

Si vs. C

- Si is less electronegative than C
- More facile nucleophilic addition at Si center

Average BDE (kcal/mol)

C-C	C-Si	Si-Si	C-F	Si-F
83	76	53	116	135
C-O	Si-O	C-H	Si-H	
86	108	83	76	

Average Bond Lengths (Å)

C-C	C-Si	C-O	Si-O
1.54	1.87	1.43	1.66

Silicon forms weak π -Bonds

- π - C-C = 65 kcal/mol
- π - C-Si = 36 kcal/mol

Siliconium Ion

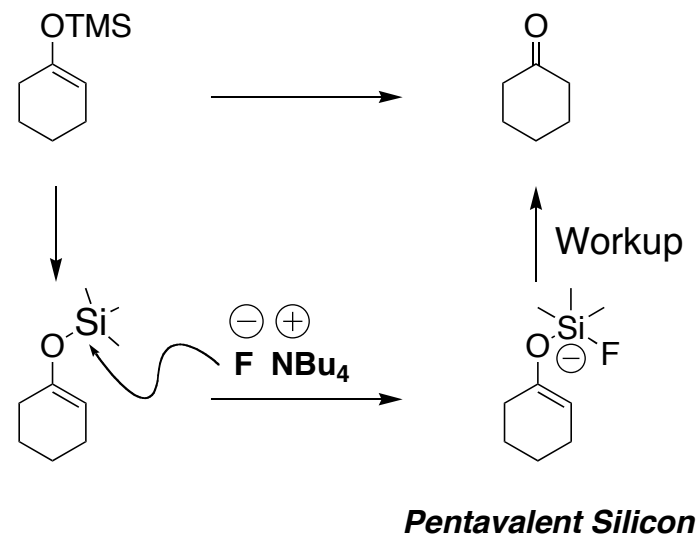
- Not believed to exist in any reaction in solution
J. Y. Corey, *J. Am. Chem. Soc.* **1975**, *97*, 3237

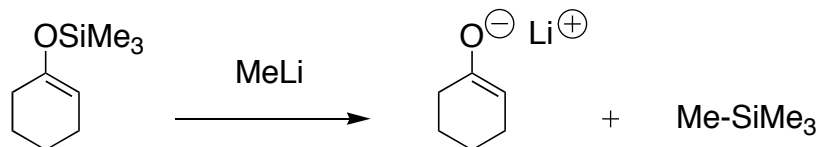
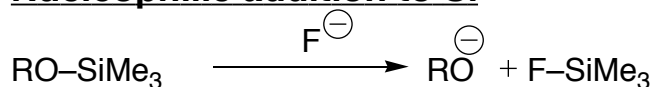
- Pentacoordinate Si compounds have been observed



- Lack of cation justified by high rate of bimolecular reactivity at Si

Mechanism of TMS Deprotection



Nucleophilic addition to Si

Duhamel et al. *J. Org. Chem.* **1996**, *61*, 2232

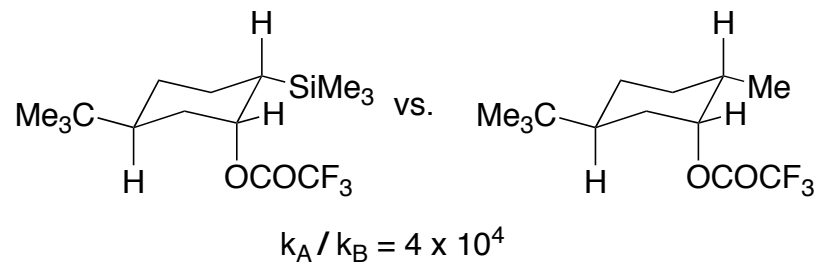
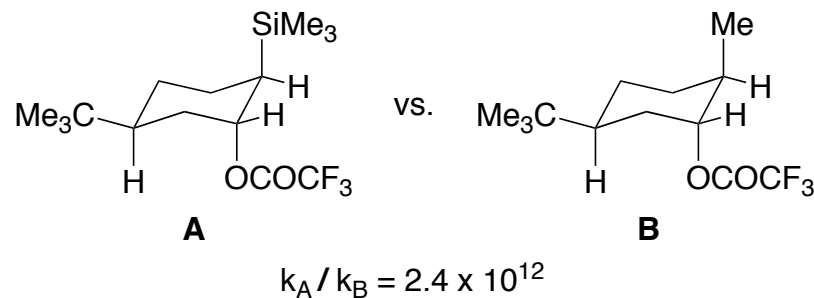
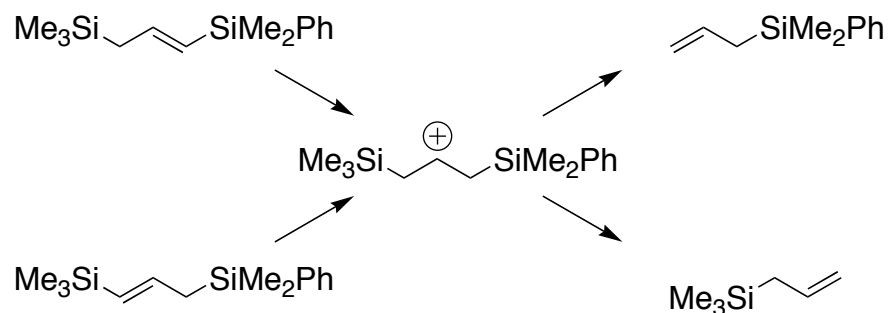
β-Silicon Effect

- Silicon stabilizes β-carbocations
- Stabilization is a result of hyperconjugation

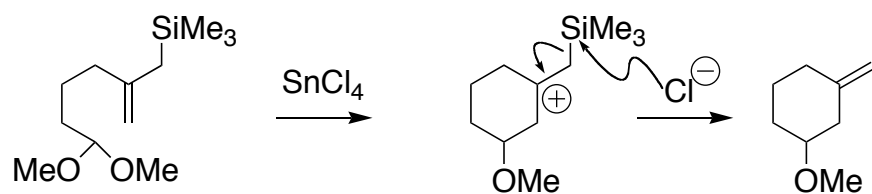


* **A** is more stable than **B** by 38 kcal/mol *

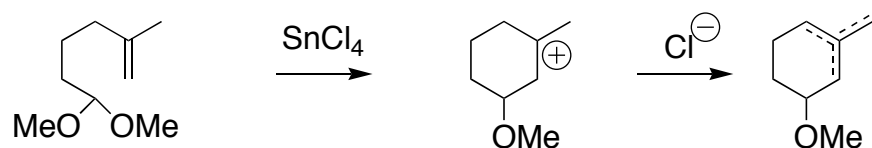
Jorgensen, *JACS*, **1986**, *107*, 1496

α-Silicon effect and SolvolysisEvidence for Stepwise mechanism

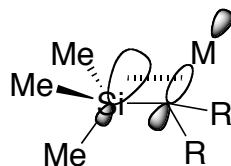
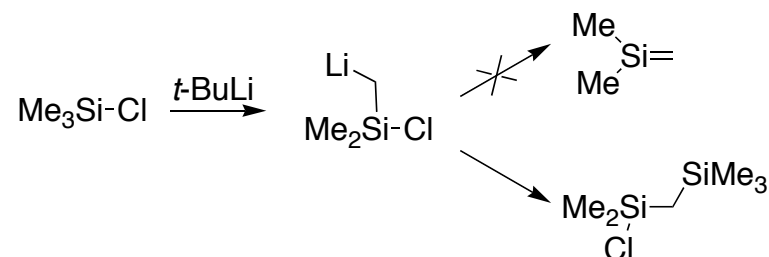
Product ratios are equal from either starting material suggesting common intermediate cation

Evidence for Rapid Nucleophilic Attack

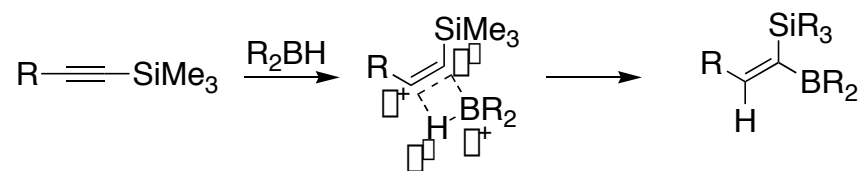
vs.

