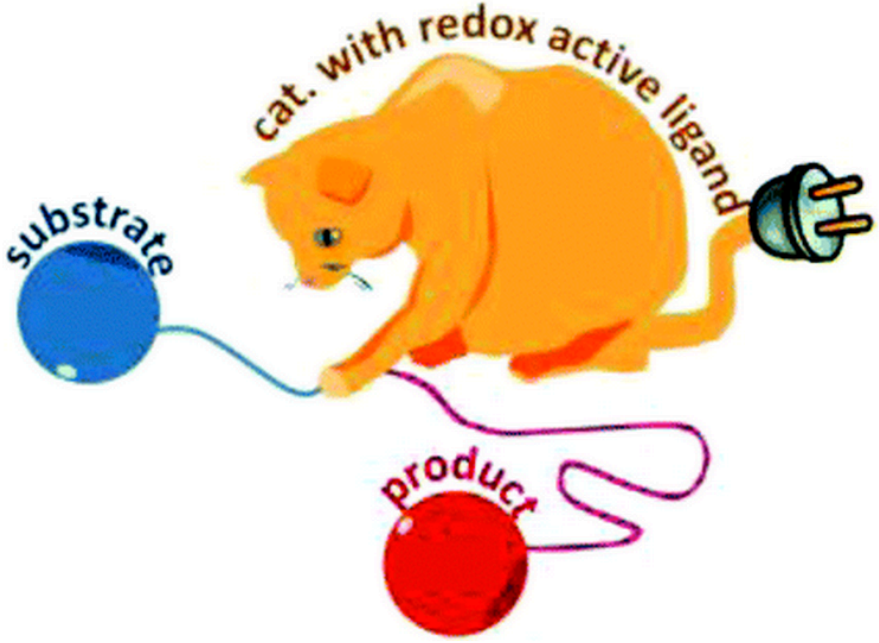
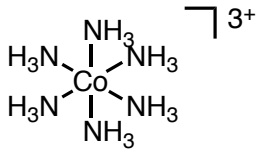
Redox-Active Ligands

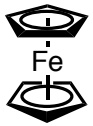


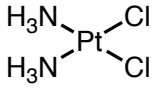
MacMillan Group Meeting
Andrew Capacci
2/4/14

Coordination Chemistry and Metal-Ligand Interactions

- The coordination of metal complexes have been described in the classical terms of Werner complexes

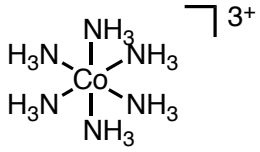


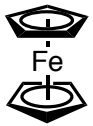


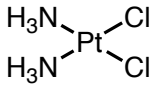


$[Co(NH_3)_6]Cl_3$ $FeCp_2$ $PtCl_2(NH_3)_2$

- Considered "innocent" ligands as the metal oxidation state is easily predicted







$[Co(NH_3)_6]Cl_3$ $FeCp_2$ $PtCl_2(NH_3)_2$

NH_3 = L type | Cp = X type | Cl = X type

overall charge = +3 | overall charge = 0 | overall charge = 0

Co(III) | Fe(II) | Pt(II)

Jørgensen, C. K. *Coord. Chem. Rev.*, **1966**, *1*, 164.
Chirik, P. J. *Inorg. Chem.*, **2011**, *50*, 9737.

Coordination Chemistry and Metal-Ligand Interactions

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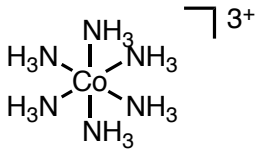

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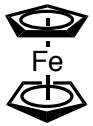
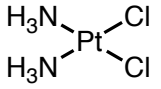


$FeCp_2$



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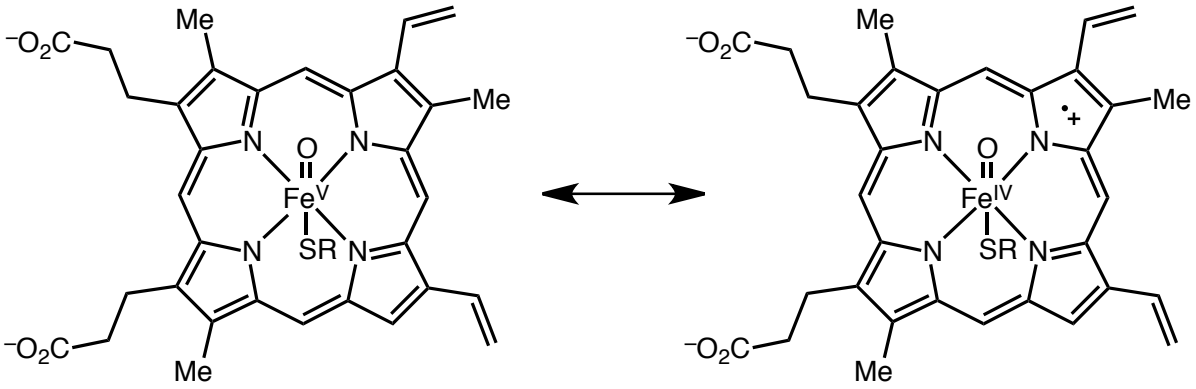
- Non-innocent ligands are classified as having experimentally determined oxidation state differ from prediction



Fe(V), neutral ligand

Fe(IV), ligand radical cation

Which oxidation state does the iron center in Compound I actually exist in?

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Non-Innocent vs. Redox-Active Ligands

- What's the difference between "noninnocent" and "redox active" ligands?

> "Redox-active, or 'noninnocent,' ligands have more energetically accessible levels that allow redox reactions to change their charge state."
>
> -Chirik, Weighardt (2010)

> "Oftentimes, the two descriptions 'redox-active' and 'noninnocent' ligands are used interchangeably in the literature. However, care must be used when using the latter because clearly defined physical oxidation states have often been established for a case where ambivalence has been implied."
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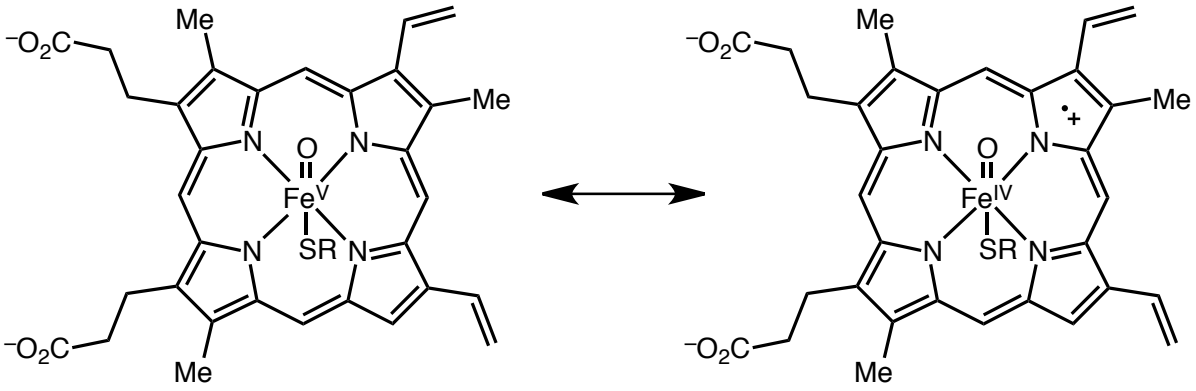

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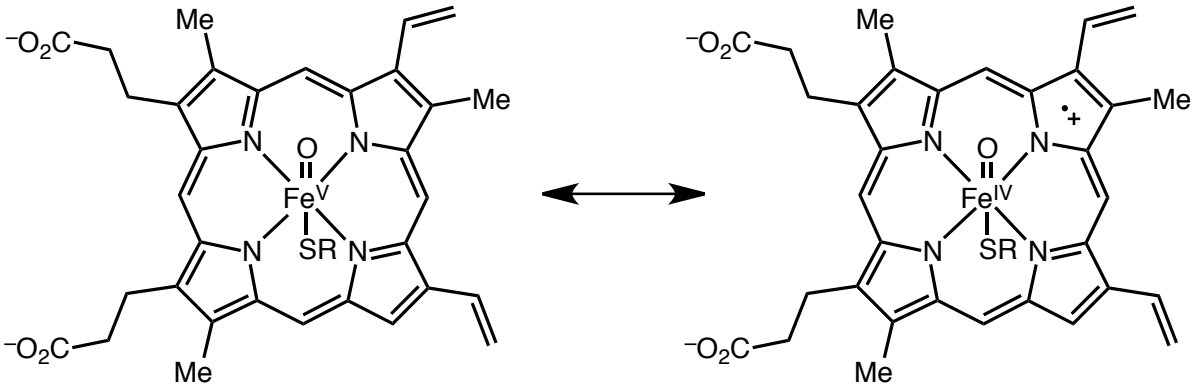

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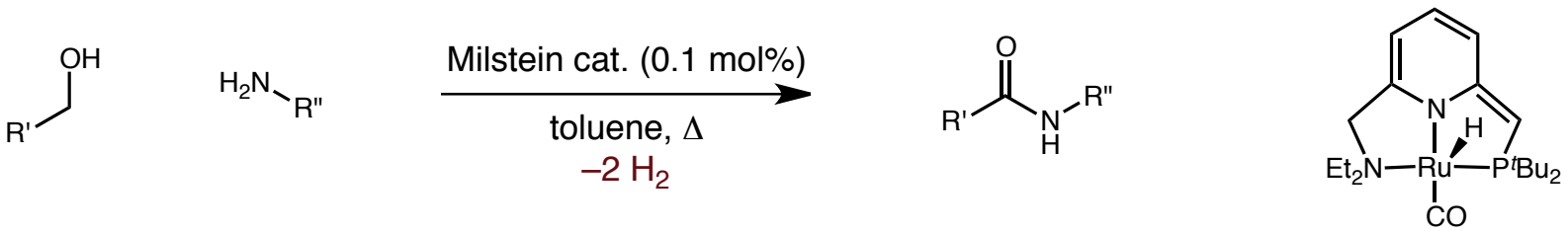
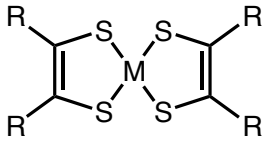


- Non-redox-active cooperative ligation is interesting but beyond the scope of this discussion

Chirik, P. J., Wieghardt, K. *Science*, **2010**, *327*, 794.
Chirik, P. J. *Inorg. Chem.*, **2011**, *50*, 9737.

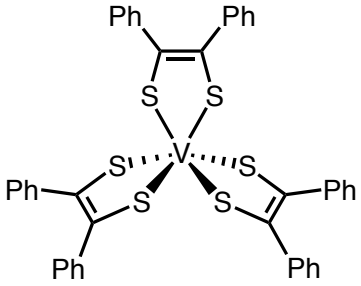
Coordination Chemistry and Metal-Ligand Interactions

- Early discovery of noninnocent ligands: metal dithiolene complexes (1960s)



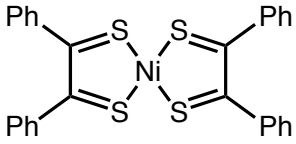
R = Ph, CN, CF_3

M = Ni, Cu, Co, Pd, Pt

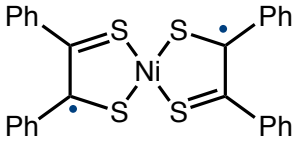


The conventional assignment of $V(S_2C_2Ph_2)_3$ would require a V(VI) metal center! ($3p^5$ valency)

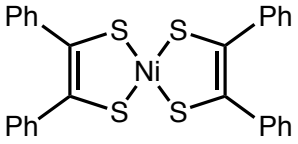
- Dithiolene complexes were examined for their spectroscopic and redox properties



Ni(0), d^{10}



Ni(II), d^8



Ni(IV), d^6

Eisenberg, R., Gray, H. B. *Inorg. Chem.*, **2011**, *50*, 9741.

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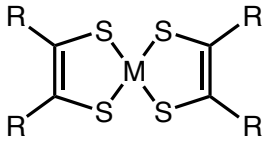

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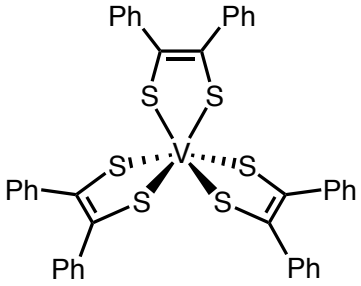

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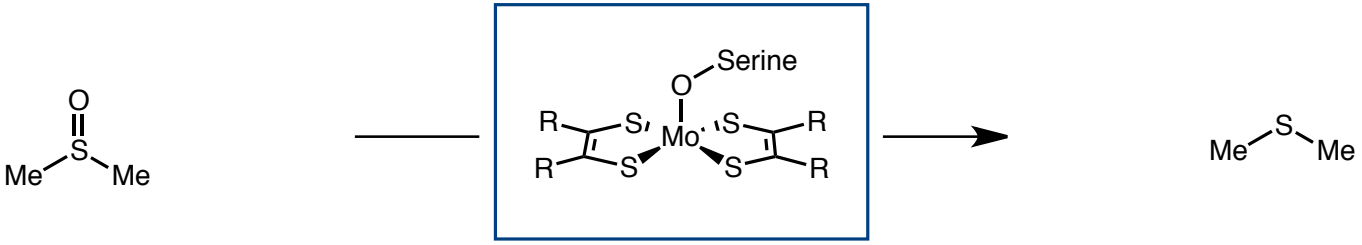
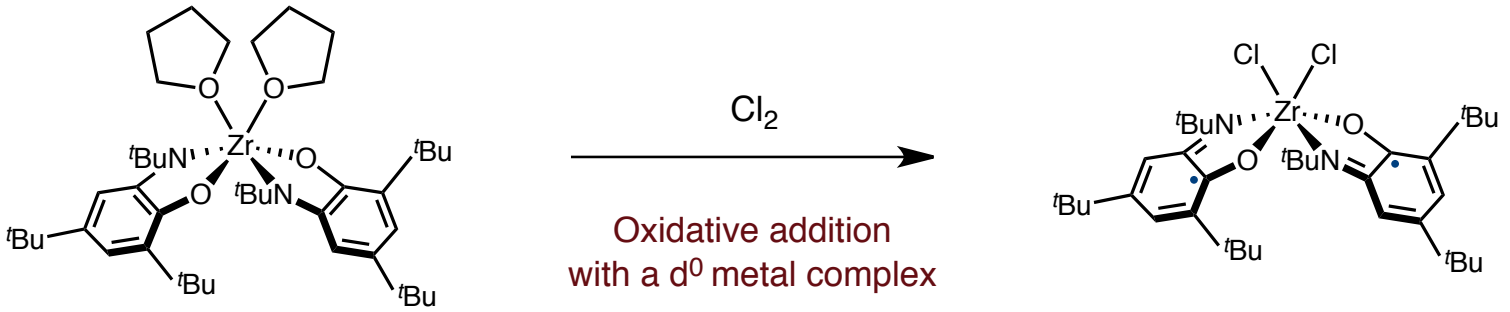
- Dithiolene complexes have applications in catalysis: Mo oxotransferases



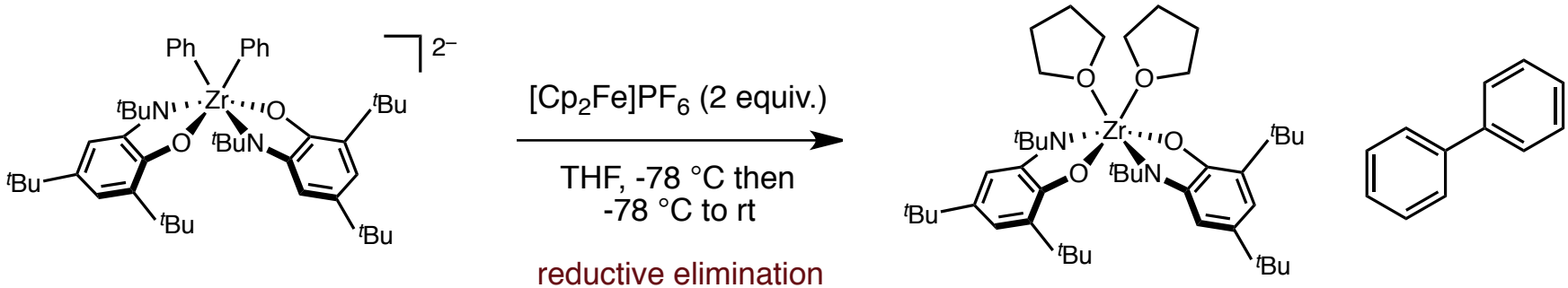
Eisenberg, R., Gray, H. B. *Inorg. Chem.*, **2011**, *50*, 9741.

