The Loss of Innocence

Finding the hidden *potential* of redox-active ligands in synthesis

Valerie A. Schmidt
Alexanian Lab Group Meeting
10 August 2010

Outline

- What are Non-Innocent Ligands?
- Bioinorganic Relevance
  - galactose oxidase
- Non-Innocent Ligands in Organic Synthesis
  - Cycloadditions
  - Reductive Cyclizations
  - Alkene Hydrogenations

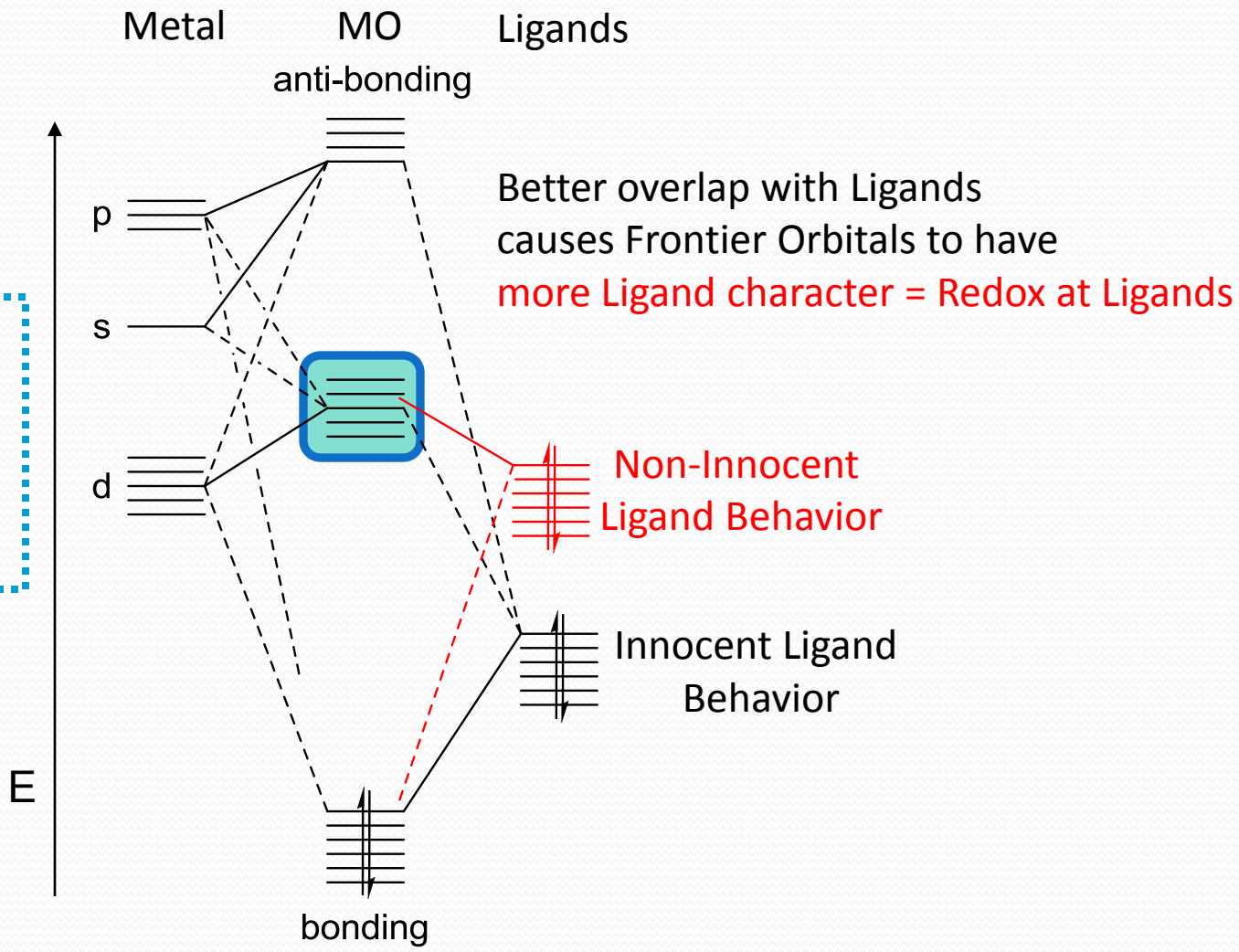
What are Non-Innocent Ligands?

- Non-innocent ligands are those with oxidation states that vary depending on their coordination environment.
- They are sometimes termed “ambi-valent.”
- Most importantly, they are redox-active.

