

Tamao-Fleming Oxidations in Organic Synthesis: Carbon-Silicon Bonds as Functional Group Masks



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Stoltz Literature Group Meeting
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Key References:

- Tamao, K; Kakui, T; Kumada, M. *JACS*, **1978**, *100*, 2268-2269.
- Tamao, K; Akita, M; Kumada, M. *JOC*, **1983**, *254*, 13-22.
- Tamao, K; Ishida, N; Tanaka, T; Kumada, M. *Organometallics*, **1983**, *2*, 1694-1696.
- Tamao, K; Kakui, T; Akita, M; Iwahara, T; Kanatani, R; Yoshida, J; Kumada, M. *Tet*, **1983**, *39*, 983-990.
- Tamao, K; Ishida, N. *JOC*, **1984**, *269*, C37-C39.
- Tamao, K; Kumada, M. *TL*, **1984**, *25*, 321-324.
- Fleming, I; Henning, R; Plaut, H. *JCS Chem. Commun.*, **1984**, 29-31.
- Fleming, I; Hill, J. H. M; Parker, D; Waterson, D. *JCS Chem Commun*, **1985**, 318-321.
- Fleming, I. *Tet. Lett.* **1987**, *36*, 4229.
- Fleming, I; Barbero, A; Walter, D; *Chem Rev*, **1997**, *97*, 2063-2192.

The Key Players



-Kohei Tamao was born in Kagawa, Japan in 1942

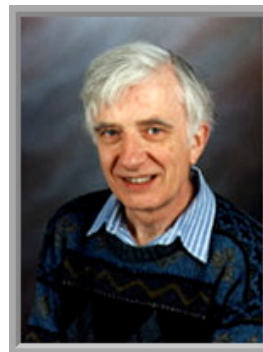
-He received his Ph.D. in 1971 from Kyoto University under the direction of Professor Makoto Kumada

-In 1970 he became an assistant professor at Kyoto University, where he has been ever since.

-His early work entailed Nickel-catalyzed cross couplings

-His later work has been focused on the functionalization of the carbon-silicon bond

-In 1993, Tamao became Full Professor at the Institute for Chemical Research, Kyoto University. He is now the Director of the Institute.



-Ian Fleming was born in Shaffordshire, England in 1935

-He studied with Dr. John Harley-Mason at Pembroke College and earned his Ph.D. in 1962.

-In 1963, he began work with Professor R.B. Woodward on the synthesis of vitamin B₁₂

-In 1964 he returned to Cambridge University and eventually became a Fellow of the Royal Society

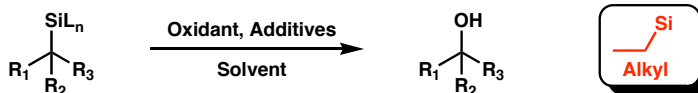
-His interests have spanned synthetic, structural, and mechanistic chemistry

-Since 1972, he has developed organosilicon chemistry

What is a Tamao-Fleming Process?

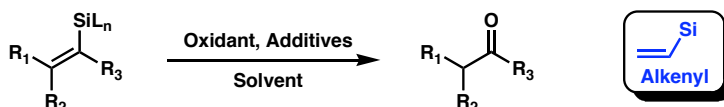
-There are two major classes of chemical transformations:

The first involves sp³ Carbon



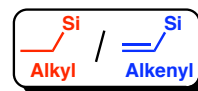
- * The product alcohol can be primary, secondary, or even tertiary
- * The oxidants, additives, and solvent can vary considerably
- * The ligands on silicon may also vary
- * parts of this talk related to sp³ processes will be indicated with the symbol shown above

The second involves sp² Carbon



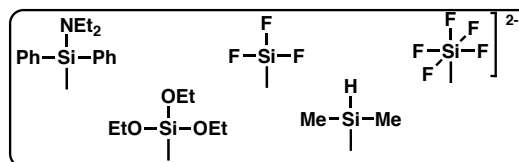
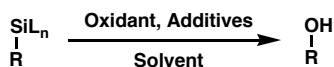
- * R₁, R₂, and R₃ are usually Carbon or Hydrogen
- * parts of this talk related to sp² processes will be indicated with the symbol shown above

Tamao Processes

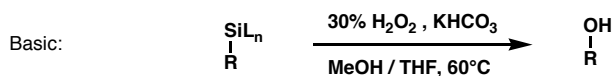
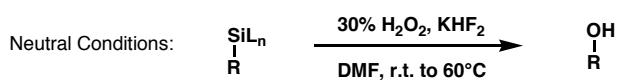
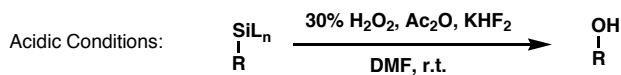


-In a Tamao Oxidation, at least one Ligand on silicon must be a heteroatom or hydrogen

Common Silicon Moieties used in Starting Materials



-The Tamao Oxidations can be carried out under a variety of pH's when H_2O_2 is the oxidant

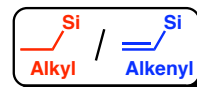


-mCPBA is also a commonly employed oxidant.

-Tamao's conditions can vary considerably

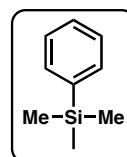
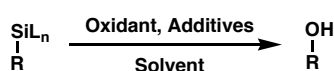
TL, 1984, 25, 321-324

Fleming Processes

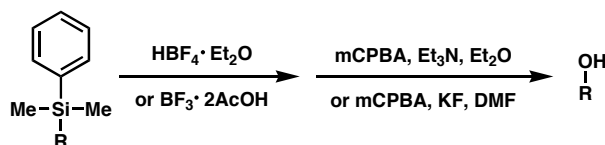


-At the beginning of a Fleming process, all of the Ligands on Silicon are carbon

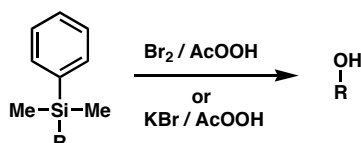
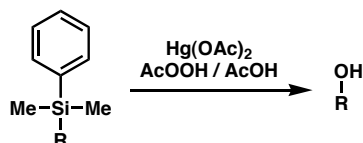
Silicon Moiety Used by Fleming:



-Fleming developed some 2-pot sequences to convert the Phenyldimethylsilyl group to an alcohol:

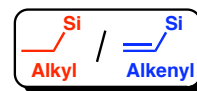


-He also developed one-pot variants:

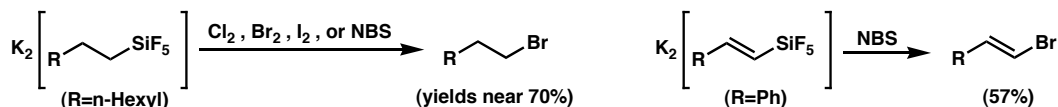


TL, 1987, 28, 4229-4232
JCS, Per. T.1, 1995, 4, 317-337

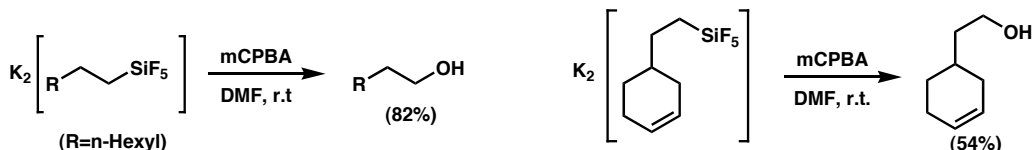
How was the Tamao Oxidation Discovered?



-Tamao was originally doing work with the halogenation of pentafluorosilicates and published the data below in January of 1978:



-In March, 1978 Tamao published results where he had used mCPBA as the oxidant instead of halogens. He found that the carbon-silicon bond could be converted to a carbon-oxygen bond.



-In 1983, Tamao demonstrated that alkyl trifluorosilanes are more reactive than their alkylpentafluorosilicate counterparts in the presence of mCPBA, giving extremely exothermic reactions, but also higher yields in several cases.

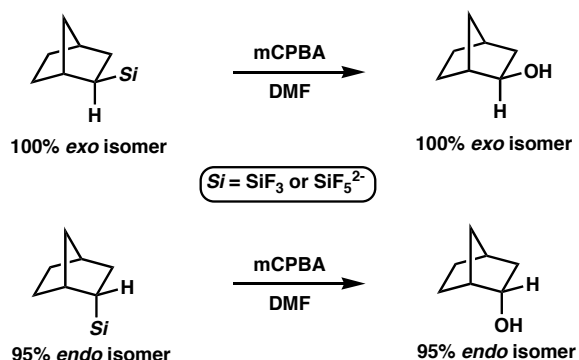


JACS, 1978, 100, 290-292
 JACS, 1978, 100, 2268-2269
 J.Orgmet.Chem, 1983, 254, 13-22

Evidence for Retention of Stereochemistry

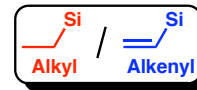


-Tamao synthesized the following norbornyl silanes and silicates and subjected them to mCPBA:

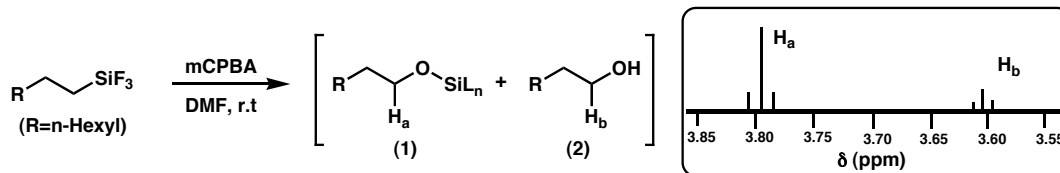


- When the starting materials above were treated with NBS or Br₂, inversion of stereochemistry was observed!

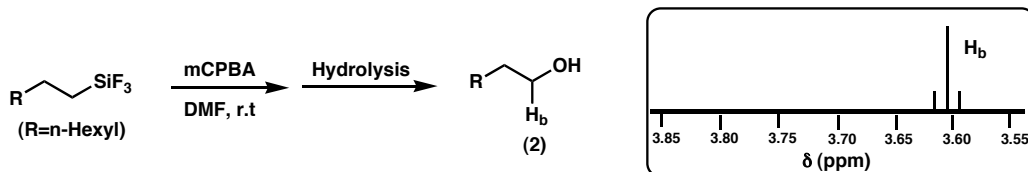
The Mechanism



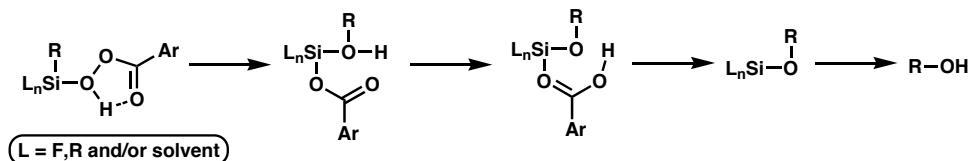
-Tamao monitored the reaction below using ^1H NMR spectroscopy immediately after addition of mCPBA



-He then carried out the hydrolysis of the reaction and followed this process by ^1H NMR

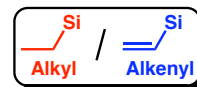


-Based on this result and the ones from the norbornyl system on the previous slide, he proposed the general mechanism below:



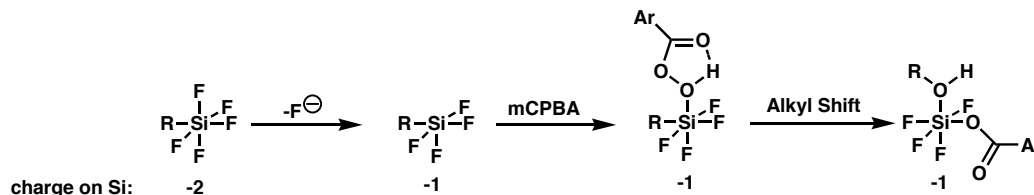
Tet, 1983, 39, 983-990

Hypervalent Silicon



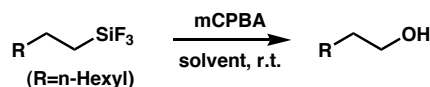
-In many Tamao-Fleming oxidations, fluoride ion is present. This can often lead to the formation of hypervalent silicon, which is silicon with a coordination number greater than 4.