Fleming et al., *JCS Chem. Com.* **1976**, 182Organosilanes Stabilize C-M Bonds

- Metallation occurs \square to silicon
- Hyperconjugation gives stability

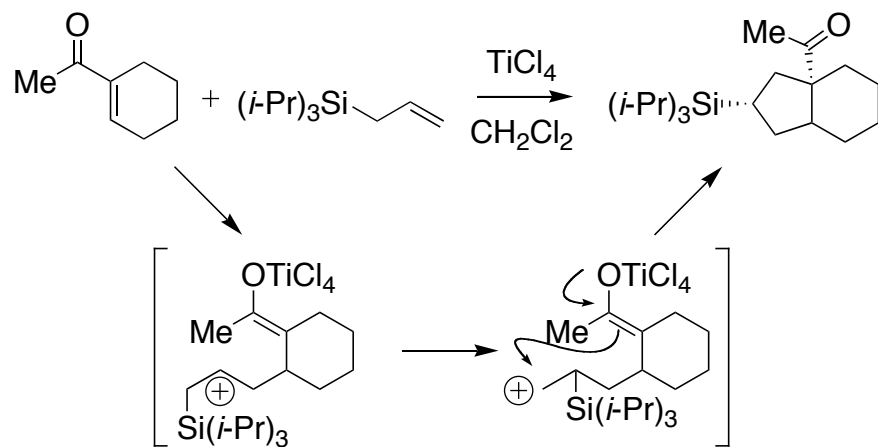
Extraordinary MetallationGornowicz et al., *J. Am. Chem. Soc.* **1968**, 90, 4478Cation-Anion Harmony

- Stabilization of \square -anion and \square -cation exemplified in regioselectivity of the hydroboration of alkynylsilanes

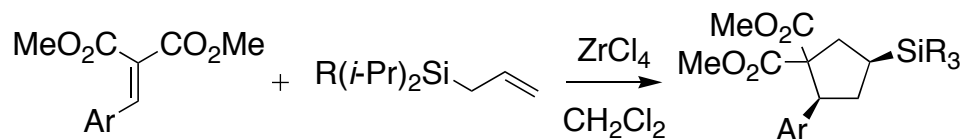
Zweifel et al., *J. Am. Chem. Soc.* **1977**, 99, 3184

Silicon Migration

- Conjugate addition can be followed by Si migration
- Migration aptitude enhanced when Si has bulky R groups



A. I. Meyers, *J. Org. Chem.* **1998**, *63*, 5517

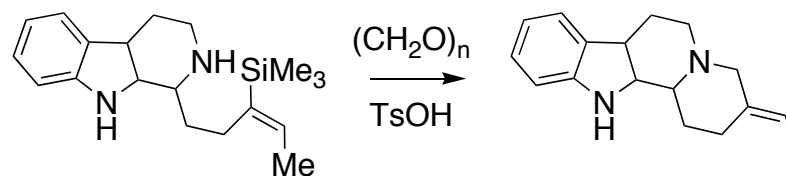
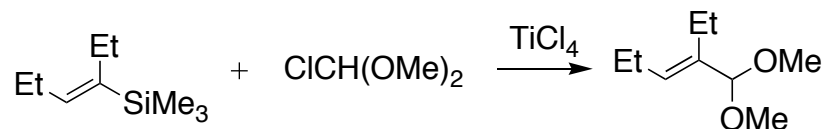


$\text{R} = i\text{-Pr, Ph}$

diastereomeric ratio 96:4, ~ 70% yield

Vinylsilane Reactivity

- React with electrophiles
- Regioselectivity governed by creation of β -carbocation
- Elimination of SiR_3 occurs with retention of initial double bond geometry due to principle of least motion
- Limited rotation also prevents eclipsing interactions between silyl group and olefin substituents

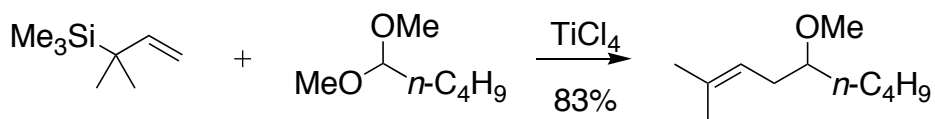
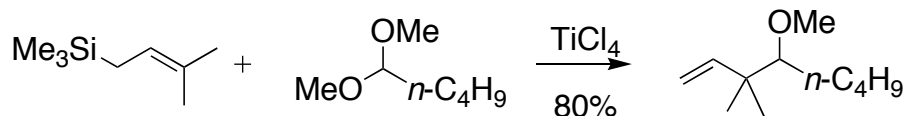
Vinylsilane Examples

Grieco et al. *J. Chem. Soc. Chem. Comm.*, **1987**, 185

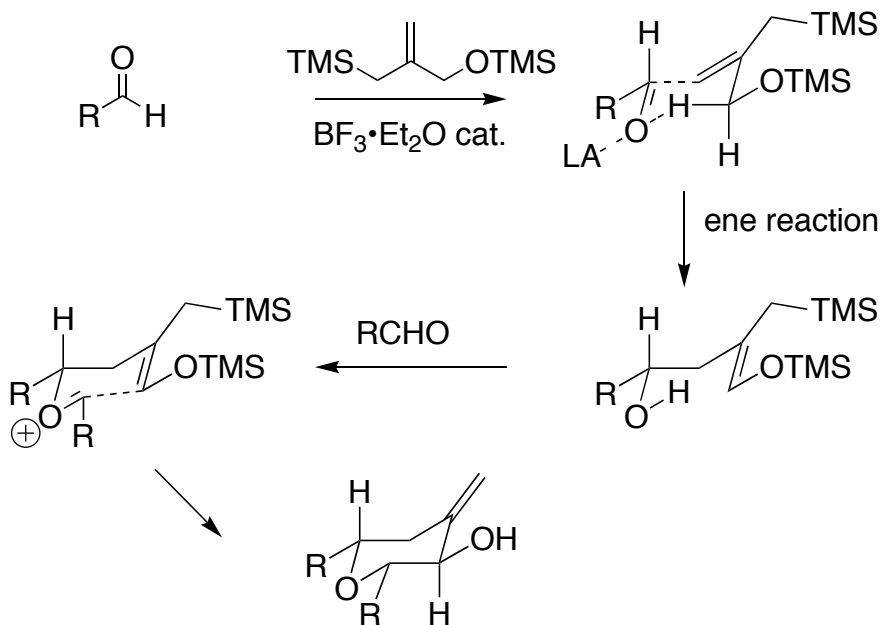
Reactions with Silicon

Sakurai Reaction

- Lewis acid catalyzed addition of allylsilanes to aldehydes and acetals

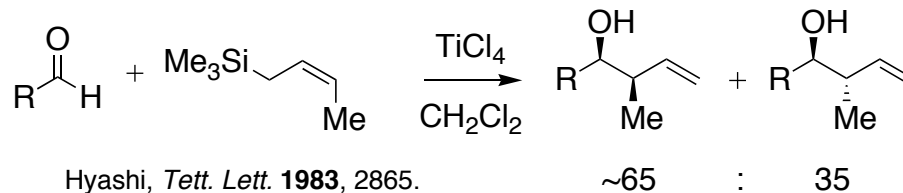
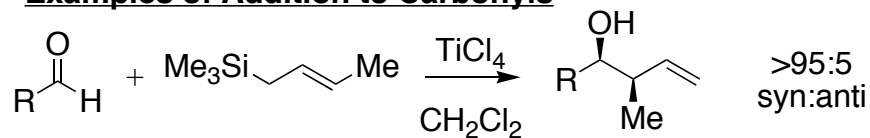


Intramolecular Sakurai Reaction



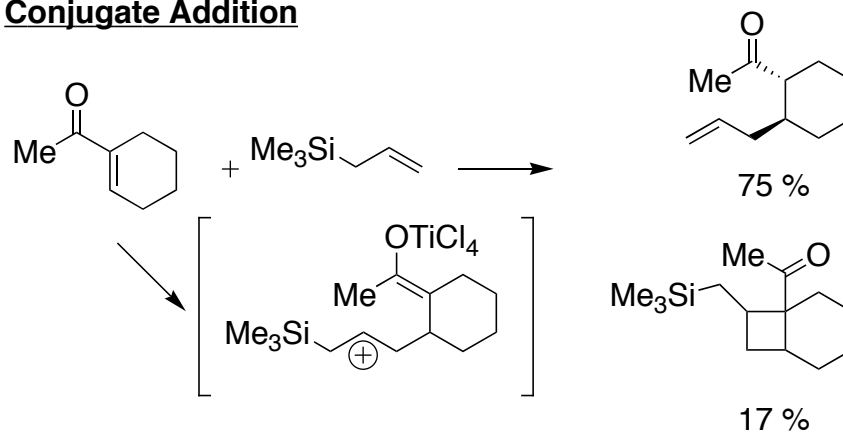
Markó et al. *Tett. Lett.*, 1992, 33, 1799

Examples of Addition to Carbonyls

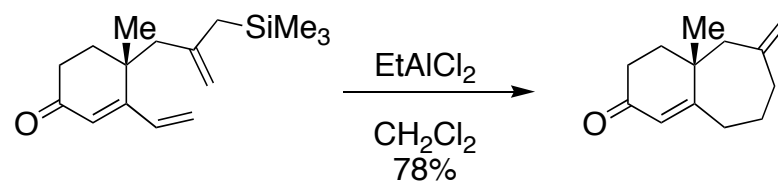


Hyashi, *Tett. Lett.* 1983, 2865.