Innocent	Non-Innocent
H_2O, NH_3, Cl^-	O_2, NO

MO Explanation

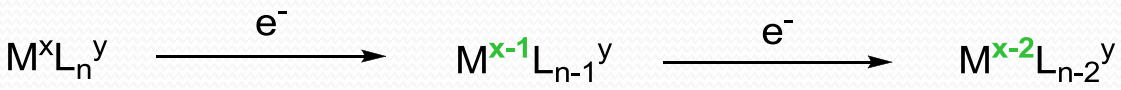
Frontier Orbital character with Innocent Ligands is dominated by the metal's d-orbitals



Crabtree, R.H. *The Organometallic Chemistry of the Transition Metals* **2005**, p. 15.
Sazama, G.T.; Betley, T.A. *Inorg. Chem.* **2010**, *49*, 2512.

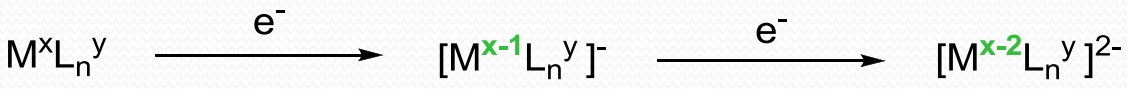
Innocent vs. Guilty Ligand Behavior

Case 1 – when L = halide



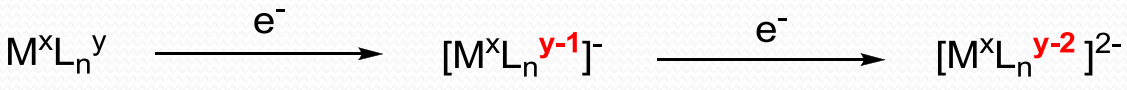
INNOCENT

Case 2 – when L = water



INNOCENT

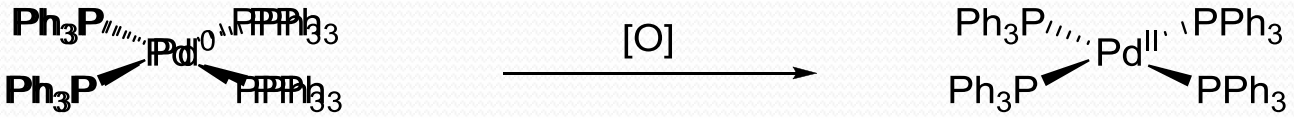
Case 3 – when L is redox active



GUILTY!!!

Assigning Oxidation States

Redox-Inactive Ligands

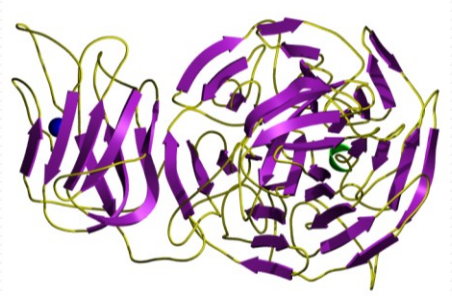


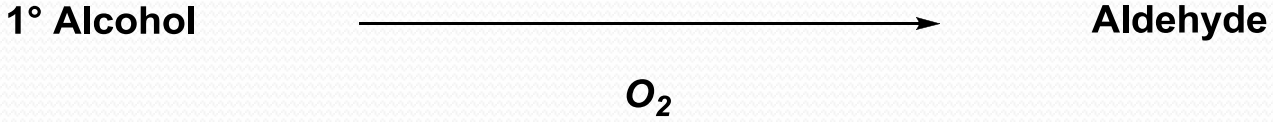
Redox-Active Ligands

Kaim, W.; Schwederski, B. *Coor. Chem. Rev.* **2010**, *254*, 1580.