Advantages of Redox-Active Ligands

- Confering noble reactivity to non-noble metals



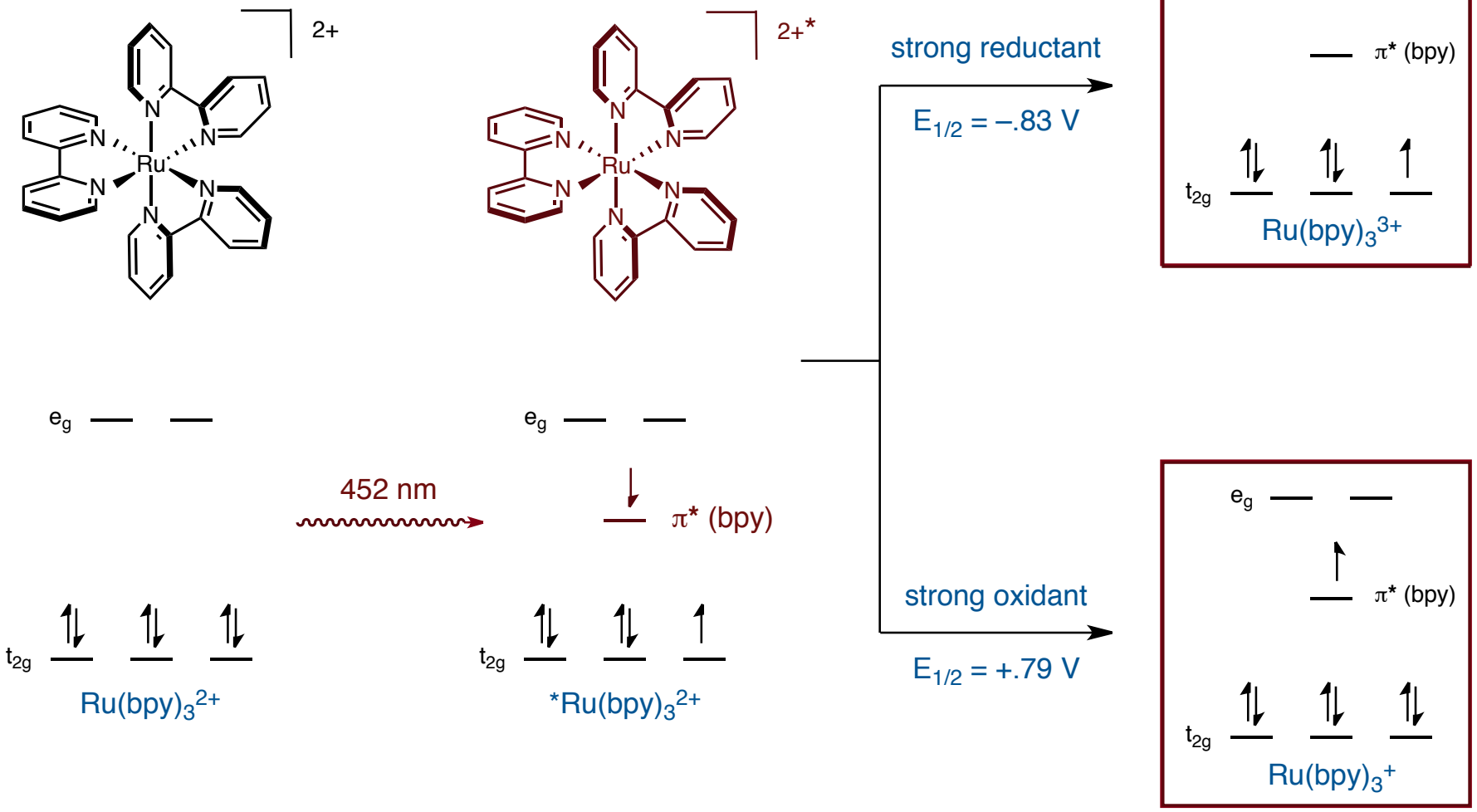
- Reductive elimination from a Zr(IV) center is also possible with redox-active ligands



Blackmore, K. J., Ziller, J. W., Heyduk, A. F. *Inorg. Chem.*, **2005**, *44*, 5559.
Haneline, M. R., Heyduk, A. F. *J. Am. Chem. Soc.*, **2006**, *128*, 8410.

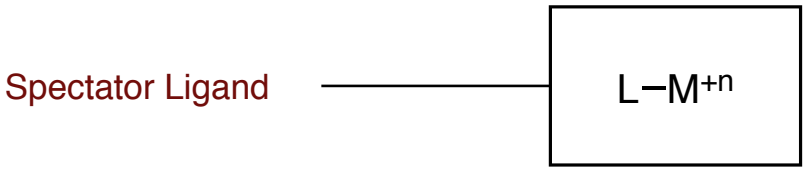
Advantages of Redox-Active Ligands

- Generation of novel reactivity:



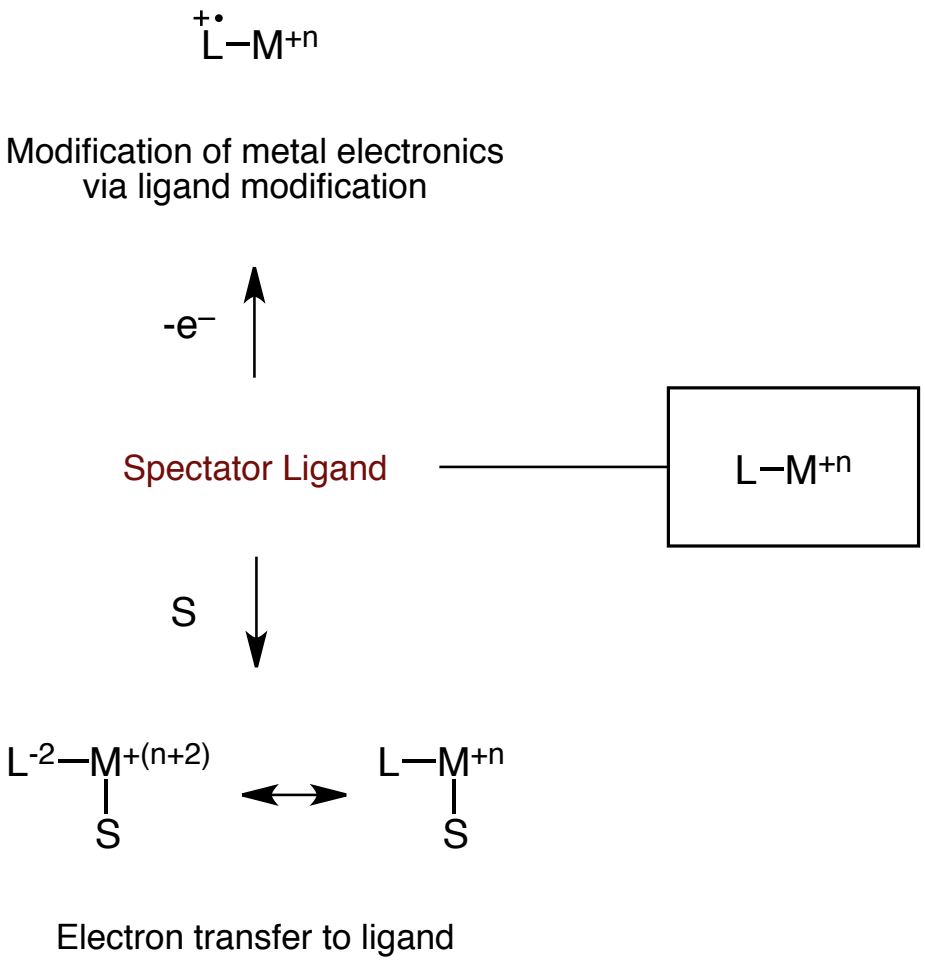
Prier, C. K., Rankic, D. A., MacMillan, D. W. C. *Chem. Rev.*, **2013**, *113*, 5322.

Classes of Redox-Active Ligands



Lyaskovskyy, V., de Bruin, B. *ACS Catal.*, **2012**, *2*, 270.
Luca, O. R., Crabtree, R. H. *Chem. Soc. Rev.*, **2013**, *42*, 1440.

Classes of Redox-Active Ligands



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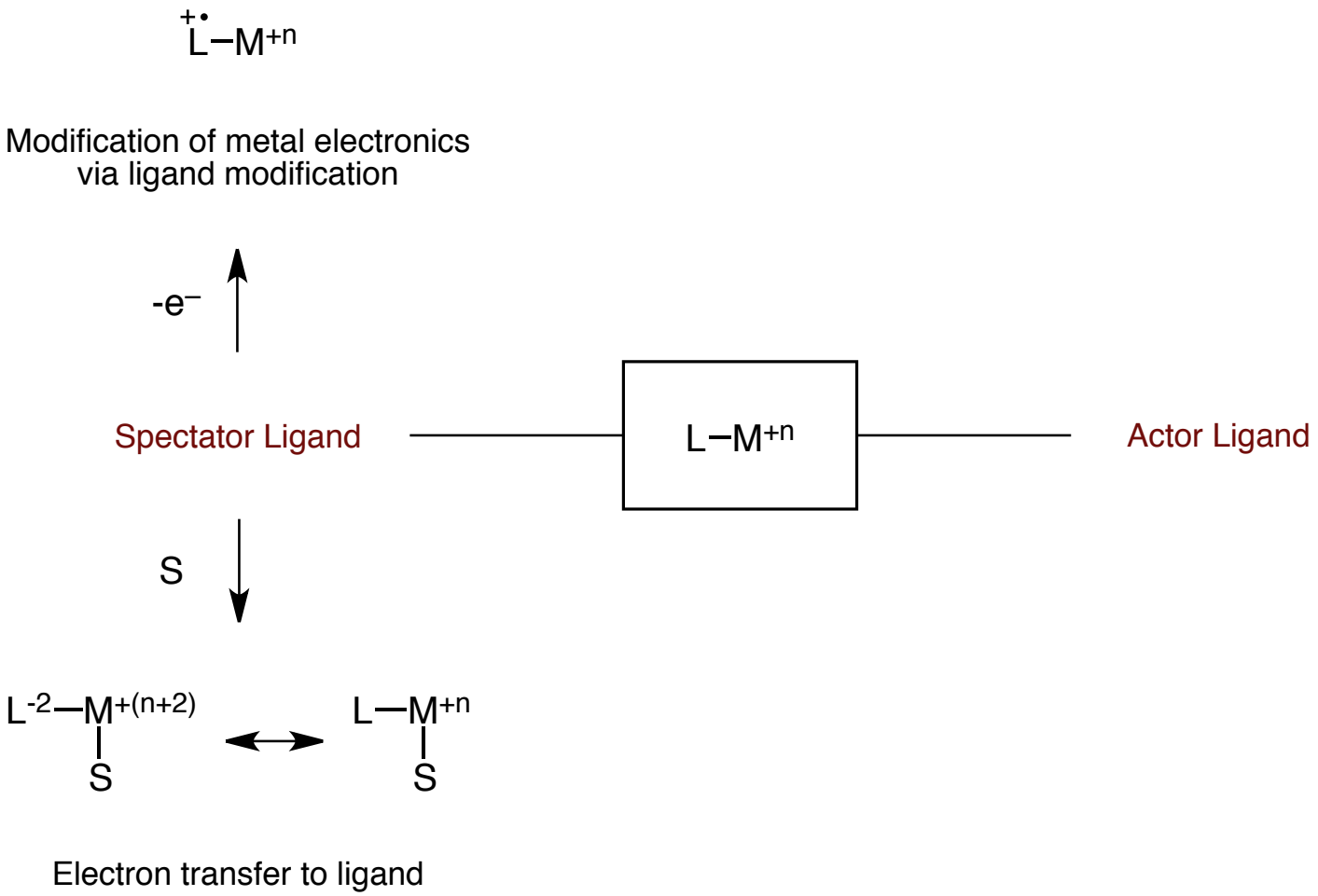

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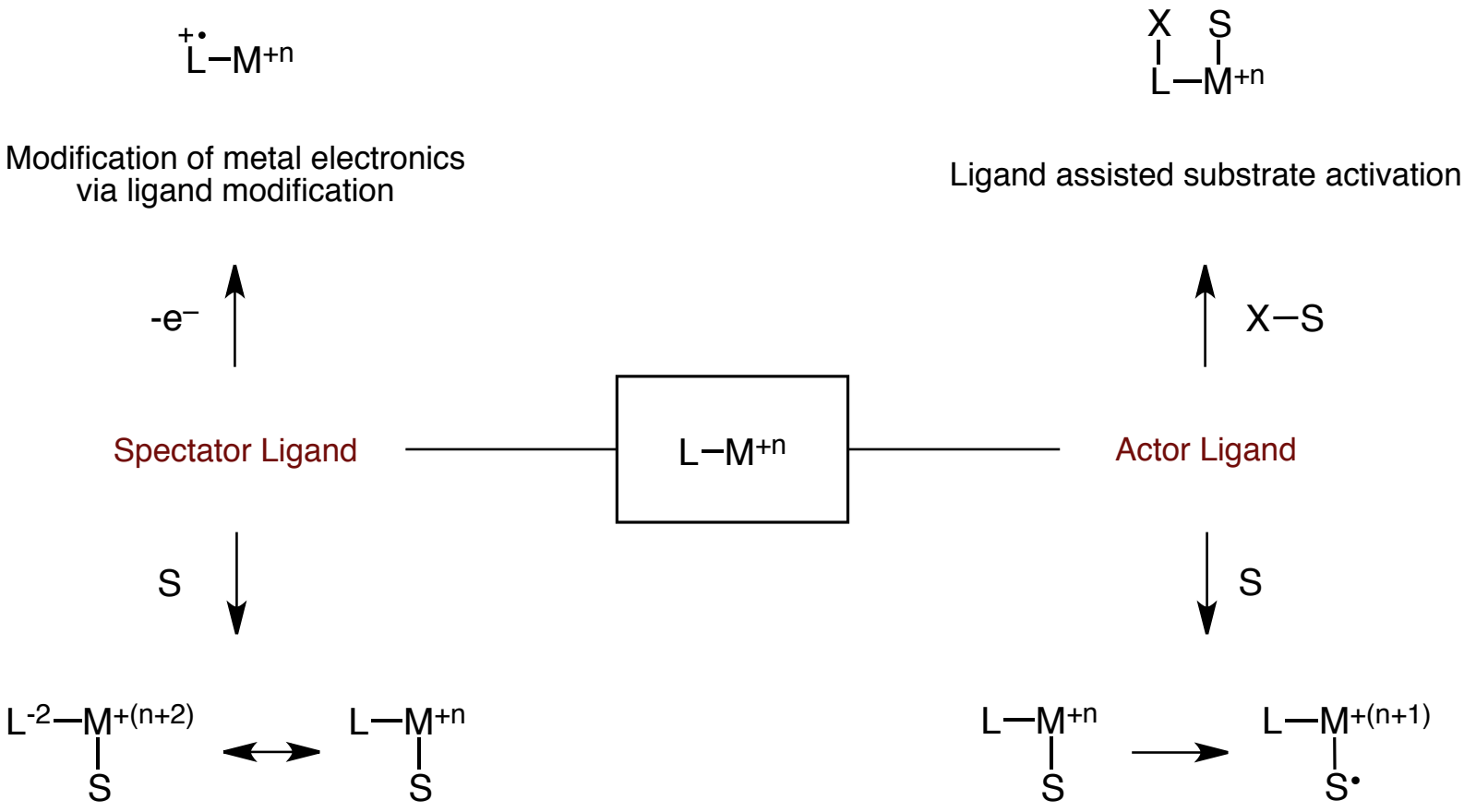

