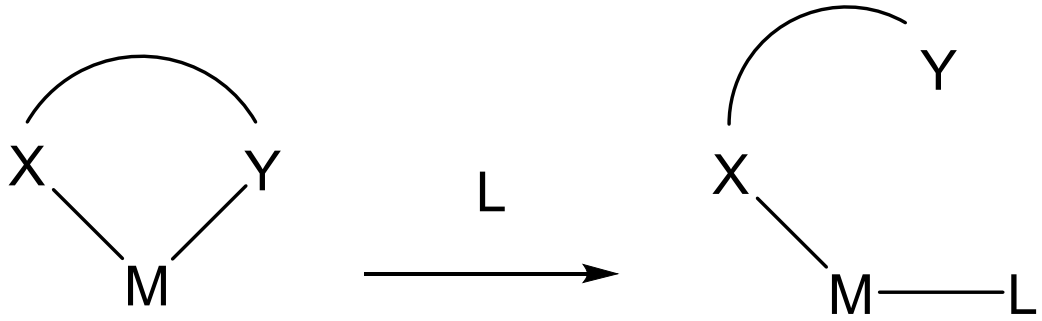
Hemilabile ligands



Douglas Baumgardner

Gilbertson Group

iCID Meeting July 15th, 2019

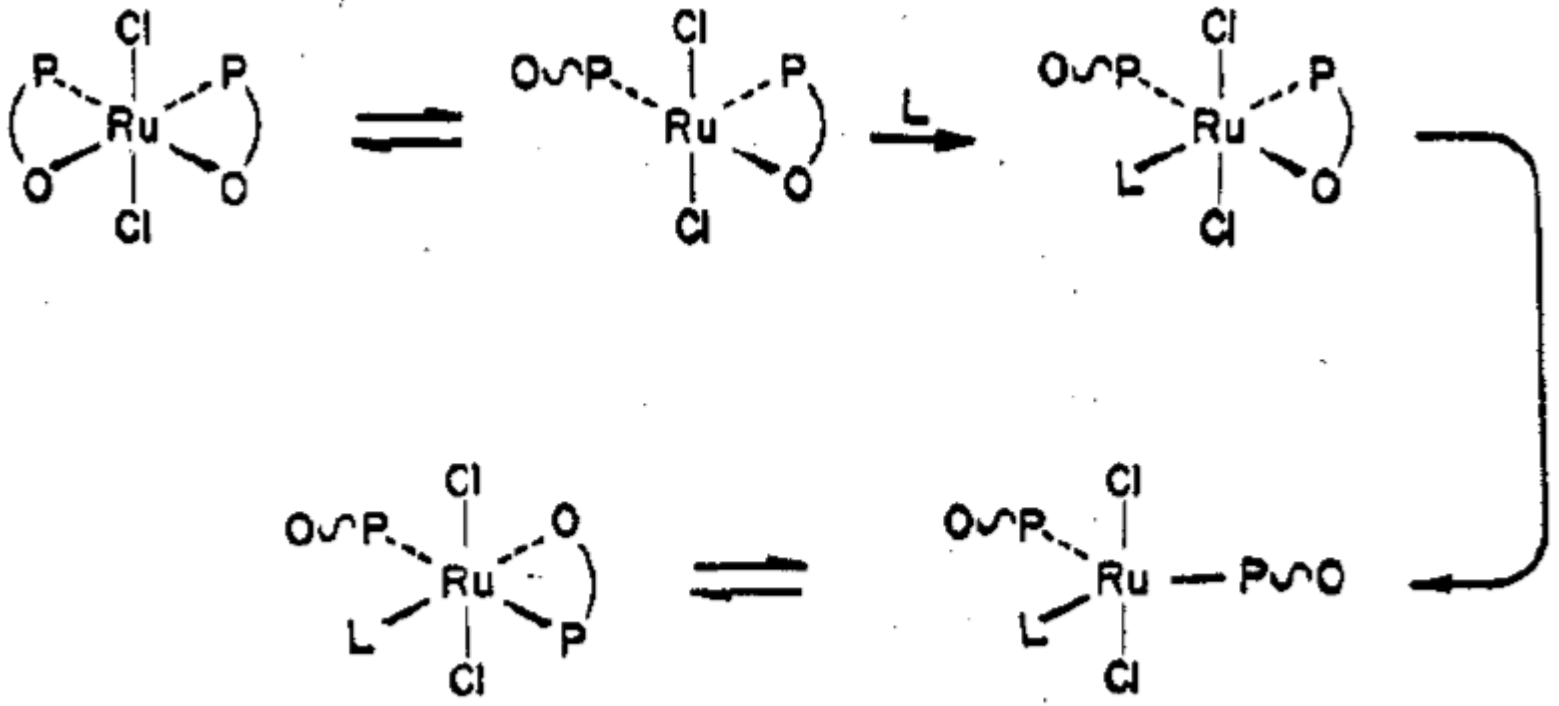
Historical context

Metal Complexes of Hemilabile Ligands. Reactivity and Structure of Dichlorobis(*o*-(diphenylphosphino)anisole)ruthenium(II)

JOHN C. JEFFREY*[1] and THOMAS B. RAUCHFUSS*[1]

Received January 26, 1979

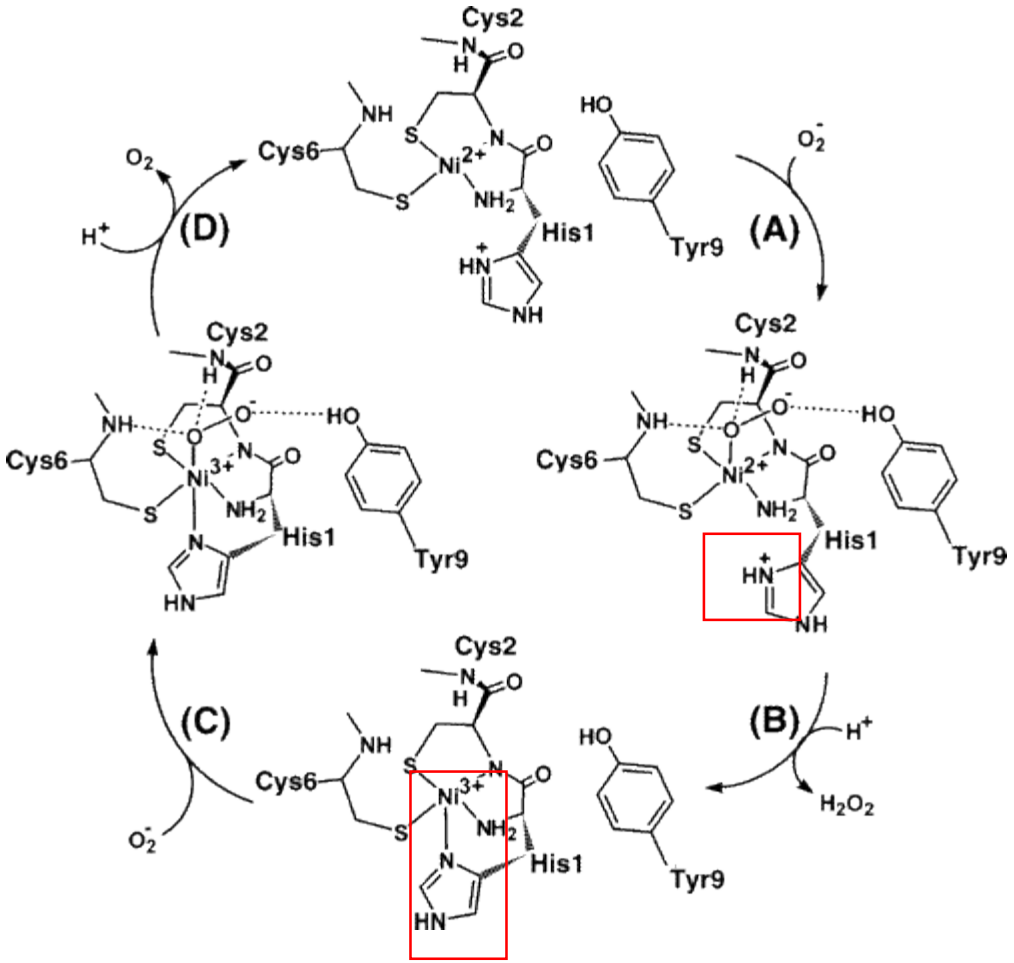
"For some time, we have investigated the chemistry of phosphine-amine and phosphine-ether ligands with the expectation that these ligands would bind well enough to allow isolation but would readily dissociate the "hard" ligand component, thus generating a vacant site for substrate binding. We call these ligands hemilabile."

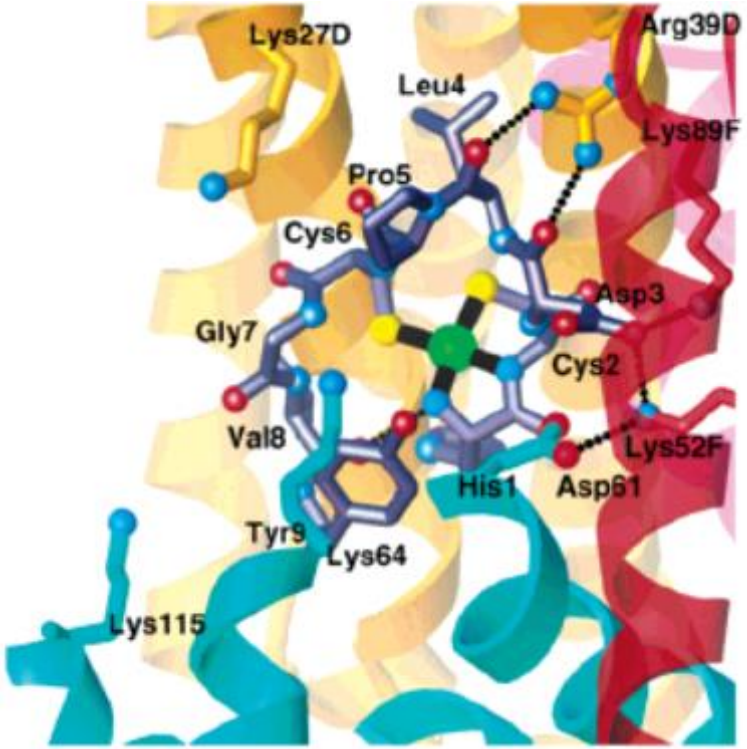


Jeffrey, J. C.; Rauchfuss, T. B. *Inorganic Chemistry* **1979**, *18* (10), 2658–2666.

