CO$_2$ Insertion Chemistry at Ruthenium Centers

$[\text{Ru}]-\text{R}$
(R = H, Me)

CO Induced Reduction of Iron Dinitrosyl Complexes

$\text{ON}_2\text{FeSR}$
$\xrightarrow{1/2\text{RSSR}}\text{ON}_2\text{FeCO}$

Samuel J. Kyran
D. J. Darensbourg Research Group

*Mettler Toledo AutoChem Information Sharing Event*
*Rice University*
*May 20, 2015*
**CO₂ Production and Utilization**

- 35 Gt/y of CO₂ is released into the atmosphere and is linked to climate change
- Geologic sequestration is seen as a long-term solution, and profitable CO₂ utilization can fund this effort
  - Inertness of CO₂ poses a challenge in its transformation
    - Need judicious choice of catalysts
- Currently ~120 Mt/y is used in industrial chemical syntheses

Adding value to a waste product

![Syntheses of Carboxylic Acids](image)

**Syntheses of Carboxylic Acids**

- First catalytic synthesis at CaRLa! (TON = 10)
- CH₃COOH
- COOH
- HCOOH
- CH₄
- x
- H₂
- MeOH
- Inorganic carbonates

---

**References**

Challenging Catalysis

Oxidative addition of hydrocarbons occur best at electron-rich late transition metal complexes

\[ [M] = \text{Ru, Rh, Pd, etc.} \]

\[
\begin{align*}
\text{CH}_4(g) + \text{CO}_2(g) & \rightarrow \text{CH}_3\text{COOH}(l) & \Delta G^{298} &= 18.0 \text{ kcal/mol} \\
\text{C}_6\text{H}_6(l) + \text{CO}_2(g) & \rightarrow \text{C}_6\text{H}_5\text{COOH}(s) & \Delta G^{298} &= 6.1 \text{ kcal/mol} \\
\text{H}_2(g) + \text{CO}_2(g) & \rightarrow \text{HCO}_2\text{H}(l) & \Delta G^{298} &= 7.6 \text{ kcal/mol}
\end{align*}
\]

Unfavorable thermodynamics will require the addition of a base to drive the reaction forward

No formic acid observed in absence of base

**CO$_2$ Insertion Step**

\[
\begin{align*}
\text{HCr(CO)}_5^- + \text{CO}_2 & \rightleftharpoons \text{HCO}_2\text{Cr(CO)}_5^- \\
\text{RW(CO)}_5^- + \text{CO}_2 & \rightarrow \text{RCO}_2\text{W(CO)}_5^- \\
R & = \text{Me, Et, Bn}
\end{align*}
\]

- Insertion into M-H bonds happens faster
- Rate of insertion increases with increasing donor ability
- Coordination of CO$_2$ is not required

**Thermodynamic preference of acetate formation via CO$_2$ insertion into [Ru]-Me bond**

Syntheses of DMPE Ligated Ru-complexes

- **[Ru₂(PMe₂Ph)₆Cl₃]Cl**
  - DMPE neat
  - 200 °C
  - **trans-Ru(dmpe)₂(H)Cl**
    - LiAlH₄
    - THF reflux

- **RuCl₃·3H₂O**
  - PMe₂Ph
  - HO
  - reflux
  - PPh₃
  - MeOH reflux
  - Ru(PPh₃)₃Cl₂
  - DMPE reflux
  - **trans-Ru(dmpe)₂(Me)Cl**
    - AlMe₃
    - reflux