-It is believed that the mCPBA binds to silicon atoms with a coordination number of 5 when extra fluoride is present. Then carbon shift occurs.



-Tamao also saw a marked solvent effect in the following reaction. DN is the solvent donicity number, a correlation to how well a solvent can contribute lone pairs.

solvent	yield(%)	DN
Benzene	23	0.1
PhNO ₂	48	4.4
Dioxane	28	14.8
Et ₂ O	12	19.2
THF	35	20.0
DMF	95	26.6
HMPA	100	38.8



-Reported yields are GC yields

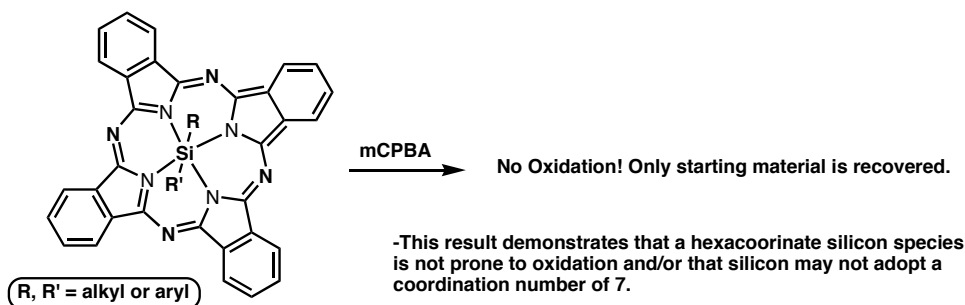
-When really donating solvents such as DMF were used, a high degree of peak broadening was seen in the ^{19}F NMR.

Tet, 1983, 39, 983-990

Alkyl / Alkenyl

$$\begin{array}{ccccccc}
 \begin{array}{c} \text{R} \\ | \\ \text{F}-\text{Si}-\text{F} \\ | \\ \text{F} \end{array} & \xrightleftharpoons{\text{Sol}} & \begin{array}{c} \text{R} \\ | \\ \text{F}-\text{Si}-\text{F} \\ | \\ \text{Sol} \end{array} & \xrightleftharpoons{\text{F}^\ominus} & \left[\begin{array}{c} \text{R} \quad \text{F} \\ | \quad | \\ \text{F}-\text{Si}-\text{F} \\ | \quad | \\ \text{F} \quad \text{Sol} \end{array} \right]^{-1} & \xrightleftharpoons{-\text{Sol}} & \left[\begin{array}{c} \text{R} \\ | \\ \text{F}-\text{Si}-\text{F} \\ | \\ \text{F} \end{array} \right]^{-1} & \xrightleftharpoons{\text{F}^\ominus} & \left[\begin{array}{c} \text{R} \quad \text{F} \quad \text{F} \\ | \quad | \quad | \\ \text{F}-\text{Si}-\text{F} \\ | \quad | \quad | \\ \text{F} \quad \text{F} \quad \text{F} \end{array} \right]^{-2} \\
 (1) & & (2) & & (3) & & (4) & & (5)
 \end{array}$$

-Tamao also synthesized phthalocyanine complexes of silicon and exposed them to mCPBA.



Tet, **1983**, 39, 983-990
J.Organomet.chem., **1988**, 341, 165-179

Chemical structure of a vinyl silane: $\text{Si}-\text{CH}=\text{CH}-\text{Alkyl}$

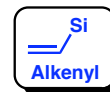
$$\begin{array}{c} \text{Me} \\ | \\ \text{R}-\text{Si}-\text{H} \\ | \\ \text{Me} \end{array} \xrightarrow[\text{MeOH/THF reflux}]{30\% \text{ H}_2\text{O}_2, \text{KHCO}_3} \begin{array}{c} \text{Me} \\ | \\ \text{R}-\text{Si}-\text{F} \\ | \\ \text{Me} \end{array} \xrightarrow[\text{MeOH/THF reflux}]{30\% \text{ H}_2\text{O}_2, \text{KHCO}_3} \begin{array}{c} \text{Me} \\ | \\ \text{R}-\text{Si}-\text{OR}' \\ | \\ \text{Me} \end{array} \xrightarrow[\text{MeOH/THF reflux}]{30\% \text{ H}_2\text{O}_2, \text{KHCO}_3}$$

$$\begin{array}{c} \text{Me} \\ | \\ \text{R}-\text{Si}-\text{OR}' \\ | \\ \text{OR}' \end{array} \xrightarrow[\text{MeOH/THF reflux}]{30\% \text{ H}_2\text{O}_2, \text{KHCO}_3} \begin{array}{c} \text{OR}' \\ | \\ \text{R}-\text{Si}-\text{OR}' \\ | \\ \text{OR}' \end{array} \xrightarrow[\text{MeOH/THF reflux}]{30\% \text{ H}_2\text{O}_2, \text{KHCO}_3} \begin{array}{c} \text{Me} \\ | \\ \text{R}-\text{Si}-\text{NEt}_2 \\ | \\ \text{Me} \end{array} \xrightarrow[\text{MeOH/THF reflux}]{30\% \text{ H}_2\text{O}_2, \text{KHCO}_3}$$

$$\begin{array}{c} \text{Me} \\ | \\ \text{R}-\text{Si}-\text{Cl} \\ | \\ \text{Me} \end{array} \xrightarrow[\text{MeOH/THF}]{30\% \text{ H}_2\text{O}_2, \text{excess KHCO}_3} \begin{array}{c} \text{Me} \\ | \\ \text{R}-\text{Si}-\text{Cl} \\ | \\ \text{Cl} \end{array} \xrightarrow[\text{then } 30\% \text{ H}_2\text{O}_2]{\text{MeOH/THF, excess KHCO}_3} \begin{array}{c} \text{Me} \quad \text{Me} \\ | \quad | \\ \text{R}-\text{Si}-\text{O}-\text{Si}-\text{Me} \\ | \quad | \\ \text{Me} \quad \text{Me} \end{array} \xrightarrow[2. \text{ CF}_3\text{COOOH}]{1. \text{ KHF}_2, \text{ TFAA}}$$

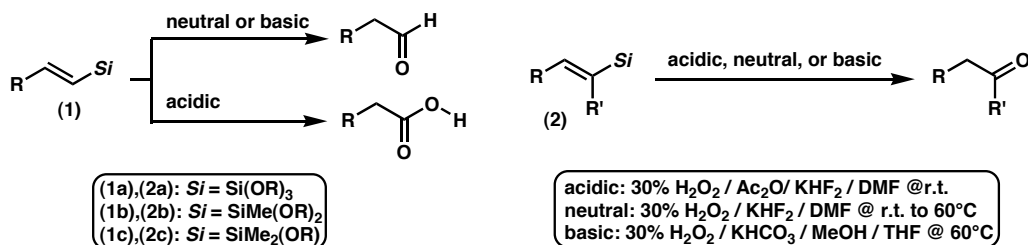
J.Orgmet.Chem, **1984**, 269, C37-C39

Alkenyl Silanes

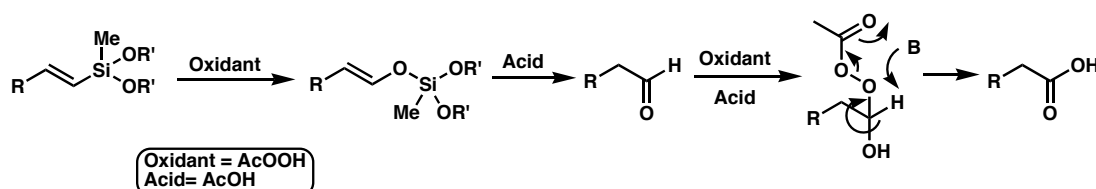


-Alkenyl silanes have different reactivity trends than alkyl silanes

-If alkenyl silanes are treated with an oxidant, a variety of different products can be obtained:

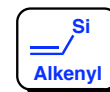


-If just two equivalents of oxidant are used on compounds of type (1b) or (1c) under acidic conditions, then only carboxylic acids are observed, indicating that an alkenyl carbon-silicon bond migrates preferentially to an alkyl carbon-silicon bond.

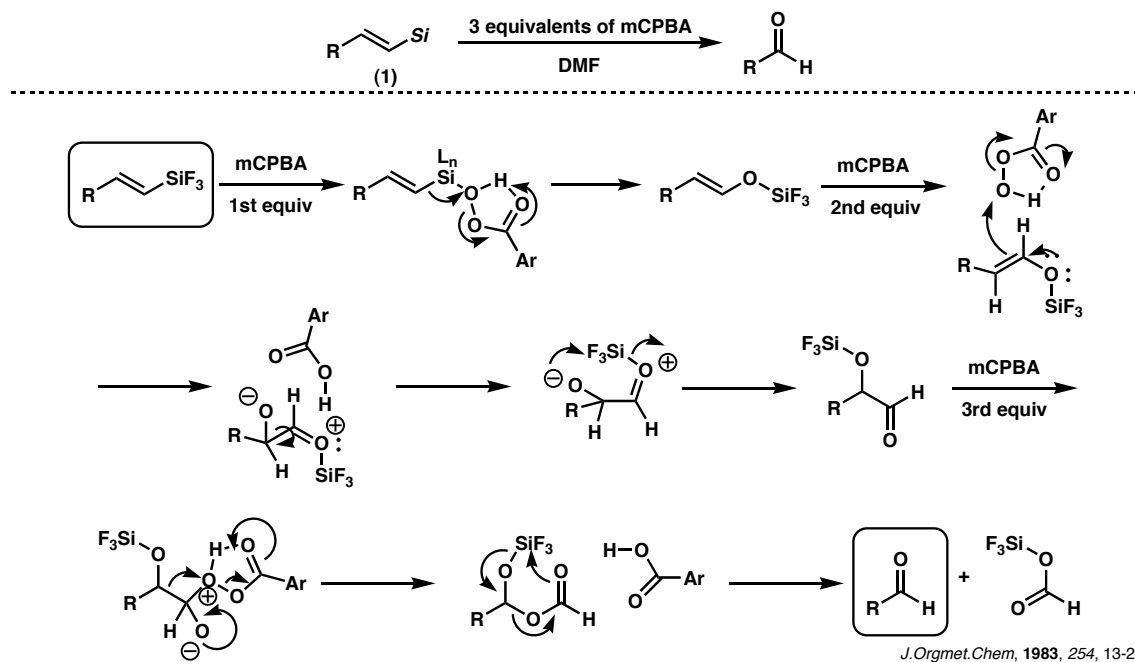


TL, 1984, 25, 321-324

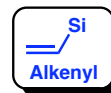
Alkenyl Silanes



-However, if compounds of type (1) are subjected to three equivalents of mCPBA in DMF, then the following dehomologation is observed:

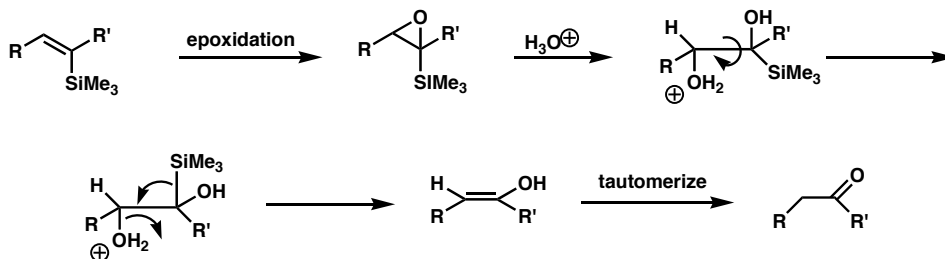


Alkenyl Silanes

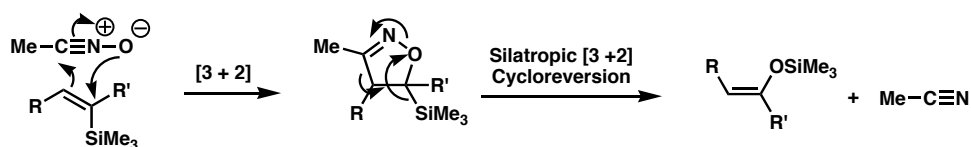


-The Tamao oxidation is mechanistically different from that of epoxidesilane or nitrile oxide oxidation:

Epoxydesilane:



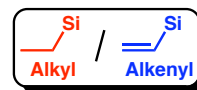
Nitrile Oxide Oxidation:



(R and R' retain their relative stereochemistry)

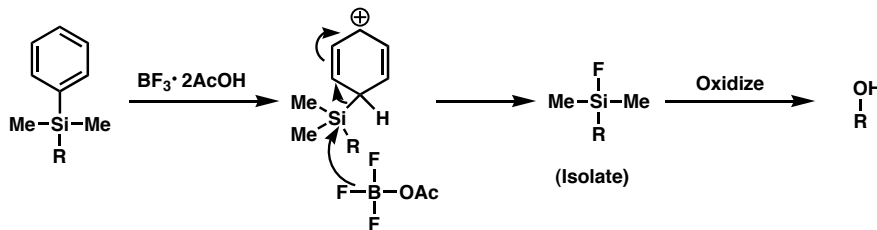
TL, 1984, 25, 321-324
J.Orgmet.Chem, 1981, 212, C51-C53

Can all the Substituents on Silicon be Carbon Atoms?

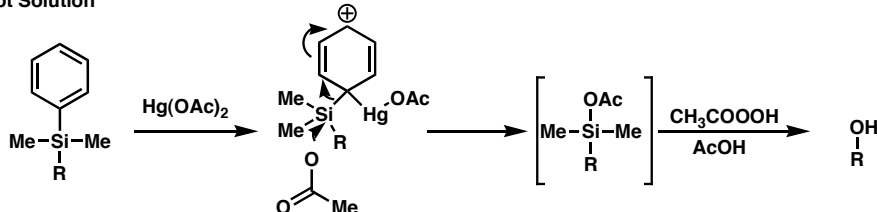


-Up to this point, Tamao had shown that it is necessary for at least one of the substituents on silicon to be a heteroatom or hydrogen. Then Fleming demonstrated something new:

2-Pot Solution



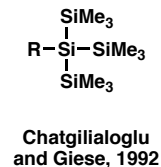
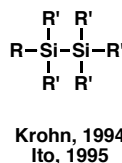
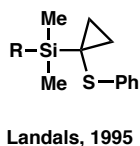
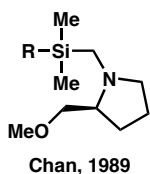
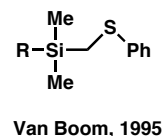
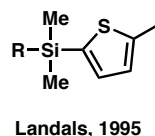
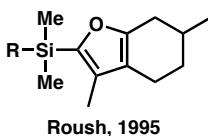
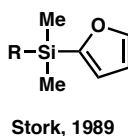
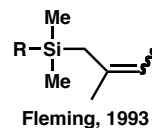
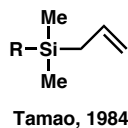
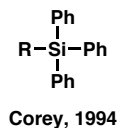
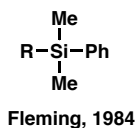
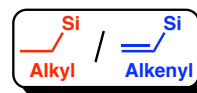
1-Pot Solution



-It is important to note that these solutions allow all-carbon-substituted silicon to be used or carried through a synthesis until just the right time, but do not skirt around the need for a heteroatom to be on the silicon just prior to oxidation!

JCS, Chem.Com., 1984, 29-31
TL, 1987, 28, 4229-4232
JCS, Per.T.1, 1995, 4, 317-337

More Silanes that can be Converted to Hydroxyl Groups

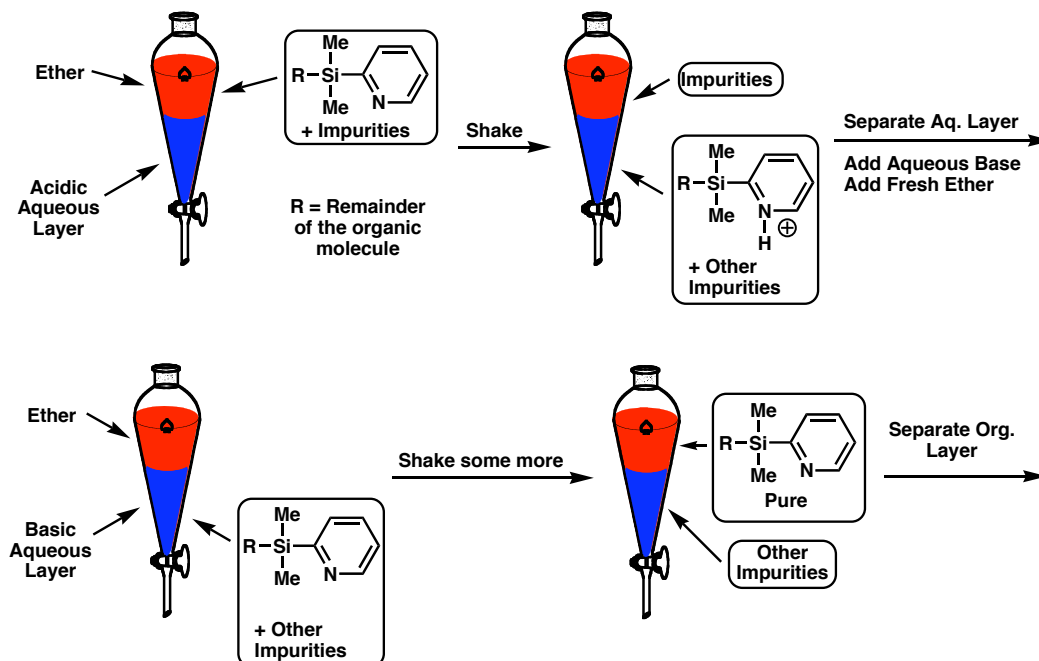


JOC, 1999, 64, 8709-8714

A Special All-Carbon Silane



-Recently a special functional group was developed that could serve as a phase tag to aid in purification.

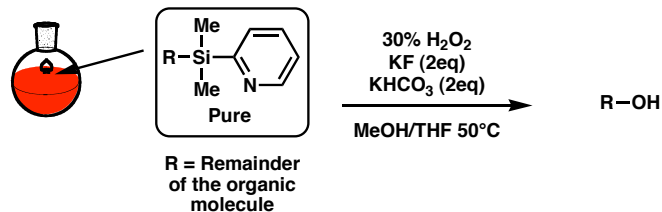


TL, 1999, 40, 3403-3406

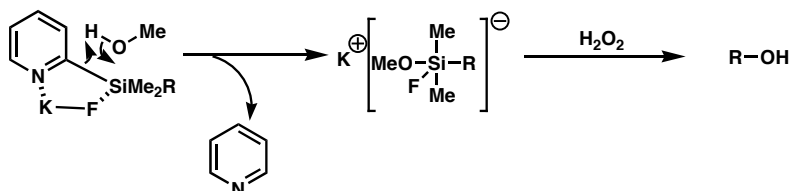
A Special All-Carbon Silane



-Once the silane has been purified using the phase-tagging procedure, a one-pot Tamao-Fleming oxidation can be performed



-The mechanism below has been hypothesized for this reaction:

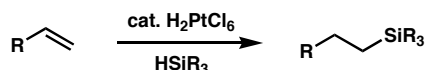


JOC, 1999, 64, 8709-8714

Hydrosilation of Alkenes

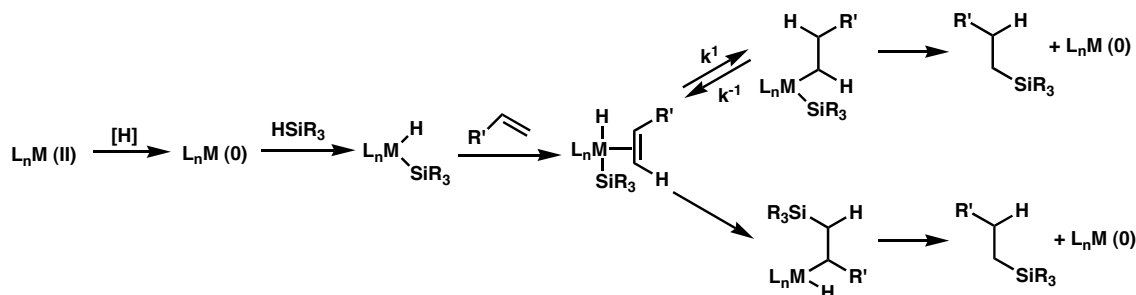


-One of the first methods devised for synthesizing alkyl silanes involved using H_2PtCl_6 (Speier's Catalyst):



-In the case of intermolecular hydrosilation of terminal olefins, the silicon usually ends up on the terminal carbon, but if the hydrosilation is intramolecular, there can be regioisomers.

-Chalk and Harrod did many mechanistic studies and elucidated the following reaction pathways:



-These reactions often begin with a low-temperature induction period, but can suddenly become exothermic as they enter the catalytic cycle above.

-These reactions can often be run neat and open to the atmosphere if Speier's or Wilkinson's Catalyst is used.

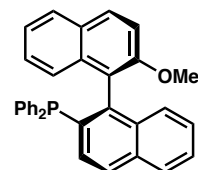
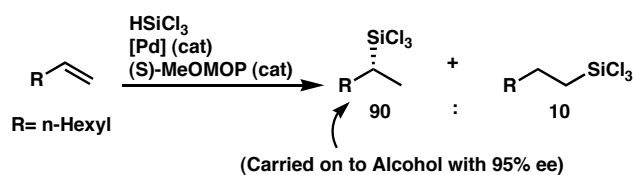
-Metals that have been used to catalyze hydrosilation include Pt, Rh, Pd, Co, Ir, and many others.

