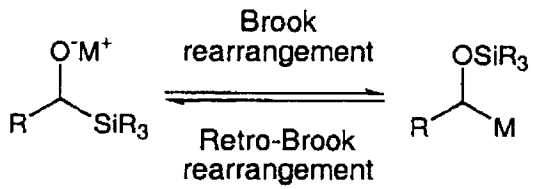
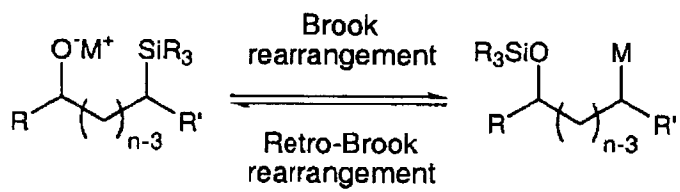
Tandem Bond Forming Strategies Utilizing the Brook Rearrangement

[1,2]-Silyl Migrations



[1,n]-Silyl Migrations



John Heemstra Jr.

12/17/02

Discovery of the Intramolecular [1,2] Anionic Migration of Silicon From Carbon to Oxygen

$$Ph_3SiK + CH_2{=}O \longrightarrow \underset{\mathbf{1}}{Ph_3SiCH_2OH}$$

$$Ph_3SiK + Ph_2CO \longrightarrow \underset{\mathbf{2}}{Ph_3SiOCHPh_2}$$

- Aliphatic aldehydes and ketones formed carbinols, **1**.
- Aromatic aldehydes and ketones formed the isomeric silyl ether **2**.

$$Ph_3SiCl + LiCHPh_2 \longrightarrow Ph_3SiCHPh_2 \xrightarrow[\text{2. AgOAc, } H_2O]{\text{1. NBS}}$$

$$\underset{\mathbf{3}}{Ph_3SiCOHPh_2} \xrightarrow{\text{Na-K}} Ph_3SiOCHPh_2$$

- Aromatic carbinol **3** rearranged rapidly when treated with trace amounts of Na-K alloy to form a silyl ether.

$$R_3Si{-}\underset{\underset{OH}{|}}{C}R_2' \longrightarrow R_3Si{-}O{-}CHR_2'$$

R = aryl, alkyl
R′ = aryl, alkyl, hydrogen
isomerizing agents: Na–K, Na, NaH, RLi, Et_2NH, R_3N

- Further investigations found that all types of silylcarbinols rearrange when treated with small amounts of active metal, organometallic reagents, or bases.

Brook, A. G. *Acc. Chem. Res.* **1974**, *7*, 77

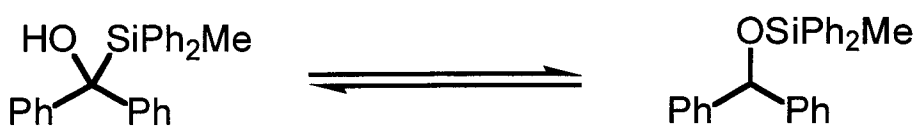
Kinetic Studies on the [1,2]-Silyl Migration

Approximate Rates of Rearrangement of Silylcarbinols in Me_2SO by Et_2NH at 36°

Carbinol	Rate, l. mol^{-1} sec^{-1}
Ph_3SiCPh_2OH	7.6
$Ph_3SiCMePhOH$	6.7×10^{-3}
$Ph_3SiCHPhOH$	5.7×10^{-3}
$Ph_3SiC(CH_2Ph)PhOH$	1.1×10^{-1}
Ph_3SiCMe_2OH	Too slow to measure
$MePh_2SiCPh_2OH$	1.2
$Me_2PhSiCPh_2OH$	2×10^{-1}
Me_3SiCPh_2OH	3.3×10^{-2}

- Rearrangement was found to obey pseudo-first-order kinetics overall.
- Increasing the amount of phenyl groups on carbon and silicon increases the rate.

E_{act} = 11.1 kcal/mol
dS = -34.2 eu



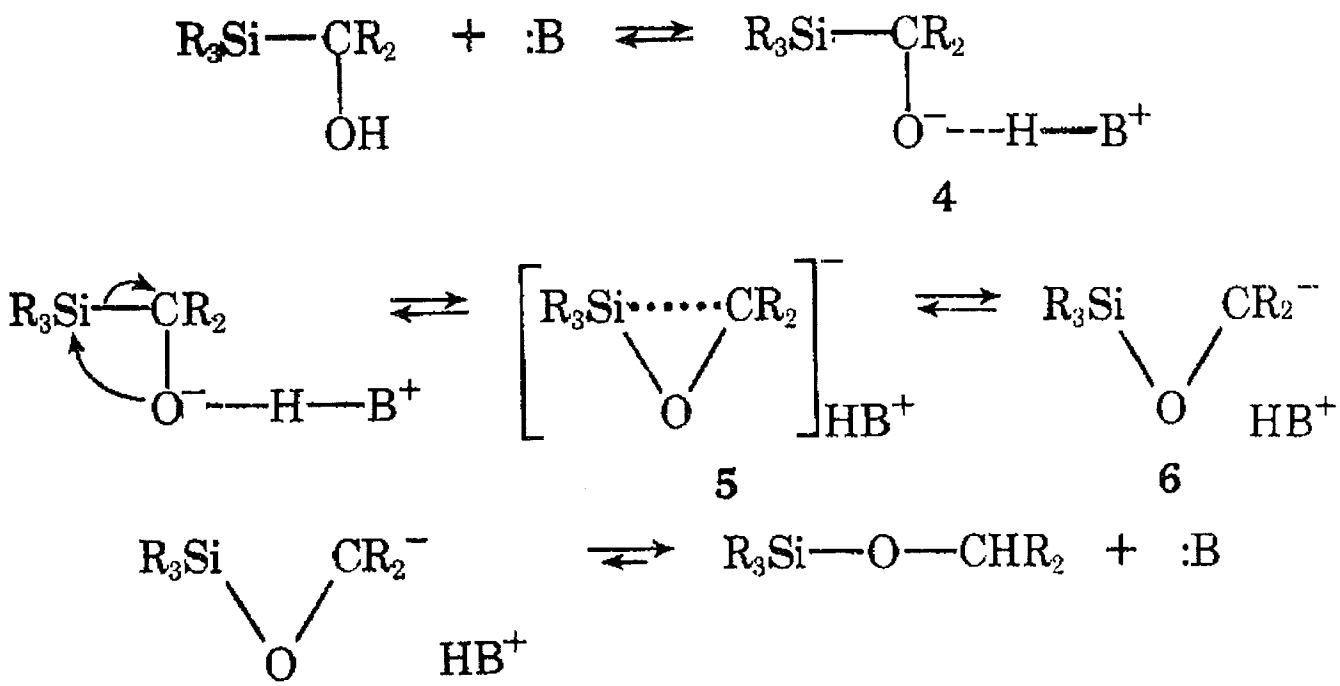
E_{act} = 8.7 kcal/mol
dS = -45.6 eu

Hammett study using σ_ρ gave values of ρ ranging from 3.4 to 4.6

- The kinetic data suggests there is a a highly ordered transition state with substantial build-up of electron density on the benzylic carbon .

Brook, A. G. *Acc. Chem. Res.* **1974**, *7*, 77

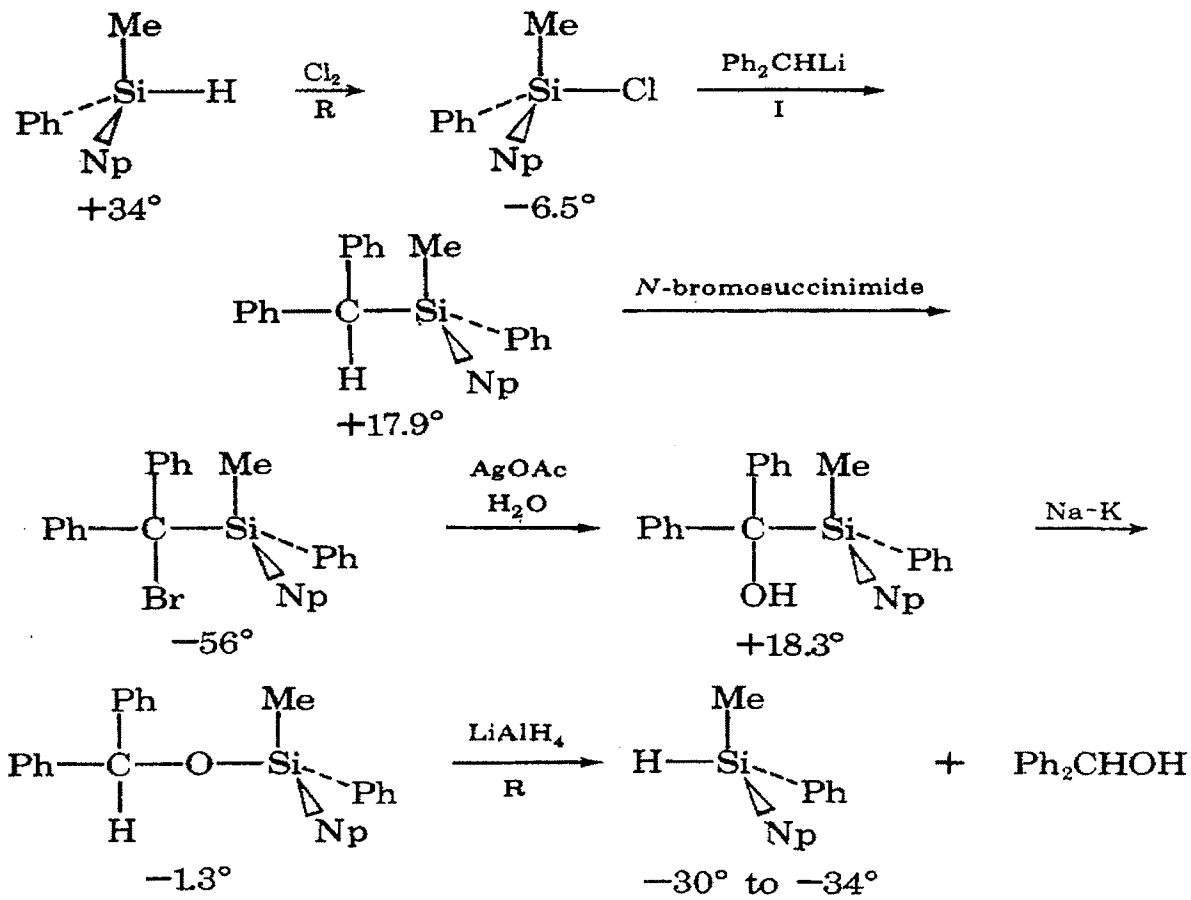
Proposed Mechanism for the 1,2 Silyl Migration



- Reactions run with catalytic amounts of base.
- Transition state **5** is proposed to have significant silicon-carbon bond breaking to account for the large positive Hammett ρ value
- The cyclic species in transition state **5** accounts for the large negative entropy of activation.

Brook, A. G. *Acc. Chem. Res.* **1974**, *7*, 77

Use of the Walden Cycle to Determine the Stereochemical Result of the Silyl Migration at Silicon

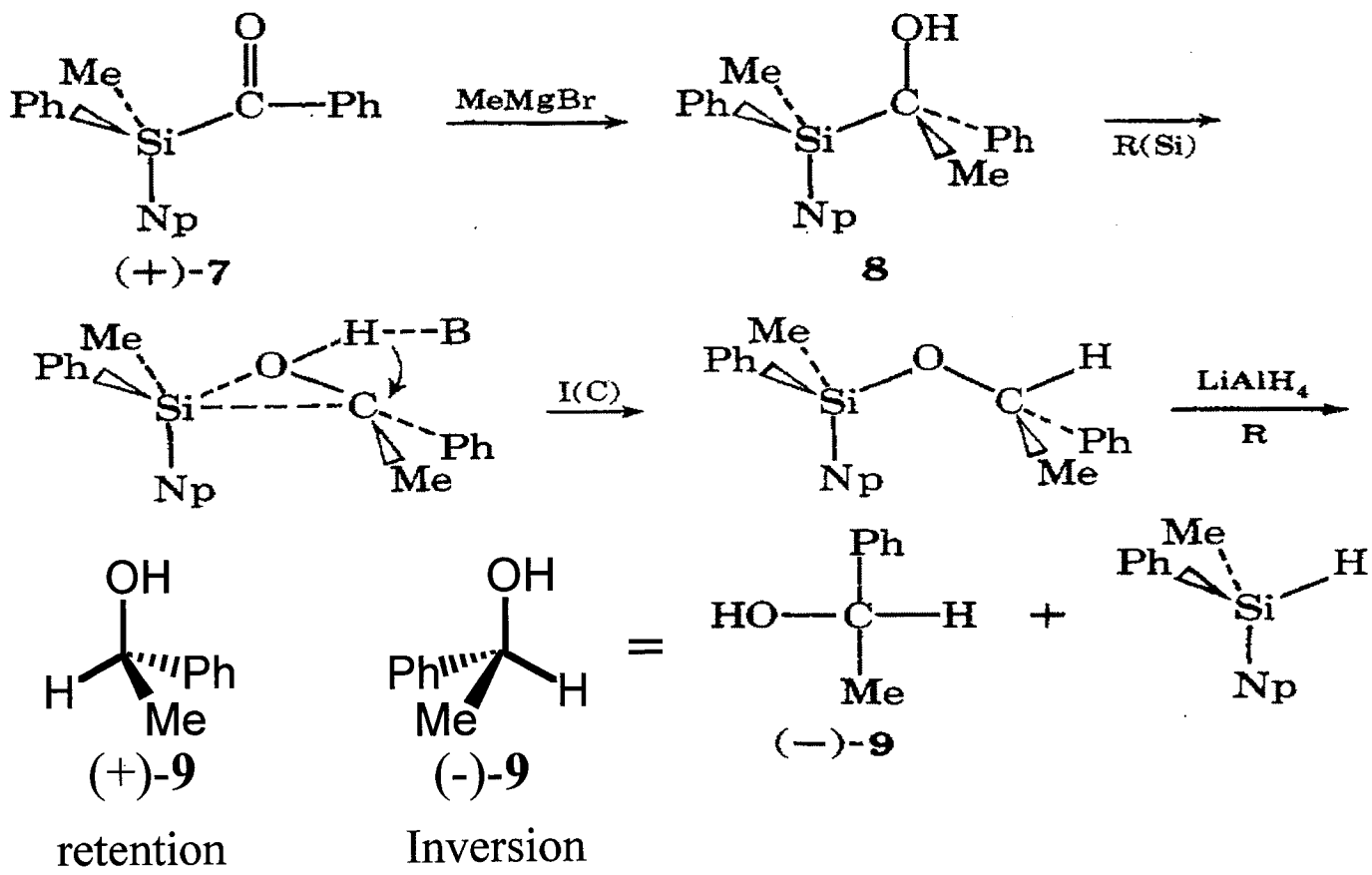


R = retention of configuration; I = inversion of configuration

Overall inversion of configuration implies the rearrangement occurs with retention of configuration at the silicon center.