Conjugate Addition



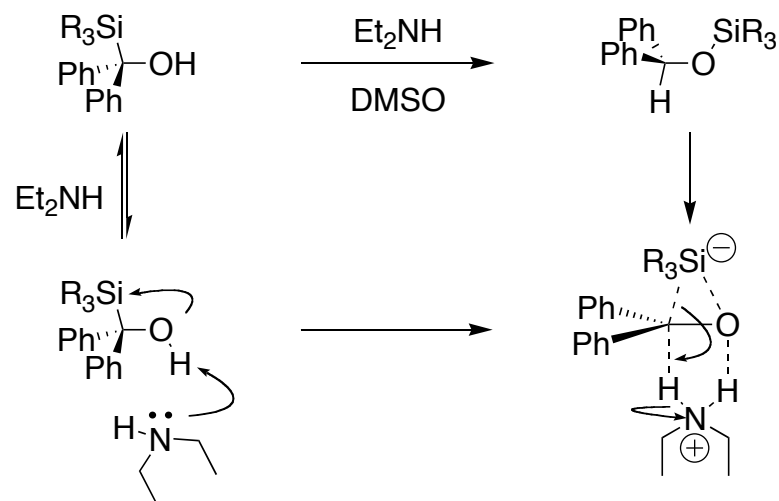
Fleming, *Org. Reactions* 1989, 37, 127-133



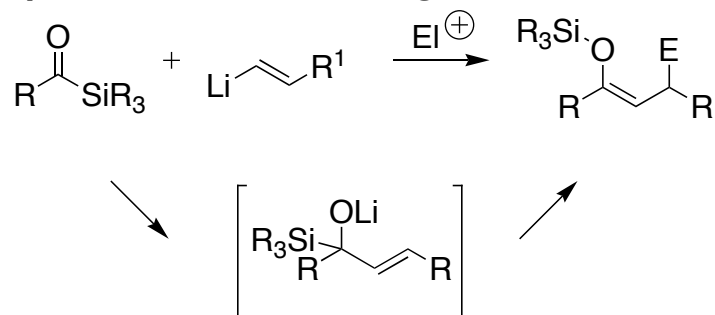
Majetich, *Tetrahedron* 1987, 43, 5621

Pioneering Work By A. G. Brook

- Rearrangement of organosilyl alcohols under base catalysis
- Retention at silicon and inversion at carbon

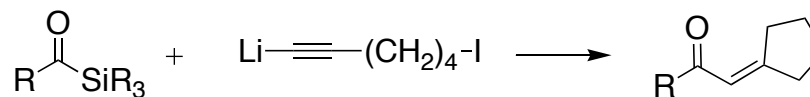


Brook, *Accts. Chem. Res.* **1974**, *7*, 77-84

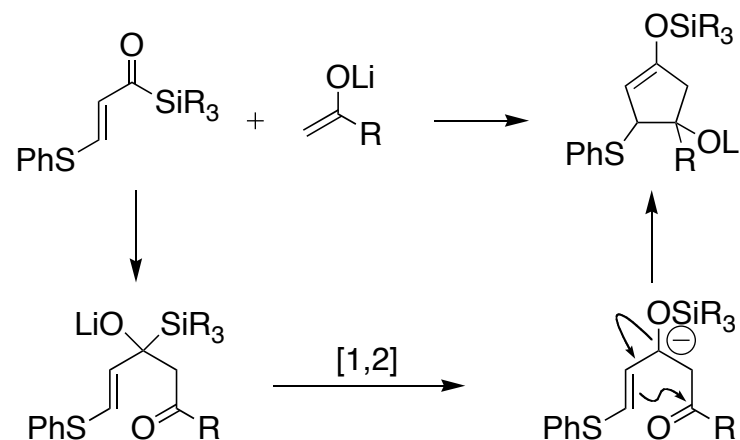
Examples of Brook Rearrangement

Moser, *Tet.* **2001**, *57*, 2065-2084

- Brook rearrangement can be used to access homoallylic enolate anions



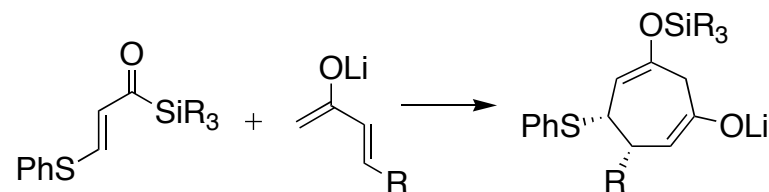
Reich, *J. Am. Chem. Soc.* **1980**, *102*, 1423



Takeda, *J. Am. Chem. Soc.* **1993**, *115*, 9351

Takeda, *Synlett.* **1994**, 178

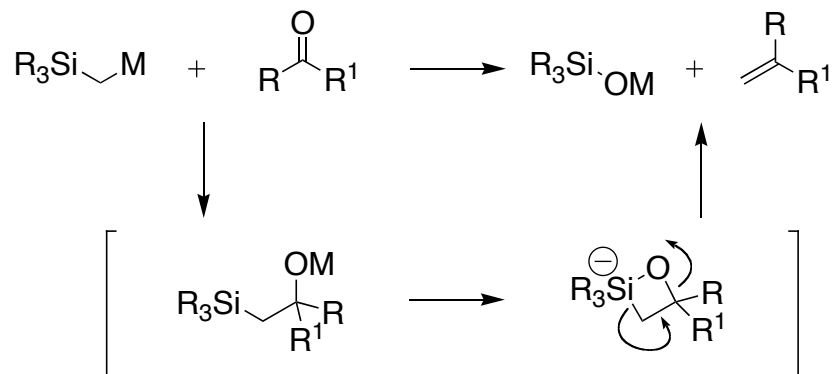
Takeda, *Synlett.* **1997**, 255



Moser, *Tett.* **2001**, *57*, 2065-2084

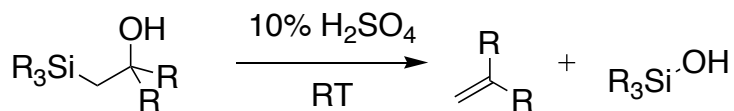
Pioneering Work By Peterson

- Investigation aimed at finding a silicon analog to phosphorous ylides
- Same cyclic four-membered transition state can be envisioned

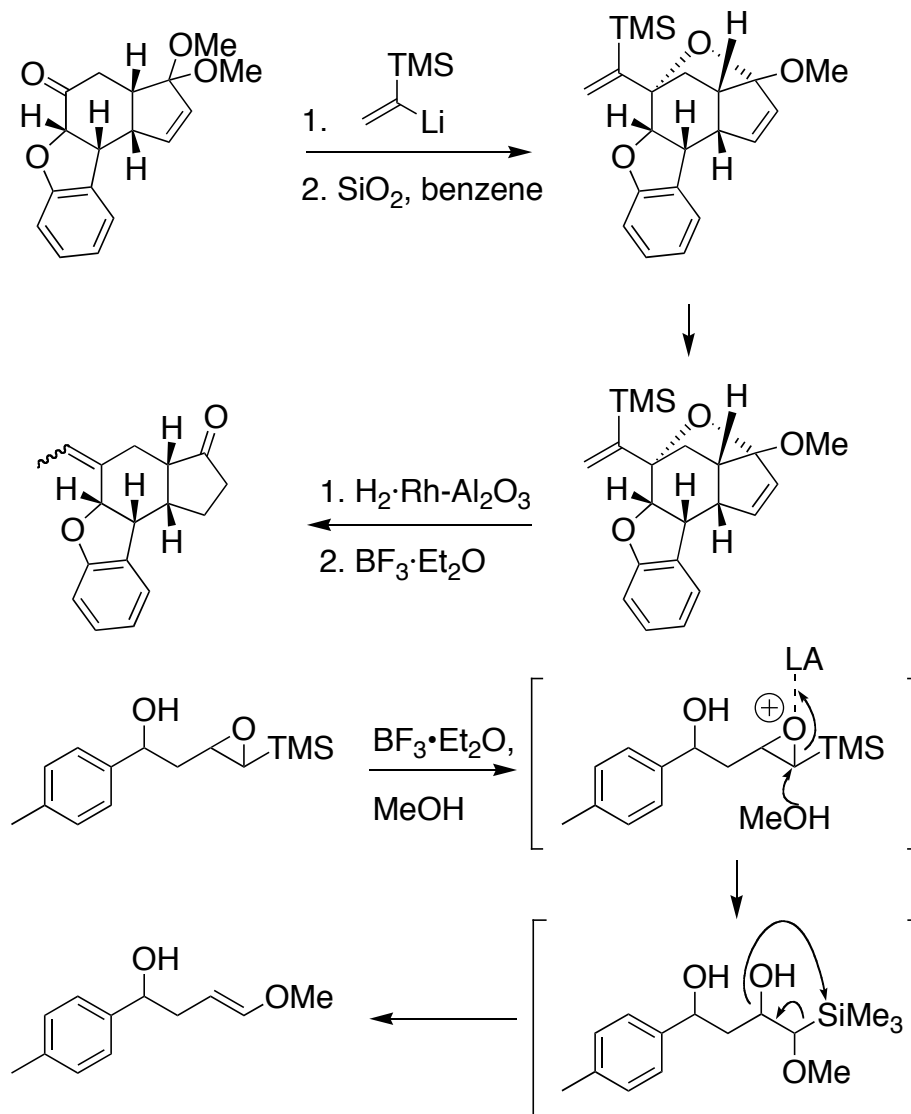


Peterson, *J. Org. Chem.* **1968**, *33*, 780-784

- Mg alkoxides are stable and do not breakdown to give olefin product
- Li, Na, and K alkoxides are reactive and breakdown to give olefin product
- β -silyl-alcohols can be converted to olefins with dilute acid