JACS, 1965, 87, 16-21

Stereocontrolled Hydrosilation of Alkenes



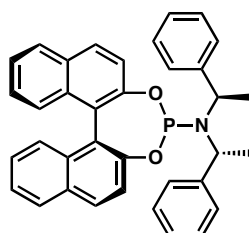
-There are a few examples of catalytic enantioselective hydrosilations. Here is one example by Hayashi:



(S)-MeO-MOP

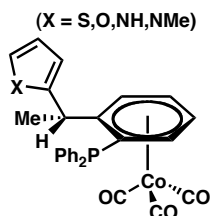
Acc.Chem.Res. 2000, 33, 354-362

-There are several other catalyst systems that allow for catalytic enantioselective hydrosilation



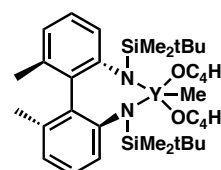
Uses [PdCl(Allyl)]₂ and HSiCl₃
Substrate Scope: Styrenes

JACS, 2002, 124, 4558-4559



Uses Pd and R₃SiH
Substrate Scope: Styrenes

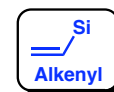
TL, 2001, 42, 6983-6986



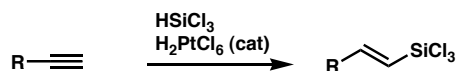
Uses PhSiH₃
Substrates Scope:
Norbornene and Styrenes

Orgmet. 1999, 18, 5661-5667

Alkyne Transformations

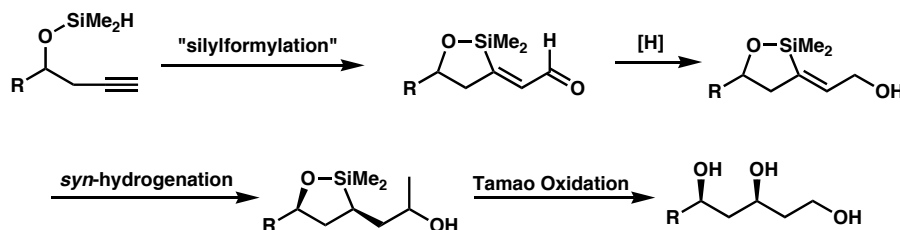


-Alkyne hydrosilation may be carried out with many of the same catalysts used for the hydrosilation of olefins.

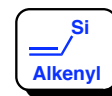


-Terminal acetylenes will hydrosilate in a *syn*-fashion under catalytic conditions (just like olefins do) and give terminal vinylsilanes when Pt or Rh are used.

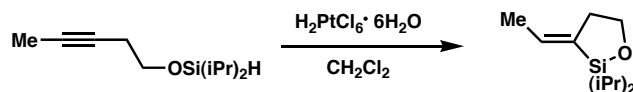
-One way to alter the regiochemistry of silation is to employ a tether as is seen in the example below:



Alkyne Transformations

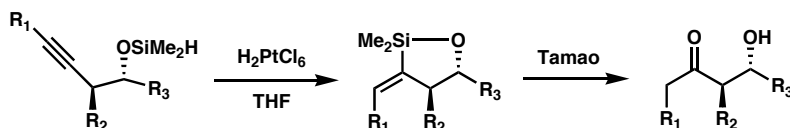


-The tethering strategy is not limited to silylformylation alone, however:



Denmark, S. E. and W. T. Pan

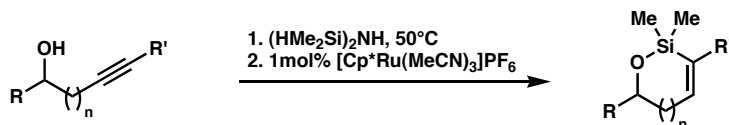
Org. Lett., 2001, 3, 61-64



Marshall, J. A. and M. M. Yanik

Org. Lett., 2000, 2, 2173-2175

-Although these examples give *exo* ring closures and *syn* hydrosilation, there is at least one example that affords *endo* ring closure with *anti* hydrosilation:

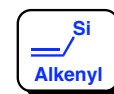


Trost, B. M. and Z. T. Ball

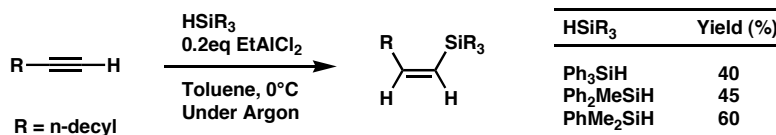
JACS, 2003, 125, 30-31

-This method by Trost is very general and shows good functional group tolerance.

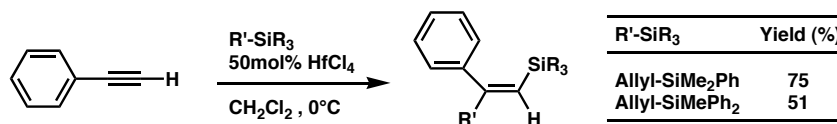
Alkyne Transformations



-Although most catalytic hydrosilations of alkynes occur in the *syn* sense, certain Lewis Acids will afford *anti* hydrosilation products that are competent starting materials for Tamao-Fleming oxidations:



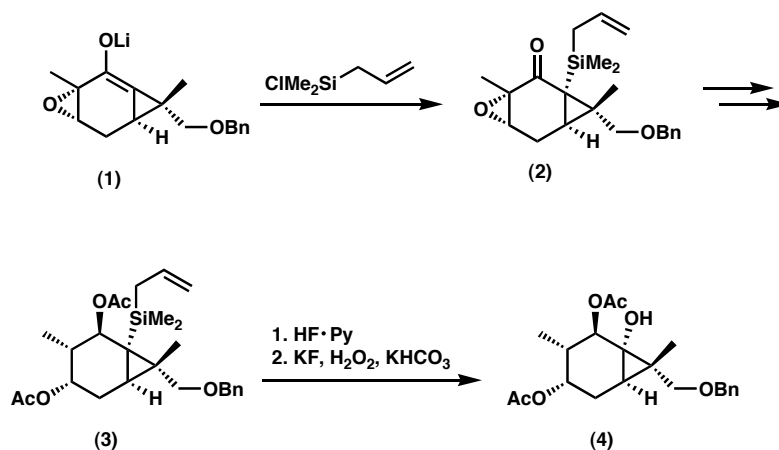
-It is also possible to carry out *trans* carbosilations of alkynes:



Electrophilic Silicon



-In a recent review by Fleming an example was shown where electrophilic silicon was brought in and converted to a hydroxyl group by means of a Tamao-Fleming process:



-The intermediate (4) was carried on in the synthesis of phorbol analogs

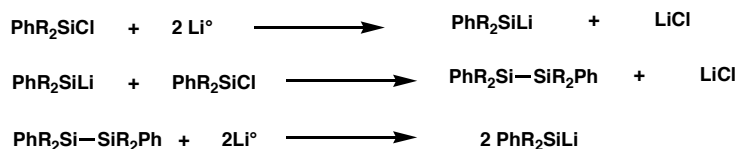
Chem.Rev., **1997**, *97*, 2063-2192

Nucleophilic Silicon



-There are many types of silyl anions that can be utilized in synthesis.

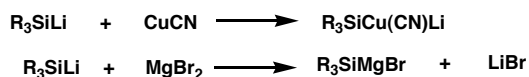
-The most typical method used to generate arylsilyl anions involves treatment of the silyl chloride with Lithium metal. The processes below are all involved in the generation of the free anion:



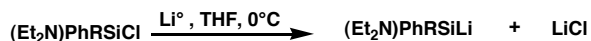
-Alkylsilyl anions may be prepared by adding alkylmetals to the appropriate disilane. Adding Lithium metal alone will not work because the Si-Si σ^* orbital is too high to accept electrons from Lithium.



-Silyl Cuprates and Grignards are prepared from the silyl lithiums as shown below:



-Another popular class of silyl anions are derived from aminosilanes:

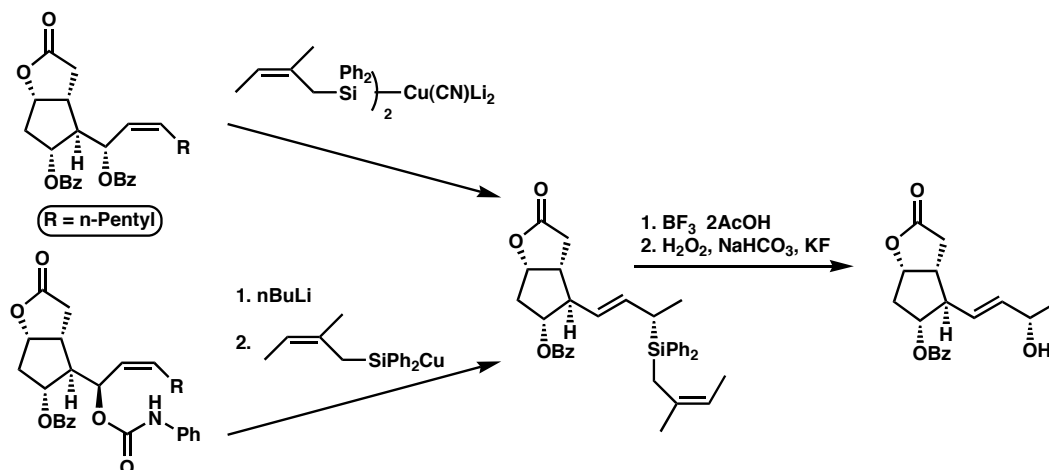


Adv.Orgmet.Chem., **1995**, *38*, 1-58

Nucleophilic Silicon



-Silyl Anions can be thought of as masked hydroxyl groups as demonstrated below:



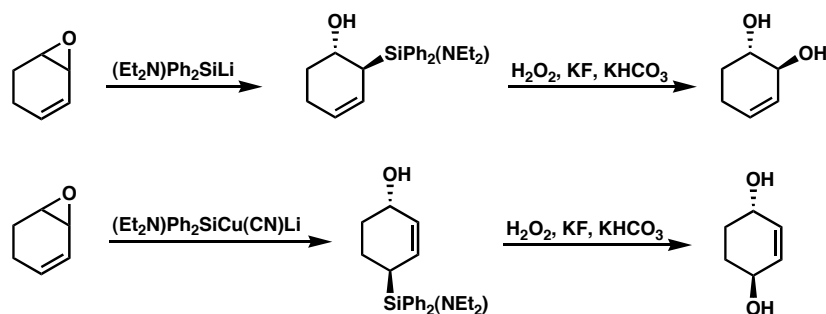
-Note that in the first case, the silyl cuprate adds *syn* to the original leaving group position, but in the second case, it adds *anti*.

