



Tuesday, July 18, 2023

Poster Session 18:00-20:00

- P-1** Preparation and conformation of calix[6]rotane
Silvio Biali, Ori Shalev
Institute of Chemistry, The Hebrew University of Jerusalem, Jerusalem, Israel
- P-2** *Flash talk*
Active role of alkali cations in the kinetics of the base-promoted berberrubine release from cucurbit[7]uril
Zsombor Miskolczy, Mónika Megyesi, **László Biczók**
Institute of Materials and Environmental Chemistry, Research Centre for Natural Sciences, Budapest, Hungary
- P-3** Moving towards auxetic calixarene-based systems
Maria Cardona¹, Ruben Gatt¹, Alessandro Casnati², Stefano Volpi², Joseph N. Grima¹
¹Metamaterials Unit, Faculty of Science, University of Malta, Msida, Malta
²Dipartimento Di Scienze Chimiche, Della Vita E Della Sostenibilita' Ambientale, University of Parma, Parma, Italy
- P-4** *Flash talk*
Novel fluorinated bambusurils: synthesis, anion binding, and transport properties
Matúš Chvojka^{1,2}, Hennie Valkenier², Vladimír Šindelář¹
¹Department of Chemistry and RECETOX, Masaryk University, Brno, Czech Republic
²École Polytechnique - Engineering of Molecular Nanosystems, Université libre de Bruxelles, Brussels, Belgium
- P-5** Modulation of the kinetic stability of host-guest complexes via light irradiation
Miriam Colaço, Patrícia Máximo, António Jorge Parola, Nuno Basílio
Department of Chemistry, NOVA University of Lisbon, Caparica, Portugal

- P-6** [Dynamic \[1\]rotaxanes based on bambusurils](#)
Arico Del Mauro, Vladimír Šindelář
Department of Chemistry and RECETOX, Masaryk University, Brno,
Czech Republic
- P-7** [Substituent electronic effect on the host-guest binding properties of the conjugated of 5,5'-bicalixarene scaffold](#)
Michal Farber, Arkadi Vigalok
Department of Organic Chemistry, Tel Aviv University, Tel Aviv, Israel
- P-8** [Multivalency in a host-guest protein-calix\[8\]arene complex](#)
Ronan Flood, Peter Crowley
Biological and Chemical Sciences, University of Galway, Galway, Ireland
- P-9** [Extraordinary control of photosensitized singlet oxygen generation by acyclic cucurbituril-like containers](#)
Daniel Guerra-Díaz¹, Nory Mariño-Ocampo¹, Vladimir Kobanov², Belinda Heyne², Felipe Andrade-Villalobos³, Angélica Fierro³, **Denis Fuentealba**¹
¹Department of Physical Chemistry, Pontificia Universidad Católica De Chile, Santiago, Chile
²Department of Chemistry, University of Calgary, Calgary, Canada
³Department of Organic Chemistry, Pontificia Universidad Católica De Chile, Santiago, Chile
- P-10** [Paramagnetic guest exchange saturation transfer \(paraGEST\) revealing hidden interactions in supramolecular host-guest systems](#)
Elad Goren, Liat Avram, Amnon Bar-Shir
¹Department of Molecular Chemistry and Materials Science, Weizmann Institute of Science, Rehovot, Israel
²Department of Chemical Research Support, Weizmann Institute of Science, Rehovot, Israel
- P-11** *Flash talk*
[Substrate-controlled and template-assisted mechanochemical synthesis of thio-hemicucurbiturils](#)
Raghuram Gujjarappa^{1,2}, Ehud Keinan², Ofer Reany¹
¹Department of Natural Sciences, The Open University of Israel, Ra'anana, Israel
²The Schulich Faculty of Chemistry, Technion-Israel Institute of Technology, Haifa, Israel
- P-12** [Hydrogen-bonded extended cavity supramolecular boxes in water based on pillar\[6\]arenes](#)
Dana Kaizerman-Kané¹, Maya Hadar¹, Ori Shalev^{1,2}, Yoram Cohen¹
¹School of Chemistry, The Sackler Faculty of Exact Sciences, Tel Aviv University, Tel Aviv, Israel
²Metabolomics Center, Core Research Facility, The Faculty of Medicine, The Hebrew University of Jerusalem, Jerusalem, Israel

- P-13** Calix[4]arenes bearing mixed aza/thia bridges
Tereza Horackova^{1,2}, Simon Pascal², Olivier Siri², Pavel Lhotak¹
¹Department of Organic Chemistry, University of Chemistry and Technology
Prague, Prague, Czech Republic
²Center Interdisciplinaire De Nanoscience De Marseille (CINaM), Aix-Marseille
Université, Marseille, France
- P-14** Improving pH stability and affecting enzymatic degradation of the anticancer prodrug capecitabine by host-guest complexation with pillararene derivatives
Inbar Horin, Yoram Cohen
Organic Chemistry, Tel-Aviv University, Tel-Aviv, Israel
- P-15** Diffusion NMR reveals the structures of the molecular aggregates of resorcin[4]arenes and pyrogallol[4]arenes in aromatic and chlorinated solvents
Inbar Horin, Sarit Slovak, Yoram Cohen
Organic Chemistry, Tel-Aviv University, Tel-Aviv, Israel
- P-16** Highly modular metallocavitands with deeply embedded metal centers
Galon Israeli, Thejasree Munikrishna, Kamal Uddin Ansari, Yuri Tulchinsky
Organic Chemistry, Hebrew University of Jerusalem, Jerusalem, Israel
- P-17** Selective electrochemical impedance sensing of perchlorate through self-assembled monolayers of semiaza-bambusuril derivatives
Raman Khurana^{1,2}, Ehud Keinan², Jurriaan Huskens³, Ofer Reany¹
¹Department of Natural Sciences, The Open University of Israel, Ra'anana, Israel
²Schulich Faculty of Chemistry, Technion - Israel Institute of Technology, Haifa, Israel
³Department of Molecules & Materials, University of Twente, Enschede, Netherlands
- P-18** Flash talk
Colorimetric differentiation of solid-state supramolecular complexes of coumarin and bimeane fluorophores
Vincent Joseph, Nathaniel Roy, Jenisha John, Flavio Grynszpan, **Mindy Levine**
Department of Chemical Sciences, Ariel University, Ariel, Israel
- P-19** Cucurbit[7]uril-mediated histidine dimerization: exploring the structure and binding mechanism
Ewelina Zaorska, **Maura Malinska**
Faculty of Chemistry, University of Warsaw, Warsaw, Poland

- P-20** Association constants between homooxacalixarenes and nitroaromatic compounds obtained by fluorescence: a critical analysis
Paula M. Marcos^{1,2}, Alexandre S. Miranda^{1,3}, José R. Ascenso⁴,
Mário N. Berberan-Santos³,
¹FCUL, Centro de Química Estrutural, Institute of Molecular Sciences, Lisboa, Portugal
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³IST, IBB-Institute for Bioengineering and Biosciences, Lisboa, Portugal
⁴IST, Centro de Química Estrutural, Institute of Molecular Sciences, Lisboa, Portugal
- P-21** *Flash talk*
Electron deficient arms of calix[4] basket for capturing toxic fluoride ion
Anita Nehra^{1,2}, Sateesh Bandaru³, Rakesh K Sharma¹
¹Chemistry, Indian Institute of Technology Jodhpur, Jodhpur, Rajasthan, India
²Chemistry, JECRC University, Jaipur, Rajasthan, India
³Computational Material Science Division, Hangzhou Dianzi University, Hangzhou, Zhejiang, China
- P-22** Bambusuril macrocycles for selective anion binding
Carola Rando¹, Jan Sokolov¹, Petr Kulhánek², Vladimír Šindelář¹
¹Department of Chemistry and RECETOX, Masaryk University, Brno, Czech Republic
²National Centre for Biomolecular Research, Masaryk University, Brno, Czech Republic
- P-23** Regulation of microtubule dynamics and function in living cells via cucurbit[7]uril host-guest molecular recognition
Akshay Saroha¹, Monica Swetha Bosco¹, Sneha Menon², Tanmoy Maity³, Subinoy Rana³, Sachin Kotak⁴, Jagannath Mondal², Sarit S. Agasti^{1,5}
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- P-24** *Flash talk*
Water-soluble pseudo-rotaxane with cucurbit[7]uril shuttling along a “dynamic” axle in response pH and light stimuli
André Seco¹, Nathan Mcclenaghan², A. Jorge Parola¹, Nuno Basílio¹
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²Institut des Sciences Moléculaires, CNRS/Univ. Bordeaux, Talence, France
- P-25** *Flash talk*
Catalytic enantioselective synthesis of inherently chiral calixarenes
Tong Shuo
Department of Chemistry, Tsinghua University, Beijing, China
- P-26** *Synthesis of novel bridged inherently chiral calixarene derivatives*
Anastasia Surina¹, Karolina Salvadori², Jan Čejka³, Ondřej Kundrat¹, Pavel Lhoták¹
¹Department of Organic Chemistry, University of Chemistry and Technology Prague, Prague, Czech Republic
²Department of Molecular Electrochemistry and Catalysis, J. Heyrovský Institute of Physical Chemistry of CAS v.v.i., Prague, Czech Republic
³Department of Solid State Chemistry, University of Chemistry and Technology Prague, Prague, Czech Republic
- P-27** *Flash talk*
Anion-recognition directed supramolecular catalysis
Qi-Qiang Wang
CAS Key Laboratory of Molecular Recognition and Function, Institute of Chemistry, Chinese Academy of Sciences, Beijing, China
- P-28** *Supramolecularly engineered platelets-hitchhiking delivery of morphology transformable peptide for tumor vascular embolization*
Ziyi Wang, Junyan Li
Institute of Chinese Medical Sciences, University of Macau, Macau, China
- P-29** *Flash talk*
Symmetry breaking during self-assembly of racemic mixture of organic cages
Shaodong Zhang
School of Chemistry and Chemical Engineering, Shanghai Jiao Tong University, China

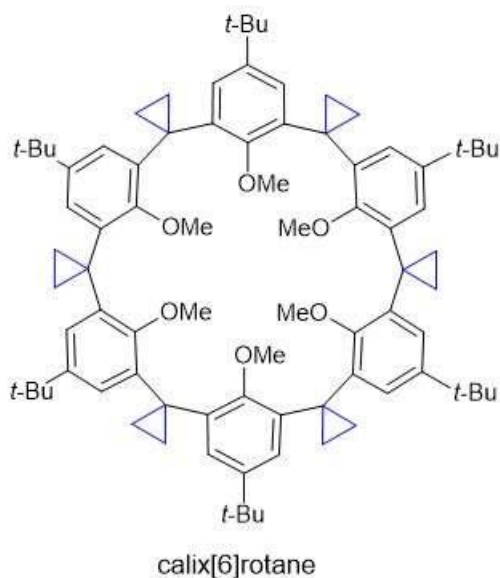
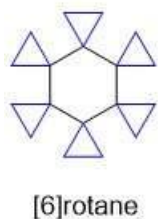
Poster Abstracts

Preparation and conformation of calix[6]rotane

Silvio Biali¹, Ori Shalev¹

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A calix[6]arene derivative with all the aryl rings interconnected by spirocyclopropyl groups (“calix[6]rotane”) was synthesized and structurally characterized. The compound was prepared via reaction of dichlorocarbene with a calix[6]arene possessing exocyclic double bonds at the bridges, followed by reductive perdechlorination of the dichlorocyclopropyl groups. Calix[6]rotane adopts in the crystal and in solution a 1,3,5-alternate conformation. The macrocycle undergoes a dynamic process consistent with a 1,3,5-alternate to 1,3,5-alternate ring inversion topomerization process that mutually exchanges the two geminal protons of a given methylene group. The presence of the spirocyclopropyl groups increases the rigidity of the macrocyclic ring.



