Dear Colleagues:

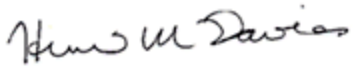
It is with great pleasure that I welcome you to the **38th National Organic Symposium**, sponsored by the Organic Division of the American Chemical Society. This is an opportunity for distinguished scholars, educators and research scientists to come together to present current research, to discuss on-going projects, to disseminate information, to share knowledge and to enjoy the camaraderie of colleagues and friends.

We are pleased to have the scenic Bloomington campus of Indiana University host this Symposium. This Symposium will be highlighted by 14 lectures and presentations by eminent researchers on a range of exciting topics at the forefront of organic chemistry research. Augmenting the lectures will be nightly poster presentations featuring over 450 participants. Considerable time will be allocated for participants to socialize with colleagues during the opening reception on Sunday evening, informal mixers on Monday, Tuesday, and Wednesday evenings and a Dinner-At-The-Fountain early Wednesday evening. We have made available a number of organized and impromptu excursions to areas throughout southern Indiana - a uniquely interesting geologic area of rolling hills, hardwood forests, limestone caves, sinkholes, and karsts. We are also offering the opportunity to spend an afternoon visiting the Eli Lilly facilities in Indianapolis.

Lectures and poster sessions will be centered in the stunning, newly renovated IU Auditorium located in the center of the IU campus surrounded by the I.M. Pei designed IU Art Museum and the world renowned Lilly Library of rare books and manuscripts.

I want to personally thank you for joining me, your friends and colleagues on the campus of Indiana University, in the academically and culturally rich town of Bloomington, Indiana, in the heartland of America, for the **38th National Organic Symposium** where outstanding science will combine with outstanding conversation among a group of outstanding scientists.

Sincerely,



Huw M. L. Davies
Larkin Professor of Organic Chemistry
University at Buffalo
State University of New York

38th National Organic Symposium
Sponsors

We wish to acknowledge the kind and generous support of the many contributing organizations.

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Lilly Research Laboratories
Dinner-at-the-Fountain
Wednesday, June 11, 2003

Indiana University
Office of the Chancellor
College of Arts and Sciences
Department of Chemistry
Opening Reception
Sunday, June 8, 2003

Special appreciation is extended to:

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38th National Organic Symposium
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Indiana University
Bloomington, Indiana
June 8-12, 2003

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38th National Organic Symposium
Exhibitors

We wish to acknowledge the following companies who have chosen to share their products and information with the Symposium participants.

Exhibitor booths will be located on the mezzanine level of the IU Auditorium.

Exhibit hours correspond with poster sessions and social mixers.

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38th National Organic Symposium
Schedule of Events

Sunday, June 8, 2003

1:00pm - 8:00pm	Registration	IU Auditorium Lobby
8:00pm - 12:00am	Poster Session A Opening Reception *Sponsored by:* *Indiana University,* *Office of the Chancellor* *College of Arts and Sciences* *Department of Chemistry*	IU Auditorium Lobby & Mezzanine
	Exhibitor booths	Mezzanine

Monday, June 9, 2003

7:30am - 10:00am	Registration	IU Auditorium Lobby
8:30am - 9:00am	**Welcome & Opening Remarks: Huw Davies**	IU Auditorium
MORNING SESSION 9:00am - 10:00am	Presiding: Huw Davies **James L. Leighton** Columbia University *Strained Silacycles: A Powerful Platform for Asymmetric and Tandem Reaction Design*	IU Auditorium
10:00am - 10:15am	Discussion	IU Auditorium
10:15am - 10:45am	Break	IU Auditorium Lobby
10:45am - 11:45am	**Larry E. Overman** University of California, Irvine *New Methods for Enantioselective Synthesis of Complex Polycyclic Molecules*	IU Auditorium
11:45am -12:00pm	Discussion	IU Auditorium

12:00pm - 1:30pm	Lunch	(on your own)
12:15pm - 5:30pm	Activities	
12:30pm - 5:30pm	Tour: Eli Lilly & Co	Indianapolis
	Golf: Scramble	Stone Crest Golf Course
	Tour: Walk in the Woods	Hoosier National Forest
	Tour: Limestone Quarry & Mill	Bybee Stone Co. & Independent Quarry
2:30pm - 5:30pm	Workshop: *Managing an Effective Job Search*	Chemistry Building Room 033
5:00pm - 7:00pm	Dinner	(on your own)
EVENING SESSION	Presiding: Andy Evans	IU Auditorium
7:00pm - 8:00pm	**Laura L. Kiessling** University of Wisconsin-Madison *Chemical Approaches to Controlling Cell Surface Interactions*	
8:00pm - 8:15pm	Discussion	IU Auditorium
8:15pm - 9:15pm	**Peter G. Schultz** The Scripps Research Institute *New Opportunities at the Interface of Chemistry and Biology*	IU Auditorium
9:15pm - 9:30pm	Discussion	IU Auditorium
9:30pm - 12:00am	Poster Session B Social Mixer *Sponsored by:* *Aldrich Chemical Company*	IU Auditorium Lobby, Mezzanine & Tents
	Exhibitor Booths	Mezzanine

Tuesday, June 10, 2003

7:00am - 8:15am	5K Run *Sponsored by:* *Bristol-Myers Squibb Co.*	Showalter Fountain
MORNING SESSION	Presiding: Mike Martinelli	IU Auditorium
8:30am - 9:30am	**David W. C. MacMillan** California Institute of Technology *Enantioselective Organocatalysis: Broadly Useful Strategies for Enantioselective Synthesis Using Organic Catalysts*	
9:30am - 9:45am	Discussion	IU Auditorium
9:45am - 10:15am	Break	IU Auditorium Lobby
10:15am - 11:15am	**Donna G. Blackmond** University of Hull *On the Origin of Asymmetric Amplification in the Autocatalytic Addition of Dialkylzincs to Pyrimidyl Aldehydes*	IU Auditorium
11:15am - 11:30am	Discussion	IU Auditorium
11:30am -12:30pm	**David A. Evans** Harvard University *Architectural & Dynamic Complexity in Organic Synthesis*	IU Auditorium
12:30pm - 12:45pm	Discussion	IU Auditorium
1:00pm - 2:00pm	Lunch	(on your own)
1:00pm - 5:30pm	Activities	
	Tour: Eli Lilly & Co.	Indianapolis
	Tour: Gypsum Mine & Co.	National Gypsum Co. Shoals, IN
2:30pm - 5:30pm	Workshop: *Fundamentals of Drug Discovery*	Chemistry Building Room 122
2:30pm - 5:30pm	Workshop: *Managing an Effective Job Search*	Chemistry Building Room 033
5:30pm - 7:30pm	Dinner	(on your own)

EVENING SESSION	Presiding: Ed Vedejs	IU Auditorium
7:30pm - 8:45pm	**Roger Adams Awardee** **Address by: Albert Eschenmoser** The Swiss Federal Institute of Technology & The Scripps Research Institute *A Sentimental Journey: From the Biogenetic Isoprene Rule to the Chemical Etiology of Nucleic Acid Structure*	
8:45pm - 9:00pm	Discussion	IU Auditorium
9:00pm - 12:00am	Poster Session C Social Mixer *Sponsored by:* *InnoCentive, Inc.*	IU Auditorium Lobby, Mezzanine & Tents
	Exhibitor Booths	Mezzanine

Wednesday, June 11, 2003

MORNING SESSION	Presiding: Jeffrey Johnston	IU Auditorium
8:30am - 9:30am	**Eric T. Kool** Stanford University *From Biomimetic Chemistry to Synthetic Biology: Mimicking the Molecules and Mechanisms of Nature*	
9:30am - 9:45am	Discussion	IU Auditorium
9:45am - 10:15am	Break	IU Auditorium Lobby
10:15am - 11:15am	**Edward Delaney** Bristol-Myers Squibb Co. *Automation and the Changing Face of Process R&D in the Pharmaceutical Industry*	IU Auditorium
11:15am - 11:30am	Discussion	IU Auditorium
11:30am - 12:30pm	**Timothy M. Swager** Massachusetts Institute of Technology *Electronic Ploymers for Sensory Applications*	IU Auditorium
12:30pm - 12:45pm	Discussion	IU Auditorium
1:00pm - 2:00pm	Lunch	(on your own)
1:00pm - 5:30pm	Activities	
	Tour: Eli Lilly & Co	Indianapolis
	Tour: Walk in the Woods	Hoosier National Forest
	Tour: Cave exploration	Blue Springs Cavern,
	Boat Trip	Bedford, IN
2:30pm - 5:30pm	Workshop: *Funding & Grant Writing*	Chemistry Building Room 033
5:30pm - 7:15pm	Dinner-at-the-Fountain *Sponsored by:* *Lilly Research Laboratories* *Music: ACS Publications*	Tents
EVENING SESSION	Presiding: Joe Gajewski	IU Auditorium
7:30pm - 8:30pm	**Ronald Breslow** Columbia University *Recent Advances in Bioorganic Chemistry*	

8:30pm - 8:45pm	Discussion	IU Auditorium
9:00pm - 12:00am	Poster Session D Social Mixer Exhibitor Booths	IU Auditorium Lobby & Mezzanine

Thursday, June 12, 2003

MORNING SESSION 9:00am - 10:00am	Presiding: Ahmed F. Abdel-Magid **John L. Wood** Yale University *Bridged Polycyclic Natural Products: Inspirational Targets for Total Synthesis*	IU Auditorium
10:00am - 10:15am	Discussion	IU Auditorium
10:15am - 10:45am	Break	IU Auditorium Lobby
10:45am - 11:45am	**Matthew D. Shair** Harvard University *Using Lessons from Nature in Organic Synthesis*	IU Auditorium
11:45am - 12:00pm	Discussion	IU Auditorium
12:00pm - 12:30pm	Closing Remarks	IU Auditorium

38th National Organic Symposium
The Roger Adams Award in Organic Chemistry

The Roger Adams Award in Organic Chemistry is sponsored jointly by the American Chemical Society, Organic Reactions, Inc., and Organic Synthesis, Inc. The award recognizes the distinguished career of Roger Adams, who played a vital role in each of these three organizations. He was Chairman of the Board of Directors as well as President of the American Chemical Society, and he co-founded *Organic Syntheses* and *Organic Reactions.*

The award is made biennially to an individual, without regard to nationality, for outstanding contributions to research in organic chemistry. The award consists of a gold medal, a sterling silver replica of the medal, and an honorarium of twenty-five thousand dollars. It is presented at the biennial National Organic Chemistry Symposium of the Division of Organic Chemistry of the American Chemical Society. The awardee is a featured lecturer in the program of the symposium.

The recipient of this year's Roger Adams Award is Professor Albert Eschenmoser of the Swiss Federal Institute of Technology and the Scripps Research Institute. His award address, entitled "A Sentimental Journey: From the Biogenetic Isoprene Rule to the Chemical Etiology of Nucleic Acid Structure," will be delivered on Tuesday evening, June 10.

38th National Organic Symposium
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	Stephen W. Kaldor	Stephen W. Kaldor

38th National Organic Symposium
Plenary Speakers

Roger Adams Awardee
Professor Albert Eschenmoser
Swiss Federal Institute of Technology
Laboratory of Organic Chemistry
ETH Hoenggerberg, HCI H309
CH-8093 Zuerich, Switzerland and
The Skaggs Institute for Chemical Biology
The Scripps Research Institute
MSC MB-16
10550 North Torrey Pines Road
La Jolla, CA 92037, USA
Presenting: Tues., June 10, 7:30 pm

Professor Donna G. Blackmond
The University of Hull
Chemistry Department
Cottingham Road
Hull, HU6 7RX, UK
Presenting: Tues., June 10, 10:15 am

Professor Ronald Breslow
Columbia University
Department of Chemistry
3000 Broadway
New York, NY 10027
Presenting: Wed., June 11, 7:30 pm

Edward Delaney
Bristol Myers-Squibb
PO Box 191
New Brunswick, NJ 08903
Presenting: Wed., June 11, 10:15 am

Professor David A. Evans
Harvard University
Department of Chemistry & Chemical Biology
12 Oxford Street
Cambridge, MA 02138
Presenting: Tues., June 10, 11:30 am

Professor Laura L. Kiessling
University of Wisconsin
Department of Chemistry & Biochemistry
1101 University Avenue
Madison, WI 53706
Presenting: Mon., June 9, 7:00 pm

Professor Eric T. Kool
Stanford University
Department of Chemistry
Stauffer I
Stanford, CA 94305
Presenting: Wed., June 11, 8:30 am

Professor James L. Leighton
Columbia University
Department of Chemistry
3000 Broadway, Mail Code 3117
New York, NY 10027
Presenting: Mon., June 9, 9:00 am

Professor David W. C. MacMillan
California Institute of Technology
Division of Chemistry & Chemical Engineering
1200 E. California Blvd
Mail Code 164-30
Pasadena, CA 91125
Presenting: Tues., June 10, 8:30 am

Professor Larry E. Overman
University of California, Irvine
Department of Chemistry
4042A Frederick Reines Hall
Irvine, CA 92697-2025
Presenting: Mon., June 9, 10:45 am

Professor Peter G. Schultz
The Scripps Research Institute
Department of Chemistry
Mail: SR-202San Diego, California
Presenting: Mon., June 9, 8:15 pm

Professor Matthew D. Shair
Harvard University
12 Oxford St.
Cambridge, MA 02138
Presenting: Thurs., June 12, 10:45 am

Professor Timothy M. Swager
MIT
Department of Chemistry
Room T18-209
Cambridge, MA 02139-4307
Presenting: Wed., June 11, 11:30 am

Professor John L.Wood
Yale University
P.O. Box 208107
New Haven, CT 06520-8107
Presenting: Thurs., June 12, 9:00 am

38th National Organic Symposium
ACS Organic Division
Graduate Fellows and Sponsors

Listed below are the thirty-three advanced graduate students who were awarded Division of Organic Chemistry Graduate Fellowships in the past two years. All of these students are here at the Symposium with poster presentations. Next to the names is listed the session and poster number where they will be presenting. Also listed are the names of their institutions, faculty research advisors, and the companies that sponsored these awards. The Division is pleased to honor these extraordinary students and to gratefully acknowledge the substantial financial support provided by their generous sponsors.

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University: University of California, Irvine
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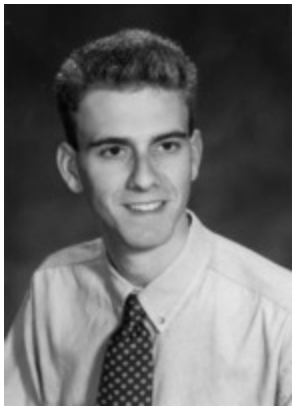

Andrew M. Harned **B106**

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University: University of Kansas
Advisor: Paul R. Hanson

Ivory D. Hills **B110**

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Advisor: Gregory C. Fu

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Advisor: Matthew Sigman

Richard J. Keaton **C52**

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University: University of Maryland
Advisor: Lawrence R. Sita

Bianca R. Sculimbrene **B56**

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Advisor: Babak Borhan

Matthew G. Woll **C50**

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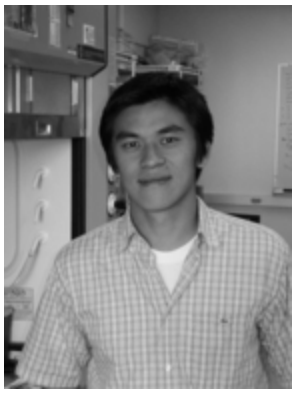

Howard C. Hang **B58**

Sponsor: DuPont Pharmaceuticals
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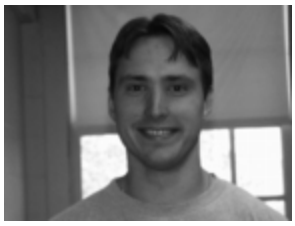
Advisor: Carolyn R. Bertozzi



Frank W. Kotch **B128**

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Scott E. Wolkenberg **B36**

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Advisor: Dale L. Boger

Aaron D. Wrobleski **A16**

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Advisor: Jeffrey Aubé

38th National Organic Symposium
Lecture Abstracts

A SENTIMENTAL JOURNEY: FROM THE BIOGENETIC ISOPRENE RULE TO THE CHEMICAL ETIOLOGY OF NUCLEIC ACID STRUCTURE

Albert Eschenmoser

Laboratory of Organic Chemistry, Swiss Federal Institute of Technology, Hönggerberg, HCI-H309, CH-8093 Zürich, Switzerland
and
The Skaggs Institute for Chemical Biology at the Scripps Research Institute, MB16, 10550 North Torrey Pines Road, La Jolla, California 92037, USA

The address will present a survey of the author's research activities in synthetic, mechanistic and biological organic chemistry from the time that he was a graduate student at ETH in 1949 – 51 up to his present activity at both ETH and the Scripps Research Institute. Chemically grown up in the inspiring environment of the legendary Ruzicka-school in classical natural product chemistry, the author has witnessed in his time major changes that organic chemistry has undergone in the last century. One of them took place while he was still a student: the ascent in chemical reasoning from the level of constitutional analogy to reasoning based on mechanistic analogy, a change that, together with the advent of conformational analysis, literally liberated natural product synthesis from the constraints of its childhood and opened the way to its coming of age in the Woodwardian era. What soon followed turned out to be the most incisive development of that time: organic chemistry began to loose a monopoly it had been holding among the physical sciences for more than a century, namely, to be the only science that possessed methods for discovering the constitutional and configurational structure of molecules. This "deregulation" in the realm of methods of structure determination initiated the explosive acceleration in the process of exploring the molecular world, an acceleration we witness still today. Within organic natural products chemistry the revolution led to self-reflection, regrouping of the forces, and to focusing on the remaining as well as newly appearing essentials: on synthesis, chemical as well as biological, target-oriented as well as methodological, on studying reactivity and function of biologically relevant molecules, on bioorganic chemistry.

Before the middle of the last century the organic chemist's attitude toward the conundrum of living organisms creating complex organic molecules was certainly no longer "vitalistic" as it had been a century before, but – I vividly remember– it still contained a distinct element of a sort of residual chemical " mysticism" in the sense that in matters of creating molecules we took for granted that Nature has ways of her own, unknown and perhaps unknowable to us, ways unfettered by the reactivity rules we were familiar with and were forced to obey in chemistry. At that time, we stood in awe before a world that, from a chemical point of view, appeared mysterious and chemically quasi-omnipotent. However, this was also the time when, on the other side of the fence that separated organic chemistry from what then became known as biochemistry, researchers started to make use of the potentials of isotopes and, in rapidly accelerating rate, to uncover the pathways of the biosynthesis of natural products, opening our eyes to the beauty of life's "organic" chemistry, and radically doing away with those residual blobs of chemical mysticism.

In retrospect, it would have been very important to look beyond that fence already quite a while before, the fence that shielded us organic chemists from being disturbed in our "pure-chemistry paradise", in our "low-molecular-weight complacency". At least in my memory, we natural product chemists had no idea of what was going on in biology in the early fifties, and it was distinctly with a kind of suspicion that in 1953 we took note of the DNA double helix proposed by the non-chemists Watson and Crick, a proposal that all at once not only described the constitutional, conformational and constellational aspects of a polymeric biomolecular structure, but also unearthed the perhaps most fundamental molecular mechanism Nature held in store for us chemists (!) to discover, namely, the pairing interaction of the nucleobases, the chemical basis of heredity.

Today, after 50 years of this discovery: all of us are aware of what happened since then: life on its material level was radically demystified by molecular biology; the ultimate "elucidation of the constitution of a natural product", that of the human genome, was accomplished; fences between the branches of molecular science do no longer exist, at least not in principle; chemistry, the study of molecules and its transformations, is being done under a great many of different names and headings, a fact that stands for the ubiquity of what is chemical in our world.

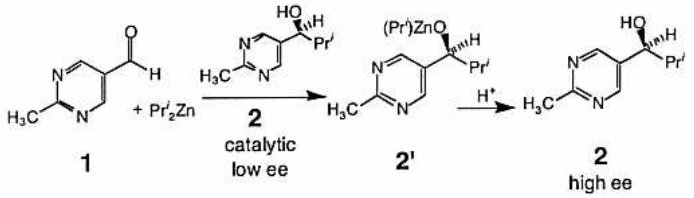
What is chemical in our world has found its supreme expression in what is biological in this world. It is the oneness of the two that came into full evidence during the second half of the century behind us. It was the author's privilege to have been a contemporary of this truly evolutionary step in science and, while pursuing his own small part of research in natural products chemistry, to have been an interested spectator of it. Since the times of Louis Pasteur and Emil Fischer, organic natural product chemists had always also been (molecular) biologists in a sense, namely, to the extent that their work was a prerequisite for, and a contribution to, the knowledge and understanding of the living. What they did, was the part of biology, only chemists could do. The modern term "chemical biology" is by no means just fashion, rather it reminds us of the task originally assigned to the branch of chemistry that was named "organic". Above all, however, the term forcefully directs us to one of the central challenges that organic chemistry will have to meet in the future, namely, to continue doing the part of biology only chemists can do.

Notes

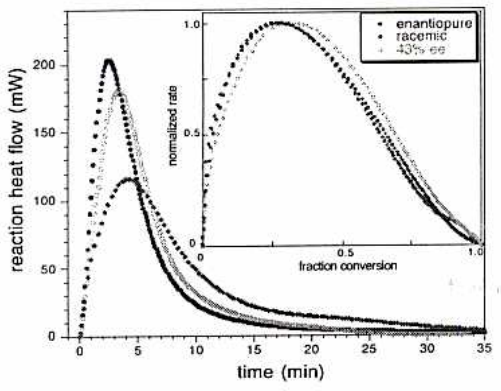
On the Origin of Asymmetric Amplification in the Autocatalytic Addition of Dialkylzincs to Pyrimidyl Aldehydes

Donna G. Blackmond
Department of Chemistry
University of Hull
Hull HU6 7RX United Kingdom
D.G.Blackmond@hull.ac.uk

Autocatalytic reactions have been implicated both in the self-replication of biological molecules[1] and in the amplification of enantiomeric excess of a chiral molecule in the prebiotic environment.[2,3] In a remarkable finding related to the latter case, Soai[4,5] has showed that pyrimidyl alcohols such as **2** may serve as both the catalyst and the product in dialkylzinc alkylations of the corresponding pyrimidyl aldehydes (Scheme 1). Alcohols such as **2** in very low enantiomeric excess have been shown to catalyze their own formation in greatly amplified enantiomeric excess.



In kinetic studies of the Soai reaction, using reaction calorimetry to monitor reaction progress (Figure 1), we[6] showed that the catalytically active species is a dimer formed by combination of two molecules of **2'**, the Zn alkoxide of **2**. Remarkably, and in contrast to examples of significant asymmetric amplification in *catalytic* reactions, we found that in this autocatalytic case there is ***no preference*** for formation of the heterochiral dimer. We determined that the origin of the asymmetric amplification rests solely on the relative inactivity of the heterochiral species as a catalyst and not on its higher stability. Achieving high selectivity by capitalizing on stability differences between complex species is a common tool in modern catalyst design; however, it is one that is unlikely to have been available to the simple molecules present in the prebiotic world. Thus amplification without this requirement, as demonstrated by our studies, may provide an important clue toward the understanding of the biochemical origin of homochirality.



$$2' + 2' \rightleftharpoons 3$$

$$[3]_{active} = ([3_{RR}] + [3_{SS}]) \qquad K_{eq} = 4 = \frac{[3_{RS}]^2}{[3_{RR}]\cdot[3_{RR}]}$$

$$rate = k\cdot[1]\cdot[Pr^i_2Zn]\cdot[3]_{active}$$

$$ee_{dx} = ee_0 \cdot \frac{[3_{RR}] - [3_{SS}]}{[3_{RR}] + [3_{SS}]}; \quad ee_{x+dx} = \frac{ee_x\cdot[2] + ee_{dx}\cdot\frac{dx}{2}\cdot[1]_0}{[2] + \frac{dx}{2}\cdot[1]_0}$$

Figure 1. Reaction rate curves for the Soai reaction.[6]

Further kinetic studies of the Soai autocatalytic reaction show that this model gives an excellent prediction of reaction rate and enantioselectivity *only* when the ratio of [Pr$^i_2$Zn] : [**1**] is close to stoichiometric. At higher [Pr$^i_2$Zn] : [**1**] ratios, the form of the experimental reaction rate profile retained the form expected for the general autocatalytic reaction (**A**+**B**+**C**→ **C**+**C**) employing *stoichiometric* ratios of **A** and **B**. The simplest model that is consistent with both our current and former observations substitutes [**1**] for [Pr$^i_2$Zn] in the rate law above (i.e., **A**+**A**+**C**→ **C**+**C**) . Remarkably, as shown in Figure 2, this gives an excellent description of the reaction for a range of [Pr$^i_2$Zn] : [**1**] ratios and different values for the initial enantiomeric excess of **2**. Figure 2 also shows that this kinetic model applied to the reaction rate data also accurately predicts the amplification of product enantiomeric excess in experiments employing enantioimpure 2.

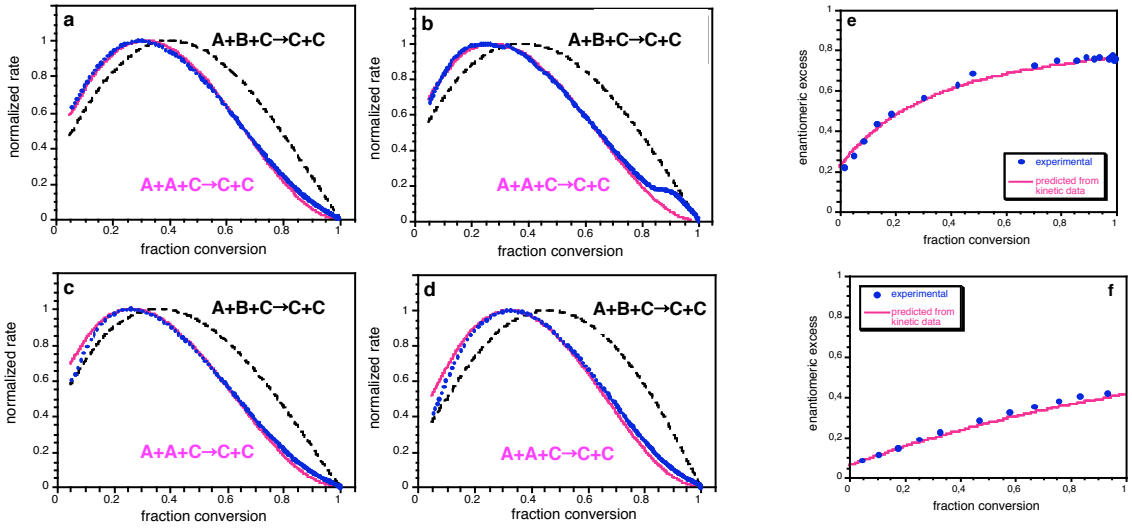
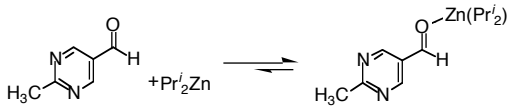


Figure 2. Reaction rate (parts a-d) and enantiomeric excess (parts e-f) as a function of fraction conversion of **1** for the reaction shown in Scheme 1. Blue circles represent experimental data points; lines represent the kinetic models: dashed black lines represent the rate equation containing [Pr$^i_2$Zn]; for the solid pink lines [Pr$^i_2$Zn] is replaced by [**1**]. Reaction progress was monitored using reaction calorimetry for reactions carried out in toluene at 298 K with [**1**]$_0$ = 0.1 M and 10 mol% **2** as catalyst, with varying initial enantiomeric excess of **2** and equivalents Pr$^i_2$Zn as noted: a) ee(**2**)$_0$ = 0.22, 1.8 equiv. Pr$^i_2$Zn; b) ee(**2**)$_0$ = 0.06, 2.0 equiv. Pr$^i_2$Zn; c) ee(**2**)$_0$ = 0.97, 2.0 equiv. Pr$^i_2$Zn; d) ee(**2**)$_0$ = 0.22, 3.6 equiv. Pr$^i_2$Zn; e) ee(**2**) as a function of conversion for the reaction shown in Figure 1a; f) ee(**2**) as a function of conversion for the reaction shown in Figure 1b.

A plausible chemical rationalization of the absence of [Pr$^i_2$Zn] in the rate law proposes the formation of a **1**-Pr$^i_2$Zn complex prior to the alkyl transfer step, possibly a nascent Zn alkoxide species **4** formed in a Lewis acid-base interaction:

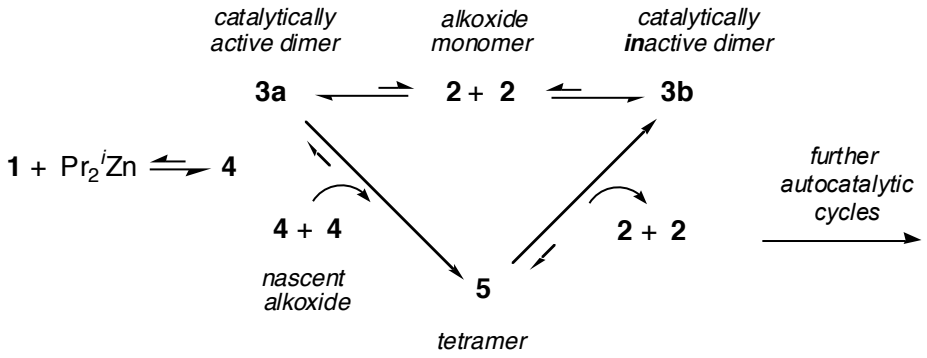


1 **4**

If this reaction is strongly driven toward the product **4**, then we can make the approximation that the concentration of **4** will be given simply by that of the limiting reagent, [**1**] (saturation kinetics in [Pr$^i_2$Zn]). This affords the rate law for an autocatalytic reaction between two

molecules of **4** and the dimeric catalyst $\mathbf{3}_{active}$, accurately describing the experimental data for both stoichiometric and non-stoichiometric ratios of **1** and Pr_2^iZn.

The suggestion that two molecules of **4** interact with the dimeric catalyst $\mathbf{3}_{active}$ state points toward a tetrameric transition state, as shown in the scheme below. This is in notable contrast to the trimeric transition state that the original rate expression suggests.[7] This tetrameric transition state bears a resemblance to the "minimal systems" for self-replication developed by von Kiedrowski[1a-b] and others for nucleic acids,[1a-c] peptides,[1e,f] small organic molecules,[1d] and ribozyme[1g] autocatalytic systems. Failure to sustain autocatalysis has been noted in many of these cases due to self-poisoning by strong binding of the catalyst-product complex or by competition from the uncatalyzed reaction. Our studies demonstrate that, unlike many of these examples, the Soai reaction is a template-directed self-replicating system that successfully maintains ideal exponential growth kinetics, and therefore high autocatalytic efficiency, over many turnovers.



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[1] a) von Kiedrowski, G., *Angew. Chem. Int. Ed. Eng*., **1986**, *25*, 932; b) von Kiedrowski, G., in *Bioorganic Frontiers,* (Springer: New York, ed. By H. Dugas), **1993**, v. 3, p. 113; ;c) Zielinski, W.S., Orgel, L.E., *Nature*, **1987**, *327*, 346; d), Wintner, E.A., Conn, M.M., Rebek, J., Jr., *J. Am. Chem. Soc*., **1994**, *116*, 8877; e) Yao, S., Ghosh, I., Zutshi, R., Chmielewski, J., *J. Am. Chem. Soc*.,**1997**, *119*, 10559; f) Saghatelian, A., Yokobayashi, Y., Soltani, K., Ghadiri, M.R., *Nature*, **2001**, *409*, 797; g),Paul, N. Joyce, G. P., *PNAS*, **2002**, *99*, 12733.

[2] a) Frank F. C.:,*Biochim. Biophys. Acta* **1953**, *11*, 459; b) Calvin M.:, *Chemical Evolution*, p. 149. Oxford University Press, Oxford 1969.

[3] ~ a recent review on spontaneous asymmetric synthesis, see Mislow, K., *Coll. Czech. Chem. Comm.,* in press.

[4] First publications: a) Soai K., Shibata T., Morioka H., Choji K.: *Nature* **1995**, *378*, 767; b) Shibata T., Choji K., Hayase T., Aizu Y., Soai K.: *Chem. Commun*. 1996, 1235; c) Shibata T., Morioka H., Hayase T., Choji K., Soai K.: *J. Am. Chem. Soc*. **1996**, *118*, 471

[5] For a recent review:) Soai K., Sato I.: *Chirality* **2002**, *14*, 548.

[6] a) Blackmond D. G., McMillan C. R., Ramdeehul S., Schorm A., Brown J. M.*: J. Am. Chem. Soc*. **2001**, *123*, 10103; b) Blackmond D. G.: *Adv. Synth. Catal.* **2002**, *344*, 156.

[7] The kinetic equations suggest that the transition state is assembled from **3**, originating from two molecules of the alkoxide **2'** plus *either* only one aldehyde molecule (**1**+PriZn) (eq. (3), hence a trimer), *or* two molecules of **4** = (**1**+PriZn) (eq. (7), hence a tetramer).

Notes

RECENT ADVANCES IN BIOORGANIC CHEMISTRY

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There are two aspects to bioorganic chemistry, depending on the direction of information flow. In one we use information from biology to inspire us into creating new chemistry, what I have called "biomimetic chemistry." In the other aspect we use our chemical skills and ideas to influence or understand biology. An important example is the invention of new medicinal compounds, an activity that has helped increase life expectancy by 50% over the last century.

In this lecture I will describe our work in those two areas. In one, we have developed mimics of enzymes that have several important features. They operate in water solution, and one type is able to direct oxidation reactions whose selectivity is dominated by the geometry of the catalyst/substrate complex, overriding the intrinsic reactivity of the substrate. Our goal in this work is to "liberate chemistry from the tyranny of functional groups." Another type of biomimetic catalyst is based on hydrophilic polymers with hydrophobic cores. This class is able to imitate the ability of enzymes to use the advantages of water for hydrophobic binding but use the non-aqueous interior of the protein to promote rapid catalytic reactions, producing "a drop of DMSO suspended in water." The result is an acceleration of the synthesis of tryptophan by transamination with an acceleration of 240,000-fold caused by the polymer.

In the second area, medicinal chemistry, we have started with the observation that DMSO is able to induce erythroleukemia cells to differentiate into normal erythrocytes, and developed this into a group of potent molecules that accomplish a number of important goals in cancer therapy with a wide range of cancer types. 1) The cancer cells cease growth. 2) They can differentiate into normal non-cancerous cells. 3) In some cases they undergo apoptosis, programmed cell death. The compounds do not show significant toxicity, are orally active, and the lead compound is now in phase 2 clinical trials, having successfully emerged from phase 1 with flying colors. The intellectual path that led to the potent compounds will be described, as well as the evidence on their mode of action and the results of animal and human trials.

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Notes

Automation and the Changing Face of Process R&D in the Pharmaceutical Industry

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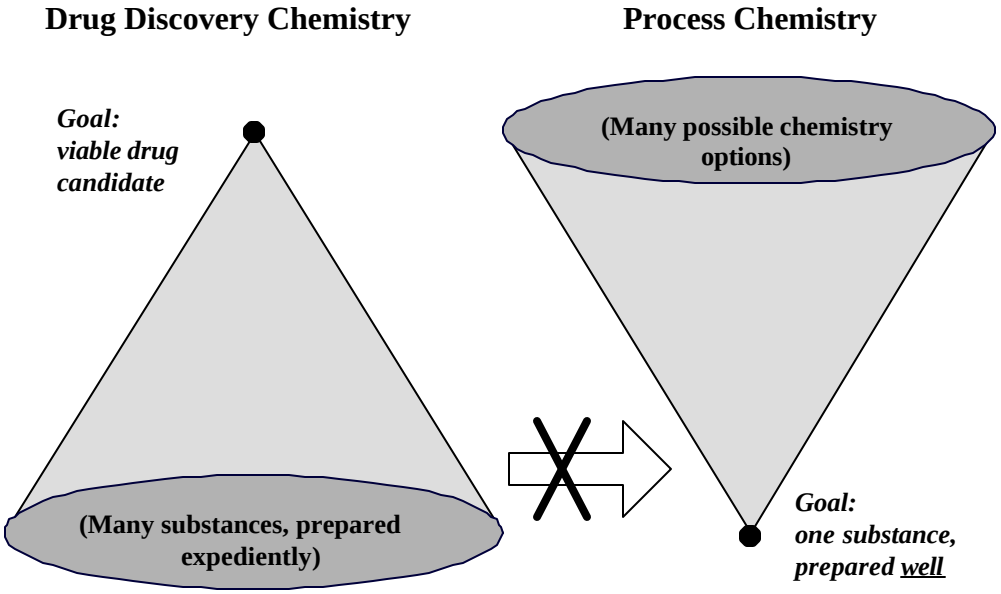
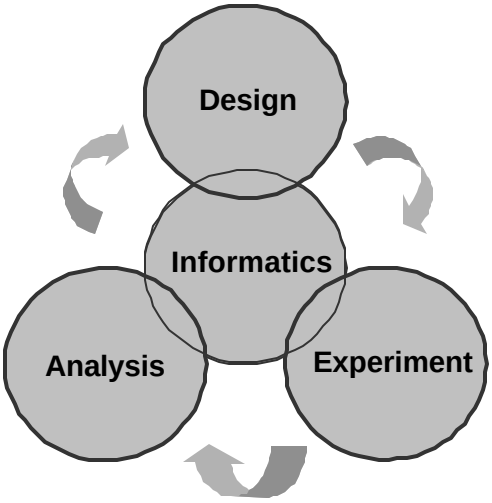
The use of automation tools in organic chemistry research has gained increased attention over the past several years within industrial pharmaceutical R&D laboratories. While concepts and adaptable robotic equipment have been available for many years, investment and development of commercial instrumentation of greater sophistication has only come about over the past decade, in parallel with the widespread adoption of combinatorial approaches that now play an important role in drug discovery efforts.

Benefits from automation are reaped in cases where a high degree of repetitiveness is involved, and such is clearly the case when identical operations can be applied in preparing large libraries of compounds based on a programmed set of reaction and work-up conditions. In contrast, process research and development activities are largely dedicated toward the identification of routes and the creation of detailed chemistry knowledge that will allow a particular entity to be prepared safely, reliably, with acceptable cost-effectiveness, and with high throughput. It is therefore not surprising to find that many tools specifically developed to support combinatorial chemistry workflow (which can be visualized as supporting the lower portion of the left cone in the figure below) do not lend themselves well to the most important aspects of process R&D:



More appropriately aligned with process R&D goals are tools that are designed for flexibility, and that simplify and organize the conduct of less differentiated, but routine functions that support *chemical experimentation* (i.e. supporting the higher end of the right cone, above). Such functions include the accurate measurement, transfer, and tracking of materials, the accurately timed sampling and analysis of reaction mixtures,

and integrated aids for both the design of experiments and the analysis of experimental data, as represented below:



The primary premise justifying the need for such tools is that process R&D chemists generally have more ideas worth exploring, and exploring in adequate depth, than their existing tool infrastructure (e.g. hood space, analytical capacity, experimental planning/tracking and data reduction tools) can support with high efficiency. Secondarily, those same constraints encourage chemists to rely most heavily on their experience and intuition, while discouraging them from logical approaches that appear attractive, but are unprecedented and therefore more risky.

While specific strategic approaches vary, pharmaceutical process R&D functions are increasingly taking advantage of commercial hardware and applying computer-based technology in ways that enable chemists to conduct broader, more detailed research while accelerating the pace of chemical knowledge acquisition. In this talk, one company's approach will be detailed, and several research examples will be presented in which the application of advanced tools played an important role in developing well-understood synthetic processes to prepare drug candidates.

Notes

ARCHITECTURAL & DYNAMIC COMPLEXITY IN ORGANIC SYNTHESIS

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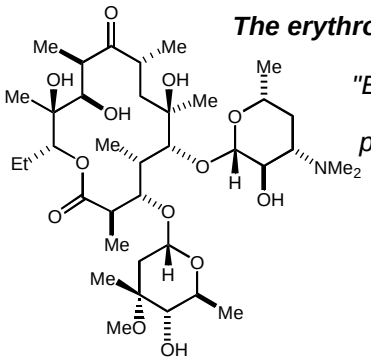
rganic chemists are frequently invited to speculate on the next frontiers in organic synthesis. t is evident from this year s list of participants that the field is moving in a number of directions. ne frontier is concerned with the application of the tools of chemical synthesis to solving problems in biology. The application of chemical synthesis to the construction of new materials with tailored physical properties represents another direction. hat about organic synthesis

The *Complexity Criterion* may be used to evaluate the state of advancement of the synthesis activity. or example, the condition of the field may be assessed on the basis of the *Architectural Complexity* that may be achieved in the synthesis of molecular targets with latest reaction-based tools. oodward s rumination on the architectural complexity embodied in the erythromycin structure signaled that this molecular target was beyond the reach of organic chemists and their reaction tools at that point in time.



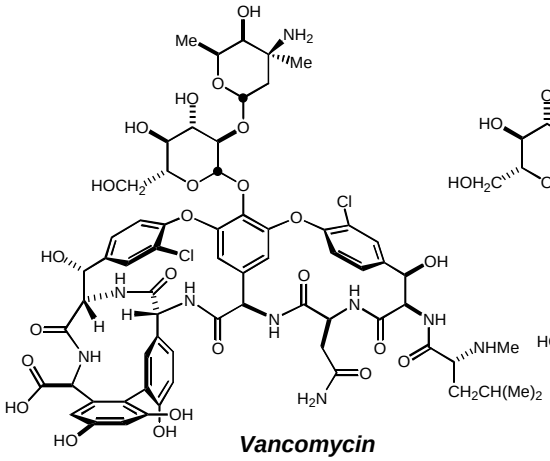
The erythromycin-A structure, as viewed by Woodward in the '50s

"Erythromycin, with all of our advantages, looks at present quite hopelessly complex, particularly in view of its plethora of asymmetric centers."

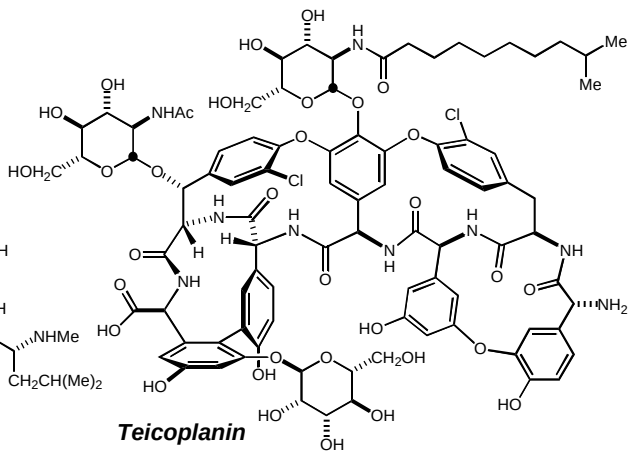
R. B. Woodward, 1956

t the personal level, the vancomycin and teicoplanin structures have provided me with a similar visceral response. t the outset of our studies in this area some years ago, these structures also appeared to us to be hopelessly complex as well. ccordingly, such structures become ideal targets for synthesis since the undertaking will drive the development of new reactions that must perform in an architecturally complex molecular environment.

Architectural Complexity: Complex molecular targets define limitations of the field



Vancomycin



Teicoplanin

The complexity criterion may also be used in the evaluation of reaction development. or example, the number of competing rate constants that might be associated with a given chemical process may be used as a gauge of the inherent complexity of the overall transformation. n this instance one is dealing with the issue of *Dynamic Complexity*. or the purpose of illustration, the pictured imide alkylation may be viewed as a four-rate constant problem wherein both enolization and enolate face selectivities must be constrained to collectively contribute to the overall stereoselectivity of the desired bond construction. f the requirements for the hydrolysis event are included, the complexity of the process further escalates. evertheless, in this example, the chemical events are regulated by reagent addition.

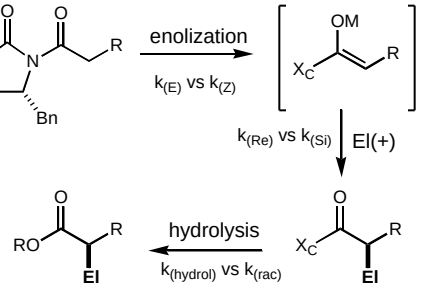
Chiral Enolate Design: A six rate constant problem

Overall enantioselection will be the sum total of the defects introduced through:

(A) Enolization selectivity: $k_{(E)}$ vs $k_{(Z)}$

(B) Enolate-El(+) face selectivity: $k_{(Re)}$ vs $k_{(Si)}$

(C) X_c removal vs racemization $k_{(hydrol)}$ vs $k_{(rac)}$

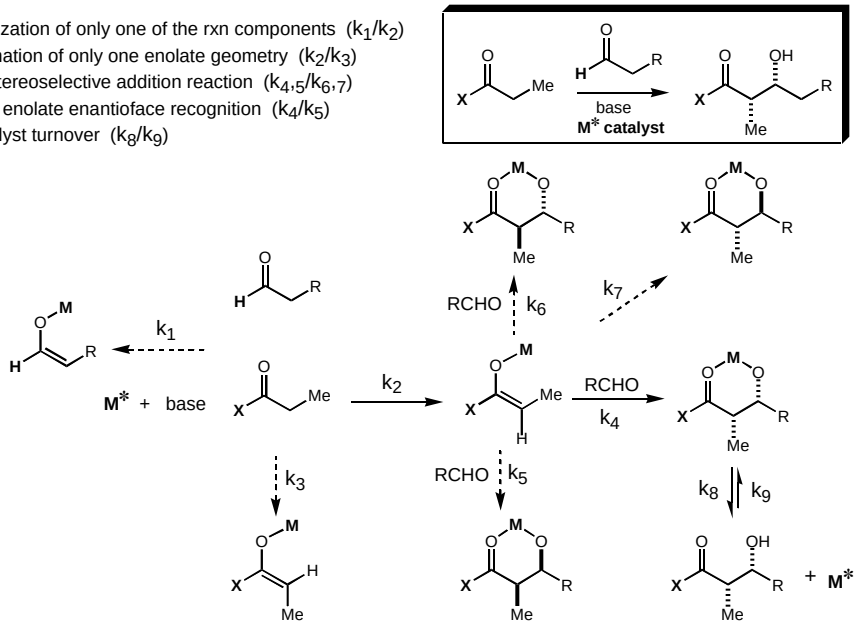


with Bartroli, Shih, *JACS* **1981**, *103*, 2127; with Ennis, Mathre, *JACS* **1982**, *104*, 1737

The *Dynamic Complexity* associated with catalytic enantioselective processes is invariably large, and the frontiers of reaction design currently encompass transformations that fall into this general family. s the graphic below illustrates, approximately nine rate constants must be appropriately tailored for an acceptable outcome.

Catalyzed Enantioselective Aldol Reactions: An nine rate constant problem

Enolization of only one of the rxn components (k_1/k_2)
Formation of only one enolate geometry (k_2/k_3)
Diastereoselective addition reaction ($k_{4,5}/k_{6,7}$)
High enolate enantioface recognition (k_4/k_5)
Catalyst turnover (k_8/k_9)



This lecture will focus on the issue of architectural and dynamic complexity in the continued development of the field of organic synthesis.

Notes

Chemical Approaches to Controlling Cell Surface Interactions

Laura L. Kiessling
University of Wisconsin-Madison

Chemical synthesis offers many approaches to investigate the combinatorial interactions of proteins encoded by genomes. Synthetic ligands that mediate the assembly of defined multi-protein complexes on the cell surface can activate or inhibit signaling pathways depending on how many and on which proteins are engaged. We have focused on the synthesis of ligands that bind multiple proteins simultaneously and thereby elicit a specific biological response. The resulting compounds have been used to investigate the consequences of protein clustering for a range of distinct cellular processes. Multivalent ligands that selectively activate or inhibit immune cell responses have been generated. Such compounds may serve as immunomodulators, functioning to augment desirable immune responses or subvert undesirable ones. Our ability to modulate biological responses depends on the development of efficient synthetic routes to the target compounds. Our recent results on ligand synthesis and a biological function will be discussed.

Notes

From Biomimetic Chemistry to Synthetic Biology: Mimicking the Molecules and Mechanisms of Nature

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I. Introduction: Toward a Synthetic Biology

Our goal is to make new molecules that mimic the structure and chemistry of natural biomacromolecules, a field often traditionally termed "biomimetic chemistry".[1] In recent years, the tools of analytical chemistry, synthetic chemistry, and molecular biology have become increasingly powerful, allowing chemists to approach molecules, mechanisms and pathways that are considerably more complex than was once possible. One direction for this field is to employ these tools to work toward ever increasing complexity: from small molecules toward larger macromolecules and to multi-molecular complexes; from simple catalytic mechanisms to multistep mechanisms to whole interconnected pathways; and from pure single molecules in solution, to defined mixtures, and finally to the incredibly complex situation inside cells. We expect that chemists will become increasingly comfortable with replacing not only small sections of macromolecules, but also with designing ever larger ones and inserting them into biological pathways, and even designing new biological pathways that function in cells. We term this trend toward increasing biomimetic complexity "synthetic biology".[2,3]

What are the reasons for mimicking natural molecules and mechanisms? First, this exercise tests our chemical understanding of the complex natural system. If the designed molecules can successfully function like the natural ones do, it suggests that we understand most of the salient features and mechanisms that make them work (or we are lucky). Second, structural mimics, such as isosteres, have a long history of usefulness in biomedical applications, and they are also being applied as tools in probing the functions of the natural systems.

Challenges in the chemistry and biology of DNA. In our laboratory, DNA serves as inspiration for the design of new molecules and reactions. The structure of the DNA double helix was discovered fifty years ago, and chemists have been making many important contributions and advances in the decades since. Thus it is fair to ask: what is left to do? What remains unknown or untested? Here are some questions we are posing:

• How do polymerase enzymes replicate DNA? What renders some of them highly accurate, while others are very sloppy?

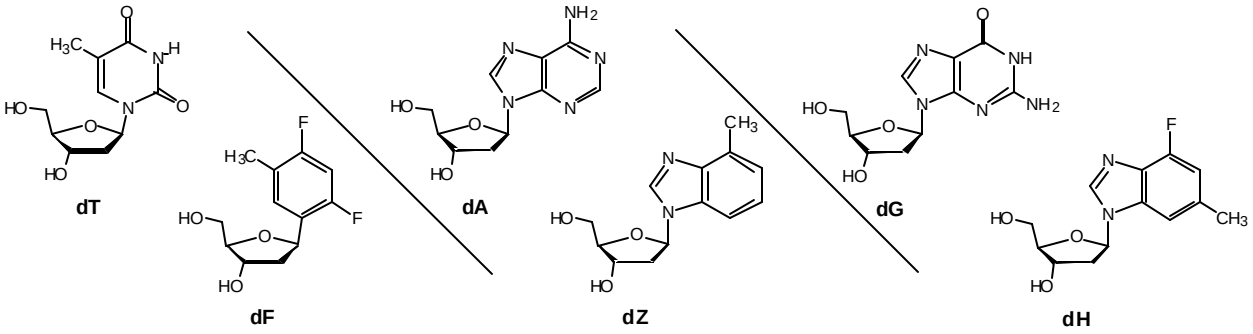
• Do we understand enough about natural DNA replication to design new molecules and pathways that can function in cells?

• Could DNA have been designed differently in nature? What other base pair structures can pair, fold and function like the natural system does?

• If DNA is a scaffold for careful arrangement of nucleobases, how can that scaffold be applied in the engineering of other useful molecular functions?

II. Mimicry of DNA Structure and Function

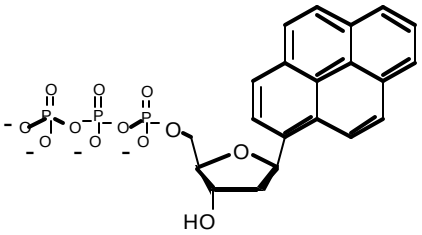
Nonpolar nucleoside isosteres. We have developed a set of nucleoside structural mimics that are nearly the same size and shape as the natural ones, but lack Watson-Crick hydrogen bonding groups.[4] The pyrimidine analogs are C-nucleosides based on substituted benzenes (see dF), and the purine analogs are indoles or benzimidazoles (dZ,dH). These compounds are quite nonpolar and show no evidence of hydrogen bonding, even with the electronegative fluorine atoms. Structural studies show that they serve as quite good mimics of the natural structures, even in the context of DNA duplexes.[5,6] Interestingly, studies of base stacking stability suggest that the nonpolar molecules stack considerably more strongly than



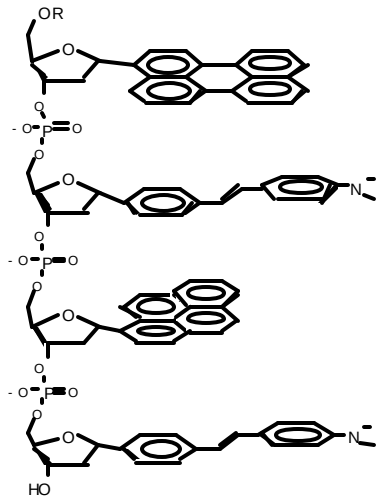
their natural (more polar) counterparts.[7]

Insights into DNA replication mechanisms. The nonpolar nucleoside isosteres such as dF or dZ are strongly destabilizing to DNA when paired opposite natural partners, confirming that hydrogen bonding groups are quite important to the stability of the double helix. Surprisingly, however, some of these molecules can be replicated with very high efficiency and fidelity by polymerase enzymes, despite the lack of Watson-Crick bonds.[7,8] Mostly recently, this has even been repeated in whole bacterial cells.[9] Such experiments have led to the once-controversial conclusion that these H-bonds are not necessary for high-fidelity transfer of genetic information. We have proposed that instead, the enzymes use steric sizes and shapes to guide them in assembling new base pairs.[10,11] This hypothesis is currently being tested with new types of DNA base analogs.

Applications of hydrophobic DNA bases. The strong stacking potential of large, flat and hydrophobic DNA base replacements allows them to be useful in stabilization of DNA helices, and in design of new DNA base pairs. Strong stackers can act as cooperative helix stabilizers when placed at the ends of natural helix-forming sequences or in loop regions. They can also be designed (with appropriate partners) to form stable hydrophobic base pairs. The first stabilizing, non-H-bonding base pair was the pyrene-abasic pair.[12] Notably, this pair can also be efficiently and specifically assembled by DNA polymerase enzymes (see pyrene nucleoside triphosphate structure, below).[13]



Fluorescent DNA base replacements. The larger, extended pi systems of some DNA base replacements leads to useful optical properties such as fluorescence. It occurred to us that if the DNA bases in a synthetic strand were all replaced by fluorescent groups, this would organize the groups for close electronic interaction. This would be expected to lead to various forms of energy transfer, yielding properties in an "oligofluor" strand that do not exist in any of the individual fluorophores (see example of oligofluor molecule at left). We are making large combinatorial libraries of such polyfluor molecules, using DNA synthesizers to assemble them, and are discovering a number of useful new fluorescence and sensing properties in some of the composite DNA-like molecules.[14]



Differently-sized DNA base replacements: toward a new genetic form? Finally, we are exploring whether DNA bases could be made larger or smaller than the natural ones,[15] and yet retain some of the natural properties such as helix-forming ability. These molecules can also be used to test the steric room inside the active sites of DNA polymerase enzymes.

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Notes

STRAINED SILACYCLES: A POWERFUL PLATFORM FOR ASYMMETRIC AND TANDEM REACTION DESIGN

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When constrained in a small ring, silicon possesses unusually high Lewis acidity useful for organic synthesis (Figure 1). Whereas previous examples have been restricted to silacyclobutanes, it has recently been found that silacyclopentane derivatives can exhibit this unusual reactivity as well. The examples provided are illustrative, and the small internal bond angle at silicon in such systems will be noted. This lecture will outline the profound implications of the discovery that 5-membered silacycles exhibit sufficiently high Lewis acidity for use in organic synthesis.

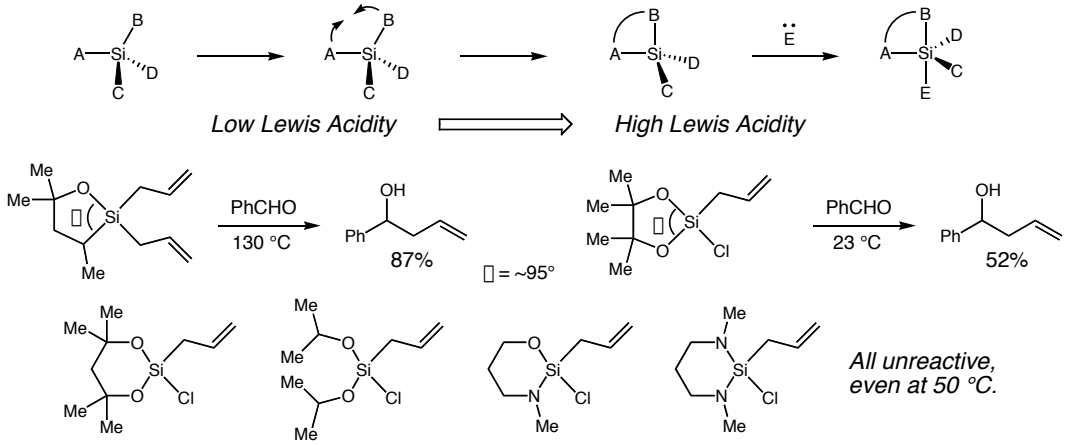

Figure 1. Strained silacycle-induced Lewis acidity, and examples of uncatalyzed aldehyde allylsilylation reactions.

A new family of reagents has been developed for the highly practical and enantioselective allylation and crotylation of aldehydes based on the concept of strained silacycle-induced Lewis acidity (Figure 2). The pseudoephedrine-derived reagent is easily prepared on large scale, is amenable to storage, and provides good enantioselectivities with aliphatic aldehydes. The cyclohexanediamine-based reagents are also easily prepared on large scale, and, importantly, are crystalline solids that may be stored for long periods of time and may be briefly be handled in air without significant decomposition. The performance of the diamine-based reagents is superior, generally providing products in 95-98% *ee* with a wide range of aldehydes, both aromatic and aliphatic.

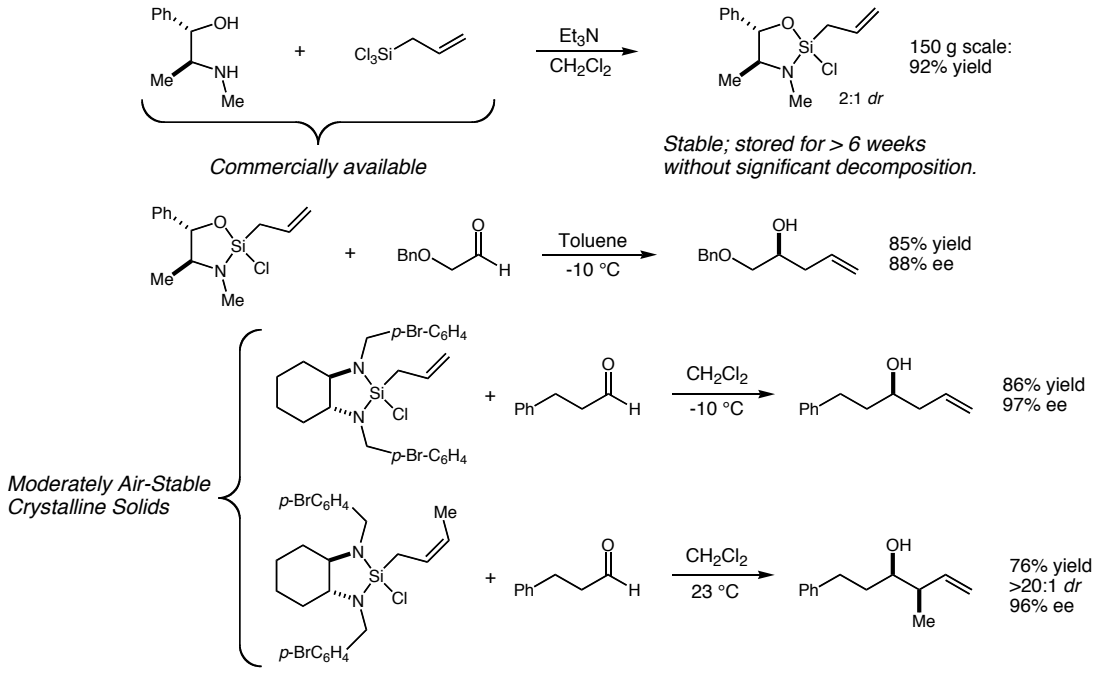

Figure 2. Reagents for asymmetric aldehyde allylation and crotylation based on strained silacycle-induced Lewis acidity.

The same pseudoephedrine-based reagent has been found to be highly versatile as it undergoes smooth reaction with acylhydrazones to provide homoallylic amine derivatives with good enantioselectivities (83-97% *ee*). The products are often crystalline and this can lead to a chromatography-free procedure giving highly enantiomerically enriched products upon a single recrystallization (Figure 3). It has been found recently that ketone-derived acylhydrazones are viable substrates as well, leading to the practical synthesis of chiral, tertiary homoallylic amines.

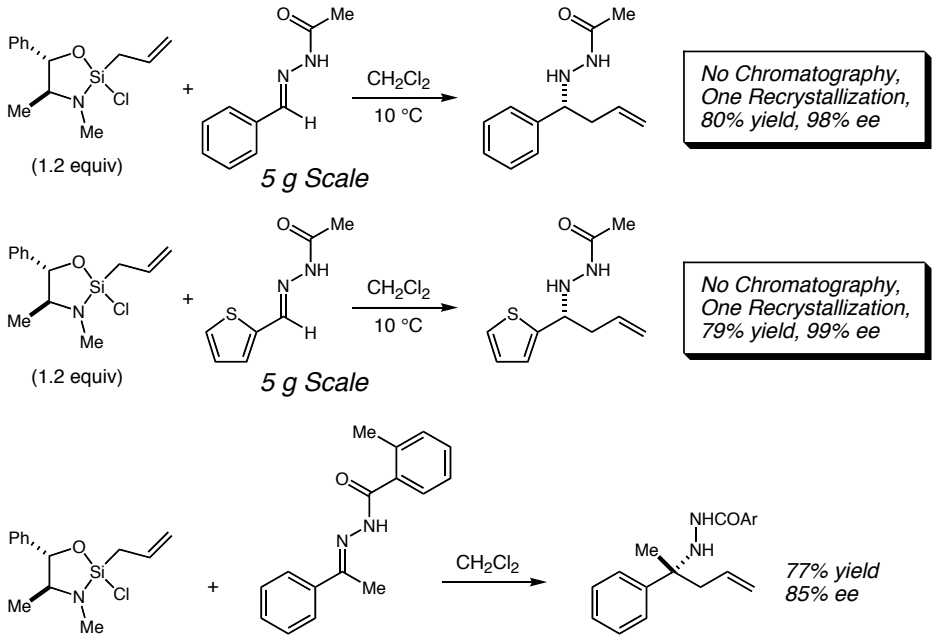

Figure 3. Enantioselective allylation of acylhydrazones using the versatile pseudoephedrine-based reagent.

Aldehyde-derived enolates are rarely employed in aldol chemistry due partly to the problem of uncontrolled oligomerization. If such a process could be controlled, a uniquely efficient approach to polyketide synthesis might result. To begin to approach this problem, we envisioned a tandem aldol-allylation reaction as outlined in Figure 4.

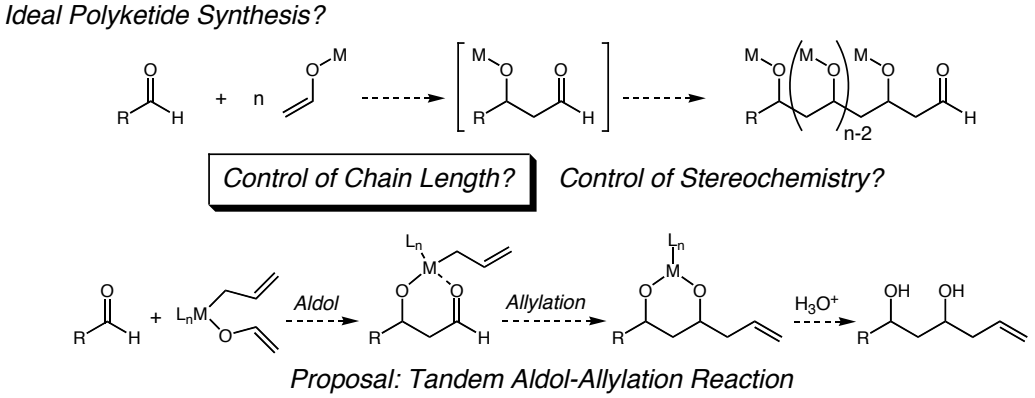

Figure 4. A new approach to the synthesis of polyketide fragments, a proposed tandem aldol-allylation reaction.

While more classical approaches to the invention of this reaction failed, strained silacycle-induced Lewis acidity proved successful. The allyl(crotyl) enolsilanes are readily prepared and quite stable, and their reactions with aldehydes are trivial experimentally giving diol products in good yield, and establishing as many as four new stereocenters with good diastereoselectivity (Figure 5).

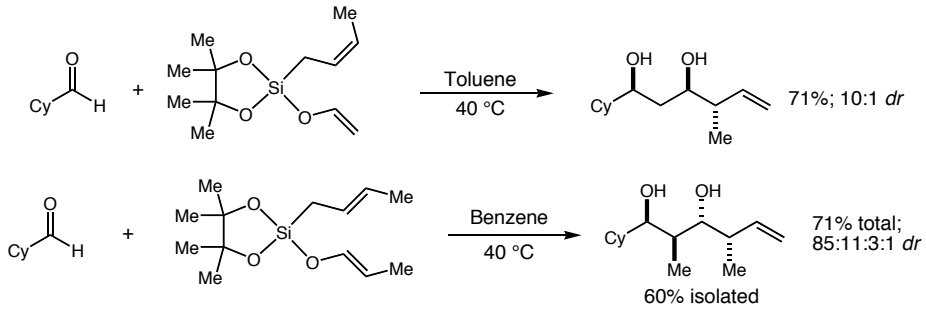

Figure 5. The tandem aldol-allylation reaction, which can establish up to four new stereocenters.

Ketone-derived enolsilanes may be employed in this chemistry as well, leading to the synthesis of tertiary alcohol stereocenters with good diastereoselectivity (Figure 6). Indeed, the use of ketone-derived enolsilanes makes possible the tandem aldol-aldol reaction, which provides highly functionalized products with excellent efficiency, and holds promise for the *in situ* reaction of the initially formed ketone products. Efforts further to develop the tandem aldol-allylation and aldol-aldol reactions and to develop enantioselective variants will be presented.

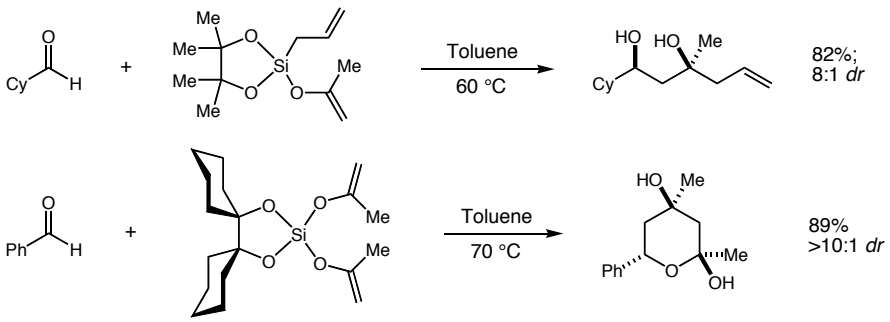

Figure 6. Ketone-derived enols in the tandem aldol-allylation reaction and the tandem aldol-aldol reaction.

Notes

Enantioselective Organocatalysis: Broadly Useful Strategies for Enantioselective Synthesis using Organic Catalysts.

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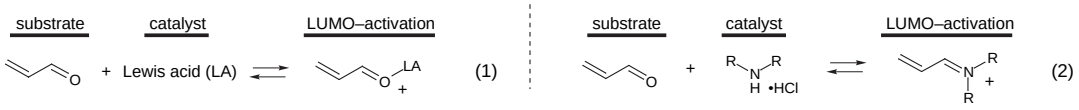
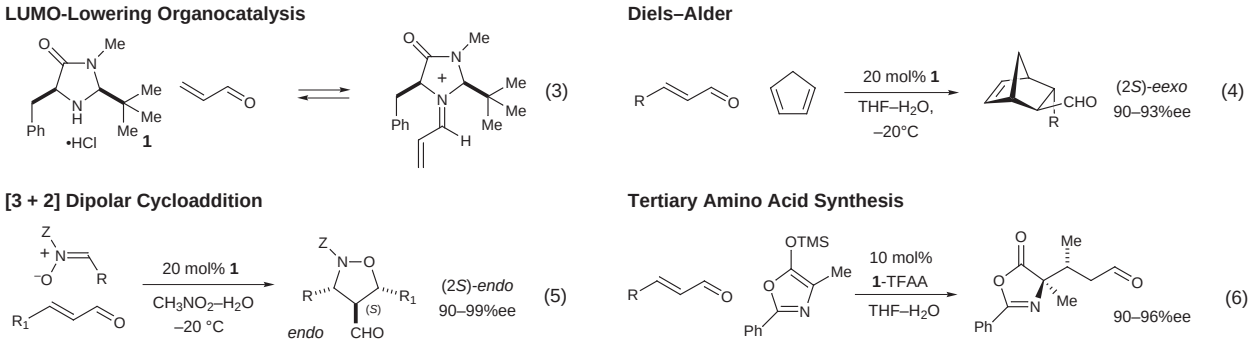
Over the past 30 years enantioselective catalysis has become one of the most important frontiers in exploratory organic synthetic research. During this time, remarkable advances have been made in the development of organometallic asymmetric catalysts that in turn have provided a wealth of enantioselective oxidation, reduction, pi-bond activation and Lewis acid catalyzed processes.[1] Surprisingly, however, relatively few asymmetric transformations have been reported which employ organic molecules as reaction catalysts,[2] despite the accordant potential for academic, economic and environmental benefit and the widespread availability of organic chemicals in enantiopure form. With this in mind, we recently embarked upon the development of new strategies for enantioselective organocatalysis that we have subsequently demonstrated to be amenable to a diverse range of asymmetric transformations. In this presentation, we will demonstrate that several organocatalytic strategies has been successfully translated to enantioselective Diels-Alder, Nitrone cycloadditions, Friedel-Crafts conjugate additions, Mukaiyama–Michael Additions, Nitrone Alkylations, cascade cyclizations, nucleophilic epoxidation reactions, direct aldehyde cross-coupling aldol reactions and a new protocol for the two step synthesis of differentially protected natural and unnatural carbohydrate architecture. We will also present new organocatalytic strategies towards the rapid construction of complex architecture including Diazonamide A.

Part A: Iminium Catalysis. We reasoned that (i) LUMO–lowering activation and (ii) the kinetic lability towards ligand substitution that enables Lewis acid–catalyst turnover (eq 1) might also be available with a carbogenic system that exists as a rapid equilibrium between an electron-deficient and a relatively electron-rich state. With this in mind, we hypothesized that the reversible formation of iminium ions from α,β-unsaturated aldehydes and amines (eq 2) might emulate the equilibrium dynamics and π-orbital electronics that are inherent to Lewis acid catalysis, thereby providing a new platform for the design of organocatalytic processes. Significantly, this analysis reveals the attractive prospect that *chiral amines might function as enantioselective catalysts for a range of transformations that traditionally utilize metal salts.*



To test this hypothesis we investigated the utility of enantiopure imidazolidinone **1** as an enantioselective catalyst for a range of transformations (eq 3) including the Diels-Alder reaction (eq 4), [3 + 2] dipolar cycloadditions (eq 5), Michael additions and conjugate addition reactions using pyrroles furans, indoles and silyloxy oxazoles (eq 6). The results of this investigation will be presented.



(1) For lead references see: (a) *Asymmetric Catalysis in Organic Synthesis*, Noyori, R. Ed; Wiley: New York, 1994. (b) *Asymmetric Synthesis*, Ojima, I. Ed.; VCH: New York, 1993.

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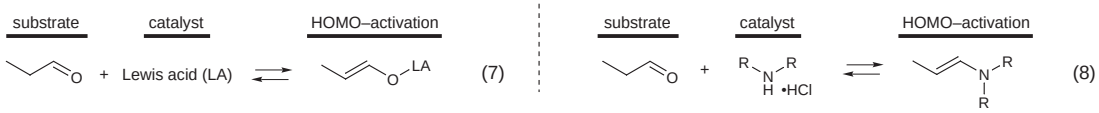
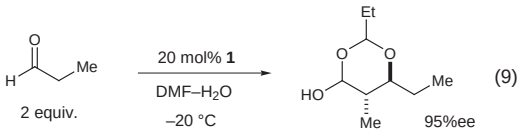
Part B: Enamine Catalysis. Over the last three decades, seminal research from the laboratories of Evans,[3] Heathcock,[4] Masamune[5] and Mukaiyama[6] have established the aldol reaction as the principal chemical reaction for the stereoselective construction of complex polyol architecture. Recently, studies by Barbas,[7] List,[8] Shibasaki[9] and Trost[10] have outlined the first examples of enantioselective direct aldol reactions, an important class of metal or proline catalyzed transformations that do not require the pregeneration of enolates or enolate equivalents. With these remarkable advances in place, a new goal for asymmetric aldol technology has become the development of catalytic methods that allow the direct coupling of aldehyde substrates[11] (eqs 9 and 10), a powerful yet elusive aldol variant that has only been accomplished within the realm of enzymatic catalysis.[12]

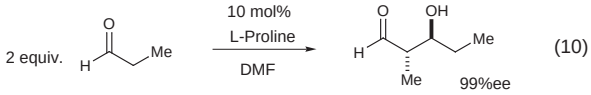


Traditionally, the enantioselective aldol coupling of non-equivalent aldehydes has been viewed as a formidable synthetic challenge on account of (i) the propensity of aldehydes to polymerize under metal catalyzed conditions and (ii) the mechanistic requirement that non-equivalent aldehydes must selectively partition into two discrete components, a nucleophilic donor and an electrophilic acceptor. In this presentation, we demonstrate that this elusive aldol sequence can be accomplished using enamine catalysis to allow the first highly enantioselective coupling of aldehyde substrates. Moreover, we highlight that excellent levels of aldol efficiency and enantioselectivity are available using either the imidazolidinone catalyst **1** or proline (eqs 9 and 10). We expect this chemical variant of the Hajos-Parrish-Barbas-List reaction[13] will provide a powerful yet operationally simple protocol for the rapid production of enantioenriched aldolate architecture.

Imidazolidinone Aldol Catalysis



Proline Aldehyde–Aldehyde Coupling



The development of a powerful new sequence that allows the construction of enantioenriched carbohydrate architecture will also be discussed. Application of this new technology to the rapid production of fully differentially protected sugar and amino-sugar moities will be highlighted.

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(3) (a) Evans, D. A.; Nelson, J. V.; Taber, T. in *Topics in Stereochemistry*, Vol. 13; John Wiley and Sons, Inc., New York, 1982; pp. 1. (b) Evans, D. A.; Vogel, E.; Nelson, J. V. *J. Am. Chem. Soc.* **1979**, *101*, 6120. (c) Evans, D. A.; Nelson, J. V.; Vogel, E.; Taber, T. R. *J. Am. Chem. Soc.* **1981**, *103*, 3099. (d) Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc.* **1981**, *103*, 2127.

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(9) (a) Yamada, Y. M. A.; Yoshikawa, N.; Sasai, H.; Shibasaki, M. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1871. (b) Yoshikawa, N.; Yamada, Y. M. A.; Das, J.; Sasai, H.; Shibasaki, M. *J. Am. Chem. Soc.* **1999**, *121*, 4168. (c) Yoshikawa, N.; Kumagai, N.; Matsunaga, S.; Moll, G.; Oshima, T.; Suzuki, T.; Shibasaki, M. *J. Am. Chem. Soc.* **2001**, *123*, 2466. (d) Yoshikawa, N.; Shibasaki, M. *Tetrahedron* **2001**, *57*, 2569.

(10) (a) Trost, B. M.; Silcoff, E. R.; Ito, H. *Org. Lett.* **2001**, *3*, 2497 (b) Trost, B. M.; Ito, H. *J. Am. Chem. Soc.* **2000**, *122*, 12003.

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Notes

NEW METHODS FOR ENANTIOSELECTIVE SYNTHESIS OF COMPLEX POLYCYCLIC MOLECULES

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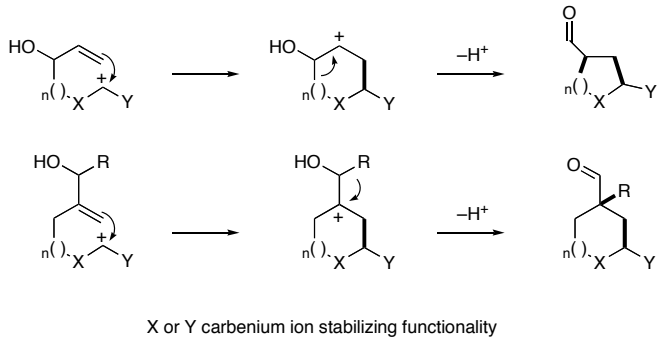
The distinctive aspect of chemistry is the ability to create new molecules and chemical systems.[1] Chemical transformations are the engine that drives our ability to further expand this universe of chemistry. A goal of contemporary organic synthesis is to prepare molecules of high complexity in a practical fashion. Achieving efficiency in the synthesis of such molecules requires: a plan (synthesis strategy) that employs the fewest number of chemical transformations, and high-yielding chemical transformations. The development of new chemical transformations is singularly important as new chemical transformations enable new synthesis strategies.

One strategy we have employed at Irvine to invent new chemical transformations is to design cascade processes in which the product of one carbon–carbon bond-forming transformation is the starting material for another. In one aspect of these studies, we have developed a suite of cyclization reactions that employ a pinacol rearrangement to terminate a cationic cyclization (Figure 1). This simple design can be implemented in various ways to prepare polycyclic products having fused, bridged or attached rings (Figure 2). The strategic use of a Prins-pinacol reaction to complete the first total syntheses of briarellin diterpenes will be discussed (Figure 3).[2]

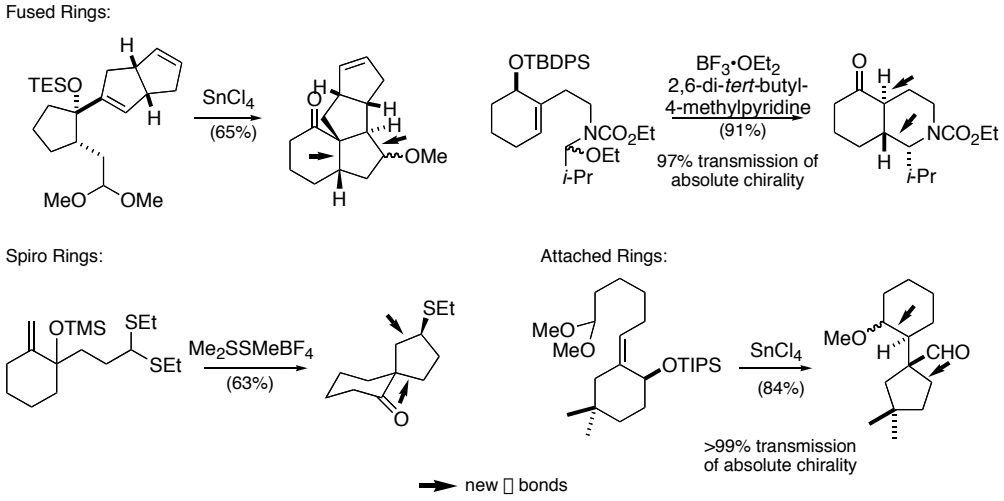


X or Y carbenium ion stabilizing functionality

Figure 1

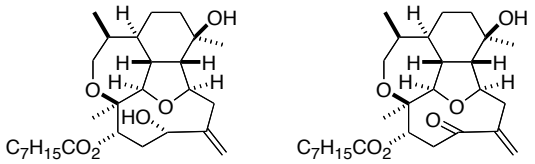
[1] *Beyond the Molecular Frontier: Challenges for Chemistry and Chemical Engineering*; Breslow, R. C. D.; Tirrell, M. V., Eds., National Academy Press, 2003.

[2] Corminboeuf, O.; Overman, L. E.; Pennington, L. D. *J. Am. Chem. Soc.* **2003**, *125*, in press.



with Hirst, Johnson *J. Am. Chem. Soc.* 1993, *115*, 2992; Minor T*etrahedron* 1997, *53*, 8927; Pennington *Can. J. Chem.* 2000, *78*, 732; Kamatani *Org. Lett.* 2001, *3*, 1229; Velthuisen unpublished (2003)

Figure 2



briarellin E briarellin F

Figure 3

Complex natural products having unusual structures have also served to stimulate our development of new chemical transformations. One recent example is the polypyrrolidinoindoline alkaloids, which have been isolated from a variety of natural sources including bacteria, fungi, and higher plants (Figure 4).[3] Characterized by the linkage of cyclotryptamine subunits through quaternary carbon centers, members of this alkaloid class exhibit two general structural motifs. The first, found in *meso*-chimonanthine and its C_2-symmetric stereoisomer (–)-chimonanthine, is a 3a,3a′-bispyrrolidinoindoline moiety that links the benzylic quaternary stereocenters of two pyrrolidinoindoline fragments (Figure 4). The second, present in higher order members of this alkaloid family, is a 3a,7-bispyrrolidinoindoline unit joining the C7 peri position of one pyrrolidinoindoline unit and the benzylic quaternary stereocenter of another. This latter motif is found in idiospermuline, quadrigemine C, and numerous other higher order polypyrrolidinoindoline alkaloids. Our recent development of new chemical

[3] Anthoni, U.; Christophersen, C.; Nielsen, P. H. In *Alkaloids: Chemical and Biological Perspectives*; Pelletier, S. W., Ed.; Wiley: New York, 1999; Vol. 14, pp 163–236.

transformations to deal with the synthetic challenges presented by the polypyrrolidinoindoline alkaloids will be discussed.[4]

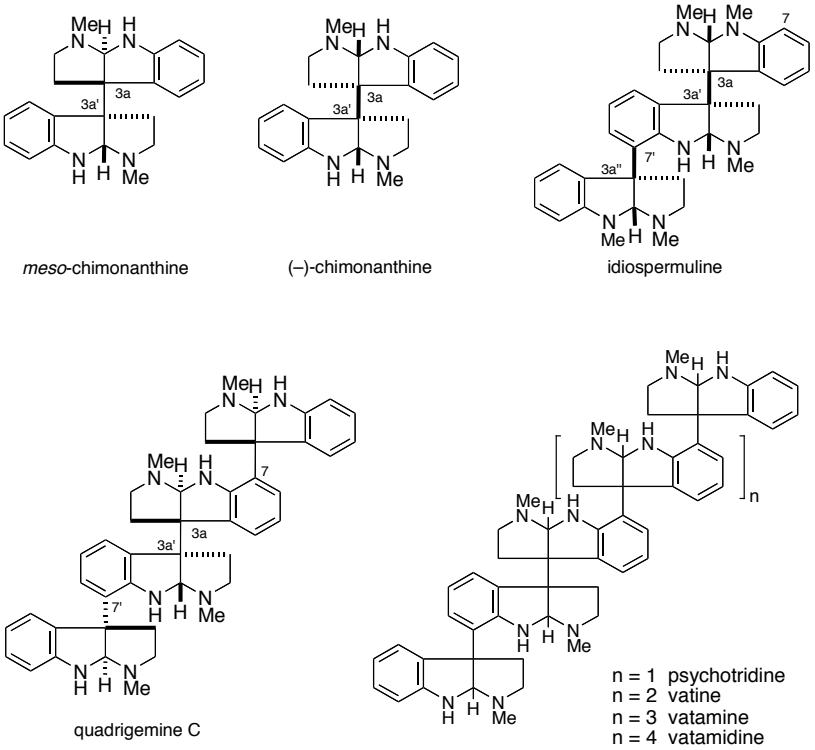


Figure 4

[4] (a) Overman, L. E.; Larrow, J. F.; Stearns, B. A.; Vance, J. M. *Angew. Chem. Int. Ed.* **2000**, *39*, 213–215. (b) Hoyt, S. B.; Overman, L. E. *Org. Lett.* **2000**, *2*, 3241–3244. (c) Lebsack, A. D.; Link, J. T.; Overman, L. E.; Stearns, B. A. *J. Am. Chem. Soc.* **2002**, *124*, 9008–9009. (d) Dounay, A. B.; Hatanaka, K.; Kodanko, J. J.; Oestreich, M.; Overman, L. E.; Pfeifer, L. A.; Weiss, M. M. *J. Am. Chem. Soc.* **2003**, *125*, in press. (e) Overman, L. E.; Peterson, E. A. *Angew. Chem., Int. Ed.* **2003**, *42*, in press. (f) Kodanko, J.; Overman, L. E. *Angew. Chem., Int. Ed.* **2003**, *42*, in press..

Notes

"NEW OPPORTUNITIES AT THE INTERFACE OF CHEMISTRY AND BIOLOGY"

Peter G. Schultz
Department of Chemistry, The Scripps Research Institute, La Jolla, CA 92037
Genomics Institute of the Novartis Research Foundation, San Diego, CA 92121

Living organisms are remarkable in their ability to generate complex structures with functions ranging from gene regulation and the immune response to photosynthesis and catalysis. The machinery of the cell when combined with the tools and principles of chemistry can be used to create molecules and assemblies of molecules with properties not yet found in nature. A number of such examples of the synergistic use of biology and chemistry will be discussed ranging from the generation of selective biological catalysts and organisms with expanded genetic codes to genomics, drug discovery and materials science.

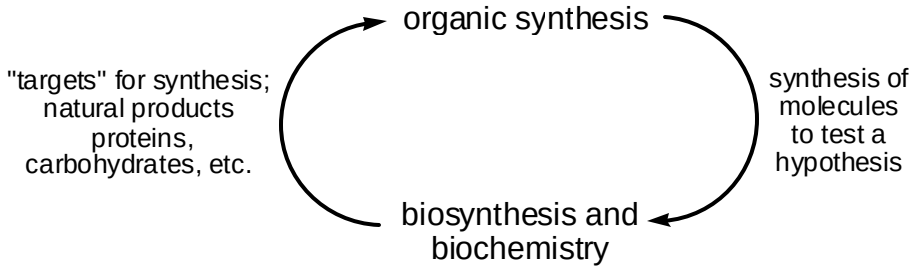
Notes

USING LESSONS FROM NATURE IN ORGANIC SYNTHESIS

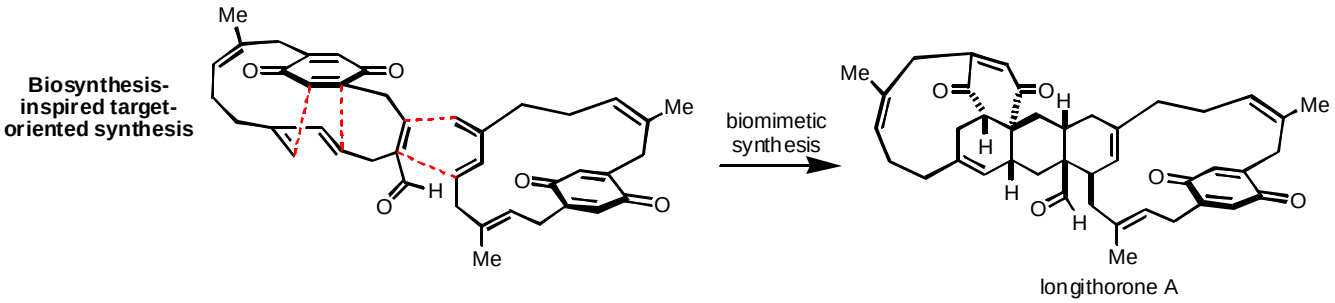
Matthew D. Shair
Department of Chemistry and Chemical Biology, Harvard University
12 Oxford Street, Cambridge, MA 02138

My lecture will describe how a synergistic relationship between organic synthesis, biosynthesis, and biochemistry has led to projects in three areas: target-oriented synthesis, catalytic reactions, and the discovery of small molecules to study cell biology.

For several decades, organic synthesis has been used to answer questions about the way in which nature assembles complex molecules. For example, Konrad Bloch used organic synthesis to prepare isotopically labeled squalene to determine the mechanism of the enzyme-catalyzed conversion of squalene to lanosterol. Chemists have also used organic synthesis to prepare intermediates believed to be generated during natural product biosynthesis in order to test its chemical feasibility. In turn, biosynthesis has provided many of the targets that have been used in the development of organic synthesis. This synergistic relationship between organic synthesis and biosynthesis has been a powerful engine for discovery in both areas.

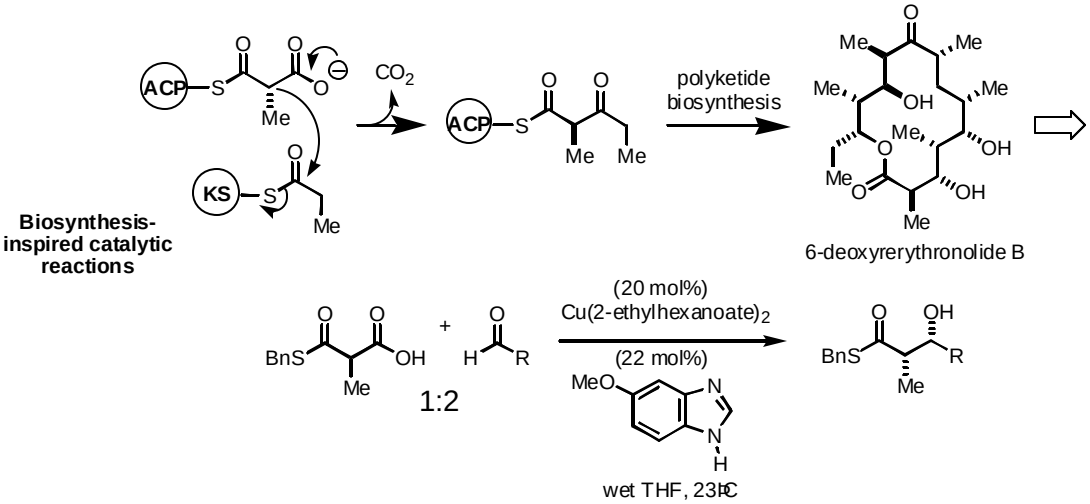


Our interest in using organic synthesis to test the chemical feasibility of a biosynthesis hypothesis brought our attention to longithorone A, a marine natural product with a unique heptacyclic structure. It was proposed by Schmitz that the biosynthesis of longithorone A involved intermolecular and transannular Diels-Alder reactions between two nearly identical paracyclophanes. Equally provocative was the possibility that the atropisomerism of both of these paracyclophanes completely, or in some part, controlled the absolute and relative stereochemistry of the natural product. We have used organic synthesis to construct paracyclophanes closely related to those believed to be involved in the biosynthesis of longithorone A and used them to test the chemical feasibility of these reactions.

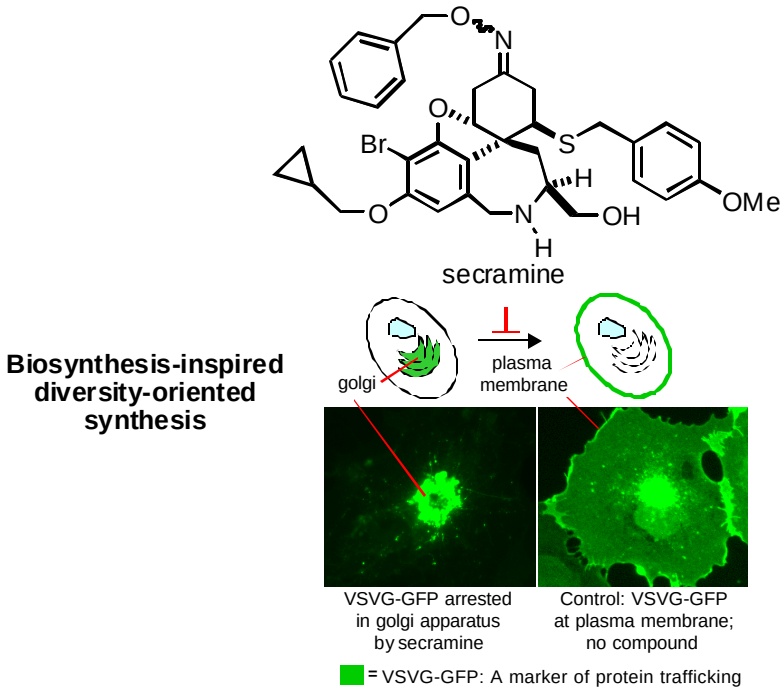


The use of biosynthesis to inspire complex molecule synthesis has a long, productive history. The application of laboratory emulation of biosyntheses to inspire useful, interesting catalytic reactions has less precedent. During fatty acid and polyketide biosynthesis, a thioester enolate, or its equivalent, is

generated from a malonic acid half thioester and it reacts with another thioester in a cross-Claisen condensation. This is the predominant C-C bond forming reaction in fatty acid and polyketide biosynthesis. It would be interesting and possibly useful to generate ester enolates or their equivalents in the laboratory under conditions that approximate those used in nature. In fact, we have succeeded in adapting nature's ester enolate precursors, malonic acid half thioesters, to a laboratory-friendly catalytic thioester aldol reaction.



The reaction is achieved using catalytic quantities (as low as 5 mol%) of commercially available Cu(2-ethylhexanoate)$_2$ and 5-methoxybenzimidazole. The reaction can be performed in wet solvents, including THF, EtOAc and acetone, open to the atmosphere, and at room temperature. The aldol reaction is diastereoselective with some aldehydes. In my lecture, I will report on the discovery of this reaction, the development of an enantioselective variant and experiments to deduce the mechanism.



Taking a departure from the ways in which biosynthesis has influenced organic synthesis; we have performed a diversity-oriented synthesis of 3000 galanthamine-like molecules using a synthesis approach that resembles its biosynthesis. The purpose of making a collection of 3000 galanthamine-like molecules was to use them in cell-based phenotypic screens to identify small molecules that would be useful in exploring cell biology. It was not known, a priori, that molecules resembling galanthamine would have any inherently new biological properties compared to the natural product, but this skeleton was chosen to demonstrate the utility of biosynthesis-inspired diversity-oriented synthesis. Since biosynthesis-inspired organic synthesis often leads to complex structures efficiently and rapidly, we believed that marrying this approach to diversity-oriented synthesis would be useful. Through cell-based screens, it was discovered that one of the galanthamine-like molecules potently disrupted the secretory pathway in mammalian cells. This molecule, named secramine, was shown to block protein trafficking from the Golgi apparatus to the plasma membrane. It is one of the first examples of diversity-oriented synthesis of a natural product-like molecule combined with cell-based screens leading to a molecule with a biological property that does not exist in the natural product. Over the last year, we have made progress in determining the mechanism by which secramine blocks protein trafficking.

Most of the small molecules that are used in cell biological research have historically come from natural products. However, recently, several examples of combining diversity-oriented organic synthesis and cell-based or protein binding-based screens, including the discovery of secramine, have demonstrated the potential for discovering useful biological “reagents” by an approach that is not beholden to the isolation of naturally occurring molecules.

Notes

Electronic Polymers For Sensory Applications

Timothy M. Swager
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e-mail: tswager@mit.edu

This lecture will describe the conceptual design and optimization of chemical sensors based upon conjugated polymers.[1] The ability of a conjugated polymer to produce gain (amplification) in a fluorescence- or resistance-based chemosensor stems from its ability to transport optical excitations or electrical charge, respectively, over large distances. These transport properties provide the increased sensitivity and versatility of conjugated polymers over small-molecule chemosensors. My program is striving to add new functional diversity to conjugated polymers and to optimize their conductive and chemoresistive properties. It is clear that this agenda requires careful optimization of polymer structure both at the molecular and supramolecular level.

In a fluorescence sensor, the migration of an optical excitation increases the probability of an encounter with an occupied binding site. We originally demonstrated this scheme making use of analyte induced quenching (Figure 1a).[2] We have also been interested in using local reductions in the polymers bandgap (E_g) to produce wavelength shifts in the polymers emission (Figure 1b).

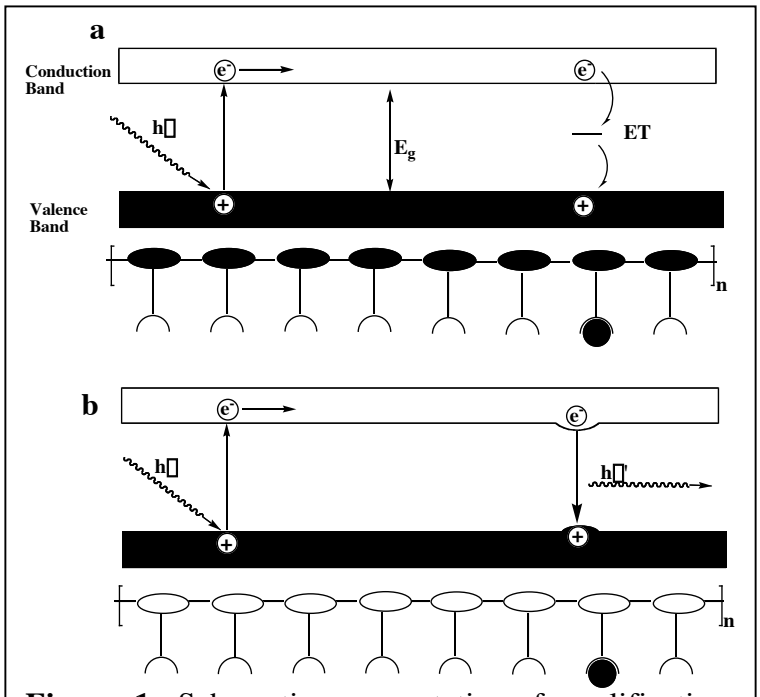


Figure 1. Schematic representation of amplification. (**a**) Excitations migrate along the polymer backbone and are quenched when they encounter an acceptor. (**b**) Excitations selectively recombine at trapping sites created by the occupation of a non-quenching analyte, which produces a local minimum in the band gap.

We continue to develop new polymers that have optimal fluorescent semiconductive polymers properties for sensor, photovoltaic, and electroluminescent applications. Previous designs described by us and others have focused on avoiding interchain interactions (3-D electronic interactions) with leads to self-quenching of fluorescence and inherent compromises in the mobility of charge and energy throughout the medium. This has restricted the performance of materials in many electrooptic applications. We now report the formation of stable highly fluorescent chiral 3-D grids using interlocking structural elements on the polymer (Figure 2).[3] Based

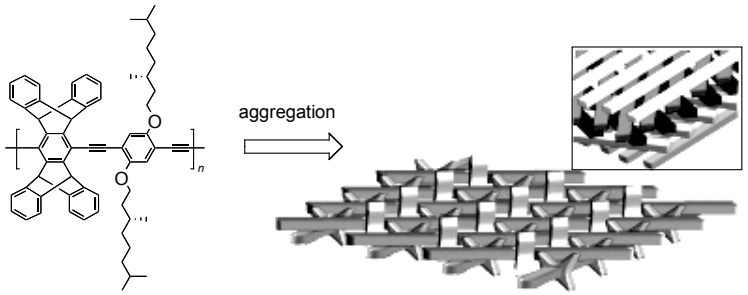


Figure 2. Aggregation of this chiral polymer creates grids that have 3-dimensional electronic structures and improved exciton and carrier mobility.

upon our investigation of 58 different polymers, we find that simple chiral polymers lacking interlocking structural elements, do not display this behavior. We have further shown that these chiral grid polymer assemblies provide superior sensory properties for the detection of the explosive TNT.[4]

To impart recognition to our polymers we have made use of a variety of molecular recognition schemes, assemblies, and reactions. Recently we have developed a polymer dosimetric sensor for the detection of fluoride ion in an effort to develop systems that could be used in nuclear nonproliferation (Figure 3). This represents an example of a reactivity-based sensor wherein the response is the result of the highly specific reaction of fluoride ions with silyl protecting groups.

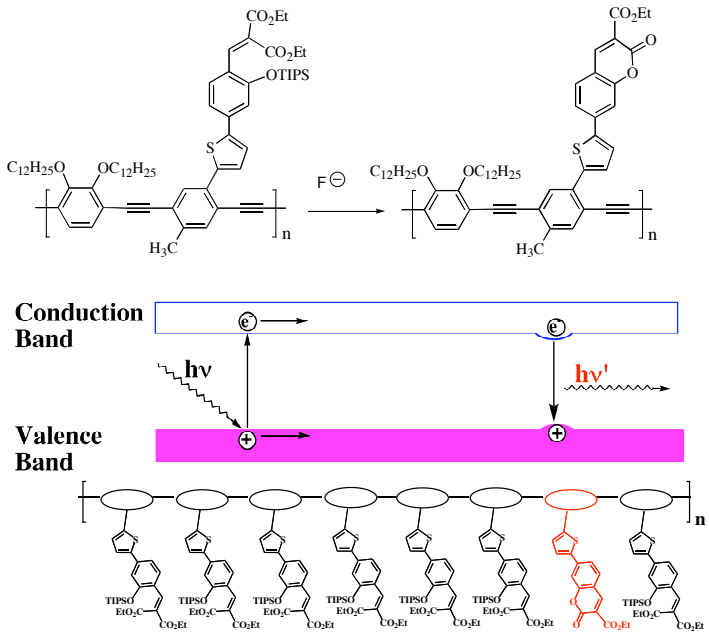
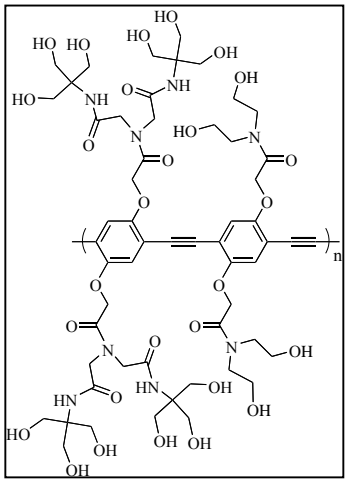


Figure 3. Fluoride ion triggered cyclization can be amplified in a conjugated polymer by energy migration to low band-gap segments of the polymer chains.

Other recognition schemes are focused on biological targets. For optimal biosensory functions we have been developing a series of water-soluble polymers. It was necessary to attach a large number of hydroxyl groups to the monomers to overcome the highly hydrophobic nature of the conjugated polymer backbone and the high affinity that these structures have for aggregation. Many water soluble polymers conjugated polymers have been produced using ionic groups. Charged groups however give rise to non-specific interactions with oppositely charged biomolecules. These new polymers are completely neutral and thereby avoid these nonspecific interactions.[5] Recent applications of these materials in biosensory schemes will be discussed.



References:

[1] (a) Swager, T. M. "The Molecular Wire Approach to Sensory Signal Amplification" *Accts. Chem. Res.* **1998**, 31, 201-7. (b) Wosnick, J. H.; Swager, T. M. "Molecular Photonic and Electronic Circuitry for Ultrasensitive Chemical Sensors" *Curr. Opinion Chem. Bio.* **2000**, 4, 711-720. (c) McQuade, D. T.; Pullen, A. E.; Swager, T. M. "Conjugated Polymer Sensory Materials" *Chem. Rev.* **2000**, 100, 2537-2574.

[2] Zhou, Q.; Swager, T. M. "A Method for Enhancing Sensitivity in Fluorescent Chemosensors: Energy Migration in Conjugated Polymers" *J. Am. Chem. Soc.* **1995**, 117, 7017-8.

[3] Zahn, S.; Swager, T. M. "Three Dimensional Electronic Delocalization in Chiral Conjugated Polymers" *Angew. Chem. Int. Ed. Engl.* **2002**, *41*, 4225-423.

[4] Yang, J.-S.; Swager, T. M. "Porous Shape Persistent Fluorescent Polymer Films: An Approach to TNT Sensory Materials " *J. Am. Chem. Soc.* **1998**, 120, 5321-5322.

[5] Kuroda, K.; Swager, T. M. "Synthesis of a Nonionic Water Soluble Semiconductive Polymer" *Chemical Commun.* **2003**, 26-27.

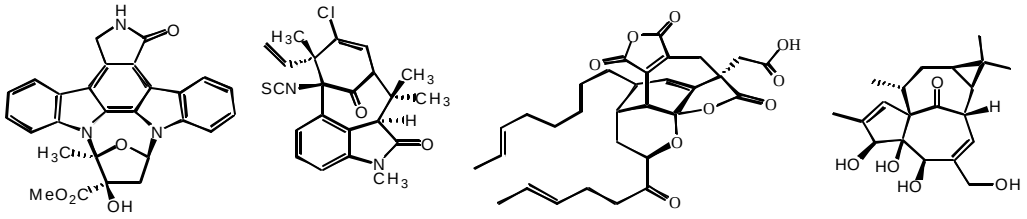
Notes

Bridged Polycyclic Natural Products: Inspirational Targets for Total Synthesis

John L. Wood
Department of Chemistry, Yale University

Over the past several years our group has been focusing on syntheses of bridged polycyclic natural products (Figure 1), molecules which have proven to be inspirational to the development of both strategies and tactics in organic synthesis. Critical to these developments has been the evolutionary nature of synthesis; the discovery of novel transformations while engaged in a synthesis often influence subsequent directions in the ongoing synthesis and the general approaches taken toward other target molecules.

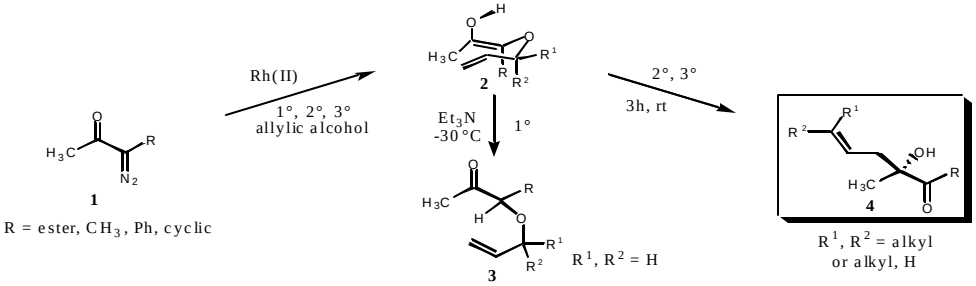
Figure 1



K252a | *N*-Methyl-welwitindolinone C Isothiocyanate | CP-263,114 | Ingenol

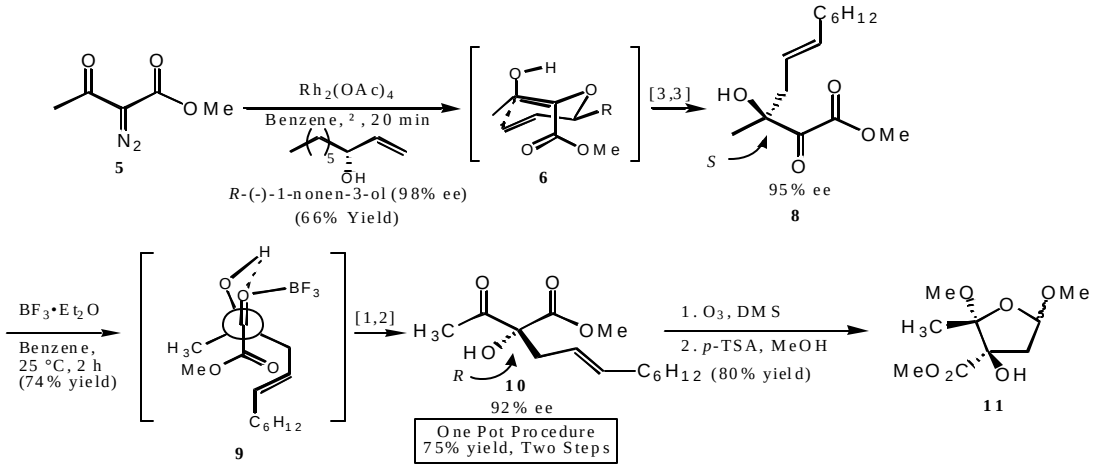
Early efforts directed toward a synthesis of K252a led to the discovery that alpha-diazo ketone derived rhodium carbenoids couple with alcohols to selectively furnish Z-enols. Of particular value to our synthetic effort was the observation that Z-enols derived from 2° and 3° allylic alcohols rapidly undergo Claisen rearrangement to the corresponding alpha-hydroxy ketones (e.g., **1 to 2 to 3**, Scheme 1).

Scheme 1

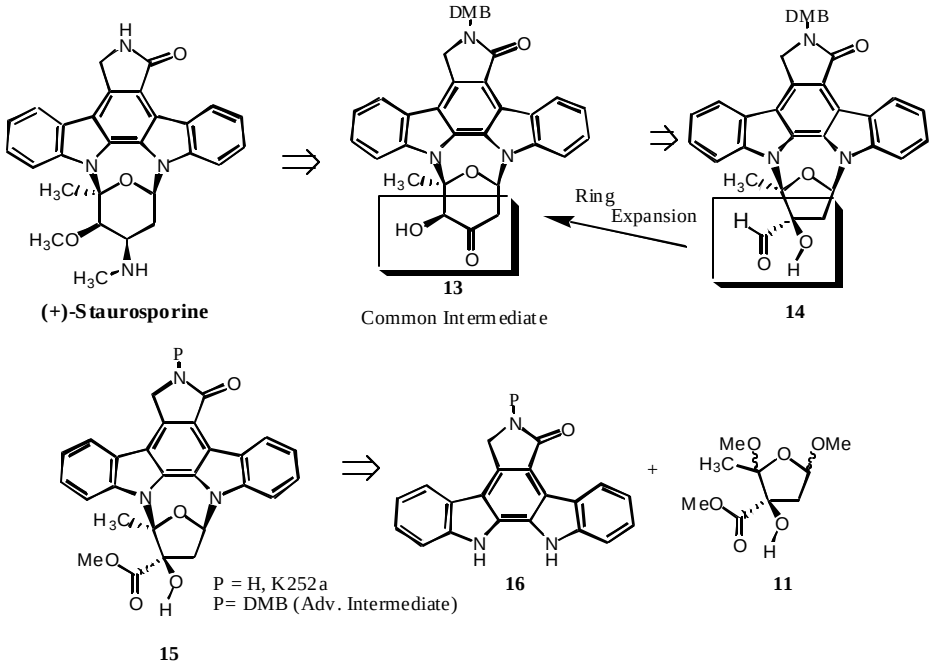


Importantly, selective enol formation coupled with the high degree of stereochemical transfer intrinsic to the Claisen rearrangement allows the preparation of enantioenriched alpha hydroxy ketones from readily available enantioenriched allylic alcohols. As illustrated in Scheme 2, this chemistry was employed in a synthesis of the K252a carbohydrate that also featured a stereoselective alpha-ketol rearrangement of the derived alpha-hydroxy ketone (e.g., **8 to 9 to 10**). This latter chemistry inspired development of a similar alpha-ketol rearrangement in a ring expansion approach to Staurosporine (e.g. **14 to 13**, Scheme 3).

Scheme 2

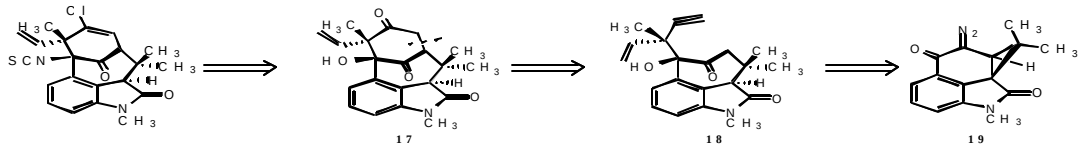


Scheme 3



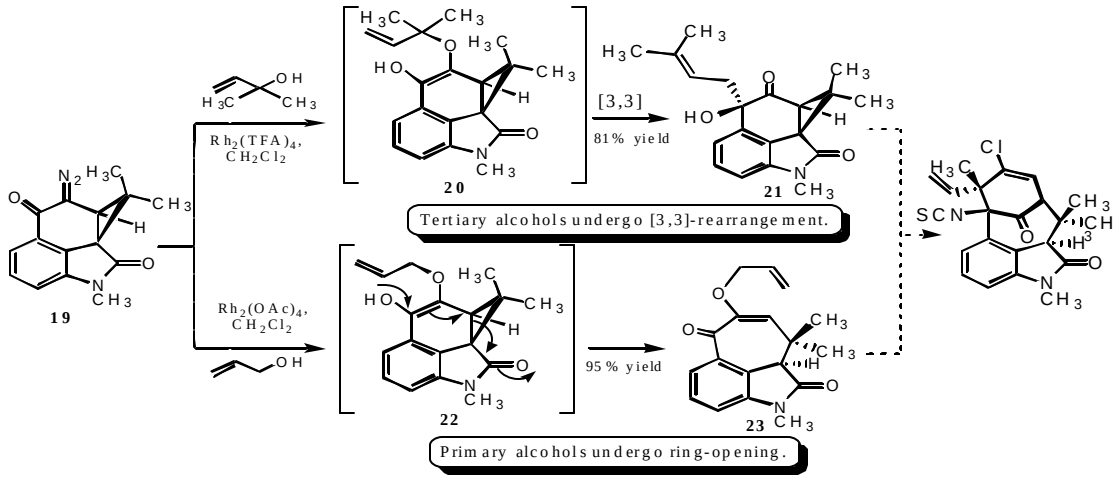
While still in the midst of the K252a synthesis we began developing an approach to the welwitindolinone alkaloids. Interested in further applications of the then recently developed rhodium initiated Claisen rearrangement we began exploring the feasibility (Scheme 4) of a late stage rearrangement that would transform alpha diazo ketone **19** to **18** an intermediate poised for conversion to welwitindolinone C.

Scheme 4



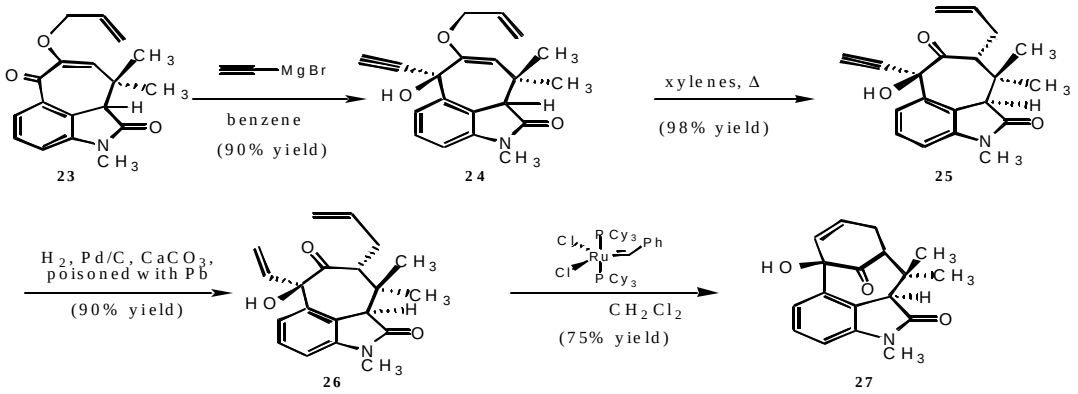
As illustrated in Scheme 5, **19** was indeed found to undergo the desired rearrangement when combined with 3° allylic alcohols. In contrast, when engaging 1° allylic alcohols under similar conditions **19** was found to furnish ring opened product **23**.

Scheme 5



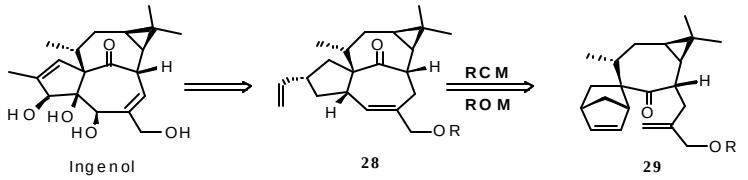
Although we continue to pursue the rhodium initiated Claisen approach to the welwitindolinones, the observed reactivity of **19** with primary allylic alcohols has also proven useful as the derived ring-opened product **23** provided facile access to the complete carbon skeleton via a four step sequence that concludes with a ring closing metathesis (RCM) reaction (Scheme 6).

Scheme 6

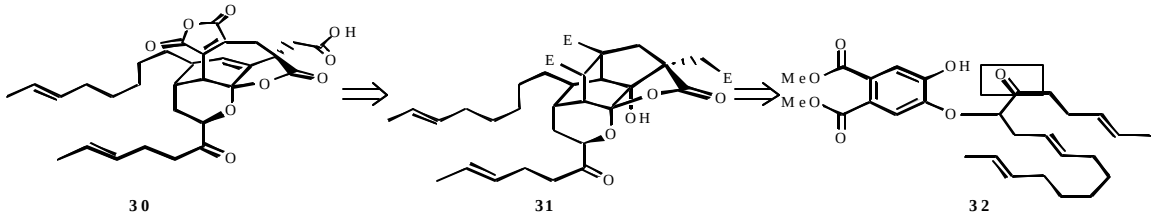


Efforts to complete the carbocyclic skeleton of the welwitindolinones coincided with the initiation of synthetic programs directed toward the tumor promoter ingenol and CP 263,114. As illustrated in Schemes 7 and 8, a ring closing metathesis-based approach to ingenol and a Claisen-inspired fragmentation approach to CP 263,114 (**30**) reflect influences of our ongoing welwitindolinone and completed staurosporine syntheses. This seminar will intermix the evolution of our overall research program with the development of synthetic approaches directed toward CP263,114 and ingenol.

Scheme 7



Scheme 8



Notes

38th National Organic Symposium
Poster Abstracts
Session A

Schedule of Presenters – Poster Session A Sunday June 8, 8 pm – 12 am

A1 PROGRESS TOWARDS THE TOTAL SYNTHESIS OF MYRIAPORONE 4
Kristen N. Fleming and Richard E. Taylor
University of Notre Dame
Department of Chemistry and Biochemistry, Notre Dame , IN 46556-5670

A2 STRUCTURALLY DIVERSE CYCLOPROPANES *VIA* HETEROATOM STABILIZATION OF HOMOALLYLIC CATION REARRANGEMENTS
Christina A. Risatti and Richard E. Taylor*
University of Notre Dame,
Department of Chemistry and Biochemistry, Notre Dame, IN 46556

A3 SYNTHETIC AND CONFORMATIONAL STUDIES OF THE CORNEXISTINS
Chen, W.; Tung, J. C; Taylor, R. E.* and Dent III, W. H.[1]
Department of Chemistry & Biochemistry, University of Notre Dame*,
Notre Dame, IN 46656 and Discovery Research, Dow Agrosciences LLC[1], Indianapolis, IN 46268-1054

A4 ALKYL CARBAMOYL OXADIAZOLIDINEDIONES: NOVEL PRE-EMERGENCE HERBICIDES
Kanu M. Patel, Elaine K. Rhoads, Thomas M. Stevenson, Tho V. Thieu, Xian J. Meng, Farah Ali, Frank T. Coppo, Chi Peng Tseng, Georgia R. Pugh, George C. Chiang, Gary D. Annis, Wonpyo Hong, Bruce L. Finkelstein, Stephen K. Gee, Morris P. Rorer, David A. Clark, Bonita M. Reeves, Matthew A. Wilson, Ja Kim, Mukesh Shah, Robert J. Pasteris and Maya Sethuraman
DuPont Crop Protection
Stine -Haskell Research Center, Newark, DE 19714

A5 CATALYTIC ASYMMETRIC SYNTHESIS WITH KETENES: THE DEVELOPMENT OF NOVEL METHODOLOGY FOR THE SYNTHESIS OF ß-LACTAMS AND ß-HALOESTERS
Andrew E. Taggi, Ahmed M. Hafez, Harald Wack, Thomas Lectka
The Johns Hopkins University
Department of Chemistry, 3400 North Charles Street, Baltimore, MD 21218

A6 A MILD, EFFICIENT METHOD FOR THE SYNTHES IS OF AROMATIC AND ALIPHATIC SULFONAMIDES
Carl Berthelette* and Wing Yan Chan
Merck Frosst Center for Therapeutic Research
16711 Trans Canada Hwy., Kirkland, Quebec, Canada, H9H 3L1

A7 SYNTHESIS OF CYCLOHEXANOINDOLES: A NOVEL CLASS OF POTENT AND SELECTIVE PROSTAGLANDIN D2 RECEPTOR (DP) ANTAGONISTS.
Boyd, M.; Berthelette, C.; Scheigetz, J.; Roy, B.; Sturino, C.; Lachance, N.
Merck Frosst Center for Therapeutic Research.
16711 Trans Canada Hwy., Kirkland, Quebec, Canada, H9H 3L1

A8 SYNTHETIC APPLICATIONS OF AN ASYMMETRIC INVERSE ELECTRON DEMAND HETERO-DIELS-ALDER REACTION
David E. Chavez and Eric N. Jacobsen
Harvard University
Department of Chemistry and Chemical Biology
Cambridge, MA USA 02138

A9 STEPS TOWARD THE SYNTHESIS OF C-GLYCOSIDE CONTAINING DENDRIMERS

Michael J. Panigot, Shang-U Kim, Alison M. Bare, Matthew D. Whiteside, Jeremy Lamb, Jason Boggs, Jennifer Faulkner, Amanda Caldwell, Robin Carlton

Department of Chemistry, Arkansas State University, State University, AR 72467

A10 EFFORTS TOWARD THE SYNTHESIS OF STEREOSELECTIVELY BETA-DEUTERATED HISTIDINE

Michael J. Panigot[1], Robert W. Curley, Jr.[2], Derek W. Barnett[2], Rikki Long[1], Jennifer L. Faulkner[1], Lesley White[1], Alistair Kent[3]

1. Department of Chemistry, Arkansas State University, State University, AR 72467
2. Division of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, The Ohio State University, Columbus, OH 43210
3. Department of Physical Science, Harding University, Searcy, AR 72149

A11 TOWARD TOTAL SYNTHESIS OF AMIDE LINKED RNA MIMICS

Eriks Rozners, Yang Liu, Qun Xu

Department of Chemistry and Chemical Biology, Northeastern University
360 Huntington Ave., Boston, MA 02115

A12 SYNTHESIS OF ARYL AND HETEROARYL ACETONITRILE AND ACETAMIDE DERIVATIVES VIA CYANOCARBONATION/HYDROGENATION OF ARYL ALDEHYDES

Stanley P. Kolis*, Marcella T. Clayton, John L. Grutsch and Margaret M. Faul

Global Chemical Process Research and Development
Eli Lilly and Company, Indianapolis, IN 46285-4813

A13 A [2+2] CYCLOADDITION ROUTE TO DIMETHYLAMINOMETHYLENE VINAMIDINIUM SALTS

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A14 A PRACTICAL EFFICIENT SYNTHESIS OF ANTI-MITOTIC COMPOUND, A-289099

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A15 SOLID STATE SULFONATION OF ARYLAMINES

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A16 EXAMINATION OF THE NOVEL REACTIVITY OF BRIDGEHEAD LACTAMS

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A17 THE DISCOVERY OF NOVEL IMMUNOSUPPRESSIVE AGENTS THROUGH BIOCATALYSIS AND CHEMO-ENZYMATIC METHODS

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A18 METABOLICALLY-STABILIZED LYSOPHOSPHATIDIC ACID ANALOGUES

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A19 COLORIMETRIC NANO-SENSORS BASED ON PHOTO-POLYMERIZABLE AMPHIPHILIC PAMAM DENDRIMERS

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A20 GENERATION AND CYCLIZATION OF IMIDOYL RADICALS DERIVED FROM PHENYLSELENYL IMIDATES

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A21 STUDIES TOWARD THE TOTAL SYNTHESIS OF CAPENSIFURANONE UTILIZING ASYMMETRIC CONJUGATE ADDITION

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A22 SYNTHETIC EFFORTS TOWARD THE TOTAL SYNTHESIS OF SPHINXOLIDE

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A23 STEREOSELECTIVE SYNTHESIS OF ß-ARYL-ß-AMINOESTERS

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A24 USING MICROFLUIDICS TO CONTROL CHEMICAL SYSTEMS IN TIME

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A25 STUDIES DIRECTED TOWARD THE SYNTHESIS OF PRIMARY AMINES FROM KETONES AND ALDEHYDES VIA REDUCTIVE AMINATION

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A26 AN EFFICIENT SYNTHESIS OF D-*THREO* AND L-*THREO*-GALACTOSYL CERAMIDES

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A27 THE DEVELOPMENT AND UTILITY OF CLICKCHEM REACTIONS IN THE SYNTHESIS OF DRUG-LIKE MOLECULES

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A28 SYNTHETIC STUDIES ON NATURALLY OCCURRING TETRAMIC ACID CONTAINING MACROLACTAMS

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A29 A NO-D* ^{1}H NMR STUDY OF THE REACTION SEQUENCE FOR PREPARATION OF THE KELLY b-TURN MIMIC

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A30 NO-D* ^{1}H NMR SPECTROSCOPIC TITRATIONS OF CARBANIONIC (RLi, RMgX) AND HYDRIDIC (LAH, DIBALH) REAGENTS

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A31 A FAMILY OF *iota*-AMINO ACIDS FOR THE CREATION OF NANOMETER-SCALE MOLECULAR ARCHITECTURES

James S. Nowick, Chris Gothard, Sang-Woo Kang, Santanu Maitra
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A32 A TOTAL SYNTHESIS OF (-)-DACTYLOLIDE [AND (-)-ZAMPANOLIDE] VIA TI(IV)-MEDIATED MACROLACTONIZATION/COUPLING OF EPOXIDE AND CARBOXYLIC ACID COMPONENTS

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A33 KINETIC LACTONIZATIONS OF PSEUDOSYMMETRIC, HIGHLY OXYGENATED AZELAIC ACIDS: THE C(1)-C(9) FRAGMENT OF PELORUSIDE A

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A34 DESIGN AND SYNTHESIS OF METHYLATED ANALOGS OF THE IMPORTANT CALCIUM RELEASE INHIBITOR, XESTOSPONGIN C

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A35 A TOTAL SYNTHESIS OF CALLIPELTOSIDE A: RING FORMATION BY ACYL KETENE MACROLACTONIZATION VERSUS RELAY RING CLOSING METATHESIS

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A36 ^{1}H NMR CHEMICAL SHIFT INCREMENTS FOR OXYGEN-CONTAINING SUBSTITUENTS: METHYLCYCLOHEXANOLS

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A37 CROSS-COUPLING OF TRIALKYL VINYL GERMANES WITH ARYL HALIDES

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A38 HIGHLY SENSITIVE FLUORESCENT ZINC SENSORS

Royzen, Maksim and Canary, James, W.
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A39 3,4-EPOXY-1-BUTENE. A VERSATILE INTERMEDIATE FOR ORGANIC SYNTHESIS

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A40 INDOLE-CONTAINING HETEROCYCLES FORMED BY A NOVEL TANDEM INDOLIC OXIDATION/CYCLIZATION REACTION

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A41 PROCESS RESEARCH AND DEVELOPMENT OFAN $\alpha_V\beta_3$ INTEGRIN ANTAGONIST

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A42 A FACILE REACTION OF (Z)-(1-BROMO-1-ALKENYL)BORONATE ESTERS WITH CYCLOPENTYL MAGNESIUM BROMIDE. AN EASY ACCESS TO ALKYL CYCLOPENTYL KETONES

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A43 ISOLATION, PURIFICATION AND CHARACTERIZATION OF A SAPONIN BIOACTIVE MOLECULE FROM CITRULLUS COLOCYNTHIS

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A44 EXPLORING NOVEL SYNTHETIC METHOD BASED ON INDIUM CHEMISTRY AND ITS APPLICATION TO THE TOTAL SYNTHESIS OF ANTILLATOXIN

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A45 EXPANDING THE GENETIC ALPHABET: SYNTHESIS AND FUNCTIONALIZATION OF 7-DEAZA-ISO-GUANINE FOR POLYMERASE IN VITRO EVOLUTION STUDIES

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A46 IAN AMINES: NEW REAGENTS FOR ORGANIC AND ORGANOMETALLIC SYNTHESIS

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A47 SELF-COMPLEMENTARY SUPRAMOLECULAR DIMERIZATION VIA EIGHT HYDROGEN BONDS

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A48 FORMATION OF SILOLES FROM DILITHIOBUTADIENE SYSTEMS AND MONOCHLOROSILANES; LOSS OF ORGANIC GROUPS FROM SILICON

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A49 AN ALLENIC PAUSON-KHAND APPROACH TO GUANACASTEPENE A

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A50 A REGIOSELECTIVE NITRATION OF (*R,R*)-*TRANS*-1-AMINO-2-INDANOL

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A51 OPTIMIZED SYNTHESIS OF AN ARYL-ALKYL AMIDINE

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A52 DEVELOPMENT OF AN ASYMMETRIC SYNTHETIC APPROACH TO 1,3,4-TRI-SUBSTITUTED IMIDAZOLIDIN-2-ONE DERIVATIVES FROM L-METHIONINE

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A53 DIAZAPENTACENE AND ITS DERIVATIVES: A NEW FAMILY OF ORGANIC SEMICONDUCTORS

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A54 VICINAL HETEROATOM FUNCTIONALIZATION OF OLEFINS USING GROUP TEN TRANSITION METALS

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A55 AN ALLENIC ALDER-ENE AND PAUSON-KHAND REACTIONS, A STRATEGY FOR RAPID ASSEMBLY OF MULTIPLE ARCHITECTURALLY UNIQUE COMPOUNDS

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A56 CONVENIENT SYNTHESES OF SIDE-CHAIN FLUORINATED BIOIMIDAZOLES

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A57 FORMAL ASYMMETRIC SYNTHESIS OF (+)-EPOXYSORBICILLINOL

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A58 SYNTHESIS OF BENZOFURYL METHYL TETRAHYDROPYRIDINES

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A59 EFFECT OF CONFORMATIONAL CONSTRAINTS ON THE REACTIVITY OF DIAZOMALONATES AND THEIR DIAZIRINE ISOMERS

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A60 A STEREOSELECTIVE INTRAMOLECULAR AZA [3 + 3] FORMAL CYCLOADDITION APPROACH TO INDOLIZIDINES AND QUINOLIZIDINES

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A61 TANDEM CARBON-CARBON BOND CONSTRUCTIONS VIA CATALYZED BROOK REARRANGEMENT REACTIONS

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A62 PROGRESS TOWARDS THE TOTAL SYNTHESIS OF THE CALLIPELTOSIDE A AGLYCONE

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A63 NOVEL COMBINATIONS OF THE NICHOLAS AND PAUSON-KHAND REACTIONS

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A64 TOTAL SYNTHESIS OF PHORBOXAZOLE A

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A65 AN ALLENIC ALDER ENE APPROACH TOWARDS THE SYNTHESIS OF CASSIOL

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A66 CLASSICAL RESOLUTION OF a-SUBSTITUTED-ß- PHENETHYLAMINES AND ß-AMINOTETRALINS: SYNTHESIS, METHODS, ^{1}H NMR ANALYSIS

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A67 STUDIES OF ENZYMES, TOXIC MOLECULES AND OTHER MACROMOLECULES OF A NEW HYBRID SOYBEAN VARIETY BY INSTRUMENTAL & CONVENTIONAL CHEMICAL METHODS.