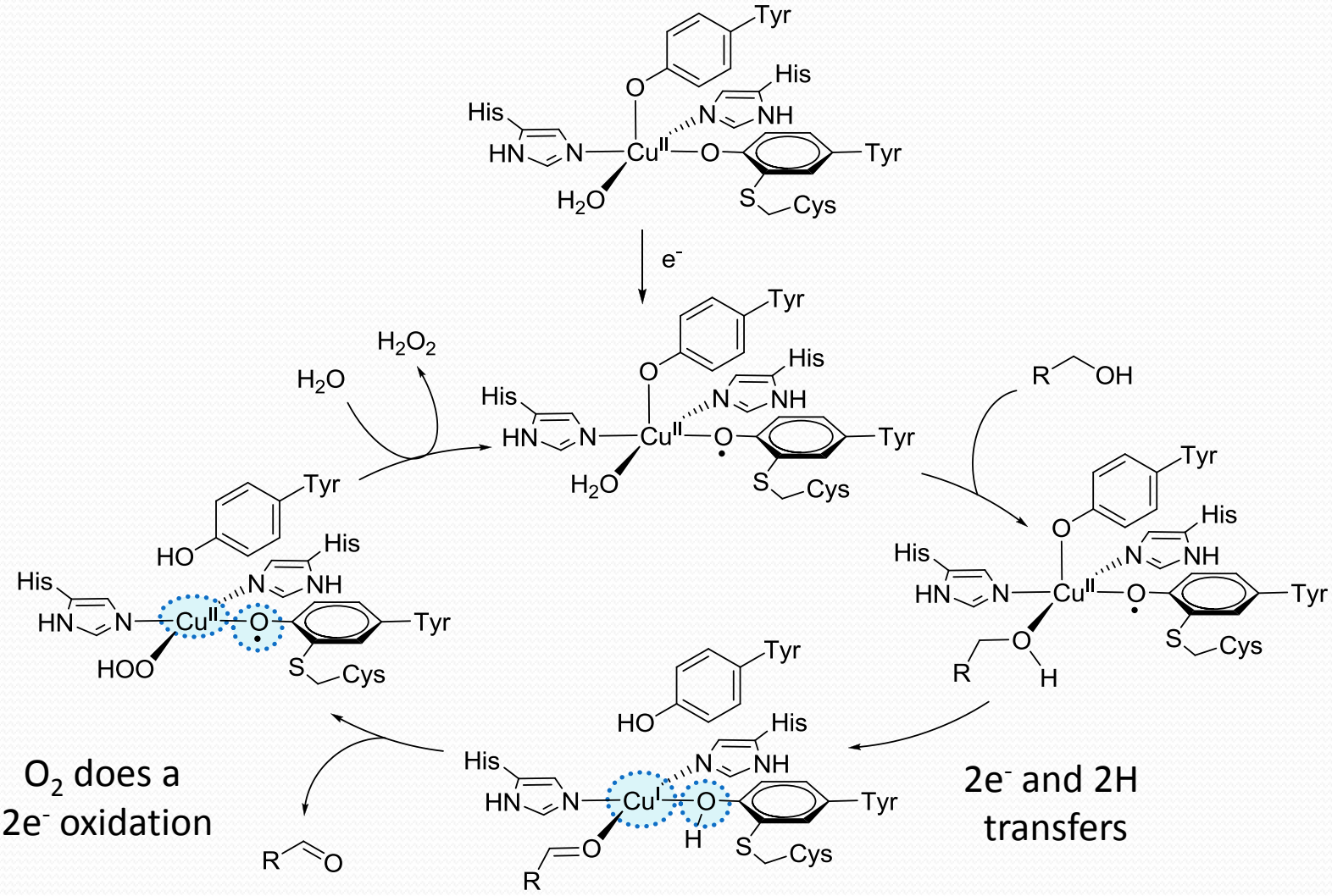
Bioinorganic Chemistry

- Enzymes are uniquely suited for NIL's
  - Utilize first-row transition-metals that are prone to undergo single-electron transfers (Fe, Cu).
  - Active sites confine radical species, preventing unselective radical chemistry.





Galactose Oxidase



Kaim, W.; Schwederski, B. *Coor. Chem. Rev.* **2010**, *254*, 1580.

Bringing Nature to the Laboratory

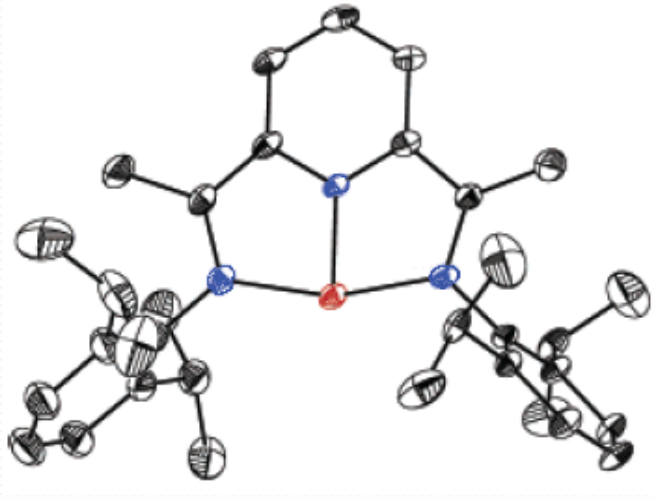
NIL's used in Organic Synthesis

Fe Bis(imino)pyridine catalyzed :