Chem.Rev., 1997, 97, 2063-2192

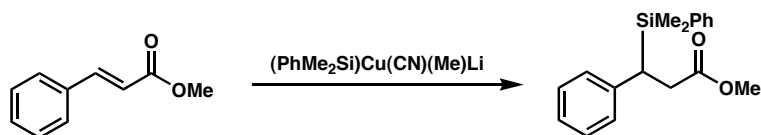
Nucleophilic Silicon



-Silyl Anions can also be added to α,β -unsaturated epoxides:



-Silyl Cuprates can add into α,β -unsaturated carbonyl compounds:

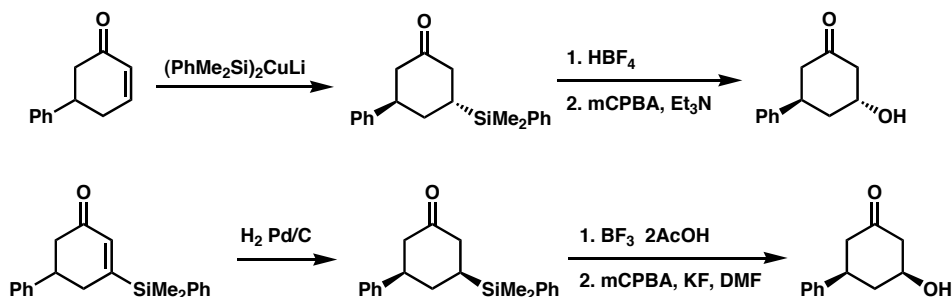


Chem.Rev., 1997, 97, 2063-2192
Adv.Orgmet.Chem., 1995, 38, 1-58

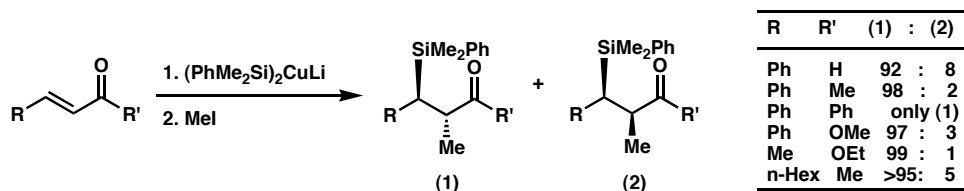
Fleming's "Aldol" Chemistry



-Fleming developed the following chemistry with six-membered rings:

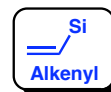


-He also developed similar chemistry with acyclic systems:



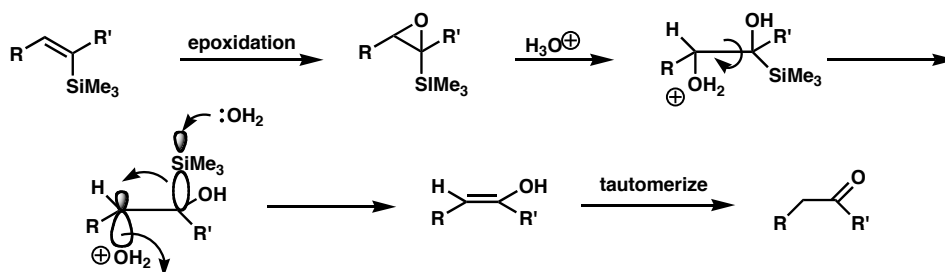
JCS.Chem.Com., 1984, 29-31
JCS.Chem.Com., 1984, 28-29

Tamao-Fleming Oxidations Used to Prepare Carbonyl Compounds

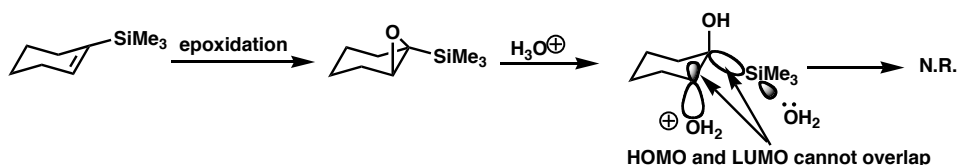


-The epoxydesilation methodology mentioned earlier allows for the preparation of acyclic ketones from vinyl silanes, but cannot be used to generate cyclic ketones due to stereoelectronic reasons:

Acyclic Mechanism:



The Cyclic Case:

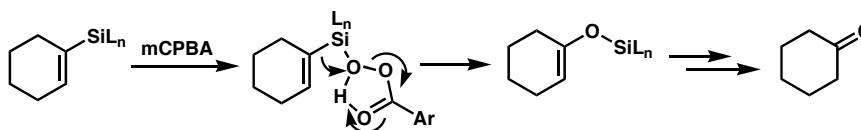


TL, 1984, 25, 321-324

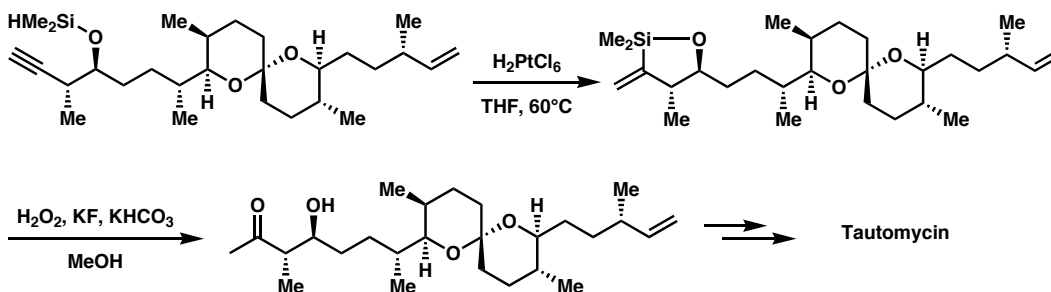
Tamao-Fleming Oxidations Used to Prepare Carbonyl Compounds



-The Tamao-Fleming oxidation, however, gives access to cyclic ketone from cyclic vinyl silanes because it goes through a different reaction pathway:



-An Intramolecular Hydrosilation of an Alkyne and Tamao Oxidation were used in the total synthesis of the Protein Phosphatase Inhibitor Tautomycin:

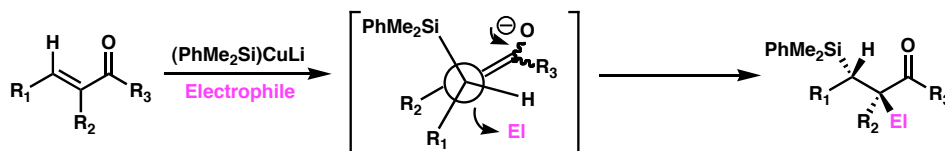


JOC, 2001, 66, 1373-1379

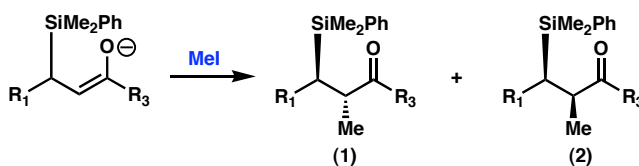
Stereoselective Reactions



-Fleming speculated that acyclic conjugate addition intermediates had a preferred conformation that could be used to explain why the formation of certain diastereomers was favored:

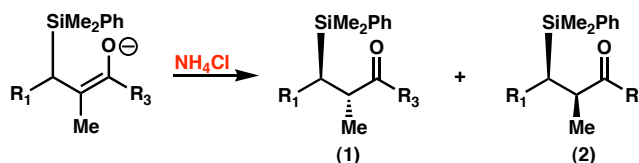


Examples:



(Enolates drawn could be either E or Z)

R ₁	R ₃	(1):(2)
Ph	OMe	97:3
Ph	Me	98:2
Ph	H	92:8
Ph	NMe ₂	97:3
Me	Me	91:9
iPr	Me	85:15



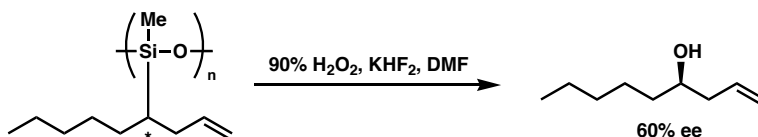
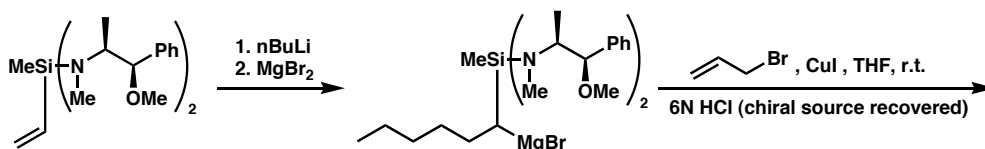
R ₁	R ₃	(1):(2)
Ph	OMe	15:85
Ph	Me	30:70
Ph	H	11:89
Ph	NMe ₂	18:82
Me	Me	13:87
iPr	Me	4:96

JCS, Chem.Com., 1985, 318-321

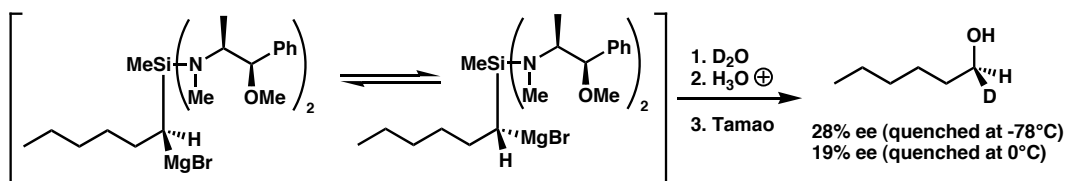
Stereoselective Reactions



-Chiral Auxiliaries have been developed where there is an optically active group attached to the silicon atom. The auxiliary can be used in a diastereoselective reaction and removed via Tamao Oxidation:



-Using isotopic quenching, the authors found that the metalated species below is in a dynamic equilibrium in which the auxiliary pushes the metal/anion to a particular diastereoface preferentially.

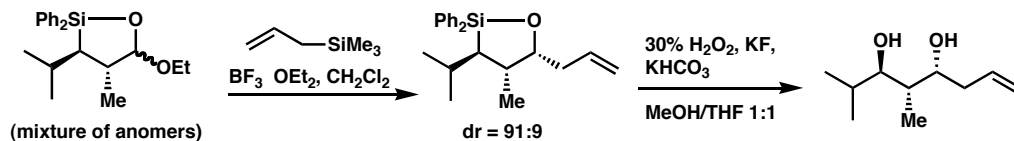
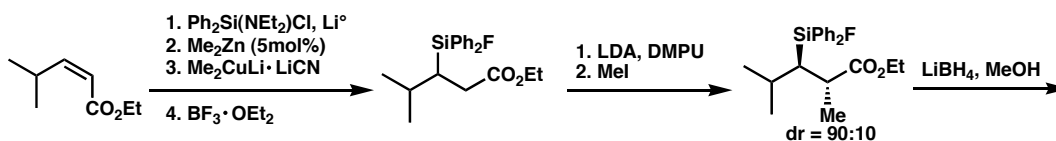


TL, 1984, 25, 1913-1916

Polyol Synthesis

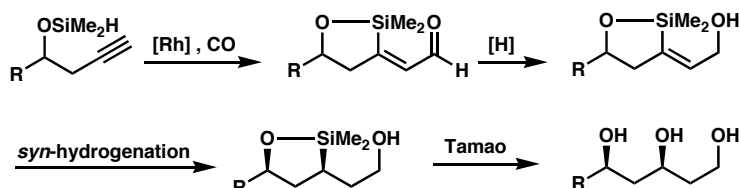


-Woerpel has used functionalized silyl anions in the synthesis of *anti*-1,3 diols:



Org. Let., 2003, 5, 4325-4327

-Hara, Moralee, and Ojima have use intramolecular silylformylation/ diastereoselective hydrogenation to synthesize *syn*-1,3 diols:

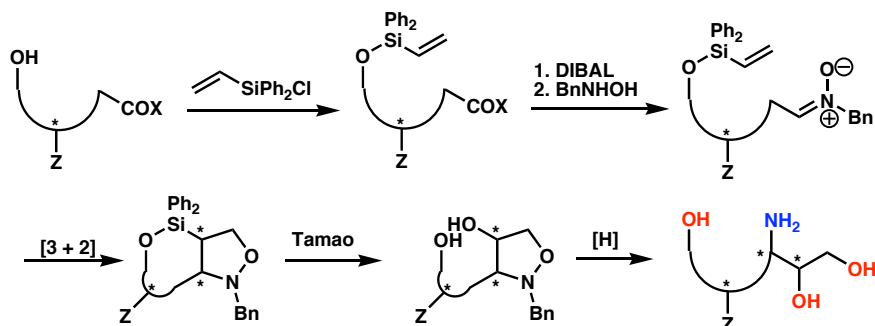


Abstracts of Papers, 222nd ACS Meeting, Chicago, 2001, ORGN-089

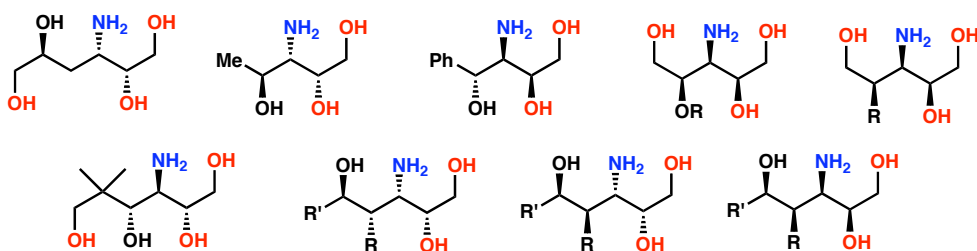
Polyol Synthesis



-The [3 + 2] cycloaddition of nitrones to olefins is yet another powerful tool used to generate complex polyols as demonstrated by Ishikawa:



-Many types of amino polyols are accessible via this methodology:

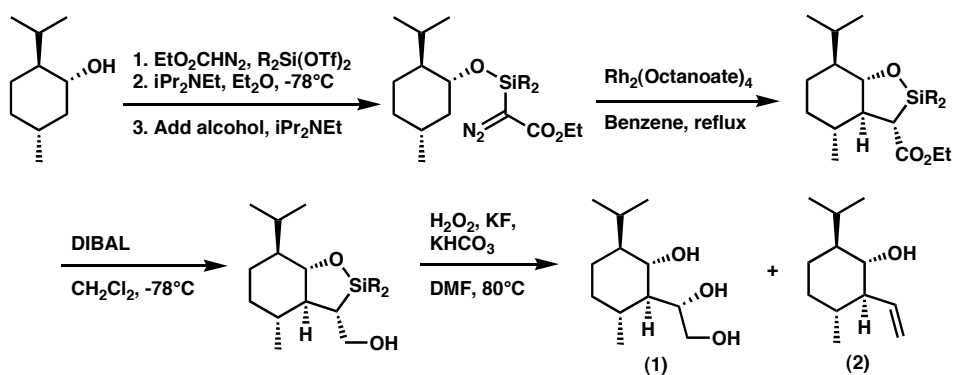


JACS, 2000, 122, 7633-7637

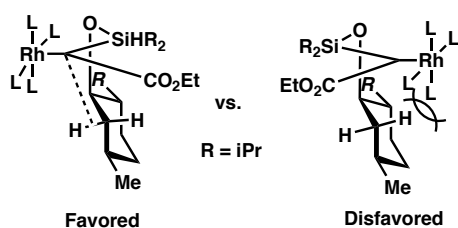
Polyol Synthesis



-It is also possible to tether silyl groups that can participate in C-H insertion reactions as Marsden has demonstrated:



-Proposed model for observed diastereoselection in the insertion step:



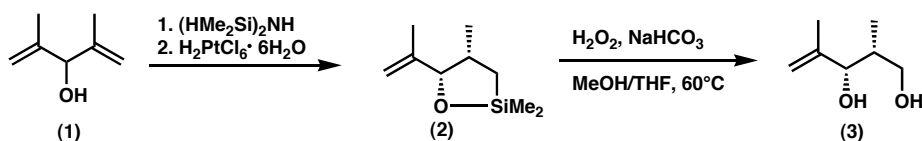
The olefinic side product (2) above arises from a Peterson elimination process

TL, 1998, 39, 5109-5112

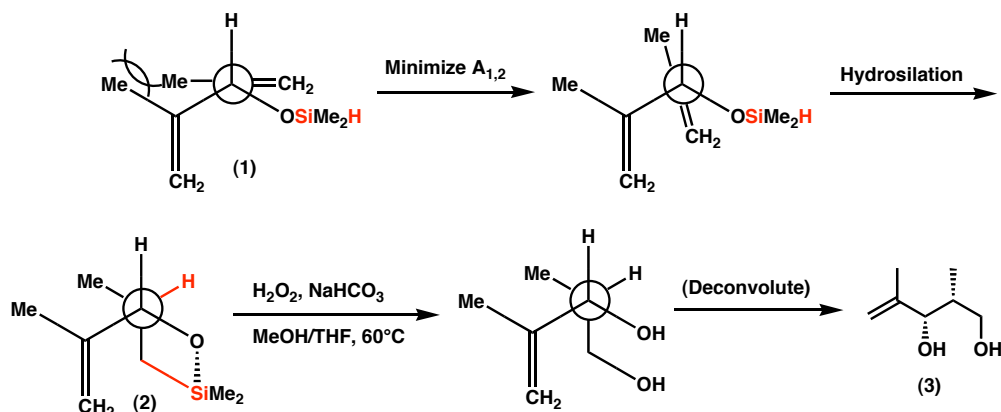
Polyol Synthesis



-Tamao has also done diastereoselective desymmetrizations of *meso*-allylic alcohols:



-The diastereoselection observed can be explained by an $A_{1,2}$ strain argument

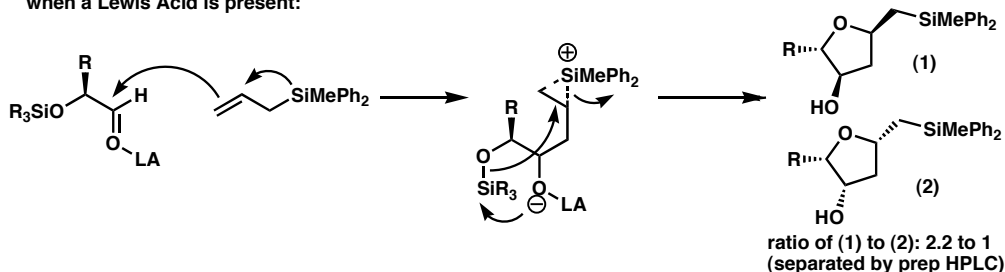


JACS, 1986, 108, 6090-6093

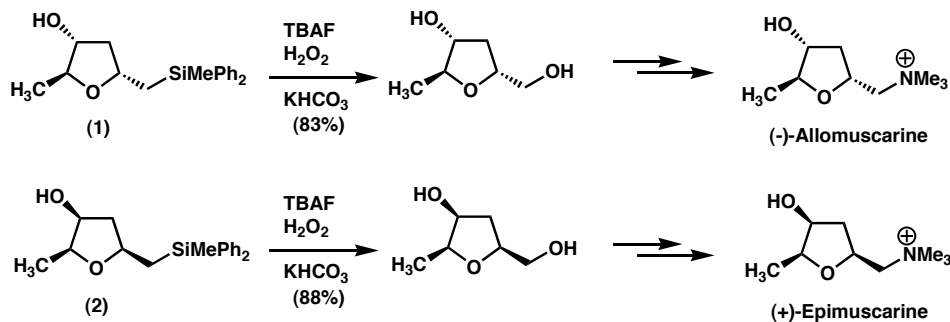
Tetrahydrofuran Synthesis



-Allylic Silanes can be added to α -siloxy aldehydes in a formal [3 + 2] sense, to give tetrahydrofurans when a Lewis Acid is present:



-This methodology, when combined with the Tamao-Fleming Oxidation allowed for the total synthesis of both (+)-Epimuscarine and (-)-Allomuscarine

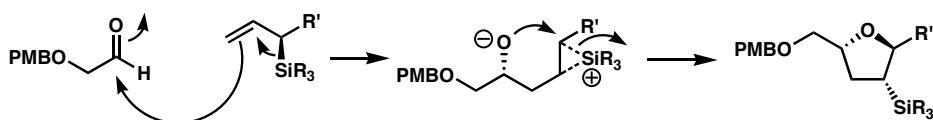


JACS, 2002, 124, 3608-3613

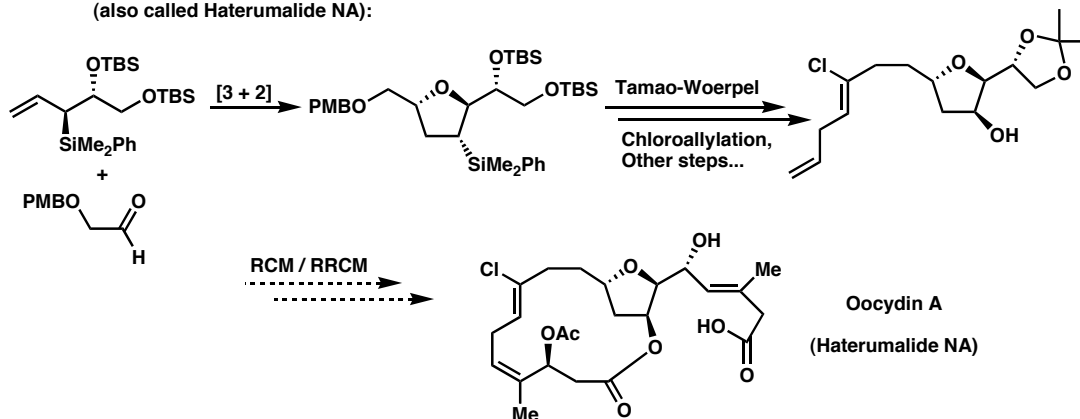
Tetrahydrofuran Synthesis



-If the α -substituent on the aldehyde is protected with a functional group that cannot migrate, the [3 + 2] cycloaddition may go through an alternative pathway that is *endo* instead of *exo*:



-This alternative methodology was applied in progress toward the total synthesis of Oocydin A (also called Haterumalide NA):