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A68 RING-CLOSING METATHESIS REACTIONS OF NOVEL YNAMIDES AND INTRAMOLECULAR OXYALLYL [4 + 3] CYCLOADDITIONS OF ALLENAMIDES

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A69 PREPARATION AND APPLICATIONS OF A POLYMER-SUPPORTED PHOSPHORYL AZIDE

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A70 LITHIATION OF 3,4-DIHYDRO-2H-PYRAN: A DENSITY FUNCTIONAL THEORY STUDY

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A71 BIO-ACTIVE MOLECULE SYNTHESIS INCORPORATING RING-CLOSING METATHESIS

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A72 C-H AMINATION METHODS FOR ORGANIC SYNTHESIS: DISCOVERY, SCOPE AND MECHANISM

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A73 SYNTHESIS OF SUBSTITUTED FARNESYLS

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A74 PROGRESS TOWARDS THE SYNTHESIS OF FUMAGILLOL VIA A RHODIUM CATALYZED FORMAL ALLENIC ALDER-ENE REACTION

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A75 SYNTHESIS OF A NOVEL UREIDOPEPTIDE HIV-1 PROTEASE INHIBITOR

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A76 STUDY OF THE CONFORMATION OF $GABA_A$-BENZODIAZEPINE RECEPTOR BIVALENT LIGANDS BY LOW TEMPERATURE NMR

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A77 A PRACTICAL SYNTHESIS ACCESSING CHEMICAL DESCRIPTOR SPACE CHARACTERIZED BY MULTIFUNCTIONALITY, FEW ROTATABLE BONDS, CHIRALITY AND PRIVILEGED STRUCTURES.

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A78 CHROMIUM(III)-CATALYZED ASYMMETRIC HETERO-ENE REACTIONS

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A79 TOWARD THE TOTAL SYNTHESIS OF LEMONOMYCIN

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A80 PALLADIUM-CATALYZED OXIDATIVE WACKER CYCLIZATIONS IN NONPOLAR ORGANIC SOLVENTS WITH MOLECULAR OXYGEN: A STEPPING STONE TO ASYMMETRIC AEROBIC CYCLIZATIONS

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A81 EXPERIMENTAL EVIDENCE FOR PYRINDINE RING-OPENING AND RECLOSURE PATHWAYS IN NITROSATIVE GUANOSINE DEAMINATION

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A82 HIGHLY ENANTIOSELECTIVE SYNTHESES OF FUNCTIONALIZED LACTAMS VIA Rh(I)-CATALYZED CYCLOISOMERIZATION OF ENYNES AND THE APPROCH TO THE SYNTHESES OF KAINIC ACIDS

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A83 THE SYNTHESIS OF SELENOXANTHONES AS PRECURSORS TO SELENORHODAMINE PHOTOSENSITIZERS FOR PHOTODYNAMIC THERAPY

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A84 THE SYNTHESIS AND APPLICATION OF A NOVEL OPTICALLY PURE *C*$_3$ SYMMETRIC PHOSPHINE LIGAND

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A85 MACROCYLIC METABOLITES FROM THE MARINE SPONGE *MYRIASTRA CLAVOSA*

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A86 A KILOGRAM SCALE SYNTHESIS OF 2-(PHENYLSULFONYL)-1,3-CYCLOHEXADIENE AND 2-(PHENYLSULFONYL)-1,3-CYCLOHEPTADIENE

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A87 STRUCTURE-ACTIVITY RELATIONSHIP STUDIES OF 3-BENZYILDENEPHATHALIDE ANALOGS

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A88 PROGRESS TOWARDS THE TOTAL SYNTHESIS OF (+)-SORANGICIN A

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A89 ASYMMETRIC SYNTHESIS OF CYCLOPENTANE AND CYCLOPROPANE PEPTIDE NUCLEIC ACID MONOMERS

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A90 NEW STEREOSELECTIVE SYNTHESES OF *CIS*- AND *TRANS*-2-METHYL-4-ARYL-PIPERIDINES

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PROGRESS TOWARDS THE TOTAL SYNTHESIS OF MYRIAPORONE 4

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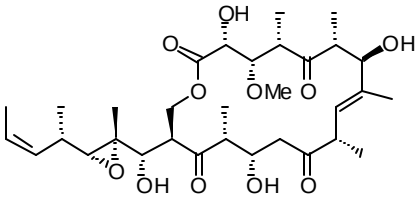
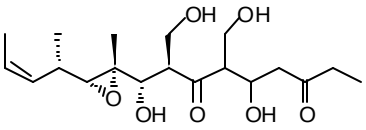
The macrolide natural product tedanolide was isolated from *Tedania ignis* (Caribbean sponge) by Schmitz in 1984 and found to be extremely cytotoxic against lymphocytic leukemia and human nasopharynx carcinoma. More recently, Rinehart reported the isolation of a class of structurally related compounds, the myriaporones. Since the myriaporones also exhibit cytotoxicity against murine leukemia, this class of compounds may represent structurally simplified tedanolide analogs. Very little is known about the biological mode of action of either tedanolide or the myriaporones, so the goal of this project is to determine whether or not they share the same biological receptor. Efforts toward these goals will be presented.



Tedanolide



Myriaporone 4

Structurally Diverse Cyclopropanes *via* Heteroatom Stabilization of Homoallylic Cation Rearrangements

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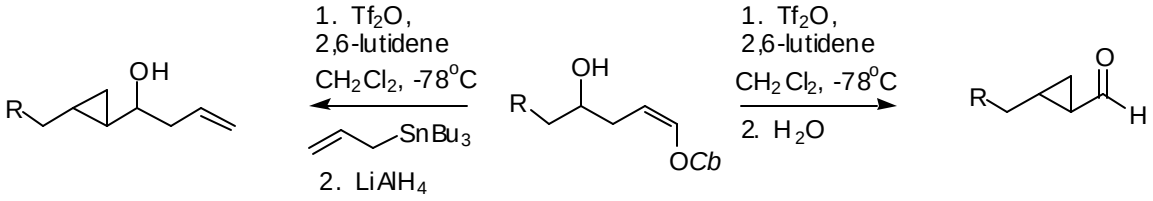
Recent advances in the area of cyclopropyl aldehyde formation via a cationic mechanism using heteroatom stabilization will be discussed. Including application toward enantiomerically enriched cyclopropyl aldehydes using chiral auxiliaries to induce asymmetry. Furthermore, trapping of intermediate oxonium ions to access structurally diverse cyclopropyl carbinols will also be introduced.



SYNTHETIC AND CONFORMATIONAL STUDIES OF THE CORNEXISTINS

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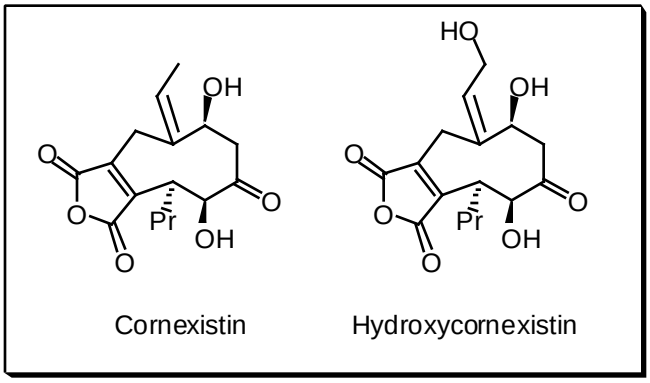
Notre Dame, IN 46656 and Discovery Research, Dow Agrosciences LLC[1], Indianapolis, IN 46268-1054.

The cornexistins are microbial natural products that show potent and selective herbicidal activity. s a part of our interest in the conformational properties of biologically active polyketides, we have begun to investigate these interesting nonadride natural products. M and computer modeling studies are being used in concert with total synthesis. ur progress towards the development of a total synthesis of cornexistin, hydroxycornexistin, and analogues as well as conformational analysis will be presented.



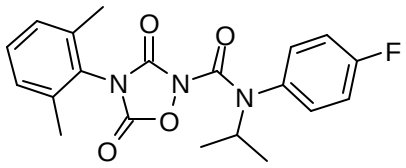
Alkyl Carbamoyl Oxadiazolidinediones: Novel Pre-Emergence Herbicides

Kanu M. Patel, Elaine K. Rhoads, Thomas M. Stevenson, Tho V. Thieu, Xian J. Meng, Farah Ali, Frank T. Coppo, Chi Peng Tseng, Georgia R. Pugh, George C. Chiang, Gary D. Annis, Wonpyo Hong, Bruce L. Finkelstein, Stephen K. Gee, Morris P. Rorer, David A. Clark, Bonita M. Reeves, Matthew A. Wilson, Ja Kim, Mukesh Shah, Robert J. Pasteris and Maya Sethuraman

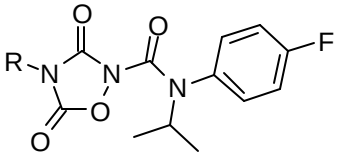
DuPont Crop Protection

Stine-Haskell Research Center, Newark, DE 19714

In the follow-up to our discovery of aryl carbamoyl oxadiazolidinediones(I) as a novel class of pre-emergence herbicides, we have found that alkyl carbamoyl oxadiazolidinediones (II) are safe and more active pre-emergence herbicides with selectivity to maize. We will discuss many routes to prepare the compounds of type (II) and present biological data for certain compounds.



(I)

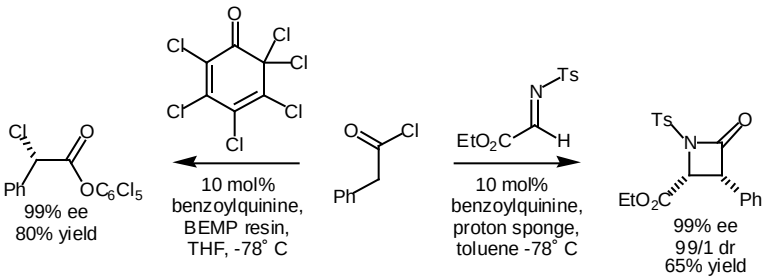


R= alkyl, alkoxy and amino

(II)

Catalytic Asymmetric Synthesis With Ketenes: The Development of Novel Methodology for the Synthesis of β-Lactams and α-Haloesters

Andrew E. Taggi, Ahmed M. Hafez, Harald Wack, Thomas Lectka
The Johns Hopkins University
Department of Chemistry, 3400 North Charles Street, Baltimore, MD 21218

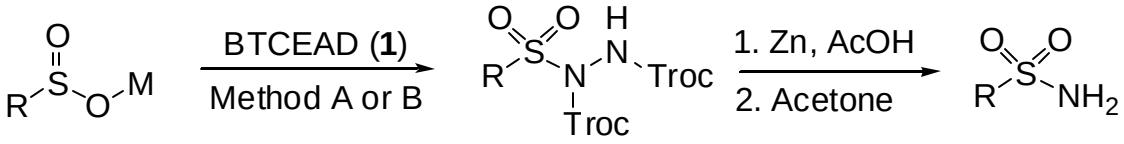


Central to this work was the development of the first catalyzed reaction of ketenes with imines to form β-lactams in extremely high enantio- and diastereoselectivity. The resultant class of β-lactams is known to inhibit serine proteases, which have been implicated in many diseases. This methodology was then adapted for use in a continuous flow system allowing for the synthesis of β-lactams using polymer-supported reagents and catalysts while obviating the need for work-up and column chromatography. inally, the same benzoylquinine-ketene catalyst system was then used as the keystone for the first catalytic asymmetric α-chlorination and α-bromination reactions resulting in enantiopure α-haloesters. These products are not only pharmaceutically active, but can also be employed as densely functionalized synthetic intermediates during the synthesis of many larger molecules.

A MILD, EFFICIENT METHOD FOR THE SYNTHESIS OF AROMATIC AND ALIPHATIC SULFONAMIDES

Carl Berthelette* and Wing Yan Chan
Merck Frosst Center for Therapeutic Research.
16711 Trans Canada Hwy., Kirkland, Quebec, Canada, H9H 3L1.

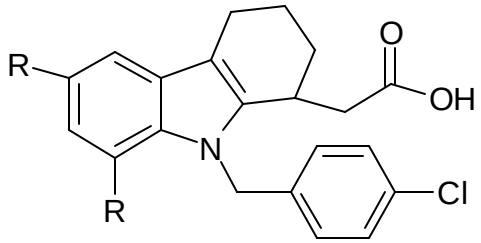
A two-step method was developed for the synthesis of aromatic and aliphatic sulfonamides from the corresponding sulfinates using bis(2,2,2-trichloroethyl) azodicarboxylate as the electrophilic nitrogen source. The intermediate hydrazides were obtained in very good yields and were cleaved under reductive conditions to yield the desired sulfonamides. A variety of substituents in the aromatic ring are well tolerated.



SYNTHESIS OF CYCLOHEXANOINDOLES: A NOVEL CLASS OF POTENT AND SELECTIVE PROSTAGLANDIN D2 RECEPTOR (DP) ANTAGONISTS.

Boyd, M.; Berthelette,. C.; Scheigetz, J.; Roy, B.; Sturino, C.; Lachance, N.
Merck Frosst Center for Therapeutic Research.
16711 Trans Canada Hwy., Kirkland, Quebec, Canada, H9H 3L1.

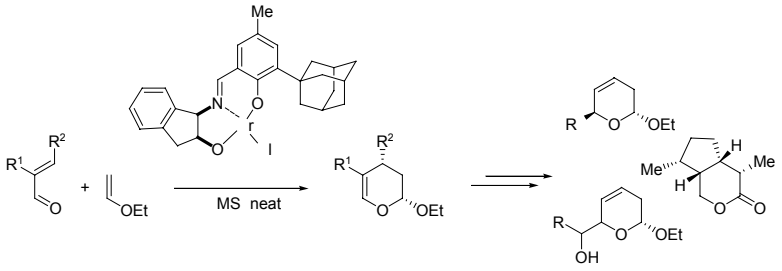
Prostaglandin D2 (PGD2) is considered to be an important mediator in various allergic diseases. Selective PGD2 receptor (DP) antagonists are useful for defining the role of PGD2 in allergic airway responses. It was discovered by high throughput screening that compounds of the basic structure 1 are potent DP antagonists. The challenges encountered in the synthesis of the compounds of this series will be described and discussed, as well as the SAR relating to potency and selectivity vs. the other prostaglandin receptors.



1

Synthetic Applications of an Asymmetric Inverse Electron Demand Hetero-Diels-Alder Reaction

David E. Chavez, Eric N. Jacobsen
Harvard University
Department of Chemistry and Chemical Biology
Cambridge, MA USA 02138



e have recently reported a highly enantio- and diastereoselective inverse electron demand hetero-Diels- lder reaction between a variety of α,β-unsaturated aldehydes and ethyl vinyl ether, catalyzed by a chiral tridentate Schiff base chromium( ) complex. e now describe several synthetic application of this methodology, including the syntheses of several iridoid natural products. The preparation and synthetic utility of chiral silyl, stannyl and other substituted dihydropyrans will also be presented.

STEPS TOWARD THE SYNTHESIS OF C-GLYCOSIDE CONTAINING DENDRIMERS

Michael J. Panigot, Shang-U Kim, Alison M. Bare, Matthew D. Whiteside, Jeremy Lamb, Jason Boggs, Jennifer Faulkner, Amanda Caldwell, Robin Carlton
Department of Chemistry, Arkansas State University, State University, AR 72467

The initial plan toward the synthesis of C-glycoside dendrimers provided intermediate structures which proved difficult to characterize by HNMR due to the relatively small difference in the number of aryl hydrogens present in the product and starting benzyl ether protected C-glycoside. Steps within this route including the preparation of alkynyl-C-glycosides containing benzyl protecting groups and their attempted Pd-catalyzed coupling to 1,3,5-tribromobenzene will be presented. Additionally a conversion of the benzyl groups to acetate groups has been reported in the literature for the C-glycoside to be used. Efforts to utilize this conversion in this particular instance will be described. Further, an alternate plan utilizing allyl-C-glycosides will be addressed. For this planned synthesis the preparation of both alpha and beta allyl-C-glucosides by known literature methods and the attempted functionalization of the alkene double bond to form a dendrimer core molecule (generation zero dendrimer) will be discussed

EFFORTS TOWARD THE SYNTHESIS OF STEREOSELECTIVELY BETA-DEUTERATED HISTIDINE

Michael J. Panigot[1], Robert W. Curley, Jr.[2], Derek W. Barnett[2], Rikki Long[1], Jennifer L. Faulkner[1], Lesley White[1], Alistair Kent[3]

1. Department of Chemistry, Arkansas State University, State University, AR 72467

2. Division of Medicinal Chemistry and Pharmacognosy, College of Pharmacy, The Ohio State University, Columbus, OH 43210

3. Department of Physical Science, Harding University, Searcy, AR 72149

Knowledge of the 3-dimensional structure of proteins under conditions mimicking a physiological environment is important in the area of structure based drug design. This analysis has often been achieved through the use of multidimensional NMR techniques. These methods require isotopically labeled amino acids to be efficient. Some isotopic labels such as 15-N and 13-C can be incorporated into amino acids by feeding bacteria feed stocks containing the isotopic labels then performing protein hydrolysis while others need to be prepared in the laboratory. The current attempt at the synthesis of stereoselectively beta deuterated histidine by the preparation of an appropriate chiral deuterated imidazole electrophile and the attempted alkylation of this electrophile by the dianion derived from ethyl hippurate will be presented. Additionally, unexpected difficulties in the synthesis of this electrophile will be described.

Toward Total Synthesis of Amide Linked RNA Mimics

Eriks Rozners, Yang Liu, Qun Xu
Department of Chemistry and Chemical Biology, Northeastern University
360 Huntington Ave., Boston, MA 02115

Replacement of the negatively charged phosphates by a neutral amide backbone will eliminate the unfavorable electrostatic repulsion between RNA helices, and will considerably improve the folding and catalytic potential of RNA. Such biopolymer mimics can be prepared using peptide type couplings of monomeric nucleoside derived amino acids **1** and **2**. The synthetic challenge is the preparation of these highly modified nucleoside analogs. In contrast to traditional routes that would use carbohydrates as starting materials, we developed a "total synthesis" approach to 3',5'-modified nucleoside amino acids (Figure). Our recent work on synthesis and properties of amide linked RNA mimics will be discussed.

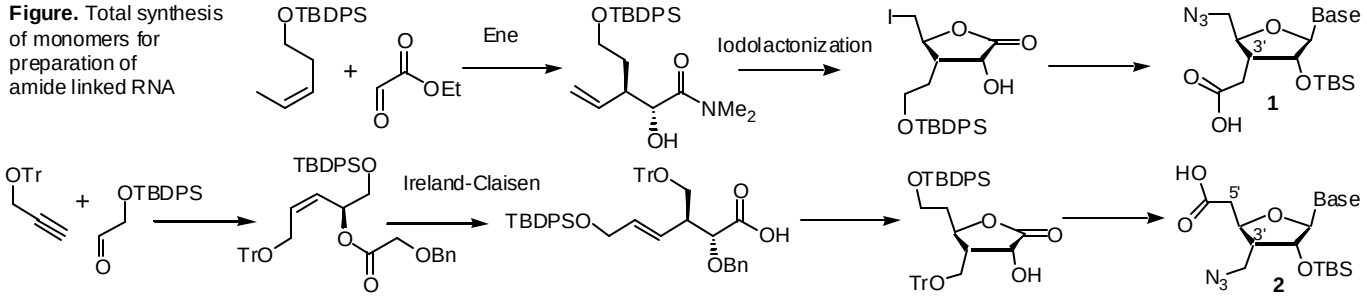
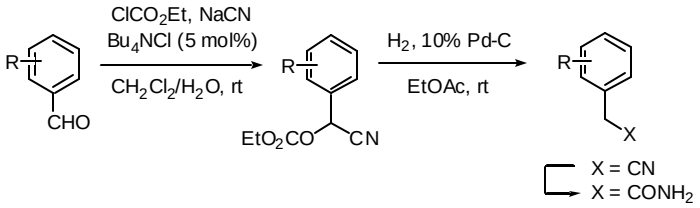


Figure. Total synthesis of monomers for preparation of amide linked RNA

SYNTHESIS OF ARYL AND HETEROARYL ACETONITRILE AND ACETAMIDE DERIVATIVES VIA CYANOCARBONATION/HYDROGENATION OF ARYL ALDEHYDES

Stanley P. Kolis*, *Marcella T. Clayton*, *John L. Grutsch and Margaret M. Faul.
Global Chemical Process Research and Development
Eli Lilly and Company, Indianapolis, IN 46285-4813



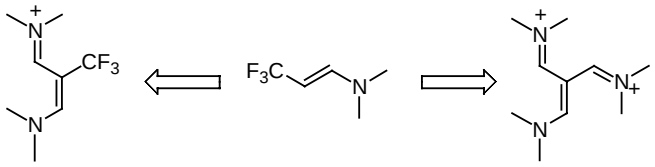
Aryl- and heteroaryl aldehydes are efficiently converted to arylacetonitriles and arylacetamides in good to excellent yield. An examination of substrate scope and application to the synthesis of indole-acetonitriles will be highlighted.

A [2+2] Cycloaddition Route to Dimethylaminomethylene Vinamidinium Salts

Ian W. Davies,* David M. Tellers,* C. Scott Shultz, Fred J. Fleitz, Dongwei Cai, and Yongkui Sun

Merck Research Laboratories, Merck & Co., Inc., PO Box 2000, Rahway, NJ 07065-0900

Trifluoropropanoic acid reacts with 1 equiv. of $POCl_3$ in DMF to generate the trifluoromethyl enamine (**7**). At this stage two reaction manifolds are available. The expected reaction with additional $POCl_3$ generates the 2-trifluoromethyl vinamidinium salt (**3c**). However, thermally driven loss of fluoride generates an iminium ion which sets the stage for a [2+2] cycloaddition to ultimately generate the dimethylaminomethylene vinamidinium salt (**1**). A detailed mechanistic picture of these two transformations will be presented.

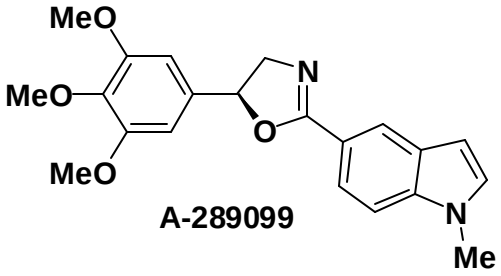


3c **7** **1**

A Practical Efficient Synthesis of Anti-Mitotic Compound, A-289099

Ashok Gupta*, Elaine Lee, Dan Plata, Yu-Ming Pu and Howard Morton
GPRD Process Chemistry, Abbott Laboratories
Department R-450, North Chicago, IL 60064

A-289099 is a chiral 2,4-diaryl oxazoline compound which is in an effective class of cytotoxic chemotherapeutic agents. An efficient and convergent synthesis of A-289099 was accomplished by the resolution of an optically active salt in 4 steps, 23% overall yield with an enantiomeric excess >97%. Evolution of the synthetic procedure will be presented.



A-289099

SOLID STATE SULFONATION OF ARYLAMINES

Gurdip Singh*, S. Prem Felix and Jaya Srivastava
Chemistry Department
D.D.U. Gorakhpur University
Gorakhpur, 273009, INDIA

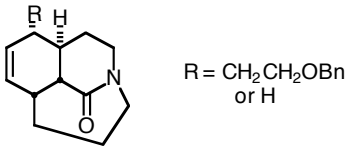
A large number of mono and di-substituted arylanilinium sulfate salts have been prepared from the corresponding arylamines by treatment with conc. H_2SO_4 at room temperature. These were characterised by elemental, gravimetric and spectral analysis. These sulfate salts yield the corresponding ring substituted aminobenzenesulfonic acids (RSABSA) when subjected to thermal energy. Thermal decomposition of these salts has been studied by various thermoanalytical techniques such as TG, DTG, DTA and DSC.
Kinetics and mechanistic aspects of all the ring substituted salts were studied. Log(k) and decomposition temperature were found to have linear relationship with pk_a values of the corresponding arylamines. It is found that most of the salts undergo transformation to the corresponding sulfonic acids in solid state via a proton transfer reaction prior to sulfonation. A reaction scheme representing the thermal decomposition pathways of these salts has been suggested.

- Corresponding author, e-mail:gsingh4us@yahoo.com
  Phone: 91-551-2202856, Fax: 91-551-2340459
  http//:quicksitebuilder.cnet.com/singhgurdip/

Examination of the Novel Reactivity of Bridgehead Lactams

Aaron D. Wrobleski, Jennifer Golden, Lei Yao, Ashley Albright and Jeffrey Aubé
Department of Medicinal Chemistry, University of Kansas
Lawrence, KS 66045-7582

The amide bond, in most cases, adopts a planar conformation and exhibits a range of well-known and extensively studied chemical properties. Placing an amide bond, however, into the bridgehead position of a polycyclic molecule may distort the amide bond from this preferred conformation and provide an opportunity to modify the reactivity of this functional group. A series of bridgehead lactams have been prepared and an investigation focusing on their reactivity has been initiated. The synthesis, structure, and reactivity of a series of related bridged amides will be investigated.



THE DISCOVERY OF NOVEL IMMUNOSUPPRESSIVE AGENTS THROUGH BIOCATALYSIS AND CHEMO-ENZYMATIC METHODS

Bruce F. Molino[1], Michael S. Hemenway[2], Peter C. Michels[2], Joseph O. Rich[2], Yuri Khmelnitsky[2], Simon N. Haydar[1]

1. Albany Molecular Research, Inc., 21 Corporate Circle, P.O. Box 15098, Albany, NY 12212. 2. Albany Molecular Research, Inc., 601 E. Kensington Road, Mount Prospect, IL 60056.

Immunosuppressive agents like cyclosporin A (CsA), tacrolimus (FK506) and sirolimus (rapamycin) have revolutionized the field of organ transplantation. However, their chronic use is associated with limiting toxicities, particularly severe in the case of CsA and FK506, which both cause nephrotoxicity and neurotoxicity. The need for a less toxic immunosuppressive agent is clear. We set out to address this need by applying our combinatorial biocatalysis technology to cyclosporin A and other lead compounds.

AMRI's combinatorial biocatalysis technology makes possible an efficient strategy for obtaining novel analogues of these immunosuppressive agents. An initial screen of 380 microbial systems and 63 selected enzyme catalysts was performed against cyclosporin A to identify novel products. The most promising reactions were rapidly identified, optimized and scaled up to provide adequate quantities of products for characterization and testing for immunosuppressive activity. This poster will present some of these novel cyclosporin A analogues, as well as semi-synthetic chemistry performed on an interesting methyl ketone derivative.

METABOLICALLY-STABILIZED LYSOPHOSPHATIDIC ACID ANALOGUES

Yong Xu, Lian Qian, and Glenn D. Prestwich
Department of Medicinal Chemistry, The niversity of tah
41 akara ay, Suite 2 , Salt ake City, tah 41 -12

Lysophosphatidic acid (LPA) is a natural phospholipid that causes a variety of physiological effects, ranging from rapid morphological changes to induction of gene expression and stimulation of cell proliferation and survival. We report novel synthetic routes for the preparation of receptor-specific agonists and antagonists for LPA receptors. In LPA analogues that cannot undergo acyl migration, the *sn*-1 or *sn*-2 hydroxy group was replaced with fluorine, difluoromethyl, *O*-methyl, or *O*-hydroxyethyloxy. In LPA analogues that are resistant to phosphatase degradation, the bridging oxygen in the monophosphate was replaced by an α-monofluoromethylene- or α,α-difluoromethylene-phosphonate moiety. The α-monofluoromethylenephosphonate analogues turned out to be unique and novel nonhydrolyzable LPA ligands, and showed surprising enantiospecific and receptor-specific biological readouts. One analogue was a long-lived hyperagonist, showing a 1000-fold higher activity than 18:1 LPA for LPA_3. In addition to direct effects on LPA receptor signaling, several analogues were potent inhibitors of lipid phosphate phosphatase, while others showed no LPA receptor activation, but were potent ligands for activation of the nuclear transcription factor, PPARγ.

COLORIMETRIC NANO-SENSORS BASED ON PHOTO-POLYMERIZABLE AMPHIPHILIC PAMAM DENDRIMERS

Abhijit Sarkar,[1] Paul S. Satoh,[2] Petar R. Dvornic[1] and Steven N. Kaganove[1]
[1]Michigan Molecular Institute
1910 W. St. Andrews Road, Midland, MI 48640
[2]Neogen Corp.
620 Leshe r Place, Lansing, MI 48912

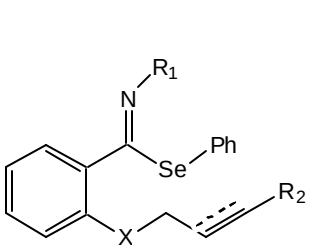
Synthetic studies aimed at the development of dendrimer-based colorimetric sensors that combine both sensory and reporter functionalities in nano-scaled macromolecular constructs are reported. Polydiacetylene segments function as colorimetric reporter units while dendrimer cores serve as structure-directing scaffolds. Because of their unique molecular architecture, high density of functionality and specificity, these sensors are expected to show enhanced sensitivity, good compatibility with analyzed media and facile fabrication and handling.

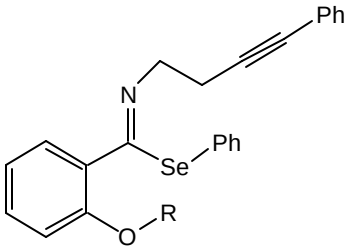
Generation and cyclization of imidoyl radicals derived from phenylselenyl imidates.

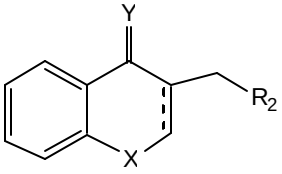
Adrian Sánchez[1], Josué Sansón[1], Javier Contreras[1], Martha Albores-Velasco[1], Joseph M. Muchowski[2].

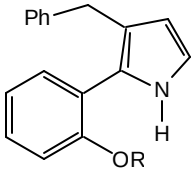
1.Facultad de Química. Universidad Nacional Autónoma de México. Circuito Interior, Ciudad Universitaria. 04510, México, D.F. 2. Roche Bioscience, 3401 Hillview Avenue, Palo Alto, Ca. 94304.

Phenylselenyl imidates 1 and 2, prepared from the imidoyl chlorides and sodium phenylselenide, served as imidoyl radical sources upon reaction with nBu_3SnH/AIBN in toluene at 100°C. The imidoyl radicals derived from 1 underwent 6-exo cyclization to 3 (Y= NR_1) isolated as the oxo compounds 3 (X=O), whereas pyrroles 4 derived from 5-exo cyclization were obtained from 2.









1 R_1=Me, Et, iPr, nBu R_2= H, Me

2.R= Me, allyl

3. Y= NR_1,O X= O, NR_2

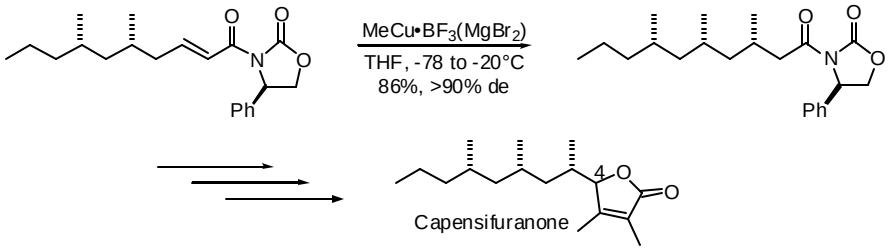
4

STUDIES TOWARD THE TOTAL SYNTHESIS OF CAPENSIFURANONE UTILIZING ASYMMETRIC CONJUGATE ADDITION

Andrea L. Nold*, Richard J. Mullins, Ryan E. Stites, David R. Williams
Indiana University, Department of Chemistry
800 E. Kirkwood Ave., Bloomington, IN, 47405, USA

Recently, our group developed a conjugate addition methodology allowing us to directly install iterative 1,3-*syn* and 1,3-*anti* methyl stereoarrangements. To probe its utility, we decided to apply this protocol in the synthesis of natural products. Capensifuranone and other metabolites isolated from the South African marine mollusk *Siphonaria capensis* have a unique structural feature—a uniform 1,3-polymethyl array. Successful application of our methodology for the synthesis of this natural product will be illustrated.

Another synthetic difficulty inherent to this molecule is the unknown stereochemistry at C-4, which requires stereoselective synthesis at this center as well. Progress toward the completion of the total synthesis of capensifuranone will be presented.

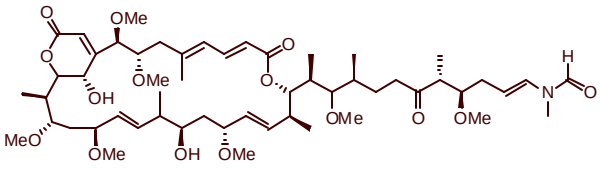


* Undergraduate researcher

Synthetic Efforts Toward the Total Synthesis of Sphinxolide

J. Alex Bates, Joel Berniac,* and *Paul Helquist
University of Notre Dame
Department of Chemistry and Biochemistry, Notre Dame, IN 46545

Many cytoxic marine natural products have been the target of total synthetic efforts by many groups due to the interesting structures and activities that they possess. The Sphinxolide family falls into this category. Sphinxolide A was isolated in 1989 by Guella and coworkers from the egg masses of an unidentified Hawaiian nudibranch and the remaining members of this family of molecules was isolated by Minale and coworkers in 1993 from the New Caledonian sponge *neosiphonia superstes*. Due to the unique mode of action and the excellent activity against several human cancer cell lines, the total synthesis of this molecule was undertaken. This molecule causes irreversible depletion of microfilaments. The total synthesis of this molecule will utilize Horner-Wadsworth-Emmons olefination reaction for the key bond forming reactions.

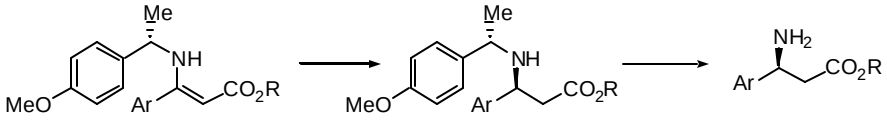


Sphinxolide

Stereoselective Synthesis of b-Aryl-b-Aminoesters

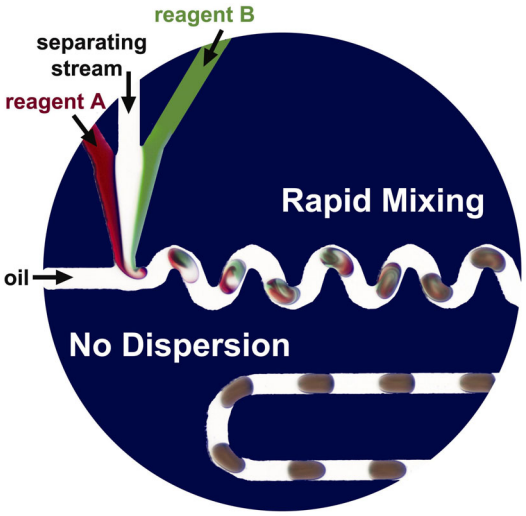
Judith H. Cohen, Ahmed F. Abdel-Magid, Harold R. Almond, Jr., Cynthia A. Maryanoff
Johnson & Johnson Pharmaceutical Research & Development, LLC
Drug Evaluation, Chemical & Pharmaceutical Development
Welsh & McKean Rds, Spring House, PA 19477

An efficient stereoselective synthesis of β-aryl-β-amino esters via reduction of enantiomerically enriched *N*-(*p*-methoxy-α-methylbenzyl)enamines by catalytic hydrogenation followed by debenzylation is described.



USING MICROFLUIDICS TO CONTROL CHEMICAL SYSTEMS IN TIME

Rustem F. Ismagilov, Helen Song, Joshua D. Tice*
Department of Chemistry, The University of Chicago, Chicago, IL 60637



We have developed a microfluidic system that can be used to control networks of chemical reactions in time. These microfluidic networks use fluid flow to convert spatial evolution of chemical systems into temporal evolution (convert distance into time). In these networks, laminar streams of several aqueous solutions of reagents are injected into a hydrophobic channel with a flow of water-immiscible oil, where the aqueous solutions spontaneously form streams of plugs separated by oil. Each plug acts as a miniature reactor with a volume of ~ 200 pL. In these pressure-driven, continuous flow microfluidic networks the reagents are mixed rapidly by chaotic advection (< 1 ms) and transported with no dispersion. This system has been validated by measuring single-turnover rate constant of RNase A. A complete reaction profile with millisecond resolution was obtained from a single spatially resolved image using less than 100 nL of solutions. This system will serve as a research tool for studying time-dependent processes -- especially those that involve complex networks -- in chemistry, biochemistry and biophysics.

STUDIES DIRECTED TOWARD THE SYNTHESIS OF PRIMARY AMINES FROM KETONES AND ALDEHYDES VIA REDUCTIVE AMINATION

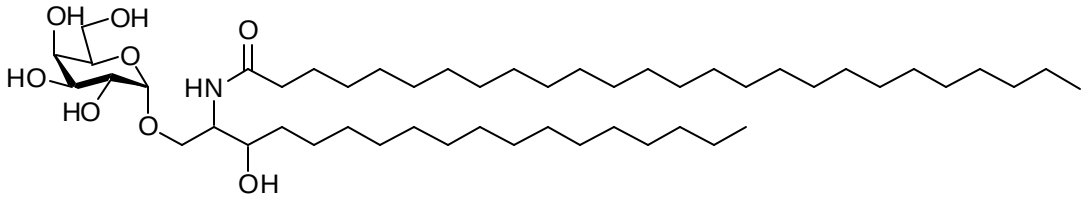
Steven J. Mehrman, Ahmed F. Abdel-Magid, Allison Mailliard, Cynthia A. Maryanoff
Johnson & Johnson Pharmaceutical Research & Development L.L.C.
Drug Evaluation – Chemical and Pharmaceutical Development
Spring House, PA 19477-0776

We reported a general and efficient methodology to perform the reductive amination of ketones and aldehydes utilizing both primary and secondary amines with sodium triacetoxyborohydride. However, the use of ammonia or ammonia equivalents to perform this reaction has been less utilized. We've also noted the reaction of ketones and aldehydes with ammonium acetate and sodium triacetoxyborohydride forms primarily the secondary amine products. We are now reporting a reductive amination procedure for the preparation of primary amines from ketones and aldehydes. . The scope and limitations of this reaction will be discussed.

AN EFFICIENT SYNTHESIS OF D-*THREO* AND L-*THREO* ? -GALACTOSYL CERAMIDES

Kuanqiang Gao, Robert M. Moriarty
Department of Chemistry, University of Illinois at Chicago
845 W. Taylor Street, 4500 SES, Chicago, IL 60607 USA

The synthesis of two a-galactosyl ceramide, *O*-(a-D-galactopyranosyl)-2-hexacosylamino-D-*threo*-1,3-octadecandiol (**1**) and *O*-(a-D-galactopyranosyl)-2-hexacosylamino-L-*threo*-1,3-octadecandiol (**2**), has been achieved. These compounds would be tested for anti-Hepatitis B and C activity. The key intermediates D-*threo* and L-*threo* dihydrosphingosines have been synthesized starting from D-serine and L-serine respectively in 5 steps and the total synthesis required only 12 steps, thus yielding final compounds in good yields.



(1) *O*-(a-D-galactopyranosyl)-2-hexacosylamino-D-*threo*-1,3-octadecandiol
(2) *O*-(a-D-galactopyranosyl)-2-hexacosylamino-L-*threo*-1,3-octadecandiol

THE DEVELOPMENT AND UTILITY OF CLICKCHEM REACTIONS IN THE SYNTHESIS OF DRUG-LIKE MOLECULES

Ramanaiah Kanamarlapudi[1], Paul Richardson[1], Haihong Jin[1], Gaznabi Khan[1], Hartmuth C. Kolb[2]

1.Lexicon Pharmaceuticals, 350 Carter Road, Princeton, New Jersey 08520

2.The Scripps Research Institute, Department of Chemistry, 10666 North Torrey Pines Road, La Jolla, Ca. 92037

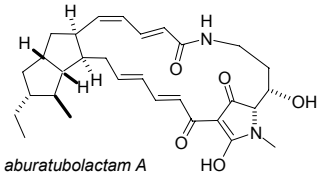
Click Chemistry reactions are defined to be modular, high yielding reactions, which are environmentally friendly and are wide in substrate scope. The reactions utilized are characterized as being easy to perform in terms of both carrying out the actual reaction as well as isolating the product. Such reactions are well suited for scale-up, and represent ideal chemical processes.

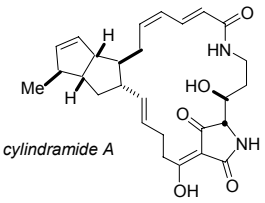
This poster will illustrate how we produce large quantities of pharmaceutically relevant building blocks in a routine fashion using these chemical reaction processes. Furthermore, we will demonstrate how minor changes in synthetic strategy can greatly simplify a process making it more amenable to scale-up. The application of Click Chemistry to a multi-step synthesis of a norstatine inhibitor will be described.

Synthetic Studies on Naturally Occurring Tetramic Acid Containing Macrolactams

Andrew J. Phillips, Amy C. Hart, James A. Henderson, and Gillian M. Nicholas*
Dept. of Chemistry and Biochemistry, University of Colorado, Boulder, CO 80309

Aburatubolactam A[1] and cylindramide A[2] are recently isolated members of a growing class of biologically active tetramic acid-containing macrolactams that also includes cylindramide A, geodin A, xanthobaccin A, ikarugamycin, discodermide, and the alteramides. Our progress towards the synthesis of these molecules employing novel tandem metathesis reactions will be presented.



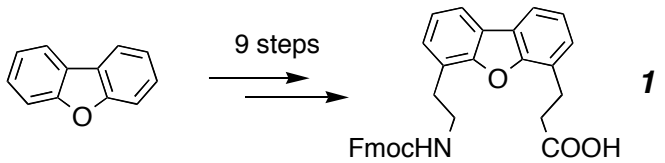


1. Bae, M.A.; Yamada, K.; Ijuin, Y.; Tsuji, T.; Yazawa, K.; Tomono, Y.; Uemura, D. *Heterocycl. Commun.* **1996**, *2*, 3152
2. Kanazawa, S.; Fusetani, N.; Matsunaga, S. *Tetrahedron Lett*. **1993**, *34*, 1065.

A No-D* ^{1}H NMR Study of the Reaction Sequence for Preparation of the Kelly -Turn Mimic

Thomas R. Hoye, Yan He, and Michael A. Puskarich

Department of Chemistry, University of Minnesota, Minneapolis, MN 55455



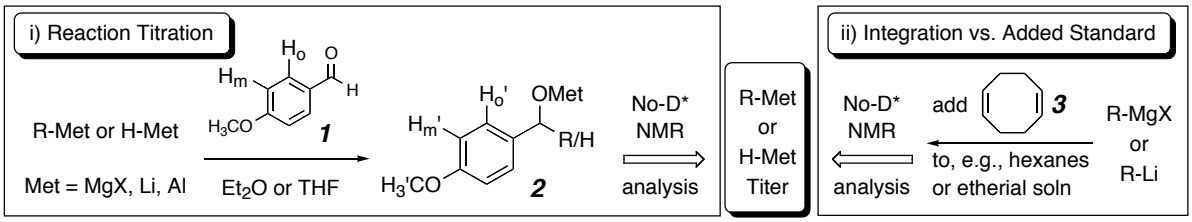
All nine steps in the reaction sequence for preparation of the Kelly -turn mimic **1** has been monitored by No-D* ^{1}H NMR spectroscopy. The sequence includes a lithiation, Heck reactions, heterogeneous hydrogenations, iodinations, and a Curtius rearrangement. This sequence demonstrates the versatility of No-D spectroscopy and includes reactions carried out in a variety of solvents (CH_2Cl_2, EtOH, Et_2O, THF, etc.). Many No-D spectra, recorded for aliquots taken directly from these reaction mixtures, will be presented to demonstrate the versatility, simplicity, and power of this technique.

* No-Deuterium

No-D* ^{1}H NMR Spectroscopic Titrations of Carbanionic (RLi, RMgX) and Hydridic (LAH, DIBALH) Reagents

Thomas R. Hoye, Andrew W. Aspaas, and Brian M. Eklov

University of Minnesota, Department of Chemistry, Minneapolis, MN 55455



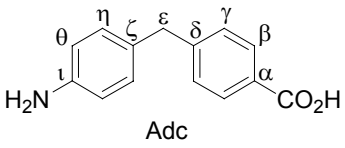
The concentration of alkyl(aryl/alkenyl)-magnesium halide, organolithium, and aluminum hydride solutions can be determined by No-D* ^{1}H NMR spectroscopy. Two methods will be described: i) Reaction Titration and ii) Integration vs. Added Standard. The former is accomplished by reacting a known volume of a solution of the nucleophile with a known excess of *para*-anisaldehyde (**1**) followed by direct analysis of the reaction solution and integration of the aromatic resonances in the new adduct **2** vs. unreacted **1**. In the second method, an internal standard for integration [like 1,5-cyclooctadiene (**3**)] is added to a solution of R-Met and the resulting solution analyzed directly by No-D* NMR spectroscopy. Both methods will be illustrated for a variety of anion solutions and the data compared with more traditional colorimetric/wet titration methods.

* No-Deuterium

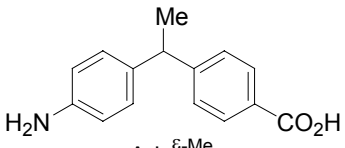
A FAMILY OF *iota*-AMINO ACIDS FOR THE CREATION OF NANOMETER-SCALE MOLECULAR ARCHITECTURES

James S. Nowick, Chris Gothard, Sang-Woo Kang, Santanu Maitra
University of California, Irvine
Department of Chemistry, Irvine, California 92697-2025

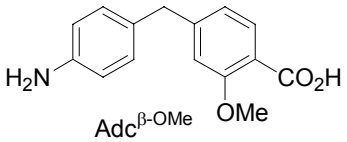
This paper introduces *aminodiphenylmethanecarboxylic acid* (Adc) and its substituted analogues as building blocks for the creation of unnatural oligomers that fold and self-assemble into nanometer-scale molecular architectures, such as rings, knots, and helices. Adc is an *iota*-amino acid, with a fixed distance of 0.95 nm between the amino and carboxyl groups, that is designed to participate in aromatic and hydrogen-bonding interactions. $Adc^{\varepsilon\text{-}Me}$ has a stereogenic center at the ε-position to control the chirality of the architectures; $Adc^{\beta\text{-}OMe}$ has a methoxy substituent at the β-position to control hydrogen bonding. The syntheses of Boc- and Fmoc-protected Adc, $Adc^{\varepsilon\text{-}Me}$, and $Adc^{\beta\text{-}OMe}$ will be described and their efficient coupling to generate oligomers will be discussed.



Adc



$Adc^{\varepsilon\text{-}Me}$

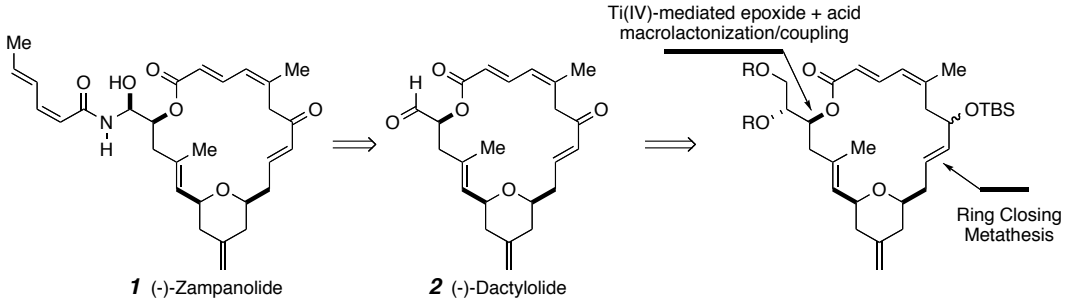


$Adc^{\beta\text{-}OMe}$

A Total Synthesis of (-)-Dactylolide [and (-)-Zampanolide] via Ti(IV)-Mediated Macrolactonization/Coupling of Epoxide and Carboxylic Acid Components

Thomas R. Hoye and Min Hu

Department of Chemistry, University of Minnesota, Minneapolis, MN 55455

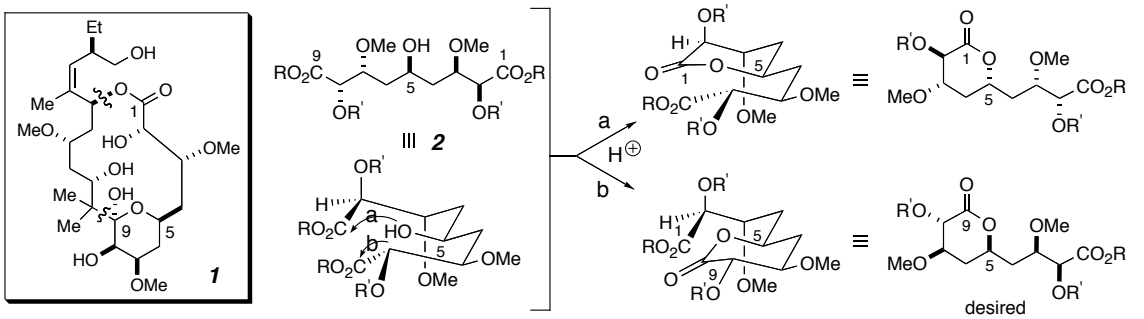


We will present a total synthesis of (-)-dactylolide (**2**) that features two distinctive macrocyclization strategies: a novel Ti(IV)-mediated *intramolecular* macrolactonization of an acid-epoxide substrate and a RCM macrocyclization of an α,β-dienediol, which was constructed by an *intermolecular* version of Ti(IV)-mediated acid/epoxide coupling reaction. Other notable features include: a proton-catalyzed, *cis*-selective Sakurai cyclization to establish the 2,6-*cis*-tetrahydropyran; a selective oxidation of allylic alcohol among a triol substrate by an oxoammonium ion; an aluminum aza-aldol addition reaction of a hexadienyl amide side chain to aldehyde (-)-**2** to construct the acyclic carbinolamide moiety in (-)-zampanolide (**1**).

Kinetic Lactonizations of Pseudosymmetric, Highly Oxygenated Azelaic Acids: the C(1)-C(9) Fragment of Peloruside A

Thomas R. Hoye and Troy D. Ryba[1]

Department of Chemistry, University of Minnesota, Minneapolis, MN, 55455



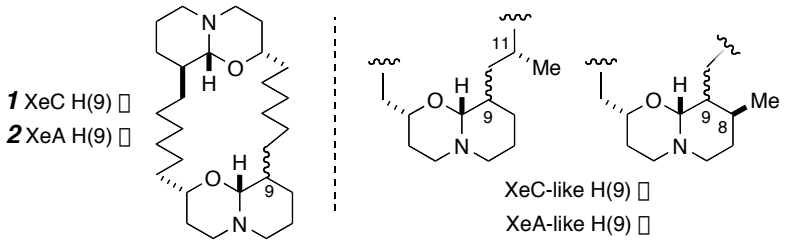
Peloruside A (**1**) is a secondary metabolite isolated from the marine sponge *Mycale hentscheli*. Recently, this macrolide has received considerable attention largely due to reports of its potent cytotoxicity and its limited availability. Our synthetic strategy has two major disconnections: the C(10)-C(20) fragment and the C(1)-C(9) fragment. C(1)-C(9) fragment assembly involves exploiting the relative rate differences for lactonization between the diastereotopic carboxyl groups in Azelaic acids **2**. Lactonization studies relevant to the synthesis of the C(1)-C(9) fragment will be presented.

[1]NIH Chemistry / Biology Interface Training Grant

Design and Synthesis of Methylated Analogs of the Important Calcium Release Inhibitor, Xestospongin C

Thomas R. Hoye and Peng Zhao

Department of Chemistry, University of Minnesota, Minneapolis, MN 55455

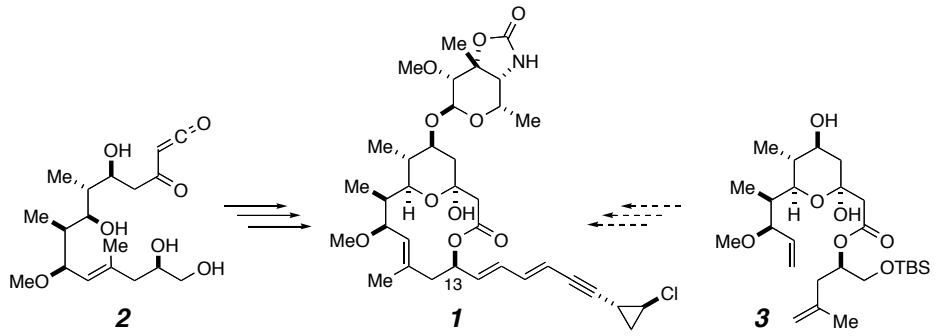


Xestospongin C (**1**, XeC) and its C(9)-epimer, xestospongin A (**2**, XeA), were isolated from the Australian sponge *Xestospongia exigua*. Recently, xestospongin C has drawn considerable attention because of its function as a potent membrane-permeable blocker of IP_3-mediated Ca^{2+} release. We have designed and prepared derivatives having the otherwise thermodynamically less favorable XeC-like relative configuration. The syntheses of 11-methyl-, 11,11'-dimethyl-, and 8,8'-dimethyl- analogs of xestospongin A and C will be presented.

A Total Synthesis of Callipeltoside A: Ring Formation by Acyl Ketene Macrolactonization Versus Relay Ring Closing Metathesis

Thomas R. Hoye, Michael E. Danielson, and Hongyu Zhao

Department of Chemistry, University of Minnesota, Minneapolis, MN 55455



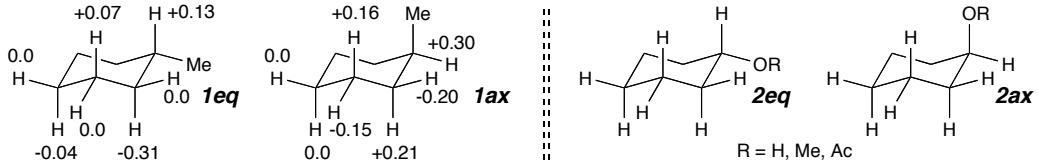
2 ***1*** ***3***

Access to the cytotoxic marine natural product callipeltoside A **(1)** has been achieved through total synthesis. Two methods of ring closure were investigated: a) acyl ketene macrolactonization and b) relay ring closing metathesis (RRCM). Unexpected selectivity was observed in the acyl ketene macrolactonization of di-, tri- and tetraol (cf. **2**) containing 1,3-dioxinones. Ring closing metathesis proved unsuitable for the task of cyclizing the parent diene **3**, necessitating the need for the design of a novel method of metathesis that we refer to as relay ring closing metathesis. Our total synthesis of callipeltoside A (**1**) will be presented with an emphasis on the two methods of ring closure.

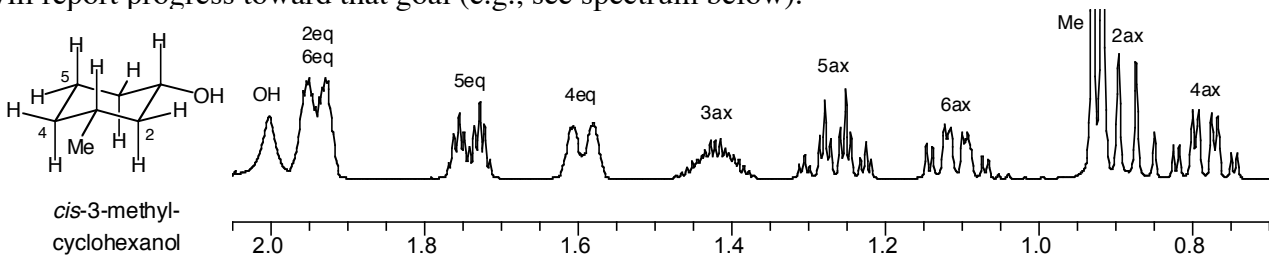
[1]H NMR Chemical Shift Increments for Oxygen-containing Substituents: Methylcyclohexanols

Thomas R. Hoye and Vadims Dvornikovs

University of Minnesota, Department of Chemistry, Minneapolis, MN 55455



From the analysis of various methylated cyclohexanes, Curtis, Dalling, and Grant derived parameters for incremental [1]H NMR chemical shifts arising from substitution of a proton by a methyl group on the cyclohexane ring (cf., **1eq** and **1ax**, *J. Org. Chem.*, **1986**, 136-142). We find these parameters to be quite useful for rationalizing/predicting the relative configuration of not only cyclohexane derivatives but other conformationally defined systems as well. We are developing a similar set of incremental shift parameters for oxygen containing substituents (cf. **2eq** and **2ax**) and will report progress toward that goal (e.g., see spectrum below).

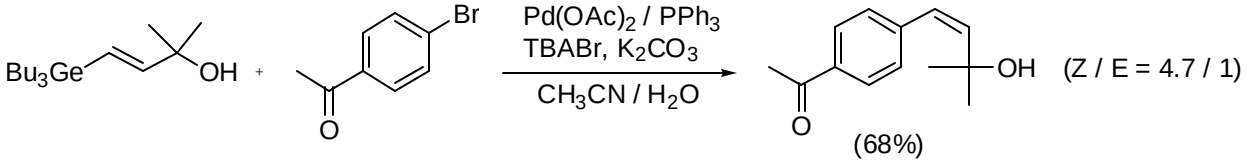


Cross-Coupling of Tri Alkyl Vinyl Germanes with Aryl Halides

Jérôme M. Lavis and Robert E. Maleczka, Jr.
Michigan State University
Department of Chemistry, East Lansing, MI 48824

Even though germanes are more stable and easier to handle than stannanes, the cross-coupling reactions of alkyl germanes has been relatively overlooked, but this is starting to change, especially with the preparations and reactions of germanotranes and trifuryl germanes. However, to the best of our knowledge, the only example of trialkyl vinyl germane coupling was reported by Kosugi who coupled tributylvinylgermane with *p*-bromotoluene to obtain *p*-methylstyrene.

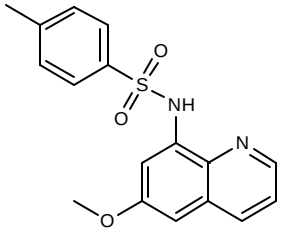
We have found that suitably substituted *E*-trialkylvinylgermanes can be coupled with aryl halides to afford predominantly *Z*-cross-coupled products. This stereochemical outcome seems to indicate that these reactions can proceed through a Heck-type mechanism.



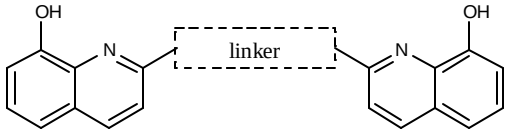
Highly Sensitive Fluorescent Zinc Sensors.

Royzen, Maksim; Canary, James, W.
New York University, Department of Chemistry, New York, NY 10003

Zinc imaging is a valuable tool for brain research. It has allowed linkage of several devastating cerebral disorders, such as Alzheimer's disease, Parkinson's disease and Amyotrophic lateral sclerosis (ALS) to abnormally high vesicular Zn^{2+} concentration. Imaging techniques rely on fluorescent Zn^{2+} sensors, the most prominent of which is N-(6-Methoxy-8-quinolinyl)-4-methylbenzenesulfonamide or TSQ. Development of better Zn^{2+} sensors may prove to be a valuable contribution to this field. One of the properties that needs improvement is sensitivity. We address this question by designing ligands based on 8-hydroxyquinaldine, a well established analytical tool for zinc chelation. It forms a 2:1 ligand- Zn^{2+} complex with binding affinity of $\log\beta_2 = 16.76$ ($\log K_1 = 8.66$, $\log K_2 = 8.1$). Incorporation of two 8-hydroxyquinaldine moieties in one ligand provides a possibility for combining binding affinities of two chelating groups thereby achieving a 1:1 ligand-metal complex with dramatically large $\log K_1$. Several ligands were synthesized according to the above-mentioned design.



TSQ

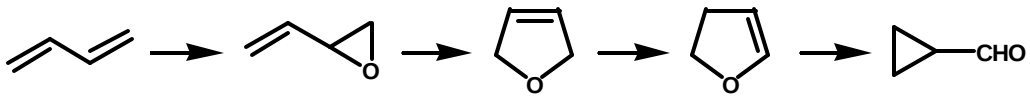


General Model of **Bis-8-hydroxyquinaldine** sensor

3,4-Epoxy-1-butene. A Versatile Intermediate for Organic Synthesis

Stephen N. Falling
Eastman Chemical Company
Research Laboratories
P.O. Box 1972
Kingsport, TN 37662-5150

An efficient, continuous, vapor-phase, air oxidation of 1,3-butadiene has recently been commercialized for the manufacture of 3,4-epoxy-1-butene (**1**). Prior to this scale-up and commercialization, the synthetic utility of epoxide **1** was relatively unexplored due its high cost of manufacture. Epoxide **1** is a versatile intermediate for the synthesis of many C_4 products traditionally produced by Reppe chemistry (via acetylene/formaldehyde condensation). Three sequential isomerizations greatly increase the number of products derived from epoxide **1**. The Lewis acid/iodide isomerization of **1** to 2,5-dihydrofuran (**2**) opens up the furan family of heterocycles. Vapor phase isomerization of **2** over a supported palladium catalyst yields 2,3-dihydrofuran (**3**). Finally thermal isomerization of **3** to cyclopropane carboxaldehyde (**4**) provides an intermediate for the production of numerous small ring products. The processes for these three isomerizations will be discussed as well as the utility of all four isomers.



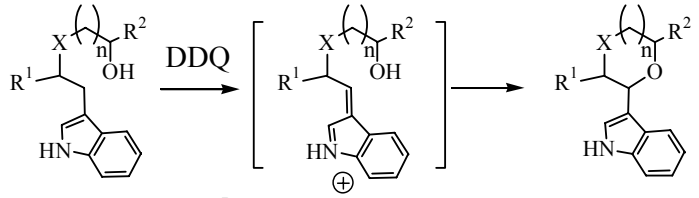
1 **2** **3** **4**

Indole-Containing Heterocycles formed by a Novel Tandem Indolic Oxidation/ Cyclization Reaction

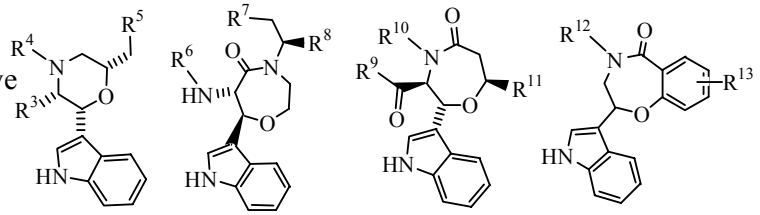
***Thomas D. Bannister*[1]**
Sepracor Inc.
111 Locke Drive, Marlborough MA 01532
[1]current employer: Suntory Pharmaceutical Research Laboratories, LLC,
One Kendall Square Building 1400W Cambridge MA 02139

3-substituted indoles bearing a terminal hydroxyl group on a 6 or seven atom chain readily oxidize with dichlorodicyanoquinone (DDQ). The indolic cation formed spontaneously cyclizes, producing novel ring systems. 6- and 7-membered rings are formed under the same reaction conditions. The stereoselectivitity of the reaction is discussed, as well as the design rationale and potential utility of the products. Conformationally constrained tryptophan peptidomimetics and analogs of biologically active acylic indole-containing compounds can be readily assembled using this methodology.

key step: (n = 1, 2)



representative products:

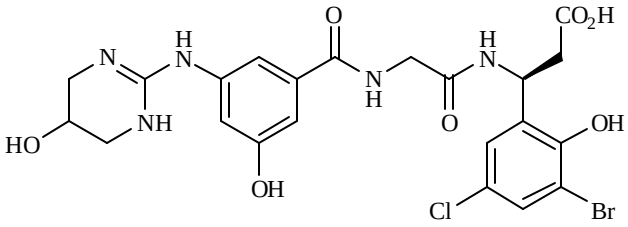


PROCESS RESEARCH AND DEVELOPMENT OFAN $a_v b_3$ INTEGRIN ANTAGONIST

Jerry D. Clark[1]*, Keith D. Anderson[1], Pierre-Jean Colson[2], Albert D. Edney[1], Donald J. Gallagher[2], Carl M. Knable[2], Christine M. Moore[2], Ajit S. Shah[1], Bruce E. Wise[2], Gerald A. Weisenburger[2]

[1]Pharmacia Corp., Global Chemical Process Research and Development
800 N. Lindbergh Blvd., St. Louis, MO 63167
[2] Pharmacia Corp., Global Chemical Process Research & Development
4901 Searle Parkway, Skokie, IL 60077

Described is the chemical process research and development studies directed toward the preparation of the $\alpha_v\beta_3$ integrin antagonist, (3S)-N-[3-Hydroxy-5-[(1,4,5,6-tetrahydro-5-hydroxy-2-pyrimidinyl)amino] benzoyl] glycyl-3-(3-bromo-5-chloro-2-hydroxy-phenyl)-β-alanine. The route developed entails a convergent, fifteen step synthesis from commercially available starting materials. The key chemistry steps employed are an efficient 4,6-tetrahydropyrimidine synthesis, a novel diastereoselective imino Reformatsky reaction, and a unique peptide bond forming reaction.



A facile reaction of (Z)-(1-bromo-1-alkenyl)boronate esters with cyclopentylmagnesium bromide. An easy access to alkyl cyclopentyl ketones

Narayan G. Bhat*

Department of Chemistry, University of Texas-Pan American, 1201 West University Drive, Edinburg, Texas 78539, USA.

Abstract

A convenient, simple synthesis of alkyl cyclopentyl ketones based on *Z*-1-bromo-1-alkenylboronate esters is developed. α-Bromo-(*Z*)-1-alkenylboronate esters readily available from the literature procedures smoothly undergo a reaction with cyclopentylmagnesium bromide in ether to provide the corresponding "ate"complexes. These "ate" complexes undergo intramolecular nucleophilic substitution reactions in the presence of sodium methoxide in methanol to provide the corresponding novel (*E*)-1-alkenylboronate esters containing cylcopentyl moiety which upon oxidation with hydrogen peroxide and sodium acetate afford the corresponding alkyl cyclopentyl ketones in good yields (70%-84%).

ISOLATION, PURIFICATION AND CHARACTERIZATION OF A SAPONIN BIOACTIVE MOLECULE FROM CITRULLUS COLOCYNTHIS.

N. Balyani, N. Saxena, P. Sahu* and N.K Saxena
Department of Post Graduate Studies and Research in Chemistry.
R.D. University Jabalpur (M.P.) 482001 INDIA

ABSTRACT

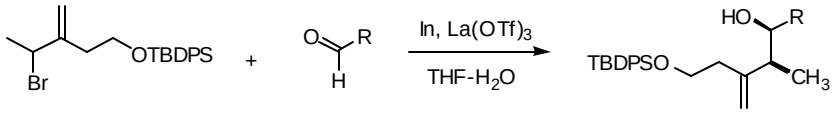
Citrullus colocynthis is a perninial herb of ethnobotanical importance in India. The bioactive saponin molecule known for its medicinal properties has been isolated, purified and characterized by IR, Mass, ^{13}C NMR and ^{1}H NMR and a tentative structure has been elucidated. Extraction of saponin was done by standard methods using petroleum ether and purification was carried out by polarity specific column chromatograhic methods using chloroform and methanol. Compound I obtained as pure saponin showed a pentacyclic terpene type structure as characterized by IR, Mass and NMR. Its M.P. was 377^{o}C and Rf 0.28. The sugar moiety attached to compound I was hydrolysed by acid giving two fractions, a glycone fraction and an aglycon fraction. The glycon fraction was identified as 2,3,4,6, tetra-*O*-methyl -D glucopyranoside, by methylation. It was further confirmed by HPLC. C-3 sugar linkage was found by ^{13}C NMR, C3 signal appeared at 74.3 ppm and was more deshielded than the other oxygenated carbons C2 (75.48 ppm) and C4 (77.8 ppm) . It is suggested that sugar is linked through the C3 - hydroxyl of the aglycone. The aglycon fraction was further analysed by IR, Mass, ^{1}H NMR, ^{13}C NMR and was confirmed to be a pentacyclic terpene. Molecular mass was determined by mass spectroscopy and was found to be 606. Unattached free sugars were identified as glucose, sucrose, verbacose, raffinose and stachyose. The identification of these sugars was done by HPLC using a carbohydrate column and ethylacetate : methanol : water (65:40:10) solvent system. A tentative structure for the isolated compound has been proposed.

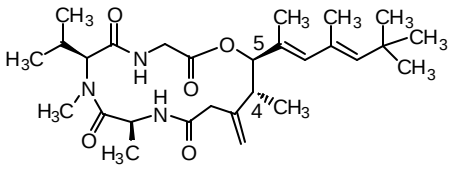
* Presenting Author

Exploring Novel Synthetic Method Based on Indium Chemistry and its Application to the Total Synthesis of Antillatoxin

Hong-Yan Song, Teck-Peng Loh*, Zheng Yin
Department of Chemistry, National University of Singapore, 3 Science Drive 3, Singapore 117543

Recent work from our group on the use of indium and indium complexes has resulted in the discovery of some novel synthetic methodologies.[1] Here we present a new reaction condition for the indium-mediated allylation of an unreactive secondary allylic bromide with aldehydes in aqueous media to afford the corresponding homoallylic alcohols in high yields and *syn* diastereoselectivity. Furthermore, it has provided an easy entry to the key intermediate for the total synthesis of antillatoxin[2] under mild and environment profitable conditions.



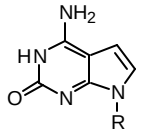


(4R,5R)-Antillatoxin

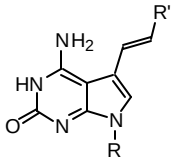
[1] (a) Loh, T. P, Hu, Q. Y and Ma, L. T. *J. Am. Chem. Soc*, **2001,** *123*, 2450-2451; (b) Loh, T. P, Tan, K. T and Hu, Q. Y, *Angew. Chem. Int. Engl. Ed*, **2001,** *40*, 2921-2922.
[2] Orjala, J.; Nagle, D. G.; Hsu, V. L.; Gervick, W. H. *J. Am. Chem. Soc.* **1995**, *117*, 8281.

EXPANDING THE GENETIC ALPHABET: SYNTHESIS AND FUNCTIONALIZATION OF 7-DEAZA-ISO-*GUANINE FOR POLYMERASE* IN VITRO *EVOLUTION STUDIES*

Theodore A. Martinot,[1] Cynthia L. Hendrickson,[2] and Steven A. Benner[1,2]
University of Florida
(1) Department of Chemistry
PO BOX 117200, Gainesville, FL 32611-7200
(2) College of Medicine, Department of Anatomy and Cell Biology



1, R = H
R = 2'-deoxy-ribose, ...



2, R = H
R = 2'-deoxy-ribose, ...
R' = NH_2, Imidazole, ...

We describe the synthesis of 7-deaza-*iso*-guanine (C^7*i*G, **1**), its respective nucleotide triphosphate and phosphoramidite. We also present work that focuses on the 7-position functionalized 7-deaza-*iso*-guanine (**2**) as well as its nucleoside, nucleotide triphosphate, and phosphoramidite.

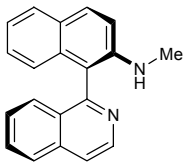
Inherent in this research is the desire to discover nucleic acids that offer properties—such as catalysis—that transcend simple information storage. In developing non-standard bases and incorporating them into DNA, we are probing whether enzymatic activity can be obtained from a *traditionally* non-catalytic system.

C^7*i*G was chosen as a synthetic target in part because of the known tautomerism of *iso*-guanine, which can often pair with thymidine (T; a mismatch) in addition to *iso*-cytidine (*i*C; a match). How will the substitution at the 7-position affect this tautomeric ambiguity? Part of the study will deal with identifying the relative ratios of each of the tautomers in solution, and comparing the value with the match/mismatch values after incorporation by DNA polymerases. Is it possible that the environment within the enzyme active site affects which tautomer is incorporated?

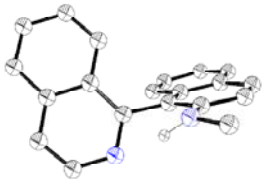
IAN AMINES: NEW REAGENTS FOR ORGANIC AND ORGANOMETALLIC SYNTHESIS

***Sarah B. Cortright*, *Jeffrey N. Johnston*[*]**
Indiana University
Department of Chemistry, 800 East Kirkwood Avenue
Bloomington, IN 47405-7102

IAN Amines, derived from *I*soquinoline and 2-*A*mino *N*aphthalene, combine the strengths of the β-diketimine framework with the axial chirality of binaphthyl systems. The ligands are easily accessible and configurationally stable. These chiral pyridines are competent ligands for a variety of coordination centers. Their diastereoselective complexation and use in a range of new reactions will be discussed.



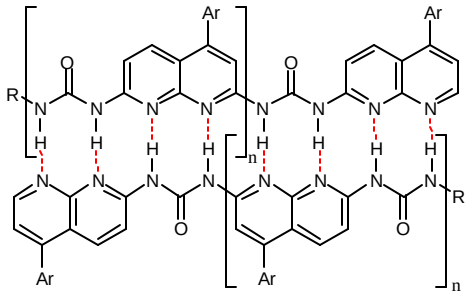
(±)-Me-IAN amine
C_1-symmetry



X-ray of Me-IAN amine

SELF-COMPLEMENTARY SUPRAMOLECULAR DIMERIZATION VIA EIGHT HYDROGEN BONDS

Michael F. Mayer, Shoji Nakashima, Elizabeth A. Unanue, and Steven C. Zimmerman
The University of Illinois at Urbana-Champaign
Department of Chemistry
600 S. Mathews Avenue, Urbana, IL 61801

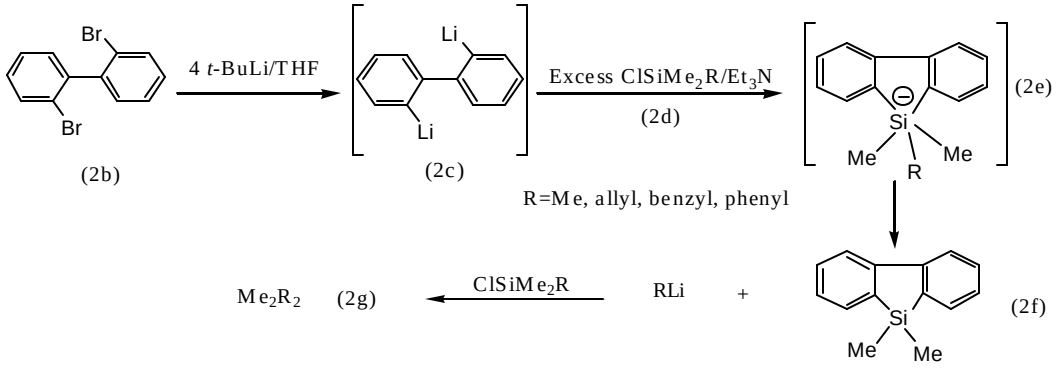


Self assembly via hydrogen bonding can provide highly stable supramolecular complexes and it is expected that as the number of hydrogen bonds increases, so does the stability of the complex. Toward this end, we now present a new method to generate discrete synthetic oligomers that are capable of pairing through the formation of multiple hydrogen bonds. Our design is based upon a repeating ureido-naphthyridine motif. This architecture provides an array of hydrogen bond donor and acceptor groups, similar to that found in natural nucleoside base pairs, but here (n=1) with an unprecedented number of contiguous donor / acceptor sites.

FORMATION OF SILOLES FROM DILITHIOBUTADIENE SYSTEMS AND MONOCHLOROSILANES; LOSS OF ORGANIC GROUPS FROM SILICON

Paul F. Hudrlik, Anne M. Hudrlik, and Donghua Dai
Department of Chemistry, Howard University, Washington DC 20059

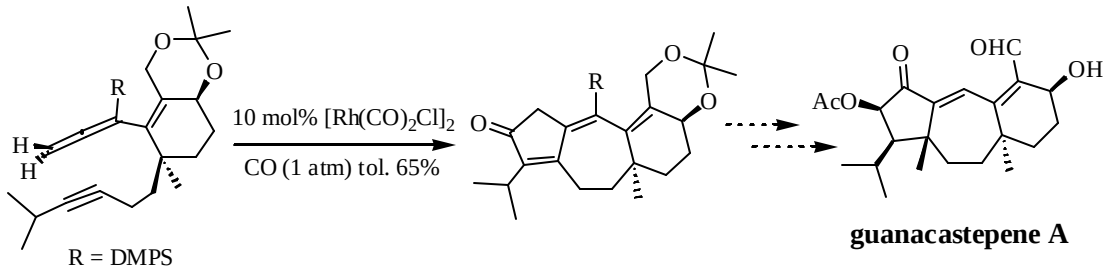
Siloles, silicon analogs of cyclopentadiene, have been of recent interest because of their dianions which appear to have aromatic character, and because of their electronic structure which makes them of interest as building blocks for conjugated systems. In the course of preparing siloles from dilithiobutadienes and dichlorosilanes, we attempted to characterize the dilithiobutadienes (e.g., 2c) by reaction with Me_3SiCl. Instead of the expected bis(trimethylsilyl)butadienes, we obtained dimethylsiloles (e.g., 2f). We have studied this reaction in several systems. The organic group which was lost from the sililcon, presumably as an organolithium, was trapped with the excess chlorosilane (to give 2g). The siloles were formed in good yields. Pentacoordinate organosilicon compounds (e.g., 2e) are presumed intermediates.



AN ALLENIC PAUSON-KHAND APPROACH TO GUANACASTEPENE A

Kay M. Brummond and Dong Gao
Department of Chemistry, University of Pittsburgh, PA 15260

Guanacastepene A, a fungal extract isolated from the branch of a *Daphnopsis americana* tree in the Guanacaste Conservation Area in Costa Rica, has shown excellent activity against methicillin-resistant *S. aureas* (MRSA) and vancomycin-resistant *E. faecalis* (VREF) pathogens. Recently, we have shown that the rhodium(I)-catalyzed allenic Pauson-Khand reaction affords seven-membered ring in high yields. We have subsequently shown that this method to form seven-membered rings can be used to access the [5-7-6] ring system of guanacastepene A. Progress directed towards the synthesis of this compound will be discussed.

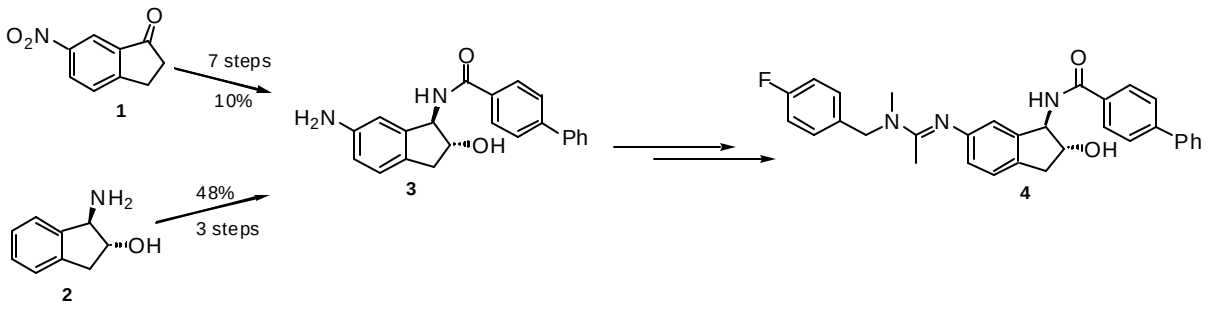


R = DMPS

guanacastepene A

A Regioselective Nitration of (*R,R*)-*trans*-1-amino-2-indanol

***Jeffrey Ward, Marvin Hansen, Sam Larsen, Stanley Kolis, Marcella Clayton, Andrew Smith, James Wright, Ryan Linder*. Global Process R & D, Eli Lilly and Co., Lilly Corporate Center, Indianapolis, IN 46285-4813**



Described are two synthetic strategies to afford aminoindanol derivative **3**, a precursor to M1 agonist clinical candidate **4**. Our early efforts proceeded through a 7 step sequence beginning with 6-nitroindanone (**1**) to afford aminoindanol derivative **3**. In comparison, a markedly regioselective nitration procedure was worked out using the available (*R,R*)-*trans*-1-amino-2-indanol (**2**) to provide **3** in 3 steps. A comparison of the advantages offered by the later nitration strategy will be discussed.

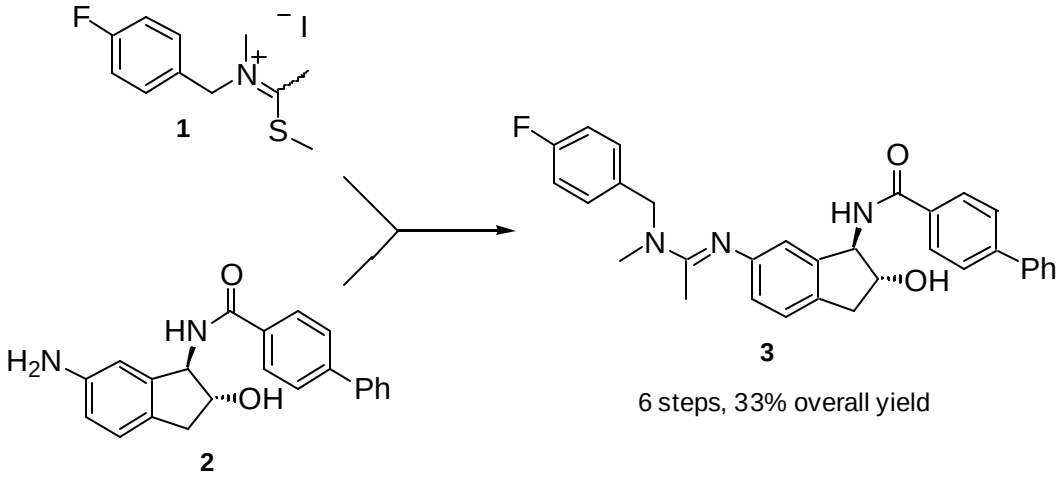
OPTIMIZED SYNTHESIS OF AN ARYL-ALKYL AMIDINE

Ryan Linder, Marvin Hansen, Jeffrey Ward, Stanley Kolis, Marcella Clayton, Phil Hoffman, Cynthia Steadham

Global Chemistry Process R&D, Eli Lilly & Company

Lilly Corporate Center, Indianapolis, IN 46285-4813

Aryl-alkyl amidine **3**, an M1 agonist in clinical development, was prepared from thioiminium salt **1** and aniline **2**. The effect of various basic promoters was examined, as well as non-traditional workup methods to isolate the free amidine. Salt **1** was prepared in two steps from N-fluorobenzyl, N-methyl acetamide, in 75% yield. Aniline **2** was prepared in three steps from (R,R)-*trans*-1-amino-2-indanol, in 48% yield.

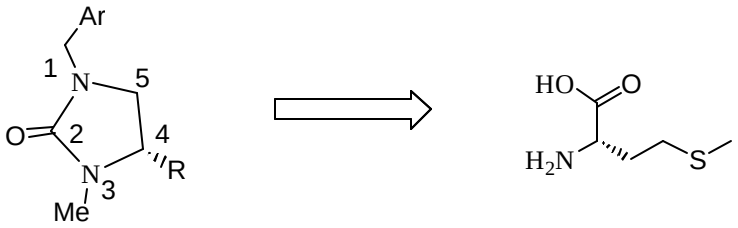


Development of an Asymmetric Synthetic Approach to 1,3,4-Tri-substituted Imidazolidin-2-one Derivatives from L-Methionine.

Sreenivasa R. Mundla,* David Mitchell, Y. John Pu, Michael A. Staszak, and Matthew D. Voss.

Global Chemical Process R&D, Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46285

Over the past several years, imidazolidin-2-one derivatives have emerged as a very important class of compounds. It is mainly because of their presence as substructures in biologically active molecules, and their use as chiral auxiliaries for asymmetric syntheses. Recently we became interested in synthesizing optically active 1,3,4-trisubstituted imidazolidin-2-ones of general structure **1** as key building blocks for incorporation into more complex drug candidates. In this poster we will present the development of an asymmetric synthetic approach to 1,3,4-tri-substituted imidazolidin-2-one derivatives (**1)** (R = CH_2CH_2SMe; CH_2CH_2I) starting from L-methionine (**2)**.



1 **2**

Diazapentacene and Its Derivatives: a New Family of Organic Semiconductors

Qian Miao, Colin Nuckolls
Department of Chemistry, Columbia University
New York, NY, 10027

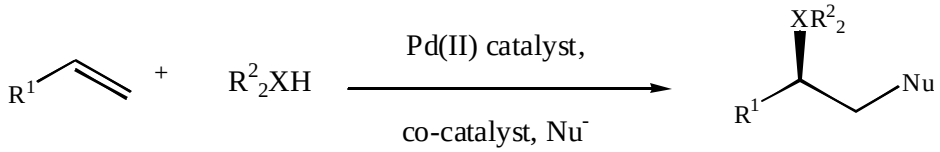
This poster details experiments on the synthesis and study of diazapentacene derivatives. lthough their structures have been essentially neglected for decades, our results show them to have a rich semi-conducting behavior. Moreover, derivatives of these compounds can be formed much more easily than those of linear acenes. ne derivative of diazapentacene forms highly ordered polycrystalline vacuum-evaporated films with conductivity of ca.1 $^{-2}\Omega^{-1}cm^{-1}$, which is several orders of magnitude higher than that of pentacene. The temperature-dependent conductivity and spectrum of thin films indicate that this derivative has a band gap of ca. .2 ev.

Several dihydro-derivatives of diazapentcene were also synthesized. packing mode very similar to that of pentacene was observed in their crystal structure. They function as p-type organic thin film transistors with field effect mobility up to ×1 $^{-3}$ cm^{2} $^{-1}s^{-1}$.

Vicinal Heteroatom Functionalization of Olefins Using Group Ten Transition Metals

Maria R. Manzoni, Thomas P. Zabawa, Sherry R. Chemler
University at Buffalo, The State University of New York
Department of Chemistry, Buffalo, NY 14260-3000

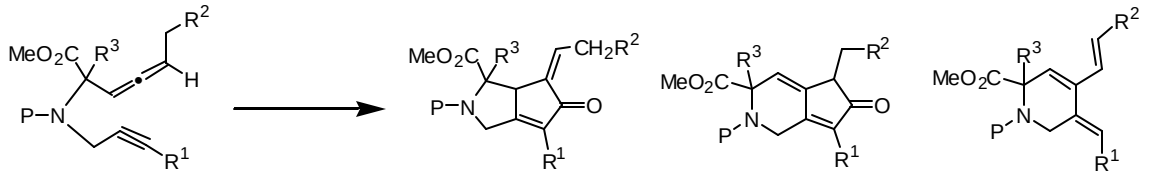
Platinum and palladium catalyzed additions of heteroatoms to olefins will be presented. Through the agency of stoichiometric amounts of inexpensive co-catalysts, the oxidation of organometallo (II) species to an organometallo (IV) species results in vicinal heteroatom functionalization . Depending upon the nature of the catalyst and co-catalyst, different products may be obtained. We are currently exploring substrate scope and product diversity. The catalytic asymmetric variants of these transformations will also be discussed. The synthesis of chiral and doubly functionalized compounds provides useful intermediates for organic synthesis and chemical library development.



AN ALLENIC ALDER-ENE AND PAUSON-KHAND REACTIONS, A STRATEGY FOR RAPID ASSEMBLY OF MULTIPLE ARCHITECTURALLY UNIQUE COMPOUNDS

Kay Brummond, Branko Mitasev
University of Pittsburgh, Department of Chemistry
Pittsburgh, PA 15260

Alkynyl allenes (**1**) which can be easily prepared starting from alpha-amino acids, undergo transition metal catalyzed cyclizations to give three different products with excellent chemoselectivity. Reaction conditions have been developed that allow for selective formation of the Pauson-Khand product with the proximal (**2**) and distal (**3**) double bond of the allene. In addition, the product of a formal Alder-ene reaction, a cross-conjugated triene (**4**) can also be formed selectively in excellent yields. These results provide a useful synthetic strategy for rapid introduction of diversity by using a single pivotal compound. These results, and the efforts to further functionalize these compounds in a diversity-oriented synthesis project, will be reported on.



1 **2** **3** **4**

CONVENIENT SYNTHESES OF SIDE-CHAIN FLUORINATED BIOIMIDAZOLES

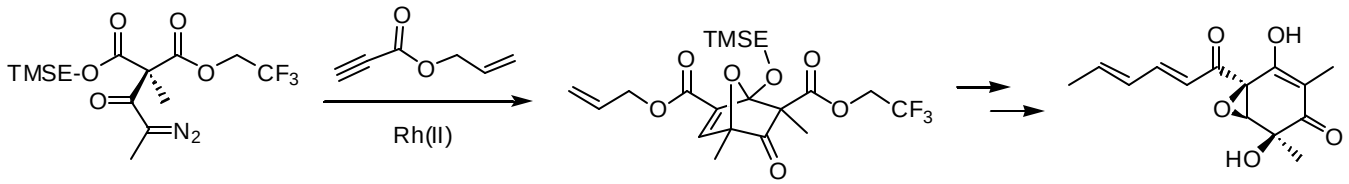
Jayan Narayanan, Bohumil Dolensky and Kenneth L. Kirk
Laboratory of Bioorganic chemistry, NIDDK, NIH, DHHS
8 Center drive, MSC 0810, Bethesda, MD, 20892

We previously have studied the syntheses and biological properties of ring-fluorinated biogenic amines and amino acids including fluorinated analogues of catecholamine, catecholamino acids (DOPAs), histamines, histidines and tryptamines. The many useful biological properties of these analogues have prompted us to extend our studies to the relatively unknown analogues of these compounds having fluorine substituted on the reactive benzylic position of the side-chain. As part of this new direction, we have investigated syntheses of such side-chain analogues of biologically important imidazoles. Analogues of histidinol have attracted interest as potential herbicidal agents and also have intriguing properties related to drug toxicity. Using "FBr" addition to double bond of vinyl imidazoles, we have prepared versatile fluorinated building blocks. These building blocks were used to prepare mono and di fluoro substituted analogues of histidinol. We will describe this work as well as our continued efforts toward the preparation of other important bioimidazoles.

FORMAL ASYMMETRIC SYNTHESIS OF (+)-EPOXYSORBICILLINOL

John L. Wood; Che-Wah Lee and Brian D. Thompson
Yale University, Department of Chemistry
New Haven, CT

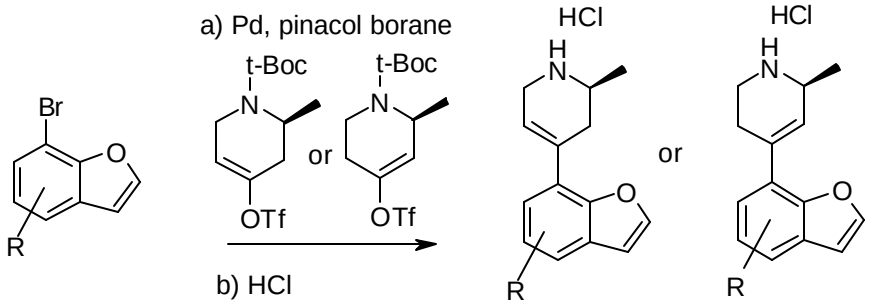
A formal asymmetric synthesis of (+)-epoxysorbicillinol (**3**) has been completed. The key step involves a highly chemoselective [3+2] cycloaddition between chirally pure α-diazoketone **1** and allyl propiolate to afford oxabicycle **2**. Further elaboration of **2** has afforded a formal intermediate which was previously reported in the total synthesis of epoxysorbicillinol.



1 **2** **3**

Synthesis of Bezofuryl Methyl Tetrahydropyridines

Brian E. Cunningham, Timothy P. Burkholder, William H. Gritton
Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285

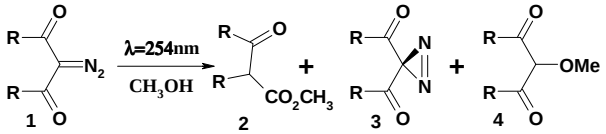


A series of benzofur-7-yl methyl substituted tetrahydropyridines were synthesized as part of our systematic side chain investigation in pursuit of 5-HT_{2C} agonists. Experimental details will be described for the preparation of the vinyl triflates and their subsequent palladium mediated coupling with the in situ generated substituted benzofuryl boranes.

EFFECT OF CONFORMATIONAL CONSTRAINTS ON THE REACTIVITY OF DIAZOMALONATES AND THEIR DIAZIRINE ISOMERS

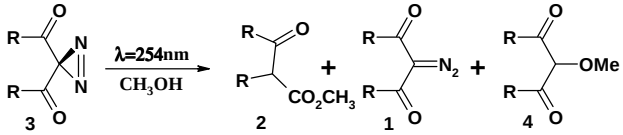
Aneta Bogdanova, Vladimir Popik
Bowling Green State University
Center for Photochemical Sciences, Bowling Green, OH 43403

Thermolysis or 254 nm irradiation of diethyl diazomalonate (**1a**) in MeOH, which can adopt three conformations, yields O-H insertion product **4a**. In contrast, decomposition of the cyclic analog of **1a**, diazo Meldrum's acid (**1b**), under identical conditions mainly results in Wolff Rearrangement (WR). Irradiation of **1a** and **1b** with 350 nm or longer wavelength light dramatically changes reactivity of both diazo compounds and isomerization into corresponding diazirines **3a** and **3b** becomes the major process. Mild heating of spirocyclic diazirine **3b** gives quantitative isomerization to **1b**, while thermolysis of acyclic **3a** in MeOH produces both diazo malonate **1a** and O-H insertion product **4a**. The photochemical reactivity of diazirines **3a** and **3b** resembles the reactivity of their diazo isomers. Photolysis of **3a** in MeOH results in the formation of O-H insertion product **4a** and diazo malonate **1a**. UV irradiation of cyclic diazirine **3b** is accompanied by WR and isomerization to **1b**. Differences in reactivities of cyclic and acyclic diazo- and diazirinomalonates will be discussed using experimental and theoretical data.



fractions in product mixture

a) R,R=OEt	0	0.10	0.90
b) R,R= 	0.91	0.06	0



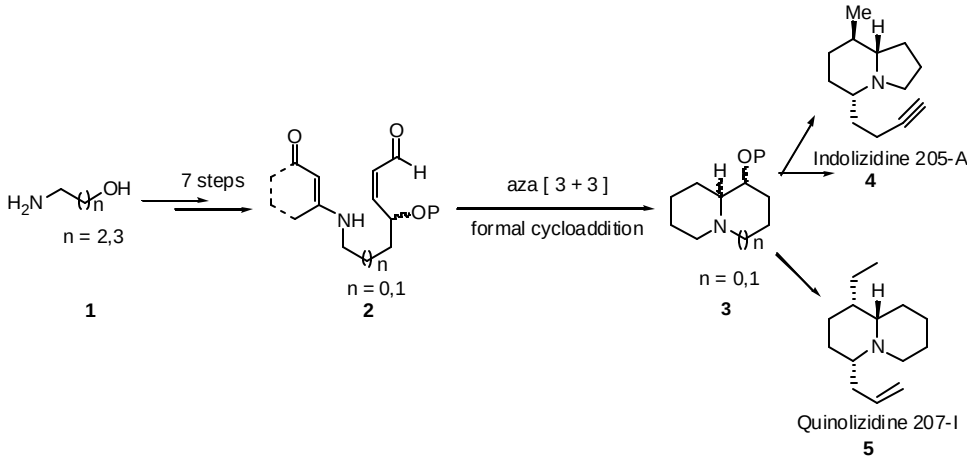
fractions in product mixture

a) R,R=OEt	0	0.01	0.99
b) R,R= 	0.93	0.04	0

A STEREOSELECTIVE INTRAMOLECULAR AZA [3 + 3] FORMAL CYCLOADDITION APPROACH TO INDOLIZIDINES AND QUINOLIZIDINES

HEATHER A. COVERDALE, XAIO-FAN YANG, LIN-LI WEI, ALEKSEY I. GERASYUTO, AND RICHARD P. HSUNG*
UNIVERSITY OF MINNESOTA-TWIN CITIES
DEPARTMENT OF CHEMISTRY, MINNEAPOLIS, MN 55455

Both indolizidine and quinolizidine frameworks **3** can be accessed via a stereoselective intramolecular aza [3 + 3] formal cycloaddition of vinylogous amide **2**. The key vinylogous amide intermediate **2** can be synthesized in 7 steps from achiral amino alcohols **1**. We examined the effects on an adjacent protected alcohol on the stereoselectivity of ring closure via the aza intramolecular cycladdition. We can apply this approach to stereoselective total synthesis of indolizidine 205-A (**4**) and quinolizidine 207-I (**5**).

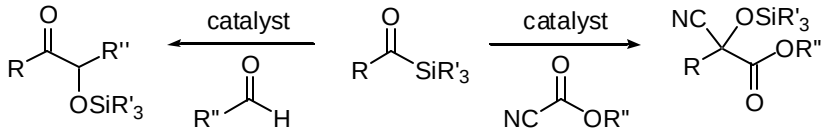


1 **2** **3** **4** **5**

TANDEM CARBON-CARBON BOND CONSTRUCTIONS VIA CATALYZED BROOK REARRANGEMENT REACTIONS

Xin Linghu, Jeffrey S. Johnson
University of North Carolina, Chapel Hill
Department of Chemistry, University of North Carolina, Chapel Hill, NC 27599-3290

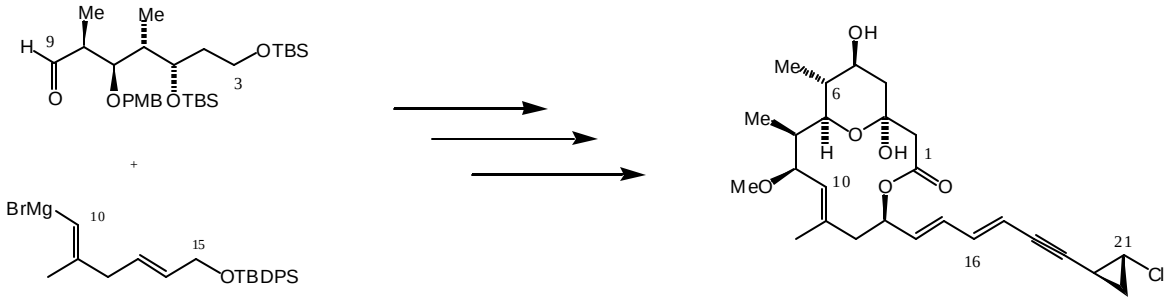
Silyloxynitrile anions generated by nucleophile-promoted Brook rearrangement of acylsilanes can be trapped by cyanoformate esters and aldehydes to afford protected tertiary carbinols and silyl-protected benzoin adducts, respectively. In both reactions, the substrate scope is relatively broad for the two reacting partners. Current efforts directed toward the development of an asymmetric variant of these new catalytic reactions will be described.



Progress Towards the Total Synthesis of the Callipeltoside A Aglycone

Patrick M. Eidam, James A. Marshall*
The University of Virginia
Department of Chemistry, Charlottesville, VA 22903

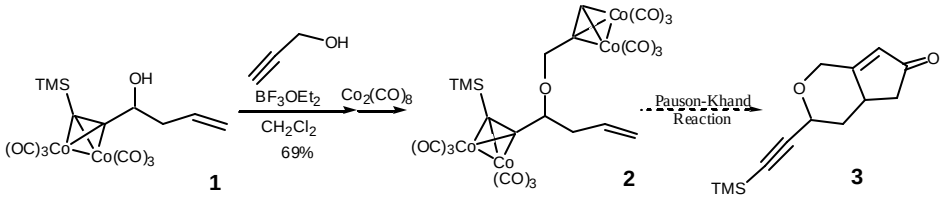
Progress towards the total synthesis of the cytotoxic marine natural product Callipeltoside A will be reported. The propionate domain of the molecule was synthesized via an allenyl metal addition to a chiral aldehyde followed by manipulation of the resulting functional handles which furnished the C3-C9 aldehyde. Addition of the C10-C15 vinyl Grignard reagent to this aldehyde and subsequent functional group transformations allowed for the completion of the C1-C15 carbon backbone. Studies regarding pyran ring closure as well as macrolactonization and side chain coupling are currently in progress.



NOVEL COMBINATIONS OF THE NICHOLAS AND PAUSON-KHAND REACTIONS

Miriam M. Quintal and Kevin M. Shea
Smith College
Clark Science Center, Northampton, MA 01063

Initially, our research focused on the selectivity of the Pauson-Khand reaction. Using an intermolecular Nicholas reaction, we introduced another alkyne in to cobalt-complexed alkyne **1**. The two cobalt-complexed alkynes can now compete in an intramolecular Pauson-Khand reaction where either a 4-5 or 6-5 ring system will be formed. We predict that the 6-5 ring system (**3)** will be the only product and are expanding this system to study a 5-5 versus 7-5 competition.



In the future we would like to combine an intramolecular Nicholas reaction with an intramolecular Pauson-Khand reaction to form a variety of carbo and heterotricyclic ring systems. The Nicholas reaction would be endocyclic, placing a cobalt complexed alkyne in a medium sized ring. The distances between alkyne and nucleophile and between alkyne and alkene would be varied to create a variety of ring sizes.

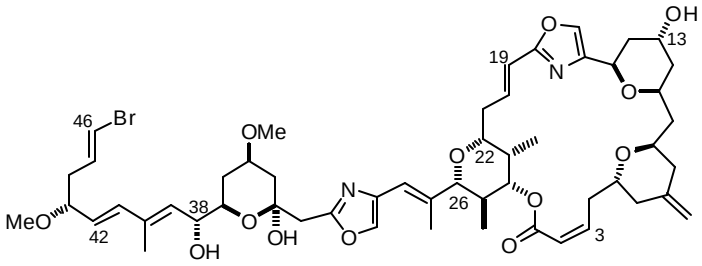
TOTAL SYNTHESIS OF PHORBOXAZOLE A

David R. Williams,* Andre A. Kiryanov, Ulrich Emde, Michael P. Clark, Martin A. Berliner and Jonathan T. Reeves

Indiana University, Department of Chemistry

800 E. Kirkwood Ave., Bloomington, IN, 47405, USA

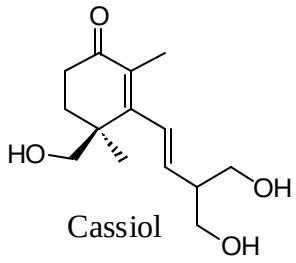
A highly convergent, stereocontrolled total synthesis of phorboxazole A has been achieved. Asymmetric allylation reactions of stannyl-derived allyldiazaborolanes are demonstrated as a powerful protocol for the enantiocontrolled assembly of functionally complex components. Key features of the overall scheme include a stereoselective cationic cyclization reaction for formation of the fully substituted C_{22}-C_{26} tetrahydropyran, and the use of a Julia olefination for incorporation of the sensitive C_{37}-C_{46} dienyl system. The novel Barbier-type coupling of an iodomethyl oxazole provides promising methodology for incorporation of the intact oxazole heterocycle.



AN ALLENIC ALDER ENE APPROACH TOWARDS THE SYNTHESIS OF CASSIOL

Thomas O. Painter and Kay M. Brummond
University of Pittsburgh
Department of Chemistry, Pittsburgh, PA 15260

Cassioside, a natural product found in the bark of *Cinnamum cassia* Blume, and its aglycone, Cassiol, have both shown antiulcer activity. Our approach towards the synthesis of Cassiol utilizes an allenic Alder ene reaction, catalyzed by a Rhodium(I) complex. This new method used to access cross-conjugated trienes, along with the synthetic progress towards Cassiol will be discussed.



Cassiol

CLASSICAL RESOLUTION OF a-SUBSTITUTED-b-PHENETHYLAMINES AND b-AMINOTETRALINS: SYNTHESIS, METHODS, ^{1}H NMR ANALYSIS

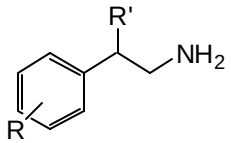
Mark A. Youngman*, Michele C. Jetter, Scott L. Dax and Jef Proost[†]

Johnson & Johnson Pharmaceutical Research and Development, LLC

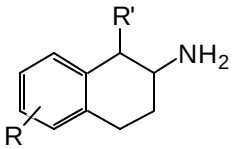
Welsh and McKean Roads, Spring House, PA USA 19477

[†]**Turnhoutseweg 30, Beerse, Belgium**

Chiral β-phenethylamines are important intermediates in the synthesis of a number of biologically active molecules. We were particularly interested in obtaining pure enantiomers of α-substituted-β-phenethylamines **1** and α-substituted-β-aminotetralins **2** for elaboration into GPCR receptor modulators. We found that the application of classical resolution techniques allowed facile separation of the racemic compounds into their enantiomers. In this poster, we present the synthesis of the racemic amines and a step-by-step "tutorial" in the method of separation of enantiomers by diastereomeric salt formation and isolation. We also discuss the efficient determination of % ee by ^{1}H NMR analysis. The resolved enantiomers were characterized by optical resolution, HPLC chromatography and single crystal X-ray diffraction analysis.



1



2

STUDIES OF ENZYMES, TOXIC MOLECULES AND OTHER MACROMOLECULES OF A NEW HYBRID SOYBEAN VARIETY BY INSTRUMENTAL & CONVENTIONAL CHEMICAL METHODS.

S.K. SINHA, N. SAXENA, C. DUBEY, R. BARDHAN* AND N.K. SAXENA
DEPARTMENT OF POST GRADUATE STUDIES AND RESEARCH
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ABSTRACT:

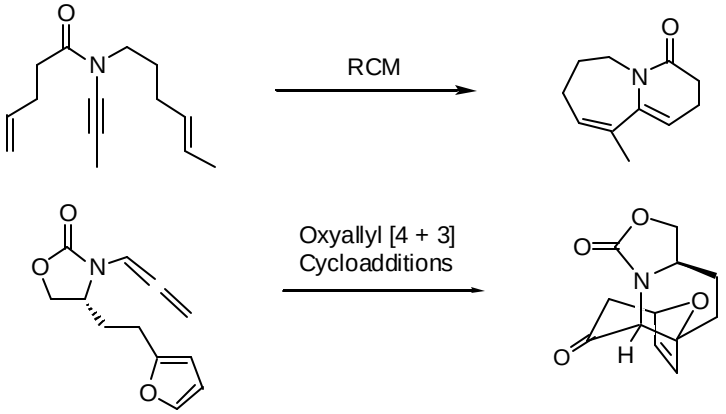
The detailed Chemical & Instrumental analysis have been employed on the seeds of Soybean JS-75-46. Two main DNA dependent enzymes RNA Polymerase and Urease & major macromolecules like lipids, proteins, carbohydrates were analyzed. It was found that the enzymes under study did not remain intact but prominent break away fraction was seen for both the enzymes. The RNA Polymerase showed a major fraction of molecular weight 220 Kda and 180 Kda & Urease showed major fraction of molecular weight of 280 Kda. The protein solubility profiles at wide range of pH were also analyzed for the seeds. Optimum solubility pHs were found to be lowest at 6.5 pH and highest at pH 11.5. Further the proteins were analyzed by HPLC for their amino acid profiles. The study also included quantitative as well as qualitative analysis of amino acids. Fatty acid profiles were done by GLC. Four toxic molecules namely cyanide, tannin content, haemaglutinating factor and trypsin inhibitor were found in Soybean JS-75-46 variety.

* Presenting Author

Ring-Closing Metathesis Reactions of Novel Ynamides and Intramolecular Oxyallyl [4 + 3] Cycloadditions of Allenamides

Jian Huang, Hui Xiong, Richard P. Hsung, Rameshkumar Chellappan, Jason A. Mulder, Tyler P. Grebe, Sunil K. Ghosh
University of Minnesota, Twin Cities
Department of Chemistry, Minneapolis, MN 55455-0431

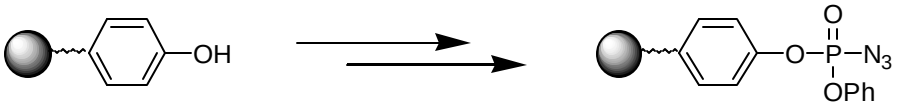
Synthetic utility of ynamides and allenamides, electron deficient variants of ynamines and allenamines, respectively, has recently attracted much attention in the literature. We report here our first successful base-promoted isomerization of propargyl amides for synthesis of them, and their applications in the ring-closing metathesis and Oxyallyl [4 + 3] Cycloadditions, respectively.



Preparation and Applications of A Polymer-supported Phosphoryl Azide

Yuhua Lu and Richard T. Taylor
Department of Chemistry & Biochemistry
Miami University, Oxford, OH 45056

A polymer-supported diphenylphosphoryl azide was prepared. This polymer-supported version of DPPA, a useful reagent for organic synthesis, exhibited high moisture tolerance and simplified the workup procedures. The synthetic application of this solid-phase reagent was explored by conversion of variety of carboxylic acids to urethanes and ureas through Curtius rearrangement reactions. Carboxylic acids bearing different functional groups (aromatic, aliphatic and heterocyclic carboxylic acids) were subjected to the reaction, and the corresponding products were obtained with satisfactory yields. Furthermore, five-membered cyclic urethane and urea derivatives were successfully prepared through intramolecular reactions with good yields and purities.



Phenol resin Polymer-supported DPPA

Lithiation of 3,4-Dihydro-2H-Pyran: a Density Functional Theory Study

Zhiqing Yan, John F. Sebastian
Miami University
Department of Chemistry and Biochemistry, Oxford, OH 45056

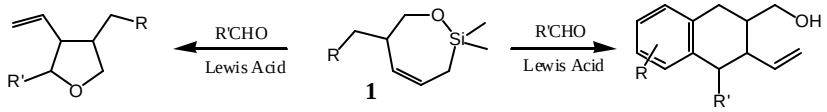
Lithiation reactions of 3,4-dihydro-2H-pyran (DHP), with methyl lithium in the gas phase and in ether solutions were investigated using geometry optimization of the reactants, transition states, and products with the density functional theory (DFT) method --- (B3LYP/6-31++G(d,p)). The calculations indicate that vinylic lithiation is kinetically favored (which is consistent with experimental result) by 0.42 kcal/mol when dimethyl ether is explicitly included in the computing system. The allylic product is predicted to be about 3.30 kcal/mol more stable than the vinylic one. Like other cyclic vinyl ethers in previous studies, we assumed that the two allylic positions in DHP are equivalent at the current level of theory (B3LYP/6-31++G(d,p)) – because the predicted energy differences between the two allylic transition structures and between the two allylic products are only 3×10^{-6} kcal/mol and 0.15 kcal/mol, respectively, which are negligible. The calculations also suggest a vinylic angle compression of 8.09°, while allylic angle expansion is not observed in the current study. The atomic charges were determined by Natural Population Analysis (NPA), using the same DFT method. The charges of the migrating hydrogens in all the transition structures are low, suggesting that the transition states are multi-center processes, which agrees with previous HF level optimizations.

Other solvation models investigated include the Onsager model, the polarized continuum model (PCM), and the isodensity polarized continuum model (IPCM). However, the results of these models yielded the allylic lithiation.

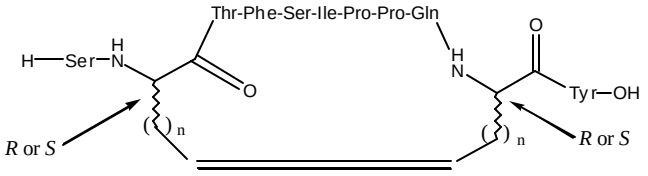
BIO-ACTIVE MOLECULE SYNTHESIS INCORPORATING RING-CLOSING METATHESIS

Steven M Miles[1], Robin J Leatherbarrow[1], Stephen P Marsden[1] & William C Coates[2]
[1]Department of Chemistry, Imperial College, London, SW7 2AZ, UK
[2]GlaxoSmithKline R&D, New Frontiers Science Park, Harlow, Essex, CM19 5AW, UK

New methodology has been developed for the transformation of RCM-derived cyclic allylsilanes (**1**) into either trisubstituted tetrahydrofuran or tetrahydronaphthalene products. Yields are good and stereoselectivities excellent, and the products contain functionality for further reaction. A family of lignan natural products has been synthesised by this convergent route , in high overall efficiency.



New methodology for microwave-assisted RCM on solid support has been developed for the synthesis of an array of macrocyclic enzyme inhibitor analogues (**2**). Based on the Bowman-Birk reactive site loop sequence, the 11-mer cyclic peptide products have the disulfide bridge of the natural inhibitor replaced by an all carbon link. Biological assay and NMR studies of the array are currently underway.



2

n=1,2,3

C-H Amination Methods for Organic Synthesis: Discovery, Scope and Mechanism

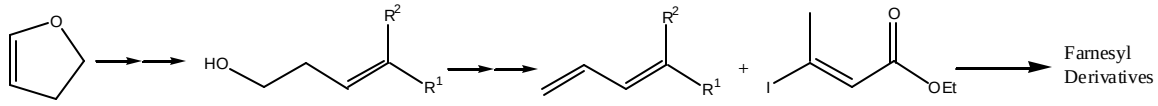
Christine G. Espino and J. Du Bois*
Department of Chemistry, Stanford University
Stanford, CA 94305-5080

A fundamental interest in developing C-H oxidation reactions applicable to the construction of complex molecules has culminated in new, highly efficient methods for the oxidative cyclization of carbamate and sulfamate esters. Using dirhodium(II) catalysts and $PhI(OAc)_2$ as the terminal oxidant, high yields of the respective oxazolidinone and oxathiazinane products are obtained. The product heterocycles are synthetically versatile materials and allow facile access to 1,2- and 1,3-difunctionalized amine derivatives. Amination of optically active substrates is stereospecific and consistent with oxidation by a metallo-nitrene species. Recent work on C-H amination has focused on: (1) mechanistic investigations; (2) development of new transition metal catalysts; and (3) examination of additional nitrogen functional groups for oxidative cyclization. Progress in each area will be presented.

SYNTHESIS OF SUBSTITUTED FARNESYLS

Josephine S. Nakhla and Kevin M. Shea*
Smith College
Department of Chemistry, Northampton, MA 01063

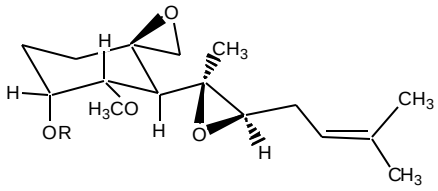
Farnesyl transferase (FTase) inhibitors are a potentially important class of anticancer drugs. FTase catalyzes the farnesylation of the Ras protein by farnesyl pyrophosphate (FPP), the natural substrate for FTase, which is a key step in the signaling mechanism controlling cell proliferation. Several research groups have synthesized compounds substituted at various positions in the farnesyl skeleton and these compounds have exhibited FTase inhibitory capabilities. Our work focuses on using known reactions to develop an efficient and flexible synthesis of a variety of substituted farnesyl derivatives for potential use as FTase inhibitors. The chemistry of Kocienski introduces the R^1 fragment via a higher order cyanocuprate. This is followed by incorporation of R^2 using various reactions; currently, we have focused on the use of Suzuki couplings to yield trisubstituted alkene 2. Alcohol **2** can easily be converted to the respective diene **3**, which after hydroboration, will be coupled with known vinyl iodide **4** via a Suzuki reaction to yield the farnesol skeleton. Future investigations will involve the synthesis of a library of compounds substituted at both R^1 and R^2 and subsequent evaluation of their FTase inhibitory activity.



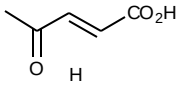
1 2 3 4

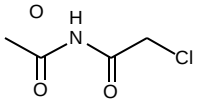
PROGRESS TOWARDS THE SYNTHESIS OF FUMAGILLOL VIA A RHODIUM CATALYZED FORMAL ALLENIC ALDER-ENE REACTION

Jamie M. McCabe and Kay M. Brummond
University of Pittsburgh
Department of Chemistry, Pittsburgh, PA 15260



1 R = H

2 R = 

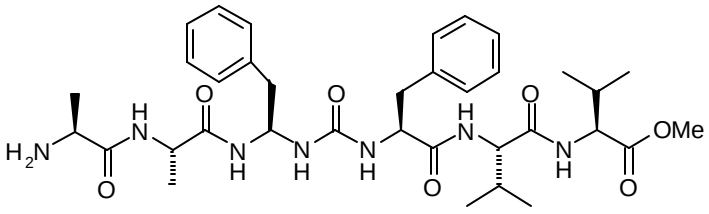
3 R = 

An allenic rhodium(I) catalyzed Alder-ene reaction has been discovered in our group. This unprecedented reaction gives very interesting substructures which contain a cyclic conjugated triene. It is predicted that this allenic Alder-ene reaction provides substructures that are uniquely suited for application to the synthesis of biologically relevant compounds, in particular fumagillin (**2**). Fumagillin is a fungal metabolite isolated in 1951 from *Aspergillus Fumagatus*, and shows potent anti-parasitic properties. Fumagillol (**1**) is not only the immediate precursor to fumagillin, but is the core cyclohexanol of an unnatural ester TNP 470 (**3**). TNP 470 displays potent angiogenesis inhibitory properties and this semi-synthetic derivative is in late stage clinical trails as an anti-tumor agent.

SYNTHESIS OF A NOVEL UREIDOPEPTIDE HIV-1 PROTEASE INHIBITOR

Adam C. Myers, Mark A. Lipton
Department of Chemistry, Purdue University
West Lafayette, IN 47907-2084

HIV-1 Protease continues to be an important target for the development of new AIDS therapies. Inhibition of the HIV-1 protease has been shown to halt viral replication and is the mode of action of many clinically important anti-HIV drugs. A novel HIV-1 protease inhibitor (1) has been designed and synthesized, employing a pseudopeptide motif previously developed in our laboratories. This motif, termed a "ureidopeptide," replaces the scissile amide bond in a known peptide substrate of HIV-1 protease with a urea linkage. Such a modification to the peptide backbone has previously been shown to inhibit proteolytic cleavage with minimal structural modification. Inhibitor 1 was made by a convergent synthesis involving an oxidative Hoffmann rearrangement to form the central urea. The synthesis of 1 and its inhibition of HIV-1 protease will be presented.



1

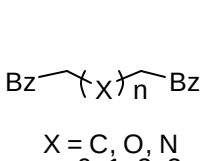
Study of the Conformation of $GABA_A$-Benzodiazepine Receptor Bivalent Ligands by Low Temperature NMR

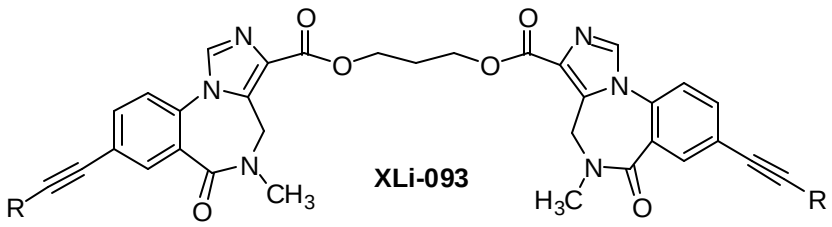
Dongmei Han[1], F. Holger Foersterling[1], Xiaoyan Li[1], Jeffery R. Descamps[2], Hui Cao[1], Jun Ma[1], Wenyuan Yin[1] and James M. Cook[1]

[1]Department of Chemistry, University of Wisconsin-Milwaukee, Milwaukee, WI, 53211

[2]Laboratory for the Structure of Matter, Naval Research Laboratory, Washington, D. C. 20375

Bivalent ligands often exhibit higher receptor binding selectivity than their monomeric counterparts. Receptor binding data has shown that XLi-093 is about 200 times more selective than the monomeric RY-80.