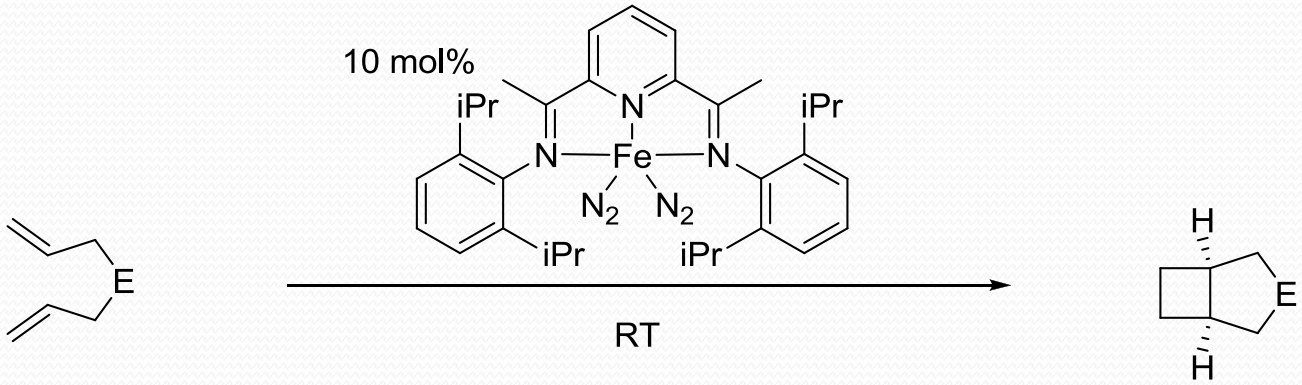
- [2+2] cycloadditions
- Reductive Cyclizations
- Alkene hydrogenations

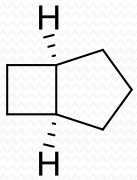
These areas are dominated by the use of Ru, Rh, Ir, Pd, Ni catalysts.

Prof. Paul J. Chirik



[2+2] Cycloadditions





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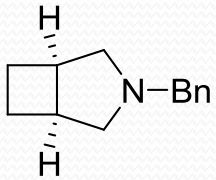

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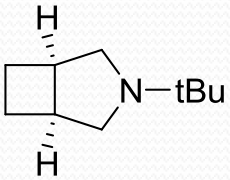

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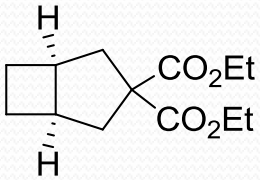

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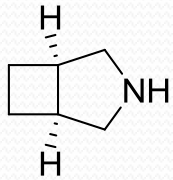
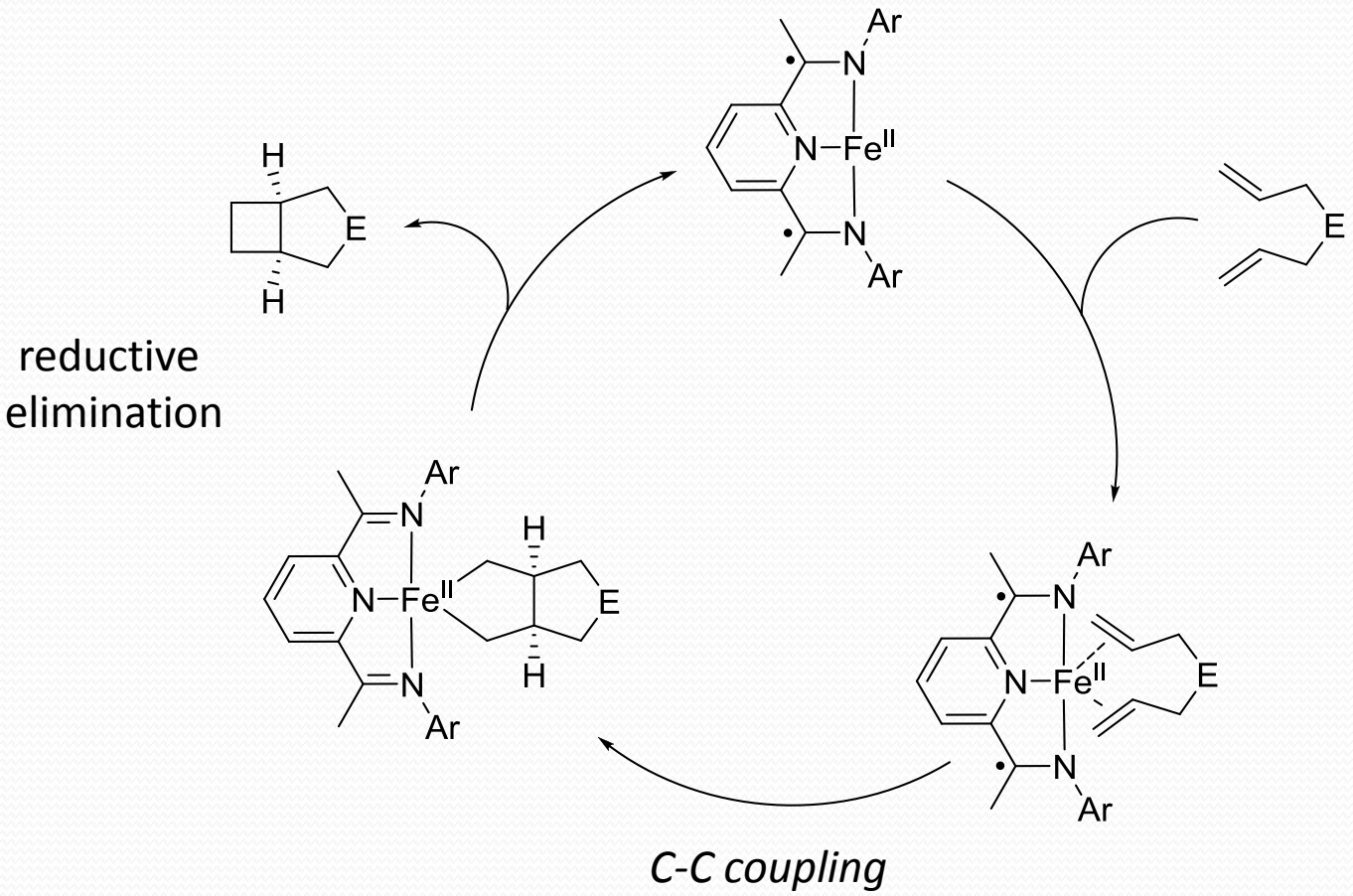


