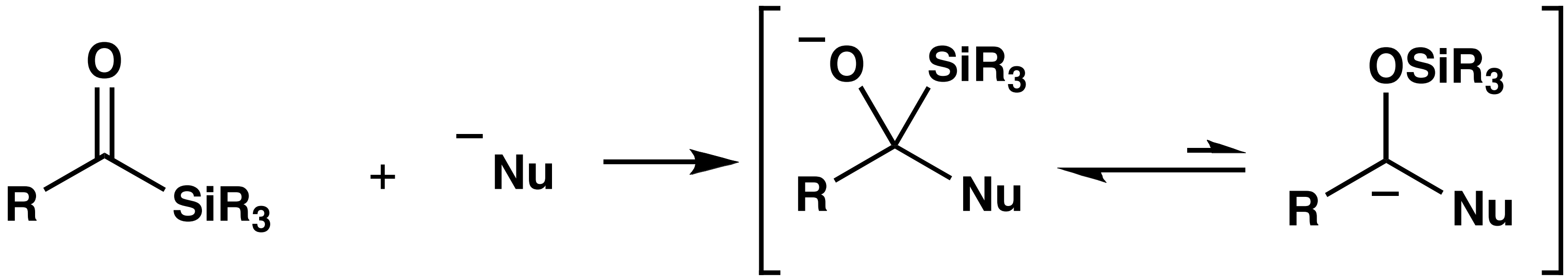
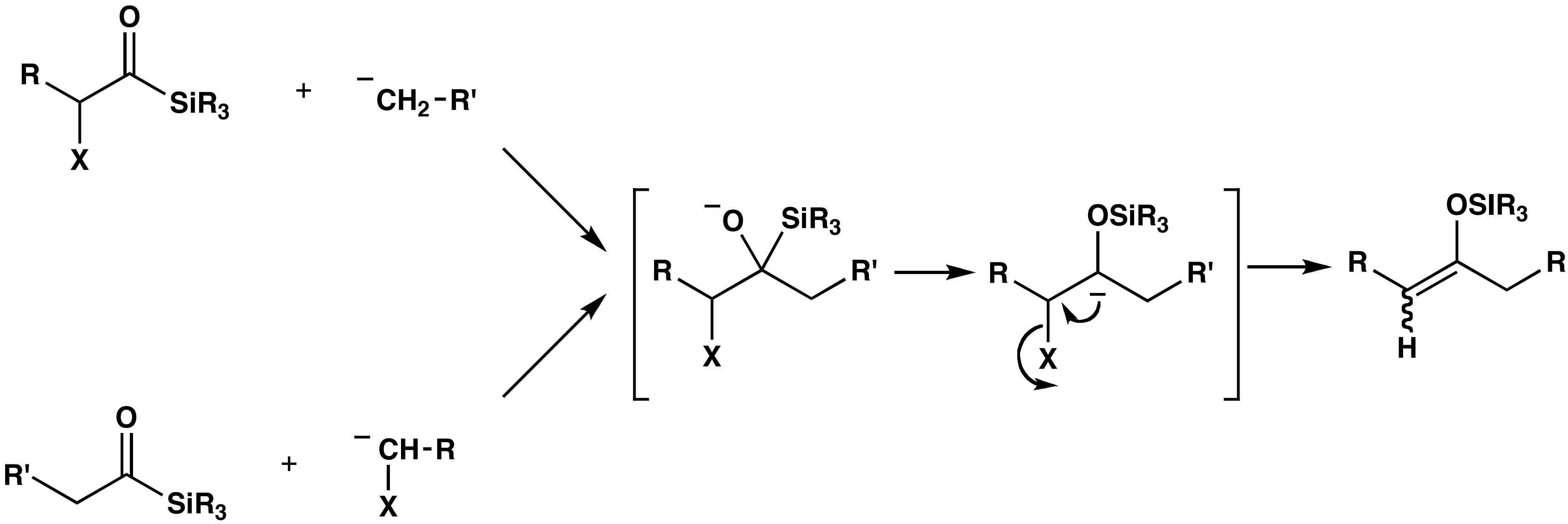


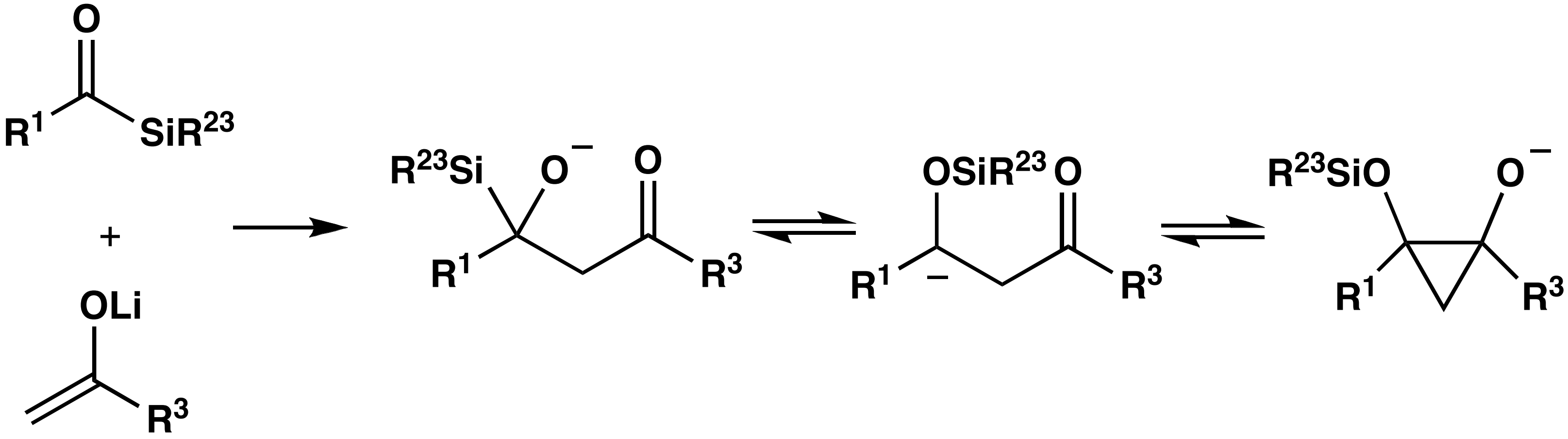
Brook rearrangement



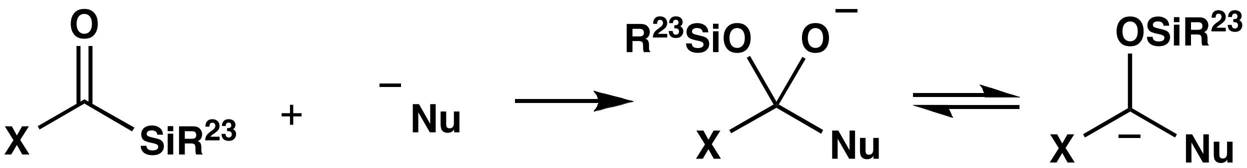
$X = \overset{+}{N}$∫$N, \overset{+}{P}R_3, SO_2Ph, CN$

Brook, A. G.; Limburg, W. W.; MacRae, D. M.; Fieldhouse, S. A. *J. Am. Chem. Soc*. **1967**, *89*, 704.
Reich, H. G.; Holtan, R. C.; Bolm, C. *J. Am. Chem. Soc*. **1990**, *112*, 5609-5617.
Nakajima, T.; Segi, M.; Sugimoto, F,; Hioki, R.; Yokota, S.; Miyashita, K. *Tetrahedron* **1993**, *37*, 8343.

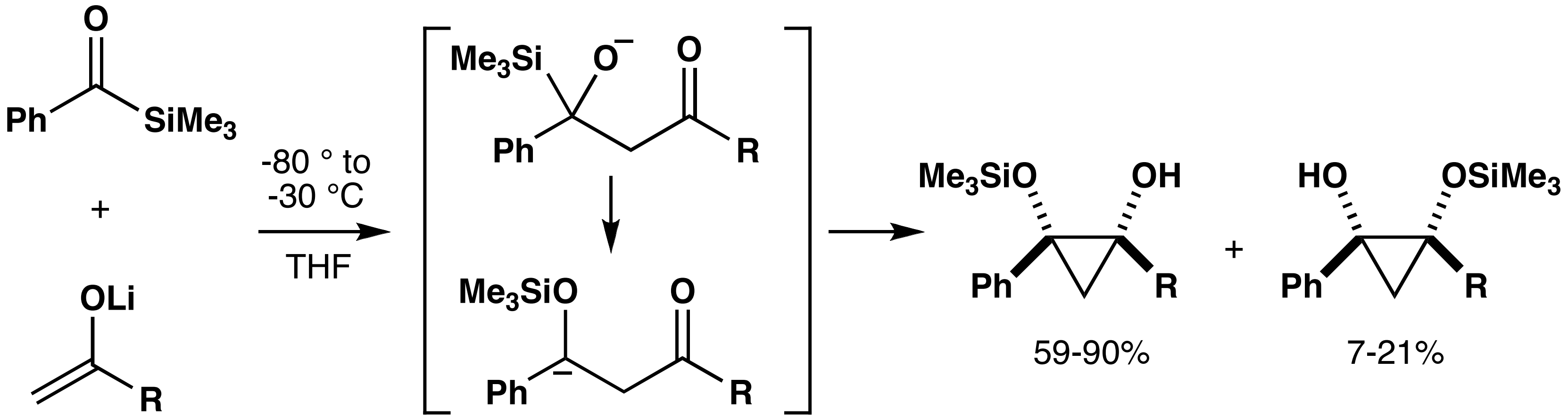
1. Use of Ketone Enolate as a Nucleophile