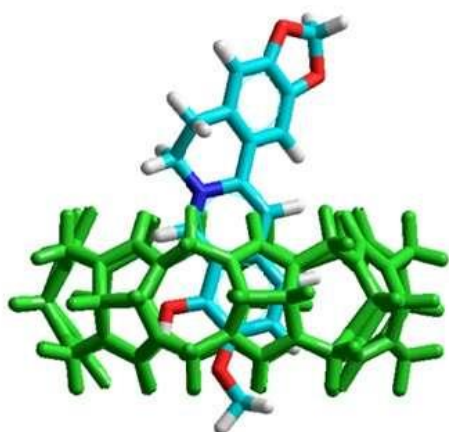
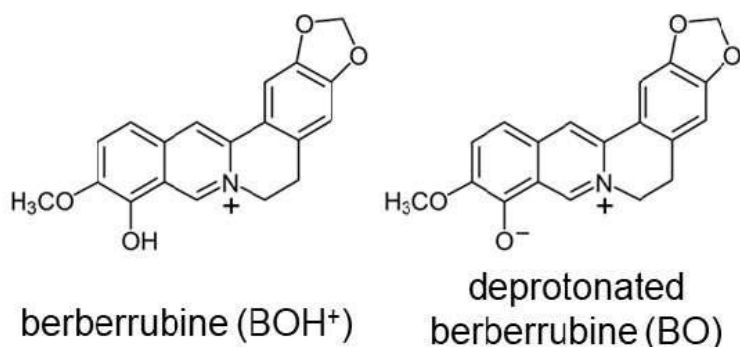
Flash talk

Active role of alkali cations in the kinetics of the base-promoted berberrubine release from cucurbit[7]uril

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Institute of Materials and Environmental Chemistry, Research Centre for Natural Sciences, Budapest, Hungary

A pH-responsive inclusion complex was created from berberrubine, a pharmacological active natural isoquinoline alkaloid and cucurbit[7]uril (CB7) macrocycle exploiting the more than four orders of magnitude larger binding affinity of the cationic guest (BOH^+) compared to the deprotonated uncharged conjugate base (BO). Since only the CB7-encapsulated BOH^+ emitted strong fluorescence, the transformation of this host-guest complex could be selectively monitored in real time by stopped-flow measurements. Systematic kinetic studies with various alkali hydroxides revealed the mechanism of base-initiated transformation of BOH^+ -CB7 complex and the rate of the reaction steps. Alkali cations expelled BOH^+ from CB7 in a pseudo-first order reaction and formed ternary complex with BOH^+ -CB7. The ternary complex was deprotonated by OH^- anions much faster than BOH^+ -CB7. The rate of the process could be tuned not only by the OH^- concentration but also by the size and amount of the alkali cation. LiOH induced the proton loss of BOH^+ -CB7 much more efficiently than NaOH or KOH. The revealed mechanistic details may be applied to other deprotonable CB7 complexes. The knowledge gained in the present study significantly contribute to the rational design of the tailor-made pH-responsive targeted delivery systems, the fabrication of stimuli-responsive materials, and the development of indicators for the monitoring of the local basicity in their microenvironment.



berberrubine (BOH^+) inclusion complex with cucurbit[7]uril

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On the auxetic behaviour of novel calixarene-based systems

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Auxeticity is a non-conventional property whereby a material becomes wider when stretched and thinner when compressed, a result of a negative Poisson's ratio (a fundamental material property which is the negative ratio of the transverse strain and axial strain).¹ The design of auxetic materials is an emerging field of research, which aims to deliver new materials with improved qualities such as enhanced fracture and vibrational damping ability, augmented resistance to indentation and synclastic curvature.² A calix[4]arene-based network system has previously been studied through molecular simulation and shown to possess auxetic behaviour when the calixarenes are linked through para-para biphenyl linkages.^{3,4} This arrangement mimics an “egg-rack” structure consisting of alternate-facing four-legged claws arranged in a square grid which opens up in all directions like an umbrella when the structure is loaded in tension (Fig. 1a). In this study, we explore a different design of calixarenes which mimic this “egg-rack” structure. Our design proposes the use of calix-tubes covalently linked together by rigid linkers and held into shape through supramolecular interactions within the structure (Fig. 1b). We study their potential auxetic behaviour through force-field based simulations and carry out a systematic study to explore the change in the mechanical properties upon modification of the constituents of the ring and on the connecting linkages. This provides a design rationale for the potential synthesis of novel calixarene-based systems which are inherently auxetic, leading the way towards novel materials with improved properties.

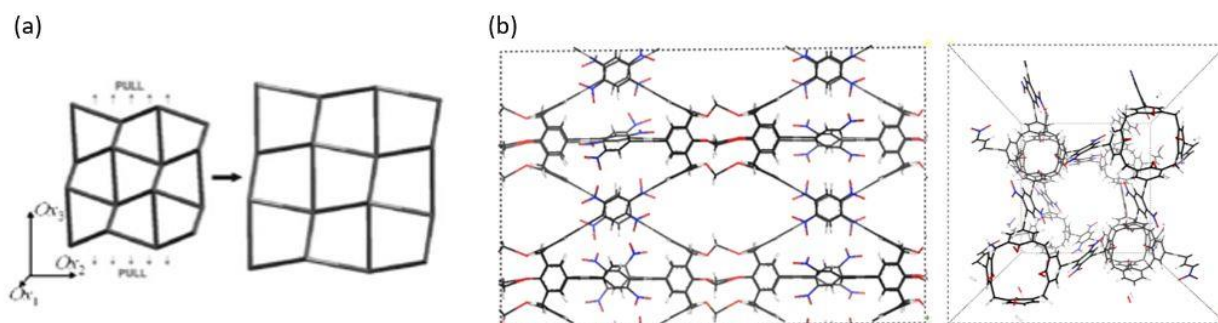


Fig. 1 (a) An illustration of mechanism in operation when the “egg-rack structure” opens up under tension. Adapted from 3. (b) Two views of a unit cell showing a representative example of the designed systems in the proposed egg rack configuration.

References

1. K.E. Evans, M.A. Nkansah, I. Hutchinson, S.C. Rodgers, *Nature*, 1991, 353, 124.
2. R. Gatt, L. Mizzi, J.I. Azzopardi, K.M. Azzopardi, D. Attard, A. Casha, J. Briffa, J.N. Grima, *Scientific Reports*, 2015, 5, 8395.
3. J.N. Grima, J.J. Williams, K.E. Evans, *Chemical Communications*, 2005, 4065-4067.
4. J.N. Grima, J.J. Williams, R. Gatt, K.E. Evans, *Molecular Simulation*, 2005, 31(13), 907-913.

Novel fluorinated bambusurils: Synthesis, anion binding, and transport properties

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Bambusurils are macrocyclic substances made of six glycoluril building units connected via methylene linkers.¹ They are appreciated for their strong anion binding in solution, which is mediated by twelve C-H...anion hydrogen bond interactions. Their anion affinity was improved even further by introduction of fluorinated substituents, leading to exceptionally high association constants ranging between 10^7 - 10^{11} M⁻¹ for Cl⁻, NO₃⁻, and HCO₃⁻ in acetonitrile.² These fluorinated substituents appended to the bambusurils did also increase their lipophilicity and, in combination with their high anion binding strength, very efficient anion transporters were obtained.

Here, fluorinated bambusuril derivatives containing strongly electron-withdrawing substituents will be presented. The low electron density inside the cavity of the bambusuril macrocycles resulted in stronger anion binding, which was comprehensively studied by a ¹H and ¹⁹F NMR spectroscopy. The effect of increased anion binding strength on anion transport properties was evaluated using liposomes, using the lucigenin assay for chloride/bicarbonate antiport studies.

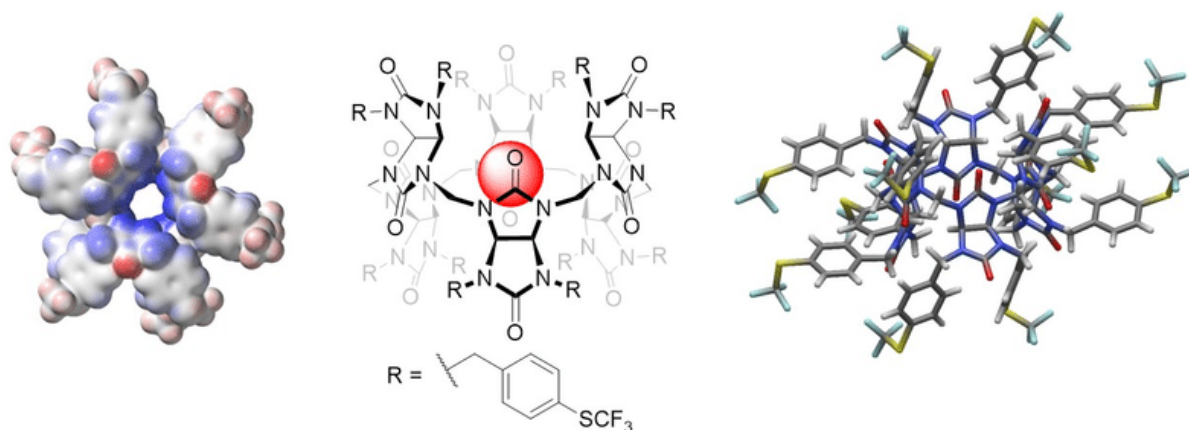


Fig. 1: An example of a fluorinated BU derivative, its electrostatic potential map (left), graphical representation of complex with an anion (middle) and crystal structure (right).

(1) Svec, J.; Necas, M.; Sindelar, V. Bambus[6]Uril. *Angew. Chem. Int. Ed.* 2010, 49 (13), 2378–2381. <https://doi.org/doi:10.1002/anie.201000420>.