quant.
with 1 equiv. Fe

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

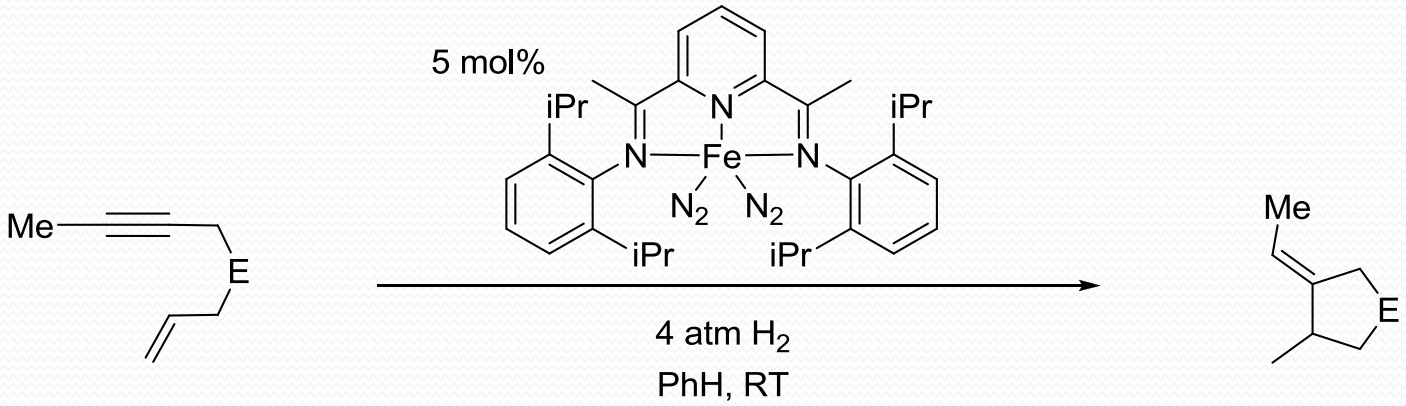
[2+2] Cycloadditions

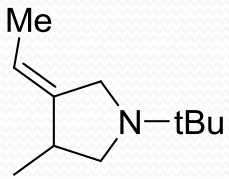


Fe^{II} oxidation state is preserved throughout, preventing formation of inactive Fe^{0} species.

