The Loss of Innocence
Finding the hidden potential of redox-active ligands in synthesis

Valerie A. Schmidt
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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.

<table>
<thead>
<tr>
<th>Innocent</th>
<th>Non-Innocent</th>
</tr>
</thead>
<tbody>
<tr>
<td>H₂O, NH₃, Cl⁻</td>
<td>O₂, NO</td>
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</tbody>
</table>
Innocent Ligand Behavior

Better overlap with Ligands causes Frontier Orbitals to have more Ligand character = Redox at Ligands

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.
Innocent vs. Guilty Ligand Behavior

Case 1 – when $L = \text{halide}$

\[
M^{x}L_{n}^{y} \xrightarrow{e^-} M^{x-1}L_{n-1}^{y} \xrightarrow{e^-} M^{x-2}L_{n-2}^{y}
\]

INNOCENT

Case 2 – when $L = \text{water}$

\[
M^{x}L_{n}^{y} \xrightarrow{e^-} [M^{x-1}L_{n}^{y}]^{-} \xrightarrow{e^-} [M^{x-2}L_{n}^{y}]^{2-}
\]

INNOCENT

Case 3 – when $L$ is redox active

\[
M^{x}L_{n}^{y} \xrightarrow{e^-} [M^{x}L_{n}^{y-1}]^{-} \xrightarrow{e^-} [M^{x}L_{n}^{y-2}]^{2-}
\]

GUILTY!!!
Assigning Oxidation States

Redox-Inactive Ligands

Redox-Active Ligands

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.

![Diagram of galactose oxidase](image-url)
Galactose Oxidase

$O_2$ does a 2e$^-$ oxidation

2e$^-$ and 2H transfers

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.
[2+2] Cycloadditions

[2+2] Cycloadditions

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

Reductive Cyclizations

Reductive Cyclizations

Reductive Cyclizations

Alkene Hydrogenations

0.3 - 5 mol%

\[
\text{Fe} \quad \text{N} \quad \text{N} \\
\text{iPr} \quad \text{iPr} \quad \text{iPr}
\]

4 atm H₂
PhH, RT

95%, 15 min.

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

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.