Brook, A. G. *Acc. Chem. Res.* **1974**, *7*, 77

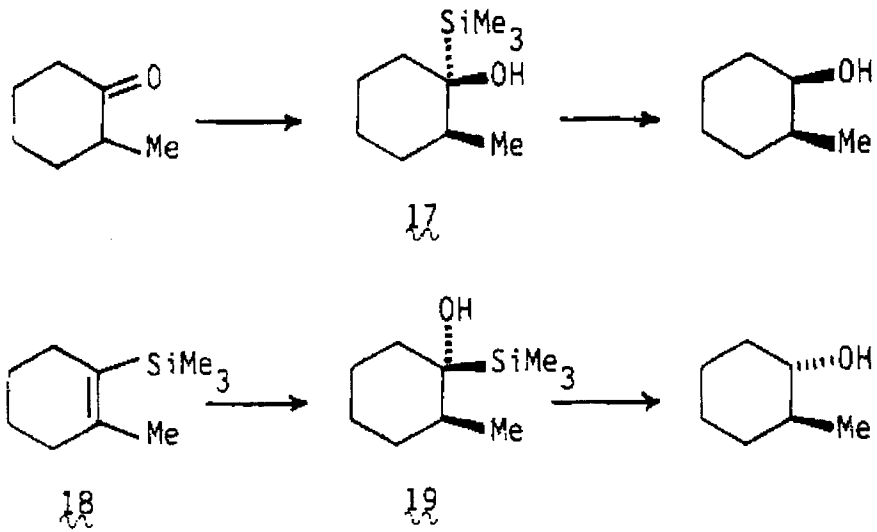
Determination of the Stereochemical Results of the Silyl Migration At Carbon



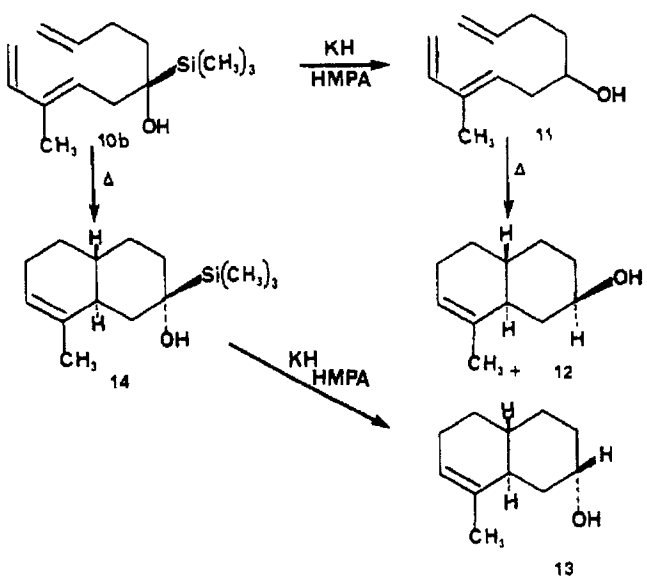
- Alcohol **8** was obtained in an 81:19 mixture of diastereomers (major isomer drawn).
- Alcohol **9** was obtained in an 80:20 mixture of enantiomers (major isomer drawn).
- Silyl migration occurs with a highly stereospecific inversion of configuration at carbon.

Brook, A. G. *Acc. Chem. Res.* **1974**, *7*, 77

Retention of Configuration at Carbon in Aliphatic Silyl [1,2] Brook Rearrangements



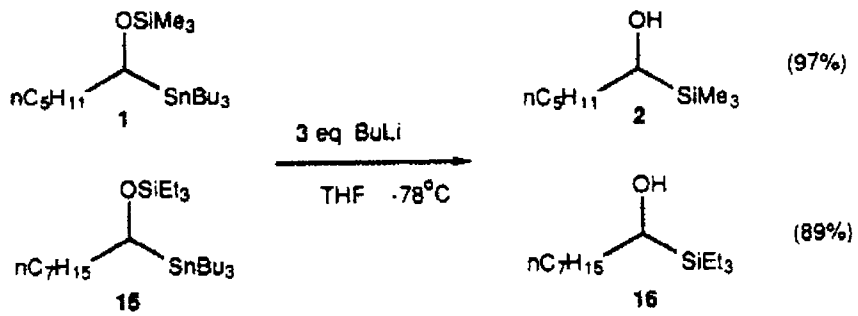
Treatment with **17** and **19** with 5% KO-*t*-Bu lead to silyl [1,2] migration followed by proteodesilylation with retention of configuration at carbon.



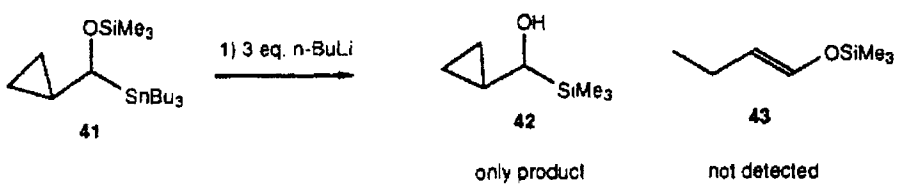
Authors propose that retention can be rationalized by kinetic equatorial protonation of the anionic intermediate to form axial alcohol **13**.

Hudrlik, P. F. et al. *J. Am. Chem. Soc.* **1982**, *104*, 6809
Snider, B.B; Deutsch, E. A. *J. Org Chem.* **1982**, *47*, 747

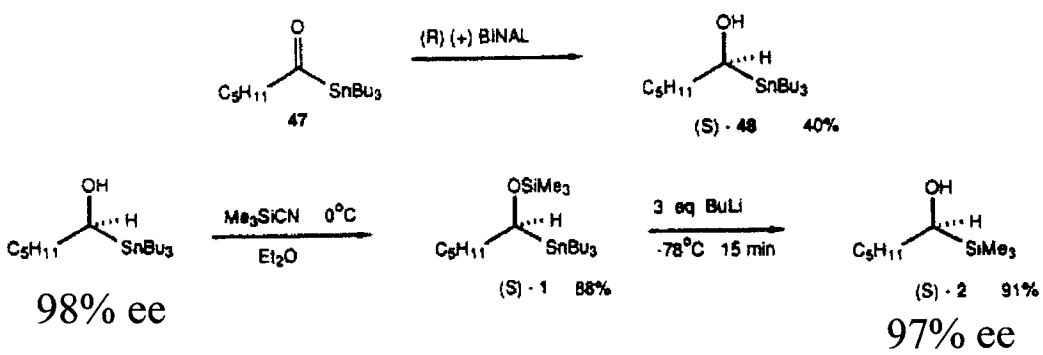
Further Mechanistic Studies of the Aliphatic Reverse Brook Rearrangement



Cross-over experiment yielded only products from an intra-molecular reaction, **2** and **16**.



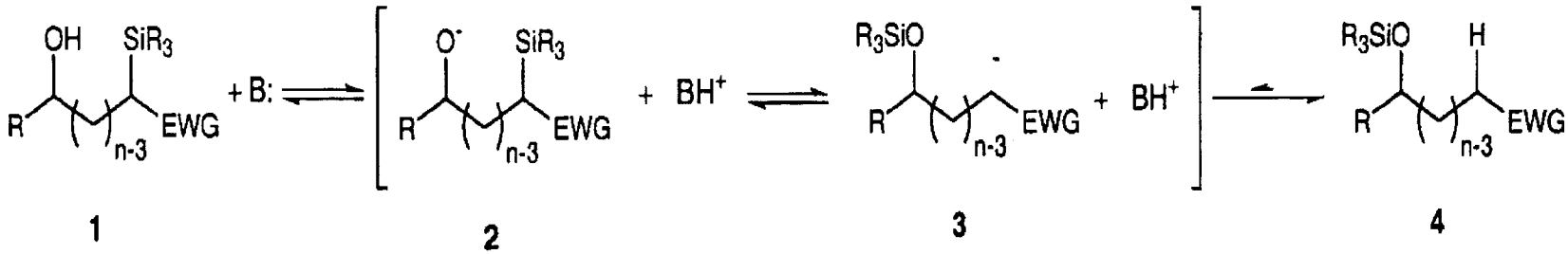
Incorporation of a radical trap revealed the rearrangement does not involve radical intermediates.



The aliphatic reverse brook rearrangement occurs with retention of configuration at carbon.

Linderman, R. J.; Ghannam, A. *J. Am. Chem Soc.* **1990**, *112*, 2392

Anionic Silyl Migration is an Equilibrium process



When catalytic amounts of base are used:

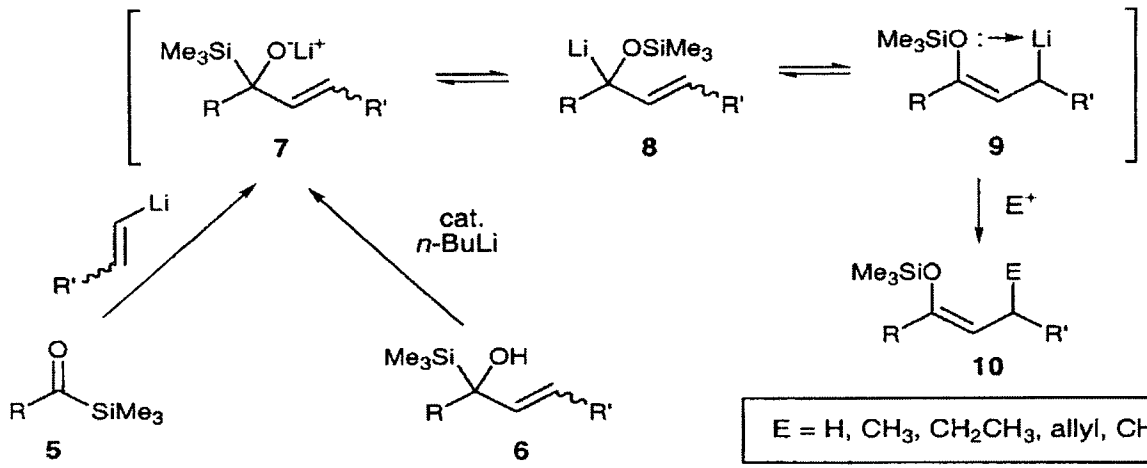
- Relative stabilities of **1** and **4** control the position of the equilibrium.
- When an EWG is present, strength of the O-Si bond (120-130 kcal/ mol) compared to the C-Si bond (75-85 kcal/mol) allows for complete conversion of the carbinol to a silyl ether.
- Carbanion **3** is rapidly and irreversibly protonated by the conjugate acid or starting alcohol.

When an excess of strong base is used:

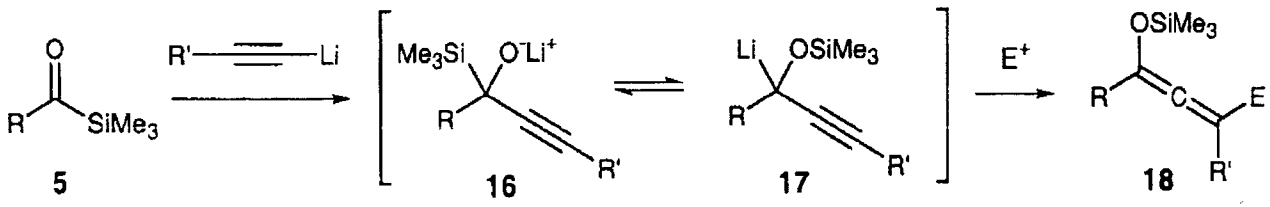
- The most important factors controlling the equilibrium are the basicity of the carbanion and the alkoxide counter ion.
- Relative stabilities of **2** and **3** control the position of the equilibrium.
- Presence of an EWG favors carbon to oxygen migration.
- Highly aggregated states and tight ion pairings (Li) favor oxygen to carbon migration.
- Weak ion pairing (K or Na), polar aprotic solvents (THF, DME, HMPA, or DMPU), or chelation of metal counterions (TMEDA or crown ethers) destabilize the alkoxide and favor carbon to oxygen migration.

Moser, W. *Tetrahedron*, **2001**, *57*, 2065

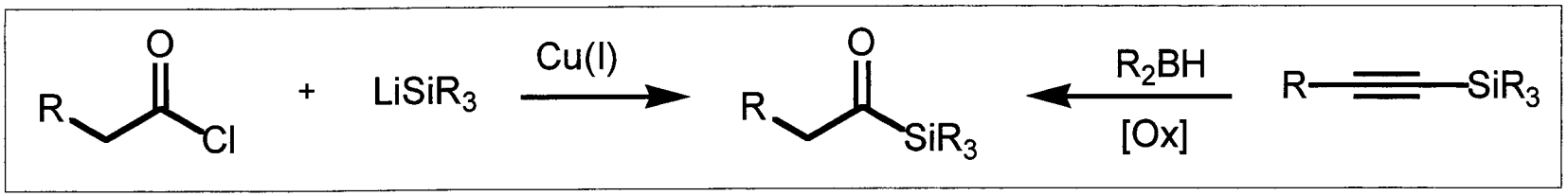
Use of [1,2] Silyl Migrations in the Formation Silyl Enol Ethers



Highly stereoselective formation of the (Z) isomer with almost exclusive γ alkylation.