Whitmore et al., *J. Am. Chem. Soc.* **1947**, *69*, 1551

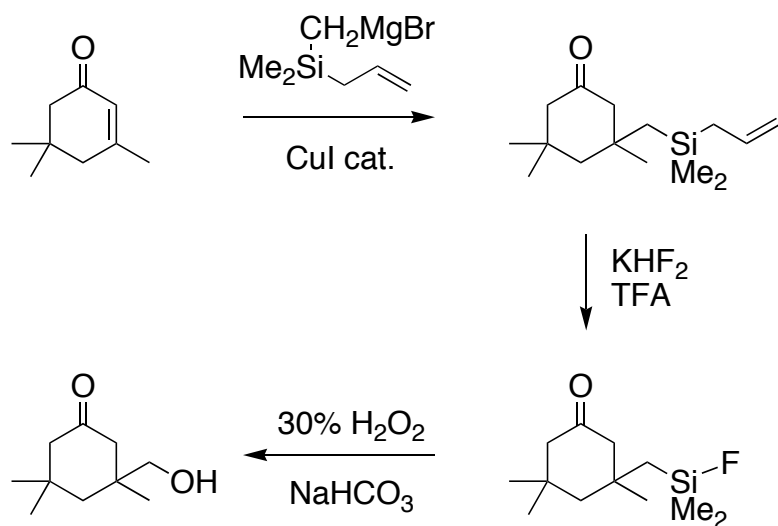


Ager, *Org. Reactions* **1990**, *38*, 1.

Tamao Oxidation

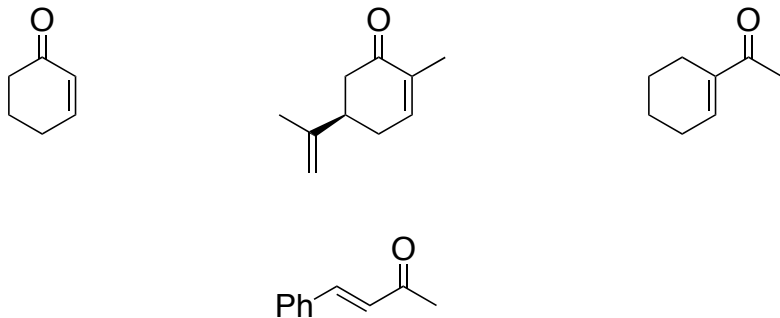
Tamao Oxidation

- Conversion of organosilanes to corresponding alcohols
- Pioneered by Tamao in 1984 (*Tett. Lett.* **1984**, 25, 4249)

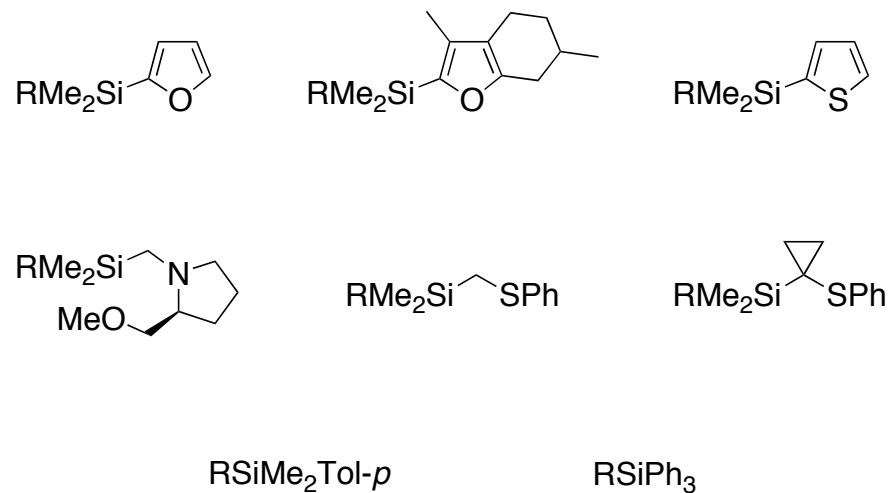


68% overall

- Other substrates used and in all cases no Bayer-Villager seen

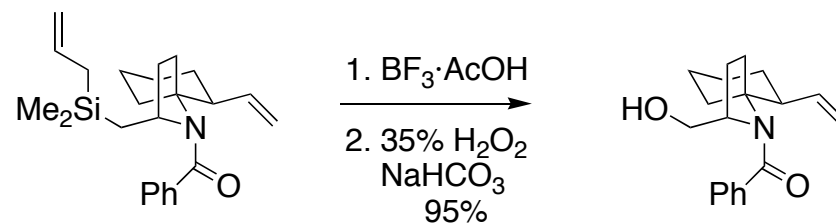


Representative Silanes

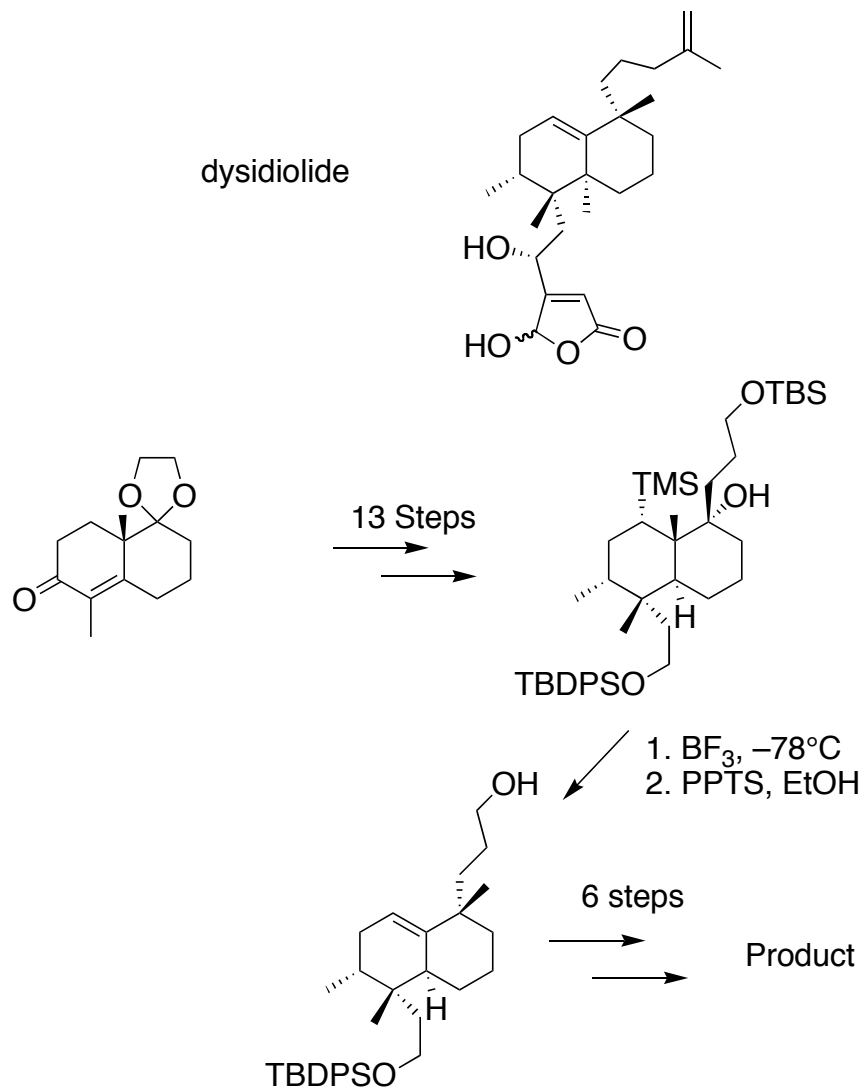
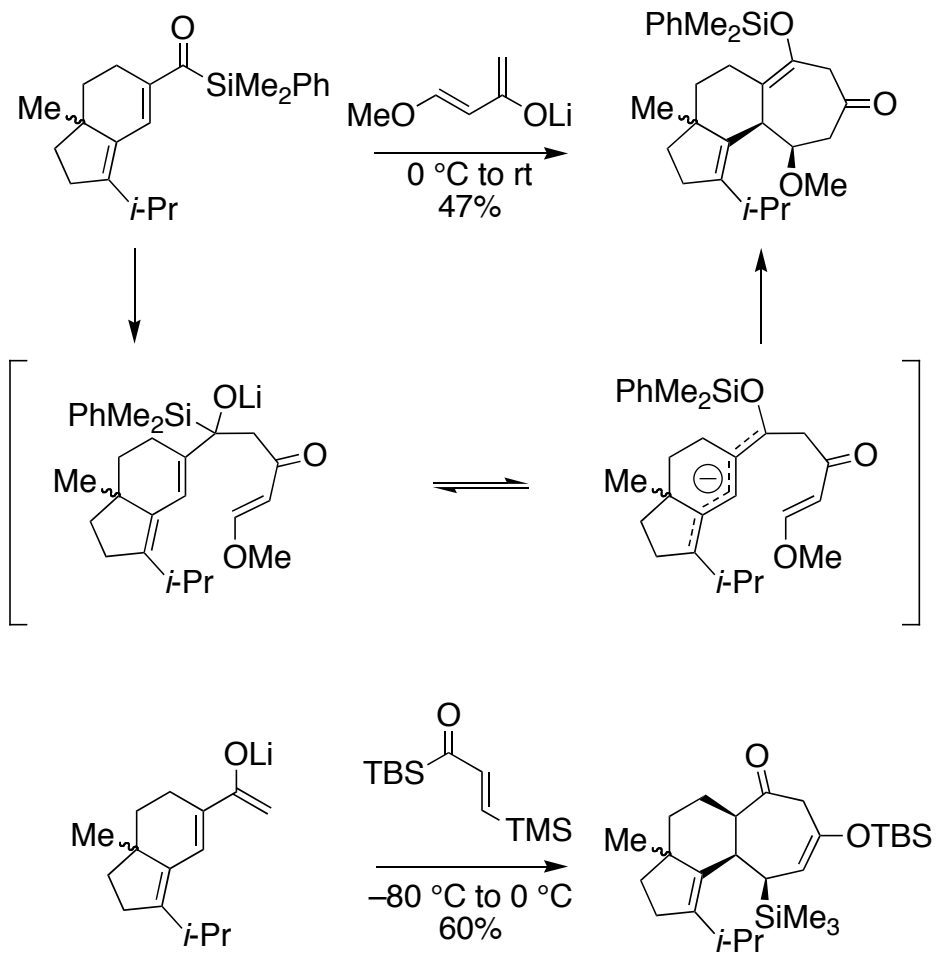