Determination of the stable or preferred conformation of bivalent ligands may help one to understand the structure-activity relationships. The conformation of ligands was determined in the solid state by X-ray crystallography. Low temperature NMR techniques were employed to explore the conformation in solution. ^{1}HNMR, ^{13}CNMR, homonuclear decoupling experiments, COSY, PECOSY, HMQC, NOESY and ROESY were run at different temperatures (from 177 K to 313 K) and in $CHCl_3$ as well as CH_2Cl_2, respectively. Analysis of the data indicated that the conformation in solution at low temperature was similar to that in the solid state.

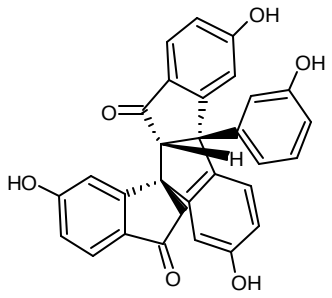
A Practical Synthesis Accessing Chemical Descriptor Space Characterized by Multifunctionality, few Rotatable Bonds, Chirality and Privileged Structures.

Clarke Slemon[1], Jean Vaugeois[2], Latchezar Trifonov[2] and Bohumil Macel[3]

[1]SiantarEnterprises; [2]Québépharma Inc.; [3]Toronto Research Chemicals Inc.

[1] P.O Box 103, Portland, ON, Canada K0G 1V0; [2] 225, avenue du Président-Kennedy, Montréal, QC, H2X 3Y8; [3]2 Brisbane Road, North York, ON, M3J 2J8

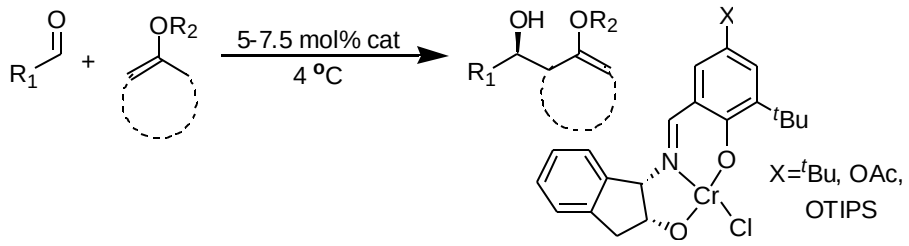
In chemical genetics it is an important problem to probe the relationship between chemical and biological descriptor spaces. Privileged structures and few rotatable bonds are attractive recognized descriptors. Polyfunctionality is important for library design. A simple scaleable synthesis has practical importance. The illustrated scaffold is made simply in chiral and achiral forms.



Chromium(III)-Catalyzed Asymmetric Hetero-Ene Reactions

Rebecca T. Ruck, Eric N. Jacobsen
Harvard University
Department of Chemistry, Cambridge, MA 02138

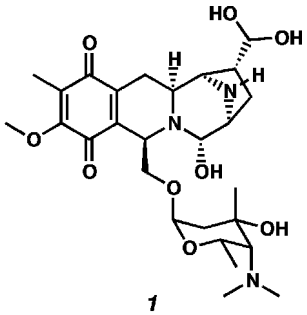
A new chromium(III)-catalyzed hetero-ene reaction is developed between 2-methoxypropene and benzaldehyde derivatives, generating ß-hydroxyenol ethers in high yields and enantioselectivities. These products are readily converted to the corresponding ß-hydroxyketones and ß-hydroxyesters. This ene reaction is extended to employ 2-trimethylsilyloxypropene as ene component. No silyl transfer product is observed. Subtle changes made to the tridentate Schiff base chiral ligand architecture facilitate the use of aliphatic aldehydes as enophiles. The resultant ß-hydroxytrimethylsilyl enol ethers are protected and employed as nucleophiles in subsequent aldol reactions. Further changes to the catalyst electronics enable the development of hetero-ene reactions between electron-deficient aryl aldehydes and cyclic trimethylsilyl enol ethers that proceed in high enantioselectivities and high anti diastereoselectivities. Detailed mechanistic and structural studies provide insight into how these hetero-ene and related hetero-Diels-Alder reactions proceed.



TOWARD THE TOTAL SYNTHESIS OF LEMONOMYCIN

Eric R. Ashley, Ernie G. Cruz, Tin Yiu Lam, Brian M. Stoltz*
California Institute of Technology
Division of Chemistry and Chemical Engineering, Pasadena, CA 91125

Our synthetic efforts toward the tetrahydroisoquinoline antitumor-antibiotic Lemonomycin (**1**) will be disclosed. The core structure of the aglycon has been constructed utilizing an auxiliary-controlled asymmetric dipolar cycloaddition, a palladium catalyzed fragment coupling reaction, and a Pictet-Spengler ring closure as key steps. A route to the 2,6-dideoxy-4-amino sugar has been developed starting from threonine. The glycoside synthesis features an exquisitely diastereoselective aldol coupling reaction.

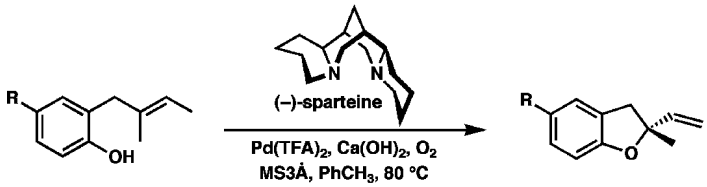


1

PALLADIUM-CATALYZED OXIDATIVE WACKER CYCLIZATIONS IN NONPOLAR ORGANIC SOLVENTS WITH MOLECULAR OXYGEN: A STEPPING STONE TO ASYMMETRIC AEROBIC CYCLIZATIONS

Raissa M. Trend, Yeeman K. Ramtohul, Eric M. Ferreira, Brian M. Stoltz*
California Institute of Technology, Division of Chemistry and Chemical Engineering
Pasadena, CA 91125

variety of Pd( )-catalyzed oxidative nucleophile olefin cyclizations proceed in excellent yield under simple aerobic conditions in nonpolar media (Pd, pyridine, and $_2$ in toluene). ucleophiles for these cyclizations include phenols, carboxylic acids, amides, and primary alcohols. The experimental conditions are operationally simple and employ a non-coordinating solvent, and thus provide entry into the realm of direct dioxygen-coupled asymmetric catalysis. nantioselective cyclizations are feasible with a Pd-sparteine system similar to that used in our previously reported enantioselective alcohol dehydrogenation. nantioselectivities of up to ee have been observed for the simple phenol olefin cyclizations.

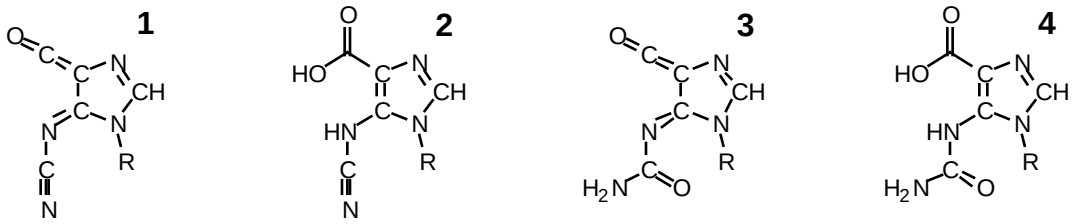


EXPERIMENTAL EVIDENCE FOR PYRINDINE RING-OPENING AND RECLOSURE PATHWAYS IN NITROSATIVE GUANOSINE DEAMINATION

Sundeep Rayat and Rainer Glaser*

Department of Chemistry, University of Missouri-Columbia, Columbia, Missouri 65211

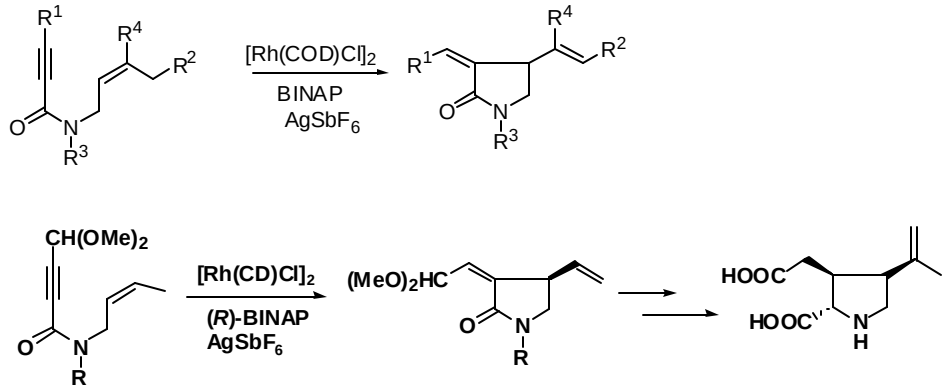
Deamination of guanosine leads to xanthosine and oxanosine. Dediazoniation of guaninediazonium ion occurs in concert with pyrimidine ring-opening and deprotonation to form **1**. The deamination product **1** contains two functional groups that are both extremely susceptible to water addition and **2** **4** are possible hydrolysis products. xanosine can be formed from **2** **4** and xanthosine can be formed from **3** and **4**. e studied the deamination of guanosine in -1 labeled water and of -1 ( ) guanosine in water to discriminate between the intermediates **2** **4** and the results of these studies are reported.



The experiments definitely exclude **4** as precursor to xanthosine formation. The experiments show that some of the oxanosine must be formed via **3** and this result demonstrates the very existence of **3**. Because of the existence of **3** and because of its chemical competence to form xanthosine, this results suggests that xanthosine can be formed by way of a pyrimidine ring-opening and reclosure mechanism.

Highly Enantioselective Syntheses of Functionalized Lactams via Rh(I)-catalyzed Cycloisomerization of Enynes and the Approch to the syntheses of Kainic Acids

Aiwen Lei, **Jason P. Waldkirch**, Minsheng He and Xumu Zhang*,
The Pennsylvania State University
Department of Chemistry, 152 Davey Laboratory, University Park, PA 16802.

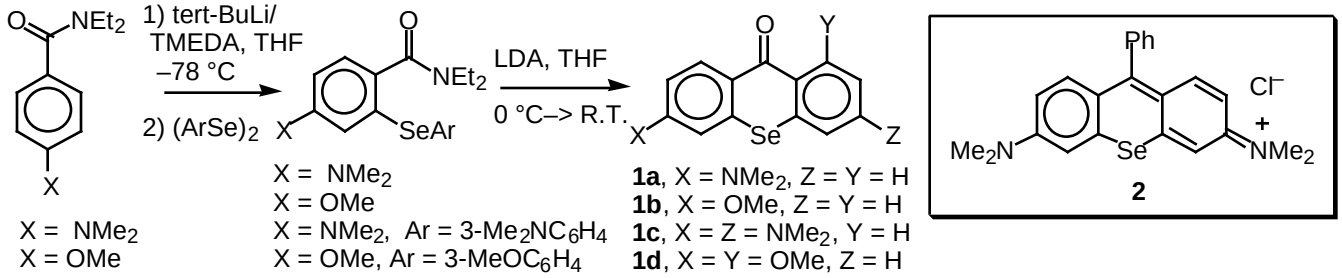


The functional lactams is one of most important heterocyclic compounds, which is an important motif in many natural products and biologically active compounds. Recently, we successfully developed Rh-catalyzed cycloisomerization reactions of Enynes, which was proven as powerful tools to produce functionalized Lactams. We found that the substituent R^3 at nitrogen is crucial for the reactions. However when R^3 is H, there are no desired products; and R^3 is Bn and Ts groups, high yield and high enantioselectivity were obtained. Our efforts for the syntheses of enantiomerically pure kainic acids appling the cycloisomerization product as key intermediate were reported in this poster.

The Synthesis of Selenoxanthones as Precursors to Selenorhodamine Photosensitizers for Photodynamic Therapy

Nancy K. Brennan, David J. Donnelly, and Michael R. Detty
University at Buffalo, The State University of New York
Department of Chemsitry, Buffalo, NY 14260-3000

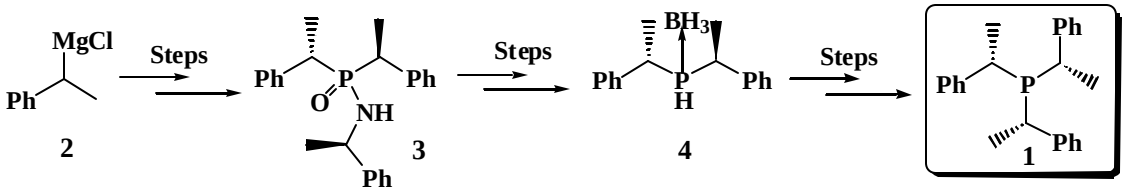
eavy-atom analogues of the rhodamines, in which the ring has been replaced by a heavier chalcogen atom, have been synthetic targets to provide photosensitizers that retain the specificity of the rhodamines for the mitochondria of cancer cells, but have longer wavelengths of absorption and higher quantum yields for the generation of singlet oxygen. e have developed a synthetic approach to selenoxanthones (**1**) via directed metallation as shown in the Scheme below. The lone-pair donating substituent is critical to the success of the directed metallation. Selenoxanthylium dye **2** and related analogues have been prepared and their biological and photophysical properties are under investigation.



THE SYNTHESIS AND APPLICATION OF A NOVEL OPTICALLY PURE C_3 SYMMETRIC PHOSPHINE LIGAND

Jonathan Charmant, Helen Eley, Paul Wyatt
University of Bristol
School of Chemistry, Cantock's Close, Bristol BS8 1TS, UK

Phosphine donors are widely used in asymmetric catalysis, but there are only a few chiral C_3 symmetric monodentate phosphine ligands. Our aim was to synthesise the C_3 symmetric monodentate phosphine ligand **1** and to investigate its applications in asymmetric catalysis. In addition to its C_3 symmetry, the chirality of **1** is adjacent to the phosphorus centre and the three α-methylbenzyl groups create a highly congested phosphorus environment that may enhance the selectivity of **1** in certain reactions.



Phosphine **1** was successfully synthesised *via* the novel *pseudo*-C_2 symmetric phosphine borane **4** that has two of the desired α-methylbenzyl units in place. Optically pure **4** was made from the Grignard **2** *via* the phosphinamide intermediate **3**. Exploiting the nucleophilic properties of phosphorus, the third α-methylbenzyl unit was successfully installed and the borane group easily removed to give optically pure **1**. Preliminary results obtained so far regarding the applications of **1** are extremely promising and work is underway to exploit the full potential of **1** as a chiral ligand in asymmetric catalysis.

Macrocylic Metabolites from the Marine Sponge *Myriastra clavosa*

Karen L. Erickson,[1] Kirk R. Gustafson,[2] Lewis K. Pannel,[3] John A. Beutler,[2] and Michael R. Boyd[2]

[1]Carlson School of Chemistry and Biochemistry, Clark University, Worcester, MA 01610

[2]Molecular Targets Drug discovery Program, National Cancer Institute, Frederick, MD 21702

[3]Laboratory of Bioorganic Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD 20892

Both aqueous and organic extracts of a Philippines collection of the marine sponge *Myriastra clavosa*, when tested in the NCI's 60-cell antitumor screen, presented a distinctive pattern of differential cytotoxicity and antiproliferative effects. This suggested the presence of compounds capable of modulating specific molecular targets and prompted a chemical investigation of the extracts. The aqueous extract yielded, in trace amounts, four dimeric dilactones, two of which proved to be identical to clavosolides A and B reported earlier [1,2]. The organic extract provided three novel cyclic octapeptides containing oxazole and/or thiazole components. The structures of these metabolites were elucidated spectroscopically, including extensive NMR analyses utilizing a variety of solvents.

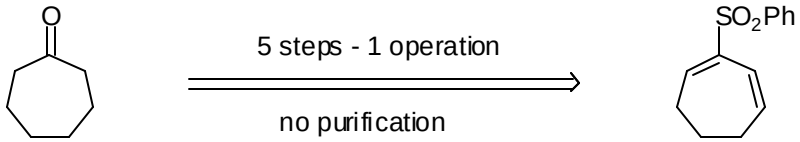
[1] Rao, M. R.; Faulkner, D. J. *J. Nat. Prod.* **2002**, *65*, 386-388.

[2] Erickson, K. L.; Gustafson, K. R.; Pannell, L. K.; Beutler, J. A.; Boyd, M. R.. *J. Nat. Prod.* **2002**, *65*, 1303-1306.

A Kilogram Scale Synthesis of 2-(Phenylsulfonyl)-1,3-cyclohexadiene and 2-(Phenylsulfonyl)-1,3-cycloheptadiene

Taesik Park, Philip L. Fuchs
Department of Chemistry, Purdue University
West Lafayette, IN, 47906

Dienyl sulfone compounds are important starting material for the synthesis of the various polypropionate segments and also their valuable chemistry was reported. Recently Meyer in our group reported economical and environmentally friendly synthesis of the compounds. The original synthesis has been further optimized and now is run at the 10 Mole scale, delivering the compounds in excess of 1 Kg per run in a single operation without any purification.

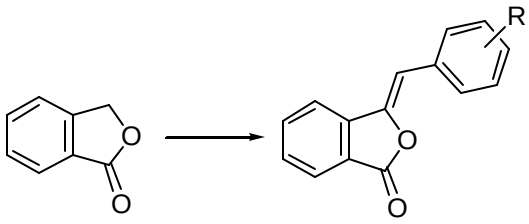


1 Kg 1.14 Kg

STRUCTURE-ACTIVITY RELATIONSHIP STUDIES OF 3-BENZYILDENEPHATHALIDE ANALOGS

Nausheena Baig, Michelle Poore, John J. Beck*
Department of Chemistry
Sweet Briar College
Sweet Briar, VA 24595

(Z)-Ligustilide, a bioactive component of several medicinal herbs of *Ligusticum* species, contains an electrophilic site that is purported to be responsible for the molecule's bioactivity. This reactivity has prompted the investigation of 3-benzylidenephthalide, a simpler version of (Z)-ligustilide. Successful bioactivity testing of 3-benzylidenephthalide has led to structure-activity relationship (SAR) studies of an entire family of benzylidene analogs in an effort to improve the bioactivity of this class of compounds. The progress of this research will be reported.

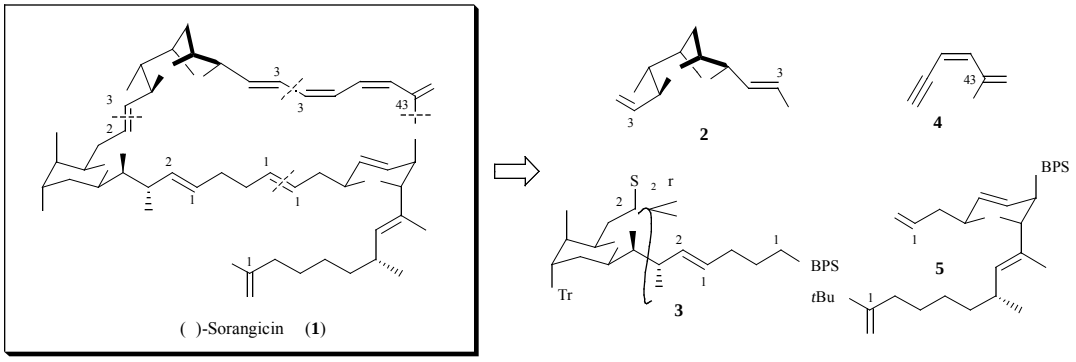


R = CH_3, OCH_3, OH, NH_2, Br, Cl, CF_3, CN, NO_2

PROGRESS TOWARDS THE TOTAL SYNTHESIS OF (+)-SORANGICIN A

Amos B. Smith III, Richard J. Fox and John A. Vanecko
University of Pennsylvania, Department of Chemistry, Philadelphia, PA 19104

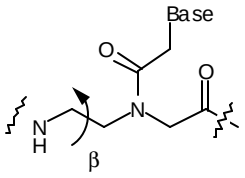
( )-Sorangicin (**1**) is the most potent congener of a novel class of antibiotics isolated from the bacteria *Sorangium cellulosom*, displaying average M C values of 1 ng m and 1 μg m against gram-positive and gram-negative bacteria respectively. ecently, we initiated efforts to develop a convergent and stereocontrolled synthesis of this novel macrolide. arly achievements include a novel, acid-catalyzed cascade of epoxide openings initiated via a Co_2(C) -alkyne complex to afford the C(3 -3) bicyclic framework. Construction of a C(1-) side chain has also been achieved. summary of these results, as well as additional progress will be presented.



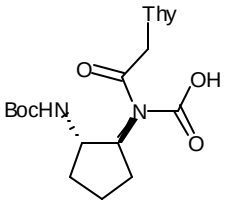
Asymmetric Synthesis of Cyclopentane and Cyclopropane Peptide Nucleic Acid Monomers

Daniel H. Appella *, Nataliya V. Larionova, Michael C. Myers, Mark A. Witschi
Department of Chemistry, Northwestern University, Evanston, Illinois 60208

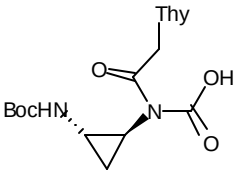
Peptide nucleic acids (PNAs) are a unique class of antisense molecules that hybridize to complementary DNA and RNA. Modifications to the PNA backbone could improve the biomedical applications of PNA by enhancing binding affinities and oligonucleotide selectivity. Our research has focused on controlling the C2-C3 dihedral angle β (**1)** by the incorportion of cyclopentane (**2**) and cyclopropane (**3**) units into the PNA backbone. The (*S*,*S*)-*trans*-configuration of the cyclopentyl and cyclopropyl PNA monomers were set by employing Yamamoto's asymmetric synthesis to form 5- and 3-membered rings. Gram quantaties of enantiomerically pure Boc protected cyclopentane and cyclopropane diamines were synthesized and converted into PNA monomers over 8 steps with a 4% overall yield. The backbone preorganization of these modified PNAs has lead to improved binding affinity for cyclopentyl-PNA and improved selectivity for cyclopropyl-PNA.



1



2



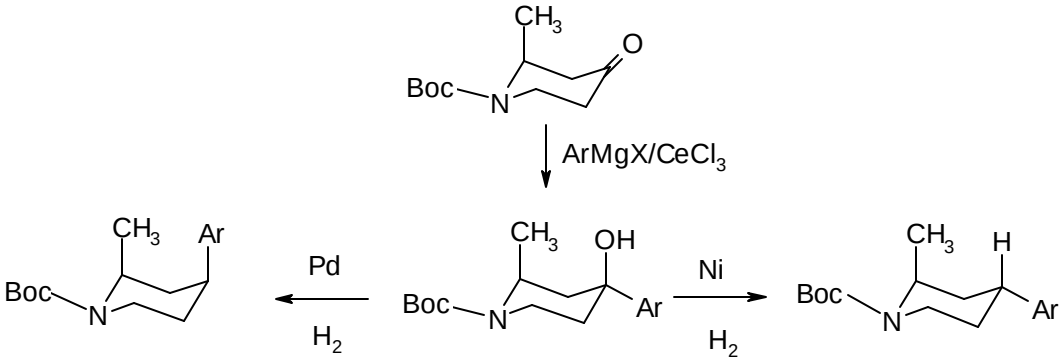
3

NEW STEREOSELECTIVE SYNTHESES OF CIS- AND TRANS-2-METHYL-4-ARYL-PIPERIDINES.

Alain Merschaert, Laurent Delhaye, Jean-Paul Kestemont, Willy Brione, Pieter Delbeke.

Chemical Process Research and Development, Lilly Research Laboratories, Lilly Development Centre, rue Granbonpré, 1348 Mont-Saint-Guibert, Belgium.

A stereoselective approach has been developed for the synthesis of *cis* and *trans* 2-methyl-4-arylpiperidines from a common intermediate. The Ni-catalyzed hydrogenolysis of *N*-Boc-2-methyl-4-aryl-4-piperidinols, obtained by addition of organometallic reagents on *N*-Boc-2-methyl-4-piperidone, affords the *trans* derivatives with up to 95% selectivity whereas the corresponding *cis* isomers are obtained in the presence of palladium catalysts.



38th National Organic Symposium
Poster Abstracts
Session B

Schedule of Presenters – Poster Session B Monday June 9, 9:30 pm – 12 am

B1 QUINONE METHIDES AND CYCLOHEXADIENONES IN SYNTHESIS: TOWARDS THE TOTAL SYNTHESIS OF SCYPHOSTATIN

Ryan W. Van De Water, Thomas R. R. Pettus
University of California, Santa Barbara
Department of Chemistry and Biochemistry
Santa Barbara, CA 93106

B2 DESIGN SYNTHESIS AND EVALUATION OF SERIES COMPOUNDS BASED ON TRIFLUOROMETHYLATED VITAMIN B_6 AS POTENTIAL NOVEL INDICATORS FOR IN VIVO AND NON-INVASIVE DETECTION OF TUMOR CELLULAR pH

Jianxin Yu, Pieter Otten, Weina Cui, Ralph P. Mason*
Department of Radiology, The University of Texas Southwestern Medical Center at Dallas, 5323 Harry Hines Blvd., Dallas, Texas 75390

B3 STEREOSELECTIVE SYNTHESIS AND EVALUATION OF FLUORINATED VITAMIN B_6 β-*D*-GALACTOSIDES AS POTENTIAL NOVEL SUBSTRATES FOR IN VIVO AND NON-INVASIVE DETECTION OF LACZ GENE EXPRESSION

Jianxin Yu, Ralph P. Mason*
Department of Radiology, The University of Texas Southwestern Medical Center at Dallas, 5323 Harry Hines Blvd., Dallas, Texas 75390

B4 A DESIGNED INHIBITOR OF PIN1 PPIASE ACTIVITY

Xiaodong J. Wang and Felicia A. Etzkorn*
Virginia Polytechnic Institute and State University
Department of Chemistry, Blacksburg, VA 24061-0212

B5 SYNTHESIS OF PHOTOCLEAVABLE PROTECTING GROUPS FOR PRIMARY ALCOHOLS WITH APPLICATIONS IN THE CONSTRUCTION OF DNA MICROARRAYS

Garrett M. Zopp, Mary K. Boyd
Loyola University Chicago
Department of Chemistry, Chicago, IL 60626

B6 SENSITIZED PHOTOLYSIS OF 1-ACYL-7-NITROINDOLINES GREATLY IMPROVES THE EFFICIENCY FOR PHOTORELEASE OF THE ALKANOIC ACID

John E.T. Corrie,[1] George Papageorgiou[1] and P. Wan[2]
1 National Institute for Medical Research, The Ridgeway, Mill Hill, London NW7 1AA, U.K.
2 Department of Chemistry, University of Victoria, Victoria, B.C., Canada V8W 3V6

B7 HIGH ASYMMETRIC INDUCTION WITH b-TURN DERIVED PALLADIUM PHOSPHINE COMPLEXES

Scott J. Greenfield and Scott R. Gilbertson
Department of Chemistry
Washington University
Saint Louis, Missouri 63130

B8 ADVANCES IN THE ASYMMETRIC CONSTRUCTION OF ARCHITECTURALLY COMPLEX NATURAL PRODUCTS: THE LITUARINES

Amos B. Smith, III, Shawn P. Walsh, and Michael Frohn
Department of Chemistry, University of Pennsylvania
Philadelphia, PA 19104-6323

B9 INFLUENCE OF A b-ALKOXY SUBSTITUENT ON THE C–H ACTIVATION CHEMISTRY OF ALKYL ETHERS: SYNTHESIS OF (*S*)-METHYL TROPINATE

Jaemoon Yang and Huw M. L. Davies*
Department of Chemistry, The State University of New York, Buffalo, New York 14260-3000

B10 SYNTHESIS OF *EE*, *EZ* AND *ET* 1,3-DIENES VIA Pd-CATALYZED CHEMOSPECIFIC REDUCTION OF p-ALLYL CHEMISTRY

Xiaojin Li and Philip L. Fuchs
Department of Chemistry, Purdue University
Department of Chemistry, 560 Oval Drive, West Lafayette, IN 47906-2084

B11 APPLICATIONS OF THE NON-ALDOL ALDOL REACTION

Alexandra van den Heuvel*, Michael E. Jung, Andrew G. Leach, K. N. Houk
University of California, Los Angeles, Department of Chemistry and Biochemistry, 405 Hilgard Ave, Los Angeles, CA 90095

B12 MONOSACCHARIDE BASED PEPTIDOMIMETICS OF SOMATOSTATIN (SRIF): INCORPORATION OF BIO ISOSTERES OF INDOLE AT C1 OF b-D-GLUCOSIDES AND POSITION EIGHT OF SRIF.

Angie R. Angeles,[1] Guoxia Han,[1] Gary Chicci,[2] Marc Kurtz,[2] Elizabeth Birzin,[2] Susan Rohrer,[2] Dennis Underwood,[3] Amos B. Smith, III[1] and Ralph F. Hirschmann[1]
[1]Department of Chemistry, University of Pennsylvania, Philadelphia, PA 19104
[2]Merck Research Laboratories , Rahway, NJ 07065
[3]Infinity Pharmaceuticals, Cambridge, MA 02139

B13 DESIGN, SYNTHESIS, AND CHARACTERIZATION OF NON-CENTROSYMMETRIC HYDROGEN-BONDED LIQUID-CRYSTALLINE POLYMERS

Jeremy R. Wolf, Tongfeng Zhao, Christopher Landorf, and Daniel J. Dyer
Southern Illinois University at Carbondale
Department of Chemistry, Carbondale, IL 62901-4409

B14 SYNTHESIS OF C-GLYCOSYL ASPARAGINES AND C-GLYCOSYL SERINES BY OLEFIN CROSS-METATHESIS

Ernest G. Nolen, Adam Kurish
Colgate University, Department of Chemistry
Hamilton, NY 13346

B15 EFFORTS TOWARD THE DESIGN AND SYNTHESIS OF BIOLOGICALLY ACTIVE PYRROLINONE-BASED b-TURN PEPTIDOMIMETICS

Amos B. Smith, III, Adam K. Charnley, Andrew B. Benowitz, Meinrad Brenner, Osamu Kikuchi, Eugen F. Mesaros, Paul A. Sprengeler, Wenyong Wang and Ralph Hirschmann
Department of Chemistry, University of Pennsylvania, Philadelphia, PA 19104

B16 EFFORTS TOWARD THE HIGH-THROUGHPUT ALKYLATION AND SCREENING OF CD4 MINIPROTEIN MIMETICS: DEVELOPMENT OF LEADS FOR RATIONAL SMALL MOLECULE DESIGN

Amos B. Smith, III,[1] Irwin M. Chaiken,[2] Jason M. Cox,[1] Uma V. Manjappara,[2] Sergey N. Savinov,[1] John A. Zuawski[2]
[1]Department of Chemistry, University of Pennsylvania, Philadelphia, PA 19104
[2]Department of Medicine, University of Pennsylvania, Philadelphia, PA 19104

B17 INVESTIGATIONS OF THE COPE REARRANGEMENT OF 1,2,6-HEPTATRIENE: RESULTS FROM DIRECT DYNAMICS TRAJECTORIES AND SULFUR DIOXIDE TRAPPING STUDIES

Stefan L. Debbert and Barry K. Carpenter
Department of Chemistry and Chemical Biology, Cornell University
Ithaca, NY 14853-1301

B18 THE FIRST TOTAL SYNTHESIS OF DRAGMACIDIN D AND PROSPECTS FOR THE PREPARATION OF OTHER DRAGMACIDIN ALKALOIDS

Neil K. Garg, Richmond Sarpong, Brian M. Stoltz*
California Institute of Technology
Division of Chemistry and Chemical Engineering, Pasadena, CA 91125

B19 NOVEL ROUTES TO 5-HYDROXYPIPERIDONE-DERIVED BUILDING BLOCKS

Richard H. Blaauw,[1] Mandy K. S. Vink,[2] Hans E. Schoemaker,[3] Floris P. J. T. Rutjes[4]
[1]Chiralix B.V., [2]University of Amsterdam, [3]DSM Research, [4]University of Nijmegen
[1]P.O. Box 31070, 6503 CB Nijmegen, The Netherlands, [2]IMC, Nieuwe Achtergracht 129, 1018 WS Amsterdam, The Netherlands, [3]P.O. Box 18, 6160 MD Geleen, The Netherlands, [4]NSRIM, Toernooiveld 1, 6525 ED Nijmegen, The Netherlands

B20 SYTHESIS, SELF-ASSEMBLY, AND ELECTRO-OPTIC SWITCHING OF ONE-DIMENSIONAL NANOSTRUCTURES

Mark L. Bushey and Colin Nuckolls
Columbia University, Department of Chemistry
New York City, NY 10027

B21 ASYMMETRIC CONJUGATE ADDITION OF AZIDE CATALYZED BY SHORT FOLDED PEPTIDES AND APPLICATIONS IN ORGANIC SYNTHESIS

David J. Guerin, Thomas E. Horstmann, Scott J. Miller
Boston College Department of Chemistry, Merkert Chemistry Center, Chestnut Hill, MA 02467

B22 SYNTHESIS AND BIOLOGICAL ACTIVITY OF NEW QUINOXALINE ANTIBIOTICS OF TRIOSTIN A ANALOGUE

YunBong Kim, SungHo Kim, YongHae Kim
Center for Molecular Design and Synthesis, School of Molecular Science(BK-21), Department of Chemistry, Korea Advanced Institute of Science and Technology, 305-701, Taejeon, Republic of Korea

B23 MECHANISTIC STUDIES OF SULFATE HYDROLYSES

Benjamin T. Burlingham,[1] Lisa M. Pratt,[2] Ernest R. Davidson,[3] Vernon J. Shiner, Jr.,[4] Jon Fong,[2] Theodore S. Widlanski[4]
[1]Mount Union College; [2]Indiana University, Bloomington; [3]University of Washington; [4]Indiana University, Bloomington
[1]Department of Chemistry, 1972 Clark Ave., Alliance, OH 44601; [2]Department of Geology, Bloomington, IN, 47405; [3]Department of Chemistry, Seattle, WA 98195-1700; [4]Department of Chemistry, Bloomington, IN, 47405

B24 INTERMOLECULAR C–H ACTIVATION AT BENZYLIC METHYL POSITIONS: SYNTHESIS OF (+)-IMPERANENE AND (-)-α-CONIDENDRIN

Qihui Jin and Huw M. L. Davies*
Department of Chemistry, The State University of New York, Buffalo, New York 14260-3000

B25 INHIBITORS FOR HISTONE DEACETYLASE

Joakim Löfstedt and Paul Helquist
University of Notre Dame , Department of Chemistry & Biochemistry
251 Nieuwland Science Hall, Notre Dame, IN 46556-5670 USA

B26 SYNTHESIS OF 3-KETO PETROMYZONOL SULFATE: A POTENT SEA LAMPREY PHEROMONE

Andrea M. Pellerito and Robert E. Maleczka, Jr.
Department of Chemistry
Michigan State University
East Lansing, MI 48823

B27 DECOMPOSITION OF SILYL DIACYL PEROXIDES: A MILD AND STEREOSELECTIVE SYNTHESIS OF SILYL ESTERS

Douglas S. Masterson and Ned A. Porter
Vanderbilt University, Department of Chemistry
Box 1822 Station B, Nashville, TN 37235

B28 NEW SIMPLE CHIRAL PHOSPHINE OXAZOLIDINE LIGAND: EASY SYNTHESIS AND APPLICATION IN THE PALLADIUM-CATALYZED ASYMMETRIC ALLYLIC ALKYLATION

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B29 ENANTIOPURE AMINES AND AMINO ACIDS BY CHIRALITY TRANSFER USING (*R*)-PHENYLGLYCINE AMIDE

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B30 CHIRAL C6 BUILDING BLOCKS BY DERIVATISATION OF AN ENANTIOPURE a,ß-UNSATURATED d-LACTONE AVAILABLE ON kg-SCALE

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B31 SYNTHESIS OF OXIRANYLKETONES BY CHALCOGENIDE-CATALYZED EPOXIDATION REACTIONS OF ß-BROMOKETONES WITH ALDEHYDES

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B32 EXPLORING NOVEL CLASS OF SOLUBLE GUANYLATE CYCLASE(SGC) ACTIVATORS---A RAPID SYNTHETIC APPROACH

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B33 A NOVEL STEREOSELECTIVE APPROACH TO THE POLYCYCLIC GUANIDINE ALKALOIDS BATZELLADINE A AND D

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B34 SYNTHESIS OF a-HYDROXYTHIOLACTAMS BY SAMARIUM(II) IODIDE MEDIATED CYCLIZATION OF ß-KETO ISOTHIOCYANATES

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B35 STEREOSELECTIVE SYNTHESIS OF POLY-HYDROXYLATED ALKALOIDS

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B36 EXPLORATIONS OF INTRAMOLECULAR DIELS–ALDER REACTIONS OF 2-AMINO-1,3,4-OXADIAZOLES: TOTAL SYNTHESIS OF ANHYDROLYCORINONE

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B37 SYNTHESIS AND BIOLOGICAL ACTIVITY OF ARYL- AND HETEROARYL[A]PYRROLO[3,4-C]CARBAZOLES

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B38 STUDIES DIRECTED TOWARDS A TOTAL SYNTHESIS OF PHOMACTIN A

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B39 SILVER TRIFLATE-MEDIATED OXAZOLIUM SALT FORMATION: SOLVENT EFFECTS AND APPLICATION TOWARD THE SYNTHESIS OF AZIRIDINOMITOSENES

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B40 MECHANISTIC STUDY OF SILYLENE TRANSFER FROM A SILACYCLOPROPANE TO AN ALKENE

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B41 CATALYTIC ENANTIOSELECTIVE CYANOSILYLATION OF KETONES AND KETOIMINES

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B42 DOUBLE CYCLOISOMERIZATION-REDUCTION AS A NOVEL AND EXPEDITIOUS ROUTE TOWARD TRICYCLIC ALKALOID STRUCTURES

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B43 NOVEL 1,2-MIGRATION OF THIO-GROUP IN ALLENYLSULFIDES: EFFICIENT SYNTHESIS OF 3-THIO-SUBSTITUTED FURANS AND PYRROLES

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B44 2,3-DIARYL-5,7-DIALKYL-PYRAZOLO[1,5-*A*]PYRIMDINES AS ERB POTENCY SELECTIVE ANTAGONISTS

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B45 HALICHONDRIN B: SYNTHESIS OF THE C1-C22 SUBUNIT VIA DESYMMETRIZATION OF (+)-CONDURITOL E

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B46 COPPER-CATALYZED ENANTIOSELECTIVE 1,4-ADDITIONS OF ORGANOZINC REAGENTS TO SUBSTITUTED ENONES

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B47 SYNTHESIS OF NEW MACROCYCLIC ALLENES

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B48 TRANSITION METAL-PROMOTED SYNTHESIS OF FUNCTIONALIZED AND UNFUNCTIONALIZED PYRIDYLALLENES

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B49 DIASTEREOSELECTIVE SYNTHESIS OF FUNCTIONALIZED a-HYDROXYALLENES BY ENOLATE OXIDATION WITH DMDO

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B50 DIASTEREOSELECTIVE GOLD-CATALYZED CYCLIZATION OF a-HYDROXYALLENES: PRECURSORS IN NATURAL PRODUCT SYNTHESIS

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B51 COLUMNAR DISCOTIC LIQUID-CRYSTALLINE OXADIAZOLE AS ELECTRON TRANSPORT MATERIALS

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B52 NOVEL DERIVATIVES AND MEDICINAL APPLICATIONS OF THE TRIMETALLIC NITRIDE ENDOHEDRAL METALLOFULLERENES

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B53 TRANSITION METAL-CATALYZED HYDRO-, SILA-, AND STANNASTANNATION OF CYCLOPROPENES: STEREO- AND REGIOSELECTIVE APPROACH TOWARD MULTISUBSTITUTED CYCLOPROPYL SYNTHONS

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B54 CATALYTIC ASYMMETRIC HYDROBORATION OF CYCLOPROPENES

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B55 SYNTHETIC STUDIES TOWARDS THE AGLYCON OF APOPTOLIDIN

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B56 ASYMMETRIC CATALYTIC PHOSPHORYLATION: SYNTHESIS OF INOSITOL PHOSPHATES

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B57 THE METHYLPYRROLIDINE APPROACH TO NATURAL PRODUCTS: STUDIES TOWARD THE SYNTHESIS OF MITOMYCIN C

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B58 CHEMICAL APPROACH TOWARDS MUCIN-TYPE *O*-LINKED GLYCOPROTEOMICS USING THE STAUDINGER LIGATION

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B59 CATALYTIC ENANTIOSELECTIVE ADDITIONS OF DIMETHYLZINC TO CARBONYL COMPOUNDS

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B60 NOVEL SYNTHETIC SCAFFOLDS FOR FURTHER DERIVATION IN DRUG DISCOVERY

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B61 ASYMMETRIC SYNTHESIS OF ALL DIASTEREOMERS OF 3-HYDROXY-2,4,6-TRIMETHYLHEPTANOIC ACID: VERIFICATION OF CONFIGURATIONAL ASSIGNMENT

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B62 EFFORTS TOWARD THE SYNTHESIS OF A SULFONAMIDE-LINKED TETRAMER OF THYMIDINE

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B63 PHOTOCYCLOADDITION REACTION TO BENZODITHIOPHENE – A ONE STEP REACTION TO ALKYNE-SUBSTITUTED CYCLOBUTENES

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B64 APPROACH TOWARDS THE TOTAL SYNTHESIS OF VILLALSTONINE

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B65 SYNTHESIS OF PROTECTED (*R*)- AND (*S*)-2-METHYLCYSTEINE VIA THE CURTIUS REARRANGEMENT

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B66 A TOTALLY AUTOMATED SOLUTION FOR NORMAL AND RP PREPARATIVE HPLC WITH ANALYTICAL PURIFICATION DETERMINATION: CLC

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B67 LINEAR FREE ENERGY RELATIONSHIPS IN THE UNDERGRADUATE ORGANIC CHEMISTRY LAB

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B68 SYNTHESIS AND CHEMICAL BIOLOGY OF THE APOPTOSIS INDUCING AGENT CYTOTRIENIN A AND ITS 15 DIASTEREOISOMERS

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B69 ASYMMETRIC SYNTHESIS OF THE LEUCASCANDROLIDE MACROLIDE

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B70 SUZUKI CROSS-COUPLING REACTIONS OF TRIARYLBORANE ADDUCTS

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B71 SUBSTITUTION REACTIONS ON THE 7*H*-DIBENZO[*de,h*]QUINOLIN-7-ONE SCAFFOLD. ARE AMINOOXOISOAPORPHINE ALKALOIDS ARTEFACTS?

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B72 SYNTHESIS OF SYMMETRIC SULFATED SUGAR PROTEIN-BINDING MOLECULES

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B73 REMODELING THE ENGRAILED HOMEODOMAIN• DNA INTERFACE

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B74 [1,4]-WITTIG REARRANGEMENTS OF a-SILYL ETHERS

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B75 FLUOROPROLINE INCORPORATION INTO THE X-POSITION OF COLLAGEN: HOW STEREOELECTRONICS AFFECT TRIPLE-HELIX STABILITY

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B76 WHAT'S NEW WITH NEOMYCIN?

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B77 SULFUR YLIDE INITIATED THIO-CLAISEN REARRANGEMENTS: SYNTHESIS OF HIGHLY SUBSTITUTED INDOLINES.

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B78 SYNTHESIS OF NOVEL FLUORINATED NITROXIDES AND APPLICATIONS TO IONOMER SUPRAMOLECULAR ASSEMBLIES

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B79 2,3-ANHYDRO-D-FURANOSIDES: SYNTHETIC AND MECHANISTIC STUDIES

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B80 A HIGHLY STEREOSELECTIVE SYNTHESIS OF NOVEL *E*-A-HALOENAMIDES VIA A MILD AND EFFICIENT HYDROHALOGENATION OF YNAMIDES

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B81 ORGANOALUMINUM REAGENTS IN VINYLSILANES SYNTHESIS

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B82 RELATIVE RATES OF BOND ROTATION AND RING CLOSURE IN THE PHOTOCYCLOADDITION INTERMEDIATES FROM C60 AND THE ISOMERIC 2,4-HEXADIENES - A REANALYSIS OF REPORTED DATA

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B83 METALLOCARBENES AND MULTICOMPONENT MANNICH REACTIONS: TWO NEW METHODS FOR THE FUNCTIONALIZATION OF NATIVE PROTEIN RESIDUES

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B84 DESIGN, SYNTHESIS AND DISCOVERY OF NOVEL HYDROXYAMIDES AS ORALLY AVAILABLE GENERAL ANESTHETICS AND ANTICONVULSANTS

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B85 ALKYLPHOSPHAZINES AS EFFECTIVE COUPLING PARTNERS; A NEW ENTRY INTO THE KOJIC AMINE BASED PEPTIDOMIMETICS

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B86 DEVELOPMENT OF LOW MOLECULAR WEIGHT HIV-1 PROTEASE DIMERIZATION INHIBITORS

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B87 A NEW USE OF CARBONYLS AS INDIRECT GEMINAL RADICAL ACCEPTORS AND PRECURSORS

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B88 SELECTIVE REACTIONS OF p-ALLYL PALLADIUM(II) INTERMEDIATES GENERATED FROM *N*-ACYLNITROSO DIELS-ALDER CYCLOADDUCTS

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B89 DYNAMIC AND THERMODYNAMIC INVESTIGATION OF ARYLLITHIUM-METALLOID ATE COMPLEXES: STUDY OF THEIR ROLE IN LITHIUM-METALLOID EXCHANGE REACTIONS.

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B90 THE THIOPYRAN ROUTE TO POLYPROPIONATES. STEREOSELECTIVE ALDOL HOMOLOGATIONS OF DIPROPIONATE SYNTHONS

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B91 DEVELOPMENT OF FACILE SYNTHETIC PATHWAYS TO PLASMENYL-TYPE LIPIDS AND THEIR UTILIZATION IN THE DEVELOPMENT OF ACID SENSITIVE VINYL ETHER BASED PEGYLATED LIPOSOMES

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B92 A SIMPLE PREPARATION OF DIAZO ESTERS

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B93 METABOLITES OF A VASOPRESSIN V2- RECEPTOR AGONIST AND ANTAGONIST

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B94 THE SYNTHESIS OF CERTAIN 3-(ß-D-RIBOFURANOSYL)-6-ARYL-4,9-DIHYDRO-9-OXO-1H-IMIDAZO[1,2a]PURINES AND A STUDY OF THEIR ANTIVIRAL ACTIVITY

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B95 STEREOSELECTIVE TOTAL SYNTHESIS OF ANTITUMOR MACROLIDE RHIZOXIN D

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B96 SYNTHESIS OF DEOXYTHIO *MYO*-INOSITOLS: PHOSPHATIDYLINOSITOL 5-PHOSPHOROTHIOLATES

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B97 PHOTOCHEMICAL PROTEIN CROSSLINKING WITH 1,8-NAPHTHALIMIDES

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B98 A STUDY TOWARD A TOTAL SYNTHESIS OF AN AZIRIDINOMITOSENE DERIVATIVE OF FK317

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B99 CONJUGATE RADICAL ADDITIONS ONTO ?-CHIRAL SUBSTRATES: PROGRESS TOWARDS THE TOTAL SYNTHESIS OF (-)-STEMOAMIDE

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B100 HELICOMIMETIC PEPTIDES AS SELECTIVE, NANOMOLAR INHIBITORS OF PROTEIN-PROTEIN INTERACTIONS

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B101 SYNTHESIS OF THIOETHER-BRIDGED PEPTIDES VIA A NOVEL REACTION OF BASE-ASSISTED DESULFURIZATION

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B102 ALKYLATED C-SUGARS AS NOVEL BIOCONJUGATES

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B103 SEMI-ORTHOGONAL SYNTHESIS OF A TETRACYCLIC ANTIMICROBIAL ANALOG

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B104 CARBENE-PHOSPHINE COMPLEXES OF IRIDIUM: THEIR SYNTHESIS AND REACTIVITY TOWARD CATALYTIC OLEFIN HYDROGENATION

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B105 STEREOSELECTIVE SYNTHESIS OF POLY-HYDROXYLATED ALKALOIDS

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B106 NORBORNENYL-TAGGED REAGENTS: TOOLS FOR ORGANIC SYNTHESIS

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B107 PALLADIUM-CATALYZED C-H BOND FUNCTIONALIZATION: AEROBIC OXIDATIVE C-C BOND FORMING REACTIONS

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B108 STILLE COUPLINGS CATALYTIC IN TIN: APPLICATION TO THE TOTAL SYNTHESIS OF MONOCILLIN I

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B109 MOLECULAR STEREOCHEMISTRY: NEW DEVELOPMENTS IN THE DETERMINATION OF ABSOLUTE CONFIGURATION AND PREDOMINANT CONFORMATIONS OF CHIRAL MOLECULES IN SOLUTION PHASE

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B110 MECHANISTIC STUDIES OF PALLADIUM-CATALYZED CROSS-COUPLINGS OF ALKYL ELECTROPHILES BEARING ß-HYDROGENS

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B111 PD-CATALYZED OXIDATION AND KINETIC RESOLUTION OF ALCOHOLS USING MOLECULAR OXYGEN

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B112 SYNTHESIS OF *S*-LINKED MUCIN GLYCOPEPTIDE CONJUGATES VIA CHEMOSELECTIVE CARBOHYDRATE-PEPTIDE LIGATION

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Urbana, IL 61801

B113 CHEMISTRY IN THE BOUNDARY LAYER: THE SPINNING TUBE-IN-TUBE REACTOR SYSTEM

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B114 ACID PROMOTED PRINS CYCLIZATIONS OF VINYLOGOUS CARBONATES TO FORM TETRAHYDROPYRANS

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100 W. 18th Ave., Columbus, OH 43210

B115 *ENDO*-REGIOSELECTIVE TANDEM OXACYCLIZATION OF POLYEPOXIDES: SILICON AS A HYDROGEN ATOM SURROGATE IN THE SYNTHESIS OF *TRANS*-FUSED OXEPANES

Jason Conley Valentine, Frank E. McDonald
Emory University
Department of Chemistry, Atlanta, GA 30322

B116 THE EVANS-TISHCHENKO REACTION: A ONE-STEP OXIDATION/MACROCYCLIZATION

Amos B. Smith, III, Dongjoo Lee, and Christopher M. Adams
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B117 THE FIRST CATALYTIC, ASYMMETRIC a-ADDITIONS OF ISOCYANIDES: LEWIS-BASE-CATALYZED, ENANTIOSELECTIVE PASSERINI-TYPE REACTIONS

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B118 TOWARD GLYCOSYLATED NANOPARTICLE LIBRARIES

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B119 ß-DEPROTONATION/MAGNESIATION OF CARBOXAMIDE ACTIVATED CYCLOALKANES

Mao-Xi Zhang, Philip E. Eaton, Naruyoshi Komiya, and Cai-Guang Yang
Department of Chemistry, The University of Chicago, Chicago, IL 60637

B120 NEW APPROACH TOWARDS AMINO CARBENES

Michael Otto and Guy Bertrand
UCR – CNRS Joint Research Laboratory, University of California, Riverside

B121 METHODOLOGIES DIRECTED TOWARD AND THE SYNTHESIS OF *N*-ACYL SULFONAMIDE-LINKED DINUCLEOSIDES AS POTENTIAL INHIBITORS OF RIBONUCLEASE A

David C. Johnson II and Theodore S. Widlanski
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Department of Chemistry, Bloomington, IN 47405

B122 DISCODERMOLIDE SYNTHETIC STUDIES. LARGE SCALE SYNTHESIS OF DISCODERMOLIDE WITHOUT HIGH PRESSURE.

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B123 STUDIES TOWARD THE SYNTHESIS OF THE SACCHAROMICIN AGLYCON

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B124 DEVELOPMENT OF CASCADE REACTIONS INVOLVING DIAZO COMPOUNDS: TANDEM BAMFORD-STEVENS-CLAISEN AND TANDEM WOLFF-COPE REARRANGEMENTS

Jeremy A. May, Richmond Sarpong and Brian M. Stoltz*
Arnold and Mabel Beckman Laboratories of Chemical Synthesis
California Institute of Technology, Division of Chemistry and Chemical Engineering
Pasadena, CA 91125

B125 SPONGISTATIN SYNTHETIC STUDIES. AN EFFICIENT SECOND-GENERATION CONSTRUCTION OF AN ADVANCED ABCD INTERMEDIATE, FRAGMENT UNION, AND FINAL ELABORATION TO (+)-SPONGISTATIN 1

Amos B. Smith, III, Chris Sfouggatakis, Wenyu Zhu, Shohei Shirikami, Victoria Doughty, and Clay Bennett
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B126 PROGRESS TOWARD THE TOTAL SYNTHESIS OF COMMUNESIN B (A.K.A. NOMOFUNGIN)

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Arnold and Mabel Beckman Laboratories of Chemical Synthesis
California Institute of Technology, Division of Chemistry and Chemical Engineering
Pasadena, CA 91125

B127 HIGHLY EFFICIENT KINETIC RESOLUTION OF ENYNES ESTER AND ENANTIOSELECTIVE SYNTHESES OF POLYFUNCTIONAL a-ALKYLENE-?-BUTYROLACTONES VIA Rh(I)-CATALYZED CYCLOISOMERIZATION APPLICATION TO FORMAL SYNTHESIS OF (-)-BLASTMYCINOLACTOL AND (+)-BLASTMYCINONE

Aiwen Lei, Minsheng He, and Xumun Zhang,*
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Department of Chemistry, 152 Davey Laboratory, University Park, PA 16802.

B128 ION BINDING AND TRANSPORT BY SYNTHETIC MOLECULAR ASSEMBLIES

Frank W. Kotch, Vladimir Sidorov, Jeffery T. Davis
Department of Chemistry and Biochemistry, University of Maryland
College Park, Maryland 20742

B129 WHEN IS A HYDROPHOBIC INTERACTION NOT A HYDROPHOBIC INTERACTION? EXAMPLES IN ß-HAIRPIN PEPTIDES

Chad D. Tatko and Marcey L. Waters
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Department of Chemistry, Chapel Hill, North Carolina 27599

B130 SYNTHETIC STUDIES DIRECTED TOWARD THE TOTAL SYNTHESIS OF AFLASTATIN A

David A. Evans, Jing Zhang, William C. Trenkle, Frank Glorius, Jason D. Burch
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Department of Chemistry & Chemical Biology, Cambridge, MA 02138

B131 TOWARDS A TOTAL SYNTHESIS OF THE IEJIMALIDES

Dirk Schweitzer, John Kane, Jamie Zigterman, Paul Helquist
University of Notre Dame
Department of Chemistry & Biochemistry, Notre Dame, IN 46556-5670

B132 STEREOSELECTIVE SYNTHESIS OF 1,2-*O*-ISOPROPYLIDENE-3-*C*-(5-PHENYL-1,24-OXADIAZOL-3-YL)-ß-*D*-PSICOPYRANOSE THROUGH A NOVEL PROCEDURE

Jianxin Yu[a]*, Zhongjun Li,[b] Wenjie Lu,[c] Suna Zhang,[b] Mengshen Cai,[b]
[a]Department of Radiology, The University of Texas Southwestern Medical Center at Dallas, 5323 Harry Hines Blvd., Dallas, Texas 75390
[b]School of Pharmaceutical Sciences, Peking University, Beijing 100083, China
[c]Dpartment of Chemistry, Wuyi University, Jiangmen 529020, China

B133 DINAPSOLINE - A STUDY ON STRUCTURE-ACTIVITY-RELATIONSHIP (SAR) AND PHARMACOLOGICAL PROFILE OF A NOVEL DOPAMINE AGONIST

Sing-Yuen Sit,* Kai Xie, Swanee Jacutin-Porte, Kenneth Boy, James Seanz, Matthew T. Taber, Amit G. Gulwadi, Carolyn D. Korpinen, Kevin D. Burris, Thaddeus F. Molski, Elaine Ryan, Cen Xu, Henry Wong, Juliang Zhu, Subramaniam Krishnananthan, Todd Verdoorn and Graham Johnson
Bristol-Myers Squibb Pharmaceutical Research Institute
5 Research Parkway, Wallingford, CT 06492-7660, USA

B134 A COMPUTER PROGRAM THAT DESIGNS SYNTHETIC ROUTES

Malcolm Bersohn[1], Daniel Gruner[1], Wataru Katouda[2], Takashi Kawai[2], Tetsuhiko Takabatake[2], and Akio Tanaka[2]
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1-98 Kasugade-naka 3-chome, Konohana-ku, Osaka, Japan 554-8558

B135 CATALYTIC ASYMMETRIC INTERMOLECULAR C–H ACTIVATION AS A SURROGATE TO THE ALDOL REACTION

Rohan E. J. Beckwith, Qihui Jin, Evan G. Antoulinakis and Huw M. L. Davies*
Department of Chemistry, University at Buffalo, The State University of New York, Buffalo, New York 14260-3000

B136 DIASTEREOSELECTIVE ADDITION OF KETONE ENOLATES TO BENZYNE: ASYMMETRIC SYNTHESIS OF BENZOCYCLOBUTENOLS

Olivier J.-C. Nicaise,* Alison L. Maddeford, Daniel J. Mans, Emilio Villa Hefti, and Robert J. Otto
Monsanto Hall, Department of Chemistry, Saint Louis University, 3501 Laclede Avenue, St. Louis, MO 63103-2010

B137 *P*-HETEROCYCLIC BUILDING BLOCKS: NOVEL SYNTHONS FOR STEREOSELECTIVE SYNTHESIS

Alan Whitehead, Matthew D. McReynolds, Joel D. Moore, Diana S. Stoianova, and Paul R. Hanson*
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1251 Wescoe Hall Drive, Lawrence, KS 66045-7582

B138 OXIDATIVE COUPLING OF RING EXPANDED GLYCALS: SEPTANOSE CARBOHYDRATES

Mark W. Peczuh and Nicole L. Snyder
University of Connecticut, Department of Chemistry, Storrs, CT 06269-3060

B139 ASYMMETRIC INTERMOLECULAR C-H ACTIVATION USING IMMOBILIZED DIRHODIUM TETRAKIS((*S*)-*N*-(DODECYLBENZENESULFONYL)-PROLINATE) AS A RECOVERABLE CATALYST

Abbas M. Walji and Huw M. L. Davies
University at Buffalo, The State University of New York
Department of Chemistry, Buffalo, NY 14260-3000

B140 A HOMOHELICAL ELECTRONIC THEORY FOR CHIRAL RECOGNITION AND ASYMMETRIC INDUCTION

David Zhigang Wang*
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B141 UNDERSTANDING ORIGIN OF ENANTIOSELECTION WITHOUT STERIC REASONING: A NEW HOMOHELICAL ELECTRONIC INDUCTION THEORY LEADING TO A SIMPLE STEREOCHEMICAL RATIONALE FOR ASYMMETRIC CARBONYLS HYDROGENATION

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B142 KINETIC RESOLUTION IS ELECTRONICALLY CONTROLLED BY HOMOHELICAL RECOGNITION

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Quinone Methides and Cyclohexadienones in Synthesis: Towards the Total Synthesis of Scyphostatin

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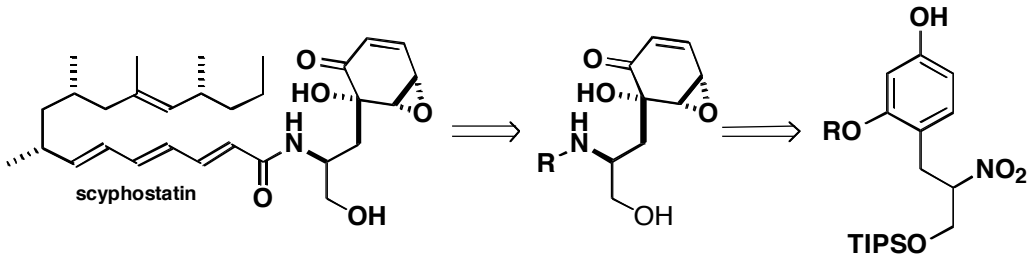
Department of Chemistry and Biochemistry
Santa Barbara, CA, 93106



Scyphostatin, a neutral sphingomyelinase inhibitor first isolated in 1997, is comprised of a highly oxidized cyclohexane ring as well as an amino alcohol side chain and fatty acid portion. Our interest in this molecule encompasses the cyclohexenone and amino alcohol core of the molecule as a testing ground for recent chemistry developed in our group. Synthetic studies to the core begin with the attachment of an amino alcohol equivalent carbon chain to resorcinol via the intermediacy of a reactive *ortho* quinone methide. Subsequent oxidative dearomatization leads to a 2,5-cyclohexadienone species that has proved to be an efficient scaffold for subsequent diastereoselective reactions. Progress towards a viable route for the synthesis of the scyphostatin core will be reported.

DESIGN, SYNTHESIS AND EVALUATION OF SERIES COMPOUNDS BASED ON TRIFLUOROMETHYLATED VITAMIN B_6 AS POTENTIAL NOVEL INDICATORS FOR IN VIVO AND NON-INVASIVE DETECTION OF TUMOR CELLULAR PH

Jianxin Yu, Pieter Otten, Weina Cui, Ralph P. Mason*
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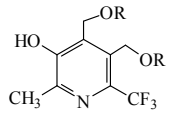
pH plays a significant role in cellular regulation and strongly influences drug uptake. Thus, the measurement of pH in tumors promises insight into developmental processes and prognostic information regarding therapeutic outcome. We have previously described the vitamin B6 analog 6-fluoropyridoxol (FPOL) [*Curr. Med. Chem*., **6**, 481, 1999] as a sensitive ^{19}F NMR pH indicator exhibiting a chemical shift range of 10 ppm. It readily crosses cell membranes and we demonstrated application to measure transmembrane pH gradients in whole blood and perfused hearts. With the goal of improving the signal-to-noise ratio, we have now evaluated a series of second generation reporters, using a CF_3-group instead of a single F-atom. The chemical shift difference between the acid and its conjugate base is 1.64 ppm compared to 10 ppm for FPOL. The rationale for the lower sensitivity is that the reporting F-atoms are not in direct π communication with the pH sensitive *para*-OH bond. The pK_a of CF_3POL is ideal at 6.82 and is insensitive to temperature. We will present synthetic strategies, molecular and spectral characteristics, and applications to cells, perfused organs, and tumors *in vivo*.



R = H, $(CH_2)_2OH$, $(CH_2)_2NH_2$, β or α-D-Glcp, $(CH_2)_2$O-D-Glcp, $(CH_2)_2$NHCSNH-D-Glcp

Acknowledgements Supported by DOD Initiative BC980020 DAMD17-99-1-9381 and NCI Pre-ICMIC P20 CA086354.

SETEREOSELECTIVE SYNTHESIS AND EVALUATION OF FLUORINATED VITAMIN B_6 β-D-GALACTOSIDES AS POTENTIALNOVEL SUBSTRATES FOR IN VIVO AND NON-INVASIVE DETECTION OF LACZ GENE EXPRESSION

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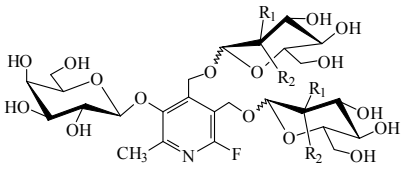
Gene therapy is generating increasing interest. However, a major issue is the success of targeting the gene to the tissue of interest, the distribution of the gene, its activity and longevity of action. The activity of most therapeutic genes is not directly detectable. A powerful tool is the incorporation of a tandem reporter gene, to reveal activity of genes of interest. While nuclear and optical imaging methods have been popularized, NMR has lagged behind. Historically, the most popular reporter gene was lacZ, which generates β-galactosidase (β-gal). Numerous biochemical assays are available to detect β-gal activity, but they have been limited to histology or *in vitro* assays. We recently demonstrated that introduction of a fluorine atom into the traditional biochemical substrate ortho-nitro-phenyl galactopyranoside (ONPG), could provide a novel enzyme activity sensor (*viz*. gene reporter) with minimal perturbation to a well-proven substrate [*ISMRM*, p71, 2002]. We have now developed a second-generation approach incorporating the ^{19}F NMR pH reporter (6-FPOL). We will present the design, synthesis and evaluation of two new fluorinated vitamin B_6 β-D-galactosides **G_1** and **G_2** as exciting substrates for *lacZ* gene expression using the ^{19}F chemical shift changes with the following characteristics: (a) the aglycone used was pH sensitive presenting the concept of gene activated local pH measurement; (b) the glycosylation at 4, 5 hydroxymethyl groups as functional parts to enhance the water solubility, ability to cross cell membranes as well as delivery effects.



G_1 R_1 = OH, R_2 = H β-D-Glucose
G_2 R_1 = H, R_2 = OH α-D-Mannose

Acknowledgements Supported by the DOD Breast Cancer Initiative and NCI Pre-ICMIC P20 CA86354.

A Designed Inhibitor of Pin1 PPIase Activity

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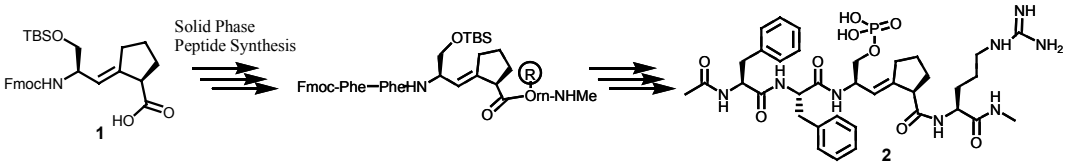
Department of Chemistry, Blacksburg, VA 24061-0212



Pin1 (protein interacting with NIMA #1) is a phosphorylation dependent peptidyl-prolyl isomerase (PPIase) discovered in 1996. It is suggested that Pin1 regulates mitosis via cis-trans isomerization of phosphoSer-Pro amide bonds in a variety of cell cycle proteins. The central role Pin1 plays in the cell cycle makes it an interesting target for inhibition, both for potential anti-cancer activity and for elucidation of the mechanism of mitosis. To understand the mechanism of Pin1 regulation in mitosis, we designed conformationally rigid (*Z*/*E*)-alkene phosphoSer-*cis*/*trans*-Pro mimics and the (*E*)-alkene mimic was incorporated into Pin1 substrate inhibitors Ac-Phe-Phe-pSer-Ψ[(*E*)CH=C]-Pro-Arg-NHMe for Pin1 inhibition. We herein describe the synthesis of dipeptide mimic FmocSer(OTBS)-Ψ[(*E*)CH=C]-ProOH **1,** synthesis of Pin1 substrate analogue Ac-Phe-Phe-pSer-Ψ[(*E*)CH=C]-Pro-Arg-NHMe **2** and the inhibition of Pin1 PPIase activity.

SYNTHESIS OF PHOTOCLEAVABLE PROTECTING GROUPS FOR PRIMARY ALCOHOLS WITH APPLICATIONS IN THE CONSTRUCTION OF DNA MICROARRAYS

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The 9-phenyl-thioxanthyl moiety (S-pixyl) is an effective protecting group (PG) for primary alcohols. It can be cleaved from the parent alcohol by photochemical methods in addition to acid catalyzed cleavage. Its regioselectivity allows specific protection of the 5'-hydroxyl group versus the 3'-hydroxyl group in deoxyribonucleosides. Further development of PGs of this type would be beneficial to the design and production of DNA chips. Several S-pixyl analogues have been synthesized to determine the effects of various substituents on the time of irradiation needed for deprotection and overall deprotection yield. This includes substitution on the aryl ring as well as the thioxanthyl backbone. The analogues will be initially tested with thymidine, and the most promising candidates will then be tested with the other nucleosides.

SENSITIZED PHOTOLYSIS OF 1-ACYL-7-NITROINDOLINES GREATLY IMPROVES THE EFFICIENCY FOR PHOTORELEASE OF THE ALKANOIC ACID

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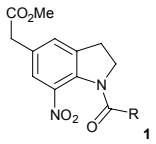
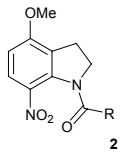
1-Acyl-7-nitroindolines (general structures **1** and **2**) are effective reagents for rapid photorelease of carboxylic acids, particularly the neuroexcitatory amino acid L-glutamate, within biological systems.[1] **1** and **2** have relative photolysis efficiencies of ~1:2.5, with the advantage for **2** mediated by combined extinction coefficient and quantum yield effects. Photocleavage involves a triplet state of the 1-acyl-7-nitroindoline[2] and to improve the efficiency of photorelease (in oxygenated conditions as required for application in biological systems), we constructed compounds in which the acylnitroindoline is linked to a triplet sensitizer (here a derivative of 4,4'-dimethoxybenzophenone). For the first conjugate, based on structure **1**, photolysis efficiency (i.e. extent of conversion in unit time) when irradiated at 300 nm (in oxygenated aqueous solution) was improved 15-fold. A comparable sensitized conjugate of **2** was ~6-fold more photosensitive than **2** alone. In both examples the acyl group is acetyl, i.e. the compounds release acetate upon photolysis. Overall, the sensitized version of **2** photolyzes at 300 nm with ~20-fold higher efficiency than the parent compound **1**.



1



2

1. Papageorgiou et al., *J. Am. Chem. Soc*. **121**, 6503-6504, 1999; Papageorgiou and Corrie, *Tetrahedron* **56**, 8197-8205, 2000; Canepari et al., *J. Physiol*. **533**, 765-772, 2001.
2. Morrison et al., *Photochem. Photobiol. Sci*. **1**, 960-969, 2002.

High Asymmetric Induction with β-Turn Derived Palladium Phosphine Complexes

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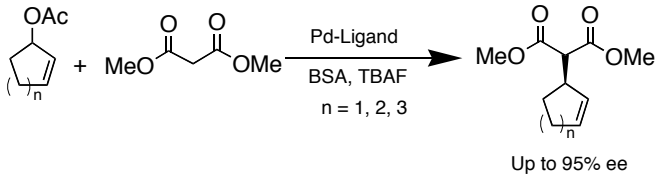
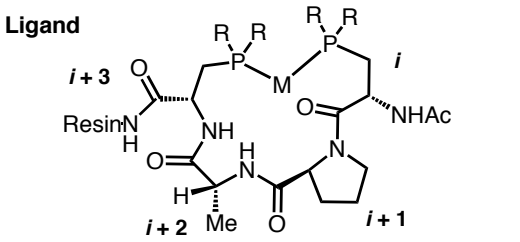
Department of Chemistry
Washington University
Saint Louis, Missouri 63130

The parallel synthesis of phosphine ligands requires the use of reactions that proceed in good yield and with high selectivity. Our group has been involved in the development of parallel methods for the discovery of asymmetric catalysts. One of the approaches taken is based on solid phase peptide synthesis. Through the use of parallel peptide synthesis a ligand that upon coordination to palladium provides high asymmetric induction in the addition of dimethylmalonate to cyclic allyl acetates has been developed.



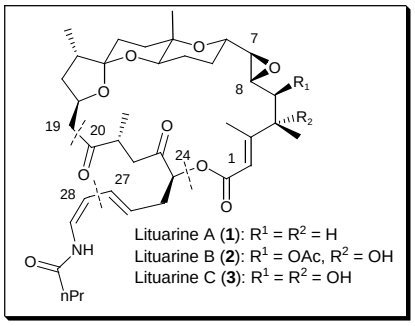


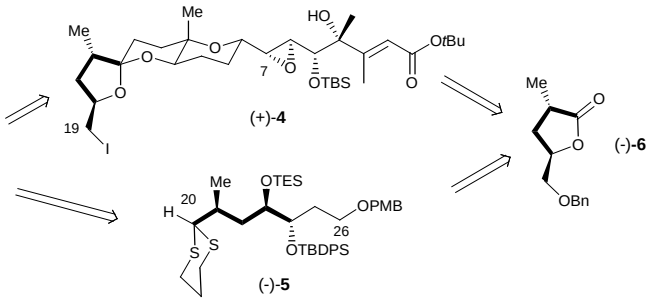
R = phenyl, 1-naphthyl, 2-naphthyl, 3,5-xylene, mesityl

ADVANCES IN THE ASYMMETRIC CONSTRUCTION OF ARCHITECTURALLY COMPLEX NATURAL PRODUCTS: THE LITUARINES

Amos B. Smith, III, Shawn P. Walsh, and Michael Frohn.
Department of Chemistry, University of Pennsylvania
Philadelphia, PA 19104-6323

The lituarines , B, and C comprise a small class of highly complex, bioactive natural products isolated from the sea pen *Lituaria australasae*. nitial screening revealed significant cytotoxicity C 1- nmol(B cells) , however, the low natural abundance has hindered further biological evaluation. ecently we initiated efforts to develop a convergent, stereocontrolled synthesis of these novel macrolides. ecent achievements include an efficient construction of ( )-**4** via sequential chemo- and regioselective oxidation of the precursor triene, in turn derived from our common tricyclic fragment[1]. Construction of (-)-**5** via common precursor (−)-**6** has also been achieved. summary of these results, as well as additional progress will be presented.





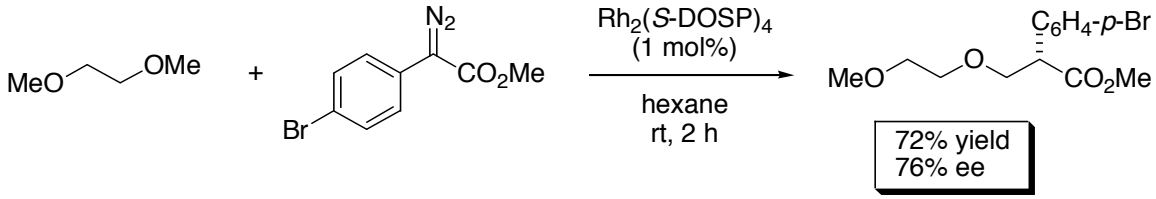
1 Smith, A.B.; Frohn, M.; *Org. Lett.* **2001**, *3(24)*, 3979-3982.

INFLUENCE OF A β-ALKOXY SUBSTITUENT ON THE C–H ACTIVATION CHEMISTRY OF ALKYL ETHERS: SYNTHESIS OF (*S*)-METHYL TROPINATE

Jaemoon Yang* and *Huw M. L. Davies*

Department of Chemistry, University at Buffalo, The State University of New York, Buffalo, New York 14260-3000

Rh_2(*S*-DOSP)$_4$ catalyzed intermolecular C–H activation of 1,2-dimethoxyethane gave a product resulting exclusively from methyl C-H insertion. The deactivating electronic effect of β-alkoxy substituents was thus studied. The C-H activation reaction of methyl *t*-butyl ether led to the concise synthesis of (*S*)-methyl tropinate and its aryl analogs.



Synthesis of *EE*, *EZ* and *ET* 1,3-Dienes via Pd-Catalyzed Chemospecific Reduction of p-Allyl Chemistry

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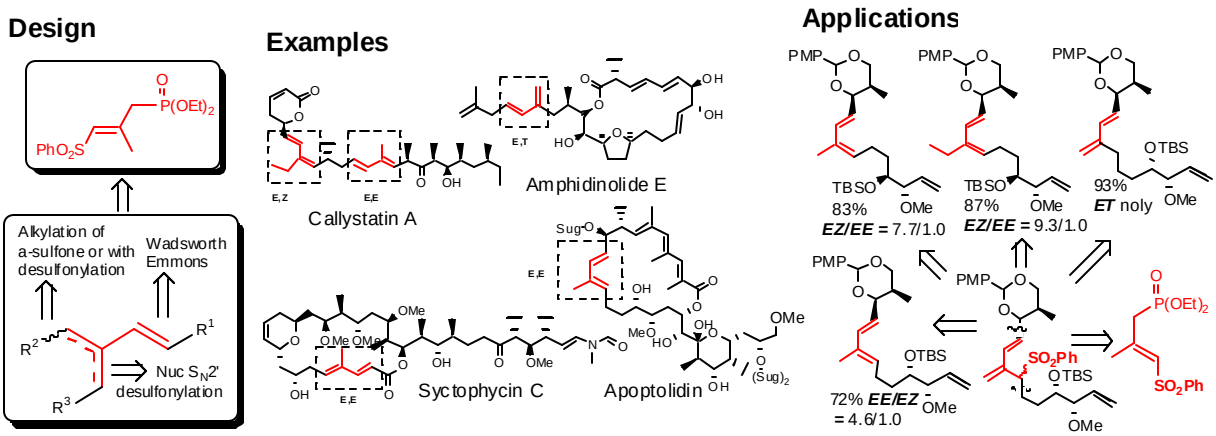
Department of Chemistry, Purdue University
Department of Chemistry, 560 Oval Drive, West Lafayette, IN 47906-2084

Trisubstituted 1,3-dienes are common components in natural products. Synthesis of the 1,3-dienes via a conjunctive strategy is described. Design and synthesis of conjunctive ?-allylphosphinoyl phenylsulfone reagent (GAPPS) will be discussed. Selective synthesis of 3-alkyl-1,3-***EE***, ***EZ*** and ***ET***-dienes using the GAPPS reagent features W. E. olefination, a-sulofonyl alkylation and ligand-directed metal-catalyzed nucleophilic desulfonylation. GAPPS was applied to synthesis of (1***E***,3***E***)-3-methyl-1,3-diene moiety of Apoptolidin.

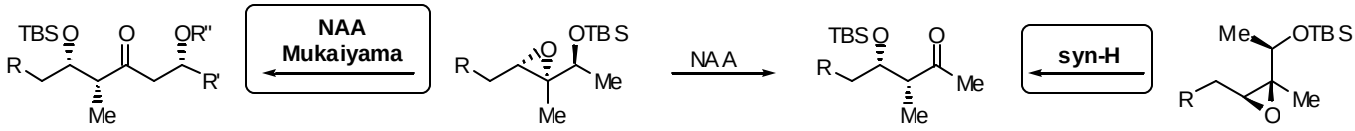


APPLICATIONS OF THE NON-ALDOL ALDOL REACTION

Alexandra van den Heuvel*, Michael E. Jung, Andrew G. Leach, K. N. Houk
University of California, Los Angeles, Department of Chemistry and Biochemistry,
405 Hilgard Ave, Los Angeles, CA 90095

The non-aldol aldol reaction permits the formation of aldol products without using the aldol condensation. It involves the rearrangement of optically active tertiary epoxide silyl ethers derived from 2-methyl allylic alcohols in the presence of a hindered base and a silyl triflate. The chirality is introduced *via* a Sharpless asymmetric epoxidation and no chiral auxiliary is necessary. When the substituent at the α position is a methyl group, one obtains selectively the *syn* methyl ketones or the β-silyloxy-silyl enol ethers. The resulting silyl enol ethers when treated with aldehydes and a catalytic amount of silyl triflate react *via* the Mukaiyama aldol condensation to yield a 5:2 ratio of diastereomeric β-silyloxy ketones.

During our study on the scope and limitations of the non-aldol aldol reaction of tertiary epoxide secondary silyl ethers, we have discovered an unprecedented rearrangement with retention of configuration at the tertiary epoxide carbon. We suggest a novel *syn* hydride migration to account for these results based on extensive theoretical calculations.



Monosaccharide Based Peptidomimetics Of Somatostatin (SRIF): Incorporation Of Bioisosteres Of Indole At C1 Of β-D-Glucosides And Position Eight Of SRIF.

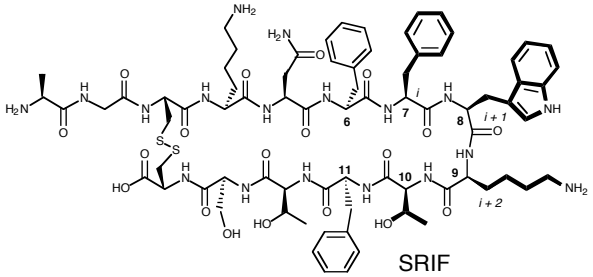
Angie R. Angeles,[1] Guoxia Han,[1] Gary Chicci,[2] Marc Kurtz,[2] Elizabeth Birzin,[2] Susan Rohrer,[2] Dennis Underwood,[3] Amos B. Smith, III[1] and Ralph F. Hirschmann.[1]

[1]Department of Chemistry, University of Pennsylvania, Philadelphia, PA 19104

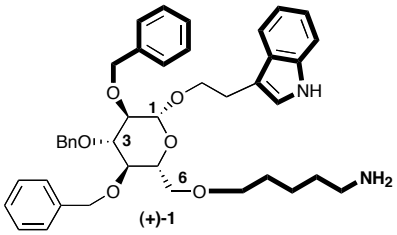
[2] Merck Research Laboratories, Rahway, NJ 07065

[3] Infinity Pharmaceuticals, Cambridge, MA 02139

Monosaccharide based peptidomimetics typified by **(+)-1** have been shown by our group to mimic the β-turn of SRIF. The indole containing sidechains of both compounds are known to play a critical role in the binding of the SRIF receptors. The methylene linker in SRIF was replaced by an ethylene linker in **(+)-1** to avoid gramine fragmentation. Using congeners not subject to fragmentation allowed us to explore the optimal chain length of the indole substituent and the promiscuity of the tryptophan binding pocket of the SRIF receptors. Modeling studies and biological assay data will be described.



SRIF



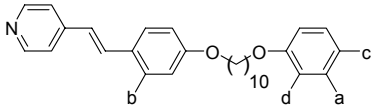
(+)-1

DESIGN, SYNTHESIS, AND CHARACTERIZATION OF NON-CENTROSYMMETRIC HYDROGEN-BONDED LIQUID-CRYSTALLINE POLYMERS

Jeremy R. Wolf, Tongfeng Zhao, Christopher Landorf, and Daniel J. Dyer
Southern Illinois University at Carbondale
Department of Chemistry, Carbondale, IL 62901-4409

Numerous emerging technologies require materials that possess one of three unique properties: nonlinear optics (NLO), pyroelectricity, and piezoelectricity. Historically, these materials consisted of inorganic crystals; however, recently organic films are being explored for these applications. In order for organic films to exhibit NLO behavior, pyroelectricity or piezoelectricity, the films must be aligned and possess polar order. Liquid crystals are molecules that possess a high degree of orientational order thus if they can be aligned in a polar fashion, the material will possess a large bulk polarization and may exhibit these useful properties.

Our design strategy and the synthesis of non-centrosymmetric hydrogen-bonded liquid-crystalline polymers 1-5 in Figure 1 will be reported in this presentation. The liquid-crystalline properties of these non-covalent polymers will be described.



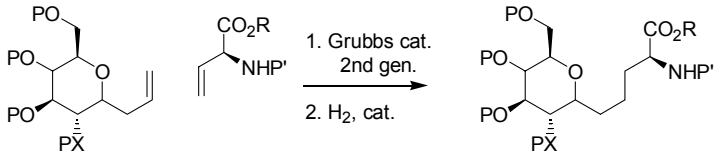
1: a=CH_3, b=H, c=CO_2H, d=H
2. a=H, b=OCH_3, c=CO_2H, d=H
3. a=CH_3, b=OCH_3, c=CO_2H, d=H
4. a=H, b=H, c=OH, d=H
5. a=CH_3, b=H, c=OH, d=CH_3

Figure 1

SYNTHESIS OF C-GLYCOSYL ASPARAGINES AND C-GLYCOSYL SERINES BY OLEFIN CROSS-METATHESIS

Ernest G. Nolen, Adam Kurish
Colgate University, Department of Chemistry
Hamilton, NY 13346

Carbon-linked glycopeptides provide increased stability toward acidic, basic, and enzymatic degradation, thus stimulating interest in this class of molecules as possible therapeutics. We report the preparation of a variety of *C*-linked glycosyl asparagines, in both the α- and β-anomeric forms, as well as α-*C*-linked N-acetylglycosyl asparagines. The syntheses utilize the second generation Grubbs catalyst for the cross metathesis of *C*-allyl glycosides and L-vinylglycines. The extension of this work to generate mimics of glycosyl serines will also be reported.



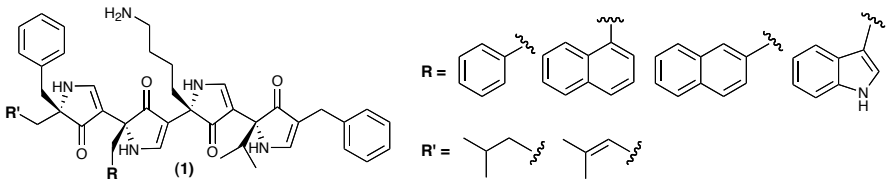
P = Ac or Bn
X = O or NH

P' = Cbz, Boc, or Fmoc
R = Me, Bn, TMSE

Efforts Toward the Design and Synthesis of Biologically Active Pyrrolinone-Based β-Turn Peptidomimetics

Amos B. Smith, III, Adam K. Charnley, Andrew B. Benowitz, Meinrad Brenner, Osamu Kikuchi, Eugen F. Mesaros, Paul A. Sprengeler, Wenyong Wang and Ralph Hirschmann
Department of Chemistry, University of Pennsylvania, Philadelphia, PA 19104

Past work in our group has established that homochiral 3,5-linked oligopyrrolinones successfully mimic the extended β-strand/β-sheet conformation of peptides and proteins, while heterochiral (i.e., alternating D,L) oligopyrrolinones exist in a β-turn like conformation both in solution and in the solid-state. Given our longstanding interest in nonpeptide peptidomimetics of SRIF, and with the goal of extending the utility of the pyrrolinone motif as a privileged nonpeptide scaffold, we have recently designed several tetrapyrrolinone SRIF mimetics (**1**). Progress toward the synthesis of the pyrrolinone-based β-turn mimetics will be presented.



[1] a) Smith, A. B., III; Guzman, M. C.; Sprengeler, P. A.; Keenan, T. P.; Holcomb, R. C.; Wood, J. L.; Carroll, P. J.; Hirschmann, R. *J. Am. Chem. Soc.* **1994**, *116*, 9947-9962. b) Smith, A. B., III; Wang, W.; Sprengeler, P. A.; Hirschmann, R. *J. Am. Chem. Soc.* **2000**, *122*, 11037-11038.

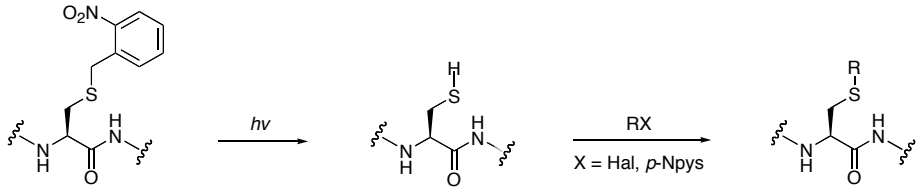
Efforts Toward the High-Throughput Alkylation and Screening of CD4 Miniprotein Mimetics: Development of Leads for Rational Small Molecule Design

Amos B. Smith, III,[1] Irwin M. Chaiken,[2] Jason M. Cox,[1] Uma V. Manjappara,[2] Sergey N. Savinov,[1] John A. Zuawski[2]

[1]Department of Chemistry, University of Pennsylvania, Philadelphia, PA 19104

[2]Department of Medicine, University of Pennsylvania, Philadelphia, PA 19104

We recently initiated a program targeting the chemical modification of miniprotein (scorpion toxin) scaffolds in an effort to enhance the potency of HIV entry inhibitors. An orthogonal deprotection-S-alkylation protocol using cysteine as a model system was developed[1] and is being applied to the scyllatoxin (ST) miniprotein scaffold [$_{20}$AGSC$_{23}$]ST. More recently we devised an on-bead ELISA using the scyllatoxin scaffold [$_{20}$AGSF$_{23}$]ST and demonstrated that this construct competes with soluble CD4 in the binding of gp120. With the development of the orthogonal deprotection-S-alkylation protocol and the feasibility of an on-bead ELISA, we are poised to begin the high-throughput alkylation and screening of miniprotein mimetics.

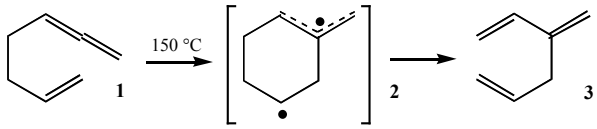


[1]Smith, A. B., III; Savinov, S. N.; Manjappara, U. V.; Chaiken, I. M. *Org. Lett.* **2002**, *4*, 4041-4044.

Investigations of the Cope Rearrangement of 1,2,6-Heptatriene: Results from Direct Dynamics Trajectories and Sulfur Dioxide Trapping Studies

Stefan L. Debbert and Barry K. Carpenter
Department of Chemistry and Chemical Biology, Cornell University
Ithaca, NY 14853-1301

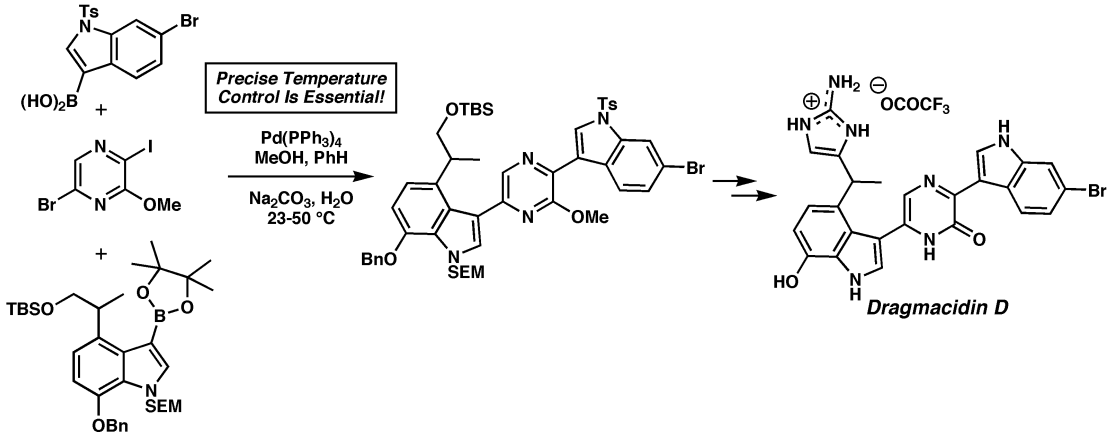
Trapping studies by Roth *et al.* employing oxygen and sulfur dioxide have led to the proposal that the nominal [3,3]-sigmatropic rearrangement of 1,2,6-heptatriene ("eneallene," **1**) to 3-methylene-1,5-hexadiene (**3**) occurs both concertedly and via biradical intermediate (**2**). However, a concerted transition structure leading directly from **1** to **3** could not be located by Hrovat and Borden at either the the (U)B3LYP or the CASSCF(8,8) levels of theory. Results from our direct-dynamics trajectories, run using both *ab initio* (CASSCF) and semiempirical (parametrized AM1) methods, suggest that a bifurcation can occur at the transition state for the formation of the biradical, allowing some trajectories to bypass the potential energy well for **2**. The calculations also suggest that a resonance between the C(3)-H out-of-plane bend and the C(4)-C(5) stretch may play a dynamically important role for those trajectories that do enter the biradical well. To test this second hypothesis, sulfur dioxide trapping experiments on the Cope rearrangement of 1,2,6-heptatriene-3-*d* are currently being carried out; the deuterium substitution is expected to mitigate the aforementioned resonance, so fewer "untrappable" trajectories would be expected for the labeled compound than for the unlabeled eneallene.



THE FIRST TOTAL SYNTHESIS OF DRAGMACIDIN D AND PROSPECTS FOR THE PREPARATION OF OTHER DRAGMACIDIN ALKALOIDS

*Neil K. Garg, Richmond Sarpong, Brian M. Stoltz**
California Institute of Technology
Division of Chemistry and Chemical Engineering, Pasadena, CA 91125

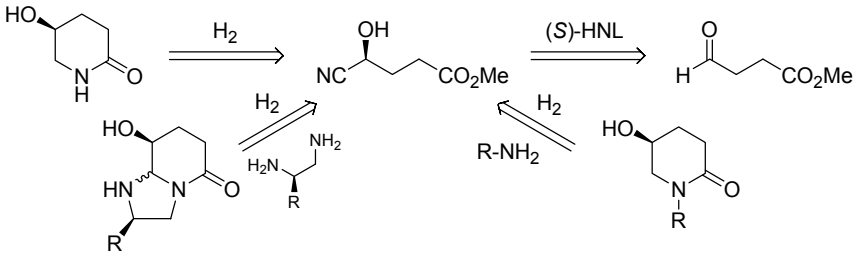
The first total synthesis of the biologically active bis-indole alkaloid dragmacidin D has been achieved. Thermal and electronic modulation dictates a series of palladium-catalyzed Suzuki cross-coupling reactions that furnishes the core structure of the complex guanidine- and aminoimidazole-containing dragmacidins. Following this key sequence, a succession of meticulously controlled final events led to the completion of dragmacidin D. We are currently applying this approach toward the total synthesis of dragmacidins E and F.



NOVEL ROUTES TO 5-HYDROXYPIPERIDONE-DERIVED BUILDING BLOCKS

Richard H. Blaauw,[1] Mandy K. S. Vink,[2] Hans E. Schoemaker,[3] Floris P. J. T. Rutjes[4]
[1] Chiralix B.V., [2] University of Amsterdam, [3] DSM Research, [4] University of Nijmegen
[1] P.O. Box 31070, 6503 CB Nijmegen, The Netherlands, [2] IMC, Nieuwe Achtergracht 129, 1018 WS Amsterdam, The Netherlands, [3] P.O. Box 18, 6160 MD Geleen, The Netherlands, [4] NSRIM, Toernooiveld 1, 6525 ED Nijmegen, The Netherlands

5-Hydroxypiperidone is a versatile building block for the preparation of potentially biologically active compounds. We detail an enantioselective biocatalytic approach towards its synthesis using (*S*)-hydroxynitrile lyase (HNL)-mediated cyanohydrin formation, followed by hydrogenation.



By adjusting the conditions of the latter step, we were able to obtain 5-hydroxypiperidone-derived (bicyclic) *N*,*N*-acetals *via* an unprecedented reductive amination of the nitrile group, as well as form *N*-alkylated 5-hydroxypiperidones in a single step from the same cyanohydrin intermediate.

SYTHESIS, SELF-ASSEMBLY, AND ELECTRO-OPTIC SWITCHING OF ONE-DIMENSIONAL NANOSTRUCTURES

Mark L. Bushey and Colin Nuckolls
Columbia University, Department of Chemistry
New York City, NY 10027

Stacked disk shaped aromatics that are surrounded by alkyl groups are the prototype of self-assembled, molecular scale wiring. Our efforts are in creating discotic liquid crystals that are held together by a combination of hydrogen bonds and π-stacking. This paper describes the first studies on a new class of crowded aromatics. Studies including the self-assembly on graphite surfaces, electro-optic switching on ITO coated glass plates, and effects of side-chains on mesophasic behavior. The switching times suggest a ferroelectric switching process in response to the applied electric field.

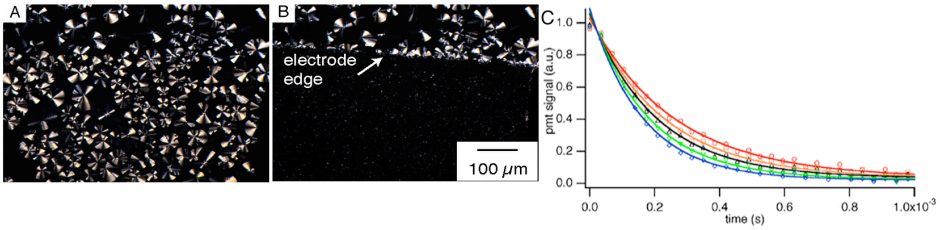
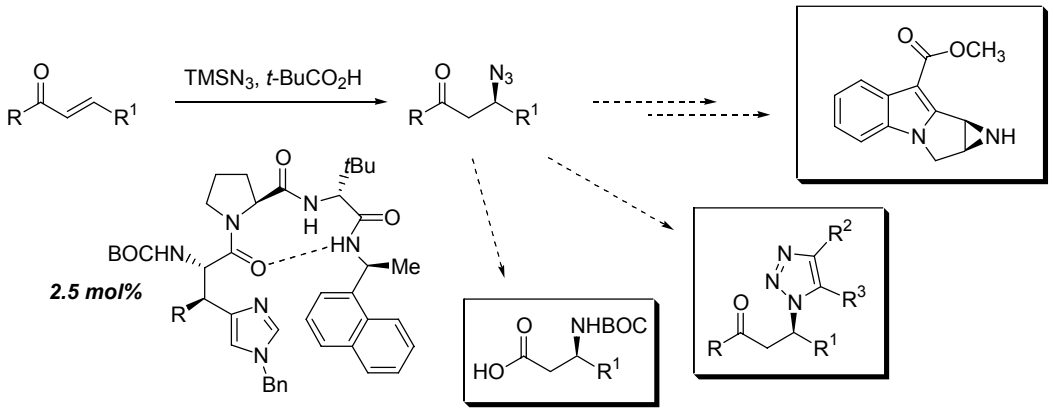


Figure 1: (A) Discotic liquid crystal at 150°C with a 0V potential on ITO; (B) Discotic liquid crystal at 150°C with a 100V potential on ITO; (C) The optical response times at 150°C at increasing electric field potentials: 64V (red) to 104V (blue).

Asymmetric Conjugate Addition of Azide Catalyzed by Short Folded Peptides and Applications in Organic Synthesis

David J. Guerin, Thomas E. Horstmann, Scott J. Miller
Boston College
Department of Chemistry, Merkert Chemistry Center, Chestnut Hill, MA 02467

The development of a peptide-catalyzed, enantioselective conjugate addition of azide is described. A tetrapeptide was developed that affords optically enriched β-azido imide products in high enantioselectivity (up to 92% ee) under mild reaction conditions using azidotrimethylsilane as the azide source. Using this methodology, efficient protocols to access optically enriched β-amino acid synthons, triazoles, and mitomycin-like targets were developed.

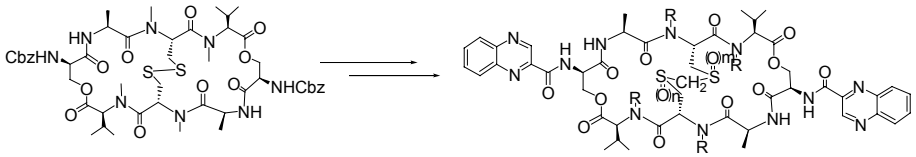


SYNTHESIS AND BIOLOGICAL ACTIVITY OF NEW QUINOXALINE ANTIBIOTICS OF TRIOSTIN A ANALOGUE

YunBong Kim, SungHo Kim, YongHae Kim

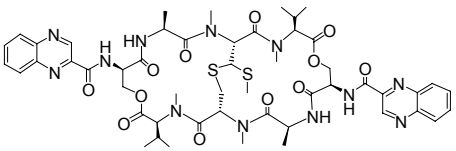
Center for Molecular Design and Synthesis, School of Molecular Science(BK-21), Department of Chemistry, Korea Advanced Institute of Science and Technology, 305-701, Taejeon, Republic of Korea

New quinoxaline antibiotics(**1**) were prepared as an triostin A analogue by modification on sulfur cross-linkage and their cytotoxicities against human cancer cell have been tested. Biological activities of 1, echinomycin, and adriamycin are compared. Some of **1** induce apoptosis of HT-29.



1

R=Alkyl or H,
m, n = 1 or 2



Echinomycin

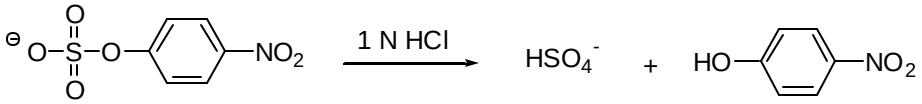
MECHANISTIC STUDIES OF SULFATE HYDROLYSIS

Benjamin T. Burlingham,[1] Lisa M. Pratt,[2] Ernest R. Davidson,[3] Vernon J. Shiner, Jr.,[4] Jon Fong,[2] Theodore S. Widlanski[4]

[1]Mount Union College; [2]Indiana University, Bloomington; [3]University of Washington; [4]Indiana University, Bloomington

[1]Department of Chemistry, 1972 Clark Ave., Alliance, OH 44601; [2]Department of Geology, Bloomington, IN, 47405; [3]Department of Chemistry, Seattle, WA 98195-1700; [4]Department of Chemistry, Bloomington, IN, 47405

A stable isotope mass spectrometry method for the determination of S-34 kinetic isotope effects in sulfate monoester hydrolysis is described. Hydrolysis of aryl sulfates under acidic conditions give large, normal S-34 kinetic isotope effect data. These data, along with inverse solvent isotope effects, are inconsistent with the currently proposed concerted mechanism involving simultaneous cleavage and proton transfer in the transition state. This method for the acquisition of S-34 kinetic isotope effects may also prove useful for studying the mechanism of other sulfuryl group transfers, including sulfatase and sulfotransferase catalyzed reactions.



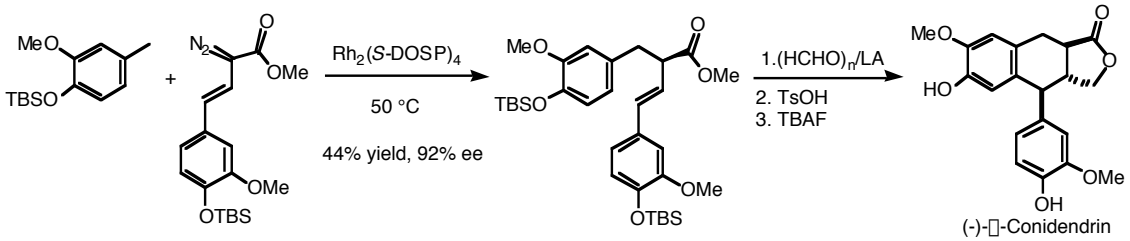
^{34}S KIE = 1.0154 +/- 0.0002; solvent k_H/k_D = 0.51 +/- 0.02

INTERMOLECULAR C–H ACTIVATION AT BENZYLIC METHYL POSITIONS: SYNTHESIS OF (+)-IMPERANENE AND (−)-Δ-CONIDENDRIN

Qihui Jin *and Huw M. L. Davies**

Department of Chemistry, University at Buffalo, The State University of New York, Buffalo, New York 14260-3000

Rh_2(*S*-DOSP)$_4$ catalyzed intermolecular C–H activation has been shown to be much more favorable at methylene positions than methyl positions. Here we described a benzylic methyl C-H insertion catalyzed by Rh_2(*S*-DOSP)$_4$. The application of this methodology has also been displayed by concise syntheses of two natural products: (+)-imperanene and (−)-Δ-conidendrin.

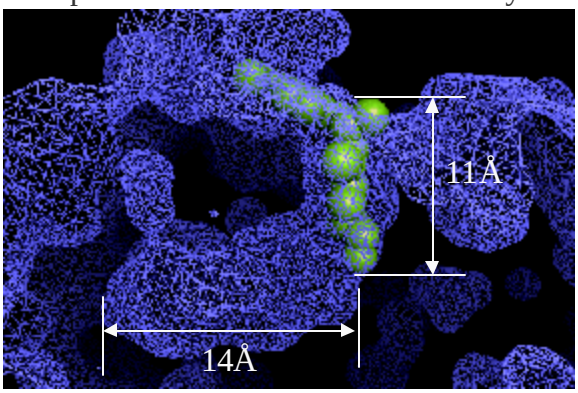


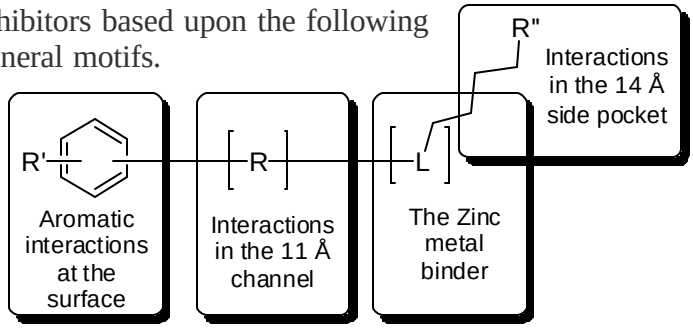
Inhibitors for Histone deacetylase

Joakim Löfstedt and Paul Helquist
University of Notre Dame, Department of Chemistry & Biochemistry
251 Nieuwland Science Hall, Notre Dame, IN 46556-5670 USA

This research project is focused on the discovery and development of small molecule inhibitors of the enzyme histone deacetylase (HDAC). The target enzymes control histone deacetylation, and by inhibiting the enzyme acetyl groups from histone proteins are not removed. HDAC inhibitors cause the accumulation of acetylated histones on DNA and counteract pathological conditions where histone acetylation levels are too low. Improper regulation of histone acetylation is associated with the development of many different types of cancer, including leukemias, lymphomas, colorectal, gastric, prostate, pancreatic, and breast. HDAC activities have been found to be defective in cancer.

SAHA, (suberoylanilide hydroxamic acid - $PhNHCO(CH_2)_6CONHOH$) is an especially well known example of a HDAC inhibitor. The enzyme active site consists of an 11 Å channel with a Zinc atom at the bottom and a perpendicular 14 Å side pocket. Our goal is to develop non-hydroxamic acid HDAC inhibitors based upon the following general motifs.

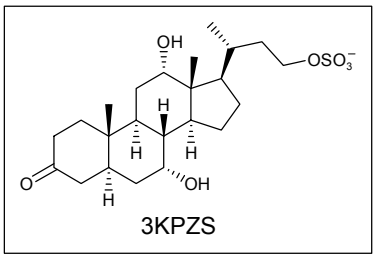




SYNTHESIS OF 3-KETO PETROMYZONOL SULFATE: A POTENT SEA LAMPREY PHEROMONE

Andrea M. Pellerito and Robert E. Maleczka, Jr.
Department of Chemistry
Michigan State University
East Lansing, MI 48823

3-Keto petromyzonol sulfate (3KPZS) has been found to be a potent pheromone secreted by the male sea lamprey. The presence of these non-indigenous, predatory fish in the upper Great Lakes has had a severe impact on the Great Lakes fishery.



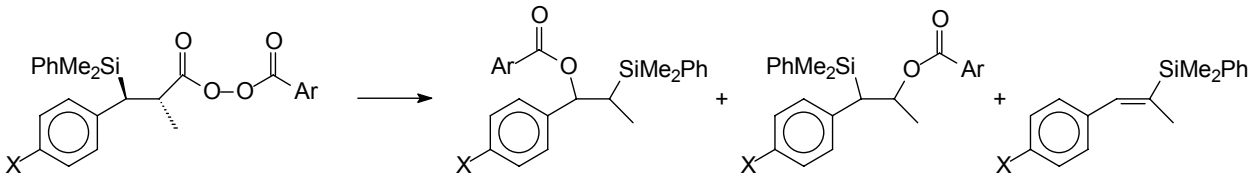
3KPZS

Although several unnatural lampricides have been found to be effective at controlling sea lamprey populations, their use has brought about public apprehension and their costs have been escalating over the past years. Consequently, we, in collaboration with Professor Weiming Li (MSU Department of Fisheries and Wildlife), have been exploring alternative methods to traditional lampricides, and believe synthetic pheromones are among the most promising methods for future lamprey control. Thus we have set out to develop an economical, environmentally friendly, large-scale synthesis of 3KPZS and its derivatives. A key feature of our synthesis is IBX oxidation of an alcohol to regioselectively afford a trisubstituted enone.

Decomposition of $-Silyl Diacyl Peroxides: A Mild and Stereoselective Synthesis of $-Silyl Esters

Douglas S. Masterson and Ned A. Porter
Vanderbilt University, Department of Chemistry
Box 1822 Station B, Nashville, TN 37235

Previous studies in our laboratories led to interest in $-silyl diacyl peroxides such as **1**. Attempted preparation of **1** using commonly employed synthetic methods failed to give the desired diacyl peroxide. Instead of the desired **1**, an inseparable mixture of **2** & **3** were isolated in 50% yield along with substantial quantities of olefin **4**. It is noteworthy that compounds **2** & **3** were obtained as an 85:15 regioisomeric mixture with high levels of diastereoselectivity. Mechanistic studies show that **1** is an initial intermediate which undergoes mild decomposition at low temperature via an ionic mechanism. Interestingly, the ratio of **2**/**3** is dependant on the para substituent X with an excellent correlation to F+. Further, more detailed, mechanistic studies will be presented.



1 (X=H) **2** **3** **4**

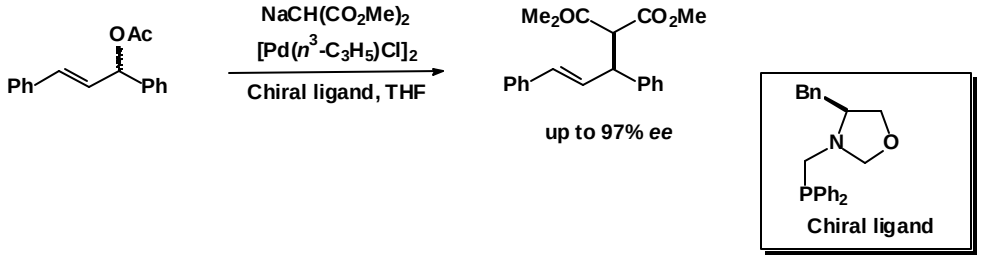
New Simple Chiral Phosphine Oxazolidine Ligand: Easy Synthesis and Application in the Palladium-Catalyzed Asymmetric Allylic Alkylation

Antonio L. Braga,* Jasquer A. Sehnem, Diogo S. Lüdtke, Rodrigo M. Rubim, Claudio C. Silveira and Miriam I. Marchi

Departamento de Química – Universidade Federal de Santa Maria – 97105-900 Santa Maria – RS – Brazil

Palladium – catalyzed allylic substitution reactions plays a central role in organic syntesis. Various chiral ligands have been applied to these substitution reactions providing high enantioselectivities.

A new P, N oxazolidine-containing ligand has been prepared in a straightforward, one-pot synthetic route, from the inexpensive and easily available L-Phenylalaninol. Furthermore this compound has been tested in the palladium-catalyzed allylic substitution reaction, furnishing the alkylated product in 98 % yield and up to 97% *ee*.

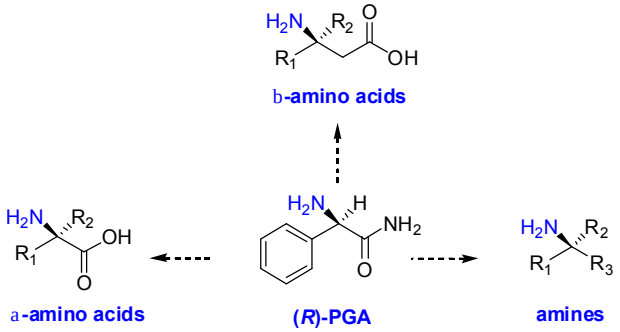


Details of the synthesis of this new aminoalcohol derived ligands as well as application in the asymmetric allylic alkylation will be presented.

ENANTIOPURE AMINES AND AMINO ACIDS BY CHIRALITY TRANSFER USING (*R*)-PHENYLGLYCINE AMIDE

Q.B. Broxterman[1], B. de Lange[1], B. Kaptein[1], M. van der Sluis[2], P.G.H. Uiterweerd[2], R.M. Kellogg[2]
[1]DSM Life Sciences - Advanced Synthesis & Catalysis
PO Box 18, 6160 MD Geleen, The Netherlands
[2]Syncom B.V.
Kadijk 3, 9747 AT Groningen, The Netherlands

The application of DSM proprietary products, like (*R*)-phenylglycine amide ((*R*)-PGA) as chiral amine donor source in the synthesis of enantiopure amino acids and other amino-functionalized compounds is presented.

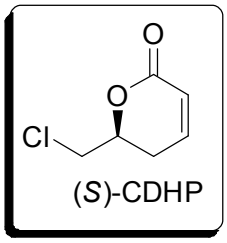


Key steps in this Chirality Transfer approach are: a) imine formation of (*R*)-PGA with for example ketones or aldehydes; b) diastereoselective reaction: addition of HCN, H_2 or organometal reagents to the imine double bond ("Chirality Transfer") and c) sacrificial removal of the chiral auxiliary. Several examples of highly diastereoselective additions followed by efficient conversions to enantiopure amines and amino acids, based on this technology, are shown on the poster.

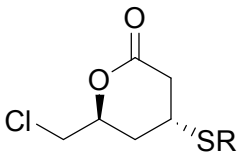
CHIRAL C_6 BUILDING BLOCKS BY DERIVATISATION OF AN ENANTIOPURE a,b-UNSATURATED d-LACTONE AVAILABLE ON KG-SCALE

Q. B. Broxterman, B. Dassen, D. Mink, M. Wolberg
DSM Life Sciences - Advanced Synthesis & Catalysis
PO Box 18, 6160 MD Geleen, NL

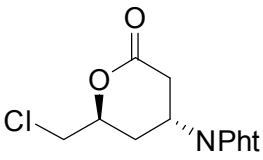
The enantiopure unsaturated lactone (*S*)-CDHP [(*S*)-6-chloromethyl-5,6-dihydropyran-2-one] is a highly functionalised intermediate available on kg-scale at DSM's "early pharma development" services unit RESCOM® (Will.Tweel-van-den@dsm.com). Its outstanding synthetic applicability originates from the presence of a conjugated double bond that allows for a variety of highly diastereoselective transformations due to the stereoelectronic effect exerted by the ring oxygen. Furthermore, the carbon chain is terminated with two functional groups of distinguishable reactivity and the chlorohydrine subunit can be considered as a masked epoxide. Some derivatisations with a focus on diastereoselective hetero-conjugate additions are presented. The products are valuable building blocks which are useful for the preparation of, e. g., deoxy-/aminosugars, hydroxylated N-heterocycles, and ß-amino acids.



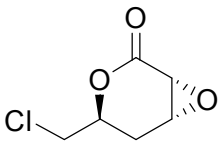
(*S*)-CDHP



R = acetyl, benzoyl



Pht = phthaloyl



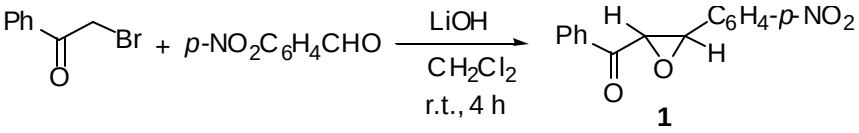
Synthesis of Oxiranylketones by Chalcogenide-Catalyzed Epoxidation Reactions of β-Bromoketones with Aldehydes

Shin-ichi Watanabe, Shinsuke Asaka, Tadashi Kataoka

Gifu Pharmaceutical University

6-1 Mitahora-higashi 5-chome, Gifu 502-8585, Japan

The asymmetric epoxidation reaction is generally regarded as one of the most important synthetic transformations and many strategies have been devised to catalyze this reaction. It is well known that chiral–sulfide catalyzed asymmetric epoxidation can be achieved by the reactions of chiral unstabilized sulfonium ylides with aldehydes. However, there is no example of the synthesis of oxiranylketones using stabilized sulfonium ylides. Therefore, we investigated the reactions of β-bromoketones with aldehydes catalyzed by chalcogenides. Enantioselectivities of epoxidation with chiral chalcogenides were also examined.



1

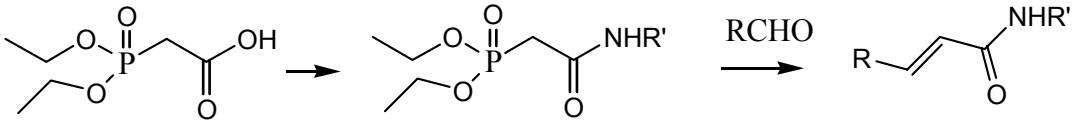
entry	Me_2S	**1**
1	———	7%
2	50 mol%	95%

EXPLORING NOVEL CLASS OF SOLUBLE GUANYLATE CYCLASE(sGC) ACTIVATORs---A RAPID SYNTHETIC APPROACH

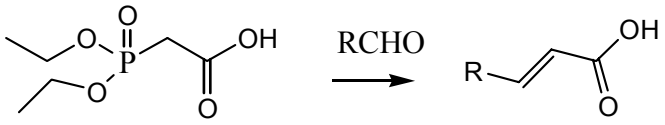
Zhiren Xia, Henry Zhang, Masaki Nakane, Teodozyj Kolasa, Jurgen Dinges.
Abbott Laboratories, Chicago, IL 60064-3500

The activation of soluble Guanylate Cyclase (sGC) will increase the conversion of guanosine 5'-triphosphate (GTP) to cyclic guanosine 3', 5'-monophosphate (cGMP), which ultimately results in penile erection. In the efforts to explore a new class of sGC activators, challenges arise for the quick establishment of SAR. It was not fast enough by using Classic Wittig reaction via ethyl [diethoxy-phosphoryl] acetic acetate for us to synthesize compound library. We then adapted two improved approaches in order to modify two different sites.

To fix amide and put different variety of aryl groups R, We used Approach I.



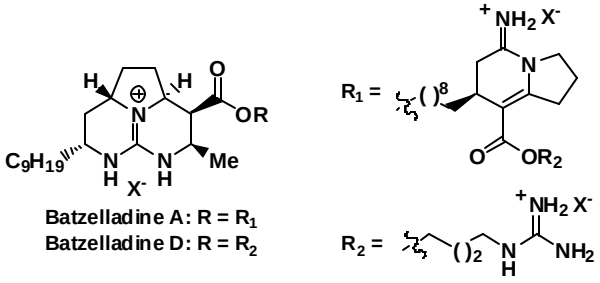
To fix the aryl group R and change the amide, we used Approach II.



A Novel Stereoselective Approach to the Polycyclic Guanidine Alkaloids Batzelladine A and D

John. E. Robinson, Bérangère Bazin, Jun Qin, P. Andrew Evans
Indiana University
Department of Chemistry, Bloomington, IN 47405

Batzelladines A-I are members of the polycyclic guanidine family of alkaloids isolated from Caribbean sponges of the genus *Batzella*. Batzelladines A and B have attracted significant attention as they exhibit micro-molar inhibition of the (HIV) gp-120 envelope protein that bind the human CD4 receptor, leading to the progressive decline of viable $CD4^+$ cells. The development of a novel stereoselective strategy for the synthesis of the polycyclic core of the batzelladines will be presented.

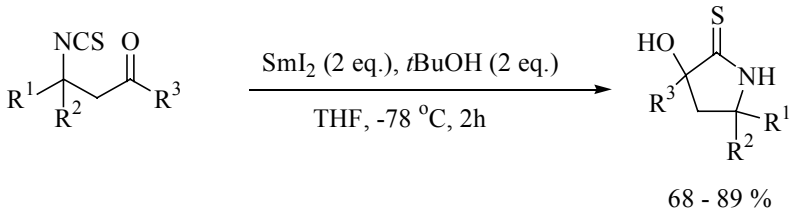


SYNTHESIS OF α-HYDROXYTHIOLACTAMS BY SAMARIUM(II) IODIDE MEDIATED CYCLIZATION OF β-KETO ISOTHIOCYANATES

Min Seok Cho, Yong Hae Kim

Center for Molecular Design and Synthesis, School of Molecular Science(BK-21), Department of Chemistry, Korea Advanced Institute of Science and Technology, 305-701, Taejon, Republic of Korea

Synthesis of thiolactams is mainly dependent on conversion of corresponding lactams. We have discovered that cyclization of β-keto isothiocyanates mediated by samarium(II) iodide provides the α-hydroxythiolactams in good yields under mild conditions. This cyclization gives high diastereoselectivities for acyclic substrates and stereospecificity for the chiral cyclic substrates.



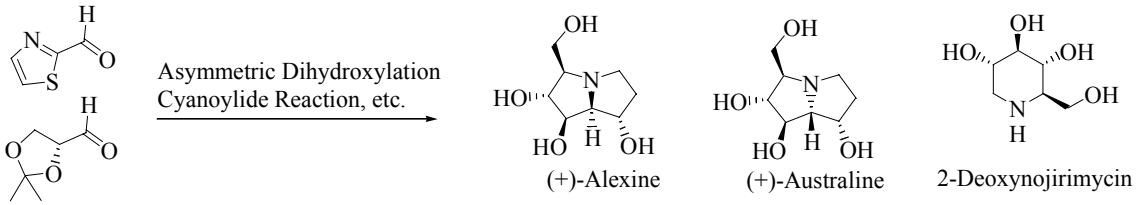
68 - 89 %

STEREOSELECTIVE SYNTHESIS OF POLY-HYDROXYLATED ALKALOIDS

Doo-Young Jung, Yong Hae Kim

Center for Molecular Design and Synthesis, School of Molecular Science(BK-21), Department of Chemistry, Korea Advanced Institute of Science and Technology, 305-701, Taejon, Republic of Korea

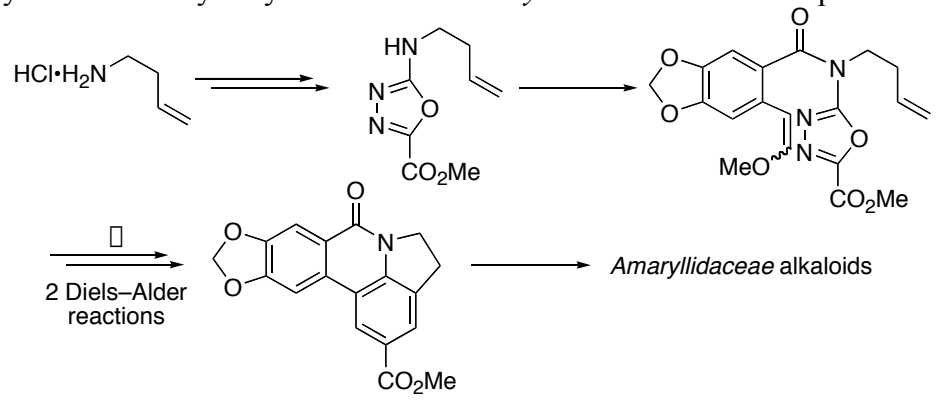
Poly-hydroxylated alkaloids have drawn much interest due to their potential biological activities and synthetic challenges imposed by their complex stereochemistry. Employing Sharpless asymmetric dihydroxylation and Wasserman's cyanoylide method as the key steps to construct molecular skeletons, we achieved concise and convergent synthesis of various poly-hydroxylated alkaloids from simple masked aldehyde equivalent.



EXPLORATIONS OF INTRAMOLECULAR DIELS–ALDER REACTIONS OF 2-AMINO-1,3,4-OXADIAZOLES: TOTAL SYNTHESIS OF ANHYDROLYCORINONE

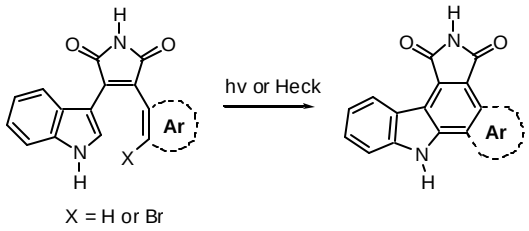
Scott E. Wolkenberg and Dale L. Boger
Department of Chemistry and The Skaggs Institute for Chemical Biology
The Scripps Research Institute
10550 N. Torrey Pines Road, La Jolla, California, 92037

In the course of studies on the cycloaddition reactivity of electron-deficient 2-amino-1,3,4-oxadiazoles, it was observed that tethered alkynyl or alkyne equivalent dienophiles generate high yields of furan products resulting from a single cycloaddition followed by elimination of N_2. The furan products, themselves reactive towards intramolecular cycloadditions, offered the potential to synthesize fused carbocyclic aromatic products in an oxadiazole → furan → benzene strategy. Application of this strategy to the synthesis of anhydrolycorinone and *Amaryllidaceae* alkaloids is presented.



SYNTHESIS AND BIOLOGICAL ACTIVITY OF ARYL- AND HETEROARYL[A]PYRROLO[3,4-C]CARBAZOLES

Concha Sanchez-Martinez,* Margaret M. Faul,* John L. Grutsch, Chuan Shih, Kevin A. Sullivan, Jeremy T. Cooper, and Stanley P. Kolis
Eli Lilly and Company, Indianapolis, IN 46285



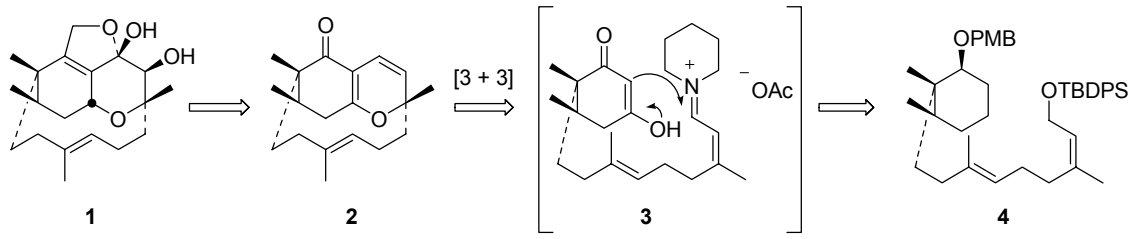
X = H or Br

Syntheses of aryl- and hetero[*a*]pyrrolo[3,4-*c*]carbazoles by photochemical oxidation and Heck cyclization are described. Photochemical oxidation of 2-naphthyl[*a*]pyrrolo[3,4-*c*]carbazoles affords two different carbazole regioisomers depending on the reaction conditions. The regiochemistry of the cyclization can be controlled using the Heck reaction.

