SAMARIUM 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

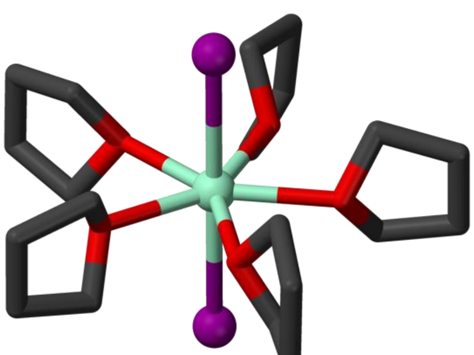
Before 1977

$$Sm \xrightarrow[\text{0.01 mm Hg}]{750^0} SmI_3$$

Kagan's Work (1977)

$$Sm \xrightarrow[\text{THF, r.t.}]{ICH_2CH_2I} SmI_2(thf)_n$$

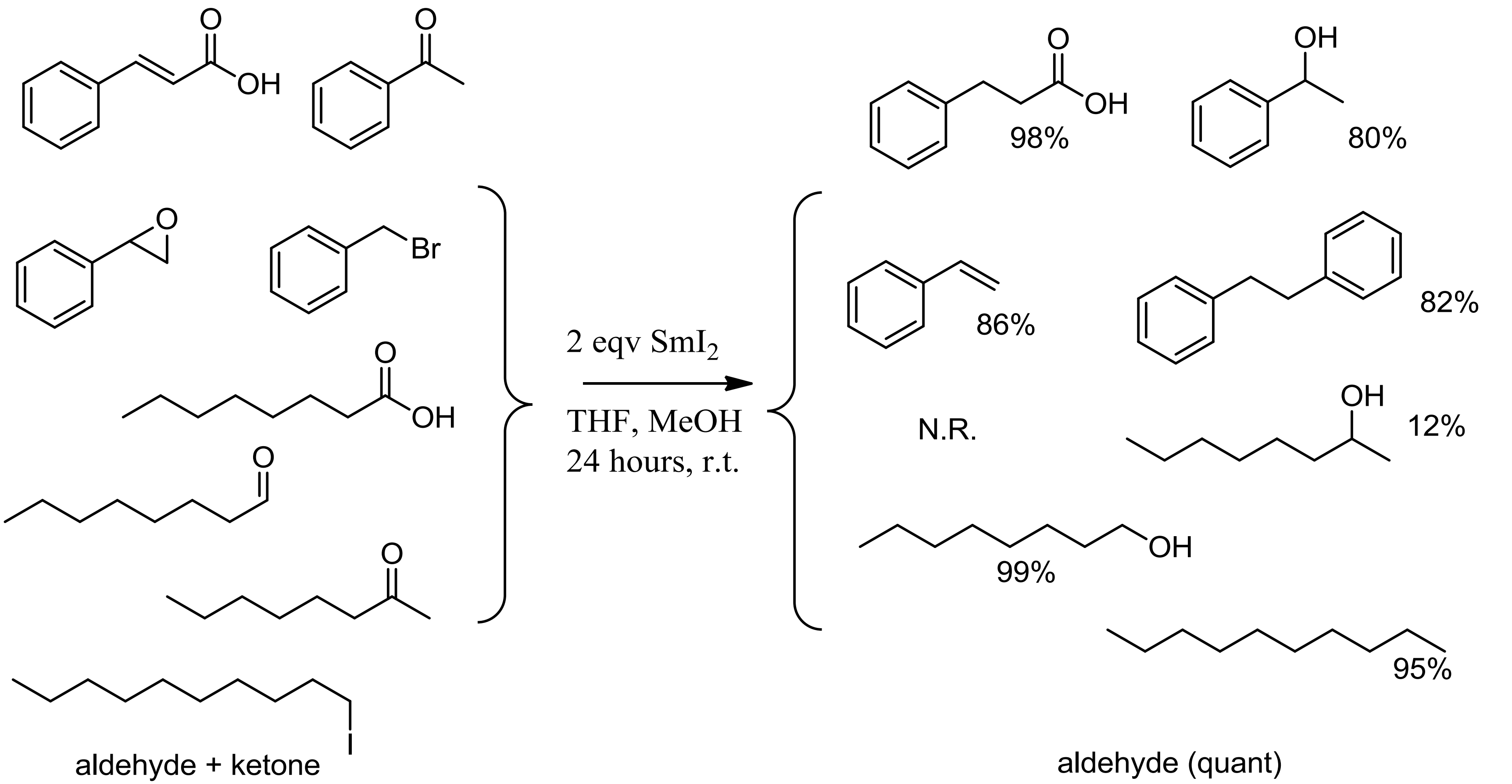
- Known by inorganic chemists since 1906
  - Ubiquitous in nature, commercial applications
- Highly dependent on solvent and additives (more later)
- Solution goes from dark blue (Sm(II)) to yellow (Sm(III)) over time
- Generally prepared and used in situ



Entry	Ln	Electron configuration of Ln	Ionic radius Ln^{II} [Å][a]	Ionic radius Ln^{III} [Å][b]	Oxophilicity D_0(Ln-O) [kcal mol^{-1}][c]	E° Ln^{III}/L^{II} [V][d]
1	Nd	$[Xe]4f^4 6s^2$	1.29	1.16	179	−2.62
2	Sm	$[Xe]4f^6 6s^2$	1.27	1.13	138	−1.55
3	Eu	$[Xe]4f^7 6s^2$	1.25	1.12	93	−0.35
4	Dy	$[Xe]4f^{10} 6s^2$	1.19	1.08	145	−2.56
5	Tm	$[Xe]4f^{13} 6s^2$	1.09	1.05	116	−2.22
6	Yb	$[Xe]4f^{14} 6s^2$	1.14	1.04	88	−1.15

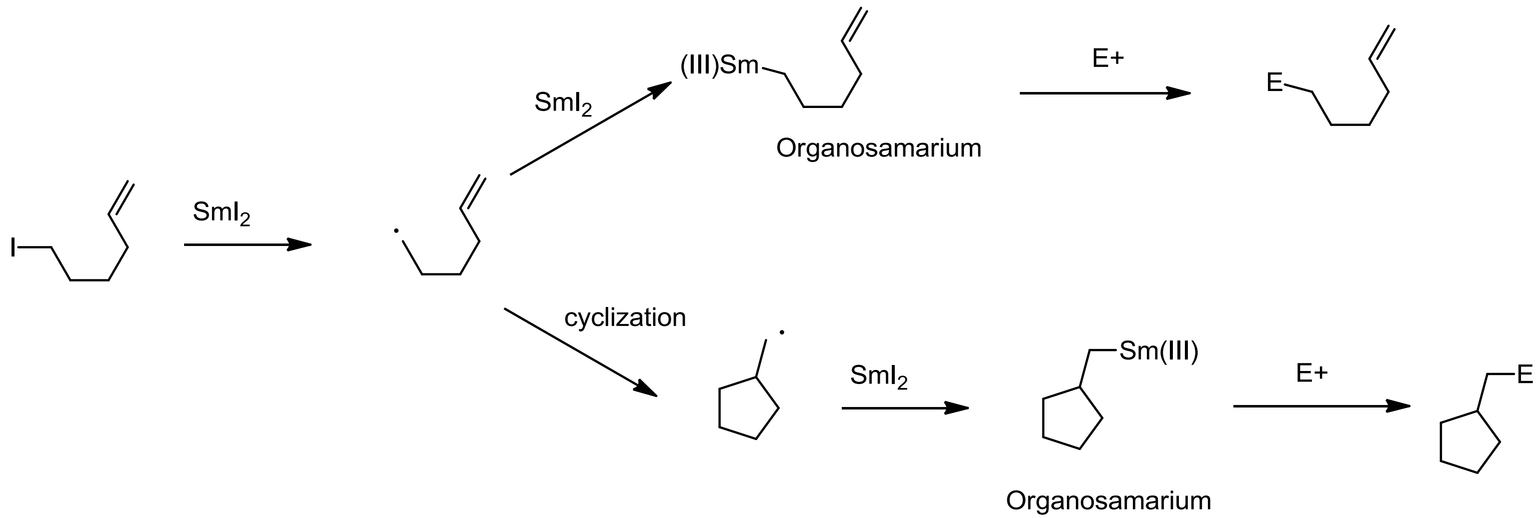
Namy, J. L., Girard, P., Kagan, H. B. *New J Chem* **1977**