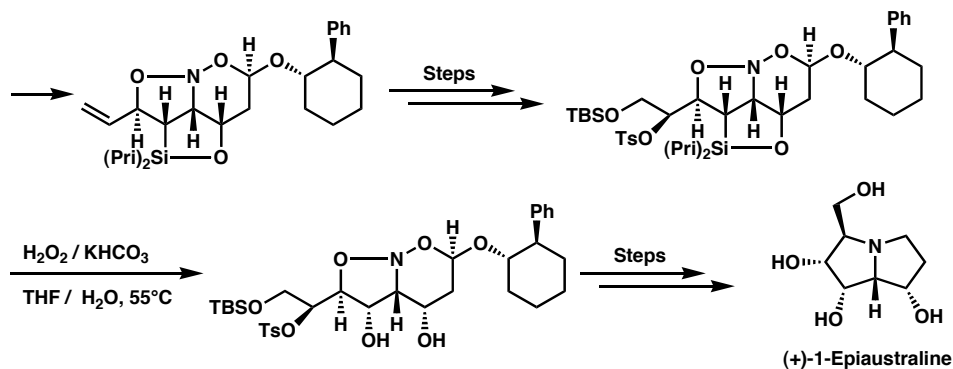
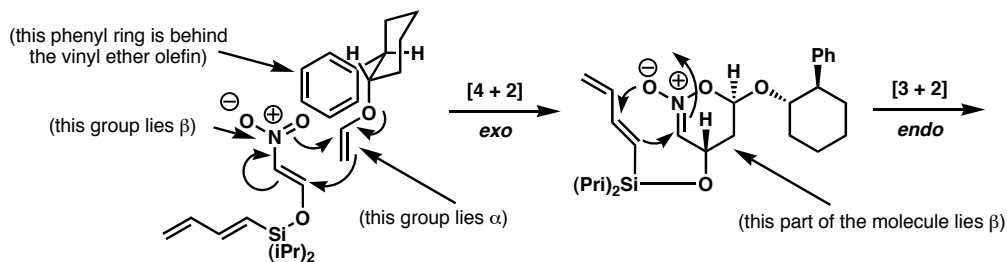


Abstracts of Papers, 226th ACS Meeting, New York, 2003, ORGN-670

Nitrone Cycloadditions

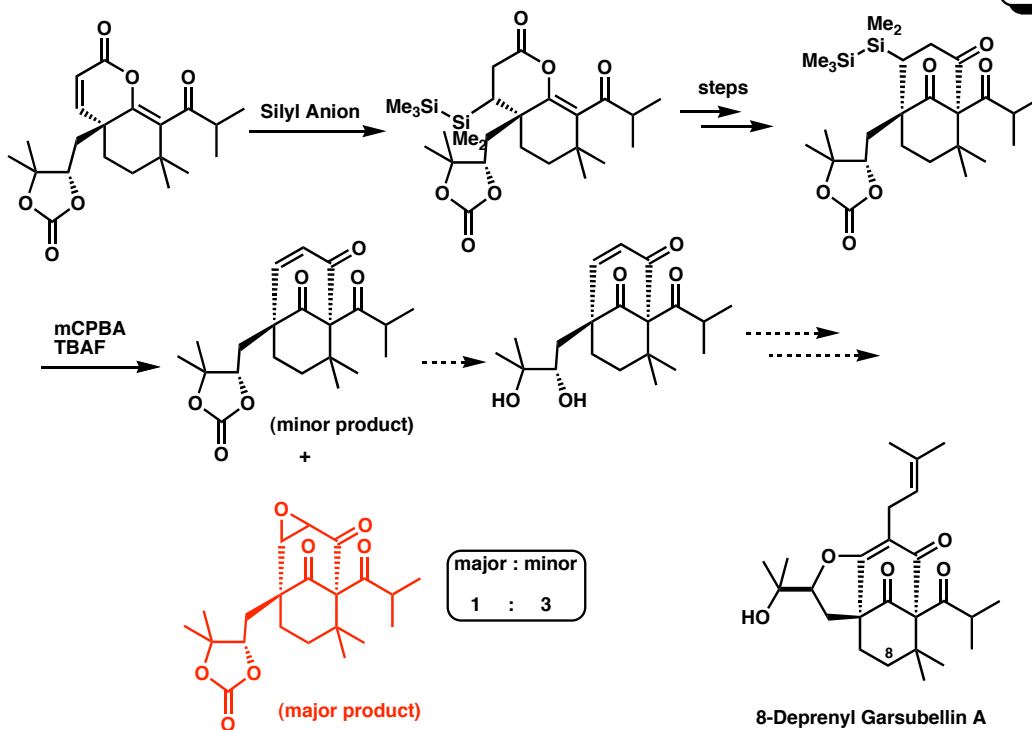


-The following series of transformations, including a Tamao oxidation was used in the total synthesis of Epiaustraline



JOC, 2001, 66, 4276-4284

8-Deprenyl Garsubellin A

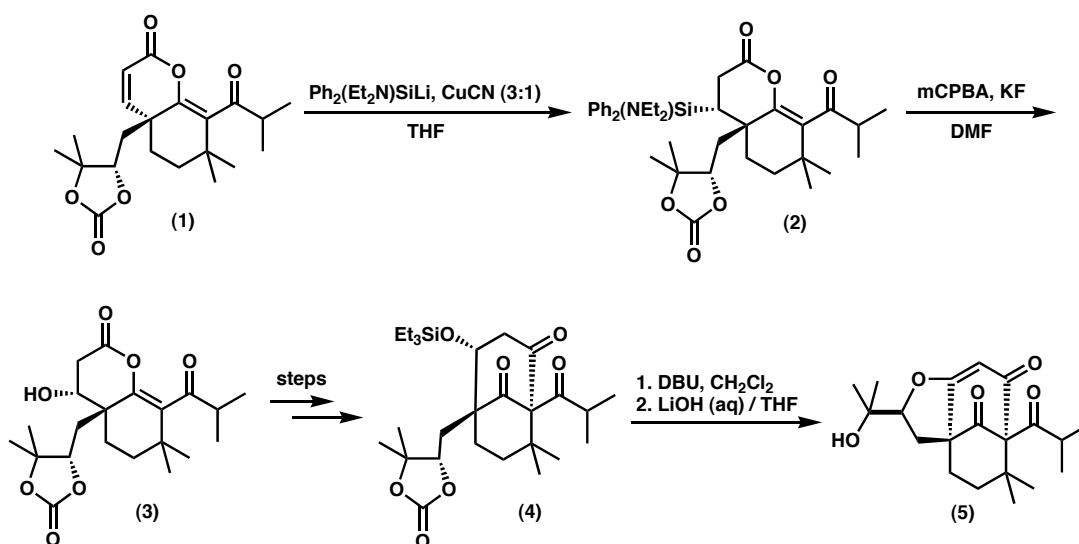


TL, 2002, 43, 3621-3624

8-Deprenyl Garsubellin A



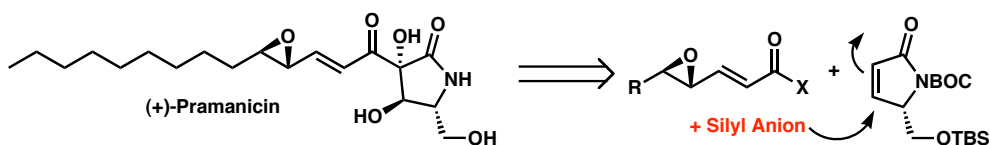
-The major problem was overoxidation promoted by the mCPBA after the β -elimination under the basic conditions with the TBAF. The authors decided to avoid β -elimination entirely!



-The intermediate (5) was successfully carried on to 8-Deprenyl Garsubellin A.

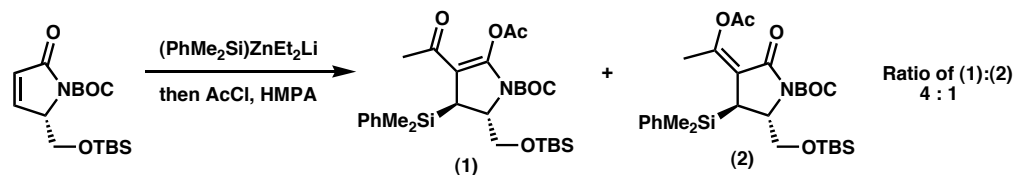
TL, 2002, 43, 3621-3624

(+)-Pramanicin

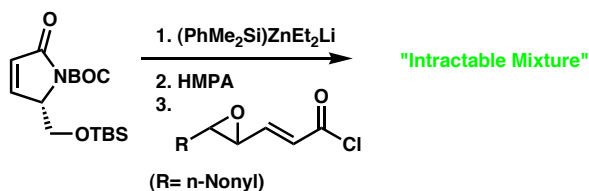


-The authors envisioned that a silyl anion could be brought in and later converted to a hydroxyl group.

-They began with a model system:



-Then they tried the real thing...

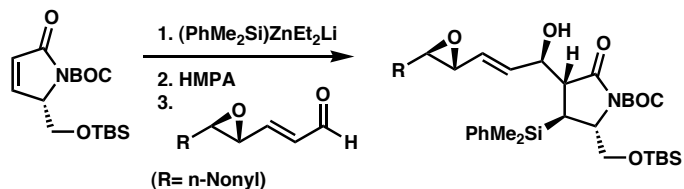


JOC, 1999, 64, 6005-6018

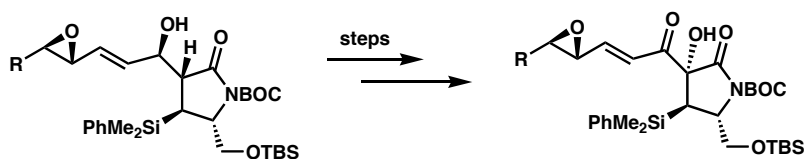
(+)-Pramanicin



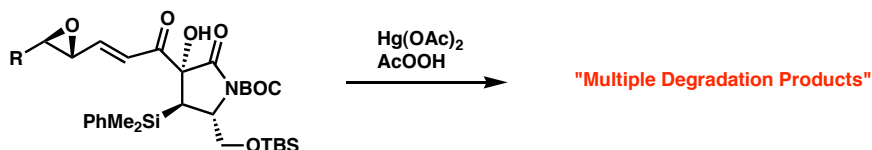
-The authors decided to bring in the epoxy piece in a different oxidation state:



-Seeing that this worked well, they elaborated the product further:



-And they got very, very close to finishing the synthesis, but...

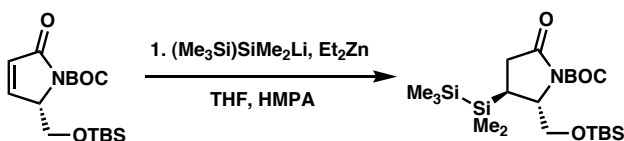


JOC, 1999, 64, 6005-6018

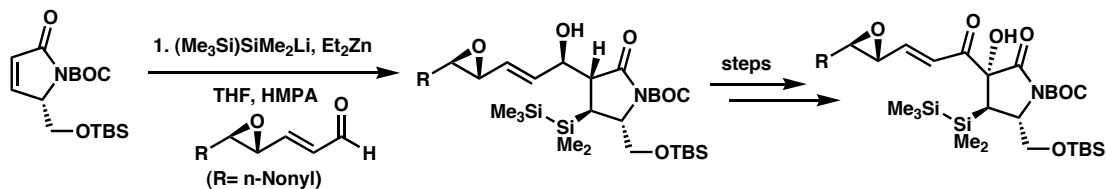
(+)-Pramanicin



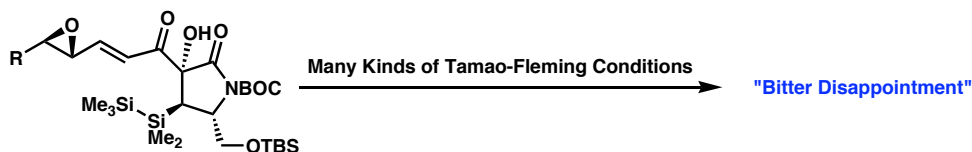
-Because they were able to get so close to the end of the synthesis, they thought that maybe another type of silane might give a more favorable outcome:



-The Silyl Anion addition went well, so they moved on with more success:



-But yet again they were unable to pull off the last step. This time the C-Si bond would just not oxidize!