- **trans-Ru(dmpe)₂(H)Me**
  - MeLi
  - RT, stir

- **trans-Ru(dmpe)₂Me₂**
  - MeLi
  - RT, stir

References:
NMR Spectra

$^{31}$P NMR

$[\text{Ru}(\text{H})\text{Me}]$

$[\text{Ru}(\text{H})\text{Cl}]$

$[\text{Ru}\text{Me}_2]$

$[\text{Ru}(\text{Me})\text{Cl}]$

$\delta = -1.18$ ppm

$^{1}J_{\text{H-P}} = 5$ Hz

$\delta = -20.7$ ppm

$^{2}J_{\text{H-P}} = 21$ Hz

$^{1H}$ NMR

$[\text{Ru}\text{Me}_2]$

$[\text{Ru}(\text{H})\text{Cl}]$

$\delta = -20.7$ ppm
CO₂ Insertion Study

1 atm CO₂

C₆H₆

Absorbance

1604 cm⁻¹

1378 cm⁻¹

Wavenumbers

Time

ReactIR iC10
CO$_2$ Insertion – Kinetic Analysis

Reaction Profiles (30 °C)

Natural log plot of abs vs. time (30 °C)

rate = $k_{obs} [\text{Ru}]$°

$k_{obs} = k [\text{CO}_2]$°

**CO₂ Insertion – High Pressure Study**

Transformation of Me signals in ¹H NMR

-1.20 ppm, 6 H, 2 Me

-1.60 ppm

2.00 ppm

**Reaction at 4.1 atm of CO₂**

$k_{obs}$ vs [CO₂] at 25 °C

$k_{obs} (s^{-1})$

- 6.8 atm
- 4.1 atm
- 1.0 atm

Complete rate expression

rate = $k [Ru]^{1} [CO₂]^{1}$
**CO₂ Insertion – Eyring Analysis**

**Rate Plots at Various Temperatures**

![Rate Plots](image)

**Eyring Plot**

\[
\ln \frac{k}{T} = \ln \frac{k_B}{h} + \frac{\Delta S^\ddagger}{R} - \frac{\Delta H^\ddagger}{RT}
\]

**Activation parameters**

\[\Delta H^\ddagger = 12.7 \pm 0.6 \text{ kcal mol}^{-1}\]
\[\Delta S^\ddagger = -31.9 \pm 2.0 \text{ e.u.}\]

**Associative Mechanism**

<table>
<thead>
<tr>
<th>T (°C)</th>
<th>[CO₂] (M)*</th>
<th>(k_{\text{obs}} \times 10^4 \text{ s}^{-1})</th>
<th>(k \times 10^4 \text{ M}^{-1} \text{ s}^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>19</td>
<td>0.118</td>
<td>0.261</td>
<td>2.21</td>
</tr>
<tr>
<td>25</td>
<td>0.111</td>
<td>0.401</td>
<td>3.61</td>
</tr>
<tr>
<td>30</td>
<td>0.106</td>
<td>0.485</td>
<td>4.57</td>
</tr>
<tr>
<td>35</td>
<td>0.101</td>
<td>0.721</td>
<td>7.15</td>
</tr>
<tr>
<td>40</td>
<td>0.095</td>
<td>0.999</td>
<td>10.5</td>
</tr>
</tbody>
</table>

**CO₂ Insertion – Effect of X ligand**

**Slower insertion due to the presence of an electron-withdrawing acetate ligand**

**Similarly, no insertion is observed for Cl-[Ru]-Me**
**CO₂ Insertion – Computational Results**

Two possible conformations of formate complexes

**immediate insertion product**

**stable by ~8 kcal/mol**
**CO₂ Insertion – Computational Results**

Free Energy Barriers (kcal/mol)

<table>
<thead>
<tr>
<th>X</th>
<th>X-[Ru]-H</th>
<th>Transition state (gas phase)</th>
<th>X-[Ru]-O₂CH</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>0</td>
<td>7.3</td>
<td>-5.1</td>
</tr>
<tr>
<td>Me</td>
<td>0</td>
<td>10.2</td>
<td>-3.3</td>
</tr>
<tr>
<td>Cl</td>
<td>0</td>
<td>27.9</td>
<td>6.4</td>
</tr>
</tbody>
</table>

*X influences both kinetics and thermodynamics of CO₂ insertion*

Supporting ligand effects

- **Poorer π-acidic ligands** (dicarbene, tmeda) favor CO₂ insertion (more exothermic)
- **APT charges on H** is a measure of its hydricity