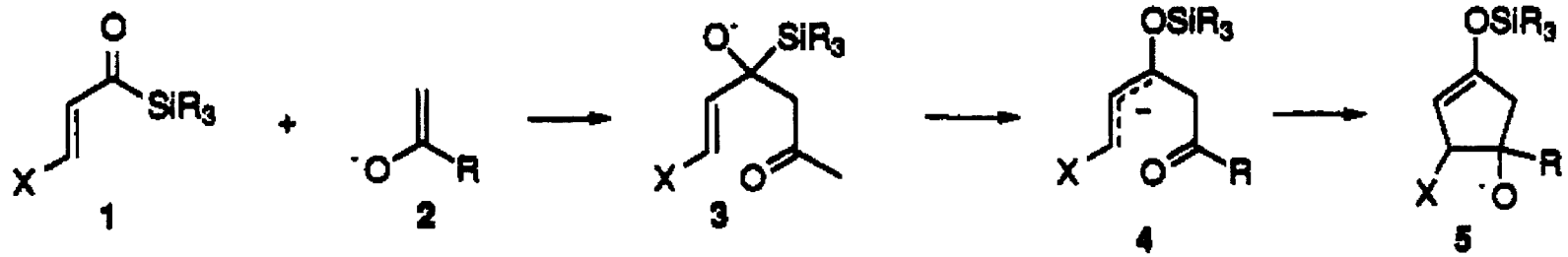
Intramolecular alkylations can also be carried out

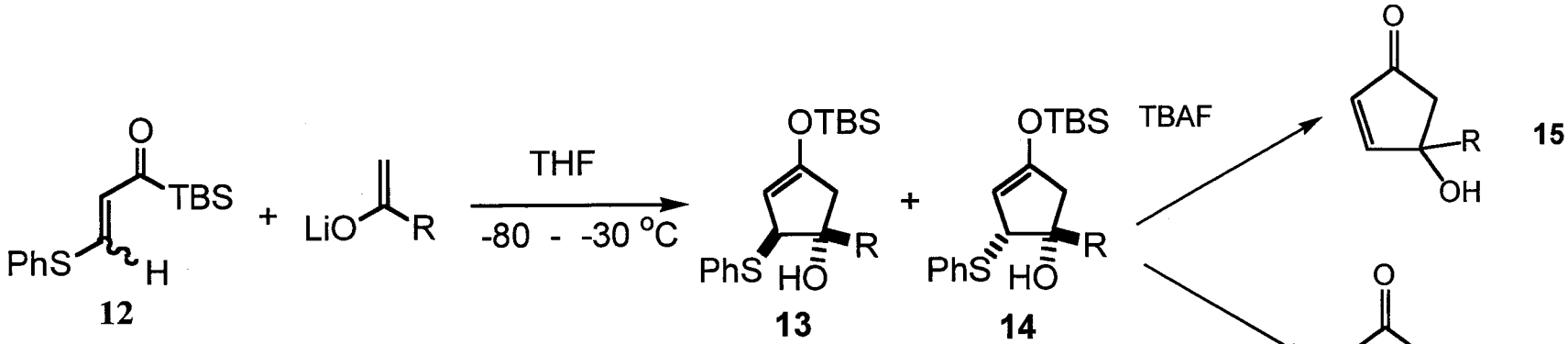


The coordination-stabilization in species **9** is believed to be the reason for the stereoselective formation of the Z isomer.

Moser, W. *Tetrahedron*, **2001**, *57*, 2065.

[1,2] Silyl Migrations in Formal [3 + 2] Annulations



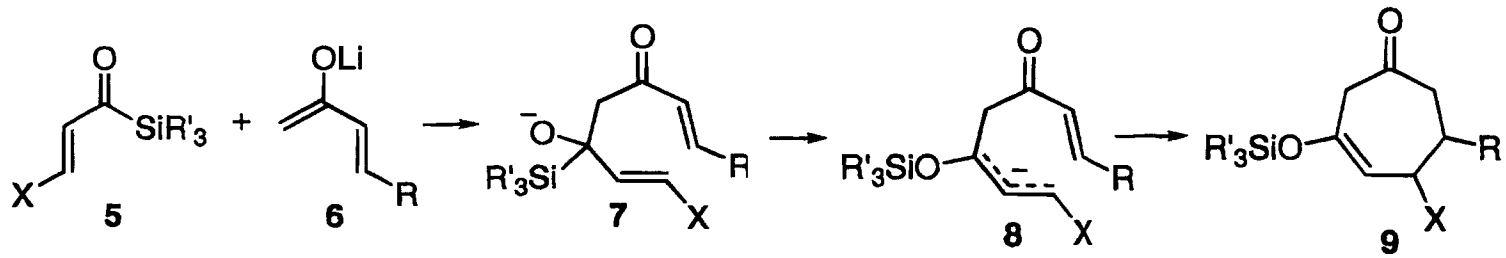


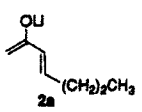
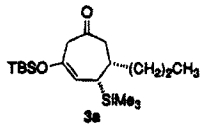
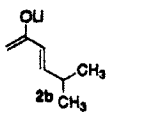
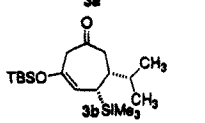
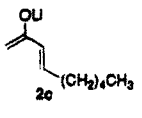
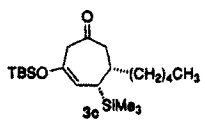
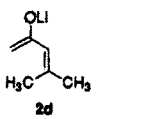
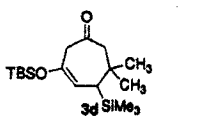
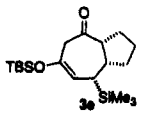
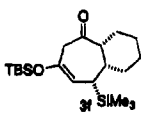
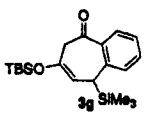
Li enolate	yield (%)			
R	13	14	15	16
i-Pr	55	19	77	79
Et	70	5	70	83
n-Pr	74	7	77	87
n-octyl	71	8	66	73

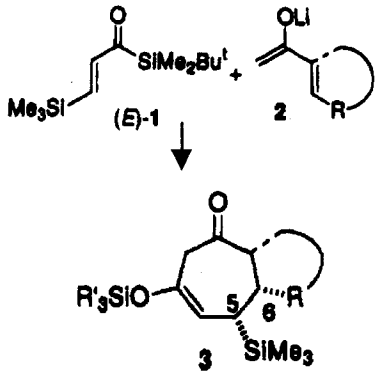
- Formal [3 + 2] annulation provides direct entry to cyclopentenol derivatives.
- Ratio of **13** to **14** is unaffected by the E/Z ratio of **12**.
- Authors could not explain predominate formation of isomer **13**.

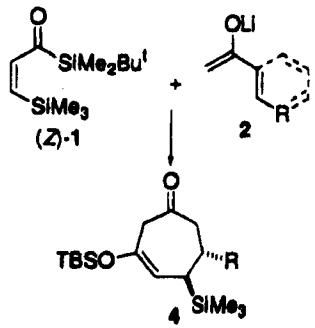
Takeda, K.; Fujisawa, M.; Yoshii, E. *J. Am. Chem. Soc.* **1993,** *115*, 9351

[1,2] Silyl Migrations in Formal [3 + 4] Annulations



entry	ketone enolate	product	yield
1	 2a	 3a	73%
2	 2b	 3b	84%
3	 2c	 3c	84%
4	 2d	 3d	65%
5	 2e	 3e	73%
6	 2f	 3f	73%
7	 2g	 3g	30%



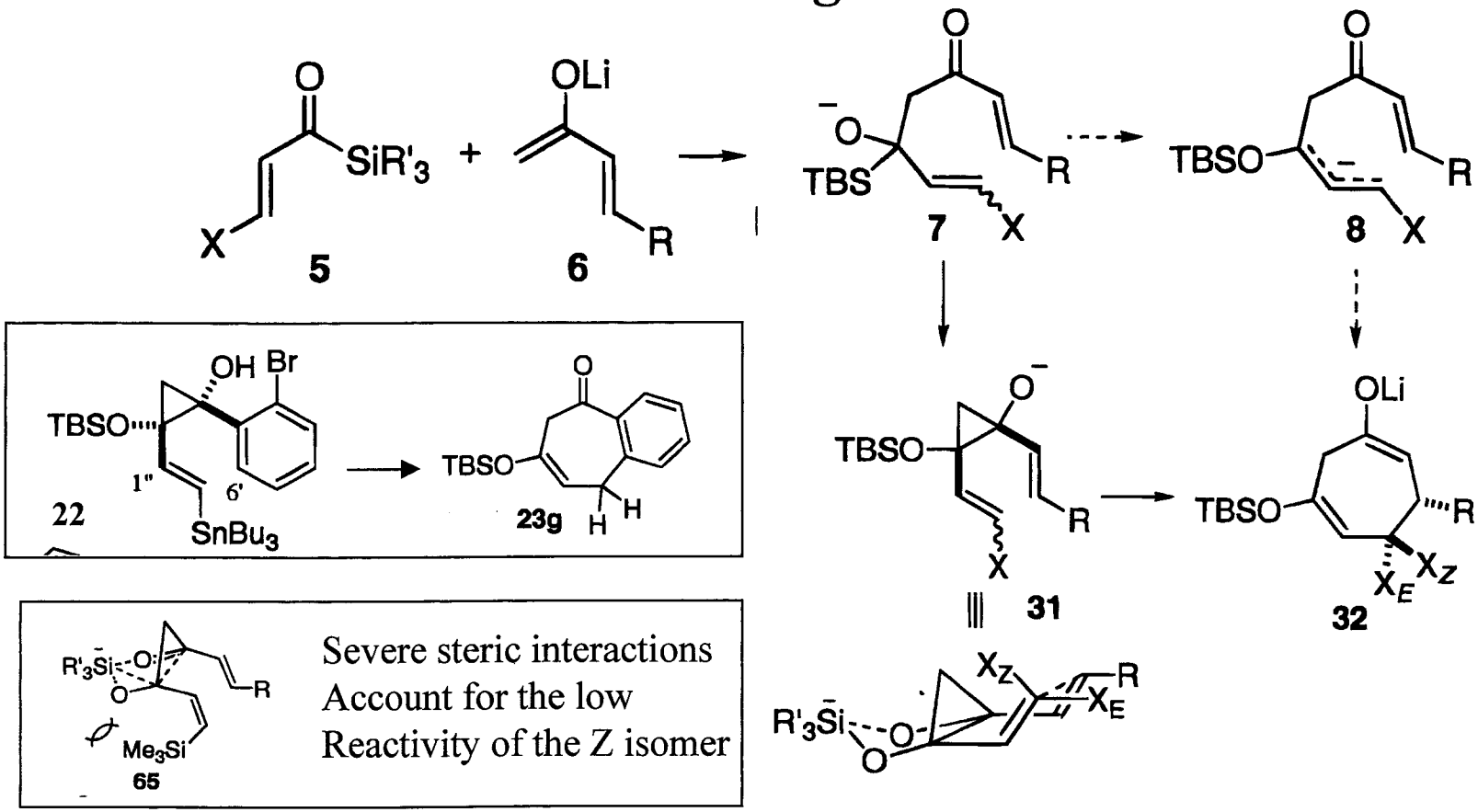


enolate[a]	product	% yield (recoverty of (*Z*)-1)
2a	4a	31 (56)
2b	4b	11 (59)
2c	4c	29 (44)
2d	4d	18 (31)
2g	4g	0 (77)

The observed stereospecificity and participation of the aromatic double bond (entry 7) cannot be rationalized using the proposed mechanism involving an intramolecular Michael addition

Takeda, K.; Takeda, M.; Nakajima, A.; Yoshii, E. *J. Am. Chem. Soc.* **1995,** *117*, 6400
Takeda, K. et .al *J. Am. Chem. Soc.* **1998,** *120*, 4947.

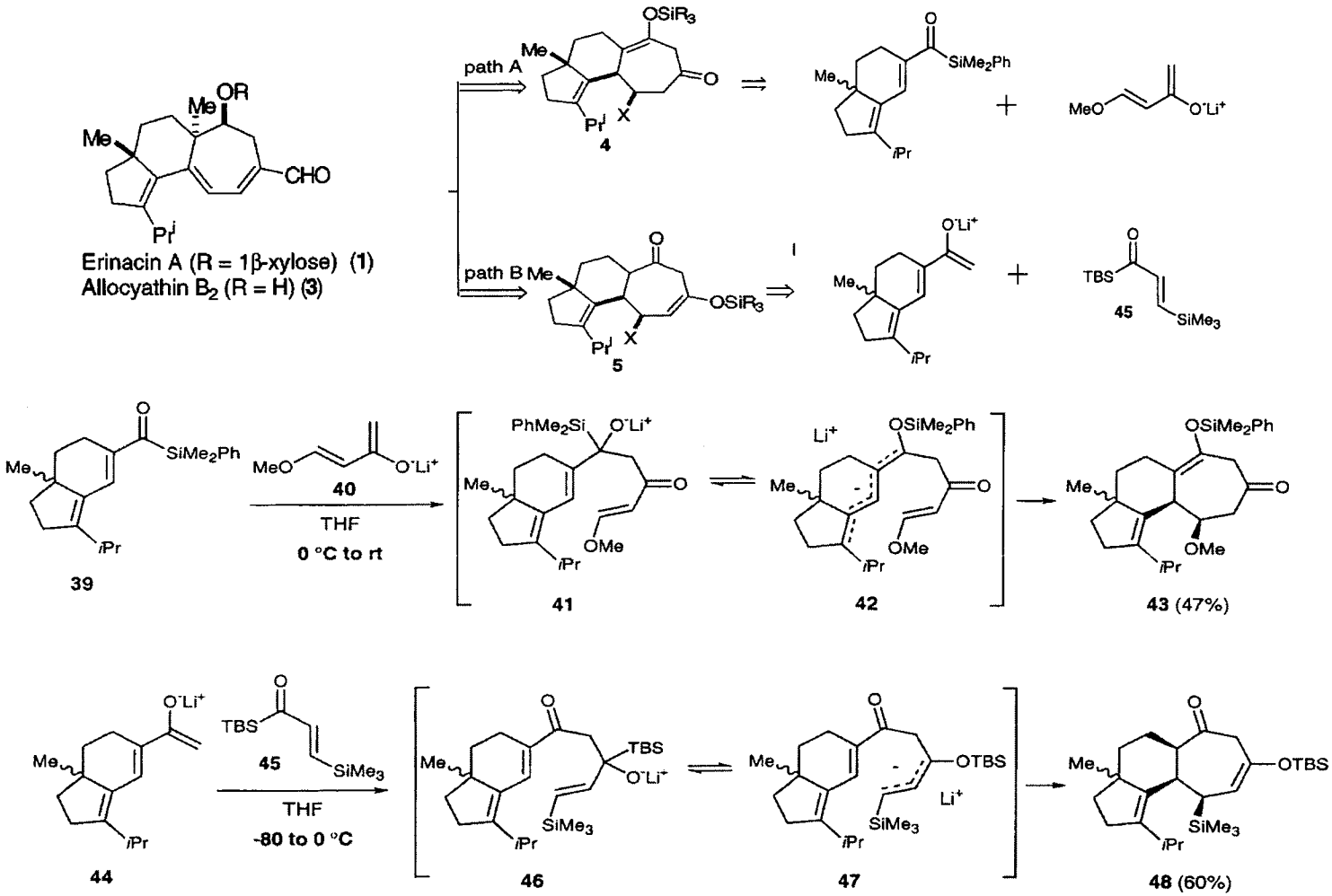
Stereospecificity is a Consequence of an Anionic Oxy-Cope Rearrangement



- Reaction proposed to involve a cylcopropanation of **6** to form 1,2-divinylcyclopropanediolate **31**, followed by a stereospecific oxyanion accelerated Cope rearrangement.
- Cyclopropanol **22** was isolated at low temperatures and found to cyclize to **23g** when warmed in the presence of THF and LDA.

