

*Redox Non-Innocent Ligands as
Electron Reservoirs in Catalysis*



*Carina Jette
Stoltz/Reisman Literature Meetings
3/9/2018*

Redox-Active Ligands: Some Definitions

Jørgenson, 1966:

"Ligands are innocent when they allow the oxidation state of the central atoms to be defined"

therefore:

non-innocent ligands: formal and spectroscopically determined oxidation state of the metal-ligand system is ambiguous

Chirik, 2010:

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

**Oxidation state ambiguity is the central aspect
to metal complexes involving redox
non-innocent ligands**

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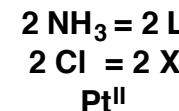
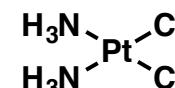
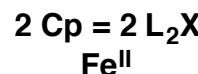
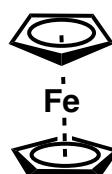
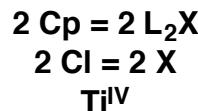
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Innocent Ligands:



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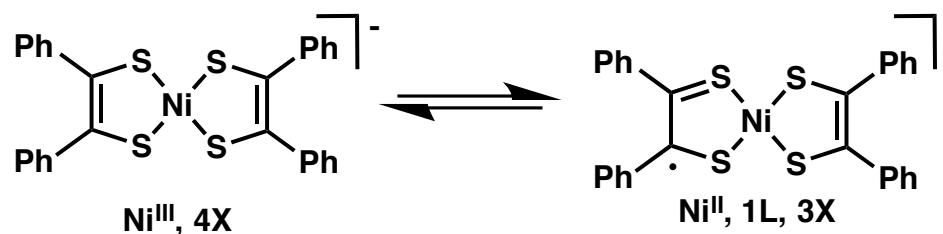
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Redox Non-Innocent Ligands:

Harry Gray, 1960's:



**which resonance structure is the main contributor?
Is the HOMO primarily ligand or metal-based?**

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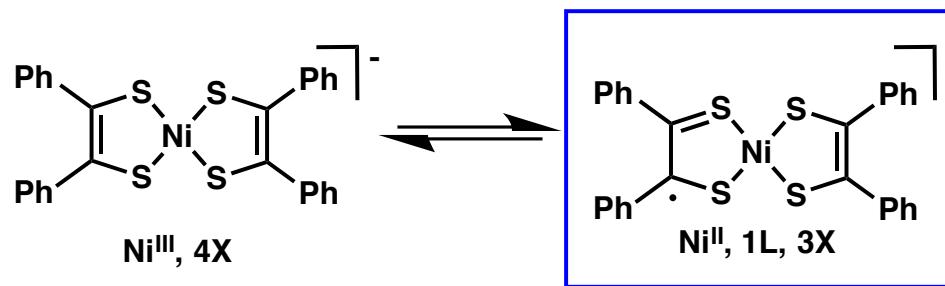
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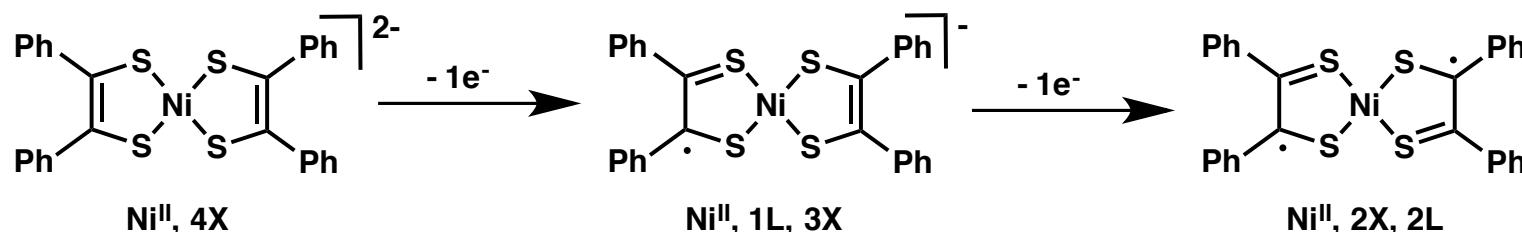
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Redox Non-Innocent Ligands:

Harry Gray, 1960's:



The ligand, rather than the metal, gets reduced!

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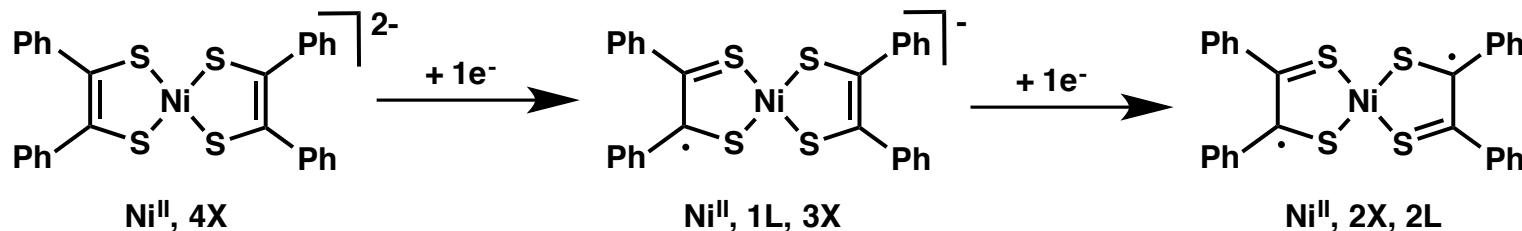
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Redox Non-Innocent Ligands:

Harry Gray, 1960's:



"Although we loved these ligands, by the end of the 1960s, we knew that they were guilty as charged!"(H.B.G., 2011)

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Redox -active ligands can be:

Non-innocent ligands: not all non-innocent ligands are redox-active today!

This term is also used to indicate the perturbation of metal coordination due to unexpected reactivity at the ligand in response to external stimuli (i.e. Protonation/deprotonation)

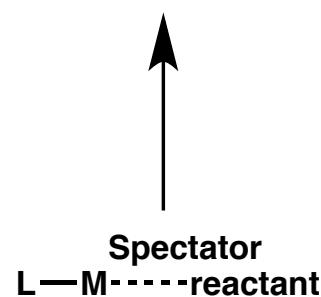
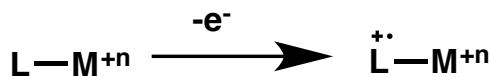
Cooperating ligands: a ligand in a metal complex that actively participates in substrate activation

Bifunctional catalysts: a catalyst comprised of two different functionalities that activate both substrates within the same scaffold

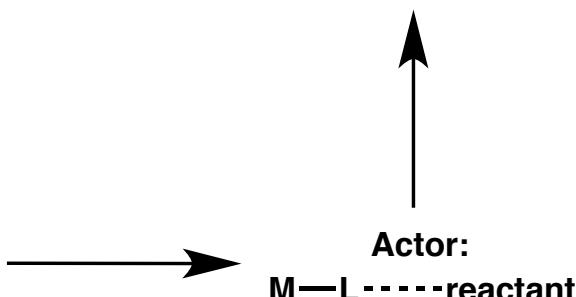
BUT: not all non-innocent ligands, cooperating ligands, and bifunctional catalysts are redox active ligands!

Types of Redox-Active Ligands

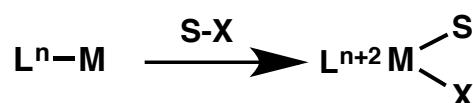
i. modulation of reactivity of metal (LA):



iii. involved in substrate bond breaking/making



ii. electron reservoir:

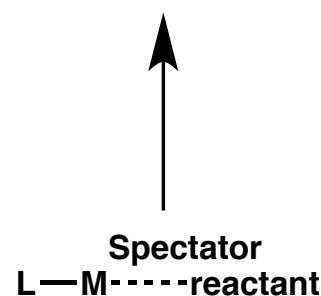


iv. reactive ligand radical



Types of Redox-Active Ligands

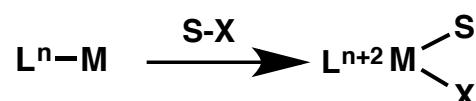
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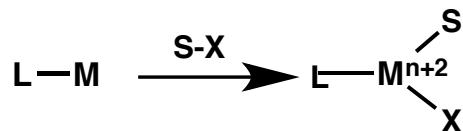


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Redox-Active Ligands as Electron Reservoirs

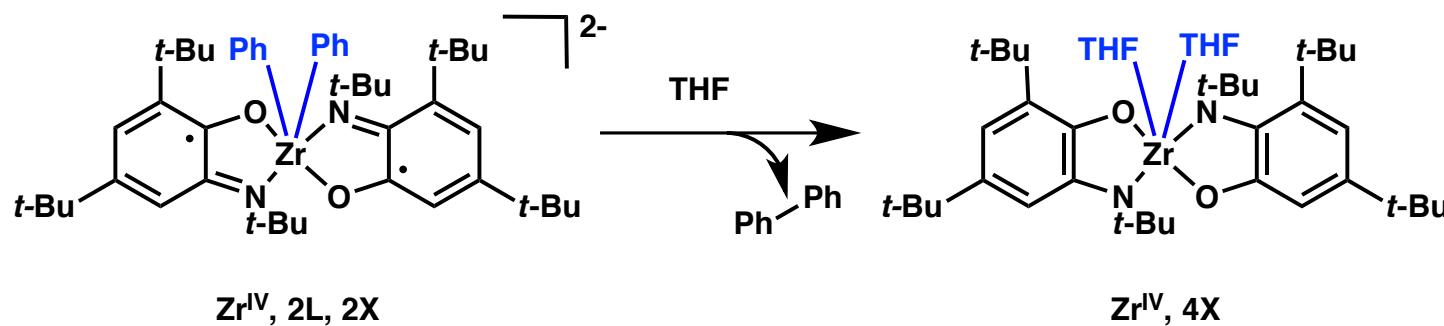
Oxidative Addition with Innocent Ligands



Oxidative Addition with Redox-Active Ligands



Reductive Elimination from Zr(IV):

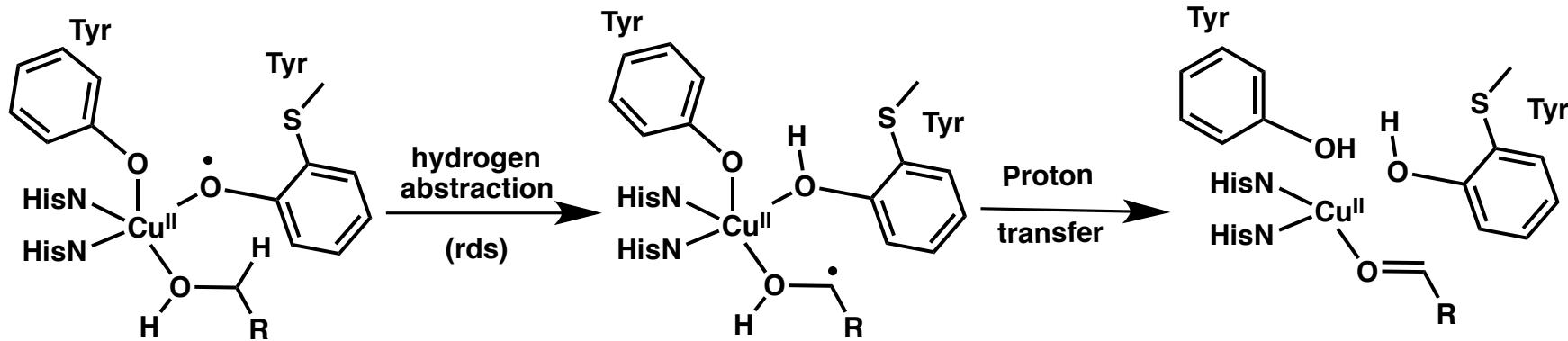


- Oxidation state of metal remains unchanged
- Ligands are not directly involved in the bond-forming process
- Store reducing equivalents in the ligand, rather than the metal
- Nature's enzymes operate close to the thermodynamic potential
- Impart novel reactivity patterns to certain transition metals

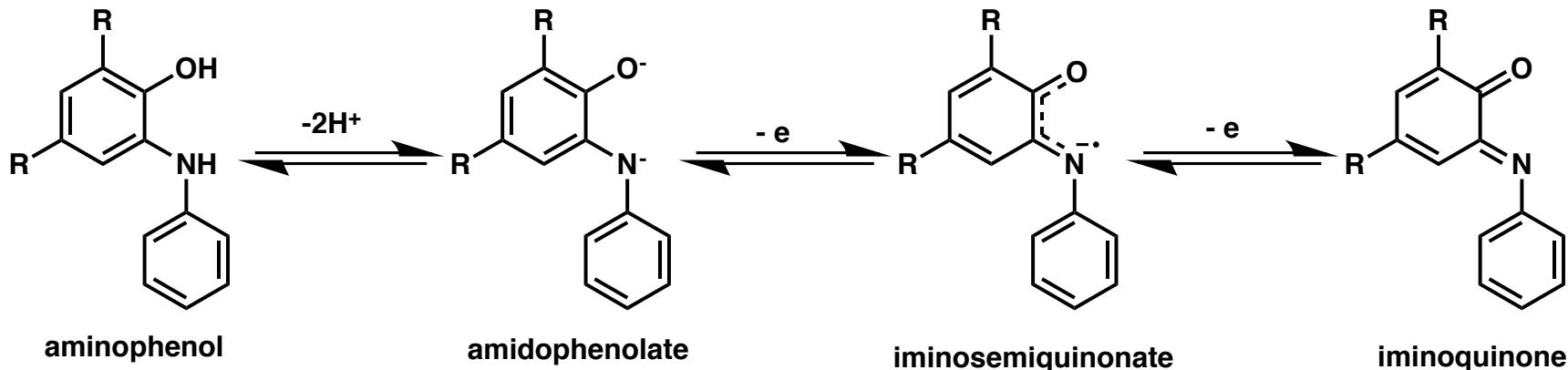
-Chirik: give noble character to first row transition metals

Aminophenols: a well-established class of redox-active ligands

- inspired by galactose oxidase:
(catalyzes the oxidation of alcohols to aldehydes)



- aminophenols shuttle between 3 distinct states:



- related to quinones (N adds another functional handle, more coordinating)