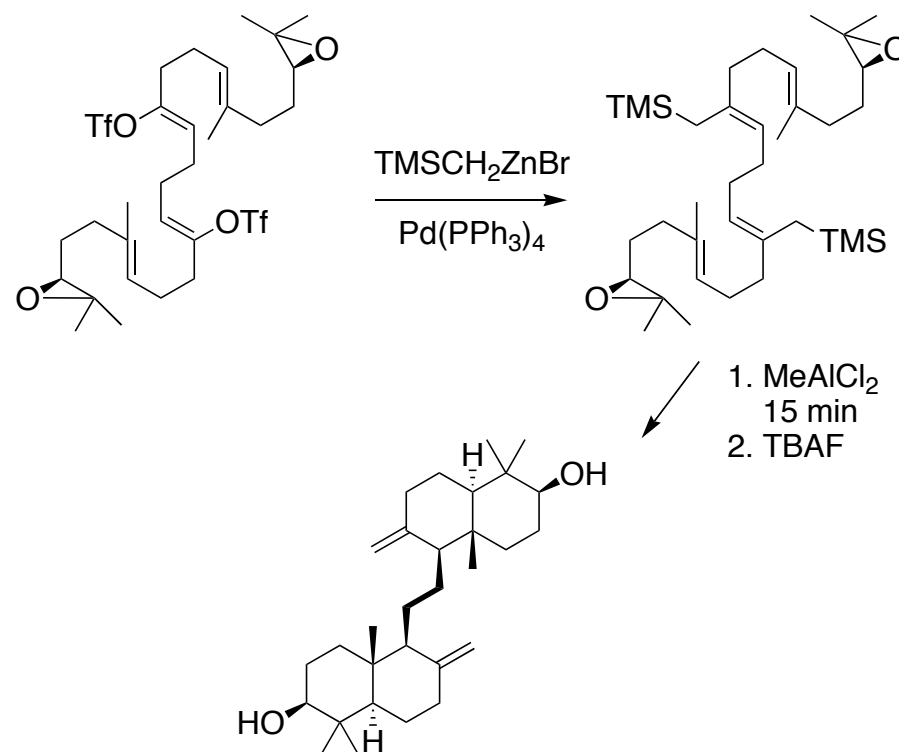
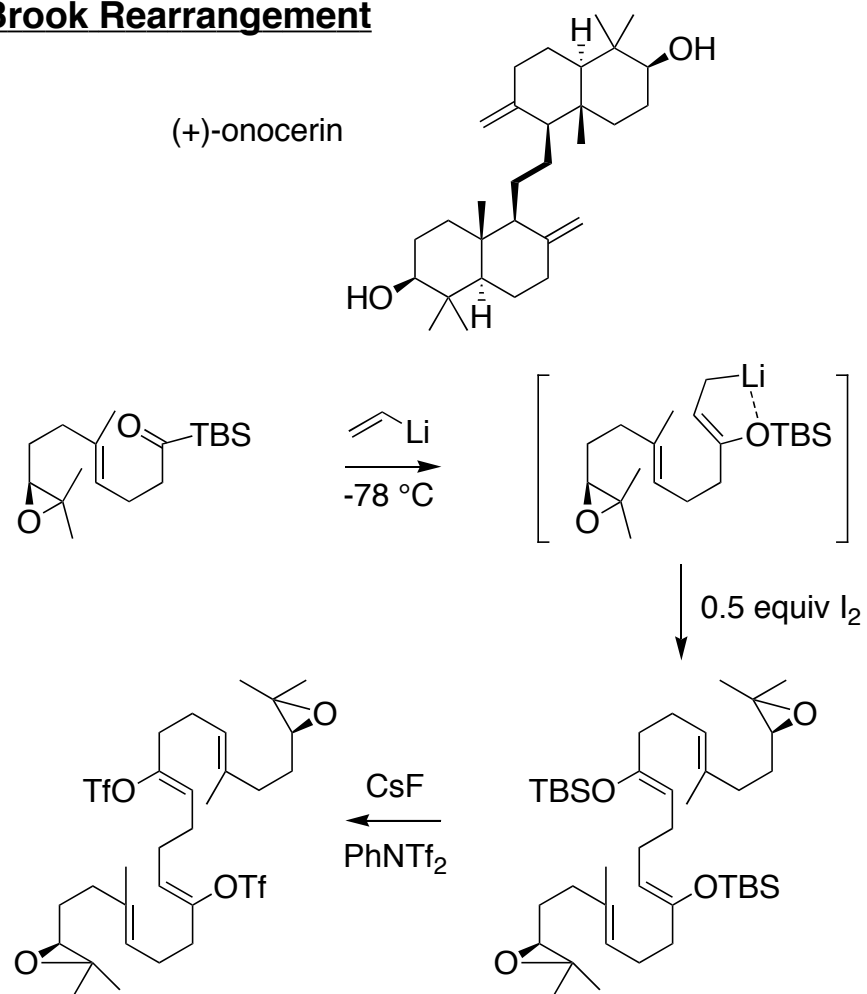
Yoshida et al. *J. Org. Chem.* **1999**, 64, 8709

Synthetic Example



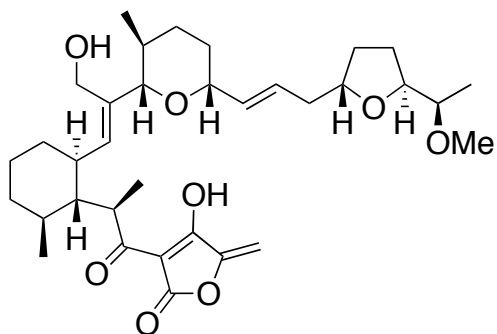
Weinreb et al. *J. Org. Chem.* **2002**, 67, 4339

Brook RearrangementCorey, Roberts, *J. Am. Chem. Soc.* **1997**, *119*, 12425 - 12431**Cyanthin Tricyclic Core**Takeda et al. *Org Lett.* **2000**, *2*, 1907