Takeda, K. et .al *J. Am. Chem. Soc.* **1998,** *120*, 4947.

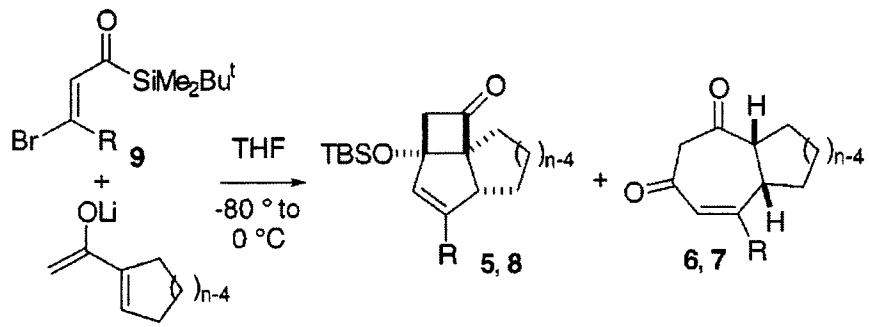
Synthesis of the Tricyclic Skeleton of Cyathins using [3 + 4] Annulations



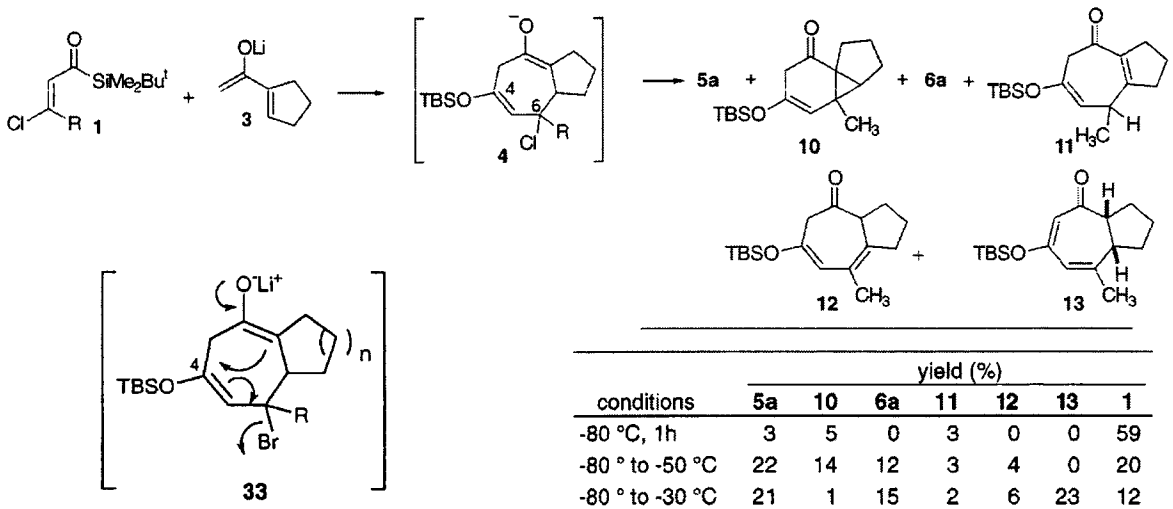
- Synthesis demonstrates the importance of the carbanion-stabilizing group at the β-position.
- Stereochemistry consistent with an anionic oxy-Cope rearrangement.

Takeda, K.; Nakane, D.; Takeda, M. *Org. Lett.* **1999**, *1*, 677
Moser, W. *Tetrahedron*, **2001**, *57*, 2065

Synthesis of Tricyclo[5.3.0.0]decanone Ring Systems using a [3 + 4] Annulation



		yield (%), n = 5		yield (%), n = 6	
	R	5	6	8	7
a	CH_3	68	0	27	45
b	*n*-Bu	49	0	27	14
c	*n*-hexyl	41	0	35	17
d	*t*-Bu	51	7	58	14
e	*c*-C_3H_5	56	0	39	32



conditions	yield (%) 5a	10	6a	11	12	13	1
-80 °C, 1h	3	5	0	3	0	0	59
-80 ° to -50 °C	22	14	12	3	4	0	20
-80 ° to -30 °C	21	1	15	2	6	23	12
-80 ° to -15 °C	27	0	43	5	0	3	3

Proposed that **5a** is formed through an Sn2' type intramolecular attack at the C-4 position of intermediate **33**. While attack at the C-6 position forms **10**, which transformation to **6a** via **11 – 13**.

Takeda, K.; Ohtani, Y. *Org. Lett.* **1999**, *1*, 677.
Moser, W. *Tetrahedron*, **2001**, *57*, 2065.

Summary of the Tandem [1,2] Silyl Migrations – Bond Forming Strategies

- Experimental data suggests a cyclic transition state with a pentacoordinate silyl species.

- The Brook rearrangement proceeds retention of configuration at silicon and aliphatic carbons, but with inversion of configuration at benyl and allyl carbons.

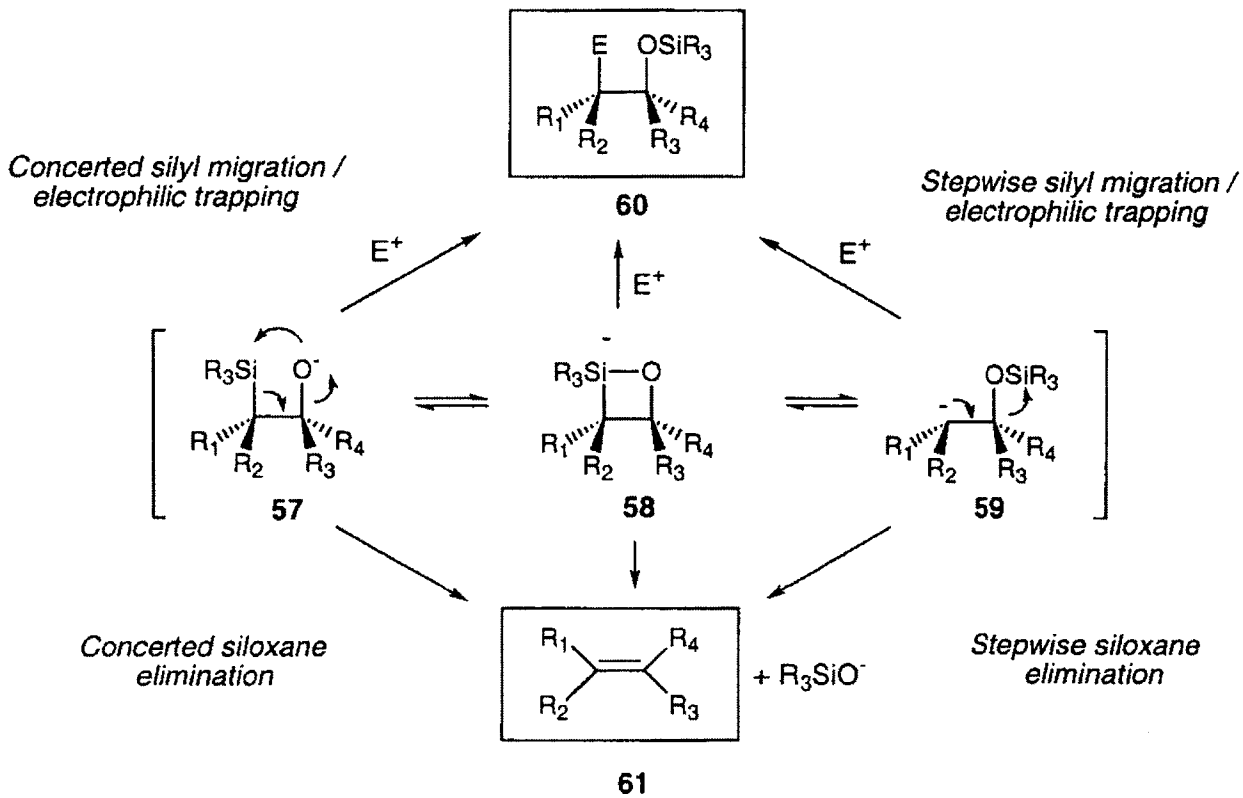
- Stereo- and regioselective formation of (Z) silyl enol ethers with subsequent γ– protonation or alkylation.

- Brook rearrangement mediated [3 + 2] and [3 +4] annulation reactions to form 5 and 7 member carbocyclic ring systems.

- The [3 + 4] annulation is proposed to go through an oxyanion-accelerated Cope rearrangement to explain the stereospecific product formation.

Moser, W. *Tetrahedron*, **2001**, *57*, 2065

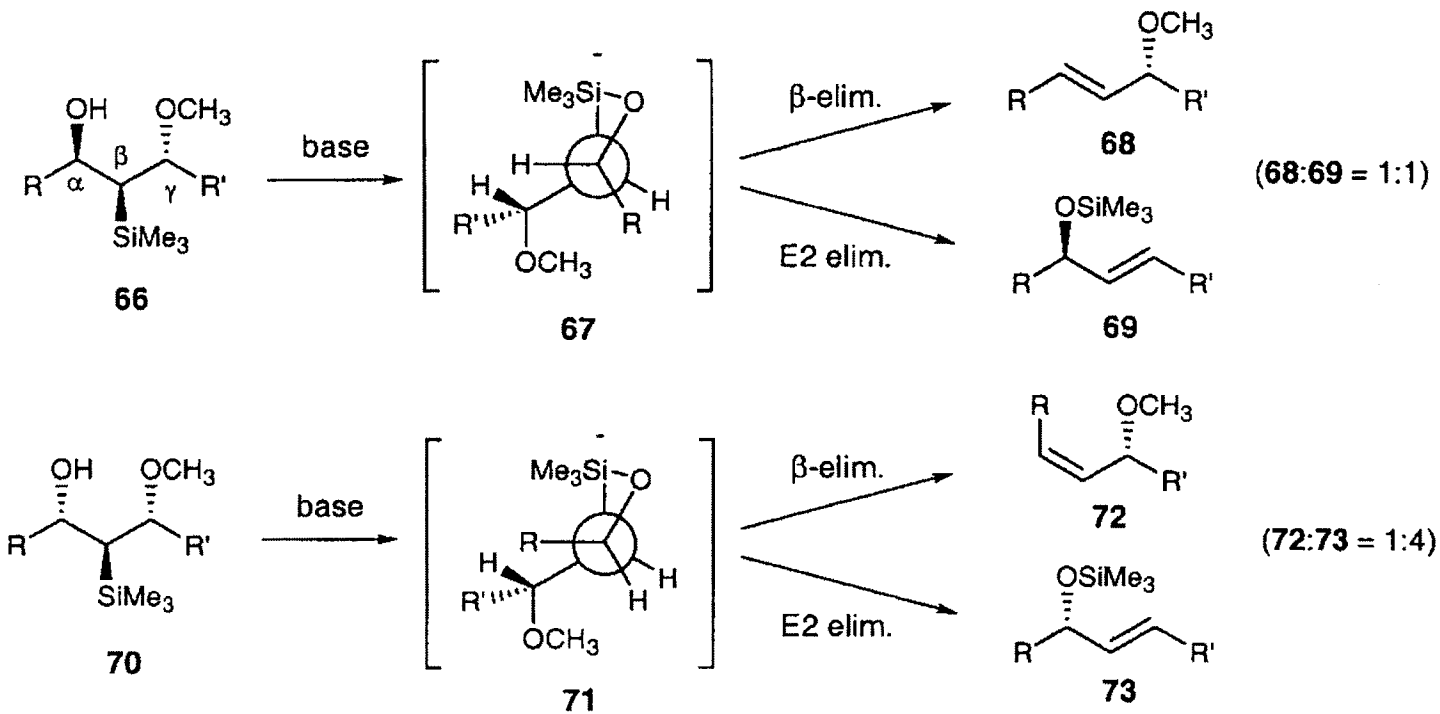
[1,3] Silyl Migrations



- The design of tandem reactions involving [1,3] silyl migrations is difficult due to competitive olefin formation via 1,2 elimination of β-silyl alkoxides.
- The exact mechanism pathway (concerted or stepwise) is still unclear.
- The structural features of the substrate determine the pathway followed.

Moser, W. *Tetrahedron*, **2001**, *57*, 2065.