STUDIES DIRECTED TOWARDS A TOTAL SYNTHESIS OF PHOMACTIN A

Kevin P. Cole and Richard P. Hsung
Department of Chemistry, The University of Minnesota
Minneapolis, MN 55455-0431

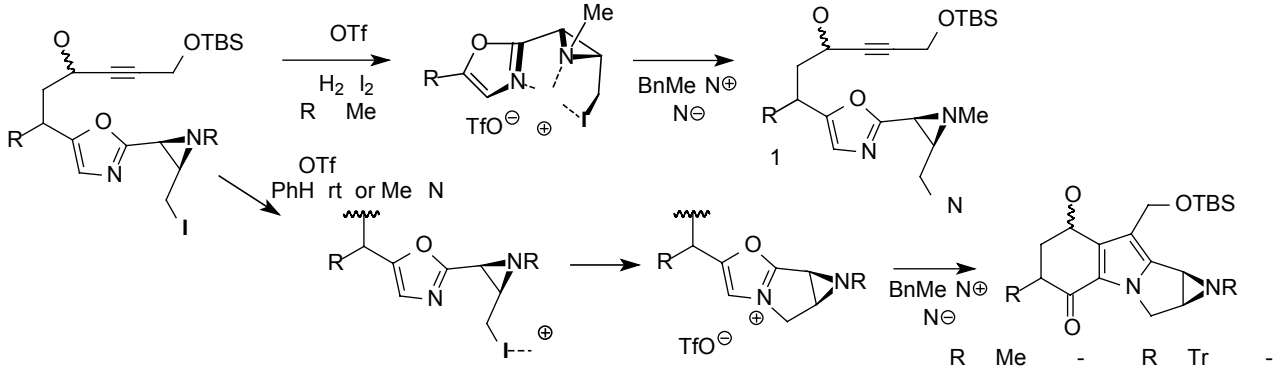
Phomactin A **(1)** was isolated in 1991 by Sugano *et. al.* and is one of a number of diterpene phomactins that, as a class, show biological activity as platelet activating antagonists. The unique architecture of the phomactin core has attracted a number of synthetic efforts that have, as of now, cumulated in two total syntheses of phomactin A. We feel that the advanced intermediate **2** could be formed *via* an intramolecular [3 + 3] cycloaddition. Preliminary data obtained using a *des*-methyl model system supports this hypothesis. Our current efforts involve the usable synthesis of cyclization precursor **4** which is highlighted by a *B*-alkyl Suzuki coupling. Progress to date will be reported in full.



Silver Triflate-Mediated Oxazolium Salt Formation:
Solvent Effects and Application Toward the Synthesis of Aziridinomitosenes

Edwin Vedejs[1], Don L. Warner[2], Amber M. Hibberd[2], Maria C. Mayes[2]
[1]Department of Chemistry, University of Michigan, Ann Arbor, MI 48109
[2]Department of Chemistry, Boise State University, Boise, ID 83725

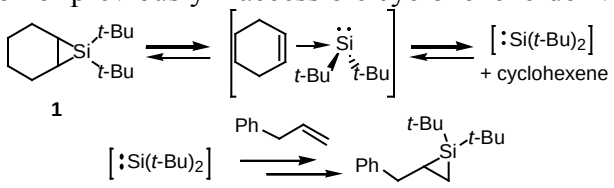
The silver triflate-mediated oxazolium salt azomethine ylide cycloaddition sequence has proven useful for the synthesis of the tetracyclic core of *N*-methyl and *N*-trityl aziridinomitosene analogs using 1, -disubstituted oxazoles as precursors. The multi-stage sequence, outlined below, produces cycloadducts containing *N*-trityl and *N*-methyl aziridines in excellent to acceptable yields, respectively. ptimization studies focused on the oxazolium salt forming reaction have resulted in an intriguing solvent dependence on rate and product profile that, in turn, has provided additional insight into the reaction mechanism. These findings and applications toward the aziridinomitosenes will be reported.



Mechanistic Study of Silylene Transfer from a Silacyclopropane to an Alkene

Tom G. Driver and K. A. Woerpel
University of California, Irvine
Department of Chemistry, Irvine, CA 92697-2025

s an alternative to the strongly reducing conditions necessary for the formation of silacyclopropanes, silylene transfer was developed as a mild, functional group tolerant method of silacyclopropanation. Di-*tert*-butylsilylene can be generated from **1** thermally or through the use of a catalytic amount of a metal salt. inetic and thermodynamic studies of the thermal reaction of **1** and allylbenzene suggested a possible mechanism for di-*tert*-butylsilylene transfer. bservable saturation kinetic behavior in allylbenzene concentration revealed the reversibility of silylene extrusion. Cycloaddition was established as a concerted electrophilic attack of silylene onto alkene through identification of a ammett ρ value to be . using σ_p constants. The sign and magnitude of the yring $\Delta S^{\neq}$ parameter (1 eu) suggested that an intermediate (such as a di-*tert*-butylsilylene alkene complex) may be formed before free silylene. The presence of a reversible silylene disassociation from **1** has synthetic consequences. emoval of the volatile cyclohexene from the reaction mixture through an evacuated headspace led to the formation of previously inaccessible cyclohexene-derived silacyclopropanes.



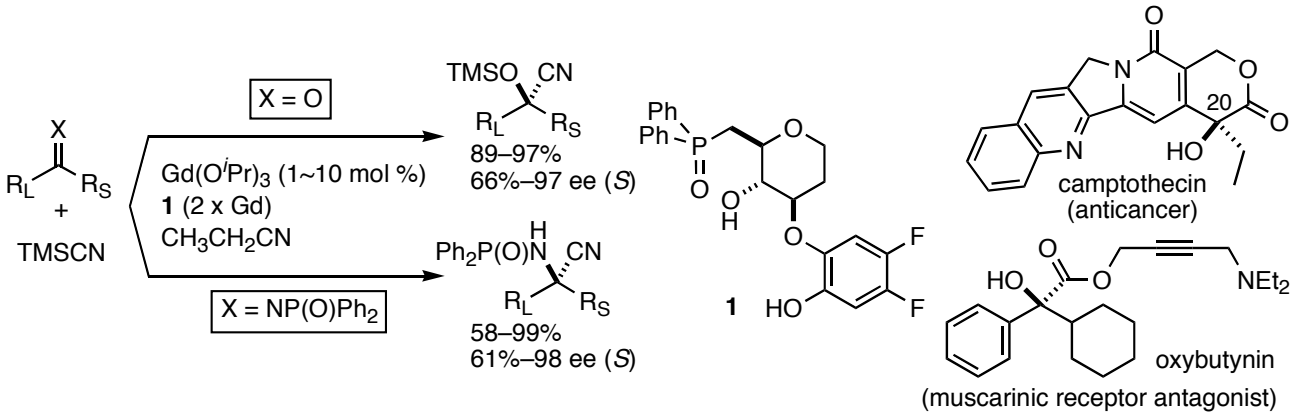
CATALYTIC ENANTIOSELECTIVE CYANOSILYLATION OF KETONES AND KETOIMINES

Motomu Kanai, Shuji Masumoto, Kazuo Yabu, Hiroyuki Usuda, Masato Suzuki, and Masakatsu Shibasaki

Graduate School of Pharmaceutical Sciences, The University of Tokyo

7–3–1 Hongo, Bunkyo–ku, Tokyo 113–0033, JAPAN

The catalyst prepared from Gd(O–*i*–Pr)$_3$ and ligand **1** in a 1:2 ratio promoted (*S*)–selective cyanosilylation of ketones with broad substrate generality. The reaction was applied to a practical synthesis of intermediates for (20*S*)–camptothecin[1] and (*S*)–oxybutynin[2]. Furthermore, the same catalyst promoted the catalytic enantioselective Strecker–type reaction of ketoimines.[3] The products are versatile precursors for various unnatural quaternary amino acids.

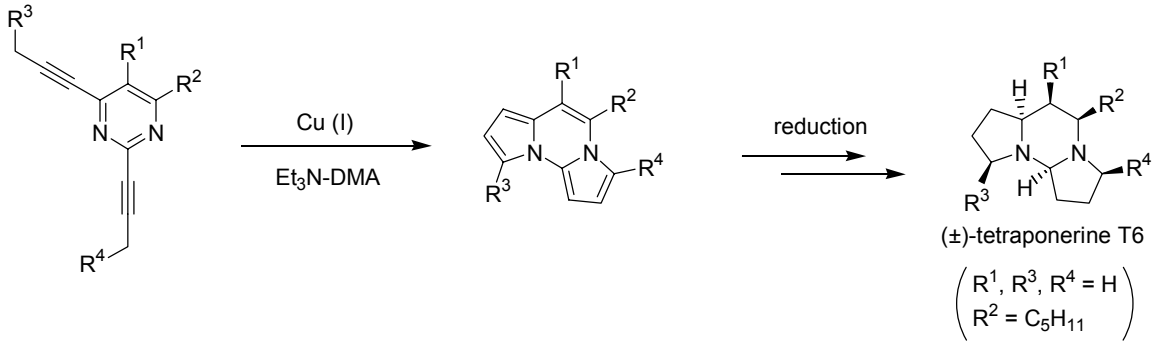


1) *Tetrahedron Lett*. **2002**, *43*, 2923; *J. Am. Chem. Soc*. **2001**, *123*, 9908. 2) *Tetrahedron Lett*. **2002**, *43*, 8647. 3) *Submitted.*

DOUBLE CYCLOISOMERIZATION-REDUCTION AS A NOVEL AND EXPEDITIOUS ROUTE TOWARD TRICYCLIC ALKALOID STRUCTURES

Joseph T. Kim, Vladimir Gevorgyan
University of Illinois at Chicago, Department of Chemistry
845 W. Taylor, Chicago, IL, 60607-7061

The first Cu-assisted double pyrrolization of bis-alkynylpyrimidine to the 5-6-5 heteroaromatic core was demonstrated. Highly selective hydrogenation/reduction of the resulting bis-pyrrolopyrimidine allowed for the short, efficient, and highly diastereoselective total synthesis of (±)-tetraponerine T6 and its derivatives. The multiple pyrrolization-reduction functionalization protocol can serve as a new, short, and efficient approach toward various polycylic alkaloid structures.



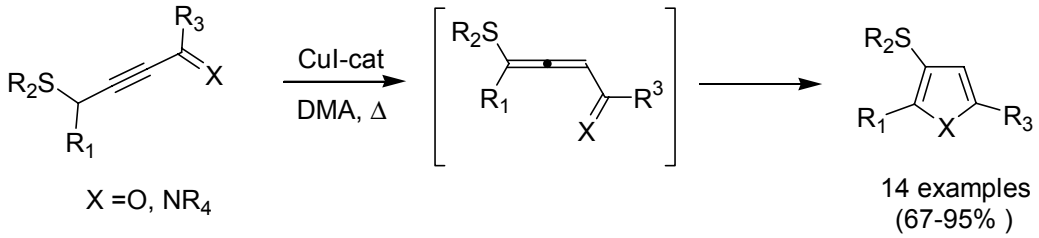
(±)-tetraponerine T6

(R^1, R^3, R^4 = H; R^2 = C_5H_{11})

NOVEL 1,2-MIGRATION OF THIO-GROUP IN ALLENYLSULFIDES: EFFICIENT SYNTHESIS OF 3-THIO-SUBSTITUTED FURANS AND PYRROLES

Joseph T. Kim, Alexander V. Kel'in, Vladimir Gevorgyan
University of Illinois at Chicago, Department of Chemistry
845 W. Taylor, Chicago, IL, 60607-7061

A novel 1,2-migration of thio-group in the keto- and iminoallenylsulfides has been discovered. Incorporation of this migration in the copper-catalyzed cycloisomerization of alkynyl ketones and -imines allows for efficient synthesis of 3-thio-substituted furans and pyrroles, an important class of heterocyclic units, previously inaccessible by standard cycloisomerization techniques. A plausible mechanism for this unusual copper-catalyzed cascade cycloisomerization reaction is proposed.



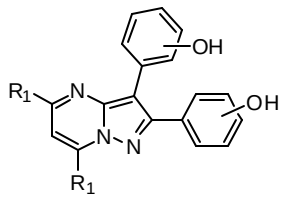
2,3-DIARYL-5,7-DIALKYL-PYRAZOLO[1,5-*a*]PYRIMDINES AS ERb POTENCY SELECTIVE ANTAGONISTS

Dennis R. Compton,[1] Shubin Sheng,[2] Natalie A. Rebacz,[1] In Young Lee,[1] John A. Katzenellenbogen,[1] Benita S. Katzenellenbogen.[2]

[1]University of Illinois Urbana-Champaign, Department of Chemistry, Urbana, IL 61801

[2]University of Illinois Urban-Champaign, Department of Molecular and Integrative Physiology, Urbana, IL 61801

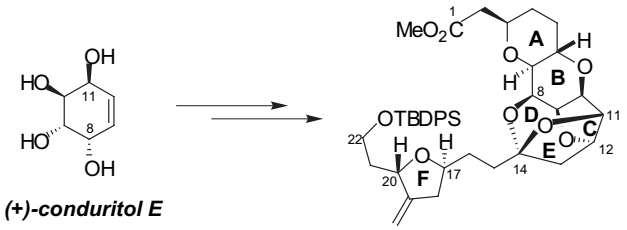
In our continued search for novel estrogen receptor (ER) ligands, we chose to investigate the pyrazolo[1,5-*a*]pyrimidine core as a scaffold for aliphatic and aromatic substituents that would lead to ER binding. A library of compounds was synthesized containing a variety of *meta* or *para* substituted phenols at the 2 and 3 positions of the core. The size of the substituents at the 5 and 7 positions were varied from small (R_1 = H) to large (R_1 = *t*-Bu). The relative binding affinities (RBA, E2 = 100%) of the ligands indicated a preference for ERβ when R_1 was small. Increasing the size of the substituent lead to a higher RBA and increased selectivity for ERα until the substituent became too large, R_1 = Ph and *t*-Bu, then a decrease in binding was seen. The ligands were found to act as potency-selective antagonists on ERβ while having little or no effect on ERα.



R_1 = H, Me, Et, *i*-Pr, CF_3, *t*-Bu, Ph

HALICHONDRIN B: SYNTHESIS OF THE C1-C22 SUBUNIT VIA DESYMMETRIZATION OF (+)-CONDURITOL E

William T. Lambert and Steven D. Burke
Department of Chemistry, University of Wisconsin-Madison
1101 University Avenue, Madison, WI 53706-1396



The C1-C22 subunit of halichondrin B has been synthesized from (+)-conduritol E in 18 steps and 1.3% overall yield. Key features of the described route include the novel ozonolytic desymmetrization of (+)-conduritol E, early-stage assembly of the C-ring, and the use of an enol ether C14-ketone surrogate as a precursor to the CDE-"caged" ketal.

Copper-Catalyzed Enantioselective 1,4-Additions of Organozinc Reagents to Substituted Enones

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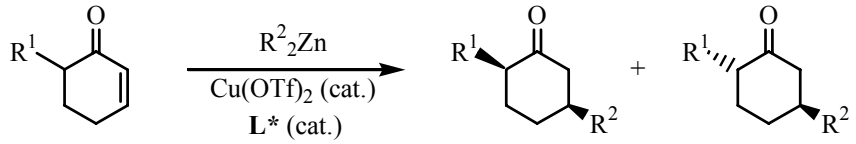
Enantioselective 1,4-additions of organozinc reagents to simple enones, catalyzed by copper(II) triflate and a chiral phosphoramidite, have recieved particular attention in recent years.[1] Here, we present the corresponding reaction of several 6-substituted cyclohex-2-enones **1** to the addition products **2**, using various phosphoramidites **L***.[2] The addition can be conducted either under kinetic resolution conditions (furnishing **2** and unreacted **1** with moderate to high enantiomeric excess) or under complete consumption of the substrate, enabling the control of both the relative and absolute configuration of the addition products **2**.



1 *cis*-**2** *trans*-**2**

[1] N. Krause, A. Hoffmann-Röder, *Synthesis* **2001**, 171-196.
[2] L. Mediavilla Urbaneja, N. Krause, *Tetrahedron Lett.* **2002**, *43*, 7887-7890

Synthesis of New Macrocyclic Allenes

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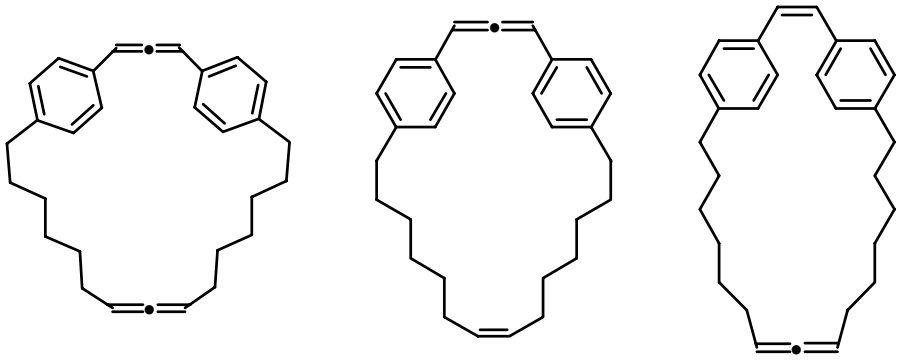
(norbert.krause@uni-dortmund.de)

Since the first synthesis of a [3_4]allenophane,[1] we are interested in macrocyclic allenes possessing different ring size and number of allenic units (e.g., **1**-**3**). Our synthetic approach involves cross-coupling reactions of stilbene derivatives, ring-closing metathesis and allene formation by Doering-Moore-Skatebøl synthesis using Seyferth's reagent $PhHgCCl_2Br$.



1 **2** **3**

[1] S. Thorand, F. Vögtle, N. Krause, *Angew. Chem.* **1999**, *111*, 3929–3931; *Angew. Chem. Int. Ed.* **1999**, *38*, 3721-3723.

Transition Metal-Promoted Synthesis of Functionalized and Unfunctionalized Pyridylallenes

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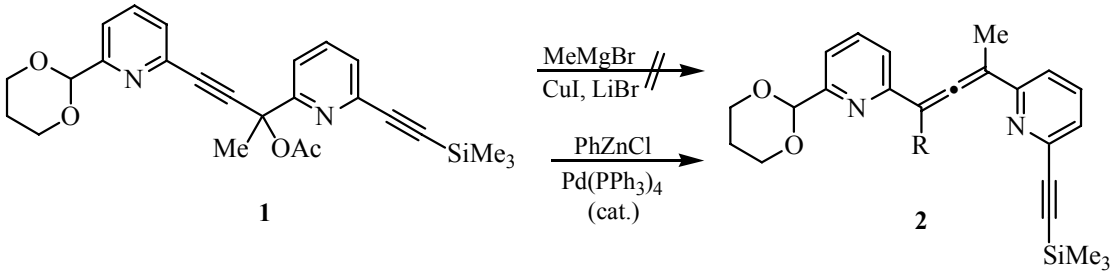
As precursor for macrocyclic host molecules bearing allenic units and pyridine rings, functionalized pyridylallenes (e.g., **2**) were required which are prepared by S_N2'-substitution of propargylic acetates like **1**.[1] Whereas the copper-mediated reaction with Grignard reagents failes in certain cases (probably due to chelation of copper species), the introduction of an phenyl group by palladium-catalyzed substitution with phenylzinc chloride proved to be a reliable method for the formation of allenic pyridines of type **2**.



[1] A. Jansen, N. Krause, *Synthesis* **2002**, 1987-1992.

Diastereoselective Synthesis of Functionalized α-Hydroxyallenes by Enolate Oxidation with DMDO

*Anja Hoffmann-Röder, Carl Deutsch, Norbert Krause**
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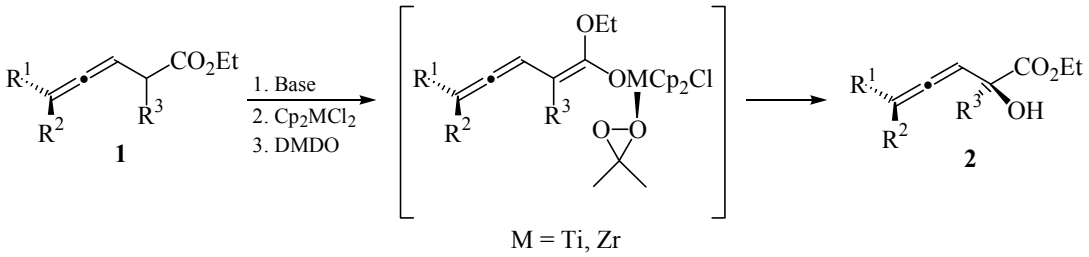
Functionalized α-hydroxyallenes are valuable synthetic precursors for 2,5-dihydrofurans, a structural motif that is found in an abundance of natural products and pharmaceuticals.[1] Recently, we have developed a new approach to α-hydroxyallenes **2** bearing an additional ester functionality by oxidation of in situ formed enolates of 3,4-dienoates **1** with dimethyl dioxirane (DMDO).[1,2] Here, the use of Cp_2ZrCl_2 instead of Cp_2TiCl_2 as transmetalating agent strongly improves the efficiency of the enolate oxidation.



[1] N. Krause, A. Hoffmann-Röder, J. Canisius, *Synthesis* **2002**, 1759-1774.
[2] N. Krause, M. Laux, A. Hoffmann-Röder, *Tetrahedron Lett.* **2000**, *41*, 9613-9616.

Diastereoselective Gold-Catalyzed Cyclization of α-Hydroxyallenes: Precursors in Natural Product Synthesis

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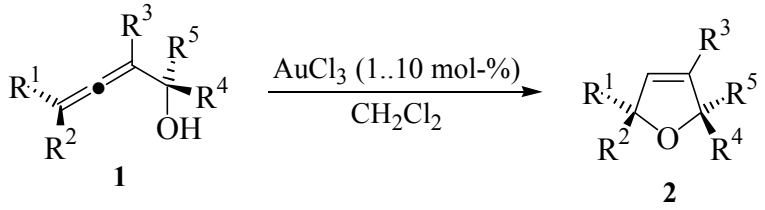
Recently, the enantioselective synthesis and transformation of chiral allenes has gained considerable interest.[1] Based on our previous work on target-oriented synthesis using functionalized allenes,[2] we have developed a new diastereoselective synthesis of 2,5-dihydrofurans **2** by gold(III)-catalyzed cyclization of α-hydroyallenes **1**.[2,3] The efficiency of this new cyclization method is illustrated in a short formal synthesis of citreoviral, a precursor of the mycotoxins citreoviridine and verrucosidine.



1 **2**

[1] A. Hoffmann-Röder, N. Krause, *Angew. Chem.* **2002**, *114*, 3057-3059; *Angew. Chem. Int. Ed.* **2002**, *41*, 2933-2935.
[2] N. Krause, A. Hoffmann-Röder, J. Canisius, *Synthesis* **2002**, 1759-1774.
[3] A. Hoffmann-Röder, N. Krause, *Org. Lett.* **2001**, *3*, 2537-2538.

COLUMNAR DISCOTIC LIQUID-CRYSTALLINE OXADIAZOLE AS ELECTRON-TRANSPORT MATERIALS

***Bilal R. Kaafarani*,[a] *Yadong Zhang*,[a] *Kim G. Jespersen*,[b] *Stephen Barlow*,[a] *Bernard Kippelen*,[b] *and Seth R. Marder*[a,b*]**

University of Arizona, Department of Chemistry, Tucson, AZ 85721

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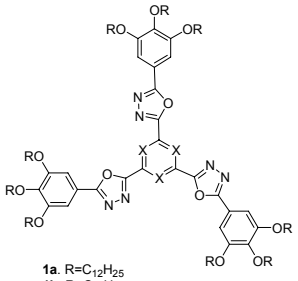
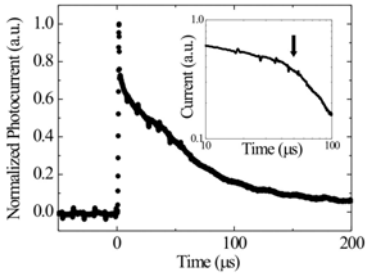
The search for organic semiconducting materials, having high carrier mobility, is crucial for a wide range of electronic applications such as light-emitting diodes, solar cells, and field-effect transistors. Discotic liquid-crystalline mesophases are two-dimensional molecules, which are often constituted of a rigid central aromatic core and extended flexible chains. These molecules usually pack in the form of well defined columns forming one-dimensional paths for charge transport along the stacked conjugated cores due to good intermolecular orbital overlap within the stacks. Organic electron-transport materials based on 1,3,4-oxadiazoles, having mobilities as high as ca. 10^{-3} $cm^2V^{-1}s^{-1}$, have been reported. Furthermore, 1,3,4-oxadiazoles have been proven to be effective as electron-transport agents in organic light-emitting diodes. We report the synthesis of a series of columnar discotic liquid-crystalline oxadiazoles **1** and new oxadiazoles with a more extended core for potential use as electron-transport materials. The time-of-flight data (shown below on the right) demonstrate that the electron mobility at room temperature of **1c** (X=CH) varies from ca. 10^{-3} to 10^{-4} $cm^2V^{-1}s^{-1}$. Other properties of these materials will be discussed.



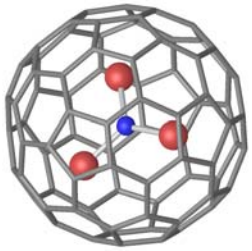
1a. R=$C_{12}H_{25}$
1b. R=$C_{10}H_{21}$
1c. R=C_8H_{17}
1d. R=C_6H_{13} X= CH, N



NOVEL DERIVATIVES AND MEDICINAL APPLICATIONS OF THE TRIMETALLIC NITRIDE ENDOHEDRAL METALLOFULLERENES

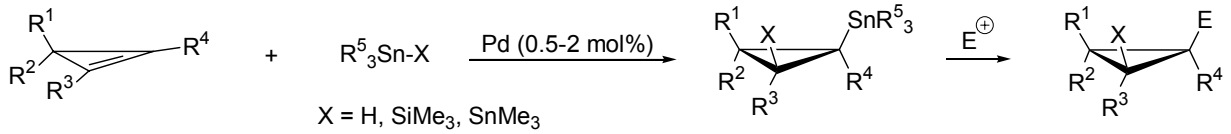
Erick B. Iezzi and Harry C. Dorn
Virginia Polytechnic Institute and State University
Department of Chemistry, Blacksburg, VA 24061

Recently, research efforts in our group have focused on the synthesis of novel organic derivatives of the trimetallic nitride endohedral metallofullerenes ($Sc_3N@C_{80}$, $Sc_3N@C_{78}$ and $Sc_3N@C_{68}$) and their applications in the field of medicine. These unique species encapsulate three metal atoms (Group III or Lanthanides) which are bound to a central nitrogen atom, yielding the formula $[A_3N]^{+6}@[C_X]^{-6}$ (where x = 68, 78 or 80). While C_{60} and traditional fullerenes are functionalized at the [6,6] ring-junctures (pyracylene-type units) of their cages, these metallofullerenes are comprised of non-conventional reactive units. In addition, only milligram amounts of these materials are available. Currently, we are planning to attach peptides and/or dendrimers to impart cage water-solubility. Metallofullerenes containing Lutetium and Gadolinium are being evaluated as potential X-ray and MRI contrasting agents.



TRANSITION METAL-CATALYZED HYDRO-, SILA-, AND STANNASTANNATION OF CYCLOPROPENES: STEREO- AND REGIOSELECTIVE APPROACH TOWARD MULTISUBSTITUTED CYCLOPROPYL SYNTHONS

Michael Rubin, Marina Rubina, and Vladimir Gevorgyan
Chemistry Department, University of Illinois at Chicago
845 West Taylor Street, Chicago, Illinois 60607-7061



Highly stereo- and regioselective transition metal-catalyzed hydro-, sila-, and stannastannation of cyclopropenes proceed very rapidly at temperatures as low as –78°C to produce up to pentasubstituted cyclopropane derivatives in very good yields. It was shown that the addition across the double bond of cyclopropene is generally controlled by steric factors and proceeds from the least hindered face. The directing effect of alkoxymethyl substituents in the hydrostannation reaction of 3,3-disubstituted cyclopropenes was demonstrated. Cyclopropylstannanes were converted into the corresponding cyclopropyllithium derivatives or cyclopropyl halides with retention of configuration. This methodology represents a powerful and atom-economic approach toward a wide variety of highly substituted stereodefined cyclopropylstannanes, important building blocks unavailable by other methods.

CATALYTIC ASYMMETRIC HYDROBORATION OF CYCLOPROPENES

Marina Rubina, Michael Rubin, and Vladimir Gevorgyan
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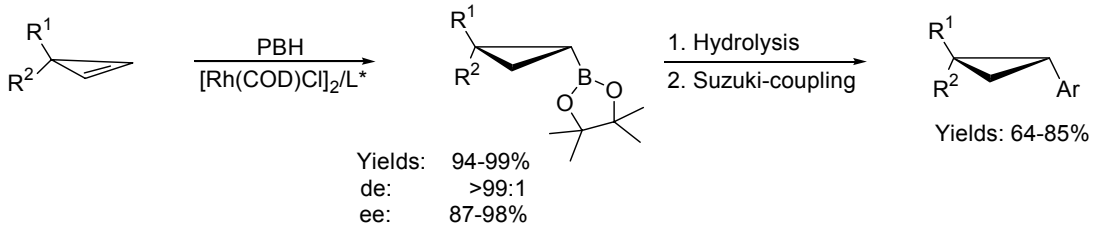
845 West Taylor Street, Chicago, Illinois 60607-7061



2,2-Disubstituted cyclopropyl boronates have been synthesized with high degrees of diastereo- and enantioselectivity via the rhodium-catalyzed asymmetric hydroboration of 3,3-disubstituted cyclopropenes. Chiral ligand effect in the hydroboration reaction has been investigated. It was demonstrated that ester and alkoxymethyl substituents serve as effective directing groups in the hydroboration reaction. The directing effect was found to be necessary in achieving high degrees of enantiomeric induction. Selected cyclopropylboronic derivatives were successfully employed in the Suzuki cross-coupling reaction to produce the corresponding optically active arylcyclopropanes in good yields.

SYNTHETIC STUDIES TOWARDS THE AGLYCON OF APOPTOLIDIN

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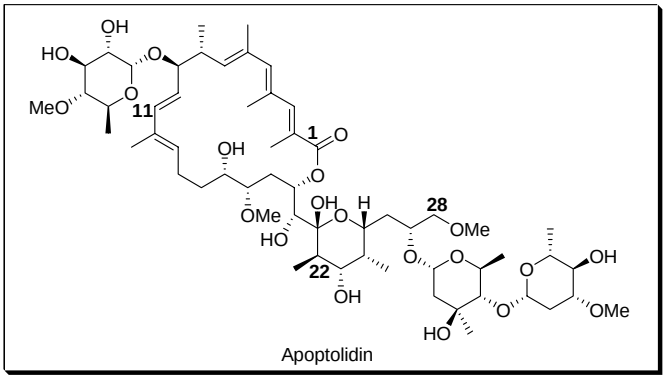
University of Notre Dame
Department of Chemistry and Biochemistry, Notre Dame, IN 46556

Apoptolidin was isolated in 1997 from *Nocardiopsis* sp. and was determined to induce apoptotic cell death in rat glia cells transformed with the E1A oncogene (IC_{50} = 11ng/ml). More recently, Kholsa and co-workers identified the mitochondrial F_1F_0 ATPase as a target to explain its unique biological function. Our research group is interested in developing a novel synthetic route to the apoptolidin aglycone in efforts to study its biological and chemical characteristics. Synthetic progress towards the aglycone is currently under investigation.

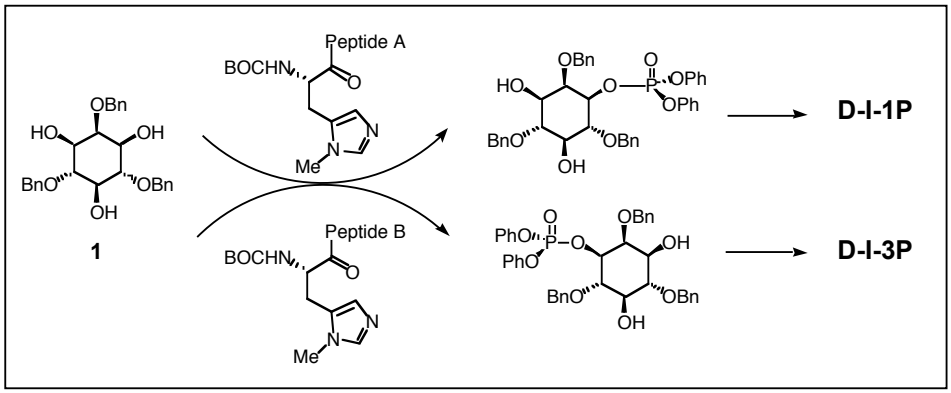


Apoptolidin

Asymmetric Catalytic Phosphorylation: Synthesis of Inositol Phosphates

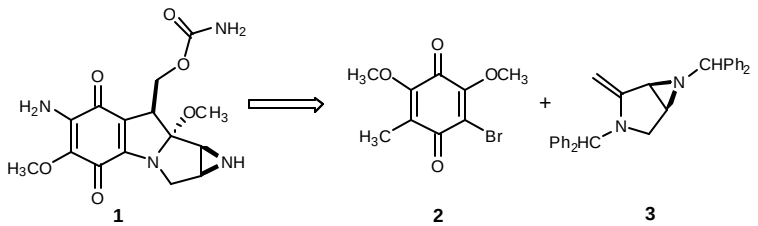
Bianca R. Sculimbrene, Adam J. Morgan, Scott J. Miller
Boston College
Department of Chemistry, Chestnut Hill MA 02467

Selectivity in the laboratory synthesis of polyfunctional molecules often pales in comparison to the remarkable control that nature exerts through its biosynthetic apparatus. Studying such problems can shed light on biological systems and improve laboratory syntheses. Nature's catalysts, enzymes, exhibit extraordinary selectivity, but are large in structure in comparison to their substrate. We sought to emulate the selectivity of enzymes while using only a few constituent amino acids in the assembly of a catalyst. We wished to demonstrate the utility of such catalysts with the synthesis of biologically active, functionality rich target molecules such as inositol phosphates. Peptide catalysts have been found that catalyze the enantiodivergent and regioselective phosphorylation of Inositol derivative (**1**). The sequential screening of random and focused peptide libraries has led to the identification of two highly selective peptides, culminating in the concise synthesis of **D-I-1P** and enantiomeric **D-I-3P**. This methodology is currently being used in the site-selective synthesis of other Inositol Phosphates.



THE METHYLPYRROLIDINE APPROACH TO NATURAL PRODUCTS: STUDIES TOWARDS THE SYNTHESIS OF MITOMYCIN C

Amie L. Williams, Jeffrey N. Johnston*
Indiana University
Department of Chemistry, 800 East Kirkwood Avenue, Bloomington, IN 47405-7102



Mitomycin C (**1**) is a potent anti-tumor agent that has been used clinically for the treatment of cancer for several decades. Since its discovery in 1956, it has also been the object of total synthesis; yet, rac-mitomycin C has succumbed only twice (Kishi, 1979 and Fukuyama, 1989). Our approach is based on disconnection of the methylpyrrolidine subunit and exploits a new acid catalyzed aziridine synthesis developed recently by us.

Chemical approach towards mucin-type *O*-linked glycoproteomics using the Staudinger ligation

Howard C. Hang[1] and Carolyn R. Bertozzi[1-3]

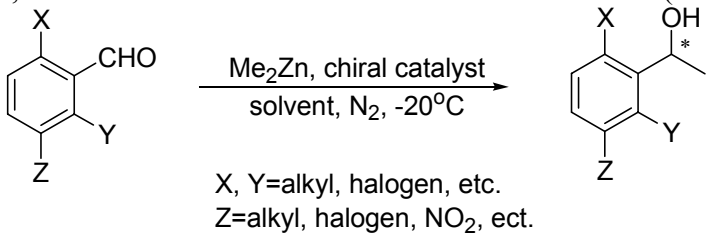
Departments of Chemistry[1] and Molecular and Cell Biology[2], Howard Hughes Medical Institute[3] University of California, Berkeley, CA 94720

Mucin-type *O*-linked glycoproteins are characterized by dense groups of oligosaccharides □-*O*-linked via *N*-acetylgalactosamine (GalNAc) to the hydroxyl group of threonine or serine side chains on proteins. These glycoproteins play vital roles in vertebrate physiology and pathology, such as lubrication and protection of epithelial cells, fertilization, cellular communication as well as in the immune response and cancer. In contrast to *N*-linked glycosylation, where a single oligosaccharyltransferase catalyzes the *en bloc* transfer of $Glc_3Man_9GlcNAc_2$ to asparagine residues of proteins bearing the consensus sequence (Asn-Xaa-Ser/Thr), a family of polypeptide *N*–acetyl-a-galactosaminyltransferases (ppGalNAcTs) initiate mucin-type *O*-linked glycosylation in which no primary consensus sequence has been identified. The development of novel methods to identify mucin-type *O*-linked glycoproteins and the sites of glycosylation would greatly facilitate our understanding of this fundamental post-translational modification. Preliminary work in our laboratory suggested the GalNAc salvage pathway in mammalian cells is permissive of unnatural analogs GalNAc, such as the ketone-isostere of GalNAc. Herein, we report the synthesis and screening of azido-GalNAc analogs for metabolic incorporation into cell surface glycoconjugates in a variety of mammalian cell lines and the application to mucin-type *O*-linked glycoproteomics

Catalytic Enantioselective Additions of Dimethylzinc to Carbonyl Compounds

Qiang Yu, Liangfu Huang, Zhiqiang Fang, Wuping Ma
SynChem, Inc., 1700 S. Mount Prospect Rd, Mount Prospect, Illinois 60018

Research focused on organozinc additions to carbonyl compounds has dramatically intensified over the past two decades. However, application of such reactions to 2,6-disubstituted benzyl aldehydes is limited and customarily results in poor enantiomeric enhancement (ee) 20-40%. In part, this is due to the steric hindrance that severely impedes the approach of the catalysts to the carbonyl group. Therefore, we have extensively studied the relationship of 2,6-disubstituted benzaldehyde substrates, catalysts, solvents, and their ratios under various reaction conditions (see below).

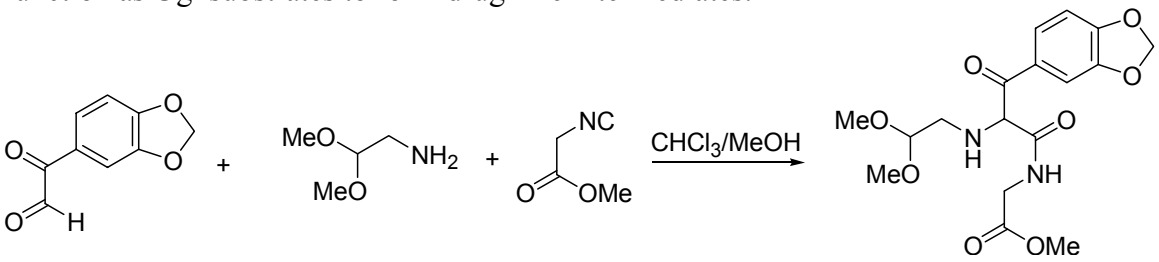


The results obtained indicate that under well controlled reaction conditions enantioselectivity may be increased from 40% ee to more than 80% ee. This result allows us to further improve the percentage of enantioselectivity for such types of molecules by converting them into appropriate derivatives.

Novel Synthetic Scaffolds for Further Derivation in Drug Discovery

Qiang Yu, Fengping Wei, Liangfu Huang, Zhiqiang Fang, and Wuping Ma
SynChem, Inc., 1700 Mount Prospect Road, Des Plaines, IL 60018

The development of high throughput screening (HTS) technology in drug discovery required the efficient, production of specific, and optimized combinatorial libraries. A new set of substrates, suitable for use in an Ugi multi component reaction (MCR), has been discovered. One typical example is illustrated below. Complementing earlier work with classical aldehydes, we now report that aromatic α-ketoaldehyes can successfully function as Ugi substrates to form drug-like intermediates.



This isocyanide based MCR one-pot reaction generated important building blocks, which bear multi functional groups and may advantageously be used for the following:

1. To provide an efficient synthesis of novel building blocks for use in drug discovery.
2. To provide multi-functional-group scaffolds for various drug-like molecules.
3. To generate numerous novel sets of libraries for use in HTS screening searching for novel drug discovery 'hits'

In addition, these scaffolds have the potential for the creation of 'super libraries' *via* further derivation.

ASYMMETRIC SYNTHESIS OF ALL DIASTEREOMERS OF 3-HYDROXY-2,4,6-TRIMETHYLHEPTANOIC ACID: VERIFICATION OF CONFIGURATIONAL ASSIGNMENT

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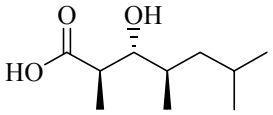
Department of Chemistry, Purdue University
West Lafayette, IN. 47906-1393

Callipeltin A, a novel marine cyclic depsipeptide isolated from a shallow water lithistid sponge, *Callipelta* sp., displays potent cytotoxicity against a broad range of human carcinoma cell lines, antiviral activity against HIV-1 (Lai strain)-infected CEM4 lymphocytes, and antifungal activity against *Fusarium oxysporum*, *Helminthosporium sativum*, *Phytophtora hevea* and *Candida albicans*. Two reports of the asymmetric synthesis of the lipidic 3-hydroxy-2,4,6-trimethylheptanoic acid of Callipeltin A, for which the relative stereochemistry was originally assigned as 2*R*,3*R*,4*S*, have recently been published. Comparison of the ^{1}H NMR to the corresponding fragment obtained from the acid hydrosylate of Callipeltin A, however, revealed the original assignment was incorrect. D'Auria *et al.* have revised the stereostructure as (2*R*,3*R*,4*R*), and confirmed their assignment by enantioselective synthesis. We herein report the first asymmetric synthesis of *all* of the diastereoisomers of 3-hydroxy-2,4,6-trimethylheptanoic acid, thereby unambiguously verifying the configurational assignment of the natural fragment.



(2*R*,3*R*,4*R*)-3-hydroxy-2,4,6-trimethylheptanoic acid

EFFORTS TOWARD THE SYNTHESIS OF A SULFONAMIDE-LINKED TETRAMER OF THYMIDINE

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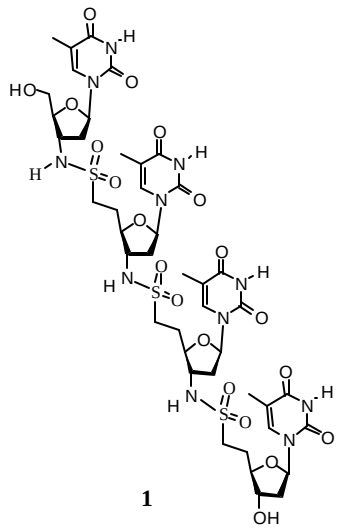
Indiana University - Department of Chemistry
800 E Kirkwood Ave. Bloomington, IN 47405

The interaction of proteins with nucleic acids is of central importance to biological processes. These processes include but are not limited to cell regulatory mechanisms, DNA damage and repair, and antigen recognition by antibodies. We sought to examine specifically the interactions of a thymidine tetramer with anti-DNA antibodies to understand the importance of the phosphate backbone for recognition of the antigen by the antibody. We will present the current efforts toward the synthesis of the sulfonamide-linked tetramer (**1**).



1

PHOTOCYCLOADDITION REACTION TO BENZODITHIOPHENE – A ONE STEP REACTION TO ALKYNE-SUBSTITUTED CYCLOBUTENES

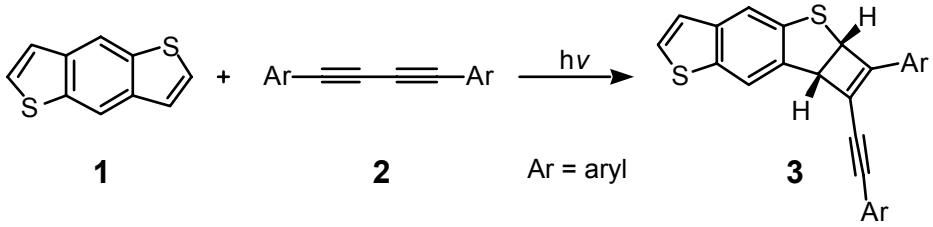
***Brigitte Wex*,[1] *Bilal R. Kaafarani*,[2] *and Douglas C. Neckers*[1*]**

[1] Bowling Green State University, Center for Photochemical Sciences, Bowling Green, OH 43403;

[2] University of Arizona, Department of Chemistry, Tucson, AZ 85721-0041

Photochemical reactions provide a facile approach to complex polycyclic systems using only solvent, sensitizer, and a light source. The photocycloaddition of dimethyl acetylenedicarboxylate to thiophene yields dimethyl phthalate, as the only reaction product. This reaction is an example of the direct conversion of a thiophene into a substituted benzene. The photocycloaddition reaction of dimethyl acetylenedicarboxylate to benzo[b]thiophene yields substituted naphthalenes upon thermal rearrangement of the photoadduct.

In this study, we report the photocycloaddition reaction of acetylenes to benzo[1,2-b:4,5-b']dithiophene. The objective is to prepare new, substituted cyclobutene derivatives that can lead to polymers with new repeat units with the inherent propensity of thermal rearrangement to a conjugated system. The photoaddition of a series of 1,4-diarylbutadiynes to benzodithiophene yields regioselective alkyne-substituted cyclobutene derivatives, which is confirmed by X-ray crystallography analysis; Scheme 1. Details of the reactions and other properties will be presented.

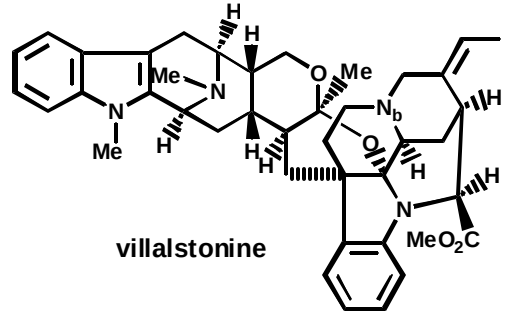


Scheme 1. Photocycloaddition of diarylbutadiyne to benzodithophene.

Approach towards the Total Synthesis of Villalstonine

Jun Ma, James M. Cook
University of Wisconsin-Milwaukee
3210 N. Cramer Street, Milwaukee, WI 53211

Bisindole alkaloids are the dimeric forms of monomeric indole alkaloids and they have been isolated from various species of plants accompanied by their monomeric progenitors. It was reported that the bisindole alkaloid macralstonine was able to lower blood pressure, besides, studies by Houghton have shown that a number of alkaloids from various parts of *Alstonia scholaris*, *A. macrophylla* and *A. glaucescens*, exhibited pronounced antiplasmodial activity. To date, villalstonine and macrocarpamine have been shown to be the most active and are much more potent than the monomeric units that comprise them. Rencent approach towards the total synthesis of villalstonine will be presented.



villalstonine

SYNTHESIS OF PROTECTED (*R*)- AND (*S*)-2-METHYLCYSTEINE VIA THE CURTIUS REARRANGEMENT

Brant L. Kedrowski
Department of Chemistry, University of Wisconsin - Oshkosh
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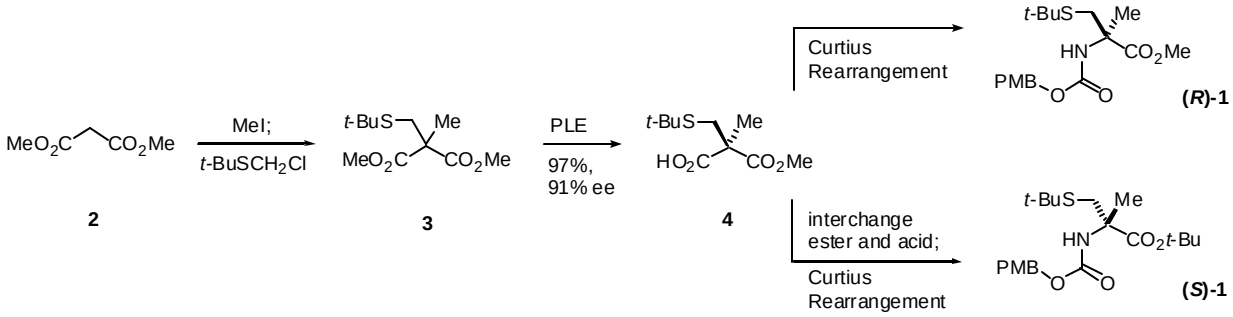
Oshkosh, Wisconsin 54901

A synthesis of differentially protected (*R*)- and (*S*)-2-methylcysteine (**1**) is described. Mono-methylation of dimethylmalonate (**2**) followed by alkylation with *t*-butylchloromethyl sulfide gave the achiral diester **3**. Selective hydrolysis of one ester with pig-liver esterase gave acid **4** in 97% chemical yield and 91% enantiomeric excess. Heating this acid with diphenylphosphoryl azide followed by 4-methoxybenzylalcohol gave protected (*R*)-2-methylcysteine **(*R*)-1**. Alternately, the acid and ester groups were interchanged and heated with diphenylphosphoryl azide followed by 4-methoxybenzylalcohol, giving protected (*S*)-2-methylcysteine **(*S*)-1**.



A Totally Automated Solution for Normal and RP Preparative HPLC with Analytical Purification Determination: cLC

Joan M. Stevens and Ben Schroeder
Gilson, Inc., 3000 W. Beltline Hwy., Middleton, WI, 53562.

It is imperative in today's world that researchers get the most bang for their buck. Many times resources are being stretched very thin as the demand to increase production goes up. Purification of compounds has largely been accomplished through liquid-based chromatography. The advantages of preparative chromatography for compound purification are well established. Reverse phase chromatography, although being the method of choice, is limited by sample capacity /injection, possible sample solubility issues and lengthy dry downs. It would be very advantageous to researchers if one could expand the capabilities of these instruments.

Researchers have shown quite an interest in implementing normal phase chromatography for compound purification. Benefits such as fast dry downs and enhanced solubility make normal phase chromatography an attractive alternative for compounds that are incompatible with RP chromatography. However does one really want additional instruments dedicated for NP? A possible solution to this dilemma is to automate the capabilities of RP and NP in one system in addition to being able to analyze the collected fraction for purity.

The cLC (comprehensive LC) system is a totally automated purification system with on-line analytical analysis of fractions, using both NP and RP environments. The cLC system requires only a little more bench space than a conventional HPLC system at about the same price. The system can automatically switch between normal and reverse phase, and is capable of accessing both pre-packed disposable silica-based columns and reverse phase columns without operator intervention. Collected fractions can then automatically be injected for determination of purity. Presentation of the system will include data representing the throughput and analysis capabilities of the system.

Authors can be reached at 1-800-445-7661
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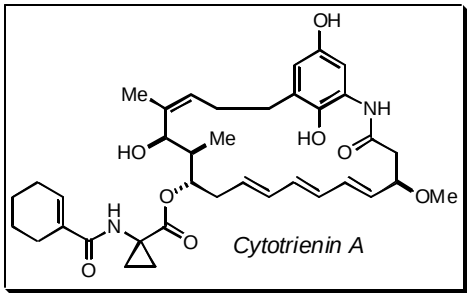
LINEAR FREE ENERGY RELATIONSHIPS IN THE UNDERGRADUATE ORGANIC CHEMISTRY LAB

Richard J. Mullins, Andrei Vedernikov and Rajesh Viswanathan
Indiana University, Department of Chemistry
800 E. Kirkwood Ave., Bloomington, IN 47405-7102

We have delineated an approach to exploring Hammett relationships which is novel in the undergraduate teaching lab. The use of competition experiments proved to be a reliable method for the construction of Hammett plots with good correlation. Reactions that were studied include the sodium borohydride reduction, methylmagnesium bromide addition and oxime formation with *para*-substituted acetophenones. The composition of reaction mixtures was established by ^{1}H NMR integrations. The use of competition experiments ensured consistency in the results, as relatively little control was required over the reaction conditions. Thus, this method provides great flexibility with regard to the compounds and reactions that may be studied.

SYNTHESIS AND CHEMICAL BIOLOGY OF THE APOPTOSIS INDUCING AGENT CYTOTRIENIN A AND ITS 15 DIASTEREOISOMERS

Jennifer V. Schaus, Gwilherm Evano, James S. Panek
Boston University, Chemistry Department and Center for Chemical Methodology Development, 590 Commonwealth Avenue, Boston, MA 02215



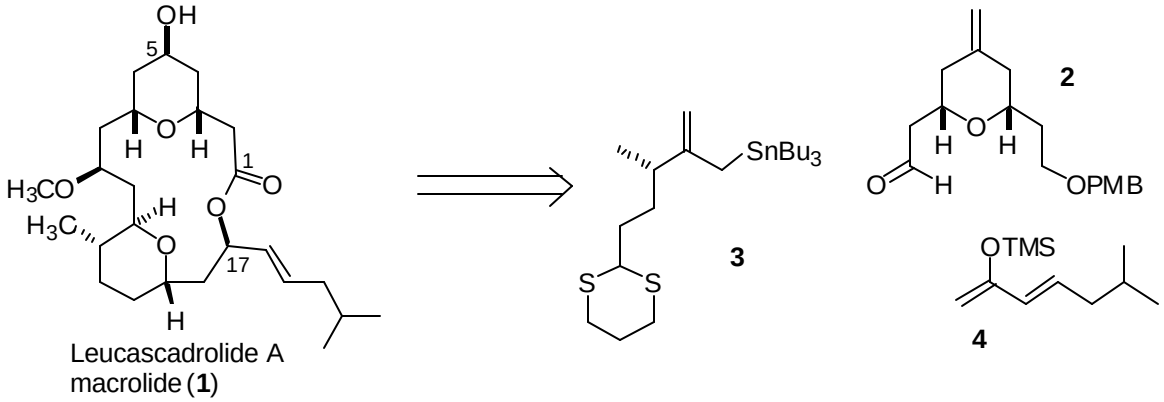
Cytotrienin A

A highly versatile synthesis of cytotrienin A, a recently disclosed apoptosis inducing agent, has been developed. The proposed synthesis allows for the generation of all possible combinations of relative and absolute stereochemical relations of C11, C12, C13 and C3. This approach will allow for not only preparation of the natural stereoisomer, whose stereochemistry has not yet been determined, but stereochemical and structural variants that can be assessed for their biological activity. All 16 diastereoisomers are currently being synthesized and will be utilized to induce cells to undergo apoptosis and can be evaluated for their effect on the mitogen-activated protein kinase pathway (MAPK) using *Saccharromyces cerevisiae* as a model organism and genome-wide transcription profiling techniques.

ASYMMETRIC SYNTHESIS OF THE LEUCASCANDROLIDE MACROLIDE

David R. Williams, Scott V. Plummer and Samarjit Patnaik
Dept. of Chemistry, Indiana University
800 E Kirkwood Ave., Bloomington IN 47406

Leucascandrolide A was isolated from a calcareous sponge in 1989 along the eastern coast of the Coral Sea in New Caledonia. It displays potent cytotoxic activity against tumor cell lines and strongly inhibits the fungus *Candida albicans*. The promising bioactivity has inspired numerous synthetic efforts towards the natural product. Our efforts for the synthesis of the macrolide of leucascandrolide (**1**) rely on a convergent asymmetric allylation/reduction strategy involving fragments **2**, **3** and **4**.



Leucascadrolide A macrolide (**1**)

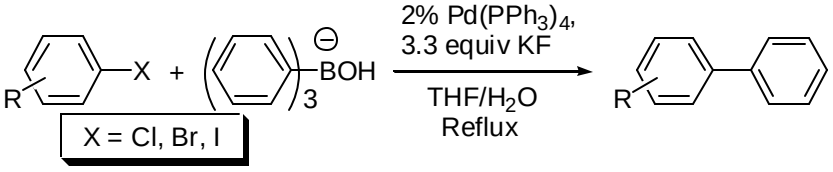
Suzuki Cross-coupling Reactions of Triarylborane Adducts

Jiangtao Hao[1], David A. Boyles[1] and John T. Bendler[2]

(1) South Dakota School of Mines and Technology, (2) United States Naval Academy

(1) Department of Chemistry and Chemical Engineering, Rapid City, SD, 57701-3995, USA, (2) Physics Department, Annapolis, MD, 21402-5026

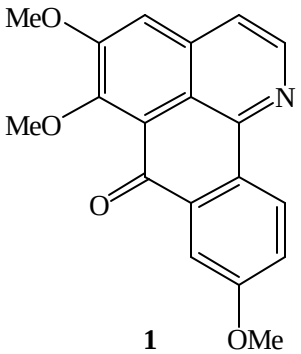
The palladium-catalyzed Suzuki cross-coupling reactions of triphenylborane sodium hydroxide and tri(4-benzyloxyphenyl)borane potassium fluoride with aryl halides proceeds readily with good yields. The adducts are air- and moisture-stable, more reactive in Suzuki reactions and can be prepared with increased overall yields and atom economy, and milder preparation conditions compared to arylboronic acid. The reaction mechanism was investigated and found all aryl group are transferable under suitable conditions.



SUBSTITUTION REACTIONS ON THE 7*H*-DIBENZO[*de,h*]QUINOLIN-7-ONE SCAFFOLD. ARE AMINOOXOISOAPORPHINE ALKALOIDS ARTEFACTS?

Eduardo Sobarzo-Sánchez, Bruce K. Cassels
University of Chile, Faculty of Sciences, Department of Chemistry, and Millennium Institute for Advanced Studies in Cell Biology and Biotechnology (CBB)
Casilla 653, Santiago, Chile

7*H*-Dibenzo[*de,h*]quinolin-7-ones or azabenzanthrones are well known as dye intermediates and have attracted some interest due to their photo- and electrochemical properties. The 7*H*-dibenzo[*de,h*]-quinolin-7-one skeleton is also present in a small group of alkaloids of uncertain biogenesis known as oxoisoaporphines, of which menisporphine (**1**) is the earliest example. More recently, a few 1-amino-substituted oxoisoaporphines such as lakshminine (**2**) have been characterized.



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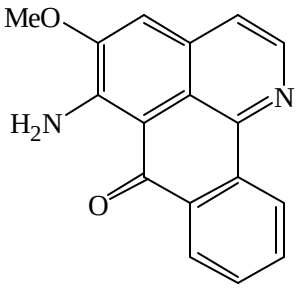


2

Experimental and quantum-chemical studies on the substitution reactions of these compounds suggest that 1-aminooxoisoaporphines may be isolation artefacts formed by the action of nitrogen nucleophiles on "normal" oxoisoaporphines bearing appropriate leaving groups at C(1).

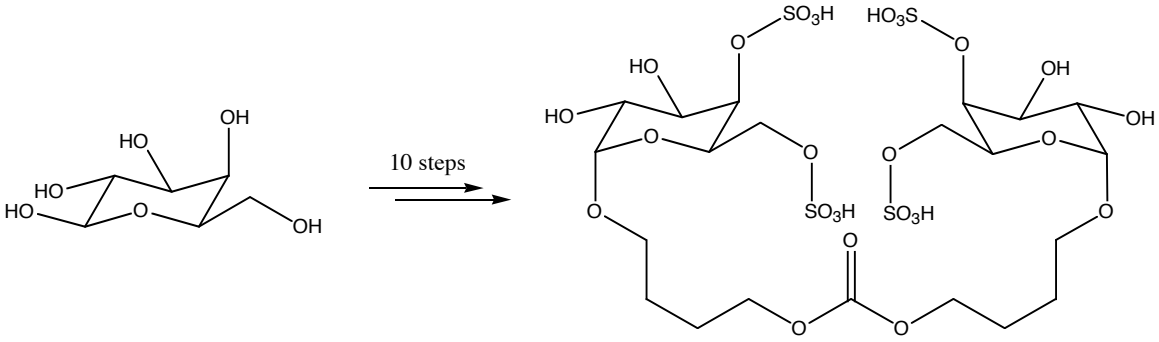
SYNTHESIS OF SYMMETRIC SULFATED SUGAR PROTEIN-BINDING MOLECULES

Alexander J. A. Cobb[1], Steven V. Ley[1], Roy Jones[2]

1. University of Cambridge, Department of Chemistry, Lensfield Road, Cambridge CB2 1EW, UK.

2. The Babraham Institute, Babraham, Cambridge CB2 4AT, UK.

The synthesis of symmetric sulfated saccharide molecules is described. It is hoped that these compounds will mimic suramin, a symmetric polysulfated ligand which inhibits the binding of spermatozoa to the zona pellucida (ZP) of superovulated eggs. Monosulfated sugars have shown to have little or no activity and it is thought that a co-operative binding effect is required. The group is a world leader in the synthesis of saccharides and a wide range of chemistry has been utilised in the synthesis of these symmetric compounds.



Scheme 1 : *Example of the synthesis of a symmetric sulfated sugar*

Remodeling the Engrailed Homeodomain•DNA Interface

Matthew D. Simon[1] and Kevan M. Shokat[1,2]
[1]University of California, Berkeley
Department of Chemistry, Berkeley, CA 94720
[2]University of California, San Francisco
Department of Cellular and Molecular Pharmacology, San Francisco, CA 94143

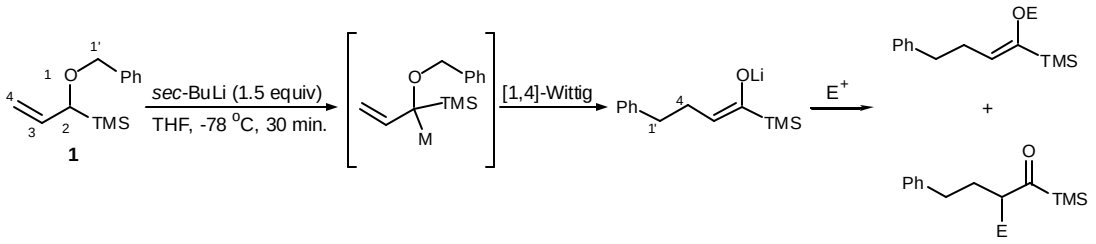
The Engrailed homeodomain•DNA interface was remodeled in a two-step process. First unnatural nucleosides with bulky appendages were introduced into the DNA in order to disrupt protein binding. A space-creating cavity at Ile47 recovered binding of Engrailed homeodomain to these unnatural DNA targets. These results support the feasibility of engineering novel functionality into a protein•DNA interface.

[1,4]-Wittig Rearrangements of α-Silyl Ethers

Edith N. Onyeozili and Robert E. Maleczka, Jr.
Michigan State University
Department of Chemistry, East Lansing, MI 48824

We have investigated the Wittig rearrangement of α-trimethylsilyl allyl ether **1** and found that with 1.5 equiv. of *sec*-BuLi, at –78 °C, in THF (0.065 M), this substrate undergoes efficient Wittig rearrangement with excellent selectivity for the [1,4]-product. Our results indicate that deprotonation of the α-silyl ether and rearrangement of the resulting lithiated species are not concurrent events. We have taken advantage of the intermediacy of an enolate species in the [1,4]-pathway to introduce various groups at the α-carbon by trapping the enolate ion with suitable electrophiles in a one-pot process.

Substitution as well as stereochemistry at the migrating carbon simultaneously impacts the selectivity of the Wittig rearrangement. Our results from this study will be presented.



Fluoroproline Incorporation into the X-Position of Collagen: How Stereoelectronics Affect Triple-Helix Stability

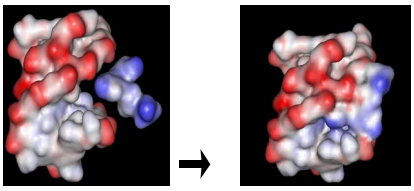
Jonathan A. Hodges[1] and Ronald T. Raines[1,2]
[1]Department of Biochemistry, University of Wisconsin-Madison, Madison, WI, 53706, U.S.A.
[2]Department of Chemistry, University of Wisconsin–Madison, Madison, WI, 53706, U.S.A.

Fluoroproline acts as a powerful tool for examining the importance of stereoelectronic effects on the stability of the collagen triple helix. The triple helix is composed of three polypeptide chains each consisting of approximately 300 repeats of the sequence (Gly–X–Y). In the Y-position, 4*R*-fluoroproline (Flp) increases the stability of the triple helix, but its stereoisomer 4*S*-fluoroproline (flp) decreases stability. The gain in stability conferred by Flp is attributed to the preference of the pyrrolidine ring in Flp to adopt a C_γ-exo ring pucker while flp prefers to adopt a C_γ-endo ring pucker. In the present work, the effects of fluoroproline incorporation into the X-position are examined. Interestingly, the results are opposite to those observed in the Y-position, as flp is stabilizing and Flp is destabilizing in the X-position. Current models describe the relationship between ring pucker, backbone dihedral angles, and triple-helix stability. The results are discussed in the context of these models.

What's New with Neomycin?

Dev P. Arya

Laboratory of Medicinal Chemistry, Department of Chemistry, Clemson University, Clemson, SC 29634



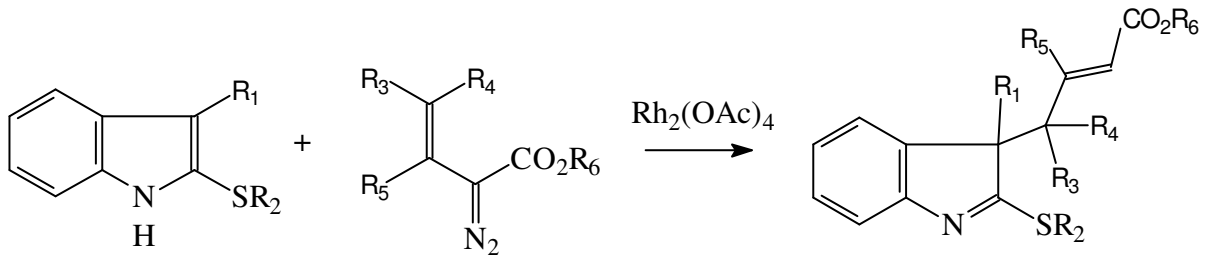
Neomycin binding to triplex Watson-Hoogsteen Groove: A Model

Aminoglycsosides have been at the vangaurd of antimicrobial therapy for fifty years. Their mechanism of action has been shown to involve binding to ribosomal RNA (16S A-site). Our work has shown that aminoglycosides bind to triplex DNA/RNA as well as hybrid duplex (DNA/RNA). This suggests that binding of aminoglycosides is not simply RNA selective, but selective for nucleic acids that can adopt an A-form. SPR, ITC and competition dialysis results of neomycin and conjugates will be presented to support this hypothesis.

Sulfur ylide initiated thio-Claisen rearrangements: Synthesis of highly substituted indolines.

Alexei V. Novikov[1], Abigail R. Kennedy[2], and Jon D. Rainier[1]
Department of Chemistry, University of Utah, 315 South 1400 East, Salt Lake City UT, 84112
1) Department of Chemistry, University of Utah, 315 South 1400 East, Salt Lake City UT, 84112
2) Exelixis, Inc., 170 Harbor Way, P.O. Box 511, So. San Francisco, CA 94083-0511

The presence of C(3) quaternary substitution in a wide variety of interesting indoline containing natural and non-natural products has inspired a number of groups, including ours, to develop new and improved routes to their synthesis. Our contributions to this area rely on the reaction of vinyl diazoacetates **2** with 2-thio-3-alkylindoles **1** in the presence of rhodium acetate leading to C(3) quaternary substituted indolines **3** (eq. 1). The reaction proceeds using mild conditions (room temperature, methylene chloride) in high yield on a variety of substrates.



1 **2** **3** (1)

This poster focuses on a more in-depth investigation of the newly discovered reaction: its scope, mechanism and potential synthetic use.

SYNTHESIS OF NOVEL FLUORINATED NITROXIDES AND APPLICATIONS TO IONOMER SUPRAMOLECULAR ASSEMBLIES

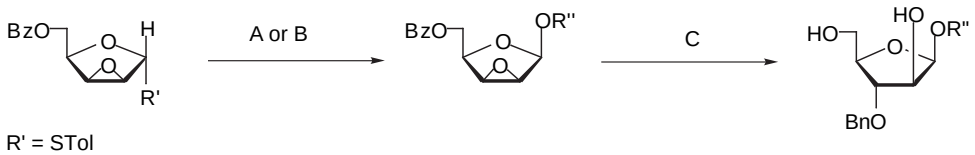
Ileana Dragutan,[1] Valerian Dragutan,[1] Ewa Szajdzinska-Pietek,[2] Jayesh G. Bokria,[3] Biji Varghese[3] and Shulamith Schlick[3]

[1]Institute of Organic Chemistry, Romanian Academy, P.O.B. 15-254, Bucharest, Romania;
[2]The Institute of Applied Radiation Chemistry, Technical University of Lodz, Lodz, Poland;
[3]Department of Chemistry, University of Detroit Mercy, Detroit, MI 48219

Specially tailored, new fluoro-substituted spin probes have been synthesized and applied to obtain structural and dynamic information on the self-assembling of Nafion type ionomers. The availability of such probes is an important asset in studies on perfluorinated surfactants, in view of the well-established repulsions occurring between hydrocarbon backbones and perfluoro counterparts. The synthetic strategy involved multi-step coupling of selected fluorinated reagents (carboxylic acids, alcohols, etc) to an array of piperidine or pyrroline nitroxide stable free radicals, each bearing at least one reactive functional group in addition to the NO**.** paramagnetic motif. ESR spectra of the nitroxides were measured in neat organic solvents, in aqueous Nafion solutions and in membranes swollen by water. The ^{14}N hyperfine splittings (A_{zz} and a_N) and line shapes were proved to respond to polarity and the presence of oxygen, respectively. The sensitivity of the line shapes relative to oxygen suggests possible use of the probes in oxymetry. Spectra of nitroxides incorporated in Nafion membranes or solutions indicated the presence of multiple sites. Probes with longer fluorinated tails penetrated deeper into the assembled polymer chains. In all cases nitroxide occurrence in polar sites has been observed.

2,3-ANHYDRO-D-FURANOSIDES: SYNTHETIC AND MECHANISTIC STUDIES

Christopher. S. Callam, Rajendrakumar R. Gadikota, Todd. L. Lowary
The Ohio State University
Department of Chemistry, Columbus, Ohio 43210



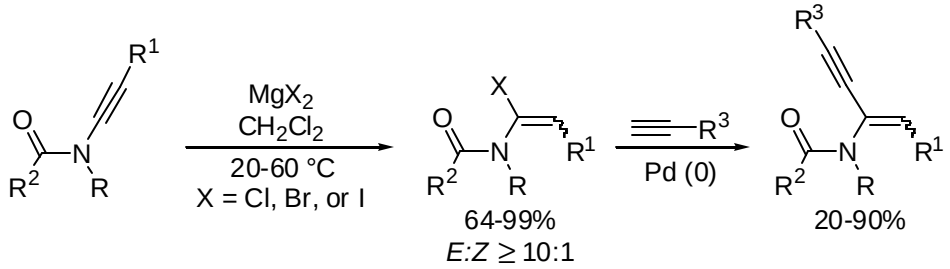
1, R' = STol
2, R' = S(O)Tol

A. i) Tf_2O, DTBMP, CH_2Cl_2, -78 °C; ii) R''OH; B. ROH, NIS, AgOTf, CH_2Cl_2, - 40 °C. C. BnOLi, (-)-spartiene

We report that 2,3-anhydrofuranose thioglycosides (e.g **1**) and glycosyl sulfoxides (e.g **2**), in which the hydroxyl groups C–2 and C–3 are "protected" as an epoxide, glycosylate alcohols with an exceptionally high degree of stereocontrol. The predominant or exclusive product of reactions with this fundamentally new class of glycosylating agent is the one in which the newly formed glycosidic bond is *cis* to the epoxide moiety. Low temperature ^{1}H, ^{13}C, ^{19}F NMR studies coupled with computational chemistry have been undertaken to gain a better understanding of the mechanism of these glycosylations reactions. We further demonstrate that subsequent nucleophilic opening of the epoxide moiety proceeds under basic conditions to give products in high yield and with good to excellent regioselectivity. In the epoxide opening reactions of glycosides with the 2,3-anhydro-β-D-*lyxo* stereochemistry the addition of (–)-sparteine to the reaction mixture dramatically enhanced the regioselectivity in favor of the *arabino* product. This represents the first example of the use of (–)-sparteine to influence the regioselectivity of an epoxide ring opening reaction with a non-carbon nucleophile. We have demonstrated the utility of this methodology through the efficient synthesis of an arabinofuranosyl hexasaccharide which is a key structural motif in two mycobacterial cell wall polysaccharides.

A HIGHLY STEREOSELECTIVE SYNTHESIS OF NOVEL *E*-a-HALOENAMIDES VIA A MILD AND EFFICIENT HYDROHALOGENATION OF YNAMIDES

Jason A. Mulder, Kimberly C.M. Kurtz, Richard P. Hsung*, Heather Coverdale, Michael O. Frederick, Lichun Shen, Craig A. Zificsak
Univerity of Minnesota
Department of Chemistry, Minneapolis, MN 55455



A highly stereoselective preparation of novel achiral and chiral *E*-a-haloenamides has been developed. Starting from the ynamide, these haloenamides may be obtained in good to excellent yields. a-haloenamides may be used in transition metal-mediated reactions, such as the Sonagashira coupling. They also provide rapid access to a-metalated enamides which could serve as a-acyl anion equivalents.

ORGANOALUMINUM REAGENTS IN VINYLSIALNES SYNTHESIS

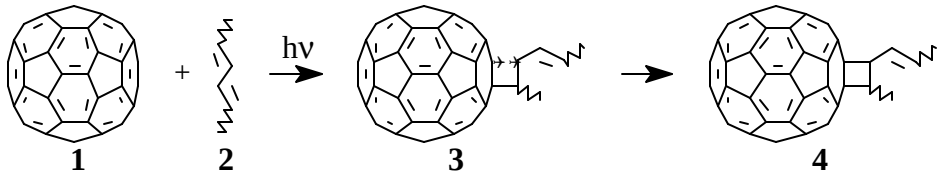
Megan Macala, Nicholas James, Joseph Haoui, , Sylvia Akbar, Desmond Kwan.
John Carroll University Chemistry department, Cleveland OH. 44118.

Vinylsilanes, versatile synthetic intermediates, play a prominent role in many natural and unnatural product syntheses (eg. antibiotics, pheromones, and terpenes). The goal of this research project is to convert various ketones to their corresponding vinylsilanes and compare the selectivity of a polar solvent to a non-polar solvent. Our approach is based primarily on the Peterson olefination reaction. The Peterson olefination converts aldehydes and ketones to desilylated alkenes under either acidic or basic conditions. Our research and Mole's work demonstrates that organoaluminum reagents are potent eliminating agents. We explored diethylaluminum chloride's reaction with β-silylalkoxides, generated in situ from the addition of (trimethylsilylmethyl) lithium to various ketones, in triethylamine (polar) and in pentane (non-polar) solvents, in a one pot synthesis.

RELATIVE RATES OF BOND ROTATION AND RING CLOSURE IN THE PHOTOCYCLOADDITION INTERMEDIATES FROM C_{60} AND THE ISOMERIC 2,4-HEXADIENES - A REANALYSIS OF REPORTED DATA

Wendell L. Dilling
Central Michigan University
Department of Chemistry, Mount Pleasant, MI 48859

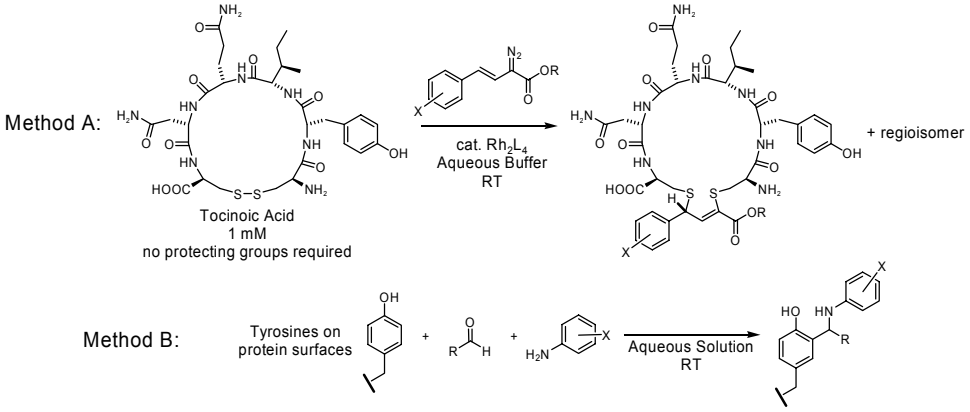
Orfanopoulos and co-workers have reported photocycloadditions of C_{60} (**1**) to several olefins. Two-step cycloadditions of triplet C_{60} were proposed for all of these reactions. These workers (*J. Am. Chem. Soc.* **1998**, *120*, 9911-9920) analyzed the product **4** distributions from C_{60} and the isomeric 2,4-hexadienes **2** by the method of Bartlett et al (*J. Am. Chem. Soc.* **1964**, *86*, 622-628) to determine a relative rate of internal rotation to ring closure of the intermediate biradical or zwitterion **3** (✻ = radical or ion). A relative rate of ~18 was calculated from the product distributions from the *cis-cis* and *trans-trans* isomers of **2**. However, these two isomers do not form a common intermediate. The analyses require the product distributions from the *cis-trans* and either the *cis-cis* or *trans-trans* isomers of **2** depending on which intermediate is being considered. Recalculation gave a relative rate of ~70 for the *trans*-propenyl intermediate. Recalculation for the *cis*-propenyl intermediate gave a negative value for the relative rate, indicating an inconsistent isomer distribution for at least one of the reactions.



1 **2** **3** **4**

METALLOCARBENES AND MULTICOMPONENT MANNICH REACTIONS: TWO NEW METHODS FOR THE FUNCTIONALIZATION OF NATIVE PROTEIN RESIDUES

John M. Antos, Neel S. Joshi, and Matthew B. Francis*
Department of Chemistry, University of California, Berkeley, CA 94720-1460, and
Materials Science Division, Lawrence Berkeley National Lab, Berkeley, CA 94720



Two new reactions for the selective bioconjugation of native protein residues will be presented. The first (Method A) features the chemoselective modification of disulfide bonds using stabilized metallocarbene intermediates, and the second (Method B) is a three component Mannich-type reaction for the selective functionalization of tyrosine residues. Both of these reactions proceed to high conversion at room temperature in buffered aqueous solution and require no protecting groups. These new bioconjugation techniques have been used to modify both cyclic peptides and small proteins.

Design, Synthesis and Discovery of Novel Hydroxyamides as Orally Available General Anesthetics and Anticonvulsants

Hilary A. Schenck,[a] Sylvia Cechova,[b] Thomas N. Pajewski,[b] James P. Stables[c] and Milton L. Brown[a]

Departments of Chemistry[a] and Anesthesiology[b], University of Virginia, Charlottesville, VA 22904, NIH[c], Division Neurological Disease and Stroke, Bethesda, MD, 20824.

Themisone, also known as Atrolactamide, was found in the 1950's to be a very potent anticonvulsant. We hypothesized a toxic metabolite based on an elimination pathway. Therefore, a fluorinated derivative was synthesized to prevent potential toxicity. Anticonvulsant testing identified analogue **1** to have potent activity (MES ED_{50} of 9.9 mg/kg, ScMET ED_{50} of 34 mg/kg and TD_{50} of 100 mg/kg). Serendipitously, general anesthesia was noted as a toxicity. With this in mind, analogue **1** was evaluated for general anesthesia. The fluorinated derivative lowered the minimum alveolar concentration (MAC) of isoflurane (1.2% in O_2) by 33% at 60 mg/kg with no hemodynamic effects at the therapeutic concentration. Therefore, a diverse range of analogues were synthesized utilizing multiple synthetic pathways to explore structure activity relationship. Asymmetric synthesis of the lead analogues was also completed. Comparative molecular field analysis was used to prioritize synthesis of second generation analogues based on [^{3}H] Batrachotoxin-A-20-a-Benzoate binding to sodium channels. Mechanisms of action explored thus far include $GABA_A$, sodium and potassium channels, lipid partitioning and protein kinase C. These results represent a novel class of orally available general anesthetics.

ALKYLPHOSPHAZINES AS EFFECTIVE COUPLING PARTNERS; A NEW ENTRY INTO THE KOJIC AMINE BASED PEPTIDOMIMETICS

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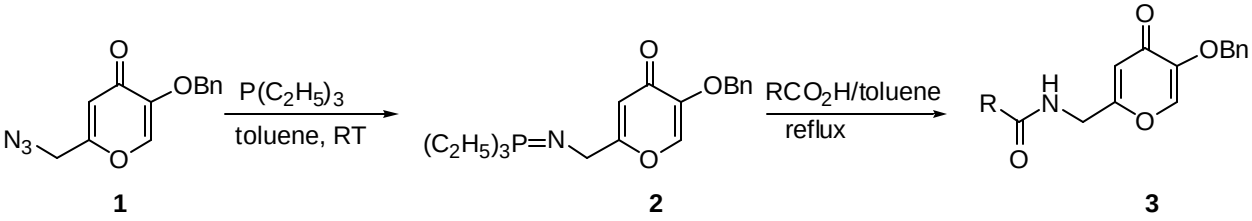
Lead Discovery Group, Procter & Gamble Pharmaceuticals, Inc.
Health Care Research Center, 8700 Mason-Montgomery road, Mason, OH 45040

There has been a single report describing the peptide coupling of Kojic amine with acids in albeit low yields (45%). Herein, an alternative method is disclosed which involved alkylphosphazines as effective coupling partners. The requisite phosphazines were synthesized from the corresponding azides via a Staudinger reaction. Once formed, the intermediate phosphazines were allowed to react with various acids in refluxing toluene (Scheme 1). The coupled products were obtained in 75-80% yield. Aliphatic as well as aromatic acids underwent the reaction to generate the coupled products. The reaction was very clean, and the only byproduct being formed was alkylphosphine oxide. One striking feature was the participation of hindered acids in the reaction to afford the desired products in good yields. Temperature and the choice of the solvent are found to be critical for this transformation.



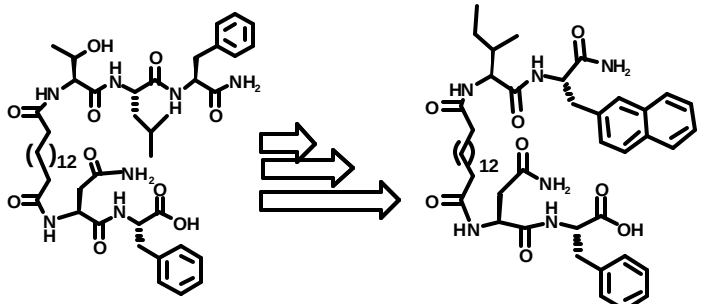
1 **2** **3**

Scheme 1

Development of Low Molecular Weight HIV-1 Protease Dimerization Inhibitors

Youseok Hwang, Song-Gil Lee, Jean Chmielewski
Purdue University
Department of Chemistry, 560 Oval Dr., West Lafayette, IN 47907-2038

The essential role of HIV protease in viral replication has made it a significant target for inhibition. The focus of our studies has been to target the dimerization interface of HIV-1 protease because disruption of the dimer will inhibit enzymatic activity. The initial strategy began with crosslinked peptides derived from the interface of HIV protease. Herein we describe the design of a focused library of agents based on a minimal pharmacophore for HIV-1 protease dimerization inhibition. A library of 70 compounds will be described. Screening and optimization of the most potent inhibitors led to compounds with Ki values in the 100-400 nM range. Fast generation of HIV-1 protease inhibitor library using disulfide bond formation will be introduced.



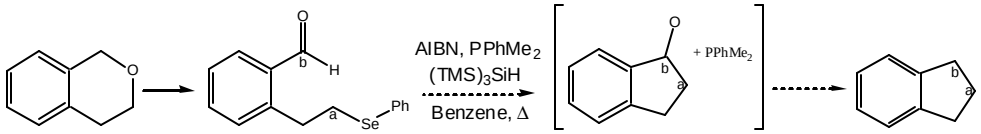
Dimerization Inhibitor
K_i = 3000 nM

Dimerization Inhibitor
K_i = 127 nM

A NEW USE OF CARBONYLS AS INDIRECT GEMINAL RADICAL ACCEPTORS AND PRECURSORS

Christina M. Longo[1], Kevin M. Shea[1], Melanie Bartow Wills[2]
[1]Smith College, Clark Science Center, Northampton, MA 01063
[2]Drew University, 36 Madison Avenue, Madison, NJ 07940

The aim of this project is the development of a new carbon-carbon bond forming radical reaction that will initially be tested on aldehyde **2** shown below. In the key radical reaction, the phenyl-selenium group will enable the formation of a radical at carbon **a** which will then react with the aldehyde to form the desired carbon-carbon bond between **a** and **b**. The second phase of the reaction sequence will involve removal of the oxygen by trapping the oxygen radical with a phosphine to ultimately produce a radical at carbon **b** that will be trapped by an intermolecular hydrogen donor to yield indan **(4)**.



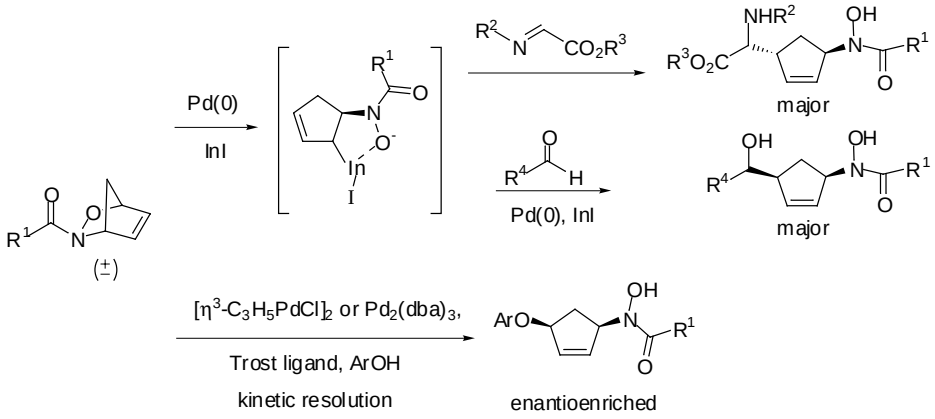
1 **2** **3** **4**

After the desired aldehyde had been prepared in five steps from isochroman **(1)**, the reaction of interest (**2→4**) was tested and yielded promising preliminary results. Once the reaction using aldehyde **2** is optimized by varying the nature of the phosphine and hydrogen donor, we will investigate the scope of this transformation by exploring the reactivity of a variety of carbonyl compounds in place of the aldehyde. We also plan to study the behavior of a radical at carbon **b** in tandem inter and intramolecular radical reactions. Overall, we hope to develop a general and flexible method for the use of carbonyls as indirect geminal radical acceptor/precursor systems.

Selective Reactions of π-Allyl Palladium(II) Intermediates Generated from *N*-Acylnitroso Diels–Alder Cycloadducts

Wenlin Lee and Marvin J. Miller*
University of Notre Dame, Department of Chemistry and Biochemistry
251Nieuwland Science Hall, Notre Dame, IN 46556-5670

The ring opened π-allyl palladium(II) species generated from *N*-Acylnitroso Diels–Alder cycloadducts have been found to undergo an umpolung when treated with indium(I) iodide and the resultant π-allyl indium(III) species would react with electrophiles such as aldehydes and imines with good diastereoselectivity. These π-allyl palladium(II) intermediates also reacted with kinetic resolution in the nucleophilic addition of phenols when Trost's ligand was used.



Dynamic and Thermodynamic Investigation of Aryllithium-Metalloid Ate Complexes: Study of their Role in Lithium-Metalloid Exchange Reactions.

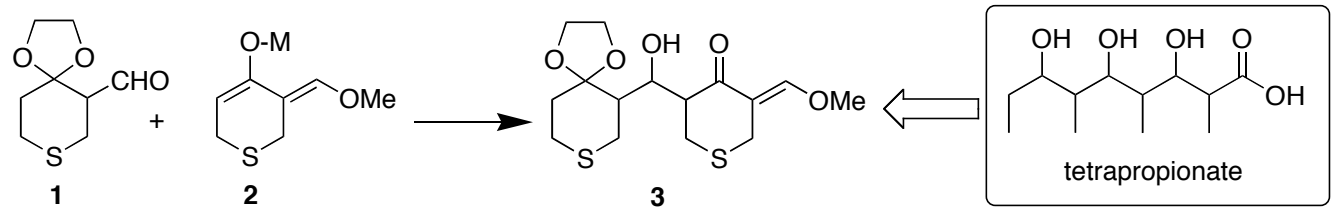
Martin J. Bevan, Hans J. Reich
University of Wisconsin-Madison
Department of Chemistry, Madison, WI 53706

Ate complexes, first proposed by Wittig, are presumptive intermediates in lithium-metalloid exchange reactions which are widely used to prepare many kinds of synthetically valuable organolithium reagents. Aryllithium ate complexes of Te, I, Sn and Sb were investigated and characterized via low temperature NMR Spectroscopy. DNMR analysis of the exchange of ArLi with Ar_2Te, Ar_3Sb, and ArI (Ar = phenyl, thienyl, or m-ethylphenyl) have shown ate complexes to be key exchange intermediates.

The Thiopyran Route to Polypropionates.
Stereoselective Aldol Homologations of Dipropionate Synthons

Dale E. Ward and Olukayode T. Akinnusi
University of Saskatchewan, Department of Chemistry
110 Science Place, Saskatoon SK S7N 5C9, CANADA

The use of cyclic sulfides as templates to facilitate certain chemical transformations is a well established strategy in organic synthesis. We have been investigating a thiopyran route to polypropionates involving sequential aldol reactions of tetrahydro-4H-thiopyran-4-one derivatives with tetrahydrothiopyran-3-carboxaldehyde derivatives, followed by desulfurization (cf. *J. Org. Chem.* **2002**, *67*, 1618). In this contribution we describe aldol reactions of the dipropionate synthons **1** and **2** under various conditions to give each of the four diasatereomers of tetrapropionate synthon **3** with good to excellent selectivity. Recent applications of this approach will be reported.



1 **2** **3**

M = Li, BR_2, $TiCl_3$, $SiMe_3$

Development of Facile Synthetic Pathways to Plasmenyl-type Lipids and Their Utilization in the Development of Acid Sensitive Vinyl Ether Based Pegylated Liposomes.

David H. Thompson, Junhwa Shin, Pochi Shum
Purdue University
Department of Chemistry, West Lafayette, IN 47907-2084

Facile and direct synthetic pathways to plasmenyl-type lipids for liposomal drug delivery and biological activity studies are described. Racemic plasmenylcholines and plasmenyl-type antitumor lipids were prepared via reductive cleavage reactions of acrolein acetals in the stereoselective formation of (*Z*)-vinyl ether linkages. Chiral plasmenylcholines were also prepared via lithioalkoxy allyl intermediates, generated from allyl ether with *sec*-BuLi, in the key (*Z*)-vinyl ether bond formation step. These two (*Z*)-vinyl ether bond forming reactions were successfully applied for the preparations of PEG-lipid conjugates linked via (*Z*)-vinyl ether bond and utilized for acid triggered release of liposomal cargo. New types of PEG-lipid conjugates having controlled acid sensitivity were rationally designed by utilizing some computational chemistry and reported kinetic data of vinyl ethers with different stereoelectronic properties. The contents release of liposomes containing these conjugates was measured by calcein release assay and the observed leakage rates suggest that control of the acid sensitivity of vinyl ether linked conjugate is a very promising approach for efficient cytoplasmic drug delivery.

A Simple Preparation of Diazo Esters

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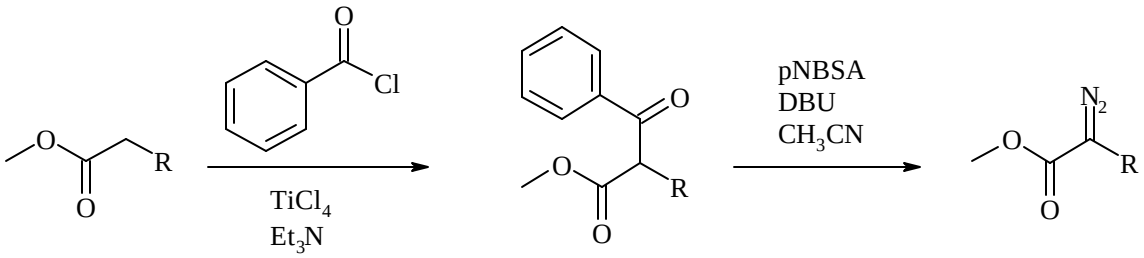
University of Delaware
Department of Chemistry and Biochemistry, Newark, DE 19716

The reaction of an ester **1** with benzoyl chloride at RT results in high yields of the benzoylated ester **2**. Diazo transfer of the crude benzoylated ester utilizing p-nitrobenzenesulfonyl azide, again at RT, affords the diazo ester **3** in good yield. Using this simplified procedure, it is easy to prepare gram quantities of diazo esters.



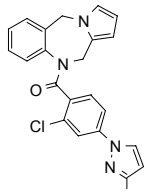
1 **2** **3**

METABOLITES OF A VASOPRESSIN V_2- RECEPTOR AGONIST AND ANTAGONIST

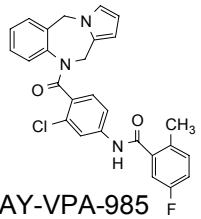
Albert J. Molinari*[†], Eugene J. Trybulski*, Jehan Bagli[‡], Susan Croce[‡], John Considine[§§], Fang Qi[§], Kadum Ali[§], William DeMaio[‡‡], and Lynne Lihotz[‡‡]

***Wyeth Research, Inc., Medicinal Chemistry, Collegeville, PA 19426; [‡]Medicinal Chemistry, Princeton, NJ 08543-8000; [§]Medicinal Chemistry, Pearl River, NY 10965; [§§]Chemical Development, Pearl River, NY 10965; [‡‡]Biotransformation, Collegeville, PA 19426**

Human vasopressin is a nona-peptide posterior pituitary regulatory hormone also known as anti-diuretic hormone. It directly and indirectly influences water balance, osmotic salt balance, and blood pressure through a series of vasopressin receptors. The V_2-receptors, located in the distal collecting tubule of the kidney, are pure aquaretic receptors balancing the re-absorption and elimination of the body's free-water content. Discovery programs were initiated to identify small molecule agonists and antagonists of this receptor subtype to treat medical conditions such as nocturnal enuresis for an agonist, and congestive heart failure and liver cirrhosis for an antagonist. The programs produced both a V_2-receptor agonist (WAY-VNA-932) and an antagonist (WAY-VPA-985), both of which underwent limited clinical trials. In the course of the project it became necessary to produce and test several metabolites associated with each program. The poster will outline the synthesis, structural validation, and testing results of several confirmed metabolites of WAY-VNA-932 and WAY-VPA-985.



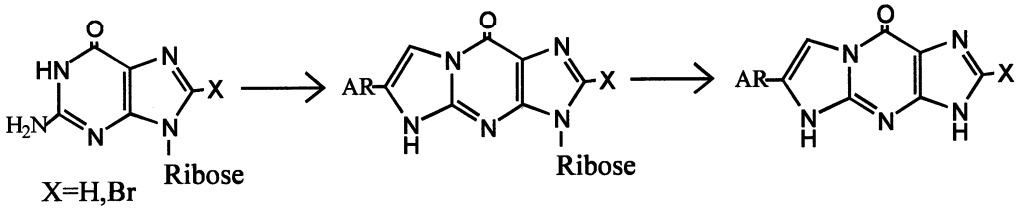
WAY-VNA-932



WAY-VPA-985

THE SYNTHESIS OF CERTAIN 3-(β-D-RIBOFURANOSYL)- 6-ARYL- 4,9-DIHYDRO-9-OXO-1H-IMIDAZO[1,2a]PURINES AND A STUDY OF THEIR ANTIVIRAL ACTIVITY

S.L. Jones [1], R.Thedford [2] and J.W. Jones [3]
1. Paul Quinn College, Department of Chemistry, Dallas, TX 75241
2. Clark-Atlanta University, Department of Chemistry, Atlanta, GA 30314
3. Baylor University, Department of Chemistry & Biochemistry, Waco, TX 76798

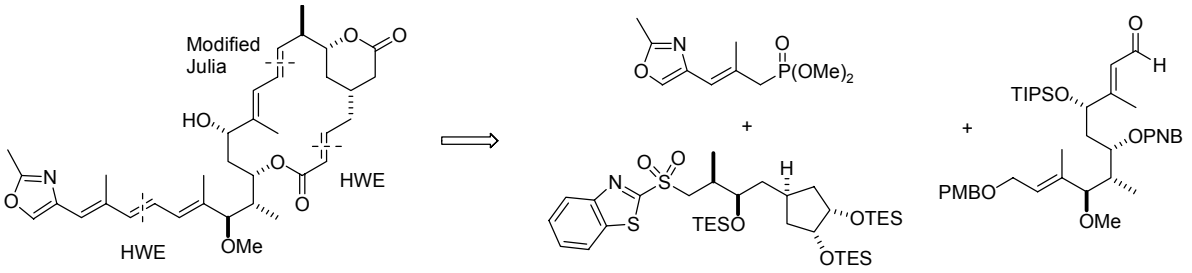


Our goal was to synthesize certain 3-(β-D-ribofuranosyl)- 6-aryl- 4,9-dihydro-9-oxo-1H-imidazo[1,2a]purines and evaluate their antiviral activity against HSV-1. A series of these so called "Y-bases" was prepared and their cytotoxicity also determined. This series focused on the preparation of a variety of aromatic substituents in position 6 of the tricyclic heterocycle. In addition, derivatives of the title compounds were synthesized including certain 2-bromo analogs and derivatives without the 3-ribosyl component. A comparison of the activity against HSV-1 was made between acylovir and the target compounds.

Stereoselective Total Synthesis of Antitumor Macrolide Rhizoxin D

Yueheng Jiang, Steven D. Burke, Jian Hong
Department of Chemistry, University of Wisconsin-Madison
1101 University Avenue, Madison, WI 53706

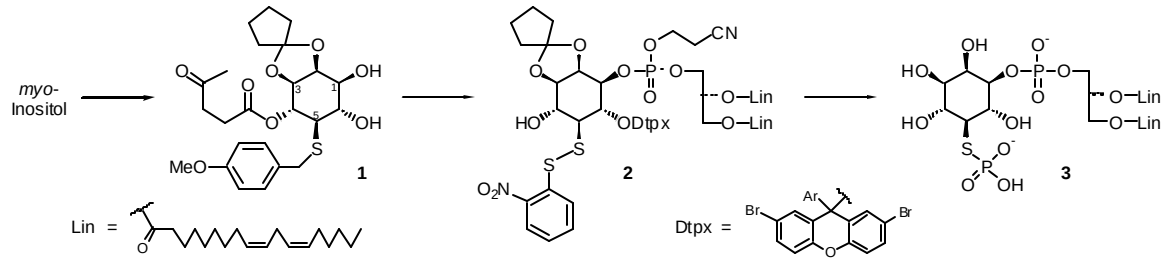
The rhizoxins constitute a class of antimitotic macrolides isolated from *Rhizopus Chinensis*. Rhizoxin binds tubulin at the vinca domain and interferes with the cell cycle by preventing tubulin polymerization. It is currently undergoing clinical evaluation. Our convergent total synthesis of rhizoxin D is described herein. Evans-Tishchenko 1,3-diol synthesis, modified Julia coupling, and intra- and intermolecular Horner-Wadsworth-Emmons (HWE) olefinations for construction of 16-membered macrolactone and all *E* triene oxazole sidechain are featured.



SYNTHESIS OF DEOXYTHIO *MYO*-INOSITOLS: PHOSPHATIDYLINOSITOL 5-PHOSPHOROTHIOLATES

Piers R.J. Gaffney, Paul Mendonça
Department of Chemistry, Imperial College London, Exhibition Road, London SW7 2AZ, United Kingdom

We report the first synthesis of phospho inositide phosphorothiolates. These were prepared from *myo*-inositol, taking care to regenerate the *myo*-configuration during replacement of oxygen with sulfur. The synthesis depends on the preparation of an appropriately fully-protected precursor that is then un-blocked in a two-step, basic then acidic treatment. This unique strategy was developed for compatiblity with the ubiquitous poly-unsaturation of mammalian phosphoinositides, but is versatile enough to preserve other sensitive functionalities.



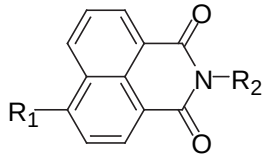
Key thioether **1** was elaborated to reactive disulfide **2** which, after total deprotection, may either be reduced to the free thiol or converted to 5-phosphorothiolate **3**.

Photochemical Protein Crosslinking with 1,8-Naphthalimides

R. Jeremy Woods, Jianxing Zhang, Charalene R. Green, Celeste Totten, Ae Gyeong Kang, Robert R. Kane

Department of Chemistry and Biochemistry and Center for Drug Discovery
P. O. Box 97348, Baylor University, Waco, TX 76798

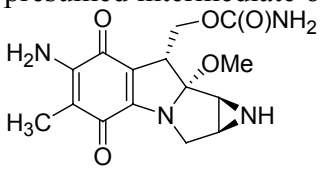
1,8-Naphthalimides are photochemically active molecules with diverse biological uses including tissue bonding and protein crosslinking. Numerous hydrophilic derivatives of 1,8-naphthalimide, with substituents on the imide nitrogen and the 4-position of the naphthalene moiety, have been synthesized and evaluated for relative abilities to photochemically induce protein crosslinking. Studies with proteins and free amino acids have been carried out in order to determine the molecular basis for crosslink formation. Tyrosine, tryptophan, and histidine have been demonstrated to be the most reactive amino acids. One of the products formed upon photochemical modification of the protein ribonuclease A has been identified as dityrosine, a well known marker of oxidative damage to proteins. Studies are underway to identify other contributing crosslinks and to delineate the molecular mechanisms of the photochemical and subsequent dark reactions leading to the crosslinks.



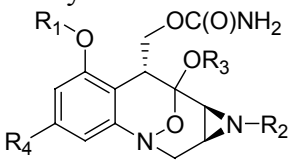
A STUDY TOWARD A TOTAL SYNTHESIS OF AN AZIRIDINOMITOSENE DERIVATIVE OF FK317

Edwin Vedejs and Musong Kim*
Department of Chemistry, University of Michigan
930 North University Ave
Ann Arbor, MI 48109

Mitomycin C, **1** is an important chemotherapeutic agent against a variety of solid tumors. The Fujisawa Pharmaceutical Co. isolated the related antitumor agents, **2** and **3**, in the late 1980's from *Streptomyces sandaensis.* In 1998, FK317 (**5**) was developed and shown to possess better antitumor activity than Mitomycin C. Although FK317 is now in advanced human clinical trials in Japan, specific mode of action is not well understood. In an effort to understand the mechanism of the FK317 we are attempting to prepare presumed intermediate **6** synthetically.

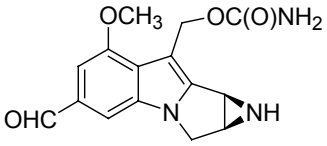


1
Mitomycin C



2 (FR66979) R_1 = H R_2= R_3 = H R_4 = CH_2OH
3 (FR900482) R_1 = H R_2= R_3 = H R_4 = CHO
4 (FK973) R_1 = Ac R_2= R_3 = Ac R_4 = CHO

5 (FK317) R_1 = CH_3 R_2= R_3 = Ac R_4 = CHO



6

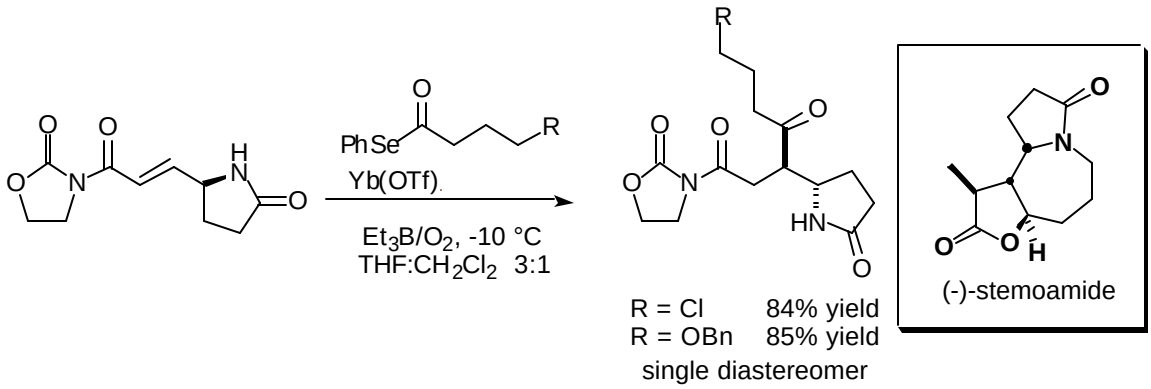
CONJUGATE RADICAL ADDITIONS ONTO g-CHIRAL SUBSTRATES: PROGRESS TOWARDS THE TOTAL SYNTHESIS OF (-)-STEMOAMIDE

Tara R. Rheault[1], Mukund P. Sibi[2]

[1]GlaxoSmithKline, 5 Moore Drive, Research Triangle Park, North Carolina 27709

[2]Department of Chemistry, North Dakota State University, Fargo, North Dakota 58105

As part of our continuing effort to develop new stereoselective radical methodologies, we examined Lewis acid-facilitated conjugate radical additions onto γ-chiral substrates using both acyl radicals and α-alkoxy radicals derived from phenyl selenides. The resultant relative stereochemistry of the radical addition at either the newly established β-center (acyl radical additions) or the β and γ-centers (α-alkoxy radical additions) were evaluated. Additionally, we extended this methodology towards the total synthesis of (-)-stemoamide.



HELICOMIMETIC PEPTIDES AS SELECTIVE, NANOMOLAR INHIBITORS OF PROTEIN-PROTEIN INTERACTIONS

Arno F. Spatola[1], Amit K. Galande[1], Kelli Bramlett[2] and Thomas P. Burris[2]

[1]Department of Chemistry and Institute for Molecular Diversity and Drug Design, University of Louisville, Louisville, KY 40292 U.S.A. and [2]Lilly Research Laboratories, Indianapolis, IN 46285 U.S.A.

Short linear peptides tend not to form stable α-helices. Yet a short, helical pentapeptide, Leu-X-X-Leu-Leu is an important structural motif found in coactivator proteins that bind to an open groove in a wide variety of nuclear receptors. Using a D-Cys, L-Cys intramolecular disulfide bridge, we have designed nonapeptides that we term helicomimetics that are not helical in water but that are induced to form a helix when bound to their target receptors [1]. One of our most potent disulfide-bridged analogs (**1**) shows a K*i* of 12 nM against estrogen receptor-alpha (ERα) [1]. While all peptides contain the 3 leucine side chains, selectivity is observed with respect to the two receptor forms, ERα and ERβ when residues adjacent to the pentapeptide core are varied. These constrained peptide analogs may represent a novel approach for the control of nuclear receptor mediated protein-protein interactions and more specifically, breast cancer.

1 H-Arg-cyclo[D-Cys-Ile-**Leu**-Cys]-Arg-**Leu**-**Leu**-Gln-NH_2

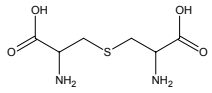
1. Spatola, A.F., Leduc, A., Wittliff, J.L., Taylor, K.G. *Proceedings of the 17th American Peptide Symposium*, 2001 P. 442 (2001).

SYNTHESIS OF THIOETHER-BRIDGED PEPTIDES VIA A NOVEL REACTION OF BASE-ASSISTED DESULFURIZATION

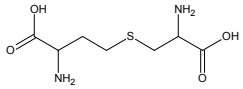
Amit K. Galande and Arno F. Spatola

Department of Chemistry and Institute for Molecular Diversity and Drug Design University of Louisville, Louisville, KY 40292 U.S.A.

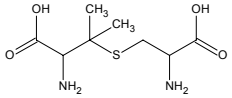
Under mild alkaline conditions, some disulfide-bridged proteins undergo facile desulfurization to produce thioether products. During our synthetic work on disulfide helicomimetics [1], we noted that mild alkaline conditions (3% aqueous ammonium hydroxide) employed for disulfide bond formation surprisingly yielded a thioether cyclic peptide. This 'base-assisted desulfurization' appears to proceed through a β-elimination where a backbone proton is abstracted by base forming a dehydroalanine residue. This is followed by Michael addition of thiolate anion to accomplish macrocyclization [2]. The cyclic thioether amino acid formed in the case of cystine disulfide peptides is known as lanthionine. More importantly, desulfurization of mixed cysteine-homocysteine disulfide peptides yields cystathionine within the peptide chain while mixed cysteine-penicillamine disulfide-bridged peptides yield "penthionine." Stereochemical aspects have been studied using 2-D NMR spectroscopy and amino acid analyses and reveal that some of the Michael additions are surprisingly stereoselective.



Lanthionine



Cystathionine



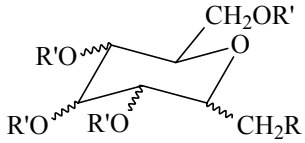
Penthionine

1. Spatola, A.F., Leduc, A., Wittliff, J.L., Taylor, K.G. *Proceedings of the 17th American Peptide Symposium*, 2001 P. 442 (2001).
2. Galande, A.K., Spatola, A.F. *Lett. Pept. Sci.*, 8, 247 (2001).

ALKYLATED C-SUGARS AS NOVEL BIOCONJUGATES

Florence M. Brunel, K. Grant Taylor, and Arno F. Spatola
Department of Chemistry and the Institute for Molecular Diversity and Drug Design
University of Louisville, Louisville, KY 40292 U.S.A.

We have recently reported the synthesis of a new class of bioconjugates that represent low molecular weight, compact, PEG-like replacements, based on a carbohydrate template. To improve overall stability, we selected C-sugars as the core unit. C-sugars are simply stabilized analogues of O-glycosides, where the exocyclic oxygen is replaced by a carbon unit. To reduce the H-bonding potential, often a detriment to membrane permeability we alkylated the 2, 3, 4, and 6 position hydroxyls. When attached to a recently designed helicomimetic peptide, we observed a surprising set of bioassay results, including improved inhibitory activity in an estrogen receptor coactivator inhibition assay [1]. More recently we have confirmed that the attachment of the bioconjugate to a peptide results in an increase in lipophilicity. These compounds may prove useful in modulating such properties as solubility, lipophilicity and biological activity of the various molecules to which they may be attached.



R= $-CO_2H$, $-NH_2$
R'= $-CH_3$, $-CH_2CH_3$, $-CH_2CF_3$...

1. Spatola, A.F., Leduc, A., Wittliff, J.L., Taylor, K.G. *Proceedings of the 17th American Peptide Symposium*, 2001 P. 442 (2001).
2. Brunel, F.M., Leduc, A.-M., Mashuta, M.S., Taylor, K.G., and Spatola, A.F., "Synthesis and Application of Alkylated C-Sugars as Peptide Bioconjugates," *Letters in Peptide Science*, Accepted for publication December 2002.

SEMI-ORHOGONAL SYNTHESIS OF A TETRACYCLIC ANTIMICROBIAL ANALOG

Peteris Romanovskis and Arno F. Spatola
Department of Chemistry and Institute for Molecular Diversity and Drug Design, University of Louisville, Louisville, KY 40292 U.S.A.

Recently Selsted and coworkers [1] reported the isolation of the first example of a head-to-tail cyclic peptide discovered in mammals (rhesus macaque leukocytes). This 18 amino acid peptide (**1**) contains three parallel disulfide bridges and possesses impressive antimicrobial activity with an IC_{50} of <2 μg/mL against S. aureus. We have previously reported the solid phase synthesis of cyclic peptides and libraries using an approach featuring side chain attachment with on-resin cyclization. But none of the residues we reported (Asp, Glu, Asn, Gln, Ser, Orn, or Tyr) are present in peptide **1**. Thus we have targeted a closely related analog with a Gln^{17} in place of Thr^{17} in order to assess a semi orthogonal synthetic strategy. In our approach we use the Fmoc method of SPPS and the methoxybenzyl-protecting group for cysteines at 3, 7, 12, and 16 and trityl for cysteines at 5 and 14. Our rationale is to test whether formation of a bicyclic analog will uniquely force formation of the remaining tetracyclic structure. Our findings tentatively confirm that this strategy has provided the desired cyclic peptide analog.

cyclo(Gly-Phe-Cys-Arg-Cys-Leu-Cys-Arg-Arg-Gly-Val-Cys-Arg-Cys-Ile-Cys-Thr-Arg)
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18

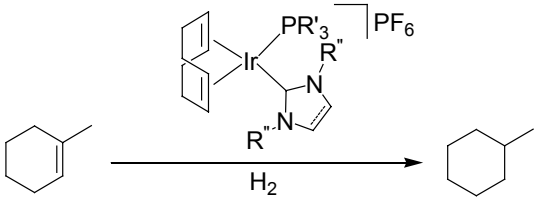
Antimicrobial Peptide **1**

1. Tang et al., *Science*, **286**, 498-503 (1999).
2. Romanovskis, P. and Spatola, A.F., *J. Peptide Res.*, **52**, 356-374 (1998).

CARBENE-PHOSPHINE COMPLEXES OF IRIDIUM: THEIR SYNTHESIS AND REACTIVITY TOWARD CATALYTIC OLEFIN HYDROGENATION

Leslie D. Vázquez-Serrano, Bridget T. Owens and Jillian M. Buriak*
Purdue University
Department of Chemistry, 560 Oval Drive, West Lafayette, IN 47907-2084

Highly active and selective hydrogenation catalysts that can effectively tackle even tetrasubstituted alkenes are important for pharmaceutical synthesis and macromolecular design. Many complexes capable of reducing mono- and disubstituted olefins and those with directing functionalities are known, but hydrogenation of simple tertiary and quaternary olefins has remained challenging. Until now, Crabtree's catalyst was the only precursor able to facilitate this transformation at room temperature under one atmosphere of hydrogen, yet suffers from a short lifetime under catalytic conditions (~1 h). Current efforts in our laboratory have yielded a first generation Ir based system with a phosphine/N-heterocyclic carbene ligand motif that accomplishes the hydrogenation of simple, highly-substituted alkenes under these conditions. Furthermore, this catalyst exhibits a longer lifetime than Crabtree's complex. We are presently developing even more reactive second generation complexes with different phosphine and N-heterocyclic carbene ligands, and non-coordinating anions. The most highly active species are being tested for reduction of imine and ketone substrates, notoriously difficult to hydrogenate under atmospheric conditions. Chiral derivatives under investigation will be discussed.

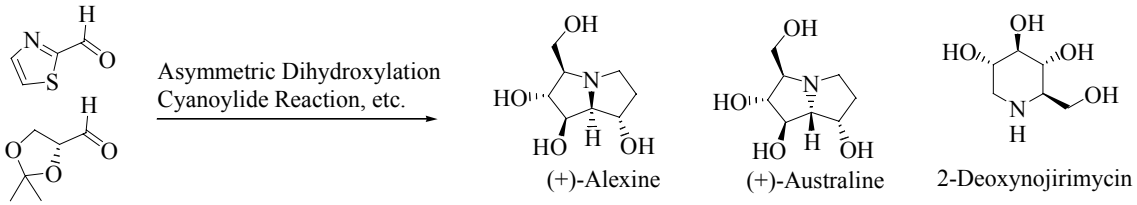


STEREOSELECTIVE SYNTHESIS OF POLY-HYDROXYLATED ALKALOIDS

Doo-Young Jung, Yong Hae Kim

Center for Molecular Design and Synthesis, School of Molecular Science(BK-21), Department of Chemistry, Korea Advanced Institute of Science and Technology, 305-701, Taejon, Republic of Korea

Poly-hydroxylated alkaloids have drawn much interest due to their potential biological activities and synthetic challenges imposed by their complex stereochemistry. Employing Sharpless asymmetric dihydroxylation and Wasserman's cyanoylide method as the key steps to construct molecular skeletons, we achieved concise and convergent synthesis of various poly-hydroxylated alkaloids from simple masked aldehyde equivalent.



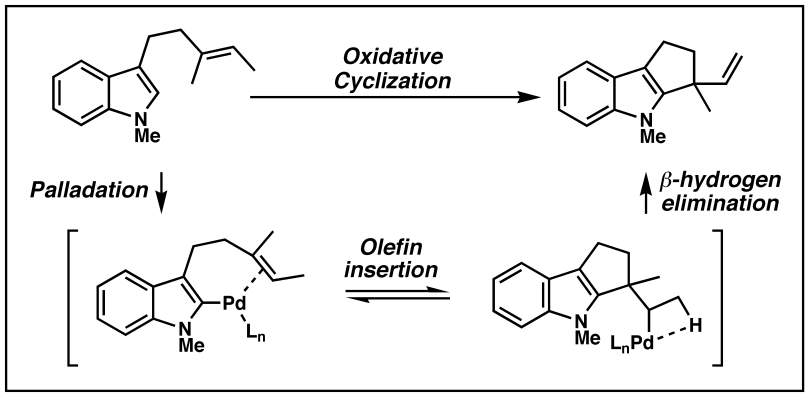
Norbornenyl-Tagged Reagents: Tools for Organic Synthesis

Andrew M. Harned,[1] *Paul R. Hanson,*[1] *Daniel L. Flynn*[2,3]
[1]**University of Kansas, Department of Chemistry**
1251 Wescoe Hall Drive, Lawrence, KS 66045-7582
[2] **NeoGenesis Pharmaceuticals, Inc. 840 Memorial Drive, Cambridge, MA 02139**
[3] **Currently at: Deciphera Pharmaceuticals, Inc., 1505 Wakarusa Drive, Lawrence, KS 66047**

Our latest results utilizing ring-opening metathesis polymerization (ROMP) as a tool for the purification of reaction products will be presented. In our approach, the norbornenyl ring system is utilized as a general chemical tag for incorporation into a wide variety of reagents, scavenging agents, capturing agents for phase-trafficking, and soluble supports. Two general strategies are being investigated: i) *in situ* ROM polymerization of norbornenyl-tagged monomers mediated by Grubbs ruthenium catalysts as an integrated and general purification operation, and ii) utilization of ROM polymerization to produce *high-load* functional oligomers with *tunable solubility profiles* that can be exploited in organic synthesis and chemical library production. Both scenarios involve solution-phase reactions, and both involve precipitation and filtration of the ROM polymer away from the reaction products.

PALLADIUM-CATALYZED C-H BOND FUNCTIONALIZATION: AEROBIC OXIDATIVE C-C BOND FORMING REACTIONS

*Eric M. Ferreira, Uttam K. Tambar, Brian M. Stoltz**
California Institute of Technology
Division of Chemistry and Chemical Engineering, Pasadena, CA 91125

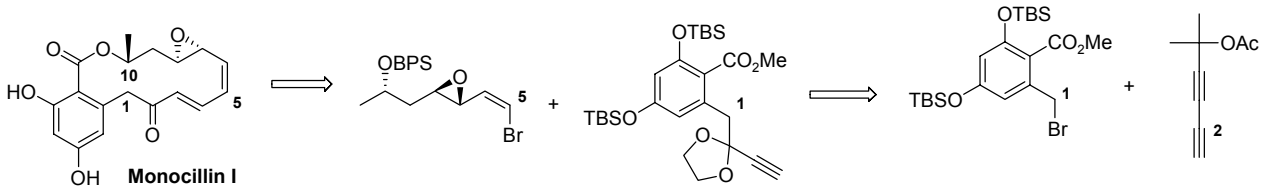


A palladium-catalyzed aerobic oxidative annulation of indoles will be described. Experiments show that a variety of factors influence these cyclizations, and in particular the electronic nature of the pyridine ligand is crucial. It is also remarkble that these oxidative cyclizations can proceed in good yield despite background oxidative decomposition patways, testament to the facile nature with which molecular oxygen can serve as the direct oxidant for Pd(0). We will also show that the mechanism most likely involves initial indole palladation (formal C-H bond activation) followed by migratory insertion and β-hydrogen elimination. This system and its application to other C-C bond forming transformations will be outlined.

STILLE COUPLINGS CATALYTIC IN TIN: APPLICATION TO THE TOTAL SYNTHESIS OF MONOCILLIN I

William P. Gallagher and Robert E. Maleczka, Jr.
Michigan State University
Department of Chemistry, East Lansing, MI 48824

Stille cross couplings are commonly employed in the preparation of natural products, new materials, etc. Despite the Stille's wide use, there are often problems associated with organostannanes (toxicity, cost, purification, etc). Our solution to the tin problem is a palladium catalyzed hydrostannation/Stille sequence that is catalytic in tin. To demonstrate our protocol's utility in the theater of total synthesis, we have embarked on a total synthesis of monocillin I. Specifically, our methodology is used in the construction of the C1–C2 and C4–C5 bonds. Recent progress in this study will be presented.



MOLECULAR STEREOCHEMISTRY: NEW DEVELOPMENTS IN THE DETERMINATION OF ABSOLUTE CONFIGURATION AND PREDOMINANT CONFORMATIONS OF CHIRAL MOLECULES IN SOLUTION PHASE

Prasad L. Polavarapu
Vanderbilt University
Department of Chemistry, Nashville, TN 37235

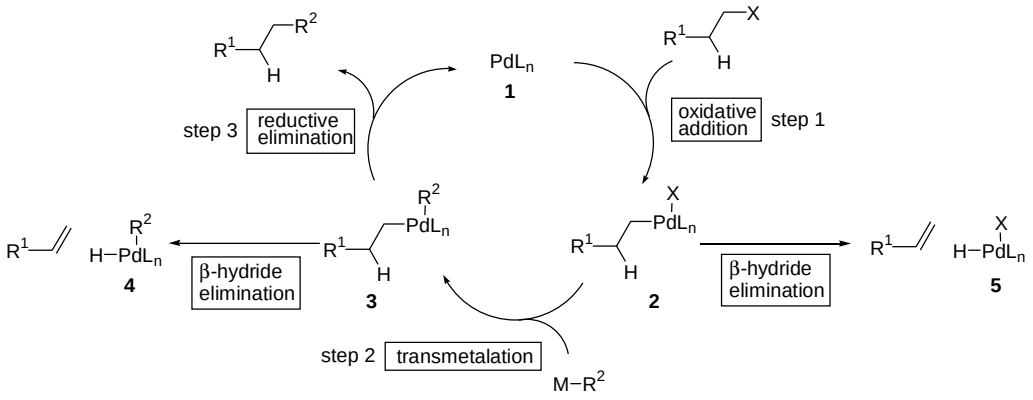
Conventionally, the absolute configuration of chiral molecules is deduced from either synthetic route used in the preparation of a chiral substance or X-ray crystal structures. In situations where individual enantiomers are separated on a chiral column or when crystals of sufficient quality cannot be obtained, one is faced with uncertainty in the absolute configuration. In the last few years, remarkable progress has been made in the deduction of absolute configuration of chiral molecules using vibrational circular dichroism[1], optical rotation[2], and vibrational Raman optical activity[3]. It is now possible to not only determine the absolute configuration unambiguously, but also to infer the predominant conformations in solution phase. In this presentation, an up-to-date summary of the recently developed capabilities to solve problems of absolute stereochemistry will be presented. The examples to be presented include a range of diverse molecules starting from the simplest chiral molecule, bromochlorofluoromethane, to large cyclic organic molecules.

[1]F. Wang, Y. Wang, P. L. Polavarapu, T. Li, J. Drabowicz, K. M. Pietrusiewicz, and K. Zygo, *J. Org. Chem* 67(8):6539 (2002);[2]P. L. Polavarapu, *Chirality* 14:768(2002);[3]P. L. Polavarapu, *Angewandte Chemie Int. Ed* 41(23),4544 (2002).

Mechanistic Studies of Palladium-Catalyzed Cross-Couplings of Alkyl Electrophiles Bearing β Hydrogens

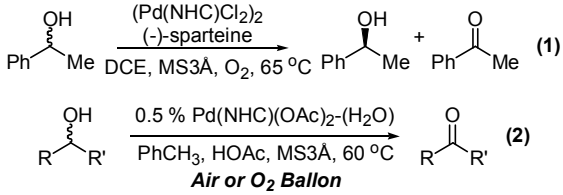
Ivory D. Hills, Matthew R. Netherton, Gregory C. Fu
Massachusetts Institute of Technology
Department of Chemistry, Cambridge, MA 02139

A proposed mechanism for the palladium-catalyzed cross coupling of alkyl electrophiles bearing β-hydrogens is presented. The isolation and characterization of key intermediates **1** and **2** is described, and an investigation determining whether by-product **5** can undergo reductive elimination to regenerate catalytically active **1** is also discussed.



Pd-Catalyzed Oxidation and Kinetic Resolution of Alcohols Using Molecular Oxygen

David R. Jensen, Matthew S. Sigman
University at Utah
Department of Chemistry, Salt Lake City, Utah 84112-0850

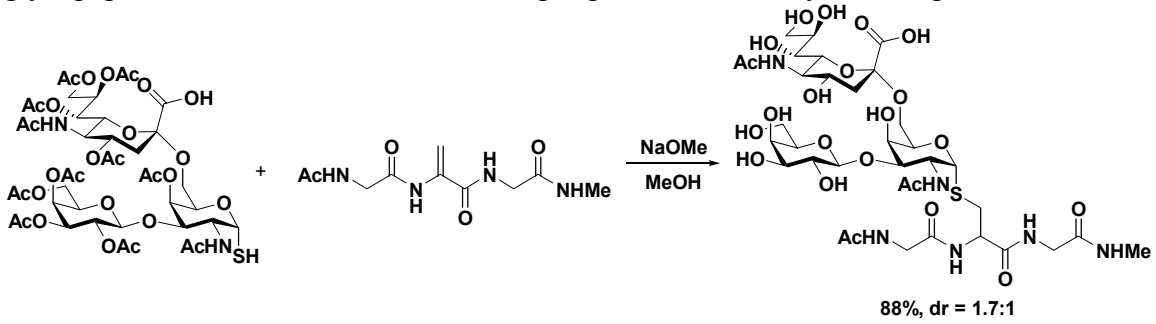


Using insight gained from the study of the mechanism of Pd-catalyzed alcohol oxidations, new catalysts for both the simple oxidation of alcohols and the oxidative kinetic resolution secondary alcohols have been developed. The catalyst for simple alcohol oxidation is more efficient than previous Pd-catalysts for alcohol oxidation, and oxidizes a variety of benzylic, allylic, and aliphatic alcohols using only 0.5 mol % of the catalyst (eq 1). Insight to why this catalyst is more effective is shown with an X-ray crystal structure where the catalyst has a bound water, implicating the catalyst can facilitate an intramolecular deprotonation. The oxidative kinetic resolution of secondary alcohols has been accomplished using 1:1 complexes of $PdCl_2$ and N-heterocyclic carbenes used in conjunction with the chiral base (-)-sparteine (eq. 2). The potential of these complexes in aerobic oxidations is highlighted by the use of a chiral Pd(II) complex and the chiral base (-)-sparteine to enhance the kinetic resolution of a racemic alcohol.