Seminal Work- Reduction Reactions



Girard, P., Namy, J. L., Kagan, H.B. *JACS*, **1980** , 2693

Proposed Reactivity

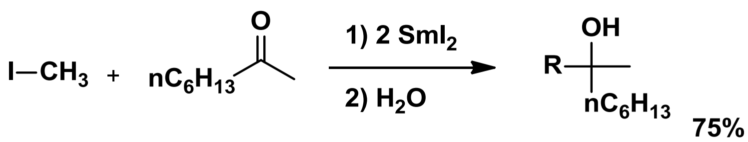


- Ability to promote one and two electron processes :
  radical/radical, radical/anionic, anionic/radical, anionic/anionic

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

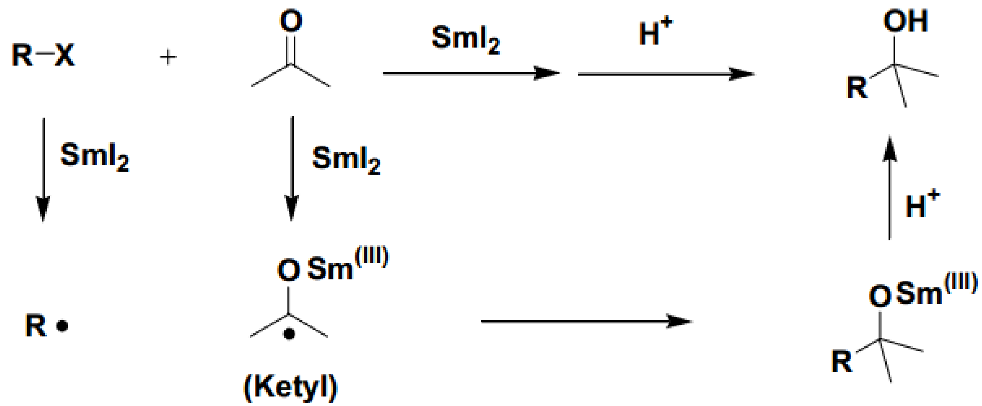
Namy, J. L., Girard, P., Kagan, H. B. *New J Chem* **1977**

Samarium Grignard and Samarium Barbier

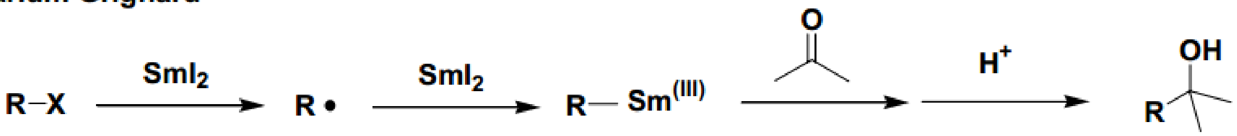


R=
n-butyl iodide 97%
n-butyl chloride 8%
sec butyl bromide 27%
tert-butyl bromide 9%

Samarium Barbier

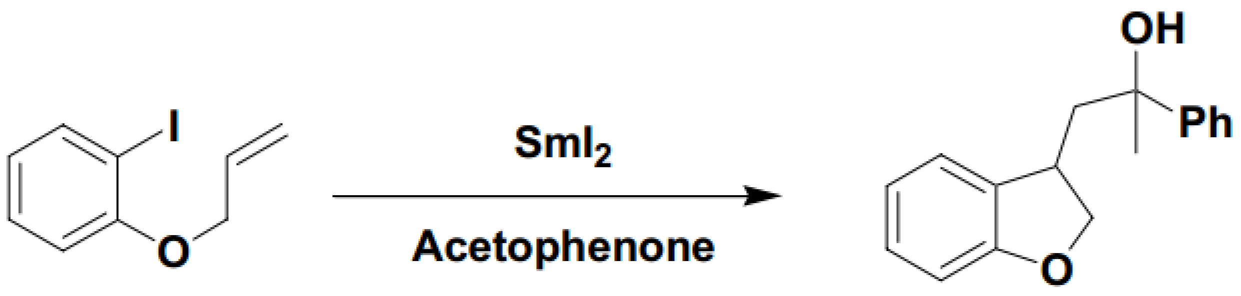


Samarium Grignard



Girard, P., Namy, J. L., Kagan, H.B. *JACS,* **1980** , 2693
Molander, G. A., Etter, J.B. *J. Org. Chem.*, **1986**, *51* (10), pp 1778–1786

Competition Reactions / Mechanistic Discovery



Sm-Barbier	Sm-Grignard
< 20%	89%

Samarium-Barbier Conditions:

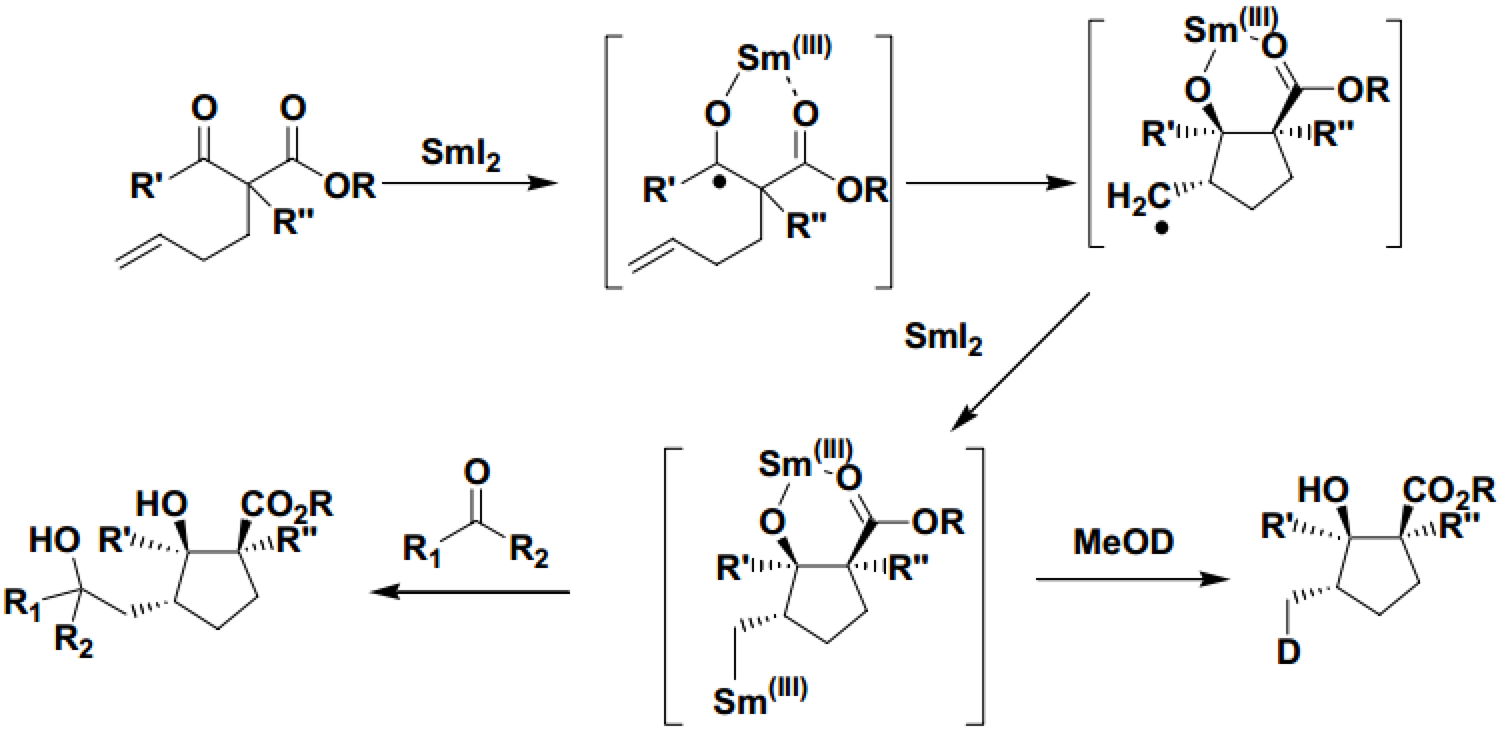
Addition of *O*-Allyl-iodobenzene **and** acetophenone to a THF solution containing Samarium diiodide and HMPA