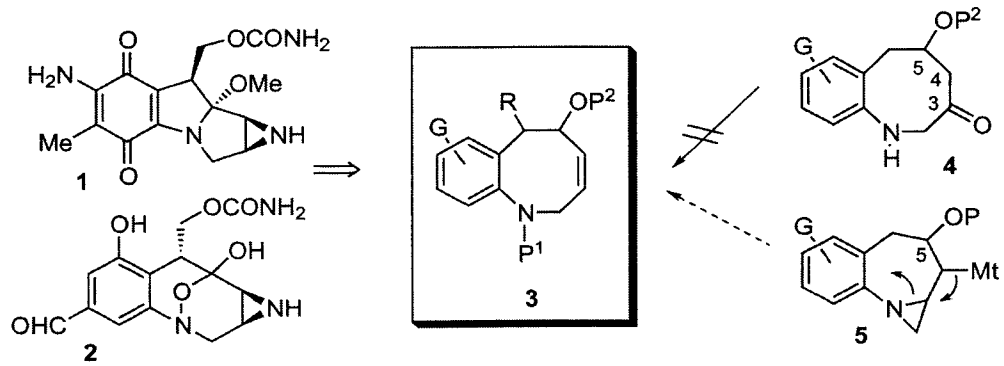
Tandem [1,3]Silyl Migration / Elimination Sequences



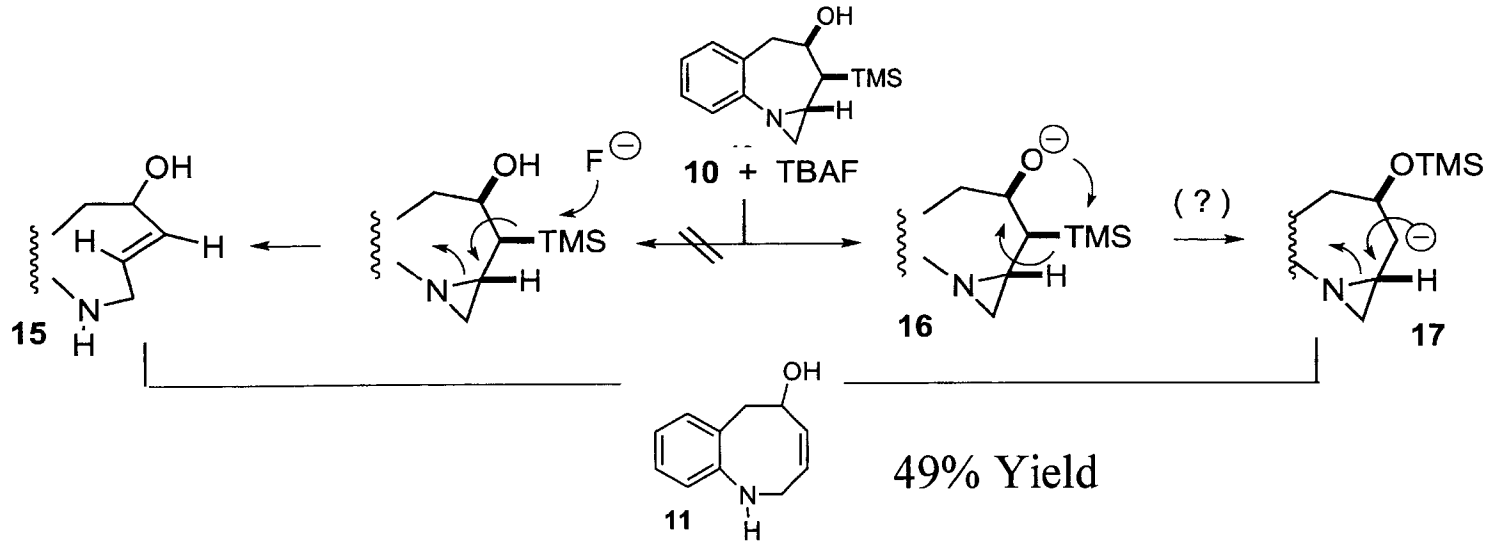
•Peterson reactions to form E alkenes **68** proceed more rapidly than to form Z alkenes **72**.
•Generally, the better the leaving group in the γ–position, the greater the preference for γ-elimination over the Peterson reaction.

Moser, W. *Tetrahedron*, **2001**, *57*, 2065.
Yamamoto, K. et al. *Tetrahedron Lett.* **1984**, *25*, 2155

Silyl [1,3] Migration Followed by a Ring Opening of a Silylated Aziridine



Method for the assembly of benzazoc-3-enes **3.**

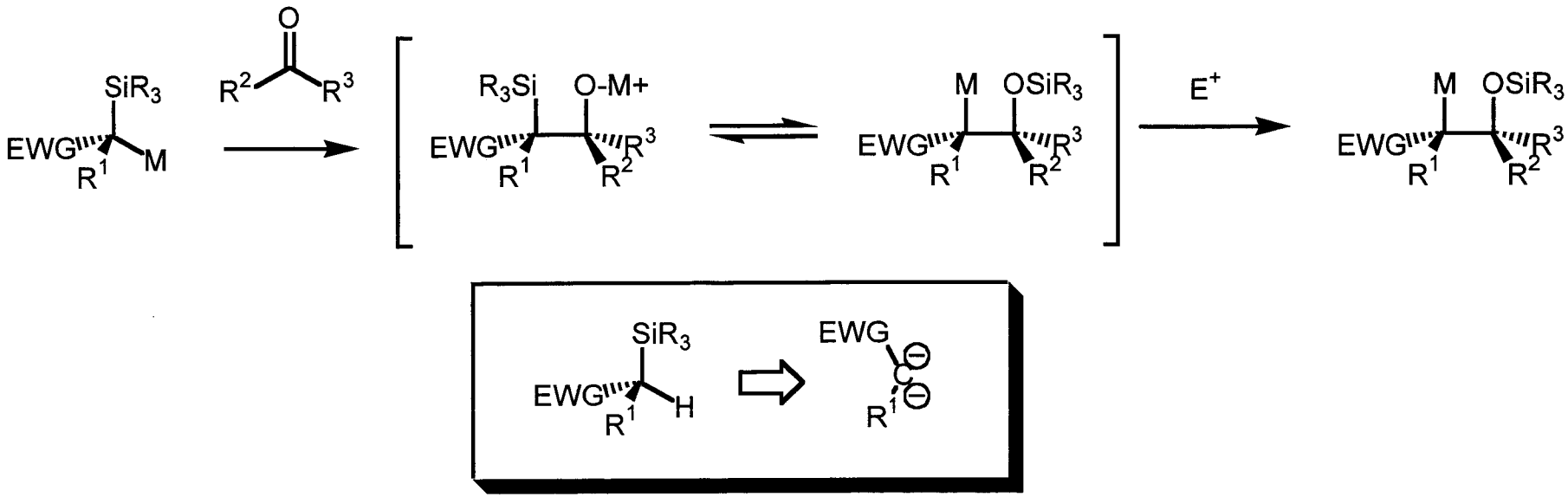


49% Yield

- Azaridine cleavage through an anti elimination process would lead to *trans*-benzazocenol **15.**
- Instead, azaridine cleavage proposed to go through a silyl [1,3] migration followed by a E2 type elimination.

Ducray, R. et al. *Tetrahedron Lett.* **2001**, *42*, 9175

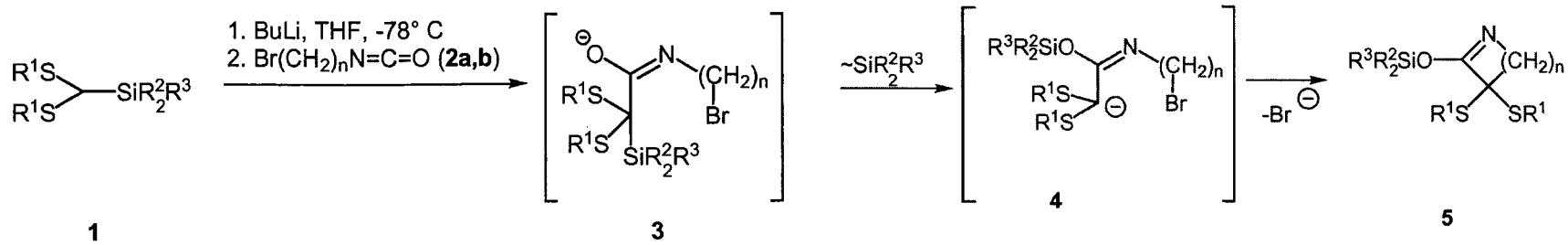
Use of [1,3] Silyl Migrations in Tandem Bis-alkylation Sequences

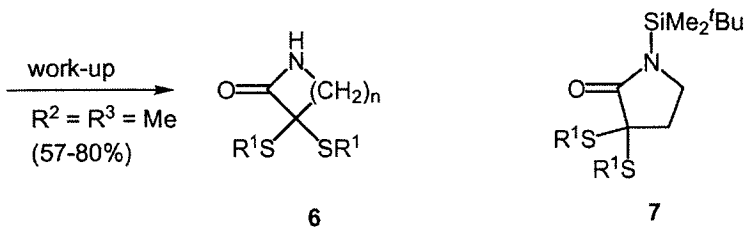


- Nucleophilic addition of silyl substituted carbanion to a carbonyl group, followed by [1,3] silyl migration and electrophilic trapping renders the silyl bearing carbon a formal dianion synthon.
- The presence of the EWG is essential for efficient carbon to oxygen migration.

Moser, W. *Tetrahedron*, **2001**, *57*, 2065.

Lactam Formation Using Silyl Migration-Intramolecular Alkylation Sequences





1a: $R^1 = R^2 = R^3 = Me$
1b: $2R^1 = (CH_2)_3$, $R^2 = R^3 = Me$
1c: $R^1 = R^2 = Me$, $R^3 = {}^tBu$

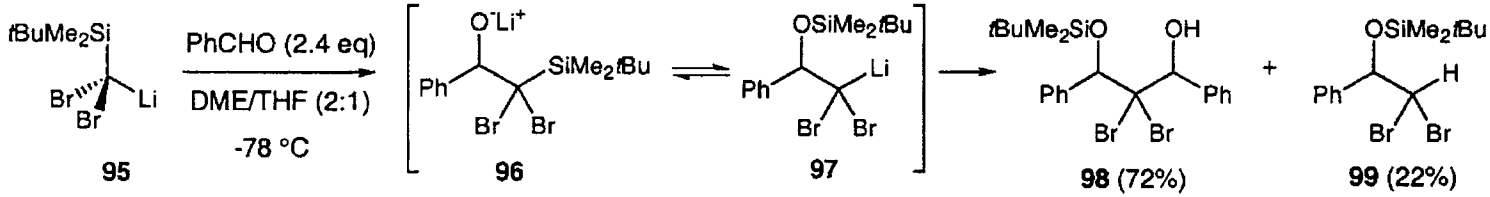
2a: n = 2
2b: n = 3

Silyl Cmpd	6	R^1	n	Yield (%)	mp (° C)
1a	**a**	Me	2	57	108-109
1b	**b**	$-(CH_2)_3-$	2	57	167
1a	**c**	Me	3	80	110
1b	**d**	$-(CH_2)_3-$	3	78	140-142

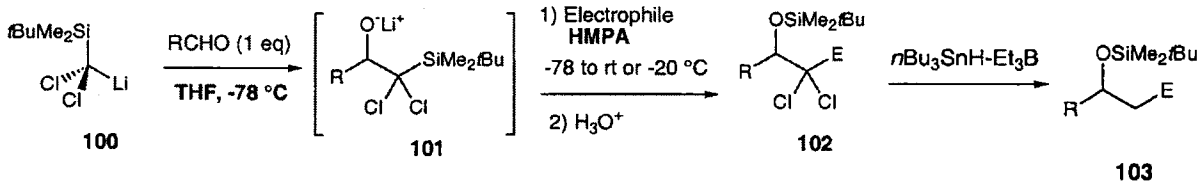
- The addition of a bis-electrophile to a silyl substituted carbanion requires selective addition to one of two sites in the initial step.
- Ketenimines formed from the competing silyloxy elimination (Peterson elimination) were not reported.

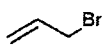
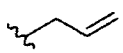
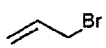
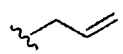
Schaumann, E.; Jung, A.; Koch, O. *Synlett*, **2000**, *1*, 92

Intermolecular Bis-Alkylations of Stabilized Silyl Migration-Generated Carbanions



•Distribution of products (1:1 adduct to 1:2 adduct) is highly dependent on the nature of the substitutents on silicon.



R	Electrophile	E	yield of **102** (%)
Ph	MeI	Me	71
Ph			70
PhCH=CH	MeI	Me	74
n-Pr			40
4-MeO-C_6H_4	PhCHO	PhCH(OH)	83
PhCH=CH	PhCHO	PhCH(OH)	73
n-Bu	PhCHO	PhCH(OH)	45

•In THF at –78 °C, **no** migration of silicon from carbon to oxygen was seen after the initial reaction with the aldehyde.

•The addition of HMPA to the reaction mixture facilitated rapid carbon to oxygen silicon migration and formation of a carbanion.

•The ability to use solvent to control silyl migration allows for unsymmetrical bis-alkylation

Oshima, K.; Utimoto, K; Shinokubo, H.; Miura, K. *Tetrahedron*, **1995**, *52*, 503
Moser, W. *Tetrahedron*, **2001**, *57*, 2065

Summary of the Tandem [1,3] Silyl Migrations – Bond Forming Strategies

- Tandem reactions using [1,3] silyl migrations is difficult due to competitive olefin formation through the Peterson reaction.