In biology

$$2\ O_2^- + 2H^+ \longrightarrow H_2O_2 + O_2$$



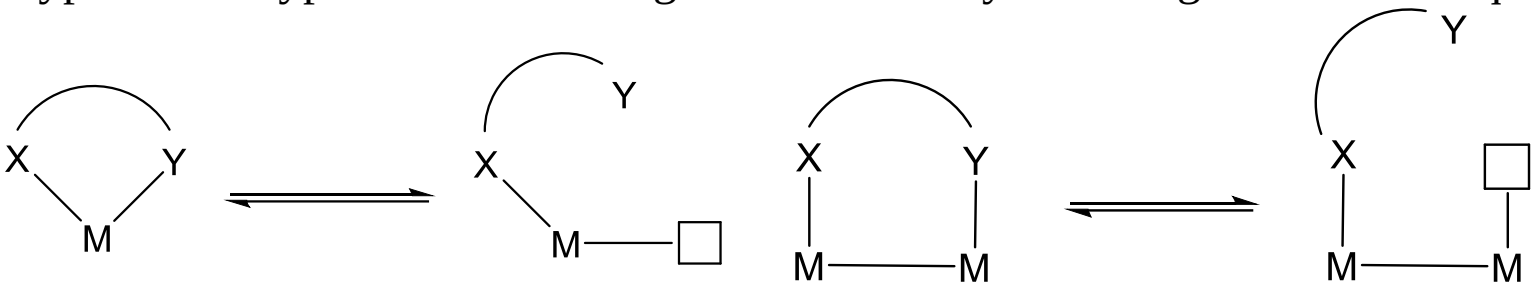


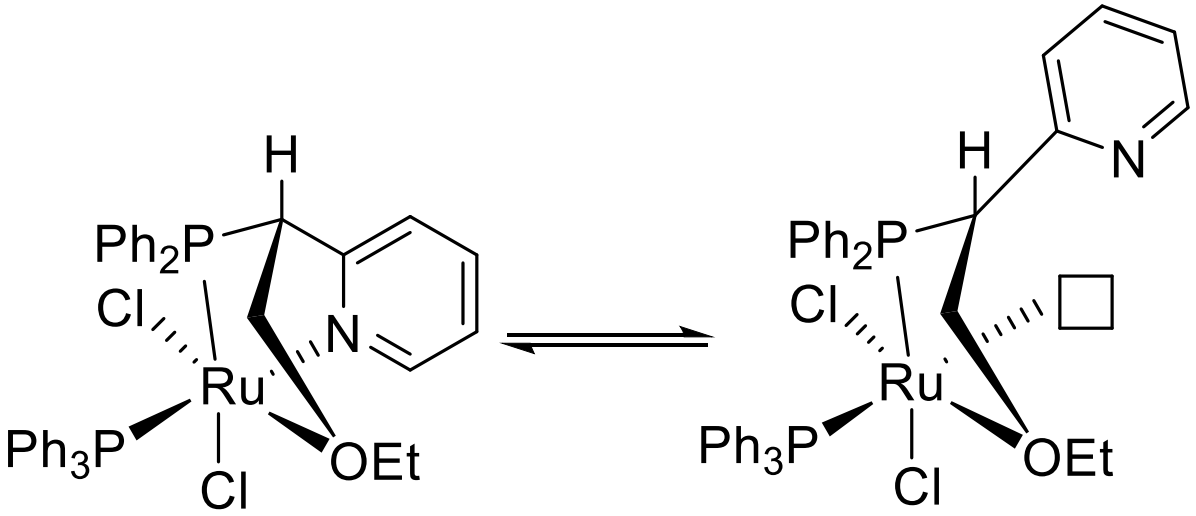
Nickel Superoxide Dismutase

Barondeau, D. P.; Kassmann, C. J.; Bruns, C. K.; Tainer, J. A.; Getzoff, E. D. . *Biochemistry* **2004**, *43* (25), 8038–8047.

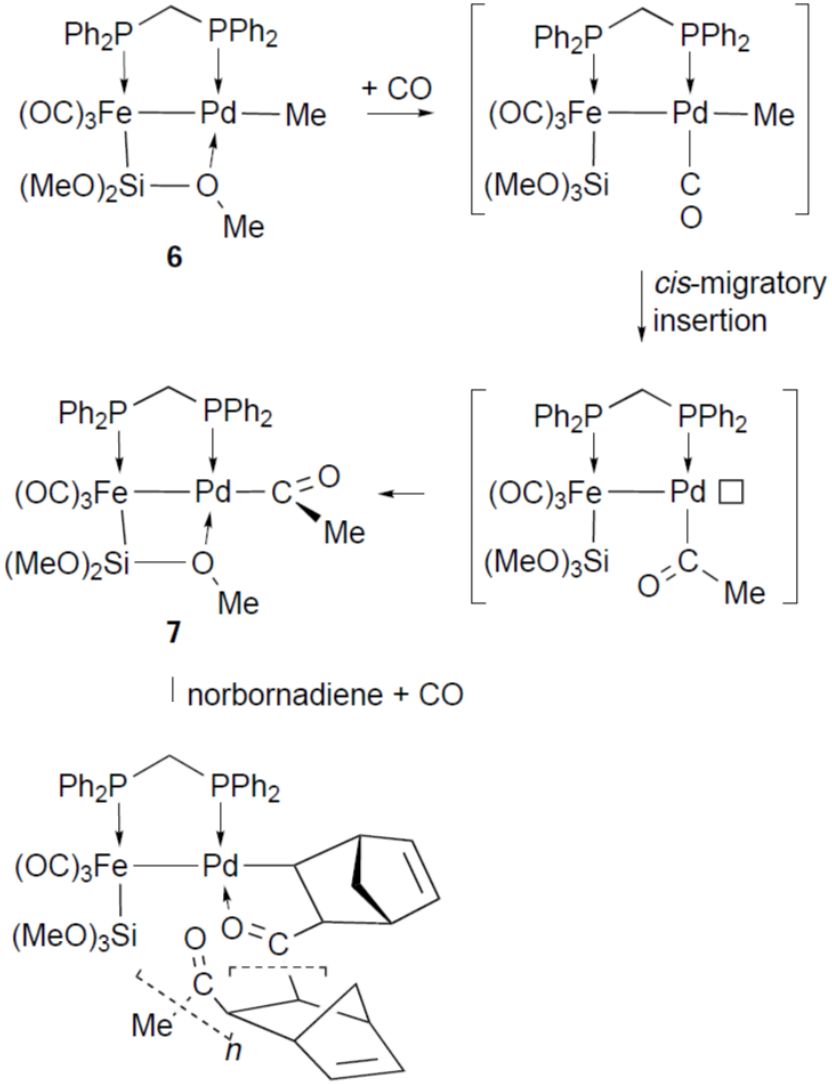
Types of hemilability

Type 1: This type of hemilabile ligand has a weakly bound ligand that is at equilibrium with an open active site.





Pyridine binds more weakly than the ether due to trans effects of triphenylphospine

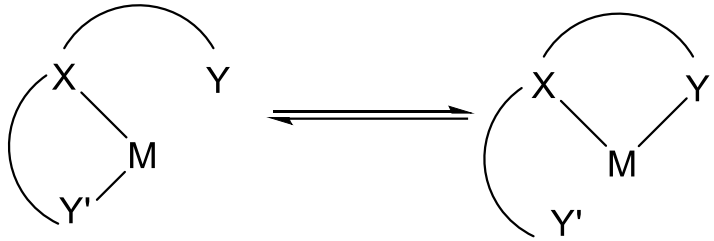


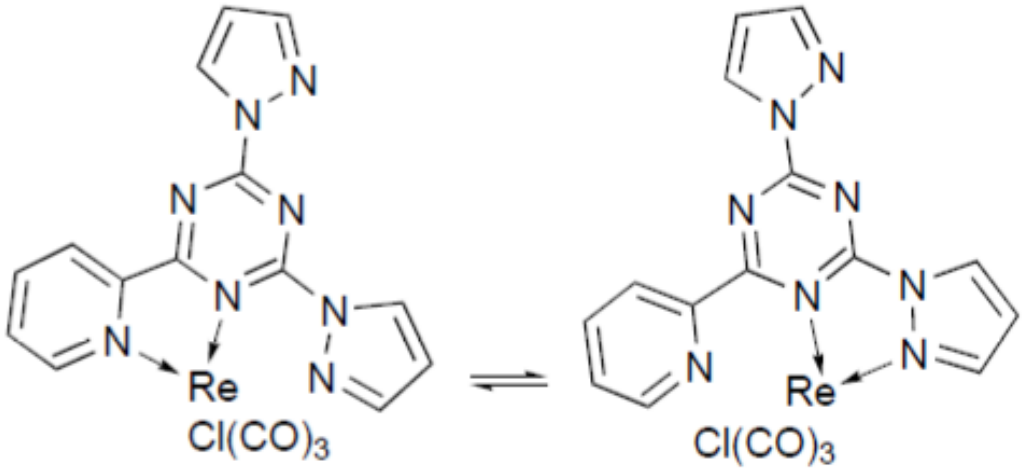
Repeated migratory insertion of CO

Braunstein, P.; Naud, F. *Angewandte Chemie International Edition* **2001**, *40* (4), 680–699.
Yang, H.; Alvarez-Gressier, M.; Lugan, N.; Mathieu, R. *Organometallics* **1997**, *16* (7), 1401–1409.
P. Braunstein, M. Knorr, T. Stährfeldt, *J. Chem. Soc. Chem. Commun.* **1994**, 1913.

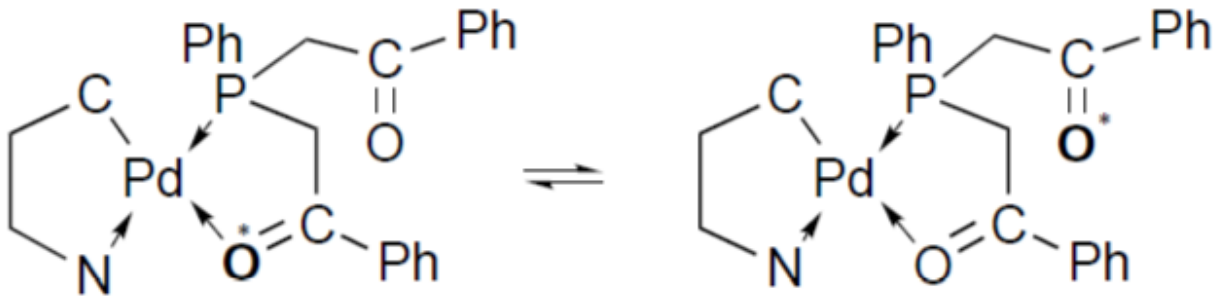
Types of hemilability

Type 2: Competing hemilabile ligands





"Tick tock"

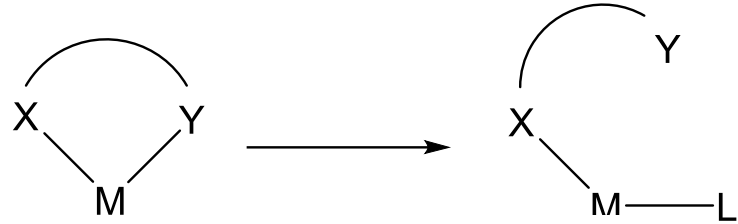


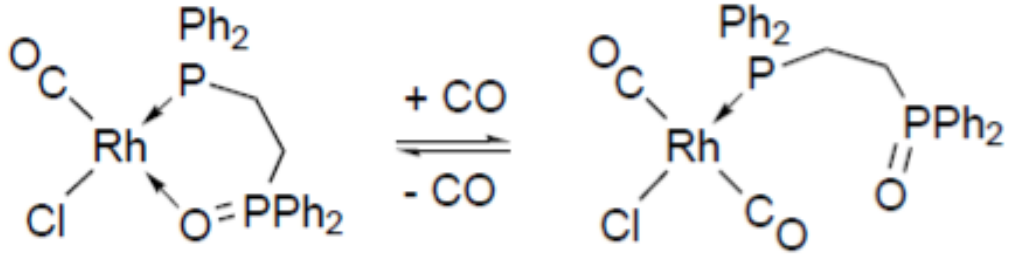
"Windshield wiper"

Braunstein, P.; Naud, F. *Angewandte Chemie International Edition* **2001**, *40* (4), 680–699.
Gelling, A.; Noble D. R.; Orell, K. G.; Osborne, A. G.; Sik, V.; *J. Chem. Soc. Dalton Trans.* **1996**, 3065.