Samarium-Grignard Conditions:

Iodobenzene was added to a solution of SmI_2/HMPA after; 5 minutes acetophenone was added

Curran, D. P., Totleben, M., *JACS*, **1992**, *114, 15*

Cyclization Reactions

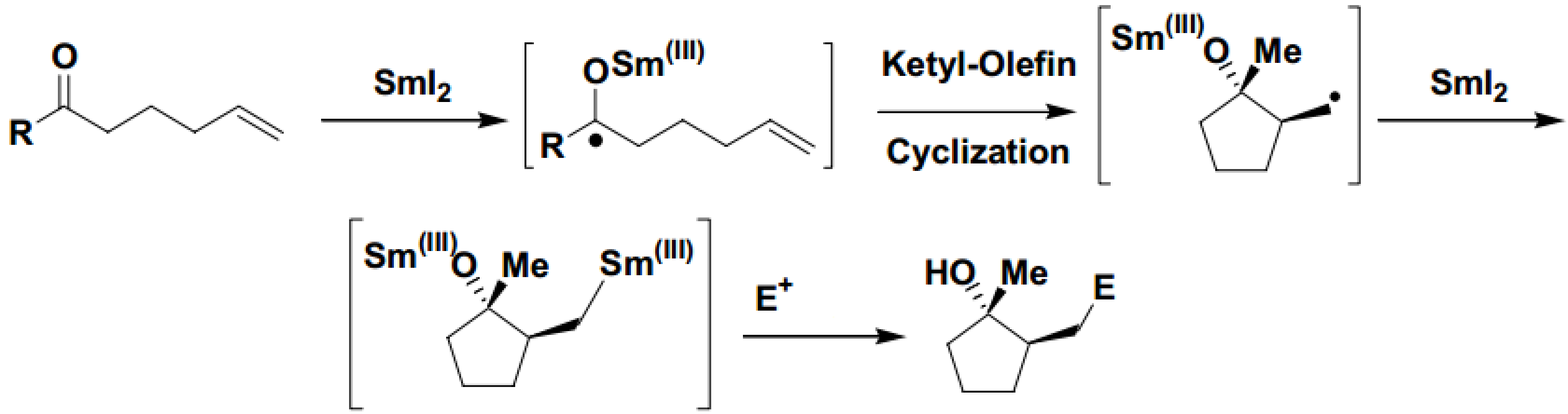


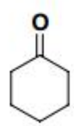
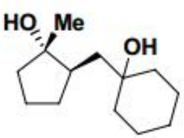
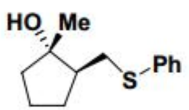
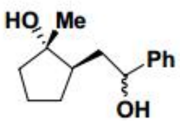
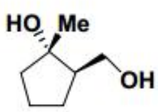
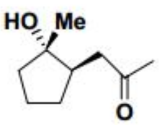
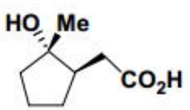
- Ester activates ketone
- Stereocontrol of 3 different centers
- Reactive electrophiles = lower yields

Ketone	% Yield	d.r.
Acetone	79	31:1
3-Pentanone	73	65:1
Diisopropyl ketone	32	>200:1
Cyclohexanone	58	200:1
Cyclopentanone	65	60:1
2-Methylcyclohexanone	75	1:1
4-*t*-Butylcyclohexanone	61	10:1

Molander, G. A.; Kenny, C. *J Org Chem.* **1991**, 56

Cyclization Reactions

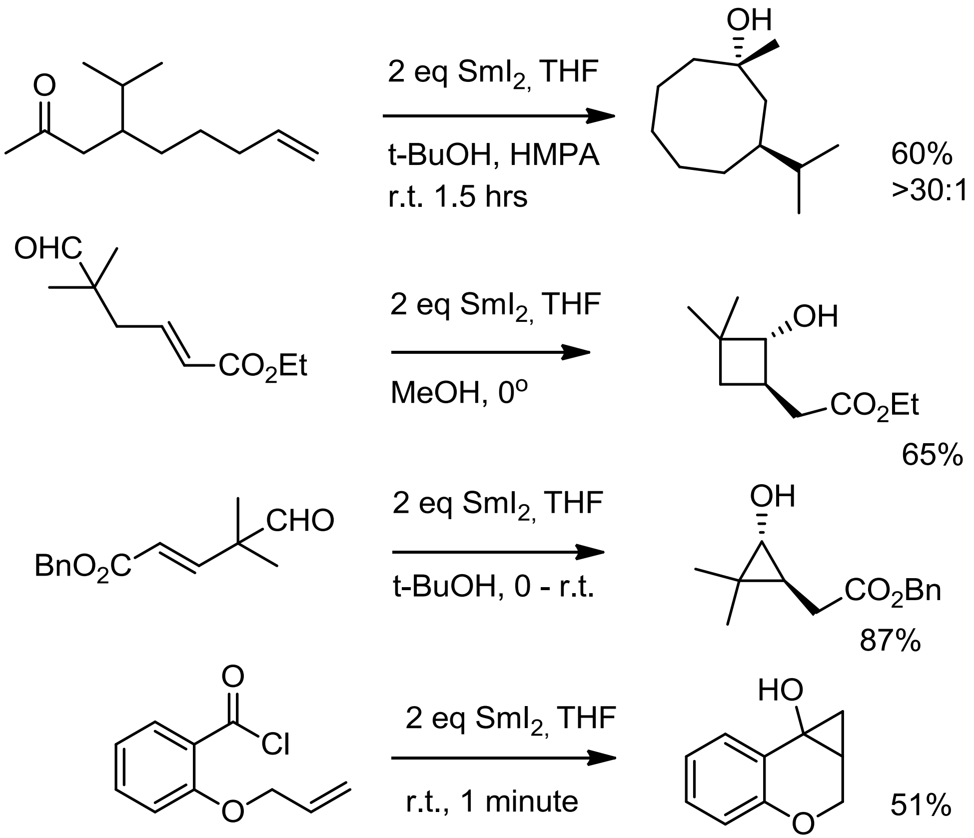


Electrophile	Product	% Yield	Electrophile	Product	% Yield
		80	$(PhS)_2$		77
PhCHO		83 (3:1)	O_2		69 (15:1)
Ac_2O (2 eq., 0 °C, 15 min)		74	CO_2		73

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

Molander, G. A.; Kenny, C. *J Org Chem.* **1992**, 57
Warner, P. *J Org Chem*, **1972**

Cyclization Reactions

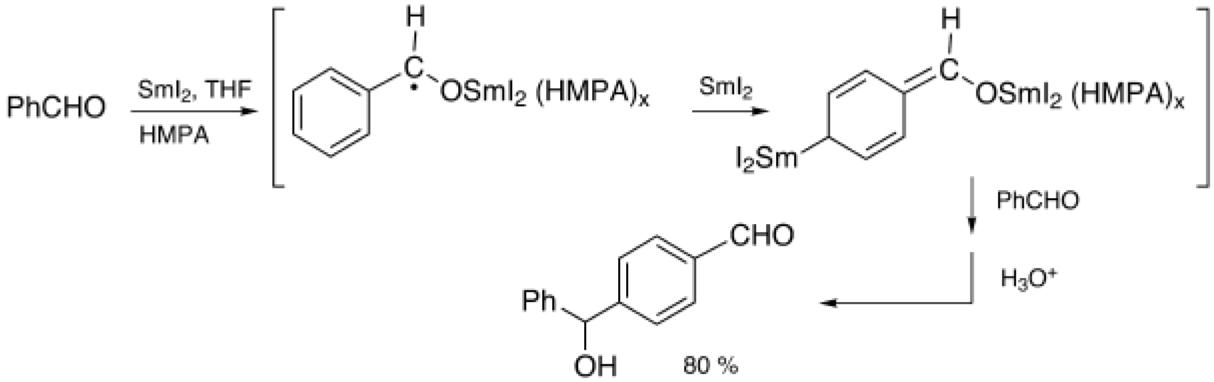


- Rings of various sizes (3,4,8) amongst variety created
- Isolated as stable, refined products
- Fast, clean reactions