SYNTHESIS OF *S*-LINKED MUCIN GLYCOPEPTIDE CONJUGATES VIA CHEMOSELECTIVE CARBOHYDRATE-PEPTIDE LIGATION

Danica P. Galonic, Wilfred A. van der Donk, David Y. Gin**
Department of Chemistry, University of Illinois at Urbana-Champaign
Urbana, IL 61801

A novel strategy for oligosaccharide-peptide ligation has been established in which α-thio-analogs of mucin glycoconjugates can be readily accessed via site-selective Michael addition of complex oligosaccharide thiolates into dehydroalanine-containing peptides. This one-pot oligosaccharide peptide ligation maintains the α-anomeric stereochemical integrity of the carbohydrate donor, and proceeds under mild conditions, providing fully deprotected oligosaccharide-peptide conjugates that are direct isosteres of the naturally occurring mucins. The rapid convergent assembly of thio-isosteres of four mucin antigen glycopeptides, T_N, T, ST_N, and 2,6-ST, highlights the efficiency of the ligation.



CHEMISTRY IN THE BOUNDARY LAYER: THE SPINNING TUBE-IN-TUBE REACTOR SYSTEM

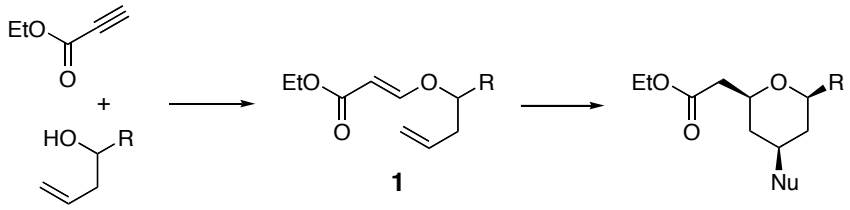
Stanley A. Sojka, Richard A. Holl, Alan N. McGrevy, Eric A. Gulliver, Nancy H. Hall
Holl Technologies Company, 1140 Avenida Acaso, Camarillo, California 93012

The boundary layer continues to be an interesting and controversial topic of current research activity. Despite differing attempts and interpretations of boundary layer characteristics, at least all agree that it is the zone of highest possible shear. Notwithstanding this generally accepted property of the boundary layer, very little is known about chemical reactions which take place in this interesting zone. This poster describes a unique process system called the Spinning-Tube-in-Tube, or STT^{TM}, process, which represents a paradigm shift away from the traditional approach of performing reactions. The patented STT^{TM} process system is a paradigm leap from volume-based to an area-based technology. Unusual acceleration of chemical kinetics have been observed when reactions are performed using this new way of doing chemistry. Applicability of the new STT^{TM} process will be across many chemical arenas. The Spinning Tube-in-Tube reactor system will be described, along with its major advantages, as well as several example reactions.

ACID PROMOTED PRINS CYCLIZATIONS OF VINYLOGOUS CARBONATES TO FORM TETRAHYDROPYRANS

Chad E. Bennett and David J. Hart*
Department of Chemistry, The Ohio State University
100 W. 18th Ave., Columbus, OH 43210

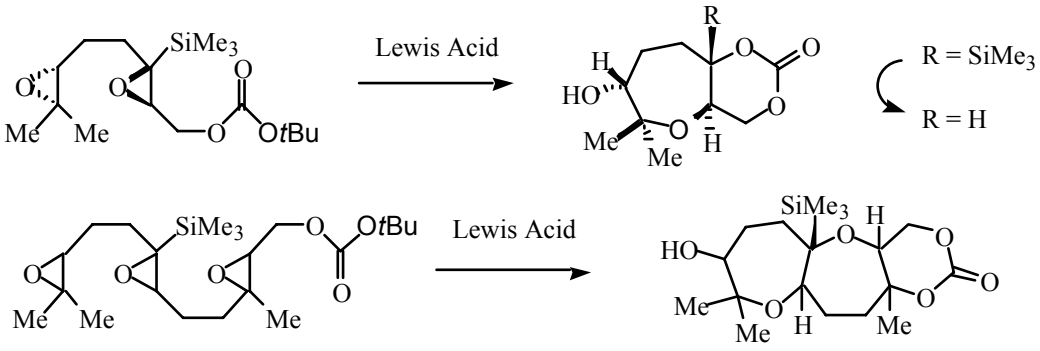
Vinylogous carbonates **1** undergo acid promoted Prins cyclizations to provide substituted tetrahydropyrans. The influences of the substituent **R** and the acid promoter have been examined. Furthermore, unique by-products of these cyclizations that reveal the presence of underlying equilibria have been isolated and identified.



Endo-Regioselective Tandem Oxacyclization of Polyepoxides: Silicon as a Hydrogen Atom Surrogate in the Synthesis of _Trans_-Fused Oxepanes

Jason Conley Valentine*, *Frank E. McDonald
Emory University
Department of Chemistry, Atlanta, GA 30322

Fused polycyclic ethers, a motif found in many marine natural products, have been hypothesized to arise biosynthetically from an oxacyclization cascade of a polyepoxide precursor. Our work has explored the use of chiral, non-racemic α,β-epoxysilanes to direct the regio and stereochemistry of Lewis acid promoted tandem oxacyclization of polyepoxides. We have also explored the stereospecific protiodesilylation of the silicon substituted oxepane products.

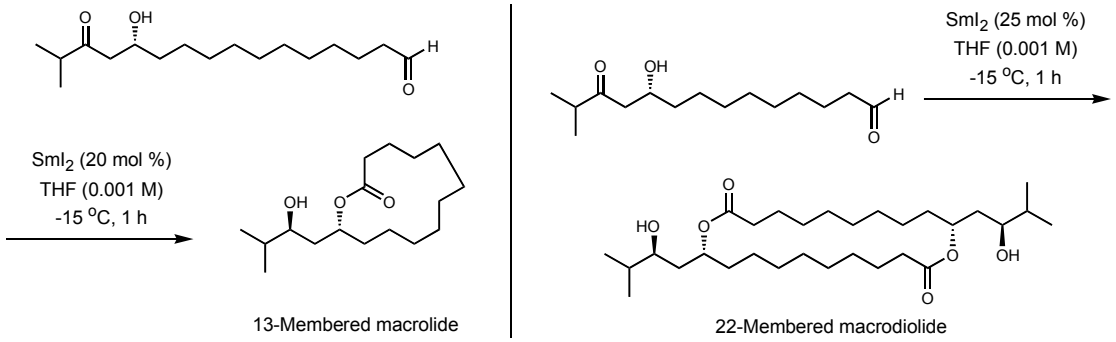


The Evans-Tishchenko Reaction: A One-Step Oxidation/Macrocyclization

Amos B. Smith, III, Dongjoo Lee, and Christopher M. Adams

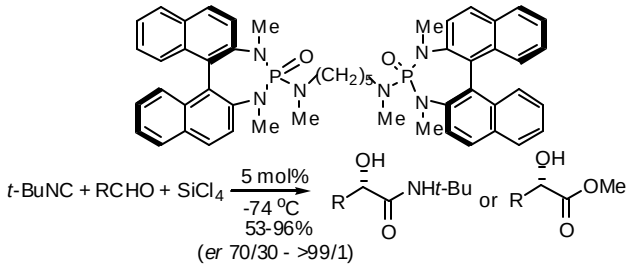
Department of Chemistry, Laboratory for Research on the Structure of Matter, and Monell Chemical Senses Center, University of Pennsylvania, Philadelphia, PA 19104-6323

Recently we have reported that the Evans-Tishchenko reaction provides an efficient and practical method to oxidize aldehydes possessing sensitive electron-rich heteroatoms to the corresponding esters (Smith, A. B., III; Lee, D.; Adams, C. M.; Kozlowski, M. C. *Org. Lett*. **2002**, *4*, 4539). Continued work in this area has led to a one-step oxidative macrocyclization tactic permitting facile access to monomeric and dimeric macrocycles.



The First Catalytic, Asymmetric a-Additions of Isocyanides: Lewis-Base-Catalyzed, Enantioselective Passerini-type Reactions

Scott E. Denmark, Yu Fan
Roger Adams Laboratory, Department of Chemistry, University of Illinois
600 South Mathews Avenue, Urbana, IL 61801

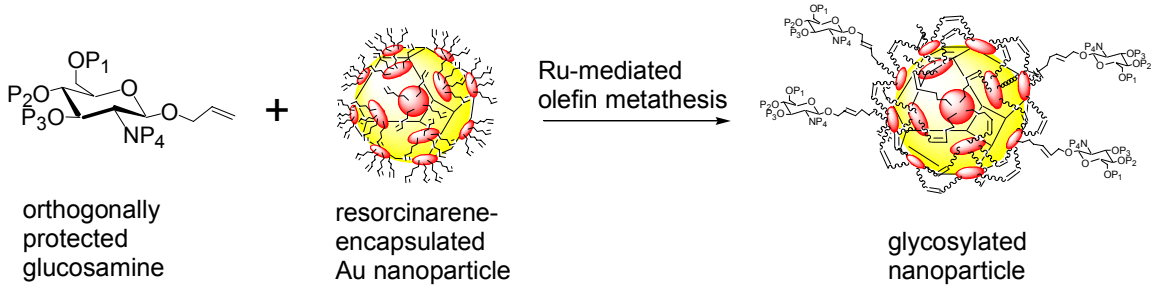


The first, catalytic, enantioselective α-additions of isocyanides to aldehydes have been demonstrated (Passerini-type reactions). The catalytic system of silicon tetrachloride and a chiral bisphosphoramide provided high yields and good to excellent enantioselectivies for the addition of *tert*-butyl isocyanide to a wide range of aldehydes (aromatic, olefinic, acetylenic, and aliphatic). Aqueous workup afforded the α-hydroxy *tert*-butyl amides whereas methanolic quench followed by basic workup afforded the α-hydroxy methyl esters.

TOWARD GLYCOSYLATED NANOPARTICLE LIBRARIES

Jesús M. Hernández-Torres, Balasubramanian Ramjee and Alexander Wei
Purdue University
Department of Chemistry, 560 Oval Drive, Purdue University, West Lafayette, IN 47907 USA.

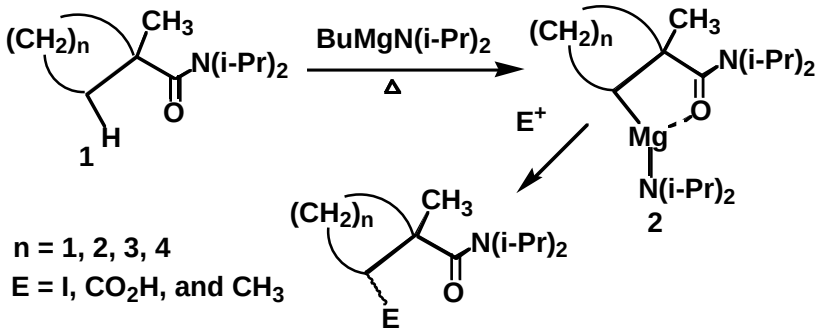
We present a strategy for generating libraries of sulfated carbohydrates on functionalized metal nanoparticles. Colloidal gold particles are extracted into organic solvents using alkene-terminated resorcinarene tetrathiols as surfactants. Olefin metathesis can crosslink the chemisorbed monolayers into robust, nondesorptive shells; it can also be used to attach ligands at variable surface densities. Here we perform olefin cross-metathesis and crosslinking in the presence of orthogonally protected alkenyl glycosides to produce glycosylated nanoparticles (GNs). Conditions for selective deprotection and sulfation can being applied to produce GN libraries with variable sulfation patterns. The physical properties of ligand-functionalized nanoparticles may offer several benefits for enhancing efforts in drug discovery and validation, and have intriguing potential in the design of multivalent inhibitors of cell-surface receptors.



β-Deprotonation/Magnesiation of Carboxamide Activated Cycloalkanes

Mao-Xi Zhang*, *Philip E. Eaton, Naruyoshi Komiya, and Cai-Guang Yang
Department of Chemistry, The University of Chicago, Chicago, IL 60637

We demonstrate for the first time that it is possible to directly deprotonate/magnesiate beta to an activating carboxamide group on saturated systems (**1**), even those that are unstrained. The reagent is $BuMgN(i\text{-}Pr)_2$: a stable, kinetically potent base, easily prepared cheaply. The carboxamide-stabilized amido-Grignards so made (**2**) are reactive towards numerous electrophiles and can be used to introduce new substitutes or functional groups with good stereoselectivity.

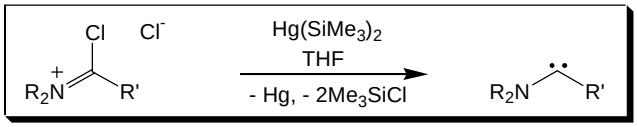


NEW APPROACH TOWARDS AMINO CARBENES

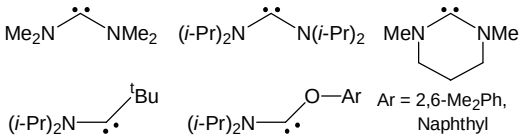
Michael Otto
Guy Bertrand
UCR – CNRS Joint Research Laboratory, University of California, Riverside

In the last 15 years, our understanding of carbene chemistry has advanced dramatically with the isolation of singlet carbenes.[a] The latter, especially diaminocarbenes, when used as ligands for transition metal centers, afford complexes with enhanced catalytic activity.[b] Here we report a new synthetic route allowing for the preparation of a variety of mono- and di-aminocarbenes.

Bis(trimethylsilyl)mercury reacts with various chloriminium chlorides leading to the corresponding carbenes:



Of particular interest, this new route allows for the characterization of the first alkylaminocarbene as well as the free bis(dimethylamino)carbene. In addition, we investigated the formation of alkali metal complexes with the 1,3-dimethyl-hexahydropyrimid-2-ylidene. The NMR data show a shift to higher field due to complexation.[c]

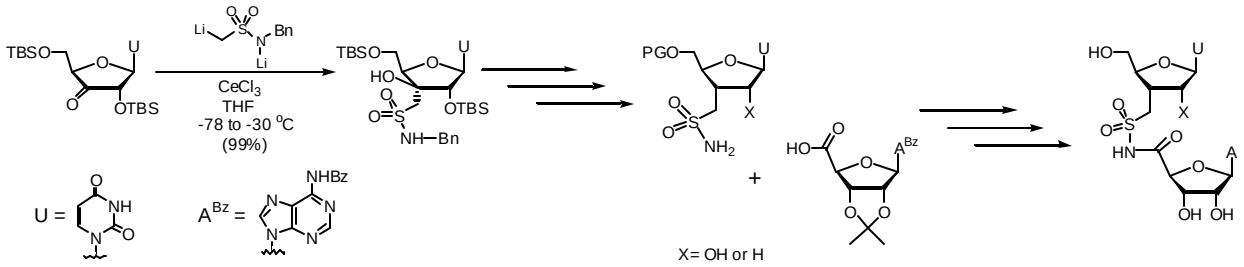


a) Bourissou, D.; Guerret, O.; Gabbai, F.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39; Arduengo III, A. J.; Harlow, R. L.; Kilne, M. *J. Am Chem. Soc.* **1991**, *113*, 361; b) Herrmann, W. A. *Angew. Chem. Int. Ed.* **2002**, *41*, 1290 ; Jafarpour, L. Nolan, S. P. *Adv. Organomet. Chem.* **2000**, *46*, 181; c) Alder, R. W.; Blake, M. E.; Bortolotti, C.; Bufali, S.; Butts, C. P.; Linehan, E.; Oliva, J. M.; Orpen, G.; Quayle, M. J. *Chem. Commun.* **1999**, 241.

METHODOLOGIES DIRECTED TOWARD AND THE SYNTHESIS OF *N*-ACYL SULFONAMIDE-LINKED DINUCLEOSIDES AS POTENTIAL INHIBITORS OF RIBONUCLEASE A

David C. Johnson II & Theodore S. Widlanski
Indiana University at Bloomington
Department of Chemistry, Bloomington, IN 47405

Some of the most potent *in vitro* inhibitors of RNase A are dinucleosides possessing pyrophosphate functionality. However, this functional group may be unsuitable for use *in vivo.* The disulfonimide, *N*-acyl sulfonamide and imide functional groups have the potential to be *in vivo*-stable surrogates of the pyrophosphate functional group. To that end, the synthesis of the first *N*-acyl sulfonamide-linked dinucleosides in ribo- and deoxyribo-forms is presented. New methodology for the condensation of sulfonamides with 5′-nucleoside carboxylic acids is presented. Additionally, methodology is presented for $CeCl_3$-mediated addition of sulfonamide dianions to carbonyl compounds of biological interest.



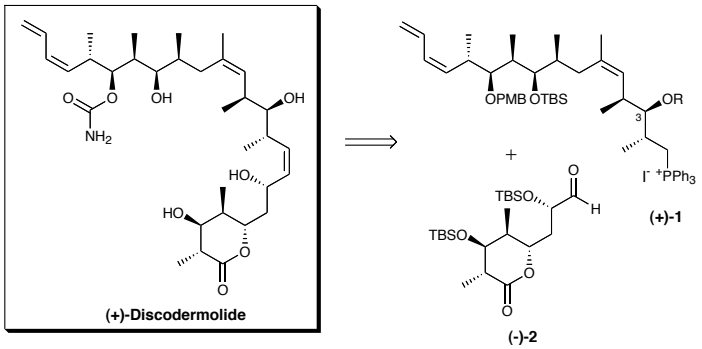
Discodermolide Synthetic Studies. Large Scale Synthesis of Discodermolide without High Pressure.

Amos B. Smith, III, [*] ***Tomoyasu Hirose, Ignacio Brouard, Scott Freeze, Mark Burlingame,*** [‡] ***Simon Shaw,*** [‡] ***Kurt Sundermann*** [‡]

Department of Chemistry, University of Pennsylvania, Philadelphia, PA 19104-6323

[‡]**Kosan Biosciences, Inc., Hayward, CA 94545**

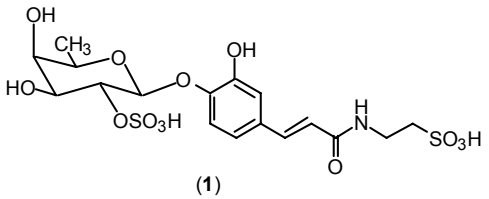
The polyhydroxylated lactone (+)-discodermolide, is a potent microtubule stabilizing agent that was first isolated from the marine sponge *Discodermia dissoluta*. It presents biological activity similar to that of clinically proven chemotherapeutic Taxol. As such, there is a demand for large quantities of this medicinally important compound to allow for clinical evaluation. Our synthetic strategy, which has been proven on a moderately large scale (1.0 g), calls for a key Wittig coupling between salt **(+)-1** and aldehyde **(-)-2**. The scalability of the synthesis of salt **(+)-1** was hindered by the necessity to use ultra-high pressure conditions in order to minimize an undesired intramolecular cyclization byproduct. Our new strategy obviates the need for ultra-high pressure, allowing salt formation under practical, scalable conditions.



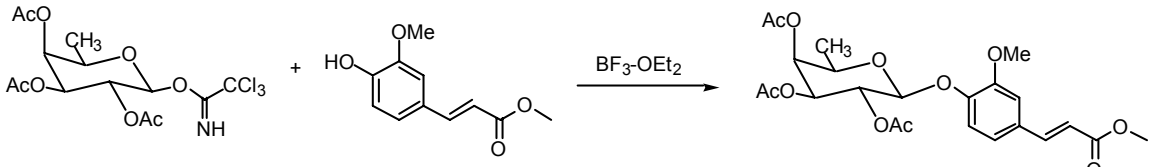
Studies Toward the Synthesis of the Saccharomicin Aglycon.

Joseph M. Pletcher, and Frank E. McDonald*
Emory University
Department of Chemistry, Atlanta, GA 30322

The structures and relative configuration of the novel heptadecaglycoside antibiotics Saccharomicins A and B were elucidated in 1998. With an aim to determine the absolute configuration of the carbohydrate components, we are exploring the synthesis of the monoglycoside degradation product (**1**). Schmidt glycosylation with triacetoxy-fucose trichloroimidate and 3-hydroxy-4-methoxy-cinnamic methyl ester stereoselectively afforded β-glycoside (**2**) in 96% yield. Progress towards the fully elaborated monoglycoside aglycon will be presented.



(**1**)



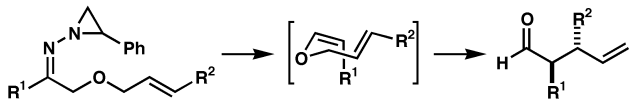
(**2**)

DEVELOPMENT OF CASCADE REACTIONS INVOLVING DIAZO COMPOUNDS: TANDEM BAMFORD-STEVENS-CLAISEN AND TANDEM WOLFF-COPE REARRANGEMENTS

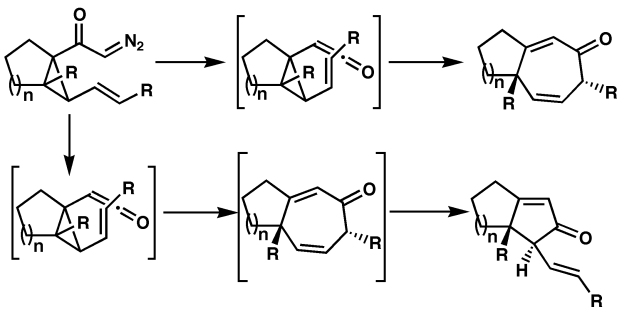
*Jeremy A. May, Richmond Sarpong and Brian M. Stoltz**
Arnold and Mabel Beckman Laboratories of Chemical Synthesis
California Institute of Technology, Division of Chemistry and Chemical Engineering
Pasadena, CA 91125

A research program utilizing diazo intermediates in a variety of cascade reactions is ongoing in our laboratory. Two applications are highlighted. The tandem Bamford-Stevens-Claisen reaction has been developed in the context of demonstrating the in situ generation of carbenes from protected hydrazones. The reaction proceeds with high yields and good diastereoselectivity for a variety of substrates. Suitable substrates will further undergo Cope or ene reactions after the Claisen rearrangement in a trio of reactions. The tandem Wolff-Cope rearrangement of cyclopropane fused bicycles affords [n,7] bicycles with appropriately situated functionality, providing an efficient entry into several natural product classes. Depending on the mode of activation, [n,5] bicycles can also be accessed by a subsequent 1,3-acyl migration.

Bamford-Stevens-Claisen



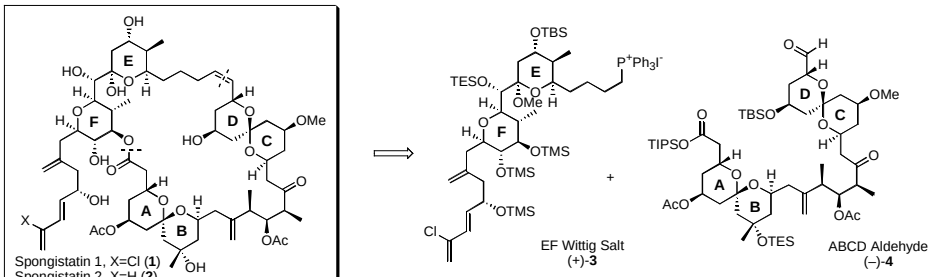
Tandem Wolff-Cope/1,3-Acyl Shift Rearrangement



Spongistatin Synthetic Studies. An Efficient Second-Generation Construction of an Advanced ABCD Intermediate, Fragment Union, and Final Elaboration to (+)-Spongistatin 1

Amos B. Smith, III, Chris Sfouggatakis, Wenyu Zhu, Shohei Shirikami, Victoria Doughty, and Clay Bennett.
Department of Chemistry, University of Pennsylvania
Philadelphia, PA 19104-6323

The spongistatins (a.k.a. altohyrtins) comprise an important family of architecturally unique bis-spiroketal macrolides that display extraordinary (subnanomolar) antitumor activities against a variety of highly chemo-resistant tumor cell lines. Due to their remarkable biological profile and extremely limited supply, the spongistatins have been the focus of considerable attention among the chemical and biological communities. ecently, we have achieved a preparatively useful synthesis of the advanced BCD fragment ( )-**4**, taking advantage of our multicomponent dithiane coupling tactic. ittig union with the phosphonium salt ( )-**3**, followed by macrolactonization and global deprotection afforded ( )-spongistatin 1 (**1**). summary of these results, as well as progress towards a modified synthesis of ( )-**3** will be presented.

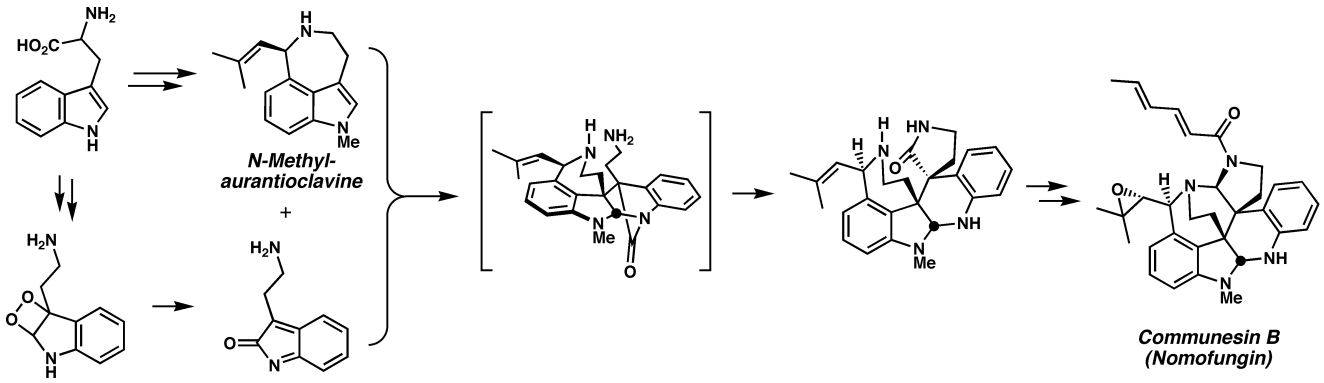


Smith, . B., hu, . Shirakami, S. Sfouggatakis, C. Doughty, . . Bennett, C.S. Sakamoto, . *Org. Lett.* **2003**, *5*, 1.

PROGRESS TOWARD THE TOTAL SYNTHESIS OF COMMUNESIN B (A.K.A. NOMOFUNGIN)

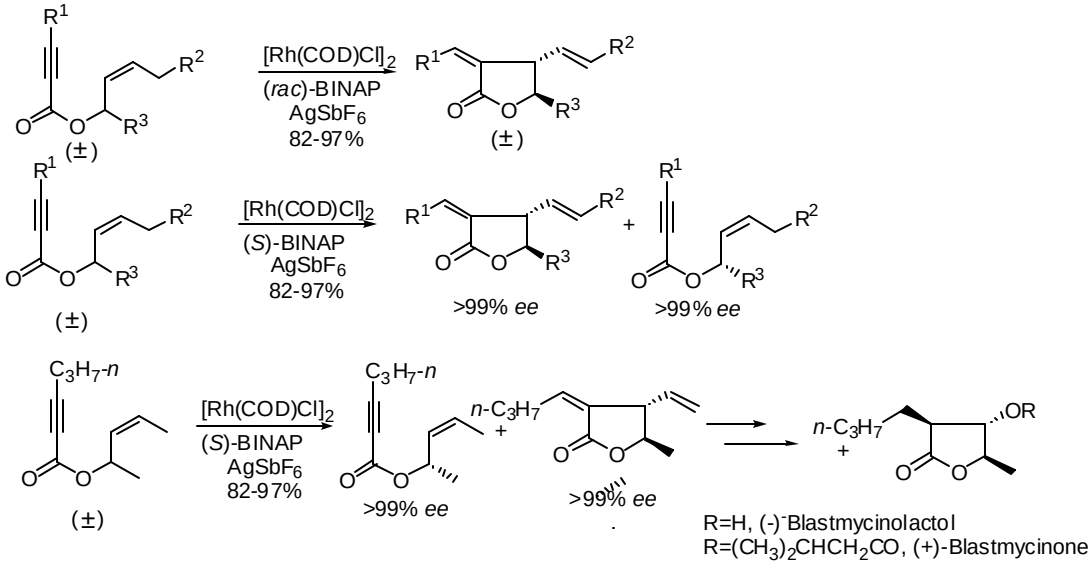
*Jeremy A. May, Ryan K. Zeidan, and Brian M. Stoltz**
Arnold and Mabel Beckman Laboratories of Chemical Synthesis
California Institute of Technology, Division of Chemistry and Chemical Engineering
Pasadena, CA 91125

The development of an approach to the alkaloid communesin B is presented. The approach is based on considerations of a possible biosynthetic sequence involving an oxidative coupling of tryptamine with a derivative of the ergot alkaloid aurantioclavine. Structure revision is also suggested for the recently isolated microfilament disrupting alkaloid nomofungin. A novel inverse-demand hetero Diels-Alder reaction using tryptophan-derived reactants forms the core of our synthetic hypothesis. Recent results show that similar Diels-Alder reactions can be carried out in the laboratory and that they are amenable to a high degree of substitution. A significant portion of the core structure of communesin B/nomofungin has been constructed using this strategy.



Highly Efficient Kinetic Resolution of Enynes Ester and Enantioselective Syntheses of ployfunctional a-Alkylene-g-butyrolactones via Rh(I)-catalyzed cycloisomerization ? Application to Formal Synthesis of (-)-Blastmycinolactol and (+)-Blastmycinone

Aiwen Lei, **Minsheng He** and Xumun Zhang*,
The Pennsylvania State University
Department of Chemistry, 152 Davey Laboratory, University Park, PA 16802.



As a type of important building block for the syntheses of biological organic compounds, such as alkaloids, macrocyclic antibiotics, pheromones, antileukemics and flavor components, the syntheses of ployfunctional, enantiomerically pure γ-substituted γ-butyrolactone unit have been attracted substantial attention. Recently, palladium (II)-catalyzed C-C formation via carbocyclization of enynes to form γ-lactones has shown its potential efficiency. Extensive studies on transition metal-catalyzed cycloisomerization have also been carried out, however, only a Rh(I)-system has been used to make γ-lactones. Furthermore, there are only few examples dealing with the formation of chiral γ-lactones. We report a highly efficient kinetic resolution and enantioselective cycloisomerization for the syntheses of ployfunctional γ-substituted lactones in over 99% *ee* and our approach for the syntheses of (-)-Blastmycinolactol and (+)-Blastmycinone.

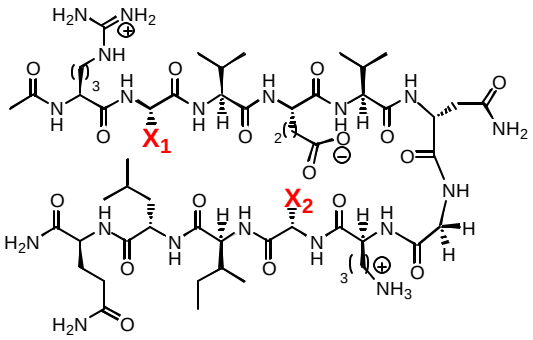
ION BINDING AND TRANSPORT BY SYNTHETIC MOLECULAR ASSEMBLIES

Frank W. Kotch, Vladimir Sidorov, Jeffery T. Davis
Department of Chemistry and Biochemistry, University of Maryland
College Park, Maryland 20742

Molecules that self-assemble into functional structures that bind and/or transport ions will be described. *Ion Binding*: A calix[4]arene-guanosine conjugate (CG **1**) was shown to dimerize in $CDCl_3$ when washed with H_2O or aqueous alkali halide solutions. The H_2O-dependent dimer functioned as a self-assembled ditopic receptor, capable of binding alkali halide salts. In the presence of $NaBPh_4$, however, CG **1** formed noncovalent polymers. Both the dimer and polymer are held together by intermolecular G-quartets. The 1,3-*alt* calix[4]arene scaffold preorganizes two appended guanosine moieties of one molecule to form quartets with two guanosines of another molecule upon cation binding, thus facilitating dimerization or polymerization. The key finding was that the resulting supramolecular structure was anion dependent, i.e. CG **1** formed a dimer with halides and a polymer with BPh_4^-. *Ion Transport*: A calix[4]arene-tetrabutylamide (calix **2**) was shown to assemble in membranes into Cl^--selective ion channels. A crystal structure of a analogous derivative suggested that the calix[4]arene core was not essential for Cl^- transport. From a series of linear oligomers based on calix **2**, but lacking the calixarene core, trimer **3** was identified as the most potent transporter, capable of supporting Cl^- transport across liposomal membranes at 6x the rate supported by calix **2**. This proved that the calix[4]arene core was not essential for the Cl^- transport function. Unlike calix **2**, trimer **3** generated a stable transmembrane potential across liposomes experiencing a Cl^- gradient.

When is a Hydrophobic Interaction NOT a Hydrophobic Interaction??Examples in b-Hairpin Peptides

Chad D. Tatko and Marcey L. Waters
University of North Carolina at Chapel Hill
Department of Chemistry, Chapel Hill, North Carolina 27599



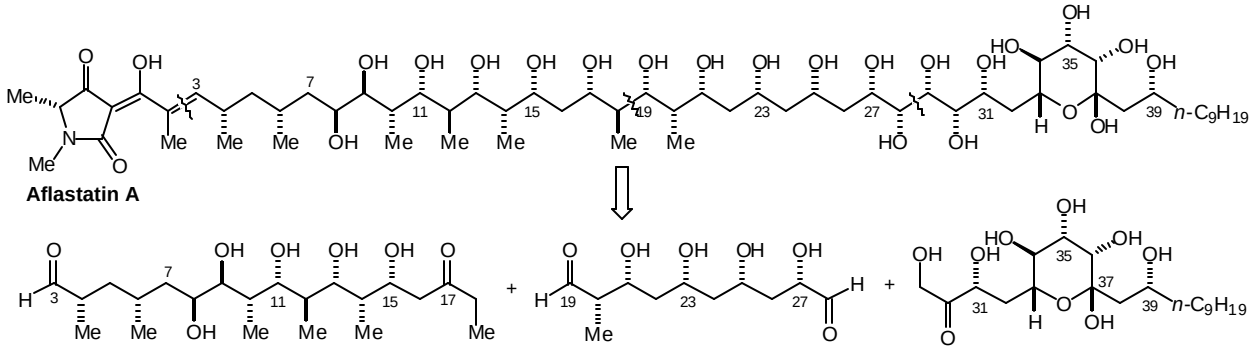
X1: Phe, Trp, Cha **X2**: Arg, Lys, Nle

Protein stability arises from the interplay of many weak forces. The shortest model of a β-sheet is an antiparallel β-hairpin and can be used to probe various non-covalent interactions. Cation-π interactions have been observed in the Protein Databank and implicated in the stabilization of protein structure, even with solvent accessibility. We sought to probe the role of the hydrophobic and cation-π interactions in a diagonal position of a β-hairpin with respect to geometry and stabilization. The interaction of Lys with an aromatic ring utilizes the Cε rather than the amine, with as many as 70% of all protein cation-π interactions involving the Cε. This has been interpreted as a hydrophobic interaction, however, we demonstrate that the amine significantly polarizes the methylene supporting the proposition that the Cε methylene is also a cation-π interaction. Strictly hydrophobic interactions investigated do not have the same folding parameters nor the specificity of interaction demonstrated by the Lys-aryl interaction. The greater surface area of Arg allows for greater overlap between an aromatic and the entire guanidium complex resulting in a parallel interaction. The interaction of cation-π complexes can be stabilizing to short peptides despite significant solvent exposure. The peptide model is well suited to investigate interactions that occur within proteins.

Synthetic Studies Directed Toward the Total Synthesis of Aflastatin A

David A. Evans, Jing Zhang, William C. Trenkle, Frank Glorius, Jason D. Burch
Harvard University
Department of Chemistry & Chemical Biology, Cambridge, MA 02138

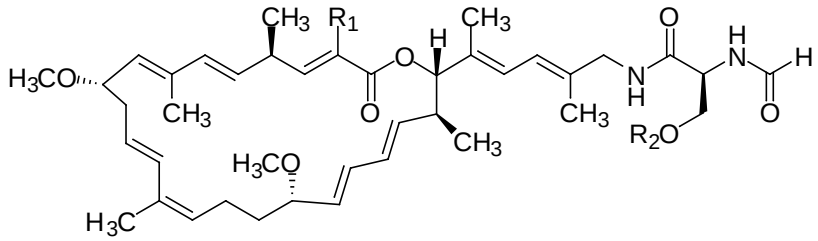
Aflastatin A was isolated by Sakuda and coworkers in 1996 from the mycelia of *Streptomyces*. It exhibits mild cytotoxic activity. Of particular interest is the ability of aflastatin A to inhibit aflatoxin production by *Aspergillus parasiticus* without affecting the growth of the fungus. Aflastatin A is a polyketide natural product notable for its stereochemical density and unusual polyol segments at C_{27}-C_{31} and C_{33}-C_{37}. Our principal disconnections of this complex molecule rely on double stereodifferentiating aldol reactions of advanced intermediates. The C_{18}-C_{19} bond will be constructed by a Felkin selective *anti* aldol reaction, and a *syn* selective oxygenated aldol addition will establish the C_{28}-C_{29} bond. The synthesis of the three major fragments via catalytic asymmetric methodologies developed in Evans lab will be presented. Preliminary fragment couplings studies will also be discussed.



Towards a Total Synthesis of the Iejimalides

Dirk Schweitzer, John Kane, Jamie Zigterman, Paul Helquist
University of Notre Dame
Department of Chemistry & Biochemistry, Notre Dame, IN 46556-5670

The Iejimalides (**1**) are a class of natural products with unique antitumor properties. We have initiated a program to accomplish their total synthesis. Progress towards this goal will be presented. Key reactions are the Julia coupling and the asymmetric Horner-Wadsworth-Emmons olefination.



1a Iejimalide A: $R_1 = R_2 = H$
1b Iejimalide B: $R_1 = CH_3$, $R_2 = H$
1c Iejimalide C: $R_1 = H$, $R_2 = SO_3Na$
1d Iejimalide D: $R_1 = CH_3$, $R_2 = SO_3Na$

STEREOSELECTIVE SYNTHESIS OF 1,2-O-ISOPROPYLIDENE-3-C-(5-PHENYL-1,2,4-OXADIAZOL-3-YL)-β-D-PSICOPYRANOSE THROUGH A NOVEL PROCEDURE

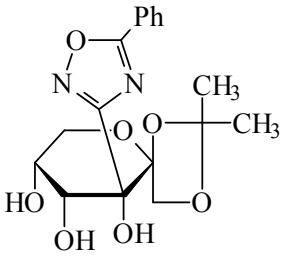
Jianxin Yu[a*], Zhongjun Li[b] Wenjie Lu[c] Suna Zhang[b] Mengshen Cai[b]

[a] Department of Radiology, The University of Texas Southwestern Medical Center at Dallas, 5323 Harry Hines Blvd., Dallas, Texas 75390-9058, E-mail: Jian-Xin.Yu@UTSouthwestern.edu

[b] School of Pharmaceutical Sciences, Peking University, Beijing 100083, China

[c] Department of Chemistry, Wuyi University, Jiangmen 529020, China

The synthesis of branched-chain sugars has attracted considerable attention[1] because of their biological importance. In addition, the incorporation of heterocyclic moieties in the carbohydrate framework has gained much importance[2,3]. Recently, a number of oxadiazolines have been reported to possess anti-HIV activity[4] prompting us to synthesize heterocyclic moieties as branched-chain links to carbohydrate fragments. We report here the stereospecific synthesis of 1,2-*O*-isopropylidene-3-C-(5-phenyl-1,2,4-oxadiazol-3-yl)-*β*-D-psicopyranose **A** through a novel neighbouring group participation and transfer approach, as well as a possible mechanism and the structural confirmation by spectroscopic data and X-ray crystallographic analysis.



A

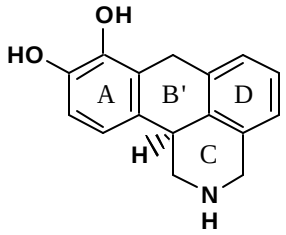
[1] Yoshimura, Y., *Adv. Carbohydr. Chem. Biochem.*, **1984**, 42, 69. [2] Sheban, M.A.E. *Adv. Heterocycl. Chem.*, **1998**, 70, 163. [3] Ashry, E.H.El.; Kilany, Y.El, *Adv. Heterocycl. Chem.*, **1998**, 69, 129. [4] Altonare, C. et al., *Chirality*, **1996**, 8, 556.

Acknowledgements Supported by the National Natural Science Foundation of China (No. 29862006).

DINAPSOLINE - A STUDY ON STRUCTURE-ACTIVITY-RELATIONSHIP (SAR) AND PHARMACOLOGICAL PROFILE OF A NOVEL DOPAMINE AGONIST

Sing-Yuen Sit,* Kai Xie, Swanee Jacutin-Porte, Kenneth Boy, James Seanz, Matthew T. Taber, Amit G. Gulwadi, Carolyn D. Korpinen, Kevin D. Burris, Thaddeus F. Molski, Elaine Ryan, Cen Xu, Henry Wong, Juliang Zhu, Subramaniam Krishnananthan, Todd Verdoorn and Graham Johnson
Bristol-Myers Squibb Pharmaceutical Research Institute
5 Research Parkway, Wallingford, CT 06492-7660, USA

DINAPSOLINE [8,9-Dihydroxy-2,3,7,11b-tetrahydro-1H-napth[1,2,3-de]isoquinoline, (±)-12], was first described by Nichols and Mailman as a novel dopamine agonist potentially useful in the treatment of Parkinson's disease. In an effort to identify a superior compound and characterize the key elements that contribute to the dopamine receptor binding affinity of dinapsoline, a variety of analogs were synthesized using a newly developed, highly convergent synthetic route. The crucial step in the new synthesis was a free-radical initiated cyclization to give the complete dinapsoline framework. The improved synthesis required half as many steps as the original procedure thus allowing for the practical preparation of dinapsoline in larger quantities. In addition, one of the late stage intermediates was resolved into a pair of enantiomers. From there, the (+)-S-isomer (**12**, absolute structure shown below) of dinapsoline was identified as the active enantiomer while the opposite (-)-R-isomer was devoid of dopamine receptor binding activity.



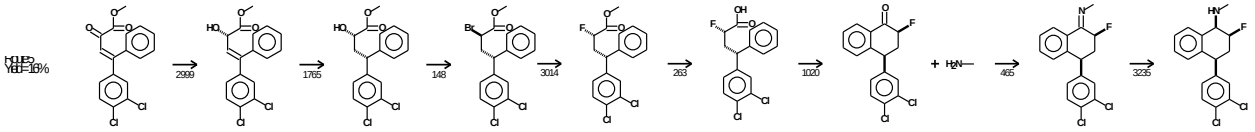
DINAPSOLINE (12)
8,9-Dihydroxy-2,3,7,11b-tetrahydro-1H-napth[1,2,3-*de*]isoquinoline

A COMPUTER PROGRAM THAT DESIGNS SYNTHETIC ROUTES

Malcolm Bersohn[1], Daniel Gruner[1], Wataru Katouda[2], Takashi Kawai[2], Tetsuhiko Takabatake[2], and Akio Tanaka[2]

[1]University of Toronto
Department of Chemistry, 80 St. George Street, Toronto, Canada M5S 3H6
[2]Organic Synthesis Research Laboratory, Sumitomo Chemical Company
1-98 Kasugade-naka 3-chome, Konohana-ku, Osaka, Japan 554-8558

The program knows almost 5000 standard reactions and can apply them to the design of syntheses of molecules with several chiral centers and many different functional groups. Besides a poster display of various already generated routes, a live computer demonstration will be available. One of the example products is fluorosertraline:

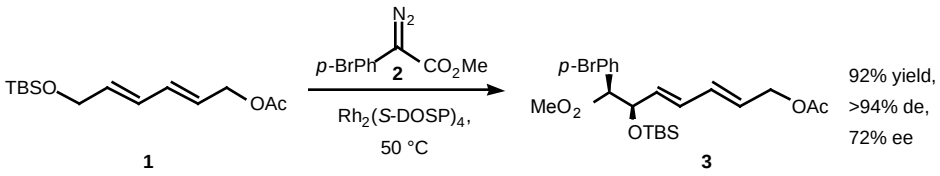


CATALYTIC ASYMMETRIC INTERMOLECULAR C–H ACTIVATION AS A SURROGATE TO THE ALDOL REACTION

Rohan E. J. Beckwith, Qihui Jin, Evan G. Antoulinakis and Huw M. L. Davies*

Department of Chemistry, University at Buffalo, The State University of New York, Buffalo, New York 14260-3000

C ctivation of silyl ethers by means of a rhodium-carbenoid induced C insertion displays high levels of regio-, diastereo- and enantioselectivity in the generation of silylated β-hydroxy esters, products classically obtained through aldol reactions. wide range of substrates are compatible with such an approach including allyl silyl ethers, tetraalkoxysilanes and simple silyl alkyl ethers. Through udicious choice of oxygen substituents remarkable site selectivity can be achieved and this has been exploited in several circumstances to illustrate the wide scope and huge potential of the chemistry. or example, the carbenoid derived from h_2(*S*-D SP)$_4$-catalyzed decomposition of **2** in the presence diene **1** results solely in the formation of β-siloxy ester **3** owing to the activating influence of the siloxy group and the deactivating influence of the acetoxy group on the neighboring methylene C bonds. eneral reactivity trends have been developed which will be useful in organic synthesis for predicting which substrates would be amenable to selective C activation.



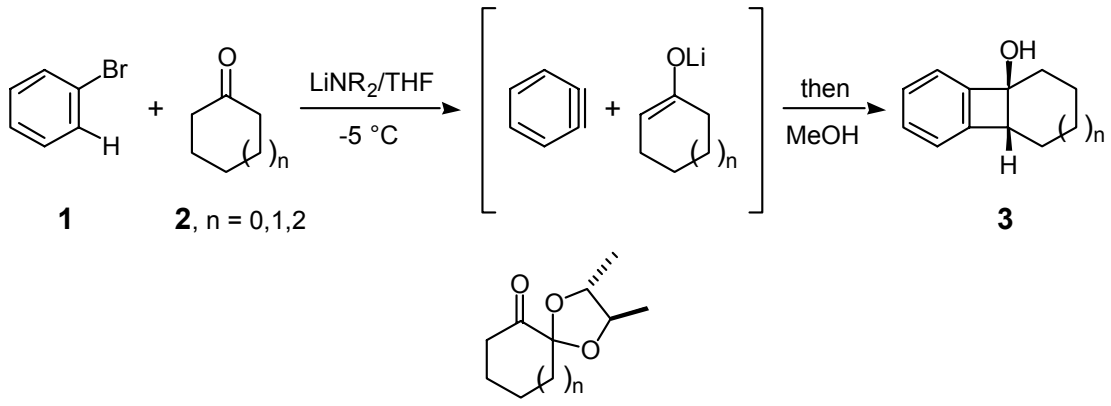
DIASTEREOSELECTIVE ADDITION OF KETONE ENOLATES TO BENZYNE: ASYMMETRIC SYNTHESIS OF BENZOCYCLOBUTENOLS

Olivier J.-C. Nicaise,* Alison L. Maddeford, Daniel J. Mans, Emilio Villa Hefti, and Robert J. Otto

Monsanto Hall, Department of Chemistry, Saint Louis University, 3501 Laclede Avenue, St. Louis, MO 63103-2010

One of our on-going research projects is directed toward the development of asymmetric aromatic elimination/addition reactions with cyclic ketone enolates. This type of transformation with substrates **1** and **2** is a one-pot reaction that involves benzyne and a lithium cyclic ketone enolate as reactive intermediates, and forms the chiral, *cis*-fused benzocyclobutenol **3**; the benzocyclobutenol motif is responsible for the biological activity of this type of compound (*e.g.*, anticonvulsive, bronchorelaxing, and β-blocking). Developing an asymmetric variant of this reaction amounts to investigate the asymmetric addition of ketone enolates to benzyne.

We will first report our preliminary work that consisted of determining the optimal reaction conditions for the formation of racemic **3** (n = 2) in high yield, and the use of 2-ketal ketones as substrates will also be presented. Then, the results obtained in the reactions of optically pure 2-ketal ketones **4** with **1** will be disclosed, showing that a high level of diastereoselectivity can be achieved in these reactions.



1 **2**, n = 0,1,2 **3**

4, n = 0,1,2

P-HETEROCYCLIC BUILDING BLOCKS: NOVEL SYNTHONS FOR STEREOSELECTIVE SYNTHESIS

Alan Whitehead, Matthew D. McReynolds, Joel D. Moore, Diana S. Stoianova, and Paul R. Hanson*
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1251 Wescoe Hall Drive, Lawrence, KS 66045-7582

The synthetic utility of nonracemic phosphorus heterocycles (*P*-heterocycles) produced via ring-closing olefin metathesis (RCM) will be presented. We have demonstrated that the inherent chemistry of phosphorus allows for the rapid functionalization of RCM-generated cyclic allyl phostone motifs en route to *P*-chiral phosphonosugars. We now report a terminus differentiation strategy utilizing RCM for the desymmetrization of 1,3-*anti*-diols employing phosphonate tethers. This terminus differentiation strategy exploits the inherent chemistry of phosphorus to construct *P*-chiral bicyclic building blocks and augments our previous work employing desymmetrization strategies on phosphorus templates. The resulting bicyclic allyl phostone framework contains a number of salient features, including endo- and exocyclic olefins for further synthetic manipulation and a temporary phosphorus tether (*P*-tether). The goal of this project is to evaluate the efficacy of these *P*-heterocyclic building blocks as 1,3-diol-containing synthons for natural product synthesis.

OXIDATIVE COUPLING OF RING EXPANDED GLYCALS: SEPTANOSE CARBOHYDRATES

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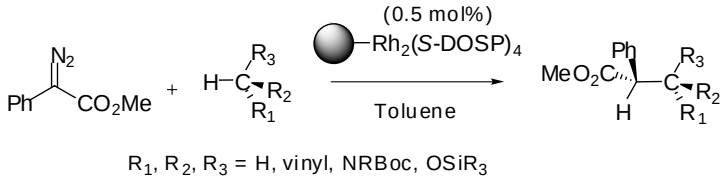
A simple synthetic route to a new family of carbohydrate based oxepines is presented. Activation of these cyclic enol ethers by DMDO and nucleophilic attack on the resulting 1,2-anhydrosugars by a number of nucleophiles will be shown. This work demonstrates a rapid entry into the synthesis of novel septanose based carbohydrates. Conformational and strucutral analysis of glucose derived methyl septanosides has been undertaken. Low energy conformations generated by molecular modeling and ab initio calculations will be compared with NMR spectra to motivate future biologically active targets. Of importance to this effort is the correlation of multiple low energy conformations to observed coupling constants.

ASYMMETRIC INTERMOLECULAR C-H ACTIVATION USING IMMOBILIZED DIRHODIUM TETRAKIS((S)-N-(DODECYLBENZENESULFONYL)-PROLINATE) AS A RECOVERABLE CATALYST

Abbas M. Walji and Huw M. L. Davies
University at Buffalo, The State University of New York
Department of Chemistry, Buffalo, NY 14260-3000



R_1, R_2, R_3 = H, vinyl, NRBoc, $OSiR_3$

Immobilization of chiral catalysts for asymmetric carbenoid transformations has attracted the interest of many research groups. Asymmetric cyclopropanation has been the standard reaction to evaluate these catalysts, with the exception of one study of asymmetric intramolecular C-H insertion with dirhodium tetracarboxamidates. Recently, we reported the immobilization of dirhodium tetraprolinates, which were highly effective for intermolecular cyclopropanations by donor/acceptor carbenoids. This led us to explore the similar heterogenization of Rh_2(*S*-DOSP)$_4$, which is the most generally effective catalyst for intermolecular C–H activation. Polymer supported Rh_2(*S*-DOSP)$_4$ is readily recycled and exhibits excellent catalytic activity for asymmetric intermolecular C–H activation by means of rhodium-carbenoid induced C–H insertion.

A homohelical electronic theory for chiral recognition and asymmetric induction

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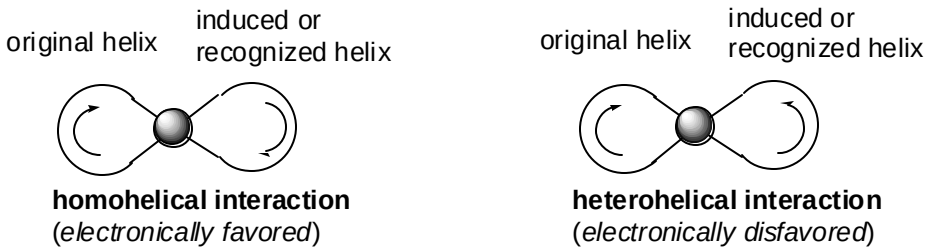
Using helical electronic effect as a tool, in this work we present an intensive literature analysis for representative systems in chiral molecular recognition and for asymmetric inductions in oxazaborolidines catalyzed ketone reduction by BH_3 and aminoalcohols catalyzed alkylation of aldehydes by Et_2Zn. The results show that chiral recognition occurs via a homohelical interaction mechanism, i.e., a chiral host is capable of recognizing a guest enantiomer of the same helical handedness through a homohelical transition state complexation. This homohelical recognition mechanism is found to be of remarkable effectiveness in predicting the retention behaviors of a wide variety of chiral HPLC separation systems: the more retained enantiomers are always the ones that form a homohelical selectand/selector diastereomeric association. In asymmetric catalysis, it is proposed that the enantiofacial complexation of a pro-chiral substrate to the catalytic center and the subsequent establishment of the product stereochemistry are electronically governed by the helical handedness of the chiral ligand employed via a homohelical induction pathway, and asymmetric induction is essentially a process in which the handedness of the original ligand is conserved. Based on the helical asymmetry of chiral ligands, catalysts can be generally categorized into two classes: being either right-handed or left-handed. For both asymmetric reactions a correlation between the ligand helical handedness and the sign of absolute stereoinduction is found.



homohelical interaction (*electronically favored*)

heterohelical interaction (*electronically disfavored*)

Understanding origin of enantioselection without steric reasoning: A new homohelical electronic induction theory leading to a simple stereochemical rationale for asymmetric carbonyls hydrogenation

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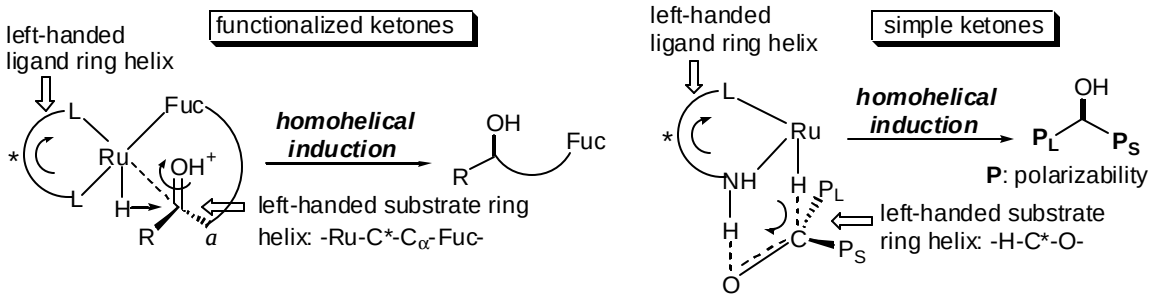
Based on well-established mechanistic studies on hydrogenation of carbonyls, a homohelical electronic induction analysis has been applied to various asymmetric catalytic systems, and an exceedingly simple and general rationale on both the catalyst helical handedness-product configuration correlation and the critical dependence of enantioselection on the substrate substituents polarizability distinction has been revealed. It holds predicting power. The empirical appreciations on catalyst design and substrate selection, together with several seemingly strange stereochemical observations in this field, have been readily understood in a clear language of polarizability and homohelical electronic induction, rather than in somewhat ambiguous steric effect-based arguments. The work presented here is expected to serve a dual role: in the practical aspect, it helps guide the chiral catalyst design from a rational angle and also aids the selection of appropriate substrates of potentials in participating highly enantioselective transformations; in the conceptual aspect, it concludes that the element of electronic control must be incorporated in our general framework of understanding on asymmetric induction thus the conventional wisdom that connects the origin of enantioselection with sole steric reasoning must be changed.



Kinetic resolution is electronically controlled by homohelical recognition

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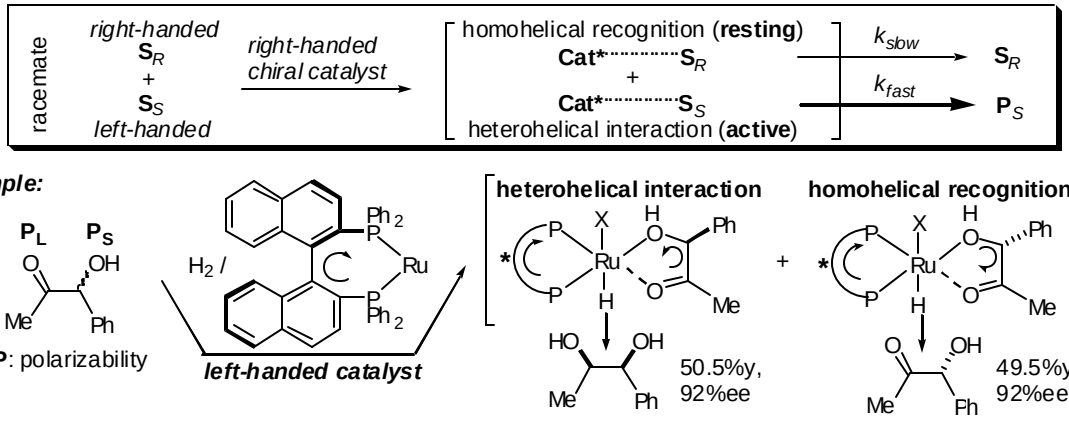
Kinetic resolution relies on a chiral catalyst's ability to discriminate the enantiomers of a racemate, chiral recognition occurs only between one enantiomer and the catalyst. The question addressed here is whether this recognition renders the corresponding enantiomer kinetically more reactive or less reactive to further reaction? A helical electronic effect analysis on a variety of most successful and reliable kinetic resolution systems (as judged by Jacobsen's recent review: *Adv. Synth. Catal.* **2001**, *343*, 5-26) clearly shows that the answer is less active: while the catalyst interacts with the oppositely handed enantiomers in a homohelical and heterohelical catalyst-substrate association, the homohelical recognition pair characterizes an energetically favorable resting state and leads to the recovery of the substrate enantiomer, and it is always the heterohelical interaction pair that undergoes faster derivatization. In other words, kinetic resolution is electronically under homohelical recognition control. The basic rationale and one illustration are shown below. This rationale is novel, simple, general and it possesses predicting power. The analysis details on these systems will be presented. Some unexpected stereochemical observations previously viewed as exceptions to the relevant empirical rules have been readily rationalized. An inherent stereochemical link between asymmetric induction and kinetic resolution is also appreciated: in a tandem process while the former dedicates to generating homohelicity via homohelical electronic induction, the latter dedicates to preserving it! This conclusion should not be surprising and might, at a more general perspective, account for the homochirality observed in nature.



38th National Organic Symposium
Poster Abstracts
Session C

Schedule of Presenters – Poster Session C Tuesday June 10, 9 pm – 12 am

C1 SYNTHESIS OF LINEAR TRIQUINANES BY ROUND TRIP RADICAL CYCLIZATIONS

Jonathan C. Tripp and Dennis P. Curran
University of Pittsburgh
Department of Chemistry, Pittsburgh, PA 15260

C2 ASYMMETRIC CONJUGATE ADDITION OF ALLYLSTANNANES

Richard J. Mullins, Nathan A. Miller, David R. Williams
Indiana University, Department of Chemistry
800 E. Kirkwood Ave., Bloomington, IN 47405-7102

C3 SUBSTITUTION REACTIONS OF 1,4-NAPHTHOQUINONES

Heather J. Crump, Cameron P. Iverson, Carolyn. B. Lauzon, Sarah J. Stadler, Bryanne L. Stills, Rachael Y. Williams, and Tetsuo Otsuki*
Department of Chemistry, Occidental College
1600 Campus Road, Los Angeles, CA 90041

C4 COUPLING OF HIGHLY CONJUGATED ALKYNES WITH CARBENE COMPLEXES

James W. Herndon, YuMei Luo, Yanshi Zhang, Binay Ghorai
New Mexico State University
Department of Chemistry & Biochemistry, MSC 3C, Las Cruces, New Mexico 88003

C5 A FOLDED, SECONDARY STRUCTURE IN STEP-GROWTH OLIGOMERS FROM COVALENTLY LINKED, CROWDED AROMATICS

Wei Zhang, Dana Horoszewski, John Decatur, and Colin Nuckolls*
Columbia University
Department of Chemistry, New York, New York 10027

C6 CONSTRUCTION OF THREE-DIMENSIONAL STRUCTURES BASED ON SPATIAL DEFINITION BY 1,2-DICARBA-*closo*-DODECABARANE (*o*-CARBORANE)

Kiminori Ohta[1], Chalermkiat Songkram[2], Kentaro Yamaguchi[3], Yasuyuki Endo[1]
[1]Faculty of Pharmaceutical Sciences, Tohoku Pharmaceutical University; [2]Graduate School of Pharmaceutical Sciences, University of Tokyo; [3]Chemical analysis Center, Chiba University
[1]4-4-1, Komatsushima, Aoba-ku, Sendai 981-8558, Japan; [2]7-3-1, Hongo, Bunkyo-ku, Tokyo 113-0033, Japan; [3]1-33, Yayoi-cho, Inage-ku, Chiba 250-8522, Japan

C7 A NO-D* ^{1}H NMR STUDY OF USEFUL SULFUR-STABILIZED ORGANOLITHIUM REAGENTS

Thomas R. Hoye, Jennifer L. Green, and Mikhail M. Voloshin
Department of Chemistry, University of Minnesota, Minneapolis, MN 55455

C8 A "BOOT CAMP" TRAINING EXERCISE IN THE HOYE GROUP: THE EPOXIDATION OF 1.0 mg OF GERANIOL

Thomas R. Hoye and Christopher S. Jeffrey
Department of Chemistry, University of Minnesota, Minneapolis, MN 55455

C9 EFFORTS TOWARD A TOTAL SYNTHESIS OF OOCYDIN A (HATERUMALIDE NA)

Thomas R. Hoye and Jizhou Wang
Department of Chemistry, University of Minnesota, Minneapolis, MN 55455

C10 A NO-D* ^{1}H NMR STUDY OF SOME ALKENYLLITHIUM AND GRIGNARD REAGENTS

Thomas R. Hoye, Ziyad F. Al-Rashid, and Mikhail M. Voloshin
Department of Chemistry, University of Minnesota, Minneapolis, MN 55455

C11 A BIOMIMETICALLY INSPIRED COPE REARRANGEMENT: CAN A BIOSYNTHETICALLY RELEVANT, ALL-CARBON [3,3]-SIGMATROPIC REORGANIZATION PROCEED UNDER AMBIENT CONDITIONS?

Thomas R. Hoye and James E. Kabrhel
Department of Chemistry, University of Minnesota, Minneapolis, MN 55455

C12 COMPLEMENTARY CROSS METATHESIS AND ORGANOCATALYSTS™ CATALYZED ENANTIOSELECTIVE INDOLE ALKYATION REACTIONS

Wen-Jing Xiao and Richard L. Pederson
Materia, Inc., Fine Chemicals R&D
12 N. Altadena Dr., Pasadena, CA 91107

C13 COMBINATORIAL SCREENING OF REAGENTS AND CATALYSTS IN HOMOGENEOUS METAL MEDIATED CROSS-COUPLING REACTIONS

Michael W. Pelter, Libbie S. W. Pelter, Regina Strug, Ken Berg, Amy Gorcowski
Purdue University Calumet
Department of Chemistry & Physics, Hammond, IN 46323

C14 SYNTHESIS AND PHOTOISOMERIZATION OF 2-*tert*-BUTYL-9-(2,2,2-TRIPHENYLETHYLIDENE)FLUORENE

Thomas W. Bell*, Rolando Procupez, Daniel J. Phillips, Vincent J. Catalano, James Barr, and Joseph I. Cline
University of Nevada, Reno
Department of Chemistry MS 216, Reno, NV 89557-0020

C15 AROMATIC BORYLATION APPLIED TO "ONE-POT" SYNTHESES OF SUBSTITUTED PHENOLS, ARYLAMINES, AND BIARYLS

Daniel Holmes, Feng Shi, G. Abbas Chotana, Robert E. Maleczka, Jr. and Milton R. Smith, III
Michigan State University
Department of Chemistry, East Lansing, MI 48824-1322

C16 TOTAL SYNTHESIS OF (–)-STEMONINE

David R. Williams and Khalida Shamim
Department of Chemistry, Indiana University, Bloomington, IN-47401

C17 THE ELECTROCHEMICAL PRODUCTION OF SUBSTITUTED LACTONES

John Brandt, Bin Liu, Kevin D. Moeller
Department of Chemistry, Washington University, Campus Box 1134,
One Brookings Drive, St. Louis, MO 63130, USA, Fax: 314-935-4481

C18 METAL COMPLEXES BEARING INDOLE MOIETIES

Valerian Dragutan[1], Ileana Dragutan[1], Taeboem Oh[2], Alex Schultz[2] and Tania Tasu[2]
[1]Romanian Academy, Institute of Organic Chemsitry, 71141 Bucharest, Romania;
[2]California State University Northridge, Department of Chemistry, Northridge, CA 91330-8262

C19 THE STUDY OF ALKOXIDE-PROMOTED ENYNE-ALLENE CYCLIZATIONS: NEXT GENERATION ISOLATED ALKENES

Michelle K. Waddell and Mark A. Lipton*
Purdue University, Department of Chemistry,
560 Oval Drive, P.O. Box 805, West Lafayette, IN 47907-2084

C20 DESIGN AND SYNTHESIS OF CYCLIC ENEDIYNES CONTAINING DIAZODICARBONYL MOIETY

Grigori Karpov, Vladimir Popik
Bowling Green State University
Center for Photochemical Sciences, Bowling Green, OH 43403

C21 NOVEL ORGANOMETALLIC COMPOUNDS AS POTENTIAL ANTITUMOR AGENTS

Valerian Dragutan[1], Ileana Dragutan[1], Mariana Danila[1], Petru Filip[1], Taeboem Oh[2], and Larry R. Sherman[3]
[1]Romanian Academy, Institute of Organic Chemistry, P.O. Box 15-254, 71141 Bucharest, Romania; [2]California State University Northridge, Department of Chemistry, Northridge, CA 91330-8262; [3]Scranton University, Department of Chemistry, Scranton, PA 18510-4626.

C22 PROGRESS TOWARDS A MODULAR SYNTHESIS OF *C*-LINKED GM AND GD GLYCOLIPID ANTIGEN DERIVATIVES

Christopher A. LeClair and Glenn J. McGarvey*
The University of Virginia
Department of Chemistry, Charlottesville, VA 22904-4319

C23 SINGLE-MOLECULE MOLECULAR MOTORS: STUDIES IN DIRECTED BOND ROTATION

Ying Lin, Jonathan Bingham, William Hallows, Jacob Cha, Mara Kelly, Matthew O Connor, Jason Gatlin, Dima Azar, Bruce Branchaud
University of Oregon
Department of Chemistry and Materials Science Institute, Eugene, OR 97403-1253

C24 INTRAMOLECULAR HYDROBORATION OF UNSATURATED AMINE BORANE COMPLEXES BY AN ALTERNATIVE MECHANISTIC PATHWAY

Edwin Vedejs and Matthew Scheideman
University of Michigan, Department of Chemistry
Ann Arbor, MI 48109

C25 SYNTHETIC AND CONFORMATIONAL STUDY OF 1,10-PHENANTHROLINE DERIVATIVES

Elke Schoffers, Eun-Joo Kim, Sun Y. Wallace
Western Michigan University
Department of Chemistry, Kalamazoo, MI 49008

C26 ARYLTHIOAMINALS AS HYDROLYTICALLY-UNSTABLE NUCLEOSIDE PRODRUGS

Hui-Min Chang and Robert R. Kane
Dept. of Chem. & Biochem and The Center for Drug Discovery
Baylor University, Waco, TX 76798

C27 SYNTHESIS AND CHARACTERIZATION OF CARBOHYDRATE-CONTAINING MATERIALS FOR DNA DELIVERY

Yemin Liu, Sathya Srinivasachari, and Theresa M. Reineke*
University of Cincinnati, Department of Chemistry
P.O. Box 210172 Cincinnati, OH 45221-0172

C28 SOLUTION-PHASE LIBRARIES BY FLUOROUS PARALLEL SYNTHESIS

Wei Zhang[1], Christine Chen[1], Zhiyong Luo[1], Tadamichi Nagashima[1], Jeffrey Irwin[1], Yimin Luo[1], Marvin Yu[1], Siva Dandapani[2], and Dennis P. Curran[2]

Fluorous Technologies, Inc.[1] and University of Pittsburgh[2]
970 William Pitt Way, Pittsburgh, PA 15238

C29 RECOGNITION PROPERTIES AND CELLULAR TRANSPORT ABILITY OF NOVEL ARTIFICIAL RECEPTORS

David B. Smithrud,* Inese Smukste, Vadims Dvornikovs, and Brian House

University of Cincinnati, Cincinnati OH 45221

C30 SOLUTION-PHASE LIBRARIES BY FLUOROUS MIXTURE SYNTHESIS

Wei Zhang, Christine Chen, Marvin S. Yu

Fluorous Technologies, Inc.
970 William Pitt Way, Pittsburgh, PA 15238

C31 NEW DEVELOPMENTS IN FLUOROUS MITSUNOBU CHEMISTRY

Siva Dandapani[1], Dennis P. Curran[1], Marvin S. Yu[2]

University of Pittsburgh[1] and Fluorous Technologies, Inc.[2]
Department of Chemistry, University of Pittsburgh, Pittsburgh, PA 15260[1]
970 William Pitt Way, Pittsburgh, PA 15238[2]

C32 DESIGN AND SYNTHESES OF CHIRAL RIGID TRIPODAL LIGANDS WITH INTERESTING PHOTOPHYSICAL PROPERTIES

Zhaohua Dai and James W. Canary

Department of Chemistry, New York University, New York, NY 10003

C33 SYNTHESIS, CHARACTERIZATION AND BINDING STUDIES OF NOVEL ORGANOMETALLIC COMPLEXES OF TECHNECIUM, RHENIUM AND COPPER LIGANDS FOR THE ESTROGEN RECEPTOR

Nathan C. Ackroyd, Michael L. Nickels, Michael A. Reynolds and John A. Katzenellenbogen*

Department of Chemistry, University of Illinois at Urbana-Champaign, Urbana, IL 61801.

C34 FULLERENE-COATED MATERIALS AS REUSABLE CATALYSTS

Anton W. Jensen, Coreen Daniels, John Berry, and Brijesh Maru

Department of Chemistry, Central Michigan University
Mount Pleasant, Michigan 48859

C35 PROGRESS TOWARDS THE TOTAL SYNTHESIS OF AMPHIDINOLIDE B1

Craig M. Crews[1,2,3], Amit K. Mandal[3], and John S. Schneekloth, Jr.[1]

Yale University, Departments of [1]Chemistry, [2]Pharmacology, and [3]Molecular, Cellular, and Developmental Biology
New Haven, CT 06520-8107

C36 SYNTHESIS OF NOVEL BENZOFURAN ANALOGS AS TUBULIN POLYMERIZATION INHIBITORS AND VASCULAR TARGETING AGENTS

Raymond J. Kessler,[1] Mallinath B. Hadimani,[1] Kevin G. Pinney,[1] Klaus Edvardsen[2]

[1]Baylor University, [2]University of Lund
[1]Department of Chemistry and Biochemistry and the Center for Drug Discovery, Waco, TX 76798-7348, [2]Department of Cell and Molecular Biology, Section for Tumor Immunology, BMC: I 12, S-221 84 Lund, Sweden

C37 SYNTHESIS OF 3-AMINO QUINAZOLINONES AS TYROSINE KINASE INHIBITORS
David S. Kuiper and Laurie A. Witucki
Grand Valley State University
Department of Chemistry, Allendale, Michigan 49401

C38 FLUOROUS-SOLUBLE CROWN ETHERS
Eric T. Hartman, T. David Bateman, Martin J. Campbell
Henderson State University
Department of Chemistry, Box 7633, Arkadelphia, AR 71999

C39 RHIZOPINE SYNTHESIS-POTENTIAL MEDIATORS FOR NITROGEN FIXATION IN PLANTS
Elke Schoffers and Venkat R. Guduru
Western Michigan University
Department of Chemistry, Kalamazoo, MI 49008.

C40 CARBOXYLATE-DIRECTED C-H ACTIVATION: ASYMMETRIC SYNTHESIS OF AN ADVANCED INTERMEDIATE FOR THE TOTAL SYNTHESIS OF ZARAGOZIC ACID Ax3
Adriana I. Velter and Duncan J. Wardrop
University of Illinois at Chicago
Department of Chemistry, 845 West Taylor Street, Chicago, IL 60607

C41 PALLADIUM CATALYZED DEOXYGENATIONS WITH A CURIOUS CHLOROBENZENE EFFECT
Ronald J. Rahaim, Jr. and Robert E. Maleczka, Jr.*
Michigan State University
Department of Chemistry, East Lansing, MI 48824

C42 DESIGNING CALIX[4]ARENE DIMERS AS MOLECULAR CAPSULES
Kevin L. Caran, Josh S. Sasine, and Suzanne B. Shuker*
School of Chemistry and Biochemistry
Georgia Institute of Technology
Atlanta, GA 30332-0400

C43 APPLICATIONS OF IONIC LIQUIDS IN ORGANIC SYNTHESIS AND CATALYSIS
Elke Schoffers, Andy LaFrate
Western Michigan University, Department of Chemistry, Kalamazoo, MI 49008

C44 SYNTHESIS OF 1,10-PHENANTHROLINE DERIVATIVES AS LIGANDS FOR ASYMMETRIC CATALYSIS
Elke Schoffers and Son D. Tran
Western Michigan University
Department of Chemistry, Kalamazoo, MI 49008

C45 OXIDATION OF INDOLE AND ALKENE SUBSTRATES BY OXODIPEROXOMOLYBDENUM-TRIALKYL(ARYL)PHOSPHINE OXIDE COMPLEXES
Christine I. Altinis-Kiraz, Luis Mora and Leslie S. Jimenez
Rutgers, The State University of New Jersey
Department of Chemistry and Chemical Biology, Piscataway, NJ 08854

C46 BUCKY BELTS: SYNTHESIS USING A CYCLODEXTRIN SCAFFOLD
Zachary E. Katsamanis, Jason A. Estrada, Nancy S. Goroff
University at Stony Brook, The State University of New York
Department of Chemistry, Stony Brook, NY 11794-3400

C47 TOWARD THE TOTAL SYNTHESIS OF (-)-DIHYDROGUAIARETIC ACID
R. Elizabeth Brewster and Suzanne B. Shuker
Georgia Institute of Technology
Department of Chemistry and Biochemistry, Atlanta, GA 30332-0400

C48 TOTAL SYNTHESIS OF (±)-MAGNOFARGESIN
Joseph P. Fritz, Edward G. Bowen, Duncan J. Wardrop
University of Illinois at Chicago
Department of Chemistry, 845 West Taylor Street, Chicago, IL 60607

C49 MICROWAVE ASSISTED CATALYTIC OXIDATIVE COUPLING OF BENZYL AMINES TO IMINES
Muralidhara Thimmaiah and Béla Török
Department of Chemistry, Michigan Technological University, 1400 Townsend Drive,
Houghton, MI 49931

C50 PROBING TERTIARY STRUCTURE IN MINIPROTEINS: DYNAMIC EXCHANGE OF SECONDARY STRUCTURAL ELEMENTS
Matthew G. Woll, Samuel H. Gellman
University of Wisconsin-Madison
Department of Chemistry, 1101 University Ave, Madison, WI 53706

C51 FACILE SYNTHESIS OF ALDEHYDES FROM ALPHA-*N,N*-DIALKYLAMINOACIDS
Brooke M. Gartland, Kristin Henry, Ciprian P. Prosecaru, William Schroeder and Robert P. Smart
Grand Valley State University
Department of Chemistry, Allendale, Michigan 49401

C52 FROM STEREOSPECIFIC, LIVING ZIEGLER-NATTA POLYMERIZATION TO ASYMMETRIC HYDROZIRCONATION: THE ROLE PLAYED BY CHIRAL ZIRCONIUM AMIDINATES
Richard J. Keaton, Yonghui Zhang, Lawrence R. Sita
University of Maryland
Department of Chemistry and Biochemistry, College Park, MD 20742

C53 TOTAL SYNTHESIS OF ACANTHODORAL BY ACYL RADICAL CYCLIZATION AND WOLFF REARRANGEMENT
Liming Zhang and Masato Koreeda
Departments of Medicinal Chemistry and Chemistry
University of Michigan, Ann Arbor, MI 48109

C54 DIASTEREOSELECTIVE NITRENIUM ION CYCLIZATIONS: APPLICATION TO THE ASYMMETRIC SYNTHESIS OF (+)-KISHI'S LACTAM AND A KEY INTERMEDIATE FOR THE PREPARATION OF FASICULARIN
Chad L. Landrie, Wenming Zhang, Duncan J. Wardrop
University of Illinois at Chicago
Department of Chemistry, 845 West Taylor Street, Chicago, IL 60607

C55 AN UNPRECEDENTED REARRANGEMENT IN THE PHOTOCYCLIZATION OF A STILBENE ANALOG
Frank B. Mallory and Colleen K. Regan
Department of Chemistry, Bryn Mawr College
Bryn Mawr, PA 19010-2899

C56 WATER SOLUBLE CALIX[4]ARENES FOR MOLECULAR RECOGNITION AND ENCAPSULATION

Suazette Reid and Suzanne B. Shuker
Georgia Institute of Technology, Department of Chemistry and Biochemistry,
Atlanta, GA 30332

C57 RESORCINARENE-ENCAPSULATED NANOPARTICLES: BUILDING BLOCKS FOR FUNCTIONAL NANOSTRUCTURES

Beomseok Kim, Steven L. Tripp, Balasubramanian Ramjee and Alexander Wei
Department of Chemistry, Purdue University, West Lafayette, IN 47907

C58 EXTENSION OF CONJUGATION AS A MEANS OF IMPROVING THE PERFORMANCE OF AN ANION SENSOR

Dmitry Aldakov and Pavel Anzenbacher, Jr.
Bowling Green State University
Department of Chemistry and Center For Photochemical Sciences, Bowling Green, OH 43403

C59 SYNTHETIC STRUCTURAL MODIFICATIONS OF THE NATURAL PRODUCT 21-BUTENYL SPINOSYN

Gary D. Crouse, Donald R. Hahn, Paul R. Graupner, Jeffery R. Gilbert, Paul Lewer, Jesse L. Balcer, Peter B. Anzeveno, John F. Daeuble, M. Paige Oliver, Thomas C. Sparks
Dow AgroSciences LLC
9330 Zionsville Road; Indianapolis, IN 46268

C60 SUZUKI CROSS-COUPLING OF ALKYL BROMIDES, CHLORIDES AND TOSYLATES WITH AKLYL AND ARYL BORONIC ACIDS USING A NOVEL CLASS OF TERTIARY PHOSPHINE LIGAND INCORPORATING A PHOSPHA-ADAMANTANE FRAMEWORK

D. A. Gerritsma, T. Brenstrum, G. Adjabeng, J. McNulty and A. Capretta
Brock University, Institute of Molecular Catalysis
500 Glenridge Avenue, St. Catharines, Ontario, Canada, L2S 3A1

C61 STEREOSELECTIVE ONE-POT SYNTHESIS OF VINYLSILANES FROM AROMATIC ALDEHYDES

Man Lung Kwan, Chiu W. Yeung, Kerry L. Breno, Kenneth M. Doxsee
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C62 A TANDEM OLEFIN ISOMERIZATION-CLAISEN REARRANGEMENT PROMOTED BY A CATIONIC IRIDIUM COMPLEX

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C63 SUZUKI CROSS-COUPLING OF ALKYL BROMIDES, CHLORIDES AND TOSYLATES WITH ALKYL-9-BBN DERIVATIVES USING A NOVEL CLASS OF TERTIARY PHOSPHINE LIGAND INCORPORATING A PHOSPHA ADAMANTANE FRAMEWORK

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C64 DEVELOPMENTS IN CARBOCYCLE SYNTHESIS FROM FUNCTIONALIZED NORBORNYLENES BY OLEFIN METATHESIS

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C65 SYNTHESIS OF PROTECTED FORMS OF ALL FOUR DIASTEROMERS OF ß-METHOXYTYROSINE

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C66 STEREOSELECTIVE RADICAL CYCLIZATIONS OF AXIALLY CHIRAL *N*-ALLYLANILIDES TO 3-SUBSTITUTED DIHYDROINDOLES WITH TRANSFER OF AXIAL CHIRALITY TO NEWLY FORMED STEREOCENTER

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C67 DESIGN AND SYNTHESIS OF PIP_2 MICELLE ANALOGS

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C68 TANDEM AROMATIC OXIDATION/DIELS-ALDER REACTIONS OF 3-(2-HYDROXYPHENYL)-PROPIONIC ACIDS. APPLICATIONS TOWARD A TOTAL SYNTHESIS OF BACCHOPETIOLONE.

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C69 SYNTHESIS OF HOMOALLYLIC AMINE DERIVATIVES BY ALLYLSILANE ADDITION TO ENANTIOPURE *N*-ACYLHYDRAZONES

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C70 COPPER CATALYZED CROSS-COUPLING REACTIONS

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C71 METHODOLOGY TO USE PARALLEL SYNTHETIC CHEMISTRY (PSC) TO PREPARE ENANTIOMERICALLY PURE EPOXIDE REAGENTS FOR USE IN PREPARING TRANSITION STATE INSERTS OF ASPARTYL PROTEASE INHIBITORS CONTAINING DIFFERENT P1 SUBSTITUENTS

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C72 APPLICATION OF Zr-CATALYZED ENANTIOSELECTIVE CARBOALUMINATION REACTION TO THE SYNTHESES OF REDUCED POLYPROPIONATES AND RELATED COMPOUNDS

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C73 a,?-CYCLOPEPTIDES CAPABLE OF FORMING PEPTIDIC NANOTUBES: THE STRUCTURAL AND THERMODYNAMIC BASIS

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C74 TOTAL SYNTHESIS OF THE ANTIBIOTIC CYTOSPORONE E

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C75 LEWIS ACID CATALYZED AND SELF-ASSEMBLED DIELS-ALDER REACTIONS (LACASA-DA). A NEW APPROACH TO ENHANCE REACTIVITY, REGIO- AND STEREOSELECTIVITY

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C76 REACTIONS OF BICYLIC AZIRIDINES WITH AMINES AND ALCOHOLS

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C77 HETEROLOGOUS EXPRESSION AND PURIFICATION OF SPAS, SPAB AND SPAC INVOLVED IN SUBTILIN BIOSYNTHESIS

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C78 DESIGN AND PERFORMANCE OF INTERFACIAL SCAFFOLDS FOR TEMPLATING 2-DIMENSIONAL CRYSTALLIZATION OF HISTIDINE-TAGGED PROTEINS

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C79 SYNTHESIS OF 2'-*C*-METHYL-ß-L-RIBONUCLEOSIDES

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C80 PRODRUGS OF THE POTENT AND SELECTIVE ANTI-HBV AGENT 2'-DEOXY-B-L-CYTIDINE (LDC): SELECTION OF THE IDEAL CANDIDATE

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C81 NOVEL MICROWAVE ASSISTED SYNTHESIS OF TRIFLUOROMETHYLATED IMINES CATALYZED BY SOLID ACIDS

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C82 ARE OPEN CHAIN CHIRAL KETONES GOOD CATALYSTS FOR ENANTIOSELECTIVE EPOXIDATIONS?

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C83 TOTAL SYNTHESIS OF KALIHINOL C

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C84 STAUDINGER LIGATION: MECHANISTIC STUDIES AND PEPTIDE IMMOBILIZATION

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C85 PHOSPHITE DEHYDROGENASE: MECHANISTIC STUDIES OF AN UNUSUAL PHOSPHORYL TRANSFER REACTION

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C86 UTILIZATION OF HIDDEN MESO-SYMMETRY TOWARDS THE SYNTHESIS OF THE C22-C36 SEGMENT OF HALICHONDRIN B

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C87 NEW CLASSES OF HISTONE DEACETYLASE INHIBITORS AS POTENTIAL ANTICANCER AGENTS

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C88 SILICON-TETHERED 6-EXO RADICAL CYCLIZATIONS OF IMINO RADICAL ACCEPTORS

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C89 TRIPLET PHOTOSENSITIZATION USING PYRONES AND IMPLICATIONS FOR PHOTOACTIVE MARINE PRODUCTS

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C90 SYNTHESIS AND PHOTOPHYSICAL PROPERTIES OF NON-COVALENTLY LINKED PORPHYRIN-FULLERENE DYADS

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C91 PHOTODEALKYLATION OF 1-*N,N*-DIALKYLAMINOANTHRAQUINONES

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C92 SYNTHESIS OF O-ARYL-ALKYNYLAMINO ACIDS BY SONOGASHIRA TYPES OF REACTION IN AQUEOUS MEDIA

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C93 ENANTIOSELECTIVE TOTAL SYNTHESIS OF ANNONACEOUS ACETOGENIN (-)-MUCOCIN

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C94 BISMUTH CATALYZED DIASTEREOSELECTIVE ETHERIFICATION REACTIONS: APPLICATION TO THE SYNTHESIS OF NON-ADJACENT AND FUSED POLYCYCLIC ETHERS

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C95 PROGRESS TOWARD THE TOTAL SYNTHESIS OF WELWITINDOLINONE A

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C96 HETEROGENEOUS CATALYTIC ENANTIOSELECTIVE HYDROGENATION OF a,ß-UNSATURATED CARBONYL COMPOUNDS BY PROLINE MODIFIED SUPPORTED PALLADIUM CATALYSTS

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C97 PHOTOCHEMISTRY OF Z-LIGUSTILIDE. BIOMIMETIC SYNTHESIS OF RILIGUSTILIDE

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C98 NOVEL CHIRAL OXATHIANE LIGANDS FOR PALLADIUM-CATALYZED ASYMMETRIC ALLYLATION

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C99 A NOVEL CHIRAL PALLADIUM-PHOSPHINOOXAZOLIDINE CATALYST FOR THE ENANTIOSELECTIVE DIELS-ALDER REACTION

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C100 INTRAMOLECULAR STAUDINGER LIGATION: A POWERFUL METHOD FOR THE RING-CLOSURE OF DIFFICULT LACTAMS

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C101 REGIO- AND STEREOSELECTIVE SYNTHESIS OF LNA GUANINE NUCLEOSIDES

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C102 STERIC ACCELERATION OF INTRAMOLECULAR CYCLISATIONS

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C103 SELECTIVE REMOVAL OF SILYL ETHERS FROM PHENOLIC HYDROXYLS WITH NAH

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C104 HIGHLY CONFIGURATION-RETAINED METHYLATION OF *TRANS*-1-BROMO(OR CHLORO)-1-SUBSTITUTED(ALKYNYL, ALKENYL, OR ARYL)-1-ENE WITH METHYLZINCS CATALYZED BY Pd(tBu$_3$P)$_2$

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C105 FLUORESCENCE SENSING OF AMMONIUM AND ORGANOAMMONIUM IONS THROUGH THE CONFORMATIONAL RESTRICTION OF TRIPODAL OXAZOLINE RECEPTORS

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C106 TOWARDS THE TOTAL SYNTHESIS OF CALLIPELTIN A AND D; ASYMMETRIC SYNTHESIS OF AGDHE, VIA VINYL SULFONES

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C107 AN IN SITU ENZYMATIC SCREENING (ISES) APPROACH TO CATALYST DEVELOPMENT

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C108 DEVELOPMENT OF POROUS FUNCTIONAL MATERIALS FOR HETEROGENEOUS CATALYSIS

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C109 PROGRESS TOWARD THE TOTAL SYNTHESIS OF SAUDIN

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C110 A COMBINATORIAL APPROACH TO NATURAL PRODUCT BASED INHIBITORS OF APOPTOSIS

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C111 C_{19} QUASSINOID MODEL STUDIES: PREPARATION OF TRANSPERHYDROINDANS VIA A VINYLOGOUS MUKAIYAMA ALDOL-FREE RADICAL CYCLIZATION ROUTE

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C112 AN IMPROVED SYNTHESIS OF ELECTRON-RICH DIARYL DITELLURIDES AND DIARYL TELLURIDES

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C113 A NOVEL 1,2 MIGRATION OF THE ACYLOXY GROUP: EFFICIENT SYNTHESIS OF TRI- AND TETRASUBSTITUTED FURANS

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C114 $B(C_6F_5)_3$-CATALYZED ALLYLATION OF SECONDARY PROPARGYLIC ACETATES WITH ALLYLSILANES

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C115 C_3-SYMMETRIC TRILACTAM SCAFFOLDS: EFFORTS TOWARD THE DEVELOPMENT OF A SMALL MOLECULE MIMIC OF DEPSIPEPTIDE MEGASYNTHETASE

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C116 RESEARCH TOWARD THE TOTAL SYNTHESIS OF LACTONAMYCIN

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C117 SYNTHESIS OF CARBOCYCLIC NUCLEOSIDE ANALOGS OF NUCLEOSIDE Q
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C118 HIGHLY SATISFACTORY ALKYNYLATION OF ALKENYL HALIDES VIA Pd-CATALYZED CROSS-COUPLING WITH ALKYNYLZINCS AND ITS CRITICAL COMPARISON WITH THE SONOGASHIRA ALKYNYLATION
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C119 SYNTHESIS AND ABSOLUTE CONFIGURATION OF 3-CHLOROBUTYNE
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C120 SYNTHESIS OF SUBSTITUTED PHENANTHROLINE LIGANDS VIA SAMARIUM-PROMOTED COUPLING WITH KETONES, ALDEHYDES, AND EPOXIDES
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C121 SN2'-AZIRIDINE RING OPENING APPROACH TO THE SOLID-PHASE SYNTHESIS OF AN *E* ALKENE PEPTIDE ISOSTERE LIBRARY
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C122 A FACILE METHOD FOR THE DEPROTECTION OF KETOXIMES USING BISMUTH BROMIDE-BISMUTH TRIFLATE
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C123 INTRAMOLECULAR ALLENE–NITRILE OXIDE CYCLOADDITIONS
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C124 METATHETICAL RING CLOSURE OF ORGANOMETALLIC COMPLEXES
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C125 NEW REAGENTS FOR ENANTIOMERIC EXCESS DETERMINATION
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C126 THE AZACYCLOPENTENYL CARBINYL RADICAL ISOMERIZATION (ACCRI): DISCOVERY, DEVELOPMENT AND POTENTIAL BIOLOGICAL IMPLICATIONS
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C127 GENERATION OF TWO READY TO SCREEN LIBRARIES VIA BIGINELLI THREE COMPONENT CONDENSATION WITH NOVEL SUBSTRATES

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C128 ACCESS TO L-SUGARS AND MIRROR-IMAGE OLIGOSACCHARIDES FROM 4-DEOXYPENTENOSIDES AND L-GLYCALS

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C129 RECENT PROGRESS IN THE SYNTHESIS OF 1,5-METHYLENESEMIBULLVALENE

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C130 THE NON-MAJORS ORGANIC COURSE: WHY DO WE DO WHAT WE DO TO THEM?

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C131 TIM: THE DISPERSED REU SITE

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C132 BIOMIMETIC STEREOSELECTIVE FORMATION OF METHYLLANTHIONINE

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C133 STUDIES TOWARDS THE TOTAL SYNTHESIS OF VIBSANINE E (1)

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C134 SYNTHESIS AND BINDING PROPERTIES OF CYCLOPENTANE-CONSTRAINED PEPTIDE NUCLEIC ACIDS

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C135 INTRA- AND INTERMOLECULAR COUPLING OF ALKENES TO HETEROCYCLES VIA C-H BOND ACTIVATION

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C136 CATALYTIC ASYMMETRIC SYNTHESIS OF A POTENT PDE IV INHIBITOR

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C137 ENANTIOSELECTIVE TOTAL SYNTHESIS OF THE PUTATIVE STRUCTURE OF LEPADIFORMINE

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C138 A SIMPLE, RAPID PROCEDURE FOR THE SYNTHESIS OF CHLOROMETHYL METHYL ETHER (MOMCl) AND OTHER CHLORO ALKYL ETHERS

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C139 SYNTHESIS AND HERBICIDAL EVALUATION OF ISOXAZOLYLTETRAZOLINONES

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C140 SYNTHESIS OF CHITIN-LIKE TETRASACCHARIDE AND ITS TETRA-*O*-METHYL DERIVATIVE

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C141 CHIRAL AZIRIDINE-2-CARBOXALDIMINE AS A VERSATILE SUBSTRATE: ASYMMETRIC SYNTHESIS OF VARIOUS NITROGEN CONTAINING HETEROCYCLES

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C142 ASYMMETRIC TANDEM MICHAEL-ALDOL REACTION TRIGGERED BY INTRAMOLECULAR MICHAEL ADDITION OF THIONES TO ENONES

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C143 STUDIES TOWARD THE DEVELOPMENT OF A GENERAL MECHANISM FOR LUMINESCENT REPORTING IN CHEMOSENSORS FOR ORGANIC SPECIES

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C144 2-(ANILINOMETHYL)IMIDAZOLINES AS ALPHA1 ADRENERGIC RECEPTOR AGONISTS: IN VITRO SAR OF THE 2' POSITION

Jason D. Speake, Michael J. Bishop, Frank Navas, Deanna T. Garrison, Eric C. Bigham, Stephen J. Hodson, David L. Saussy, Jim A. Liacos, Paul E. Irving, and Doug Minick

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C145 NEW SYNTHETIC METHODS OF SELENIUM- AND SULFUR-CONTAINING COMPOUNDS USING NOVEL SELENIUM AND SULFUR TRANSFER REAGENTS

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C146 DIASTEREOSELECTIVE PAUSON-KHAND REACTIONS OF YNAMIDES

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C147 SYNTHESIS OF THE CARBOCYCLIC CORE OF THE CORNEXISTINS USING RING-CLOSING METATHESIS

Frederic J. Marlin and J. Stephen Clark

Nottingham University
School of Chemistry, Nottingham NG7 2RD, England

C148 TOTAL SYNTHESIS AND PRECURSOR-DIRECTED BIOSYNTHESIS OF EPOTHILONE ANALOGUES

Annette Vitale Brown, Sreenivasulu Bandaru, Florence Morel, and Richard E. Taylor*

University of Notre Dame
Department of Chemistry and Biochemistry, Notre Dame, IN 46556

C149 SYNTHESIS OF NOVEL INDOLYL-ISOQUINOLINYL/QUINOLINYLPYRROLE-2, 5 DIONES AND CORRESPONDING CARBAZOLE ANALOGS PROVIDE POTENT AND SELECTIVE KINASE INHIBITORS

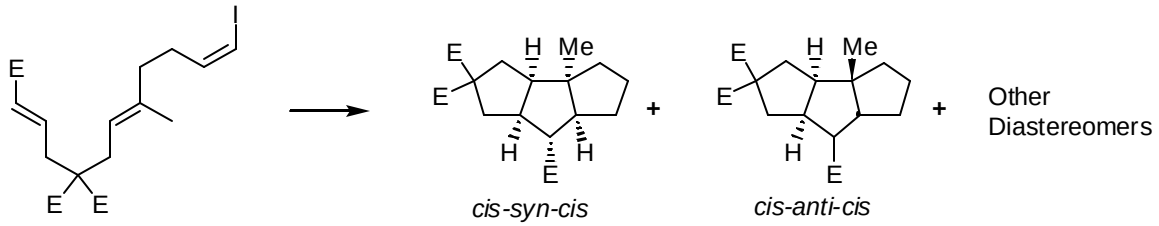
Scott E. Conner, Guoxin Zhu, Xun Zho, Chuan Shih, Timothy Burkholder, Harold B. Brooks, Charles D. Spencer, Scott A. Watkins, Eileen Considine, Jack A. Dempsey, Cathy Ogg, Bharvin Patel, Richard M. Schultz, Karen L. Huss, Ron Kaplan, Shehnaz Khan, Bryan D. Anderson, and Robert M. Campbell

Lilly Research Laboratories, A Division of Eli Lilly & Company
Lilly Corporate Center, Indianapolis, Indiana 46285, USA

Synthesis of Linear Triquinanes by Round Trip Radical Cyclizations

Jonathan C. Tripp, Dennis P. Curran
University of Pittsburgh
Department of Chemistry, Pittsburgh, PA 15260

Diastereoselective synthesis of linear triquinanes by cascade radical reactions from acyclic precursors is complicated by the formation of multiple diastereomers. It was recently reported that when precursor **1** was subjected to radical cyclization conditions at different temperatures, different product ratios were obtained.



1

E = CO_2Me

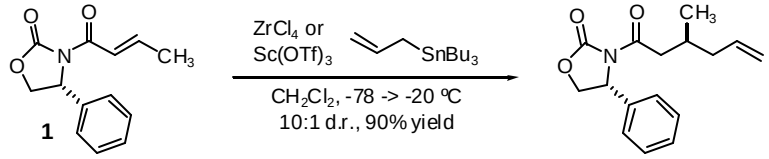
red. agent	Init.	T (ºC)	***cis-syn-cis***	***cis-anti-cis***	**other**	Yield (%)
Bu_3SnH	AIBN	80	4	3	4	80
Bu_3SnH	Et_3B	rt	4	3	0	83

In trying to reproduce this work, we saw no difference in the diastereoselectivity with four tricycles being formed under either conditions. Our results show that prematurely reduced radical products are mistakenly assigned as the additional tricyclic diastereomers. In addition we have explored two model systems that probe the stereoselectivity of the key, second 5-*exo* radical cyclization.

ASYMMETRIC CONJUGATE ADDITION OF ALLYLSTANNANES

Richard J. Mullins, Nathan A. Miller, David R. Williams
Indiana University, Department of Chemistry
800 E. Kirkwood Ave., Bloomington, IN 47405-7102

Our goals in natural product synthesis have recently focused on conjugate addition processes where asymmetry is controlled by the use of the 4-phenyl-oxazolidinone chiral auxiliary. In this well-studied area, relatively little attention has been paid to Lewis acid promoted conjugate additions of allylstannanes. Using either zirconium(IV) chloride or scandium(III) triflate, the reactions of allyltri-*n*-butyl stannane with **1** were found to proceed with high diastereoselectivity and in good yield. Surprisingly, the stereochemical outcome of these reactions was opposite to that which was expected based on the widely accepted model for the role played by the chiral auxiliary.



A useful model for proving the stereochemistry of products of conjugate additions to **1** based on ^{1}H NMR will be presented. The utility of this methodology for the preparation of complex intermediates for natural products total synthesis will be demonstrated.

SUBSTITUTION REACTIONS OF 1,4-NAPHTHOQUINONES

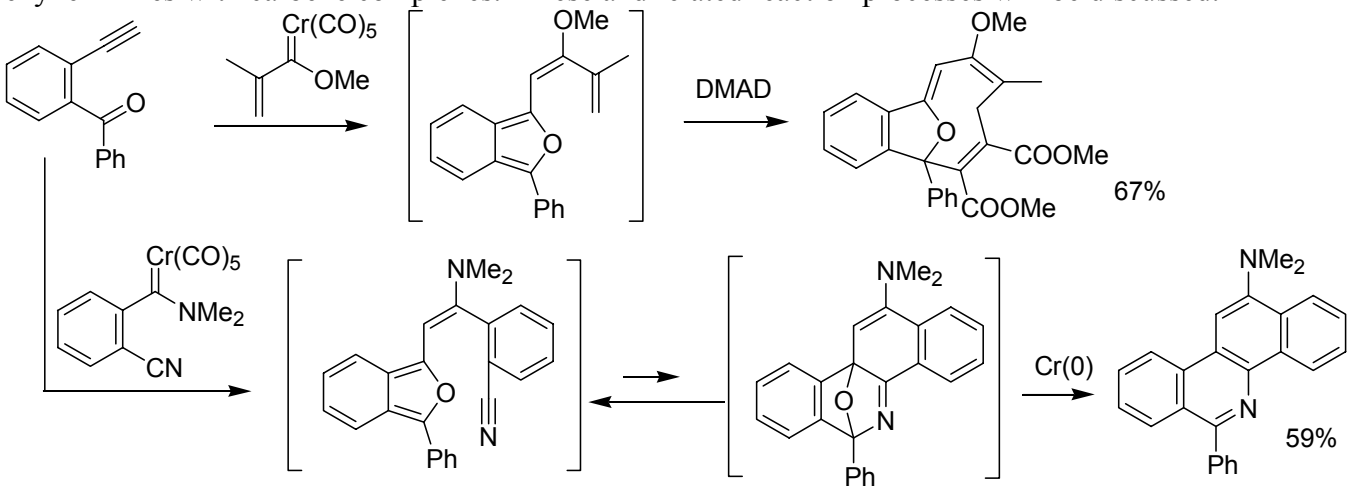
Heather J. Crump, Cameron P. Iverson, Carolyn. B. Lauzon, Sarah J. Stadler, Bryanne L. Stills, Rachael Y. Williams, and Tetsuo Otsuki*
Department of Chemistry, Occidental College
1600 Campus Road, Los Angeles, CA 90041

The substitution reaction of 1,4-naphthoquinones is an important step toward the synthesis of biologically active 1,4-naphthoquinone derivatives. Although there are many reports, there is no systematic study that allows us to introduce a specific substituent at a specific position. Here, we study the substitution reactions at the 2- and/or the 3-position of 1,4-naphthoquinones to establish a method of introducing a specific substituent at a specific position. When 2-bromo-3-methoxy-1,4-naphthoquinone is reacted with an alkylamine in methanol, 3-methoxy group is replaced with an alkylamino group, whereas 2-bromine atom is substituted by an alkylthio group in the reaction of an alkylthiol in the presence of an amine. By applying these two substitution reactions sequentially, we are able to synthesize 2-alkylamino-3-alkylthio-1,4-naphthoquinone in an excellent yield, starting from 2-bromo-3-methoxy-1,4-naphthoquionone. Under illumination of light, on the other hand, the reaction of 2-bromo-3-methoxy-1,4-naphthoquinone with an alkylamine yields 2-alkylamino-3-methoxy-1,4-naphthoquinone through the replacement of 2-bromine atom with an alkylamino group. Obviously, the reaction mechanisms governing each substitution reaction are different. In the reaction with an alkylamine, interestingly, the 3-methyl group of 2-bromo-3-methyl-1,4-naphthoquinone is replaced with an alkylamino group to form 2-alkylamino-3-bromo-1,4-naphthoquinone. In the presence of a tertiary amine, an alkanedithiol such as 1,2-ethanedithiol reacts with various 2- and/or 3-halogenated 1,4-naphthoquinones, yielding 2,3,9,10-tetrahydro-1,4-dithiaanthracene-9,10-dione.

COUPLING OF HIGHLY CONJUGATED ALKYNES WITH CARBENE COMPLEXES

James W. Herndon, YuMei Luo, Yanshi Zhang, Binay Ghorai
New Mexico State University
Department of Chemistry & Biochemistry, MSC 3C, Las Cruces, New Mexico 88003

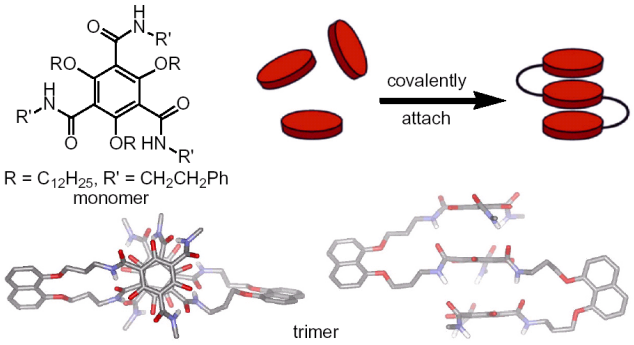
For several years the coupling of carbene complexes with highly conjugated alkynes has been investigated in this laboratory. Recent highlights include the tandem [8+2] cycloaddition from the three-component coupling of 2-ethylylbenzophenone, a novel synthesis of isoquinolines from 2-ethynylbenzaldehyde derivatives and β-cyanocarbene complexes, and preparation of pyrroles from enyne-imines with carbene complexes. These and related reaction processes will be discussed.



A FOLDED, SECONDARY STRUCTURE IN STEP-GROWTH OLIGOMERS FROM COVALENTLY LINKED, CROWDED AROMATICS

*Wei Zhang, Dana Horoszewski, John Decatur, and Colin Nuckolls**
Columbia University
Department of Chemistry, New York, New York 10027

This study delineates general methods to create a new class of folded oligomers by covalently attaching overcrowded aromatics to each other. Crucial to observing the secondary structure in these oligomers was the employment of C-shaped linkers. These linkers preorganize the strands to form intramolecular hydrogen bonds. In solution, one- and two-dimensional ^{1}H NMR data show well-defined columnar conformations. The side chains in these oligomers are critical for the secondary structure to emerge in solution. Using tris(dodecyloxy)phenethyl side chains in combination with *tert*-butyl side chains in the terminal subunit provides a soluble trimer and prevents intermolecular association above millimolar concentrations. This new folding motif, formed through a synergy between hydrogen bonds and π-stacking, is so robust that even dimers have secondary structure in solution.



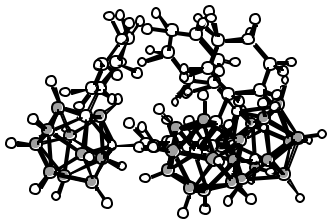
Construction of Three-dimensional Structures Based on Spatial Definition by 1,2-Dicarba-*closo*-dodecabarane (*o*-Carborane)

***Kiminori Ohta*[1], *Chalermkiat Songkram*[2], *Kentaro Yamaguchi*[3], *Yasuyuki Endo*[1]**

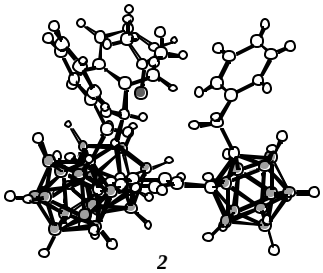
[1]Faculty of Pharmaceutical Sciences, Tohoku Pharmaceutical University; [2]Graduate School of Pharmaceutical Sciences, University of Tokyo; [3]Chemical analysis Center, Chiba University

[1]4-4-1, Komatsushima, Aoba-ku, Sendai 981-8558, Japan; [2]7-3-1, Hongo, Bunkyo - ku, Tokyo 113-0033, Japan; [3]1-33, Yayoi-cho, Inage-ku, Chiba 250-8522, Japan

The icosahedral carboranes (dicarba-*closo*-dodecaboranes) have attracted considerable attention in both their fundamental properties and their wide-ranging potential applications. The rigid geometries of the *ortho*, *meta* and *para* isomers of carboranes make excellent candidates in supramolecular chemistry. Here we show that 1,3,5-tris(2-phenyl-*o*-carboran-1-yl)benzene (**1**) and 1,3,5-tris(2-benzyl-*o*-carboran-1-yl) benzene (**2**) have *syn* conformations of all the terminal benzene rings, despite their steric overcrowding, and forms a cavity covered with four benzene rings. Moreover, we discovered that the compound (**2**) has the ability to entrap the small molecules such as acetone into the central cavity in crystalline state. The terminal phenyl and benzyl groups make a profound role to determine the *syn* stereochemistry by hydrophobic interactions, such as edge-to-face interaction between terminal benzene rings. Based on the results described here, it can be designed and synthesized carborane-containing molecules that provide a nature as a host molecule in supramolecular chemistry.



1

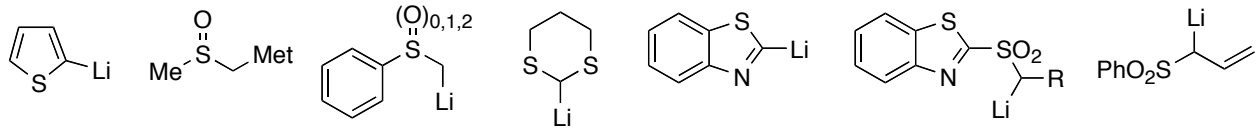


2

A No-D* ^{1}H NMR Study of Useful Sulfur-Stabilized Organolithium Reagents

Thomas R. Hoye, Jennifer L. Green, and Mikhail M. Voloshin

Department of Chemistry, University of Minnesota, Minneapolis, MN 55455



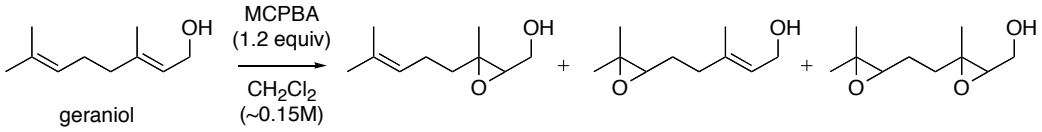
Sulfur-stabilized organolithium reagents like those shown above are useful in a wide variety of synthetic methods. No-D* proton NMR studies of the formation, stability, and reactivity of various of these carbanions will be presented.

* No-Deuterium

A "Boot Camp" Training Exercise in the Hoye Group: The Epoxidation of 1.0 mg of Geraniol

Thomas R. Hoye and Christopher S. Jeffrey

Department of Chemistry, University of Minnesota, Minneapolis, MN 55455



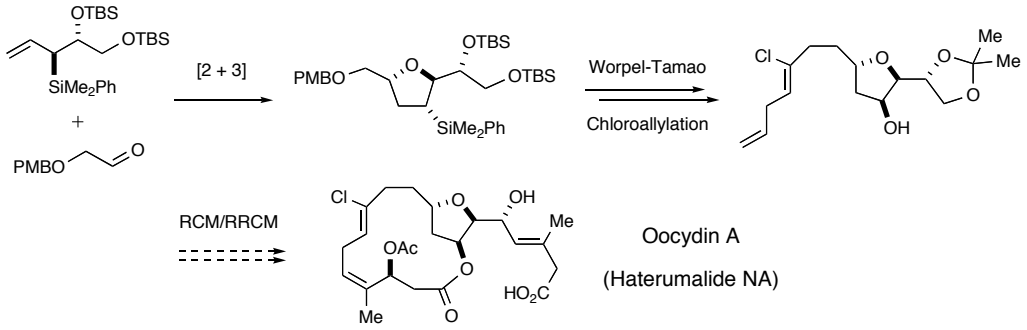
geraniol

The typical student embarking on graduate study today has had a meaningful undergraduate research experience. However, very few have designed and executed a reaction on small scale. Our working hypothesis is that the ability to confidently design, execute, isolate, purify, and characterize the reactions and their products at the, say, 1 mg level correlates with greater levels of success in many aspects of synthetic chemistry research. Therefore, we have identified an exercise that permits a student to gain such experience long before the skill is critically needed. Specifically, all new researchers entering our laboratory are encouraged to perform the above epoxidation reaction, using less than two equivalents of *m*-chloroperoxybenzoic acid (MCPBA), to separate the epoxide products, and to characterize them by GC/MS and ^{1}H NMR spectroscopy. Aspects of this empowerment experience will be presented.

Efforts Toward a Total Synthesis of Oocydin A (Haterumalide NA)

Thomas R. Hoye and Jizhou Wang

Department of Chemistry, University of Minnesota, Minneapolis, MN 55455

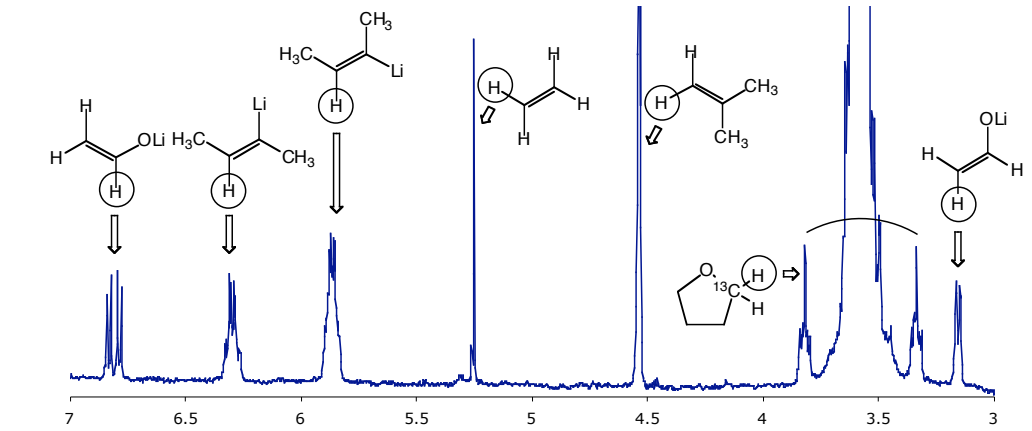


Oocydin A (haterumalide NA), a potent anti-fungal agent, was isolated from two unrelated organisms, an epiphyte (bacterium) and an Okinawan sponge. The key reactions in our synthesis efforts to date include a [2 +3] cyclization between secondary allylic silane and aldehyde partners (*a la* Roush), a palladium-catalyzed chloroallylation to set the *Z*-chloroalkene geometry, and a Tamao oxidation under Woerpel conditions. RCM and RRCM (relay ring-closing metathesis) are under study to close the 14-membered macrolactone.

A No-D* ^{1}H NMR Study of Some Alkenyllithium and Grignard Reagents

Thomas R. Hoye, Ziyad F. Al-Rashid, and Mikhail M. Voloshin

Department of Chemistry, University of Minnesota, Minneapolis, MN 55455



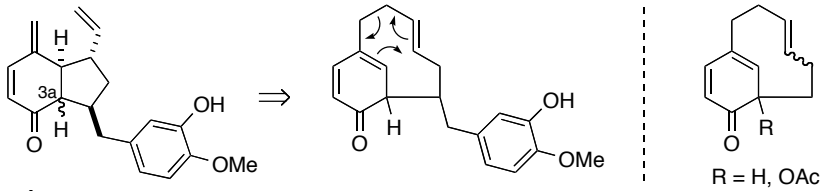
No-D* ^{1}H NMR spectroscopy of alkenyllithiums and alkenylmagnesium halides permits direct observation of, e.g., i) the concentration (titer) of these solutions vs. natural abundance $^{13}C\mathit{H}_{n}$ solvent peaks or added internal standard, ii) the integrity of the double bond geometry, and iii) stability/storage issues in various solvents. Various examples will be presented.

* No-Deuterium

A Biomimetically Inspired Cope Rearrangement: Can a Biosynthetically Relevant, All-carbon [3,3]-Sigmatropic Reorganization Proceed Under Ambient Conditions?

Thomas R. Hoye and James E. Kabrhel

Department of Chemistry, University of Minnesota, Minneapolis, MN 55455



1a H(3a) □

1b H(3a) □

2

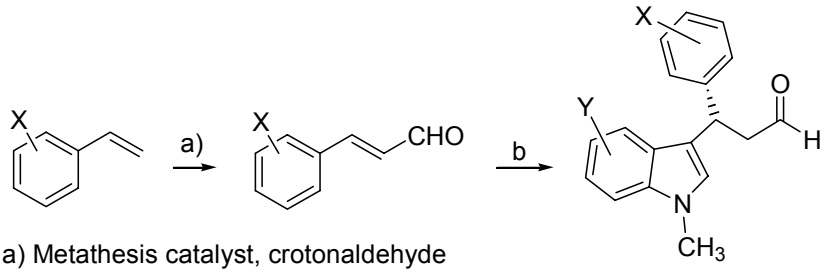
3

Otteliones A and B (**1a** and **1b**) have been isolated from *Ottelia alismoides*, an aquatic plant from the Nile River. Other compounds (diarylheptanoids) isolated from the same species have led us to propose a biosynthetic pathway to the ottelione skeleton. A key feature of our hypothesis is a [3.3]-sigmatropic rearrangement within **2**. Studies toward the synthesis of compounds like **3**, with which we intend to establish the rates of rearrangements like that of **2** to **1** will be presented.

Complementary Cross Metathesis and OrganoCatalysts™ Catalyzed Enantioselective Indole Alkyation Reactions

Wen-Jing Xiao* and *Richard L. Pederson
Materia, Inc., Fine Chemicals R&D
12 N. Altadena Dr., Pasadena, CA 91107

The chiral indole framework is acknowledged as a privileged pharmacophore and is represented in 40 medical agents of broad therapeutic action.[1] Chiral indoles are difficult to prepare by traditional synthetic techniques; however, David MacMillan's group, at Caltech, has developed a class of highly enantioselective imidazolidinone catalysts, trade-named OrganoCatalysts™, that catalyze a broad range of enantioselective chemical reactions,[2] including enantioselective indole alkylations.[3] We were interested in expanding the enantioselective indole alkylations to generate valuable pharmaceutical intermediates for drug discovery. Novel α,β-unsaturated aldehydes, which serve as substrates in these reactions, were not readily available and represented a limitation to the powerful OrganoCatalysis™ technology. In this poster, we will present the preparation of novel α,β-unsaturated aldehydes via olefin cross metathesis and the synthesis of valuable chiral indole compounds via OrganoCatalysis™.



a) Metathesis catalyst, crotonaldehyde
b) Organocatalyst, indole

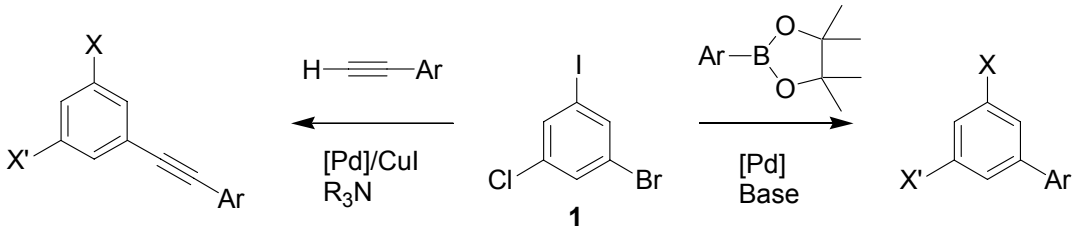
86% to 94%ee

1) For lead references, see: Kleeman. A,; Engel, J.; Kutscher, B.; Reichert, D.; Pharmaceutical Substances, 4th Ed..; Thieme: New York, 2001. 2) Paras, N.A.; MacMillan, D.W.C *J. Am. Chem. Soc*. **2001**, *123*, 4370. 3) Austin, J.F.; MacMillan, D.W.C *J. Am. Chem. Soc*. **2002**, *124*, 1172. 4) Chatterjee, A.K.; Morgan, J.P.; Scholl, M.; Grubbs, R.H. *J. Am. Chem. Soc*. **2000**, *122*, 3783.

COMBINATORIAL SCREENING OF REAGENTS AND CATALYSTS IN HOMOGENEOUS METAL MEDIATED CROSS-COUPLING REACTIONS

Michael W. Pelter, Libbie S. W. Pelter, Regina Strug, Ken Berg, Amy Gorcowski
Purdue University Calumet
Department of Chemistry & Physics, Hammond, IN 46323

In this presentation, progress towards efficient and controlled syntheses of molecular wires and single molecule components will be discussed. Initial studies will be presented that explore the efficiency and selectivity of carbon-carbon bond forming reactions using a combinatorial approach to evaluate the effect of subtle variation in reaction conditions and choice of catalyst. The use of a single substrate with three different halogens to serve as reaction sites has not been previously investigated. A more efficient synthesis of 1-bromo-3-chloro-5-iodobenzene (**1**) has provided a means to synthesize this substrate in sufficient quantities for studies of metal mediated cross-coupling reactions. We employ both solution-phase and solid-phase chemistry to investigate the utility of both Suzuki and Sonogashira cross-coupling reactions. Using a combinatorial approach, the reactivity at each halogenated site will be probed through subtle variation in reaction conditions and choice of catalyst.



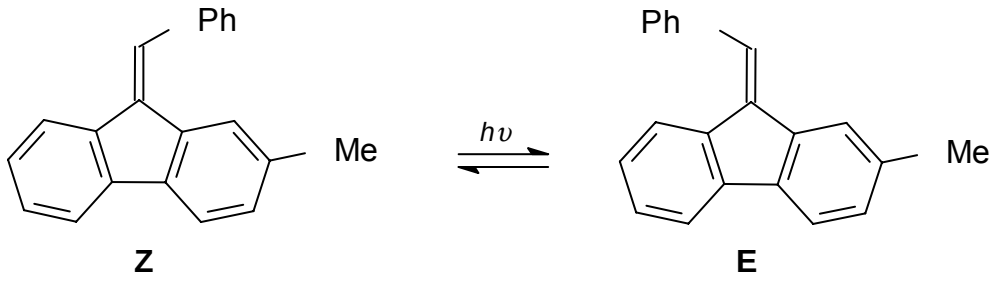
SYNTHESIS AND PHOTOISOMERIZATION OF 2-*TERT*-BUTYL-9-(2,2,2-TRIPHENYLETHYLIDENE)FLUORENE

Thomas W. Bell, Rolando Procupez, Daniel J. Phillips, Vincent J. Catalano, James Barr, and Joseph I. Cline*

University of Nevada, Reno

Department of Chemistry/MS 216, Reno, NV 89557-0020

ight mediated interconversion of cis and trans stilbene and other 1,2-diarylethenes has been well studied, but photoisomerization of 1,1-diarylethenes has scarcely been investigated. n order to evaluate the sterically geared alkene -(2,2,2-triphenylethylidene)fluorene[1] as a chromophore for use in light-driven molecular motors, we synthesized the 2-*tert*-butyl derivative in five steps from fluorene. Separation of the and stereoisomers by chromatography and crystallization gave pure samples of each for structure determination and measurement of photoisomerization and fluorescence quantum yields.

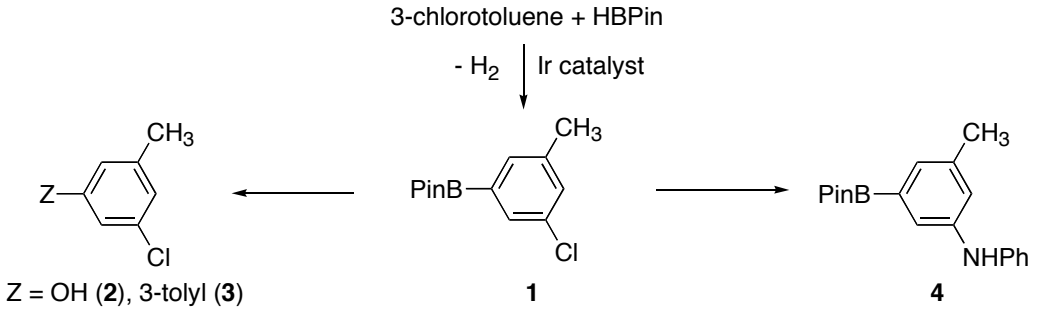


1. T. . Bell, . . Catalano, M. .B. Drew, and D. . Phillips, *Chem. Eur. J*. **2002**, *8*, 1- .

Aromatic Borylation Applied to "One-Pot" Syntheses of Substituted Phenols, Arylamines, and Biaryls

Daniel Holmes, Feng Shi, G. Abbas Chotana, Robert E. Maleczka, Jr. and Milton R. Smith, III
Michigan State University
Department of Chemistry, East Lansing, MI 48824-1322

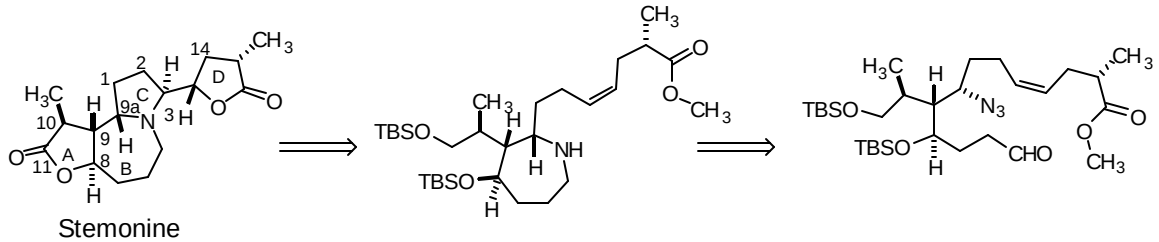
In Ir-catalyzed dehydrogenative borylations, where boranes and sp^2-C–H bonds couple generating H_2 and sp^2-C–$B(OR)_2$ species, unique regioselectivities result primarily from steric effects of the substrate. We have found that the Ir catalysts utilized in these reactions are so exquisitely selective for C–H activation that subsequent transformations, some of which are metal-catalyzed, can be performed using crude reaction mixtures to afford high yields of desired products. For example, 3-chlorotoluene is selectively activated at the 5-position and with pinacolborane provides the corresponding pinacolate ester, **1**. Crude reaction mixtures of compound **1** can be converted to phenol **2** by reaction with Oxone®, biaryl **3** using a Miyaura-Suzuki coupling, or aryl amine **4** via a Buchwald-Hartwig amination with aniline. The scope of this chemistry will be outlined and extensions to other "one-pot" transformations will be presented.