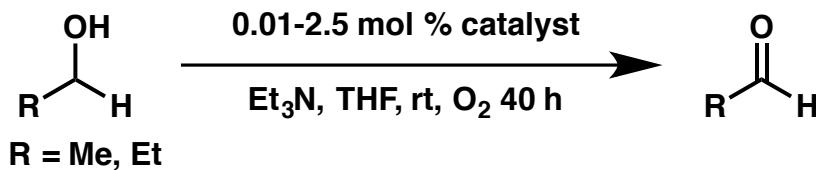
- iminoquinones have lower reduction potential

- fine tune M-L complex (electrophilicity, bond lengths)

- complex synthesis varies

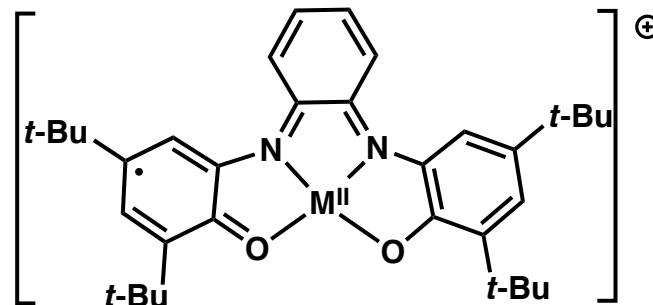
- Cu, Ni, Fe, Pt, Pd, Ru, Os

Copper and Zinc-catalyzed Aerobic oxidation of alcohols



confirmed by EPR, Magnetic and electrochemical data
stoichiometric (anaerobic conditions), catalytic (aerobic)

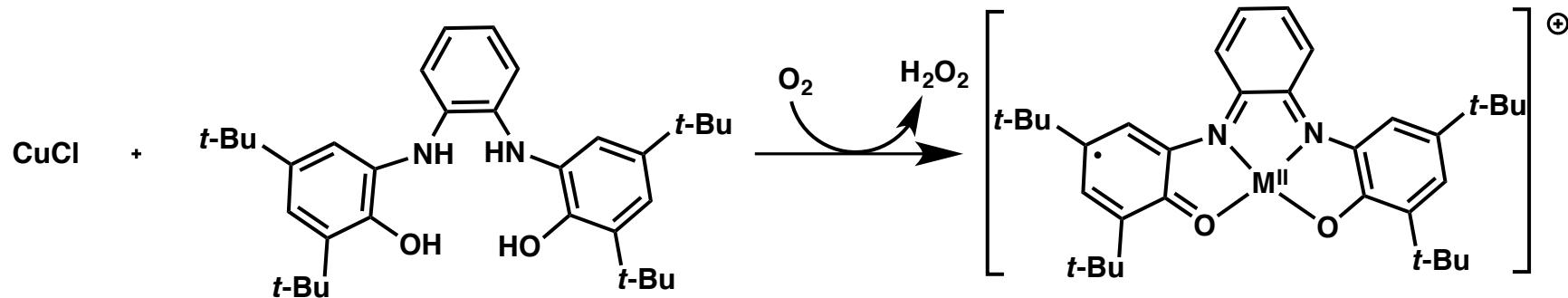
catalysts:



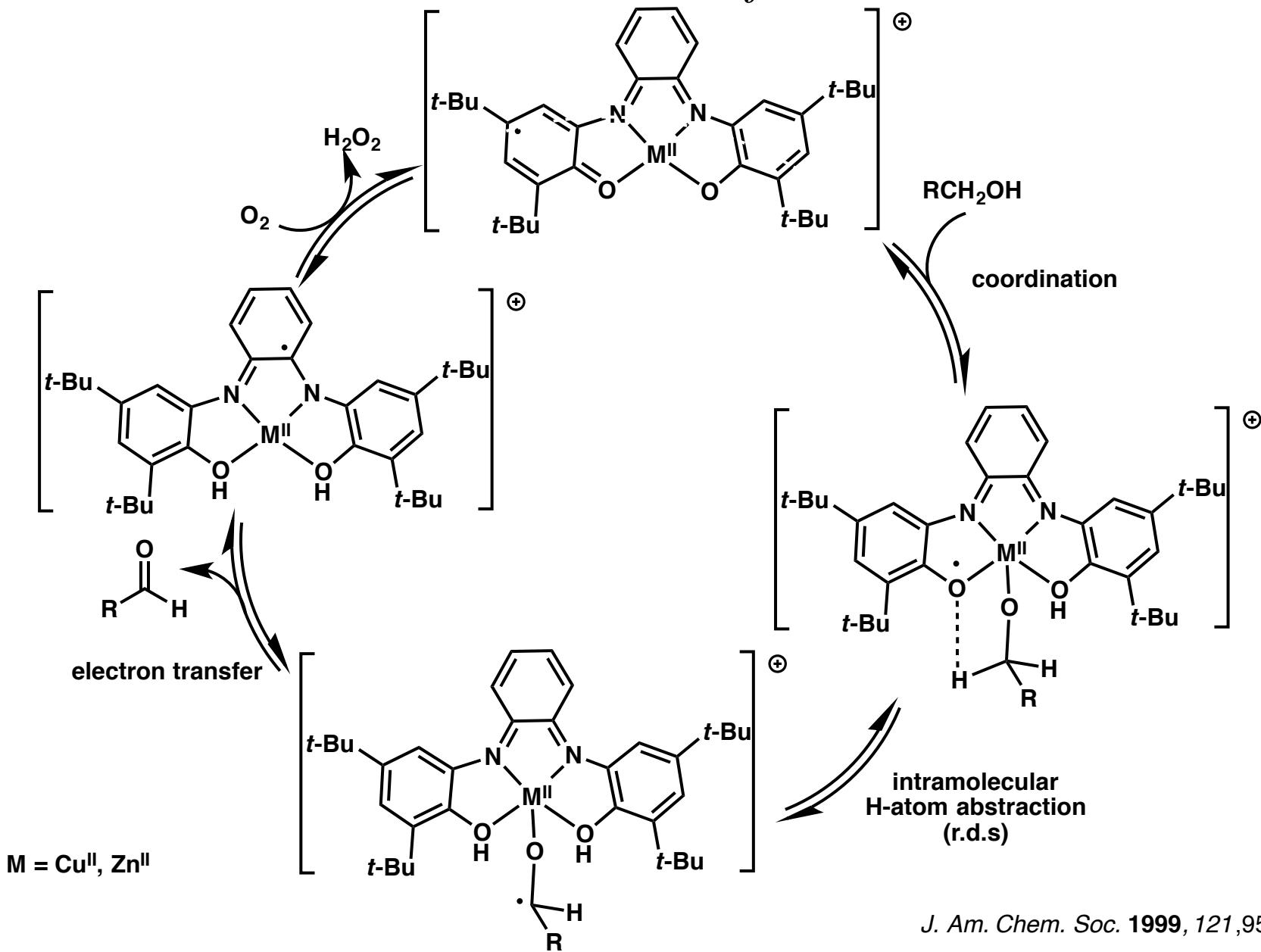
M = Cu^{II}, TOF = 0.03 s⁻¹ (5000 turnovers in 50 h)
M = Zn^{II}, TOF = 0.002 s⁻¹

can access 5 different ligand-centered oxidation states (both Zn and Cu)

Active Cu catalyst generated from:

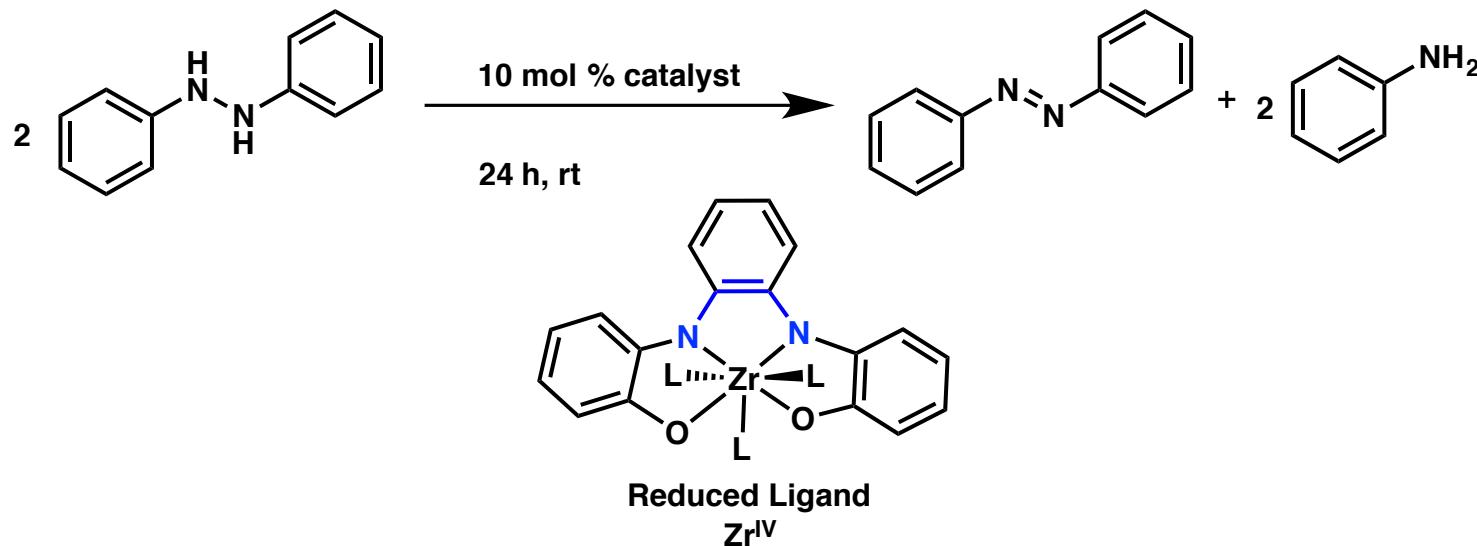


Mechanism for the aerobic oxidation of alcohols



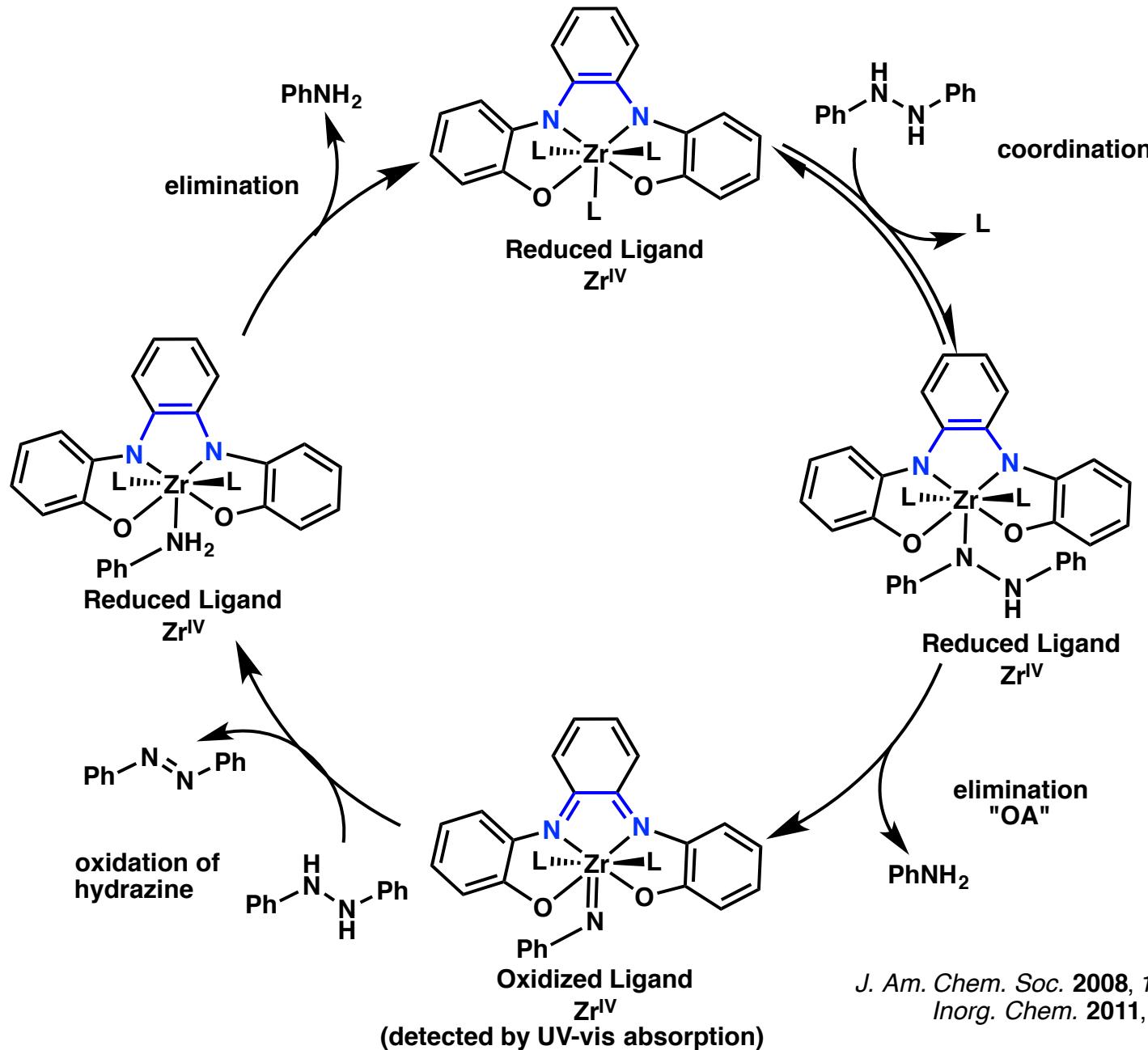
OA to Zr(IV): disproportionation of hydrazine

Heyduk and coworkers, 2008



- d⁰ metal catalyzing a multielectron reaction through the use of ligand-based valence changes
- disproportionation is thermodynamically favorable
- electrophilic metal coupled with redox properties of the ligand
- control reactions with Zr(Cl₄(THF)₂, Zr(O*t*-Bu)₄, Zr(NMePh) resulted in NR

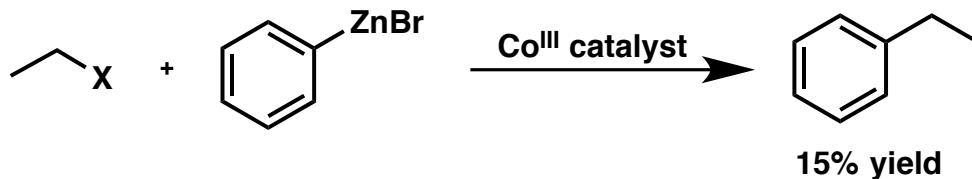
OA to Zr(IV): disproportionation of hydrazine