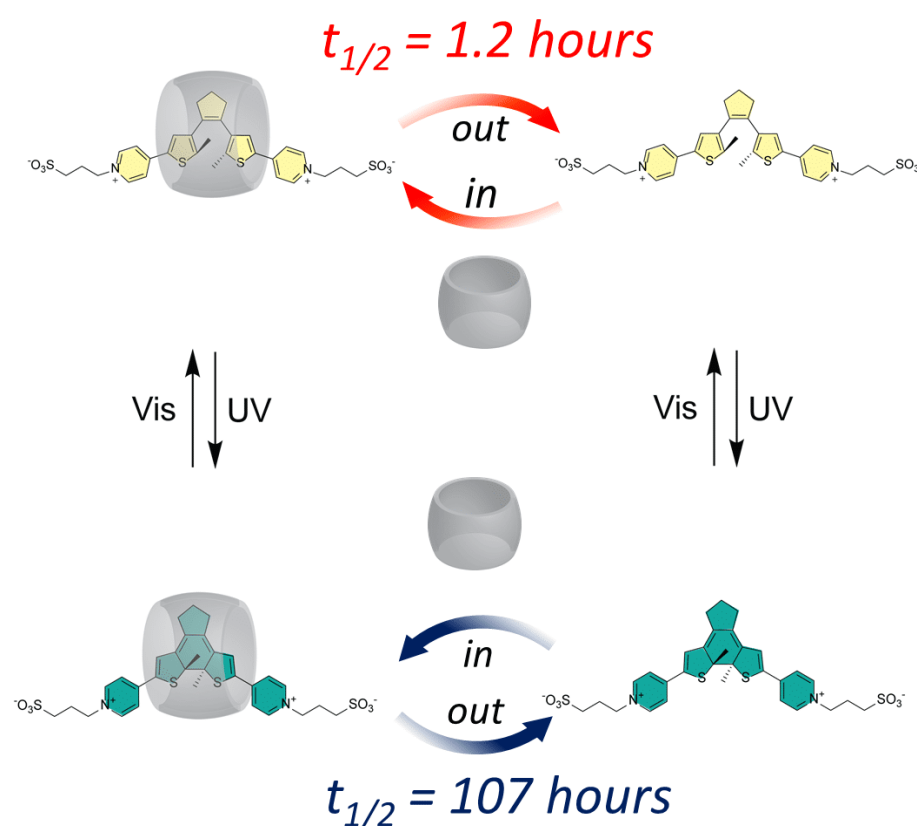
(2) Valkenier, H.; Akrawi, O.; Jurček, P.; Sleziaková, K.; Lízal, T.; Bartik, K.; Šindelář, V. Fluorinated Bambusurils as Highly Effective and Selective Transmembrane Cl⁻/HCO₃⁻ Antiporters. *Chem* 2019, 5 (2), 429–444. <https://doi.org/10.1016/j.chempr.2018.11.008>.

Modulation of the kinetic stability of host-guest complexes via light irradiation

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The formation of host-guest complexes is often thermodynamically controlled and therefore the design of supramolecular systems based on these interactions is usually based on the knowledge about their equilibrium constants. However, the formation of supramolecular complexes under out-of-equilibrium conditions can be required to develop more complex systems, such as mechanically interlocked molecules and molecular machines, which are remarkable building blocks for advanced materials and drug delivery devices. Therefore, a deep understanding about the mechanisms and kinetics of host-guest complexation is crucial.

In this communication, we present a detailed study on the binding mechanism between the synthetic macrocyclic host cucurbit[8]uril (CB8) and photoswitchable dithienylethene (DTE) guests in water. The presence of two negatively charged side arms in the DTE increases the activation barrier for its inclusion in the host, slowing down the overall kinetics, without significantly affecting the thermodynamic stability of the complexes[1]. The photochemical properties of the guests allow a control over the complexation affinity and kinetics by means of visible or near infrared light (NIR), converting the colored ring-closed isomers into their fluorescent open forms. This photoinduced *ciclo*reversion reaction result in a decrease in the stability of the 1:1 complexes from nano to micromolar range[2] and, as well, a parallel increase in the dissociation kinetics (from 107 to 1.2 hours of half-life time). Additionally, the conformational flexibility of the DTE open isomer allowed the emergence of out-of-equilibrium complexes in unusual three-dimensional arrangements that otherwise could not be observed.



[1] Colaço, M. et al. (2021) Chem. Eur. J., 27, 9550-9555

[2] Máximo, P. et al. (2022) Org. Chem. Front., 9, 4238-4249

Dynamic [1]rotaxanes based on bambusurils

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Rotaxanes are intriguing class of mechanically interlocked molecules consisting of a macrocyclic wheel threaded by the axle and having numerous applications.¹ We recently reported a novel [2]rotaxane system² that combines a reversible hypervalent iodine covalent bond with anion recognition properties of bambus[6]uril macrocycles. Here, we present our recently published results³ on [1]rotaxanes consisted of racemic monofunctionalized bambus[6]urils appended with a single arm bearing aliphatic carboxylic group (Figure 1). The arm was transformed into a bis(acyloxy)iodate(I) anionic moiety that is threaded through the bambus[6]uril cavity. We investigated the possibility of component exchange to facilitate carboxylic acid triggered release. The synthesis of a new enantiomerically pure monofunctionalized bambus[6]uril and enantiomerically pure [1]rotaxanes based on the hypervalent iodine axle will also be described.

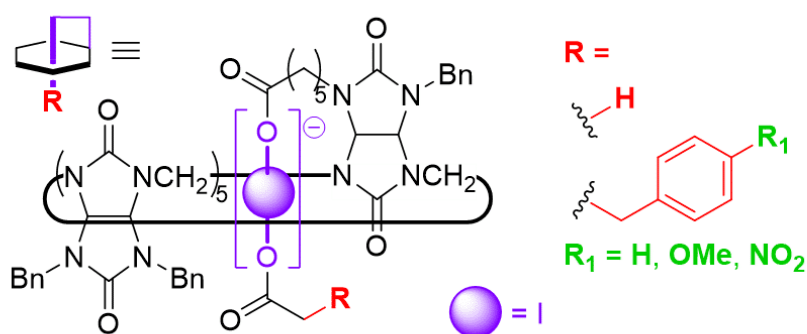


Figure 1 Representation of the prepared [1]rotaxanes.

This work was supported by the Czech Science Foundation (No. GA20-13922S).

- (1) Erbas-Cakmak, S.; Leigh, D. A.; McTernan, C. T.; Nussbaumer, A. L. Artificial Molecular Machines. *Chem. Rev.* 2015, 115 (18), 10081–10206.
- (2) Kandrnálová, M.; Kokan, Z.; Havel, V.; Nečas, M.; Šindelář, V. Hypervalent Iodine Based Reversible Covalent Bond in Rotaxane Synthesis. *Angewandte Chemie International Edition* 2019, 58 (50), 18182–18185.
- (3) Mauro, A. D.; Kokan, Z.; Šindelář, V. Dynamic [1]Rotaxanes via a Reversible Covalent Bond and Host–Guest Anion Recognition. *Chem. Commun.* 2022, 58 (23), 3815–3818.

Substituent electronic effect on the host-guest binding properties of the conjugated of 5,5'-bicalixarene scaffold

Michal Farber¹, Arkadi Vigalok¹

Department of Organic Chemistry, Tel Aviv University, Tel Aviv, Israel

Although host-guest complexation of small molecules and ions within the cavities of various calixarene compounds has been known for several decades, substituent electronic effect on this complexation remains unexplored. As an attachment of a substituent at either lower or upper rim of a calixarene cavity invariably leads to steric and/or conformational changes, the studies of the substituent's electronic properties on the host-guest complexation become complicated. Our group previously reported the preparation of fluorescent oxygen-depleted 5,5'-bicalixarene scaffolds which showed strong fluorescence response to the presence of organic cations and gaseous nitric oxide.¹ The conjugated structure of these bicalixarenes (Figure 1) also make them ideal candidates for the studies of the substituent electronic effect on the host-guest complexation. Here, we present the first studies of such effect, including the correlation between the substituent's Hammett constant and complexation strength.

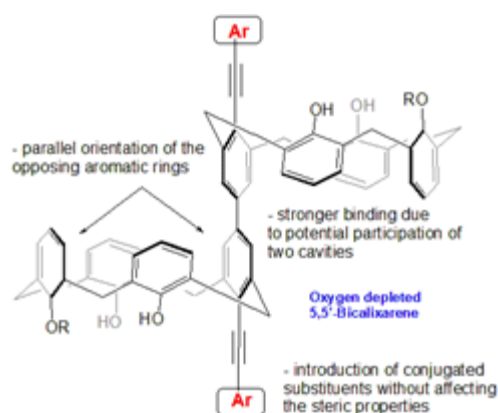


Figure 1

(1) Molad, A.; Goldberg, I.; Vigalok, A. Tubular Conjugated Polymer for Chemosensory Applications. *J. Am. Chem. Soc.* 2012, 134, 7290–7292; Ahuja, B. B.; Vigalok, A. Fluorescent Calixarene Scaffolds for NO Detection in Protic Media, *Angew. Chem. Int. Ed.* 2019, 58, 2774–2778; Baheti, A.; Dobrovetsky, R.; Vigalok, A. Fluorophore-Appendant 5,5'-Bicalixarene Scaffolds for Host-Guest Sensing of Nitric Oxide, *Org. Lett.* 2020, 22, 9706–9711.

Multivalency in a host–guest protein–calix[8]arene complex

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Protein recognition by water-soluble (multivalent) calixarenes is a topic of broad interest.^{1,2} We have shown that the anionic sulfonato-calix[8]arene (**sclx₈**, 1.5 kDa) induces the assembly and crystallization of different types of proteins.² The six-bladed β -propeller *Ralstonia solanacearum* lectin (RSL) co-crystallises with **sclx₈** in three distinct crystal forms, two of which rely exclusively on protein – calixarene complexation.³ Here, we tested **sclx₈** complexation with a five-bladed β -propeller. A mutant of the designed pentamer PDB 5c2n⁴ (~25 kDa) was selected for study. Despite the symmetry mismatch between the protein (*C*5) and macrocycle (*C*8), a tight 1:1 complex is formed (Figure 1). The calixarene sits in a shallow pocket and overlaps with the central water channel (a feature common to β -propeller proteins). Thus, the protein acts as the host and the macrocycle is the guest. Each protein monomer contributes 120–180 Å² to the interface area with the calixarene, resulting in a total of 900 Å² - the largest protein–calixarene interface observed to date. Solution-state NMR experiments confirm the binding site and suggest a micromolar dissociation constant. Apparently, multivalent interactions are important in this unexpected complex.

