SAMARIIUM DIIODIDE: DISCOVERY AND APPLICATIONS

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Wednesday Night Live Literature Series
Dong Group, February 2013
Outline

• Introduction and Discovery
• Early Reactions and Applications
• Modifications
• Applications in Natural Products
• Expansion to Other Lanthanides (II)
Discovery and Early Applications

Before 1977

\[ \text{Sm} \xrightarrow{750^0 \text{C}, 0.01 \text{ mm Hg}} \text{Sml}_3 \]

Kagan's Work (1977)

\[ \text{Sm} \xrightarrow{\text{ICH}_2\text{CH}_2\text{I}, \text{THF, r.t.}} \text{Sml}_2(\text{thf})_n \]

- Known by inorganic chemists since 1906
  - Ubiquitous in nature, commercial applications
- Highly dependent on solvent and additives (more later)
- Solution goes from dark blue (Sm(II)) to yellow (Sm(III)) over time
- Generally prepared and used in situ

Seminal Work - Reduction Reactions

Proposed Reactivity

- Ability to promote one and two electron processes:
  - radical/radical, radical/anionic, anionic/radical, anionic/anionic

- Promotes several reaction types:
  - Radical Cyclizations, Ketyl-Olefin Coupling, Pinacols, Aldol-type, Barbier-Type, Cycloadditions, etc
Samarium Grignard and Samarium Barbier

\[
\text{I} - \text{CH}_3 + \text{nC}_6\text{H}_{13} \text{CO} \xrightarrow{1) 2 \text{SmI}_2} \xrightarrow{2) \text{H}_2\text{O}} \text{OH} \quad \text{R} = \text{n-butyl iodide} \quad 97% \\
\text{n-butyl chloride} \quad 8% \\
\text{sec butyl bromide} \quad 27% \\
\text{tert-butyl bromide} \quad 9%
\]

\[\text{Samarium Barbier}\]

\[
\text{R-X} + \text{C}_2\text{H}_4\text{CO} \xrightarrow{\text{SmI}_2} \text{H}^+ \text{OH} \xrightarrow{\text{H}^+} \text{R}\text{OH}
\]

\[\text{Samarium Grignard}\]

\[
\text{R-X} \xrightarrow{\text{SmI}_2} \text{R} \cdot \xrightarrow{\text{SmI}_2} \text{R-Sm}^{(\text{III})} \xrightarrow{\text{H}^+} \text{R-OH}
\]

Competition Reactions / Mechanistic Discovery

Samarium-Barbier Conditions:
Addition of $O$-Allyl-iodobenzene and acetophenone to a THF solution containing Samarium diiodide and HMPA

Samarium-Grignard Conditions:
Iodobenzene was added to a solution of $Sml_2$/HMPA after; 5 minutes acetophenone was added

Curran, D. P., Totleben, M., JACS, 1992, 114, 15
Cyclization Reactions

- Ester activates ketone
- Stereocontrol of 3 different centers
- Reactive electrophiles = lower yields

Cyclization Reactions

- Also forms:
  - Cyclohexanol
  - Cis fused
    - [3,0,3]
Cyclization Reactions

- Rings of various sizes (3,4,8) amongst variety created
- Isolated as stable, refined products
- Fast, clean reactions

Villar, H., Guibe, F., *Tet Lett.* **2002**, *43*
Influence of Additives

- Addition of HMPA accelerates reactivity and aids in selectivity (Also TMU, DMPU)

\[
\text{PhCHO} \xrightarrow{\text{Sml}_2, \text{THF/ HMPA}} \text{PhCHO} \xrightarrow{\text{Sml}_2} \text{PhCHO} + \text{H}_3\text{O}^+ \]

- Select solvents for preparation - THP shows no competing side reactions (ie ring opening)
- Addition of alcohols (MeOH or t-BuOH) is essential for desired product distribution via in situ protonation of intermediates or products
- Recent discoveries into complex combinations
  - Water/tertiary amine/SmI\(_2\) reductions in under 10 seconds
  - Rarely, if ever, have acid additives been used

Yang, S. M., Fang, J. M. J. Org. Chem. 1999, 64, 394
Kamochi, Y., Kudo, T., Tetrahedron 1992, 48
Metal Salts and Catalytic Variants

- 1980- Fe(III) & 1996- Ni(II) in catalytic amounts:

![Chemical structures with Sml₂ and Ni₂ (cat) THF reactions]

- Mg/Zn/Mischmetall

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Reformatsky-Type Reactions

Molander, G. H., Hahn, G. *J Org Chem*.
Moslin, Jamison, *JACS*, 2006, 128
Pinacol-Like

$\text{R}_1\text{C}O\text{C}\text{R}_2\xrightarrow{\text{Sml}_2} \text{O}^\cdot\text{Sm}^\cdot\text{O}\xrightarrow{\text{Sml}_2} \text{HO}\text{OH}$

Carbonyl-Alkene Reactions

\[ \text{Sml}_2, \text{HMPA, THF} \quad (93\%, 1.4:1) \]
\[ \text{add PhSH} \quad 71\% \]

via

\[ \text{I}_2\text{SmO} \]

\[ \text{Me} \]

\[ \text{O} \]

\[ \text{Bn} \]

\[ \text{Me} \]

\[ \text{O} \]

\[ \text{Bn} \]

\[ \text{Me} \]

\[ \text{O} \]

\[ \text{Bn} \]

\[ \text{patchoulenone} \]

\[ \text{Me} \]

\[ \text{O} \]

\[ \text{Bn} \]

\[ \text{Me} \]

\[ \text{O} \]

\[ \text{Bn} \]

\[ \text{Me} \]

\[ \text{O} \]

\[ \text{Bn} \]

\[ \text{Me} \]

\[ \text{O} \]

\[ \text{Bn} \]

\[ \text{Me} \]

\[ \text{O} \]

\[ \text{Bn} \]

\[ \text{Me} \]

\[ \text{O} \]

\[ \text{Bn} \]

\[ \text{Me} \]

\[ \text{O} \]

\[ \text{Bn} \]

\[ \text{Me} \]

\[ \text{O} \]

\[ \text{Bn} \]

Banwell, M, McLeod, M. *Chem Comm.* **1998** 1851-1852

Elimination Reactions

Reductive Deconjugation

Successive Single-Electron Reductions

Cascade Reactions


Cascade Reactions


A Transition Metal!

- First ever organosamarium generated from organopalladium to undergo elimination/fragmentation

Beyond SmI₂: SmBr₂

SmBr₂ – 0.57 V stronger reductant than iodine equivalent

Miller, R. S. et al., JACS, 2000, 122, 7718
Cha, J. Y., Yeoman, J. T. S., Reisman, S. E., JACS, 2011, 133
Beyond SmI$_2$: DyI$_2$

- Redox potential: Dy -2.5 V, Mg -2.4 V, Na -2.7 V, K -2.9 V

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Mander, L. N. *Comprehensive Organic Syntheses* Vol. 8
Beyond SmI$_2$: NdI$_2$

- NdI$_2$ -2.6 V reduction potential (strongest lanthanide to date)

Conclusions and Future Outlook

• Extremely powerful reactivity-
  • Highly tunable via optimization of reaction conditions
  • Conceptually attractive, but also overwhelming

• Limitations still exist-
  • Price/molecular weight of Sm
  • Poor catalytic activity

• Future advances-
  • Photoinduced Reductions
  • Redox-active ligands

• “We hope that divalent lanthanide derivatives could form novel class of useful reagents for organic synthesis”
Thank You! Questions?