Molander, G. A., Kenny, C. *JACS* **1994,** 59
Johnston, D., et al. *J Chem Soc.* **2000**, 681
Villar, H., Guibe, F., *Tet Lett.* **2002**, 43
Kagan, H. B., et al., *Tet Lett* **1988**, 29

Influence of Additives

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

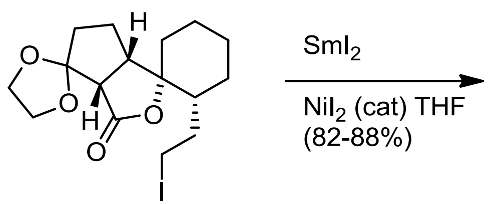


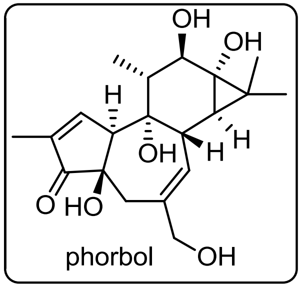
- Select solvents for preparation- THP shows no competing side reactions (ie ring opening)
- Addition of alcohols (MeOH or t-BuOH) is essential for desired product distribution via in situ protonation of intermediates or products
- Recent discoveries into complex combinations
  - Water/tertiary amine/SmI_2 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
Dahlen, A., Hilmersson, G., *Chem Eur J.,* **2003** , *9*
Kamochi, Y., Kudo, T., *Tetrahedron* **1992**, *48*

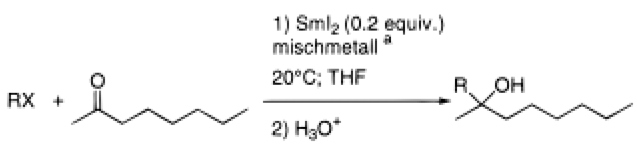
Metal Salts and Catalytic Variants

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

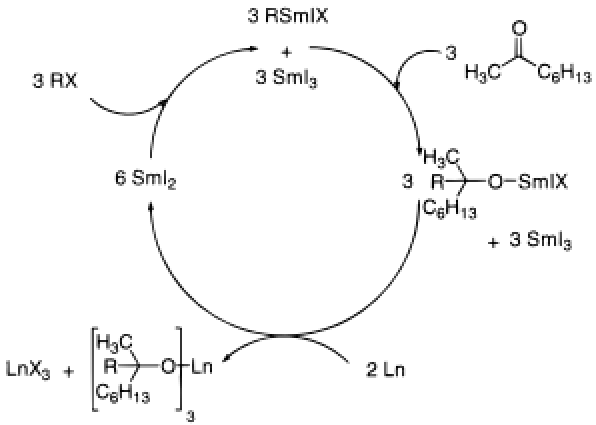




- Mg/Zn/Mischmetall

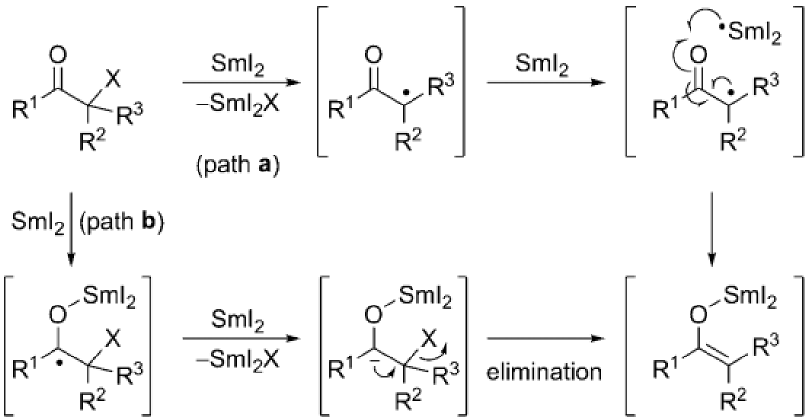


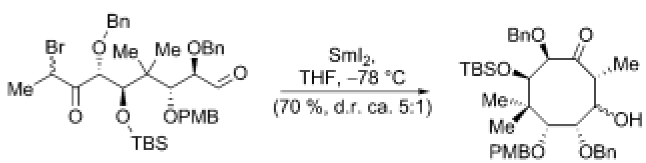
run	RX	reaction conditions[a]	isolated yields of products (%)
1	allyl iodide	1.5 h then 0.5 h	90
2	allyl bromide	3.5 h then 0.5 h	91
3	benzyl bromide	3.0 h then 0.5 h	91
4	ethyl iodide	3.5 h then 1 h	52
5	ethyl iodide	6.5 h then 1 h	67
6	ethyl iodide	2.5 h then 1 h	67[b]

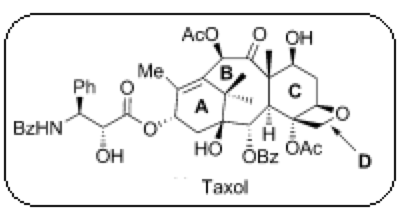


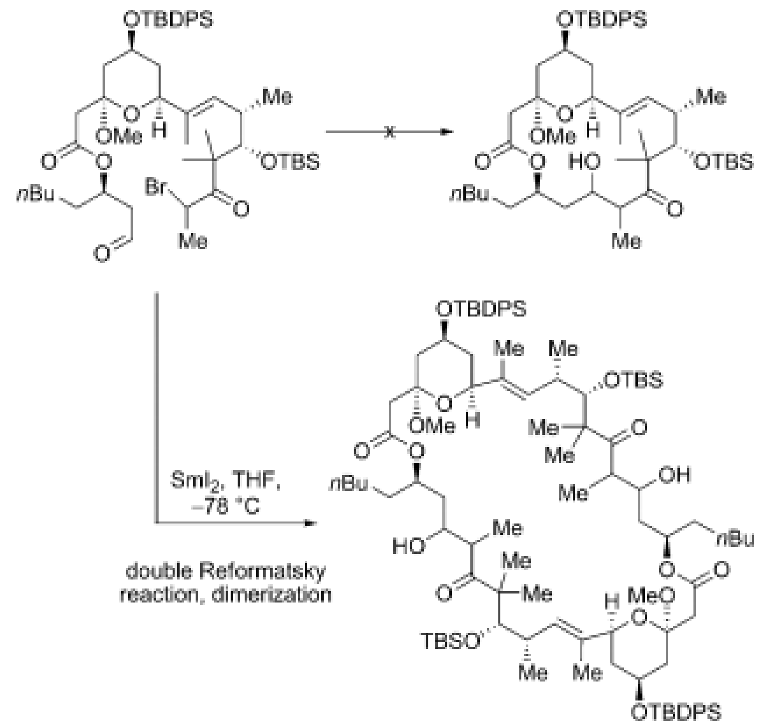
Carroll, G. L., Little, R. D., *Org Lett*, **2000**, 2
Nomura, R., et al., *JACS* **1996**, 118
Helion, F., Namy, J. L. *J Org. Chem.*, **1999**, 64