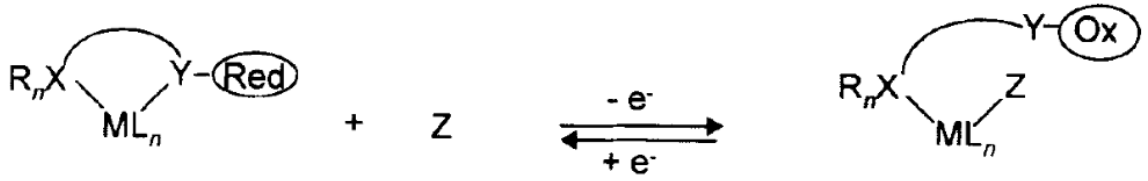
Types of hemilability

Type 3: The weakly bound portion of the hemilabile ligand is displaced by a substrate, including electrons



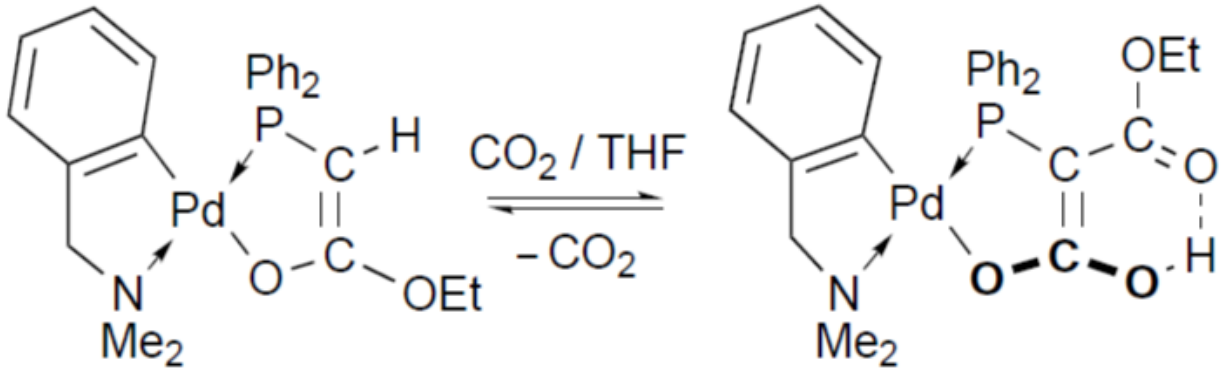


CO displaces oxide

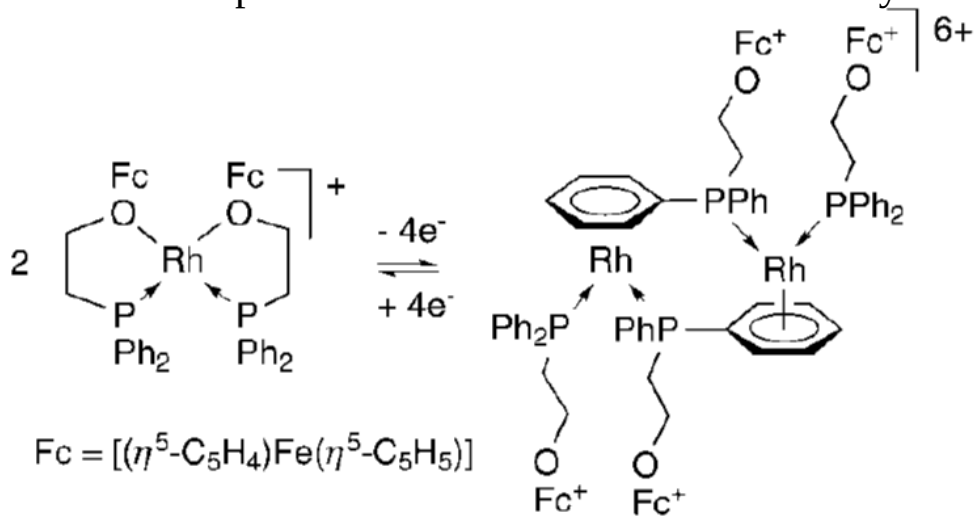


R = substituent of tunable electronic nature
X = substitutionally inert group
Y = substitutionally labile group
Z = ligand or solvent

Generic description of electron activated hemilability



CO inserts into hemilabile ligand

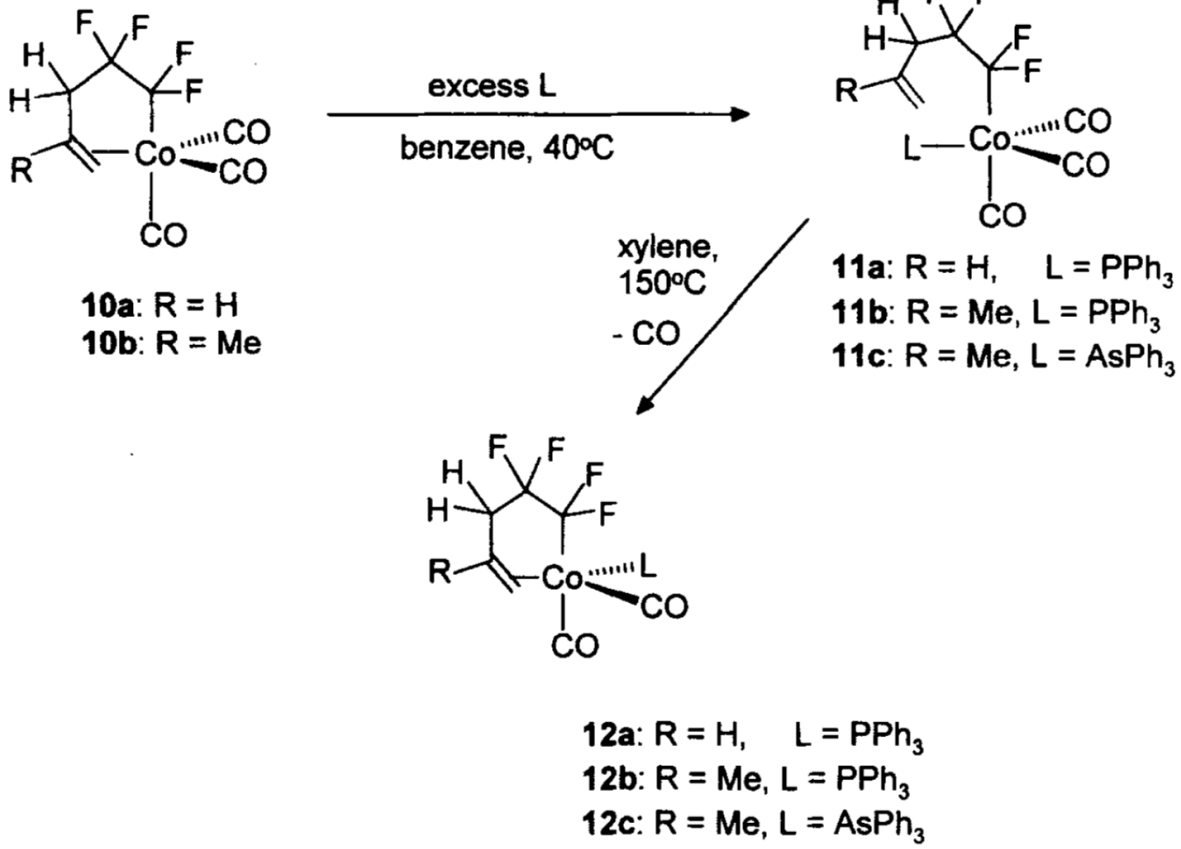


Fc = [(η^5-C_5H_4)Fe(η^5-C_5H_5)]