J. Am. Chem. Soc. **2008**, *130*, 2728-2729.
Inorg. Chem. **2011**, *50*, 9849-9863.

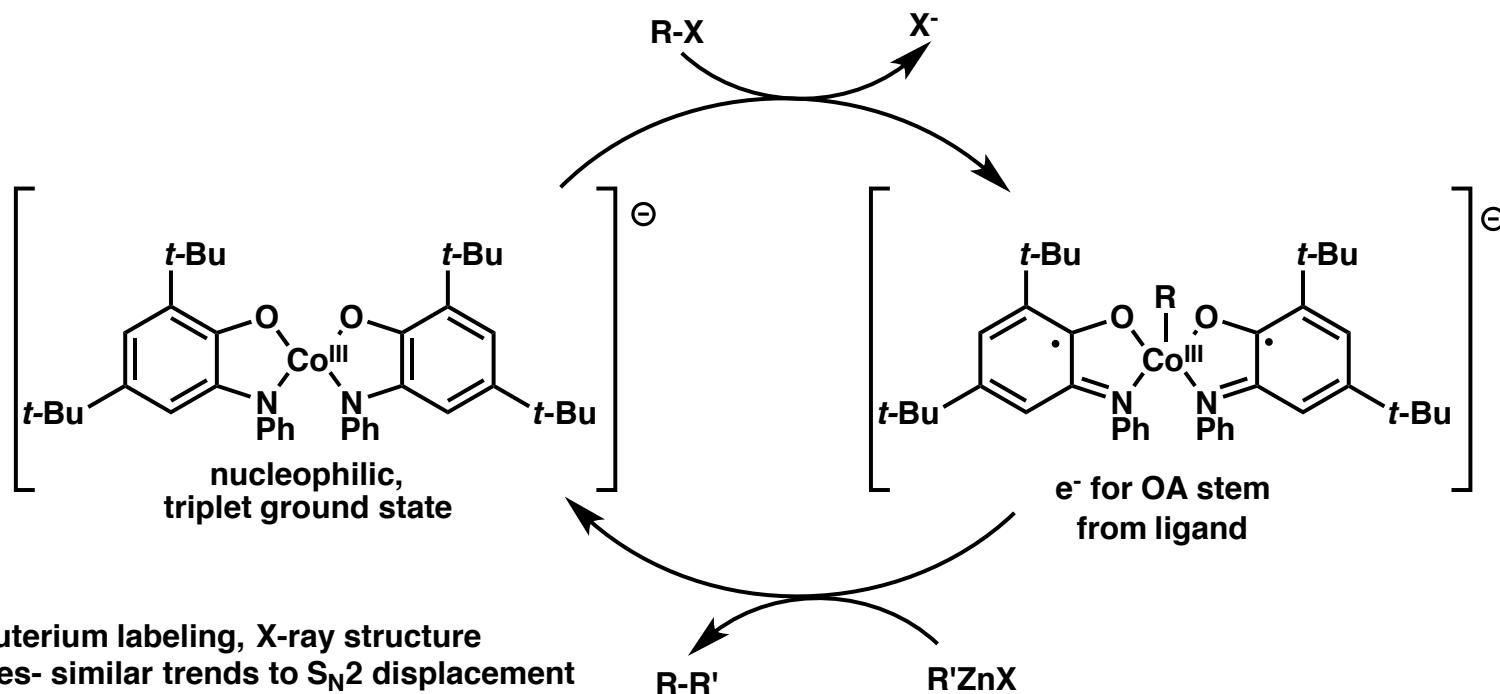
Negishi couplings with Co^{III}

Soper and coworkers, 2010:



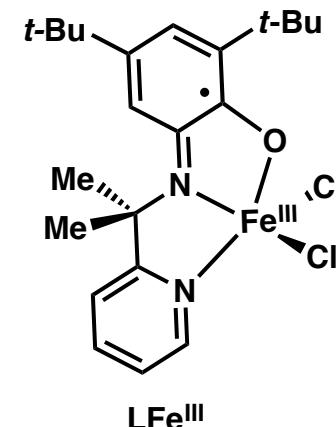
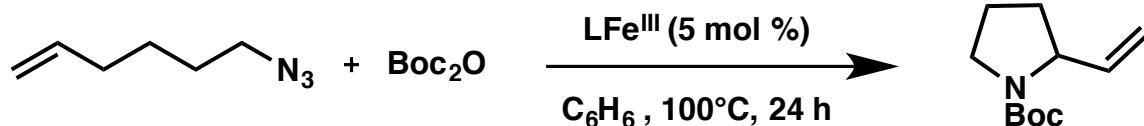
Mechanism: Ligand centered radical

pseudo oxidative addition

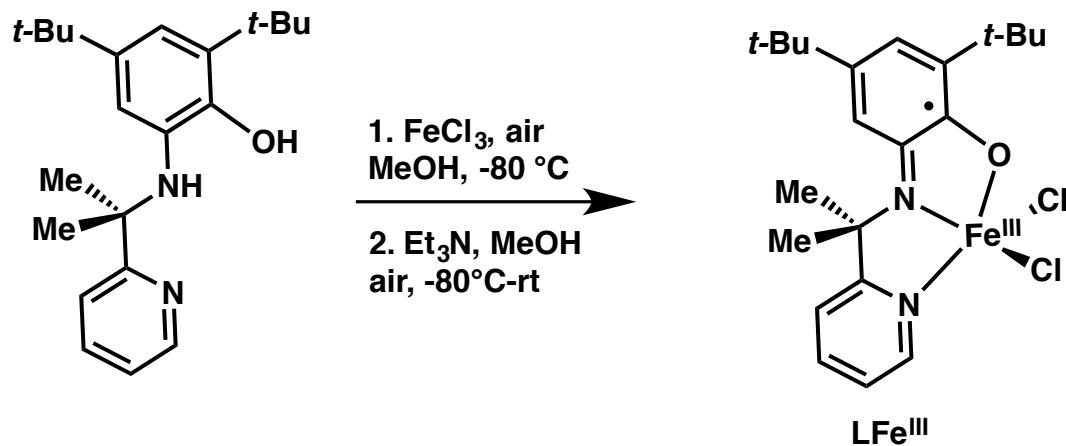


ESI-MS, deuterium labeling, X-ray structure
mech studies- similar trends to $\text{S}_{\text{N}}2$ displacement
no follow up reports

Fe(III)-catalyzed synthesis of N-Heterocycles



Catalyst synthesis:



Characterized by:

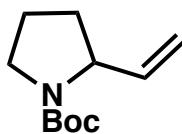
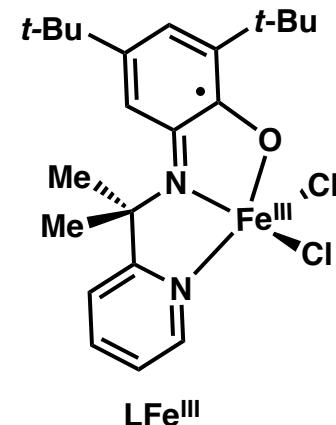
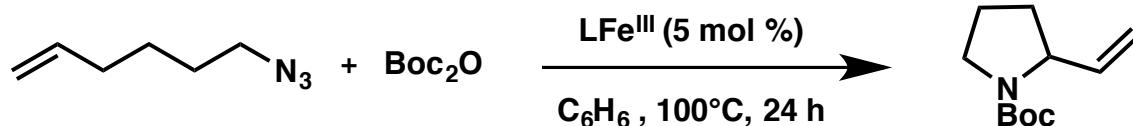
- UV-vis spectroscopy (semiquinone)
- Magnetic susceptibility ($S = 2$ ground state)
- confirmed spin by SQUID and Mössbauer
- X-ray structure determination (geometry, BL's)
- DFT calculations (5.3 kcals to $S= 3$)
- Löwdin population analysis (4 unpaired electrons)
- CV for $1e^-$ reduction and oxidation potentials

air stable, recyclable catalyst

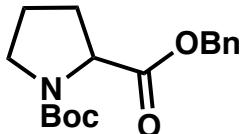
- linear, Boc protected amine was the main byproduct
- for Pd version see: J. Am. Chem. Soc. 2014, 136, 11574- 11577.