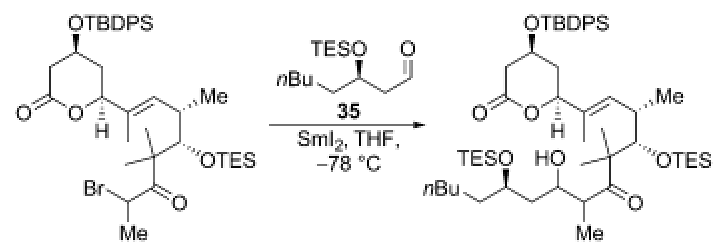
Reformatsky-Type Reactions





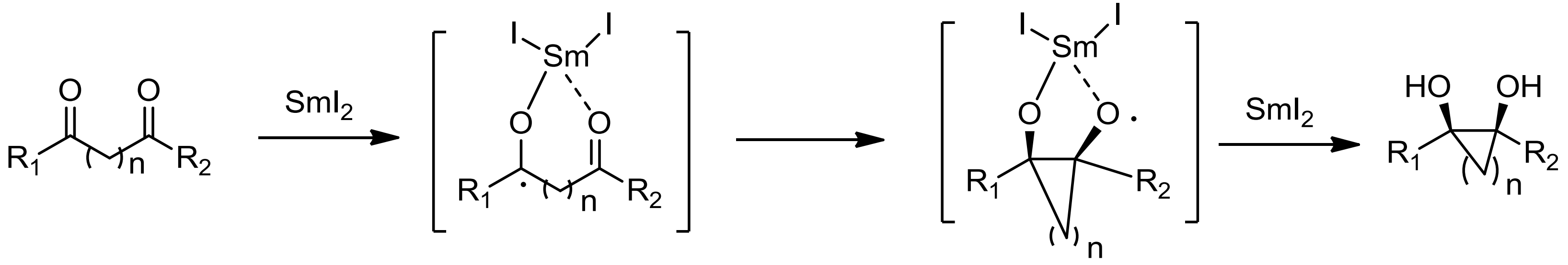


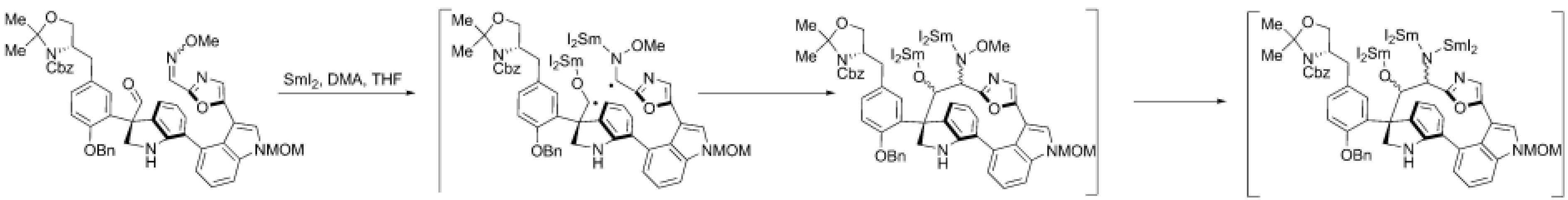


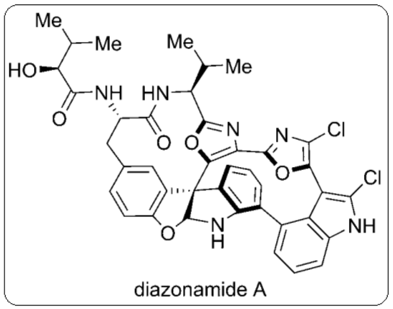


Molander, G. H., Hahn, G. *J Org Ch em .* Moslin, Jamison, *JACS*, **2006**, *128* Mukaiyama, T., et al., *Proc. Jpn. Acad., Ser. B.*, **1997**, 73

Pinacol-Like

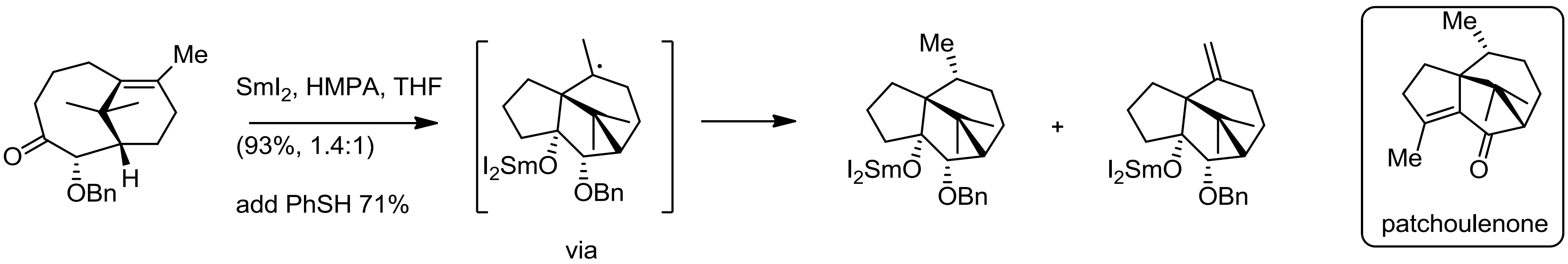


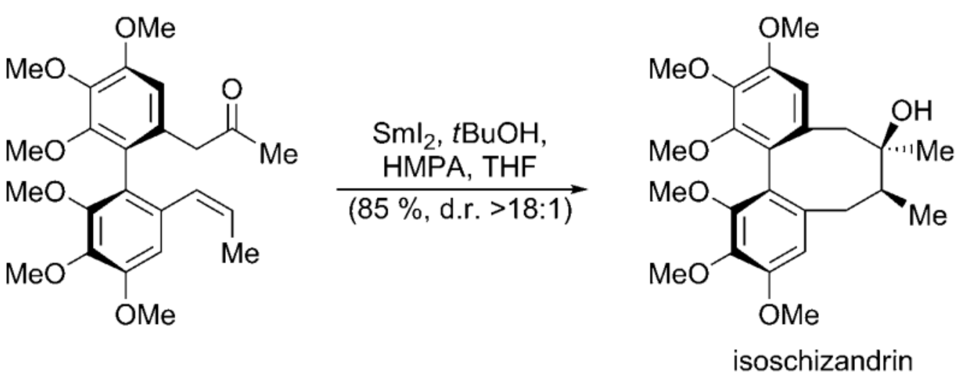


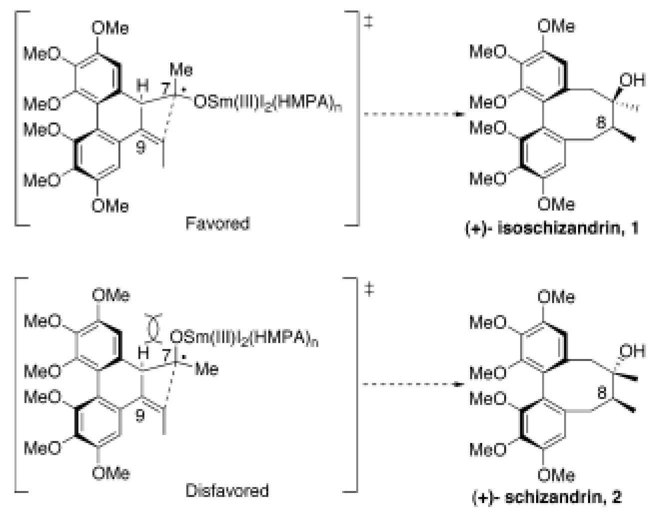


Molander, G. A., Kenny, C., *J Org Chem*, **1988**, 53
Nicolaou, K. C., et al. *Angew Chem* **2001**, 113

Carbonyl-Alkene Reactions





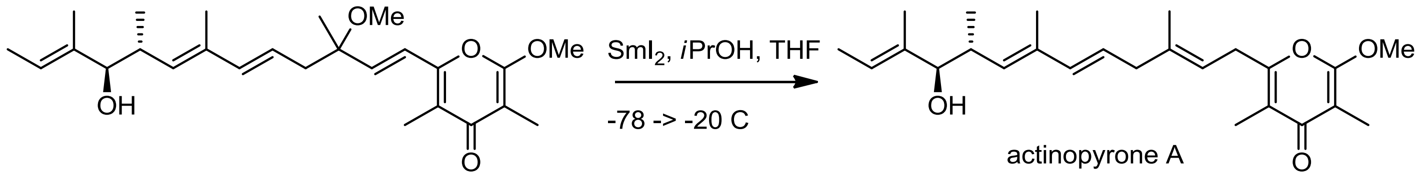


Banwell, M, McLeod, M. *Chem Comm.* **1998** 1851-1852

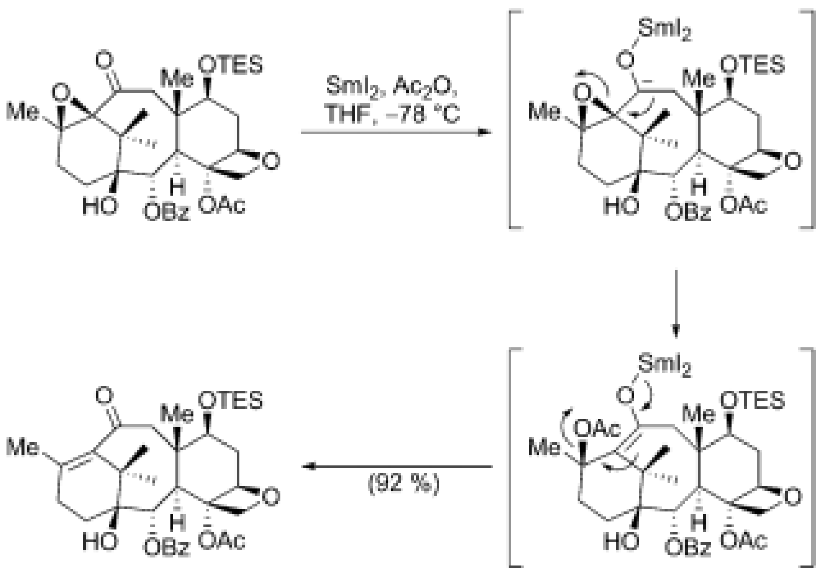
Molander, G. A., et al. *J Org Chem.* **2003**, *68*