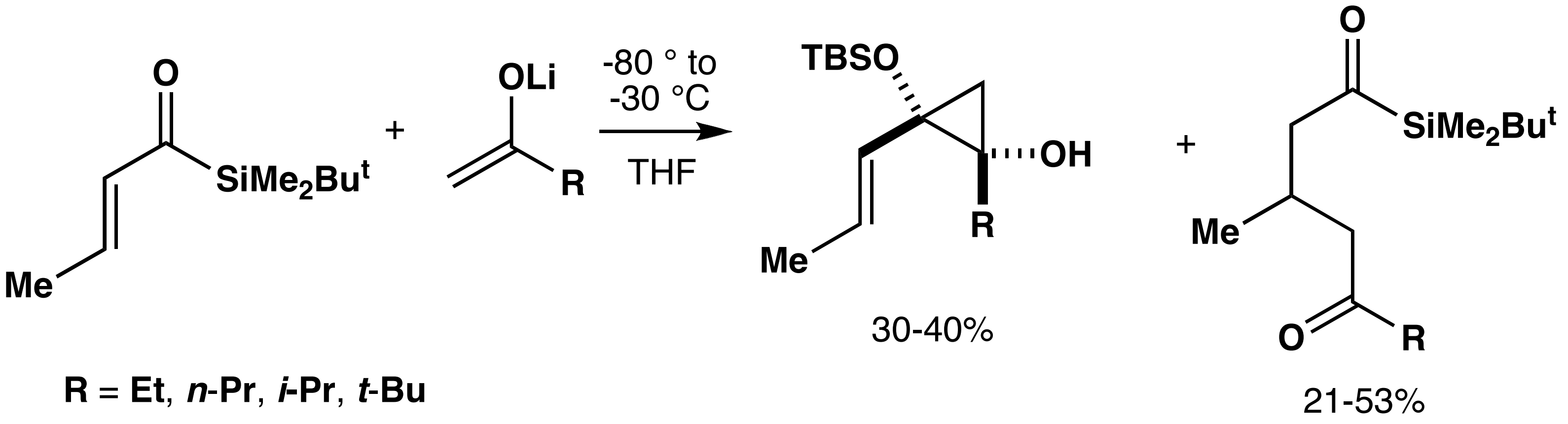


2. Introduction of Carbanion-Stabilizing Heteroatom



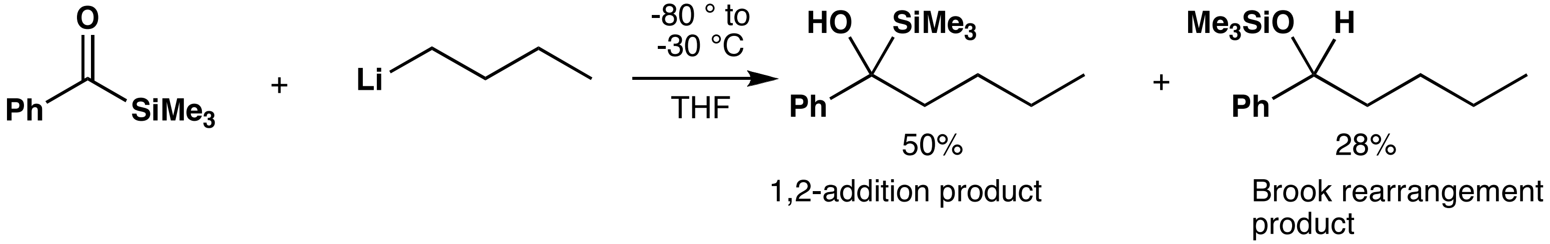
X = SPh, $SiMe_3$, $P(O)(OMe)_2$

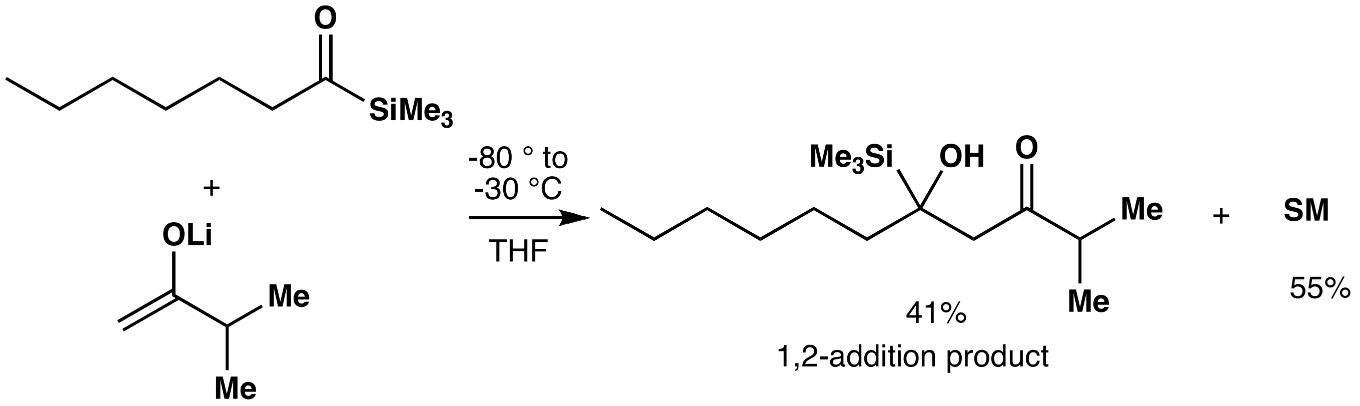


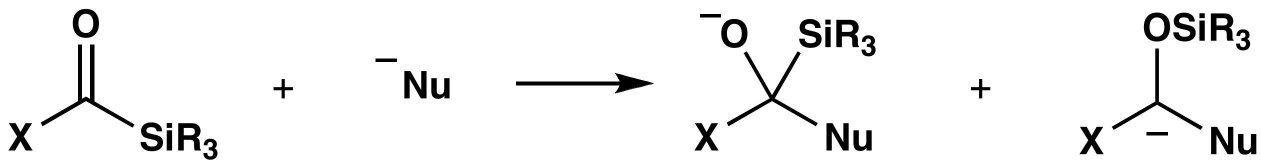


R = **Et**, ***n*-Pr**, ***i*-Pr**, ***t*-Bu**

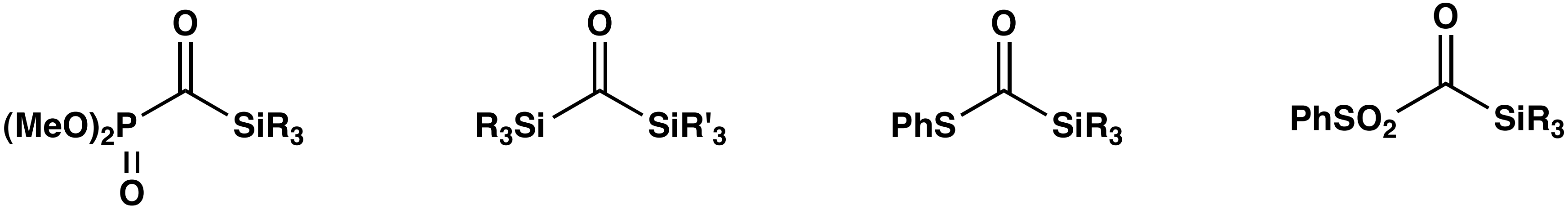
Takeda, K.; Nakatani, J.; Nakamura, H.; Sako, K.; Yoshii, E.; Yamaguchi, K. *Synlett* **1993**, 8

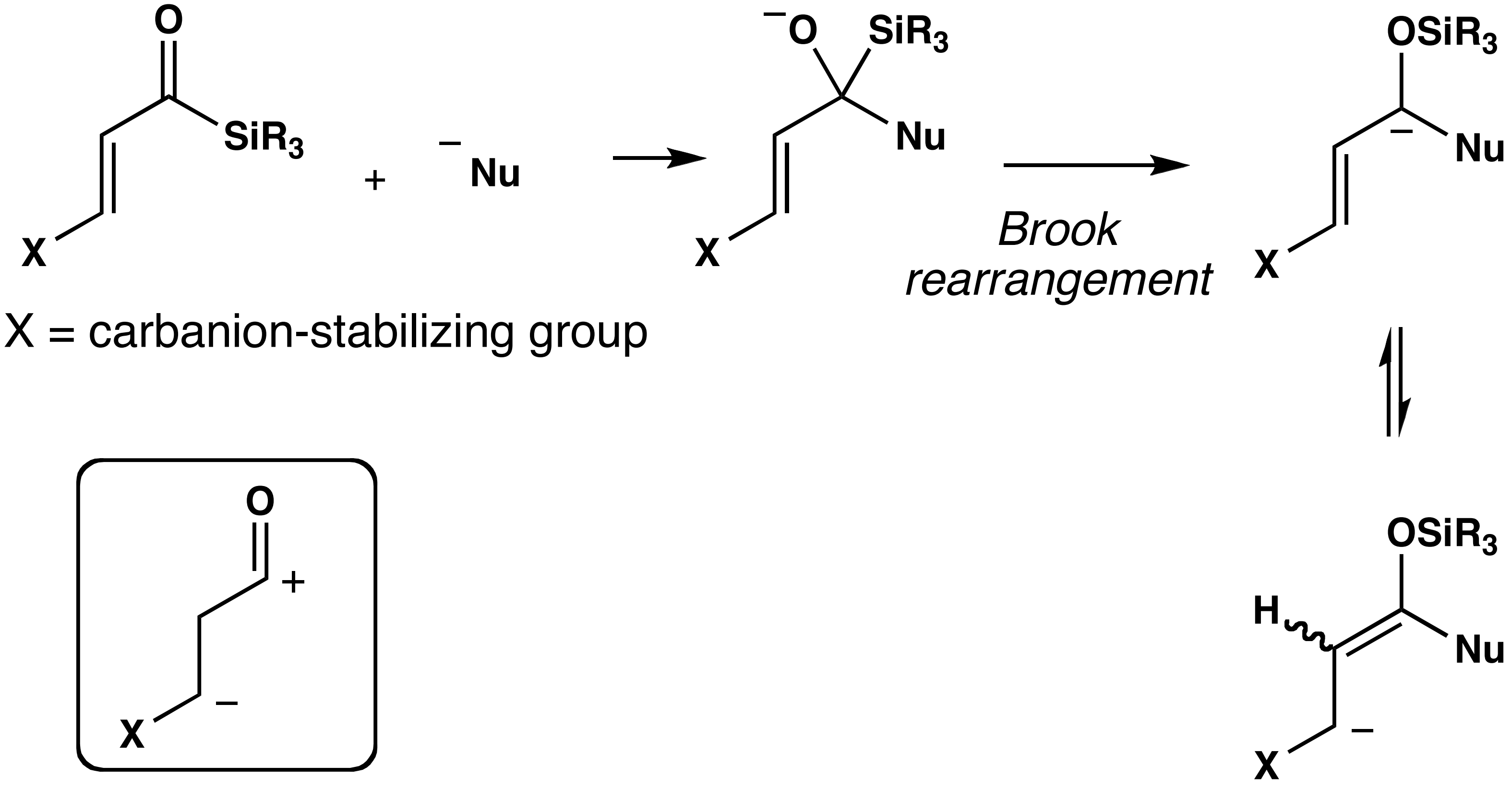

Ph
SiMe3
O
+
Li
-80 ° to
-30 °C
THF
HO
SiMe3
Ph
50%
1,2-addition product
+
Me3SiO
H
Ph
28%
Brook rearrangement
product


O
SiMe3
+
OLi
Me
Me
-80 ° to
-30 °C
THF
Me3Si
OH
O
Me
Me
41%
1,2-addition product
+
SM
55%