Fe(III)-catalyzed synthesis of N-Heterocycles

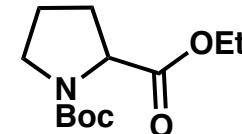
Van der Vlugt et. al, 2017



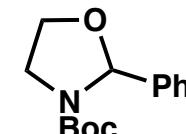
96% yield



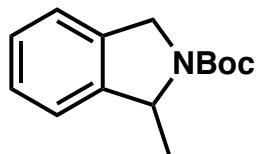
51% yield



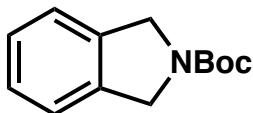
39% yield



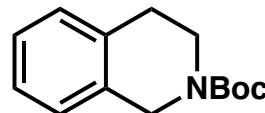
90% yield



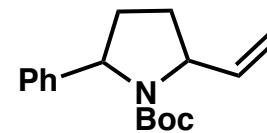
48% yield



46% yield



44% yield



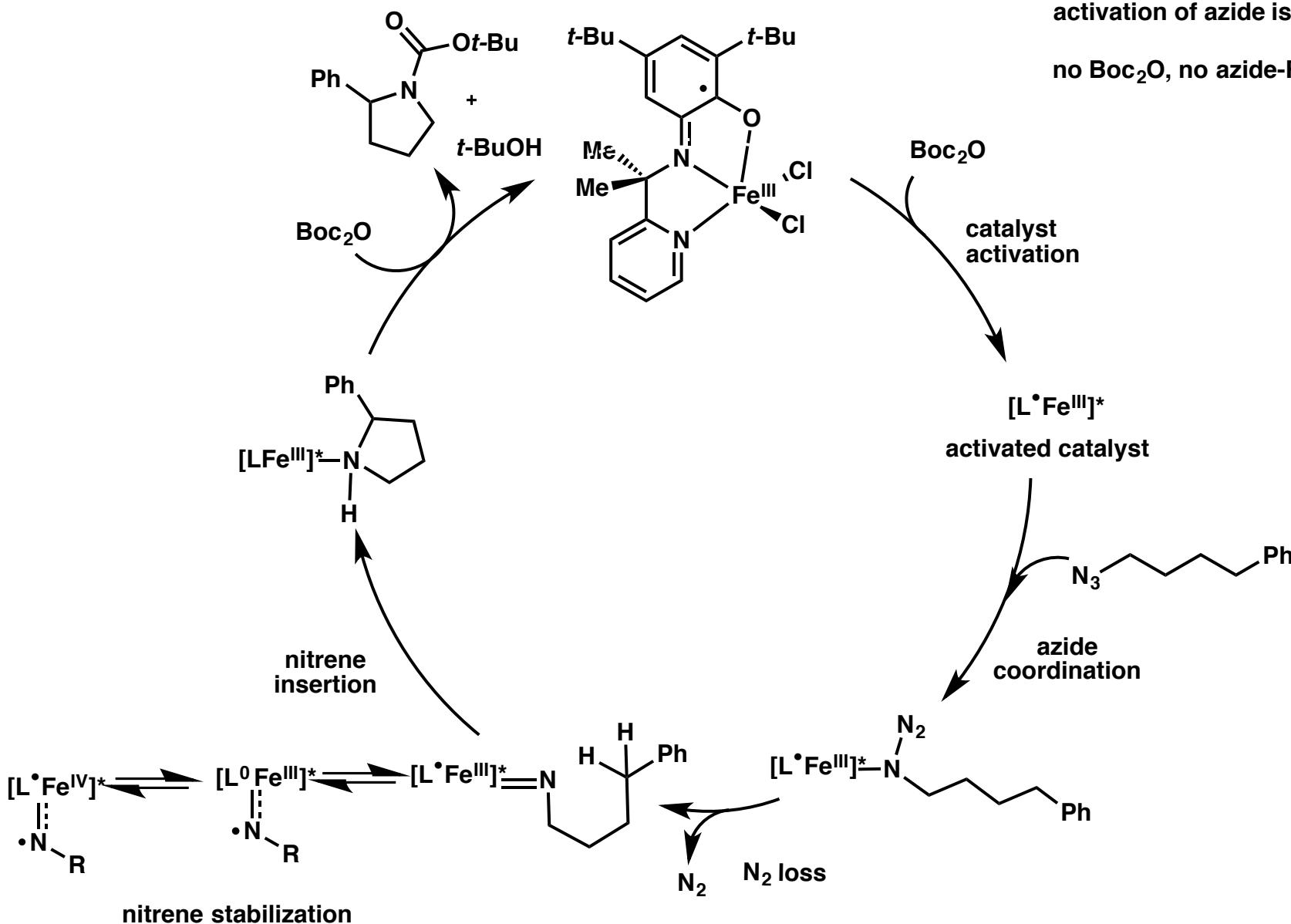
95% yield

air stable, recyclable catalyst

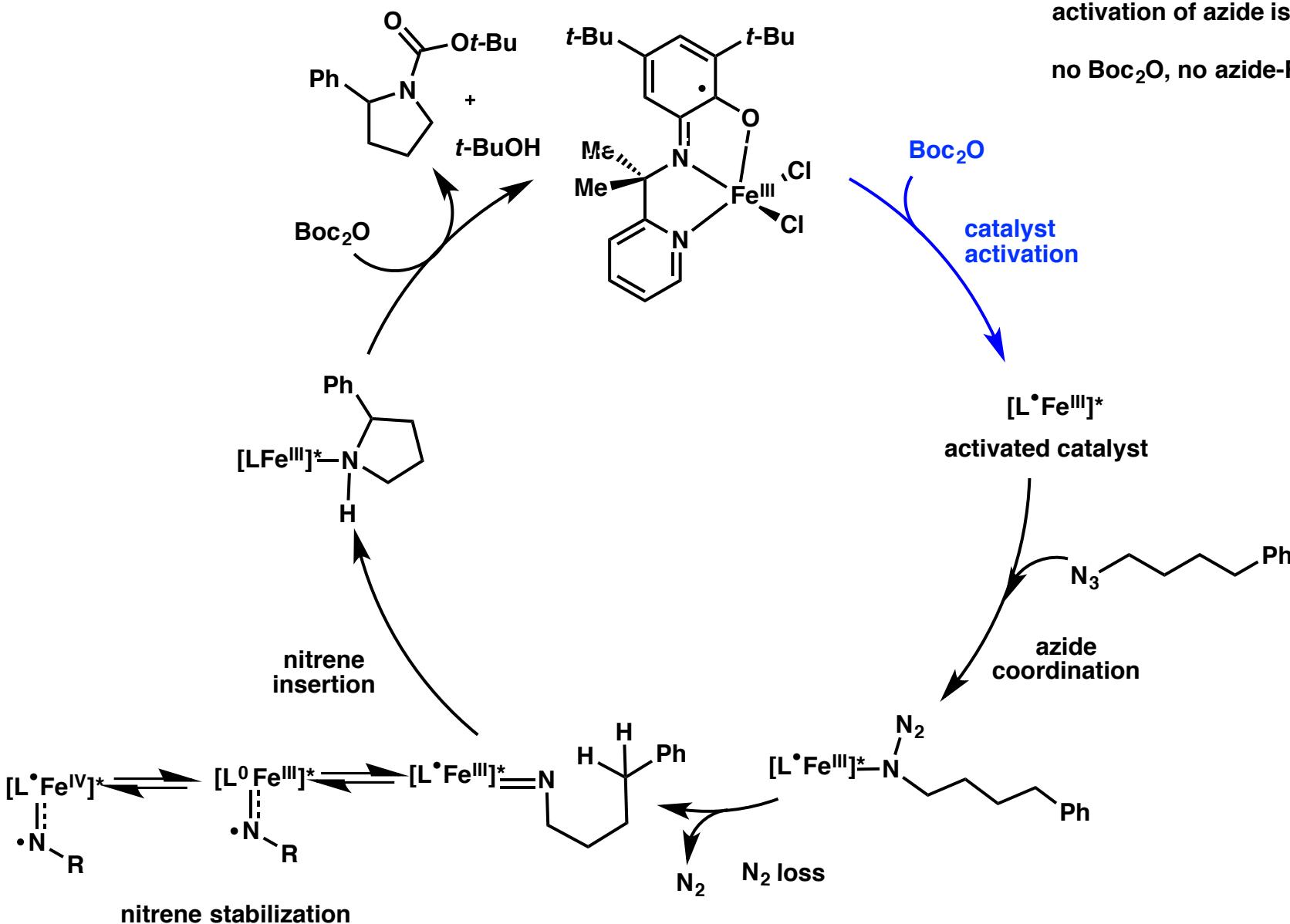
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Fe(III)-catalyzed synthesis of N-Heterocycles



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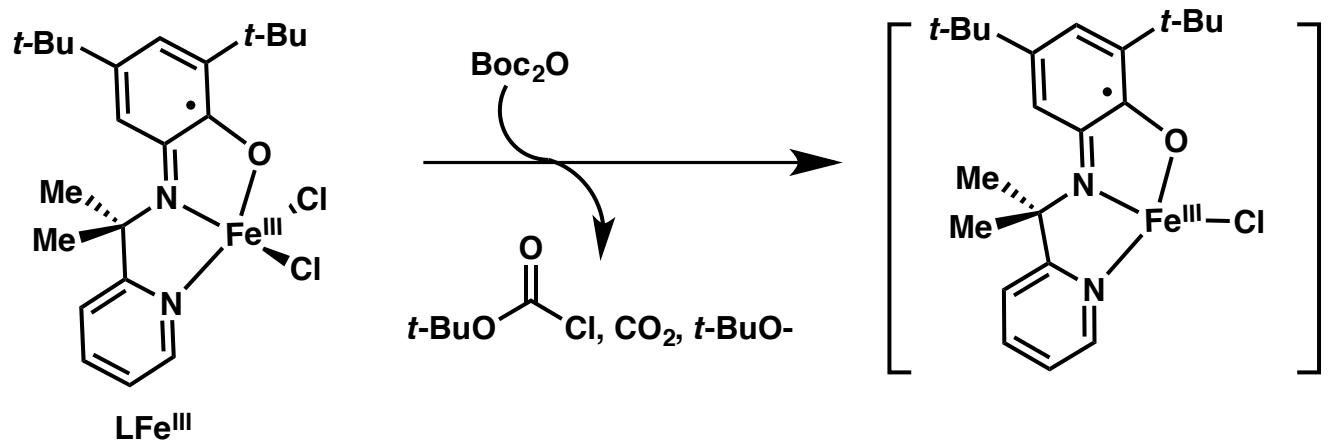


**zero-order in substrate:
activation of azide is not rds**

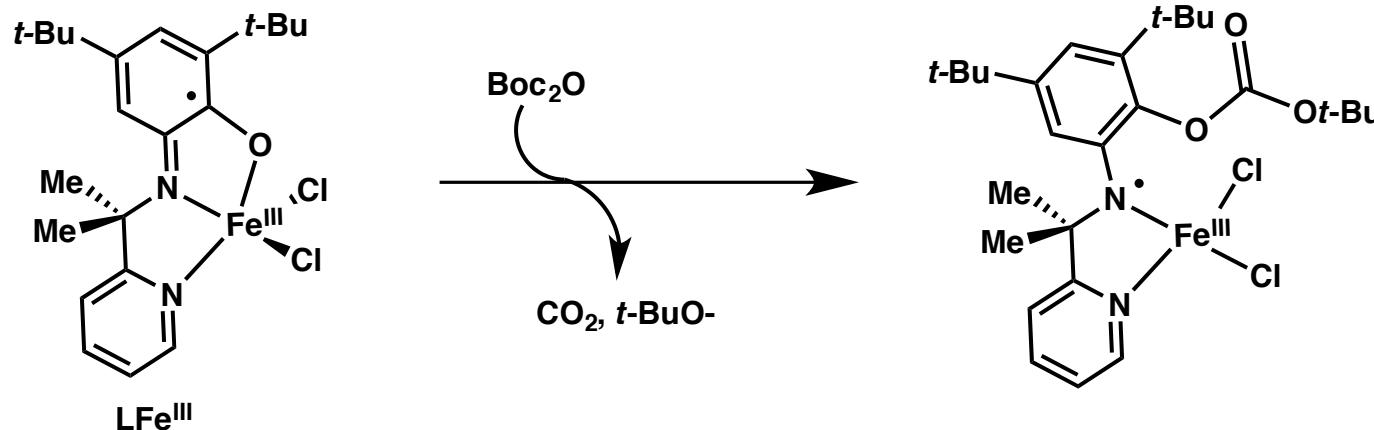
no Boc₂O, no azide-Fe complex

Fe(III)-catalyzed synthesis of N-Heterocycles: Possible modes of catalyst activation

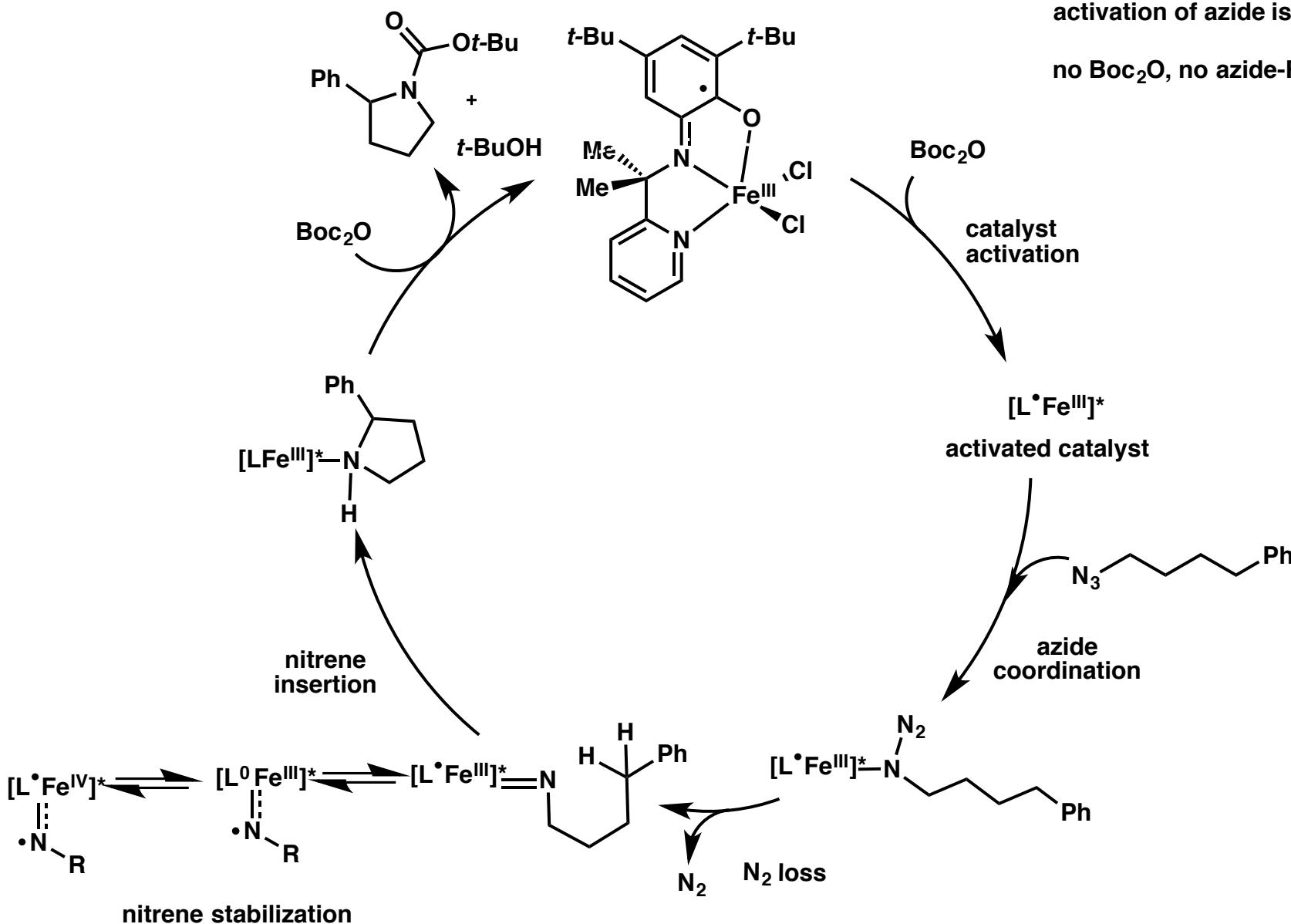
Chloride Dissociation



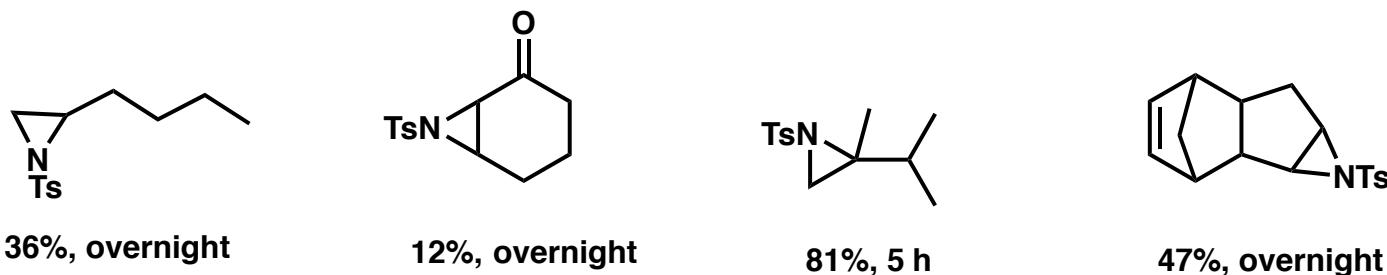
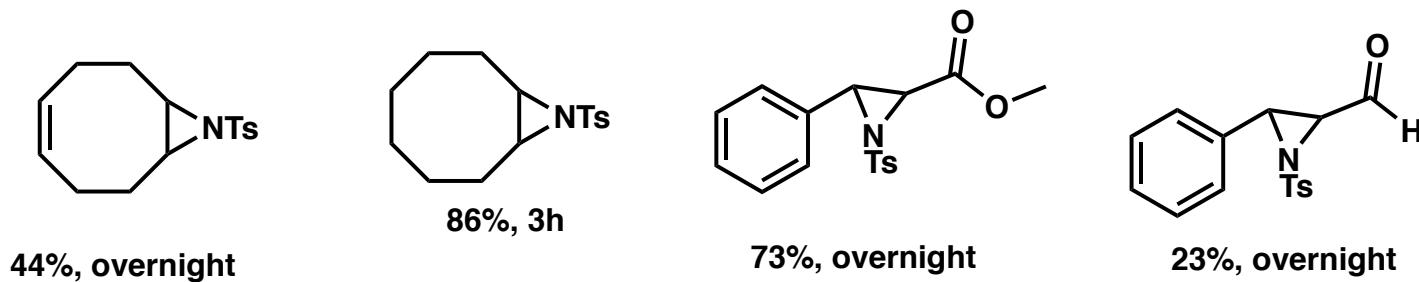
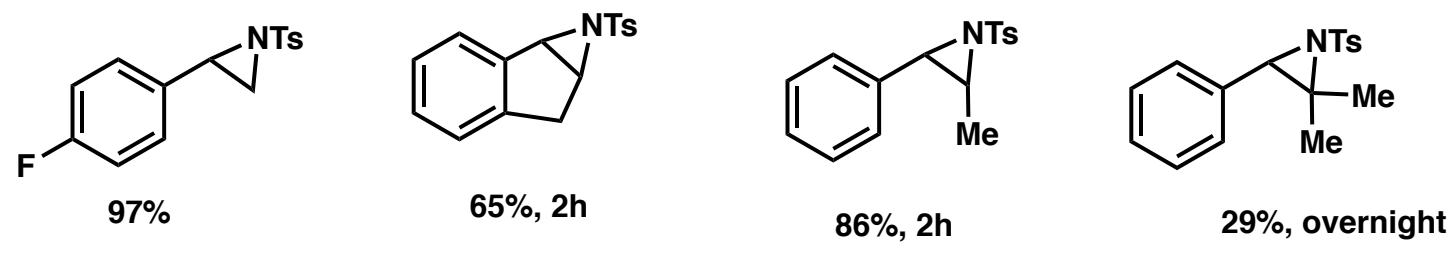
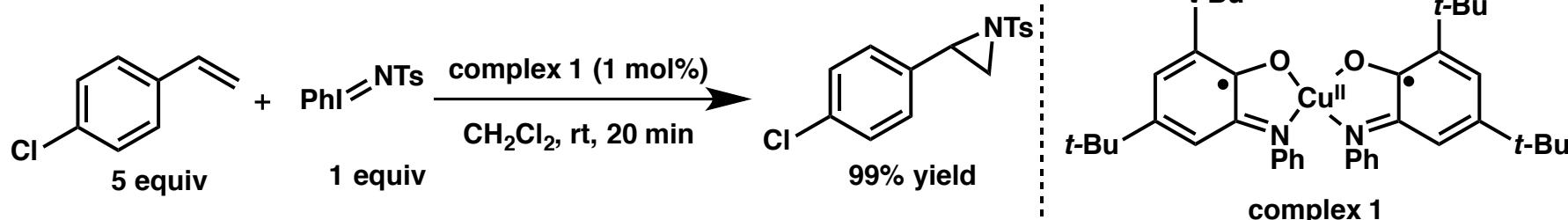
Reaction with the Ligand