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

Reductive Cyclizations





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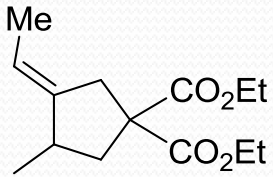

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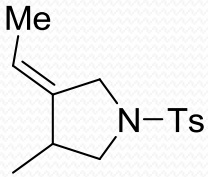

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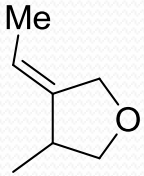

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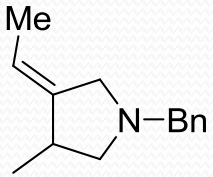
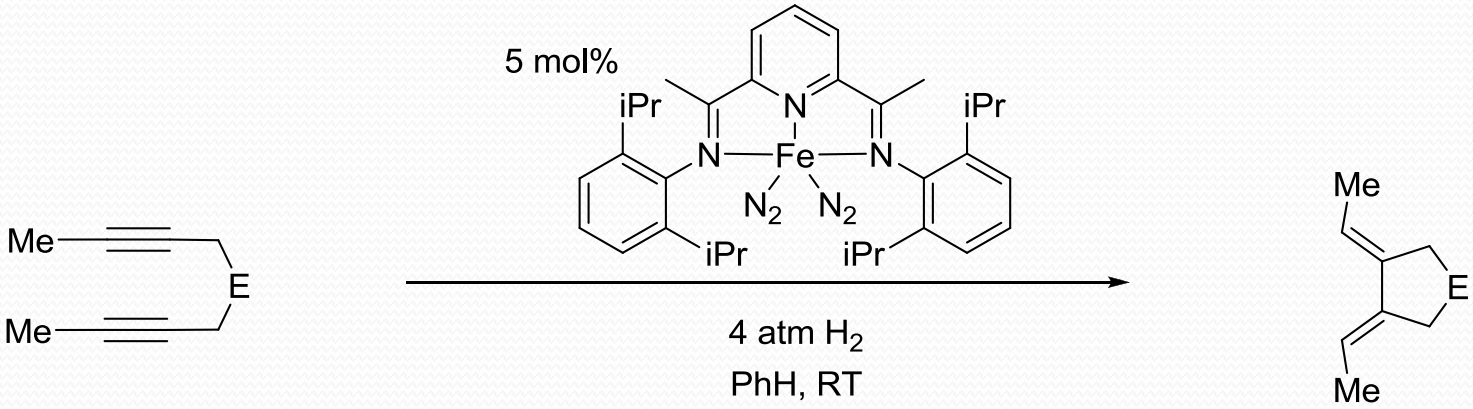
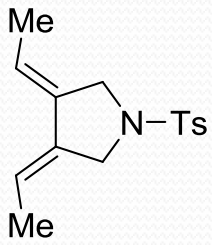


71%

Sylvester, K.T.; Chirik, P.J. *J. Am. Chem. Soc.* **2009**, 8772.

Reductive Cyclizations





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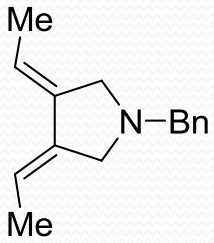

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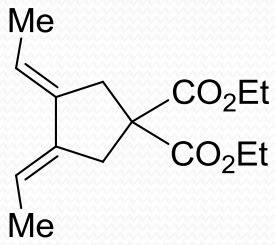