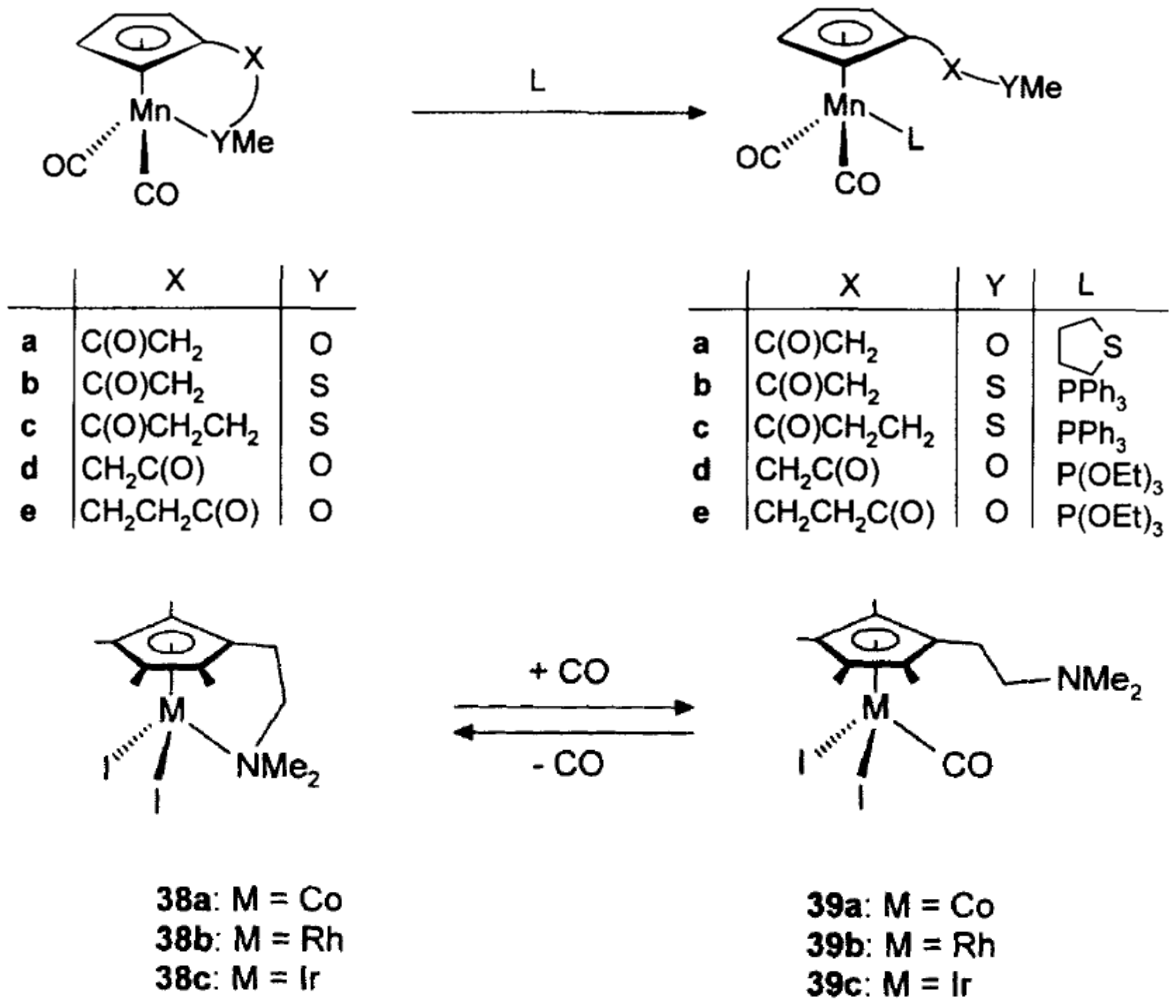
Electron mediated dimerization

Slone, C. S.; Weinberger, D. A.; Mirkin, C. A. *Progress in Inorganic Chemistry*; Karlin, K. D., Ed.; John Wiley & Sons, Inc.: Hoboken, NJ, USA, 2007; pp 233–350.
Braunstein, P.; Naud, F. *Angewandte Chemie International Edition* **2001**, *40* (4), 680–699.

Carbon anchored hemilabile ligands



Elimination of CO



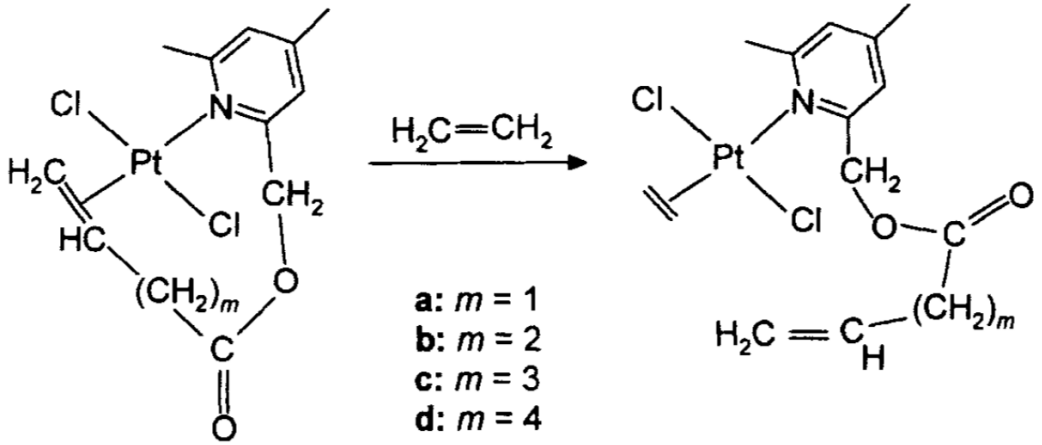
	X	Y
a	$C(O)CH_2$	O
b	$C(O)CH_2$	S
c	$C(O)CH_2CH_2$	S
d	$CH_2C(O)$	O
e	$CH_2CH_2C(O)$	O

	X	Y	L
a	$C(O)CH_2$	O	S
b	$C(O)CH_2$	S	PPh_3
c	$C(O)CH_2CH_2$	S	PPh_3
d	$CH_2C(O)$	O	$P(OEt)_3$
e	$CH_2CH_2C(O)$	O	$P(OEt)_3$

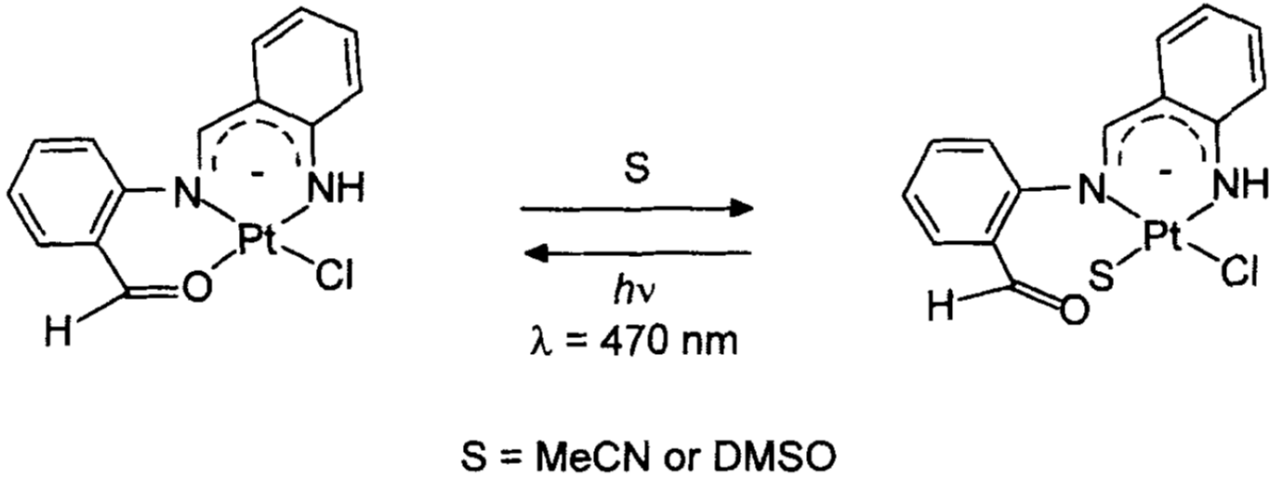
Hemilabile piano stool complexes

Slone, C. S.; Weinberger, D. A.; Mirkin, C. A. *Progress in Inorganic Chemistry*; Karlin, K. D., Ed.; John Wiley & Sons, Inc.: Hoboken, NJ, USA, 2007; pp 233–350.
Greco, A.; Green, M.; Stone, F. G. A.; *J. Chem. Soc.*, **1971,** (A), 3476
Pang, Z.; Burkey, T. J.; Johnston, R. F.; *Organometallics*. **1997,** 16

Nitrogen anchored hemilabile ligands

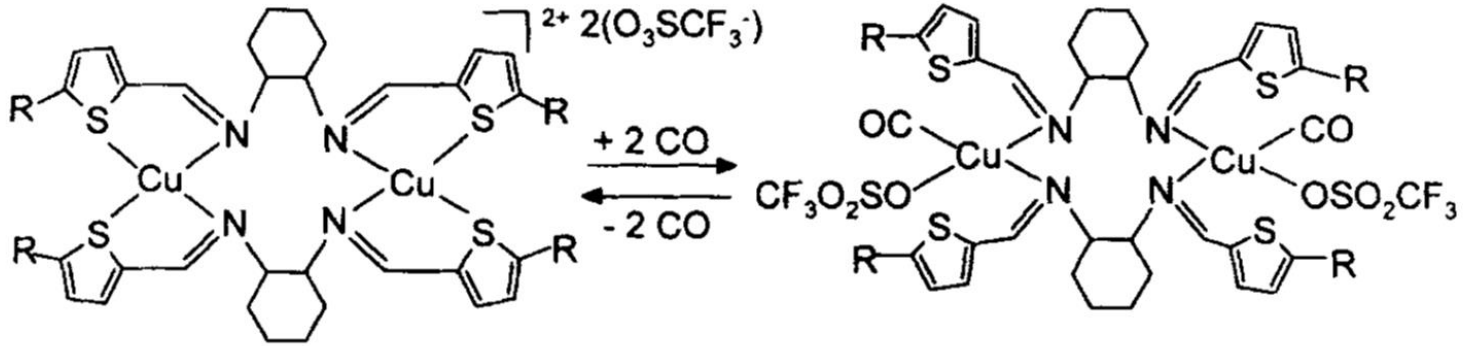


Reversible ethylene binding



S = MeCN or DMSO

Very stable, able to cycle up to 15 times



73a: R = H
73b: R = Me

74a: R = H
74b: R = Me

Biological macromolecule Cu(I) site mimicry

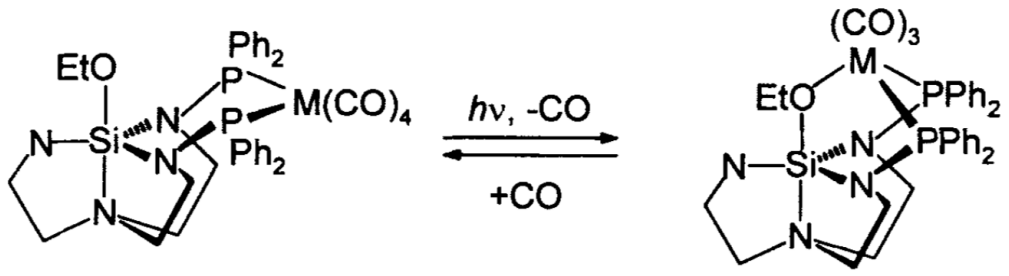
Slone, C. S.; Weinberger, D. A.; Mirkin, C. A. *Progress in Inorganic Chemistry*; Karlin, K. D., Ed.; John Wiley & Sons, Inc.: Hoboken, NJ, USA, 2007; pp 233–350.