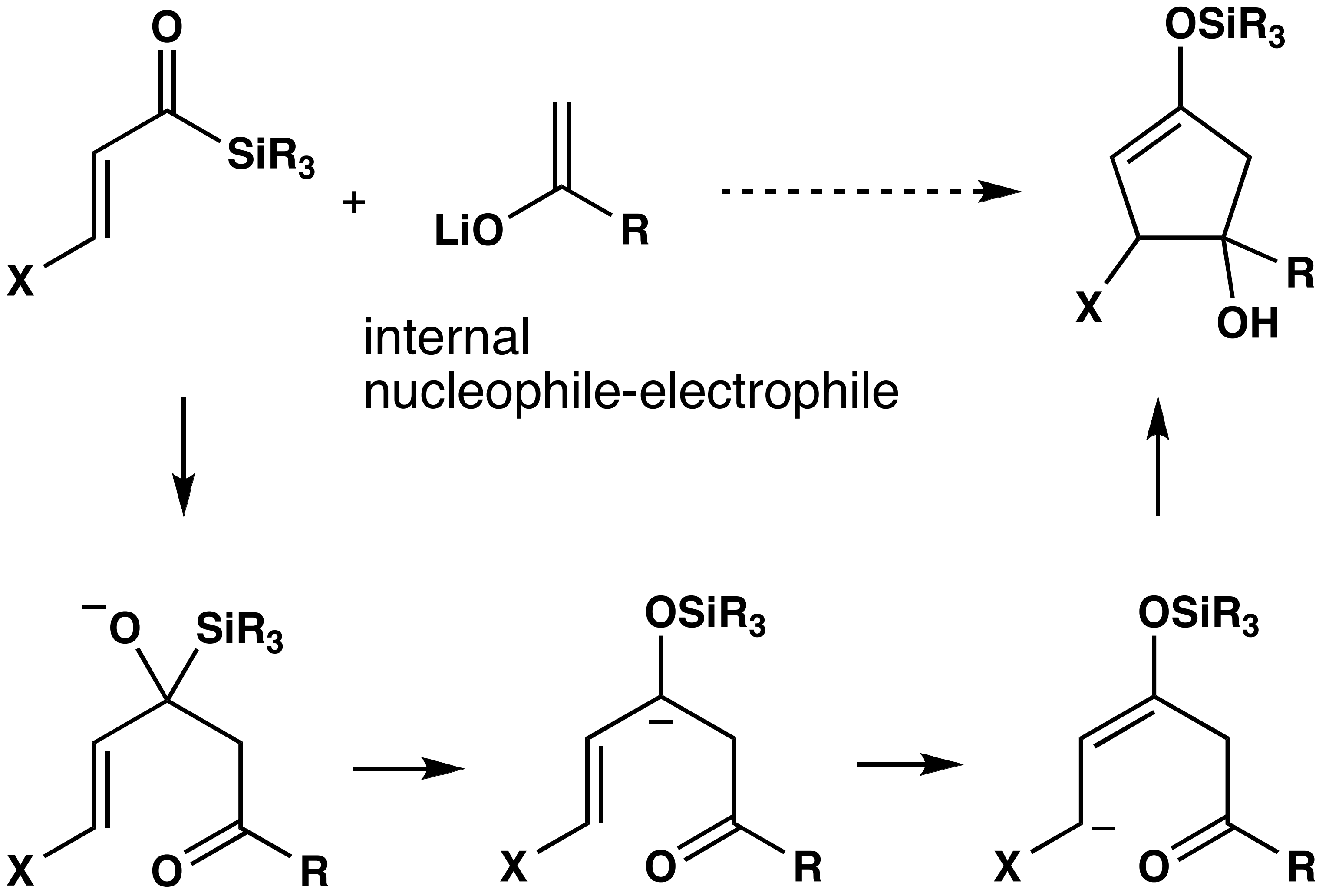
X = anion-stabilizing heteroatom





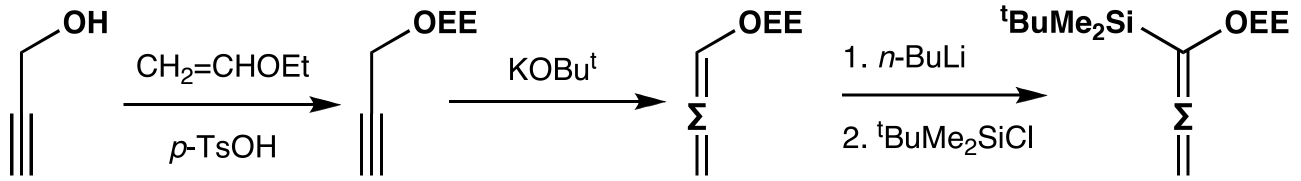
X = carbanion-stabilizing group

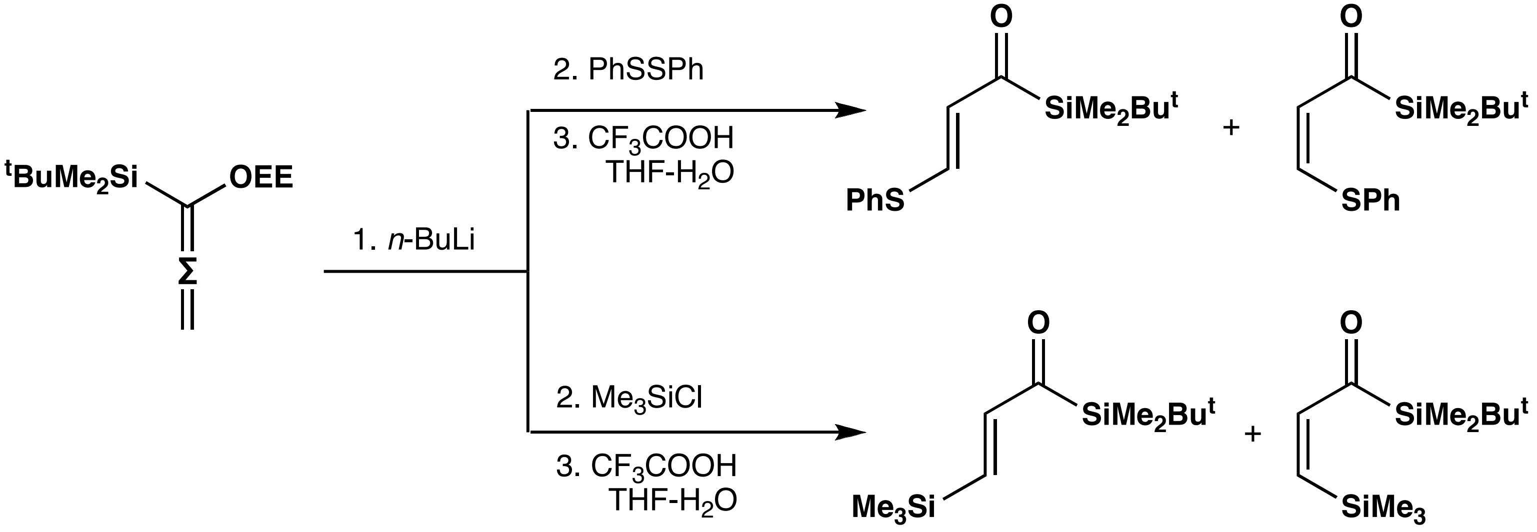
1,3-dipole



internal
nucleophile-electrophile

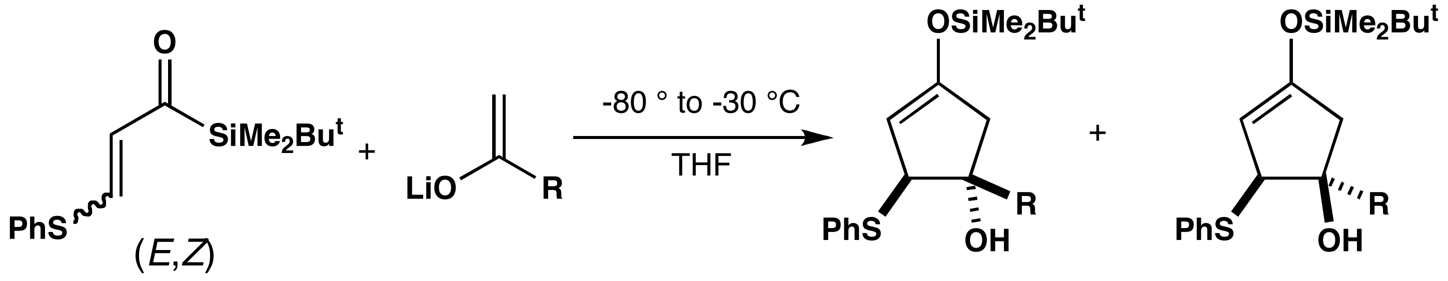
Preparation of b-(Phenylthio)- and b-(Trimethylsilyl)-Acryloylsilanes

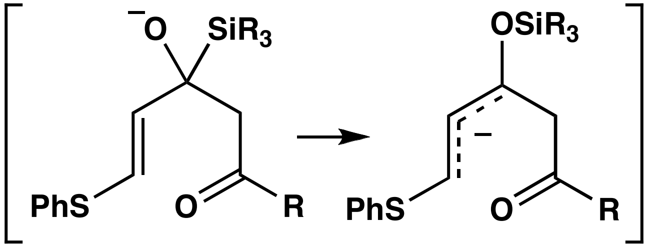




Reich, H. J.; Kelly, M. J.; Olson, R. E.; Holtan, R. C. *Tetrahedron* **1983**, *39*, 949-960

[3 + 2] Annulation Using Reaction of (b-Phenylthio)acryloyl)silanes and Lithium Enolates

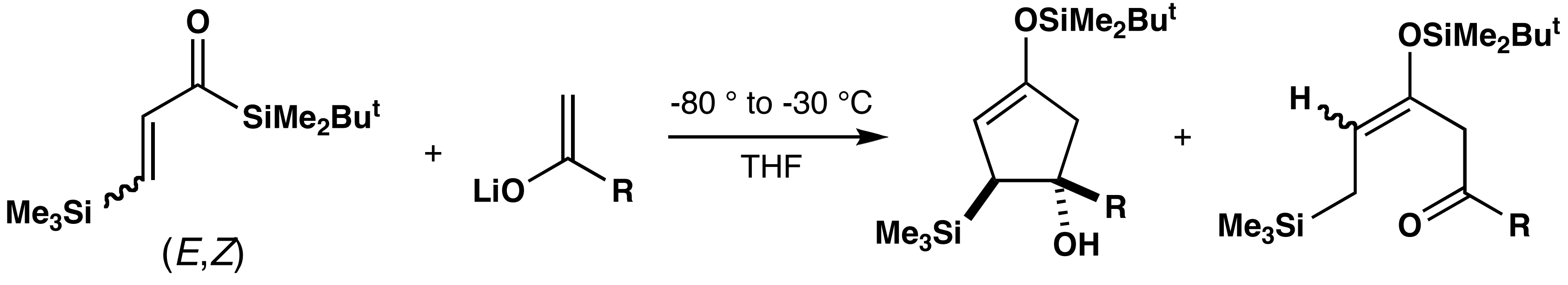


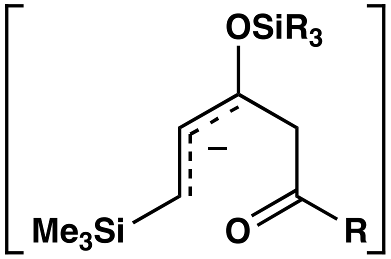


Et	70%	5%
Pr	74%	7%
***i*-Pr**	55%	19%
***n*-octyl**	71%	8%

Takeda, K.; Fujisawa, Makino, T.; Yoshii, E.; Yamaguchi, K. *J. Am. Chem. Soc*. **1993**, *115*, 9351-9352.