TOTAL SYNTHESIS OF (–)-STEMONINE

D. R. Williams and Khalida Shamim
Indiana University, Bloomington, IN-47401

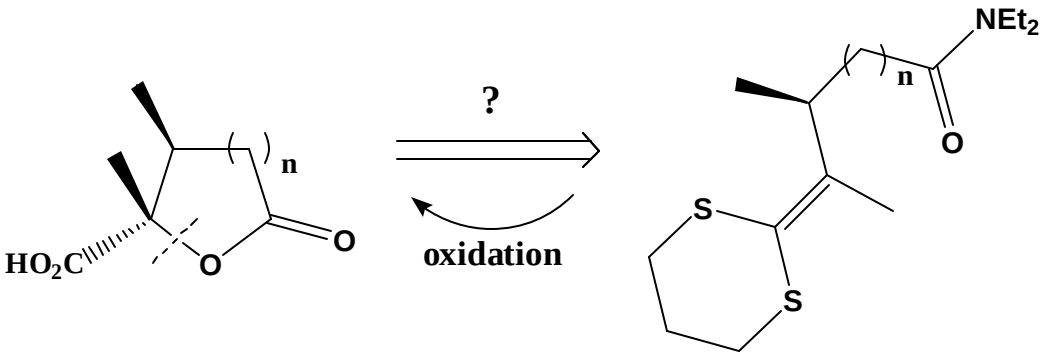
The stemona alkaloids represent a class of polycyclic alkaloids isolated from the *Stemonaceae* family, a collection of monocotyledonous plants, used in Chinese and Japanese folk medicine. This family of alkaloids is used for the treatment of respiratory diseases and as anthelmintics. Recently, we have completed the total synthesis of a family member (–)-stemonine. The synthesis involves the construction of the azepine core by a Staudinger/aza-Wittig reaction which is followed by imine reduction. The resultant secondary amine is then used in a tandem ring closing sequence initiated by iodine to form the pyrrolidino-butyrolactone ring system of the natural product.



The Electrochemical Production of Substituted Lactones

John Brandt, Bin Liu, Kevin D. Moeller
Department of Chemistry, Washington University, Campus Box 1134,
One Brookings Drive, St. Louis, MO 63130, USA, Fax: 314-935-4481
jdbrandt@artsci.wustl.edu, moeller@wuchem.wustl.edu

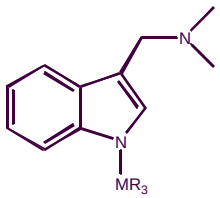
We have found that amide carbonyls efficiently trap radical cations that are derived from ketene dithioacetals. The reactions lead to lactone products and are capable of generating highly hindered carbons. Are such reactions useful for synthesizing substituted furanone natural products? The poster presented will focus on the optimal conditions for effecting the cyclization, potential mechanisms for the reaction, and developing synthetic strategies for capitalizing on the unique synthetic advantages offered by the reactions.



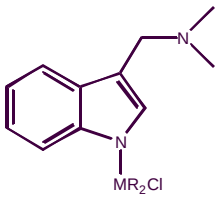
METAL COMPLEXES BEARING INDOLE MOIETIES

Valerian Dragutan[1], *Ileana Dragutan*[1], *Taeboem Oh*[2], *Alex Schultz*[2] *and Tania Tasu*[2]
[1]**Romanian Academy, Institute of Organic Chemsitry, 71141 Bucharest, Romania;**
[2]**California State University Northridge, Department of Chemistry, Northridge, CA 91330-8262**

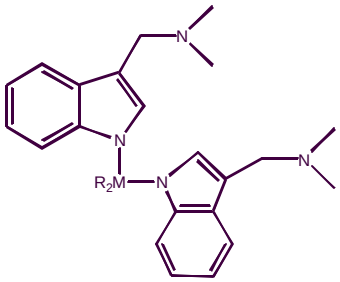
In order to evaluate the effect of ergot alkaloids on the activity of antitumor organometallic compounds based on main group IV metals, this work focuses on the synthesis and characterization of Si, Ge and Sn complexes having as the ligands indole derivatives structurally related to the ergot alkaloids. Representative examples of metal complexes from the below four groups containing as ligands 3-dimethylaminomethyl-indole (gramine) and 3-cyannomethyl-indole residues associated to triphenylgermanium (**1a**), tri-n-butylgermanium (**1b**), triphenyltin (**1c**), tri-n-butyltin (**1d**), diphenyltin (**2a**,**3a**), di-n-butyltin (**2b**,**3b**) and tri-isopropylsilyl (**4a**) are highlighted.



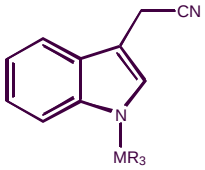
1 a. M = Ge, R = Ph
b. M = Ge, R = n-Bu
c. M = Sn, R = Ph
d. M = Sn, R = n-Bu



2 a. M = Sn, R = Ph
b. M = Sn, R = n-Bu



3 a. M = Sn, R = Ph
b. M = Sn, R = n-Bu



4 a. M = Si, R = i-Pr

THE STUDY OF ALKOXIDE-PROMOTED ENYNE-ALLENE CYCLIZATIONS: NEXT GENERATION ISOLATED ALKENES

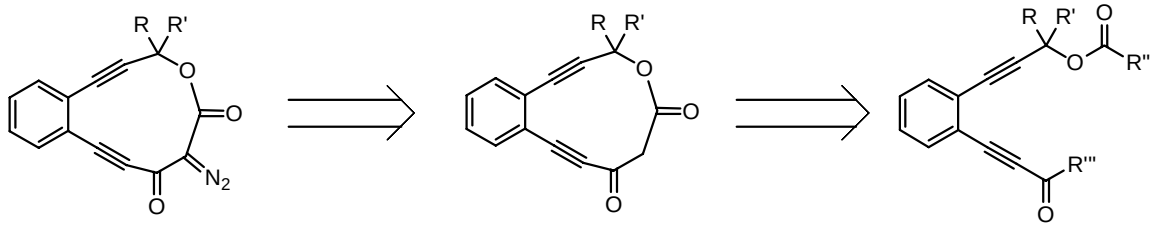
Michelle K. Waddell and Mark A. Lipton*
Purdue University,
Department of Chemistry,
560 Oval Drive, P.O. Box 805, West Lafayette, IN 47907-2084

The ene-diyne antitumor antibiotics, including the neocarzinostatin A chromophore, calicheamicin γ1, esperamicin A1, and dynemicin A, undergo a cycloaromatization of the carbocyclic core to generate a p-benzyne diradical, except NCS A which forms an indenyl diradical which cleaves the DNA backbone by hydrogen atom abstraction. Extensive study of these enediyne natural products led to the discovery that cycloaromatization occurs by two separate mechanisms, named the Bergman and Myers cyclizations. In our research group we have designed a simple model system that consists of a carbocyclic core bearing an enyne-allene moiety. The cyclization of oxyanion-substituted benzannulated enyne-allenes was previously studied in our group and was shown to undergo a C_2-C_6 cyclization rather than the expected C_2-C_7 (Myers) cyclization. The goal of this research is to synthesize an enyne-allenolate, which is composed of an isolated alkene within a cyclohexene ring and an oxyanion substituent. The cyclization products of this compound will be compared with cyclopentannulated and benzannulated derivatives previously studied in our group.

DESIGN AND SYNTHESIS OF CYCLIC ENEDIYNES CONTAINING DIAZODICARBONYL MOIETY

Grigori Karpov, Vladimir Popik
Bowling Green State University
Center for Photochemical Sciences, Bowling Green, OH 43403

A new approach to the design of photoactivatable synthetic enediyne antibiotics has been suggested. Photo-Wolff reaction can be used for efficient photochemical ring contraction of inactive eleven-membered cyclic enediynes into reactive ten-membered structures. Synthetic approaches to the α-diazo-β-dicarbonyl containing enediyne compound, the 3-diazo-2,4-dioxa-benz[7,8]-1-oxacycloundeca-5,9-diyne **(1)**, and the current progress of this work will be discussed. A key step, namely the cyclization of acyclic precursors **(3)** with a pre-formed Z-enediyne fragment into an eleven-membered cyclic enediyne-1,3-dione **(2)** by means of aldol, Claisen and Reformatsky ring closure reactions, has been explored.



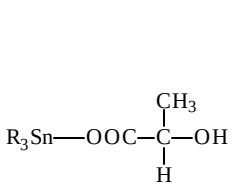
R,R' = H, CH_3; R" = CH_3, CH_2Br ; R'" = H, OCH_2CF_3, OPh, $OC_6H_4NO_2$

NOVEL ORGANOMETALLIC COMPOUNDS AS POTENTIAL ANTITUMOR AGENTS

Valerian Dragutan[1], Ileana Dragutan[1], Mariana Danila[1], Petru Filip[1], Taeboem Oh[2], and Larry R. Sherman[3]

[1]Romanian Academy, Institute of Organic Chemistry, P.O. Box 15-254, 71141 Bucharest, Romania; [2]California State University Northridge, Department of Chemistry, Northridge, CA 91330-8262; [3]Scranton University, Department of Chemistry, Scranton, PA 18510-4626.

Design and synthesis of novel bioactive organometallic compounds of group IV metals (Sn, Ge) comprising an array of selected ligands are described. Among the latter, ligands deriving from hydroxycarboxylic acids or amino acids are important because they are prone to increase the antitumor activity of the parent organometallics through a controlled release of the active metal species into the malignant cell. The overall result is a better assimilation of the bioactive organometallic compound, a higher efficiency of its action at the target site and a reduced toxicity. Synthesis and structural characterization by spectroscopic methods of organotin (e.g. **1**-**5**) and organogermanium complexes based on organo-metal chlorides R_xMCl_{4-x} (M = Sn, Ge; R = n-Bu, Ph) and hydroxycarboxylic acids or amino acids (L-lactic acid, L-ascorbic acid, D-gluconic acid, D,L-glucoheptanoic acid, L-glutamic acid etc.) or the corresponding sodium or calcium salts are discussed in detail.



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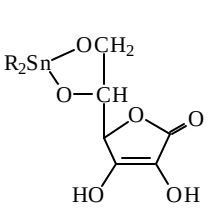

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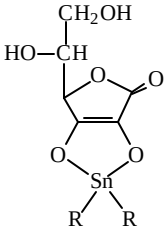

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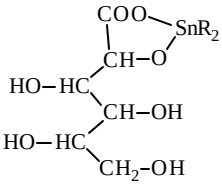

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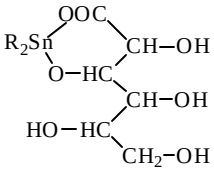
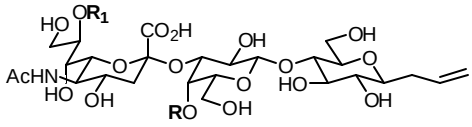


5

Progress Towards a Modular Synthesis of *C*-Linked GM and GD Glycolipid Antigen Derivatives

Christopher A. LeClair*, *Glenn J. McGarvey*
The University of Virginia
Department of Chemistry, Charlottesville, VA 22904-4319

Over the past two decades, numerous tumor associated glycolipid antigens have been identified. The most common being GM_2, GM_3, GD_2, GD_3 which are over expressed on the cell membranes of most melanomas and Fucosyl GM_1 which is a highly specific marker for small cell lung cancer cells. Consequently, these glycolipid antigens are worthwhile targets in the development of synthetic cancer vaccines. Unfortunately, *O*-linked glycolipids have the inherent problem of hydrolytic cleavage *in vivo.* Our research is directed toward the development of a facile and convergent synthesis of *C*-linked gangliosides, which are not prone to β-elimination, from inexpensive and readily available starting materials. Of major importance in this endeavor is the ability to stereoselectively and stereoconvergently install *C*-glycosidic linkages but current methods are lacking especially for the more difficult β-glycoside. The synthesis of α and β-*C*-glycosides from a common sulfoxide precursor has been under development. This *C*-glycosidic sulfoxide methodology is currently being applied to the modular synthesis of *C*-allyl analogues of the GM_2, GM_3, GD_2, GD_3, and fucosyl GM_1 glycolipid antigens.



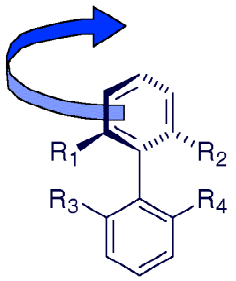
GM_3 antigen: R=H, R_1=H
GM_2 antigen: R=β-2-acetamido-D-galactosyl-(1->4), R_1=H
GD_3 antigen: R=H, R_1=α-*N*-acetylneuraminic acid-(2->8)
GD_2 antigen: R=β-2-acetamido-D-galactosyl-(1->4), R_1=α-*N*-acetylneuraminic acid-(2->8)
Fucosyl GM_1 antigen: R=β-L-fucosyl-(1->2)-β-D-galactosyl-(1->3)-β-2-acetamido-D-galactosyl-(1->4), R_1=H

SINGLE-MOLECULE MOLECULAR MOTORS: STUDIES IN DIRECTED BOND ROTATION

Ying Lin, Jonathan Bingham, William Hallows, Jacob Cha, Mara Kelly, Matthew O Connor, Jason Gatlin, Dima Azar, Bruce Branchaud

University of Oregon

Department of Chemistry and Materials Science Institute, Eugene, OR 97403-1253



An important field in nanotechnology is the development of molecular devices that mimic the function of macroscopic devices. In Nature there are many spectacular examples of molecular devices, including molecular switches and, especially, molecular motors. Biological molecular motors are multi-molecular machines. Each biological molecular motor is composed of several different types of proteins, often with multiple copies of each protein.

We are working on creating synthetic non-biological molecular motors. Part of the inspiration for this project comes from biology. Part comes from recent developments in nanochemistry and nanotechnology.

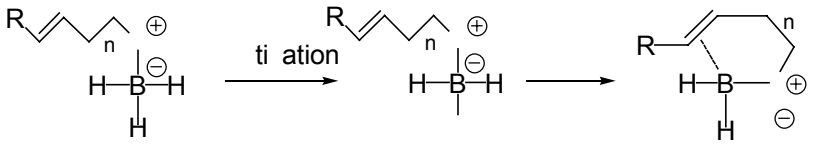
We are focusing on single-molecule rotary motors. Our approach uses energy-driven diastereoselective reactions with chiral molecules to drive bond rotation in a preferred direction.

This poster presents results from current work on directed bond rotation. We are examining different reactions that can direct rotation of the aryl-aryl bond in biaryls in 90-degree increments in a preferred direction. Iterative sequences of such reactions could be used to create functional molecular motors, with net repeated 360-degree rotation about the aryl-aryl bond in one direction.

Intramolecular Hydroboration of Unsaturated Amine Borane Complexes by an Alternative Mechanistic Pathway

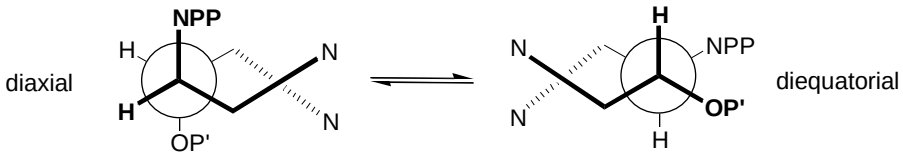
Edwin Vedejs, Matthew Scheideman
University of Michigan, Department of Chemistry
Ann Arbor, MI 48109

odine promoted intramolecular hydroboration of unsaturated amine boranes via a novel pathway has been demonstrated. pon activation, a B-iodoborane intermediate forms that is capable of internal displacement of the iodide leaving group. This results in a proposed cationic borane-alkene π-complex envisioned to be a direct precursor to the hydroborated products. The regio- and stereochemistry obtained following oxidation to amino alcohols is consistent with an intramolecular reaction. Studies involving related methods of activation and substrate reactivity will be presented.



Synthetic and Conformational Study of 1,10-Phenanthroline Derivatives

Elke Schoffers, Eun-Joo Kim, Sun Y. Wallace
Western Michigan University
Department of Chemistry, Kalamazoo, MI 49008

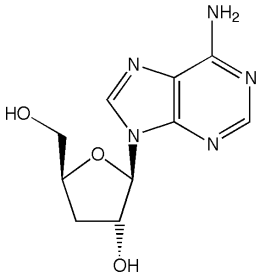


symmetric catalysis has been a very useful tool in the development of single stereoisomers and will continue to impact ma or advancements in the pharmaceutical industry. The goal of our study is to identify and characterize new potential ligands for asymmetric catalysis by utilizing the 1,1 -phenanthroline scaffold. This presentation will address the preparation of , -disubstituted phenanthrolines and the effect of protecting groups (P,P) on conformational preferences (diaxial, diequatorial).

Arylthioaminals as Hydrolytically-Unstable Nucleoside Prodrugs

Hui-Min Chang and Robert R. Kane
Dept. of Chem. & Biochem and The Center for Drug Discovery
Baylor University, Waco, TX 76798

Cordycepin (3'-deoxyadenosine, **1**) is a potent anti-leukemic, anti-fungal, and anti-parasitic nucleosidic antibiotic. Unfortunately, the biological activity of cordycepin is attenuated by its rapid conversion to 3'-deoxyinosine by adenosine deaminase (ADA). We have synthesized a series of *N*-aminal and *N*-thioaminal cordycepin analogues and have found that certain of these are slowly hydrolyzed to efficiently reveal the parent drug. These compounds are not substrates for ADA and retain activity against cancer cell lines, presumably due to their conversion to cordycepin. The most promising compounds are aryl thioaminals (**2**), which exhibit enhanced activity in the absence of ADA inhibition.



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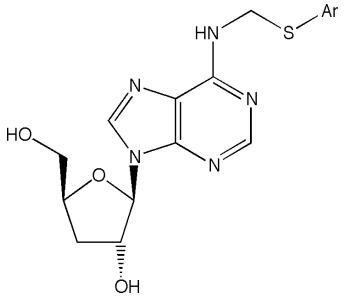


2

SYNTHESIS AND CHARACTERIZATION OF CARBOHYDRATE-CONTAINING MATERIALS FOR DNA DELIVERY

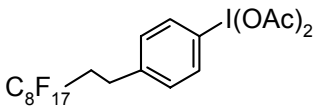
Yemin Liu, Sathya Srinivasachari, and Theresa M. Reineke*
University of Cincinnati, Department of Chemistry
P.O. Box 210172 Cincinnati, OH 45221-0172

Synthetic organic materials, such as polymers and dendrimers, show promise for use in many applications, such as for the delivery of therapeutic genetic material. It has been demonstrated that polymers and dendrimers can readily bind DNA, compact it into structures that facilitate cellular uptake, and efficiently release DNA within cells. Synthetic materials are of particular interest for gene delivery because of the dangers and problems associated with conventional viral nucleic acid delivery systems. Although the use of synthetic DNA delivery vehicles shows great promise, little is known about how or why subtle changes in the structures on molecular level influence the toxicity and gene delivery efficiency to a large degree. Here, a series of tartrate, galactarate, and beta-cyclodextrin-containing polymers and dendrimers, specifically designed for gene delivery, are presented. These structures were systematically created to elucidate structure-property relationships and to facilitate non-toxic and enhanced cellular delivery of nucleic acids. The synthesis, structural characterization, and DNA-binding properties of these materials will be presented. In addition, the toxicity and DNA delivery using these materials with mammalian cell lines will be discussed.

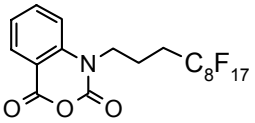
SOLUTION-PHASE LIBRARIES BY FLUOROUS PARALLEL SYNTHESIS

Wei Zhang[1], Christine Chen[1], Zhiyong Luo[1], Tadamichi Nagashima[1], Jeffrey Irwin[1], Yimin Luo[1], Marvin Yu[1], Siva Dandapani[2], and Dennis P. Curran[2]
Fluorous Technologies, Inc.[1] and University of Pittsburgh[2]
970 William Pitt Way, Pittsburgh, PA 15238

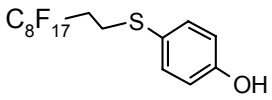
Fluorous chemistry successfully combines the characteristics of solution-phase reactivity with solid-phase like separations. Fluorous synthesis has the following unique features: favorable homogeneous reaction kinetics, intermediate analysis capability, easy product separation, and minimal chemistry development. A series of fluorous compounds, including fluorous reagents, scavengers, and protecting groups has been recently developed at FTI and University of Pittsburgh. This presentation provides several examples to demonstrate the utility of fluorous chemistry in solution phase parallel synthesis. The advantages and limitations of fluorous chemistry versus other commonly employed methods are highlighted.



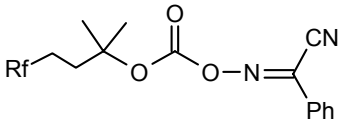
F-reagent



F-Scavenger



F-tag



F-Protecting groups

Recognition Properties and Cellular Transport Ability of Novel Artificial Receptors

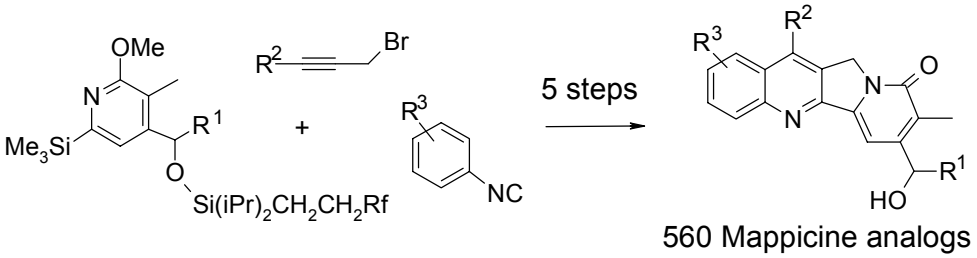
David B. Smithrud,* Inese Smukste, Vadims Dvornikovs, and Brian House University of Cincinnati, Cincinnati OH 45221

There continues to be a great demand for synthetic agents that recognize targeted compounds as well as proteins. These artificial receptors could be key components in affinity chromatography and sensors, act as catalysts, or agents that transport drugs across cell membranes. We have created a new class of binding agents that highlight a convergent arrangement of recognition elements that adjust to provide maximum binding free energy with a guest. Experiments have shown that a convergent arrangement of functional groups provides for a greater binding free energy for guest recognition than a divergent arrangement. Furthermore, the dynamic component of the binding agents does not detract significantly from the binding free energy. These binding agents also efficiently transport fluorescein and some fluorescein derivatives into eukaryotic cells. Most likely, the ability of the functional groups to adjust to their environment, e.g., cell membrane and aqueous milieu, is responsible for the observed transportation.

SOLUTION-PHASE LIBRARIES BY FLUOROUS MIXTURE SYNTHESIS

Wei Zhang, Christine Chen, Marvin S. Yu
Fluorous Technologies, Inc.
970 William Pitt Way, Pittsburgh, PA 15238

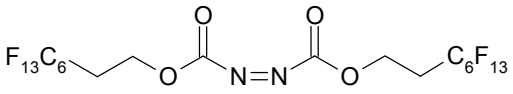
The synthesis and isolation of a 560-compound library using fluorous mixture synthesis (FMS) is described. The basis of this new mixture synthesis technique is the separation of compounds based on fluorine content using a fluorous sorbent. In fluorous mixture synthesis members of a series of unique substrate/fluorous tag pairs are mixed, carried through a series of synthetic transformations and separated using HPLC based on the fluorine content of the tag. A final de-tagging step facilitated by fluorous solid phase extraction results in individual compounds of high purity. These techniques are the first mixture techniques to allow solution phase synthesis yet still allow for both the separation and identification of the final product.



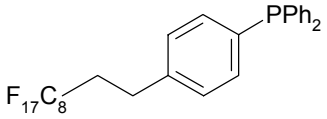
NEW DEVELOPMENTS IN FLUOROUS MITSUNOBU CHEMISTRY

Siva Dandapani[1], Dennis P. Curran[1], Marvin S. Yu[2]
University of Pittsburgh[1] and Fluorous Technologies, Inc.[2]
Department of Chemistry, University of Pittsburgh, Pittsburgh, PA 15260[1]
970 William Pitt Way, Pittsburgh, PA 15238[2]

The Mitsunobu reaction remains one of the most utilized reactions for the inversion of stereocenters and for the formation of carbon-heteroatom single bonds. The major drawback of the traditional Mitsunobu reaction is the removal of the phosphine oxide and hydrazine by-products. The use of fluorous versions of both TPP and DEAD has resulted in a fluorous version of the Mitsunobu that retains nearly all of the characteristics of the traditional reaction with the added benefit of easy removal of the by-products. Studies directed toward the development of new fluorous DEAD reagents and the removal of their by-products will be presented. The fluorous Mitsunobu will be compared with the traditional Mitsunobu and other alternatives to the Mitsunobu to define the advantages and limitations of the fluorous version. Recommendations regarding which fluorous DEAD are appropriate for specific applications will be made.



f-DEAD

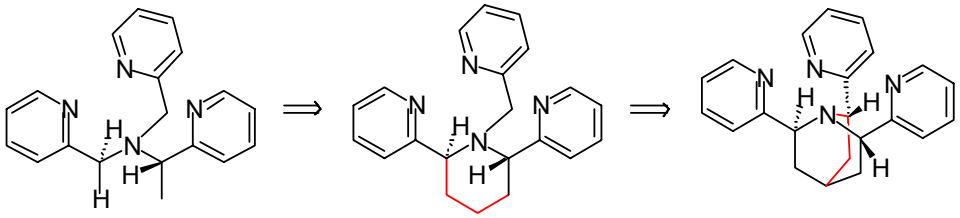


f-TPP

DESIGN AND SYNTHESES OF CHIRAL RIGID TRIPODAL LIGANDS WITH INTERESTING PHOTOPHYSICAL PROPERTIES

Zhaohua Dai and James W. Canary
Department of Chemistry, New York University, New York, NY 10003
zd210@nyu.edu

Our interest in the incorporation of a chiral bias in tripodal ligands has been extended to rigid systems containing piperidine and quinuclidine rings. In our previous studies, compound **2** was shown to bind copper and zinc ions, forming propeller-shaped complexes. The new piperidine and quinuclidine systems possess additional chiral centers and display interesting fluorescence and circular dichroism properies. These rigid compounds provide an opportunity to differentiate the relative binding energies of certain metal ions. Thus, stereochemistry is used to pre-organize the receptors to achieve metal ion selectivity.



2 **piperidines** **quinuclidines**

SYNTHESIS, CHARACTERIZATION AND BINDING STUDIES OF NOVEL ORGANOMETALLIC COMPLEXES OF TECHNECIUM, RHENIUM AND COPPER LIGANDS FOR THE ESTROGEN RECEPTOR

Nathan C. Ackroyd, Michael L. Nickels, Michael A. Reynolds and John A. Katzenellenbogen*.

Department of Chemistry, University of Illinois at Urbana-Champaign, Urbana, IL 61801.

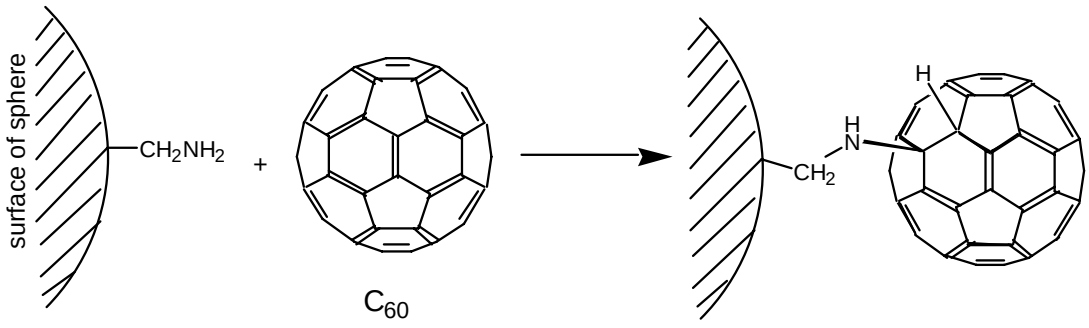
It is known that 60-70% of breast tumors contain significant concentrations of estrogen receptor (ER), and effective methods for determining the ER content of tumors are needed, so that the most effective but least morbid therapy for a particular patient can be selected. Currently, biopsy followed by bioassay or immunoassay is used to determine tumor ER concentration. An alternative, non-invasive approach would be to use functional imaging to determine ER levels in tumors.

Our efforts in developing substituted-cyclopentadienyl (Cp) and 1,4,7-triazacyclononane (tacn) ligands which have an affinity for ER and that can be labeled with radio-isotopes of Tc, Re, and Cu will be described. The uniqueness of our approach involves the placement of the radio-label in the ligand core as opposed to pendant-style radio labels in which the radionuclide is attached to a known estrogen receptor binding ligand through the use of a tether. The synthesis, characterization of these complexes and their relevance to radiopharmaceutical design will be discussed.

FULLERENE-COATED MATERIALS AS REUSABLE CATALYSTS

Anton W. Jensen, Coreen Daniels, John Berry, and Brijesh Maru
Department of Chemistry, Central Michigan University
Mount Pleasant, Michigan 48859

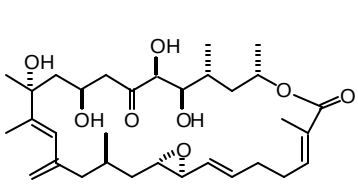
Heterogeneous photocatalysts that convert ground state oxygen to singlet oxygen ($^1O_2$) have been prepared. The catalysts facilitate various singlet oxygenation reactions such as: the Ene reaction, the Diels-Alder reaction, and others. The catalysts are made by coating either aminomethylated poly(styrene-co-divinylbenzene) beads or PAMAM dendrimers with fullerene-C_{60}. Catalysts for aqueous photooxidations are made by reacting the initial catalysts with poly(allylamine) to create an outer layer that is more hydrophilic. Stereoselective photooxidations are achieved by coating the outer layer with cyclodextrins.



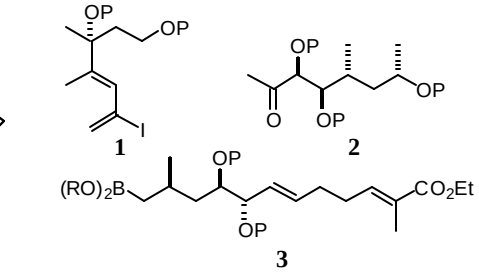
Progress Towards the Total Synthesis of Amphidinolide B1

Craig M. Crews[1,2,3], Amit K. Mandal[3], and John S. Schneekloth, Jr.[1]
Yale University, Departments of [1]Chemistry, [2]Pharmacology, and [3]Molecular, Cellular, and Developmental Biology
New Haven, CT 06520-8107

A convergent route to the synthesis of amphidinolide B1 has been devised, implementing a novel diastereoselective hydroboration/Suzuki-Miayura reaction. Progress towards the synthesis and coupling of fragments **1**,**2**, and **3** will be presented.



Amphidinolide B1



SYNTHESIS OF NOVEL BENZOFURAN ANALOGS AS TUBULIN POLYMERIZATION INHIBITORS AND VASCULAR TARGETING AGENTS

Raymond J. Kessler, [1] ***Mallinath B. Hadimani,*** [1] ***Kevin G. Pinney,*** [1] ***Klaus Edvardsen*** [2]
[1]Baylor University, [2]University of Lund
[1]Department of Chemistry and Biochemistry and the Center for Drug Discovery, Waco, TX 76798-7348, [2]Department of Cell and Molecular Biology, Section for Tumor Immunology, BMC: I 12, S-221 84 Lund, Sweden

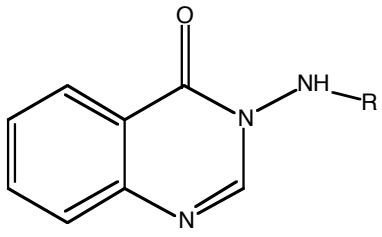
Vascular targeting is an approach to the treatment of cancer that focuses on selective disruption of blood flow to tumor cells, which deprives them of the nutrients and oxygen necessary to sustain metabolic function and survival. This disruption occurs when the endothelial cells lining the tumor vascular undergo a change in shape from flat to round, thereby physically impeding the flow of blood. Agents that inhibit the formation of microtubules, which play a key role in providing a cytoskeleton that maintains cell shape, induce endothelial cell rounding. These agents bind the protein tubulin that comprises microtubules and thus prevent the ongoing polymerization of the microtubules. While microtubule assembly is thus arrested, depolymerization at the other end continues resulting in cytoskeletal collapse and endothelial cell shape change. Several tubulin binding benzofuran-based phosphate prodrugs have been synthesized which are structurally modeled after the potent vascular targeting agents combretastatin A-4 and combretastatin A-1 prodrugs (CA-4P/CA-1P respectively). Synthetic details, biological evaluation, and a discussion of vascular targeting as it relates to tubulin binding agents will be presented.

SYNTHESIS OF 3-AMINO QUINAZOLINONES AS TYROSINE KINASE INHIBITORS

David S. Kuiper, Laurie A. Witucki
Grand Valley State University
Department of Chemistry, Allendale, Michigan 49401

The protein kinase family of enzymes is a target of pharmaceutical interest due to the active role protein kinases play in many diseases, including cancer. These enzymes are involved in cellular processes such as cell proliferation, differentiation, metabolism, and immune response; therefore making them viable candidates for small molecule inhibition. The target for our studies is the SH1 domain of protein tyrosine kinases; this is the location of both the ATP binding pocket and the protein substrate-binding groove. The synthesis of small heterocyclic molecules, which may act as ATP competitive inhibitors specific for tyrosine kinases, is the subject of this investigation. The synthesized compounds are 3-amino quinazolinone derivatives such as 3-amino-3,4-dihydro-4-quinazolinone and 3-amino-3,4-dihydro-2-methyl-4-quinazolinone. Derivitization at the 3-amino position (see structure below) of these parent quinazolinones produced a variety of compounds. Determination of the biological activity of these molecules as inhibitors of Src family tyrosine kinases is currently underway.

3-Amino quinazolinone:



FLUOROUS-SOLUBLE CROWN ETHERS

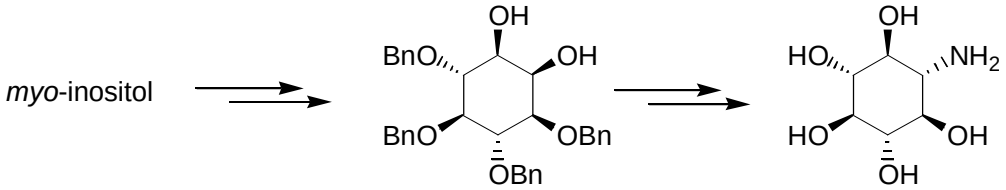
Eric T. Hartman, T. David Bateman, Martin J. Campbell
Henderson State University
Department of Chemistry, Box 7633, Arkadelphia, AR 71999

As part of a research program in Green chemistry, we are developing a series of crown ethers designed to have enhanced solubility in fluorous systems. Fluorous-phase systems use perfluorocarbons in place of hydrocarbons for two-phase synthetic work. Crown ethers and other multidentate ligands have found applications as phase-transfer catalysts, and metal ion scavengers in such systems. Traditional crown ethers have enhanced organic phase solubility when appended with long hydrocarbon tails. Such compounds have unacceptably low solubility in the new fluorous systems. Work on other compounds has demonstrated that, analogous to the hydrocarbon systems, appended perfluorinated side groups significantly enhance fluorous-phase solubility. Eugenol, a naturally occurring and readily available monoprotected allylcatechol, serves as the basis for the synthesis of a new series of crown ethers bearing allyl groups. Radical initiated addition of perfluoroalkyl tails to the allyl groups gives crown ethers of enhanced fluorous-phase solubility without adversely affecting cation complexation.

Rhizopine Synthesis-Potential Mediators for Nitrogen Fixation in Plants

Elke Schoffers, Venkat R. Guduru
Western Michigan University
Department of Chemistry, Kalamazoo, MI 49008.

This research pro ect aims to develop novel and efficient syntheses of inosamine derivatives (rhizopines). The preparation of specific rhizopines would help elucidate bacterial expression of rhizopine catabolism and degradation genes and their biochemical role during nitrogen fixation. e are investigating regio and stereoselective transformations of *myo*-inositol, utilizing organostannanes as key intermediates towards rhizopine **2.**

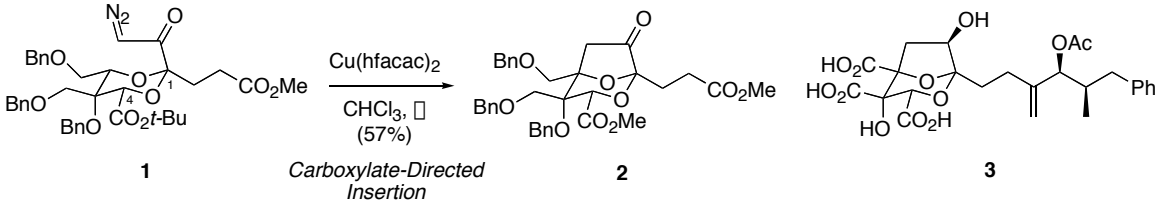


1 **2**

Carboxylate-Directed C-H Activation: Asymmetric Synthesis of an Advanced Intermediate for the Total Synthesis of Zaragozic Acid Ax3

Adriana I. Velter and Duncan J. Wardrop
University of Illinois at Chicago
Department of Chemistry, 845 West Taylor Street, Chicago, IL 60607

Although the carbenoid species generated from □-diazo ketone **1** can potentially undergo insertion into one of four different sets of C-H bonds, diazo decomposition with $Cu(hfacac)_2$ leads to the selective formation of bicycle **2** in reasonable yield. In this case, C-H insertion at the C-4 position of the dioxane ring and into the C-1 sidechain is inhibited by the presence of the carboxylate groups. In addition to a discussion of the regioselectivity of this reaction, the application of this remarkable transformation in the context of our ongoing total synthesis of zaragozic acid A_X3 (**3**) will also be presented.



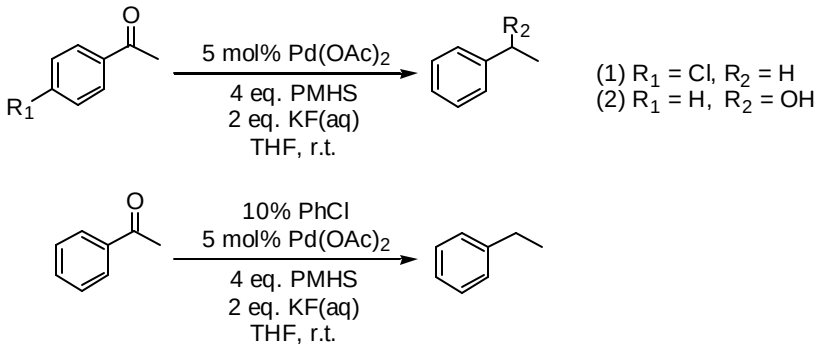
1 **2** **3**

Palladium Catalyzed Deoxygenations with a Curious Chlorobenzene Effect

Ronald J. Rahaim, Jr. and Robert E. Maleczka, Jr.*

Michigan State University

Department of Chemistry, East Lansing, MI 48824



During our work on palladium catalyzed dehalogenations with polymethylhydrosiloxane (PMHS), we discovered that the combination of catalytic $Pd(OAc)_2$, PMHS, and KF can promote deoxygenations. Exploring these conditions further revealed that the presence of an aryl chloro substituent or even the addition of catalytic chlorobenzene facilitates the process. Studies aimed at understanding the role of chlorobenzene and the scope of the deoxygenations will be presented.

DESIGNING CALIX[4]ARENE DIMERS AS MOLECULAR CAPSULES

Kevin L. Caran, Josh S. Sasine, and Suzanne B. Shuker*
School of Chemistry and Biochemistry
Georgia Institute of Technology
Atlanta, GA 30332-0400

The association of organic molecules through noncovalent interactions is becoming increasingly important for the development of novel structures for information storage, molecular transport, sensing, and the assembly of supramolecular structures. Several calixarene derivatives alkylated on the lower rim and variously substituted on the upper rim have been synthesized. Mixtures of these derivatized calixarenes with complementary functional groups form dimers through hydrogen-bonding, hydrophobic interactions and/or ion pairing at their upper rims. Encapsulation of organic guest molecules within the cavity of these dimers suggests their potential use as molecular capsules. Some of our derivatives contain aromatic or amino acid spacers between the calixarene and the charged groups on some or all of the upper rim positions. Varying the identity of and location of functional groups allows us to tune the shape and strength of the dimers. These studies will provide a toolbox of dimers of different size and association constant.

Applications of Ionic Liquids in Organic Synthesis and Catalysis

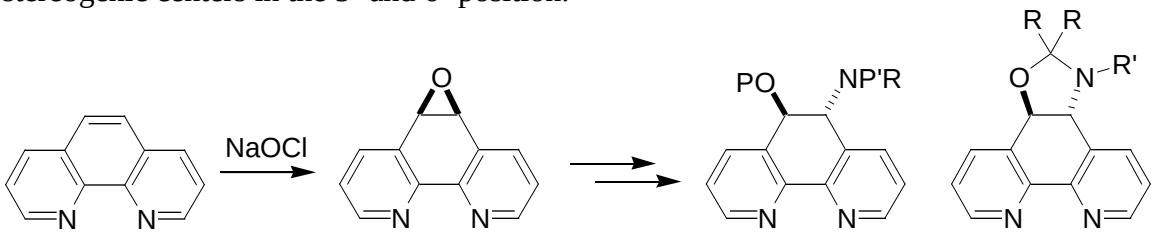
Elke Schoffers, Andy LaFrate
Western Michigan University
Department of Chemistry, Kalamazoo, MI 49008

Known and novel room temperature ionic liquids were investigated as solvents for organic transformations. Ionic liquids possess several advantages over conventional organic solvents including: high thermal stability, lack of vapor pressure at ambient temperatures, customizable solubility for liquid-liquid extractions, and the ability to be recycled. Palladium-catalyzed coupling reactions of simple aryl halide systems and modified artificial nucleosides with aryl amines were studied in ionic liquids. We also investigated the use of ionic liquids as an alternative to polar organic solvents (i.e. DMF or DMSO) for reactions involving other polar intermediates.

Synthesis of 1,10-Phenanthroline Derivatives as Ligands for Asymmetric Catalysis

Elke Schoffers, Son D. Tran
Western Michigan University
Department of Chemistry, Kalamazoo, MI 49008

We are investigating the preparation of 1,10-phenanthroline derivatives that can be employed for asymmetric catalysis. The ring-opening reaction of 1,10-phenanthroline epoxide serves as a key transformation to study novel bidentate nitrogen ligands bearing stereogenic centers in the 5- and 6- position.

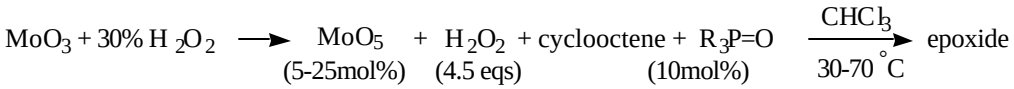


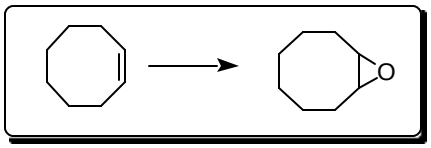
OXIDATION OF INDOLE AND ALKENE SUBSTRATES BY OXODIPEROXOMOLYBDENUM · TRIALKYL(ARYL)PHOSPHINE OXIDE COMPLEXES

Christine I. Altinis-Kiraz, Luis Mora and Leslie S. Jimenez
Rutgers, The State University of New Jersey
Department of Chemistry and Chemical Biology, Piscataway, NJ 08854

A number of $MoO_5 \cdot O{=}PR_3 \cdot H_2O$(or MeOH) (R = Me, Et, Pr, Bu, Ph) complexes have been prepared and shown to oxidize both indole and alkene substrates. A catalytic cycle under biphasic conditions (water/chloroform) has been developed in which a catalytic amount of the phosphine oxide ligand and MoO_5 solution is used along with hydrogen peroxide or *t*-butyl hydroperoxide as the stoichiometric oxidant. Alkene substrates gave isolated yields of 58-95% of the corresponding epoxides.

Catalytic Epoxidation Under Biphasic Conditions

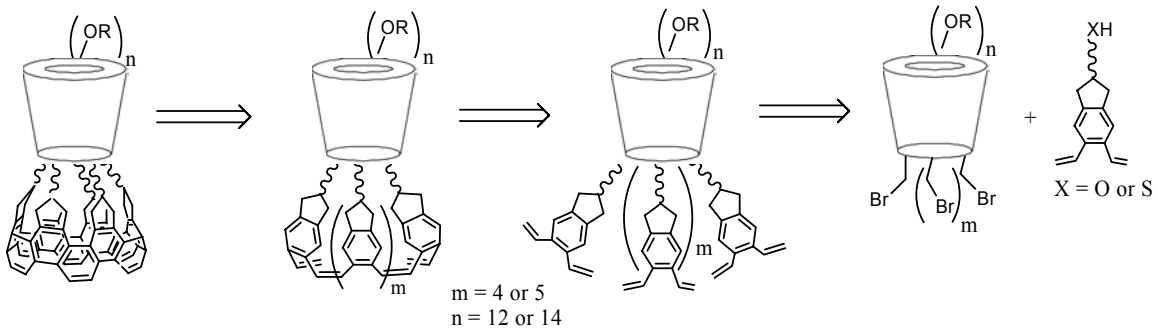




Bucky Belts: Synthesis Using a Cyclodextrin Scaffold

Zachary E. Katsamanis, Jason A. Estrada, Nancy S. Goroff
University at Stony Brook, The State University of New York
Department of Chemistry, Stony Brook, NY 11794-3400

Bucky belts form a new class of three dimensional aromatic compounds that potentially have the ability to serve as semiconductors. The synthetic approach is to align building blocks in the desired orientation by use of a cyclodextrin scaffold. Modified α-, and β-cyclodextrin derivatives have been prepared to allow for attachment of the tethered aromatic building blocks. Current research focuses on methods for this attachment via ether or thioether linkages.



TOWARD THE TOTAL SYNTHESIS OF (-)-DIHYDROGUAIARETIC ACID

R. Elizabeth Brewster, Suzanne B. Shuker
Georgia Institute of Technology
Department of Chemistry and Biochemistry, Atlanta, GA 30332-0400

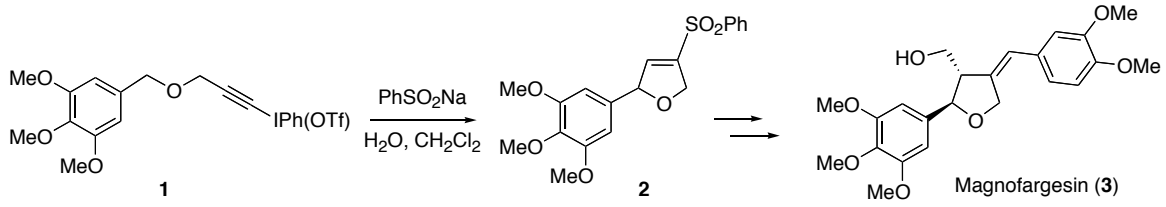
Until recently, it was widely believed that herbivory on freshwater macrophytes was low. Freshwater plants were thought to be low in nutritive value and to have a tough, unpalatable texture. Due to this misconception, these aquatic plants were not believed to display chemical defenses against herbivores. Recent studies, though, have shown that many freshwater plants, including the angiosperm *Saururus cernuus*, display these types of chemical defenses and therefore must contain toxic or unpalatable secondary metabolites.

Saururus cernuus has long been used as a folk remedy for inflammation, as a sedative, and as a poultice for tumors. Additionally, *Saururus cernuus* has been found to deter feeding by crayfish. The lignoid metabolite (-)-dihydroguaiaretic acid, which was isolated from *Saururus cernuus*, was also shown to deter crayfish feeding. Currently, (-)-dihydroguaiaretic acid is being synthesized, along with structural analogs, and will be screened for biological activity.

Total Synthesis of (±)-Magnofargesin

Joseph P. Fritz, Edward G. Bowen, Duncan J. Wardrop
University of Illinois at Chicago
Department of Chemistry, 845 West Taylor Street, Chicago, IL 60607

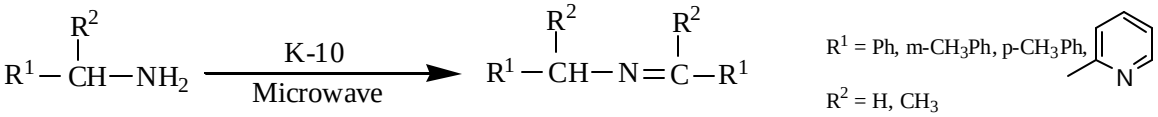
A novel method for the construction of 2,5-dihydrofurans **2**, using the chemistry of 3-alkoxy-1-alkynyliodonium triflates **1**, will be presented. Treatment of **1**, generated *in situ* from the corresponding alkynylstannane, with aqueous sodium phenylsulfinate generates an alkylidenecarbene intermediate, which undergoes intramolecular [1,5]-C-H insertion to form the 3-phenylsufonyl-2,5-dihydrofuran **2**. This methodology is compatible with a range of functional groups and the products are useful building blocks for the preparation of natural products. By way of illustration, the application of this chemistry to the total synthesis of magnofargesin (**3**), a potent antagonist of the platelet aggregating factor receptor, will be disclosed.



MICROWAVE ASSISTED CATALYTIC OXIDATIVE COUPLING OF BENZYL AMINES TO IMINES

Muralidhara Thimmaiah and Béla Török,
Department of Chemistry, Michigan Technological University, 1400 Townsend Drive, Houghton, MI 49931, Fax: 906-487-2061,mthimmai@mtu.edu, btorok@mtu.edu

The synthesis of imines received great attention due to their potential in variety of applications. Herein we describe a novel, new method for the synthesis of imines by direct oxidative coupling of aromatic and non aromatic amines. Our method is based on the application of a powerful solid acid(K-10 montmorillonite) as catalyst and microwave irradiation as energy source. During preliminary experiments it was found that the reactions proceeded with significantly higher rate under microwave conditions than in a conventional thermal reaction. Using our method the oxidative coupling of a wide variety of aromatic and non aromatic amines were carried out, the imines were isolated in excellent yields(up to 95%). Based on the detailed investigation of benzyl amine coupling, the role of experimental variables and the role of catalyst will also be discussed.



Reactions with non-aromatic amines such as cyclopentylamine, cyclohexylamine and butyl amine will also be shown

Probing Tertiary Structure in Miniproteins: Dynamic Exchange of Secondary Structural Elements

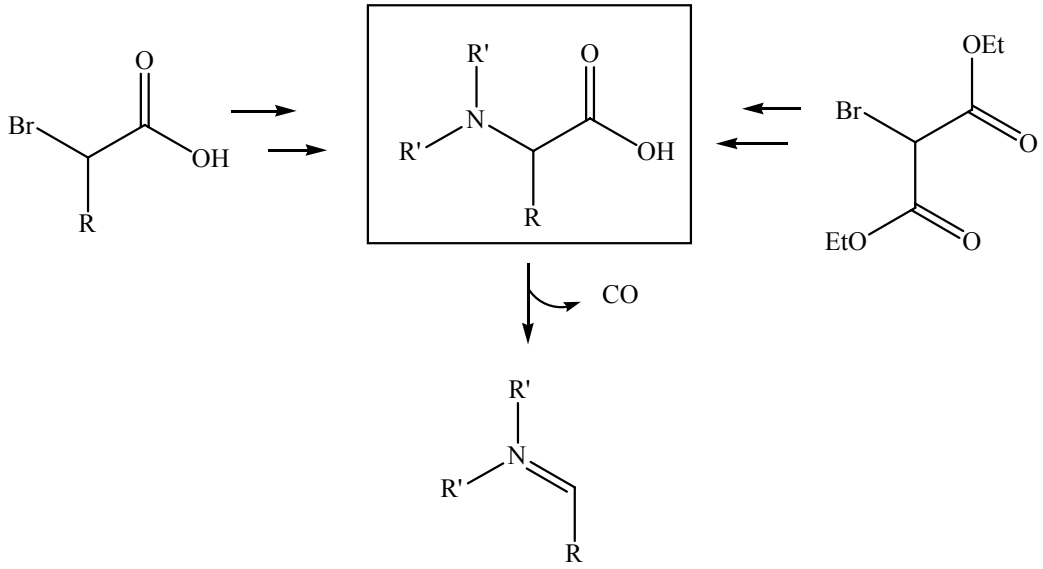
Matthew G. Woll, Samuel H. Gellman
University of Wisconsin-Madison
Department of Chemistry, 1101 University Ave, Madison, WI 53706

A new method which allows the dynamic exchange of secondary structural elements in solution has been developed to study tertiary structure in small proteins. A reversible thioester linkage has been engineered into the peptide backbone of the loop segment of bovine pancreatic polypeptide (bPP), a 36 residue protein. The short loop segment connects a type II polyproline helix to an α-helix. These two helices interact via hydrophobic packing to form a compact and stable tertiary structure. Under appropriate conditions, dynamic exchange between the native α-helical segment of bPP and a designed mutant α-helix can readily occur. The energetic contributions of individual amino acid side chains to the global fold can be probed by making the appropriate amino acid mutations. This new method is fundamentally different than the typical denaturation experiments used to probe the stability of tertiary structure since peptides remain in their native states throughout the experiment.

FACILE SYNTHESIS OF ALDEHYDES FROM ALPHA-N,N-DIALKYLAMINOACIDS

Brooke M. Gartland, Kristin Henry, Ciprian P. Prosecaru, William Schroeder and Robert P. Smart
Grand Valley State University
Department of Chemistry, Allendale, Michigan 49401

Treatment of alpha-N,N-dialkylaminoacids with dicyclohexyldiimide at room temperature leads to a rapid evolution of carbon monoxide and the formation of iminium salts. The reactions of these intermediates and their conversion to aldehydes are under study.



From Stereospecific, Living Ziegler-Natta Polymerization to Asymmetric Hydrozirconation: The Role Played by Chiral Zirconium Amidinates

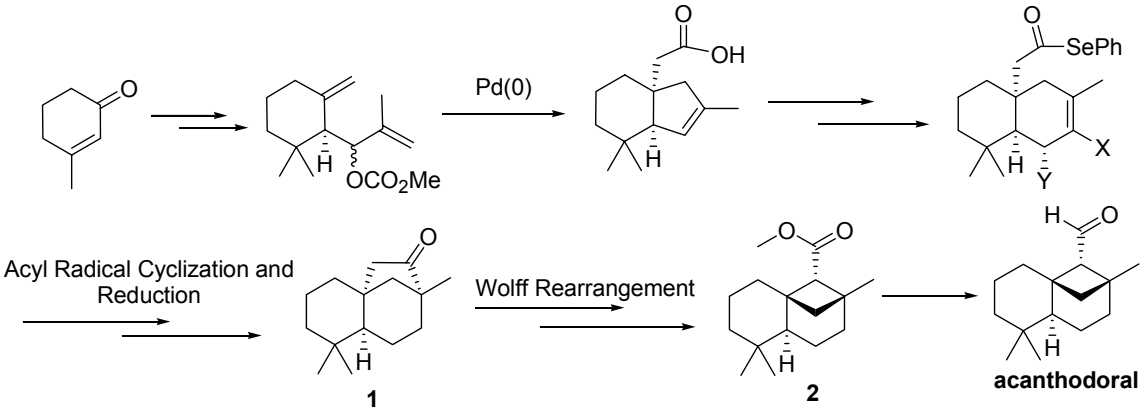
Richard J. Keaton, Yonghui Zhang, Lawrence R. Sita
University of Maryland
Department of Chemistry and Biochemistry, College Park, MD 20742

Our group has recently been involved in the development of cyclopentadienyl zirconium amidinates that can serve as highly active initiators for the stereospecific and living Ziegler-Natta polymerization of α-olefins. Central to the mechanism by which these complexes operate is the absence of termination by β-hydride elimination during polymerization, as further substantiated by the synthesis of a series of neutral and cationic species bearing alkyl substituents with β-hydrogens that are stable to both β-hydride elimination and structural isomerization. Given this unique stability toward β-hydride elimination, and the highly stereodifferentiating environment that is possible with chiral C_1-symmetric derivatives, recent efforts have been directed towards the design and synthesis of complexes for the asymmetric hydrozirconation of internal alkenes and subsequent heteroatom functionalization. Results obtained from both lines of studies will be presented.

Total Synthesis of Acanthodoral by Acyl Radical Cyclization and Wolff Rearrangement

Liming Zhang, Masato Koreeda
Departments of Medicinal Chemistry and Chemistry
University of Michigan, Ann Arbor, MI 48109

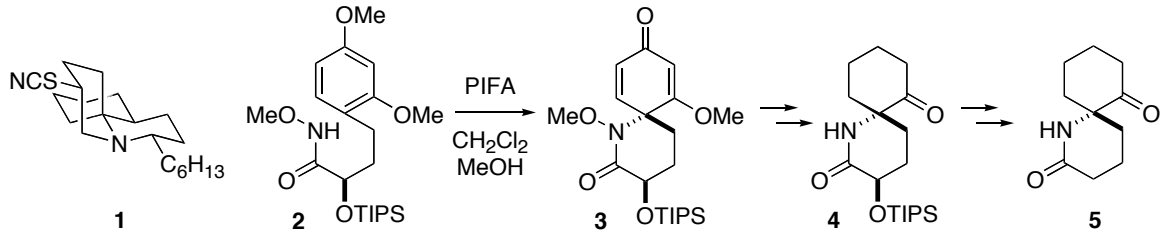
Acanthodoral was isolated from Dorid Nudibranch *Acanthodoris nanaimoensis* and, together with two other biogenetically related sesquiterpenoids, showed significant antibacterial and antifungal activities. It contains a highly strained bicyclo [3.1.1] ring system, four stereogenetic centers and three quaternary carbon centers. Our approach to its total synthesis involves Pd-catalyzed metalla-ene reaction, efficient acyl radical 5-exo-trig cyclization to form the cyclopentanone (**1**) and ring contraction of **1** by Wolff rearrangement to cyclobutanecarboxylate **2**, which is further converted to the natural product, acanthodoral.



Diastereoselective Nitrenium Ion Cyclizations: Application to the Asymmetric Synthesis of (+)-Kishi's Lactam and a Key Intermediate for the Preparation of Fasicularin

Chad L. Landrie, Wenming Zhang, Duncan J. Wardrop
University of Illinois at Chicago
Department of Chemistry, 845 West Taylor Street, Chicago, IL 60607

The 1-azaspiro[5.5]undecane ring system forms the substructure of a number of biologically active natural products including histrionicotoxin and the cytotoxic marine natural product fasicularin (**1**). The asymmetric synthesis of **4**, a key building block for the preparation of fasicularin, and (+)-Kishi's ketolactam (**5**), an intermediate in the first total synthesis of perhydrohistrionicotoxin, will be presented. The key step in this synthetic route is the diastereoselective azaspirocyclization of *N*-methoxy-□arylbutanoamide **2** to form azaspirodienone **3**, which is believed to proceed through the intermediacy of an *N*-acylnitrenium ion. Our progress towards the total asymmetric synthesis of (-)-fasicularin (**1**) will also be disclosed.

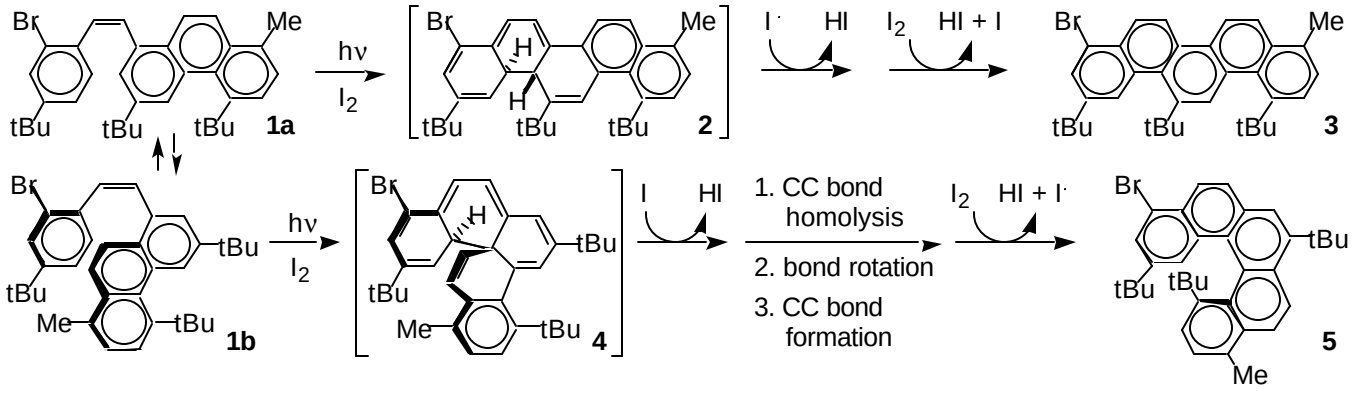


Diastereoselectivty = 9:1

AN UNPRECEDENTED REARRANGEMENT IN THE PHOTOCYCLIZATION OF A STILBENE ANALOG

Frank B. Mallory and Colleen K. Regan
Department of Chemistry, Bryn Mawr College
Bryn Mawr, PA 19010-2899

In our attempted synthesis of picene **3** by photocyclization of diarylethylene **1** and oxidative trapping of the transient dihydroaromatic intermediate **2**, we encountered a startling and unprecedented rearrangement that produced comparable amounts of **3** and pentahelicene **5**; the structure of **5** was established by single-crystal X-ray analysis. We suggest that the first step on the pathway to **5** is photocyclization of rotamer **1b** to give intermediate **4**. This appears to be the first example of a stilbene-like photocyclization in which the new CC bond is made to an angular carbon in a polycyclic aromatic ring. Our studies of the scope and mechanism of this remarkable new rearrangement will be presented.



WATER SOLUBLE CALIX[4]ARENES FOR MOLECULAR RECOGNITION AND ENCAPSULATION

Suazette Reid, Suzanne B. Shuker
Georgia Institute of Technology, Department of Chemistry and Biochemistry, Atlanta, GA 30332

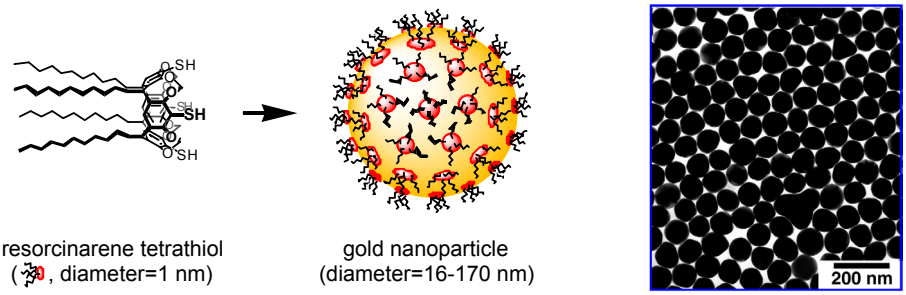
Macromolecular structures such as calixarenes that can self-assemble to form capsular structures by hydrogen bonding, metal coordination, covalent and ionic interactions are becoming increasingly important in sensing and transport. We have been designing calixarenes that can form homodimers, heterodimers and interdigitated dimers of various shapes and sizes.

We are now designing calix[4]arenes that are capable of forming dimers in aqueous solution. These calix[4]arenes are functionalized on the lower rim with hydoxyethyl groups and on the upper rim with charged groups and urea functionalities. Examples of charged groups include carboxylate and amino acids. Dimerization occurs when calixarenes with complementary functional groups are combined. Potential applications for these compounds include drug delivery and transport and encapsulation of biologically important molecules.

Resorcinarene-Encapsulated Nanoparticles: Building Blocks for Functional Nanostructures

Beomseok Kim, Steven L. Tripp, Balasubramanian Ramjee and Alexander Wei
Department of Chemistry, Purdue University, West Lafayette, IN 47907

We have developed a class of macrocyclic surfactants known as resorcinarenes for enhancing the dispersion and self-assembly of metal nanoparticles into well-defined assemblies. This includes two-dimensional arrays of colloidal Au particles as large as 170 nm with size-tunable plasmonic responses, and the self-assembly of ferromagnetic Co particles into nanosized "bracelets." Particles within these ensembles are strongly coupled and give rise to intriguing physical properties such as surface-enhanced Raman scattering (SERS) and chiral magnetic nanodomains. Nanomaterials are currently being developed for applications in chemical sensing and drug screening.



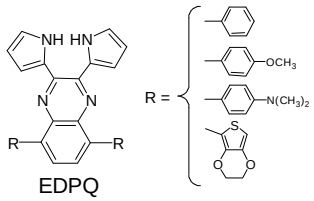
resorcinarene tetrathiol
(, diameter=1 nm)

gold nanoparticle
(diameter=16-170 nm)

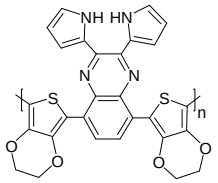
Extension of Conjugation as a Means Of Improving the Performance of an Anion Sensor

Dmitry Aldakov and Pavel Anzenbacher, Jr.
Bowling Green State University
Department of Chemistry and Center For Photochemical Sciences, Bowling Green, OH 43403

The development of anion sensors is of high importance since they play vital roles in virtually any field of modern industry, health and environment. The performance of the sensors can be improved via modification of the receptor and/or signaling parts. Aimed at the latter strategy, on the basis of a known fluorescent anion sensor, 2,3-di(pyrrole-2-yl)quinoxaline (DPQ), a series of oligomers with extended conjugation (EDPQs) was synthesized as follows: diBr-phenylenediamine, obtained from reduced benzothiodiazole, was condensed with dipyrrolyl dione to afford diBr-DPQ. The latter was coupled with various aryl substituents by Pd-catalyzed Stille coupling. The variation of substituents at 5,8- positions of quinoxaline ring enables to tune the fluorescent response upon binding of analyte originating from their different electronic effects. This modification also permits to increase the intensity of the emission as well as anion binding efficiency. Further modification of the sensor involved electrooxidative generation of a conjugated polymer material (poly-BEDOT-DPQ) capable of anion sensing in organic and aqueous media. The polymer was characterized and its performance was studied by UV-NIR absorption spectrometry and electrochemical quartz crystal microbalance (EQCM).



EDPQ



Poly-BEDOT-DPQ

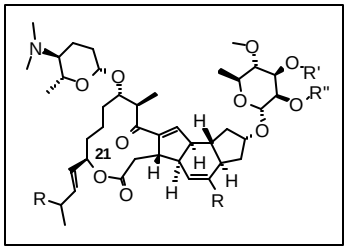
SYNTHETIC STRUCTURAL MODIFICATIONS OF THE NATURAL PRODUCT 21-BUTENYL SPINOSYN

Gary D. Crouse, Donald R. Hahn, Paul R. Graupner, Jeffery R. Gilbert, Paul Lewer, Jesse L. Balcer, Peter B. Anzeveno, John F. Daeuble, M. Paige Oliver, Thomas C. Sparks

Dow AgroSciences LLC

9330 Zionsville Road; Indianapolis, IN 46268

The 21-butenyl spinosyns are novel compounds that have been isolated from *Saccharopolyspora spinosa*. These molecules are unique from the known insecticidal compounds, spinosyns, due to the presence of the 21-butenyl side chain. The focus of the butenyl spinosyn SAR included broadening its spectrum of insecticidal activity to include sap-feeding, as well as, chewing pests. Four sections of the butenyl spinosyn molecule were targeted for modification: the rhamnose sugar, the forosamine sugar, the butenyl side chain, and the core 5-6 unsaturated ring system.



SUZUKI CROSS-COUPLING OF ALKYL BROMIDES, CHLORIDES AND TOSYLATES WITH AKLYL AND ARYL BORONIC ACIDS USING A NOVEL CLASS OF TERTIARY PHOSPHINE LIGAND INCORPORATING A PHOSPHA-ADAMANTANE FRAMEWORK.

D. A. Gerritsma, T. Brenstrum, G. Adjabeng, J. McNulty and A. Capretta
Brock University, Institute of Molecular Catalysis
500 Glenridge Avenue, St. Catharines, Ontario, Canada, L2S 3A1

The Suzuki reaction is a versatile method for the formation of carbon-carbon bonds. Palladium catalyzed couplings in which the halide is bonded to an sp^3- rather than sp^2-hybridized carbon are much less common due to the slower rate of oxidative addition of alkyl halides to palladium and the possibility for β-hydride elimination of the alkyl-palladium complex. It is postulated that oxidative addition of alkyl halides and reductive elimination of product both involve low-coordinate Pd(0) reactive intermediates, the formation of which are favoured by sterically hindered, electron rich phosphine ligands. Facile substitution at phosphorous in phospha-adamantane has allowed for the convenient synthesis of a library of suitably bulky tertiary phosphine ligands. Through the use of a catalytic system incorporating these novel ligands and palladium(II) acetate, an array of alkyl bromides, chlorides and tosylates possessing β-hydrogens were coupled cleanly and in high yield with a variety of alkyl and aryl boronic acids. Alkyl bromides coupled at room temperature, tosylates at 50 ^{o}C and alkyl chlorides at 90 ^{0}C. The reaction conditions tolerate a range of functional groups including alkenes, esters and nitriles.

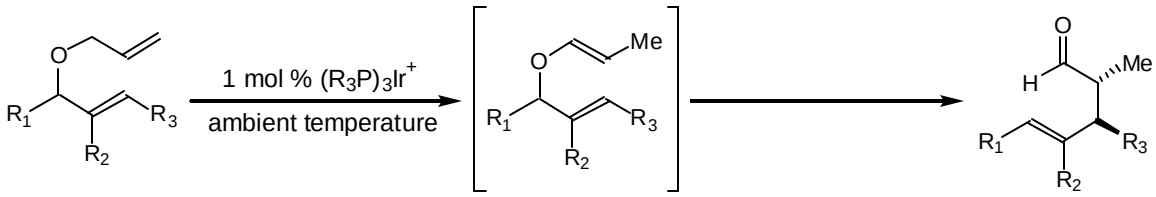
STEREOSELECTIVE ONE-POT SYNTHESIS OF VINYLSILANES FROM AROMATIC ALDEHYDES

Man Lung Kwan, Chiu W. Yeung, Kerry L. Breno, Kenneth M. Doxsee.
Department of Chemistry, University of Oregon, Eugene OR. 97403.

Vinylsilanes serve as convenient vinyl anion equivalents, but procedures for their stereoselective synthesis from aldehydes are scarce. A variety of aromatic aldehydes are converted to the corresponding vinylsilanes in a one-pot procedure involving the addition of (trimethylsilylmethyl) lithium to the aldehyde followed by treatment with Cp_2TiCH_2*$AlMe_2Cl$ ("Tebbe's reagent"). Halide and alkoxide substituents are tolerated, and (E)-vinylsilanes are formed exclusively in good yield.

A TANDEM OLEFIN ISOMERIZATION-CLAISEN REARRANGEMENT PROMOTED BY A CATIONIC IRIDIUM COMPLEX

Christopher J. Bungard*, *Kan Wang, and Scott G. Nelson*
University of Pittsburgh
Department of Chemistry
Chevron Science Center
Pittsburgh, PA 15260

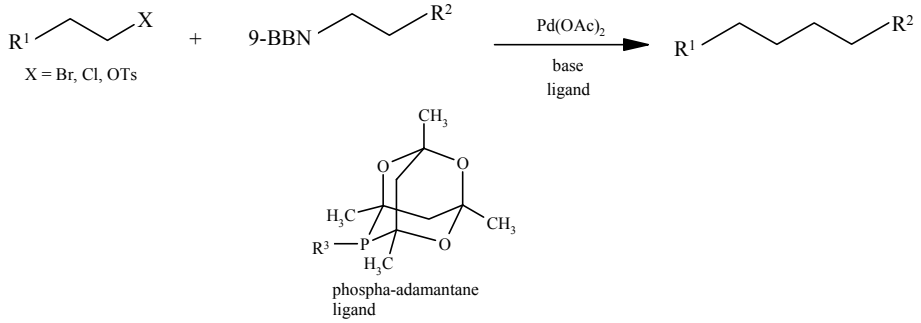


Treatment of a variety of bisallyl ethers with 1 mol % of a cationic iridium phosphine complex, results in isomerization of the monosubstituted allyl ether to afford the corresponding (*E*)-vinyl ether. The aforementioned iridium catalyst also promotes an ensuing Claisen rearrangement of the resulting allylvinyl ethers. This proceeds at ambient temperature and provides γ,δ-unsaturated aldehydes in good yields and of high diastereomeric purity (up to 20:1). Catalyst development and substrate generality will be discussed.

SUZUKI CROSS-COUPLING OF ALKYL BROMIDES, CHLORIDES AND TOSYLATES WITH ALKYL-9-BBN DERIVATIVES USING A NOVEL CLASS OF TERTIARY PHOSPHINE LIGAND INCORPORATING A PHOSPHA-ADAMANTANE FRAMEWORK.

***T. Brenstrum*, D. Gerritsma, G. Adjabeng, J. McNulty and A. Capretta**
Brock University, Department of Chemistry
500 Glenridge Avenue, St. Catharines, Ontario, Canada, L2S 3A1

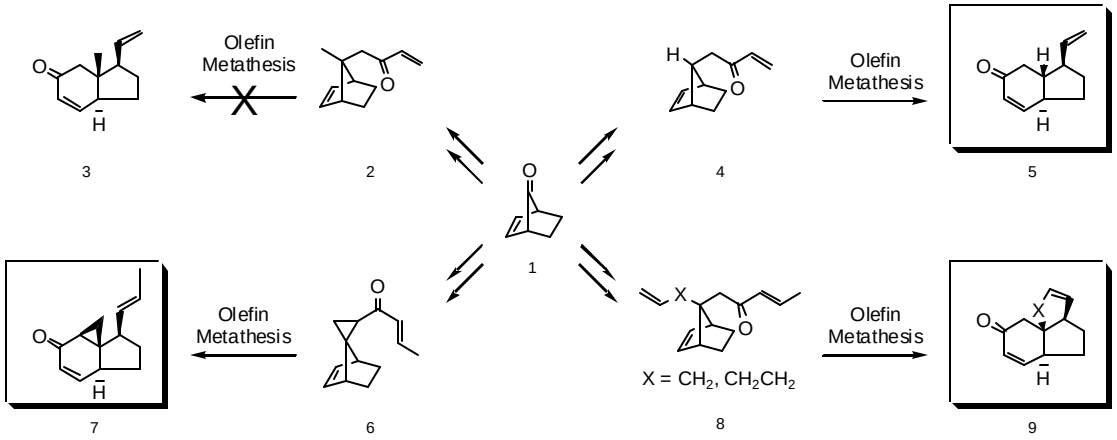
The Suzuki reaction is a versatile method for the formation of carbon-carbon bonds. Palladium catalyzed couplings in which the halide is bonded to an sp^3- rather than sp^2-hybridized carbon are much less common due to the slower rate of oxidative addition of alkyl halides to palladium and the possibility for β-hydride elimination of the alkyl-palladium complex. It is postulated that oxidative addition of alkyl halides and reductive elimination of product both involve low-coordinate Pd(0) reactive intermediates, the formation of which are favoured by sterically hindered, electron rich phosphine ligands. Facile substitution at phosphorous in phospha-adamantane has allowed for the convenient synthesis of a library of suitably bulky tertiary phosphine ligands. Through the use of a catalytic system incorporating these novel ligands and palladium(II) acetate, an array of alkyl bromides, chlorides and tosylates possessing β-hydrogens were coupled cleanly and in high yield with a variety of alkyl-9-BBN derivatives. Alkyl bromides coupled at room temperature, tosylates at 50 ^{o}C and alkyl chlorides at 90 ^{0}C. The reaction conditions tolerate a range of functional groups including alkenes, esters and nitriles.



DEVELOPMENTS IN CARBOCYCLE SYNTHESIS FROM FUNCTIONALIZED NORBORNYLENES BY OLEFIN METATHESIS

Jeremy Holtsclaw and Masato Koreeda
University of Michigan
Department of Chemistry, Ann Arbor, Michigan 48108-1055

A strategy is being developed that uses olefin metathesis technologies to provide efficient access to bicyclic and tricyclic carbocycles. These carbocyclic intermediates are a rapid entryway into the synthesis of steroids, such as desogestrel, and the magellanane class polycyclic alkaloids. This synthetic approach utilizes the readily available 7-norbornenone (**1**) to provide functionalized norbornylene intermediates that are then exposed to an appropriate olefin metathesis catalyst to yield the desired carbocyclic framework.



SYNTHESIS OF PROTECTED FORMS OF ALL FOUR DIASTEROMERS OF ß - METHOXYTYROSINE

Ravi Krishnamoorthy, Alan G. Benson, Robert L. Ferguson and Mark A. Lipton*

Purdue University, Department of Chemistry, West Lafayette, IN-47907

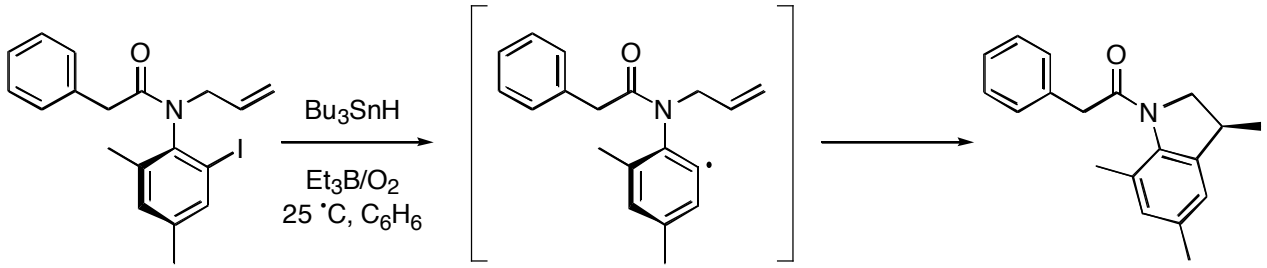
Abstract

ß-Methoxytyrosine is an important constituent of the novel cyclic depsipeptides callipeltins A and B and papuamides A and B. Even though the structures of callipeltin A and B are elucidated, the configuration of ß-methoxytyrosine is yet to be assigned. Our synthesis adapts Boger's synthesis of ß-hydroxytyrosine, which involves condensation of a Schöllkopf reagent with 4-benzyloxybenzaldehyde. Further methylation, acid hydrolysis and a transesterification reaction gives enantiomerically and diasteromerically pure protected products in a seven step sequence with an overall 30% yield .

Stereoselective Radical Cyclizations of Axially Chiral *N*-Allylanilides to 3-Substituted Dihydroindoles with Transfer of Axial Chirality to Newly Formed Stereocenter

Andre J. B. Lapierre, Christine H.-T. Chen, Ali Ates, Dennis P. Curran
University of Pittsburgh
Department of Chemistry, Pittsburgh, PA 15260

The rapidity of 5-*exo* radical cyclizations offers unique opportunities for asymmetric transformations. Axially chiral anilide **P-1** exhibits slow rotation about the *N*–aryl bond such that conformationally stable enantiomers can be chromatographically isolated and manipulated at room temperature. When submitted to radical cyclization conditions enantioenriched dihydroindole **S-2** is generated with faithful transfer of axial chirality to the newly formed stereocenter. This occurs despite an intermediate **1a** that would possess a low *N*-aryl bond rotation barrier and be expected to racemize at room temperature.



P-1 (97 % ee) **1a** **S-2** (87 % ee)
(90 % ee corrected)

n.go.com

Design and Synthesis of PIP_2 Micelle Analogs

Sarah A. Webb, Lewis J. Belcher, Nichole K. Stewart, Chris T. Ross, Yehia S. Mechref, Milos V. Novotny and Martha G. Oakley

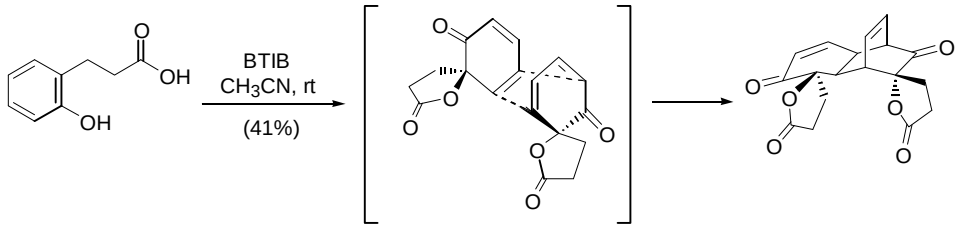
Indiana University

Department of Chemistry, Bloomington, IN 47405

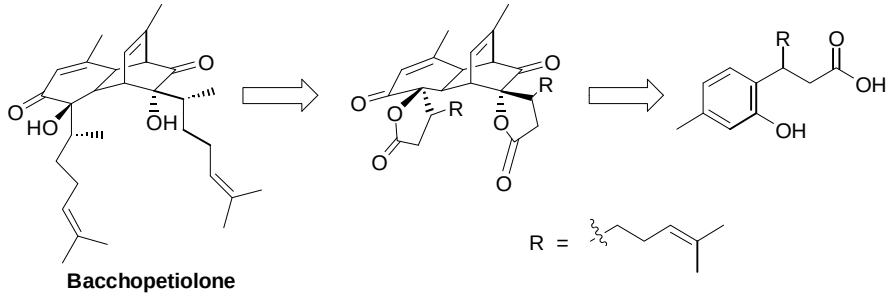
Although phosphoinositide lipids are crucial components of many signal transduction pathways, the mechanisms by which they recognize their target proteins and modulate their functions are largely unknown. We are examining the interactions of phosphatidylinositol-4,5-bisphosphate (PIP_2) and related lipids with various soluble cytoskeletal proteins involved in the regulation of actin polymerization, such as profilin. Evidence shows that multiple copies of PIP_2 bind to profilin, suggesting that multivalency is important for this protein-lipid interaction. To study this interaction, we have prepared polymeric derivatives to mimic PIP_2 micelles. PIP_2 headgroups have been attached to a dendrimeric scaffold via a diamine, 3,4-diethoxy-3-cyclobutene-1,2-dione, linker and the purification and characterization of these highly charged dendrimers is described.

TANDEM AROMATIC OXIDATION/DIELS-ALDER REACTIONS OF 3-(2-HYDROXYPHENYL)-PROPIONIC ACIDS. APPLICATIONS TOWARD A TOTAL SYNTHESIS OF BACCHOPETIOLONE.

John L. Wood, Amélie Bérubé, Ioana Drutu*
Department of Chemistry, Yale University
PO BOX 208107, New Haven, CT 06520-8107, USA



Drutu, I.; Njardson, J. T.; Wood, J.L. *Org. Lett.* **2002**, *4*493-496.



Bacchopetiolone

Synthesis of Homoallylic Amine Derivatives by Allylsilane Addition to Enantiopure N-Acylhydrazones

Hui Ding and Gregory K. Friestad
Department of Chemistry, University of Vermont, Burlington, Vermont 05405

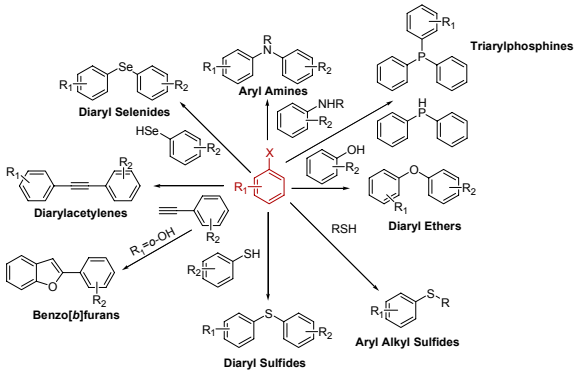
Direct asymmetric amine synthesis by addition to the C=N bond of imino derivatives holds promise for improved access to chiral amines. Stereoselective synthesis of homoallylic amines were developed from allylsilane addition to enantiopure N-acylhydrazones with dual activation by fluoride and indium triflate. Useful chiral building blocks for natural product synthesis were prepared from the homoallylic amine adducts. Specific examples include trifluoroacetyl- or benzoyl-activated N-N bond cleavage, Wacker oxidation and N-allylation. The products of N-allylation were further transformed into enantiopure functionalized piperidines using olefin metathesis.

COPPER CATALYZED CROSS-COUPLING REACTIONS

*Craig G. Bates, Rattan K. Gujadhur, Derek Van Allen, Pranorm Saejueng and D. Venkataraman**

University of Massachusetts – Amherst

Department of Chemistry, Amherst, MA 01003

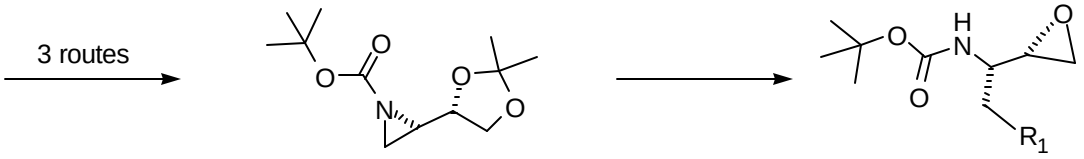


We have developed copper(I)-phenanthroline and copper(I)-neocuproine complexes as catalysts for many cross-coupling reactions (see Chart above). In comparison to palladium chemistry, these protocols are simple, mild and avoid the use of air-sensitive and expensive phosphine ligands or additives. Moreover, these protocols also accommodate substrates that do not undergo coupling by palladium catalysts. Furthermore, there is an economic attractiveness for using copper over noble metals such as palladium. We are currently exploring the utility of this chemistry to other important cross-coupling reactions.

METHODOLOGY TO USE PARALLEL SYNTHETIC CHEMISTRY (PSC) TO PREPARE ENANTIOMERICALLY PURE EPOXIDE REAGENTS FOR USE IN PREPARING TRANSITION STATE INSERTS OF ASPARTYL PROTEASE INHIBITORS CONTAINING DIFFERENT P1 SUBSTITUENTS

Christina M. Roels*, Arthur G. Romero, Cuong V. Lu, Jiong J. Chen, Eric P. Seest, Matthew R. Hester, Lester A. Dolak, Fusen Han
Pharmacia, 7000 Portage Road, Kalamazoo, MI 49001-0199

Transition state inserts (TSI) are key structural moieties in the development of aspartyl protease enzyme inhibitors (e.g. renin, HIV protease). ß-Amino alcohol TSIs, particularly with variations at the P1 (R_1) position, are difficult to prepare due to complexity of two fixed chiral centers and introducing a key carbon-carbon bond formation as late in the synthesis as possible. Methodologies were developed to use **1**, a boc protected aziridine, as an enantiomerically pure late stage intermediate that could be used to prepare numerous single diastereomer epoxide reagents introducing the various R_1 groups late in the synthesis. Three routes were developed in parallel to prepare multi-gram quantities of **1**. Two routes require resolution on a chiral HPLC column. To prepare the epoxide reagents (**2**), **1** was opened with various Cu(I) catalyzed Grignard reagents, followed by an interesting ion-exchange work up (Ps-SO_3H) to isolate the alkylated product; a subsequent one-pot procedure afforded the P1 epoxides.



1 **2**

Application of Zr-Catalyzed Enantioselective Carboalumination Reaction to the Syntheses of Reduced Polypropionates and Related Compounds

Ze Tan, Bo Liang, Marina Magnin-Lachaux, and Ei-ichi Negishi*
Herbert C. Brown Laboratories of Chemistry,
Purdue University, West Lafayette, IN 47907

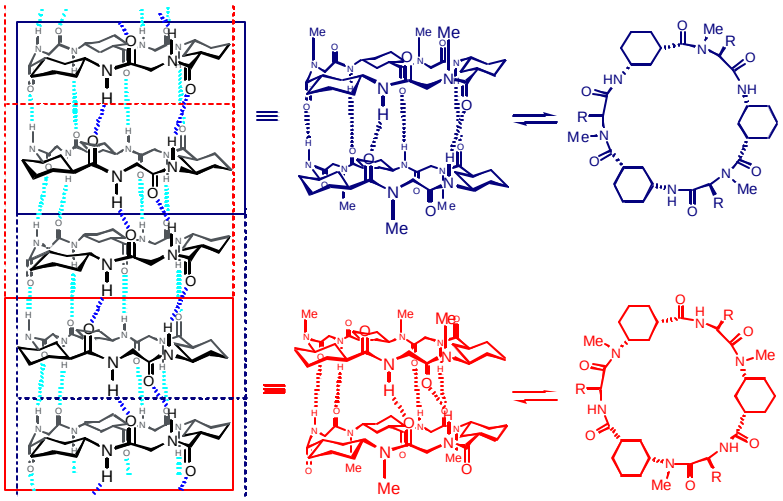
Herein we report a highly efficient and straightforward method to construct the reduced polypropionate units which are present in a wide variety of naturally occurring compounds. Previous syntheses of type of compounds typically involve the use of stoichiometric amount of chiral auxiliary or enzymatic kinetic resolution. Our approach critically hinged on the use of the Zr-catalyzed enantioselective carboalumination reaction which has been discovered and developed recently in our group. This novel methodology now permits efficient and stereoselective syntheses of a number of natural products and their part structures such as TMG-151, (+)-sambutoxin, supellapyrone, etc.

a ,g-CYCLOPEPTIDES CAPABLE OF FORMING PEPTIDIC NANOTUBES: THE STRUCTURAL AND THERMODINAMIC BASIS

Manuel Amorín, Roberto J. Brea, Luis Castedo, Juan R. Granja

Departamento de Química Orgánica e Unidade Asociada ó C.S.I.C, Facultade de Química, Universidade de Santiago, 15782 Santiago de Compostela, SPAIN

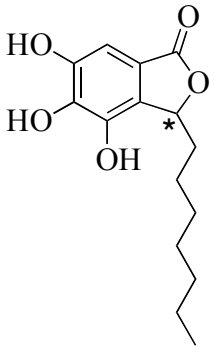
In the present communication, we will describe the studies realized with cyclopeptide made of alternating alpha- and gamma-amino acids. These peptides, when they are selectively N-alkylated in their peptide back-bone, self-assembled into cylindrical structures which serve as models for a new class of self-assembled peptide nanotubes (SPN). A principal characteristic of these particular nanotubes is that they possess an internal cavity of hydrophobic character. This work was supported by Ministerios de Educación y Ciencia, and Ciencia y Tecnología and the Xunta de Galicia under projects PB97-0524, SAF2001-3120 and PGIDT00PXI20912PR. We also thank the Spanish MEC for the award of a fellowship to M.A.



Total Synthesis of the Antibiotic Cytosporone E

Jeffrey D. Hall, Nasar A. Siddiqi, M. Faisal Siddiqi, Nathan W. Duncan-Gould, Justin K. Wyatt*
College of Charleston
Department of Chemistry and Biochemistry, 66 George St., Charleston, SC 29424

The racemic and enantioselective synthesis of the novel antibiotic trihydroxybenzene lactone cytosporone E, which was isolated from the cultures of endophytes CR200 (*Cytospora* sp.) and CR146 (*Diaporthe* sp.). The phthalide skeleton was prepared utilizing the Meyers *ortho*-alkylation of a chiral aromatic oxazoline and the results will be described.

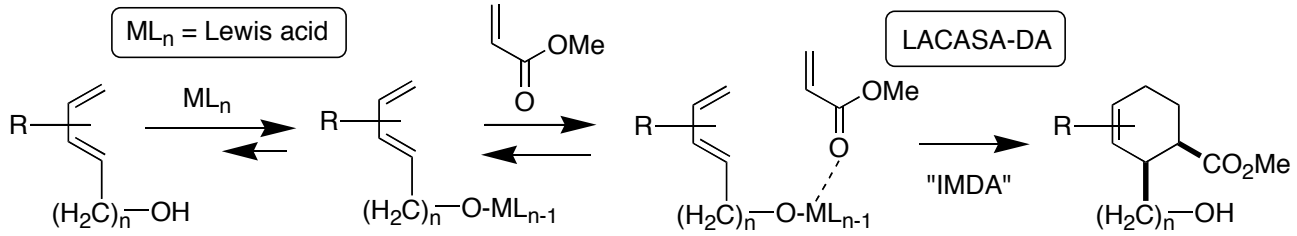


Cytosporone E

Lewis Acid Catalyzed and Self-Assembled Diels-Alder Reactions (LACASA-DA). A New Approach to Enhance Reactivity, Regio- and Stereoselectivity

Dale E. Ward, Michael S. Souweha, and M. Saeed Abaee
University of Saskatchewan, Department of Chemistry
110 Science Place, Saskatoon SK S7N 5C9, CANADA

The Diels-Alder (DA) reaction is perhaps the most powerful and versatile reaction in the synthetic chemist's arsenal, in part because of the continuous evolution of strategies to improve reactivity and selectivity. We have been developing a new strategy to control Diels-Alder reactions based on simultaneous coordination of the diene and dienophile components to a Lewis Acid to achieve both self-assembly and catalysis of the reaction (LACASA-DA; cf. *Org. Lett.* **2000**, *2*, 3937). In this contribution we report the results of our systematic study to identify conditions for high selectivity and present compelling evidence that the mechanism for selective cycloaddition involves Lewis acid catalysis of a self-assembled complex.



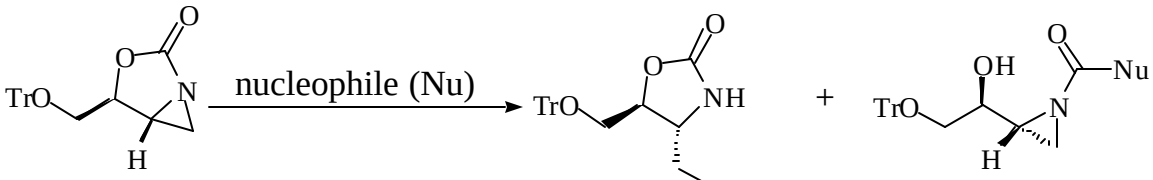
REACTIONS OF BICYLIC AZIRIDINES WITH AMINES AND ALCOHOLS

Jeffrey A. Frick[1], Stephen C. Bergmeier[2], Junfeng Huang[2], Steven J. Katz[2], Nicholas R. Van Malderen[2], and Scott M. Brombosz[1]

[1]Illinois Wesleyan University, Department of Chemistry, Bloomington, IL 61701

[2]Ohio University, Department of Chemistry and Biochemistry, Athens, OH 45701

The ring opening reaction of 3-oxa-1-azabicyclo[3.1.0]-hexan-2-ones (**1**) with amines and alcohols was examined. The predominant product of amine opening reactions was the oxazolidinone (**2**), although the aziridine (**3**) formed in some cases. When **1** is opened with alcohols, the oxazolidinone (**2**) predominates. We will present specific results for the amine opening reactions, detailing the scope of reaction. Preliminary results of the alcohol opening reactions will also be presented.



1 **2** **3**

Heterologous Expression And Purification Of SpaS, SpaB And SpaC Involved In Subtilin Biosynthesis

Champak Chatterjee, Moushumi Paul, Lili Xie, Nicole M. Okeley, Rashna Balsara, Wilfred A. van der Donk.
University of Illinois at Urbana-Champaign
Department of Chemistry, Urbana, IL 61801

Lantibiotics are peptide antibiotics that contain thioether bridges, termed lanthionines, putatively generated by the Michael addition of cysteines to dehydrated serine and threonine residues in the pre-lantibiotic peptide. The post-translational modifications observed are proposed to involve the proteins LanB and LanC that are attributed the functions of dehydration and cyclization, respectively. In our effort to elucidate the mechanism of biosynthesis of the lantibiotic subtilin we report the first heterologous expression in *Escherichia coli* and characterization of the putative dehydratase and cyclase proteins, SpaB and SpaC, respectively. The solubility of SpaB was increased dramatically when co-expressed with GroEL/ES and soluble His_6-tagged SpaB was purified. The oligomerization state of SpaB in solution is at least dimeric. Antibodies raised against the pure proteins were employed to observe the physical interaction between SpaC and SpaB by coimmunoprecipitation experiments. SpaC is monomeric in solution and contains stoichiometric zinc. EXAFS analysis suggests that two cysteines and possibly two histidines are involved in the zinc coordination sphere. SpaC mutants were constructed to determine the possible role of zinc in activating cysteine thiols of the substrate toward intramolecular Michael addition. SpaS, the proposed substrate for SpaB and SpaC, was overexpressed in *E. coli* as an intein-fusion protein and isolated after thiol-induced cleavage. Expressed protein ligation was employed to obtain biotinylated analogs of SpaS as novel substrates for lantibiotic formation.

Design and Performance of Interfacial Scaffolds for Templating 2-Dimensional Crystallization of Histidine-Tagged Proteins

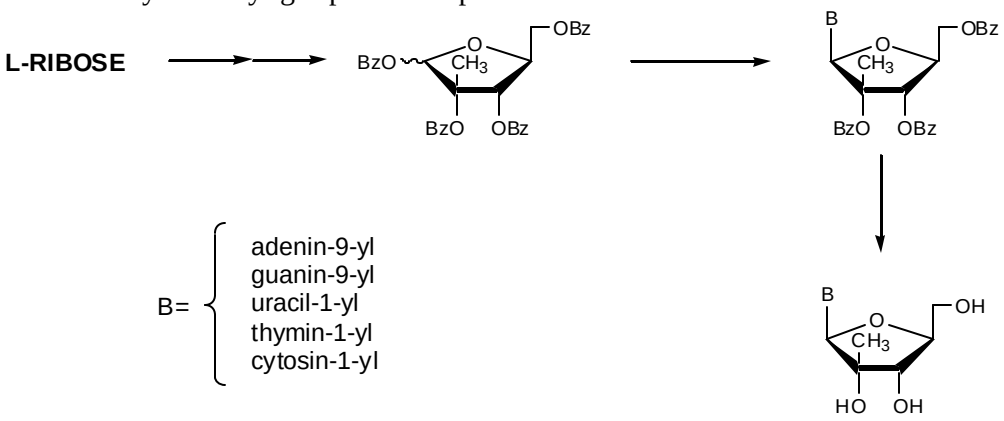
Mingkang Zhou, Joseph Franses, Saubhik Haldar, Jong-Mok Kim and David Thompson*
Purdue University
Department of Chemistry, West Lafayette, IN 47907-2084

In order to overcome the kinetic limitations of traditional 2D protein crystallization (lateral lipid diffusion), we have developed a new strategy using a site-hopping mechanism of inclusion ligands and modified cyclodextrins as a way to promote the formation of more highly ordered aggregates. Histidine-tagged green fluorescent protein (His-tag GFP) was expressed for testing this new crystallization strategy. Several novel chelating lipids were designed and synthesized. These materials were then tested for their ability to influence His-tag GFP crystallization due to interfacial templating effects using monolayer film balance, AFM, cryo-FESEM, and TEM methods. We find that different ß-cyclodextrin/NTA monolayers are capable of influencing the size and crystallinity of protein aggregations formed at the air-water interface. These studies show that interfacial design can profoundly affect the crystallization behavior of His-tag GFP.

SYNTHESIS OF 2'-*C*-METHYL-β-L-RIBONUCLEOSIDES

D. Bardiot, S. Benzaria, C. Pierra, G. Gosselin
Laboratoire Coopératif Idenix-CNRS-Université Montpellier II, 34095 Montpellier cedex 5, France

Nucleoside analogues play an important role in the treatment of various cancers and viral infections. In the search for new nucleoside analogues with potential biological activity, we have developed a convergent multi-step sequence for the preparation of a novel series of unnatural L-nucleosides branched by a methyl group in the 2' position.

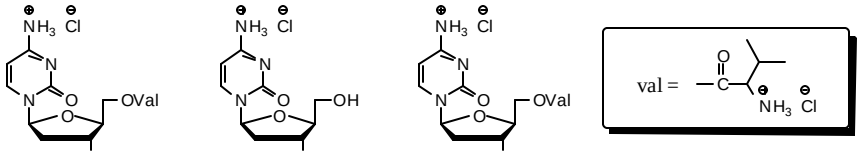


Details on the synthesis of the titled compounds will be presented in this poster.

PRODRUGS OF THE POTENT AND SELECTIVE ANTI-HBV AGENT 2'-DEOXY-b-L-CYTIDINE (LdC): SELECTION OF THE IDEAL CANDIDATE

***S. Benzaria*, [1] *C. Pierra*, [1] *E. Cretton-Scott*, [2] *E.G. Bridges*, [2] *D. Standring*, [2] *and G. Gosselin*[1]**
[1] Laboratoire Coopératif Idenix-CNRS-Université Montpellier II, 34095 Montpellier cedex 5, France; [2] Idenix Pharmaceuticals, Cambridge, USA

Since the discovery of the potent anti-HBV activity of 2'-deoxy-β-L-cytidine (L-dC), our efforts have been devoted to the improvement of its low (≈ 16% in monkey) oral bioavailability. In this regard, we have synthesized different valinyl ester derivatives of L-dC: the 3'-mono-, the 5'-mono-, and the 3',5'-di-*O*-L-valinyl esters. All three compounds showed improved oral bioavailability and increased systemic delivery of L-dC. Accordingly, it seemed interesting to study their comparative physical and pharmacokinetic properties in order to select the ideal candidate for further development.



In all cases, the 3'-val-LdC showed similar or better properties compared to the 5'- and to the 3',5'-val derivatives. Based on the ease of its synthesis, on its physico-chemical properties and on its pharmacokinetic profile in the monkey, 3'-val-LdC is the most promising studied prodrug of LdC and is currently being developed as a new anti-HBV agent.

NOVEL MICROWAVE ASSISTED SYNTHESIS OF TRIFLUOROMETHYLATED IMINES CATALYZED BY SOLID ACIDS

Markku A. Savolainen[1], Jinbo Hu[2], G. K. Surya Prakash[2], George A. Olah[2], Béla Török[1]
[1]Department of Chemistry, Michigan Technological University, 1400 Townsend Drive, Houghton, MI 49931, [2]University of Southern California, Los Angeles, CA
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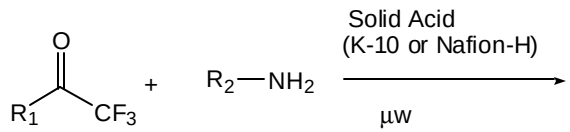
A novel solid acid catalyzed microwave assisted synthesis of trifluoromethylated imines is described. The target compounds are of high synthetic potential, as important building blocks in the synthesis of trifluoromethylated amines. Due to the highly deactivating character of the trifluoromethyl group, the conventional methods (PTSA catalysis, Dean-Stark apparatus) all failed, even after an extended reaction time (170 h).

Our new method is based on using powerful solid acids, K-10 and Nafion-H, as catalysts. The use of microwave irradiation has drastically reduced reaction time (30-60 min) and the amount of by-products. Also, the solvent-free conditions ensured easy isolation of the products. Most K-10-catalyzed reactions gave good to excellent yields (up to 95%). However, in the case where R_1=9-anthracenyl the reaction did not proceed with K-10, so the more powerful, superacidic Nafion-H was used. This technique was proven to be successful, giving the expected product in good yield (up to 75%). The novelty of the method will be illustrated by using a wide variety of α,α,α-trifluoroketones in condensation with benzyl- and chiral α-methylbenzyl amines.



R_1 = Ph, naphthyl-, 4-tolyl-, 2-thiophenyl-, 2-pyrrolyl-, 3-indolyl-, 9-anthracenyl, $PhCH_2$, 4-ClPh-, 4-BrPh-, EtO_2CCH_2-

R_2=$PhCH_2$-, $Ph(CH_3)CH$- (both (*R*) and (*S*))

Are Open Chain Chiral Ketones Good Catalysts for Enantioselective Epoxidations?

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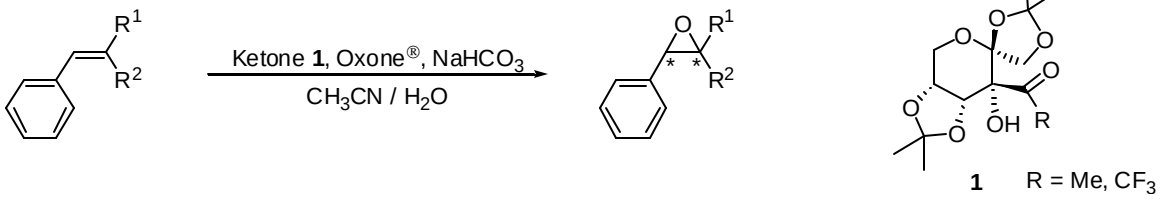
University of Texas at San Antonio
Department of Chemistry, San Antonio, TX 78249-0663

In recent years, great progresses have been achieved in ketone-catalyzed asymmetric epoxidations. All the successful catalysts developed so far are cyclic ketones. Although some of these ketones generate very impressive enantioselectivities in asymmetric epoxidations, their cyclic structures limit their varieties and make the structure modification very difficult. On the other hand, open chain chiral ketones would offer more structure varieties and be ready to modify. These two features are essential for designing more reactive and persist catalysts. While open chain chiral ketones have been tried at the very beginning of dioxirane chemistry, the enantioselectivities obtained so far are much inferior (<20% ee). In an effort to improve their enantioselectivities we have synthesized chiral ketones **1** and achieved good enantioselectivity in asymmetric epoxidations with these ketones. The synthesis of ketones **1** and the results of asymmetric epoxidations will be reported and the mechanism of the epoxidation will be discussed.

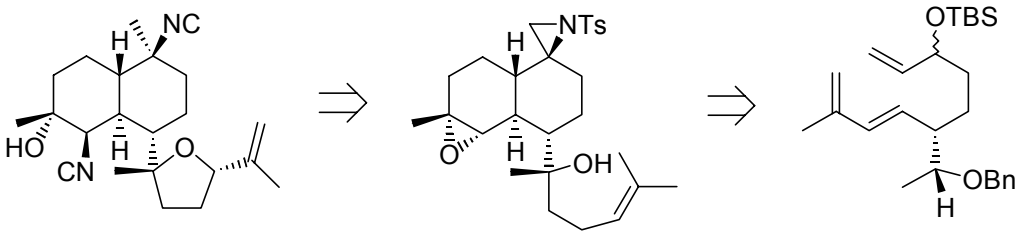


1 R = Me, CF_3

TOTAL SYNTHESIS OF KALIHINOL C

John L. Wood, Ryan D. White, Gregg F. Keaney, and Corin D. Slown
Yale University, Department of Chemistry
225 Prospect Street, P.O. Box 208107, New Haven, CT 06520-8107

The total synthesis of the marine diterpenoid kalihinol C has been achieved. The decalin core, established via an intramolecular Diels-Alder cycloaddition, was used to direct the installation of the requisite functionality through a series of substrate-controlled, diastereoselective reactions.



Kalihinol C

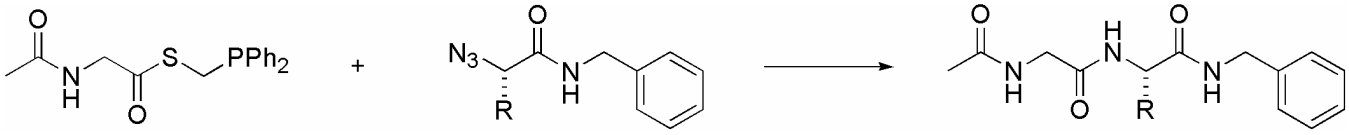
Staudinger Ligation: Mechanistic Studies and Peptide Immobilization

Matthew B. Soellner[1], *Bradley L. Nilsson*[1], *Kimberly A. Dickson*[2], *Ronald T. Raines*[1,2]

[1]**Department of Chemistry, 1101 University Avenue, University of Wisconsin-Madison, Madison WI 53706, USA**

[2]**Department of Biochemistry, 433 Babcock Drive, University of Wisconsin-Madison, Madison WI 53706, USA**

The Staudinger ligation of peptides with a C-terminal phosphinothioester and an N-terminal azide is an emerging method in protein chemistry. The Staudinger ligation is shown to have no reliance on specific amino acid residues, provide nearly quantitative yield of peptide product, have a half-life of minutes at room temperature, and proceed without detectable epimerization. Here, Staudinger ligations are studied by NMR spectroscopy in an effort to determine the reaction rate and compare a range of Staudinger ligation reagents. In addition, the Staudinger ligation is used for the site-specific, covalent immobilization of azido-peptides to a glass surface. These results demonstrate the potential for the total synthesis of proteins from peptide fragments as well as the facile use of the Staudinger ligation in the immobilization of peptide or protein analytes.



PHOSPHITE DEHYDROGENASE: MECHANISTIC STUDIES OF AN UNUSUAL PHOSPHORYL TRANSFER REACTION

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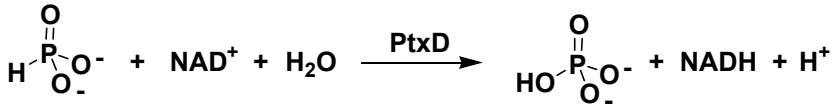
Department of Chemistry, University of Illinois at Urbana-Champaign
600 S. Mathews Ave., Urbana, IL 61801

Phosphite Dehydrogenase (PtxD) oxidizes phosphite (hydrogen phosphonate) to phosphate while concomitantly reducing NAD^+ to NADH. This reaction is highly unusual in that it is the only enzymatic phosphorus redox chemistry observed in nature.

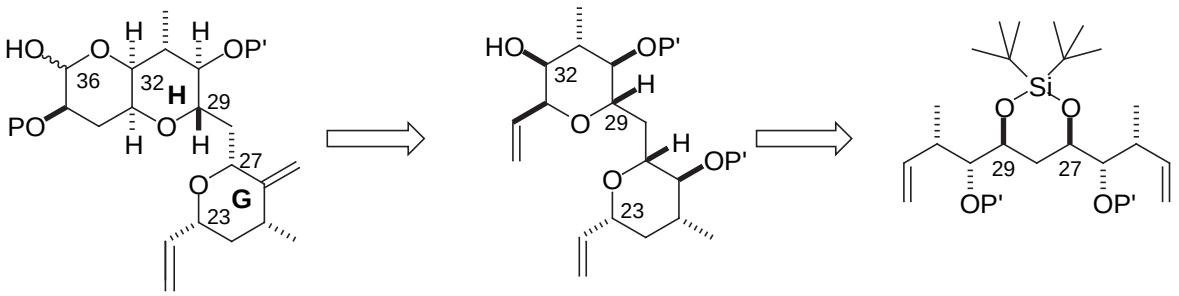
Based on sequence homology (23-49%) with the 2-hydroxyacid NAD^+-dependent dehydrogenase family, three putative catalytic residues are proposed (Arg237, Glu266, His292). In an effort to determine the mechanism of this unusual reaction, the effects of protonation state on the rate of the reaction have been studied in both H_2O and D_2O. The effect of protonation state on binding ability has also been studied. It was observed that two distinct protonation states of active site residues are necessary for optimum binding and catalysis. Additionally, six mutants derived from site-directed mutagenesis of the putative catalytic residues have been characterized. Kinetic assays show that all His292 mutants are inactive while Arg237 and Glu266 are likely involved in phosphite binding.



Utilization of Hidden Meso-Symmetry Towards the Synthesis of the C22-C36 Segment of Halichondrin B

Valerie A. Keller, Steven D. Burke
University of Wisconsin-Madison
Department of Chemistry
1101 University Ave., Madison, WI 53706

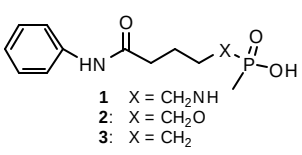
Close inspection of the G-H ring system of halichondrin B reveals masked meso-symmetry centering around C28 which has been exploited in a rapid and concise route towards the synthesis of the C22-C36 subunit. Two-directional synthesis is used to rapidly build an acyclic skeleton containing most of the correct stereogenic centers for this ring system. Desymmetrization of the meso substrate facilitates the introduction of the key C32 oxygen functionality, which was difficult to achieve with a related cyclic substrate. Asymmetric Pd(0)-mediated cyclization is proposed to concurrently form the G and H pyran rings while correctly setting the C23 and C33 stereocenters.



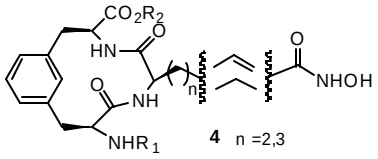
NEW CLASSES OF HISTONE DEACETYLASE INHIBITORS AS POTENTIAL ANTICANCER AGENTS

Galina V. Kapustin, Felicia A. Etzkorn
Virginia Tech, Department of Chemistry, Blacksburg, VA 24061-0212

Histone deacetylases (HDACs) are a growing family of enzymes that mediate the availability of chromatin to the transcriptional machinery. HDAC inhibitors appear to activate multiple cellular pathways, leading to growth arrest and apoptosis and have drawn a lot of attention in the past two years as promising therapeutic anticancer agents. The mechanism proposed for the histone deacetylation by HDACs is similar to that known for zinc proteases. Three new analogs of suberoylanilide hydroxamic acid, phosphonamidate, phosphonate, and phosphinate (**1-3**), were synthesized in order to test these compounds as HDAC inhibitors. We also designed and synthesized a series of hybrid molecules **4** as HDAC inhibitors employing the cyclic γ-turn motif previously developed in our laboratory. The synthesis of compound **4** involves the cascade of the Horner-Emmons olefination, asymmetric hydrogenation, and incorporation of the α-aminosuberic, α-aminoazelaic acids or their unsaturated analogs. The synthesis of compounds **1-4** and their enzyme inhibitory activity will be presented.



1 X = CH_2NH
2: X = CH_2O
3: X = CH_2

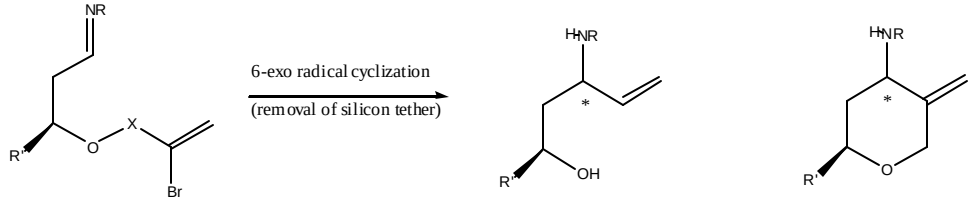


4 n =2,3

SILICON-TETHERED 6-EXO RADICAL CYCLIZATIONS OF IMINO RADICAL ACCEPTORS

Alex K. Mathies and Gregory K. Friestad
Department of Chemistry, University of Vermont
Burlington, Vermont 05405

Radical addition to C=N bonds offers potential for efficient access to multifunctional chiral building blocks under mild conditions. In previous work, a silicon tether approach for diastereocontrol has been successful for 5-exo cyclizations starting from α-hydroxy-hydrazones. In this study, 6-exo radical cyclizations to β-hydroxyhydrazones and O-benzyl oxime ethers were explored using the silicon tether approach. Vinyl radicals were found to give more efficient cyclization than alkyl radicals. Several different vinyl radical generation methods were compared with respect to diastereoselectivity and yield, including thiyl addition to an ethynyl group and halogen atom abstraction from a vinyl bromide by tributyltin hydride.

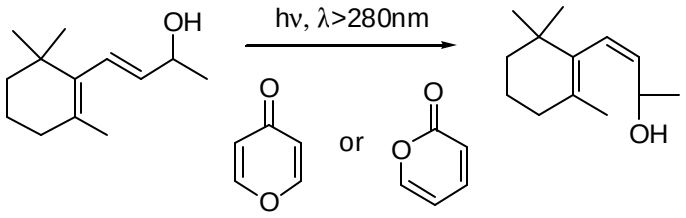


R = -NBn_2, -NPh_2, -N(Me)Bz, -OBn
R' = H, Me
X = -$SiMe_2$- , -CH_2-

Triplet Photosensitization Using Pyrones and Implications for Photoactive Marine Products

Dan Zuidema, Paul Jones
Wake Forest University
Department of Chemistry, Winston-Salem, NC 27109

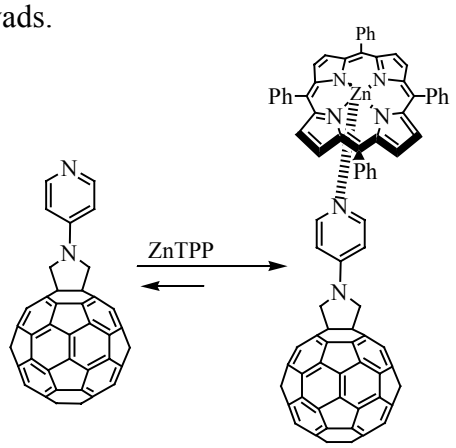
A number of polyketide natural products contain pyrone moieties. Several of these are known to be photochemically active in nature. For example, photodeoxytridachione, a polypropionate biosynthesized by *Tridachia diomedea*, is photochemically produced from deoxytridachione. Both molecules possess a γ-pyrone ring This suggests the possibility that pyrones found in nature are capable of acting as photosensitizers. We have investigated this possibility and found that some pyrones do, indeed, act as triplet sensitizers in model reactions. For example, (*E*)-ionol is completely converted to (*Z*)-ionol when irradiated in the presence of α- or γ-pyrones. An analysis of the photosensitizing capabilities of these polyketides is presented and the implications for marine photochemistry are presented.



SYNTHESIS AND PHOTOPHYSICAL PROPERTIES OF NON-COVALENTLY LINKED PORPHYRIN-FULLERENE DYADS

Shaun MacMahon, Fatma T. Tat, Stephen R. Wilson and David I Schuster
New York University
100 Washington Square East, NYU Department of Chemistry, New York, NY 10003

In the pursuit of artificial photosynthetic reaction centers, non-covalent supramolecular systems displaying photoinduced energy and electron transfer processes have attracted considerable attention. Fullerenes make particularly suitable building blocks for the construction of such multi-component systems because of their three-dimensional structure, relatively low reduction potentials, and strong electronic acceptor properties. In the present study, we have synthesized the first pyridyl-substituted fulleropyrrolidine derivative capable of forming a stable self-assembled linear complex with zinc tetraphenyl porphyrin [ZnTPP] via the axial ligation method. Ligand **1** is also used to complex a variety of covalently linked ZnTPP-C_{60} dyads.

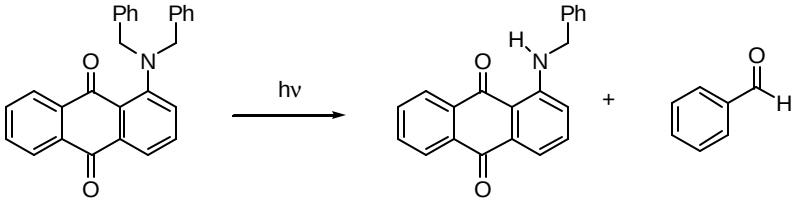


Complexation of ligand **1** with ZnTPP.

Photodealkylation of 1-N,N-*dialkylaminoanthraquinones*

John Reynolds, Robert Brinson, Paul Jones
Wake Forest University
Department of Chemistry, Winston-Salem, NC 27109

Blankespoor has shown that 1-alkoxyanthraquinones can be photochemically dealkylated to produce 1-hydroxyanthraquinone and the corresponding aldehyde. The reaction proceeds *via* intramolecular hydrogen abstraction and electron transfer. There are reports that a similar reaction occurs with 1-*N*,*N*-diakylaminoanthraquinones,[1] while a second report disputes this claim.[2] We have confirmed that a number of 1-*N*,*N*-dilakylaminoanthraquinones (including diethyl-, dibenzyl-, and *N*-methyl *N*-allylaminoanthraquinones) do, in fact, undergo dealkylation when irradiated ($\lambda > 300$ nm). Furthermore, the dealkylation is regioselective. For example, *N*-methyl-*N*-allylaminoanthraquinone loses only the allyl group when irradiated. The results of our investigation of the photochemistry of these molecules are presented.

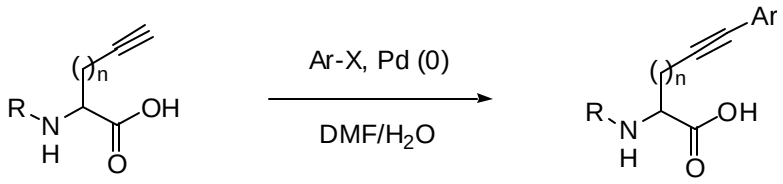


[1] Gritsan, N.P.; Bazhin, N.M. *Akad. Nauk SSR Izvestia*, **1982**, *12*, 115-120.
[2] Davies, A.K.; McKellar, J.F.; Phillips, G.O. *Proc. Roy. Soc. Lond. A*, **1971**, *323*, 69-87.

SYNTHESIS OF W-ARYL-ALKYNYLAMINO ACIDS BY SONOGASHIRA TYPES OF REACTION IN AQUEOUS MEDIA

Roberto J. Brea Fernández, and Juan R. Granja
Departamento de Química Orgánica e Unidade Asociada ó C.S.I.C, Facultade de Química, Universidade de Santiago, 15782 Santiago de Compostela, SPAIN

The remarkable structural and functional diversity of protein architecture suggest the enticing goal of constructing synthetic variants. Crucial to the *de novo* design of functional polypeptides is the availability of synthetic motifs with defined secondary and tertiary structure.[1] For small peptides, control of structure can be achieved by modification of a polypeptide with unnatural residues. Seeking to produce peptides with side chain groups featuring aryl or heteroaryl substituents with useful properties for monitoring or control of peptide structure or induce new catalytic activity, we study a Sonogashira[2] cross-coupling reaction of amino acid bearing an alkynyl side chain with appropriated halides. In this communication, we will present the efficient derivatitation of such amino acids with a wide variety of (hetero)aryl halides by cross-coupling reactions catalyzed by palladium on carbon (10% Pd/C) in aqueous media. [Supported by the grants from the Xunta de Galicia (PGIDT00PXI20912PR) and the Spanish Ministry of Education and Science (PB97-0524 y SAF2001-3120)].

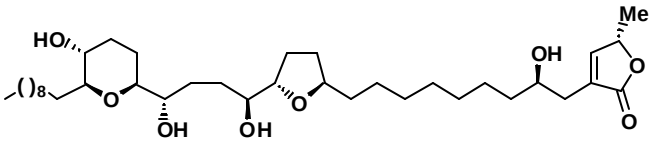


[1] De Alba, E.; Santoro, J.; Rico, M.; Jiménez, M. A. *Protein Sci.* **1999**, *8*, 854-865; Mezo, A.R.; Ottesen, J.J.; Imperiali, B. *J. Am. Chem. Soc.* **2001**, *123*, 1002-1003
[2] Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467-4470

Enantioselective Total Synthesis of Annonaceous Acetogenin (-)-Mucocin

Alexei I. Polosukhin, Hai-Ren Zhang, Santosh J. Gharpure, P. Andrew Evans
Indiana University
Department of Chemistry, Bloomington, IN 47405

We have developed a triply convergent 12 step enantioselective total synthesis of the potent antitumor agent (-)-mucocin. The total synthesis utilized a temporary silicon-tethered ring-closing metathesis (*TST-RCM*) as a key cross-coupling to accomplish the synthesis of the skeleton. The 3-hydroxy-2,6-disubstituted tetrahydropyran unit was constructed using a novel diastereoselective bismuth catalyzed reductive etherification reaction. The complete synthetic details of this approach will be presented.



(-)-Mucocin

Bismuth Catalyzed Diastereoselective Etherification Reactions: Application to the Synthesis of Non-Adjacent and Fused Polycyclic Ethers

Santosh J. Gharpure[1], Robert J. Hinkle[2], Jian Cui[1], P. Andrew Evans[1]

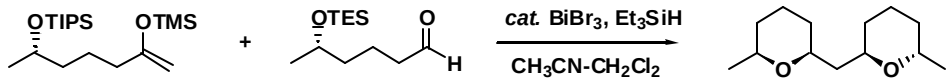
1. Indiana University

2. College of William and Mary

1. Department of Chemistry, Bloomington, IN 47405

2. Department of Chemistry, Williamsburg, VA 23187

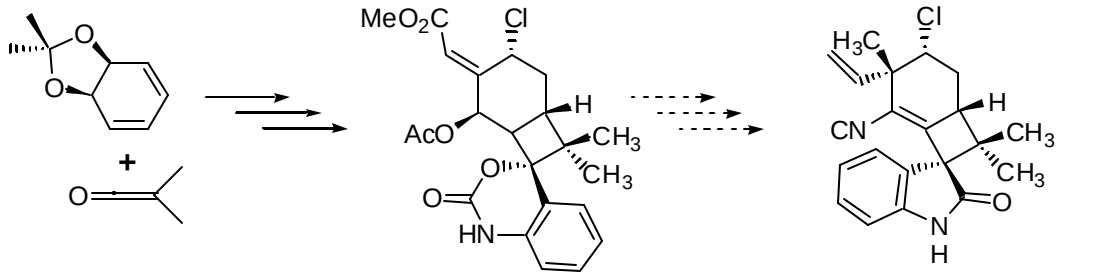
The construction of *cis*- and *trans*-cyclic ethers, present in biologically-active natural products, remains an important synthetic goal. We have developed a new bismuth catalyzed intramolecular reductive etherification and tandem cyclization-addition strategies to provide rapid entry into either *cis*- or *trans*-2,6-disubstituted cyclic ether systems. The scope and limitations of these transformations will be presented.



PROGRESS TOWARD THE TOTAL SYNTHESIS OF WELWITINDOLINONE A

John L. Wood, Sarah E. Reisman, Joseph M. Ready, Makoto Hirata, Kazuhiko Tamaki, Mathew M. Weiss
Yale University, Department of Chemistry
PO Box 208107, New Haven, CT 06520-8107

A highly functionalized intermediate (**1**) containing the [4.2.0] bicylcic ring system and handle to the requisite oxindole of the antifungal marine metabolite Welwitindolinone A (**2**) was prepared from simple starting materials. These results and ongoing work toward the total synthesis of **2** will be presented.