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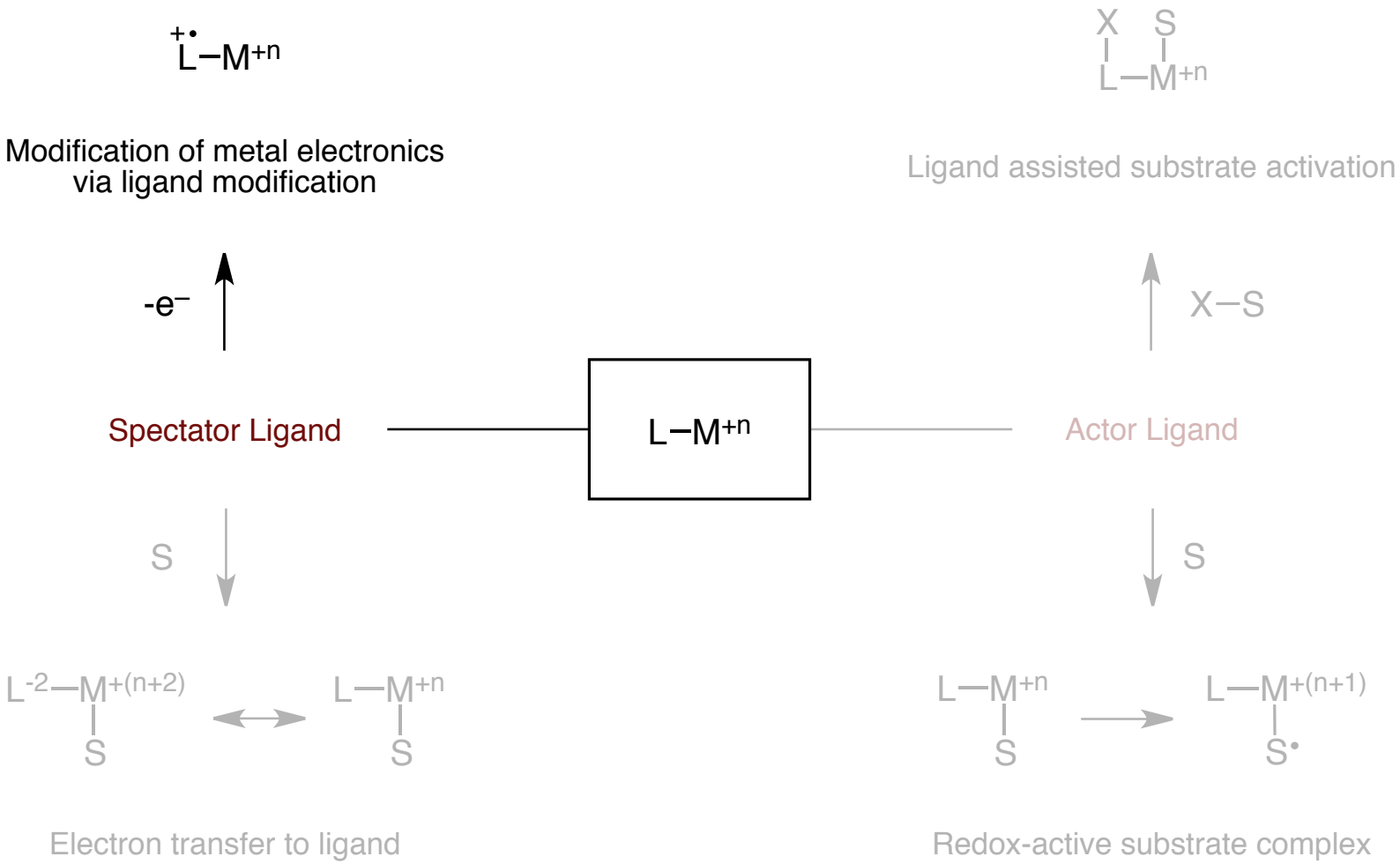

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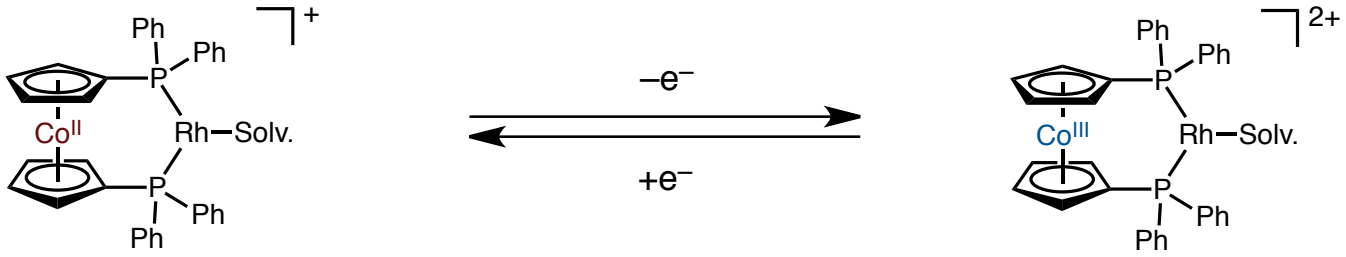
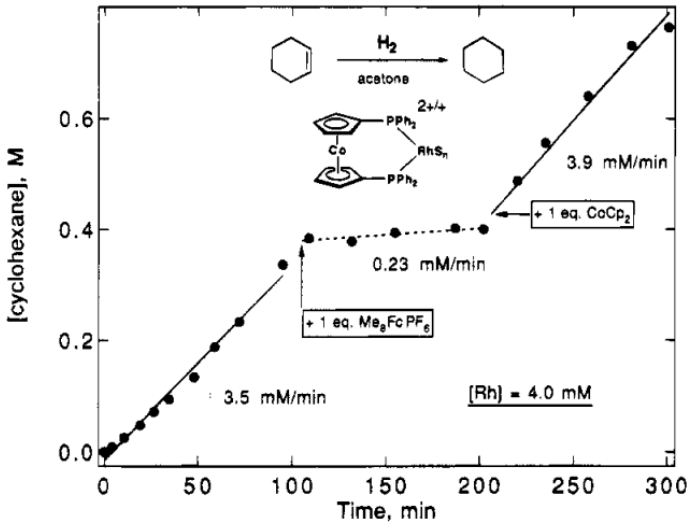
Ligand Controlled Modification of Catalytic Activity

- Early studies by Wrighton in rhodium catalyzed processes





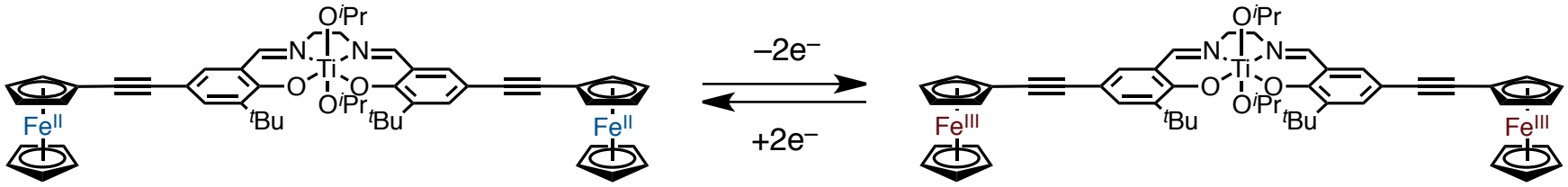
- Reduced catalyst complex is 16 times more reactive towards alkene hydrogenation

- Oxidized catalyst complex was found to be more reactive for ketone hydrosilylation

Lorkovic, I. M., Duff, R. R., Wrighton, M. S. *J. Am. Chem. Soc.*, **1995**, *117*, 3617.

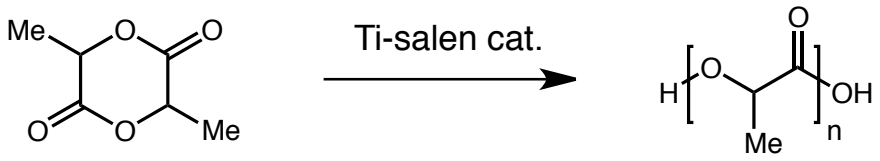
Ligand Controlled Modification of Catalytic Activity

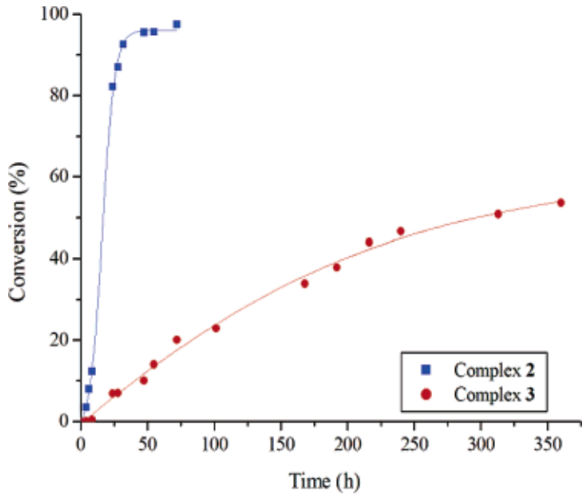
- Use of redox-active ligands as switches in Lewis acid mediated polymerizations



Active catalyst

Inactive catalyst





- An efficient redox switch would be desirable for the controlled synthesis of block copolymers

Gregson, C. K. A., Gibson, V. C., Long, N. J. Marshall, E. L., Oxford, P. J., White, A. J. P. *J. Am. Chem. Soc.*, **2006**, *128*, 7410.

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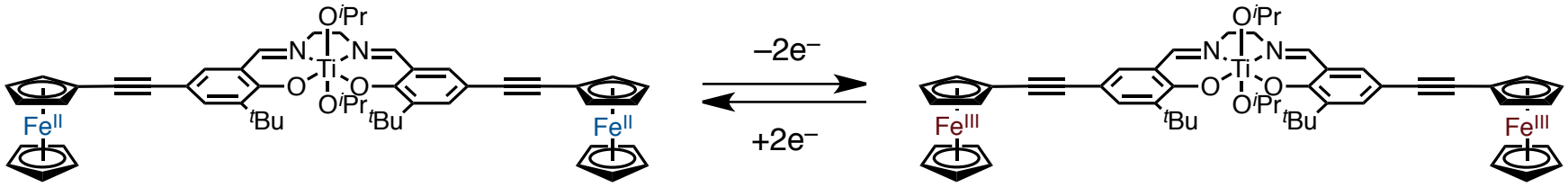

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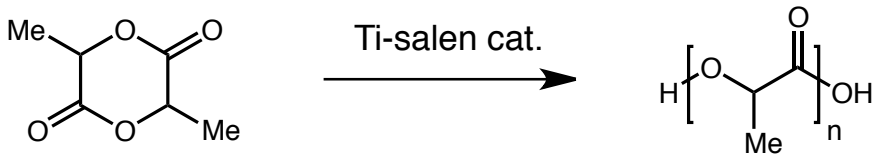

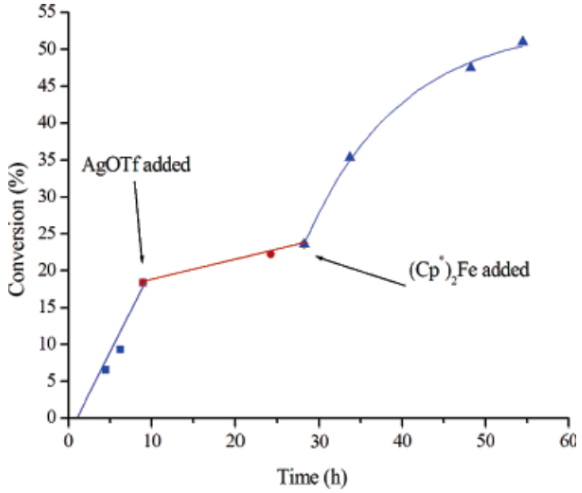

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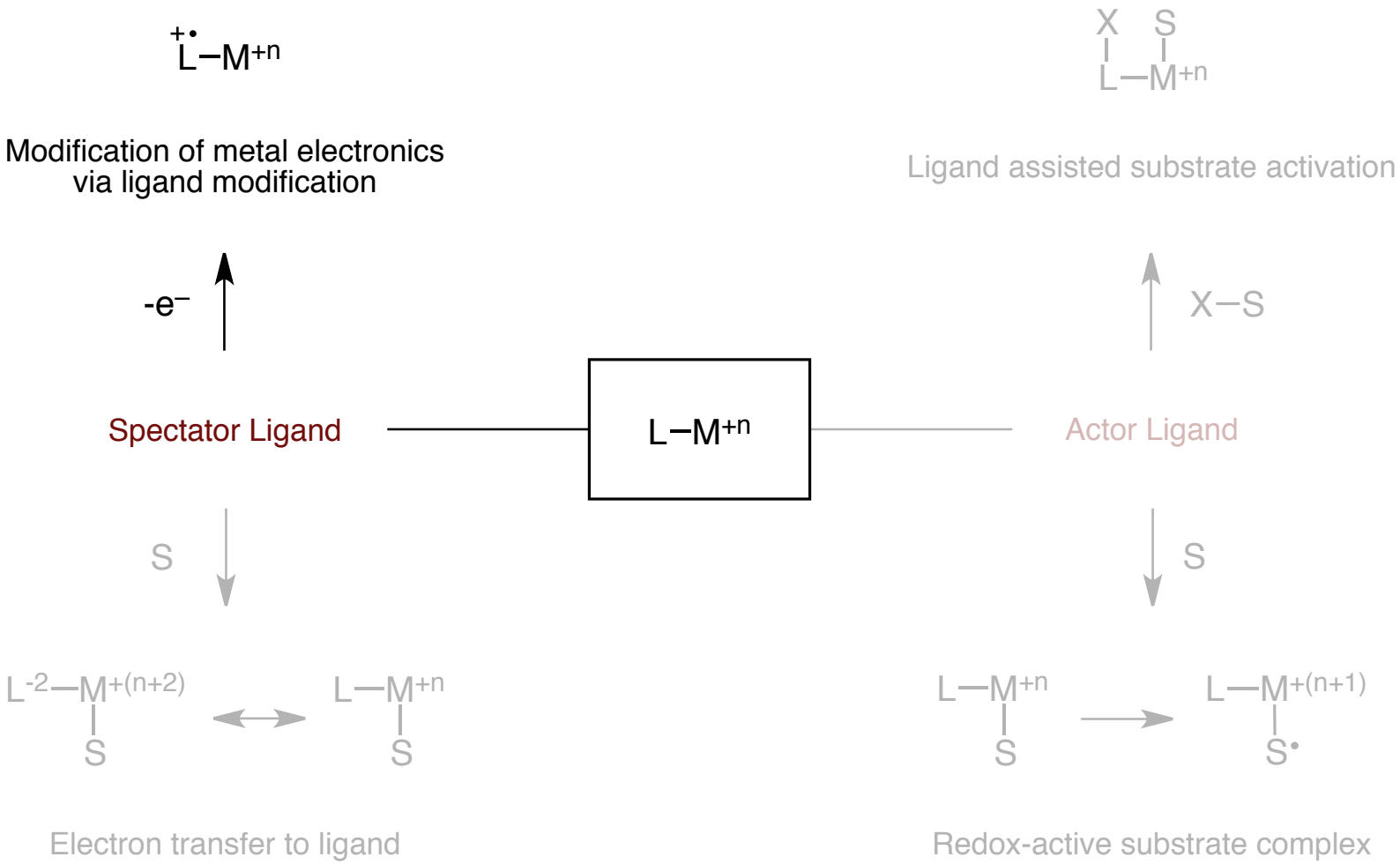
Gregson, C. K. A., Gibson, V. C., Long, N. J. Marshall, E. L., Oxford, P. J., White, A. J. P. *J. Am. Chem. Soc.*, **2006**, *128*, 7410.