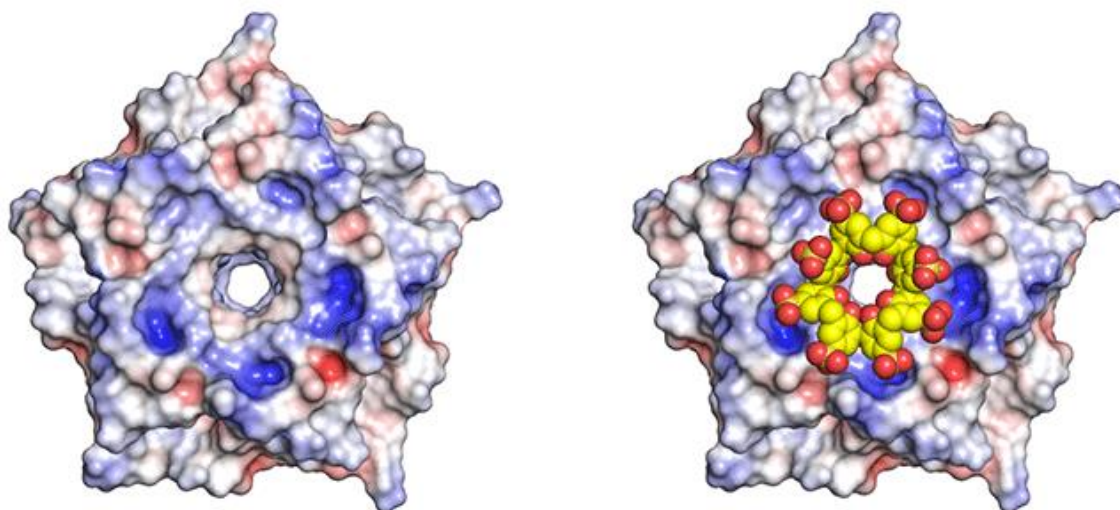


Figure 1: Crystal structures of the pure pentamer (left) and the pentamer–**sclx₈** complex (right). The protein is shown as a surface coloured by electrostatic potential.

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1. L. Baldini, A. Casnati, F. Sansone, and R. Ungaro, *Chem. Soc. Rev.* 2007, 36, 254–266.
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3. K. O. Ramberg, S. Engilberge, T. Skorek, and P. B. Crowley, *J. Am. Chem. Soc.* 2021, 143, 1896–1907.
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Extraordinary control of photosensitized singlet oxygen generation by acyclic cucurbituril-like containers

Daniel Guerra-Díaz¹, Nory Mariño-Ocampo¹, Vladimir Kobanov², Belinda Heyne², Felipe Andrade-Villalobos³, Angélica Fierro³, **Denis Fuentealba**¹

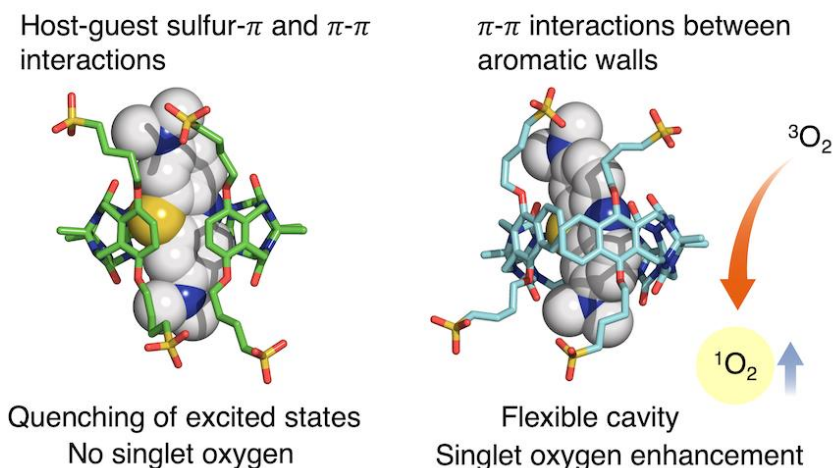
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³*Department of Organic Chemistry, Pontificia Universidad Católica De Chile, Santiago, Chile*

Supramolecular control of singlet oxygen generation is incredibly valuable for several fields with broad applications and thus still challenging. However, macrocyclic inclusion complexes inherently restrict the interaction of photosensitizers with surrounding oxygen in the media. To circumvent this issue, we turned our attention in this work to acyclic cucurbituril-like containers and uncover their properties as supramolecular hosts for photosensitizers with extraordinary control of their photophysics, including singlet oxygen generation. Thermodynamic and photo-physical studies were carried out showing that these acyclic containers compare very favorably to benchmark macrocycles such as cucurbiturils and cyclodextrins in terms of their binding affinities and supramolecular control of singlet oxygen generation. Acyclic container with terminal naphthalene walls offers a similar cavity to cucurbit[7]uril and the same carbonyl-lined portals for a tight binding of phenothiazinium dye methylene blue and stabilizing its singlet and triplet excited states. Thus, generation of singlet oxygen for this container is higher than for other macrocycles and even higher than the free photosensitizer. While the acyclic container with smaller terminal benzene walls, stacks over the dye through sulfur- π and π - π interactions deactivating the singlet and triplet excited states, thus showing the lowest generation of singlet oxygen out of all of the studied systems. Due to the great water solubility and biocompatibility of these systems, they possess great potential for novel applications in photocatalysis, synthesis, and biomedical fields, among others.

<https://doi.org/10.1021/acs.jpcc.3c00583>



Paramagnetic guest exchange saturation transfer (paraGEST) revealing hidden interactions in supramolecular host-guest systems

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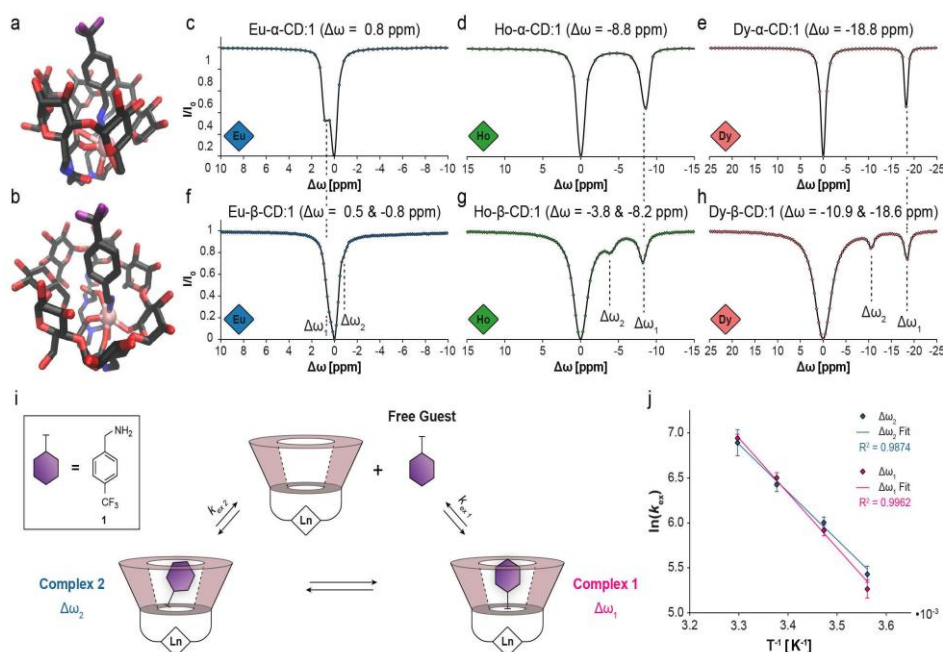
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The implementation of supramolecular architectures in a desired field is driven by dynamic processes, providing them with unique properties. However, studies of such processes, particularly in host-guest systems, are limited for specific dynamic regimes, primarily due to the inaccessibility of proper analytical tools. Therefore, robust approaches, which can be easily and extensively used for the quantitative evaluations of kinetic characteristics of such molecular systems, are greatly needed.

Previously, we have established and exploited the fluorine-19 guest exchange saturation transfer (¹⁹F-GEST) technique to study slow-to-intermediate exchanging host-guest systems¹ and expanded it into ¹⁹F-paraGEST by introducing paramagnetic lanthanides to host-guest systems of α -cyclodextrins (α -CDs)², adopting the principles of the paraCEST MRI approach³.

Here, we use ¹⁹F-paraGEST to investigate guest exchange in systems of Ln- α -CDs (Fig. 1a) and Ln- β -CDs (Fig. 1b), exhibiting intermediate-to-fast exchange rates in the NMR time scale (well-above the currently applicable limit). Specifically, we adapted the same lanthanide modification for two types of CD macrocycles, characterized by different cavity sizes, and studied their ¹⁹F-paraGEST features utilizing the same ¹⁹F-guest. Benefitting from the increasing pseudo-contact shift (PCS) effects of specific lanthanides, we were able to increase the spectral resolution of ¹⁹F-GEST (Fig. 1c-e and Fig 1f-h), which, consequently, revealed two distinct populations of bound ¹⁹F-guests in Ln- β -CDs. This observation, not obtainable for Ln- α -CDs, could not be detected with other analytical tools such as mass spectrometry, 1D-NMR, diffusion measurements, and UV-vis spectroscopy, emphasizing the uniqueness of ¹⁹F-paraGEST as an analytical tool for studying binding kinetics in supramolecular assemblies.

The observations summarized here imply different CDs-binding geometries for a given guest in Ln- β -CDs (Fig. 1i), characterized by similar activation energies (Fig. 1j), and highlight the importance of ¹⁹F-paraGEST not only as a tool for future development of non-fluorescent-CD-based-sensing but also for studying “NMR-invisible” host-guest systems.



Flash talk

Substrate-controlled and template-assisted mechanochemical synthesis of *thio*-hemicucurbiturils

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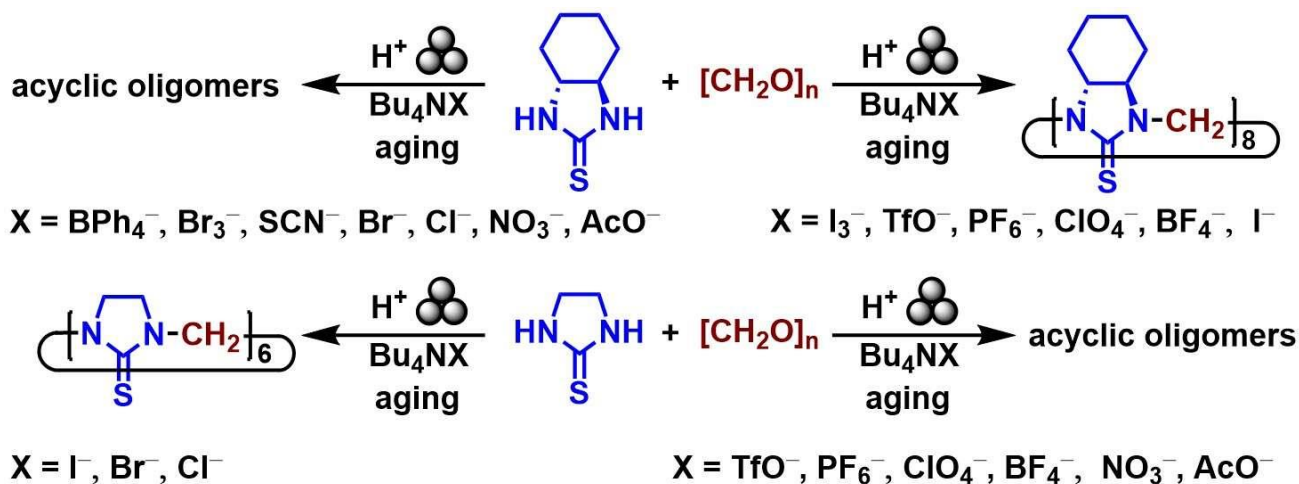
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Hemicucurbiturils (hemiCB[n]s) consist single hoop of methylene linkers interconnecting 2-imidazolidone (ethylene urea) subunits. In contrast to the rigid pumpkin shape of cucurbiturils and their affinity toward cationic species, the structure of hemiCB[n] adopts an alternating conformation and encapsulates anions. To date, selected 2-imidazolidone derivatives were successfully cyclooligomerized, and the size of the resulting macrocycles was controlled by the anion-template nature.