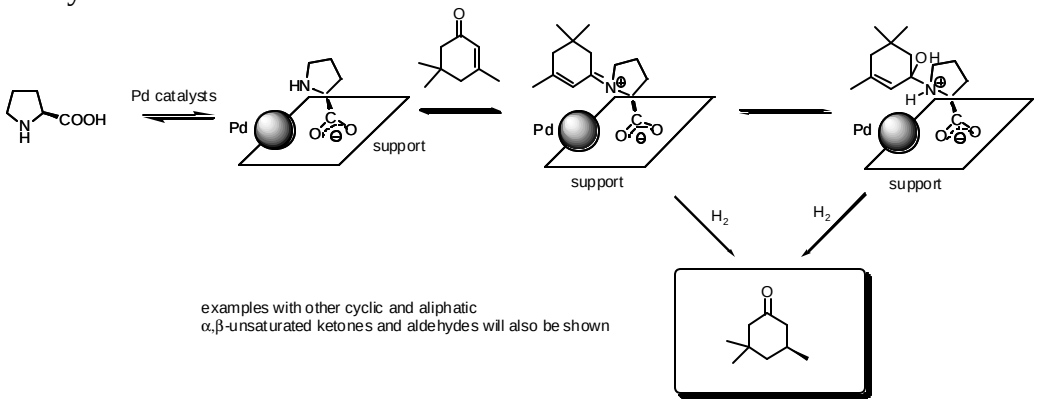


1 Welwitindolinone A (**2**)

HETEROGENEOUS CATALYTIC ENANTIOSELECTIVE HYDROGENATION OF a ,b -UNSATURATED CARBONYL COMPOUNDS BY PROLINE MODIFIED SUPPORTED PALLADIUM CATALYSTS

Shilpa Mhadgut and Béla Török
Department of Chemistry, Michigan Technological University, 1400 Townsend Drive, Houghton, MI 49931, *scmhadgu@mtu.edu*, *btorok@mtu.edu*

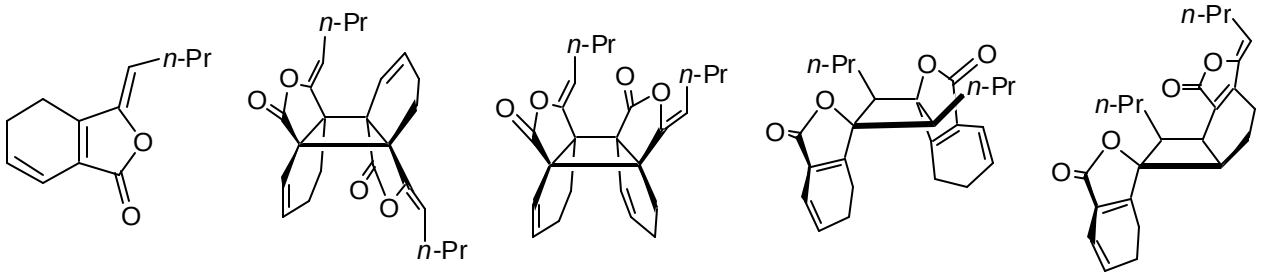
The enantioselective hydrogenation of α,β-unsaturated carbonyl compounds by proline modified Pd catalysts is described. The effects of different experimental variables, such as catalyst support, hydrogen pressure, solvent, presonication method were investigated. As a test reaction, the enantioselective hydrogenation of 3,3,5-trimethyl-2-cyclohexen-1-one (isophorone) was selected. The presonication of commercial supported Pd catalysts modified by proline and proline derivatives resulted in enhanced enantioselectivity providing good ee values (up to 91% ee) under mild experimental conditions. It was found in the presonication εxπεριμεντσ τηατ τηε αδσορπτιον οφ προλινε ον τηε χαταλψστσ συρφαχε ισ οφ χ ρυχιαλ ιμπορτανχε. Βασεδ ον τηε εξπεριμενταλ δατα ωε προποσε τηατ τηε ενηα νχεδ προλινε αδσορπτιον ισ τηε μαφορ φαχτορ φορ τηε ιμπροϖεδ χαταλψστ περφ ορμανχε. Βασεδ ον τηε ρεσυλτσ οβταινεδ ιν τηε τεστ ρεαχτιον, τηε εναντιοσελεχ τιϖε ηψδρογενατιον οφ σεϖεραλ χψχλιχ ανδ αλιπηατιχ α,β-unsaturated ketones and aldehydes will be shown.



***Photochemistry of Z-Ligustilide. Biomimetic Synthesis of Riligustilide*.**

Ricardo Figueroa and Guillermo Delgado
Instituto de Química de la Universidad Nacional Autónoma de México.
Circuito Exterior, Ciudad Universitaria. Coyoacán 04510. México, D. F.

The photoreaction of *Z*-ligustilide (**1**), a bioactive phthalide isolated from several Umbelliferae plants used in traditional medicine, using hexane or acetone as solvents, afforded mainly the dimeric products **2**-**5**, derived from a $\pi 2s + \pi 2s$ cycloaddition with high regio-, *endo/exo,* and chemo- selectivities. The structures were determined by crystallographic and spectroscopic analysis. The production of the natural racemic phthalide riligustilide (**6**) in the transformation supports its proposed biogenesis.



1 **2** **3** **4** **5**

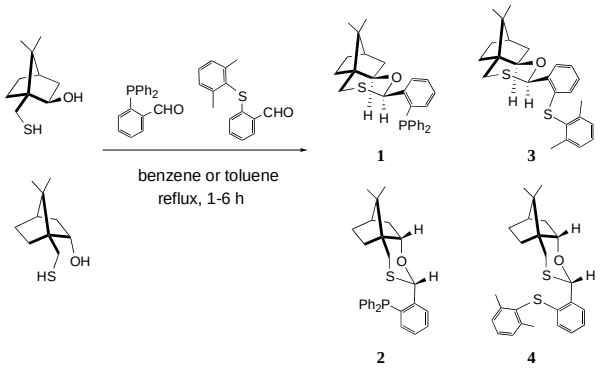
A Novel Chiral Oxathiane Ligands for Palladium-Catalyzed Asymmetric Allylation

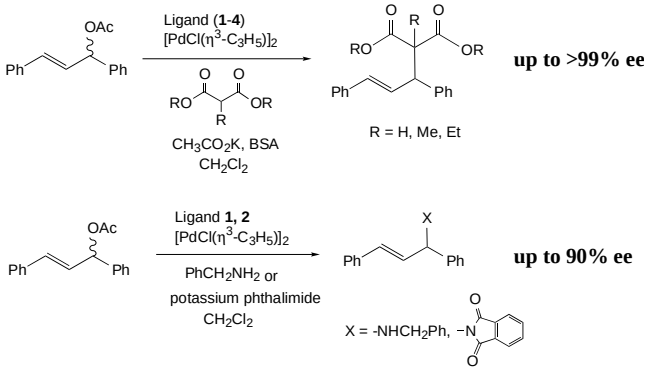
Yuko Okuyama,[a] Hiroto Nakano,[a] Kouichi Takahashi,[a] Hiroshi Hongo[a] and Chizuko Kabuto[b]

[a] Tohoku Pharmaceutical University, 4-4-1 Komatsushima, Aoba-ku, Sendai 981-8558, Japan

[b] Instrumental Analysis Center for Chemistry, Graduate School of Science, Tohoku University, Aoba, Aramaki, Aoba-ku, Sendai 980-8578, Japan

novel chiral S-P typed phosphinooxathiane and S-S typed sulfideoxathiane ligands (**1-4**) were synthesized easily by the condensations of (1*S*)-(-)-mercaptoisoborneol or (1*S*)-(-)-mercaptoborneol with 2-diphenylphosphinobenzaldehyde or 2-(2, -xylyl)thiobenzaldehyde in good to excellent yields. Pd-catalyzed asymmetric alkylation and amination using these ligands of 1,3-diphenyl-2-propenyl acetate with carbon and amino nucleophiles gave products in good yields with a high level of enantioselectivity (up to ee).





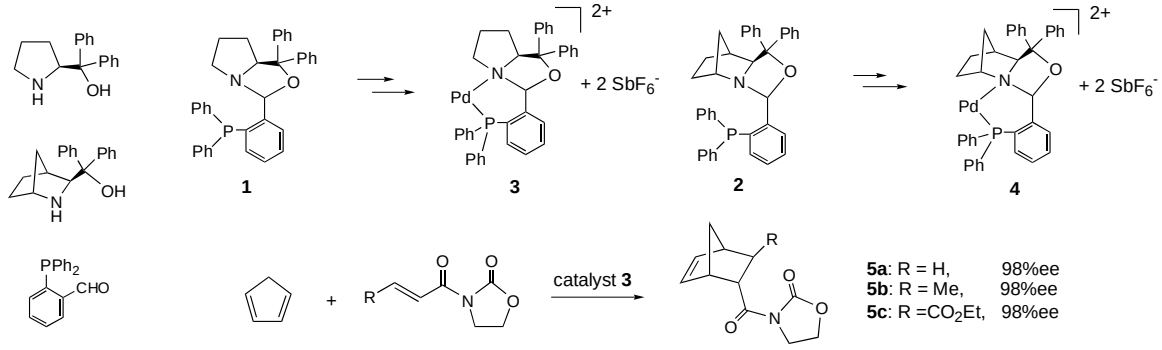
A Novel Chiral Palladium-Phosphinooxazolidine Catalyst for The Enantioselective Diels-Alder Reaction

Hiroto Nakano,[a] Yuko Okuyama,[a] Yuichiro Suzuki,[a] Reiko Fujita,[a] and Chizuko Kabuto[b]

[a] Tohoku Pharmaceutical University, 4-4-1 Komatsushima, Aoba-ku, Sendai 981-8558, Japan

[b] Instrumental Analysis Center for Chemistry, Graduate School of Science, Tohoku University, Aoba, Aramaki, Aoba-ku, Sendai 980-8578, Japan

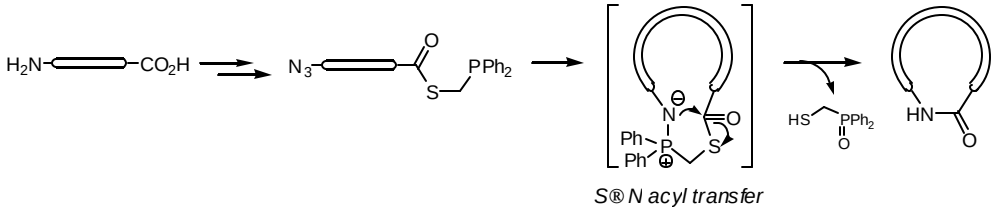
novel class of -P typed chiral ligand, phosphinooxazolidines (**1** and **2**), were designed and synthesized easily by the condensations of (*S*)-1,1-diphenyl(2-pyrrolidinyl)methanol and 2-azanorbornylmethanol with 2-(diphenylphosphino)benzaldehyde. nantioselective Diels- lder (D) reactions of cyclopentadiene with a range of acyl-1,3-oxazolidin-2-one dienophiles using chiral cationic complexes (**3** and **4**) derived from ligands **1** and **2** gave the adducts (**5a-c**) in good chemical yields and enantioselectivity (ee).



Intramolecular Staudinger Ligation:
a Powerful Method for the Ring-Closure of Difficult Lactams

Olivier David, Wim J. N. Meester, Hans E. Schoemaker, Henk Hiemstra and Jan H. van Maarseveen
Institut for Molecular Chemistry, University of Amsterdam,
Nieuwe Achtergracht 129, 1018 WS Amsterdam.

Directly inspired by the promising Staudinger ligation reaction[1,2], we want to present an *intramolecular* version hereof.
This new "Staudinger macrolactamization" efficiently ring-closes 7 to 9 membered *medium sized* lactams which cannot be obtained in a practical manner using traditional methods.



S® N acyl transfer

The intramolecular Staudinger ligation auxiliary design will be discussed together with applications in the synthesis of aliphatic lactams and bislactams of the homodiketopiperazine series.

1. Bertozzi, C.R. et al. *Science*, **2000**, *287*, 2007.
2. Raines, R.T. et al. *Journal of Organic Chemistry*, **2002**, *67*, 4993.

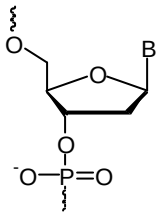
Regio- and Stereoselective Synthesis of LNA Guanine Nucleosides

Christoph Rosenbohm and Troels Koch

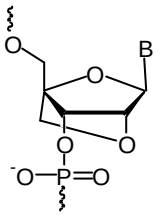
Cureon A/S

Fruebjergvej 3, DK-2100 Copenhagen, Denmark

Locked Nucleic Acid (LNA) is the single nucleic acid modification that contributes the highest affinity ever obtained by Watson-Crick hydrogen bonding. Recently, LNA oligomers have shown very promising therapeutic properties as antisense drugs.



DNA



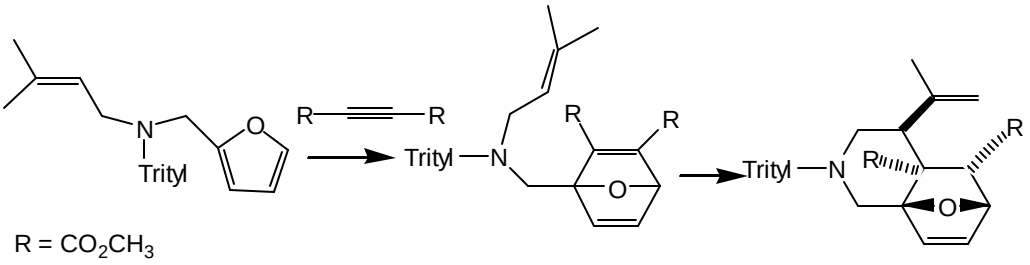
LNA

Efficient syntheses of the LNA thymine, cytosine and adenine phosphoramidites has been achieved resulting in significantly improved overall yields. However, the efficient synthesis of the LNA guanine monomer has required more attention due to poor regioselectivity in the nucleobase coupling step. A stereo- and regioselective high yielding synthesis of the LNA guanine nucleosides has now been devised employing 2-amino-6-chloropurine as glycosyl acceptor providing useful intermediates for the preparation of nucleosides with modified nucleobases (e.g. 2,6-diaminopurine).

Steric Acceleration of Intramolecular Cyclisations

Graham Smith and Peter G. Sammes
Dept. of Chemistry, University of Surrey, Guildford, Surrey, GU5 7XH, UK.

Steric buttressing can be exploited to facilitate intramolecular cyclisations by suitable manipulation of entropic and enthalpic factors. Previously we have used this technique to promote **Diels-Alder** reactions. We are now using this technique to effect **ene** reactions under mild, selective conditions. For example the reaction outlined in Scheme 1 proceeds at room temperature in good yield and with stereoselective control.



$R = CO_2CH_3$

Scheme 1

Extension of this methodology to the synthesis of substituted pyrrolidines is currently in hand. Use of suitable steric buttresses allows these reactions to proceed at lower temperatures and with greater selectivity than has previously been reported.

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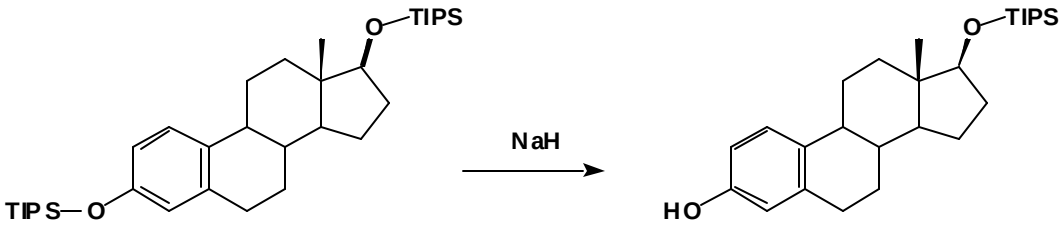
Selective Removal of Silyl Ethers from Phenolic Hydroxyls with NaH

Paula Kiuru*, *Kristiina Wähälä
Department of Chemistry, Organic Chemistry Laboratory, P.O. Box 55,
FIN-00014 University of Helsinki, Finland
e-mail: kristiina.wahala@helsinki.fi

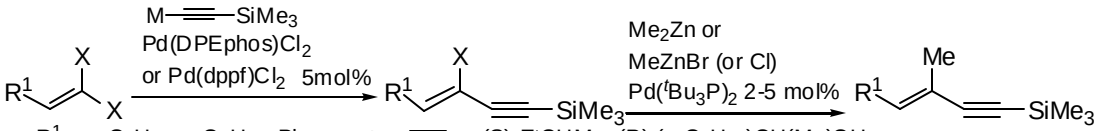
Silyl ethers as protection groups have been considered to survive well basic conditions. We report here a selective removal of TIPS and TBDPS ethers by NaH from phenolic hydroxyls in the presence of aliphatic silyl protected hydroxyls, eg. estradiol.



Highly Configuration-Retained Methylation of *trans*-1-Bromo(or Chloro)-1-Substituted(Alkynyl, Alkenyl, or Aryl)-1-Ene with Methylzincs Catalyzed by Pd(^{t}Bu$_3$P)$_2$

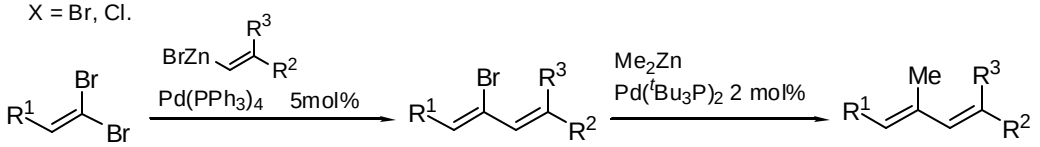
Ji-cheng Shi and Ei-ichi Negishi
Herbert C. Brown Laboratories of Chemistry, Purdue University, West Lafayette, IN 47907-1393

We present here a new protocol to the unit of *trans*-1,2-disubstituted-1-methyl-1-ene, which is often observed in natural products, through two-stage Pd-catalyzed cross-coupling of 1,1-dibromo(chloro)-1-alkene: 1) *trans*-selective alkynylation (eq. 1), alkenylation (eq. 2), and arylation (eq. 3), 2) followed by methylation. The use of Pd(^{t}Bu$_3$P)$_2$ was crucial in achieving stereospecific methylation in high yield and nearly 100% retention of configuration.



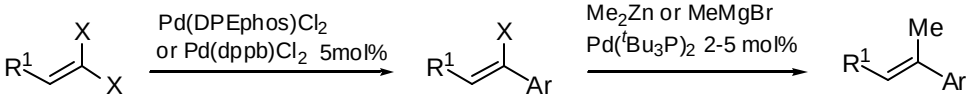
(1)

R^1 = *n*-C_9H_{19}, *n*-C_6H_{13}, Ph, Me_3Si—≡—, (*S*)-EtCHMe, (*R*)-(*n*-C_7H_{15})CH(Me)CH_2.
M = H or ZnBr (Cl).
X = Br, Cl.



(2)

R^1 = Me_3Si—≡— .
R^2 = $TBSOCH_2$, R^3 = H; R^2 = *n*-C_8H_{17}, R^3 = H; R^2 = Ph, R^3 = Me; R^2 = $TBSOCH_2CH_2CH_2$, R^3 = Me;



(3)

R^1 = *n*-C_6H_{13}, Ph, Me_3Si—≡—, (*S*)-EtCHMe.
Ar = Ph, 2-thienyl, 2-thiazoyl.
X = Br, Cl.

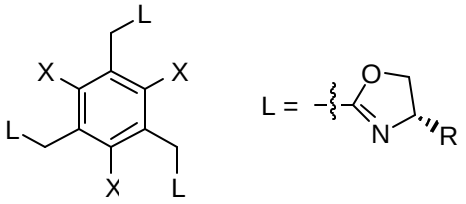
Fluorescence Sensing of Ammonium and Organoammonium Ions Through the Conformational Restriction of Tripodal Oxazoline Receptors

Hui-young Ku, Yusin Kim, Sung-Gon Kim, Yun-Ho Lee, Kyo Han Ahn

Pohang University of Science & Technology (POSTECH)

Department of Chemistry and Center for Integrated Molecular Systems, Division of Molecular and Life Science, San 31 Hyoja-dong, Pohang 790-784, Republic of Korea

A new class of fluorescence sensing system for ammonium and organoammonium ions has been disclosed, which operates mainly through the conformational restriction of tripodal receptors. Tripodal oxazoline **1** shows a significant fluorescence enhancement upon binding NH_4^+ but little response towards K^+, Na^+, and Mg^{2+} ions. Tripodal oxazoline **2** shows chiral discrimination in fluorescence upon binding enantiomeric organoammonium ions. Further elaboration of the benzene fluorophore into more conjugated derivatives (**3** and **4**) and preliminary sensing studies will be presented.

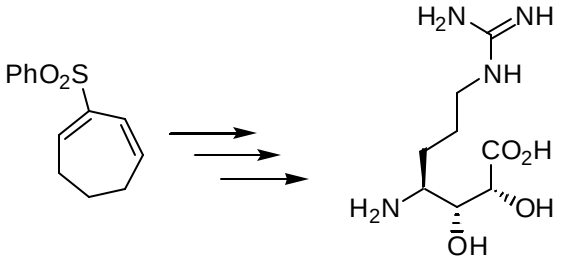


1, X = Me; R = Me
2, X = Me; R = Ph
3, X = CH=CH-Ph; R = Me
4, X = CH=CH-Ph; R = Ph

Towards the Total Synthesis of Callipeltin A and D; Asymmetric Synthesis of AGDHE, via Vinyl Sulfones.

Ángel I. Morales-Ramos, Mark A. Lipton, Phillip L. Fuchs
Purdue University
Department of Chemistry, West Lafayette, IN 47906-1393

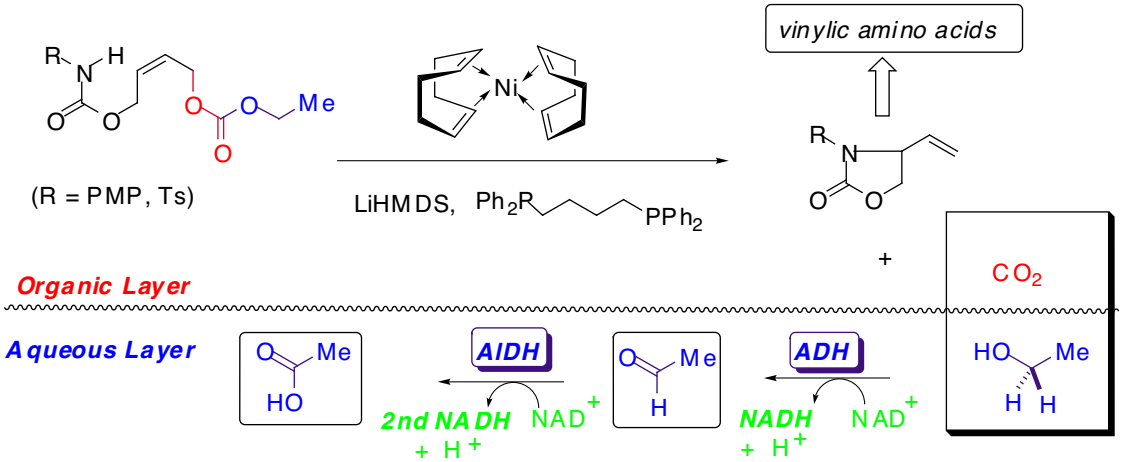
Callipeltin A, a cyclic depsidecapeptide isolated from the marine lithistida sponges Callipelta sp. and Latruncula sp. was shown to possess antifungal and anti-HIV activity as well as cytotoxicity against selected human carcinoma cell lines. The side chain attached to the macrocycle, recently isolated as callipeltin D, is essential for anti-HIV activity. A key residue in the side chain is the novel amino acid (2*R*,3*R*,4*S*)-4-amido-7-guanidino-2,3-dihydroxyheptanoic acid (AGDHE), which we herein report a new asymmetric synthesis of AGDHE via vinyl sulfone chemistry as well as progress towards the solid phase synthesis of callipeltin D.



An In Situ Enzymatic Screening (ISES) Approach to Catalyst Development.

David B. Berkowitz, Gourhari Maiti, Mohua Bose & Sungjo Choi
Department of Chemistry
University of Nebraska
Lincoln, NE 68588-0304

Described is a method for enzymatically monitoring of a set of organic reactions of interest, in parallel. An ISES screen can be conveniently run under biphasic conditions with the organic transformation under study taking place in an organic layer and the reporting enzyme(s) located in a neighboring aqueous layer. For example, as illustrated below, in a Tsuji-Trost-



type reaction, employing an ethyl carbonate leaving group, turnover leads to release of ethanol. The ethanol is detected by the sequential action of two reporting enzymes, alcohol dehydrogenase and aldehyde dehydrogenase. Two molecules of NADH are thereby formed and can be spectroscopically observed at 340 nm. Use of a multicell-changer allows for the collection of nearly continuous relative kinetic data for 6-12 reactions in parallel. Using this ISES approach, conditions for a Ni(0)-promoted allylic amination have been uncovered and fine-tuned with respect to ligand and nitrogen protecting group. This constitutes a new synthetic entry into alpha,beta-unsaturated amino acids, targets of considerable interest to us and others as potential inhibitors of pyridoxal phosphate (vitamin B_6)-dependent enzymes. The further development of this chemistry and its application to targets of this vinylic amino acid class will be presented.

DEVELOPMENT OF POROUS FUNCTIONAL MATERIALS FOR HETEROGENEOUS CATALYSIS

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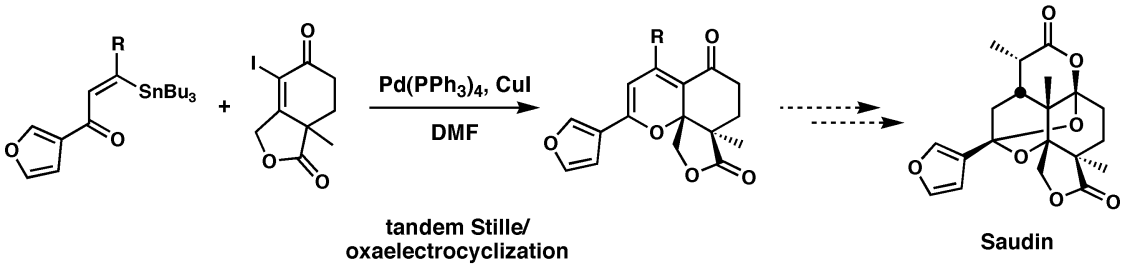
University of Kansas
Department of Chemistry
1251 Wescoe Drive
Lawrence, KS 66045-7582

mmobilization of metal complexes in porous hosts has proven to be an effective method for generating new materials with beneficial properties. ecent advances in this area have included the fabrication of materials for separation and sensor applications. ne continuing challenge in this field is to develop catalytic porous materials, where the active sites contain coordinatively unsaturated metal centers. nterest in creating catalytic polymeric hosts has grown because of their potential for reuse, long storage life, and potential for enhanced stereoselectivity. e are using template copolymerization methods to immobilize metal complexes in porous organic and inorganic hosts for use as heterogeneous catalysts. Catalytic studies with these materials are incorporating immobilized systems that have functioned well in homogeneous conditions giving a basis for comparison. Presented is the use of template copolymerization methods to immobilize chiral salen complexes as templates within porous organic hosts. Materials containing various percentages of template have been spectroscopically characterized and their function has been tested in the hydrolytic kinetic resolution of a few epoxides. Preliminary results suggest reactivity and selectivity dependence on the percentage of template immobilized in the host.

PROGRESS TOWARD THE TOTAL SYNTHESIS OF SAUDIN

*Uttam K. Tambar, Taichi Kano, John F. Zepernick, Brian M. Stoltz**
California Institute of Technology
Division of Chemistry and Chemical Engineering, Pasadena, CA 91125

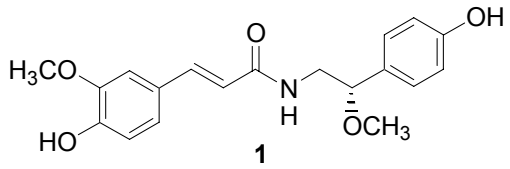
Saudin is a caged diterpenoid that exhibits potent hypoglycemogenic activity, which makes it a potential lead for the treatment of diabetes mellitus. We will describe our progress toward the total synthesis of this natural product. Our convergent and stereoselective strategy highlights a novel tandem Stille/oxaelectrocyclization reaction, which builds the core of saudin in one diastereoselective step from simple substrates. Currently we are developing this novel tandem step into a general method for synthesizing highly substituted pyrans in a stereoselective fashion. We will also discuss our efforts to advance the product of the Stille/oxaelectrocyclization reaction to saudin.



A COMBINATORIAL APPROACH TO NATURAL PRODUCT BASED INHIBITORS OF APOPTOSIS

Vitaliy Nesterenko, Paul J. Hergenrother
Department of Chemistry, University of Illinois Urbana-Champaign
Roger Adams Laboratory,
University of Illinois, Urbana, IL 61801

Apoptosis (programmed cell death) is a vital pathway for multicellular organisms. Aberrant apoptosis has been implicated in a number of disease states, including Alzheimer's disease, Parkinson's disease, and a variety of cancers. Although there are a number of small molecules that induce apoptosis, comparably fewer examples of small molecule inhibitors are known. We are seeking to identify highly potent, pathway specific inhibitors of apoptosis. As a starting point in this endeavor, we have constructed a combinatorial library of ~1000 compounds that are based on the structure of a natural product known to inhibit etoposide induced apoptosis (compound **1**). In the course of creating this library an efficient protocol for the asymmetric synthesis of 1-aryl-2-amino ethanol derivatives was developed, using a pH-controlled asymmetric aminohydroxylation of styrene substrates. With the appropriate building blocks in hand, the combinatorial library was created in parallel, and subsequently screened in apoptosis inhibition assays.

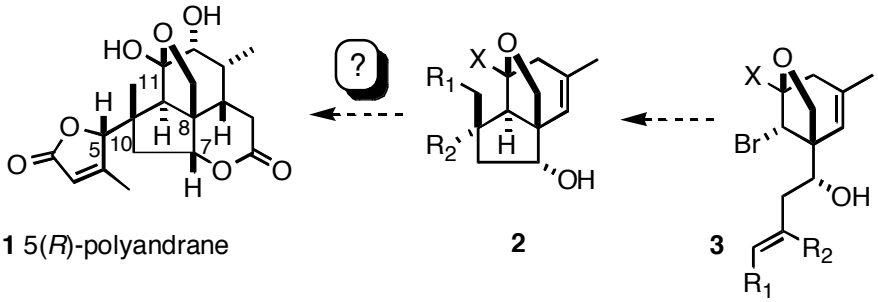


1

C_{19} QUASSINOID MODEL STUDIES: PREPARATION OF TRANS-PERHYDROINDANS VIA A VINYLOGOUS MUKAIYAMA ALDOL-FREE RADICAL CYCLIZATION ROUTE

Matthew G. Donahue and David J. Hart
The Ohio State University Department of Chemistry
100 W. 18th Ave, Columbus, OH 43210

We have been investigating a unified approach to the C_{19} and C_{20} quassinoids that involves an extension of a free radical cyclization chemistry previously developed in our laboratories. The plan for the polyandranes involves preparation of *trans*-perhydroindans of type **2** via free radical cyclization of substrates of type **3**. Structures of type **3** have been prepared in a six-step sequence featuring a titanium tetrachloride promoted vinylogous Mukaiyama aldol reaction.



1 5(*R*)-polyandrane **2** **3**

AN IMPROVED SYNTHESIS OF ELECTRON-RICH DIARYL DITELLURIDES AND DIARYL TELLURIDES

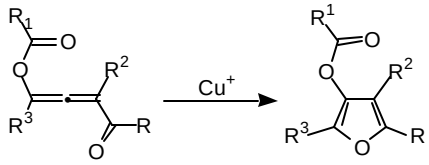
Margaret E. Logan, Elizabeth A. Gregory, Stacy A. Morrill, Andrea N. Topolnycky
SUNY College at Brockport, Brockport, NY 14420

Diaryl tellurides, particularly those substituted with electron-donating groups, are known to have good antioxidant properties, and to act as catalysts for oxidations with hydrogen peroxide. Electron-rich diaryl ditellurides are useful in the synthesis of unsymmetrical tellurides having similar properties. In order to prepare amino-substituted diaryl ditellurides and tellurides that are more electron-rich and thus would be predicted to have improved antioxidant and catalytic properties, a general synthetic route that would lead to the two classes of compounds in good yield and purity was needed. An improved synthetic route to amino-substituted diaryl ditellurides and tellurides has been developed and applied to the synthesis of five target molecules. In addition, the route has been used to prepare the telluride and ditelluride from N-methyltetrahydroquinoline and julolidine, in which the lone pair of electrons on nitrogen is increasingly constrained to overlap with the π system. Preliminary evaluation of the antioxidant properties of the resulting tellurides in both one-electron and two-electron assays showed that the ease of oxidation correlates with the electron-donating ability of the nitrogen.

A NOVEL 1,2 MIGRATION OF THE ACYLOXY GROUP: EFFICIENT SYNTHESIS OF TRI- AND TETRASUBSTITUTED FURANS

Anna W. Sromek, Alexander V. Kel'in, Vladimir Gevorgyan
University of Illinois at Chicago
Department of Chemistry
845 W. Taylor St.
Chicago, IL 60609

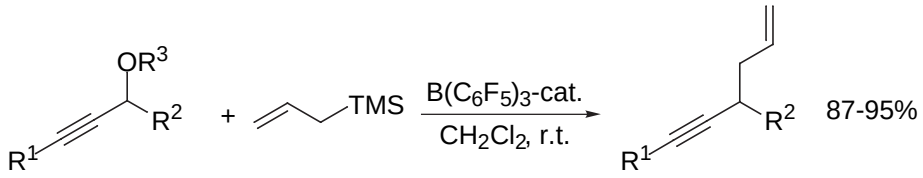
Pyrroles and furans are ubiquitous heterocyclic units widely used in materials science and found in many naturally occurring and biologically important molecules. Our group has recently developed a novel and efficient Cu(I) catalyzed cycloisomerization of alkynyl ketones and imines into the corresponding 2,5 disubstituted heterocycles. While investigating ways to further introduce functionality onto the heterocycle, an allenyl acyloxy group was found to undergo an unusual "1,2" migration to yield the corresponding tri- and tetrasubstituted heterocycle as a single regioisomers.

A number of ester groups  smoothly undergo this novel and unusual "1,2" migration producing multisubstituted furans as single regioisomers. The scope of this method will be shown and a plausible mechanism for this novel cascade transformation will be discussed.

$B(C_6F_5)_3$-Catalyzed Allylation of Secondary Propargylic Acetates with Allylsilanes

Todd Schwier, Michael Rubin, Vladimir Gevorgyan
University of Illinois at Chicago
Department of Chemistry, Chicago, IL 60607-7061

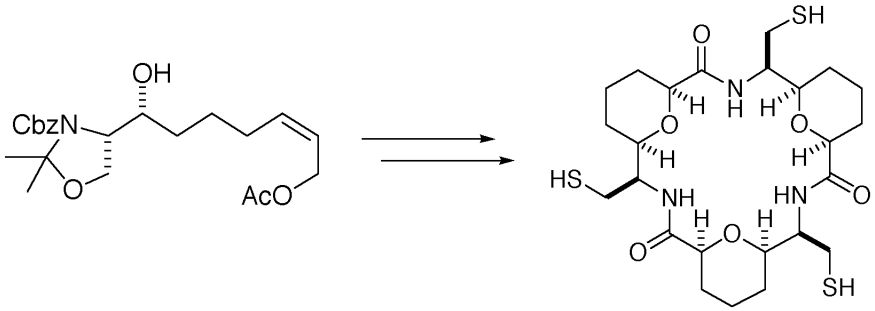
An efficient method for the allylation of secondary propargylic alcohol derivatives with allylsilanes in the presence of a catalytic amount of the Lewis acid, $B(C_6F_5)_3$, has been developed. This methodology allows for the preparation of 1,5-enynes in good yields. The scope and limitations of this protocol will be discussed in regards to functional group tolerance and type of leaving group.



C_3-Symmetric Trilactam Scaffolds: Efforts Toward the Development of a Small Molecule Mimic of Depsipeptide Megasynthetase

John E. Campbell and Steven D. Burke*
University of Wisconsin- Madison
Department of Chemistry, Madison, WI 53706

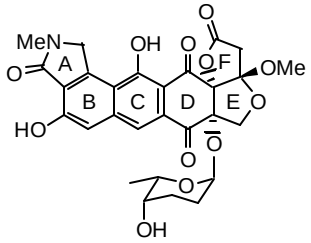
Efficient modular synthesis of conformationally preorganized, C_3-symmetric trilactams is reported. The allyl acetate cyclization substrate was synthesized in five steps from Garner's L-serine derived aldehyde. After chiral ligand-mediated, palladium cyclization, the resulting hydropyran units were transformed into orthogonally protected amino acids for iterative coupling. The final macrolactamization was accomplished using HATU/HOAt under high dilution conditions. Completion of the macrotrithiol involved a Mitsunobu displacement of three primary hydroxyl groups with thiolacetic acid followed by subsequent reduction of the resulting trithiolacetate to the trithiol with methanolic HCl.



RESEARCH TOWARD THE TOTAL SYNTHESIS OF LACTONAMYCIN

Jay P. Deville and Victor Behar*
Rice University
Department of Chemistry MS-60, Houston, Texas 77251-1892

Synthetic studies on the promising antibiotic, lactonamycin, are presented. Lactonamycin, isolated in a screen for new antibiotics active against drug resistant bacterial strains, exhibits potent antimicrobial activity against vancomycin-resistant *Enterococcus* and methicillin-resistant *Staphylococcus aureus*. The ABCD-ring system of the natural product was synthesized in an efficient manner utilizing a powerful tandem conjugate cyanide addition-Dieckmann condensation of an alkynyl diester to afford a fully functionalized anthracene. Subsequent chemoselective reduction of the cyano group with spontaneous lactam formation affords the tetracyclic core of lactonamycin. In addition to our synthesis of the ABCD-ring system, progress toward the highly oxygenated EF-ring system will be presented. An advanced intermediate toward a model of the CDEF-ring system has been synthesized utilizing a 3+2 dipolar cycloaddition of a nitrile oxide with a trisubstituted quinone as the key step.

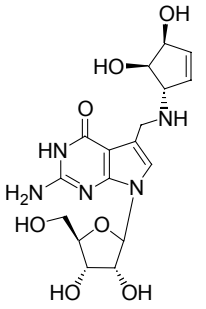


(+)-Lactonamycin

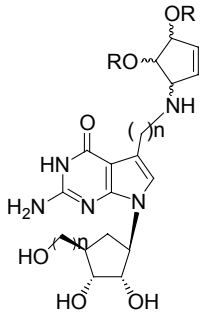
Synthesis of Carbocyclic Nucleoside Analogs of Nucleoside Q

Kyung-Hee Kim and Marvin J. Miller
University of Notre Dame
Department of Chemistry and Biochemistry, Notre Dame, Indiana 46556

Carbocyclic nucleosides are one of the important classes of modified nucleosides and have attracted much attention in development of new antiviral and antitumor agents. Naturally occurring nucleoside Q shows biological activity related to tumor growth although the definitive role of nucleoside Q is yet unknown. Nucleoside Q is a remarkably modified nucleoside with 7-deazaguanosine containing an amino methyl cyclopentendiol side chain. Some carbocyclic nucleosides have been designed as synthetic analogs of natural nucleoside Q. Due to the similarity of the structure, carbocyclic nucleoside analogs might show biological activities. Progress in synthesis of these carbocyclic nucleoside analogs is reported that will highlight recent developments in acylnitroso cycloaddition chemistry.



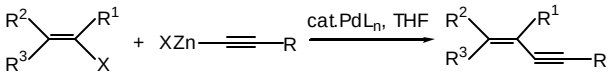
nucleoside Q



analogs of carbocyclic nucleoside Q (n=0,1)

Highly Satisfactory Alkynylation of Alkenyl Halides via Pd-Catalyzed Cross-Coupling with Alkynylzincs and Its Critical Comparison with the Sonogashira Alkynylation

Mingxing Qian, Fanxing Zeng, Luigi Anastasia, David Babinski, and Ei-ichi Negishi*
Herbert C. Brown laboratories of Chemistry, Purdue University, West Lafayette, IN 47907



R = COOMe, COOEt, COPh, COC_6H_{11}-*c*, CH=CMeCOOEt, CH=CHCH=CMeCOOEt, Ph, *n*-Hex.
R^1, R^2, R^3 = C, H, or Br. X = halogens or OTf.

The Pd-catalyzed alkynylation of various alkenyl halides and triflates as well as heteroaryl and alkynyl iodides with alkynylzincs proceeds well even with alkynyl derivatives containing electron-withdrawing groups. The reaction appears to be highly general. No stereoisomerization was detected in any of the reactions with potentially isomerizable alkenyl halides. Noteworthy is that the corresponding Sonogashira reactions under various reported conditions are significantly less satisfactory in all cases performed in this study.

SYNTHESIS AND ABSOLUTE CONFIGURATION OF 3-CHLOROBUTYNE

Jiangtao He, Prasad L. Polavarapu
Vanderbilt University
Department of Chemistry, Vanderbilt University, Nashville, TN 37235

(+)-3-chlorobutyne was synthesized by reaction between (S)-(-)-3-butyn-2-ol and 1-chloro-N,N,2-trimethyl-1-propenylamine. To determine the absolute configuration of (+)-3-chlorobutyne, the specific rotation of 3-chlorobutyne at infinite dilution has been measured in both carbon tetrachloride and methanol. The specific rotation of 3-chlorobutyne was calculated by density function theory using B3LYP functional and three large basis set: 6-311++G(2d,2p), AUG-cc-pVDZ, and AUG-cc-pVTZ. These results suggest that the absolute configuration of 3-chlorobutyne is (R)-(+). To further confirm the assignment of absolute configuration, the vibrational absorption and circular dichroism spectra of 3-chlorobutyne were measured in carbon tetrachloride solution in the 2000-900 cm^{-1}. The absorption and VCD spectra of (R)-3-chlorobutyne were also calculated by density function theory using B3LYP functional and three large basis set: 6-311++G(2d,2p), AUG-cc-pVDZ, and AUG-cc-pVTZ. The experimental spectra for (+)-3-chlorobutyne are in complete agreement with the calculated spectra of (R)-3-chlorobutyne. This confirms the absolute configuration of 3-chlorobutyne determined from optical rotation. These results demonstrate that the molecular stereochemistry of organic molecules can be conveniently established by the combined use of ab initio calculations and experimental measurements on either optical rotation or vibrational circular dichroism.

Synthesis of Substituted Phenanthroline Ligands via Samarium-Promoted Coupling with Ketones, Aldehydes, and Epoxides

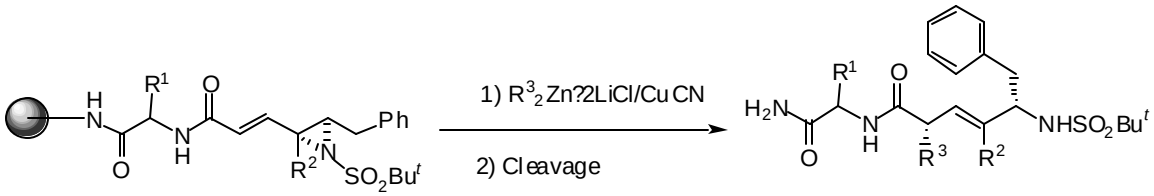
Jeremy A. Weitgenant, Jonathan Mortison, David J. O'Neill, and Paul Helquist*
University of Notre Dame, Department of Chemistry and Biochemistry
251 Nieuwland Science Hall, , Notre Dame, IN 46556

It has been shown that treatment of 1,10-phenanthroline with samarium diiodide followed by addition of various ketones provides 2-(1-hydroxyldialkyl)-1,10-phenanthrolines. These samarium-promoted reactions have now been expanded to include coupling with aldehydes and epoxides. The coupling with aldehydes cleanly provides monosubstituted phenanthroline derivatives, whereas the coupling with epoxides provides both the mono and disubstituted products depending on reaction conditions. These reactions can be used to generate a wide array of substituted phenanthrolines, which in-turn can be used as chiral ligands in metal-promoted reactions.

S_N2'-Aziridine Ring Opening Approach to the Solid-Phase Synthesis of an *E*-Alkene Peptide Isostere Library

Bryan H. Wakefield, Ruth L. Nunes and Peter Wipf
University of Pittsburgh, Department of Chemistry, Pittsburgh, PA 15260

Here we describe our attempts to construct a library of E-alkene peptide isosteres based on the L-685,458 γ-secretase inhibitor. This work illustrates the first application of our previously explored alkenyl aziridine ring opening approach, via S_N2' cuprate addition, in the preparation of a compound library. Also, this is the first use of a *t*-butylsulfonyl group as an aziridine activating group for this ring opening.

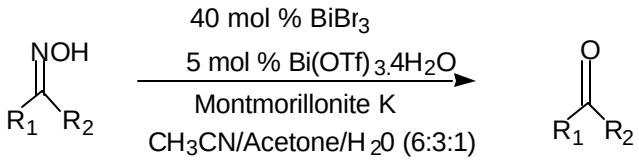


R^1 = α-Bn, β-Bn, α-*i*-Bu, β-*i*-Bu
R^2 = Me or H
R^3 = Me,Et or Phe

A FACILE METHOD FOR THE DEPROTECTION OF KETOXIMES USING BISMUTH BROMIDE-BISMUTH TRIFLATE

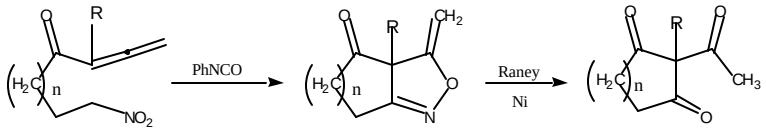
Joshua N. Arnold, Patrick D. Hayes, Robert L. Kohaus and Ram S. Mohan
Illinois Wesleyan University
Department of Chemistry, Bloomington, IL 61701

Ketones are obtained in good yields by treatment of oximes with 40 mol % $BiBr_3$ and 5 mol % $Bi(OTf)_3$ in CH_3CN/acetone/H_2O (6:3:1). Since oximes can be obtained from non-carbonyl compounds, this method also constitutes a useful synthesis of ketones. Advantages of this method include the use of relatively non-toxic and inexpensive bismuth salts as catalysts. The results of this study will be presented.



David G.J.Young, Dongmiao Zeng *Intramolecular Allene–Nitrile Oxide Cycloadditions*
University of Tennessee, Knoxville;
Department of Chemistry, Knoxville TN 37996

Intramolecular [3+2] cycloadditions involving allenes reacting with nitrile oxides were studied. An acyclic model study showed the preference of the reaction for reacting with the more remote pi bond of the allene. A cyclic model for Garsubellin A showed that the remote pi bond preference could be overturned in cases where bridgehead olefins were potential products. X-ray crystal structure of an advanced intermediate confirmed the assembly of the bridged bicyclononanone related to garsubellin.



19 **20** **21**

Metathetical Ring Closure of Organometallic Complexes

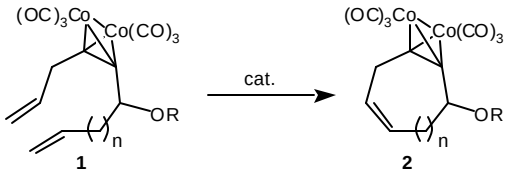
David G.J. Young,[1] Joseph A. Burlison;[1] Ulf Peters[2]

1. University of Tennessee, Knoxville;2. Cornell University

Department of Chemistry, Knoxville TN 37996

Department of Chemistry, Ithaca, NY 14853-1301

The ring closing metathesis of several dienes linked by a dicobalt hexacarbonyl complex was studied. The results showed that alcohols, esters, ketones and silyl ethers were compatible with ring closure using either Grubbs' or Schrock's catalysts in the presence of the organometallic building block. Products were subjected to transformations such as the Pauson-Khand reaction.



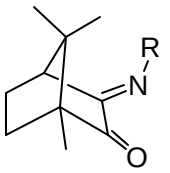
1 **2**

NEW REAGENTS FOR ENANTIOMERIC EXCESS DETERMINATION

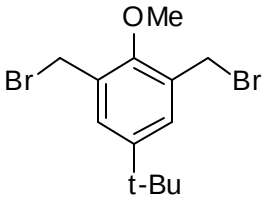
Brian E. Love, Robert A. Bills, Nicole Wilkerson, Darrell M. Campanella
Department of Chemistry, East Carolina University
Greenville, NC 27858

Several chiral primary amines have been condensed with optically active camphorquinone to yield monoimines (**1**). ^{13}C NMR spectra of (**1**) show baseline-resolved peaks for C-3 of the two diastereomeric products. The relative areas of these two peaks correspond well with the relative amounts of the two enantiomers in the starting amine.

BINOL has been allowed to react with dihalide (**2**) to produce (**3**). The methoxy peaks of diastereomeric forms of (**3**) are baseline-resolved in their ^{1}H NMR spectra. The relative areas of these two methoxy peaks can be correlated with the ee of the BINOL used in the reaction.



(1)



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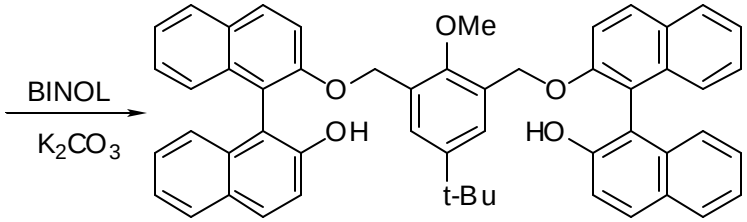
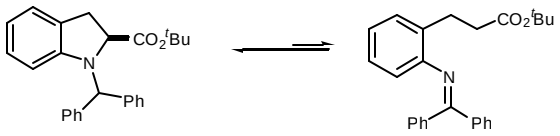


(3)

THE AZACYCLOPENTENYL CARBINYL RADICAL ISOMERIZATION (ACCRI): DISCOVERY, DEVELOPMENT AND POTENTIAL BIOLOGICAL IMPLICATIONS

Rajesh Viswanathan, Daniel Mutnick and Jeffrey N. Johnston
Indiana University,
Department of Chemistry, 800 E. Kirkwood Ave. Bloomington, IN 47405-7102

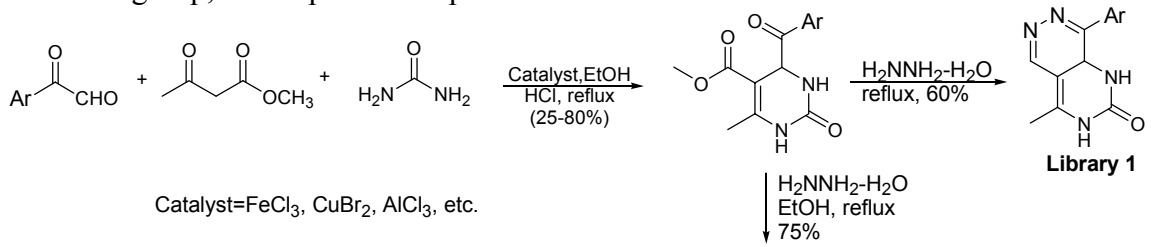


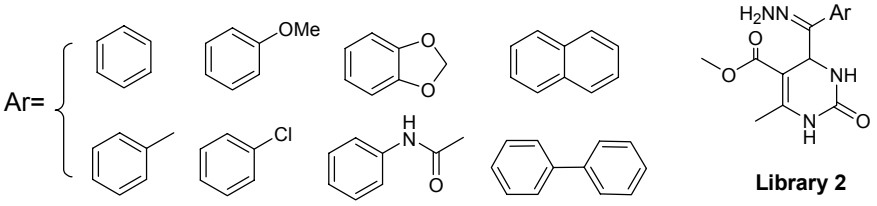
Discovery of a new α-amino acid epimerization will be described. Dependence on steric and electronic factors are studied using appropriate substituent modifications. Alternate mechanisms are considered and disproved through definitive experiments. Analogies are drawn between these isomerizations and those occurring in lysine 2,3-amino mutase. A provocative mechanism by which peptidal amino acids may be epimerized post-translationally is proposed based on these studies.

Generation of Two Ready to Screen Libraries via Biginelli Three Component Condensation with Novel Substrates

Qiang Yu, Liangfu Huang, Min Yang, Zhiqiang Fang, and Wuping Ma
SynChem, Inc., 1700 Mount Prospect Rd., Des Plaines, IL 60018

Previously, we have reported the first application of arylglyoxals as substrates in the Biginelli multi-component reactions (MCRs) with low to moderate yields. Extensive studies using various combinations of Lewis acids and solvents, led to significant improvements in the reaction yields and we have developed a scalable isolation procedure. The obtained dihydropyrimidine products thus possess an extra ketone functional group, which provides a potential site for further transformation.



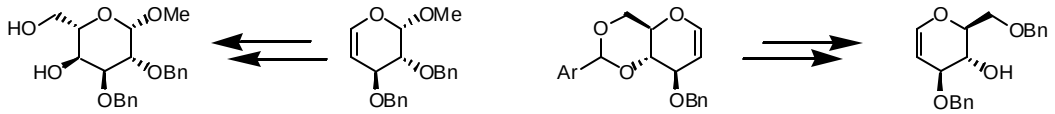


We have applied a combinatorial chemistry approach to exploit this extra ketone functionality to generate two sets of ready-to-screen libraries for anti-cancer and anti-AIDS purposes.

Access to L-Sugars and Mirror-Image Oligosaccharides from 4-Deoxypentenosides and L-Glycals

Fabien P. Boulineau, Alexander Wei
Purdue University, Department of Chemistry
560 Oval Drive, West Lafayette IN 47907-2084

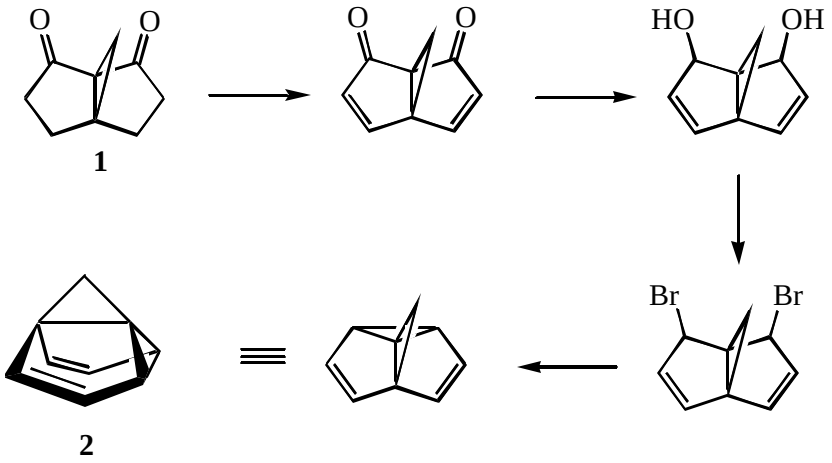
L-sugars are rare carbohydrates that are often present in biologically active compounds. Existing synthetic approaches typically involve acyclic intermediates that lead to diastereomeric mixtures upon cyclization of adducts. We have developed an efficient and general strategy for the stereocontrolled synthesis of L-pyranosides via novel cyclic enol ether intermediates (4-deoxypentenosides and L-glycals). Key steps involve oxidation/decarboxylative elimination of the C5 hydroxymethyl group, and stereoselective one-carbon homologation. A variety of 4-deoxypentenosides could be derived from several D-pyranosides and epoxidized with high facioselectivity in good to high yields. L-glycals could be synthesized from D-glucals in 35% overall yield in a readily scalable fashion. These unsaturated carbohydrate derivatives are being used in the construction of mirror-image (left-handed) oligosaccharides and other unnatural carbohydrate analogs, to demonstrate their potential in carbohydrate-based drug design.



RECENT PROGRESS IN THE SYNTHESIS OF 1,5-METHYLENESEMIBULLVALENE

Aaron W. Amick, Mitchell D. Somers, Derik K. Frantz, I. David Reingold
Juniata College
Department of Chemistry, Huntingdon, PA 16652

[3.3.1]Propellane-2,8-dione (**1**) can be made in five steps in moderate yield by undergraduates by a route previously reported. We have discovered appropriate conditions for the oxidation, reduction, and (we think) substitution steps outlined below. It remains to do these on large enough scale to attempt the ring closure to the semibullvalene under a variety of conditions. 1,5-Methylenesemibullvalene (**2**) is predicted to be a neutral bis(homo)aromatic compound, or, perhaps, a ground state triplet diradical.



1

2

THE NON-MAJORS ORGANIC COURSE: WHY DO WE DO WHAT WE DO TO THEM?

I. David Reingold
Juniata College
Department of Chemistry, Huntingdon, PA 16652

Most larger universities split the organic chemistry class into a section for chemistry majors and another for non-majors, mostly biologists and prehealth students. But despite the different career goals of the clientele, the non-majors' course usually covers almost entirely the same selection of material as the majors' course, including a great deal of chemistry that is of no use or interest to the students in the class. I propose here that the non-majors' course deliberately focus on its audience, and emphasize bioorganic chemistry while deemphasizing the more esoteric topics of interest only to chemists.

TIM: THE DISPERSED REU SITE

I. David Reingold,[1] Ronald Brisbois,[2] Nancy Mills,[3] Thomas Mitzel,[4] Kathleen Mondanaro,[5] K. C. Russell[6]

[1]Juniata College, [2]Macalester College, [3]Trinity University, [4]Trinity College, [5]Saint Michael's College, [6]Northern Kentucky University

Departments of Chemistry, [1]Huntingdon, PA 16652, [2]St. Paul, MN, [3]San Antonio, TX, [4]Hartford, CT, [5]Colchester, VT, [6]Highland Heights, KY

Eighteen members of the TIM Consortium have come to this conference as part of an experimental Research Experiences for Undergraduates (REU) Site funded by the NSF. The unique features of this site are

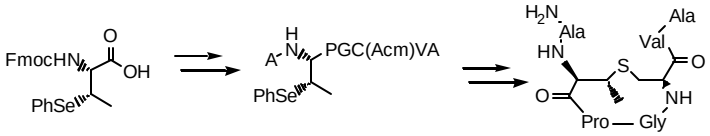
- Commonality of research interests among the participants
- Location at six different institutions
- Two to three group meetings a summer
- Attendance at this conference (odd years) or Reaction Mechanisms Conference (even)
- Participation of major researcher in meetings

This poster will describe the details of the consortium and introduce the readers to our chemistry.

BIOMIMETIC STEREOSELECTIVE FORMATION OF METHYLLANTHIONINE

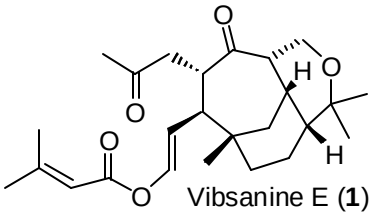
Hao Zhou and Wilfred A. van der Donk
Department of Chemistry, University of Illinois at Urbana-Champaign,
600 South Mathews Avenue, Urbana, IL 61801

Fmoc-(2R,3S)-3-methyl-Se-phenylselenocysteine was used for the synthesis of dehydrobutyrine (Dhb)-containing peptides. Biomimetic cyclization via Michael addition of Cys to a Dhb yielded the B-ring of the lantibiotic subtilin as a single diastereomer. The methyllanthionine product was shown to have the natural configuration by preparation of the authentic stereoisomer. The formation of a single isomer suggests that the prepeptide has a strong intrinsic preference for the stereochemistry observed in lantibiotics.



STUDIES TOWARDS THE TOTAL SYNTHESIS OF VIBSANINE E (1)

Øystein Loe and Huw M. L. Davies
University at Buffalo, The State University of New York
Department of Chemistry, Buffalo, NY 14260-3000



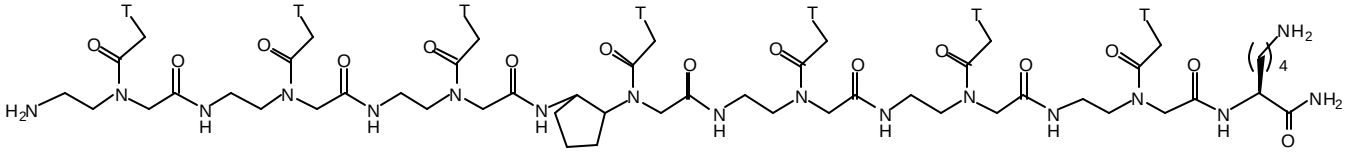
Vibsanine E (**1**)

Vibsanine E (**1**) is a diterpene of the Vibsanine class and is a potential drug for the treatment of Alzheimer's disease. Key reactions in the progress towards **1** involve a formal [3+4] cycloaddition to furnish the seven-membered ring of the target molecule. The [3+4] cycloaddition is a rhodium-carbenoid induced cyclopropanation of an alkene and the resulting divinyl cyclopropane undergoes a Cope-rearrangement to furnish the seven-membered ring. Manipulation of this molecule sets the stage for a Lewis acid catalyzed heteronuclear Diels-Alder reaction to furnish the tricyclic system. This product is made suitable for a UV-assisted [4+2] cycloaddition, which sets up the desired stereochemistry of the two side-chains of the target molecule.

Synthesis and Binding Properties of Cyclopentane -Constrained Peptide Nucleic Acids.

Daniel H. Appella *, Nataliya V. Larionova, Michael C. Myers, Mark A. Witschi
Department of Chemistry, Northwestern University, Evanston, Illinois 60208

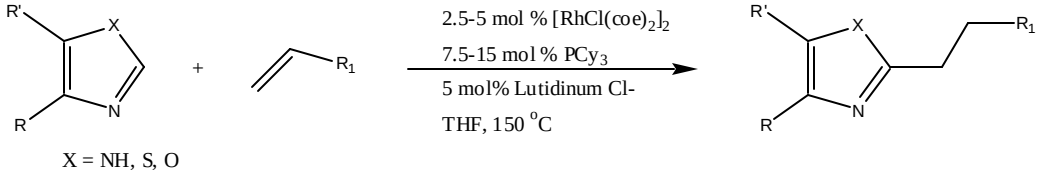
The polyamide backbone of Peptide Nucleic Acids (PNAs) is a good structural mimic of the ribose-phosphate backbone of nucleic acids. Therefore, PNA has attracted wide attention for development of antisense and antigene drugs, and in gene diagnostics.
PNAs are achiral nucleic acid mimics with backbones consisting of partly flexible aminoethyl glycine units. Incorporating the aminoethyl portion of the backbone into a cyclopentane ring conformationally constrains the PNA backbone. Cyclopentane modified PNA forms hybrid complexes with complementary DNA or RNA. The binding affinity of a modified PNA heptamer containing (*S*,*S*)-cyclopentyl residues was compared to PNA containing aminoethyl glycine residues. Incorporation of cyclopentyl residues results in a significant increase in thermal stability of PNA-DNA (or RNA) complexes. Incorporation of only one cyclopentyl residue in the middle of PNA increases the melting temperature of PNA-DNA complex by 10 ºC. Thermal stabilities and molecular modeling indicate that the structure constrained by the cyclopentyl group is well suited for DNA hybridization. In addition, Circular Dichroism data were obtained to determine the effects of cyclopentane modification on the structure of PNA-DNA (or RNA) complexes.



Intra- and Intermolecular Coupling of Alkenes to Heterocycles Via C-H bond Activation

Kian L. Tan, Robert G. Bergman, Jonathan A. Ellman
University of California-Berkeley
Department of Chemistry, Berkeley, CA 94720

Metal catalyzed C-H activation has recently been applied as a method for the formation of carbon-carbon bonds. We have developed an intramolecular cyclization that couples a vinyl carbon of a tethered alkene to a benzimidazole ring via a novel and selective C-H bond activation. This reaction was successful with a wide range of substrates, allowing for the synthesis of a variety of annulated heterocycles in good yield. Subsequent to this work, we extended the scope of the reaction to include an intermolecular variant. A wide range of heterocycles was employed in the reaction, and a variety of functional groups can be incorporated on the alkene coupling partner, including ester, nitriles, and acetals. Investigation into the mechanism of the intramolecular reaction revealed that the active catalyst was a *N*-heterocyclic carbene Rh (I) complex. This is a rare example in which an *N*-heterocyclic carbene is not acting as an ancillary ligand, but rather as an intermediate in a catalytic cycle.

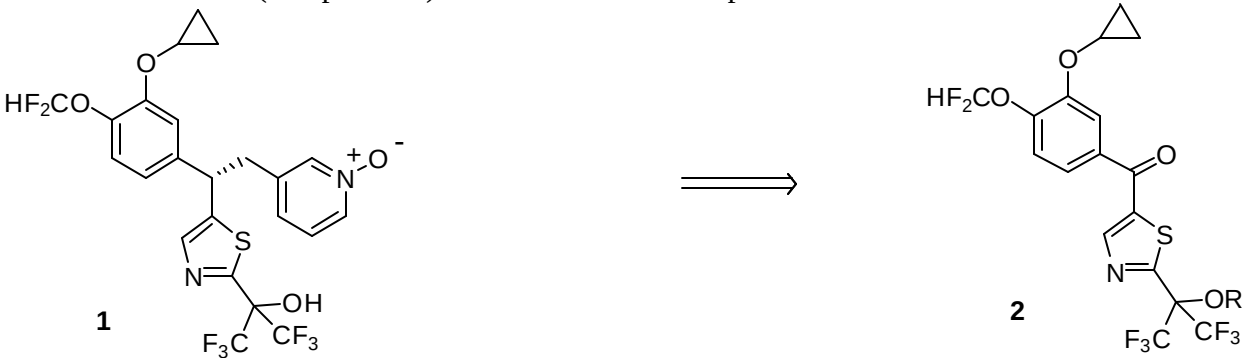


Catalytic Asymmetric Synthesis of a Potent PDE IV Inhibitor

Cheng-yi Chen*, Robbie Chen, Philippe Dagneau†, Lisa Frey, Karen Marcantonio, Paul O'Shea†, Amelie Roy†, Lushi Tan, Debera Wallace, Dalian Zhao, Rich Tillyer, Edward. J. J. Grabowski, and Ulf Do lling

Department of Process Research, Merck Research Laboratories, P.O. Box 2000, Rahway N. J. 07065, USA
†Department of Process Research, *Merck Frosst Centre for Therapeutic Research, P.O. Box 1005, Pointe Claire-Dorval, Québec, H9R 4P8, Canada*

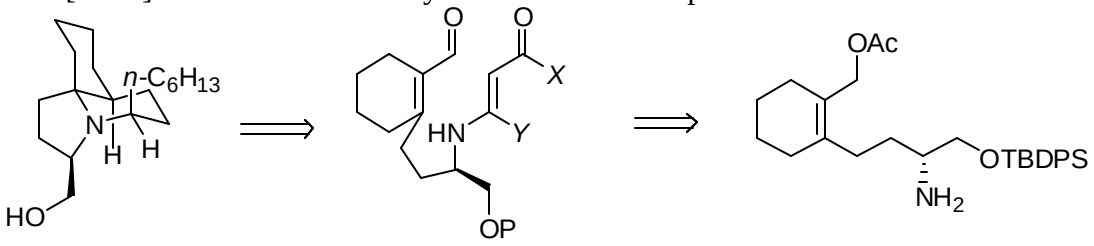
A practical, catalytic, asymmetric synthesis for the large scale preparation of a PDE-IV inhibitor (compound **1**) from ketone **2** will be presented.



Enantioselective Total Synthesis of the Putative Structure of Lepadiformine

Jiashi Wang, Richard Hsung, Heather Coverdale, Jia Liu
207 Pleasant St. S.E. , Department of Chemistry
University of Minnesota, Minneapolis, MN 55455

A enantioselective total synthesis of the putative structure of lepadiformine through a formal [3 + 3] intramolecular aza-cycloaddition will be presented.



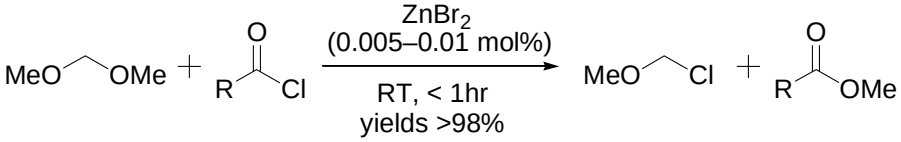
Putative Structure of Lepadiformine

***X*= OMe or Me**
***Y*= *n*-C_6H_{13} or H**

A SIMPLE, RAPID PROCEDURE FOR THE SYNTHESIS OF CHLOROMETHYL METHYL ETHER (MOMCl) AND OTHER CHLORO ALKYL ETHERS

Katherine Belecki and Martin A. Berliner
Chemical Research and Development
Pfizer Global Research and Development
Groton, CT 06340

Chloromethyl methyl ether (MOMCl) and other chloro alkyl ethers can be prepared rapidly and in >95% yield by the $ZnBr_2$-catalyzed exchange reaction between acetals and acid halides. Reactions are typically complete in less than one hour using ≤0.005 mol% catalyst on small (mmol) and large (>1 mol) scale. The solutions of chloro alkyl ethers thus obtained can be utilized without isolation in base-mediated reactions where the presence of the ester by-product does not interfere, including alkylations of alcohols, phenols, thiols and enolates. Since this procedure is conducted in one pot and the excess reagent is decomposed on workup, exposure issues arising from the handling of these potentially carcinogenic reagents can be avoided.



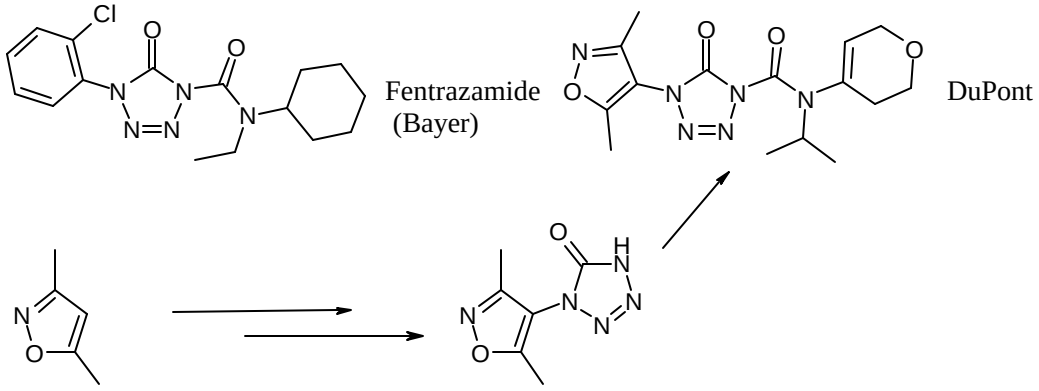
Synthesis and Herbicidal Evaluation of Isoxazolyltetrazolinones

Jill D. Coleman, Christina M. Dubas-Cordery, T.G. Murali Dhar, Donna L. Piotrowski, Hyeong B. Kim and Morris P. Rorer

DuPont Crop Protection

Stine Haskell Research Center, Newark, DE. 19714

Carbamoyltetrazolinones such as Bayer's Fentrazamide are effective rice herbicides. At DuPont, we have investigated novel isoxazolyltetrazolinones. Several synthetic routes have been developed to make the 3,5-disubstituted isoxazolyl groups. We have also developed a novel route for introducing the carbamoyl moiety in a regiochemically-controlled manner using 4-methoxytetrazolinones. Many of the isoxazolyltetrazolinones are highly active herbicides with especially good activity on grasses.



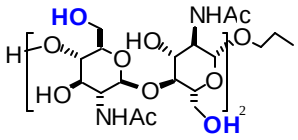
Synthesis of Chitin-Like Tetrasaccharide and Its Tetra-O-Methyl Derivative

Siong-Tern Liew, Alexander Wei

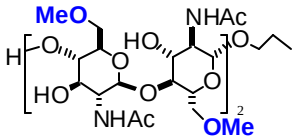
Purdue University

Department of Chemistry, 560 Oval Drive, West Lafayette, IN 47907-2084

Chitin is known to crystallize in two polymorphic forms, α and β. The α polymorph is widely believed to be stabilized by inter-sheet O6-O6 hydrogen bondings, but this has never been fully confirmed. By capping the C6 hydroxyls as methyl ethers and removing their hydrogen bonding potential, we should be able to determine whether such side-chain interactions can influence chitin polymorphism. Here we describe a concise synthesis of two tetrasaccharide derivatives from commercially available D-glucosamine hydrochloride. In the course of this synthesis, we have identified an anomalous deactivating effect of a remote thiophenyl group on glycoside coupling.



Control tetrasaccharide



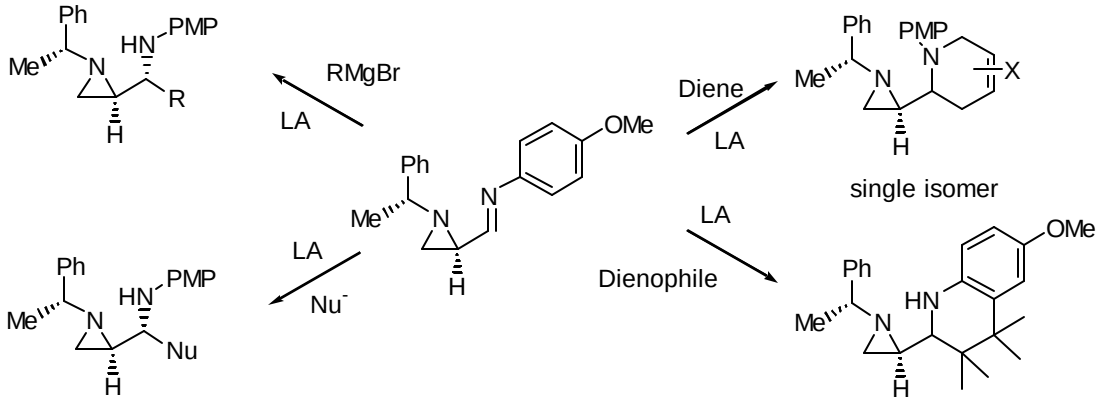
capped tetrasaccharide

Chiral Aziridine-2-carboxaldimine as A Versatile Substrate: Asymmetric Synthesis of Various Nitrogen Containing Heterocycles

Man-Jin Suh[1], Heui-Yoon Noh[1], Hyun-Joon Ha[1], and Won Koo Lee[2]

[1]Department of Chemistry, Hankuk University of Foreign Studies, Yongin, 449-791, Korea, [2]Department of Chemistry, Sogang University, Seoul 121-742, Korea,

Readily available enantiomerically pure Aziridine-2-carboxaldimine was served as a versatile substrate for nucleophilic additions and aza-Diels-Alder reactions to provide various nitrogen containing compounds. The absolute configuration of the new stereogenic center was determined after regioselective ring opening followed by cyclic urea formation.



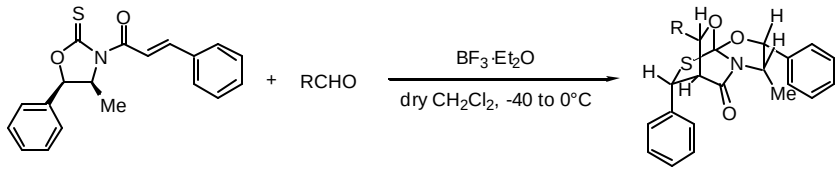
Asymmetric Tandem Michael-Aldol Reaction Triggered by Intramolecular Michael Addition of Thiones to Enones

Hironori Kinoshita, Sayaka Kinoshita, Takashi Osamura, Tadashi Kataoka

Gifu Pharmaceutical University

6-1 Mitahora-higashi 5-chome, Gifu 502-8585, Japan

Recently, we reported a new reaction, namely chalcogeno-Morita-Baylis-Hillman reaction, involving the intramolecular Michael addition of a chalcogenide group to an enone or ynone moiety in the presence of $BF_3 \cdot Et_2O$. On the other hand, thioureas and chalcogenopyran-4-thiones were useful for the tandem Michael-aldol reaction. If optically active alkenes having thioketone are used for the tandem Michael-aldol reaction, formation of products with multi chiral centers can be anticipated. Therefore, we examined reactions of *N*-enonyl-thiazolidine- or oxazolidine-2-thiones with aldehydes.



1 **2** (59-93%)

STUDIES TOWARD THE DEVELOPMENT OF A GENERAL MECHANISM FOR LUMINESCENT REPORTING IN CHEMOSENSORS FOR ORGANIC SPECIES

Diana L Nersesian, Alan W Schwabacher
University at Milwaukee, The State University of Wisconsin
Department of Chemistry, 3210 N. Cramer, Milwaukee, WI. 53211,
awschwab@uwm.edu

Lanthanide complexes show intense phosphorescence that is quenched efficiently by water directly ligated to the metal. Metal complexation has been shown to be an effective mechanism for induction of an ordered conformation of a suitably designed organic species, compatible with binding of organic guests into the so formed binding site. Metal serves in a structural and a functional role: guest ligation to metal enhances binding. If an appropriate lanthanide-ligand complex were used to organize a binding site, binding could be signaled by a change in luminescence. Solution and solid phase spectrometric studies will be described, validating the general scheme.

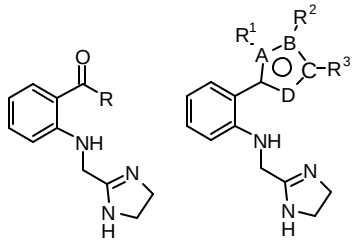
2-(Anilinomethyl)imidazolines as Alpha1 Adrenergic Receptor Agonists: In Vitro SAR of the 2' Position

Jason D. Speake, Michael J. Bishop, Frank Navas, Deanna T. Garrison, Eric C. Bigham, Stephen J. Hodson, David L. Saussy, Jim A. Liacos, Paul E. Irving, and Doug Minick

GlaxoSmithKline Research and Development

Five Moore Drive, PO Box 13398, Research Triangle Park, NC 27709-3398

The structure-activity relationship of 2'-ester and amide, as well as pyrrole, pyrazole and triazole, substituted 2-(anilinomethyl)imidazolines as α_1 adrenergic agonists was investigated. The size and orientation of substituents, as well as the position of the heteroatoms were found to have a profound effect on the potency and selectivity of the molecules. Potent α_{1A} subtype selective agonists have been identified.

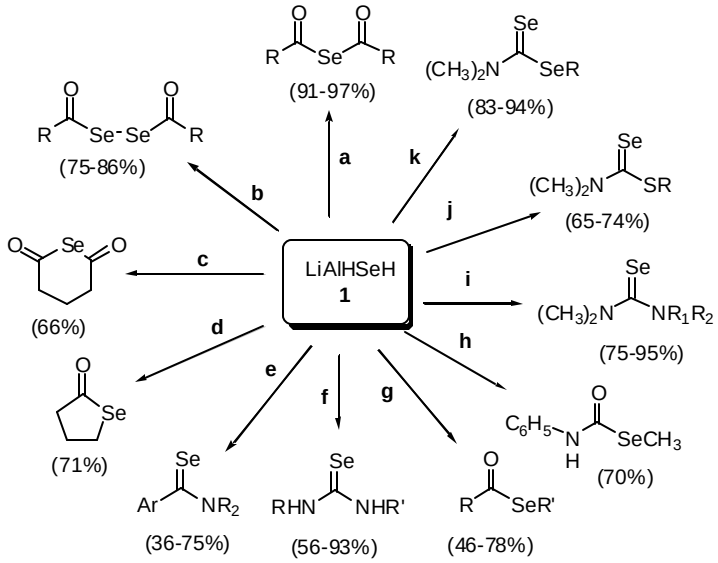


New Synthetic Methods of Selenium- and Sulfur-Containing Compounds Using Novel Selenium and Sulfur Transfer Reagents

Mamoru Koketsu, Hideharu Ishihara

Department of Chemistry, Faculty of Engineering, Gifu University, Gifu, 501-1193 JAPAN

Recently, we developed a novel selenium transfer reagent,[1] LiAlHSeH **1** which is generated by the stirring of selenium powder with $LiAlH_4$ in THF. This reagent is useful for preparing a variety of different selenium containing compounds (Figure). Also we confirmed that LiAlHSH **2** behaves similarly to LiAlHSeH, and represents an excellent reagent for the introduction of sulfur. Here we report new synthetic methods of various selnium- and sulfur-containing compounds using novel selenium and sulfur transfer reagents.

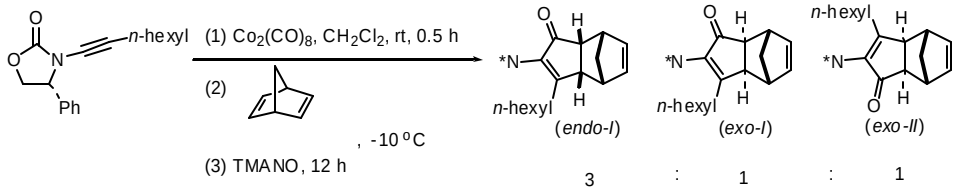


[1] H. Ishihara, M. Koketsu, Y. Fukuta and F. Nada, *J. Am. Chem. Soc.*, **123**, 8408-8409 (2001).

Diastereoselective Pauson-Khand Reactions of Ynamides

Lichum Shen, Richard Hsung
University of Minnesota, Department of Chemistry, Minneapolis, MN 55455

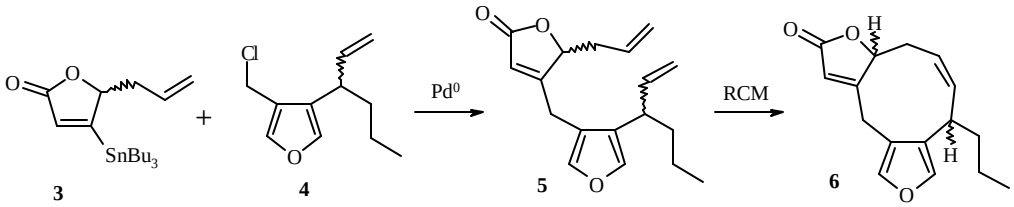
Pauson-Khand reactions of ynamides with norbornadiene gave highly regioselective and diastereoselective products.



SYNTHESIS OF THE CARBOCYCLIC CORE OF THE CORNEXISTINS USING RING-CLOSING METATHESIS

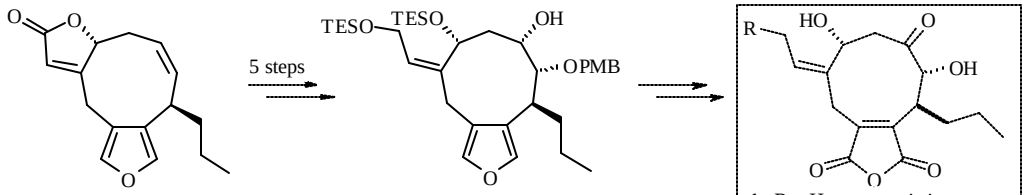
Frederic J. Marlin, J. Stephen Clark
Nottingham University
School of Chemistry, Nottingham NG7 2RD, England

The 9-membered carbocyclic core (**6**) of phytotoxic natural products cornexistin (**1**) and hydroxycornextin (**2**) has been constructed using the novel sequence palladium-mediated sp^2-sp^3 fragment coupling and ring-closing diene metathesis.[1]



3 **4** **5** **6**

The desired diastereoisomer **6a** has been successfully elaborated to give the alcohol **7** in 5 steps. Oxidation of both the free hydroxyl group and the furan ring, followed by removal of the protecting groups should then deliver (±)-hydroxycornexistin.



6a **7**

(1) Clark, J.S.; Marlin, F.; Nay, B.; Wilson, C. *Org. Lett*. **2003**, *5*, 89.

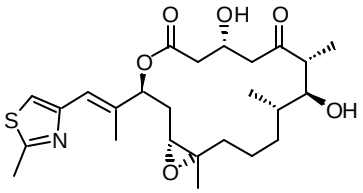
Total Synthesis and Precursor-Directed Biosynthesis of Epothilone Analogues

Annette Vitale Brown*, *Sreenivasulu Bandaru, Florence Morel, and Richard E. Taylor.*

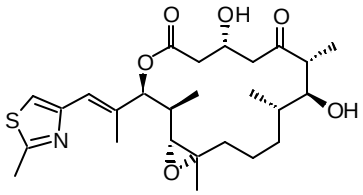
University of Notre Dame

Department of Chemistry and Biochemistry, Notre Dame, IN 46556

The epothilones are a novel class of anti-cancer natural products which are of much synthetic and clinical interest. Our program has exploited NMR and computer-based conformational studies to design analogues which probe the conformational requirements of tubulin binding. Recent results have provided novel leads with cytotoxicity equipotent to the natural product. Currently, we are exploring new synthetic and biosynthetic methods for the production of the novel epothilone analogues. Results along both routes will be presented.



Epothilone B



C14-Me Epothilone B

SYNTHESIS OF NOVEL INDOLYL-ISOQUINOLINYL/QUINOLINYL-PYRROLE-2, 5 DIONES AND CORRESPONDING CARBAZOLE ANALOGS PROVIDE POTENT AND SELECTIVE KINASE INHIBITORS

Scott E. Conner, Guoxin Zhu, Xun Zho, Chuan Shih, Timothy Burkholder, Harold B. Brooks, Charles D. Spencer, Scott A. Watkins, Eileen Considine, Jack A. Dempsey, Cathy Ogg, Bharvin Patel, Richard M. Schultz, Karen L. Huss, Ron Kaplan, Shehnaz Khan, Bryan D. Anderson, and Robert M. Campbell.
Lilly Research Laboratories, A Division of Eli Lilly & Company
Lilly Corporate Center, Indianapolis, Indiana 46285, USA

The synthetic pathway and subsequent biological activity of a series of indolyl-isoquinolinyl/quinolinyl-pyrrole-2, 5 diones and the corresponding carbazole analogs are described. The initial design template for these compounds originated from observations of X-ray co-crystal structure of the human CDK2(cyclin dependent kinase) and the natural product staurosporin. Key hydrogen bonding interactions between both the carbonyl group and acidic proton of the maleimide functional group were seen in the ATP binding pocket of CDK2. Since the ATP binding sites are thought to be highly conserved among the family of serine-threonine protein kinases, the maleimide portion of the molecule was kept constant in the design. Novel maleimides containing quinoline and isoquinoline moieties were explored in an effort to probe secondary binding sites within this family of kinases, and thus provide some selectivity among them.

38th National Organic Symposium
Poster Abstracts
Session D

Schedule of Presenters – Poster Session D **Wednesday June 11, 9 pm – 12 am**

D1 CATALYTIC ENANTIOSELECTIVE DIBORATION OF ALKENES: ACCESS TO VERSATILE REACTIVE CHEMICAL INTERMEDIATES
Jeremy B. Morgan, Steven P. Miller, and James P. Morken
The University of North Carolina at Chapel Hill
Department of Chemistry, Chapel Hill, NC 27599-3290

D2 HAMMETT STUDIES OF ENANTIOCONTROL BY PHOX LIGANDS IN Pd-CATALYZED ALLYLIC SUBSTITUTION REACTIONS
Paul B. Armstrong, Ryan N. Constantine, Naomi Kim and Richard C. Bunt
Middlebury College
Department of Chemistry & Biochemistry, Middlebury, VT 05753.

D3 PROGRESS TOWARD THE TOTAL SYNTHESIS OF THE PHOMOIDRIDES
John L. Wood, Ivar M. McDonald, David A. Spiegel, Nobuaki Taniguchi, Jon Njardarson, and Munenori Inoue
Yale University, Department of Chemistry
New Haven, CT 06520-8107

D4 PACKING REACTIVITY INTO THE NITROALDOL: HENRY CONSTRUCTION OF MULTIFUNCTIONAL INTERMEDIATES FOR ANNULATION REACTIONS
Frederick A. Luzzio and Joel P. Ott
University of Louisville
Department of Chemistry, Louisville, KY 40292

D5 THE THIOPYRAN ROUTE TO POLYPROPIONATES. DESYMMETRIZATION OF *MESO* HEXAPROPIONATE SYNTHONS BY ENANTIOSELECTIVE ENOLIZATION
Dale E. Ward, H. Martin Gillis, and K. Saravanan
University of Saskatchewan, Department of Chemistry
110 Science Place, Saskatoon SK S7N 5C9, CANADA

D6 REMARKABLE BISMUTH NITRATE-CATALYZED PROTECTION OF CARBONYL COMPOUNDS: DIASTEREOSELECTIVE SYNTHESIS
Bimal K. Banik
The University of Texas, M. D. Anderson Cancer Center, Department of Molecular Pathology,
1515 Holcombe Blvd., Box # 89, Houston, TX 77030;

D7 MOLECULAR IODINE-CATALYZED HIGHLY EFFICIENT MICHAEL REACTION OF INDOLES: A REMARKABLE MILD AND SOLVENT-FREE CONDITION
Bimal K. Banik
The University of Texas, M. D. Anderson Cancer Center, Department of Molecular Pathology,
1515 Holcombe Blvd., Box # 89, Houston, TX 77030;

D8 DOUBLE DIASTEREO-DIFFERENTIATION IN LEWIS BASE CATALYZED ALDOL ADDITIONS
Shinji Fujimori and Scott E. Denmark*
Roger Adams Laboratory, Department of Chemistry, University of Illinois at Urbana-Champaign
Urbana, IL 61801

D9 INITIAL STUDIES OF TANDEM RADIAL CYCLIZATIONS INITIATED BY RADICAL CATIONS
Bradley A. Scates, Wenhua Chu, Michelle Monnens, Kevin D. Moeller
Department of Chemistry, Washington University, One Brooking Drive, St. Louis, MO 63130,

D10 DEUTERATED ALKYLRESORCINOLS FOR ANALYSIS OF WHOLE GRAIN PRODUCTS

Kirsti Parikka and Kristiina Wähälä
Laboratory of Organic Chemistry, Department of Chemistry, P.O. Box 55
FIN-00014-University of Helsinki, Finland.

D11 SUPRAMOLECULAR HOST-GUEST STRATEGY TO CONJUGATED LINEAR POLYMERS

Sean M. Curtis, Joseph W. Lauher, Frank W. Fowler
State University of New York, Stony Brook
Department of Chemistry
Stony Brook, NY 11794-3400

D12 BICYCLO[2.2.2]OCTANES AND AMPHIPATHIC BENZENES AS ESTROGEN RECEPTOR COACTIVATOR BINDING INHIBITORS

Margaret L. Collins, Alice L. Rodriguez, John A. Katzenellenbogen
University of Illinois at Urbana -Champaign
Department of Chemistry, Urbana, IL 61801

D13 THE SYNTHESIS OF INDOLE ESTROGENS TO PROBE NON-GENOMIC ACTIONS OF THE ESTROGEN RECEPTOR

Bridget G. Trogden, Sung Hoon Kim, John A. Katzenellenbogen
University of Illinois at Urbana -Champaign
Department of Chemistry, Urbana, Illinois 61801

D14 CD INVESTIGATION OF DESS-MARTIN PERIODINANE OXIDATION

Nicole Reed, Robert Rapp, Christian Hamann, and Pamela Artz
Albright College
Department of Chemistry and Biochemistry, Reading, PA 19604

D15 COPPER CATALYZED AMINATION OF ARYL HALIDES AND SELECTIVE AMINATION OF ARYL DIHALIDES AND DIAMINES WITH 2-*N,N*-DIMETHYLAMINOETHANOL AS SOLVENT

Zhikuan Lu, Robert J. Twieg, Songping D. Huang
Department of Chemistry, Kent State University, Kent, OH 44242-0001

D16 a,?-CYCLOPEPTIDES CAPABLE OF FORMING PEPTIDIC NANOTUBES: THE STRUCTURAL AND THERMODINAMIC BASIS

Manuel Amorín, Roberto J. Brea, Luis Castedo, Juan R. Granja
Departamento de Química Orgánica e Unidade Asociada ó C.S.I.C, Facultade de Química, Universidade de Santiago, 15782 Santiago de Compostela, SPAIN

D17 DESIGN AND SYNTHESIS OF NOVEL GADOLINIUM LIPIDS FOR IMAGING LIPOSOME DELIVERY

Morag Oliver,[1] Michael R. Jorgensen,[2] Po-Wah So,[3] Jimmy Bell,[3] Andrew Miller[1]
Imperial College London
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D18 REMARKABLY MILD CARBONYL-ENE REACTION USING *N,N*-DIALLYLAMINOARYLKETONES

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D19 SYNTHESIS AND CYCLOAROMATIZATION OF A CYCLIC ENYNE-ALLENE PRODRUG

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D20 TOTAL SYNTHESIS OF (-)-*E*-15,16-DIHYDROMINQUARTYNOIC ACID

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D21 5-DEHYDRO-1,3-QUINODIMETHANE: AN ORGANIC MOLECULE WITH AN OPENSHELL DOUBLET GROUND STATE

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D22 THE SYNTHESIS OF POTENTIAL NEW ß-LACTAM ANALOGUES (ISOXAZOLIDINE-3,5-DICARBOXYLIC ACIDS) POSSESSING ANTIBACTERIAL ACTIVITY

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D23 PROCESS DEVELOPMENT OF 10098274: AN ADDENDUM FOR *EKTACOLOR* PAPER

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D24 REDUCTIVE CLEAVAGE OF THE EXOCYCLIC ESTER OF UK-2A

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D25 PROGRESS TOWARD THE TOTAL SYNTHESIS OF INGENOL

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D26 SYNTHESIS OF TRANSITION STATE ANALOGS AS INHIBITORS OF CYCLOPHILIN

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D27 AN EFFICIENT METHOD FOR THE CONVERSION OF AN ARYL PHENOL TO AN ARYL CYCLOPROPYL ETHER. THE FINAL STEPS IN THE SYNTHESIS OF A NK1 RECEPTOR ANTAGONIST.

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D28 NOVEL, ENDOSOMOLYTICALLY-ACTIVE, SUGAR-BASED LIPIDS FOR NON-VIRAL GENE THERAPY

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D29 STUDIES TOWARD THE TOTAL SYNTHESIS OF SCABRONINE A

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D30 DIASTEREOSELECTIVE RHODIUM-CATALYZED ALLYLIC ALKYLATION REACTIONS USING COPPER(I) ENOLATES

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D31 STEREOSPECIFIC RHODIUM-CATALYZED ALLYLIC ETHERIFICATION REACTIONS USING COPPER(I) ALKOXIDES

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D32 RHODIUM-CATALYZED CARBOCYCLIZATION REACTIONS

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D33 DIELS-ALDER SYNTHESIS - MINI SCALE EXPERIMENTS TO STUDY THE EFFICACY OF SOLVENT/CATALYST SYSTEMS AND THE REDUCTION OF HAZARDOUS WASTE

Anthony Masulaitis, Jeffrey Stewart, Taha Ahmad, Carina Neto, Arpit Patel, Kirtiben Solanki, and Treva Pamer
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D34 SYNTHESIS OF ANTI-AIDS DIARYLSULFONES

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D35 REVERSING THE POLARITY OF ENOLATE EQUIVALENTS: THE USE OF *N,O*-KETENE ACETALS IN INTRAMOLECULAR ANODIC OLEFIN COUPLING REACTIONS.

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D36 THE SYNTHESIS OF NOVEL NITRO AND AMINO COMBRETASTATIN A-4 ANALOGS

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D37 THE CONVERSION OF AZIDES TO DIAZONIUM IONS UNDER NEUTRAL CONDITIONS

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D38 PHYTOALEXINS FROM WILD AND CULTIVATED CRUCIFERS: ISOLATION, STRUCTURE DETERMINATION, SYNTHESIS, AND BIOSYNTHESIS

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D39 STUDIES TOWARD THE TOTAL SYNTHESIS OF ASPIDOSPERMIDINE

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D40 FREE RADICAL-MEDIATED VINYL AMINATION

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D41 NEW INSIGHTS INTO IMINIUM CATALYSIS: ENANTIOSELECTIVE ORGANOCATALYTIC [1,3]–DIPOLAR CYCLOADDITION AND *EXO* SELECTIVE CYCLOADDITION REACTIONS

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D42 REACTIVITY OF (BICYCLO[5.1.0]OCTADIENYL)$Fe(CO)_2L$ CATIONS: PREPARATION OF A CONFORMATIONALLY RESTRICTED GLUTAMATE ANALOG

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D43 INVESTIGATIONS INTO THE SCOPE AND ORIGINS OF DIASTEREOSELECTIVITY IN SPIROCYCLE-FORMING INTRAMOLECULAR HECK REACTIONS.

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D44 CHEMOSELECTIVE CONJUGATE REDUCTION OF a,ß-UNSATURATED CARBONYL COMPOUNDS WITH POLYMETHYLHYDROSILOXANE

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D45 2,6-BIS-HYDRAZINOPYRIDINE AS A REACTANT IN FORMING BISPYRAZOLEPYRIDINE LIGANDS

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D46 EPIQUINAMIDE: A NOVEL NICOTINIC AGONIST FROM AN ECUADORIAN FROG, *EPIPEDOBATES TRICOLOR.*

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D47 TELLURIUM-TRIGGERED REACTIONS OF CYCLOPROPANEMETHANOL DERIVATIVES AND HALOACETATE ESTERS OF GLYCIDOLS

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D48 A COPPER-CATALYZED AMIDATION OF HALOALKYNES AND SUBSEQUENT SAUCY-MARBET REARRANGEMENT TOWARDS THE SYNTHESIS OF CHIRAL ALLENES

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D49 *DE NOVO* DESIGN OF AN ANTIPARALLEL HOMODIMERIC COILED COIL

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D50 Pd-CATALYZED HIGHLY STEREOSELECTIVE TANDEM ALKENYLATION-ALKYLATION OF 1,1-DIHALO-1-ALKENES TO GIVE CONJUGATE DIENES CONTAINING EITHER AN *E*- OR A *Z*- TRISUBSTITUTED ALKENE MOIETY

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D51 2,3-DIBROMO-1-(PHENYLSULFONYL)PROPENE (DBP) AS A VERSATILE REAGENT FOR THE PREPARATION OF 2,4-DISUBSTITUTED FURANS

Aaron VanZanten, Ryan Harrington, Adam Kiefer, David Carlson, Bill Andrews, Claude Ogoe and S. Shaun Murphree

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D52 TOWARD THE SYNTHESIS OF A C_3-SYMMETRIC TRIVALENT HIV-GP41 LIGAND

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D53 CASCADE SYNTHESIS OF FUNCTIONALIZED AMINO CYCLOPROPANES

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D54 MILD COPPER-FREE SONOGASHIRA COUPLING OF ARYL BROMIDES

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D55 SYNTHESIS OF A NEW 5-IA PRECURSOR USING TRIMETHYLSILYL IODIDE AS BENZYLOXYCARBONYL DEBLOCKING AGENT

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D56 REGIOSPECIFIC SYNTHESIS OF D3 AND D6 *RRR*-gamma-TOCOPHEROL FOR *IN VIVO* STUDIES OF TOCOPHEROL METABOLISM

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D57 AN EFFICIENT SYNTHESIS OF A DOXORUBICIN-PEPTIDE CONJUGATE AND THE EFFECT OF MIXING ADDITIVES ON EDC-MEDIATED AMIDE FORMATION

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D58 APPLICATION OF FLUOROUS MIXTURE SYNTHESIS FOR ACCESSING NATURAL PRODUCTS AND THEIR STEREOISOMERS – TOTAL SYNTHESIS OF SIXTEEN STEREOISOMERS OF SEX PHEROMONE OF PINE SAWFLY.

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D59 DESIGN AND SYNTHESIS OF NEW THIAZOLE-CONTAINING, GABA SELECTIVE IONOPHORE

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D60 AN AZOPHENOL BASED-CHROMOGENIC PYROPHOSPHATE SENSOR IN WATER

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D61 SYNTHESIS AND DIFFUSION MEASUREMENTS OF FLEXIBLE TETRAETHER ACYCLIC BISPHOSPHOCHOLINES.

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D62 A ONE-POT DIASTEREOSELECTIVE SYNTHESIS OF *CIS*-3-HEXENES-1,6-DIOLS VIA AN UNUSUALLY REACTIVE ORGANOZINC INTERMEDIATE

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D63 STRUCTURAL EFFECTS IN REACTIONS OF DIAZO-CARBONYL COMPOUNDS WITH ALDEHYDES

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D64 STUDIES TOWARD THE SYNTHESIS OF AZADIRACHTIN: SUCCESSFUL FORMATION OF THE CROWDED C8-C14 BOND USING RADICAL AND ORGANOMETALLIC CHEMISTRY

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D65 PROGRESS TOWARD THE TOTAL SYNTHESIS OF GARSUBELLIN A AND RELATED PHLOROGLUCINS

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D66 UTILIZATION OF THE [2,3] STILL-WITTIG REARRANGEMENT TO TRANSFORM 2- TO 2,3- SUBSTITUTED FURAN DERIVATIVES

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D67 REGIOCONTROLLED SULFENYLATION OF METALLATED INDOLES WITH METHYL METHANETHIOSULFONATE

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D68 CRYSTALLIZATION-INDUCED ASYMMETRIC TRANSFORMATION OF AMINOAZEPINONES

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D69 A HIGHLY CONVERGENT SYNTHESIS FOR HYDROXAMATE-DERIVED SIDEROPHORES

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D70 PHENYL THIAZOLYL UREA AND CARBAMATE DERIVATIVES AS NEW INHIBITORS OF BACTERIAL CELL WALL BIOSYNTHESIS

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D71 DESIGN AND SYNTHESIS OF NOVEL, SUBTYPE-SELECTIVE SPHINGOSINE-1-PHOSPHATE RECEPTOR AGONISTS AND ANTAGONISTS

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D72 NOVEL OXIDATIVE PATHWAYS UTILIZING OSMIUM TETROXIDE AND OXONE

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D73 SYNTHESIS OF 5-CYANOIMINO-IMIDAZOLE-4-CARBOXAMIDE AND THEIR CYCLIZATION TO PURINES

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D74 SYNTHESIS OF NEW CHIRAL ALIPHATIC AMINO DISELENIDES AND THEIR APPLICATION AS CATALYSTS IN THE ENANTIOSELECTIVE ADDITION OF DIETHYLZINC TO ALDEHYDES

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D75 FACILE SINGLE-POT PREPARATION OF TERTIARY AMINES USING NOVEL TITANIUM (IV) ISOPROPOXIDE AND SODIUM BOROHYDRIDE REAGENT SYSTEM

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D76 THE STUDY TOWARD AN ENENTIOSELECTIVE TOTAL SYNTHESIS OF (+)-CYLINDRICINE C VIA TANDEM MANNICH CONDENSATION STRATEGY

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D77 SYNTHESIS OF AlQ_3 DERIVATIVES WITH EXTENDED TUNABLE CHROMOPHORES

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D78 NOVEL STEREOSELECTIVE SYNTHESIS OF 1-(ß-D- AND a-L-GLYCOPYRANOSYL)-5-METHYL-1H-1,2,4-TRIAZOLES

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D79 H3 ANTAGONIST—PROCESS RESEARCH FOR THE SYNTHESIS OF A-304121

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D80 ENANTIOSELECTIVE TOTAL SYNTHYSES OF PHOMOPSOLIDE A-E

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D81 RING ENLARGEMENT OF SULFUR-CONTAINING MACROCYCLES VIA RHODIUM-CATALYZED STEVENS REARRANGEMENT

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D82 MECHANISTIC STUDY OF UNUSUAL DESILYLATION OF α-SILYLOXY ß-AMINO CARBOXYLIC ACID DERIVATIVES

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D83 COPPER AND PALLADIUM CATALYZED INTRAMOLECULAR ARYL GUANIDINYLATION: AN EFFICIENT METHOD FOR THE SYNTHESIS OF 2-AMINOBENZIMIDAZOLES

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D84 HIGH THROUGHPUT PROCESS OPTIMIZATION FOR THE FINE CHEMICAL AND PHARMACEUTICAL INDUSTRIES

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D85 CYCLOHEXADIENE-1-CARBOXAMIDES IN SYNTHESIS OF BIOLOGICALLY ACTIVE COMPOUNDS

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D86 DE NOVO SYNTHESIS OF GALACTO-PAPULACANDIN USING SHARPLESS CATALYTIC ASYMMETRIC DIHYDROXYLATION

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D87 SECOND CYCLE LIGANDS FOR OSMIUM CATALYZED OLEFIN DIHYDROXYLATION AND AMINOHYDROXYLATION

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D88 PALLADIUM CATALYZED OXIDATIVE KINETIC RESOLUTION OF SECONDARY BENZYLIC ALCOHOLS

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D89 DE NOVO SYNTHESIS OF DISACCHARIDES AND TRISACCHARIDES USING PALLADIUM CATALYZED GLYCOSIDATION

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D90 STUDIES DIRECTED TOWARD THE SYNTHESIS OF PRIMARY AMINES FROM KETONES AND ALDEHYDES VIA REDUCTIVE AMINATION

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CATALYTIC ENANTIOSELECTIVE DIBORATION OF ALKENES: ACCESS TO VERSATILE REACTIVE CHEMICAL INTERMEDIATES

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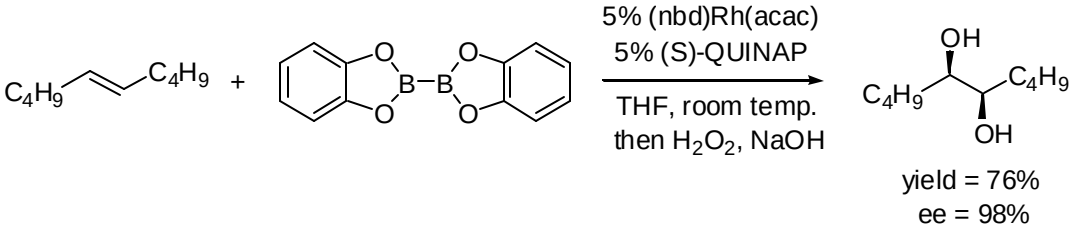
The ability to convert simple alkenes into valuable functionalized synthetic intermediates in a non-racemic fashion is important in organic chemistry. Recognizing the importance of this problem and that carbon-boron bonds allow for transformation into a number of functional groups, catalytic enantioselective diboration of unsaturated organic molecules has recently come under investigation in our laboratory. Based upon consideration of a putative reaction mechanism, a series of chiral group 9 complexes is employed in the diboration of unactivated alkenes. A catalyst system comprised of (nbd)Rh(acac) and (S)-QUINAP facilitates the addition of bis(catecholato)diboron to olefins of various substitution patterns, leading to the first example of a catalytic asymmetric diboration. Oxidation of the carbon-boron bonds yields the resulting 1,2-diols with up to 98% ee. Work focused on other functionalizations of the organo(bis)boronate intermediates and efforts directed towards increasing catalyst efficiency will also be displayed.



HAMMETT STUDIES OF ENANTIOCONTROL BY PHOX LIGANDS IN PD-CATALYZED ALLYLIC SUBSTITUTION REACTIONS

Paul B. Armstrong, Ryan N. Constantine, Naomi Kim and Richard C. Bunt
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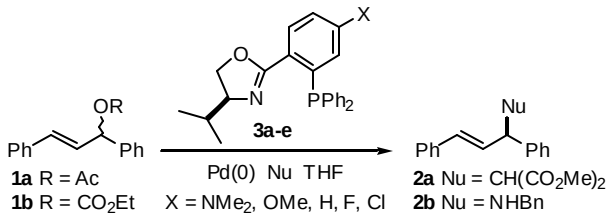

Electronically modified phosphinooxazoline (PHOX) ligands **3a-e** were synthesized to probe the mechanism of the enantioselective palladium-catalyzed allylic alkylation and amination reactions. Alkylation with dimethyl sodiomalonate produced only a small variation in the ee (**2a**: 89.3% to 93.4%), but amination with benzylamine gave a much wider variation in the ee (**2b**: 16.4% to 66.6%). Hammett analysis suggests that the substituents interact more significantly with phosphorus and supports a combined electronic and steric basis for enantioselection.

PROGRESS TOWARD THE TOTAL SYNTHESIS OF THE PHOMOIDRIDES

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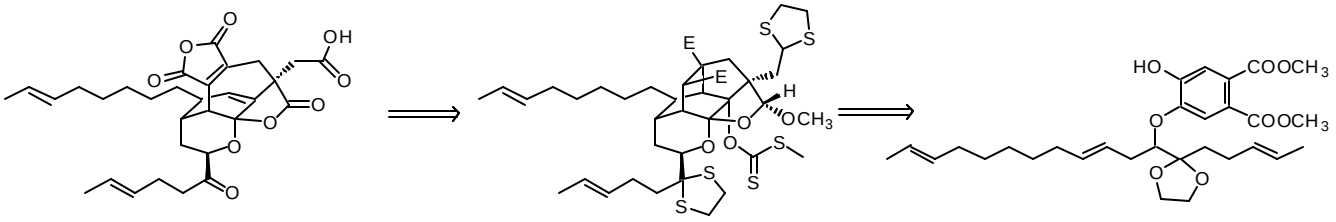
New Haven, CT 06520-8107

The Phomoidrides display activity against both ras farnesyltransferase and squalene synthase and contain a unique carbocyclic core containing a bridgehead olefin. We have shown in model systems that this carbocyclic core can be accessed via fragmentation of xanthate-containing isotwistanes. Herein we describe the efficient synthesis of phenol **3** and its conversion to xanthate **2**, containing every carbon-carbon bond found in the natural product. Recent progress toward the total synthesis will be presented.



Phoimoidride D
(**1**)

(**2**)

(**3**)

Packing Reactivity into the Nitroaldol: Henry Construction of Multifunctional Intermediates for Annulation Reactions

Frederick A. Luzzio, Joel P. Ott
University of Louisville
Department of Chemistry, Louisville, KY 40292

The nitroaldol (Henry reaction) is one of the best expedients for carbon-carbon bond formation between two fragments having sensitive and diverse functionality.[1,2] The mild nature of the reaction allows for significant latitude when each coupling partner contains functionality protected as acetals, ketals, esters, orthoesters and an array of ether protection such as benzyl and trialkyl silyl groups. The key components of a synthetic sequence which includes a nitroaldol reaction are further transformation of the nitro-alkanol function itself. Our present interests in nitroaldol chemistry involves effective manipulation of the nitroalkanol group so that annulation reactions, either azacyclic or carbocyclic, may be accomplished. With the inclusion of suitably-disposed functional groups which are either electrophilic or radical-accepting, we have designed nitroaldols which are potential key intermediates for the requisite cyclizations. The design and synthesis of a diverse array of coupling partners, having either the functionalized nitro or carbonyl components and their utilization in cyclization reactions will be presented.

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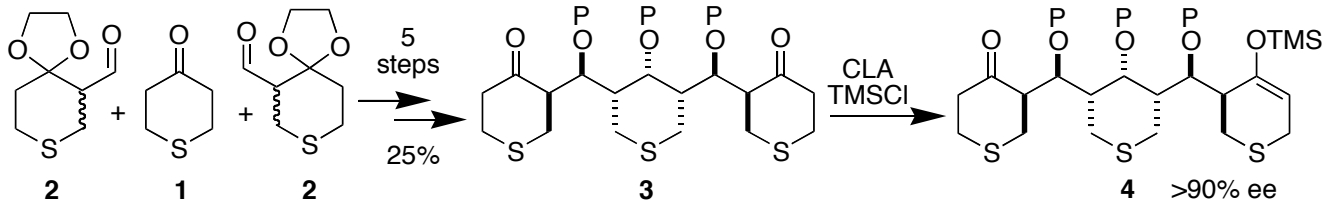
2. Luzzio, F. A. *Tetrahedron* **2001**, *57*, 915-945.

The Thiopyran Route to Polypropionates.
Desymmetrization of *Meso* Hexapropionate Synthons by Enantioselective Enolization

Dale E. Ward, H. Martin Gillis, and K. Saravanan
University of Saskatchewan, Department of Chemistry
110 Science Place, Saskatoon SK S7N 5C9, CANADA

We have been investigating a thiopyran route to polypropionates involving sequential two-directional aldol reactions of tetrahydro-4H-thiopyran-4-one derivatives with tetrahydrothiopyran-3-caboxaldehyde derivatives followed by desulfurization. (cf. *Org. Lett.* **2000**, *2*, 1325). In this contribution we describe the synthesis of a meso diketone (**3**) and its desymmetrization by enantioselective enolization using a chiral lithium amide (CLA) base. Using this approach, a highly enantiomerically enriched hexapropionate synthon (**4**) can be readily prepared in six steps from assembly of simple precursors (**1**, **2**). Recent applications will be reported.

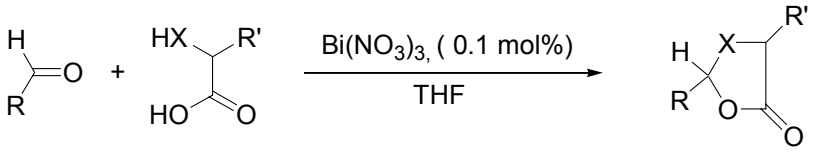


REMARKABLE BISMUTH NITRATE-CATALYZED PROTECTION OF CARBONYL COMPOUNDS: DIASTEREOSELECTIVE SYNTHESIS

Bimal K. Banik

The University of Texas, M. D. Anderson Cancer Center, Department of Molecular Pathology, 1515 Holcombe Blvd., Box # 89, Houston, TX 77030; E-mail: bbanik@mail.mdanderson.org

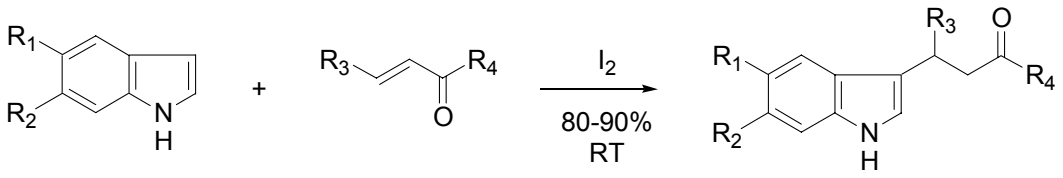
The protection of carbonyl groups plays an important role in organic and medicinal chemistry. In spite of these efforts, protection as acetal, 1-3-dioxalane, mixed ketals, and thioketal remains the most practical choice. In general, this method requires protic, Lewis acids or acidic catalysts. The most important shortcomings of the acid-induced methods are the long reaction time and conditions that require a high temperature and stoichiometric amount of reagents. In this paper, we describe our study of the protection of carbonyl compounds as acetal, dioxalone, mixed ketal and thioketal using a general bismuth nitrate method at room temperature. In addition, using this method a facile diastereoselective synthesis of ketal-types of compounds has also been achieved. Notably, bismuth nitrate has been found to be highly effective in the protection of aldehydes and ketones, even with 0.1 mol% of the reagent. In conformity of hypothesis, our bismuth nitrate-catalyzed reaction produced a diastereoselective mixture of *cis* and *trans* (85:15) dioxolanones and oxathiolanones.



MOLECULAR IODINE-CATALYZED HIGHLY EFFICIENT MICHAEL REACTION OF INDOLES: A REMARKABLE MILD AND SOLVENT-FREE CONDITION

Bimal K. Banik
The University of Texas, M. D. Anderson Cancer Center, Department of Molecular Pathology, 1515 Holcombe Blvd., Box # 89, Houston, TX 77030; E-mail: bbanik@mail.mdanderson.org

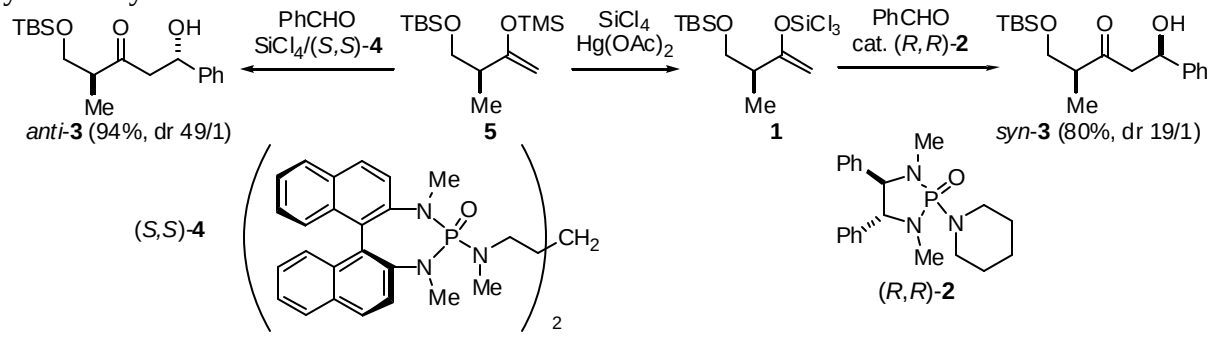
The Michael reaction is one of the most important reactions in organic chemistry. In general, this type of conjugate addition reaction of nucleophiles to unsaturated carbonyl compounds requires basic conditions or acidic catalysts. Some of these methods require stoichiometric amounts of the reagents, and many side reactions can occur if the reactive partners are sensitive. In connection with our ongoing research to develop iodine-catalyzed organic transformations, we herein report an extremely convenient Michael reaction of indoles using solvent-free conditions. In general, the reactions took place at the 3-position of the indole ring when this position was unoccupied. When a methyl group occupied the 3-position, the reaction took place at C_2 position. In contrast to the existing methods using acidic catalysts or reagents, this method is very rapid, simple, high-yielding, environmentally friendly, oxygen and moisture tolerant.



DOUBLE DIASTEREO-DIFFERENTIATION IN LEWIS BASE CATALYZED ALDOL ADDITIONS

Shinji Fujimori and Scott E. Denmark*
Roger Adams Laboratory, Department of Chemistry, University of Illinois at Urbana-Champaign
Urbana, IL 61801

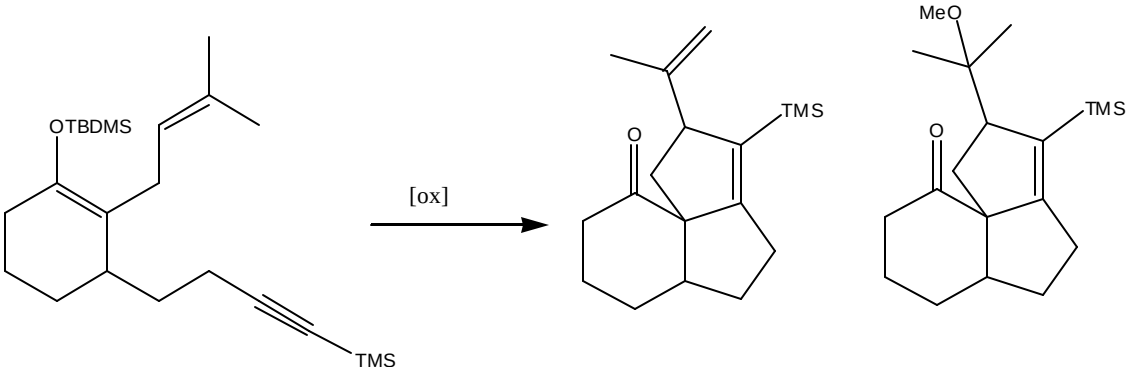
The aldol addition of chiral trichlorosilyl enolate **1** to benzaldehyde under catalysis by (*R,R*)-**2** gives 1,4-*syn* product (*syn*-**3**) in good diastereoselectivity. The diastereomeric adduct *anti*-**3** could be obtained using the enantiomeric catalyst, albeit with attenuated selectivity. Recent reports from these laboratories have described a new Mukaiyama-type aldol reaction employing $SiCl_4$ and a catalytic amount of a chiral phosphoramide (**4**). Using this catalyst system, the addition of the chiral TMS enol ether **5** to benzaldehyde affords *anti*-**3** with excellent selectivity. Thus, these two Lewis base catalyzed aldol reactions allow for complementary and highly stereoselective preparation of both diastereomers from a common TMS enol ether. This principle has been applied to other enol silyl ethers derived from chiral methyl and ethyl ketones.



Initial Studies of Tandem Radial Cyclizations Initiated by Radical Cations

Bradley A. Scates, Wenhua Chu, Michelle Monnens, Kevin D. Moeller
Department of Chemistry, Washington University, One Brooking Drive, St. Louis, MO 63130, Fax: 314-935-4481

Radical cations generated by electrochemical oxidation have been used to initiate tandem cyclization reactions. The reactions utilize alkynes as the trapping group for the initial radical cation, a transformation that leads to a reactive vinyl radical that triggers the formation of the second ring. The tricylcic core of the molecule paniculatine has been used as a model system for investigating the cyclizations. Progress toward the synthesis of this ring system, evidence for the mechanism of the initial cyclization, and the compatibility of the reaction with different terminating olefins will be discussed.



DEUTERATED ALKYLRESORCINOLS FOR ANALYSIS OF WHOLE GRAIN PRODUCTS

Kirsti Parikka and Kristiina Wähälä
Laboratory of Organic Chemistry, Department of Chemistry, P.O. Box 55
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Alk(en)ylresorcinols are phenolic lipids that have an odd numbered n-alkyl or alkenyl side chain at resorcinol C-5. They are found in 11 families of plants, e.g. the family *Gramineae* (cereal grains: rye, wheat and triticale).[1] Alkylresorcinols are found in the outer part of the grain kernel and are therefore only present in high amounts in whole grain products.[2-3]
Alkylresorcinols are biologically active compounds[1] and their beneficial health effects have now raised interest. Alkylresorcinols may be a factor in the protective effects of whole-grain foods against certain cancers and heart disease.[4] Recently alkylresorcinols have been determined from human fluid.[5] Analytical and metabolic studies of alkylresorcinols and their biological activity require deuterolabelled analogues of these compounds. We have developed different deuterolabelling techniques and investigated the isotopical and isomerical stability and purity of the products.

References

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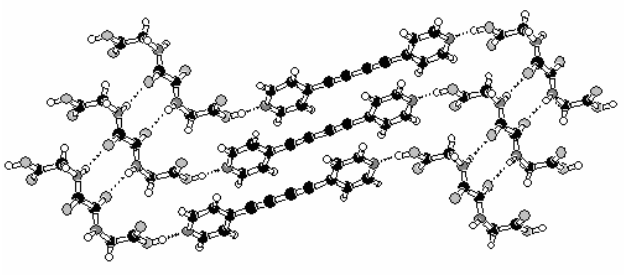
3. A. B. Ross, A. Kamal-Eldin, C. Jung, M. J. Shepherd and P. Åman, *J. Sci. Food Agric*. 2001, 81, 1405
4. L. Marquart, J. L. Slavin and R. G. Fulcher, Whole-grain foods in health and disease, AACC, St Paul, 2002
5. A. -M. Linko, K. Parikka, K. Wähälä and H. Adlercreutz, *Anal. Biochem*. 2002, 308, 307

Supramolecular Host-Guest Strategy to Conjugated Linear Polymers

Sean M. Curtis, Joseph W. Lauher, Frank W. Fowler
State University of New York, Stony Brook
Department of Chemistry
Stony Brook, NY 11794-3400

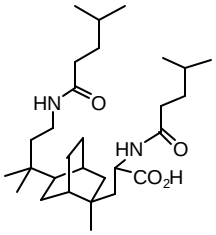
The production of conjugated linear polymers requires the pre-organization of monomeric molecules. This pre-organization can only be achieved in the solid-state, thereby making supramolecular strategies a crucial design element in the production of these polymers. A two-molecule supramolecular system has been developed for this required pre-organization of monomeric or guest molecules. The organization and packing of the guest molecules is achieved by forming a reliable hydrogen bond network with a second host molecule, generating a crystalline supramolecular moiety. It is within this moiety that a topochemical polymerization can implemented to produce conjugated linear polymers.

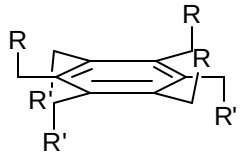


BICYCLO[2.2.2]OCTANES AND AMPHIPATHIC BENZENES AS ESTROGEN RECEPTOR COACTIVATOR BINDING INHIBITORS

Margaret L. Collins, Alice L. Rodriguez, John A. Katzenellenbogen
University of Illinois at Urbana-Champaign
Department of Chemistry, Urbana, IL 61801

The estrogen receptor (ER) plays an important biological role in various tissues including the brain, uterus, bone and breast. It would be advantageous to regulate the ER in order to help control diseases associated with these tissues such as breast cancer. A novel approach to this problem is to target the interaction of coactivators with agonist bound ER. Blocking estrogen action at this level could be useful for circumventing hormonal resistance encountered in cancer treatment because it targets a point in the signal transduction pathway subsequent to hormone binding. Small molecule coactivator binding inhibitors were designed based on the analysis of the crystal structure of the coactivator's conserved LXXLL (L = leucine, X = any amino acid) motif with ER. The key hydrophobic and hydrogen bonding moieties were incorporated onto a variety of cores including bicyclo[2.2.2]octane and benzene. A fluorescence-based assay was used to evaluate the ability of the coactivator binding inhibitors to inhibit the ER-coactivator interaction.



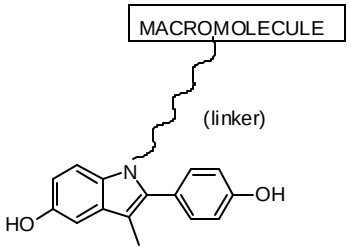


R = Hydrophilic
R' = Hydrophobic

The Synthesis of Indole Estrogens to Probe Non-Genomic Actions of the Estrogen Receptor

Bridget G. Trogden, Sung Hoon Kim, John A. Katzenellenbogen
University of Illinois
Department of Chemistry, Urbana, Illinois 61801

The estrogen receptor (ER) is a ligand-regulated transcription factor located in many tissues. In addition to its direct nuclear gene regulatory roles, the ER can also carry out transcription-independent functions by activating other signaling pathways. These non-genomic effects are likely mediated through a membrane-bound ER (mER), but prior methods of studying this interaction have not always given definitive results. We have designed indole ER ligands which can be attached to a variety of macromolecules in order to study these effects. Differential synthesis of 2-phenyl indoles with various N-linker regions combined with ER binding affinity studies should allow for an optimized indole estrogen-macromolecular conjugate to explore the role(s) of the mER. The synthesis of indoles with three classes of linker regions – alkyl, phenyl, or benzyl – with various alkyl caps has been accomplished and binding data obtained for these ER ligands.