Classes of Redox-Active Ligands



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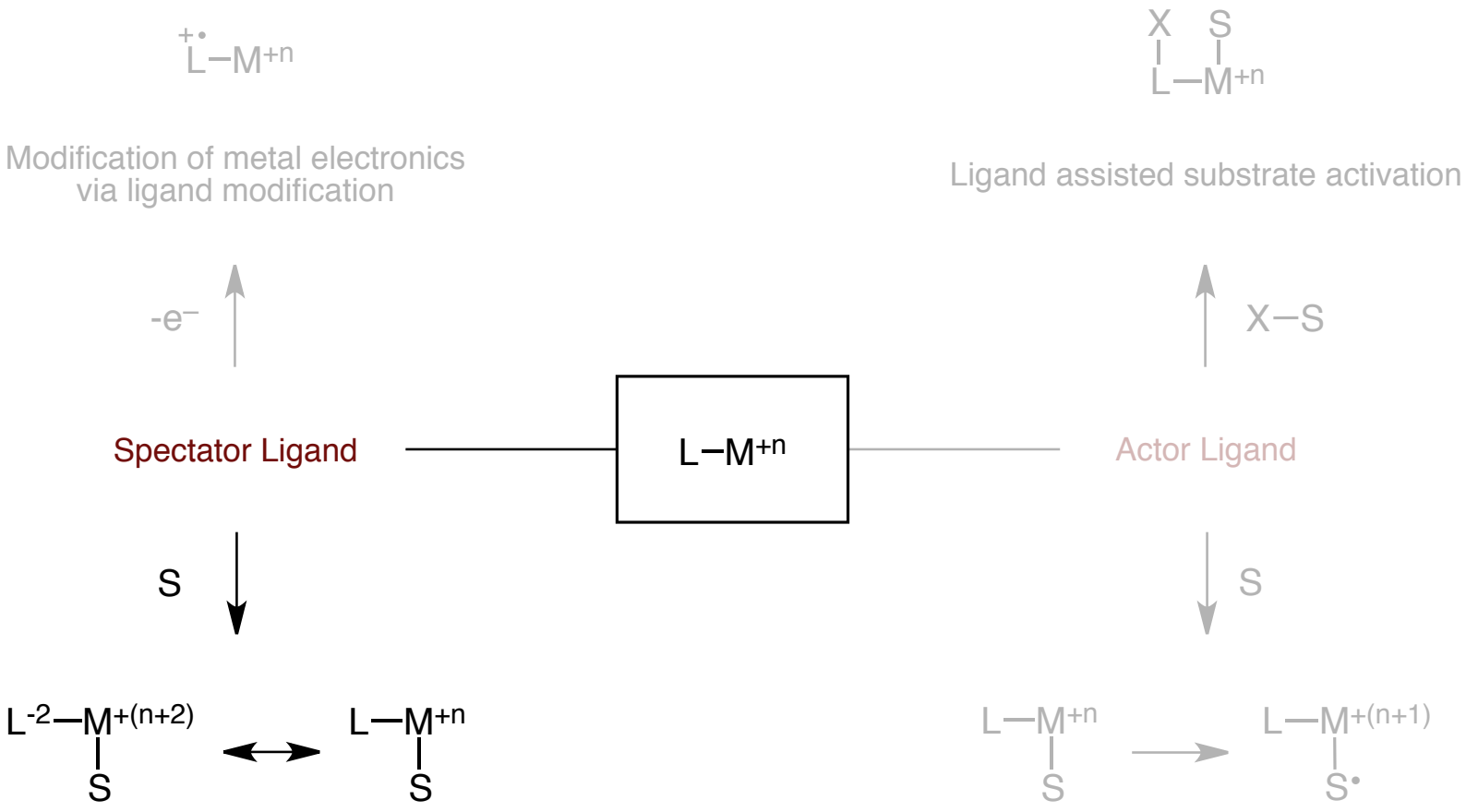

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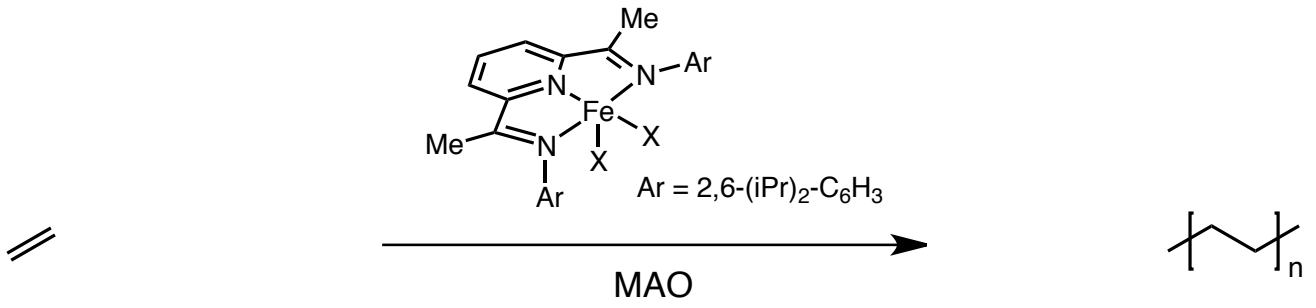
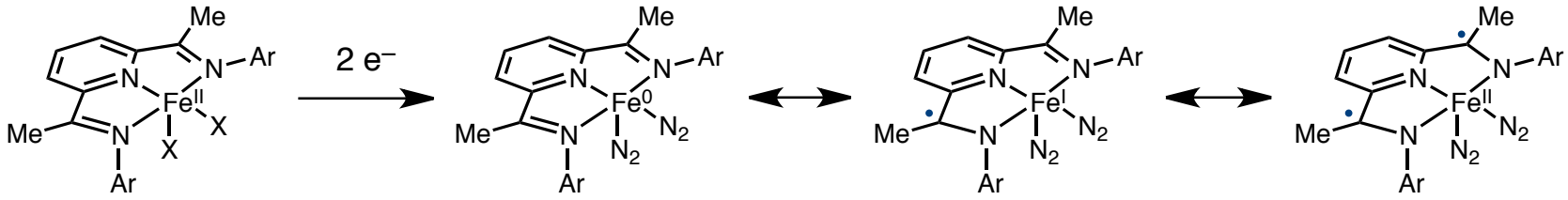
Luca, O. R., Crabtree, R. H. *Chem. Soc. Rev.*, **2013**, *42*, 1440.

Redox Active Bis(imino)-Pyridine Ligand with Iron(II)

- Brookhart developed bulky pyridine diimine ligands for use in polymerization



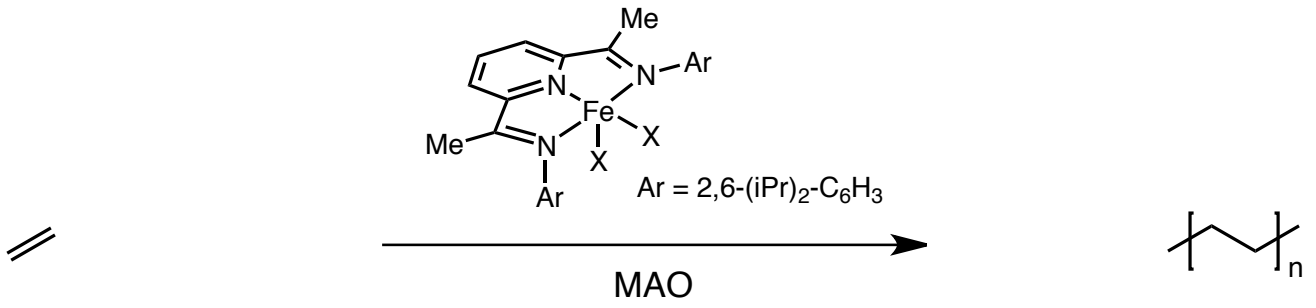
- In 2006, involvement of the PDI ligand upon two-electron reduction of the iron complex was established



Small, B. L., Brookhart, M., Bennett, A. M. A. *J. Am. Chem. Soc.*, **1998**, *120*, 4049.
Bart, S. C., Chlopek, K., Bill, E., Bouwkamp, M. W., Lobkovsky, E., Neese, F., Wieghardt, K., Chirik, P. J. *J. Am. Chem. Soc.*, **2006**, *128*, 13901.

Redox Active Bis(imino)-Pyridine Ligand with Iron(II)

- Brookhart developed bulky pyridine diimine ligands for use in polymerization



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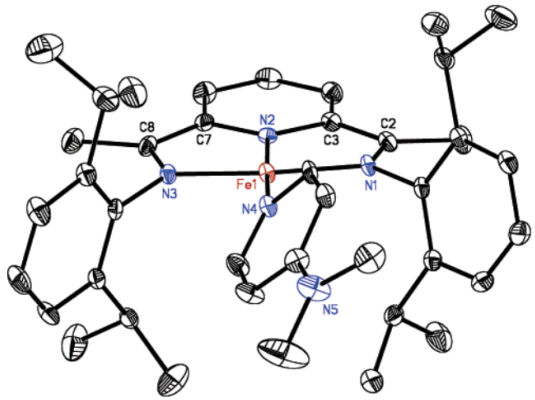
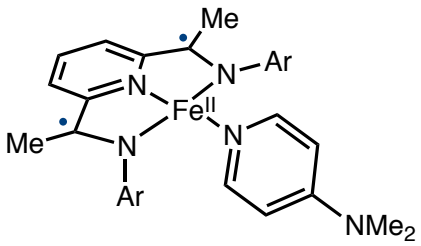
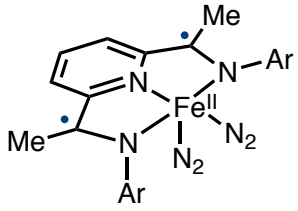




vs.

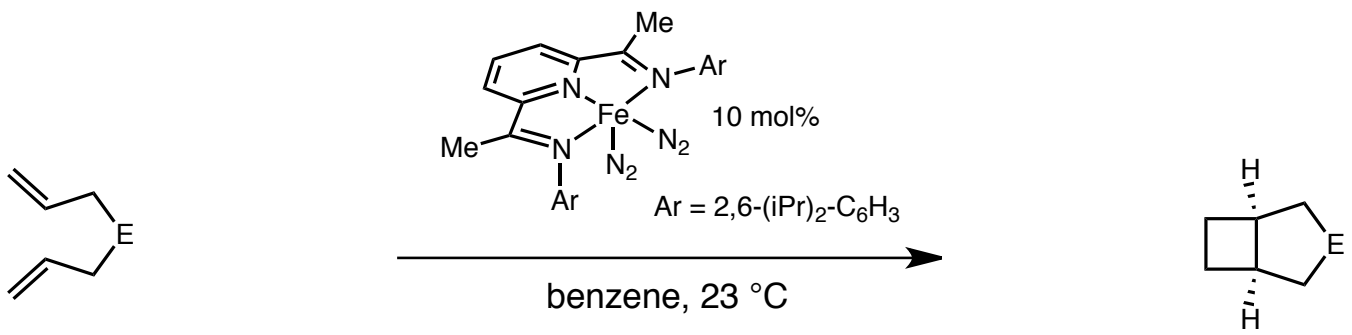


major resonance form

Small, B. L., Brookhart, M., Bennett, A. M. A. *J. Am. Chem. Soc.*, **1998**, *120*, 4049.
Bart, S. C., Chlopek, K., Bill, E., Bouwkamp, M. W., Lobkovsky, E., Neese, F., Wieghardt, K., Chirik, P. J. *J. Am. Chem. Soc.*, **2006**, *128*, 13901.

Redox Active Bis(imino)-Pyridine Ligand with Iron(II)

- Chirik has developed bis(imino)-pyridine iron(II) dinitrogen complexes with unique reactivity



E =	Time (min)	Conv. (%)	TOF (h^{-1})
CH_2	300	92	1.8
NBn	26	90	21
NtBu	< 5	> 95	> 240
$C(CO_2Et)_2$	141	> 95	4

Bouwkamp, M. W., Bowman, A. C., Lobkovsky, E., Chirik, P. J. *J. Am. Chem. Soc.*, **2006**, *128*, 13340.

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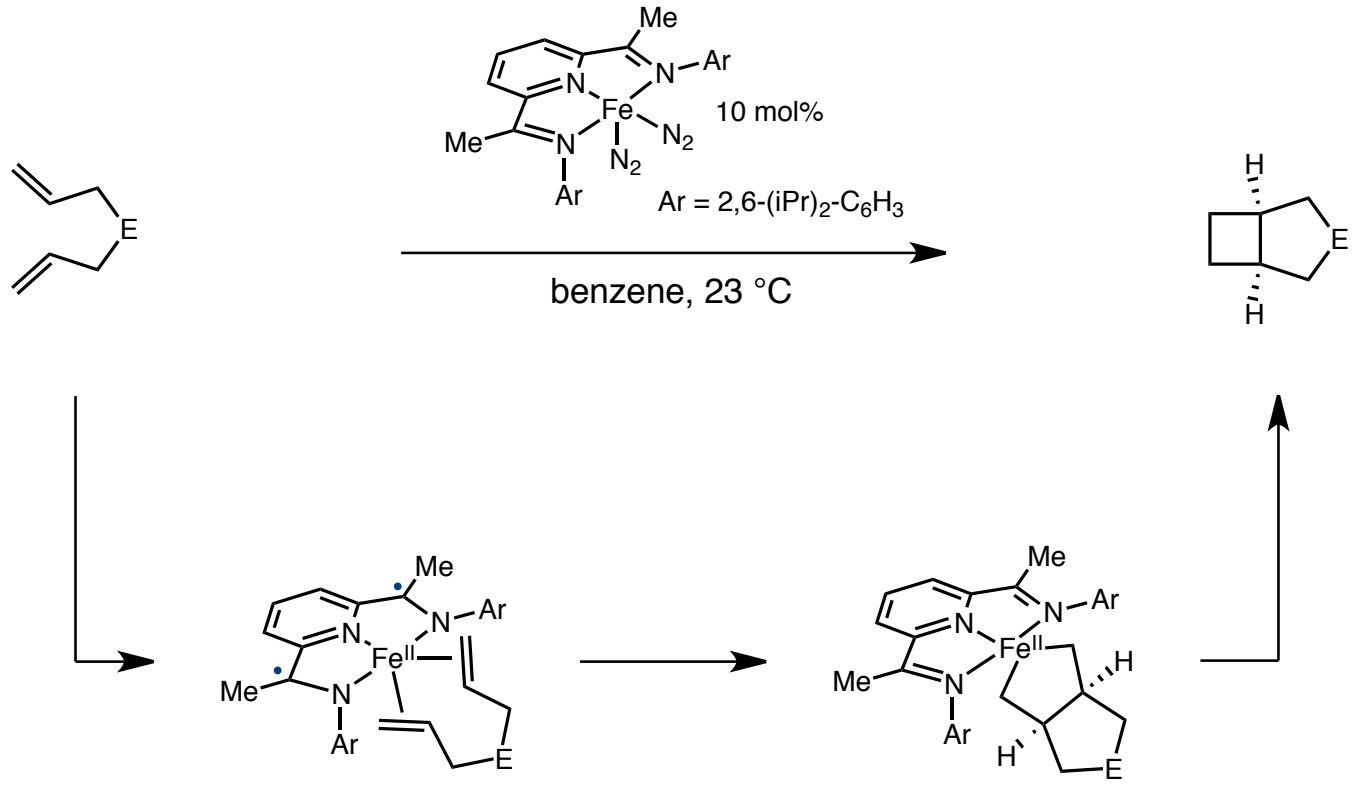

- PDI ligand acts as an electron sink to enable metallocene formation and reductive elimination

Bouwkamp, M. W., Bowman, A. C., Lobkovsky, E., Chirik, P. J. *J. Am. Chem. Soc.*, **2006**, *128*, 13340.