Fe(III)-catalyzed synthesis of N-Heterocycles



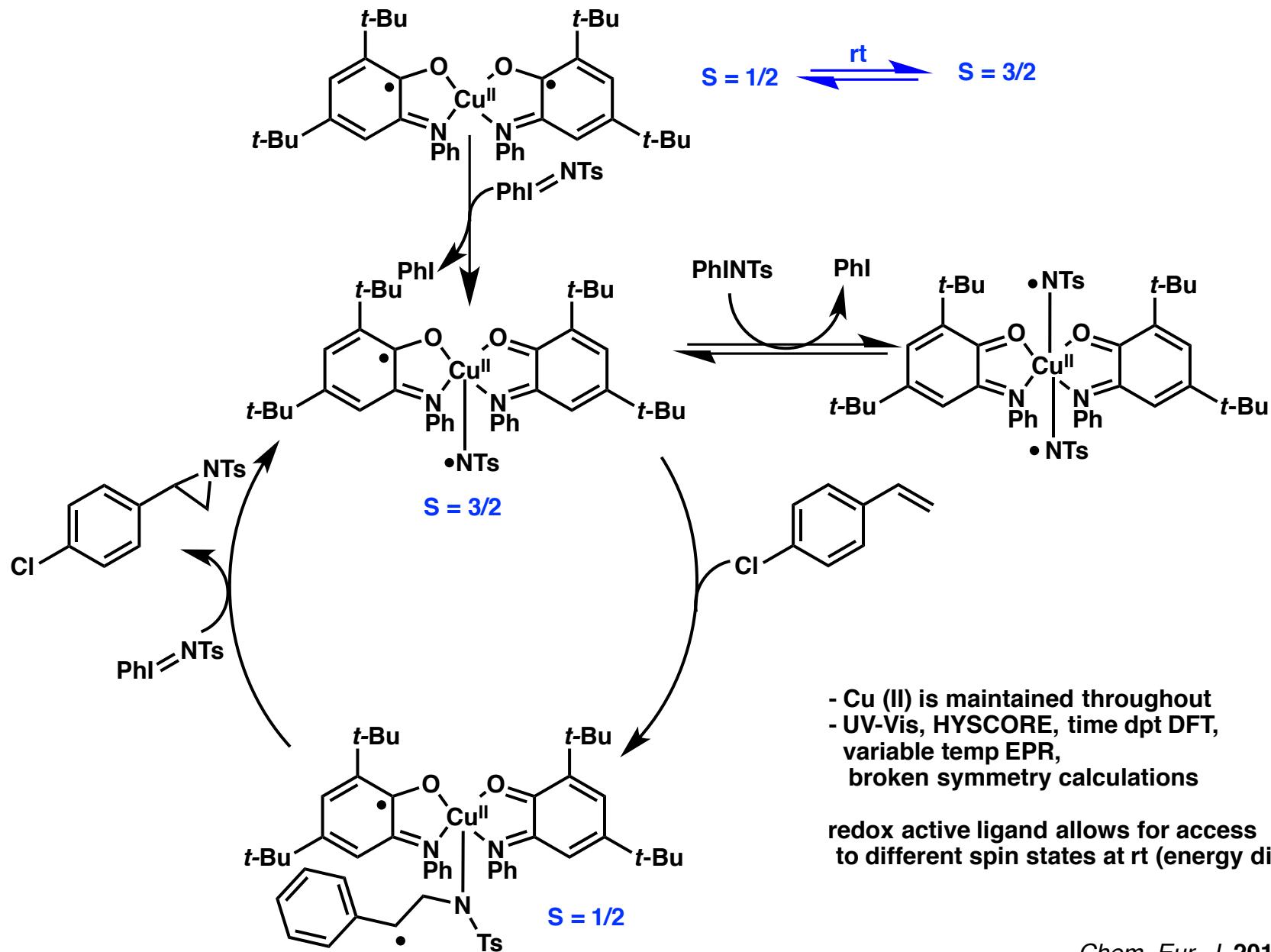
Copper-Catalyzed Aziridination



* reaction is not air sensitive, all run under air

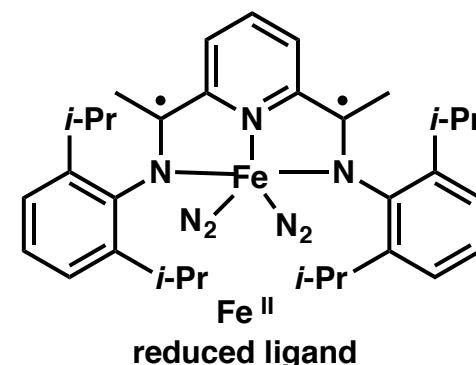
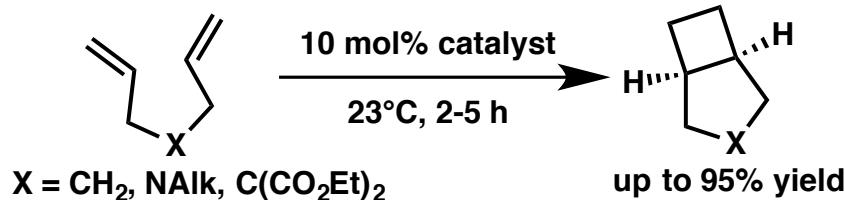
Chem. Eur. J. 2018, 24, 1-6.

Copper-Catalyzed Aziridination: Redox Active ligand for spin fluxionality

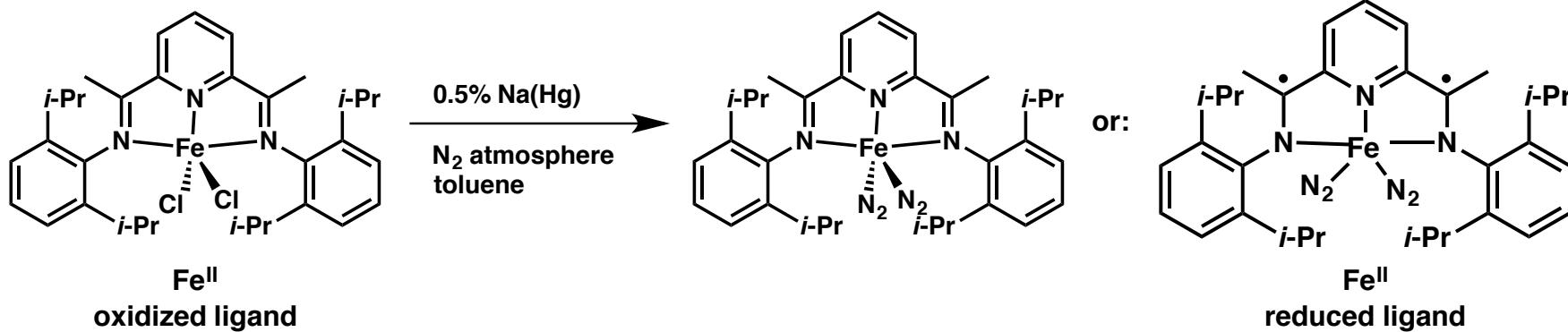


2,6-Diiminepyridine Ligand as an Electron Reservoir

Chirik and coworkers, 2006:

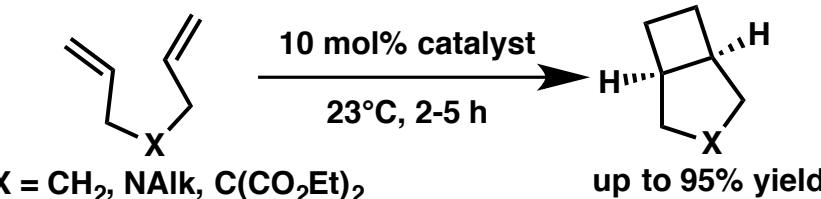


Catalyst Synthesis:



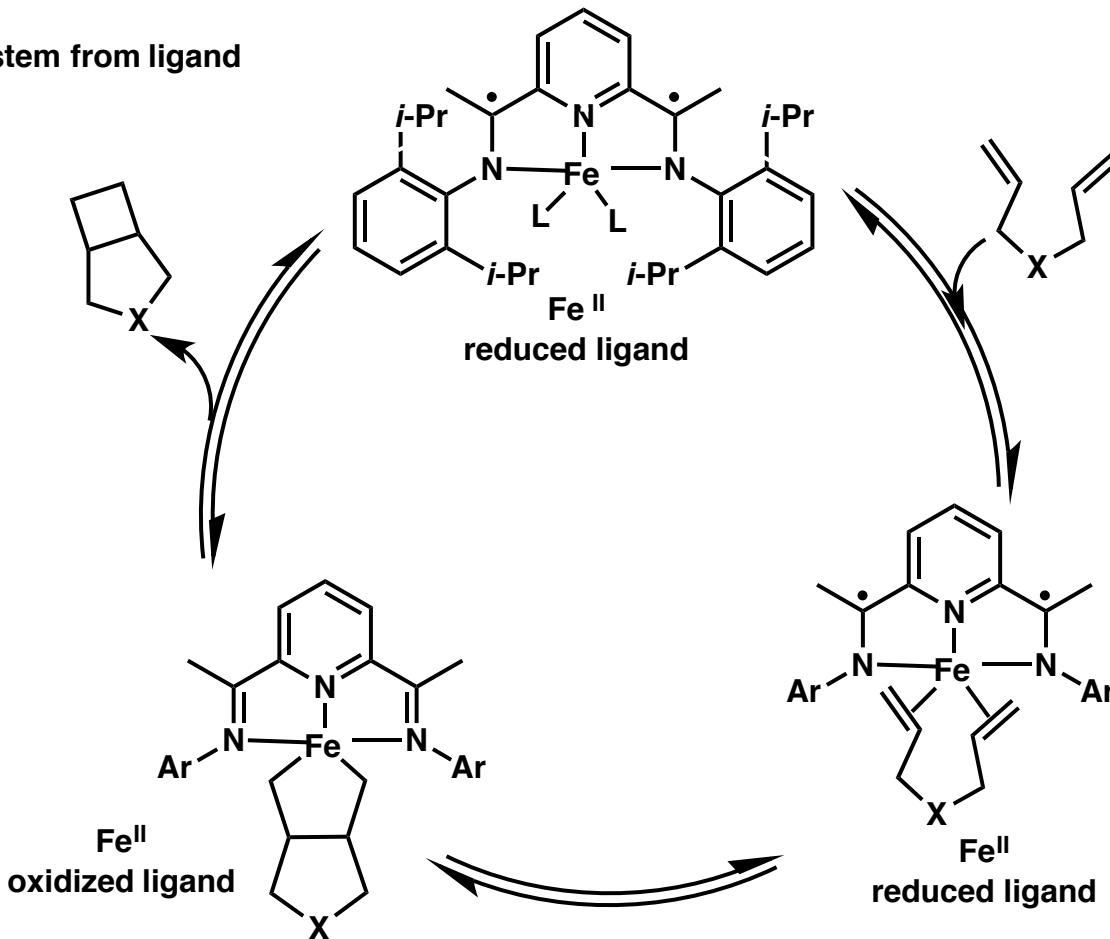
The ligand stores two reducing equivalents in an iron(II) complex!

2,6-Diiminepyridine Ligand as an Electron Reservoir



- energetically favorable Fe^{II}

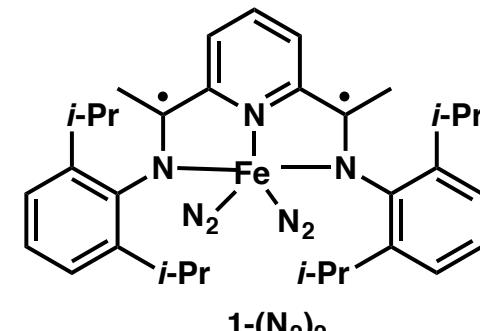
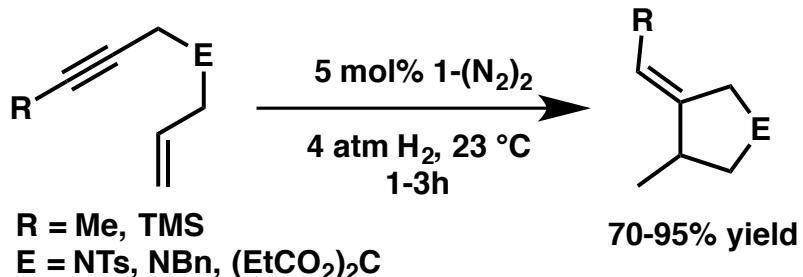
- electrons for OA/ RE stem from ligand



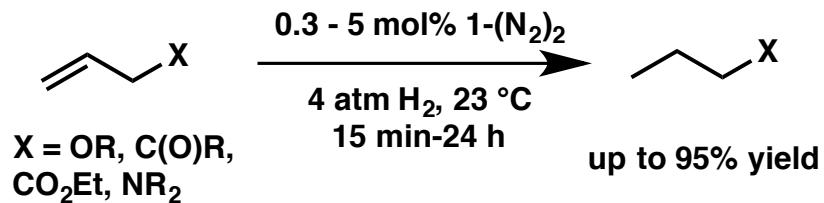
- DFT, experimental,
spectroscopic,
crystal structure