Chottard, J. C.; Mulliez, E.; Girault. J. P.; Mansuy, D.; *J. Chem. Soc. Chem. Commun.*, **1974**, 780

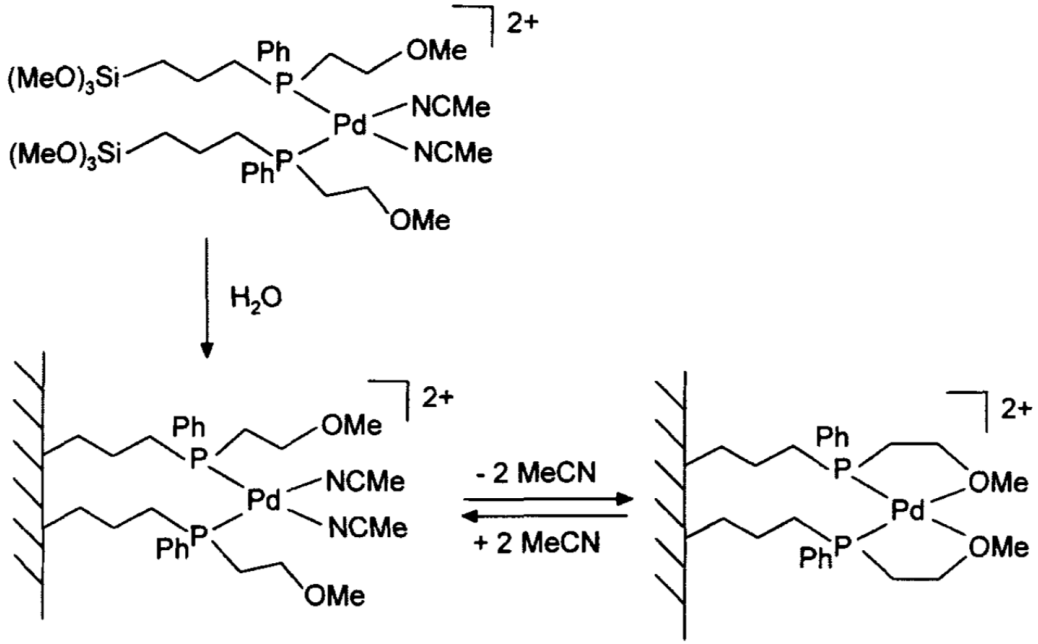
W. G. Rohly and K. B. Mertes, *J. Am. Chem. Soc.*, **1980**, 102

Van Stein, G. C.; Van Koten, G.; Blank, F.; Taylor, L. C.; Vrieze, K.; Spek, A. L.; Duisenberg, A. J. M.; Schreurs, A. M. M.; Kojić-Prodić, B.; Brevard, C.. *Inorganica Chimica Acta* **1985**, *98* (2), 107–120.

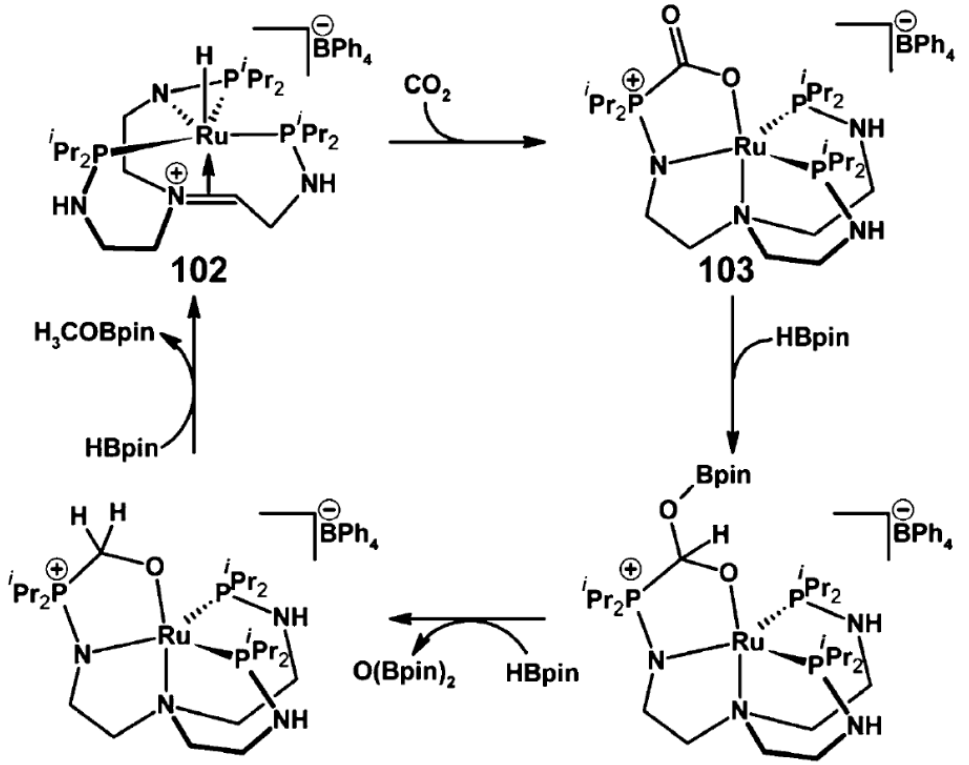
Phosphorus anchored hemilabile ligands



Reversible CO binding



Reversible acetonitrile binding, active in the copolymerization of CO and ethylene without solvent



CO_2 activation

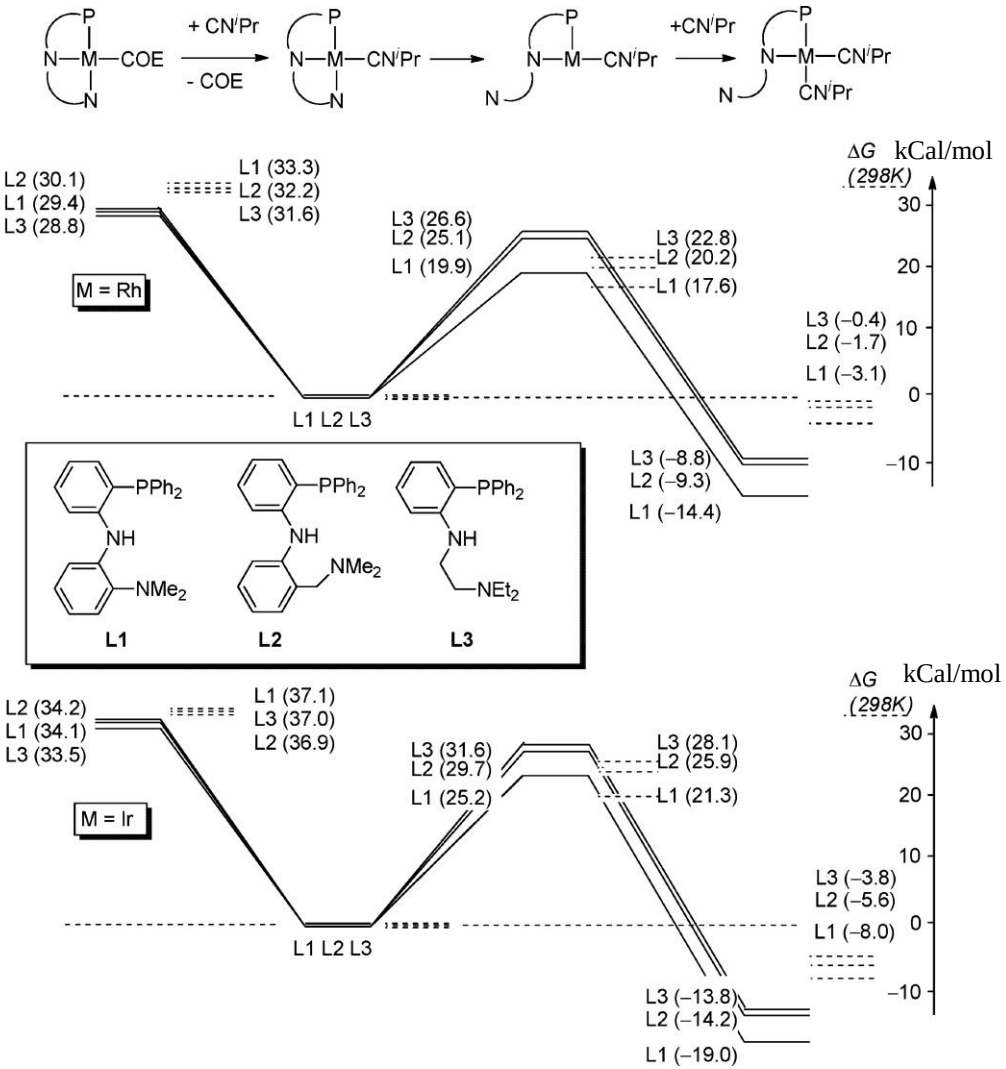
Annibale, V. T.; Song, D. *RSC Advances* **2013**, *3* (29), 11432.

Gudat, D.; Daniels, L. M.; Verkade, J. G.; *Organometallics*, **1990**, 1464 (9)

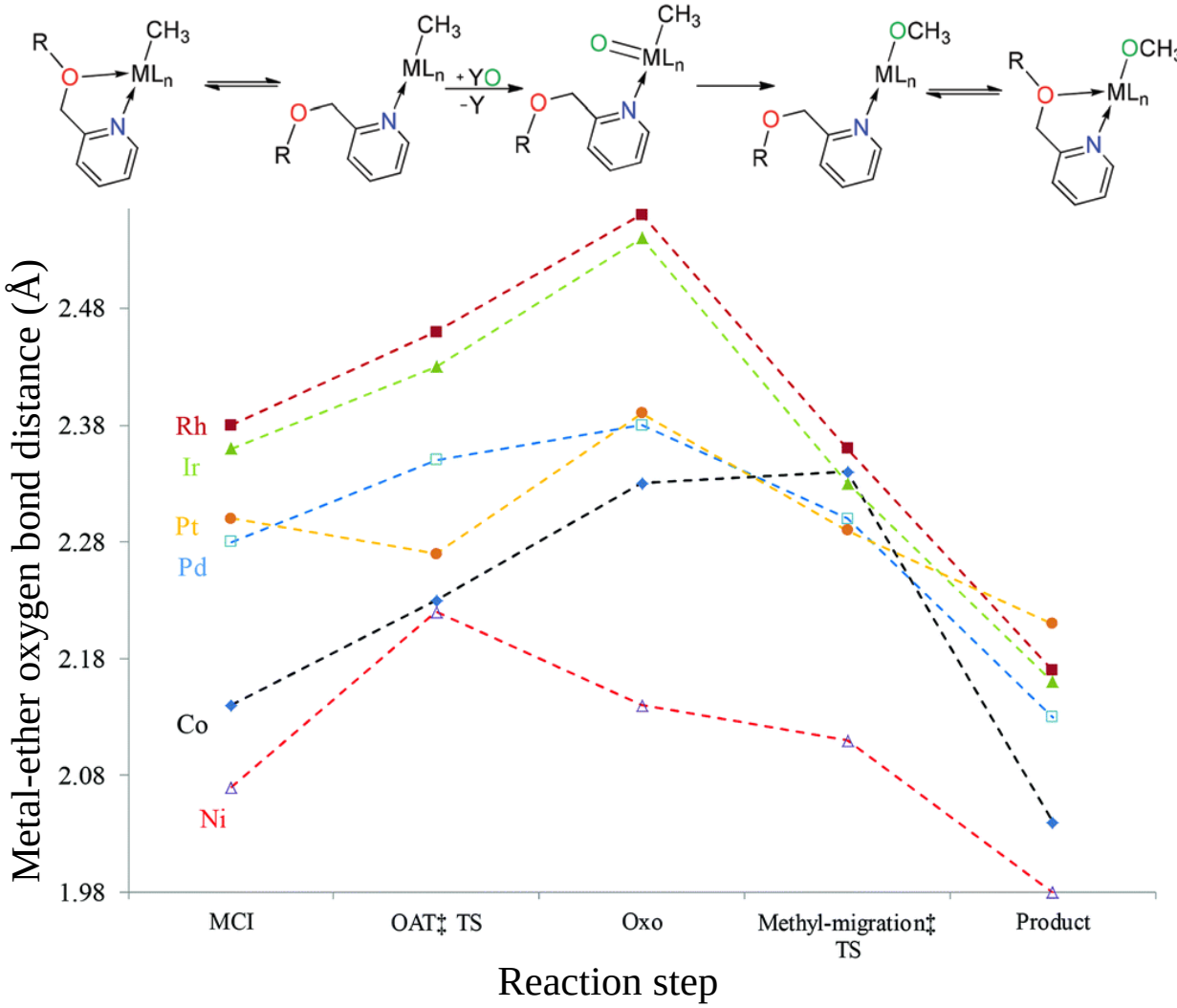
Lindner, E.; Schreiber, R.; Schneller, T.; Wegner, P.; Mayer, H. A.; Göpel, W.; Ziegler, C. *Inorg. Chem.* **1996**, *35* (2), 514–525.