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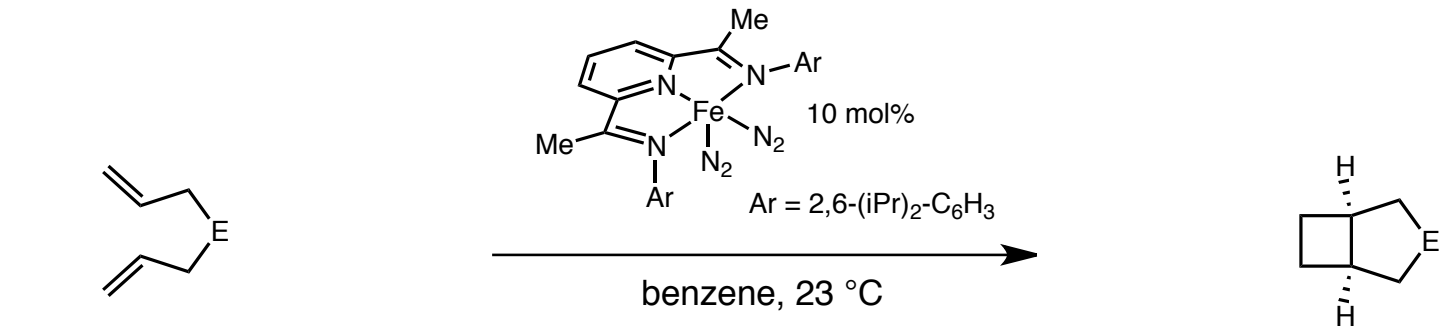
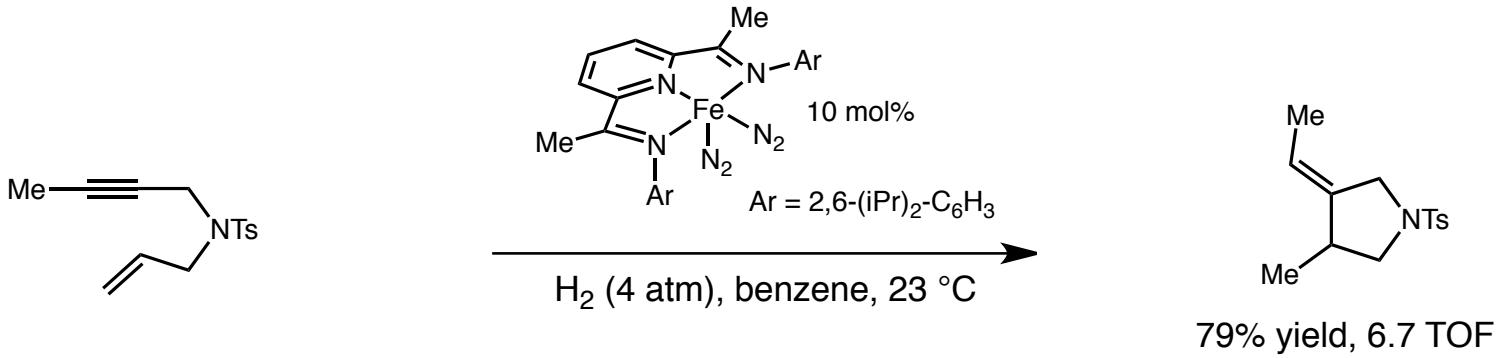


- Reductive enyne cyclizations are also possible via similar mechanism

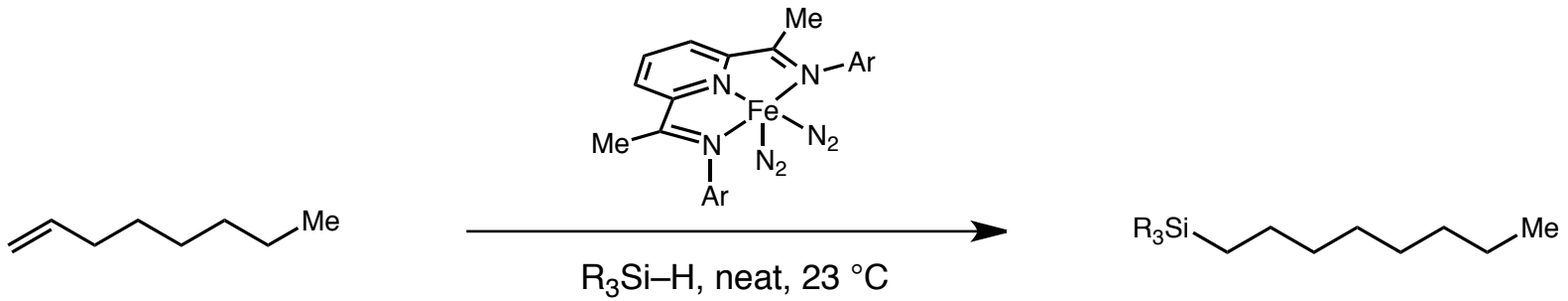


79% yield, 6.7 TOF

Sylvester, K. T., Chirik, P. J. *J. Am. Chem. Soc.*, **2009**, *131*, 8772.
Bouwkamp, M. W., Bowman, A. C., Lobkovsky, E., Chirik, P. J. *J. Am. Chem. Soc.*, **2006**, *128*, 13340.

Redox Active Bis(imino)-Pyridine Ligand with Iron(II)

- Terminal alkene hydrosilylation for use in industrial applications



- One of the largest-scale applications of homogeneous catalysis
- Used to produce a range of silicone-based surfactants, fluids, molding products, release coatings, and pressure-sensitive adhesives
- Current production relies upon the use of Nobel metal catalysts (Pt, Pd, Ru, and Rh)
- Estimated that industry consumed 5.6 metric tons of Pt in 2007

Tondreau, A. M., Atienza, C. C. H., Weller, K. J., Nye, S. A., Lewis, K. M., Delis, J. G. P., Chirik, P. J. *Science*, **2012**, *335,* 6068, 567.

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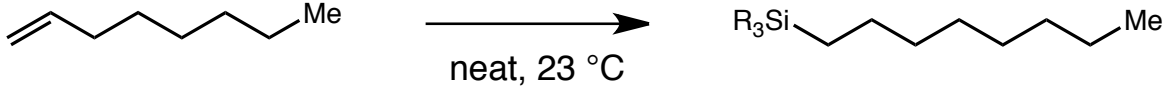
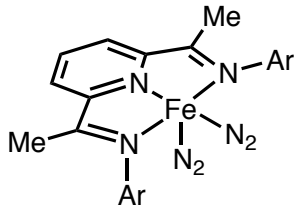
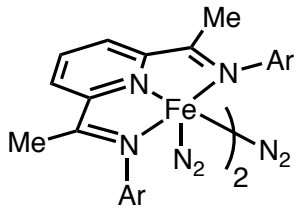




1, Ar = 2,6-$(iPr)_2$-C_6H_3

Catalyst	mol %	Silane	Time	Yield (GC)
1	0.05	$(TMSO)_2MeSiH$	15 min	> 98%
1	0.04	$(EtO)_3SiH$	15 min	96%
1	0.03	Et_3SiH	1 hr	trace
2	0.02	Et_3SiH	15 min	9%
3	0.02	Et_3SiH	45 min	> 98%
3	0.004	$(TMSO)_2MeSiH$	15 min	> 98%



Ar = 2,6-$(Et)_2$-C_6H_3, **2**
Ar = 2,6-$(Me)_2$-C_6H_3, **3**

25,000 turnovers

Tondreau, A. M., Atienza, C. C. H., Weller, K. J., Nye, S. A., Lewis, K. M., Delis, J. G. P., Chirik, P. J. *Science*, **2012**, *335,* 6068, 567.

Redox Active Bis(imino)-Pyridine Ligand with Iron(II)

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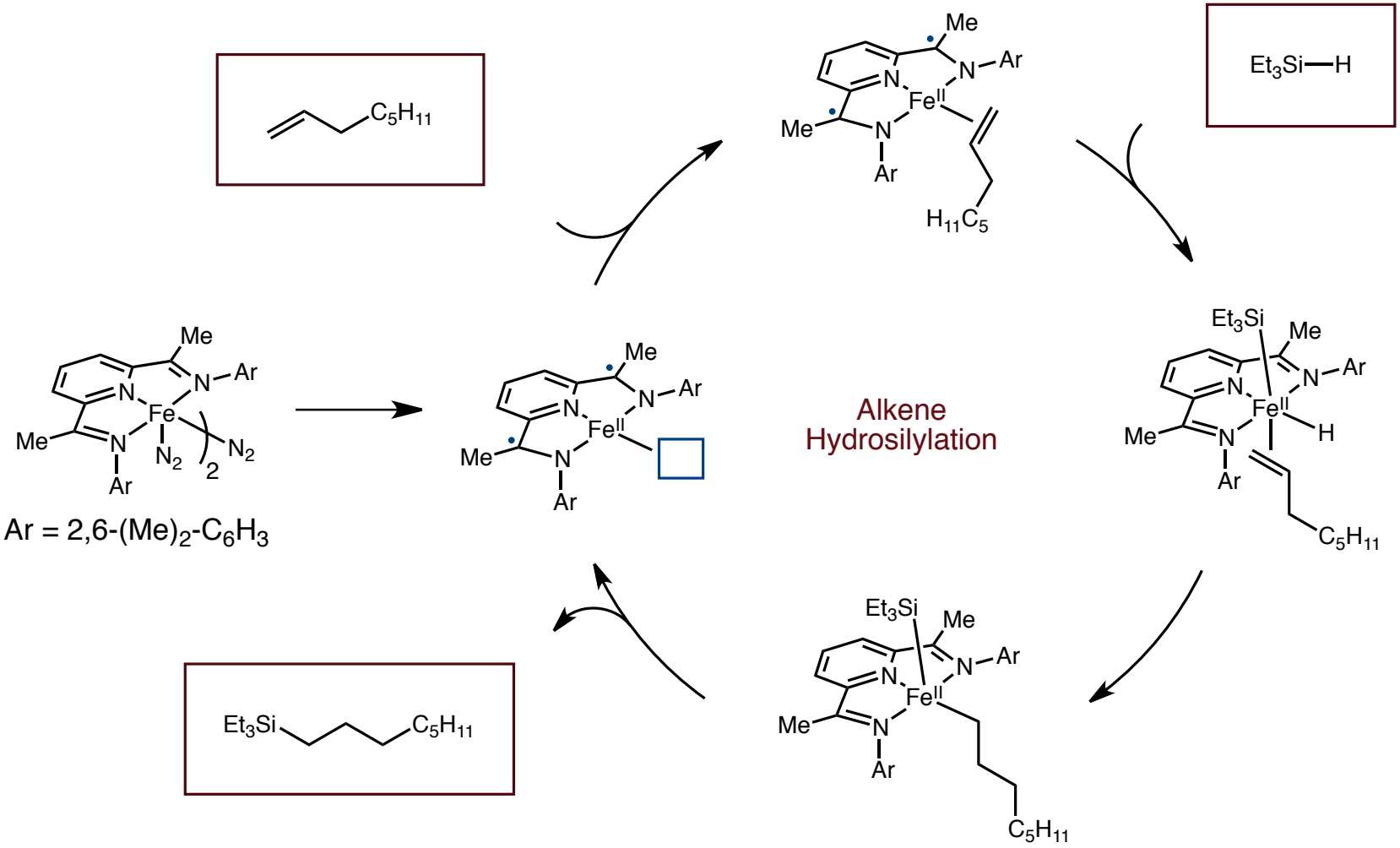

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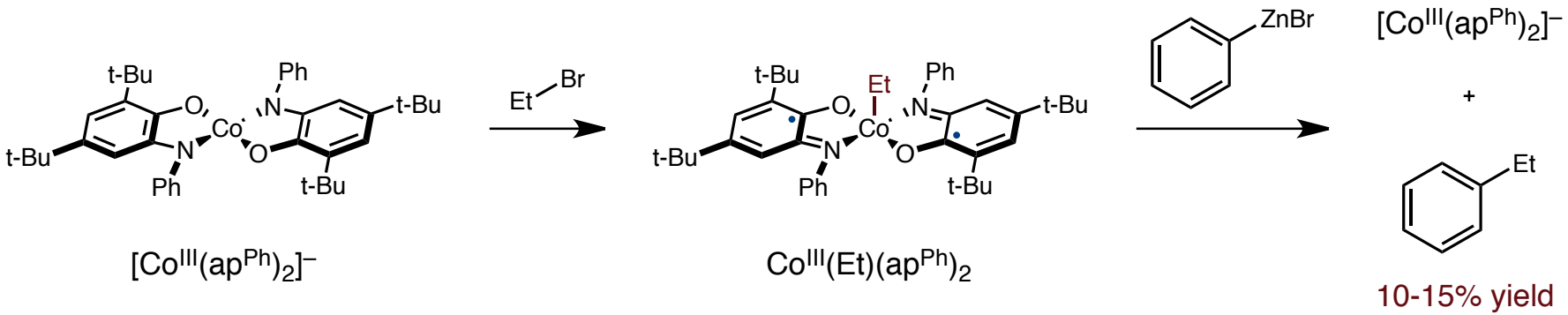
Negishi-type Coupling Using Cobalt(III)

- Breakthrough use of Cobalt(III) for alkyl halide oxidative addition and reductive elimination

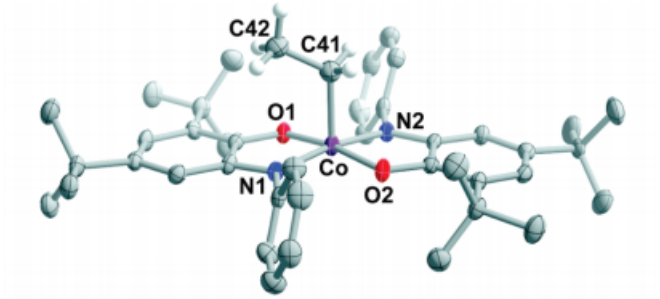


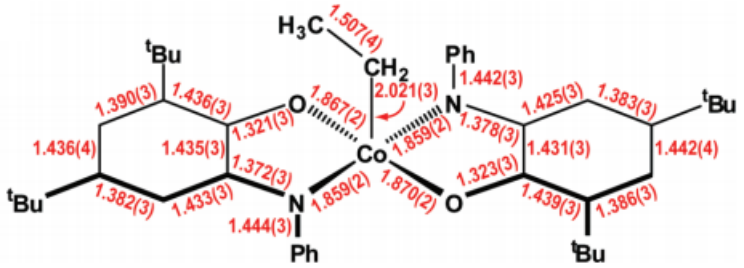
$[Co^{III}(ap^{Ph})_2]^-$

$Co^{III}(Et)(ap^{Ph})_2$

$[Co^{III}(ap^{Ph})_2]^-$ + Et

- Oxidative addition results in formation of semiquinonate complex





Smith, A. L., Hardcastle, K. I., Soper, J. D. *J. Am. Chem. Soc.*, **2010**, *132*, 14358.

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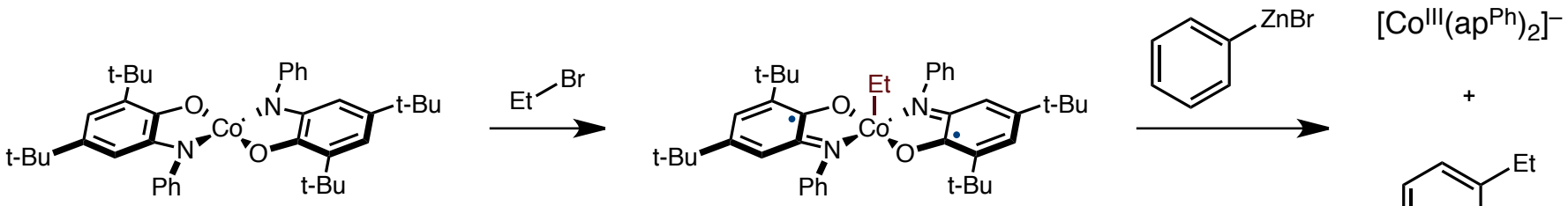

$[Co^{III}(ap^{Ph})_2]^-$ $Co^{III}(Et)(ap^{Ph})_2$

10-15% yield

- Oxidative addition highly responsive to sterics

Alkyl electrophile:	CH_3I, CH_3OTf	EtI	EtBr	i-PrI	BnBr	BnCl
Reaction Time:	< 30 sec	<1 min	1 hr	3 hrs	24 hrs	> 48 hrs

- Oxidative addition likely occurs through an S_N2 type mechanism

Smith, A. L., Hardcastle, K. I., Soper, J. D. *J. Am. Chem. Soc.*, **2010**, *132*, 14358.