Transition state for Ru(dmpe)₂H₂ leading to carboxylation. Distances: Ru-H (a) 2.471 Å; Ru-C (b) 2.936 Å; Ru-O (c) 3.003 Å; Ru-H (d) 1.575 Å.
Summary and Future Directions

- Less electron-donating ligands retard the rate of carboxylation
- Acetate formations have higher barriers but are more exothermic than formates
- Theoretical data corroborates experimental work

- Thermodynamic preference on other late transition metal species

- Conditions for carboxylic acid release from the metal center

- Synthesis of cis-isomers

- Ultimate goal of designing a catalytic system with experimental and computational insights
CO$_2$ Insertion Chemistry at Ruthenium Centers

$[\text{Ru}]-R$

($R = \text{H, Me}$)

CO Induced Reduction of Iron Dinitrosyl Complexes

$\text{CO}$

$\text{ON}$

$\text{Fe}$

$\text{SR}$

$\text{L}$

$\text{ON}$

$\text{Fe}$

$\text{CO}$

$\text{L}$

$\text{1/2 RSSR}$


JACS 2013, 135, 8423-8430.

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Nitric Oxide: From Noxious Pollutant to Vital Messenger

“NO wonder!! nitric oxide is the lightest molecule- and the first gas-known to act as a biological messenger in mammals”

Nobel Prize 1998:
Furchgott, Ignarro and Murad "for their discoveries concerning nitric oxide as a signalling molecule in the cardiovascular system"

Endogenous Synthesis of NO: Nitric Oxide Synthase Family

nNOS: neurotransmission

\[
\text{L-arginine} \xrightarrow{\text{NADPH + O}_2 \ - \ H_2O} \text{N}^\omega\text{-hydroxy-L-arginine} \xrightarrow{1/2 \text{NADPH + O}_2 \ - \ H_2O} \text{L-citrulline}
\]

Daff, S. Nitric Oxide 2010, 23, 1.
Vanin, A. F. Nitric Oxide 2009, 21, 1.

Lifetime of uncomplexed NO in cellular environment: 2 ms to 2 s

Stabilization, storage and transport of NO

S-nitrosothiols (RSNOs) and Dinitrosyl iron complexes (DNICs)

Daff, S. Nitric Oxide 2010, 23, 1.
Vanin, A. F. Nitric Oxide 2009, 21, 1.

17
Discovery of Dinitrosyl Iron Complexes in Biological Systems

EPR signals observed from animal tissues and yeast cells in the 1960’s matched that of thiol-containing Fe-NO complexes

Formation in vivo

- NO binding to protein-based iron centers or iron-sulfur cluster-containing proteins
- Studies have relied on the paramagnetism and characteristic EPR signal of biological DNICs; other diamagnetic DNICs may go unnoticed

SR = cysteine, glutathione

Characteristic EPR signal, g = 2.03

Problems in biological DNIC studies:

- Biological DNICs are difficult to extract and isolate

Vanin, A. F. Nitric Oxide 2009, 21, 1.
Synthetic Analogues of Dinitrosyl Iron Complexes

High molecular weight protein-bound DNICs detected by their EPR signals:

<table>
<thead>
<tr>
<th>Name</th>
<th>Coordination Environment</th>
<th>EPR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bovine serum albumin</td>
<td>S/S</td>
<td>2.01, 2.04</td>
</tr>
<tr>
<td>Sox R</td>
<td>S/N</td>
<td>2.01, 2.04, 2.05</td>
</tr>
<tr>
<td>Mammalian ferrochelatase</td>
<td>N/N</td>
<td>2.01, 2.35, 2.055</td>
</tr>
<tr>
<td>Aconitase</td>
<td>S/S</td>
<td>2.03</td>
</tr>
<tr>
<td>FNR</td>
<td>S/S</td>
<td>2.014, 2.033</td>
</tr>
<tr>
<td>Succinate-Q reductase</td>
<td>S/S</td>
<td>2.012, 2.031, 2.037</td>
</tr>
<tr>
<td>Mammalian ferritin</td>
<td>N/N</td>
<td>2.004, 2.034, 2.016</td>
</tr>
<tr>
<td>Fur</td>
<td>S/S</td>
<td>2.016, 2.034, 2.038</td>
</tr>
<tr>
<td>Iron-quinone complex of photosystem II</td>
<td>S/S</td>
<td>2.04</td>
</tr>
<tr>
<td>Sox R</td>
<td>S/S</td>
<td>2.014, 2.033</td>
</tr>
<tr>
<td>Mammalian ferritin</td>
<td>N or O</td>
<td>2.015, 2.033, 2.055</td>
</tr>
<tr>
<td>Fur</td>
<td>N/N</td>
<td>2.017, 2.032, 2.042</td>
</tr>
<tr>
<td>Iron-quinone complex of photosystem II</td>
<td>N/N</td>
<td>2.01, 2.03, 2.05</td>
</tr>
</tbody>
</table>

S, N, O donor ligand environment

<table>
<thead>
<tr>
<th>Oxidized</th>
<th>Reduced</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPR active</td>
<td>EPR silent</td>
</tr>
<tr>
<td>NO release</td>
<td>NO storage</td>
</tr>
</tbody>
</table>

Anionic | Neutral | Cationic

Anionic

Neutral

Cationic

Neutal

Anionic

Synthetic Analogues of Dinitrosyl Iron Complexes

**Exploration of N-Donors: Analogues of Histidine-Containing DNICs**

Fe(CO)\textsubscript{2}(NO)\textsubscript{2} + {Fe(NO)\textsubscript{2}}\textsuperscript{10} \rightarrow \text{Extremely air sensitive} \rightarrow \{Fe(NO)\textsubscript{2}\}\textsuperscript{10} \rightarrow \{Fe(NO)\textsubscript{2}\}\textsuperscript{9}

---


Li, L. *Comments on Inorganic Chemistry* 2002, 23, 335.
NHC DNICs as Analogues Of Histidine-containing DNICs

- NHC stabilize both \(\{\text{Fe(NO)}_2\}_9\) and \(\{\text{Fe(NO)}_2\}_{10}\) DNICs
- Similar steric and electron donor properties between imidazoles and NHCs

NHCs are suitable mimics of imidazoles / histidines!

Inter-conversion of \( \{\text{Fe(NO)}_2\}_9/\{\text{Fe(NO)}_2\}_10 \)

\[
\begin{array}{c}
\{\text{Fe(NO)}_2\}_9 \\
\text{Oxidized} \\
\text{EPR active}
\end{array}
\quad \quad
\begin{array}{c}
\{\text{Fe(NO)}_2\}_10 \\
\text{Reduced} \\
\text{EPR silent}
\end{array}
\]

- In biology: implications on governing the role of the DNIC as an NO-release agent or as reservoirs of NO

- For \([ (RS)_2\text{Fe(NO)}_2 ]^- \), reduction requires strong reducing agent (ex: Sodium-biphenyl) and good incoming nucleophile (excess PR$_3$).
**CO Induced Inter-conversion of \( \{\text{Fe(NO)}_2\}^9/\{\text{Fe(NO)}_2\}^{10} \)**

\[
\begin{align*}
\text{EPR: } g &= 2.03 \quad (1) \quad \{\text{Fe(NO)}_2\}^9 \\
\text{paramagnetic} \\
\text{CO} &\rightarrow \text{1/2 PhSSPh} \quad \rightarrow \text{CO} \\
\text{1H NMR: reduced complex} &\quad &\text{diamagnetic} \\
\end{align*}
\]

- CO is also a regulatory and signaling molecule
- Interactions between CO & NO producing enzymes in biological milieu are noted*

\[
\begin{align*}
\text{IR Spectra (THF)} \\
\text{Wavenumber (cm}^{-1}) \\
\end{align*}
\]