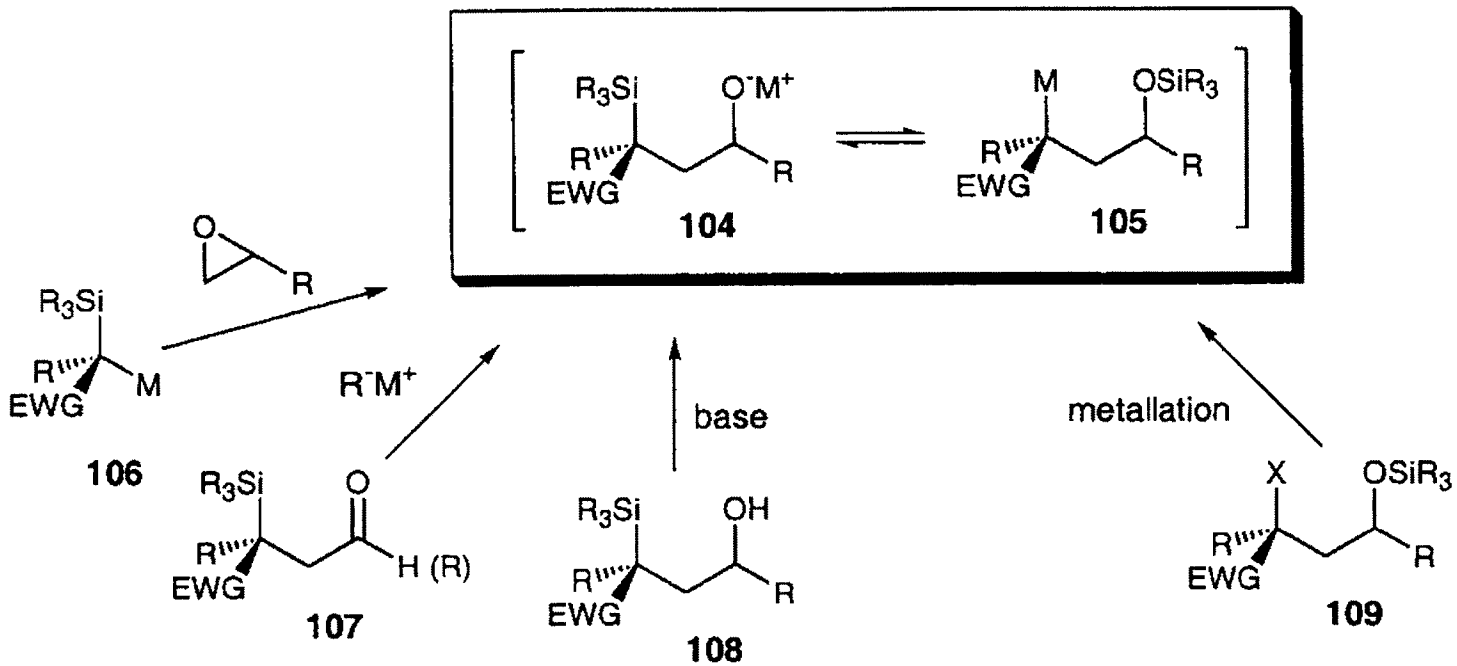
∞β-silyl alcohols with a leaving group in the γ-position can undergo silyl migration - elimination reactions to form allyl silyl ethers.

- Silyl lithium reagents bearing a carbanion stabilizing group can facilitate carbon to oxygen migration and be used as dianion synthons.

- The choice of solvent can control the silyl migration step and be used for the bis-alkylation of a methylene dianion with two different electrophiles in a one-pot reaction.

Moser, W. *Tetrahedron*, **2001**, *57*, 2065

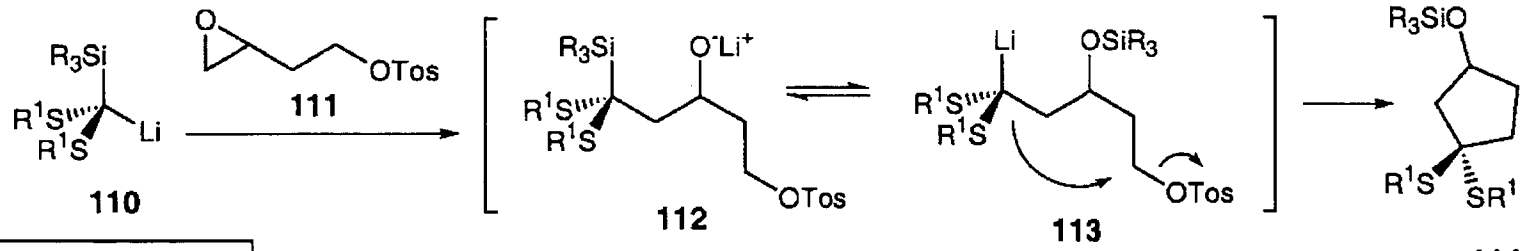
[1,4] Silyl Migrations



•The large variety of methods to form the necessary anionic precursors and the absence of competing side reactions has lead to a variety of applications of the Anionic [1,4] silyl migrations tandem reactions.

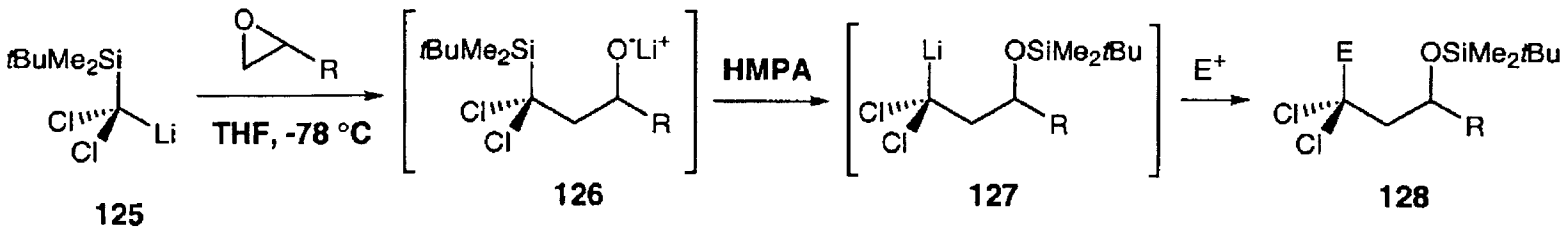
Moser, W. *Tetrahedron*, **2001**, *57*, 2065

Tandem nucleophilic Addition – 1,4 Silyl Migration – Intra- and Intermolecular alkylations



$R^1 = CH_3, -(CH_2)_3-$

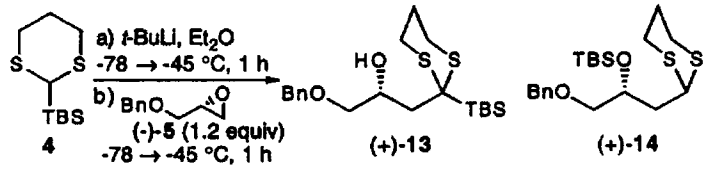
- Formal [4 + 1] Synthesis of Substituted cyclopentanols
- Secondary tosylates can also be used with a slight decrease in yield.
- Attempts to form cyclohexanols and cycloheptanols were mildly successful.



- Electrophilic trapping with CH_3I, PhCHO, and HCOOiPr gave adducts in good yields.
- Solvent control of the silyl migration allows for efficient bis-alkylation.

Oshima, K.; Utimoto, K; Shinokubo, H.; Miura, K. *Tetrahedron*, **1995**, *52*, 503
Moser, W. *Tetrahedron*, **2001**, *57*, 2065.

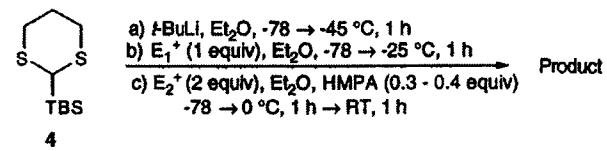
Unsymmetrical Linchpin Coupling of Silyl Dithianes



Entry	Solvent	Additive[a]	Yield **13** (%)	Yield **14** (%)
1	THF	-	60	-
2	Et_2O	-	74	-
3	Et_2O	HMPA	9	56
4	Et_2O	DMPU	12	66

[a] Following step b, the reaction mixture was cooled to −78 °C, treated with 0.3−0.4 equiv of additive in Et_2O, and warmed to −45 °C for 1 h.

Unsymmetrical coupling is possible with solvent controlled [1,4] silyl migration.

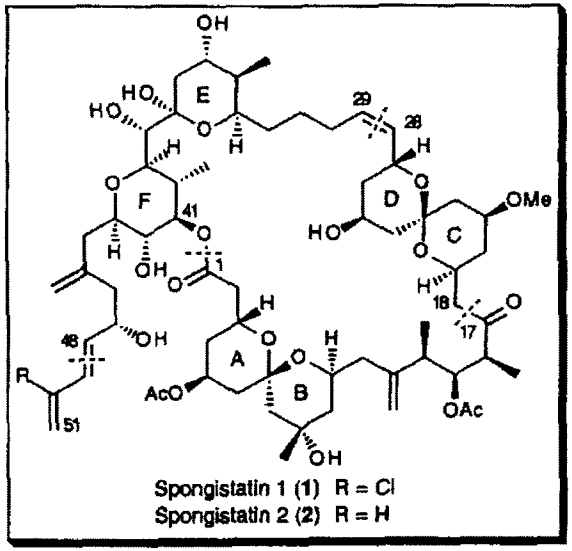


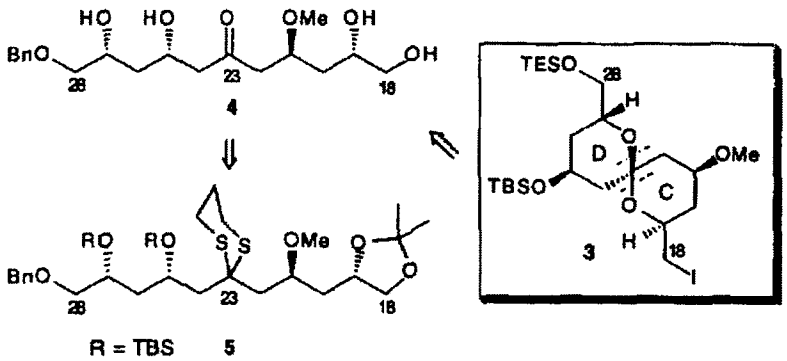
Entry	E_1^+	E_2^+	Product	Yield (%)[b]
1	(-)-5	(-)-15	(+)-16	56
2	(-)-5	(-)-17	(+)-18	74
3	(-)-5	19	(+)-20	62
4[a]	(-)-5	(-)-21	(+)-22	60
5[a]	(-)-5	(+)-23	(+)-24	71
6	(+)-25	(-)-26	(+)-27	59

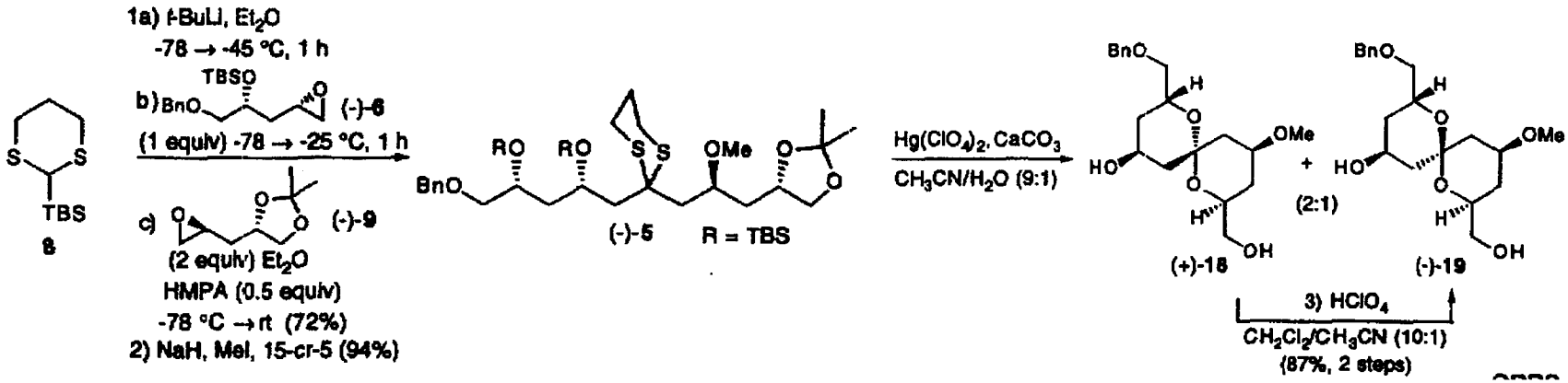
[a] Only 1 equiv of E_2^+ was used. [b] After chromatography.