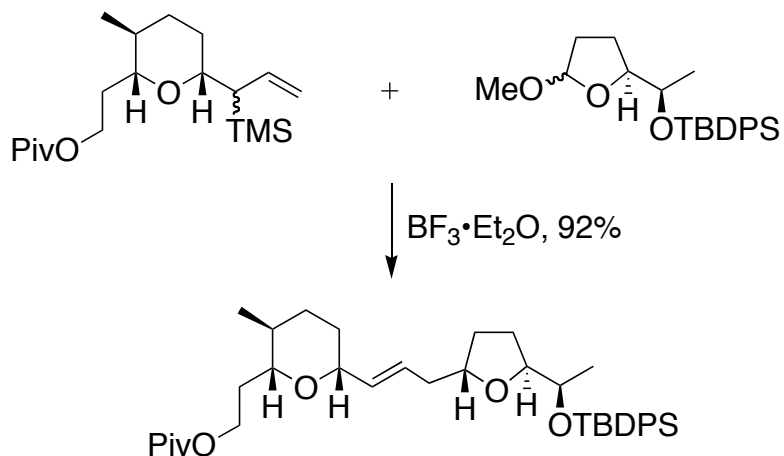
Brook Rearrangement

Mi, Schreiber, Corey, *J. Am. Chem. Soc.* **2002**, *124*, 11290-11291

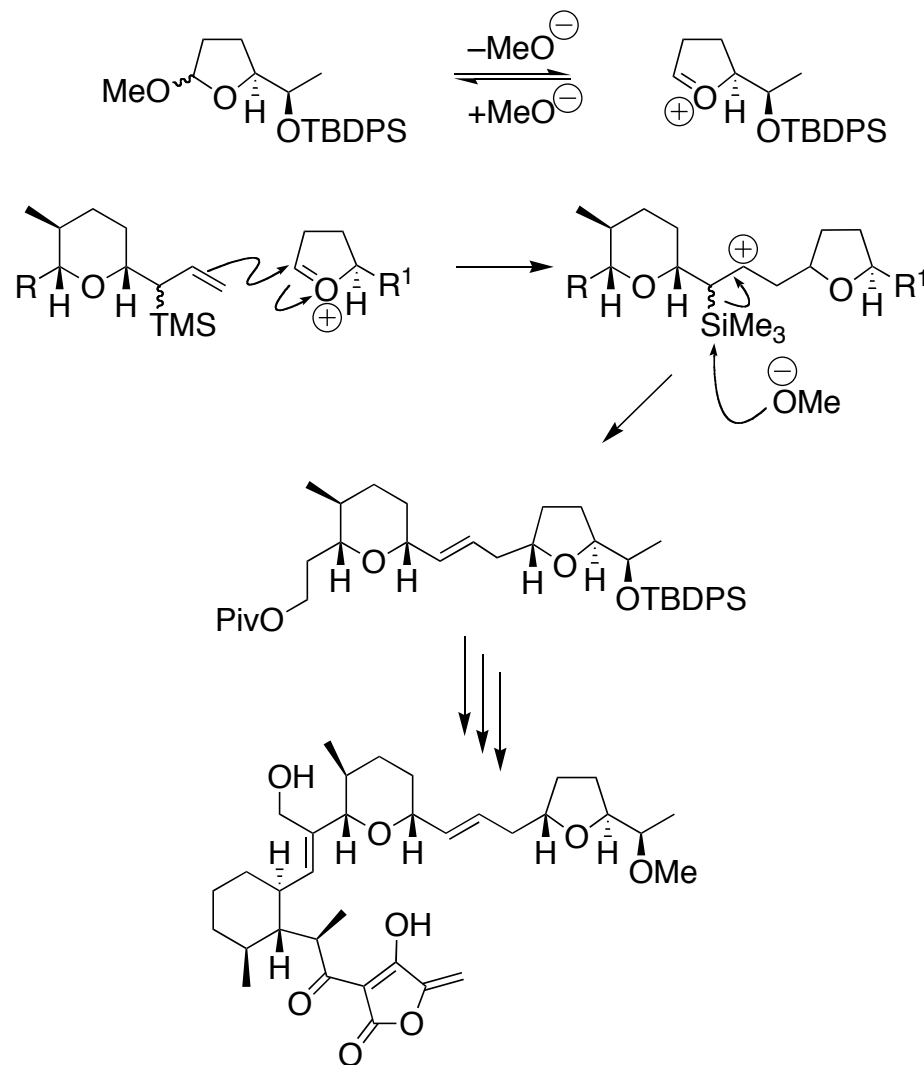
- Properties of silicon exploited
- β -carbocation stabilization
- β -anion stability

(+)-Tetronomycin

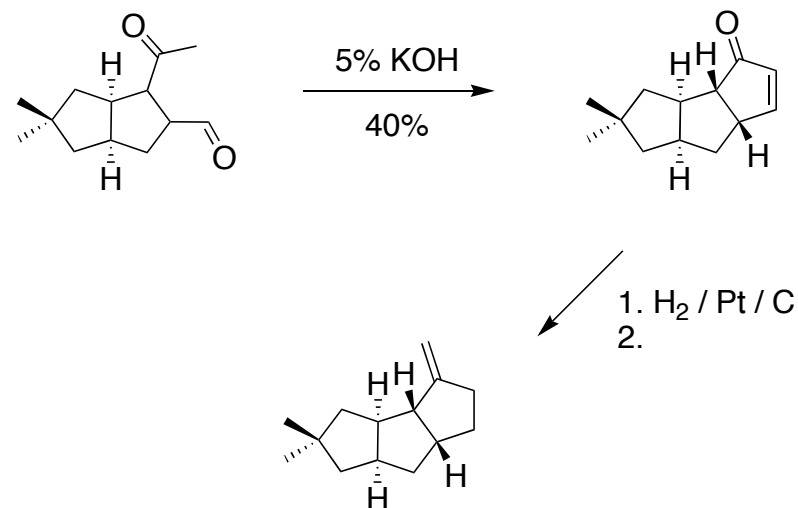
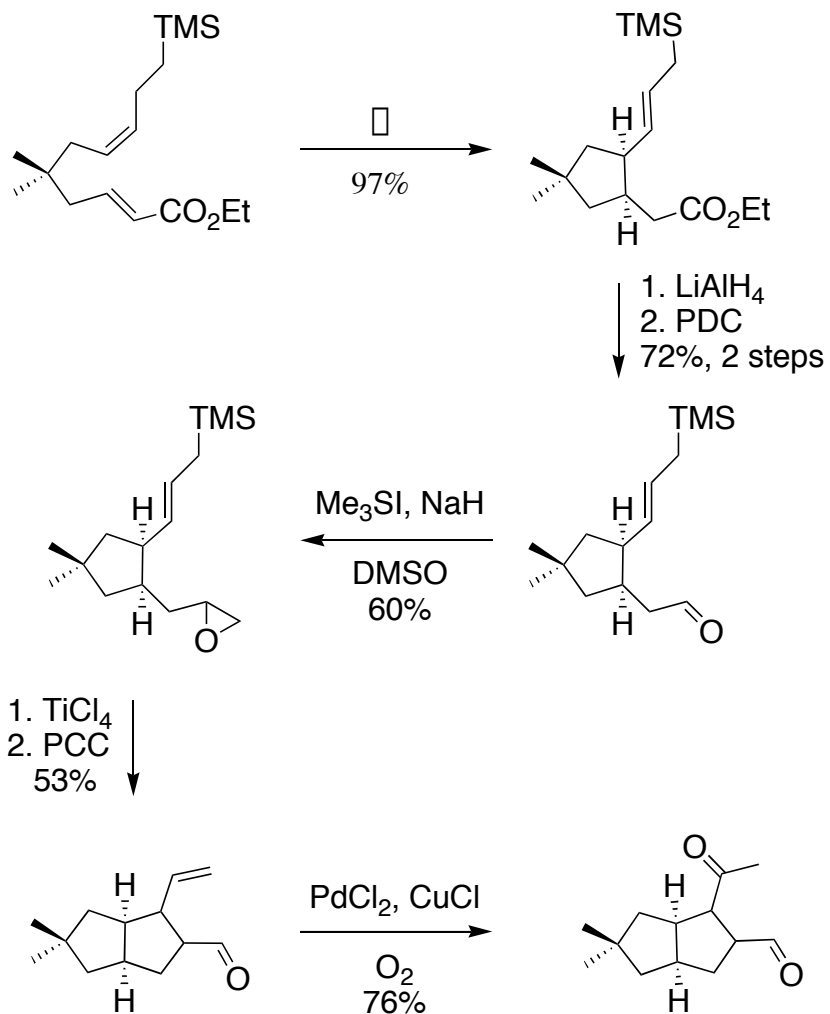
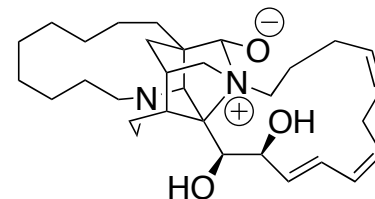
- Key coupling step in convergent synthesis uses allylsilane coupling reaction



- Stabilization of σ cation



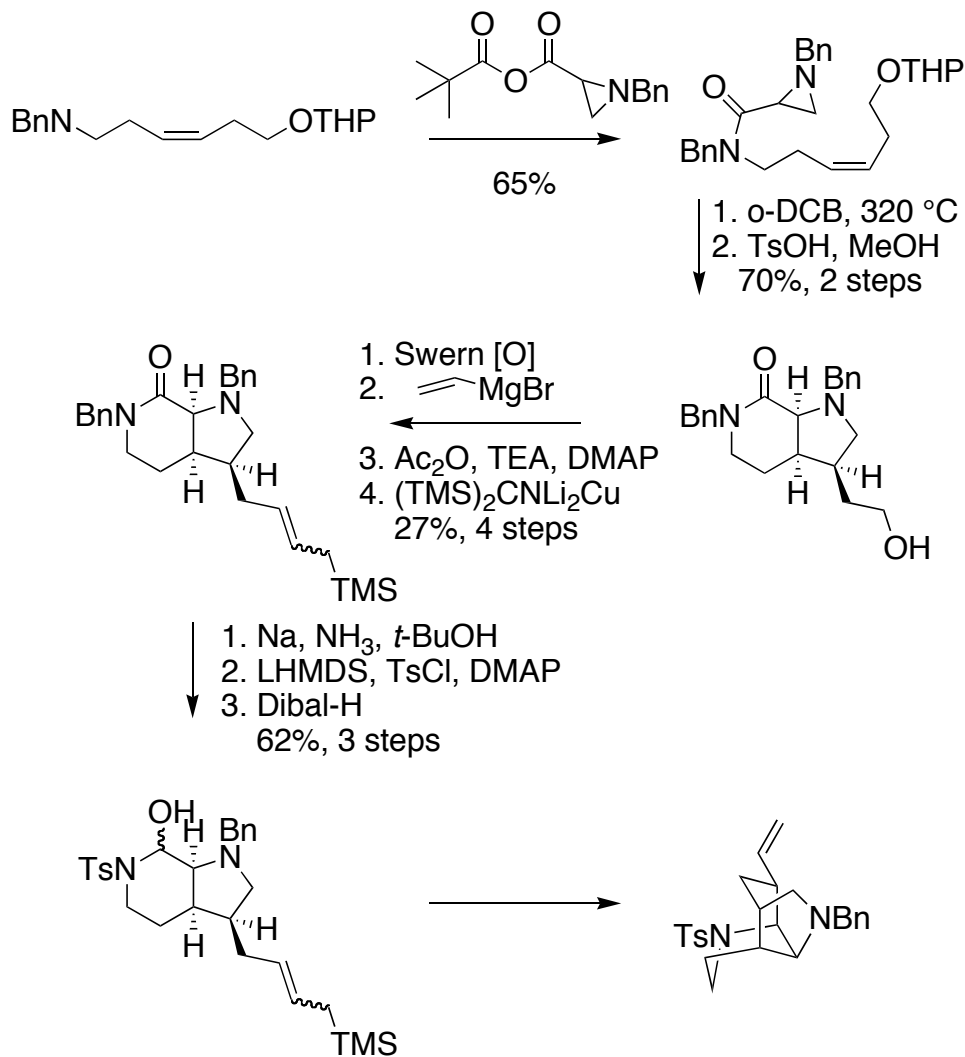
Yoshi et al. *J. Org. Chem.* **1992**, *57*, 2888