Negishi-type Coupling Using Cobalt(III)

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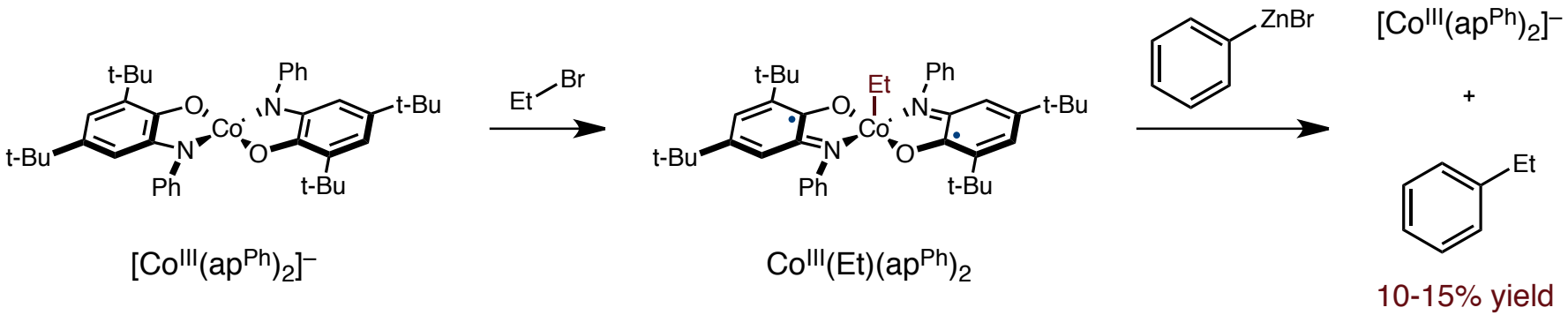


$[Co^{III}(ap^{Ph})_2]^-$

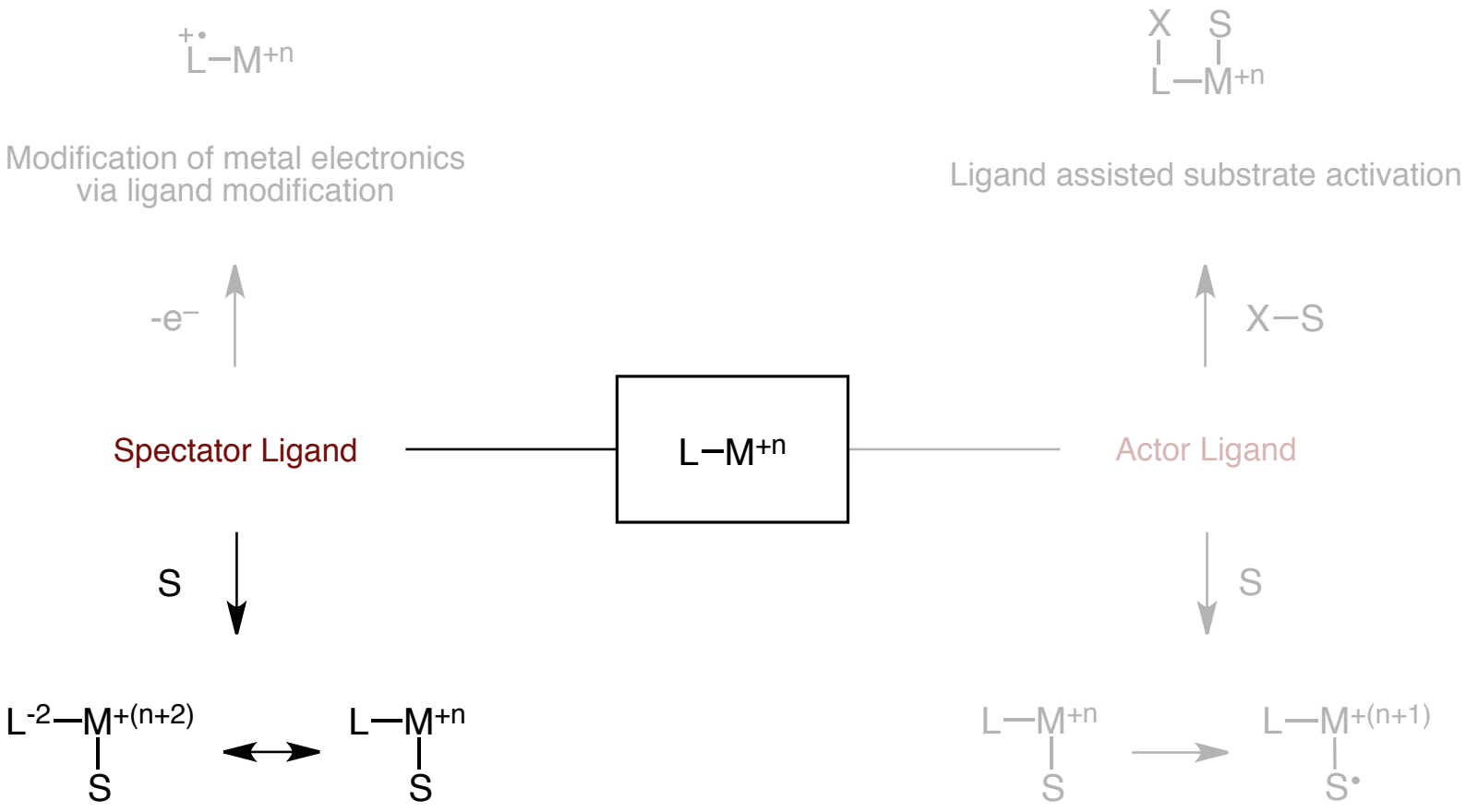
$Co^{III}(Et)(ap^{Ph})_2$

- Treatment with organozinc reagents induces reductive elimination in low yield

PhZnBr (equiv.)	$Co^{III}(Et)(ap^{Ph})_2$ remaining	Ph–Et yield
2	20%	11%
4	7%	15%
6	3%	15%
10	2%	15%

Smith, A. L., Hardcastle, K. I., Soper, J. D. *J. Am. Chem. Soc.*, **2010**, *132*, 14358.

Classes of Redox-Active Ligands



Lyaskovskyy, V., de Bruin, B. *ACS Catal.*, **2012**, *2*, 270.
Luca, O. R., Crabtree, R. H. *Chem. Soc. Rev.*, **2013**, *42*, 1440.

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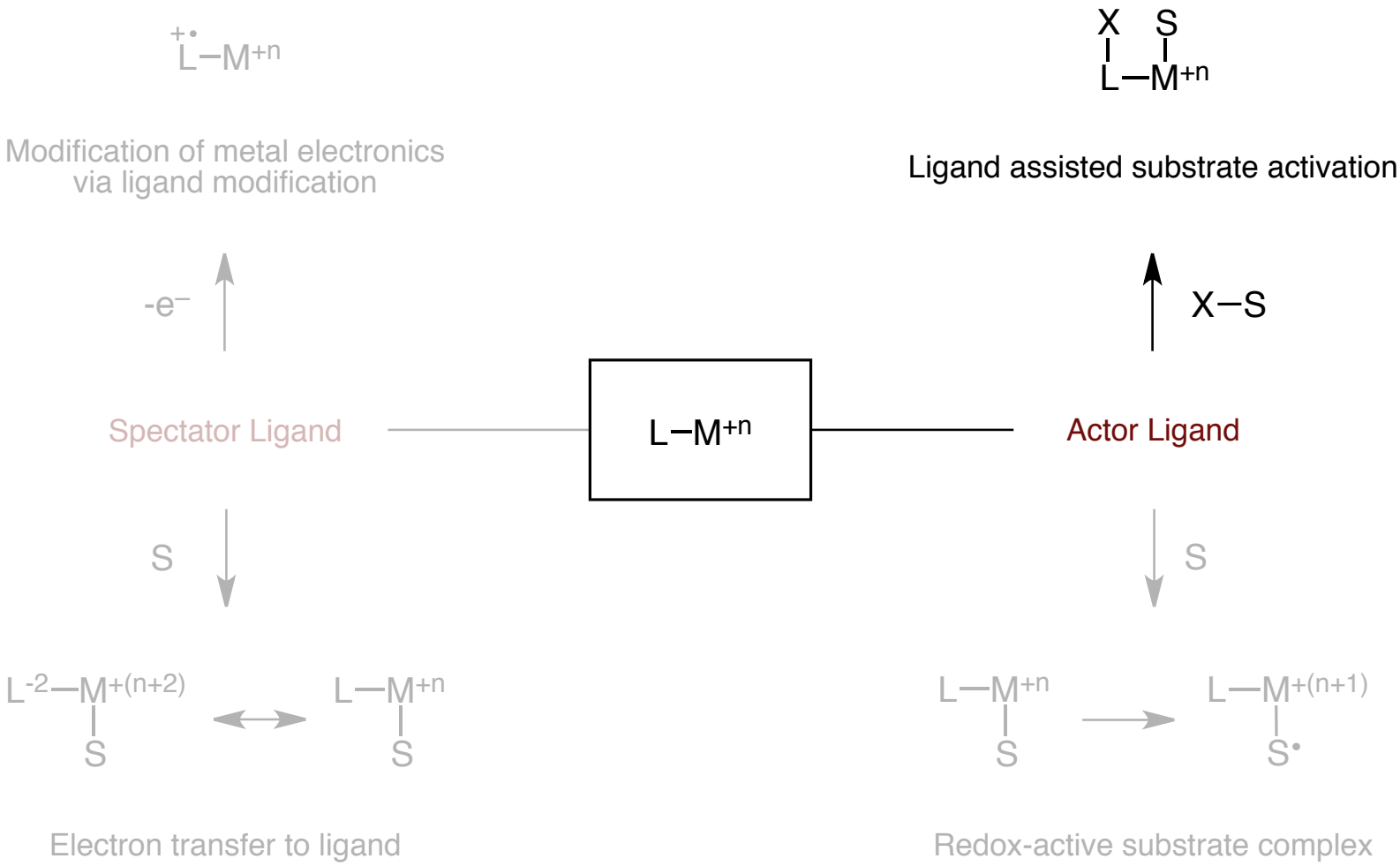

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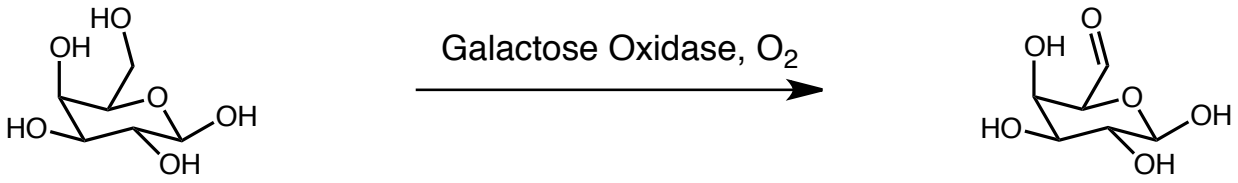
Redox-Active Ligand in Actor Role During Catalysis

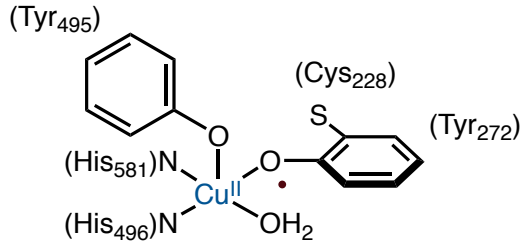
- Novel reactivity derived from ligand centered radical in nature



- Galactose oxidase, isolated from a fungal form, is a copper(II) containing enzyme which catalyzes the oxidation of primary alcohols to aldehydes

- This enzyme has been found to utilize a redox active tyrosine residue to facilitate the 2-electron oxidation process

Catalytically active form of enzyme:



Wachter, R. M., Montagne-Smith, M. P., Branchaud, B. P. *J. Am. Chem. Soc.*, **1997**, *119*, 7743.

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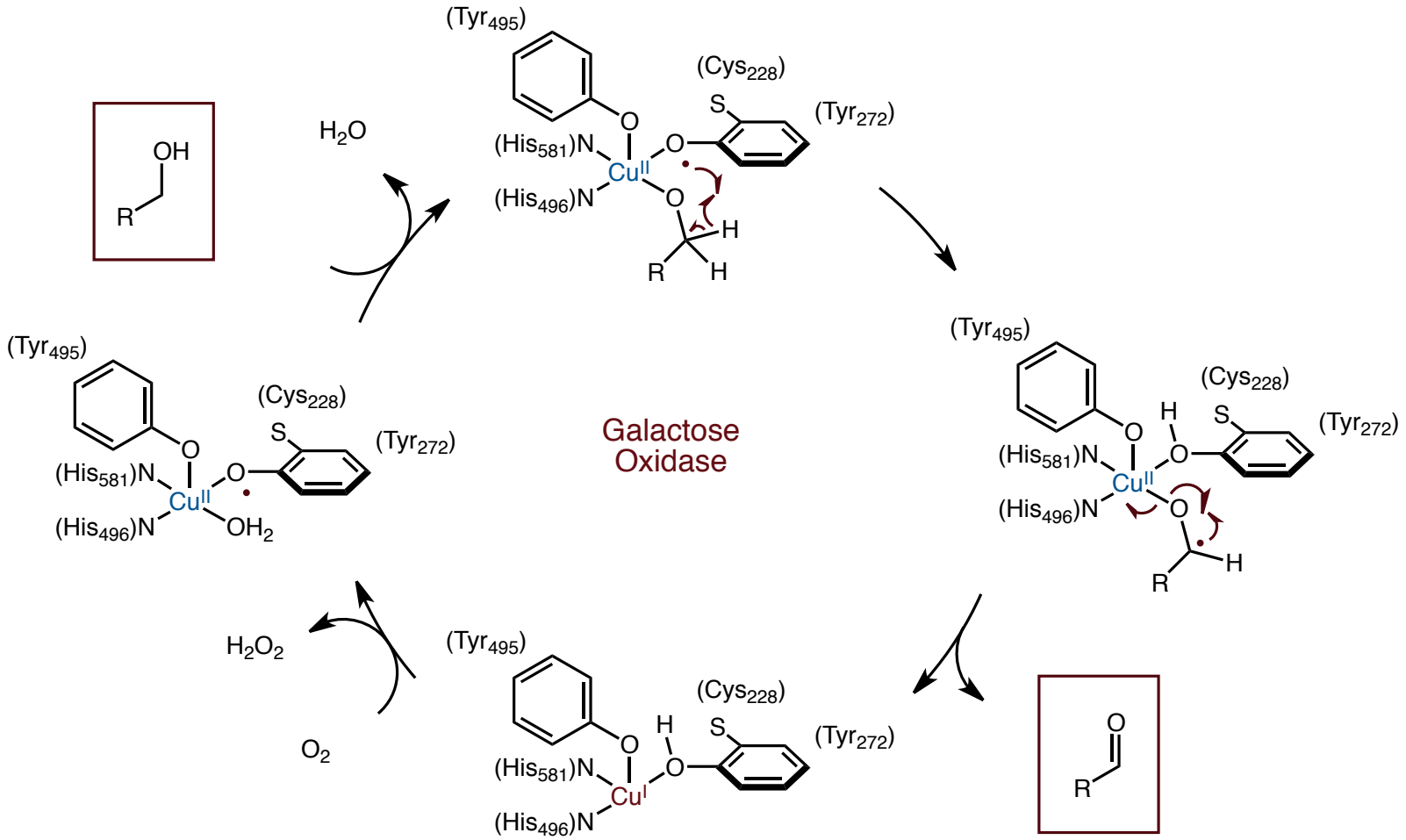