Slone, C. S.; Weinberger, D. A.; Mirkin, C. A. *Progress in Inorganic Chemistry*; Karlin, K. D., Ed.; John Wiley & Sons, Inc.: Hoboken, NJ, USA, 2007; pp 233–350.

Hemilabile bond energetics



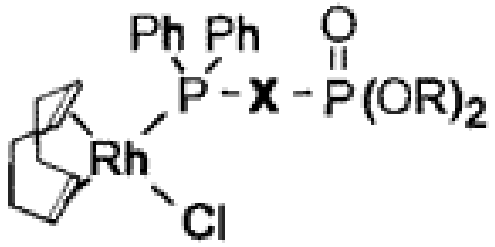
Calculated energies of (formal) intermediates for the reaction of the COE complexes [M(**L**)(COE)] (M = Rh, Ir; **L** = **L1**–**L3**) with isopropyl isocyanide.



Oxy-insertion reaction and calculated bond distances

M. Prince, B.; Brent Gunnoe, T.; R. Cundari, T. *Dalton Transactions* **2014**, *43* (20), 7608–7614.
Lindner, R.; van den Bosch, B.; Lutz, M.; Reek, J. N. H.; van der Vlugt, J. I. *Organometallics* **2011**, *30* (3), 499–510.

Hemilabile bond energetics

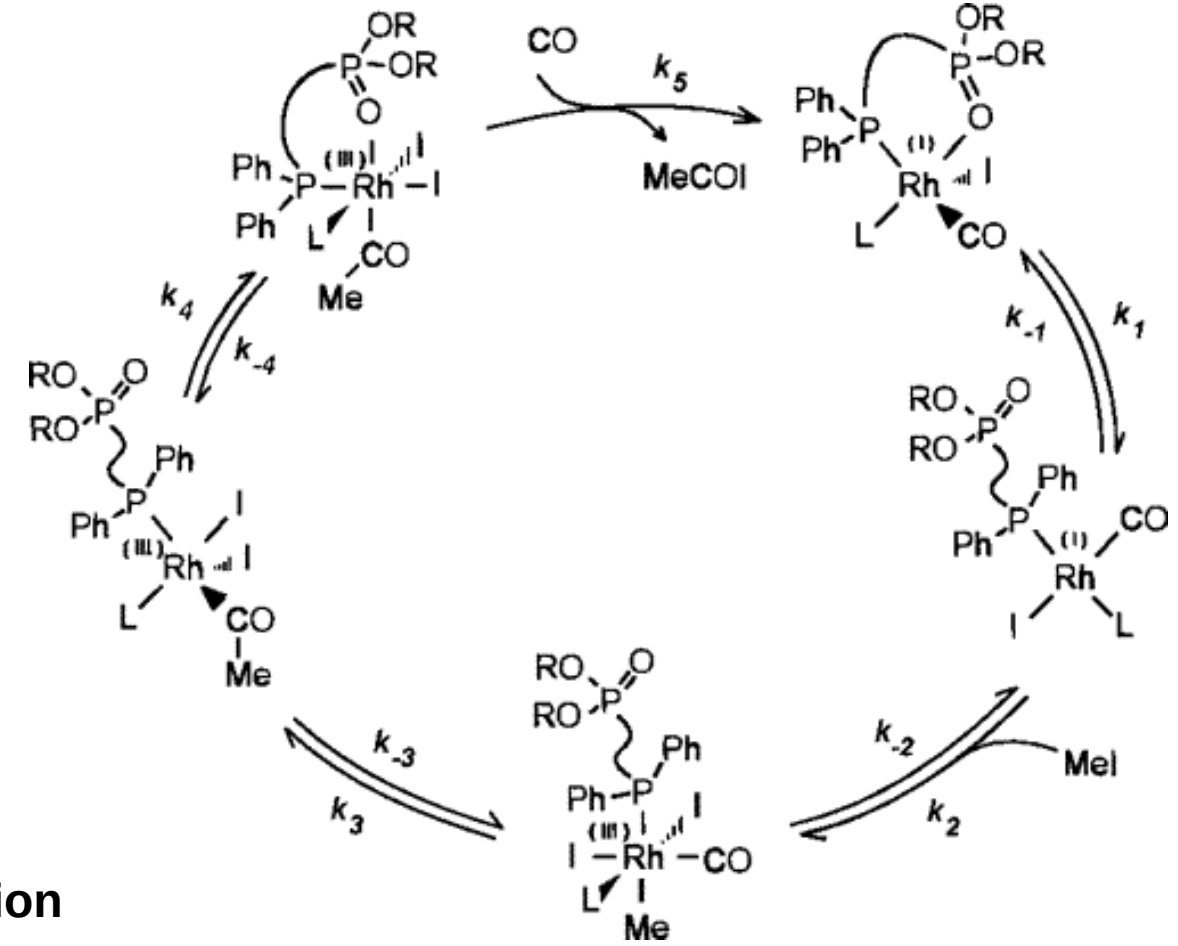


2a - d

a-d = methyl through butyl
substituent at "X"

Ligand Effects on Activation Parameters in Homogeneous Rh-Catalyzed Methanol Carbonylation

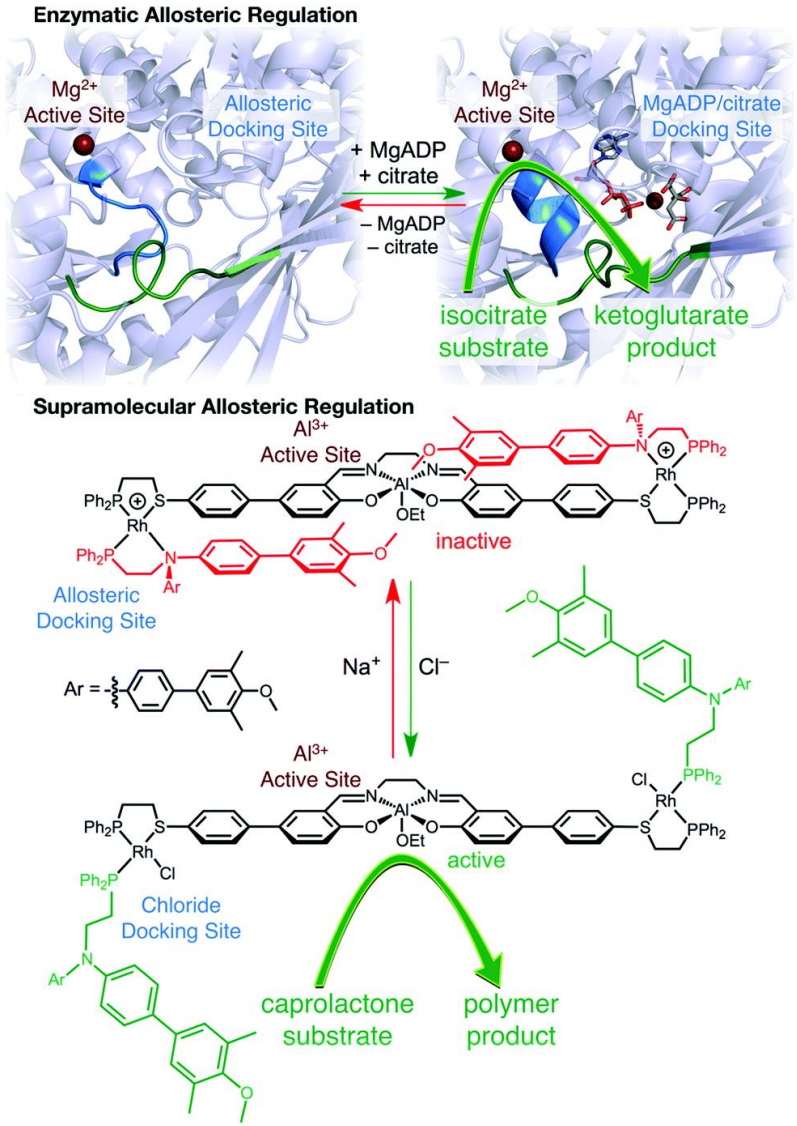
	PPh_3[c]	dppe[d]	2a	2b	2c	2d
$\Delta H^{\ddagger}$ (kJ/mol)	54.9 ± 5.4	27.5 ± 6.2	38.6 ± 3.4	55.2 ± 5.2	61.8 ± 5.3	76.0 ± 9.1
$\Delta S^{\ddagger}$ (J/mol/K)	−141 ± 13	−211 ± 15	−179 ± 8	−141 ± 12	−126 ± 12	−90 ± 22