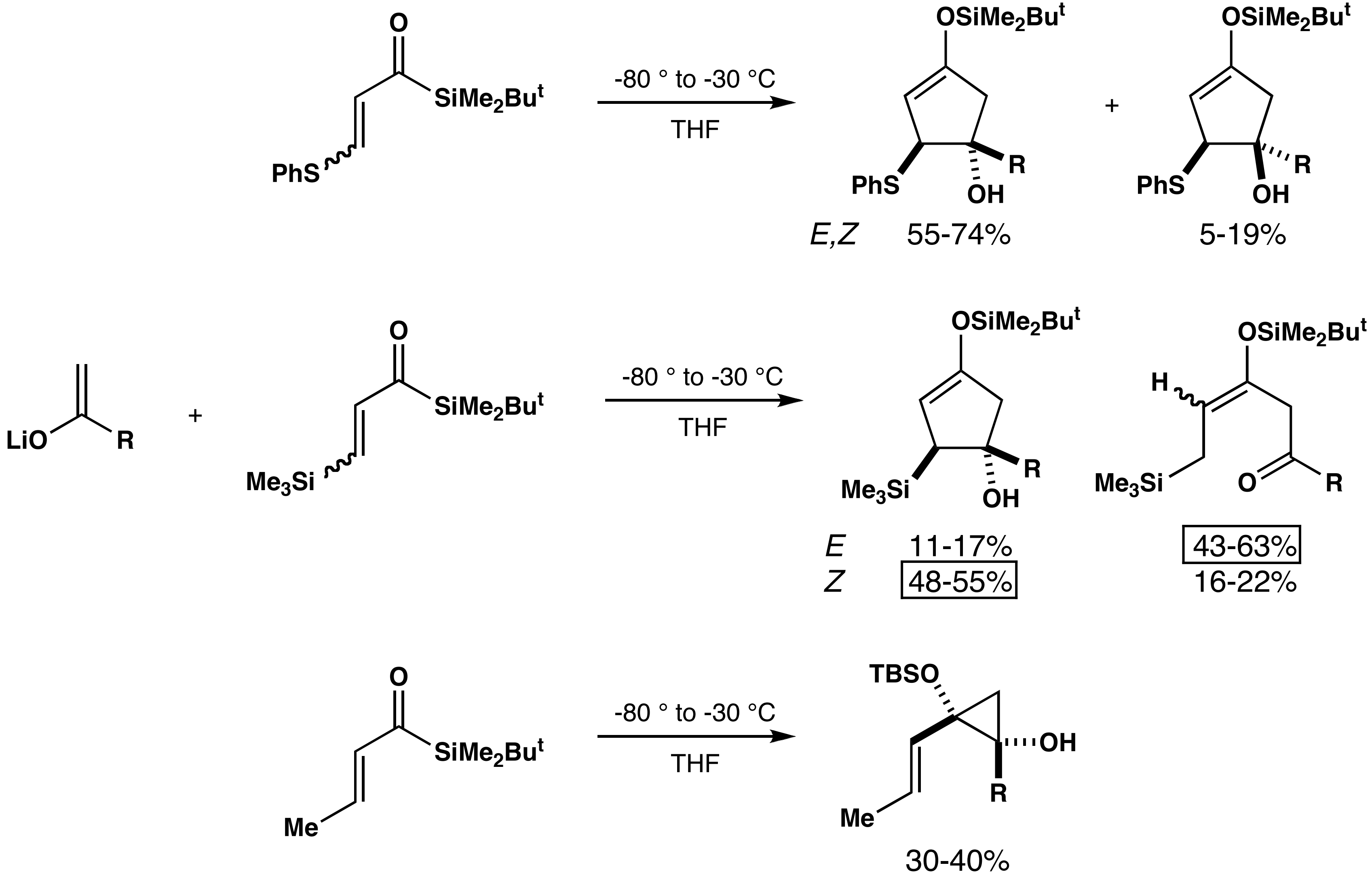
[3 + 2] Annulation Using Reaction of (b-Trimethylsilyl)acryloyl)silane and Lithium Enolates



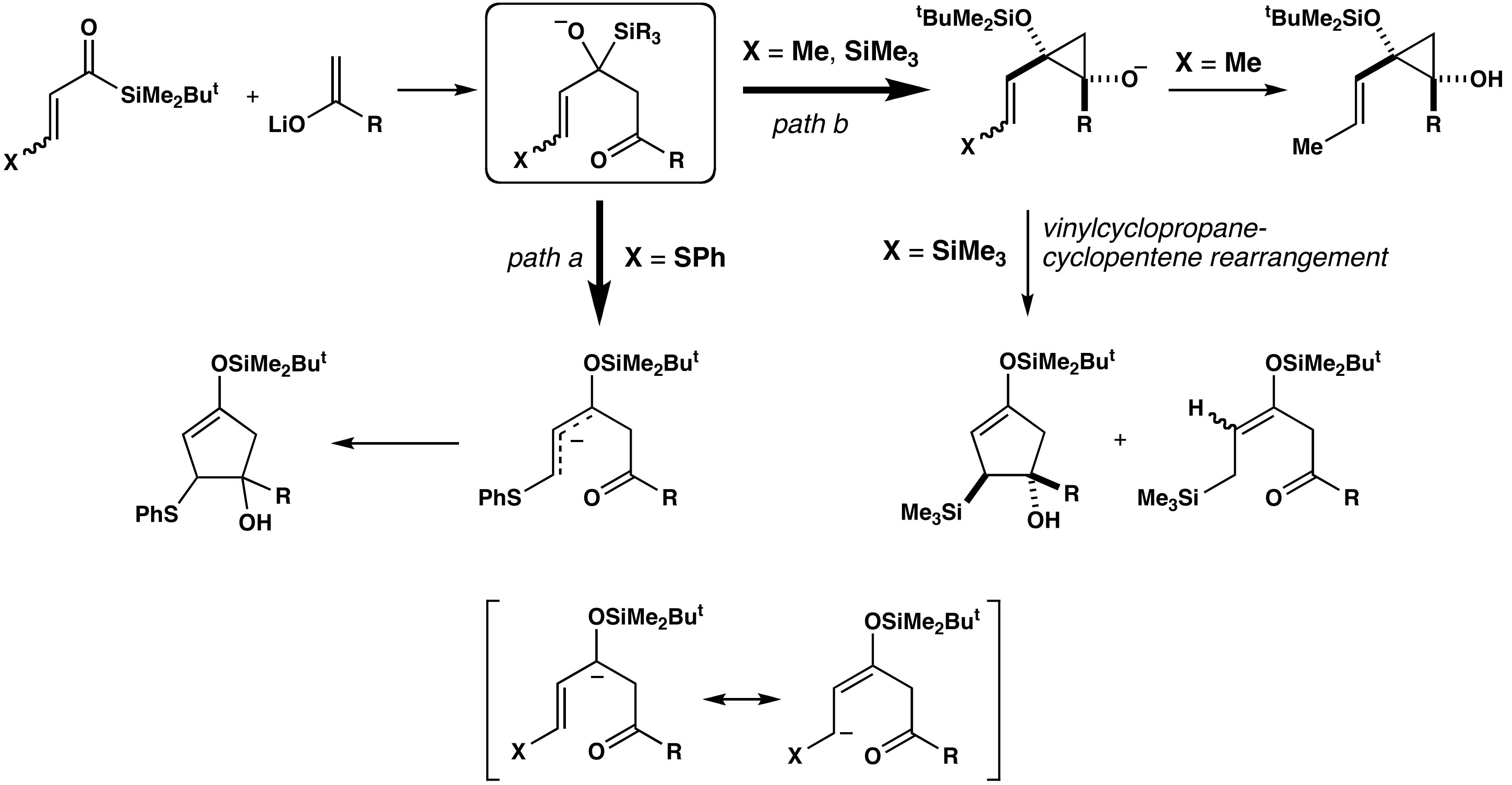


E	Et	17%	43%
	n-Pr	11%	57%
	i-Pr	14%	63%
Z	Et	48%	16%
	n-Pr	55%	22%
	i-Pr	51%	21%

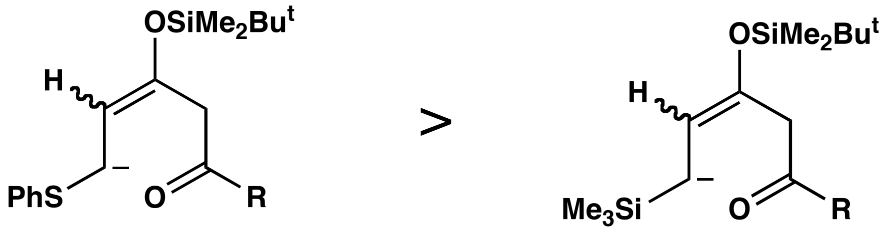
Summary of the Reaction of b-Substituted-Acryloylsilanes with Lithium Enolate of Methyl Ketones



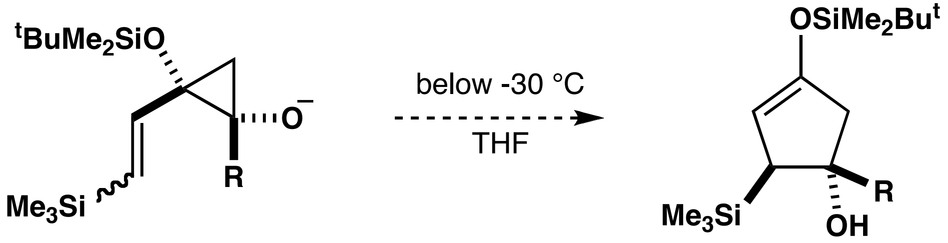
A Proposed Reaction Pathway for the [3 + 2] Annulation Using b-Phenylthio- and b-Trimethylsilyl-Acryloylsilanes