Smith III, A. B.; Boldi, A. M. *J. Am. Chem. Soc.* **1997**, *119*, 6925

Synthesis of the C(18-28) Spiroketal in Spongistatin Using A One Pot Bis-Alkylation of a Silyl Dithiane



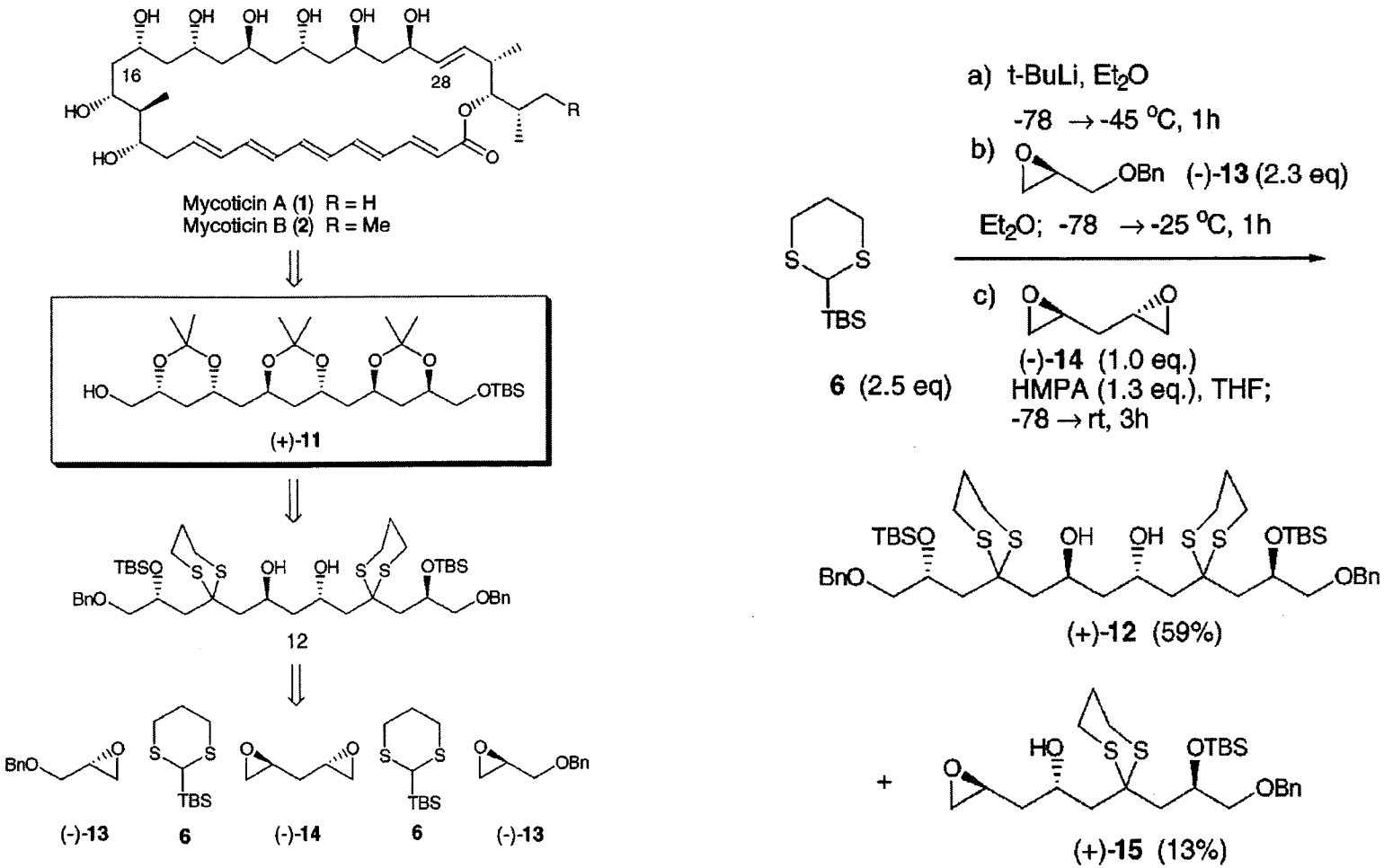




The one pot bis-alkylation method provided the coupled product in yields superior to the stepwise process (72% : 20%).

Smith III, A. B. et al. *Tetrahedron Letters*, **1997**, *38*, 8671

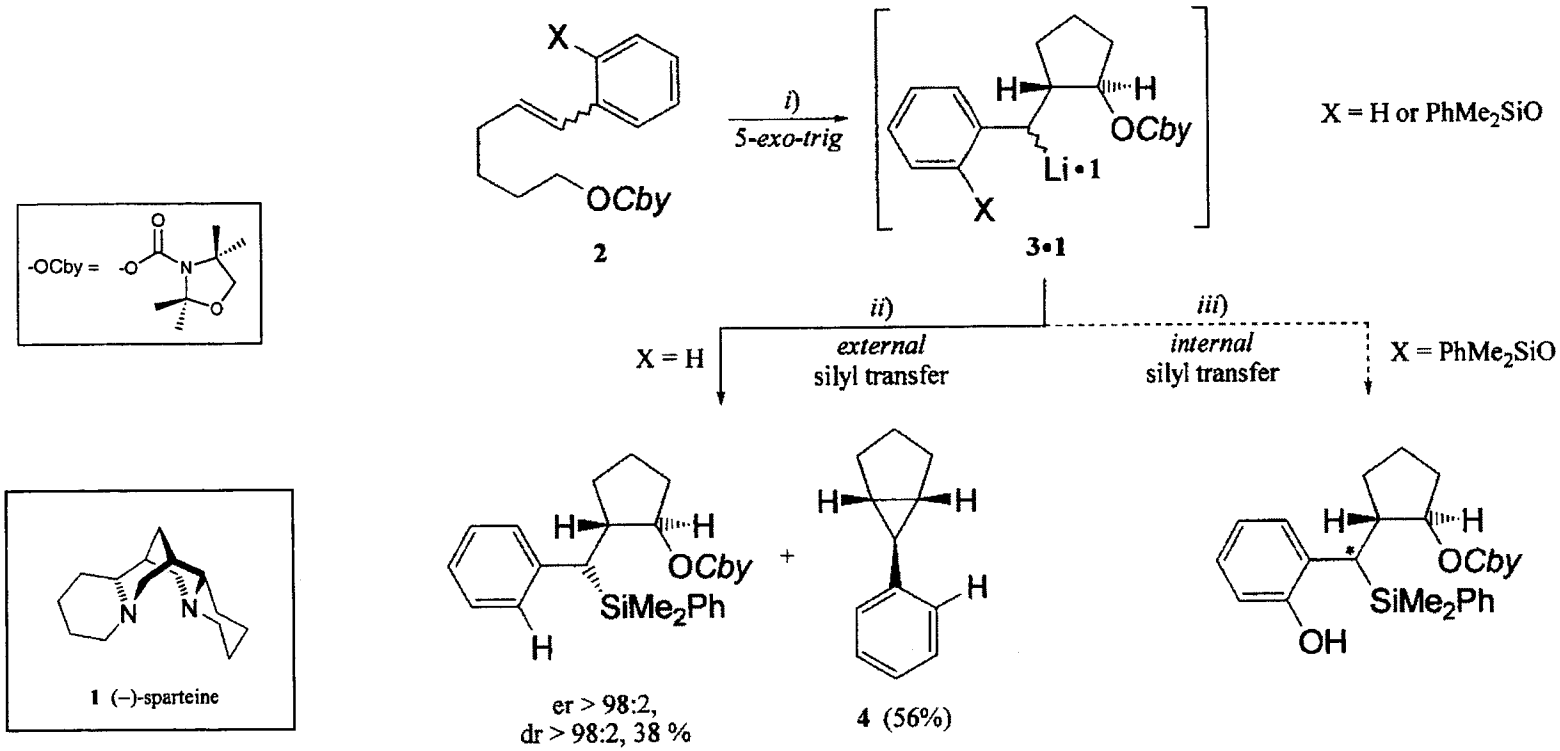
Synthesis of Extended 1,3 Hydroxylated Chains Using Multicomponent Linchpin Coupling of Silyl Dithianes



The synthesis of (+)-11 was achieved in an eight step synthesis, five fewer than The previously reported route, in an overall yield of 17%

Smith III, A. B.; Pitram, S. M. *Org. Lett.* **1999**, *1*, 2001

An Asymmetric Cylcocarbolithiation Coupled to a Stereospecific *retro*-[1,4]-Brook Rearrangement

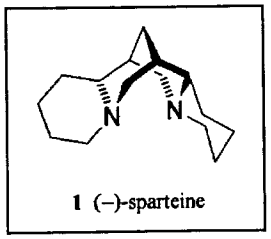


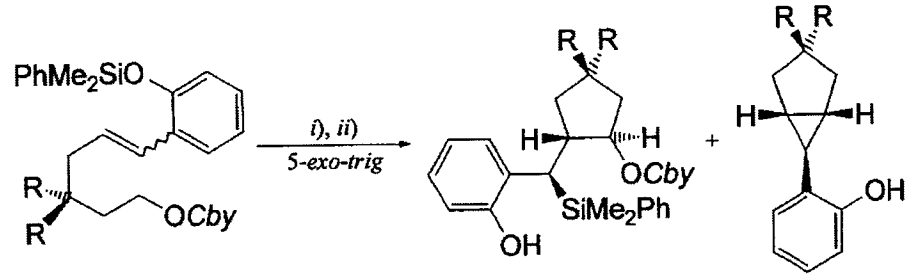
i) *s*-BuLi/**1**, Et_2O, $-78°$, several hours. *ii*) $PhMe_2SiCl$, $-78°$, then r.t. *iii*) MeOH, $-78°$, then r.t.

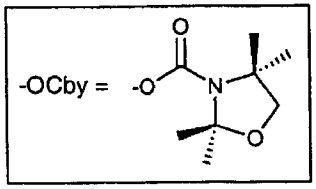
An *internal* silyl group delivery to the anionic carbon via a retro-Brook mechanism was proposed to suppress formation of **4.**

Hoppe, D.;Kleinfield, S. H.; Wegelius, E. *Helv. Chim. Acta* **1999**, *82*, 2413

A Retro-[1,4]-Brook Rearrangement in a Stereoselective Tandem Reaction







i) *s*-BuLi/**1** or *s*-BuLi/*N,N,N′,N′*-Tetramethylethylenediamine (**11**), Et_2O, $-78°$, then $-40°$, several hours. *ii*) MeOH, $-78°$, then r.t. See also the *Table*.

Table 1. *Domino-Type Reaction Sequence of the Hex-5-enyl Carbamates* **2**

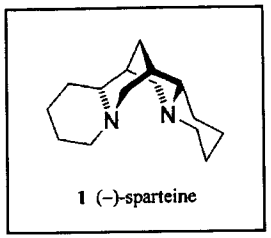
Entry	*Alkene*	R	(*E*/*Z*)-Ratio[a])	Carbocycle	er[b])	dr[c])	Yield/%	
							2	**8**
1	(*E*/*Z*)-**2a**	H	50:50	**8a**	>98:2	>99:1	16	58[d])
2	(*E*)-**2a**	H	90:10	**8a**	>98:2	>99:1	17	60
3	(*Z*)-**2b**	Me	30:70	**8b**	>98:2	>99:1	40	47
4[e])	(*E*/*Z*)-**2a**	H	50:50	*rac*-**8a**	–	>99:1	–	8[f])
5[e])	(*Z*)-**2b**	Me	30:70	*rac*-**8b**	–	>99:1	–	50

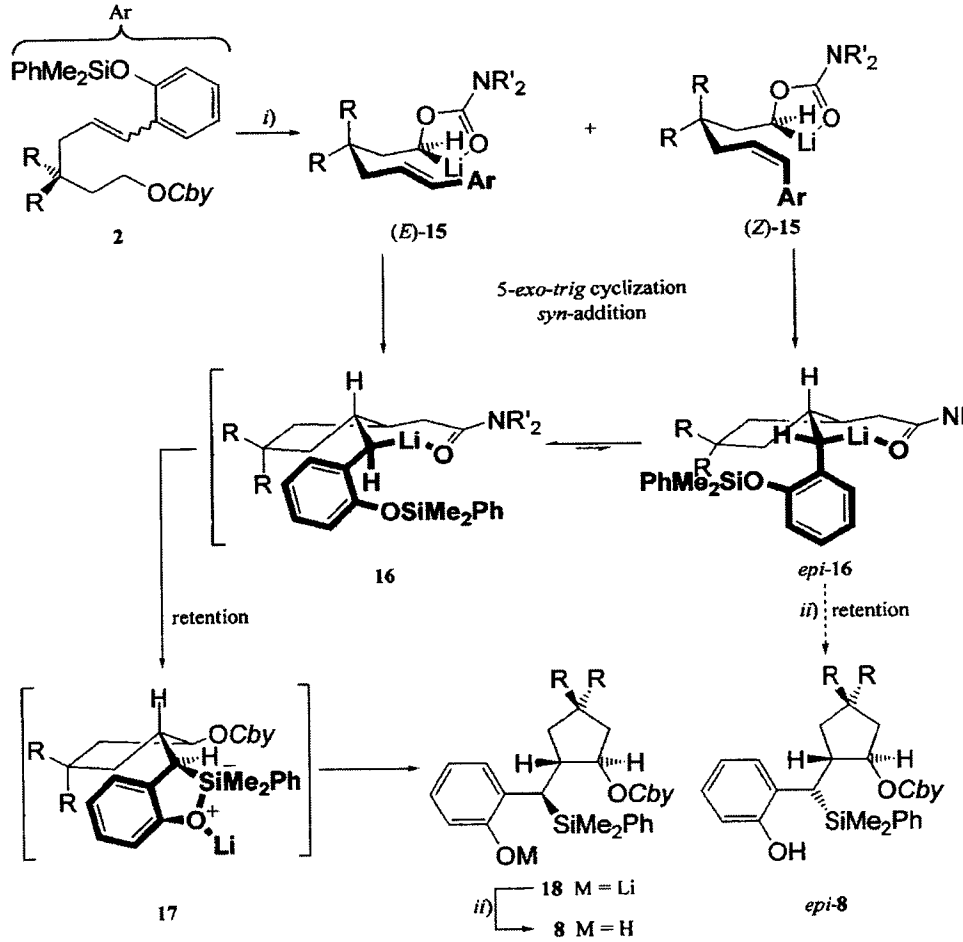
[a]) Determined from the ^{1}H-NMR spectra. [b]) Determined from the ^{1}H- and ^{19}F-NMR spectra of the Mosher esters by comparison with the racemates. [c]) Determined by GC analysis and from the ^{1}H-NMR spectra. [d]) The bicyclic product **9a** was formed in 9% yield. [e]) These experiments were carried out in the presence of TMEDA (**11**) instead of (–)-sparteine (**1**). [f]) The 1,3-cycloelimination is highly favored in the presence of a 'small' diamine such as **11**.

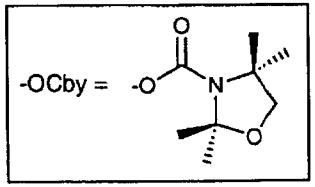
- The relative and absolute configuration of cyclized product is independent of alkene geometry.
- The intramolecular 1,4 oxygen to carbon migration is thermodynamically favored and must be kinetically faster than the 1,3-cycloelimination process.

Hoppe, D.;Kleinfield, S. H.; Wegelius, E. *Helv. Chim. Acta* **1999**, *82*, 2413

A *Stereoretentive* mechanism for the *retro*-[1,4]-Brook Rearrangement







i) *s*-BuLi/**1**, Et_2O, $-78°$, then $-40°$, several hours. *ii*) MeOH, $-78°$, then r.t. Ligands (*e.g.*, **1**) at the Li-center are omitted for the sake of clarity.

- The cyclization step produces two configurationally labile epimers **16** and *epi*-**16**.
- Steric interactions favor silyl migration from epimer **16** with retention of configuration.

Hoppe, D.;Kleinfield, S. H.; Wegelius, E. *Helv. Chim. Acta* **1999**, *82*, 2413

Summary of the Tandem [1,4] Silyl Migrations – Bond Forming Strategies

- Nucleophilic addition – 1,4 silyl migration – intramolecular alkylation can be used to form substituted cyclopentanols.