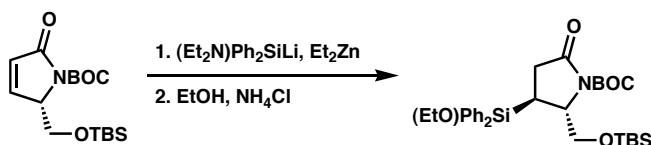


JOC, 1999, 64, 6005-6018

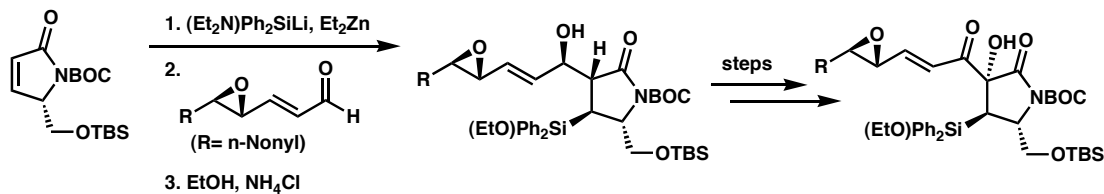
(+)-Pramanicin



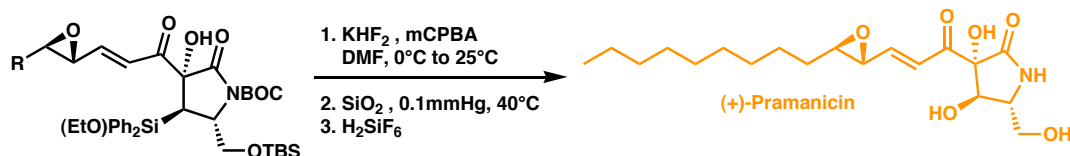
-Where many chemists would have surrendered, the authors continued their assault:



-And yet again they met with early successes:

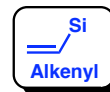


-Could they pull off the last step?

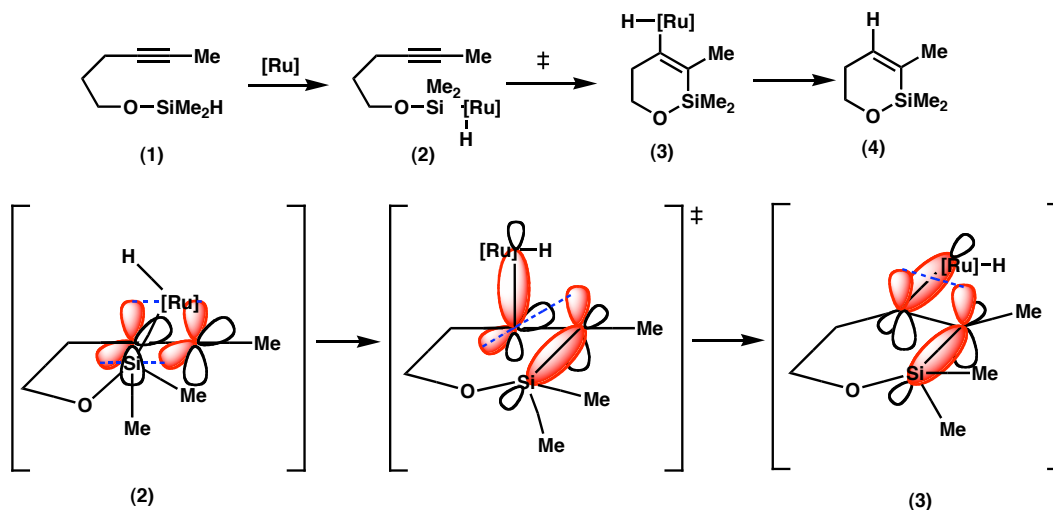


JOC, 1999, 64, 6005-6018

Alkyne Transformations



-Trost's best hypothesis about the mechanism of this hydrosilylation is that the Ru-Si bond is adding across BOTH π -systems of the alkyne:

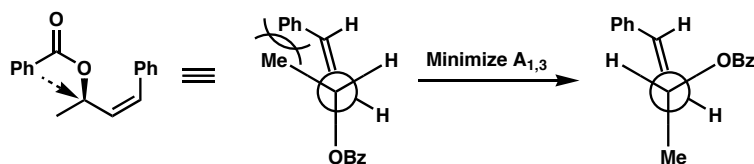


JACS, 2003, 125, 30-31

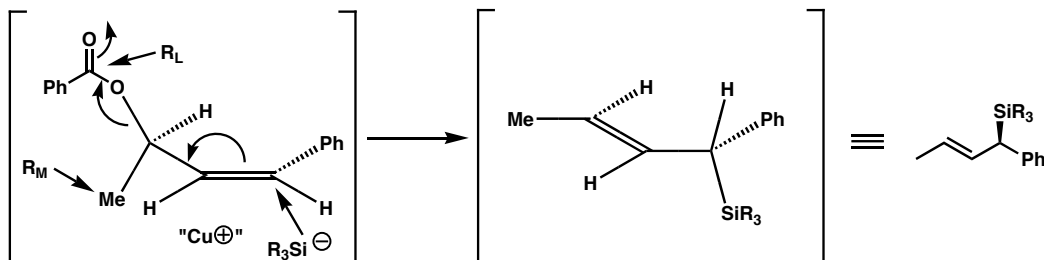
Nucleophilic Silicon



-The stereoselection shown on the previous slide can be explained as follows:



-The Silane approaches the least hindered face

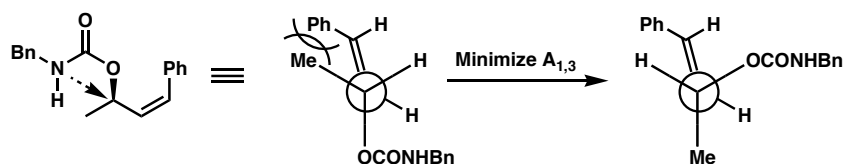


Chem. Rev., 1997, 97, 2063-2192

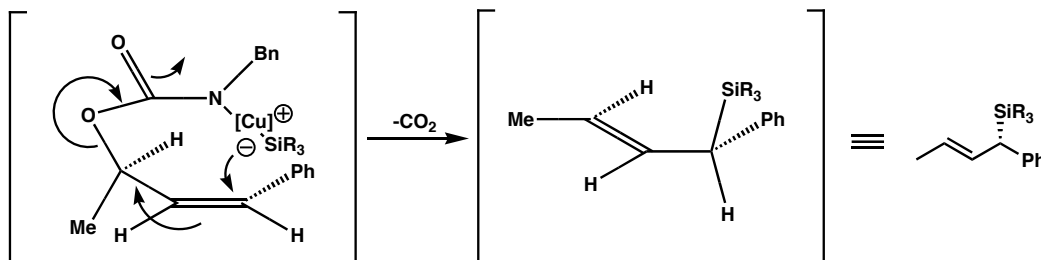
Nucleophilic Silicon



-In the case of the carbamate, the reaction sets up in a similar way:



-The Cuprate, however, is now directed to the opposite face of the olefin.



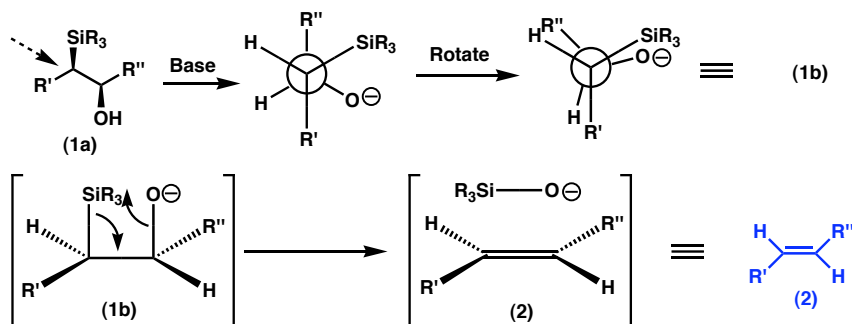
-In both the benzoate and carbamate cases, *trans*-disubstituted olefins are less stereospecific.

Chem. Rev., 1997, 97, 2063-2192

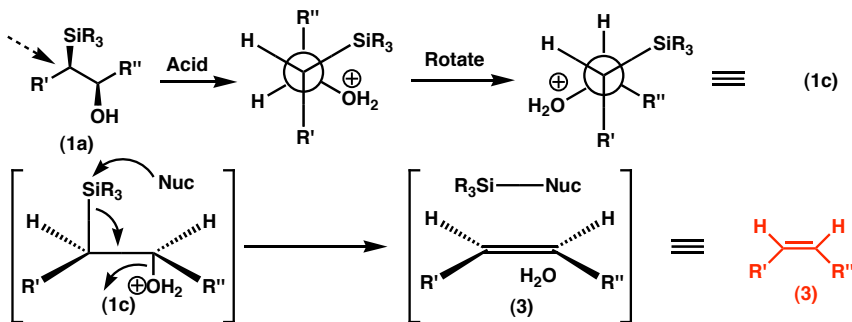
The Peterson Olefination



-Under Basic Conditions, the following reaction pathway occurs:



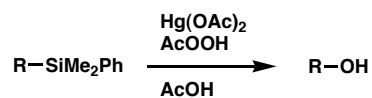
-Under Acidic Conditions, a different mechanism is involved:



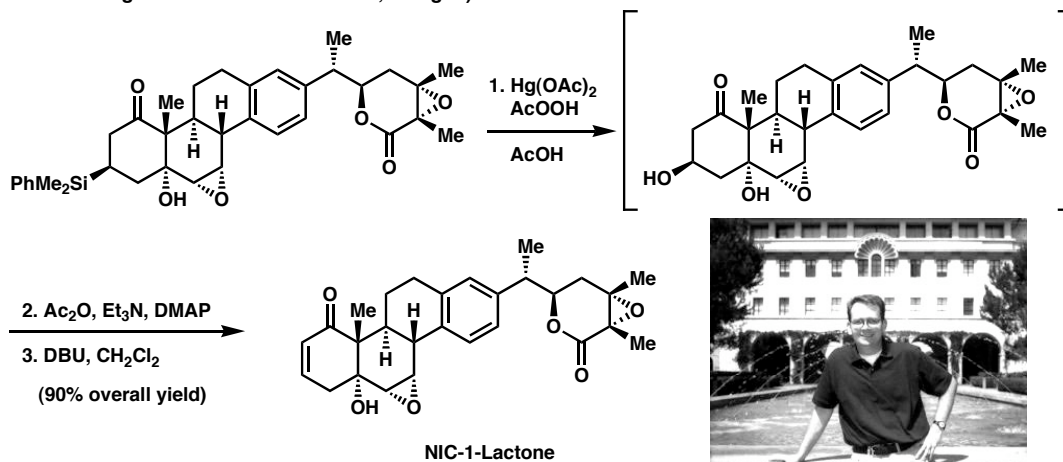
Look Familiar?



-Someone we know once called the reaction below "A Classic":



-He might have been a little biased, though :)



Stoltz, B. M.; Kano, T.; Corey, E. J. *JACS*, **2000**, *122*, 9044-9045.