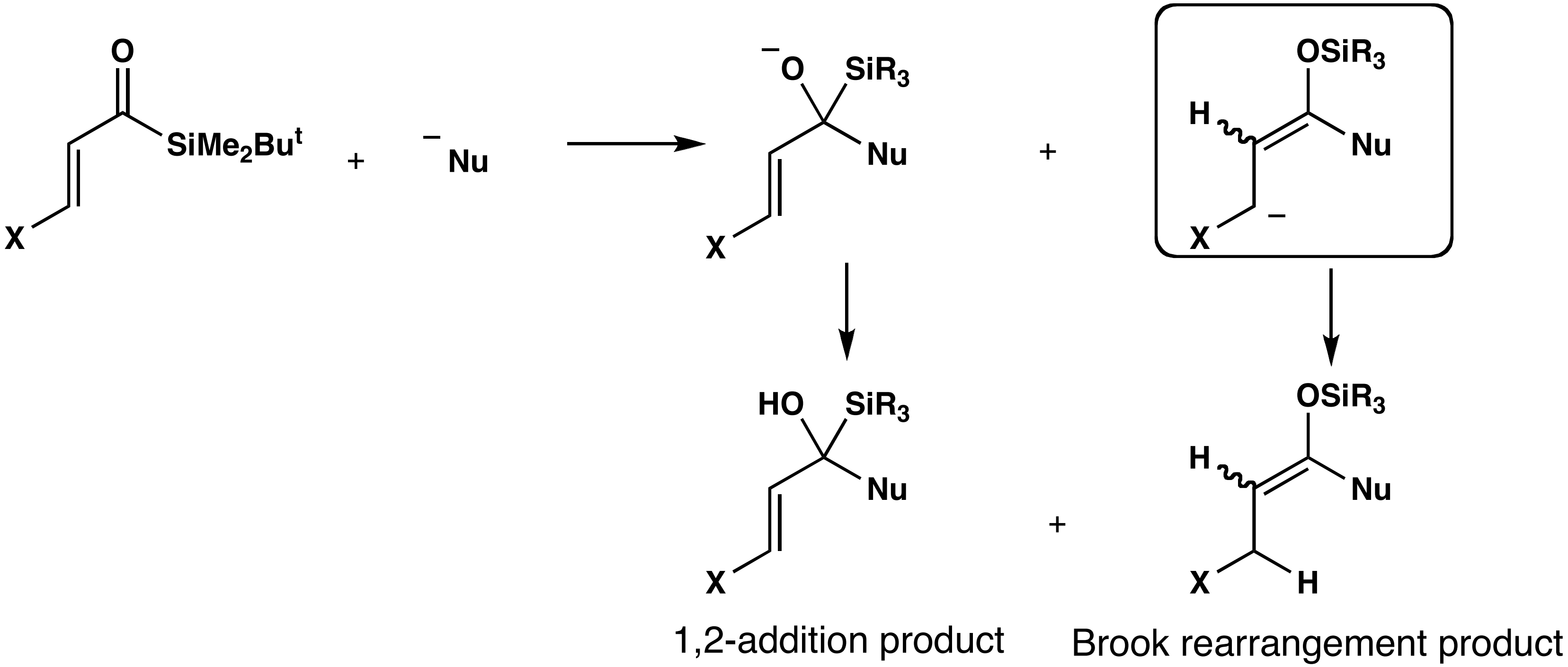


1. Does the phenylthio group stabilize the a-carbanion more strongly does than the trimethylsilyl group?

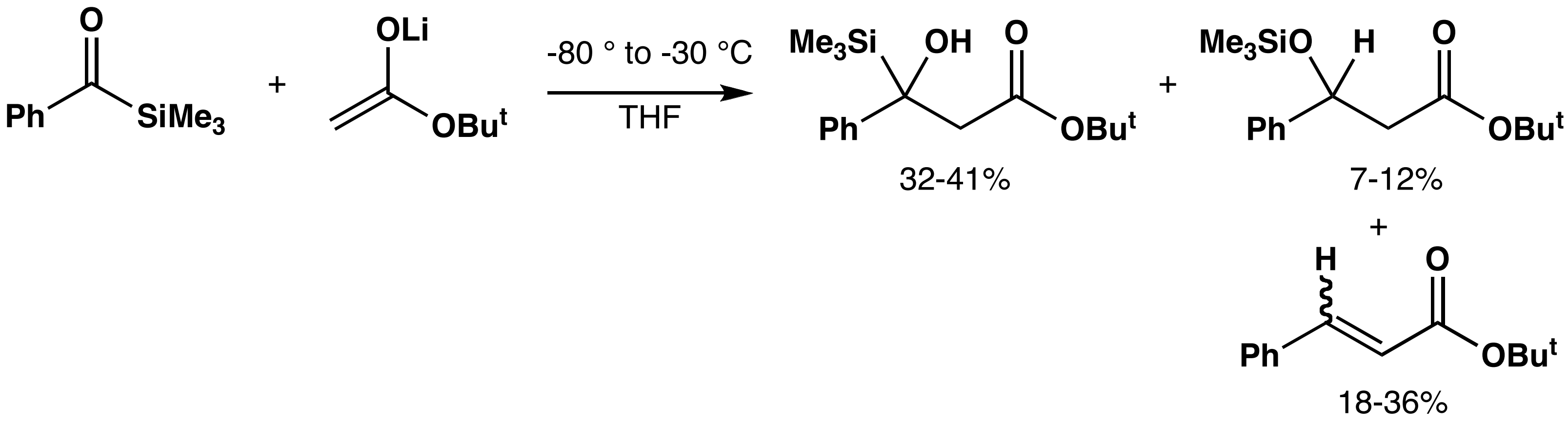


2. Does the oxyanion accelerated vinylcyclopropane rearrangement occur at low temperatures below -30 °C?



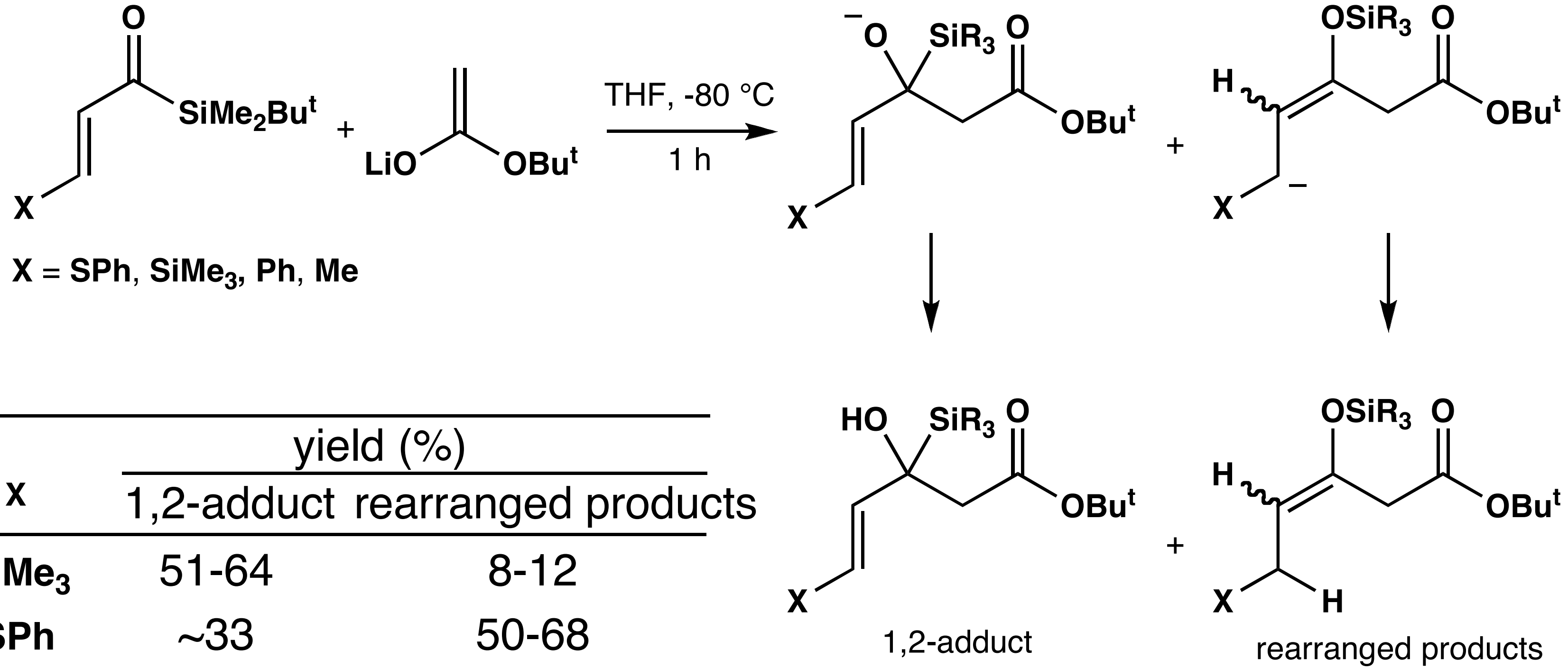


O
SiMe2But
X
+
−Nu
−O
SiR3
Nu
X
+
OSiR3
H
Nu
X
−
HO
SiR3
Nu
X
+
OSiR3
H
Nu
X
H
1,2-addition product
Brook rearrangement product



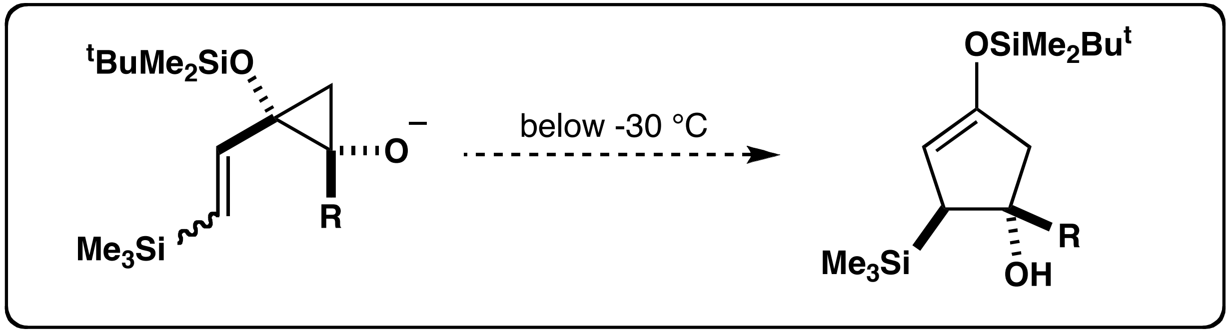
O
Ph
SiMe3
+
OLi
OBut
-80 ° to -30 °C
THF
Me3Si
OH
O
Ph
OBut
32-41%
+
Me3SiO
H
O
Ph
OBut
7-12%
+
H
O
Ph
OBut
18-36%