Here we present the synthesis of *thio*-hemiCB[n] ($n = 6, 8$) employing the heteroatom replacement approach.¹ However, the commonly used synthetic methodology for cyclooligomerization of imidazolidone-2-thione and its derivatives is not applicable because the substrates are acid-sensitive. Instead, we applied a mechanochemical approach that involves solid-phase reactants in a nearly solvent-free environment. Optimization reactions included the effect of the templating agent, the nature of the acid catalyst, aging duration and temperature. Under the optimized reaction conditions, we successfully prepared 6- and 8-membered *thio*-hemiCB[n]s in high selectivity. Ring-size selectivity was attributed to the nature of the building block. Acyclic oligomers vs. macrocycles were determined by choice of anion template. X-ray studies and isothermal titration calorimetry (ITC) confirmed the selective anion-binding affinities of each *thio*-hemiCB[n] homolog.



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Hydrogen-bonded extended cavity supramolecular boxes in water based on pillar[6]arenes

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Self-assembled supramolecular cages and containers can serve as discrete and confined space in which new chemistry and catalysis can occur.¹ Therefore, the preparation of such systems in aqueous environment is paramount.² Following our previous work on the subject,³ here we present the preparation and characterization of new pillar[6]arene-based supramolecular hexagonal boxes (SHBs) in water having extended cavities that are held together by hydrogen bonds. These boxes are based on different extended amino derivatives of pillar[6]arene that serve as the core of the systems and mellitic acid and benzene pentacarboxylic acid that serve as the lids. Initially, the host-guest interactions of these pillar[6]arene derivatives with 1, ω -bi-functionalized alkane guests was assessed. Then, the behavior of the guests after the addition of the lid compound and in presence of the “closed” box was studied. From these experiments we could draw conclusions on the relative affinity of the guests and the relative stability of the different extended self-assembled supramolecular boxes formed.

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Calix[4]arenes bearing mixed aza/thia bridges

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The well-established chemistry of classical calixarenes can be reasonably changed by the introduction of heteroatoms instead of the common CH₂ bridging units, which results in significant changes in the macrocycle behaviour (cavity size, electronic properties). For instance, thiacalixarenes exhibit distinct complexation and conformational properties due to the presence of sulfur bridges. Azacalixarenes are of growing interest as they can form quinoid type structures and can be stabilized in the form of a zwitterion by subsequent intramolecular proton transfer. The aim of this work is the synthesis of calixarenes combining properties of the both macrocyclic compounds together within a single molecule to obtain unprecedented fused multicalixarenes. Such systems can find the application mainly in the preparation of new types of receptors. We focused our attention also towards the inherently chiral azacalixarenes which are interesting candidates for the supramolecular recognition and extends the heteracalixarene family.

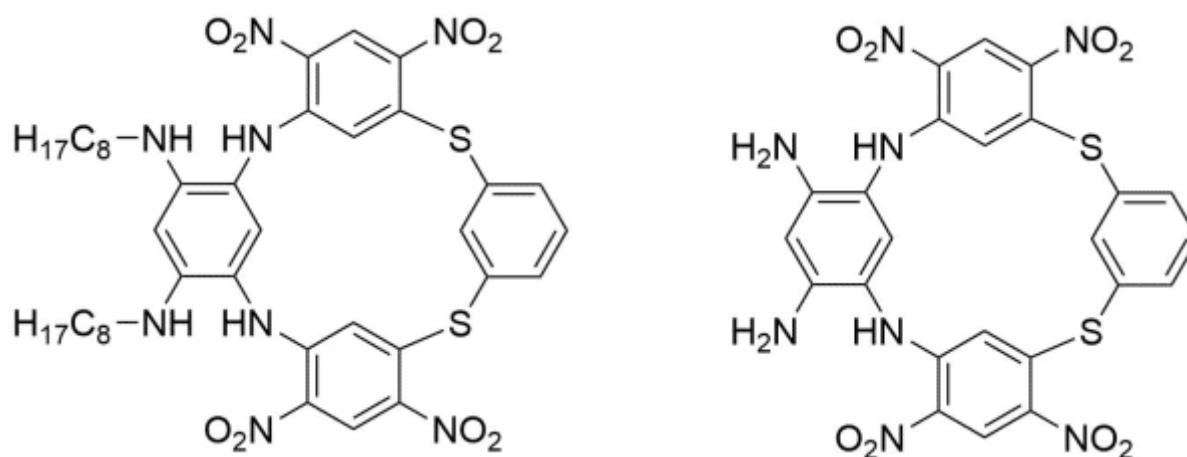


Figure 1: The example of prepared fused heteracalixarenes

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Improving pH stability and affecting enzymatic degradation of the anticancer prodrug capecitabine by host-guest complexation with pillararene derivatives

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Cancer is currently a leading cause of death, and the number of cancer cases is expected to grow in the future. Indeed, overcoming cancer is a long and persistent struggle.¹ Supramolecular chemotherapy based on host-guest chemistry is a new strategy to fight cancer.² Capecitabine (**1**) is an oral prodrug of 5-fluorouracil for cancer patients.³ It is administrated in high doses (due to short elimination half-life of 0.5-1 h) and causes severe adverse effects.³ Nevertheless, the sales of **1** world-wide exceed \$1 billion in 2021.^{3c} Here, we hypothesized based on its structure that capecitabine is suitable for encapsulation in pillar[5]arene (P5A) derivatives, in aqueous solution. Pillararens are cylindrical macrocyclic hosts, first synthesized by Ogoshi in 2008.⁴ We chose four derivatives of P5A and used ¹H-,¹⁹F- NMR and isothermal titration calorimetry to study the complexation of these P5A's with **1**. We evaluated the effect of the complexation on the chemical characteristics and stability of **1** by following its decomposition rate, at acidic pH, and in the presence of the enzyme carboxylesterase (the first enzyme in the cascade of reactions leading from the prodrug to the active drug). We found that three of the P5A's we have tested protect **1** significantly from acidic degradation. We also found that the same derivatives can affect the enzymatic hydrolysis of **1** in a variable manner. These results demonstrates that complexation of **1** by P5A derivatives can affect the clinical use of this anti-cancer prodrug.

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Diffusion NMR reveals the structures of the molecular aggregates of resorcin[4]arenes and pyrogallol[4]arenes in aromatic and chlorinated solvents

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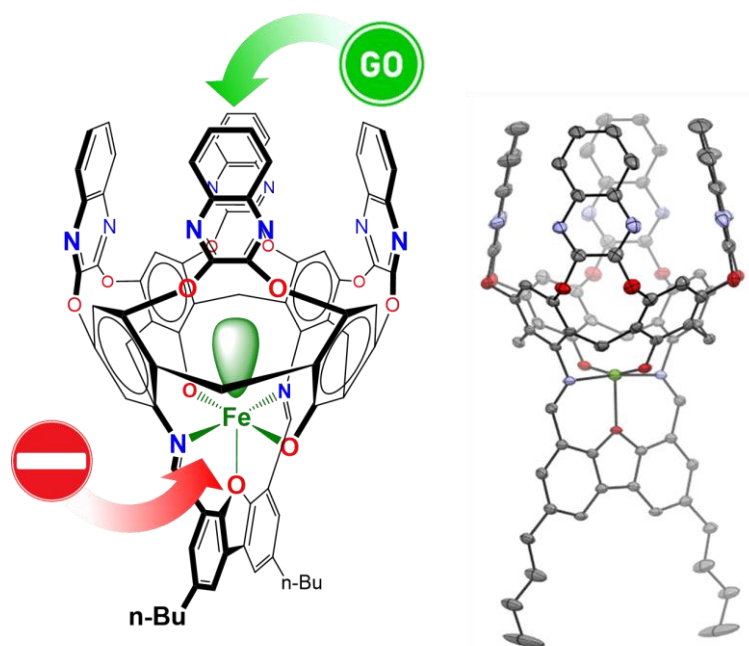
Resorcinarenes and pyrogallolarenes forms fascinating structures in the solid-state as shown by the Atwood and Mattay groups.¹ Diffusion NMR² has been instrumental in probing the hexameric nature of such systems in solution.³ In the last decade Tiefenbacher and others demonstrated the catalytic abilities of resorcinarene,⁴ which made this macrocycle even more important to the scientific community. Recently, Sakurai and his group suggested, based on SANS or SAXS, that C₁₁-resorcin[4]arene (**1**) forms octameric micellar and not capsular aggregates in toluene.⁵ Here, we have used NMR spectroscopy (protonated solvent ¹H-NMR, diffusion and DOSY) to study the self-assembly of **1** and C₁₁-pyrogallol[4]arene (**2**) in benzene, toluene, and in chloroform.⁶ Our findings revealed that **1** self-assembles into two types of aggregates in aromatic solvents, the major species being an hexameric capsule and the minor one appears to be an octameric aggregate. We showed that hexameric capsules are the only type of aggregates found for **1** and **2** in chloroform. Also, hexameric capsules are the only type of aggregates for **2** in benzene and toluene. Our findings demonstrate the importance of using appropriate reference when using diffusion NMR and how essential is to use protonated solvent ¹H-NMR when studying capsular structures.

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Highly modular metallocavitands with deeply embedded metal centers

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Designing simple homogeneous catalysts that incorporate structural motifs, analogous to key ones found in metalloenzymes, remains a significant challenge for chemists to this day. For this purpose, cavitand-based architectures have significant potential, due to their ability to emulate the flexible hydrophobic pocket present in many enzymatic systems. This is due to the known vase-kite equilibrium exhibited by these compounds in solution. However, very few examples exist which manage to fully combine the unique supramolecular capabilities of such systems with the chemical reactivity of organometallic complexes. Herein we report the design and synthesis of a conceptually-novel cavitand-based multidentate ligand architecture, capable of fully embedding a coordinatively unsaturated metal center via a rigid coordination cage deep within its cavity, in a way that only enables accessing the metal center from within the macrocyclic pore. By utilizing a modular approach to ligand design, a series of novel cavitands, varying in the nature of the coordinating groups in the primary sphere of the metal center, was prepared. This ligand architecture exhibits a high degree of affinity towards divalent and trivalent 1st row transition metals. The resulting complexes are stable in a coordinatively unsaturated form, with the metal centers possessing a vacant coordination site within the molecular cavity of the ligand. Through various crystal structures obtained, the ability to incorporate different small guest molecules into the vacant coordination site of the metal centers is demonstrated.



Selective electrochemical impedance sensing of perchlorate through self-assembled monolayers of semiaza-bambusuril derivatives

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Salts containing perchlorate anions are persistent pollutants threatening human health by impairing the thyroid gland's function over long-term exposure. Consequently, many analytical methods were developed for detecting perchlorates in water sources, soil, and food products. High-throughput electrochemical techniques are also attractive for developing and easily operating sensory devices.