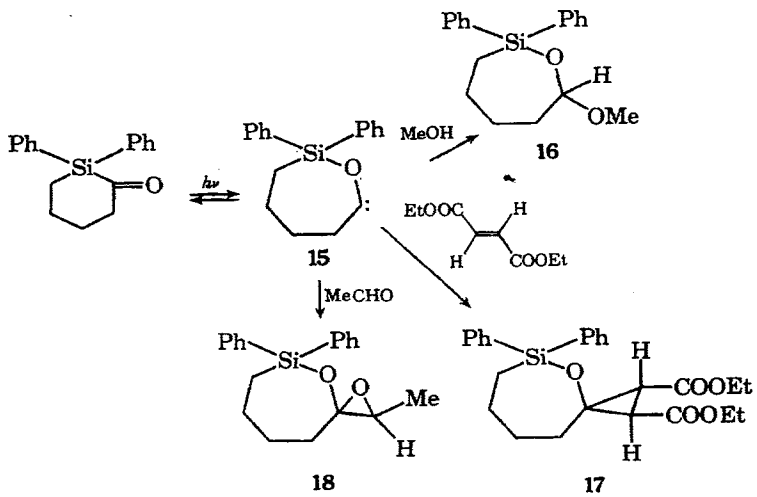
- Solvent controlled 1,4 silyl migration can be used for unsymmetrical inter-molecular bis-alkylations.

- Silyl dithianes can be used in one-pot multicomponent coupling sequence, and then converted to ketones or alcohols.

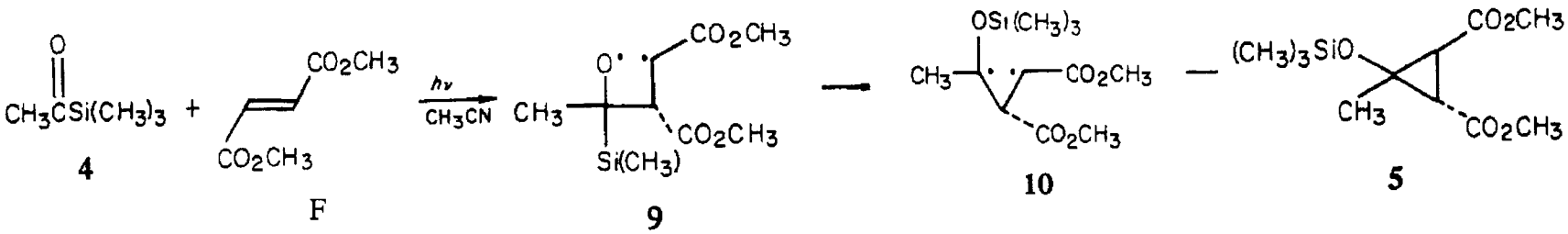
- A *retro*-Brook rearrangement can be for the rapid internal delivery of silyl group to trap a carbanion.

Moser, W. *Tetrahedron*, **2001**, *57*, 2065

The First Proposal of a Radical [1,2] Brook rearrangement



•Originally Brook and co-workers proposed the reaction proceeded through a nucleophilic siloxycarbene intermediate **15**.



•Later studies by Dalton and Bourque presented data that was better explained by a mechanism involving a radical [1,2] Brook rearrangement. Further evidence for a radical mechanism has also been provided by ESR spectroscopy.

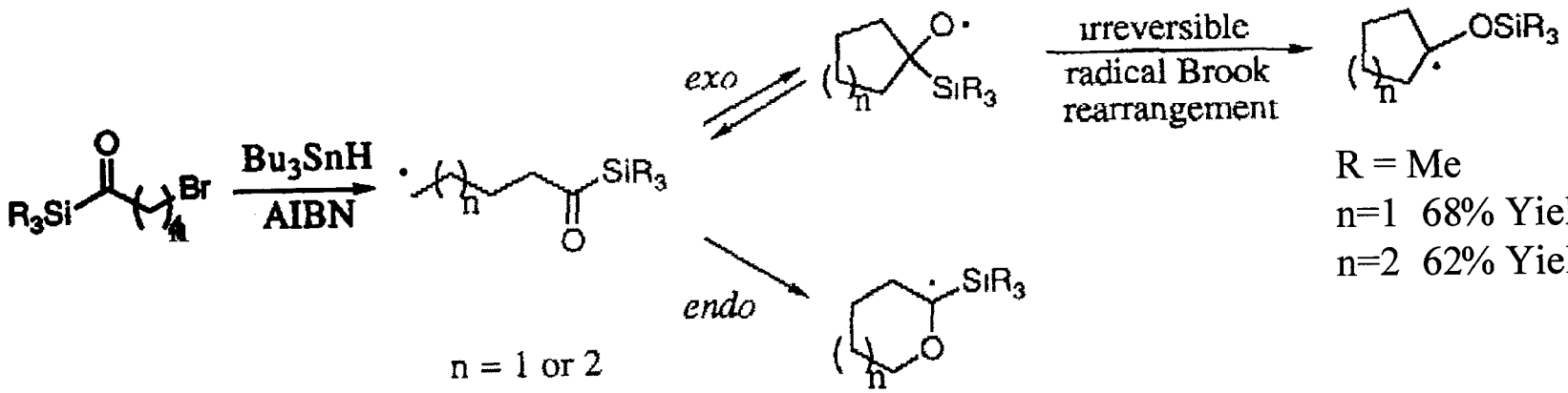
Brook, A. G. et al. *Can. J. Chem.* **1971**, *49*, 1618
Dalton, J. C.; Bourque, R. A. *J. Am. Chem. Soc.* **1981**, *103*, 699
Harris, J. M., et.al. *J. Chem. Soc., Perkin Trans.* 2 **1993**, 2119

Silyl-Migration Mediated Radical Cyclizations

$k_1 = 8.7 \times 10^5\ s^{-1}$ (80°C)
$k_{-1} = 4.7 \times 10^8\ s^{-1}$ (80°C)

$k_2 = 1.0 \times 10^6\ s^{-1}$ (80°C)
$k_{-2} = 1.1 \times 10^7\ s^{-1}$ (80°C)

Radical additions to carbonyls are reversible and fragmentation rates are faster than cyclization rates



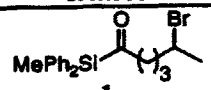
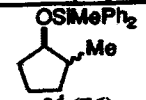
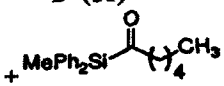
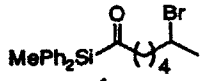
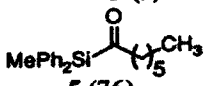
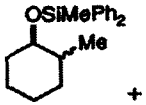
R = Me
n=1 68% Yield
n=2 62% Yield

not detected

- Unlike anionic Brook rearrangement, radical Brook rearrangements are not reversible.
- The radical [1,2]brook rearrangement was used to trap the alkoxy radical as soon as it was formed.

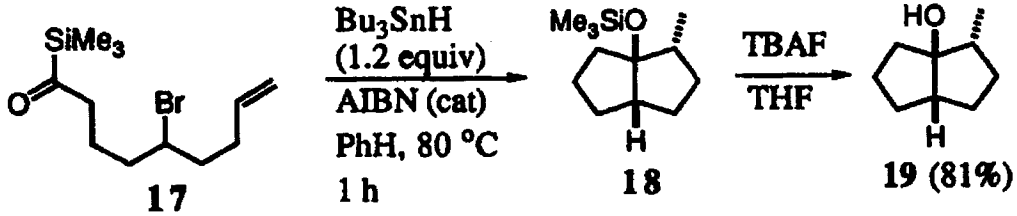
Tsai, Y.; Cherng, C. *Tetrahedron Lett.* **1991**, *32*, 3515

Radical Cyclizations Involving Secondary Radicals

entry	bromide	conc. (M)[b]	time (h)[c]	product (% yield)
1	 1	0.05	6	 2[d] (76)
2	1	0.5	0.5	2[d] (81)
3[e]	1	0.5	0.5[f]	2[d] (94) +  3 (5)
4	 4	0.5	0.5	 5 (76)
5	4	0.02	2	 6[g] (51) + 5 (42)
6	4	0.01	2	6[g] (57) + 5 (39)

[a]Please see reference 1 for general procedure. [b]Final concentration relative to the bromide. [c]Addition time of the tributyltin hydride solution. [d]A *cis/trans* (55/45) mixture (ref. 5). [e]Performed by direct mixing of the reagents in benzene and heated at 80 °C. [f]Reaction time. [g]A *cis/trans* (30/70) mixture (ref. 6).

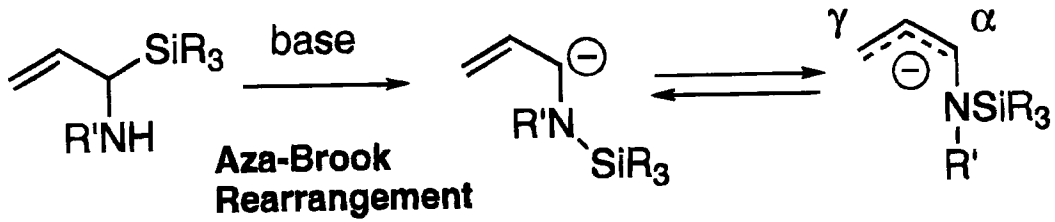
Five-member rings are formed in good yields while large amounts of elimination products are seen in reactions to form six-member rings

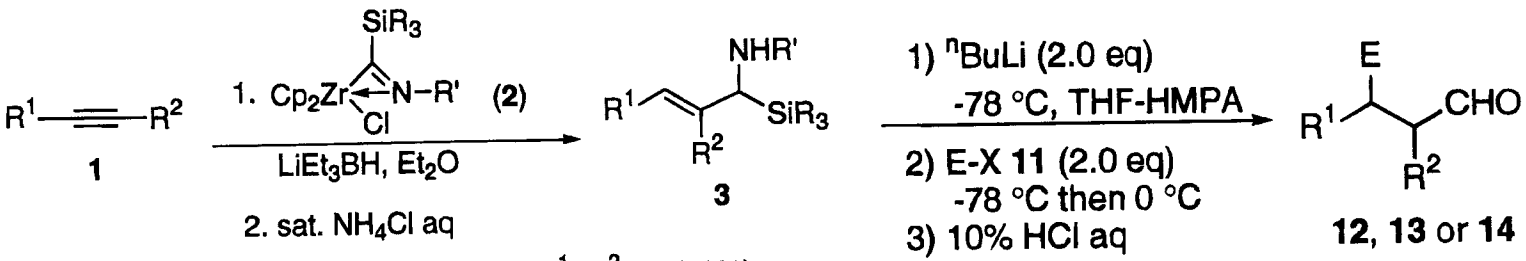


The resultant a-siloxy radicals can also participate in a second intramolecular bond forming reaction to create bicyclic compounds.

Tsai, Y.; Tang, K.; Jiaang, W. *Tetrahedron Lett.* **1993**, *34*, 1303 .

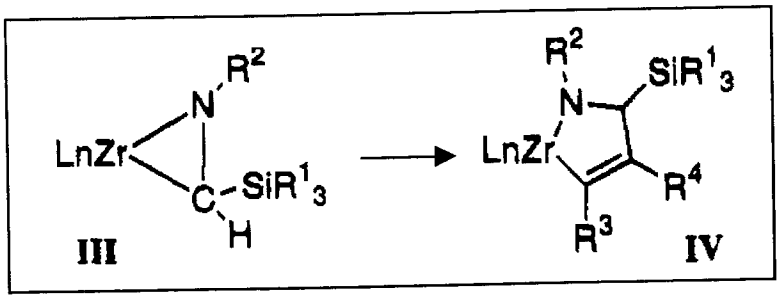
Tandem Aza-Brook Rearrangement-Alkylation Reaction





1a; $R^1=R^2=Pr$
1b; $R^1=Ph$, $R^2={}^nC_5H_{11}$
1c; $R^1={}^nC_5H_{11}$, $R^2=H$

3a; $R^1=R^2=Pr$ (73%)
3b; $R^1=Ph$, $R^2={}^nC_5H_{11}$ (78%)
3c; $R^1={}^nC_5H_{11}$, $R^2=H$ (37%)



run	substrate	E–X **11**	product yield (%)
1	**3a**, $R^1 = R^2 = Pr$	$BnO(CH_2)_3$–I (**11b**)	**12b** (67)
2	**3a**	$BnO(CH_2)_3$–Br (**11b'**)	**12b** (59)
3	**3b**, $R^1 = Ph$, $R_2 = {}^nC_5H_{11}$	$CH_2{=}CHCH_2$–Br (**11c**)	**13** (92)
4	**3c**, $R^1 = {}^nC_5H_{11}$, $R_2 = H$	$BnO(CH_2)_3$–I (**11b**)	**14** (36)[a]
5	**3a**	$CH_2{=}CHCH_2$–Br (**11c**)	**12c** (66)
6	**3a**	Bn–Br (**11d**)	**12d** (51)
7	**3a**	Pr–Br (**11e**)	**12e** (59)
8	**3a**	$Ph(CH_2)_3$–Br (**11f**)	**12f** (57)

[a] The yield of the corresponding alcohol ($NaBH_4$/MeOH).

Functional groups can introduced at both carbons of an alkyne using a aza-Brook rearrangement of an (α-silylallyl)amine, **3**.

Mori, M.; Honda, T. *J. Org. Chem.* **1996**, *61*, 1196

Summary of the Tandem radical Silyl and Aza-Brook Migration – Bond Forming Strategies

- The irreversibility of radical Brook rearrangement allows them to be used as internal radical traps to form carbocyclic ring systems.

- The trapped a siloxy radical can also be used in additional bond forming reactions to form bicyclic compounds.

- Aza-Brook rearrangements have been used in the functionalization of alkynes.

- The lack of general method to make α-, β-, and γ- silyl amine precursors and the decreased strength of the N-Si bond makes implementation of the Aza-Brook rearrangement strategy difficult

Moser, W. *Tetrahedron*, **2001**, *57*, 2065