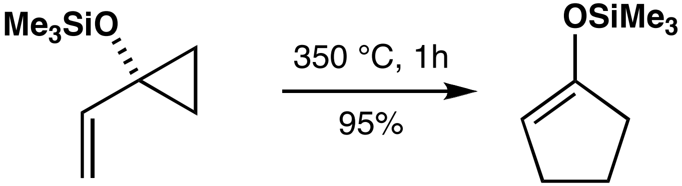
Reaction of b-Substituted-Acryloysilanes with Lithium Enolate of *t*-Butyl Acetate



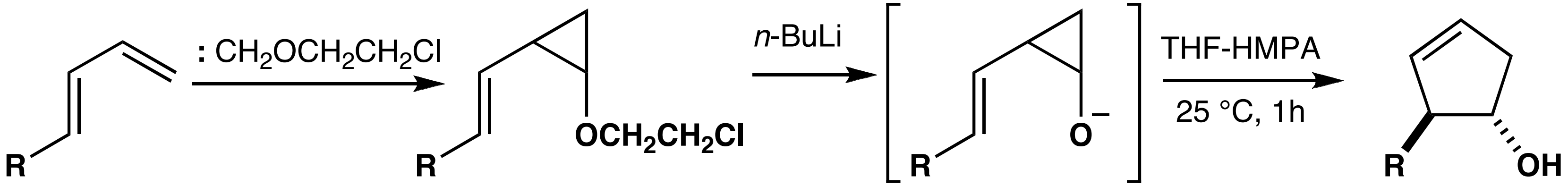
X	yield (%)	
	1,2-adduct	rearranged products
$SiMe_3$	51-64	8-12
SPh	~33	50-68
Me	90	0

Vinylcyclopropane-Cyclopentene Rearrangement

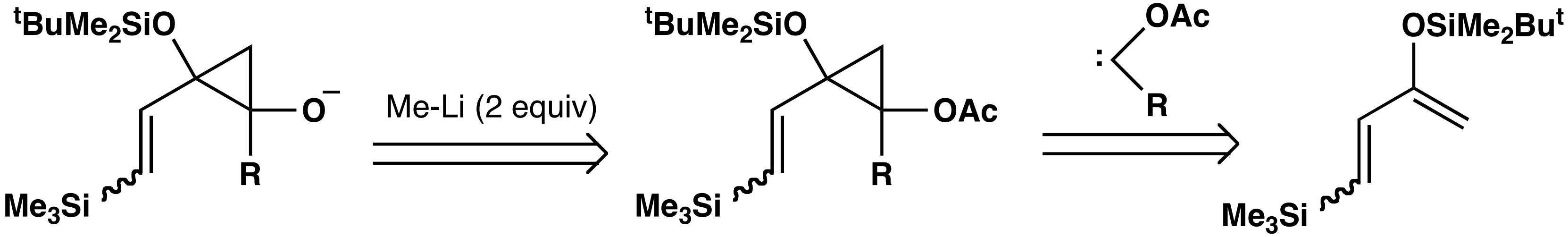




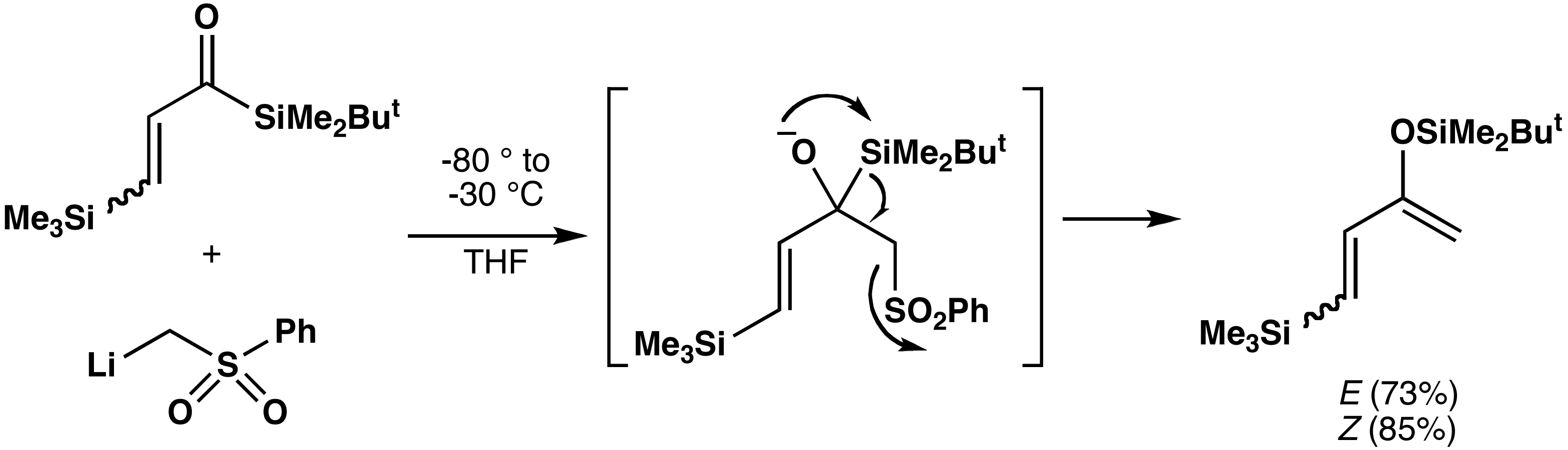
Girard, C.; Amice, P.; Barnier, J. P. Conia, J. M. *Tetrahedron Lett*. **1974**, 3329.



Danheiser, R. L.; Davilla, C. M.; Auchus, R. J.; Kadonaga, J. T. *J. Am. Chem. Soc*. **103**, 2443 (1981).

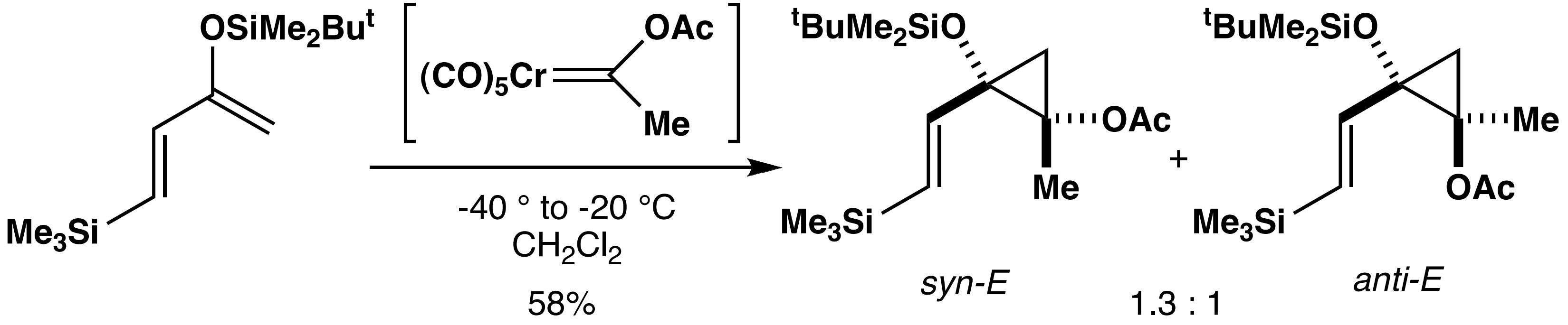


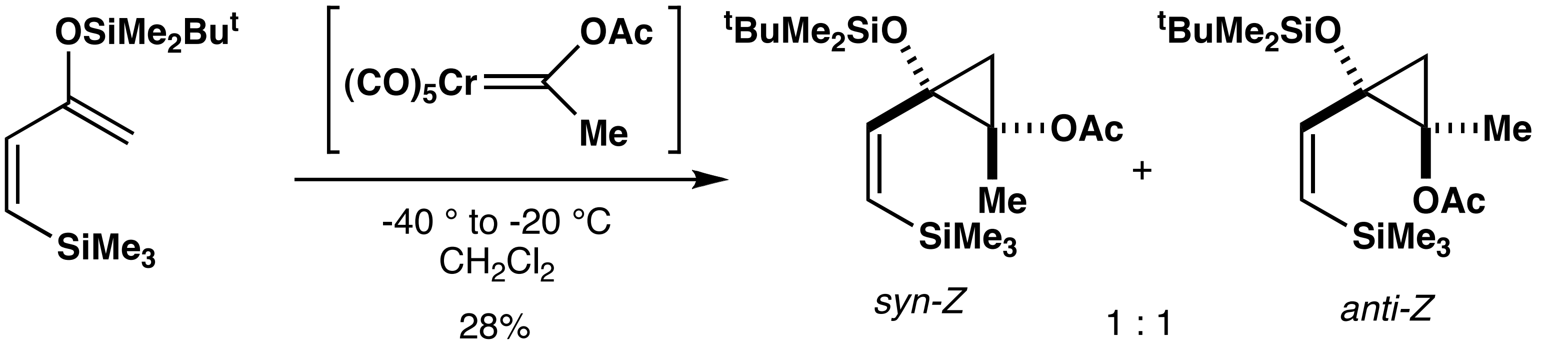
cf . Murray, C. K.; Yang, D. C.; Wulff, W. D. *J. Am. Chem. Soc.* **1990**, *112*, 5660-5662.

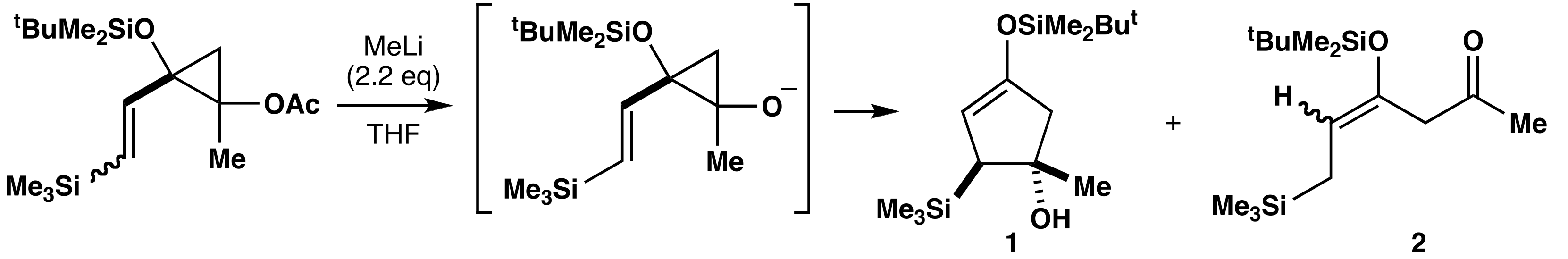


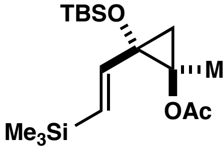
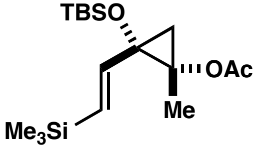
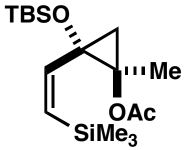
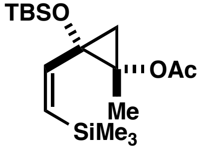
cf . Reich, H. J.; Holtan, R. C.; Bolm, C. *J. Am. Chem. Soc.* **1990**, *112*, 5609-5617.