2,6-Diiminepyridine Ligand as an Electron Reservoir

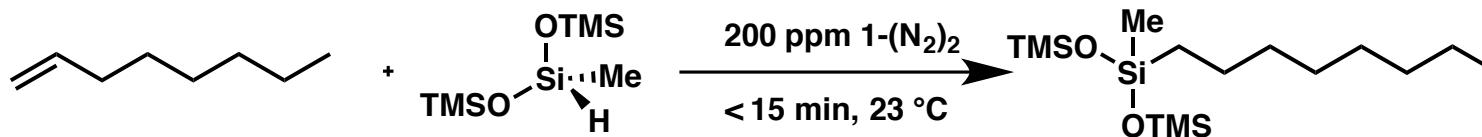
1,6- enyne cycloaddition



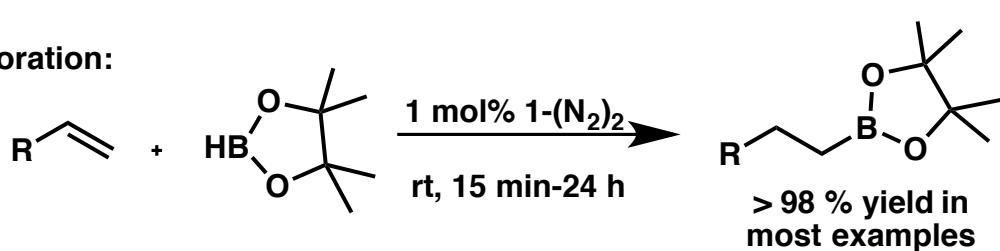
Hydrogenation of olefins:



Hydrosilylation:

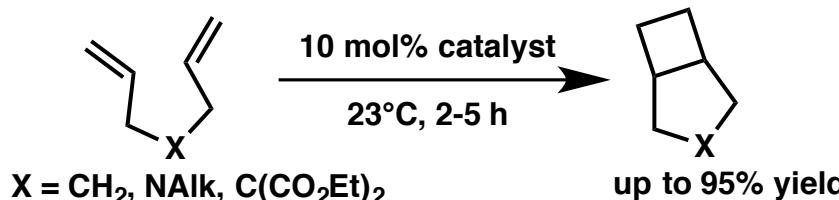


Hydroboration:

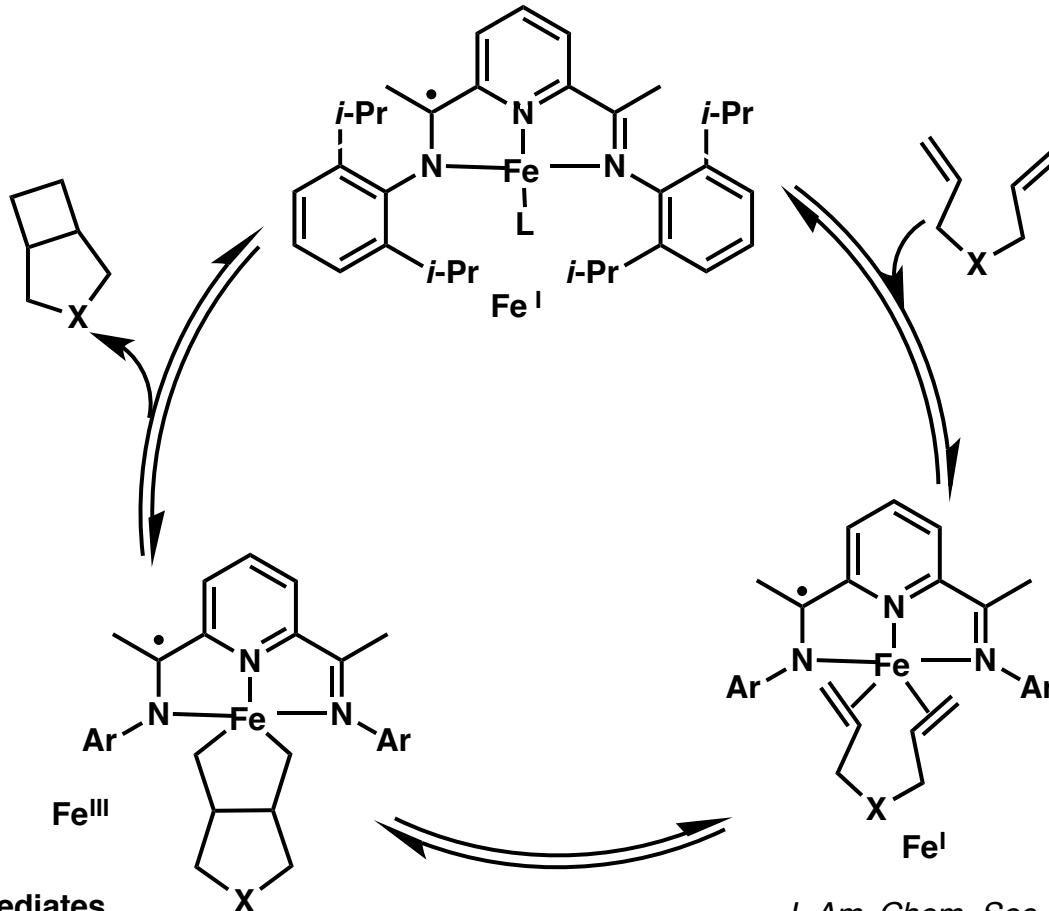


J. Am. Chem. Soc. 2009, 131, 8772-8774.
Organometallics, 2008, 27, 1470-1478.
Science, 2012, 335, 567-570.
ACS Catal. 2012, 2, 2169-2172.
Org. Lett. 2013, 15, 2680-2683.

2,6-Diiminepyridine Ligand as an Electron Reservoir: The Real Story



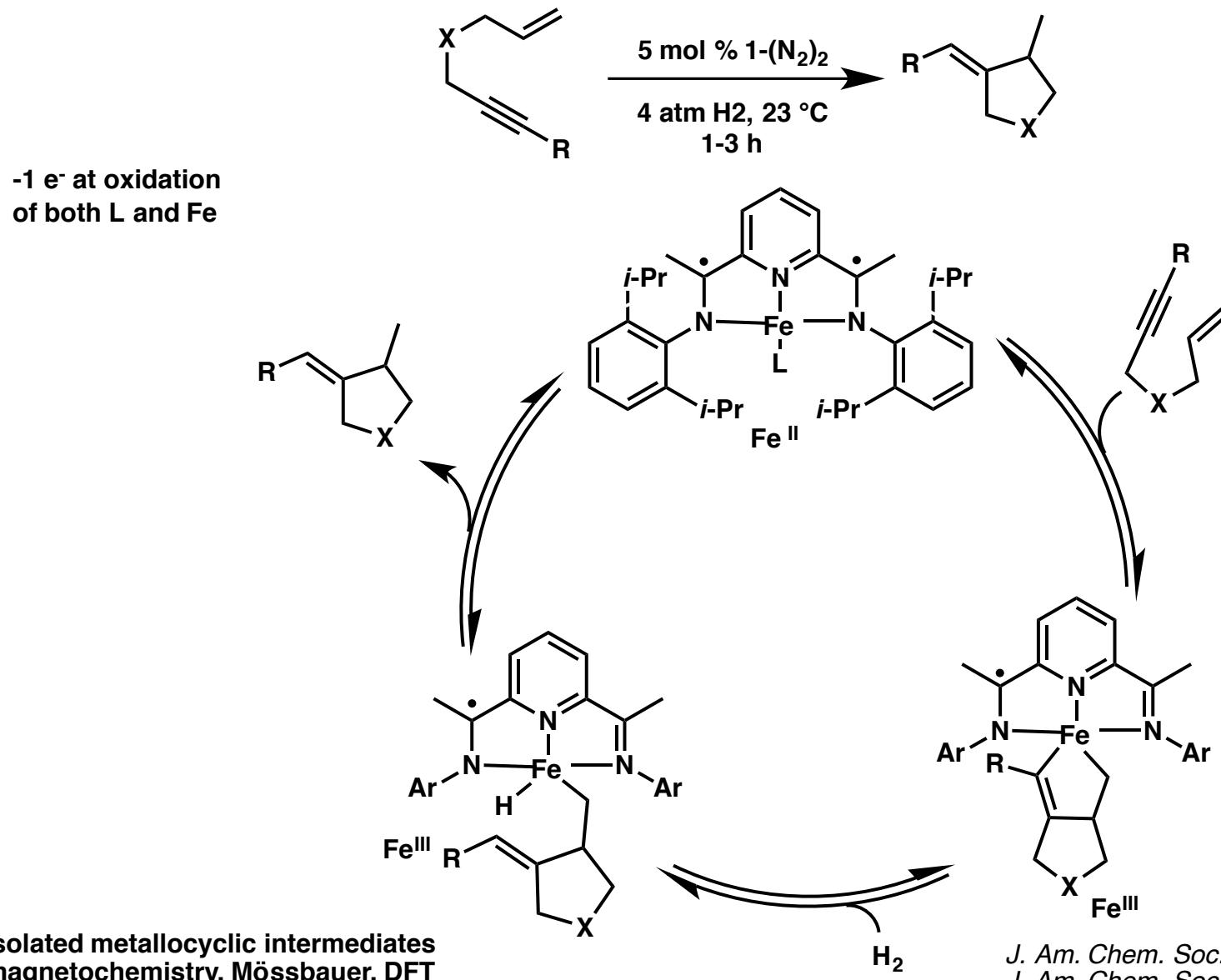
- Ligand helps adopt Fe^{III} -
- C-C RE over β -H elim.
- Ligand prevents $\text{Fe}(0)$ OS



- Isolated metallocyclic intermediates
- magnetochemistry, Mössbauer, DFT

J. Am. Chem. Soc. **2012**, *134*, 17125-17137.
J. Am. Chem. Soc. **2006**, *128*, 13340-13341.
J. Am. Chem. Soc. **2013**, *135*, 4862-4877.

2,6-Diiminepyridine Ligand as an Electron Reservoir: The Real Story

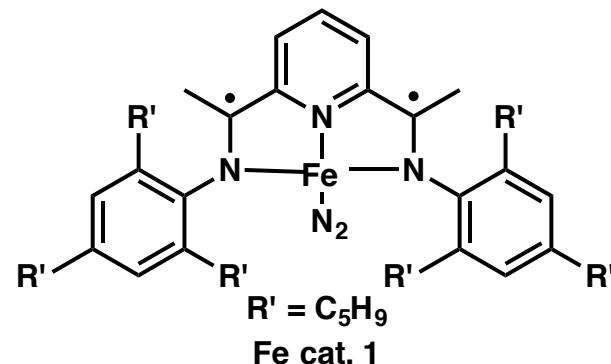
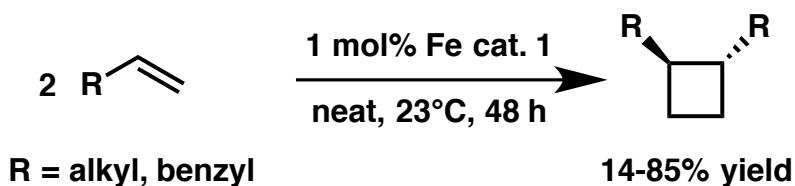


-Isolated metallocyclic intermediates
-magnetochemistry, Mössbauer, DFT

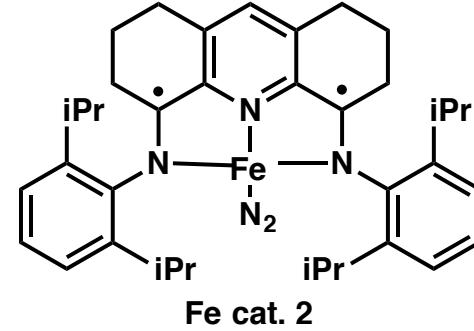
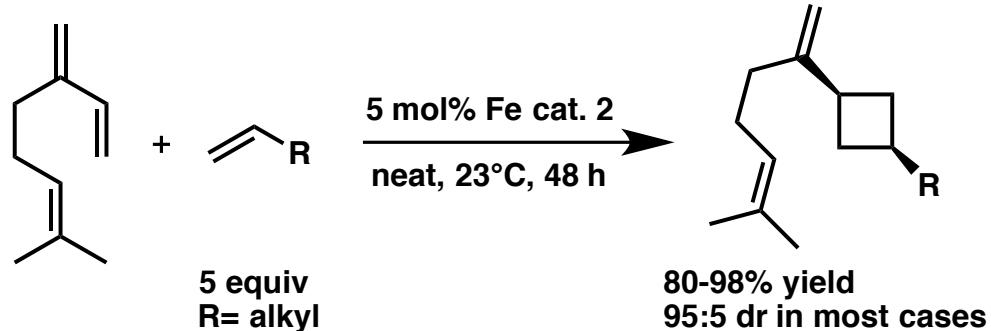
J. Am. Chem. Soc. **2012**, *134*, 17125-17137.
J. Am. Chem. Soc. **2006**, *128*, 13340-13341.
J. Am. Chem. Soc. **2013**, *135*, 4862-4877.