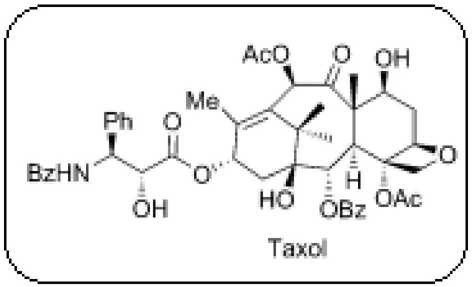
Elimination Reactions

Reductive Deconjugation



Successive Single-Electron Reductions



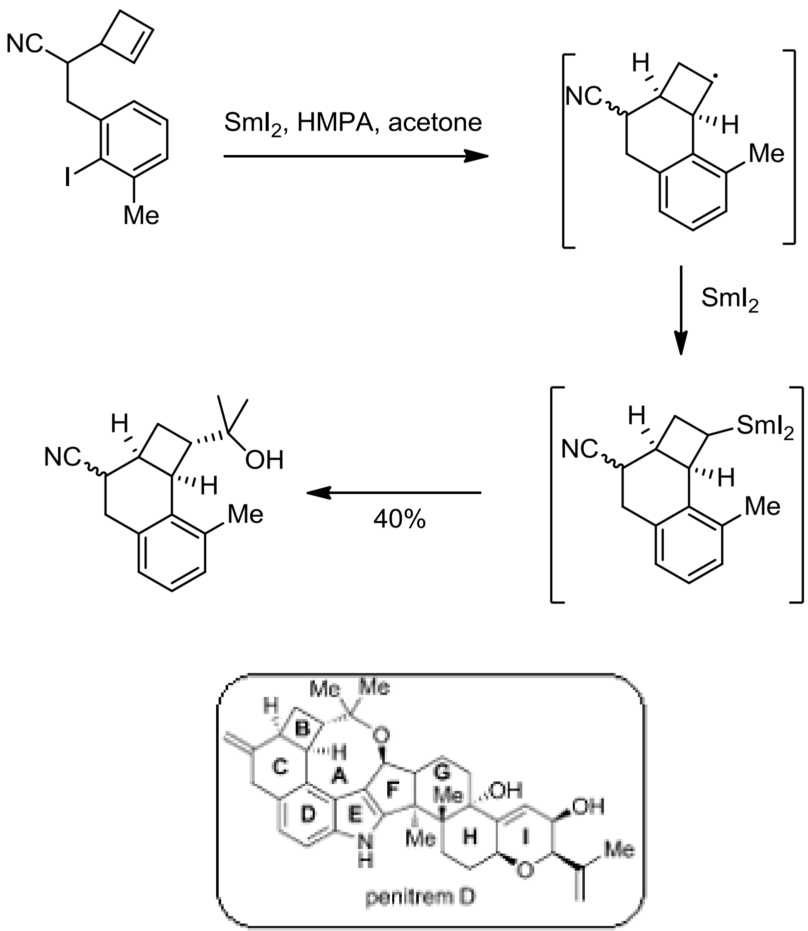


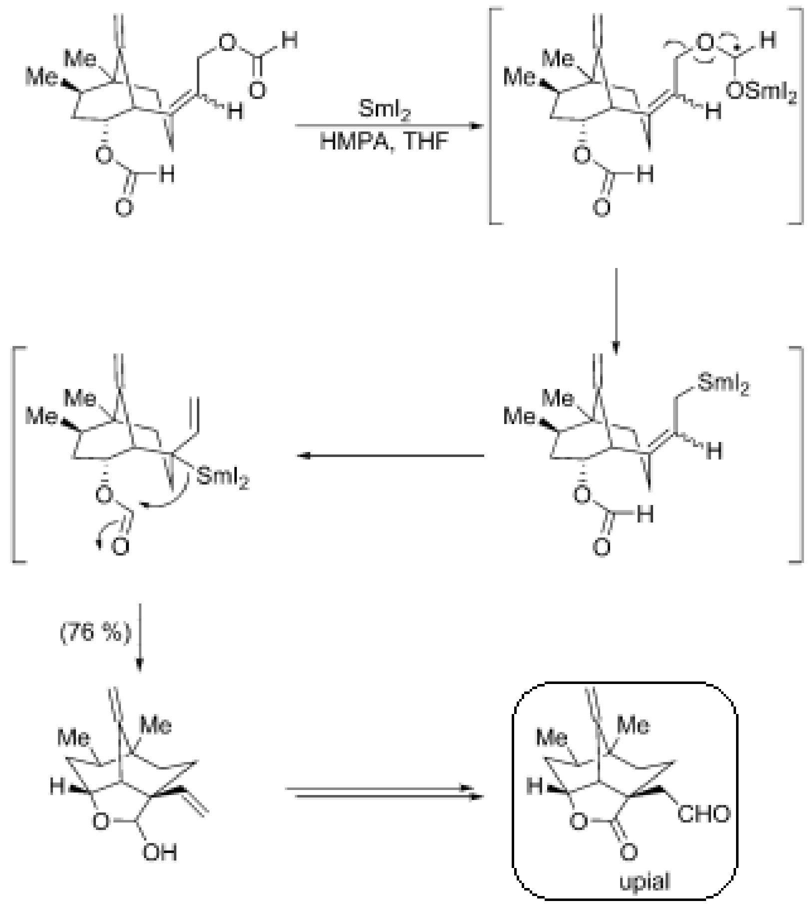
Hosokawa, S., et al. *Tet Lett* **2006**, 47