CD INVESTIGATION OF DESS-MARTIN PERIODINANE OXIDATION

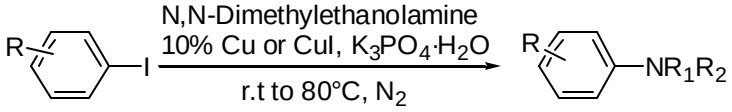
Nicole Reed, Robert Rapp, Christian Hamann, and Pamela Artz
Albright College
Department of Chemistry and Biochemistry, Reading, PA 19604

We describe an experiment that introduces Dess-Martin periodinane chemistry and circular dichroism spectropolarimetry in to the sophomore organic chemistry curriculum. The Dess-Martin reaction (Dess & Martin, 1983, *J. Org. Chem.*, **48**, 4155) was selected because it affords safer laboratory conditions and easier purification steps than chromic acid or bleach. Half of the organic chemistry laboratory group performed the oxidation with (-)-menthol and the other half used (+)-menthol to produce (-)- and (+)-menthone, respectively. Instrumental analysis of the products was performed using infrared spectroscopy, gas chromatography/mass spectrometry, and circular dichroism spectropolarimetry. The CD spectra for reactant and product were compared, as were the spectra for the product enantiomeric ketones. The large change in the CD spectrum of the product compared to the reactant was diagnostic for a successful oxidation. The students were able to interpret CD data even when percent oxidation was 50 – 70%. The CD spectra of the enantiomeric products were idential in shape, but opposite in sign due to the distinct optical activity of each molecule. An assessment tool was administered before and after the laboratory to evaluate student learning outcomes. These data suggest that students increased their knowledge of CD theory and practice after performing this laboratory and that they improved their understanding of stereochemistry, optically active compounds and alcohol oxidation.

Copper Catalyzed Amination of Aryl Halides and Selective Amination of Aryl Dihalides and Diamines with 2-N,N-dimethylaminoethanol as Solvent

Zhikuan Lu, Robert J. Twieg, Songping D. Huang

Department of Chemistry, Kent State University, Kent, OH 44242-0001



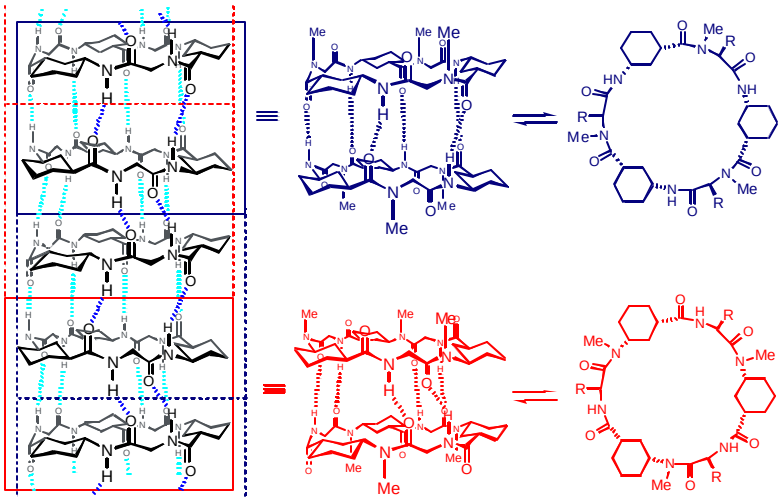
A copper-catalyzed amination of aryl iodides under mild conditions using N,N-dimethylethanolamine as solvent is described. We have studied this reaction in detail varying the copper source, base, water content and other parameters as well as the scope of useful amine and aryl halide structures. A variety of 4-halo-N,N-cycloalkylanilines were synthesized for further elaboration into chromophores for photonic applications. Diamines with both primary and secondary amino groups react preferentially at the primary amine with aryl iodides. Lower yields and selectivity are observed for amination of aryl bromides using this method.

a ,g-CYCLOPEPTIDES CAPABLE OF FORMING PEPTIDIC NANOTUBES: THE STRUCTURAL AND THERMODINAMIC BASIS

Manuel Amorín, Roberto J. Brea, Luis Castedo, Juan R. Granja

Departamento de Química Orgánica e Unidade Asociada ó C.S.I.C, Facultade de Química, Universidade de Santiago, 15782 Santiago de Compostela, SPAIN

In the present communication, we will describe the studies realized with cyclopeptide made of alternating alpha- and gamma-amino acids. These peptides, when they are selectively N-alkylated in their peptide back-bone, self-assembled into cylindrical structures which serve as models for a new class of self-assembled peptide nanotubes (SPN). A principal characteristic of these particular nanotubes is that they possess an internal cavity of hydrophobic character. This work was supported by Ministerios de Educación y Ciencia, and Ciencia y Tecnología and the Xunta de Galicia under projects PB97-0524, SAF2001-3120 and PGIDT00PXI20912PR. We also thank the Spanish MEC for the award of a fellowship to M.A.



DESIGN AND SYNTHESIS OF NOVEL GADOLINIUM LIPIDS FOR IMAGING LIPOSOME DELIVERY

Morag Oliver, [1] ***Michael R. Jorgensen,*** [2] ***Po-Wah So,*** [3] ***Jimmy Bell,*** [3] ***Andrew Miller*** [1]
Imperial College London
[1] **Genetic Therapies Centre, Department of Chemistry, South Kensington, London, SW7 2AZ, UK**
[2] **IC-Vec Ltd., Flowers Building, Armstrong Road, South Kensington, London, SW7 2AZ, UK**
[3] **MRI Unit, Clinical Sciences Centre, Hammersmith Hospital, London, W12 OHS, UK**

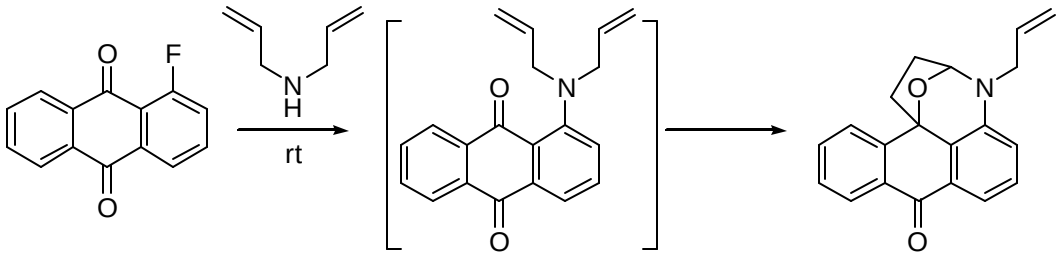
Liposomes are artificially constructed spheres of lipid bilayers enclosing an aqueous compartment, frequently used for the delivery of drugs and nucleic acids into cells. An important development for liposome technology is the ability to monitor both their pharmcokinetic behaviour and site of delivery. This could potentially be achieved by the development of a new liposome membrane consisting of labelled components, such as a contrast agent for Magnetic Resonance Imaging (MRI). The aim of this research is to design and synthesise a series of gadolinium lipids for the incorporation into the liposome membrane. Lipids will be analysed by MRI, both individually and within the liposome membrane allowing elucidation of a structure-activity relationship for these compounds. Successful candidates will then be used in experiments imaging liposome delivery both *in vitro* and *in vivo*.

The structure of our imaging agents comprises a simple phospholipid or cholesterol-based lipid, bonded through the lipid head group to an octadentate ligand, namely DOTA or DTPA, which permits coordination of the Gd metal ion. Currently we are developing a novel solid phase synthesis methodology for the functionalisation of DOTA or DTPA. This will permit the development of new lipids with varying linkers and functionality.

Remarkably Mild Carbonyl-Ene Reaction
Using* N,N-*diallylaminoarylketones

Robert Brinson, Paul Jones
Wake Forest University
Department of Chemistry, Winston-Salem, NC 27109

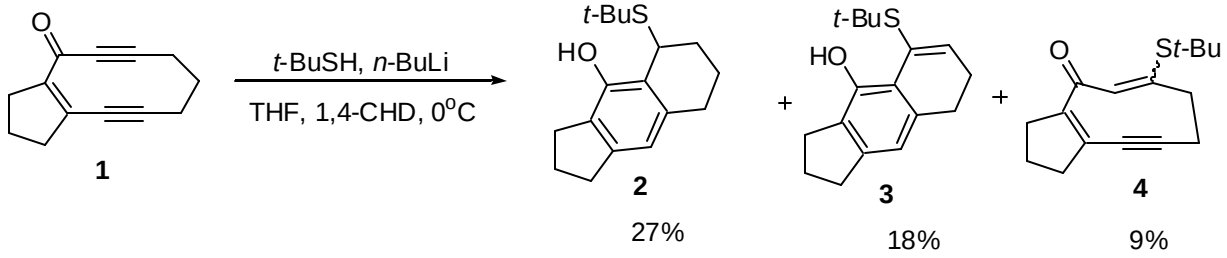
The carbonyl-ene reaction of allylamines with tethered carbonyl groups is an efficient means of preparing azepines and oxazines. These important structural types, found in many natural products that exhibit biological activity, have been prepared using high temperature carbonyl-ene reactions to produce hydroxydihydroazepines. These can be further cyclized to oxazines under mild conditions. We have discovered a novel, ambient temperature method for the construction of azepine and oxazine substructures using *N,N*-diallylated amines. This dramatic increase in rate appears to be due to enforced proximity of one alkene to the carbonyl. Our results describing the scope and limitations of the reaction are presented.



SYNTHESIS AND CYCLOAROMATIZATION OF A CYCLIC ENYNE-ALLENE PRODRUG

Tefsit Bekele and Mark A. Lipton*
Purdue University
Department of Chemistry, West Lafayette, IN 47907

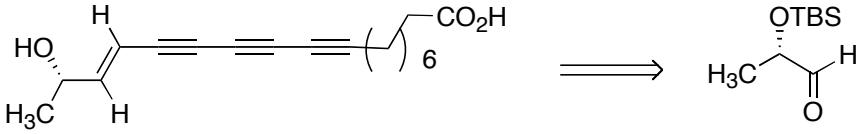
Abstract: A simple and stable cyclic enediynone (**1**) has been synthesized using an intramolecular Nozaki-Hiyama-Kishi cyclization as the key step. Reaction with a thiolate nucleophile led to rapid cycloaromatization of **1**. Trapping experiments using 1,4-cyclohexadiene support the intermediacy of an aromatic diradical in the cycloaromatization.



TOTAL SYNTHESIS OF (-)-*E*-15,16-DIHYDROMINQUARTYNOIC ACID

Benjamin W. Gung,* Godwin Kumi
Department of Chemistry and Biochemistry, Miami University
Oxford, Ohio 45056

The potent anti-cancer entriyne natural product, (*S*)-*E*-15,16-dihydrominquartynoic acid (**1**), is synthesized in 5 linear steps from the known aldehyde **2**. The key step is an one-pot desilylation-Cadiot-Chodkiewicz coupling to construct the entriyne unit without the isolation of the diyne intermediate.

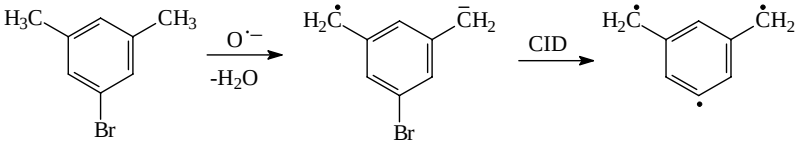


1 **2**

5-DEHYDRO-1,3-QUINODIMETHANE: AN ORGANIC MOLECULE WITH AN OPEN-SHELL DOUBLET GROUND STATE

Tamara E. Munsch and Paul G. Wenthold
Purdue University
Department of Chemistry, West Lafayette, IN 47907-2084

In this work, we describe gas-phase studies of the thermochemistry of 5-dehydro-1,3-quinodimethane. With a $\pi^1\pi^1\sigma^1$ molecular configuration, 5-dehydro-1,3-quinodimethane is the first known example of an "open-shell" doublet ground state for an organic molecule. The enthalpy of formation of 5-dehydro-1,3-quinodimethane has been determined using a flowing afterglow-triple quadrupole instrument. The 5-bromo-1,3-quinodimethane negative ion was generated by the reaction of $O^{\bullet -}$ with 5-bromo-*m*-xylene.

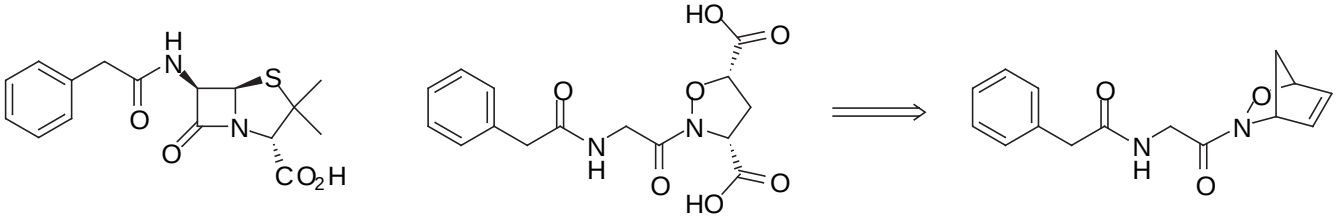


Collision-induced dissocation (CID) threshold energy measurements with the 5-bromo-1,3-quinodimethane ion was used to determine the enthalpy of formation for 5-dehydro-1,3-quinodimethane. Preliminary data gives an enthalpy of formation of 136 kcal/mol. The measured enthalphy of formation indicates that the C-H bond dissociation energy at the 5-position for *m*-xylylene is 107 kcal/mol, which is similar to the C-H bond dissociation energy at the *meta*-position for benzyl radical. The strength to the third C-H bond indicates that there is weak, indirect interaction between the π- and σ-systems in the triradical

The Synthesis of Potential New β-Lactam Analogues (Isoxazolidine-3,5-dicarboxylic Acids) Possessing Antibacterial Activity

George Nora, Marvin J. Miller
University of Notre Dame, Department of Chemistry and Biochemistry
251 Nieuwland Science Hall, Notre Dame, IN 46556-5670

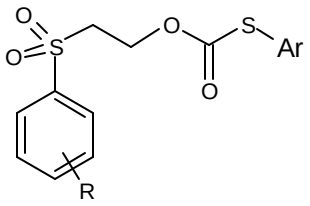
The structural similarities between β-lactam antibiotics such as penicillin **1** and isoxazolidine-3,5-dicarboxylic **2** acids leads to the hypothesis that isoxazolidine-3,5-dicarboxylic acids could be structural analogs to β-lactam antibiotics. The synthesis of isoxazolidine-3,5-dicarboxylic acids *via* an acylnitroso Diels Alder adduct **3** and subsequent biological testing have shown that they are inhibitors of *E. Coli* X580 but lack broad spectrum activity. The synthesis of modified isoxazolidines, that may improve the broad spectrum activity is in progress.



1 **2** **3**

PROCESS DEVELOPMENT OF 10098274: AN ADDENDUM FOR *EKTACOLOR* PAPER

Muhunthan Sathiosatham
Eastman Kodak Company
Rochester, NY 14652

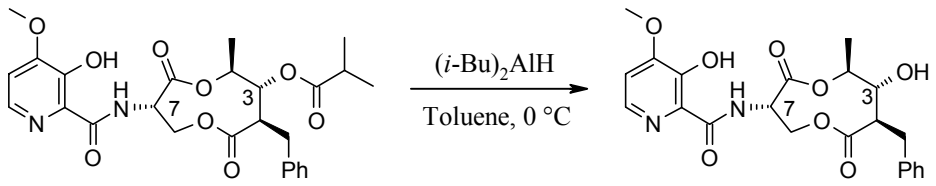


10098274 is a photographically active compound. This poster will discuss the development of the manufacturing process, design of experiments (DOEs) for optimization, and scale-up of TETT.

REDUCTIVE CLEAVAGE OF THE EXOCYCLIC ESTER OF UK-2A

Kevin G. Meyer[1], Noormohamed M. Niyaz[1], Carl V. Deamicis[1], Richard B. Rogers[1], David E. Podhorez[2]

[1]Dow AgroSciences LLC
9330 Zionsville Road, Indianapolis, IN 46268
[2]The Dow Chemical Company
1710 Dow Center, Midland, MI 48674



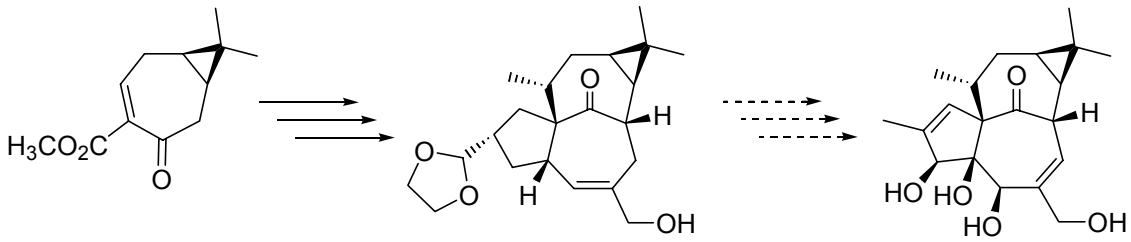
UK-2A (1) **2**

UK-2A (**1**) is a natural product isolated from *Streptomyces sp.* 517-02 and has drawn considerable attention as an agricultural fungicide. Other UK-2 compounds, which vary only in the type of ester at C-3, demonstrate different levels of fungicidal activity, verifying the C-3 site as a target of synthesis exploitation. Preparation of robust C-3 derivatives required the selective removal of the isobutryl ester without affecting the bis-lactone. A brief study of reducing agents revealed diisobutylaluminum hydride as the reagent of choice. Four equivalents of reducing agent at 0 °C in toluene followed by a careful acid quench converted UK-2A smoothly into **2**. The process was ramped up to supply kilogram quantities of **2**, which provided sufficient amounts of UK-2A derivatives for field testing.

PROGRESS TOWARD THE TOTAL SYNTHESIS OF INGENOL

John L. Wood, Haifeng Tang, Andrew Nickel, Toru Maruyama, Prescott Murphy, and Blake Greene
Yale University, Department of Chemistry
New Haven, CT 06520-8107

An efficient route from enone **1** to tetracycle **2**, which contains the entire carbon skeleton of ingenol, has been developed. The synthesis of **2** and attempts to convert it to the natural product will be presented.

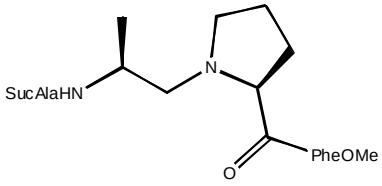


1 **2** Ingenol

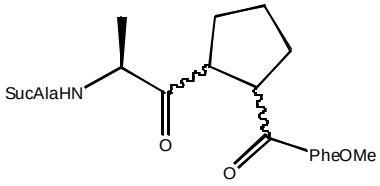
SYNTHESIS OF TRANSITION STATE ANALOGS AS INHIBITORS OF CYCLOPHILIN

Marc Lannuzel, Kezia Sterling, Felicia A. Etzkorn[*]
Virginia Tech, Department of Chemistry, Blacksburg, VA 24061

Peptidyl Prolyl Isomerases (PPIases) are enzymes catalyzing the cis-trans interconversion of the amino acyl-prolyl amide bond in both peptides and proteins and are involved in many biological processes. The first PPIase discovered, Cyclophilin, is the main receptor of the immunosuppressive undecapeptide Cyclosporin A and hence, is implicated in immunosuppression. We have designed and synthesized two transition state analogs, the reduced amide **1,** and the ketone **2.** The four diastereomers of **2** were separated by HPLC.



1

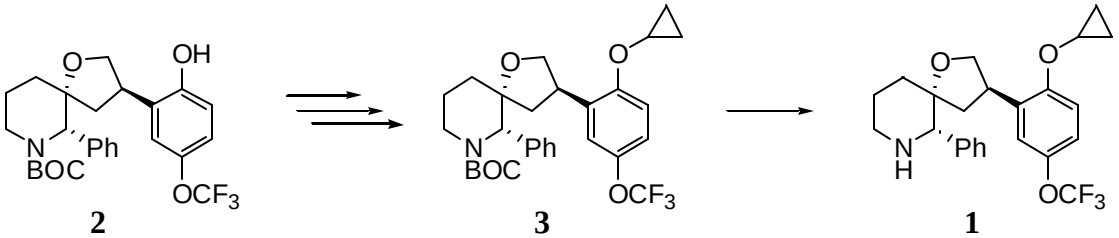


2

An Efficient Method for the Conversion of an Aryl Phenol to an Aryl Cyclopropyl Ether. The Final Steps in the Synthesis of a NK_1 Receptor Antagonist.

Mark Cameron,*[1] Michael.S. Ashwood[2], Ian.F. Cottrell[2],
Ulf.H. Dolling[1],Andrew.W. Gibson[2] ,Simon.A. Johnson[2] and Derek. J. Kennedy[2]
[1]Department of Process Research, Merck Research Laboratories, Merck & Co. Inc., P.O. Box 2000, Rahway, N.J. 07065, U.S.A.
[2]Department of Process Research, Merck Sharp and Dohme Research Laboratories, Hertford Road, Hoddesdon, Hertfordshire, EN11 9BU, UK.

Substance P, a peptide neurotransmitter that binds preferentially to the NK_1 receptor is widely distributed in the central and peripheral nervous systems as well as gastrointestinal tissue. Consequently, NK_1 receptor antagonists may represent a major new therapeutic use in the treatment of depression, pain, migraine and nausea. Our interest in this field required an efficient synthesis of NK_1 antagonist **1.** The final steps in the synthesis required the efficient conversion of the aryl phenol **2** to the aryl cyclopropyl ether **3**. Subsequent deprotection affords **1**. We, herein, report a highly efficient four-step conversion of **2** to **1** in 72-77% yield. The factors influencing yield and final purity of **1** are discussed.



2 **3** **1**

NOVEL, ENDOSOMOLYTICALLY-ACTIVE, SUGAR-BASED LIPIDS FOR NON-VIRAL GENE THERAPY

Steven Fletcher,[1] Michael R. Jorgensen,[2] Andrew D. Miller[1]
Imperial College London
[1]Genetic Therapies Centre, Department of Chemistry, South Kensington, London, SW7 2AZ, UK
[2]IC-Vec Ltd., Flowers Building, Armstrong Road, South Kensington, London, SW7 2AZ, UK

Cationic liposomes are proving to be successful alternatives to viruses as delivery vehicles for nucleic acids. The cationic charge is required to condense the therapeutic gene and to facilitate escape from the endosome, the organelle through which the liposomes are internalised, however this charge also promotes liposome destruction in the blood. Therefore, we propose to mask temporarily this positive charge, through exploiting the fall in pH as the endosome matures into the digestive lysosome, by incorporating the maleic acid functionality into the head groups of two lipids, namely DOPE (zwitterionic) and cholesterylamine (cationic). The resulting acid-labile, anionic maleamates will be formulated into liposomes with our cationic lipid CDAN, so that only the minimal positive charge necessary to condense the therapeutic gene is presented. Upon internalisation and endosome maturation, the concomitant fall in pH will facilitate cleavage of the maleamates, regenerating DOPE or cholesterylamine, thereby revealing the full cationic nature of the liposome.

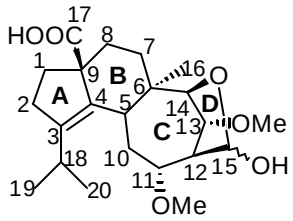
We have prepared two novel, anionic, galactose-based, acid-labile lipids. Incorporation of galactose (to impart steric stabilisation on the resultant liposomes) was achieved by modifying the maleic acid moiety into an acid-labile linker, enabling conjugation of the lipid to the sugar. Due to the highly convergent nature of the synthetic route, different lipids and sugars may be easily substituted.

Studies Toward the Total Synthesis of Scabronine A

Eli A. C. Ron[1], Francis Johnson[1,2]

1.State university of New York at Stony Brook
Department of Chemistry, Stony Brook, NY 11794-3400
2.State university of New York at Stony Brook
Department of Pharmacology, Stony Brook, NY 11794-3400

Investigations of compounds that have the ability to stimulate the *in vivo* production of NGF are at the forefront of a number of drug development programs. It is hoped that substances that can direct control of the endogenous production of NGF can be found. Of these substances members of the eranicine and scabronine families have proven to be potent stimulators of NGF synthesis. Therefore a convenient and efficient total synthesis is required not only for the drug itself but also for the generation of structural variants. In addition having the material generally available should help to clarify the mechanisms underlying the biological synthesis and secretion of NGF. The scabronine family so far consists of seven members termed scabronines A – G. All members of the scabronine family are diterpenoids that posses a cyathane skeleton consisting of angularly condensed five, six, and seven membered rings. Scabronine A has nine stereocenters and in contrast to the others, has an additional lactal ring.

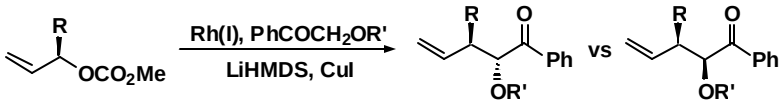


Scabronine A

Diastereoselective Rhodium-Catalyzed Allylic Alkylation Reactions Using Copper(I) Enolates

Michael J. Lawler, David K. Leahy, P. Andrew Evans
Indiana University
Department of Chemistry, Bloomington, IN 47405

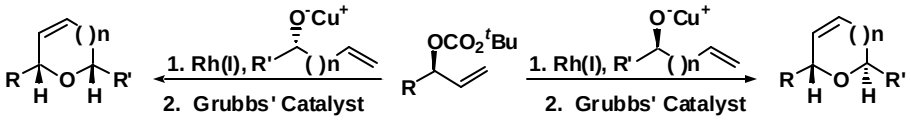
The transition metal-catalyzed allylic alkylation represents a fundamentally important cross-coupling reaction for the construction of carbon-carbon bonds. We have developed a new diastereoselective rhodium-catalyzed allylic alkylation of acyclic unsymmetrical allylic alcohol derivatives using copper(I) enolates. The reaction's broad scope and application towards target directed synthesis will be presented.



Stereospecific Rhodium-Catalyzed Allylic Etherification Reactions Using Copper(I) Alkoxides

David K. Leahy, Daisuke Uraguchi, William J. Andrews, P. Andrew Evans
Indiana University
Department of Chemistry, Bloomington, IN 47405

The transition metal-catalyzed allylic etherification represents a fundamentally important cross-coupling reaction for the construction of carbon-oxygen bonds. We have developed a new stereospecific rhodium-catalyzed allylic etherification of acyclic unsymmetrical allylic alcohol derivatives using copper(I) alkoxides. The reaction's scope and application towards cyclic ether containing natural products will be presented.



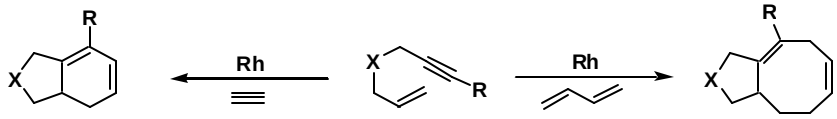
Rhodium-Catalyzed Carbocyclization Reactions

Aleem N. Fazal, Erich W. Baum, James R. Sawyer, John E. Robinson, P. Andrew Evans

Indiana University

Department of Chemistry, Bloomington, IN 47405

Transition metal-catalyzed carbocyclizations are among the most powerful transformations available for target directed synthesis. Significant attention has been given to rhodium-catalyzed carbocyclization reactions due to their unique selectivity and synthetic versatility. Current research is focused on the synthesis of bicyclic compound from tethered enyne derivatives *via* intermolecular [4+2+2] and [2+2+2] cyclizations. The scope and limitation of these transformations will be presented.



DIELS-ALDER SYNTHESIS - MINI SCALE EXPERIMENTS TO STUDY THE EFFICACY OF SOLVENT/CATALYST SYSTEMS AND THE REDUCTION OF HAZARDOUS WASTE

Anthony Masulaitis, Jeffrey Stewart, Taha Ahmad, Carina Neto, Arpit Patel, Kirtiben Solanki and Treva Pamer

New Jersey City University, Department of Chemistry, Jersey City, NJ 07305

The NJCU settlement agreement with the US Environmental Protection Agency resulting from alleged hazardous waste violations includes a Supplemental Environmental Project to modify organic chemistry experiments using mini scale, defined as a 2.0 g limit on the amount of starting materials. Prior experience with the important Diels-Alder reaction from micro scale texts yielded unsatisfactory results.

A team of undergraduate research students undertook a study to modify macro scale procedures down the mini scale conditions designed to provide experimental parameters for the full class and to learn about the effect of scale on the course of a reaction that requires heat. Three sets of adducts: 3-sulfolene, 1,3-cyclopentadiene and 1,3-cyclohexadiene were each reacted with maleic anhydride. Solvent/catalyst systems studied were xylene, xylene/HCl, xylene/$ZnCl_2$, water, and water/HCl.

Products were analyzed using FTIR and GC-MS along with physical properties. Future studies of chiral products using LC-MS with chiral columns are planned.

SYNTHESIS OF ANTI-AIDS DIARYLSULFONES

Geetha T. Mukundan*, Murray Zanger
Department of Chemistry and Biochemistry
University of the Sciences in Philadelphia
600 South 43rd Street, Philadelphia, PA 19104-4495

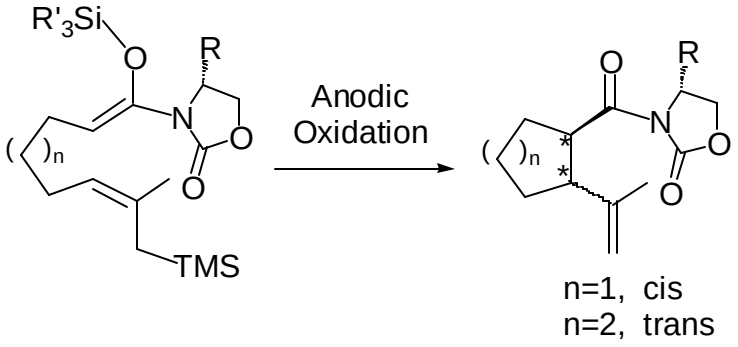
Diarylsulfones, one among several novel classes of non-nucleoside inhibitors of HIV type 1 reverse transcriptase (NNRTIs) exhibit less toxicity, more selectivity and similar biological activity than the nucleoside inhibitors of HIV type 1 reverse transcriptase (NRTIs) such as AZT, ddC, ddI etc., that were described as first anti-HIV compounds. Structural activity relationship studies (SAR) on the lead compound, 2-nitrophenyl phenylsulfone (NPPS) led to a number of compounds with remarkable results. The most active compound, NSC 667952 was selected as the lead compound for further study in this series.

In this research, four molecules designed and predicted as having greater activity by Free-Wilson approach – a mathematical equation employed in quantitative structure activity relationship (QSAR) studies than NSC 667952 are synthesized and tested for their anti-HIV activities. The results of anti-HIV evaluation have shown that the Free-Wilson approach is not a good method to predict activities for this class of compounds. As a consequence attempts are currently underway using computational techniques to design more potent drug molecules in the diarylsulfone family.

Reversing the Polarity of Enolate Equivalents: The Use of N,O-Ketene Acetals in Intramolecular Anodic Olefin Coupling Reactions.

Yung-tzung Huang, Kevin D. Moeller
Department of Chemistry, Washington University, Campus Box 1134,
One Brookings Drive, St. Louis, MO 63130, USA, Fax: 314-935-4481
yhuang@artsci.wustl.edu, moeller@wuchem.wustl.edu

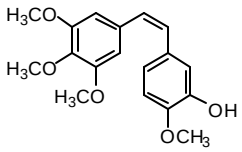
While intramolecular anodic olefin coupling reactions have proven to be useful tools for generating new C-C bonds, asymmetric variants on the reactions have not been studied. Are such reactions feasible? In an effort to address this question, we have begun to study the compatibility of the reactions with ketene acetal moieties. In this way, we hope to take advantage of the chiral auxiliaries that have already been developed in connection with both asymmetric aldol and alkylation reactions. In this paper, the utility of oxazolidinone derived ketene acetal equivalents as initiating groups for the anodic olefin coupling reaction will be discussed.



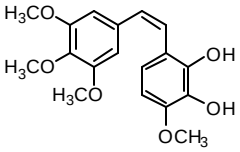
THE SYNTHESIS OF NOVEL NITRO AND AMINO COMBRETASTATIN A-4 ANALOGS

Keith A. Monk, Charles M. Garner
Baylor University
Department of Chemistry and Biochemistry, Waco, TX 76798

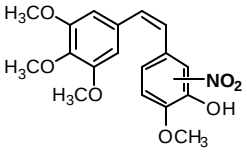
Combretastatin A-4 and Combretastatin A-1, cis-stilbenoid natural products derived from the South African tree *Combretum caffrum*, have been shown to display potent cytotoxicity against a variety of cancer cell lines. Combretastatin A-4 and A-1 are tubulin binding agents, which target tumor vasculature and induce cell death through the reduction of blood flow through the tumor. The Combretastatins are thus attractive lead compounds for the development of novel analogs. Our research is focused on the synthesis of nitro and amino derivatives of Combretastatin A-4, where the variations are made in the B-ring. Numerous compounds have been prepared along with the corresponding pro-drugs. Biological evaluation shows effective *in vivo* blood flow shutdown and potent tubulin inhibition for some of these analogs. The scope of these chemical transformations, biological evaluation, and discussion of vascular targeting will be presented.



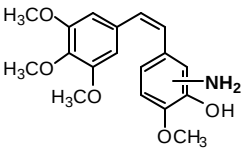
Combretastatin A-4



Combretastatin A-1



Nitro CA-4 Analogs

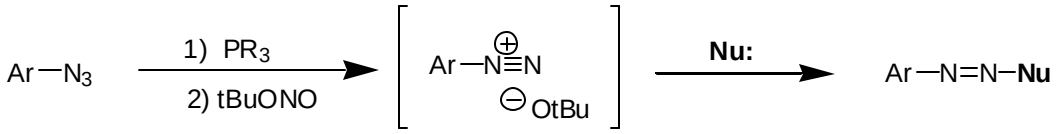


Amino CA-4 Analogs

THE CONVERSION OF AZIDES TO DIAZONIUM IONS UNDER NEUTRAL CONDITIONS

Michele N. Williams and Mark A. Lipton
Department of Chemistry, Purdue University
West Lafayette, IN 47907

Diazonium ions are a widely used functional group in organic synthesis transformations. Their synthesis routinely involves strongly acidic conditions that may be undesirable for acid sensitive compounds. A novel procedure has been developed for the synthesis of diazonium by the formal abstraction of N from azides. This novel methodology involves the conversion of aryl azides to Staudinger intermediates that react under neutral conditions or under Lewis acid catalysis to form synthetically useful diazonium ions. These ions were isolated and characterized as their diazo adducts.



PHYTOALEXINS FROM WILD AND CULTIVATED CRUCIFERS: ISOLATION, STRUCTURE DETERMINATION, SYNTHESIS, AND BIOSYNTHESIS

M. S. C. Pedras, S. Montaut, P. B. Chumala, and P. K. W. Ahiahonu
University of Saskatchewan, Department of Chemistry, Saskatoon, Canada
E-mail: soledade.pedras@usask.ca

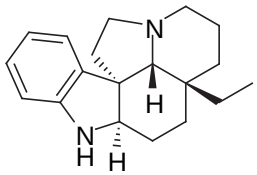
Phytoalexins, plant secondary metabolites synthesized *de novo* in response to diverse forms of stress, are an important component of a plant's chemical and biochemical defense mechanisms. The plant family Cruciferae comprises a large number of economically important oilseed crops as well as condiments and vegetables. Chemical characterization of metabolites from crucifers has unraveled a remarkable array of phytoalexins biogenetically derived from tryptophan and containing both nitrogen and sulfur. Our search for phytoalexins from cruciferous plants resistant to economically important fungal diseases, lead us to examine stinkweed or pennycress and dog mustard, potential sources of disease resistance against Phoma blackleg and Sclerotinia stem rot, respectively. Blackleg and stem rot of crucifers occur worldwide and can be particularly devastating for oilseed crops. Hence, it is of enormous importance to determine the chemical traits responsible for the disease resistance of both stinkweed and dog mustard, as such agronomically important traits are transferable to canola. Furthermore, rutabaga is a well known cruciferous vegetable from which no phytoalexins have been reported to date.

Thus, we analyzed the phytoalexins elicited in rutabaga roots, stinkweed, and dog mustard and identified several known and three new phytoalexins. Furthermore, we have synthesized these metabolites and established their biosynthetic relationships utilizing deuterated indolyl precursors. Results of these studies will be presented and implications will be discussed.

Studies Toward The Total Synthesis of Aspidospermidine

Aaron Aponick and William H. Pearson
Department of Chemistry, The University of Michigan
930 N. University Avenue, Ann Arbor, MI 48109

The *Aspidosperma* family of alkaloids is a structurally diverse set of natural products with varying biological activity. The parent compound, aspidospermidine, is devoid of sensitive functional groups but retains the complex pentacyclic core, and for this reason has been the focus of numerous synthetic endeavors. As part of an ongoing project aimed at exploring the use of 2-azaallylstannanes as precursors to 2-azaallyllithiums in [π4s+π2s] cycloaddition reactions, we have developed an approach to the synthesis of the aspidosperma family of alkaloids. The progress of our synthetic studies towards the total synthesis of aspidospermidine will be presented.

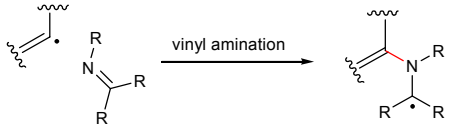


Aspidospermidine

FREE RADICAL-MEDIATED VINYL AMINATION

Benjamin M. Nugent, Jeffrey N. Johnston*
Indiana University
Department of Chemistry, 800 East Kirkwood Avenue Bloomington, IN 47405-7102

Methods for the formation of vinyl-nitrogen bonds have received less attention than the analogous aryl-nitrogen bond formation despite the importance of enamines as intermediates in organic synthesis. Existing methodologies such as metal-mediated cross-couplings and hydroamination provide only partial solutions. Free radical-mediated vinyl amination offers a mild, pH-neutral route to *N*,*N*-dialkyl enamines. This study demonstrates the potential of vinyl radical addition to the nitrogen of azomethines to generate a variety of architecturally diverse enamines (eq 1).

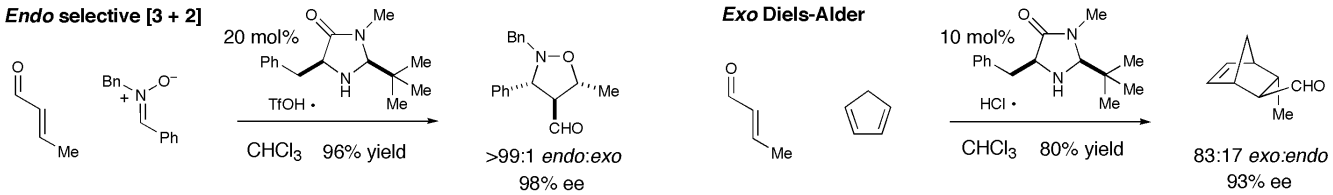


(1)

NEW INSIGHTS INTO IMINIUM CATALYSIS: ENANTIOSELECTIVE ORGANOCATALYTIC [1,3]–DIPOLAR CYCLOADDITION AND *EXO* SELECTIVE CYCLOADDITION REACTIONS

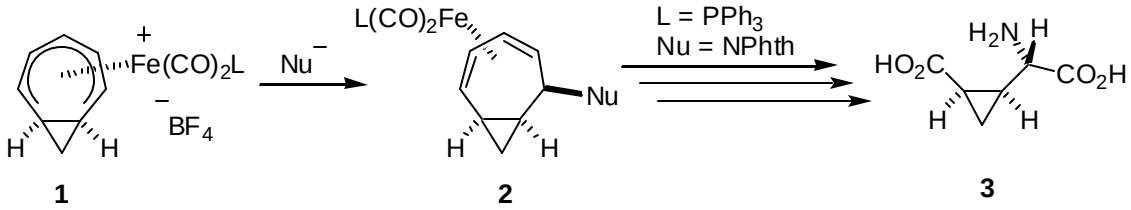
John J. M. Wiener, Wendy S. Jen, David W. C. MacMillan
California Institute of Technology
Department of Chemistry, Mail Code 164-30, Pasadena, CA 91125

Isoxazolidines are useful synthons for the construction of amino acids, β-lactams, amino carbohydrates, and alkaloids. In an extension of the LUMO-lowering organocatalysis strategy developed in our laboratories, we can now access this structural motif in an enantioselective catalytic fashion via a [1,3]–dipolar cycloaddition reaction between nitrones and α,β-unsaturated aldehydes using a chiral imidazolidinone catalyst. This process has allowed, for the first time, simple aldehydes to function as dipolarophiles in a [3+2] nitrone cycloaddition. Additional studies demonstrate the increased catalytic activity and selectivity of a second-generation imidazolidinone catalyst; this catalyst has also enabled the development of the first *exo*-selective, enantioselective catalytic nitrone and Diels-Alder cycloaddition reactions.



REACTIVITY OF (BICYCLO[5.1.0]OCTADIENYL)Fe(CO)$_2$L CATIONS: PREPARATION OF A CONFORMATIONALLY RESTRICTED GLUTAMATE ANALOG

Nathaniel J. Wallock, William A. Donaldson
Marquette University
Department of Chemistry, Milwaukee, WI 53201-1881



1 **2** **3**

The preparation and reactivity of **1** (L = CO, PPh_3, NMDPP) with a variety of nucleophiles will be described, as well as synthetic applications of the nucleophilic addition products. Specifically, addition of potassium phthalimide to the dienyl terminus of **1** gave a key intermediate used in the synthesis of a conformationally restricted glutamate analog: *cis*-2-(2'-carboxycyclopropyl)glycine (**3**).

Investigations into the Scope and Origins of Diastereoselectivity in Spirocycle-Forming Intramolecular Heck Reactions.

Larry E. Overman and Donald A. Watson
University of California, Irvine
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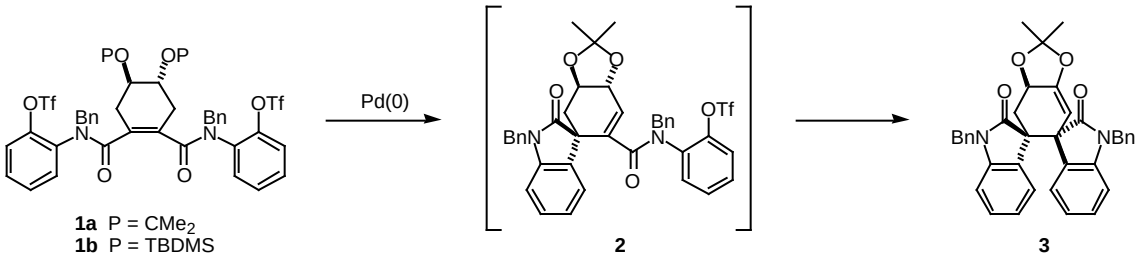
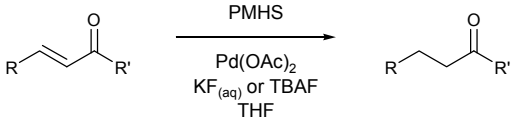
ntramolecular eck reactions that form spirocyclic ring systems in a substrate-directed diastereoselective fashion are rare. Consequently, the origins of the diastereoselection in these systems are poorly understood. The recent report of the diastereoselective double eck cyclization of acetonide **1a** to form **3** has been investigated in greater detail. Several factors contribute to high diastereoselection in this reaction. irst, a moderate preference exists for migratory insertion to occur to form a pseudoaxial C-C bond in conformationally rigid systems. Second, steric interactions vicinal to the site of migratory insertion can reinforce this inherent diastereoselectivity. This latter effect contributes significantly to diastereoselection in the cyclization of **1a**. Third, remote substituent effects of the non-reacting amide substituent of **1a** further modulate the selectivity of the cyclization to form intermediate **2**. Studies of the cyclization of the related TBDMS-protected congener **1b** also will be described.



Chemoselective Conjugate Reduction of α,β-Unsaturated Carbonyl Compounds with Polymethylhydrosiloxane

Jill Muchnij, Robert E. Maleczka, Jr.
Michigan State University
Department of Chemistry, East Lansing, MI 48824

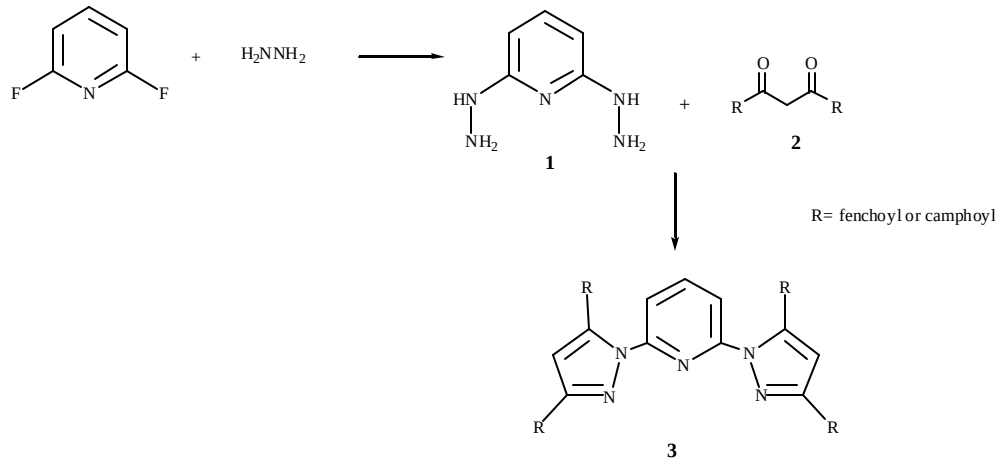
Polymethylhydrosiloxane (PMHS) is a versatile and inexpensive reducing agent. Reaction of PMHS with a fluoride source such as TBAF or $KF_{(aq)}$ allows for formation of the hypercoordinate silicon specie that facilitates reduction under $Pd(OAc)_2$ catalysis. Hypercordinate PMHS allows for selective room temperature 1,4-reductions of α,β-unsaturated carbonyl compounds without the need for additional additives such as copper or tin.



2,6-BIS-HYDRAZINOPYRIDINE AS A REACTANT IN FORMING BIS-PYRAZOLEPYRIDINE LIGANDS

Charles Garner, Kimberly Brien
Baylor University Department of Chemistry and Biochemistry
P.O Box 97348, Waco, TX 76798

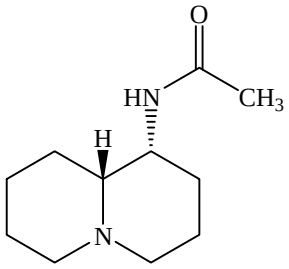
2,6-Bis hydrazinopyridine (**1**) has been made and characterized. The compound was then reacted with both fenchyl and camphor diketones (**2**) to form bis-pyrazolpyridine ligands (**3**). The synthesis of the hydrazinopyridine and the ligands will be described.



EPIQUINAMIDE: A NOVEL NICOTINIC AGONIST FROM AN ECUADORIAN FROG, *EPIPEDOBATES TRICOLOR.*

Richard W. Fitch*, Hugo Martin Garraffo, Thomas F. Spande, Herman J.C. Yeh, and John W. Daly*.
Section on Pharmacodynamics, Laboratory of Bioorganic Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892. Department of Health and Human Services, USA.

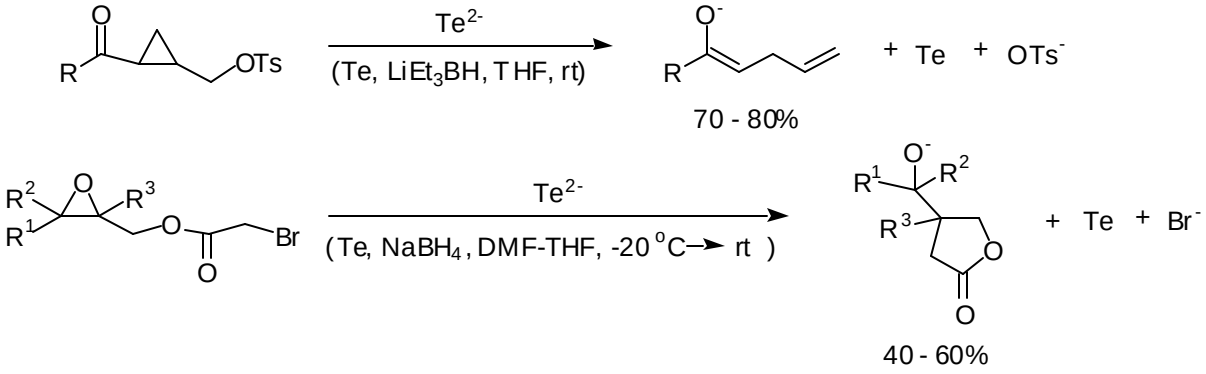
Analytical HPLC fractionation combined with a 96-well fluorescent bioassay screen has been developed and used for the separation and screening of natural product extracts. This method was used to guide the isolation of a novel quinolizidine alkaloid from the methanolic skin extracts of *E. tricolor*. The structure was determined based on MS, IR, and NMR analyses as 1-acetamidoquinolizidine. We have named this compound epiquinamide, reflecting its origin and structure.



TELLURIUM-TRIGGERED REACTIONS OF CYCLOPROPANEMETHANOL DERIVATIVES AND HALOACETATE ESTERS OF GLYCIDOLS

Mahesh G. Malusare, Qun Li, Donald C. Dittmer
Syracuse University
Department of Chemistry, Room 1-014 CST, Syracuse, NY 13244

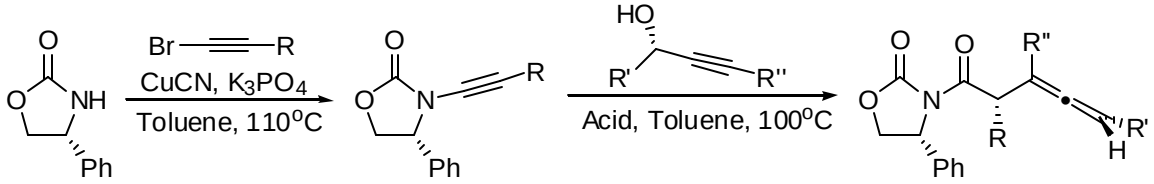
Treatment of acylcyclopropanemethanol tosylates with telluride ion under mild conditions yields ring opened enolates capable of being trapped. Similar treatment of haloacetate esters of glycidols (oxiranemethanols) produces an ester enolate, which can undergo intramolecular reaction with the epoxide ring to yield lactone alcohols. The potential exists for fixing the stereochemistry of specific stereogenic centers.



A Copper-Catalyzed Amidation of Haloalkynes and Subsequent Saucy-Marbet Rearrangement Towards the Synthesis of Chiral Allenes

Michael O. Frederick, Richard P. Hsung, Jason A. Mulder
University of Minnesota
207 Pleasant St. NE
Minneapolis, MN 55455

We have developed a copper-catalyzed amidation of haloalkynes for the synthesis of chiral ynamides in good to excellent yields. Ynamides are a very useful class of organic compounds that can undergo a wide variety of reactions. One such reaction is an acid-promoted Saucy-Marbet rearrangement with propargyl alcohols providing access to chiral allenes.



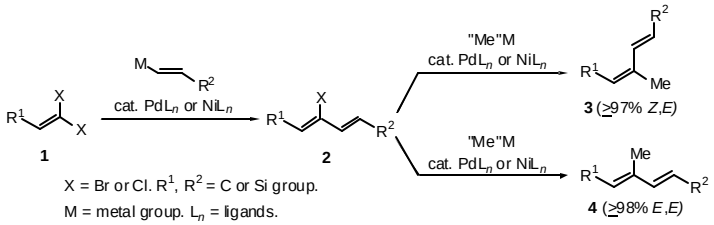
DE NOVO DESIGN OF AN ANTIPARALLEL HOMODIMERIC COILED COIL

Daniel Gurnon, Jennifer Challgren, and Martha Oakley
Indiana Univeristy
Chemistry Dept., Bloomington, IN, 47405

Coiled coils are formed by two or more a-helices wrapped around one another that associate in a parallel or antiparallel relative orientation. Coiled coils occur in nature as the dominant motif in fibrous proteins and as mediators of oligomerization. Synthetic coiled coils have been engineered for applications ranging from affinity purification to the inhibition of viral membrane fusion. For such applications, there is a need for control of coiled coil topology. In contrast to the parallel Leucine Zipper class of proteins, none of the short coiled-coil domains in naturally occurring antiparallel coiled coils have been shown to be sufficient for dimerization without undergoing further self-association [Hollenbeck, J.J.; Oakley, M.G. (2001) COSB *11*, 450-7].We have designed a coiled coil that provides an antiparallel counterpart to the leucine zipper class of peptides. Our design features a charged residue at an interior position, which has recently been shown to specify a dimer at a relatively low cost to stability [McClain, D.L; Gurnon, D.G; Oakley, M.G.; (2002) JMB *324*, 257-70][Campbell, K.M.; Sholders, A.J.; Lumb, K.J. (2002) Biochemistry *41*, 4866-71]. An antiparallel alignment of a-helices is specified through the simultaneous application of Coulombic and hydrophobic components at the helical interface. The resulting peptide, NAPH, forms a highly stable antiparallel homodimer as judged by CD and equilibrium sedimentation experiments. Chemical denaturation experiments show the designed peptide to be 2 kcal/mol more stable than the parallel Leucine Zipper GCN4. In addition, unlike many model coiled coils, the antiparallel homodimer can be expressed in bacterial cells .

Pd-Catalyzed Highly Stereoselective Tandem Alkenylation-Alkylation of 1,1-Dihalo-1-alkenes to Give Conjugate Dienes Containing either an *E*- or a *Z*- Trisubstituted Alkene Moiety

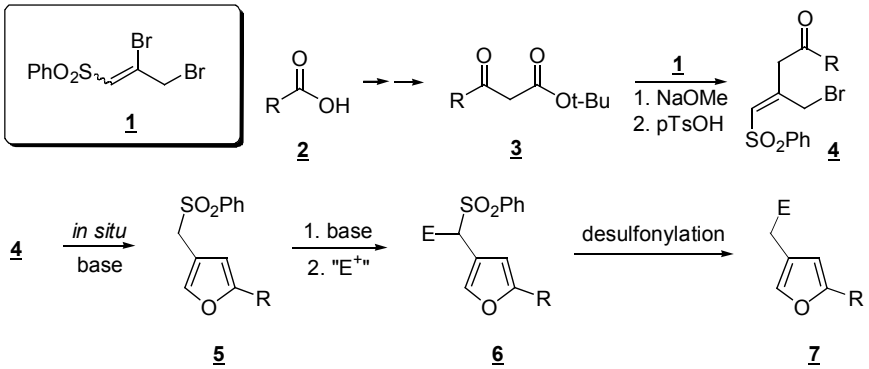
*Xingzhong Zeng, Qian Hu, Mingxing Qian, Ei-ichi Negishi**
Herbert C. Brown Laboratories of Chemistry,
Purdue University, West Lafayette, IN 47907



Herein we report an unprecedented tandem *trans*-selective alkenylation-methylation process of 1,1-dihalo-1-alkenes (**1**) leading to the synthesis of conjugate dienes containing either an *E*- or a *Z*-trisubstituted alkene moiety (**3** or **4**). In cases where conventional catalysts for Pd-catalyzed cross-coupling, such as $Pd(PPh_3)_4$, $Pd(TFP)_2Cl_2$ and $Pd(dppf)Cl_2$ as well as more recently introduced Pd catalysts, such as $Pd(DPEphos)Cl_2$, are used, methylation with either MeZnBr or MeZnCl is accompanied by nearly complete stereoisomerization ($\geq$97%) leading to the formation of *Z*-trisubstituted alkenes. This tandem alkenylation-methylation sequence can be achieved either in one pot or in two steps. In sharp contrast with these results, stereoselective synthesis of 2-halo-1,3-dienes (**2**) as in the above tandem reaction followed by methylation in a separate step in the presence of a catalytic amount of $Pd(t\text{-}Bu_3P)_2$ leads to complete retention of stereochemistry to afford conjugated dienes containing $\geq$98% *E*- trisubstituted alkene moiety.

2,3-DIBROMO-1-(PHENYLSULFONYL)PROPENE (DBP) AS A VERSATILE REAGENT FOR THE PREPARATION OF 2,4-DISUBSTITUTED FURANS

Aaron VanZanten, Ryan Harrington, Adam Kiefer, David Carlson, Bill Andrews, Claude Ogoe and S. Shaun Murphree
Department of Chemistry, Allegheny College, 520 N. Main St., Meadville, PA 16335

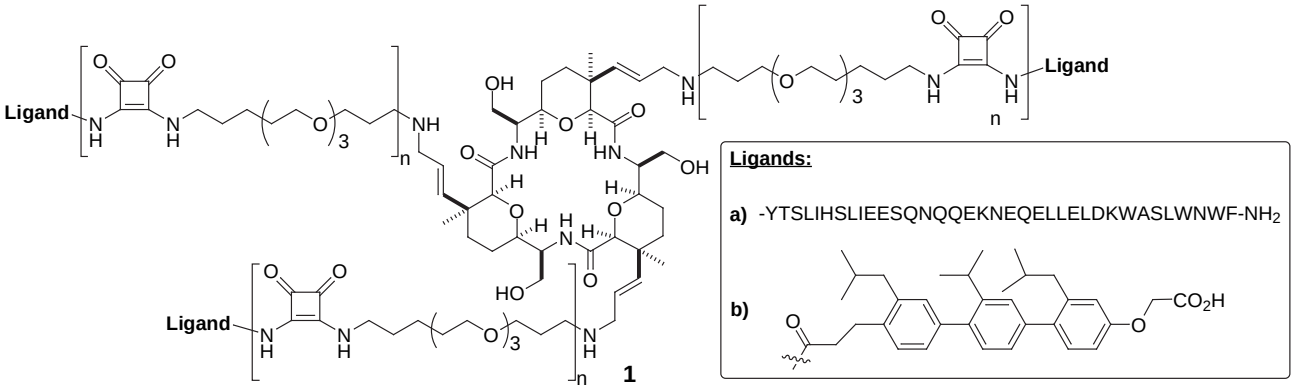


Carboxylic acids (**2**) are converted to 1,3-ketoesters by known methodologies. These active methylene compounds add to the vinylic position of 2,3-dibromo-1-(phenylsulfonyl)propene (DBP, **1**) to form Michael adducts (**4**), which cyclize under basic conditions to afford 2,4-disubstitued furans (**5**). Deprotonation at the α-sulfonyl position furnishes a stabilized carbanion, which may be captured by a variety of electrophiles (**"E^+"**) to give the adducts **6**. Subsequent desulfonylation yields 2,4-disubstitued furans (**7**) with variable substitution at the 2- and 4-positions.

Toward the Synthesis of a C_3-Symmetric Trivalent HIV-gp41 Ligand

*Andrew J. Hawk and Steven D. Burke**
University of Wisconsin – Madison
Department of Chemistry, Madison, WI 53706

The HIV entry process, directly directly by the homotrimeric fusion protein gp41, is a promising therapeutic target recently focused on by many researchers. However, many aspects of the mechanism remain unclear. A convergently oriented trimeric ligand display would aid in the elucidation of the interactions between trimeric the HIV envelope glycoprotein complexes in pore formation. Previous work in the Burke group involving ligand displays on C_3-symmetric scaffolds suggest that triamide macrocycles **1** would be ideally suited trimeric ligand displays for gp41. These ligand displays allow for variation both in linker and ligand on a well-defined scaffold. Synthetic efforts toward the scaffold and more detailed context will be presented.

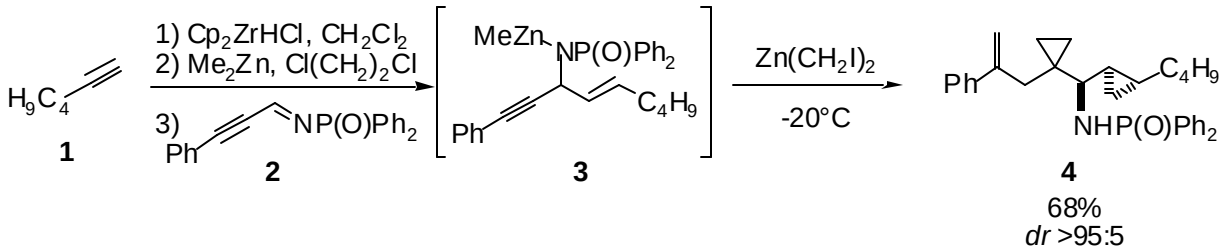


1

Cascade Synthesis of Functionalized Amino Cyclopropanes

Corey R. J. Stephenson, Kazuo Okumura and Peter Wipf
University of Pittsburgh, Department of Chemistry, Pittsburgh, PA 15260

The dimethylzinc mediated addition of alkenyl zirconocenes to α-β-acetylenic imine **2** provides metalated amide **3** (not isolated) which subsequently reacts with iodomethylzinc to afford compound **4** in good yield and excellent diastereoselectivity. During the course of this reaction, 9 new carbon-carbon bonds are formed incorporating 5 methylene units into the product **4**. The scope of the reaction along with mechanistic details will be presented.



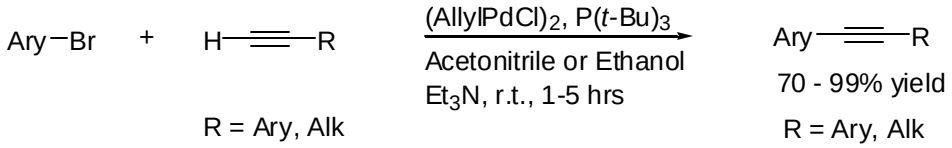
1 **2** **3** **4**

68%
dr >95:5

Mild Copper-Free Sonogashira Coupling of Aryl Bromides

Arash Soheili*, Jennifer Albaneze-Walker, Jerry A. Murry, Dave L. Hughes, and Rich Tillyer
Process Research, Merck Research Laboratories
Rahway, New Jersey 07065

We recently required a robust aryl halide alkyne coupling in conjunction with the synthesis of a drug candidate. Employing literature procedures with copper as a co-catalyst resulted in Glaser homocoupling of alkyne as a significant side reaction. The use of zinc as a co-catalyst produced only moderate yields. Copper free conditions as reported by Herrmann (*Eur. J. Org. Chem.* **2000**, 3679-3681), resulted in large amount of alkyne polymerization. Therefore, it seemed necessary to develop new reaction conditions to accommodate this transformation. A screen of solvents showed that the most rapid coupling times were obtained in either ethanol or acetonitrile. Tri-alkyl bases like triethylamine afforded the fastest reaction time while inorganic bases like cesium carbonate resulted in low yields. The best system for conversion of aryl bromides was found to be $(AllylPdCl)_2$ with $P(t\text{-}Bu)_3$ in acetonitrile with triethylamine as the base. In this poster we present the optimized Sonogashira coupling of several terminal acetylenes with a variety of aryl bromides. Reactions proceed at room temperature with good to excellent yields.

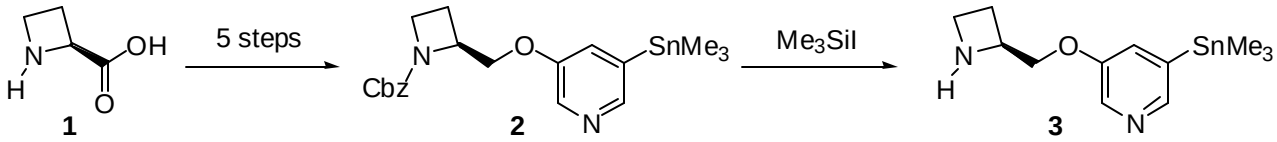


SYNTHESIS OF A NEW 5-IA PRECURSOR USING TRIMETHYLSILYL IODIDE AS BENZYLOXYCARBONYL DEBLOCKING AGENT

Eric Brenner, Ronald M. Baldwin and Gilles Tamagnan
Yale University, School of Medicine, VA Connecticut HCS (116A2)
950 Campbell Avenue, New Haven, CT 06516

The iodinated analog (*S*)-5-[^{123}I]iodo-3-(2-azetidinylmethoxy)pyridine of A-85380 ([I^{123}]5-IA) is a new SPECT tracer studied on human subjects because of its high specificity for the a_4b_2 subnicotinic acetylcholine receptors, which play an important role in neurodegenerative diseases and in tobacco dependence. At present the methods described in the literature require two steps to afford [I^{123}]5-IA, one step to label a *N*-protected precursor and another one to release the amino group.

We realized the synthesis of a new precursor **3**, obtained in 64% overall yield in six steps starting from (*S*)-2-azetidine carboxylic acid **1**. The key step of this synthesis is the last one with the release of the amine function using iodotrimethylsilane since no reaction occurs by catalytic hydrogenolysis. The last step afford **3** in 92% yield without removal of the stannyl moiety. This new precursor presents the advantages to be synthesized in good overall yield and to lead directly [I^{123}]5-IA after the labeling step.



REGIOSPECIFIC SYNTHESIS OF d3 AND d6 *RRR*-gamma-TOCOPHEROL FOR *IN VIVO* STUDIES OF TOCOPHEROL METABOLISM

Rachel Parsons and Jeffrey Atkinson
Department of Chemistry and Centre for Biotechnology, Brock University, St.Catharines, Ontario, Canada, L2S 3A1

Tocopherols are widely distributed plant lipids that exist as a family of four differentially methylated chromanols known as alpha-, beta-, gamma- and delta-tocopherol. Despite obtaining large amounts of gamma-tocopherol, mammals differentially retain alpha-tocopherol in their tissues due to a selective uptake of this isomer, and the fast metabolism and excretion of gamma-tocopherol. One of the most useful techniques to follow the fate of ingested tocopherols in mammals is the use of specifically deuterated forms, which allow the mass spectral analysis of fractions extracted from plasma. We have previously prepared dideuterated gamma-tocopherol by the reduction of a chromene form of the vitamin, but it would be useful to have three or more deuterons in the biological tracer to enable more facile mass spectral analysis and also more sophisticated experiments with other tocopherols and stereoisomers. Synthesizing the trideuteromethyl version of gamma-tocopherol is difficult because of the unfavourable regiochemistry involved in preparing either the 7,8-dimethylchroman structure from tocol or 2,3-dimethylhydroquinone, which is a precursor for a condensation with phytol during the preparation of vitamin E. In order to circumvent this problem we have devised a way of preparing 2,3-di(trideuteromethyl)-1,4-hydroquinone using the cyclobutendione methodology of Leibeskind and Moore. In brief, the diisopropyl ester of squaric acid is reacted with two equivalents of trideuteromethyl lithium in separate steps with appropriate protection of intermediates to prepare a di(trideuteromethylcyclobutenedione that when reacted with acetylide and ring expanded by thermolysis provides the required hydroquinone. Preparation of the complete tocopherol utilizes Trosts chiral palladium catalysts followed by ring closure.

AN EFFICIENT SYNTHESIS OF A DOXORUBICIN-PEPTIDE CONJUGATE AND THE EFFECT OF MIXING ADDITIVES ON EDC-MEDIATED AMIDE FORMATION

D.R. Lieberman[1], B.C. Bishop[1], M.C. Cameron[2], I.F.Cottrell[1], U.H. Dolling[2], D. Hands[1], J.E. Lynch[2], R.A. Reamer[2], M.A Robbins[2], Y.-J Shi[2], R.P. Volante[2] and R.D. Wilson[1]

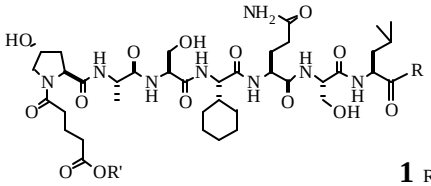
[1]Department of Process Research, Merck Sharp and Dohme

[1]Hertford Road, Hoddesdon, EN11 9BU, UK

[2]Department of Process Research, Merck Research Laboratories

[2]PO Box 2000, Rahway, NJ 07065

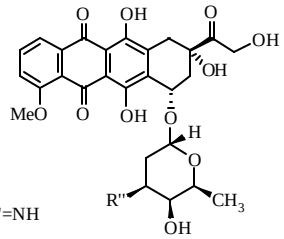
An efficient synthesis of the sodium salt of the doxorubicin-peptide conjugate **1**, useful for the treatment of prostate cancer is described. The EDC-mediated amide formation between the heptapeptide (**2**) and doxorubicin (**3**) as the key step has been extensively studied employing peptide-coupling additives, such as 1-hydroxybenzotriazole (HOBt), 1-hydroxy-7-azabenzotriazole (HOAt) and 2-hydroxypyridine N-oxide (HOPO). Surprisingly, mixing the additives HOAt and HOPO produced the best results.



2 R=OH; R'=Fm

Heptapeptide chain

1 R=Dox; R'=H; R''=NH



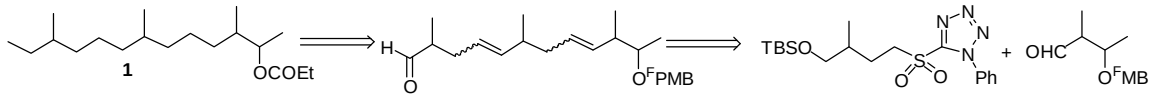
3 R''=NH_2

Doxorubicin moiety

Application of Fluorous Mixture Synthesis for Accessing Natural Products and Their Stereoisomers – Total Synthesis of Sixteen Stereoisomers of Sex Pheromone of Pine Sawfly.

Sivaraman Dandapani, Mario Jeske, Dennis P. Curran
Department of Chemistry, University of Pittsburgh, Pittsburgh, PA 15260

The sex pheromone of pine sawfly (**1**) has four stereocenters and hence a total of sixteen possible stereoisomers. All the sixteen stereoisomers have been synthesized by split-parallel Fluorous Mixture Synthesis (FMS). Four different fluorous *p*-methoxy benzyl protecting groups were used as tags. Julia olefination was used as the key segment coupling reaction.



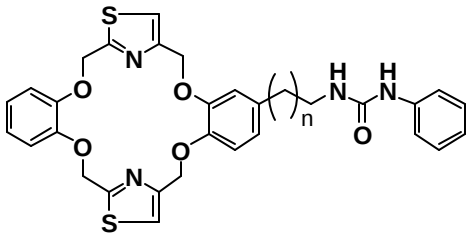
DESIGN AND SYNTHESIS OF NEW THIAZOLE-CONTAINING, GABA SELECTIVE IONOPHORE

Hong-Seok Kim, Ki Soo Kim, Young-Rea Yi

Kyungpook National University

Department of Industrial Chemistry, Taegu 702-701, Korea

GABA (γ-butyric acid) is the well known inhibitory neurotransmitter in the mammalian central nervous system where it exerts its effects through ionotropic ($GABA_{A/C}$) receptors, to produce fast synaptic inhibition. A novel ditopic receptor in which thiazolodibenzocrown ether (TDBC) and urea are connected with methylene spacers has been synthesized and characterized The binding studies of ditopic TDBC receptors were carried out with ^1H NMR experiment for amino acids including β-alanine, GABA, and 6-aminocapric acids.



An Azophenol Based-Chromogenic Pyrophosphate Sensor in Water

Dong Hoon Lee, Ja Hyun Im and Jong-In Hong*

School of Chemistry, College of Natural Sciences, Seoul National University, Seoul 151-747, Korea

Pyrophosphate anion (PPi), in particular, participates in several bioenergetic and metabolic processes, such as the synthesis of cyclic AMP as a second messenger from ATP with the concomitant release of PPi and the production of calcium pyrophosphate dihydrate (CPPD) crystals. It is these crystals deposition that are frequently detected in patients with osteoarthropathy or pseudogout. This diversity of function, both beneficial and otherwise, is why the detection of PPi is the main focus of many research groups today. While PPi analyses such as ion chromatography remains important, there is mounting incentive to find alternative means of analysis, including those based on the use of selective chemosensors. Particularly useful would be systems that can recognize PPi in an aqueous solution and signal its presence via an optical signal. We present a new azophenol-based chromogenic PPi sensor, which shows a high sensitivity and selectivity for PPi over other anions in aqueous solvent of wide pH range.

Synthesis and Diffusion Measurements of
Flexible Tetraether Acyclic Bisphosphocholines.

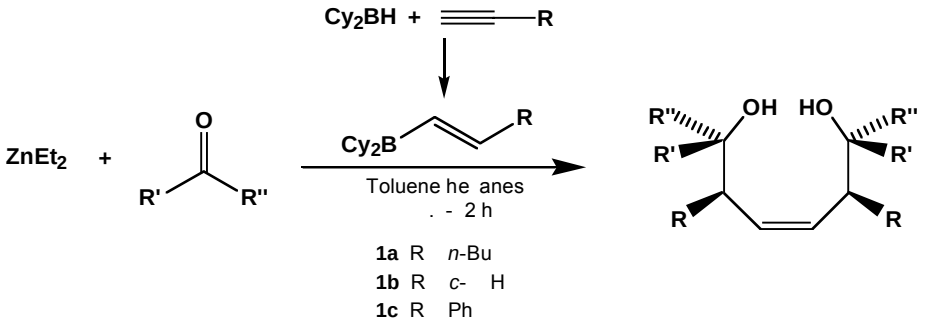
Febo-Ayala, Wilma; Bradley, Scott A.; Patwardhan, Aniruddha; Thompson, David H.
Purdue University, Department of Chemistry, West Lafayette, IN 47907

Tetraether bisphosphocholines (also known as bolaamphiphiles) are underway via an efficient synthesis for structure-function determination studies. Prior studies from this lab have shown that fluid phase bolaamphiphile vesicles are impermeable to encapsulated ions on the days timescale. This property makes these materials promising candidates for the development of stabilized bolaamphiphile-based supported membrane sensors, since they will produce films that are more stable than conventional supported bilayer membranes, while retaining lateral mobility in the membrane phase. We will apply pulsed-field gradient NMR (PFG-NMR) methods for the determination of lateral diffusion coefficients for vesicles made from tetraether bolaamphiphiles. These studies are aimed at developing an understanding of how bolaamphiphile molecular structure affects the diffusion coefficients of these compounds and to correlate these properties with the physical stability of their membranes.

A One-Pot Diastereoselective Synthesis of *cis*-3-Hexenes-1,6-diols via an Unusually Reactive Organozinc Intermediate

*Celina García, Eric R. Libra, Patrick J. Carroll, and Patrick J. Walsh**
P. Roy and Diane T. Vagelos Laboratories, Department of Chemistry, University of Pennsylvania, 231 South 34th Street, Philadelphia, PA 19104-6323

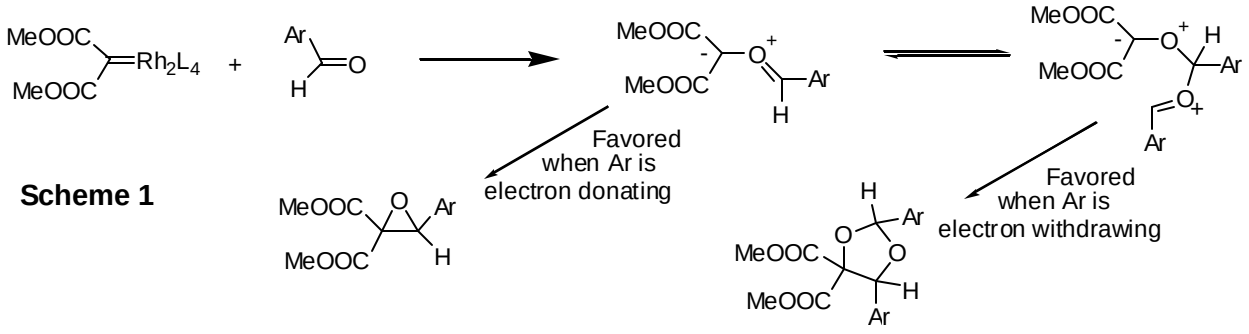
highly diastereoselective method for the synthesis of *cis*-3-hexene-1, -diols has been developed. The diols are made in a one-pot procedure involving hydroboration of a terminal alkyne and transmetalation to zinc to give a divinylzinc intermediate. This intermediate undergoes reductive elimination, forming a C C bond. n the presence of ketones or aldehydes, the proposed intermediate metallocyclopentene is trapped via a double insertion of the carbonyl substrate. orkup provides the *meso*-1, -endiols in 4 - yield. This new reaction proceeds with excellent control of diastereoselectivity over four stereocenters and the double bond geometry.



Structural Effects in Reactions of Diazo-Carbonyl Compounds with Aldehydes

Jonathan A. Brekan, Michael P. Doyle
University of Arizona
Department of Chemistry, Tucson, AZ 85721-0041

We have recently demonstrated epoxide formation in the dirhodium(II)-catalyzed [2+1]-cycloaddition of aldehydes/ketones with the carbene derived from methyl styryldiazoacetate (***Organic Lett.*** **2001**, ***3***, 933). Product yields were high, and this reaction was extended to aziridine formation from imines. We have now extended this reaction methodology to reactions of vinyl ether analogues of vinyldiazoacetates, as well as to diazoacetoacetates and diazomalonate. We observe epoxide formation from diazomalonate in high yields and are able to direct product formation to dioxolanes. Diazoacetoacetates form dioxolenes.



Scheme 1

Studies Toward the Synthesis of Azadirachtin: Successful Formation of the Crowded C8-C14 Bond Using Radical and Organometallic Chemistry

K.C. Nicolaou,[1,2] A.J. Roecker,[1] Markus Follmann,[1] Holger Monenschein,[1] Prasuna Guntupalli,[1] Kevin W. Hunt,[1] Rachid Baati[1]

[1] The Scripps Research Institute
Department of Chemistry and The Skaggs Institute for Chemical Biology
La Jolla, CA 92307

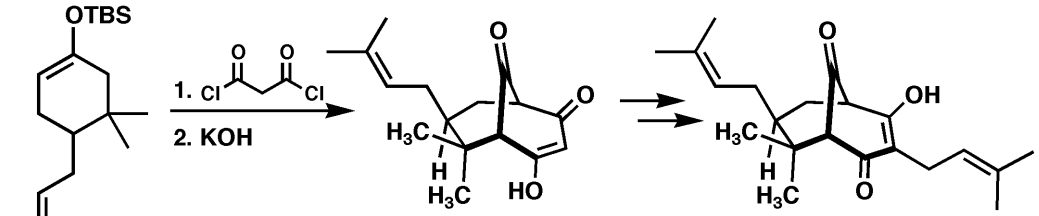
[2] University of California, San Diego
Department of Chemistry and Biochemistry
La Jolla, CA 92093

Isolated from the seeds of the neem tree, azadirachtin exhibits potent insect antifeedant activity and growth inhibitory properties across a broad range of insect species while having low mammalian toxicity. Due to these important biological actions and its imposing molecular architecture, azadirachtin has elicited considerable interest from the synthetic community. Despite nearly twenty years of effort, azadirachtin still remains elusive to total synthesis, with its crowded C8-C14 bond bridging its two domains being the main obstacle. Herein, we will report successful model studies on an intramolecular formation of the C8-C14 bond of azadirachtin via radical and organometallic chemistry.

Progress toward the Total Synthesis of Garsubellin A and Related Phloroglucins

Sarah J. Spessard, Govindasamy Sekar, and Brian M. Stoltz*
California Institute of Technology
Division of Chemistry and Chemical Engineering, Pasadena, CA 91125

A highly diastereoselective single-step cyclization reaction provides access to the bicyclo[3.3.1]nonane core of the polyprenylated natural product garsubellin A. Further elaboration to a more functionalized analogue involves a sequential Claisen rearrangement/Grubbs olefin metathesis strategy. Additionally, this strategy can be extended to the preparation of the bis-quaternary carbon array found at the bridgehead positions of the phloroglucin natural products. Progress on a more stepwise approach will also be discussed.



Relative Stereoconfiguration Determined by X-Ray

Utilization of the [2,3] Still-Wittig Rearrangement to Transform 2- to 2,3- Substituted Furan Derivatives

Patrick Caruana, Alison J. Frontier
University of Rochester, Department of Chemistry, Rochester, NY 14627

Substituted furans are important building blocks in the synthesis of natural products; yet the efficient synthesis of certain substitution patterns can be elusive. For example, 2,3- di and 2,3,5- trisusbtituted furan systems are often difficult to access. The application of the [2,3] Still-Wittig rearrangement as a solution to this problem is described. The scope, utility, and details of this transformation will be presented, along with potential applications to the synthesis of natural products.

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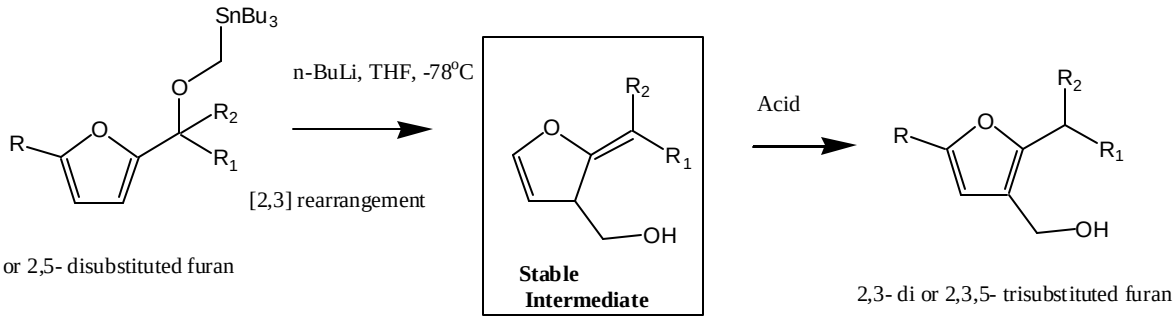
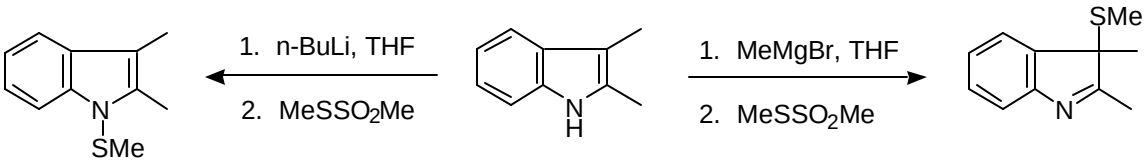


REGIOCONTROLLED SULFENYLATION OF METALLATED INDOLES WITH METHYL METHANETHIOSULFONATE

Jonathon S. Russel, Julie M. Gapinski, Jeremy O. Swanson, Matthew W. Soyk
Division of Natural Science, Saint Norbert College
100 Grant Street, De Pere, WI 54115

The preparation of 3-methylsulfenylindoles and 2,3-dialkyl-3-methylsulfenylindolenines has been reported using methanesulfenyl chloride as the sulfenylating agent. These procedures are complicated by the necessity of generating methanesulfenyl chloride from toxic precursors (e.g., sulfuryl chloride and dimethyl disulfide or methanethiol and chlorine gas) that require special handling. We have found that commercially available methyl methanethiosulfonate is a convenient reagent for sulfenylation of metallated indoles. Sulfenylation can be directed selectively to indole C3 using indole magnesium salts. Alternatively, treatment of the corresponding lithium salts of indole with methyl methanethiosulfonate affords N-sulfenylindoles.

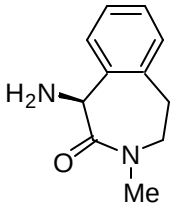


Crystallization-Induced Asymmetric Transformation of Aminoazepinones

Thomas M. Koenig, David Mitchell,* Lynne A. Hay, Andrew H. Fray, William D. Miller, [1]James E. Audia, [1]Jeffrey S. Nissen, [1]Stacey L. McDaniel, [1]Almudena E. Rubio, [1]Melinda J. Hope

Global Chemical Process R&D, [1]Discovery Chemistry Research, Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, Indiana 46285

Two efficient and practical syntheses of structurally similar aminobenzoazepinone (**1**) and aminophenylazepinone (**2**) were established providing the enantiopure compounds via a crystallization-induced asymmetric transformation (dynamic resolution). This resolution process, when applicable provides an attractive alternative to the classical resolution or asymmetric synthesis. Racemic aminobenzoazepinone (**1**) was prepared with >98% *ee* and in >80 % yield. Racemic aminophenylazepinone (**2**) was resolved with 97% *ee* and in 72% yield.



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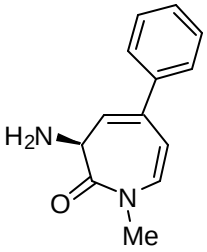


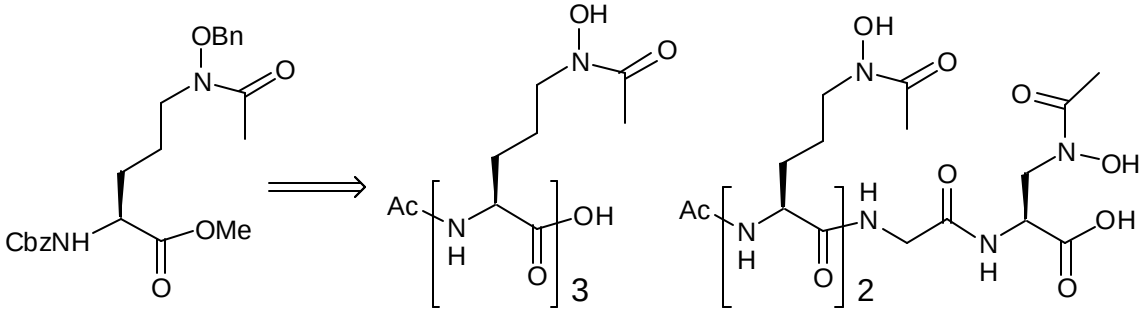
2

A Highly Convergent Synthesis for Hydroxamate-Derived Siderophores

Pingyu Ding, Paul Helquist, Marvin J. Miller

Walther Cancer Research Center, University of Notre Dame, Notre Dame, IN 46556

Siderophores are secreted by organisms as microbial iron transport agents to solubilize iron(III) under iron-deficient conditions. Hydroxamate-based siderophores form strong, selective complex with Fe(III). Syntheses of siderophores as drug delivery agents and diagnostic agents are of considerable interest. In our effort to synthesize new hydroxamate-derived siderophores, we have recently synthesized the fully protected amino acid (**1**) from L-ornithine in good yield. This compound served as useful synthetic intermediate for the synthesis of the corresponding dipeptide and tripeptides in excellent yields. Using this method, siderophores **2** and **3** were efficiently prepared. This method could also be extended for the synthesis of their analogues.



1 **2** **3**

Phenyl Thiazolyl Urea and Carbamate Derivatives as New Inhibitors of Bacterial Cell Wall Biosynthesis

Zhong Li, Gerardo D. Francisco, Nancy H. Eudy, J. Donald Albright, Alan Katz, Pornpen Labthavikul, Peter Petersen, Anatory Severin, Guy Singh, Youjun Yang, Beth Rasmussen, Yang-I Lin, Tarek S. Mansour

Chemical Sciences and Infectious Diseases, Wyeth Research

Pearl River, NY 10965, USA

Over fifty phenyl thiazolyl urea and carbamate derivatives were synthesized for evaluation as new inhibitors of bacterial cell wall biosynthesis. Many of them demonstrated good activity against MurA and MurB and gram-positive bacteria including MRSA, VRE and PRSP. 3,4-Difluorophenyl 5-cyanothiazolyl urea with clog P of 2.64 demonstrated antibacterial activity against both gram-positive and gram-negative bacteria.

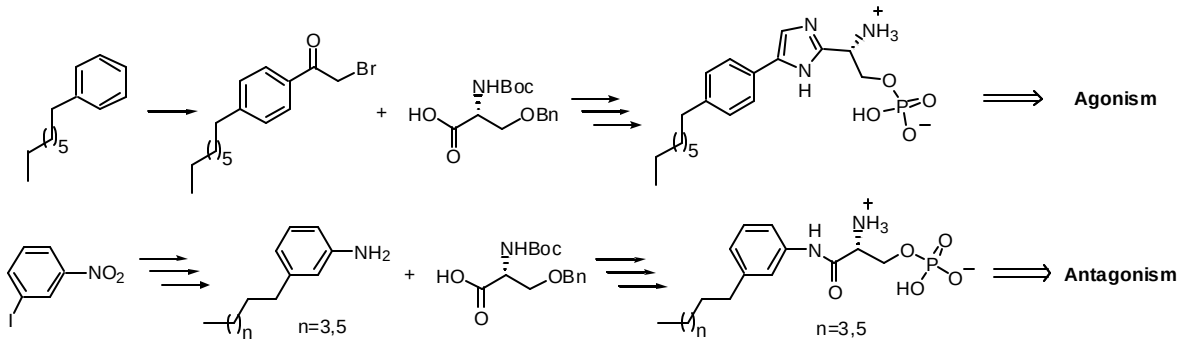
Design and Synthesis of Novel, Subtype-Selective Sphingosine-1-Phosphate Receptor Agonists and Antagonists

***Jeremy Clemens*[1], *Michael D. Davis*[2], *Kevin R. Lynch*[2], *Timothy L. Macdonald*[1]**

(1) Department of Chemistry, University of Virginia, P.O. Box 400319, McCormick Road, Charlottesville, VA 22904-319, Fax: 434-982-2302, jjc3n@virginia.edu;

(2) Department of Pharmacology, University of Virginia

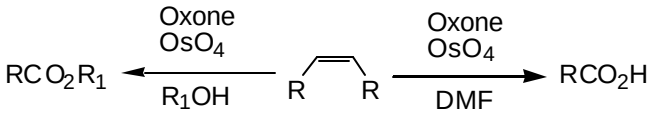
Sphingosine-1-phosphate (S1P), an intercellular signaling molecule as well as an intracellular second messenger, is regarded as an important regulator in a wide variety of biological functions including platelet aggregation, wound healing, immune modulation, and angiogenesis. Extracellular S1P induces biological effects through its interaction with five specific seven transmembrane G-protein coupled receptors, namely $S1P_{1\text{-}5}$. Structure-activity relationship (SAR) studies on S1P have led us to the synthesis of potent $S1P_1$, $S1P_4$, and $S1P_5$ agonists as well as $S1P_1$ and $S1P_3$ antagonists. Synthetic strategies towards the biologically active molecules will be described.

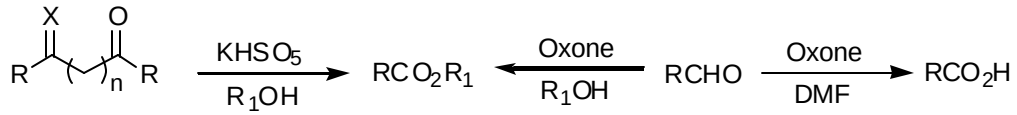


NOVEL OXIDATIVE PATHWAYS UTILIZING OSMIUM TETROXIDE AND OXONE

Benjamin R. Travis, Babak Borhan
Michigan State University
Department of Chemistry, East Lansing, MI 48824

OsO_4 is a well studied catalytic oxidizing agent primarily used to prepare vicinal diols form olefins via the UpJohn procedure. These intermediate diols are also well known to undergo C-C bond cleavage through the addition of co-oxidant's like $NaIO_4$ to prepare aldehydes. However, the direct oxidative cleavage of olefins that mimics ozonolysis has not been a productive process. A focus in our laboratory is to cleave olefins directly to prepare aldehydes, acids, esters and lactones by using catalytic OsO_4 and other appropriate co-oxidants. Additionally, we have identified that α- and β-diones or ketols also undergo similar oxidative scission albeit without OsO_4. Recent progress towards the preparation of aldehydes, acids, esters and lactones, along with mechanistic studies and practical applications of such chemistry will be discussed.



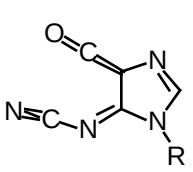


X = O or OH,H
n = 0,1

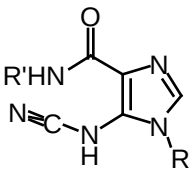
SYNTHESIS OF 5-CYANOIMINO-IMIDAZOLE-4-CARBOXAMIDE AND THEIR CYCLIZATION TO PURINES

Ming Qian and Rainer Glaser*
Department of Chemistry, University of Missouri-Columbia, Columbia, Missouri 65211

ur theoretical studies suggest that the dediazoniation of guaninediazonium ion occurs with concomitant pyrimidine ring-opening and deprotonation to form cyanoimines **1**. e are now testing our hypothesis experimentally. Since compounds **1** are extremely reactive, we are exploring the chemistry of their addition products, the cyanoamines **2**. Specifically, we synthesized cyanoimine **2** (C $_2$- -C $_2$- C $_2$- ,) from **3** and characterized *pure* **2** by M , , MS and MS MS. e found that **2** easily cyclizes to guanines **4** and isoguanines **5**. f the acid were used instead of the carboxamide **2**, then oxanosine and xanthine were formed in analogy to the formations of **4** and **5**, respectively. ence, the present results support our hypothesis that guanine deamination may involve pyrimidine ring-opening and reclosure. f the reaction of **1** to **2** involved a D base (, C or) as the primary amine, then this guanine formation would result in a cross-link. The model reaction of **2** to **4** with thus provides a first indication of the possible existence of a new class of cross-links.



1



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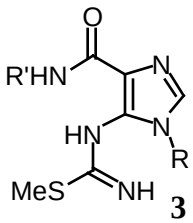

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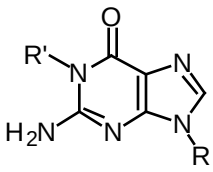

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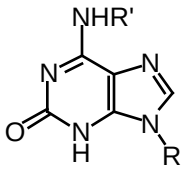


5

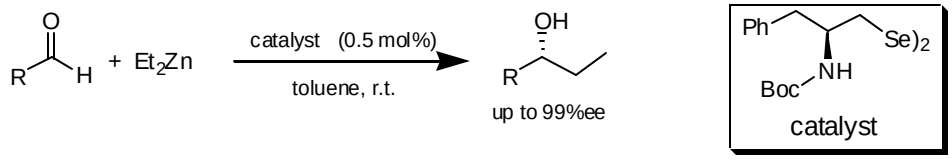
Synthesis of New Chiral Aliphatic Amino Diselenides and their Application as Catalysts in the Enantioselective Addition of Diethylzinc to Aldehydes

Antonio L. Braga,* Marcio W. Paixão, Diogo S. Lüdtke, Claudio C. Silveira and Oscar E. D. Rodrigues.

Departamento de Química, Universidade Federal de Santa Maria, Santa Maria, RS, 97105-900, Brazil

The catalytic enantioselective addition of diethylzinc to prochiral aldehydes has proven to be a useful strategy to obtain optically active secondary alcohols. Over the past years many chiral catalysts have been designed and successfully used in this reaction.

Herein we report the synthesis of a new set of chiral aliphatic ß-amino diselenides starting from commercially available natural L-aminoacids in a short synthetic route. These ß-amino diselenides were used in the diethylzinc addition to several aldehydes and the secondary alcohols were obtained in high yields and up to 99% *ee*.



Details of the ligands synthesis as well as the asymmetric diethylzinc addition will be presented.

FACILE SINGLE-POT PREPARATION OF TERTIARY AMINES USING NOVEL TITANIUM (IV) ISOPROPOXIDE AND SODIUM BOROHYDRIDE REAGENT SYSTEM

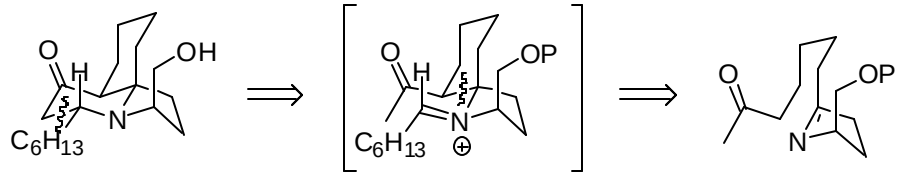
Hephzibah J. Kumpaty*, Sukanta Bhattacharyya[1]
(*Department of Chemistry, University Of Wisconsin-Whitewater, WI, 53190;
[1]Argonaut Technologies, 887 Industrial Road, Suite G, San Carlos, CA 94070)

Development of mild and effective reagent system for the reductive amination reactions remains as an important theme in chemical research. Methods available in the literature for the generation of tertiary amines suffer from several limitations such as their compatibility with acid sensitive functional groups, cost, toxicity and the difficulty involved in the work-up procedure. We herein report a high yielding one-pot procedure for the synthesis of N-alkyl tetrahydroisoquinoline derivatives using a novel reagent system titanium (IV) isopropoxide/sodium borohydride. Remarkable advantages of the present method include mild, neutral non-aqueous reaction conditions, simple work-up procedure and the use of safe and inexpensive reagents. In our research we have tried both conventional and microwave methods for the synthesis of tertiary amines. Microwave conditions gave only 40-50 % product yields; however, conventional reaction conditions provided excellent yields. Experimental and reaction details will be discussed.

The Study Toward an Enentioselective Total Synthesis of (+)-Cylindricine C via. Tandem Mannich Condensation Strategy

Jia Liu, Richard Hsung
Department of Chemistry, University of Minnesota
Minneapolis, MN 55455

The investigation of a new approach toward an enantioselective total synthesis of (+)-cylindricine C via. an intramolecular tandem Mannich condensation strategy will be presented.

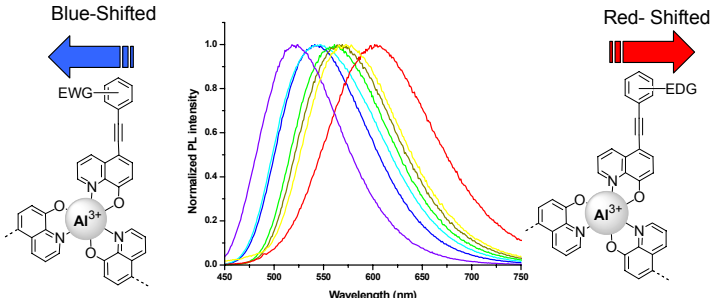


(+)-cylindricine C

SYNTHESIS OF AlQ_3 DERIVATIVES WITH EXTENDED TUNABLE CHROMOPHORES

Radek Pohl, Victor Montes and Pavel Anzenbacher, Jr.
Bowling Green State University
Department of Chemistry and Center for Photochemical Sciences. Bowling Green, OH 43402.

8-quinolinolate aluminum(III) (AlQ_3) is an important electroluminophore of great utility in the fabrication of OLED-based displays. The fabrication of full color OLED-based displays is predicated upon availability of suitable red, green, and blue emitters. We present our strategy toward synthesizing quinolinolate-based electroluminophores with tunable emission wavelengths via attachment of electron-donating or –withdrawing aryl or arylethynyl substituents to the 5-position of the quinolinolate ligand. Methods for the synthesis of 5-aryl and 5-arylethynyl-8-hydroxyquinolines were developed using Sonogashira-Hagihara, Suzuki, and Stille couplings. The synthesis departs from an O-protected 5-bromoquinolinolate derivative followed by Pd-mediated couplings and selective deprotection. The protective groups were selected with respect to coupling conditions and subsequent easy removal. The synthetic strategy also includes different pathways for the synthesis of electron-deficient and electron-rich ligands. A successful tuning in the emission color was achieved: the emission wavelength was found to correlate with the Hammett constant of the respective substituents, providing a powerful strategy for prediction of the optical properties of new electroluminophores.



NOVEL STEREOSELECTIVE SYNTHESIS OF 1-(β-D- AND α-L-GLYCOPYRANOSYL)-5-METHYL-1H-1,2,4-TRIAZOLES

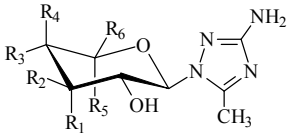
Jianxin Yu[a*], Zhongjun Li[b] Wenjie Lu[c] Suna Zhang[b] Mengshen Cai[b]

[a] Department of Radiology, The University of Texas Southwestern Medical Center at Dallas, 5323 Harry Hines Blvd., Dallas, Texas 75390-9058, E-mail: Jian-Xin.Yu@UTSouthwestern.edu

[b] School of Pharmaceutical Sciences, Peking University, Beijing 100083, China

[c] Department of Chemistry, Wuyi University, Jiangmen 529020, China

1-*β*-D-ribofuranosyl-*1H*-1,2,4-triazole-3-carboxamide (Virazole, Ribavirin®), a broad spectrum antiviral agent, also inhibits replication of HIV in human T lymphocytes and displays some antitumor activity in mice. Thus synthesis approaches to this molecule and its related derivatives have attracted considerable attention[1~3]. Here, We report facile, novel procedures for the stereoselective synthesis of 1-(*β*-D- and *α*-L-glycopyranosyl) -5-methyl-*1H*-1,2,4-triazoles **1**~**3**, which are closely related to 1-*β*-D-ribofuranosyl-*1H*-1,2,4-triazole-3-carboxamide and present preliminary *in vitro* antitumor and immuno activities.



1 $R_1=R_4=R_5=R_6=H$, $R_2=R_3=OH$
2 $R_1=R_4=OH$, $R_2=R_3=R_6=H$, $R_5=CH_3$
3 $R_1=R_4=R_5=H$, $R_2=R_3=OH$, $R_6=CH_2OH$

[1] Fuertes, M.*et al.*, *J. Carb. Nucl.*, **1996**, 3, 169. [2] Smith, R. A.; Kirkpatrick, W.(*Eds*.), *Ribavirin, a Broad Spectrum Antiviral Agent*, Academic Press, New York, **1980**. [3] Smith, R. A.; Knight, V.; Smith, J.A.D.(*Eds*.), *Clinical Applications of Ribavirin*, Academic Press, New York, **1984**.

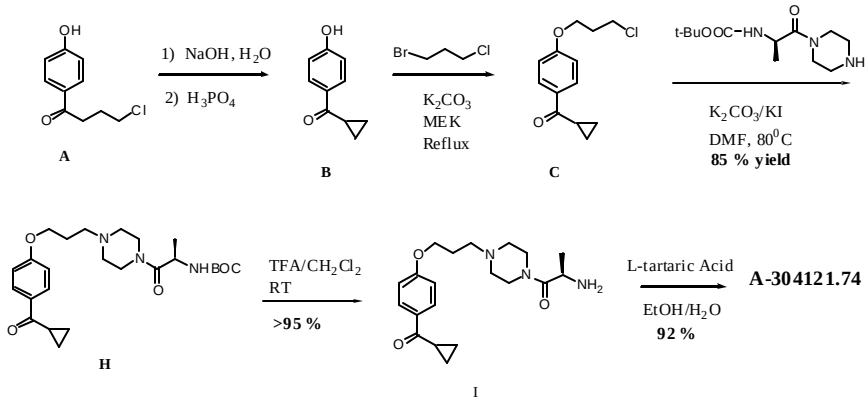
Acknowledgements Supported by the National Natural Science Foundation of China (No. 29862006).

H3 ANTAGONIST—PROCESS RESEARCH FOR THE SYNTHESIS OF A-304121

Sou-Jen Chang*, Dilinie P. Fernando and Steve King,
Ramin Faghih, Katheleen Phelan, Youssef L. Bennani(Neuroscience Research)

Process Research and Development, Global Pharmaceutical Research and Development, Abbott Laboratories, 1401 Sheridan Rd, North Chicago, IL 60064

An efficient synthesis for an investigational H3 antagonist for the treatment of attention deficit hyperactivity disorder, A-304121, is presented beginning with anisol. An interesting interconversion of chlorobutanonephenol (A) and hydroxybutanonephenol is discovered with the mechanism proposed.



ENANTIOSELECTIVE TOTAL SYNTHYESIS OF PHOMOPSOLIDE A-E

Miaosheng Li and George A. O'Doherty
Department of Chemistry, West Virginia University
Morgantown, WV 26506-6045

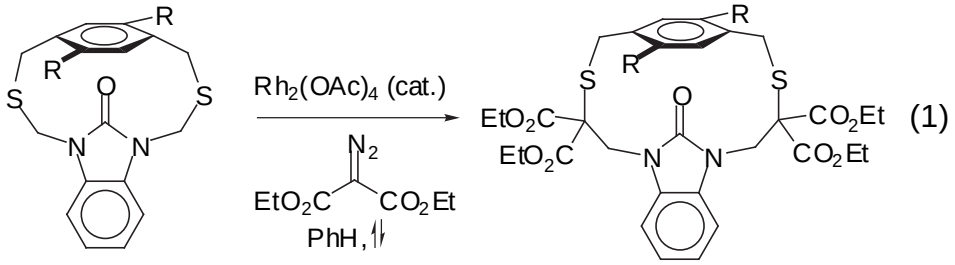
1a: cis, R = O; **Phomopsolide A**
1b: trans, R = OH; **Phomopsolide B**
1c: trans, R = O; **Phomopsolide C**
1d: 6,7-dihydro, R = OH; **Phomopsolide D**
1e: 6,7-dihydro, R = O; **Phomopsolide E**

An enantioselective approach toward the total synthesis of a Phomopsolide will be described. The key steps involved the Sharpless catalytic asymmetric dihydroxylation on the dienone, followed by a Noyori catalytic asymmetric hydrogenation of a furyl ketone. The resulting triols can be stereoselectively transformed into lactones via a diastereoselective oxidation and reductive sequence, which features an Achmatowicz reaction.

Ring Enlargement of Sulfur-Containing Macrocycles via Rhodium-Catalyzed Stevens Rearrangement

Keisha K. Ellis and Steven T. Diver
University at Buffalo, The State University of New York
Department of Chemistry, Buffalo, NY 14260-3000

Our group is interested in the synthesis and application of *N*-heterocyclic carbenes both as ligands and as catalysts. Herein, we report our efforts towards the synthesis of a *N*-heterocyclic carbene ligand that is incorporated inside the pocket of a cyclophane environment. Conversion of the novel [2.2]heterocyclophanes[1] into their corresponding *N*-heterocyclic carbenes was thwarted due to macrocyclic ring strain. To overcome this difficulty, the macrocycle was expanded through a double Stevens rearrangement (eq 1). Carbene insertion was achieved through $Rh_2(OAc)_4$-catalyzed decomposition of diazoesters which proceeds via sulfonium ylide intermediates. The rearrangement was found to be completely regioselective.



(1)

[1]Ellis, K. K.; Wilke, B.; Zhang, Y.; Diver, S. T. *Org. Lett.* **2000**, *2,* 3785-3788.

Mechanistic Study of Unusual Desilylation of a -Silyloxy b -Amino Carboxylic Acid Derivatives

H. Marlon Zhong,* Michael N. Greco,† and Bruce E. Maryanoff†

***Drug Evaluation, Chemical and Pharmaceutical Development, †Drug Discovery,**

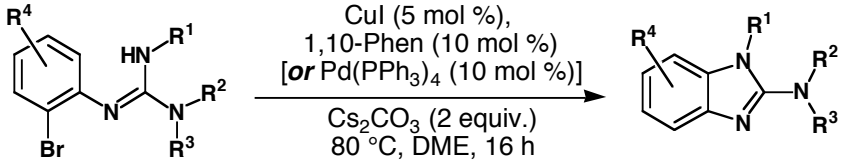
Johnson & Johnson Pharmaceutical Research & Development, LLC, Spring House, PA 19477

Abstract: Saponification and mild acidification of α-silyloxy homo-arginine derivative revealed an unusual lability of the silyl protecting group. A systematic study of related substrates indicates that hydrogen bonding between the α-amino hydrogen and the carbonyl oxygen is critical for facile desilylation. A mechanism involving neighboring group participation of NH and carboxyl groups is proposed.

Copper and Palladium Catalyzed Intramolecular Aryl Guanidinylation: An Efficient Method for the Synthesis of 2-Aminobenzimidazoles

Ghotas Evindar, Robert A. Batey*
Davenport Research Laboratories, Department of Chemistry, University of Toronto, 80 St. George Street, Toronto, Ontario, M5S 3H6, Canada

The formation of 2-aminobenzimidazoles via intramolecular C–N bond formation between an aryl halide and a guanidine moiety can be achieved through either copper or palladium catalysis. Inexpensive copper salts, such as CuI, are generally superior to the use of palladium catalysts. Regioselective cyclizations, where R_3 = H, can be achieved in high yield under CuI / 1,10-phenanthroline catalyzed conditions, whereas palladium catalysis results in the formation of regioisomeric products. This methodology has been applied to the synthesis of the histamine H1-receptor antagonist astemizole (Hismanal) and, its highly active metabolite, norastemizole. This work is the first serious study of metal catalyzed arylation of guanidines, and is one of a handful of examples of copper catalyzed cyclizations involving C-N bond formation.



High Throughput Process Optimization for the Fine Chemical and Pharmaceutical Industries

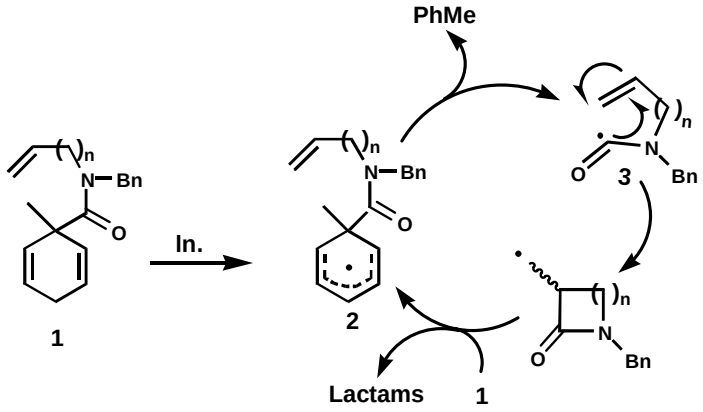
Peter Desrosiers
Symyx Technologies, 3100 Central Expressway, Santa Clara CA 95051

Process optimization consists of identifying a combination of chemicals (e.g. catalysts, reagents, solvents, etc.) and conditions (e.g. time, temperature, and pressure, etc.) that results in a high yield and/or purity of a desired product. Often a time consuming and expensive task, Symyx Technologies is currently applying its expertise in high through screening to develop a fully integrated workflow for process optimization. Designed to allow hundreds of mg scale reactions to be run in parallel and analyzed using proprietary rapid serial and parallel analytical techniques, this system greatly reduces the time and material needed to find the optimum conditions for a given organic transformation. Consisting of reactor loading and sample preparation robots, primary and secondary screening reactors capable of operating at temperatures and pressures of up to 180oC and 1000 psi, and a suite of analytical devices all linked by the Symyx Renaissance™ suite, this system can be used for a wide range of reactions including: hydrogenations (homogenous and heterogeneous, enantioselective), oxidations, alkylations, and Lewis acid catalyzed reactions. A detailed description of the hardware and software components system along with selected examples illustrating the use of the systems will be provided.

Cyclohexadiene-1-carboxamides in Synthesis of Biologically active compounds

Antonio F. Bella, Leon V. Jackson and John C. Walton*
University of St. Andrews, School of Chemistry, St. Andrews, Fife, KY16 9ST, UK

ur work mainly focuses on the use of amidocyclohexadienes for syntheses of lactams and related biologically active compounds.



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mides containing oxime ether functionality have also been exploited. ing closure onto oxime ether functionality is much faster than hex- enyl cyclisation[2] leading to improved lactam yields.

These two procedures are being compared for several lactam ring sizes. adical chains which involve oxime ether double bond seem well suited for the preparation of β-lactam antibiotics because small ring formation are efficient and because the product lactams can contain nitrogen functionality at C (3)-exactly as required in many antibiotics of this class.

eferences

1. P. . Baguley, . C. alton, *Angew. Chem. Int. Ed*. **1998**, 3 , 3 2.
2. . . allis, . M. Brinza, *Tetrahedron*, **1997**, 3, 1 43.

DE NOVO SYNTHESIS OF GALACTO-*PAPULACANDIN USING SHARPLESS CATALYTIC ASYMMETRIC DIHYDROXYLATION*

Md. Moinuddin Ahmed and George A. O'Doherty
Department of Chemistry, West Virginia University
Morgantown, WV 26506-6045

***galacto*-papulacandin**

The papulacandins are a group of naturally occurring glycolipid-antifungal agents isolated from the fermentation of broths of *Papularia spherosperma* and *Dictyochaeta simplex*. Herein, we will describe our recent efforts toward the synthesis of the *galacto*-isomer of the core spiroketal ring system. Our synthesis of the *galacto*-papulacandin ring system relies on regioselective Sharpless catalytic asymmetric dihydroxylation followed by a diastereoselective dihydroxylation using the Upjohn condition to establish the absolute and relative stereochemistry. The synthesis is completed by one-pot deprotection/spiroketal formation followed by per-debenzylation.

Second Cycle Ligands for Osmium Catalyzed Olefin Dihydroxylation and Aminohydroxylation

Peng Wu, Robert Hilgraf, Valery V. Fokin and K. Barry Sharpless
Department of Chemistry and the Skaggs Institute for Chemical Biology
The Scripps Reserch Institute, La Jolla, CA 92037

Mechanistic studies reveal that two catalytic cycles are involved in the osmium-catalyzed olefin dihydroxylation and aminohydroxylation. Cinchona alkaloid ligands keep the catalysis in the first, enantioselective, catalytic cycle. However, slow hydolysis of the Os(VI) monoglycolate (monoazaglycolate) intermediates often shunts the catalysis into the second catalytic cycle, resulting in poor enantioselectivity (and, in the case of aminohydroxylation, poor chemoselectivity).

To improve the efficiency and reliability of the osmium-catalyzed oxidations of olefins, we devised a series of ligands which force the catalysis into the second catalytic cycle. *N*-Sulfonyl □, □-hydroxyaminoacid derivatives proved to be useful in controlling these 2nd cycle processes. The new ligands have been studied in both dihydroxylation and aminohydroxylation, showing excellent catalytic turnover and moderate to good enantioselectivity.

PALLADIUM CATALYZED OXIDATIVE KINETIC RESOLUTION OF SECONDARY BENZYLIC ALCOHOLS

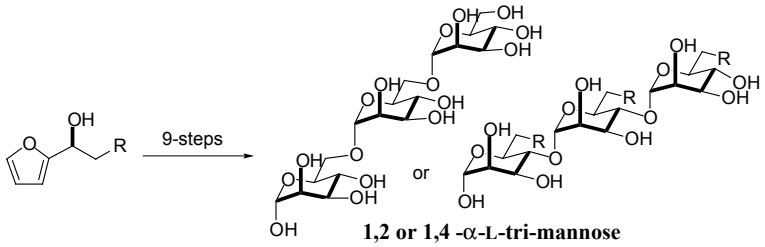
Jeffrey T. Bagdanoff, Eric M. Ferreira, Dan Caspi, Ryan McFadden, David Ebner, Brian M. Stoltz*

California Institute of Technology, Division of Chemistry and Chemical Engineering, Pasadena, CA, 91125

As part of a generalized program aimed at developing metal catalyzed enantioselective oxidation reactions, we have discovered a palladium catalyzed oxidative kinetic resolution of secondary benzylic alcohols. In a racemic mixture of secondary alcohols, one enantiomer is selectively oxidized over the other, providing a ketone and an enantioenriched alcohol as resolution products. While the process effectively oxidizes secondary benzylic alcohols to high enantiomeric excess, we have undertaken careful optimization studies aimed at reducing reaction times and temperatures, while increasing the substrate scope and selectivity of the process.

DE NOVO SYNTHESIS OF DISACCHARIDES AND TRISACCHARIDES USING PALLADIUM CATALYZED GLYCOSIDATION

R. Satheesh Babu and George A. O'Doherty
Department of Chemistry, West Virginia University
Morgantown, WV 26506-6045



Unnatural 1,2- and 1,4-α-L-*manno*-disaccharides and 1,2- and 1,4-α-L-*manno*-trisaccharides were synthesized from furan alcohols using a palladium catalyzed glycosidation reaction. The 1,2- and 1,4-α-L-*manno*-disaccharides were achieved in 7 total steps starting from a furan alcohol. Similarly, 1,2- and 1,4-α-L-*manno*-trisaccharides were also synthesized in 9 total steps using a sequential palladium catalyzed glycosidation reaction. Key to the overall efficiency of this process are the use of diastereoselective Luche reductions and diastereoselective dihydroxylation reactions, in tandem.

STUDIES DIRECTED TOWARD THE SYNTHESIS OF PRIMARY AMINES FROM KETONES AND ALDEHYDES VIA REDUCTIVE AMINATION

Steven J. Mehrman, Ahmed F. Abdel-Magid, Allison Mailliard, Cynthia A. Maryanoff
Johnson & Johnson Pharmaceutical Research & Development L.L.C.
Drug Evaluation – Chemical and Pharmaceutical Development
Spring House, PA 19477-0776

We reported a general and efficient methodology to perform the reductive amination of ketones and aldehydes utilizing both primary and secondary amines with sodium triacetoxyborohydride. However, the use of ammonia or ammonia equivalents to perform this reaction has been less utilized. We've also noted the reaction of ketones and aldehydes with ammonium acetate and sodium triacetoxyborohydride forms primarily the secondary amine products. We are now reporting a reductive amination procedure for the preparation of primary amines from ketones and aldehydes. . The scope and limitations of this reaction will be discussed.

38th National Organic Symposium
General Information

Security
Badges must be worn during all Symposium events.

Alcohol – Campus Policies
All visitors are subject to the Indiana University alcohol policies. Alcohol will be available during the poster sessions, social mixers and Dinner-at-the-Fountain and may not be removed from designated areas. Walking across campus with alcoholic beverages is prohibited. Violations of the policies will be handled by IUPD.

Concierge
Concierge will be available to assist you in planning excursions, locating restaurants, making reservations, planning travel and responding to your questions.
Location: IU Auditorium Lobby
Hours:

Sunday, June 8th	1:00pm – 8:00pm
Monday, June 9th	7:30am – 8:30am
	10:15am – 11:45am
	12:00pm – 2:00pm
	5:00pm – 7:00pm
Tuesday, June 10th	7:30am – 8:30am
	9:45am – 10:15am
	12:45pm – 2:00pm
	5:00pm – 7:30pm
Wednesday, June 11th	7:30am – 8:30am
	9:45am – 10:15am
	12:45pm – 2:00pm
	5:00pm – 7:30pm
Thursday, June 12th	8:00am – 9:00am
	10:15am – 10:45am

Internet/Email Access

Wireless
Wireless internet connection is available in the Indiana Memorial Union provided that your laptop is equipped with a wireless card. Your card must be 802.11b. Cards are available for purchase in the IU Bookstore (located in the Indiana Memorial Union) for $65.00 - $75.00 dollars.

When you turn on your laptop in the IMU:

- Click on icon in your taskbar representing wireless card.
- Choose from a list of available networks.
- Select network name "NOS2003"
- You will be asked to fill in a field with a WEP key, which is 671203.

Email and Internet Room

Hard wire internet access will be available in Chemistry Building Room 046. The room will be staffed and opened during non-session hours.

Hours available:

Sunday, June 8th	1:00 pm – 8:00 pm
Monday, June 9th	12:15 pm – 7:00 pm
Tuesday, June 10th	1:00 pm – 7:30 pm
Wednesday, June 11th	1:00 pm – 7:30 pm

Poster Setup and Teardown

Session A: Sunday, June 8th
Setup: IU Auditorium Lobby and Mezzanine
1:00 pm – 6:00 pm
Teardown: 12:00 am – 7:30 am

Session B: Monday, June 9th
Setup: IU Auditorium Lobby and Mezzanine
8:00 am – 6:00 pm
Tents
2:00 pm – 6:00 pm
Teardown: 12:00 am – 7:30 am

Session C: Tuesday, June 10th
Setup: IU Auditorium Lobby, Mezzanine and Tents
8:00 am – 6:00 pm
Teardown: 12:00 am – 7:30 am

Session D: Wednesday, June 11th
Setup: IU Auditorium and Mezzanine
8:00 am – 6:00 pm
Teardown: 12:00 am – 7:30 am

Note: Limited poster supplies are available from the concierge. We will not be held responsible for unremoved posters.

Volunteers

Indiana University Department of Chemistry student volunteers can be recognized by their crimson NOS 2003 T-shirts. They will be available throughout the Symposium to assist you.

Eating on campus

Wright Food Court
Wright Food Court is located at the corner of 10th and Jordan. It offers a variety of eating options, including a pizza venue, deli, Dunkin Donuts, Chinese, spud, soup and salad bar.

Monday – Saturday	7:00 am – 7:00 pm
Sunday	9:00 am – 7:00 pm

Note: Credit cards are not accepted.

Indiana Memorial Union
The IMU offers the following food options:

Sugar and Spice Coffee Shop

Monday – Friday	8:00 am – 5:00 pm
Saturday & Sunday	11:00 am – 5:00 pm

Charleston Market

Monday – Friday	7:00 am -10:00 am; 11:00 am – 2:00 pm
Saturday & Sunday	7:00 am – 11:00 am

Burger King

Monday – Friday	10:00 am – 6:30 pm

Pizza Hut

Monday – Friday	10:00 am – 2:00 pm

SubConnection

Monday – Saturday	10:00 am – 2:00 pm

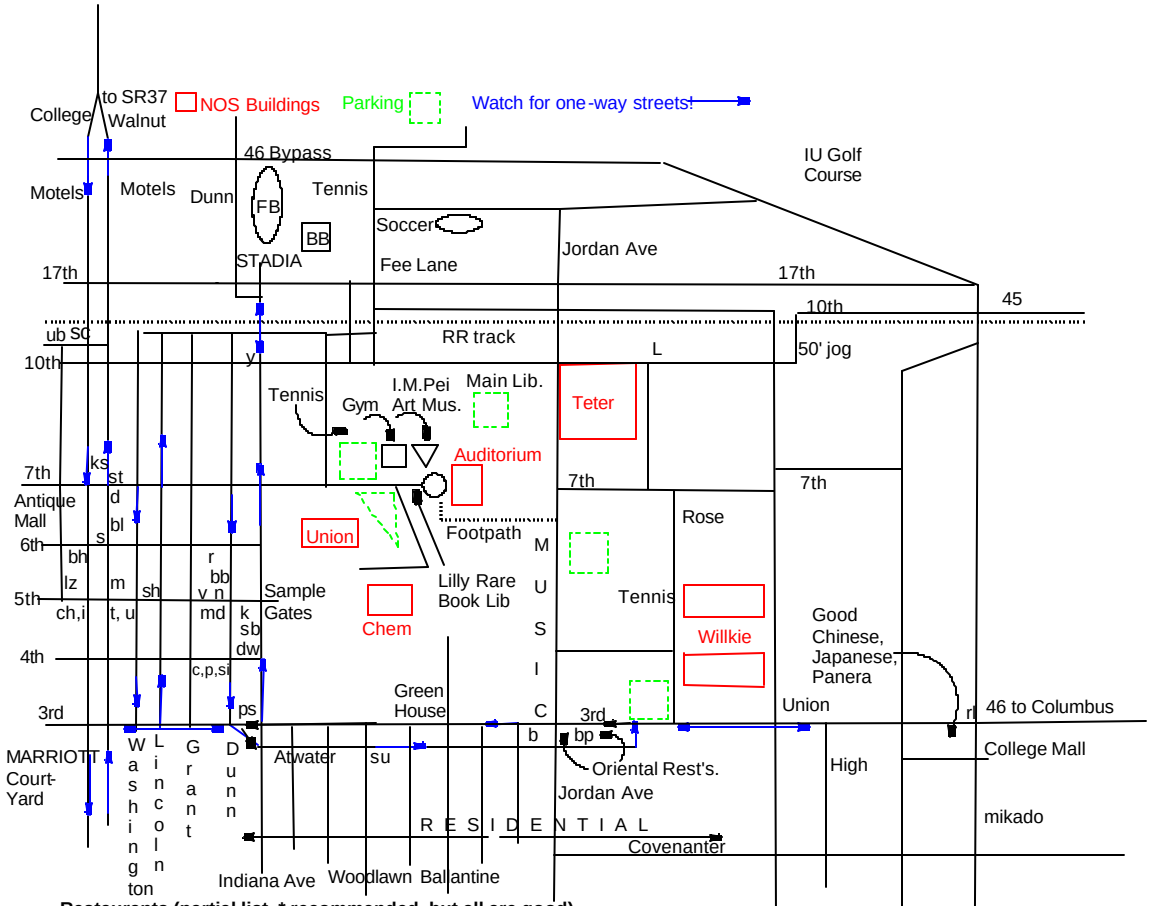
Note: Credit cards are not accepted at any of the above.

Tudor Room – Buffet Lunch

Monday – Friday	11:30 am – 1:00 pm
Sunday brunch	10:30 am – 1:30 pm

Note: Credit cards accepted.

Bloomington and Campus Map
(and partial restaurant guide)



Restaurants (partial list, * recommended, but all are good)

b-Bear's*
bb-Bloomington Bagel
bp-Bear's Pizza*
bl-BlueBird-bar-music
bh-Bakehouse-lunch
c-Casablanca*
ch-Crazy Horse
d-Divino's-upscale
dw-Dagwood's Sandwich
i-Irish Lion*
k-Kilroy's
ks-Kilroy's Sports

L-Lennies*
lz-Little Zagreb-Best Beef*
m-Malibu Grille-upscale
mikado-upscale*
md-macdonalds
n-Nick's-The Campus Bar*
p-Puccinis-upscale*
ps-Penn Station Sandwich
rl-Red Lobster
r-Runcible Spoon
s-Samira-Afgan-affordable*

sb-Starbucks
sc-Scholar's Inn-upscale*
si-Siam House-Thai*
sh-Shanti-Indian*
st-Scotty's Bar & Grille
su-Subway
t-Trojan Horse-Gyros*
u-Uptown-upscale*
ub-Upland Brewing Co
v-Village Pantry-B & L
y-Yogi's Bar & Grille

Important Phone Numbers

Emergencies	911
IUPD	855-4111
Indiana Memorial Union Front Desk	(812) 856-6381
Bloomington Shuttle (to Indy airport)	(800) 589-6004
Classic Touch Limousine	(800) 319-0082
Local Car Rental (Ace)	(812) 335-1501

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