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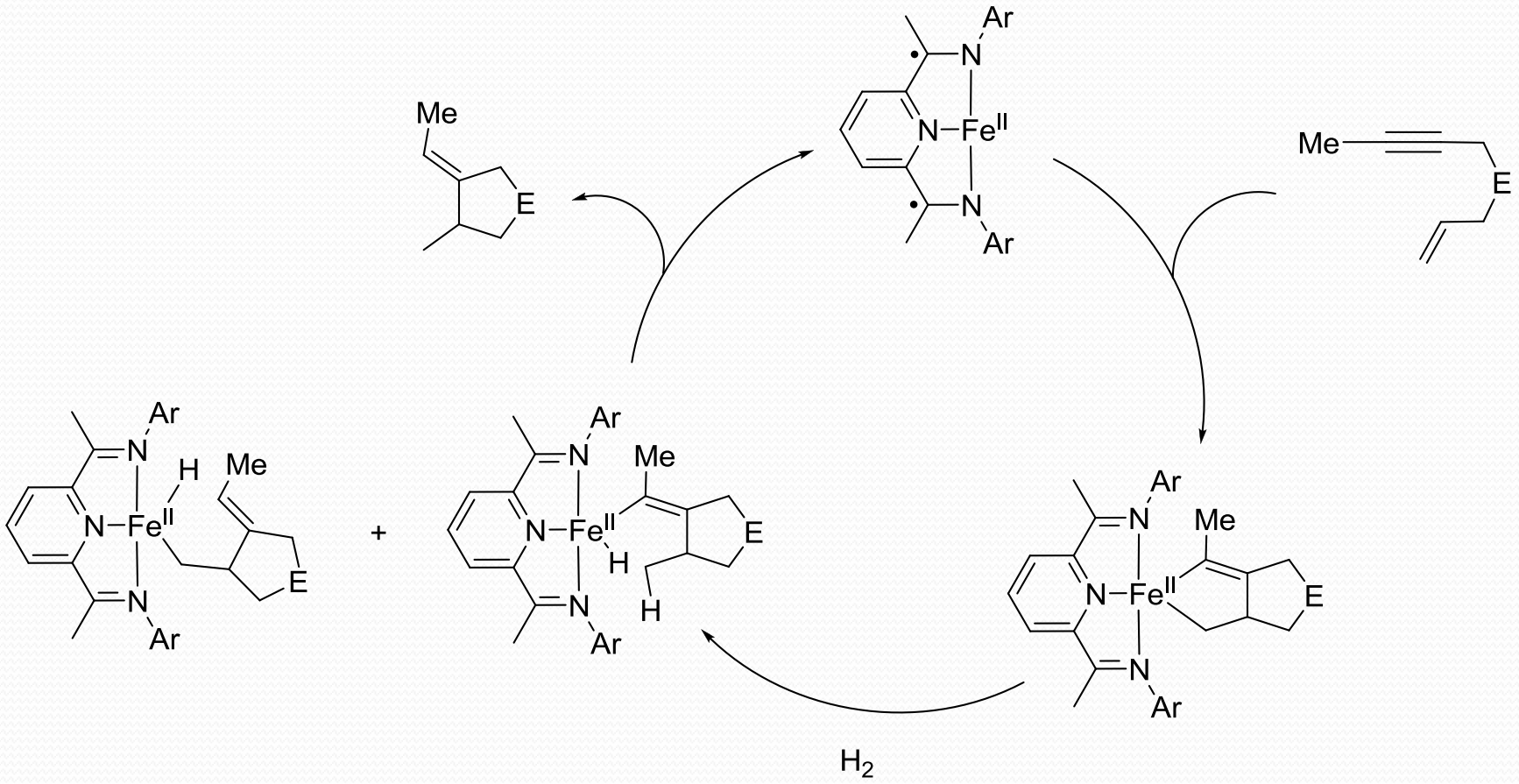
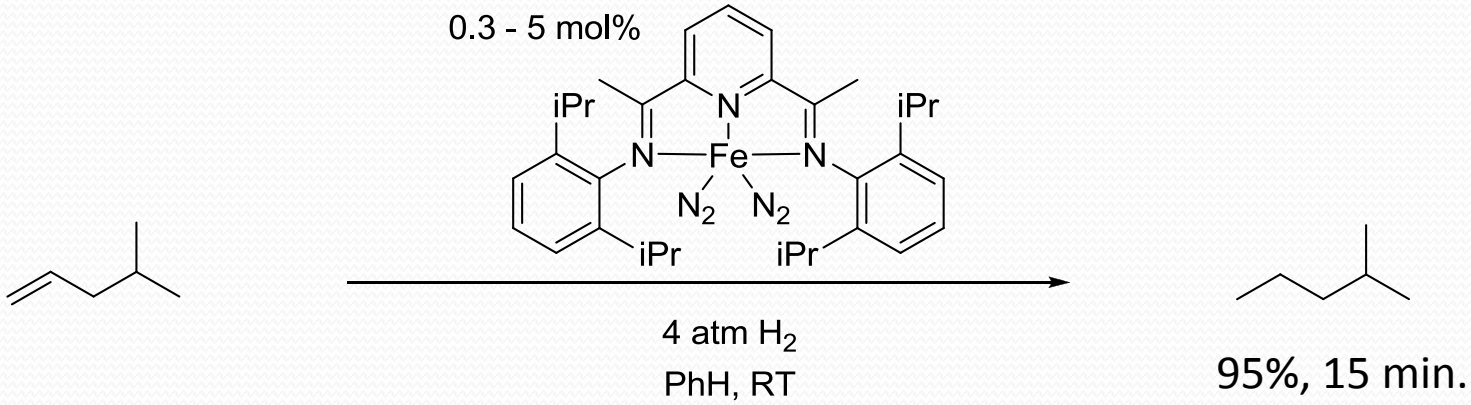
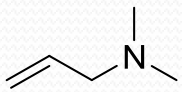
Reductive Cyclizations



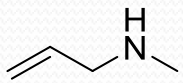
Sylvester, K.T.; Chirik, P.J. *J. Am. Chem. Soc.* **2009**, 8772.

Alkene Hydrogenations

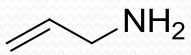




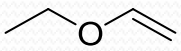
95%, 15 min.