Otaka, A., et al. *Chem Comm*, **2003**, 1834-1835

Masters, J. L., Danishefsky, S., et al., *Angew Chem* **1995** *107*

Cascade Reactions

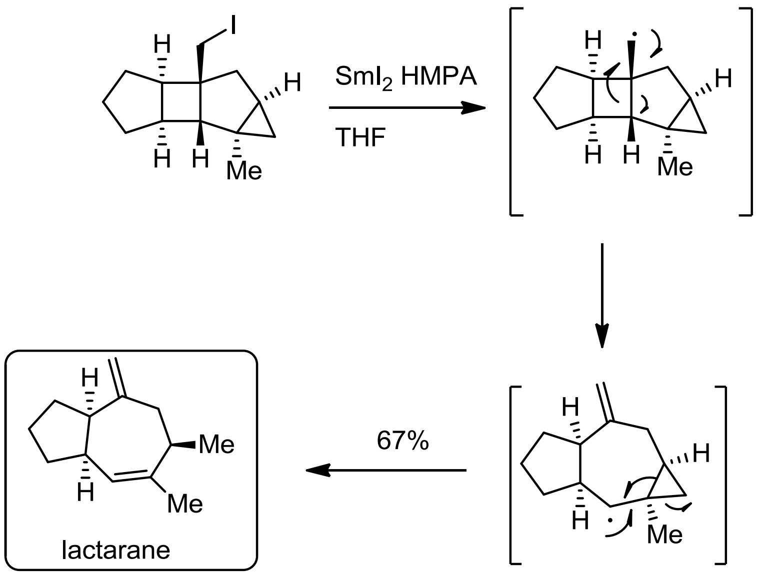


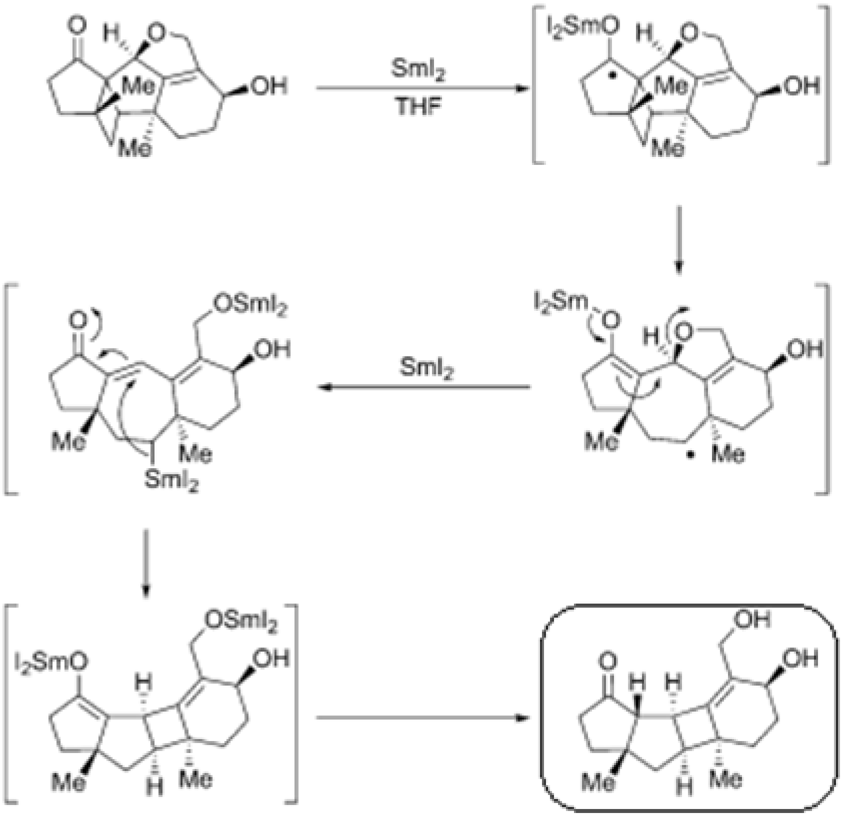


Curran, D. P., et al. *J Org Chem*, **2004**, 69

Nagaoka, H., Shibuya, K., Yamada, Y., *Tet Lett* **1993**, 34

Cascade Reactions



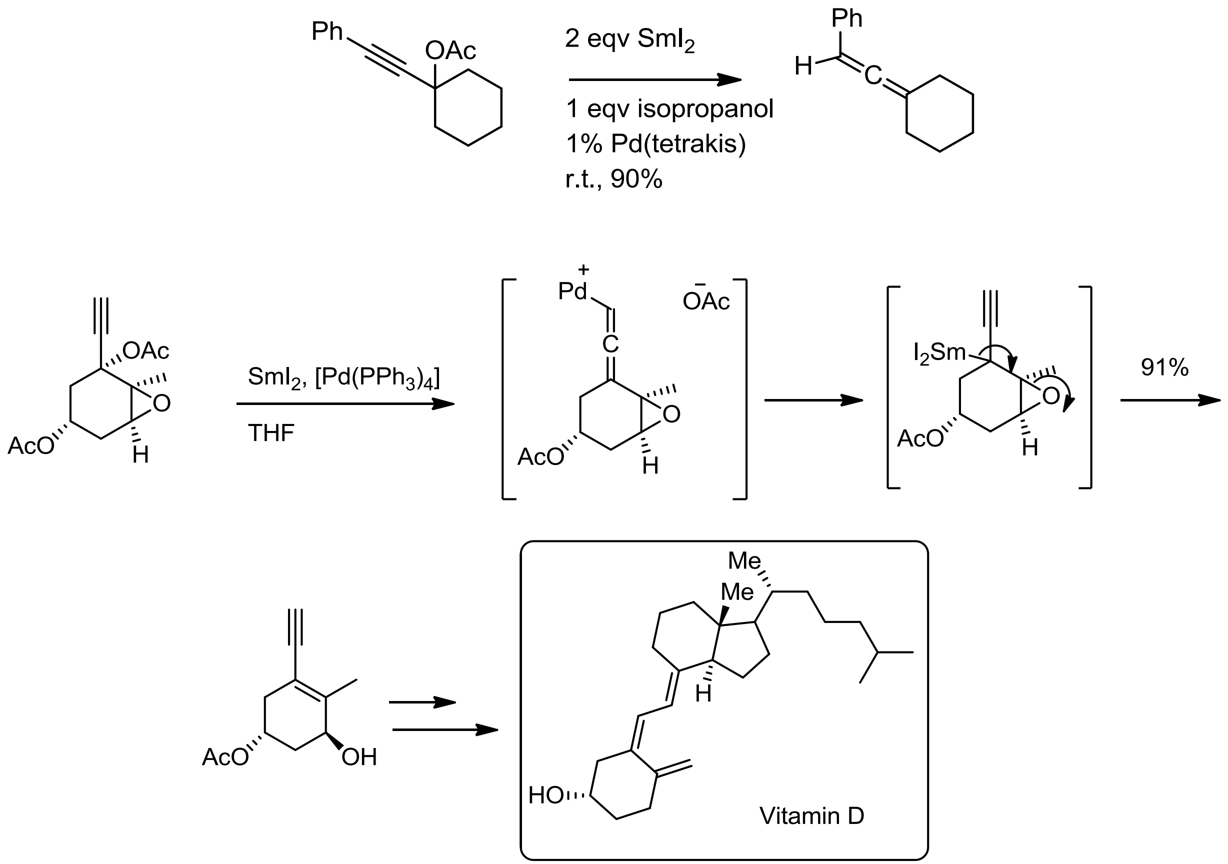


guanacastapene

Lange, G. L., Corelli, N., *Tet Lett*, **2007**, 48

Shipe, W. D., Sorensen, E. J., *JACS*, **2006,** 128

A Transition Metal!

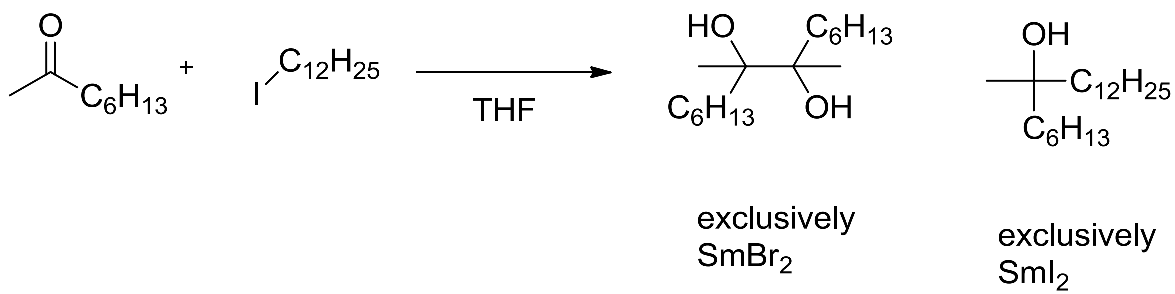


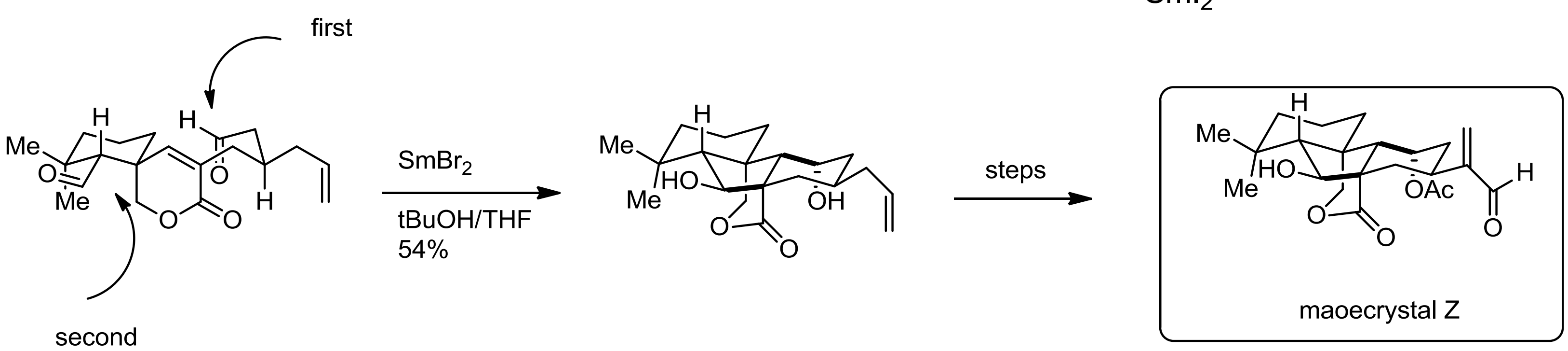
- First ever organosamarium generated from organopalladium to undergo elimination/fragmentation