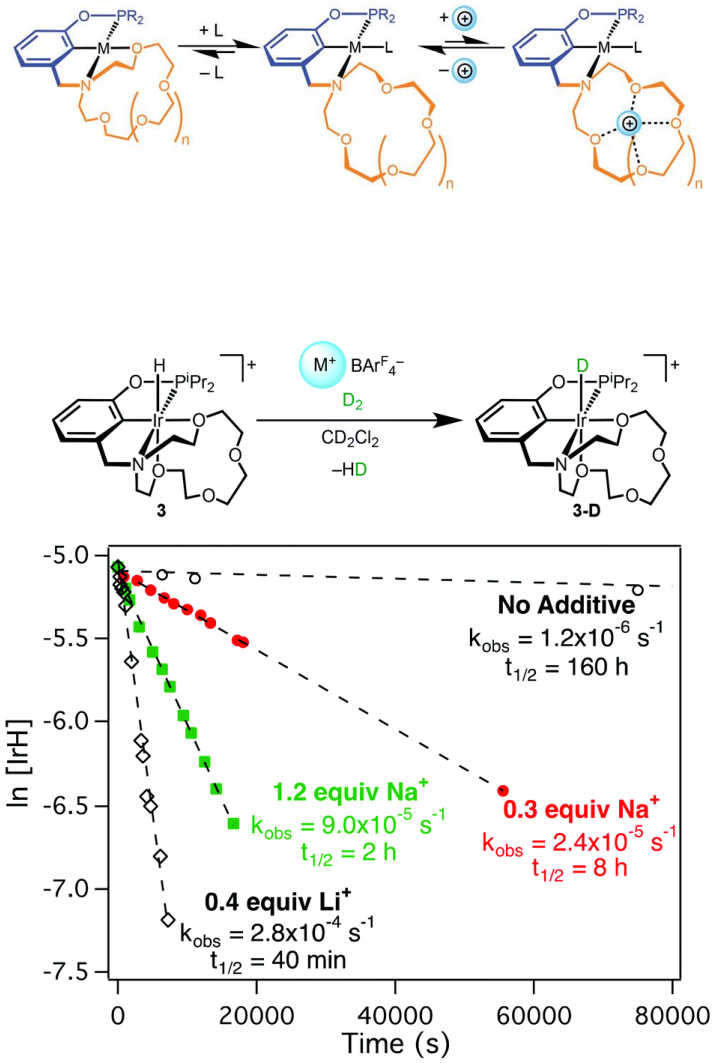


Carbonylation of methanol

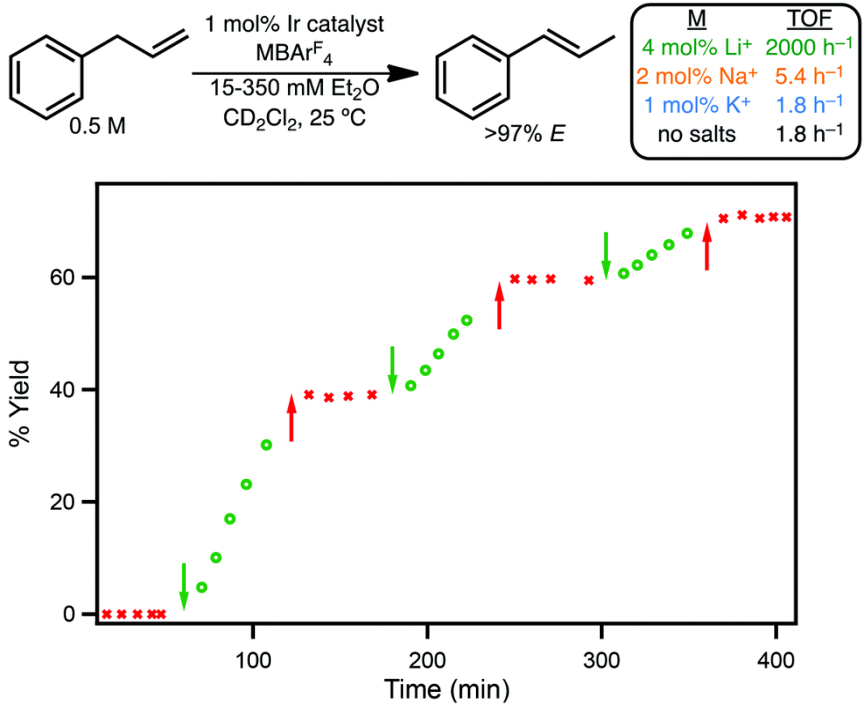
Bischoff, S.; Weigt, A.; Miessner, H.; Lücke, B. *Energy Fuels* **1996**, *10* (3), 520–523.

Allosteric like regulation





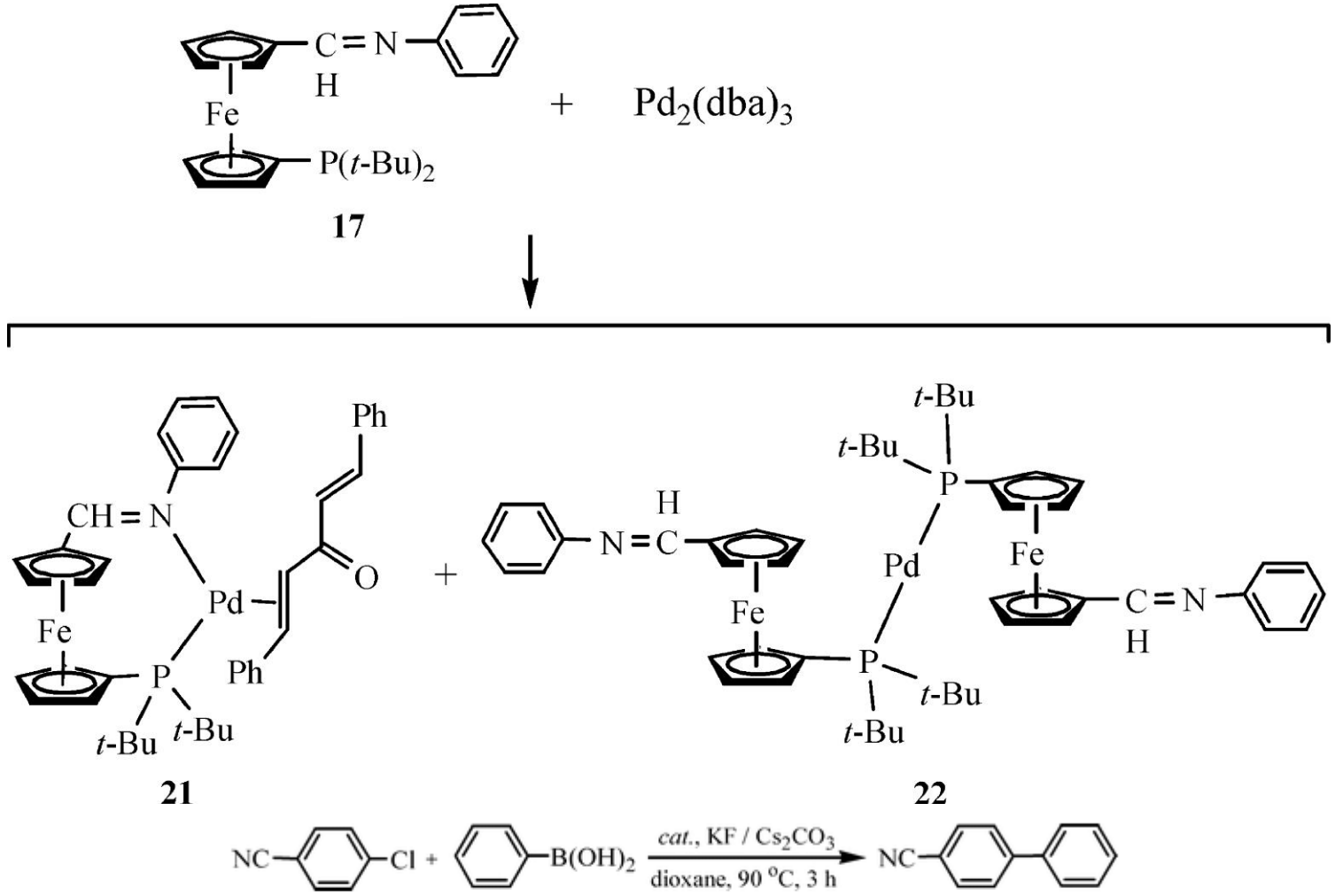
Initial rates of reaction



Switchable allylbenzene isomerization catalyzed by iridium pincer-crown ether species. A 0.5 M allylbenzene solution in CD_2Cl_2 was charged with 5 mM κ^4-(^{15c5}NCOP^{iPr})Ir(H)(Cl) (**2**) and monitored by ^{1}H NMR spectroscopy. Green down arrows mark the time when 2 equiv. of $NaBAr^F_4$ was added to switch on catalysis. Red up arrows mark the time at which 2 equiv. of PPNCl were added to switch off catalysis

Miller, A. J. M. *Dalton Trans.* **2017**, *46* (36), 11987–12000.

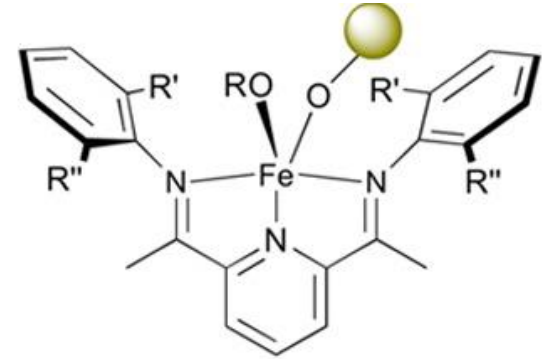
Suzuki coupling



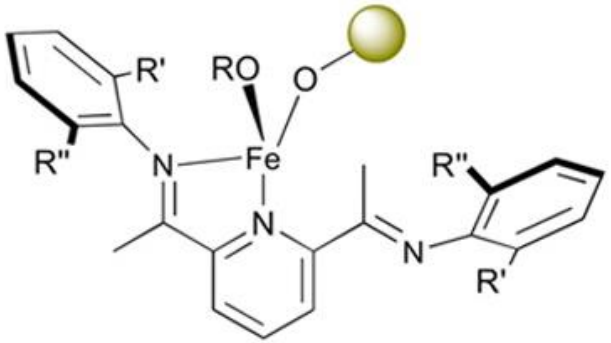
catalyst	21	22
0.25 mol % (Pd)	**98%**	**100% yield**
0.01 mol % (Pd)	**52%**	**100% yield**

Weng, Z.; Teo, S.; Hor, T. S. A. *Acc. Chem. Res.* **2007**, *40* (8), 676–684.

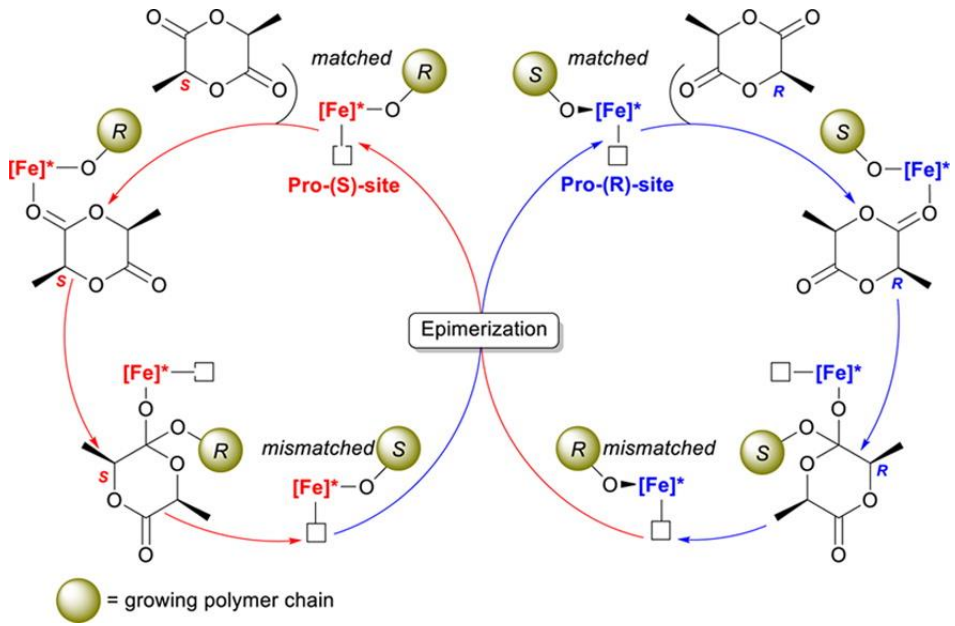
Polymerization with hemilabile ligands

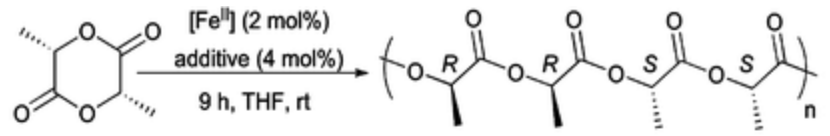


C_s-symmetric achiral



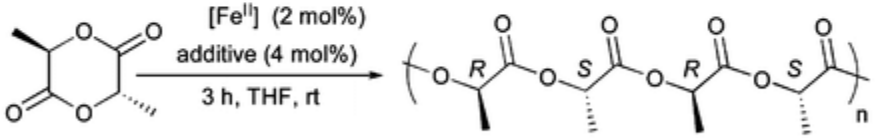
C_1-symmetric chiral





(*rac*)-lactide — heterotactic poly(lactic acid)