(±)-HirsuteneSarkar et al. *Tett. Lett.*, 1990, 31, 3461**(±)-Sarain A Core Scaffold**

Sarain A

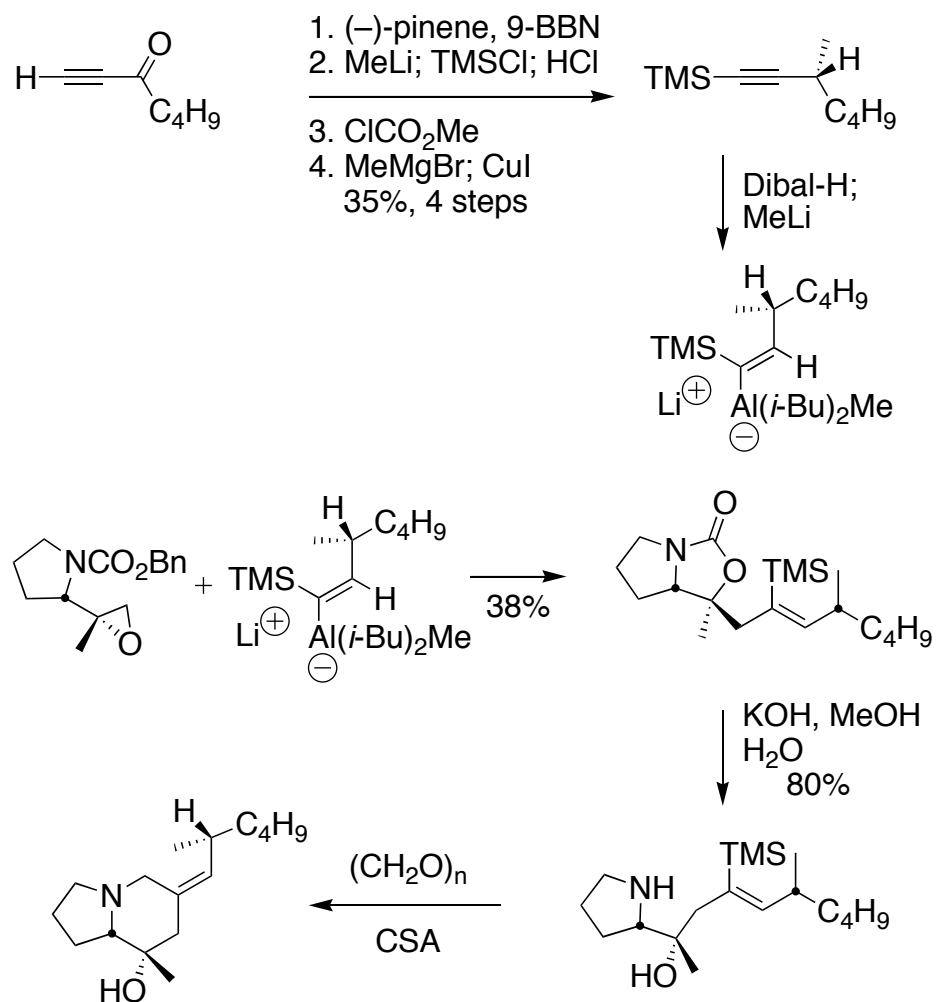
Silicon in Synthesis

(±)-Sarain A Core Scaffold



Weinreb et al., *J. Org. Chem.*, **1991**, *56*, 3210

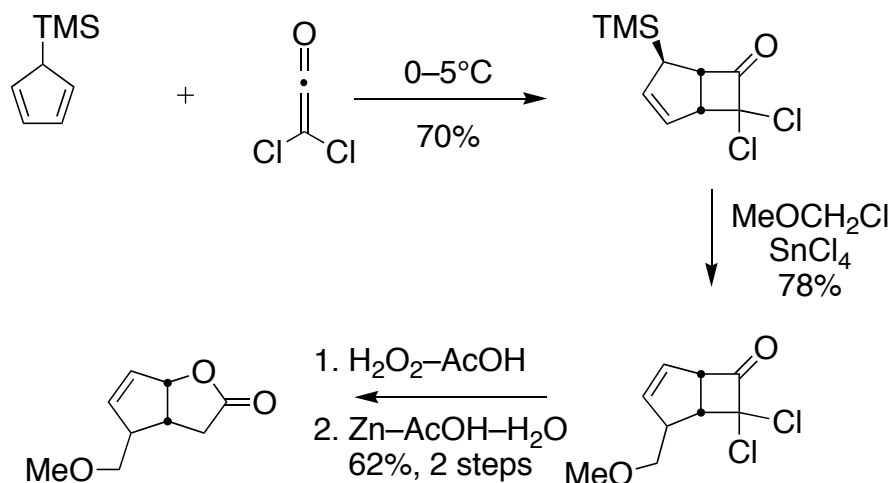
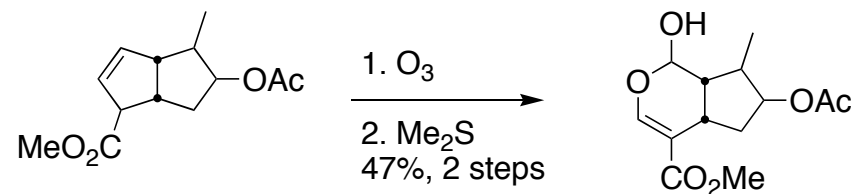
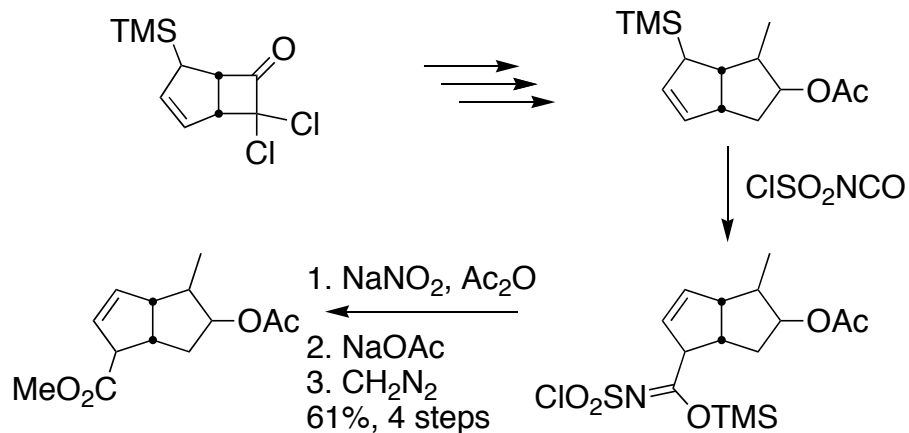
(+)-Pumiliotoxin A



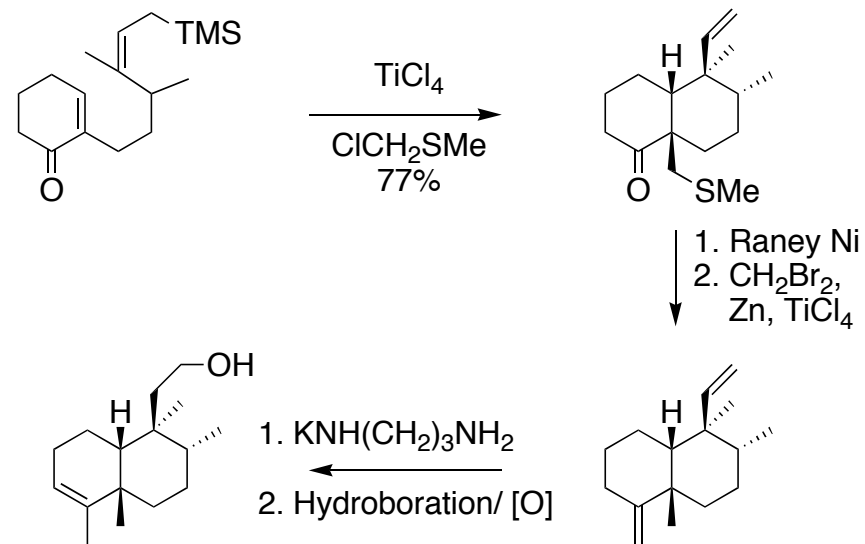
Overman et al., *J. Org. Chem.*, **1985**, *50*, 3670