Okamura, W. H., et al., *J Org Chem*, **1989,** 54
Tabuchi, T., Inanaga, J., *Tet Lett*, **1986**, 27
Tabuchi, T., Inanaga, J.,*Tet Lett* **1986**, 27, 43

Beyond SmI_2: $SmBr_2$

$SmBr_2$ –0.57 V stronger reductant than iodine equivalent

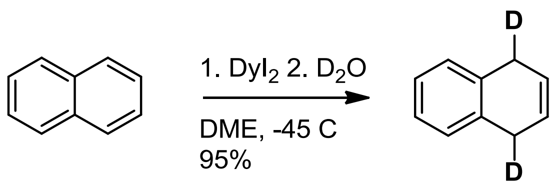


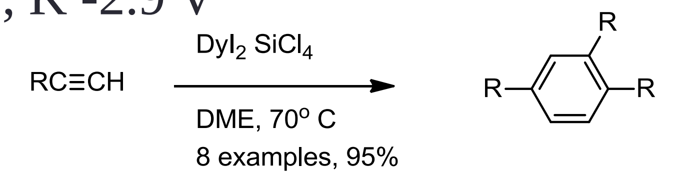


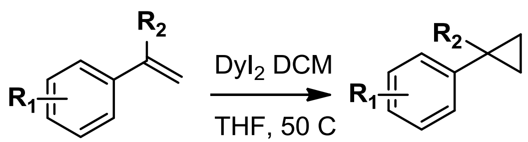
Miller, R. S. et al., *JACS* , **2000**, 122, 7718
Cha, J. Y., Yeoman, J. T. S., Reisman, S. E., *JACS*, **2011,** 133

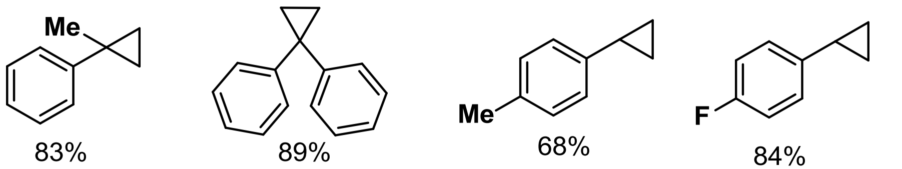
Beyond SmI_2: DyI_2

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

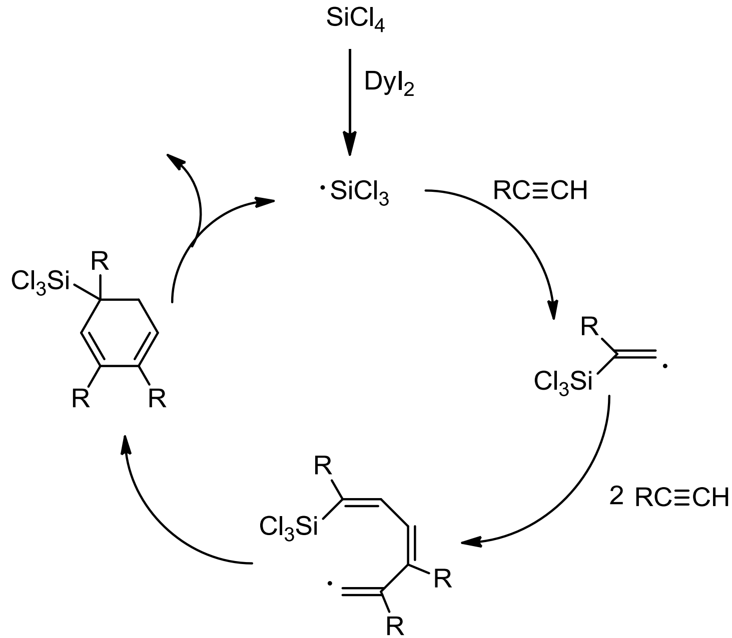




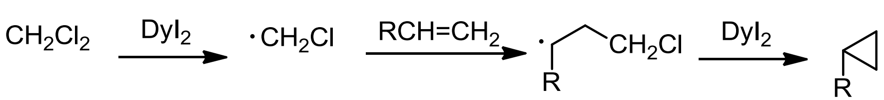




proposed mech.



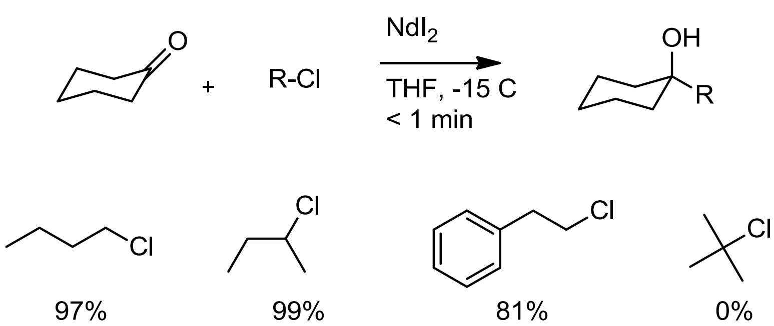
proposed mechanism



Mander, L. N. *Comprehensive Organic Syntheses Vol. 8*
Xiang, X., et al., *Organometallics*, **2008**, 27, 1959
Zhu, Z. et al., *Chem Commun*, **2006**, 2066

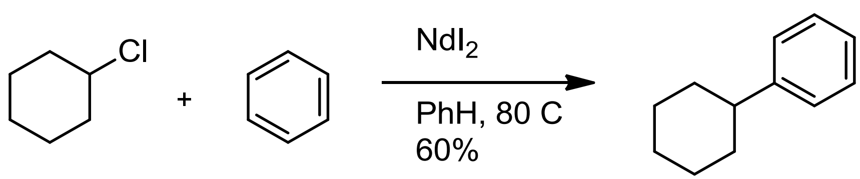
Beyond SmI_2: NdI_2

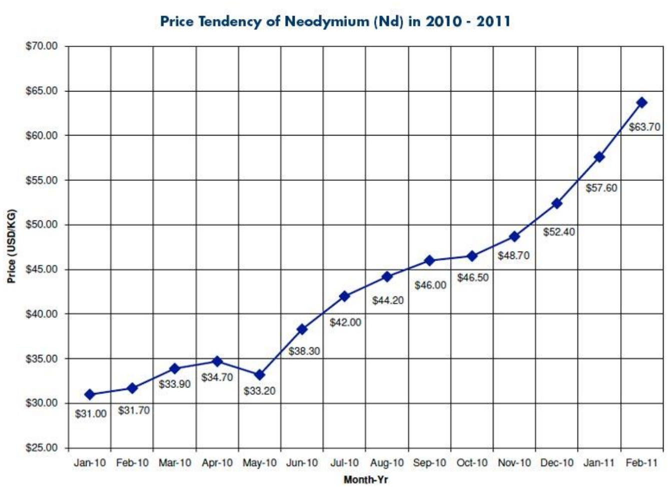
- NdI_2 -2.6 V reduction potential (strongest lanthanide to date)



Entry	Reagent	E° (Ln^{III}/L^{II})[a]	Unactivated R-Cl[b]	Birch reduction
1	$[SmI_2(hmpa)]$	−2.05 V	−	−
2	TmI_2	−2.22 V	+	−
3	DyI_2	−2.56 V	+	+
4	NdI_2	−2.62 V	+	+

[a] For entry 1 values are vs $Ag/AgNO_3$ in THF;[20b] for entries 2–4 values are vs NHE.[67] [b] For entry 1: 25 °C, 18 h; for entry 2: 0 °C, 1 h; for entries 3 and 4: < 0 °C, < 5 s.





Evans, W. J., et al., *Org Lett*, **2003**, 5
Bochkarev, M. N., et al., *Polyhedron* **2006**, 25

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?