In Situ IR Analysis

3D stack plots at 60 °C in toluene

1992
1768 → 1753
1720 → 1708

High pressure study with ASI® ReactIR 1000
A Bimolecular Process

Activation parameters

\[ \Delta H^\ddagger = 7.80 \pm 0.16 \text{ kcal/mol} \]

\[ \Delta S^\ddagger = -45.0 \pm 0.5 \text{ e.u.} \]

Small $\Delta H^\ddagger$ and large negative $\Delta S^\ddagger$:

*Associative nature of the mechanism*

\[ \Delta G^\ddagger (298 \text{ K}) = 21.2 \pm 0.2 \text{ kcal/mol} \]
Computational Investigations

- A five-coordinate, 19-electron intermediate with NO ligands accommodating excess charge.
- Disulfide formation is the driving force of the reaction.

The transition state, \([1-3]^\dagger\), contains a bonding interaction between a \(\pi\) orbital on the Fe(NO)\(_2\) unit and the \(\pi^*\) orbital of the CO.

- Nucleophilic attack of the Fe on the CO stabilizes the addition of the poor nucleophile.
Alterning Electronics at the \{\text{Fe(NO)}_2\} Unit

**More** electron density at \{\text{Fe(NO)}_2\} unit:

\[\text{faster rate}\]

**Less** electron density at \{\text{Fe(NO)}_2\} unit:

\[\text{slower rate}\]
Synthesis of para substituted aryl thiolates: \((\text{slMes})(S-C_6H_4X)\text{Fe(NO)}_2\)

<table>
<thead>
<tr>
<th></th>
<th>a</th>
<th>b</th>
<th>c</th>
<th>d</th>
<th>e</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td>OCH₃</td>
<td>CH₃</td>
<td>Cl</td>
<td>CF₃</td>
<td>NO₂</td>
</tr>
<tr>
<td>(\sigma_p)</td>
<td>-0.268</td>
<td>-0.170</td>
<td>0.230</td>
<td>0.540</td>
<td>0.778</td>
</tr>
</tbody>
</table>

EDG | EWG
Crystallized in concentrated ether or THF with layered hexanes via slow cooling at -35 °C
**IR Spectroscopy**

\[ \{\text{Fe(NO)}_2\}^9 \]

1 (a-e)

Systematic increase in NO stretching frequencies with stronger electron-withdrawing groups
Cyclic Voltammetry

Recorded in 2 mM THF solutions with 100 mM [n-Bu₄N][BF₄] as the supporting electrolyte. Potentials measured relative to a Ag⁰/AgNO₃ electrode using a glassy carbon electrode. Referenced to Cp₂Fe/ Cp₂Fe⁺ (E₁/₂ = 0.00 V vs Ag/AgNO₃ in THF)

IR and CV confirm changes in electron density occurring at the Fe(NO)$_2$ unit upon variation of substituent at a remote position.
**Kinetic Studies**

Determining reaction rates of 1a-1e towards CO induced reduction

Reaction profile of 2, $v_{CO} = 1992$ cm$^{-1}$ in a toluene solution of 1b and CO at 60 °C

Linear natural log plot of absorption data versus time over three half-lives. $R^2 = 0.991$
### Hammett Analysis of Reaction Rates

<table>
<thead>
<tr>
<th>Complex</th>
<th>Substituent</th>
<th>$k_{obs} \times 10^3$ (s$^{-1}$)</th>
<th>$k \times 10^3$ (M$^{-1}$ s$^{-1}$)</th>
<th>$t_{1/2}$ (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>OCH$_3$</td>
<td>0.103 ± 0.012</td>
<td>12.9 ± 1.5</td>
<td>1.9</td>
</tr>
<tr>
<td>1b</td>
<td>CH$_3$</td>
<td>0.0555 ± 0.0030</td>
<td>6.95 ± 0.38</td>
<td>3.5</td>
</tr>
<tr>
<td>1c</td>
<td>H</td>
<td>0.0603</td>
<td>7.56</td>
<td>3.2</td>
</tr>
<tr>
<td>1d</td>
<td>Cl</td>
<td>0.0424</td>
<td>5.31</td>
<td>4.5</td>
</tr>
<tr>
<td>1e</td>
<td>CF$_3$</td>
<td>0.0172</td>
<td>2.16</td>
<td>11.2</td>
</tr>
<tr>
<td>1f</td>
<td>NO$_2$</td>
<td>0.00270</td>
<td>0.338</td>
<td>71.4</td>
</tr>
</tbody>
</table>