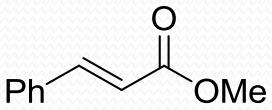
95%, 60 min.



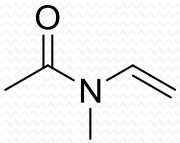
20%, 1 day



>99%, 5 min.



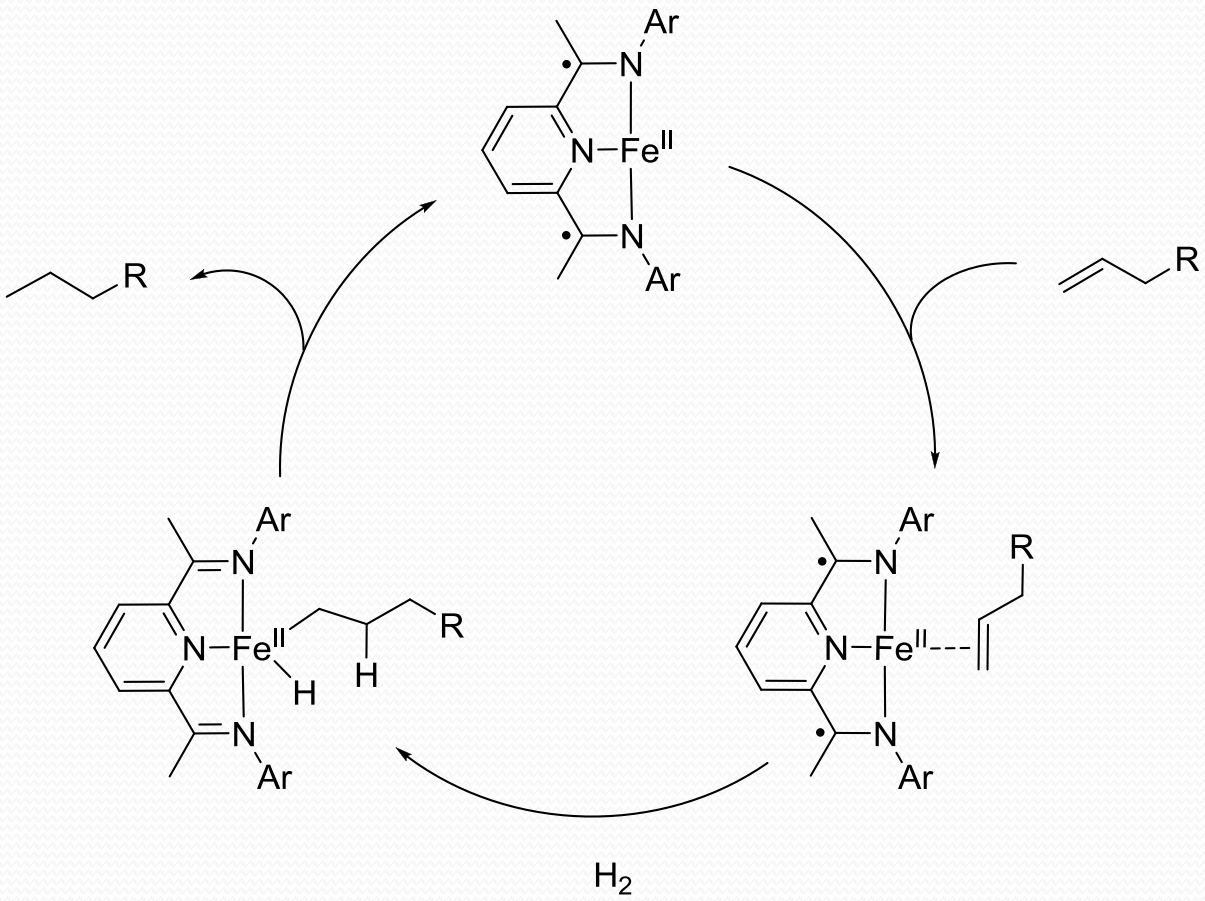
>99%, 5 min.



87%, 4h

Trovitch, R.J.; Lobkovsky, E.; Bill, E.; Chirik, P.J. *Organometallics,* **2008**, 1470.

Alkene Hydrogenations



Trovitch, R.J.; Lobkovsky, E.; Bill, E.; Chirik, P.J. *Organometallics,* **2008**, 1470.

Summary

- Non-Innocent Ligand orbitals mix with metal d-orbitals allowing redox processes to occur at the ligands instead of the metal center.
- Nature uses NIL's.
  - galactose oxidase
- NIL's can allow catalysts to accomplish $2e^-$ transformations using metals that generally facilitate single electron transfers.