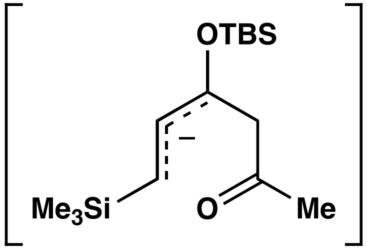
Preparation of 2-(2-(Trimethylsilyl)ethenyl)cyclopropyl Acetates

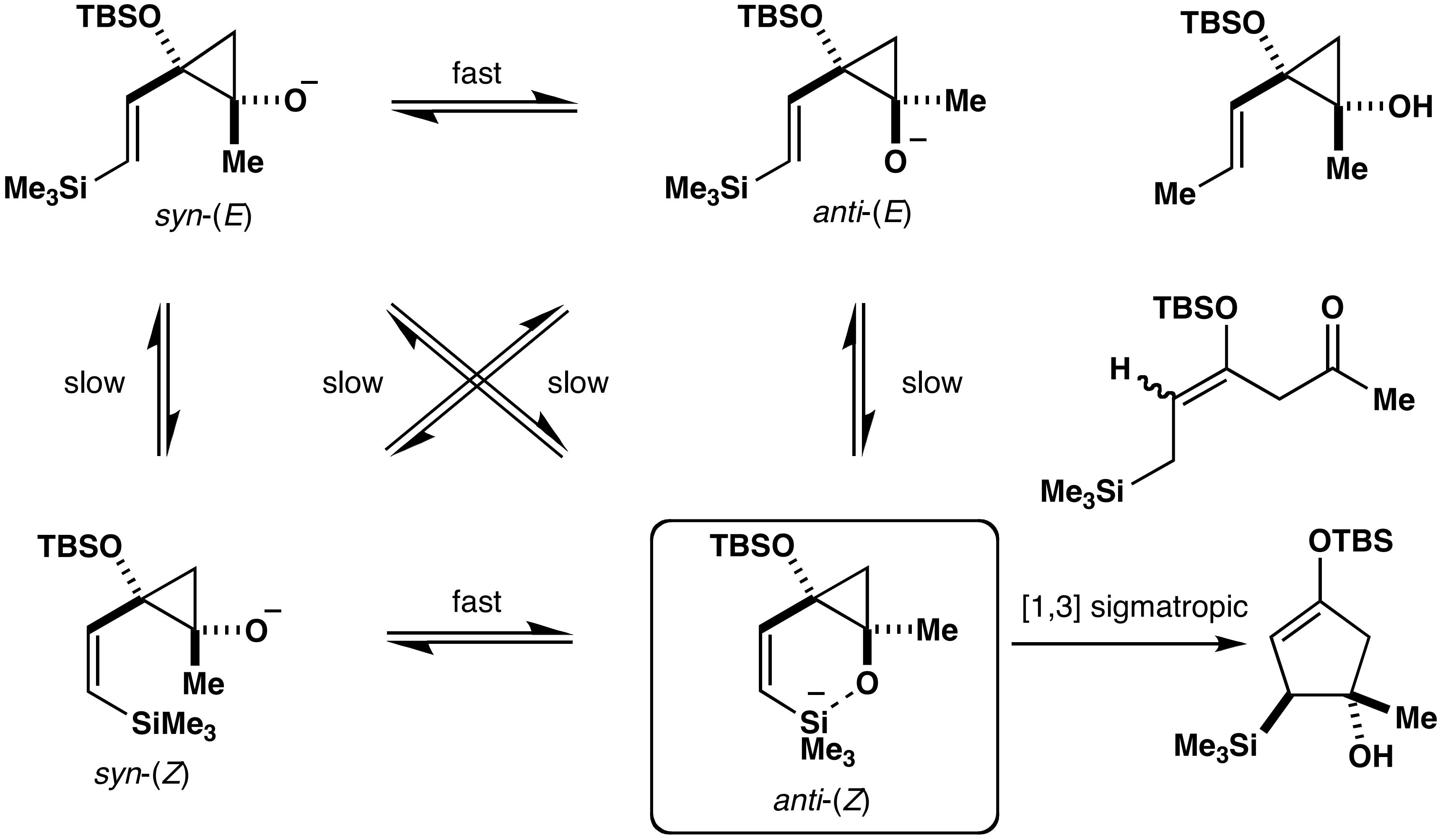




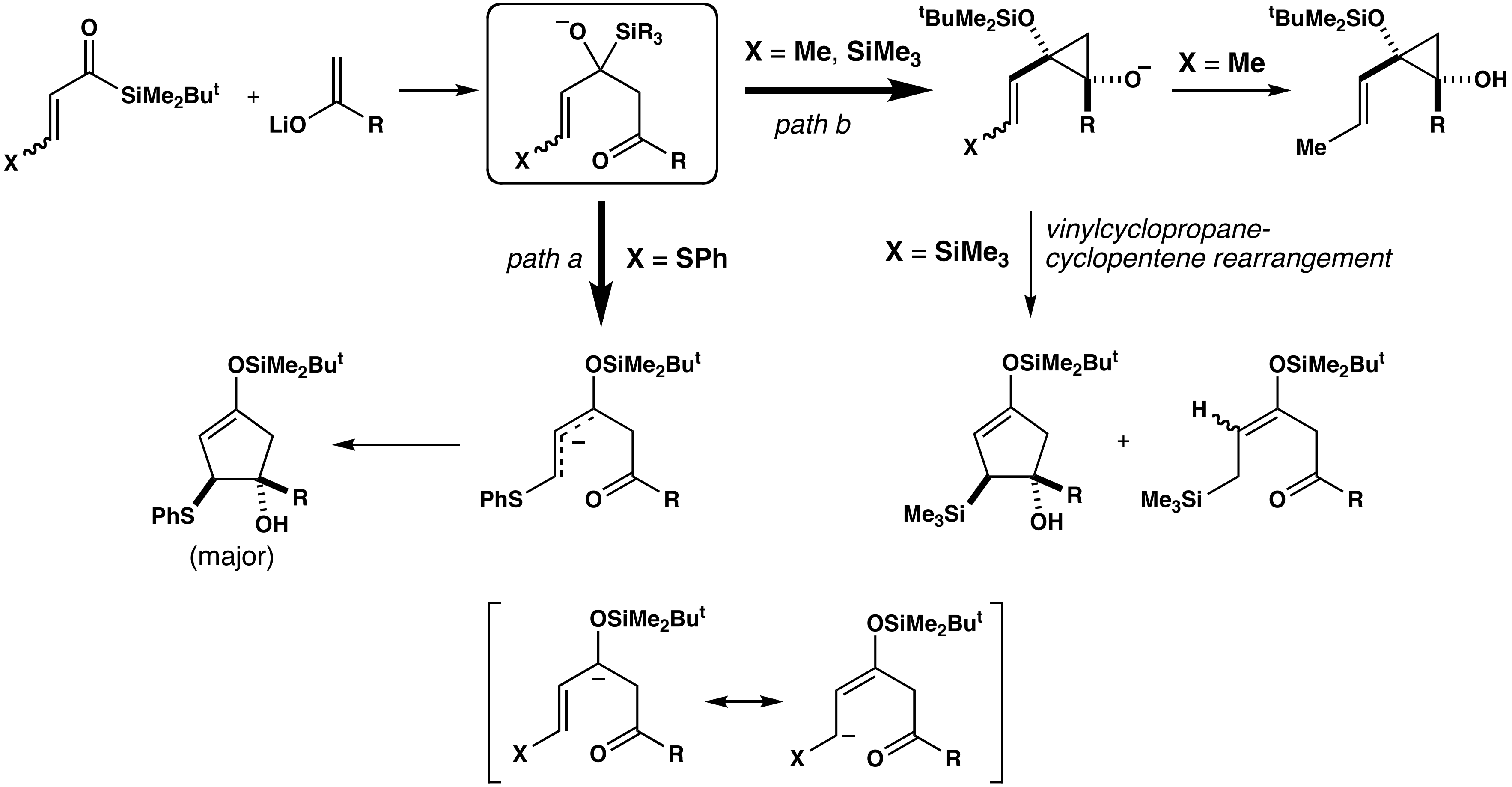


entry	cyclopropyl acetate		conditions	yield (%)	
				1	**2**
1		*anti-E*	-80 °C, 30 min	0	89
2			-80 ° to -30 °C	63	34
3		*syn-E*	-80 °C, 30 min	0	81
4			-80 ° to -30 °C	54	31
5		*anti-Z*	-80 °C, 30 min	59	10
6			-80 ° to -30 °C	76	14
7		*syn-Z*	-80 °C, 30 min	52	20
8			-80 ° to -30 °C	76	16

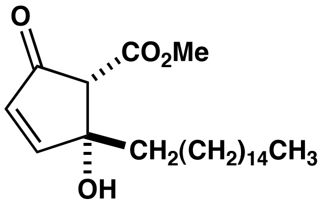



TBSO
O−
Me
Me3Si
syn-(E)
fast
TBSO
Me
O−
Me3Si
anti-(E)
TBSO
OH
Me
Me
slow
slow
slow
slow
TBSO
O
H
Me
Me3Si
TBSO
O−
Me
SiMe3
syn-(Z)
fast
TBSO
Me
O
−
Si
Me3
anti-(Z)
[1,3] sigmatropic
OTBS
Me
Me3Si
OH

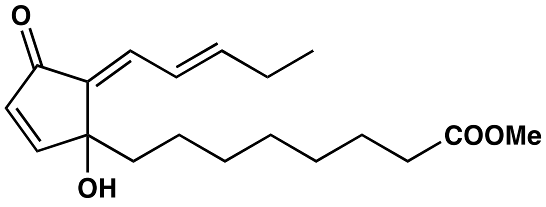
A Proposed Reaction Pathway for the [3 + 2] Annulation Using b-Phenylthio- and b-Trimethylsilyl-Acryloylsilanes