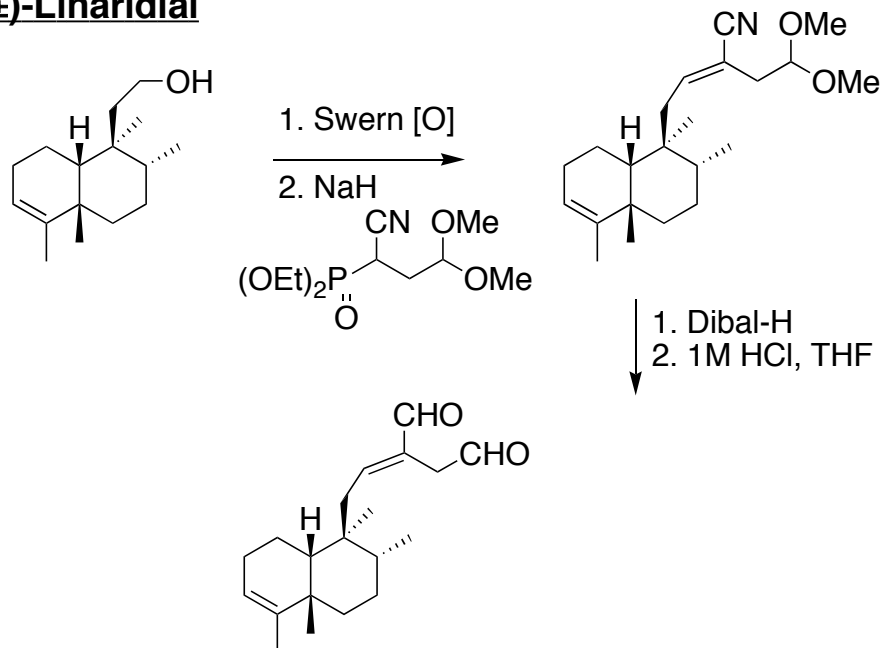
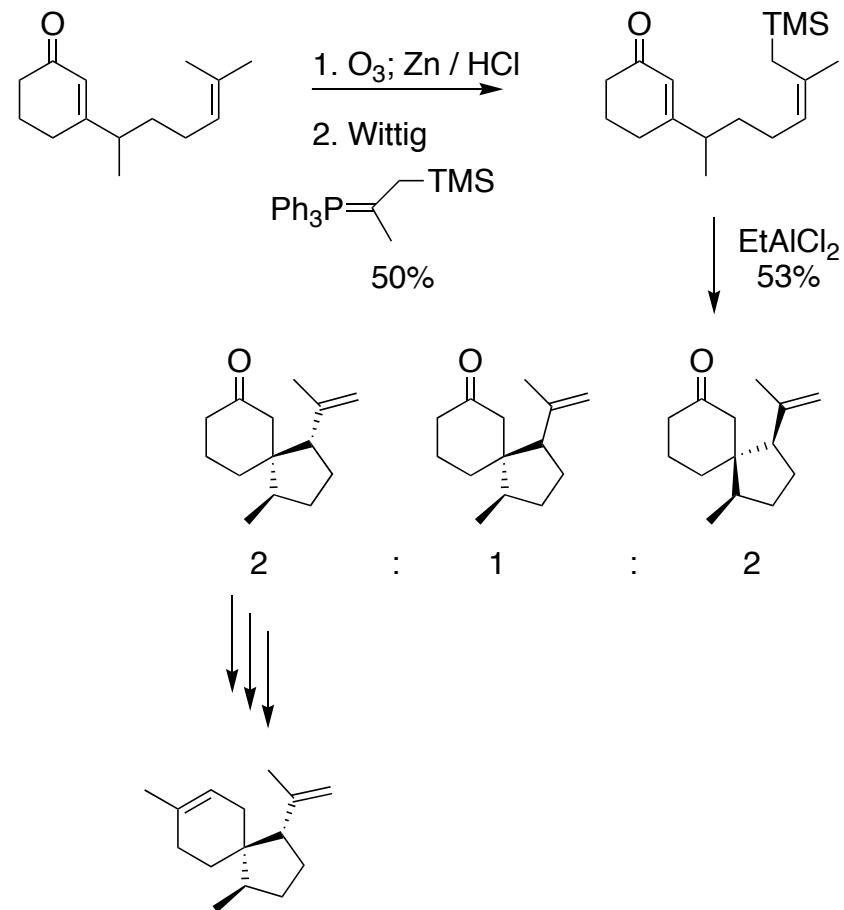
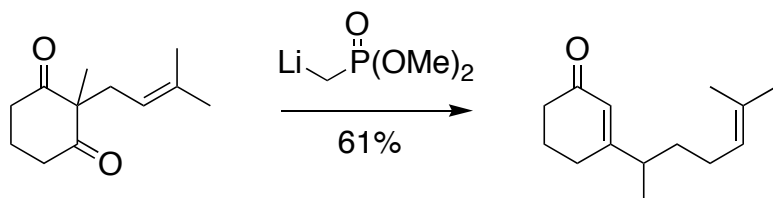
Prostaglandins

- Fleming contributed greatly to the field of organosilicon chemistry

**Loganin**

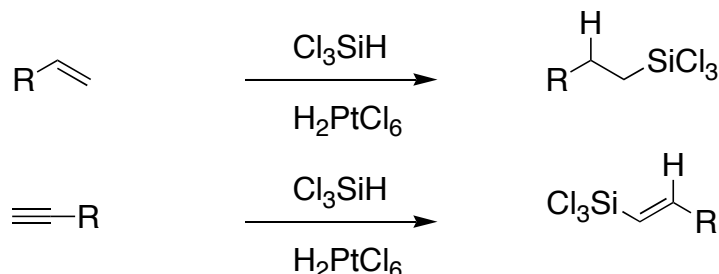
Fleming, *J. Chem. Soc. Chem. Comm.*, **1977**, 79 - 80
 Fleming, *J. Chem. Soc. Chem. Comm.*, **1977**, 81

(±)-Linaridial

(±)-LinaridialTokoroyama et al. *Tett. Lett.*, **1987**, *28*, 6645**(±)- β -Acoradiene**Yamamoto et al. *J. Org. Chem.*, **1990**, *55*, 3971

Hydrosilation

- Metal and radical catalyzed addition to alkenes and alkynes
- Metal catalysis is done at room temperature and best yields obtained with trichloro and methylchlorosilanes
- Addition of methyl grignard converts chlorosilanes to TMS



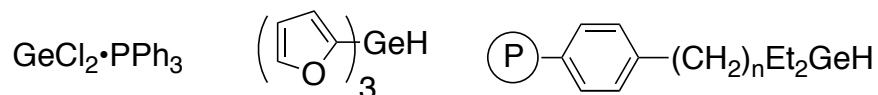
Chalk; Harrod; *J. Am. Chem. Soc.* **1965**, *87*, 16

- Cr(CO)₆ with light gives 1,4 reduction of dienes

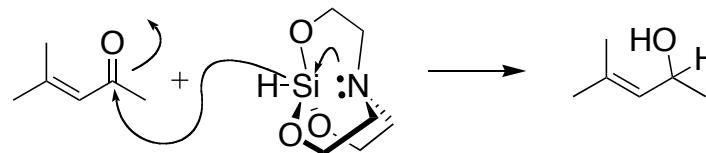
Germanes and Dehalogenation

- Organohalides can also be reduced with various organogermanes
- Can be used catalytically with PPh₃ for reduction of C–X bond
- Reactivity of halide I > Br > Cl > F
- Solid support methods can be used
- Similar reactivity to silanes
- Furanylgermane reduces C–X bond under mild conditions

- "Common" Germanes

**Reduction with Silanes**

- Catalysis needed for convenient rates
- Catalysts include TBAF, protic and Lewis acids, Wilkinson's cat, silatrane

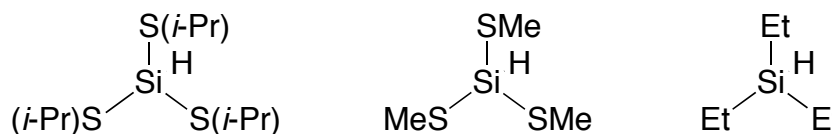


Attar-Bashi et al. *Organometallic Chem.* **1976**, *117*, C87

Silanes and Dehalogenation

- Organohalides can be reduced with various organosilanes
- Radical mechanism of hydrodehalogenation
- Reactivity of halide I > Br > Cl > F
- Reactions are fast and clean often giving quantitative yields

- Common Silanes



- Common Radical Initiators

AIBN

Dibenzoylperoxide

- Phenylsilane is also used
- Reactions with phenylsilane are refluxed neat with a radical initiator