	[Fe^{II}]	Additive	Cone angle[13]	M_n (kg/mol)	M_w/M_n	P_s[a] (%)
1[b]	**3**	*p*-$MeOC_6H_4OH$	-	9.08	1.42	50
2	**3**	Ph_3SiOH	145	42.9	1.31	66
3	**4**	Ph_3SiOH	145	29.1	1.45	69
4	**4**	$MePh_2SiOH$	136	15.7	1.38	75
5	**4**	Et_3SiOH	132	10.1	1.46	58
6	**4**	$Me_2PhSiOH$	122	9.0	1.50	64
7	**5**	Ph_3SiOH	145	43.1	1.40	73

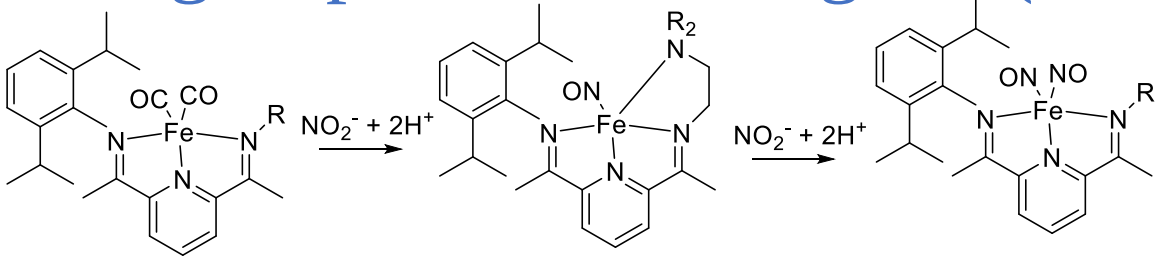


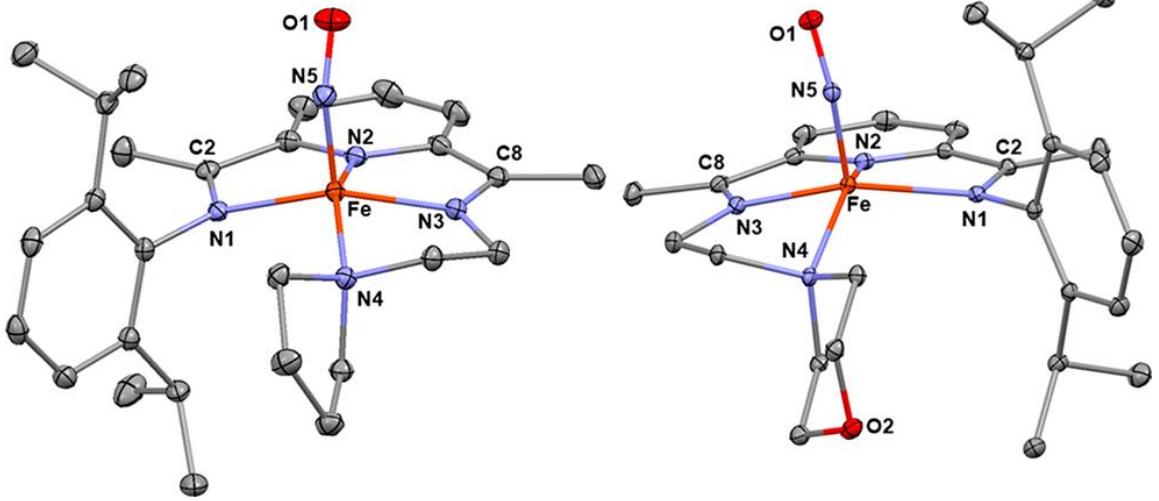
(*meso*)-lactide — syndiotactic poly(lactic acid)

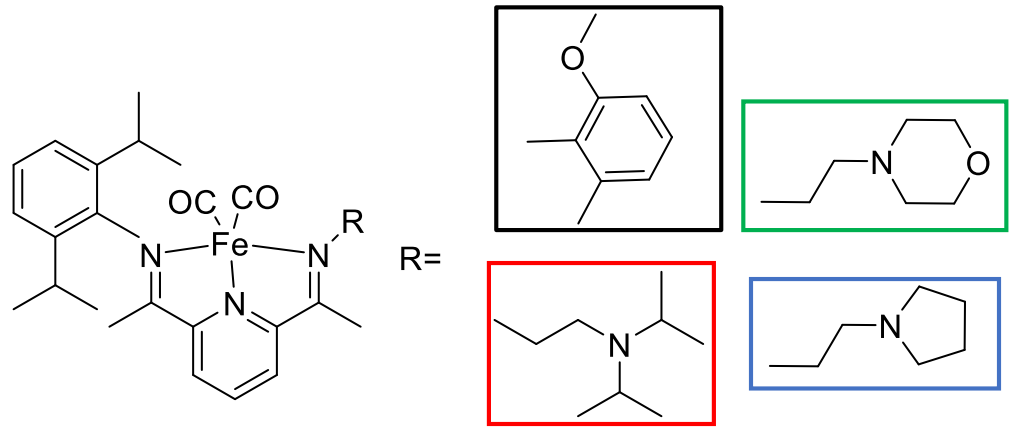
8	**4**	*p*-$MeOC_6H_4OH$	-	9.04	1.25	67
9	**4**	Ph_3SiOH	145	54.4	1.43	88
10	**4**	$MePh_2SiOH$	136	7.0	1.52	82
11	**4**	Et_3SiOH	132	11.5	1.62	92
12	**4**	$Me_2PhSiOH$	122	8.6	1.40	85
13	**5**	Ph_3SiOH	145	39.2	1.60	70

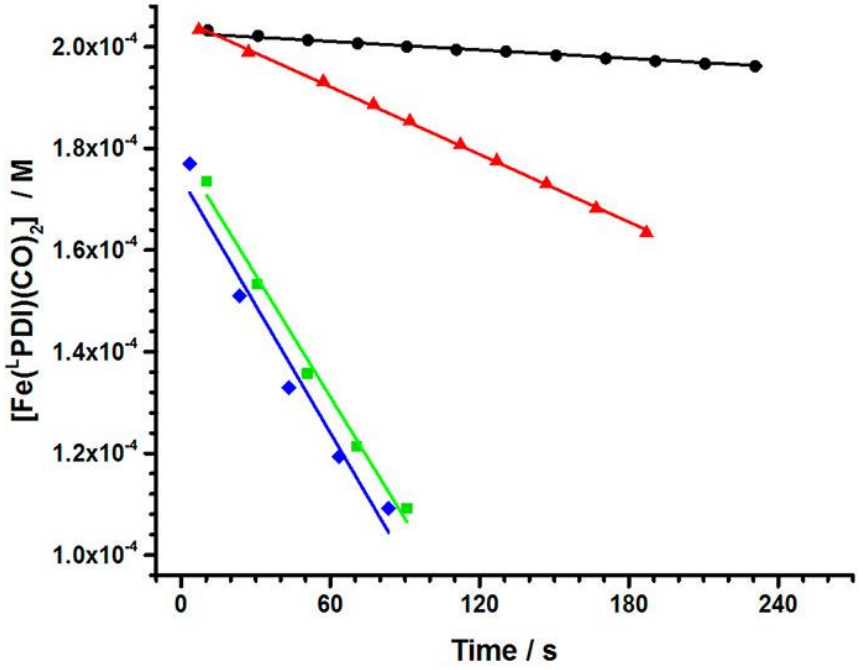
Manna, C. M.; Kaur, A.; Yablon, L. M.; Haeffner, F.; Li, B.; Byers, J. A. *J. Am. Chem. Soc.* **2015**, *137* (45), 14232–14235.

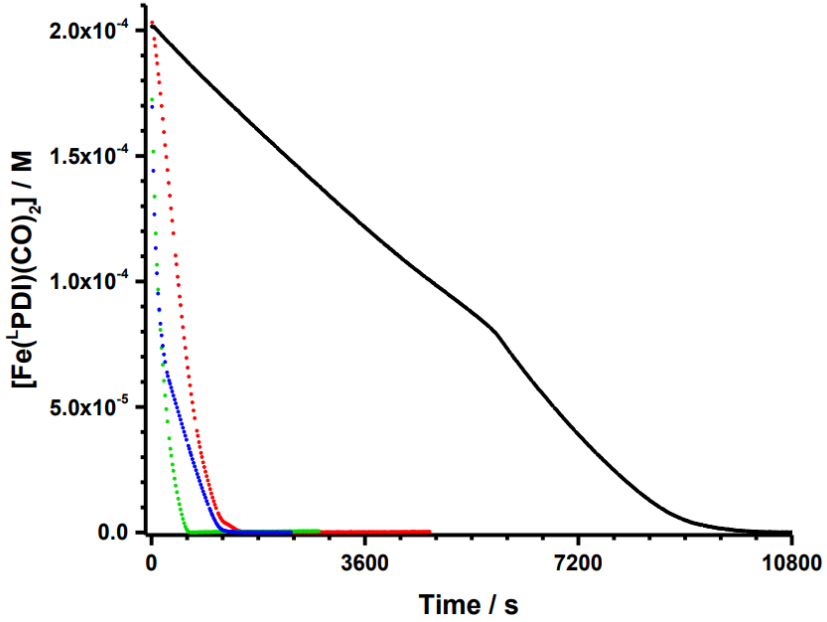
Gilbertson group hemilabile ligand (MNIC)











Conclusions and Outcomes

Hemilabile ligands can:

- Increase stability
- Allow access to active sites that would otherwise be obscured
- Lead to different reactivity
- Probe binding pathways of biomolecules
- Allow for isolation of reactive intermediates
- Have more sites that can be poisoned in catalysis
- Be less predictable

Design principles to consider when designing hemilabile ligands:

- **Hard/Soft Acid/Base theory**
- **Trans influence**
- **Ring strain/angles**
- **Sterics**
- **Electronics (donating/withdrawing)**
- **Entropic effects/floppiness**
- **Redox states/activity**
- **Preferred geometry of Metal**