2,6-Diiminepyridine Ligand as an Electron Reservoir: Intermolecular 2+2

Homo-dimerization:



Hetero-coupling:



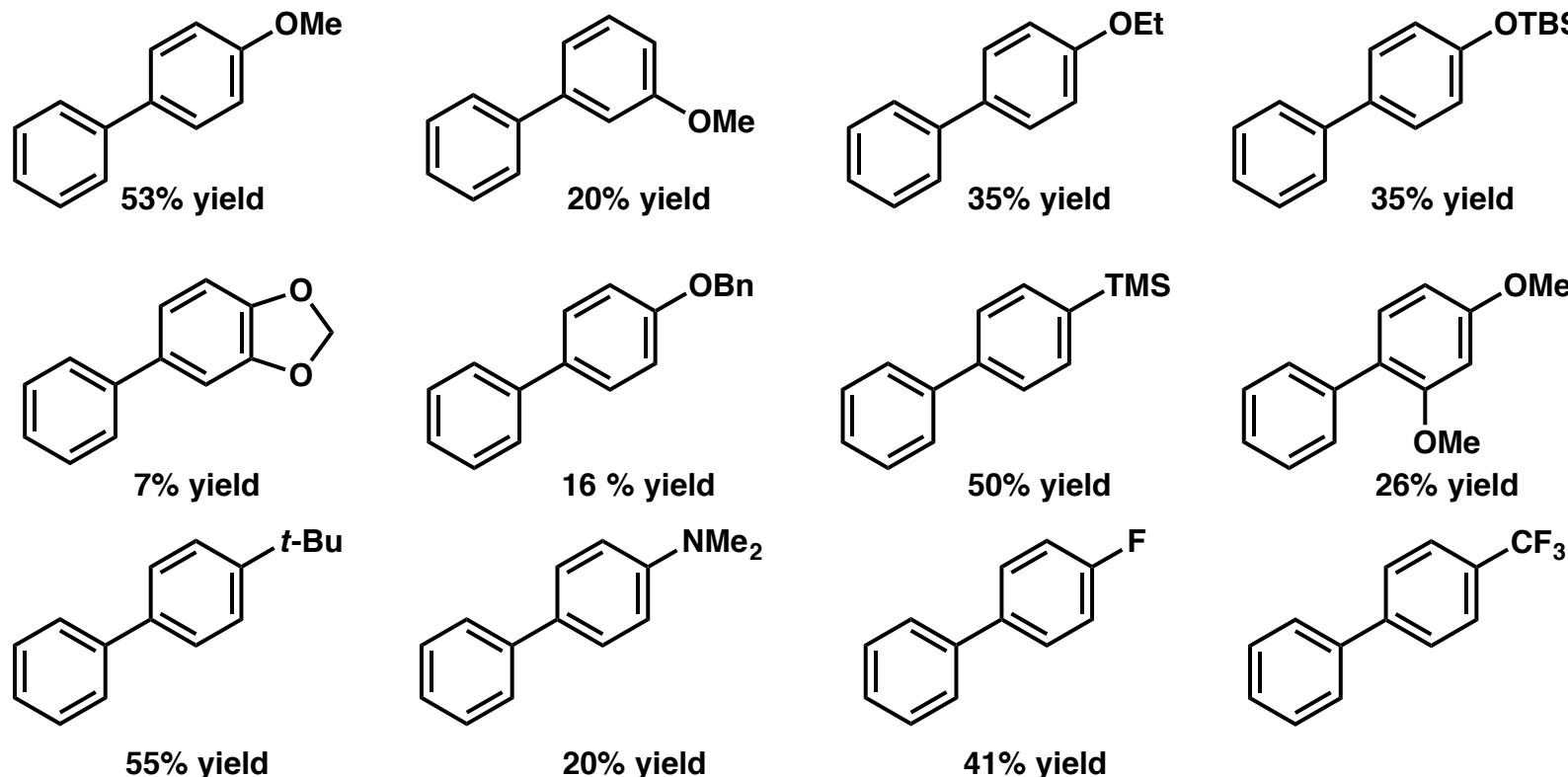
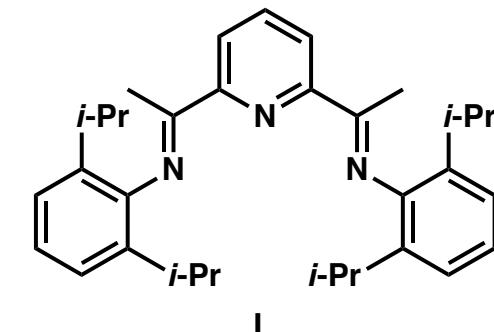
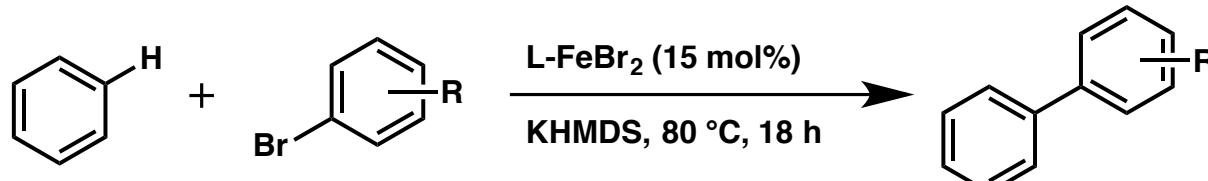
**no homo-dimerization
no 4+2 cycloaddition products**

With Cobalt: *J. Am. Chem. Soc.* **2015**, *137*, 7903-7914.
ACS Catal., **2016**, *6*, 2632-2636.

Science, **2015**, *349*, 960-963.

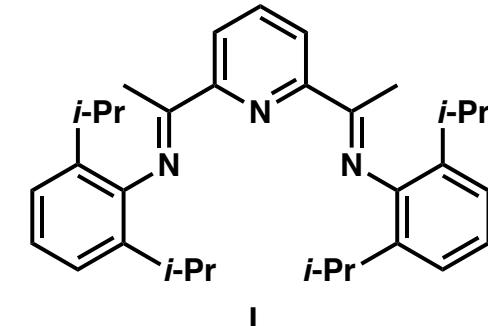
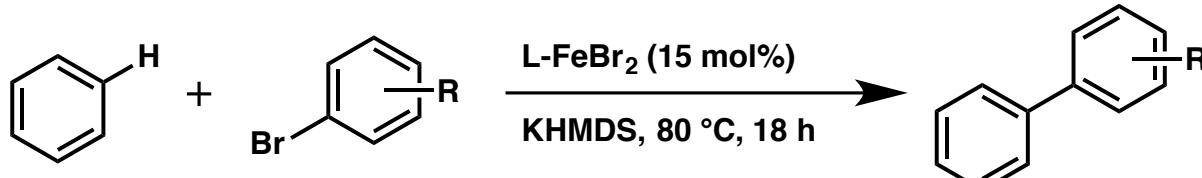
Fe-catalyzed C-H activation/arylation

Fensterbank et al, 2014

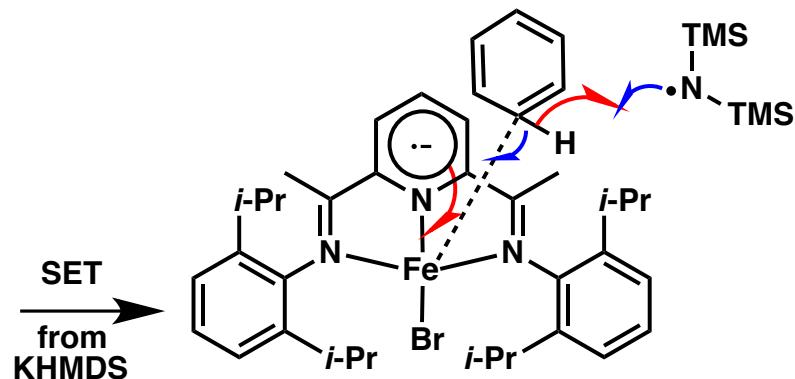


Fe-catalyzed C-H activation/arylation

Fensterbank et al, 2014



May proceed through a metal-based inner-sphere C-H activation

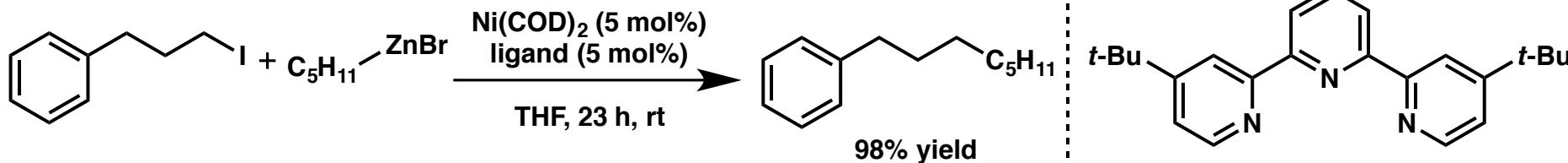


Mechanistic studies show:

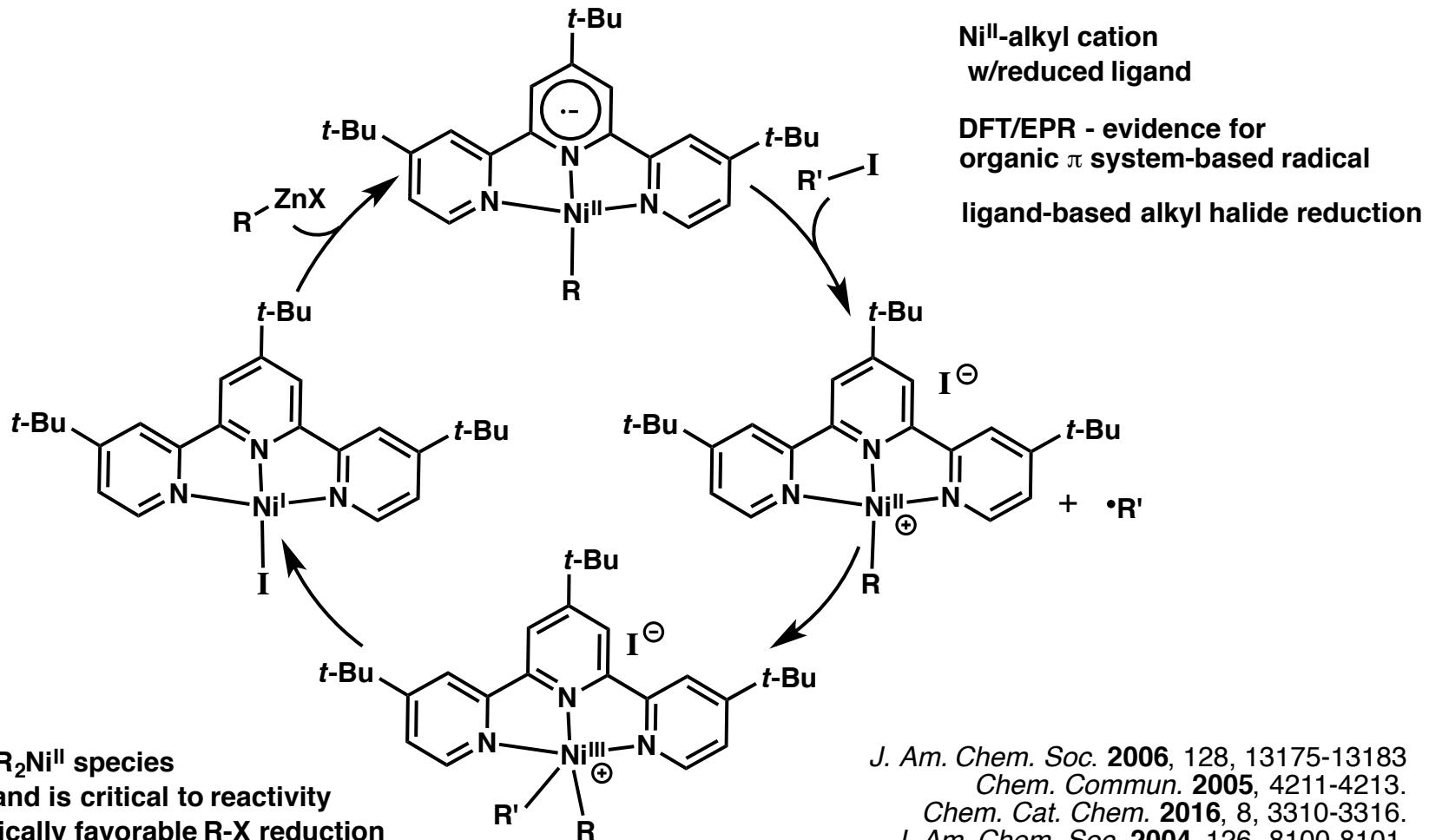
- structure of the base is more important than basicity
- not a homolytic aromatic substitution
- spectroscopy- ligand centered radical
- DFT calculations-
 - electron transfer from base to starting complex (ligand-centered radical)
 - H-abstraction to form Fe-C bond

Ni-catalyzed $C(sp^3)$ - $C(sp^3)$ cross couplings

Vicic and coworkers, 2006:



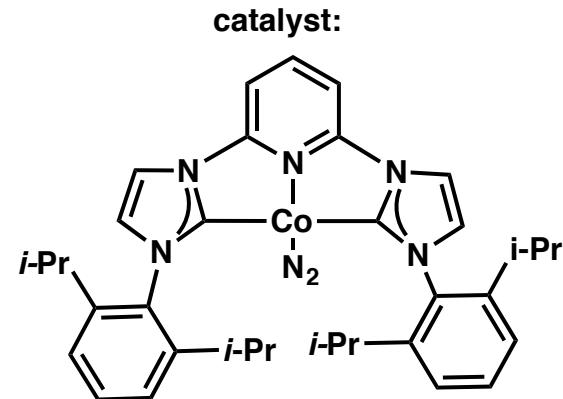
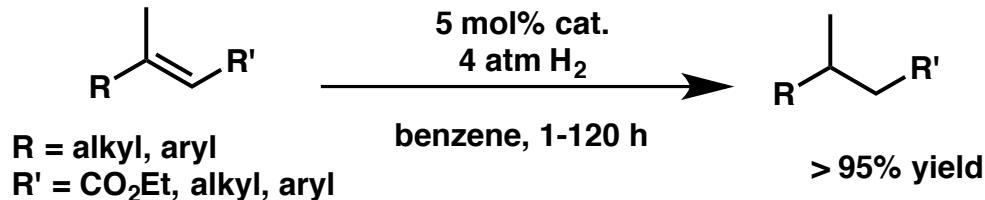
Mechanism:



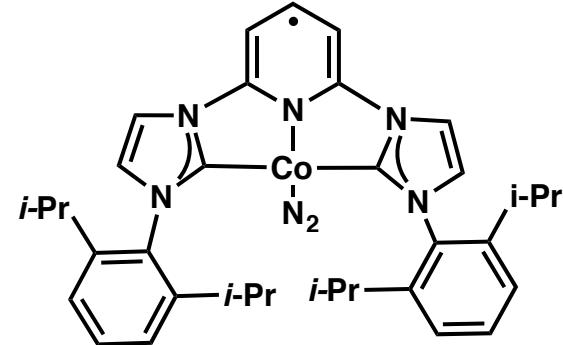
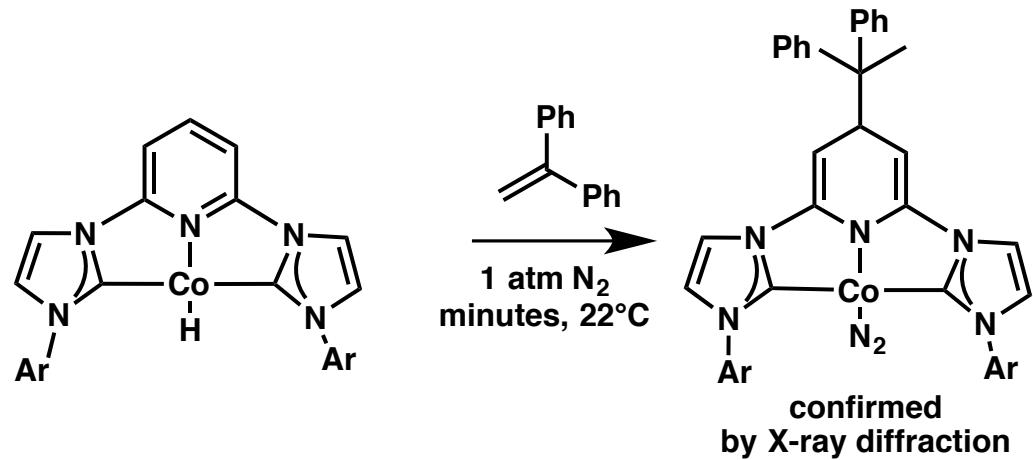
J. Am. Chem. Soc. 2006, 128, 13175-13183
Chem. Commun. 2005, 4211-4213.
Chem. Cat. Chem. 2016, 8, 3310-3316.
J. Am. Chem. Soc. 2004, 126, 8100-8101.