- Negative $\rho$ implies a diminution of negative charge at the reaction center in RDS
- Loss of negative charge at the Fe(NO)$_2$ unit as result of its nucleophilic attack on CO

\[
\rho = -0.831 \\
R^2 = 0.901
\]
Summary and Conclusions

- Reduction of a \{Fe(NO)\textsubscript{2}\}\textsuperscript{9} complex under mild conditions

  
  \[
  \begin{align*}
  \text{ON} & \quad \text{Fe} \quad \text{SPh} \\
  \text{CO} & \quad \text{Toluene} \quad 50 ^\circ \text{C, 1 d} \\
  - & \quad 1/2 \text{PhSSPh}
  \end{align*}
  \]

- Systematic increase in the electron density of the \{Fe(NO)\textsubscript{2}\}\textsuperscript{9} core shows an enhancement of reaction rate

- Bimolecular process initiated by the “attack” of the frontier orbitals of Fe(NO)\textsubscript{2} on the vacant \(\pi^*\) orbitals of the entering CO ligand – experimental tests prove computational hypothesis

Mechanistic understanding of a potential model for the “cross talk” of intracellular gaseotransmitters

- Nitric Oxide Synthase
- Fe-S cluster
- DNICs
- NO transfer agent
- NO storage
- Heme-oxygenase enzymes

\[\text{NO} \quad \text{Fe-S cluster} \quad \text{DNICs} \quad \{\text{Fe(NO)}\textsubscript{2}\}\textsuperscript{9} \quad \text{e}^- \quad \{\text{Fe(NO)}\textsubscript{2}\}\textsuperscript{10} \quad \text{CO}\]

[1-3]*
Acknowledgements

- Prof. Donald J. Darensbourg
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  - Dr. Andrew Yeung
  - Dr. Ryan Bethel
- Mettler Toledo AutoChem
- Rice University
- Audience

Funding
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[Ru]-R
(R = H, Me)

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Redox States of Nitric Oxide

\[
\begin{align*}
\text{N} &= \text{O} \\
S &= 0
\end{align*}
\]

\[\xrightarrow{-e^-} \]

\[
\begin{align*}
\text{N} &= \cdot \text{O} \\
S &= 1/2
\end{align*}
\]

\[
\xrightarrow{+e^-} \\
\begin{align*}
\text{N} &= \cdot \text{O}^- \\
\text{Fe}^{III}(\text{NO})^{-} &\quad \text{or} \quad \text{N} &= \cdot \text{O}^-
\end{align*}
\]

\[
\begin{align*}
\text{S} &= 0 \\
\text{S} &= 1
\end{align*}
\]

\[
\begin{align*}
\left[\text{Fe}^{I}(\text{NO})^+\right]^{2+} &\quad \left[\text{Fe}^{II}(\text{NO})^0\right]^{2+} &\quad \left[\text{Fe}^{III}(\text{NO})^-\right]^{2+}
\end{align*}
\]

Enemark/Feltham notation: \(\{M(\text{NO})_x\}^n\)

\[n = \# \text{ of metal } d \text{ orbital } e^- + \# \text{ } e^- \text{ in NO } \pi^* \text{ orbital}\]

\[
\begin{align*}
\{\text{Fe}^{I}(\text{NO})^+\}^7 &\quad \{\text{Fe}^{II}(\text{NO})^0\}^7 &\quad \{\text{Fe}^{III}(\text{NO})^-\}^7
\end{align*}
\]