Here we report the synthesis of new semiaza-bambusurils (BUs) equipped with surface anchoring groups, such as thioether or disulfide groups and their implementation into SAM-based electrochemical anion sensing layers. We characterized the interactions at the interface between the anchoring groups of semiaza-BUs and the metal substrate via Cyclic voltammetry (CV) with Fe(CN)₆^{3-/4-} as a redox probe together with X-ray photoelectron spectroscopy (XPS), atomic force microscopy (AFM) and ellipsometry techniques. Data showed that the anion receptors' packing patterns on the gold strongly depend on the anchoring group. Electrochemical impedance spectroscopy (EIS) supported by CV measurements, was used for detecting perchlorate anion in aqueous solutions.

With short thioether alkyl chains, no interfacial solid-liquid electrochemical activities were detected. In contrast, SAMs based on semiaza-BUs equipped with either aryl thioether or lipoic chains followed a significant change in their CV and impedance plots upon titration of perchlorate. Both SAMs showed high selectivity compared to other inorganic anions.

Interestingly, the impedance behaviour of the lipoic SAM were depend upon the concentration of incubating solution and was significantly more sensitive at 1 mM concentration of lipoic semiaza-BUs incubating solution to detect the perchlorate concentration (down to 2-4 mM), which was explained by the highly compact, dense monolayer film due to cross-linking between disulfide moieties. This crosslinking phenomenon could be an elegant solution for pinholes and defects commonly associated with SAMs. The SAMs of the disulfide-substituted semiaza-BU provided a way to tune the dynamic range and sensitivity of anion detection by variation of their thickness. Remarkably, strong binding of perchlorate anion over other anions was detected with SAMs of the semiaza-BU.

Flash talk

Colorimetric differentiation of solid-state supramolecular complexes of coumarin and bimeane fluorophores

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Supramolecular complexation of small-molecule fluorophores in macrocyclic hosts has the potential to dramatically alter the photophysical properties of such fluorophores, their stability, and a variety of other physicochemical properties. Our research groups have pioneered the development of novel bimeane and coumarin fluorophores, the supramolecular complexation of such fluorophores in cyclodextrin hosts, and the use of these fluorophores as highly effective fluorescent and colorimetric sensors. The majority of our research to date has focused on investigating solution-state complexation, which has the advantage of facilitating a multitude of spectroscopic analytical techniques, while the majority of our effective sensors operate in the solid-state. Our work reported herein aims at bridging the gap between solution-state complexation and solid-state chemical sensing, through the rational formation, analysis, and optimization of solid-state supramolecular complexes. These complexes, formed from a variety of calixarene and cyclodextrin hosts combined with bimeane and coumarin fluorophores, display unique solid-state properties, particularly for methyl-beta-cyclodextrin combined with an aldehyde-substituted coumarin. A detailed analysis of these results provides both improved understanding of solid-state complexation, including critical differences between cyclodextrin and calixarene scaffolds, as well as critical information for the development and optimization of next-generation supramolecular sensors.

Cucurbit[7]uril-mediated histidine dimerization: exploring the structure and binding mechanism

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Cucurbit[7,8]urils have been shown to form inclusion complexes with hydrophobic amino acids and peptides containing those residues at the N-terminus. However, the binding affinity of histidine residues to cucurbit[7,8]urils has not been extensively studied, despite their common use in protein purification. In this study, we explored the binding affinity of histidine residues to CB7 and CB8 using X-ray diffraction experiments and isothermal titration calorimetry. It revealed that the binding of histidine to CB7 and CB8 was weak, with equilibrium dissociation constants (K_d) in the range of 10^{-3} M. However, we observed that CB7 readily formed crystals in the presence of histidine in solution, indicating its binding capability. Our X-ray diffraction experiments showed the formation of a network of $\pi \dots \pi$ and hydrogen bonds between CB7 and two histidine residues (Figure 1), challenging the previous notion that only CB8 is large enough to accommodate two rings. Furthermore, our isothermal titration calorimetry measurements showed that the binding of dipeptides containing histidine at the C-terminus to CB7 and CB8 exhibited a stronger binding affinity, with equilibrium K_d in the range of 10^{-6} M. In contrast, dipeptides with histidine at the N-terminus exhibited weaker binding, with K_d values in the range of 10^{-3} M, likely due to steric hindrance. These findings highlight the potential of CB7 as a host molecule for binding histidine-containing molecules, particularly in crystal engineering and drug delivery applications.

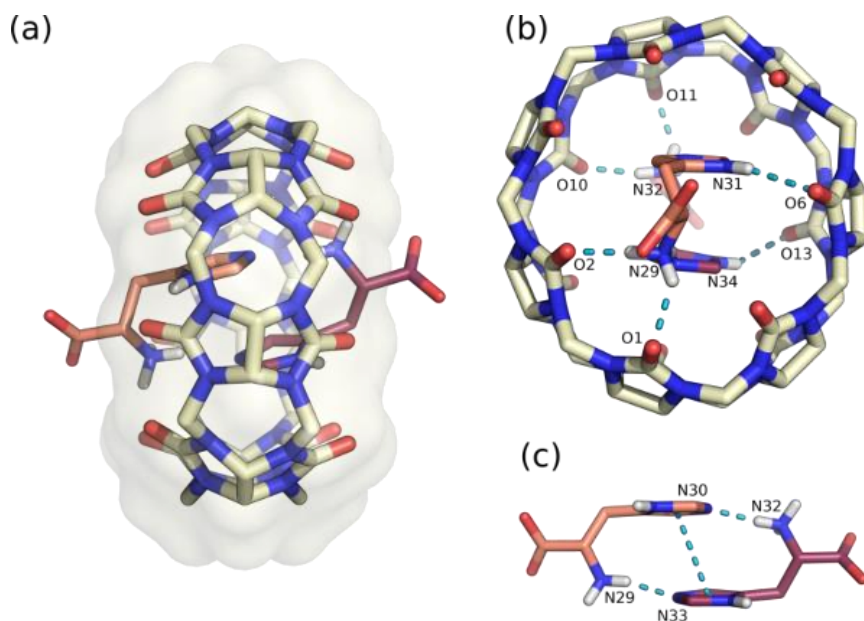


Figure 1. L-His@CB7 in the asymmetric part of the unit cell of the crystal structure with host-guest ratio 1:2. The CB7 molecule is drawn in stick representation, with van der Waals surfaces shown (a). Hydrogen bonds and $\pi \dots \pi$ stacking interactions shown as a blue dashed lines between L-His and CB7 (b) and between two L-His (c). Atoms involved in the most important intramolecular interactions between the guest and host are labelled. Non-polar hydrogen and water atoms removed for clarity.

Association constants between homooxacalixarenes and nitroaromatic compounds obtained by fluorescence: a critical analysis

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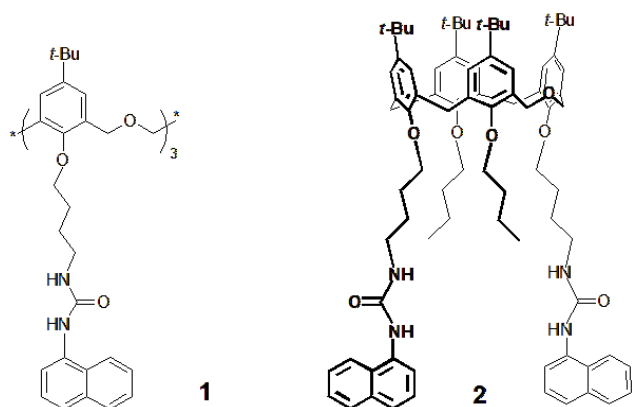
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The detection of explosives is a major task in the fight against terrorism and in homeland security. Nitroaromatic compounds (NACs), such as trinitrotoluene (TNT), dinitrotoluene (DNT) and trinitrophenol (TNP), are common explosives used for military purposes and are the principal components of unexploded landmines. They are also considered environmental pollutants.

Low-cost detection techniques, with high portability, high sensitivity and selectivity are needed for in-field analyte effective sensing. Luminescence-based methods fulfil these requirements.¹ Lately, a broad range of fluorescence sensors for explosive monitoring have been developed based on calixarenes.² Fluorophores like naphthalene, anthracene and pyrene are among the most incorporated in the calixarene framework, leading to potential fluorescent probes for NACs.

In the course of our recent studies on anion binding by fluorescent homooxacalixarenes,^{3,4} we have investigated the possible recognition of nitroaromatic compounds by these receptors. This work reports the binding behaviour of two ureido-hexahomotrioxacalix[3]arene (1) and dihomooxacalix[4]-arene (2) derivatives containing naphthyl residues at the lower rim, towards selected NAC's. Their affinity (or lack of it) was determined by UV-Vis absorption, fluorescence and NMR spectroscopy. Conflicting results between the usual approach in fluorescence studies and the other methods prompted us to conduct a broader study.



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Flash talk

A modular approach towards the total synthesis of conjugated carbon nanocones from calixarenes

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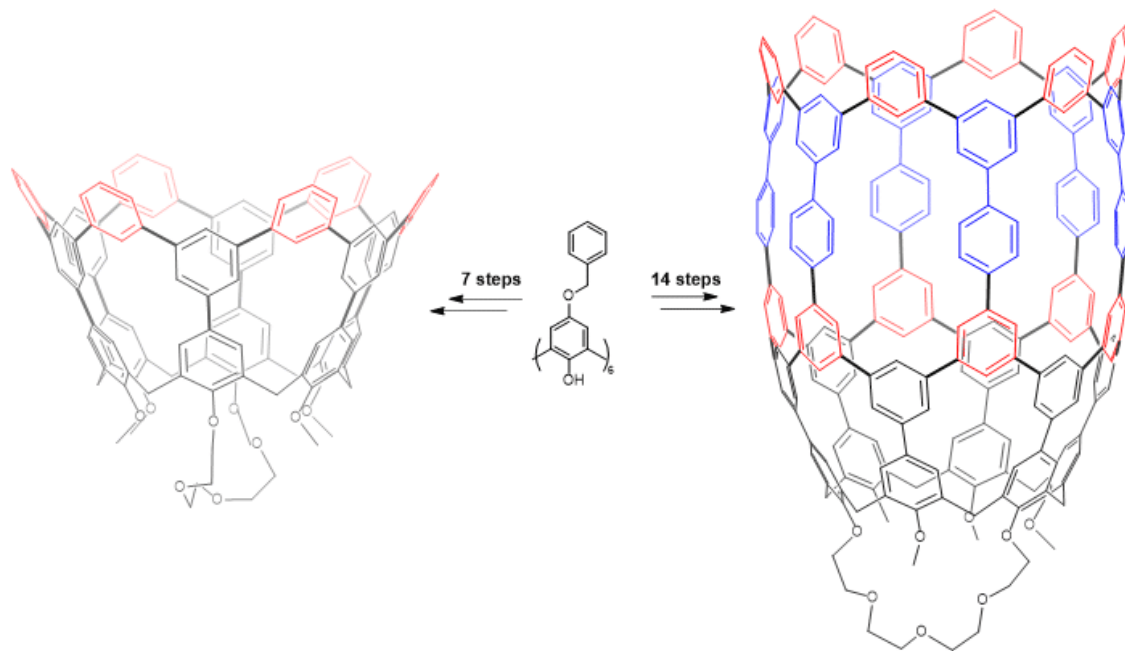
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With recent developments in the synthesis of carbon-rich nanostructures, extensive strategies have been undertaken to control and direct their outstanding optoelectronic properties which depend on the geometry parameters (diameter, chirality, winding mode, etc.).