Catalytic Hydrogenation with Bis(arylimidazol-2-ylidene)pyridine Co complexes

Chirik and coworkers:



Evidence for Pyridyl-based Radical intermediate:



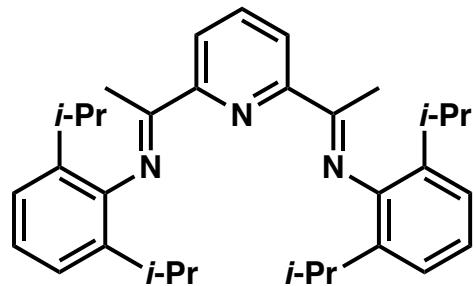
- NMR analysis of intermediates,
- EPR: ligand-centered radical
- X-ray crystal structure
- spin density calculations
- DFT

Chiral cobalt hydrogenation catalysts:
J. Am. Chem. Soc. 2012, 134, 4561-4564.
J. Am. Chem. Soc. 2013, 135, 13168-13184.

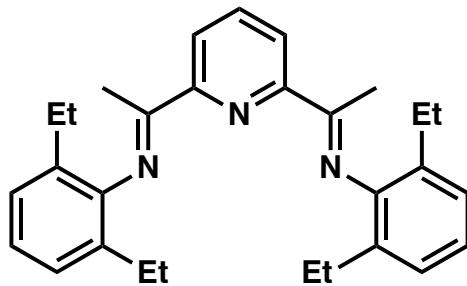
*What about more common ligands such as
BOX/ PyBox?*

What about more common ligands such as BOX/ PyBox?

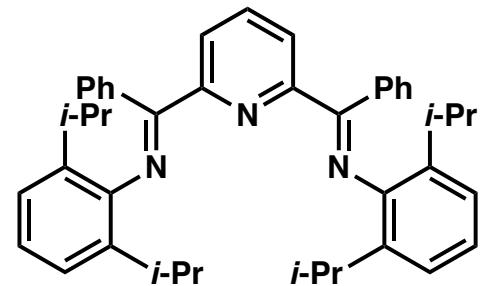
Reduction Potentials of free ligands:



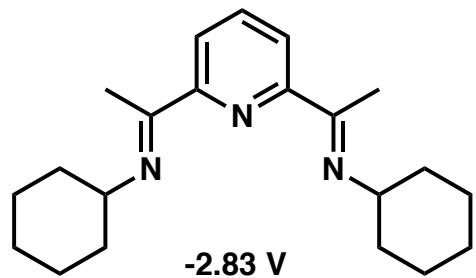
-2.62 V



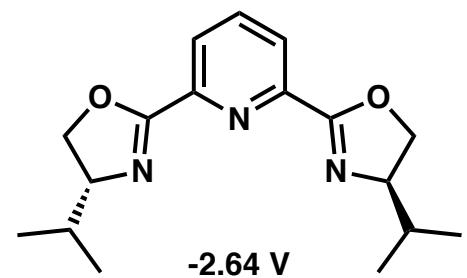
-2.72 V



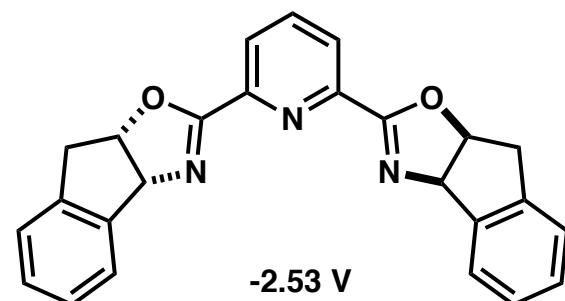
-2.55 V



-2.83 V



-2.64 V



-2.53 V

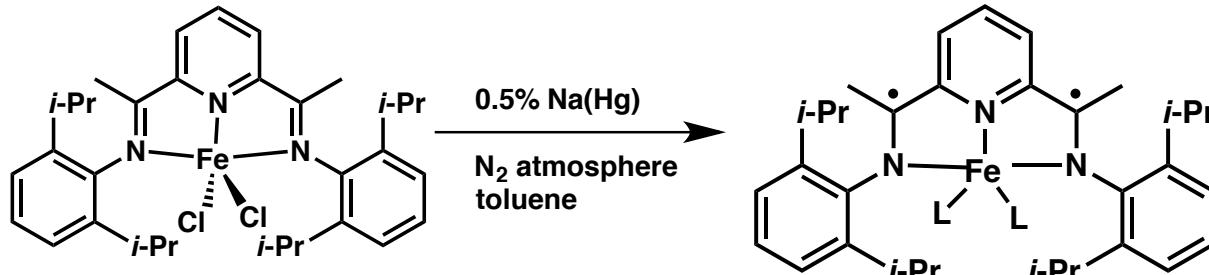
Cyclic voltammograms were recorded in THF solution (~1 mM in compound) with $[n\text{Bu}_4\text{N}]^+\text{PF}_6^-$ electrolyte (~0.1 M), using a 3 mm glassy carbon working electrode, Pt wire counter electrode, and Ag/Ag^+ reference electrode. Values are reported versus ferrocene/ferrocinium

Remember: $\Delta G = -nFE$, the more positive the RP, the greater the affinity for electrons or tendency to be reduced

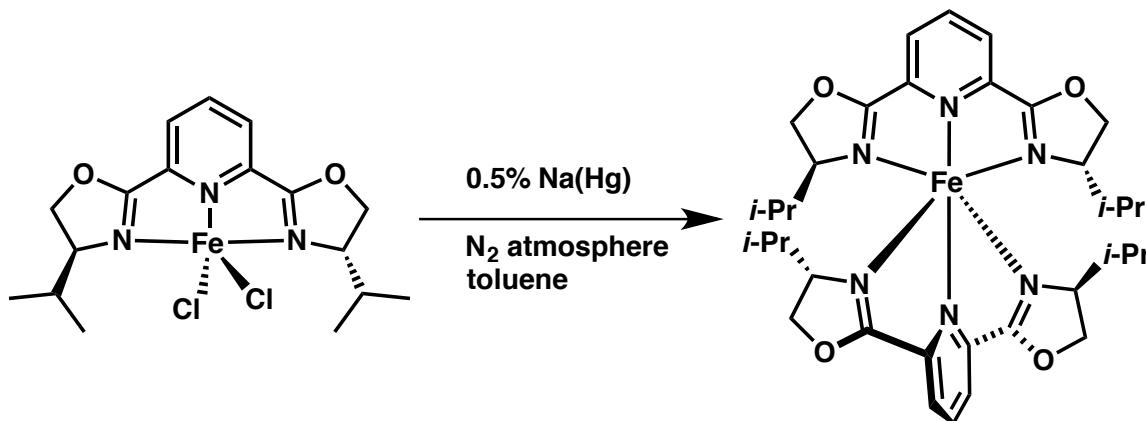
- more electron rich ligands, lower RP
- PyBox ligands fall within the range of the bis(imino)pyridine ligands

What about more common ligands such as BOX/ PyBox?

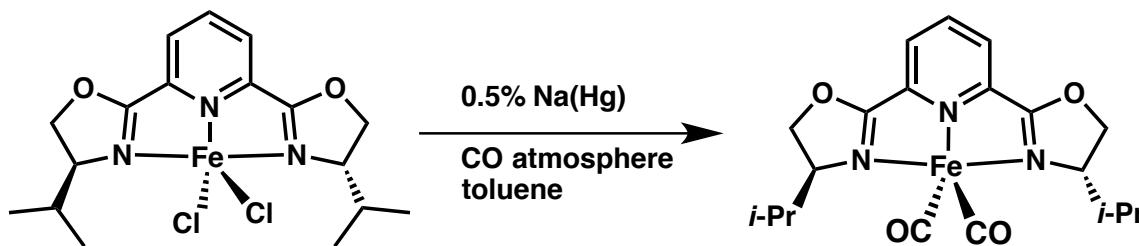
Synthesis of the reduced Fe(PyBOX) complexes:



Chirik and coworkers:
synthesis of active Fe catalyst for
2+2, alkene hydrogenation,
etc.



only bis(chelate) was isolated under a wide variety of reduction conditions

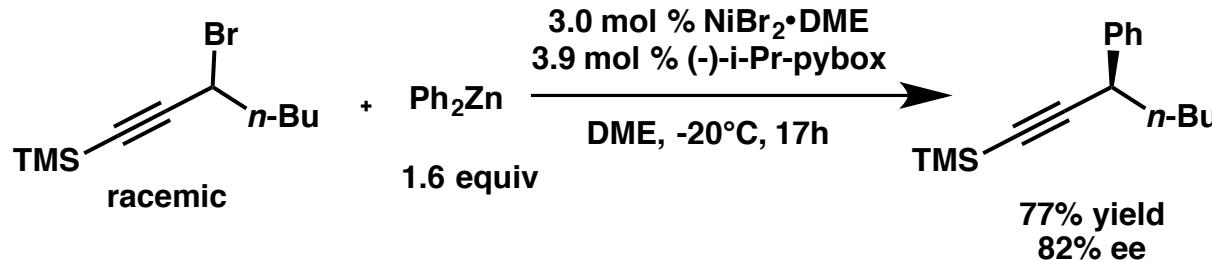


compared IR-stretching frequency
- ligands are more electron
donating than bis(imino)pyridine,
less likely to be reduced

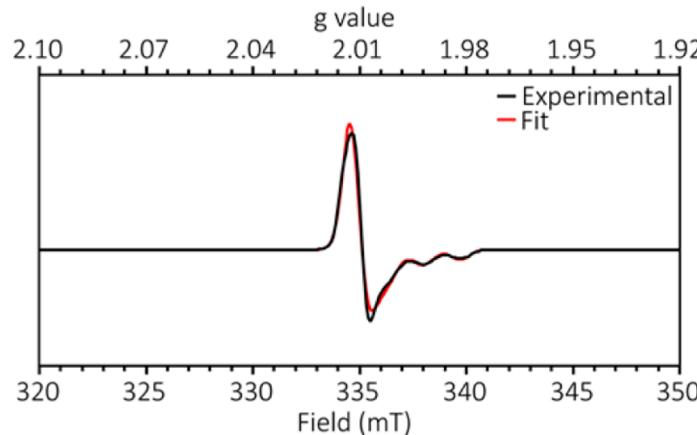
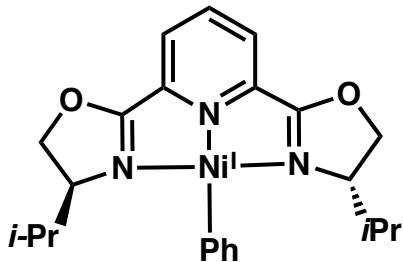
- PyBox and BOX exhibited decent reactivity but low enantioselectivity in hydrosilylation of ketones
- not as efficient as bis(imino)pyridines, more info is needed to confirm similar reaction pathway
- bis(chelate) formation is principal catalyst deactivation pathway

What About more common ligands such as PyBox/ Box?

Greg Fu (2014):



EPR spectrum of proposed intermediate:



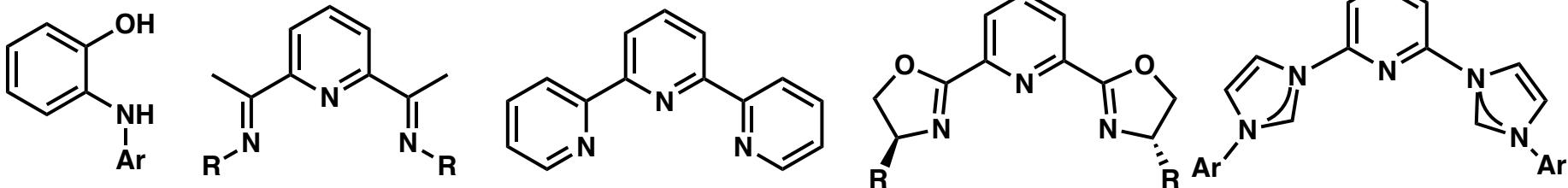
revised mechanism doesn't involve this intermediate

EPR spectrum of (-)-i-Pr-pyboxNiI(Ph) (2; black) and corresponding fit (red). Fit parameters: $g_1 = 2.0067$, $g_2 = 2.0075$, $g_3 = 1.9889$, ^{14}N coupling (MHz) = 0.0205, 0.0124, 47.2047, line width = 0.9929. X-band EPR spectra were collected at 77 K in a toluene glass at $\omega_{\text{rf}} = 9.411$ GHz at 2 mW power and a modulation amplitude of 2 G.
(reproduced from JACS, 2014, 136, 16588-16593)

axial signal at $g = 2.00$, indicative of coupling to a single ^{14}N in one g component, which is consistent with a largely ligand-centered radical

Outlook

Ligand Characteristics:



- high degree of delocalization
- Nitrogen is key!

Overall conclusions:

- Limited scope-
- How should they be studied?
 - sterics: Tolman angle, % buried volume, etc
 - electronics:
 - Crabtree: CV of free ligand, ligand bound to redox-inactive metal
 - establish OS, ID radical ligands, physical/chemical consequences
- Role of Metal in the reaction- structural stability or crucial role?
- Versatile new tools

Some Reviews:

Fensterbank, *Chem. Cat. Chem.* **2016**, *8*, 3310- 3316.

Crabtree, *Chem. Soc. Rev.* **2013**, *42*, 1440-1459.

Caulton, *Eur. J. Inorg. Chem.* **2012**, 435-443.

Kaim. *Inorg. Chem.* **2011**, *50*, 9752-9765.

Ward, *Angew. Chem. Int. Ed.* **2012**, *51*, 10228-10234.

van der Vlugt, *Chem. Soc. Rev.*, **2015**, *44*, 6886-6915.

de Bruin, *ACS Catal.* **2012**, *2*, 270-279.