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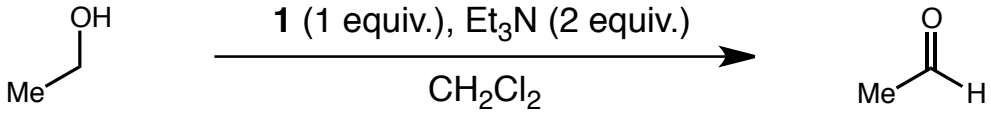
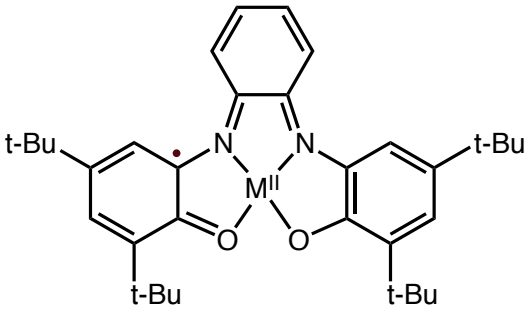
Substrate Participation as a Redox-Active Ligand

- Synthetic galactose oxidase mimics enable alcohol oxidation



>95% yield



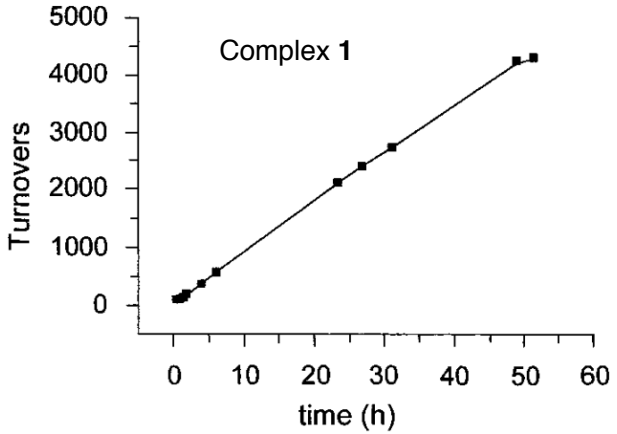
M = Cu, **1**
Zn, **2**

- The copper(II) complex (**1**) is capable of quantitatively oxidizing primary alcohols to the corresponding aldehyde

- Complex **2**, with a redox inactive zinc(II) is also capable of oxidizing primary alcohols (approx. 150 TON in 24 hrs).

- Kinetic studies show a k_H/k_D of 54 for methanol oxidation using complex **1** indicating H-atom abstraction as the rate determining step in the process

Catalytic ethanol oxidation:



Chaudhuri, P., Hess, M., Müller, J., Hildenbrand, K., Bill, E., Weyhermüller, T., Wieghardt, K. *J. Am. Chem. Soc.*, **1999**, *121*, 9599.

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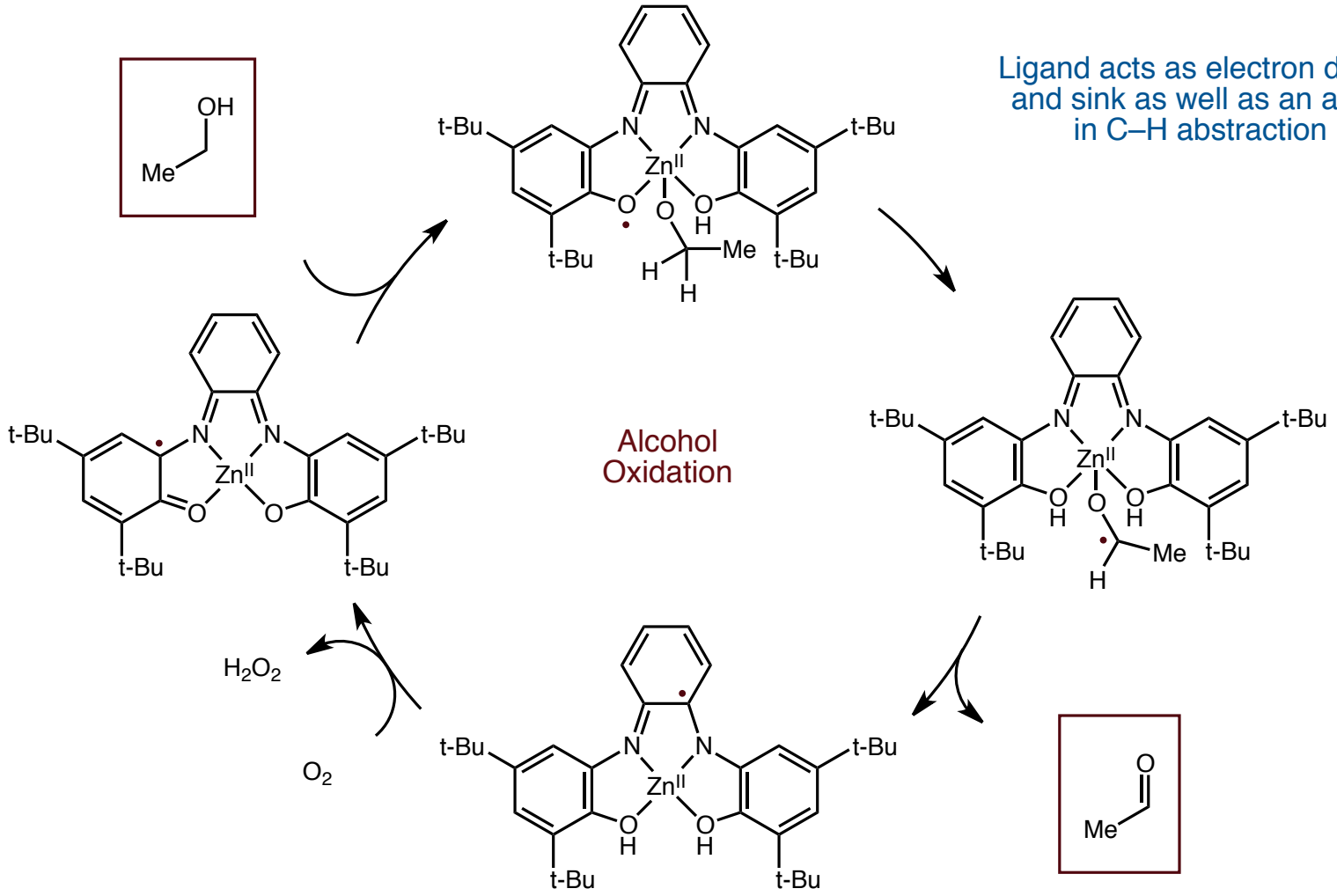

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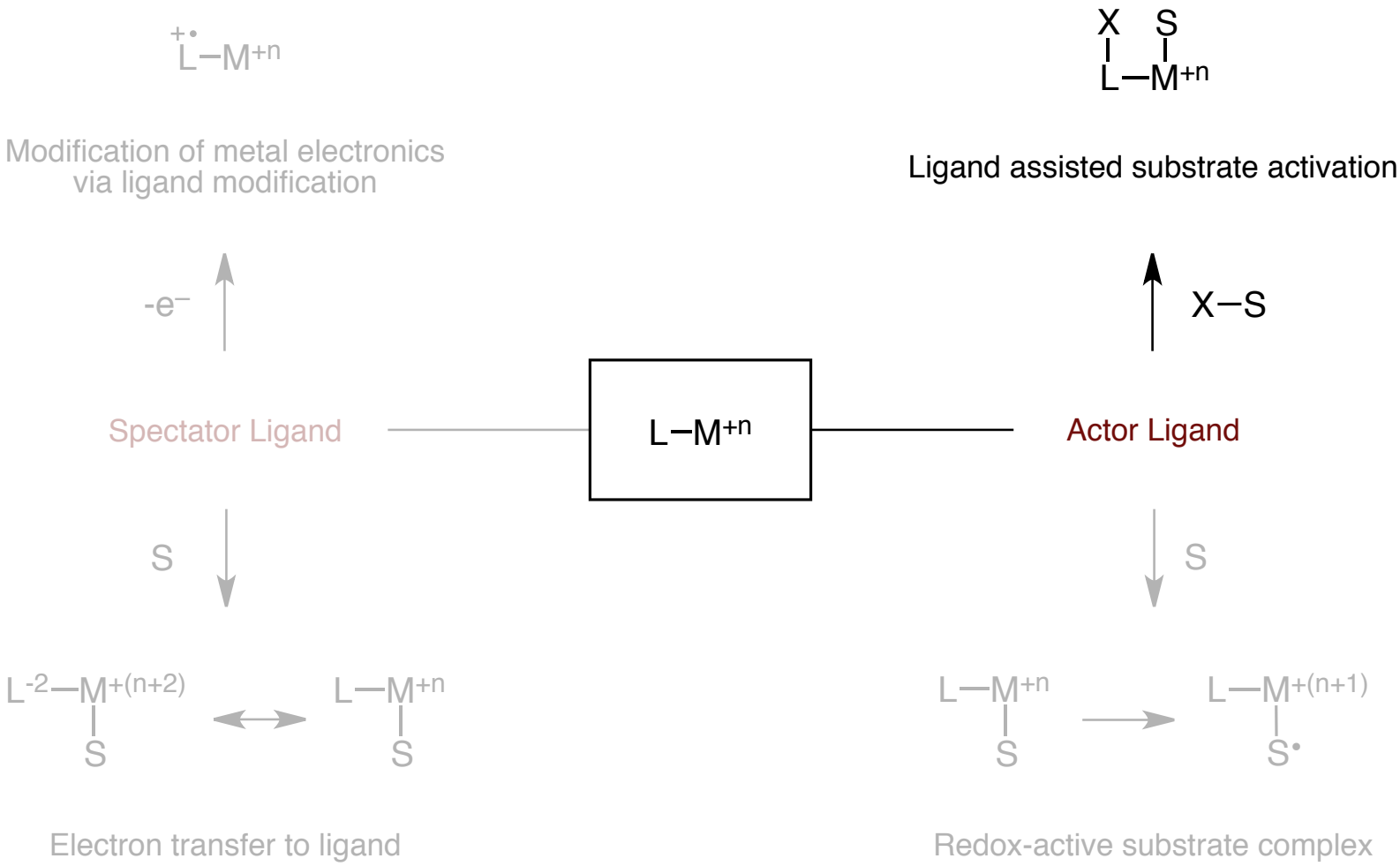
Classes of Redox-Active Ligands



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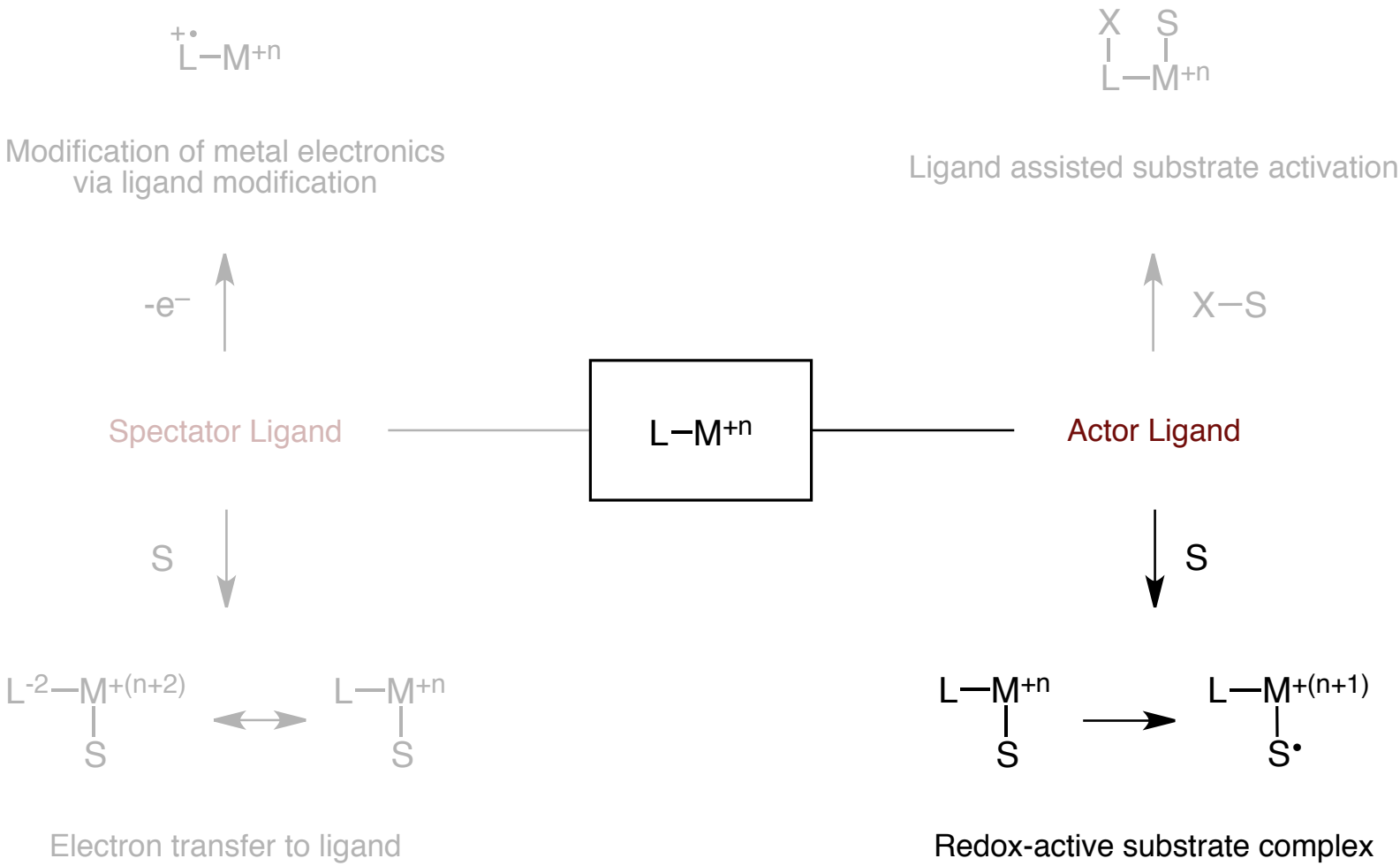

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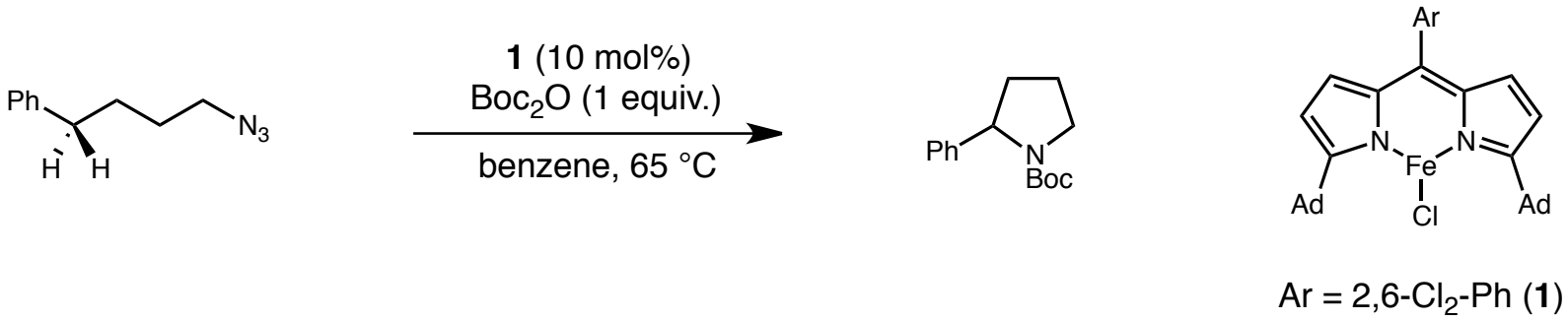
Substrate Participation as a Redox-Active Ligand

- Novel reactivity derived from ligand cetered nitrogen radical

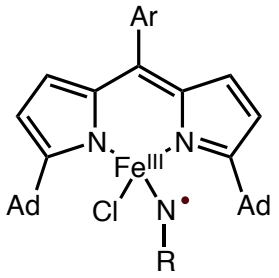


Ar = 2,6-Cl_2-Ph (**1**)

- Highly reactive Fe^{III}–N• system enable the direct functionalization of alkanes in an analagous manner to cytochrome P450 Fe^{IV}–O reactive center

- Dipyrrolomethane ligand is thought to behave redox-innocently from previous DFT studies

Key intermediate:



King, E. R., Hennessy, E. T., Betley, T. A. *J. Am. Chem. Soc.*, **2011**, *133*, 4917.
Hennessy, E. T., Betley, T. A. *Science*, **2013**, *340*, 591.