In this context, based on our recent publication[1] we developed a new method for the synthesis of conjugated carbon nanocones, using preassembled aromatic units organized on a calixarene template. First, using calixarenes offers powerful templating strategies to build lengthened, diameter-controlled, and functional conjugated structures. Moreover, it allows for avoiding many of the difficulties encountered in the current syntheses of “classical” Single-Walled Carbon Nanotubes SWCNTs. Second, the calixarene rings are directly involved in the conjugated system, increasing its rigidity and reinforcing its electronic potential. Furthermore, the large cavity of these structures can be used in host-guest chemistry.

Last, the rigidity of the preassembled aromatic units reduces the number of steps during the final assembly of the conjugated ring. This considerably improves the yields.

Photophysical studies and DFT analysis of these new nanocones suggest interesting electronic and optical behaviors.



Scheme : Synthetic route of the two carbon nanocones starting from calix[6]arene.

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Flash talk

Electron deficient arms of calix[4] basket for capturing toxic fluoride ion

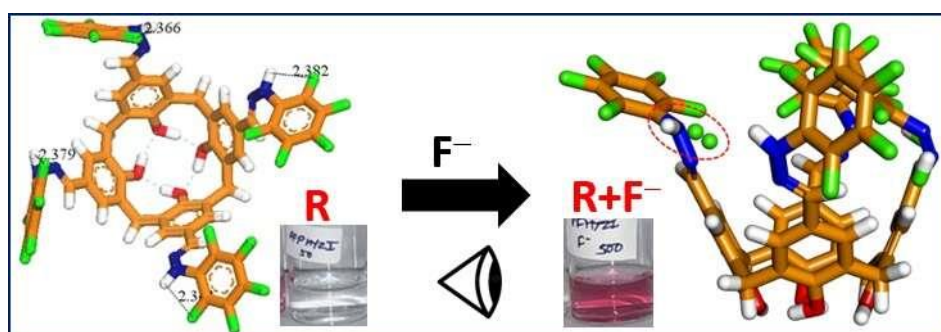
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Owing to a stable cone conformation of calix[4]arene, it is one of the most widely used macrocycles for highly selective recognition of ions.[1] Moreover, a broad range of anion sensors have been developed using the calix[4] platform.[2] Intake of excess fluoride is highly toxic and detrimental to human body. Therefore, its detection is crucial. Here we present a neutral electron-deficient receptor of calix[4]arene, R is synthesized and characterized. The R showed naked eye detection of fluoride by giving instant deep pink color among other 19 anions studied in acetonitrile. No interference of other anions is observed. Two isosbestic absorption points in the UV-vis studies implied transition from free R to fluoride complexed species. The fluoride interacted with electron-deficient centres identified by ¹H & ¹⁹F NMR studies. Variable temperature NMR studies revealed the formation of HF₂⁻ when ten equivalent of fluoride is added to the R. The fluoride ion bound species along with counter ion are detected by ESI-MS. DFT calculations demonstrate the strong interaction of F⁻ ions with the R and an optical absorption shift towards longer wavelengths in R+F⁻ complexes as revealed by TD-DFT studies as shown in the Scheme 1.[3]



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Bambusuril macrocycles for selective anion binding

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Six membered bambusurils are macrocyclic compounds consisting of six glycoluril units held together by six methylene bridges.¹ These compounds are characterized by an electropositive cavity that allows them to bind to inorganic anions of different sizes, such as small fluoride and large iodide. This behavior is due to the relatively high flexibility of the macrocycle, which can adapt to anions of different sizes and shapes. The selectivity of bambusurils for different anions has remained constant regardless of the type of substituent attached to their portals. Recently, we reported the synthesis of chiral bambusurils bearing spacious 1-phenylethyl groups, which provide the macrocycles with higher rigidity compared to the former derivatives.² Herein, we show that these chiral bambusurils BU1 and BU2 (Fig. 1) bind inorganic anions with very different selectivity than previously prepared bambusurils derivatives.

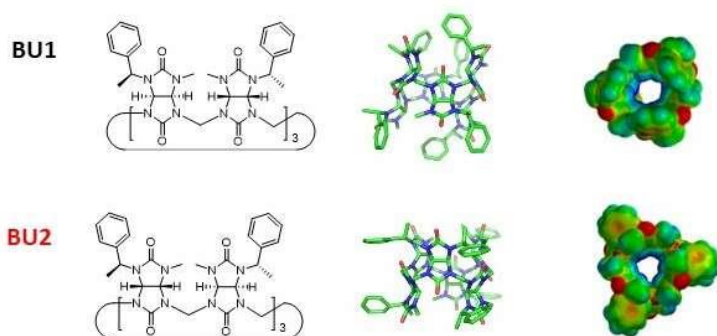


Fig. 1 Schematic representation and electrostatic surface potential of BU1 and BU2

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Regulation of microtubule dynamics and function in living cells via cucurbit[7]uril host-guest molecular recognition

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Protein regulation, as well as their assembly and dynamics, are responsible for nearly every function and developmental programme in biological systems. Synthetic control over these processes is an important aspect to understand as well as gain control over them. Through the reversible connection of complementary components, host-guest recognition provides an enticing method for achieving this control. In this study, we were able to build a biochemical regulator that efficiently allows supramolecular control and regulation of microtubule dynamics in a complex live cell environment. We have targeted the cytoskeleton protein Microtubules (MTs) as they contribute significantly to vital cellular processes like cellular motility, intracellular trafficking and cellular proliferation. We covalently modified docetaxel, a well-known small molecule that stabilises MTs against depolymerization, to create a microtubule-binding docetaxel analogue by incorporating p-xylenediamine into its side chain at the 3'-amine position. This analogue upon complexation with cucurbit[7]uril (CB[7]) form a non-toxic complex. This complex can be disassembled to restore the activity of docetaxel analogue by an external chemical stimuli, the higher affinity orthogonal guest of CB[7], 1-adamantylamine (ADA) which enables the release of the bound docetaxel analogue from CB[7] host. We thoroughly investigated intracellular function of this host-guest complex by using GFP-tagged MTs. To achieve the spatiotemporal control over the MT activity we have used photo-caged adamantylamine (^CADA) which upon 365 nm light irradiation delivers the higher affinity guest ADA. Further to use this system in the therapeutic study, we have used gold nanoparticles which were covalently modified with ADA which help to release the bound docetaxel analogue. Overall we were able to build a CB[7] mediated host-guest biochemical regulator that efficiently allows supramolecular control and regulation of protein dynamics in a complex live cell environment.

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Flash talk

Water-soluble pseudo-rotaxane with cucurbit[7]uril shuttling along a “dynamic” axle in response pH and light stimuli

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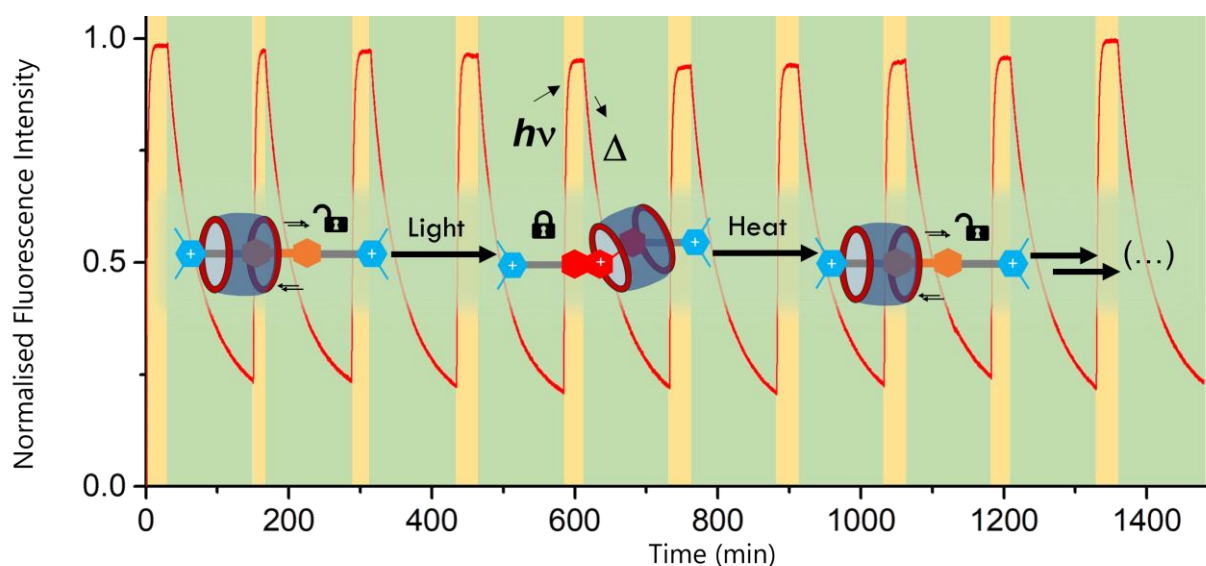
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Rotaxanes and pseudo-rotaxanes are among the most well studied types of supramolecular devices and cucurbiturils have proven over the last two decades that they are an ideal macrocycle to build this kind of devices in aqueous media, something that still presents a challenge in the field. In this work we will present a pseudo-rotaxane assembled from a cucurbit[7]uril, CB7, wheel and a 2-hydroxychalcone based axle.

This 2-hydroxychalcone based axle was designed to take advantage of the pH dependence and light sensitivity that are characteristics of these compounds, related to the anthocyanin's family multistate [1]. Indeed, while the chalcone is stable at neutral pH and has a measured affinity constant towards CB7 of $K_{11}=1.2 \times 10^5 \text{ M}^{-1}$, at very acidic pH ($K_{11}=1.5 \times 10^8 \text{ M}^{-1}$).

This flavylium form is also highly fluorescent on its own ($QY_{\text{free}} = 0.29$) and upon 1:1 complexation the quantum yield increases drastically to an almost unitarian quantum yield ($QY_{11} = 0.97$) [2].

Considering these stark differences in affinity, we can work at an intermediate pH where we start with the chalcone form and use light to promote the formation of the flavylium in a metastable equilibrium that eventually reverts to the chalcone form. That causes the CB7 wheel to switch from a loose binding on the chalcone, to a locked conformation on the flavylium and back to a loose binding on the chalcone again, and so on, as shown by the cycling experiment in the picture below.