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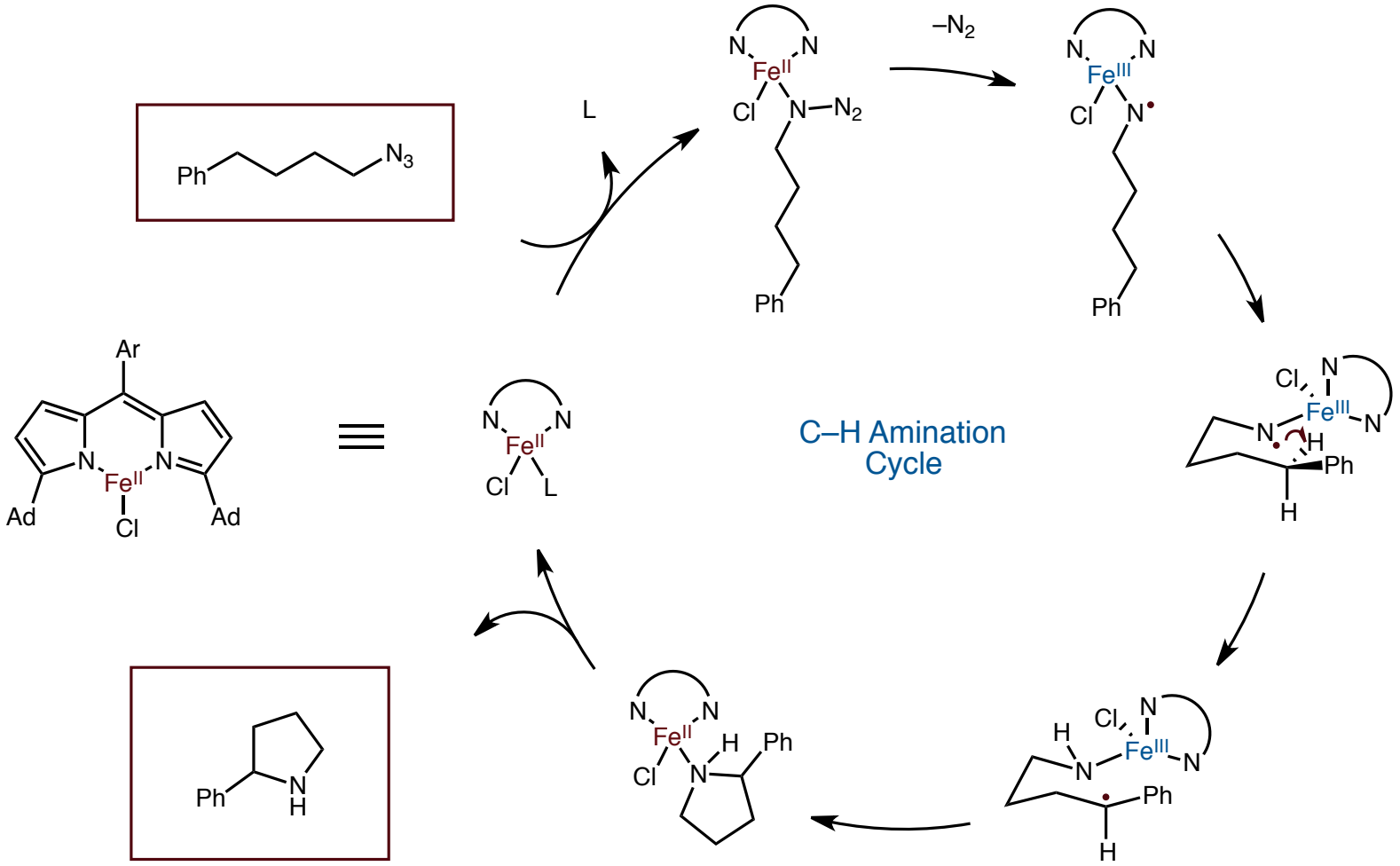

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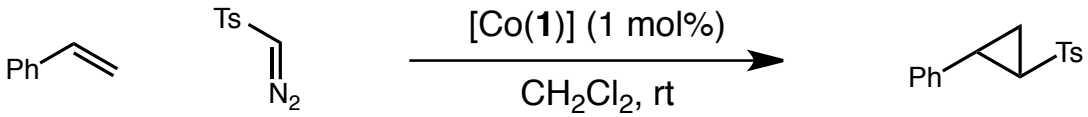
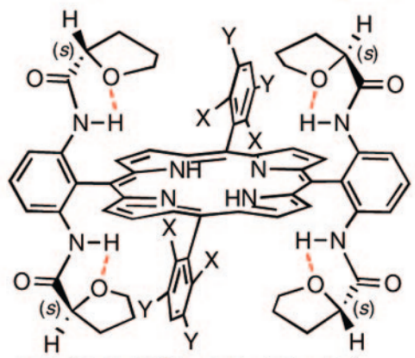
Hennessy, E. T., Betley, T. A. *Science*, **2013**, *340*, 591.

Substrate Participation as a Redox-Active Ligand

- Novel reactivity derived from ligand-centered carbene radical





X = OMe, Y = H, **1**

- Generation of carbenes using cobalt porphyrin complexes result in carbene with significant ligand centered radical character

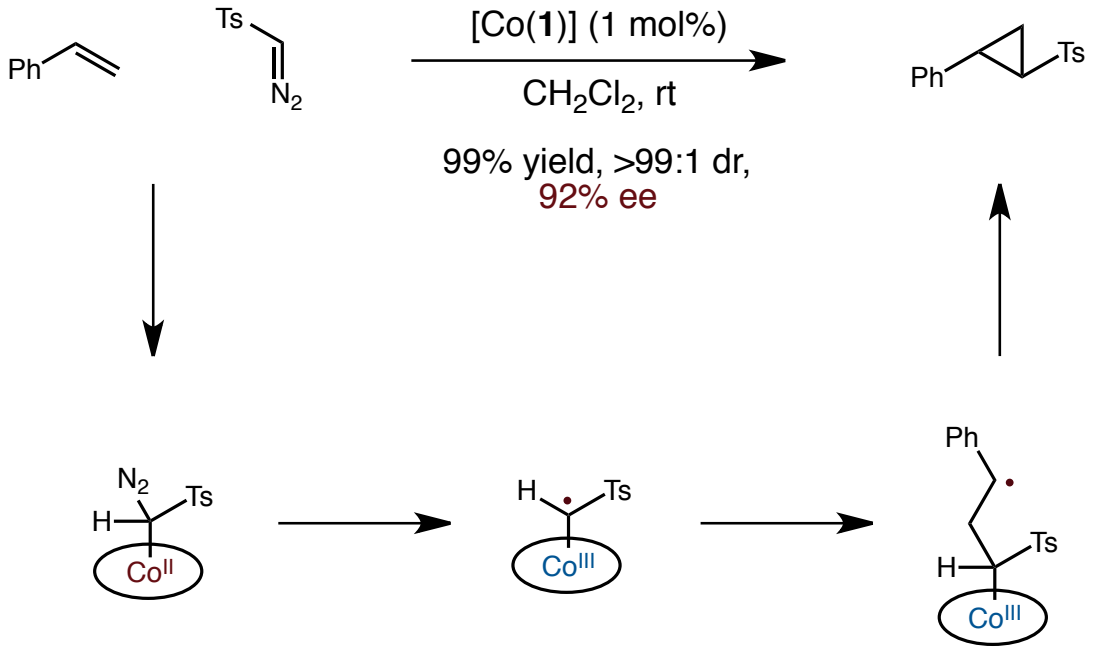
- Radical nature of the reaction mechanism necessitates large chiral pockets in order to achieve high selectivity

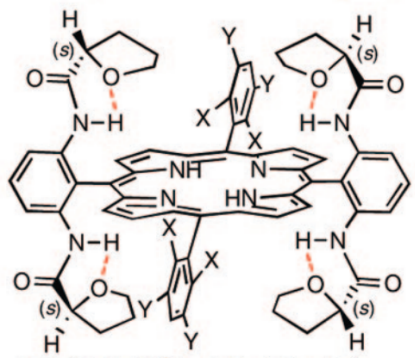
- Formation of nitrene ligands is also possible and can insert into activated C–H bonds

Zhu, S., Ruppel, J. V., Lu, H., Wojtas, L., Zhang, X. P. *J. Am. Chem. Soc.*, **2008**, *130*, 5042.

Substrate Participation as a Redox-Active Ligand

- Novel reactivity derived from ligand-centered carbene radical





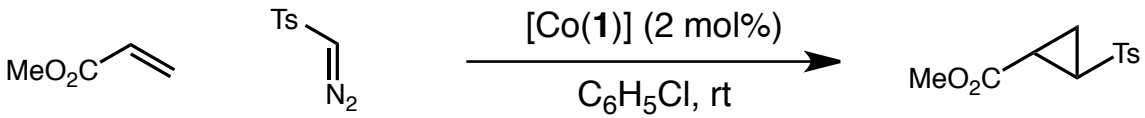
X = OMe, Y = H, **1**

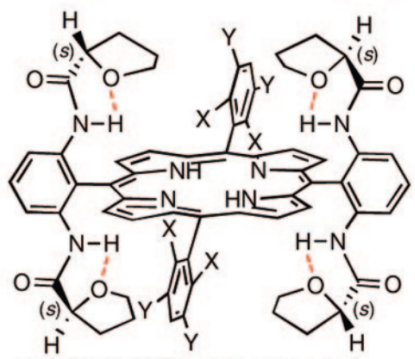
- Loss of nitrogen results in electron transfer from Co(II) center and formation of carbon centered radical

Zhu, S., Ruppel, J. V., Lu, H., Wojtas, L., Zhang, X. P. *J. Am. Chem. Soc.*, **2008**, *130*, 5042.

Substrate Participation as a Redox-Active Ligand

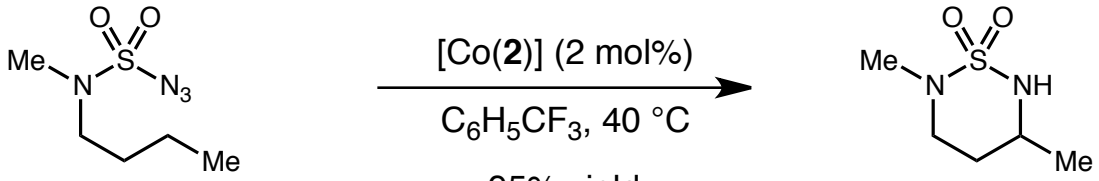
- Novel reactivity derived from ligand-centered carbene radical

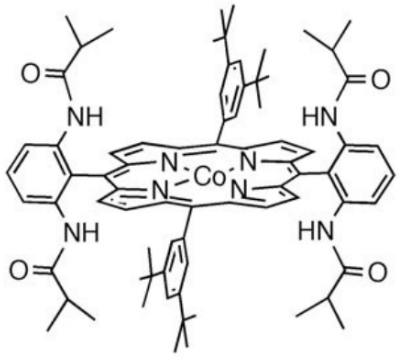




X = OMe, Y = H, **1**

- Nitrene based systems proceed through a similar process





Co(**2**)

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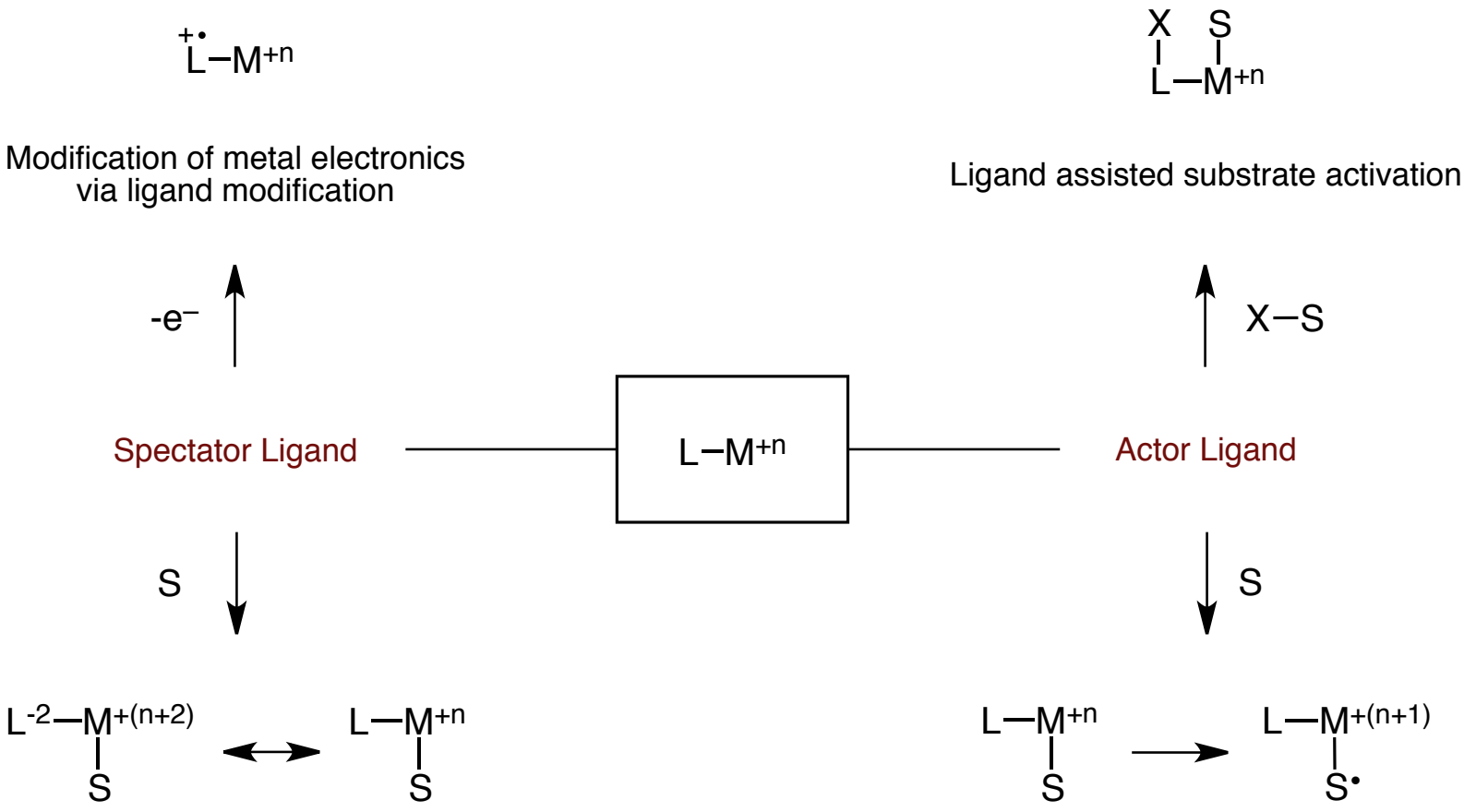
Classes of Redox-Active Ligands



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