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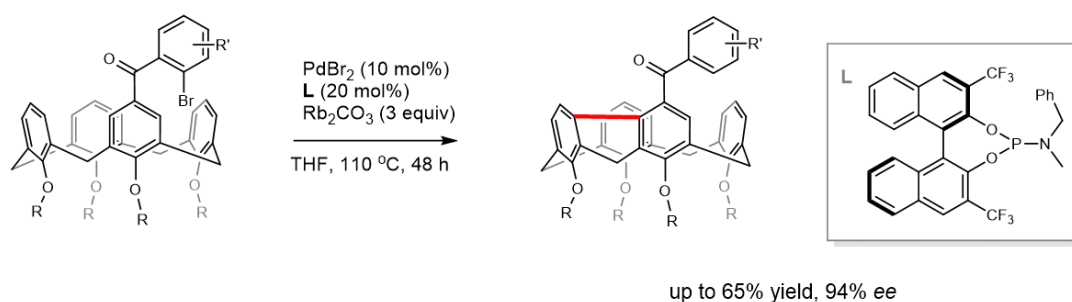
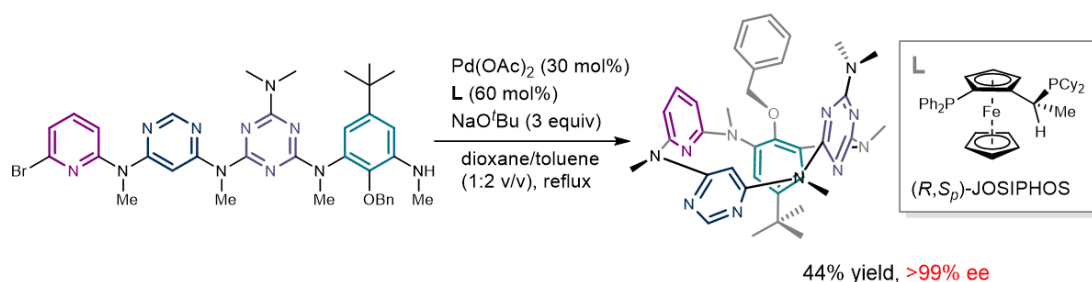
Flash talk

Catalytic enantioselective synthesis of inherently chiral calixarenes

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Owing to their unique chiral structures and chiral recognition properties, inherently chiral macrocycles have drawn growing attention since the term was coined in 1994. The efficient synthesis of highly enantiopure inherently chiral macrocycles, however, still remains challenging till now. We aim to establish and develop the methodology for the catalytic enantioselective synthesis of inherently chiral calixarenes. To showcase the potential of fragment coupling strategy to create diverse inherently chiral structures, we designed an ABCD-type linear tetramer which contains benzene, pyridine, pyrimidine, and triazine rings. Starting with this linear tetramer, we have developed a catalytic enantioselective intramolecular Buchwald-Hartwig C-N bond forming reaction for the highly enantioselective de novo synthesis of ABCD-type inherently chiral tetraazacalix[4]aromatics. Starting from unchiral macrocycles, we have also developed asymmetric post-macrocyclization transformation for the construction of inherently chiral macrocycles.[1] Under the catalysis of PdBr₂ and a chiral phosphoramidite ligand, the upper-rim mono-(2-bromoaryl)-substituted calix[4]arene derivatives underwent a facile enantioselective desymmetrization reaction to afford 9H-fluorene-embedded inherently chiral calixarenes in good yields with excellent enantioselectivities.[2] The so obtained inherently chiral macrocycles are useful scaffolds for the fabrication of circularly polarized luminescence (CPL) materials.[1-4] The outcomes opened new opportunities for the design and synthesis of novel CPL materials based on the inherently chiral calixarene skeleton.



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Synthesis of novel bridged inherently chiral calixarene derivatives

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Bridged derivatives of calixarenes present a unique substitution pattern that leads to highly distorted cavities, offering new possibilities for supramolecular chemistry applications. This project deals with the synthesis of new bridged inherently chiral calixarenes via regioselective mercuration of tetraalkylated calix[4]arenes.

The first part of this work is focused on synthesis of meta-substituted derivatives using Sonogashira reaction of the corresponding halogen substituted calix[4]arenes, which are then bridged by reaction with diphenyl diselenide and ferric chloride. The influence of functional groups on the course of the reaction was studied. The second method of bridging the upper rim involves the gold-catalysed cyclization to provide an anthracene motif within the macrocycle molecule.

The properties of the newly prepared compounds were investigated for their possible use in supramolecular chemistry. Inherently chiral substances were separated on a chiral HPLC, the complexation properties towards selected guests were assessed using the ¹H NMR or UV/Vis titration experiments. Several macrocycles in this project contain selenium atoms, which have a significant impact on the redox properties of substances. Therefore, the electrochemical methods were also employed to study these macrocycles.

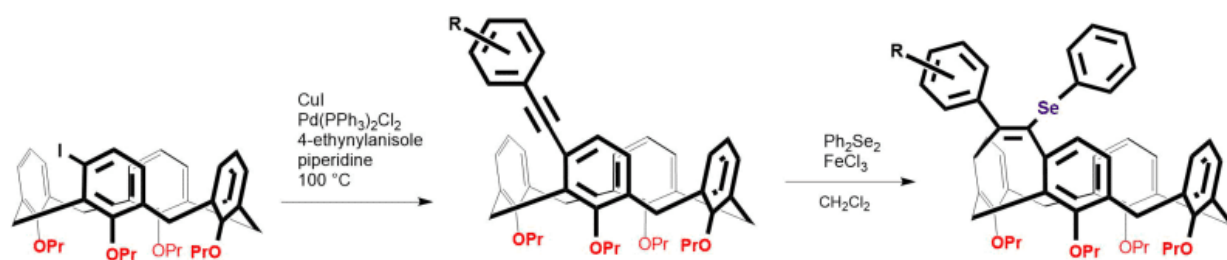


Figure 1. Synthesis of bridged derivatives of calixarenes

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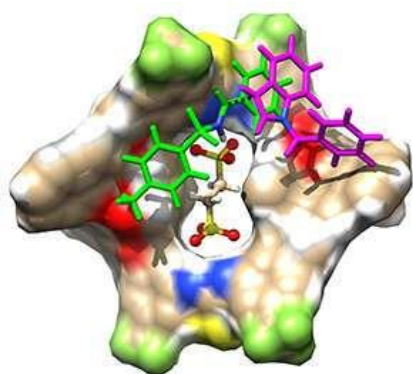
Flash talk

Anion-recognition directed supramolecular catalysis

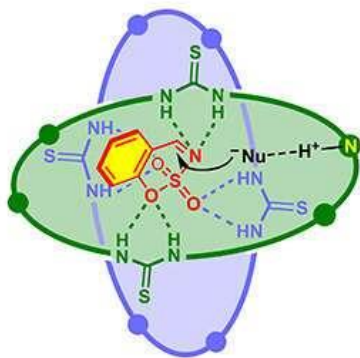
Qi-Qiang Wang

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Chinese Academy of Sciences, Beijing, China

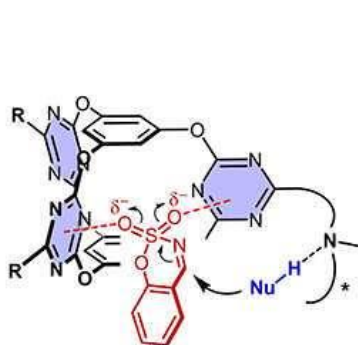
Our research focuses on the construction of functional macrocycles and cages with enzyme-mimetic pocket and specific recognition ability for boosting highly efficient and selective supramolecular catalysis. Different from the use of conventional, cation-relevant interactions or hydrophobic effects, we came up with anion-recognition direction by taking inspiration from the recent development of anion supramolecular chemistry. The advantages of anions, including rich variety, diverse geometry and multiple interaction sites, are taken for manipulating a sophisticated activation network. Following this concept, we have developed hydrogen-bonding macrocycle-enabled counteranion trapping and substrate-induced assembly catalysis systems with great efficiency and excellent stereocontrol.^[1-3] Moreover, exploiting of emerging anion- π interactions for driving highly efficient and selective catalysis was also achieved.^[4-6] Cooperative anion- π activation was realized by building molecular cage catalysts with electron-deficient π -cavity. It paves a way to push the novel anion- π activation toward more practical and useful catalyst design and applications.



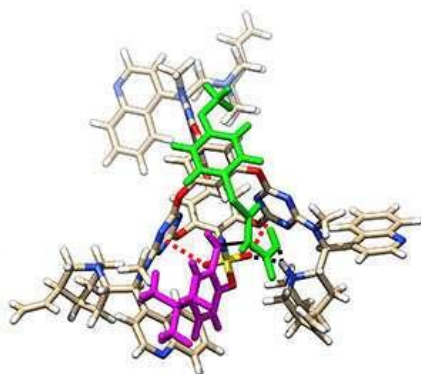
Macrocycle-enabled
Counteranion trapping catalysis



Substrate-induced
assembly catalysis



Cooperative anion- π catalysis



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Supramolecularly engineered platelets-hitchhiking delivery of morphology transformable peptide for tumor vascular embolization

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Tumor embolization therapy is a promising non-interventional anticancer modality, demonstrating effective tumor growth and metastasis inhibition by blocking oxygen, nutrient supplies and restraining angiogenesis. However, current strategies, mostly based on in situ embolization construction, showed imprecise and inadequate tumor obstruction, leading to unsatisfied embolization therapy. Inspired by natural coagulation process, which achieved by platelets activating and fabricating with fibrin, herein, we developed a supramolecular strategy for hitchhiking delivery of platelets with artificial fibrin (morphology transformable peptide) for effective tumor vascular embolization. Platelets-hitchhiking delivery is mediated via host-guest interactions between cyclodextrin (CD) and adamantane (ADA) modified on the surface of peptide-assembled nanoparticles and platelets, respectively. Under acid tumor microenvironment, the peptide-assembled nanoparticles could transform to fiber-like structure, imitating the function of fibrin to induce strong embolization together with platelets. Benefiting by the hemorrhage targeting of platelets, the proposed embolization strategy suppresses tumor growth and metastasis obviously on post-surgical tumor-bearing mice. Therefore, this supramolecularly engineered platelets-hitchhiking delivery system may be a promising antitumor embolization treatment, and more importantly, it might offer new insights for biomimicking behaviors constructed in situ.

Flash talk

Symmetry breaking during self-assembly of racemic mixture of organic cages

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Symmetry breaking is a process in which the symmetry of a system decreases spontaneously, and the study of symmetry breaking can provide important cognitive tools for the search of new materials, thus attracting widespread interest in physics, chemistry, and materials science. Symmetry breaking is relative and only valid when the temporal and/or spatial scales of the system are explicitly defined, and we herein use the self-assembly process of organic cage and cage catenanes to illustrate this relativity and to elucidate how the symmetry of racemic mixtures is broken at specific temporal, spatial, and logical levels. Symmetry is one of the most universal and important norms in the universe, and deviation from it requires a "driving force to achieve inhomogeneous properties", and we illustrate the driving force of non-covalent interactions in this process through the spontaneous chiral resolution of racemic mixtures of molecular cages during crystallization. Symmetry breaking is an important way to generate phenomena that provide rational design guidance for many functions, which we interpret through the generation of second-order nonlinear optics and ferroelectricity/piezoelectricity in the assembly of organic-cage racemates.