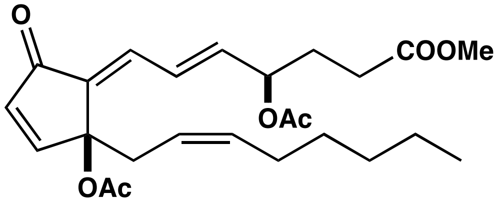
Application of the [3 + 2] Annulaton to Synthesis of Natural Products



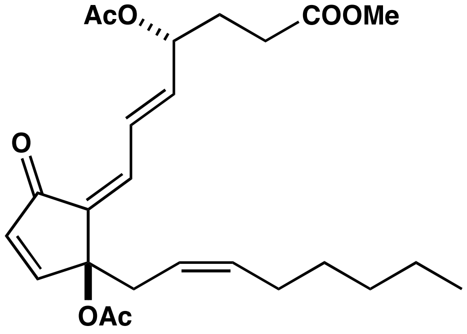
Untenone A[1]



Chromomoric acid DII methyl ester[2]



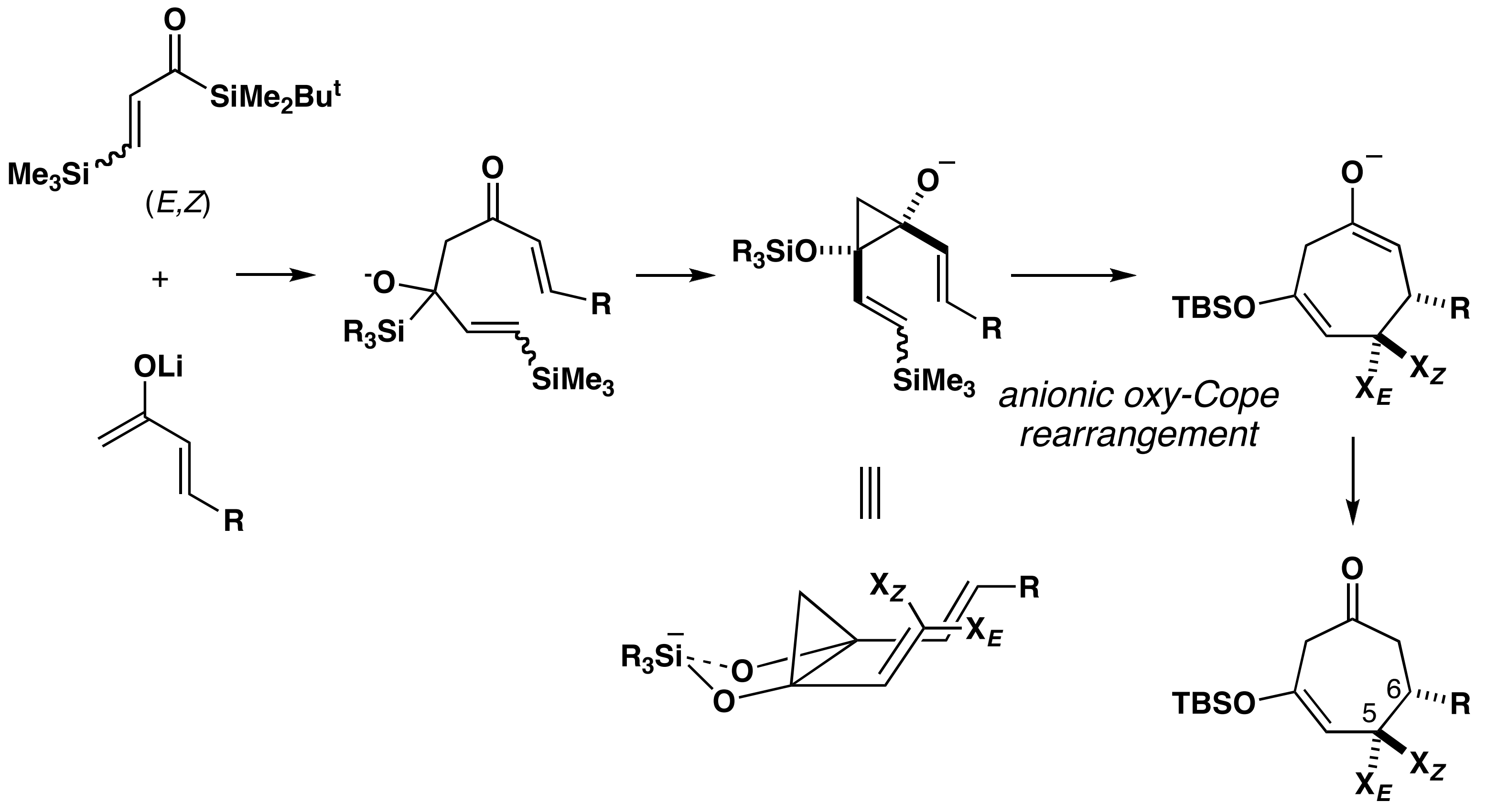
Clavulone II[3]



Clavulone III[3]

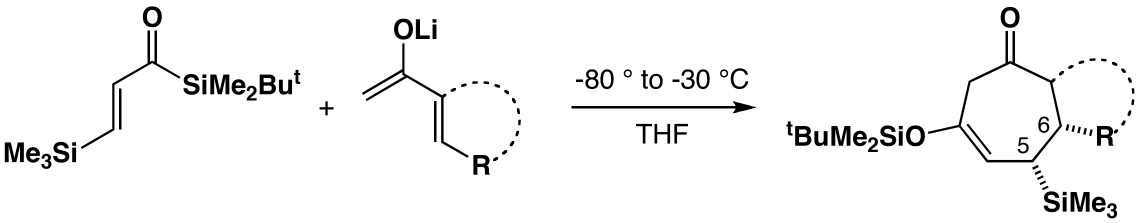
1. Takeda, K.; Nakayama, I.; Yoshii, E. *Synlett* **1994**, 178.
2. Takeda, K.; Fujisawa, M.; Makino, T.; Yoshii, E.; Yamaguchi, K. *J. Am. Chem. Soc*. **1993**, *115*, 9351-9352.
3. Takeda, K; Kitagawa, K.; Yoshii, E. *20th International Symposium on the Chemistry of Natural Products*, 1996, 9, Chicago.

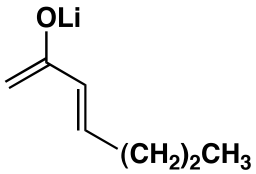
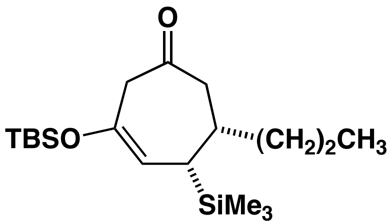
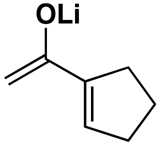
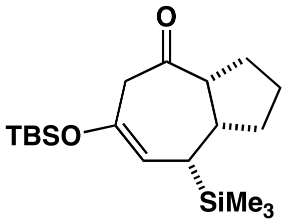
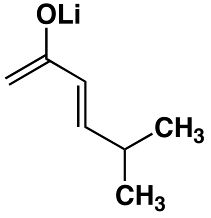
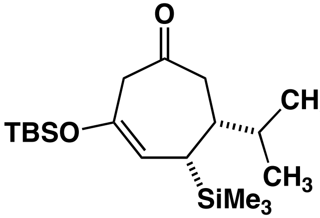
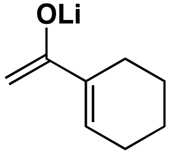
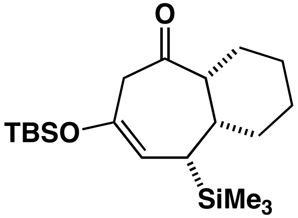
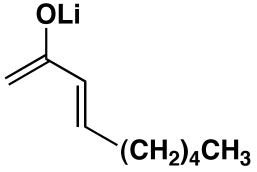
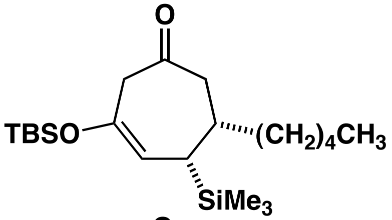
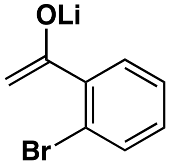
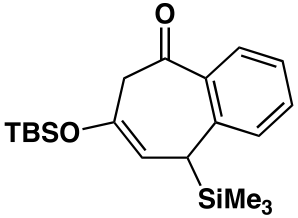
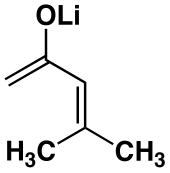
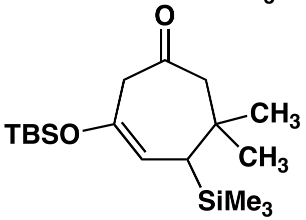
[3 + 4] Annulation Using Reaction of (b-(Trimethylsilyl)acryloyl)silanes with the Lithium Enolate of Alkenyl Methyl Ketone

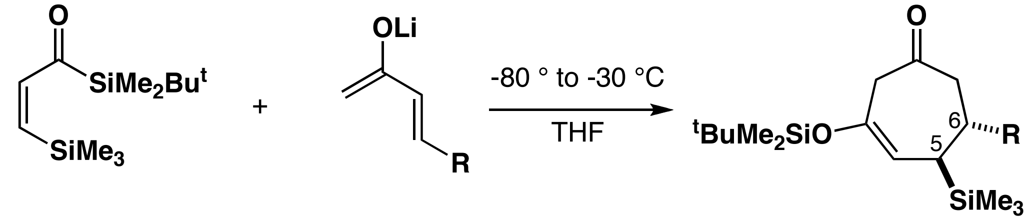


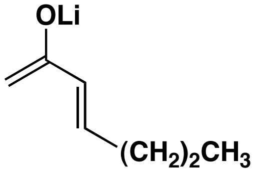
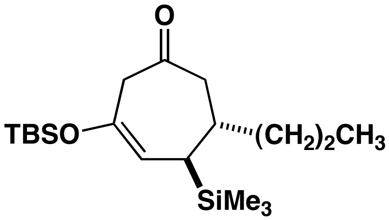
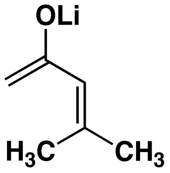
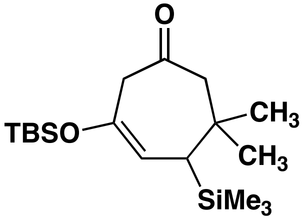
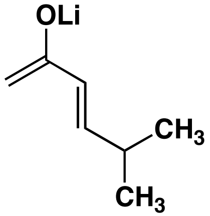
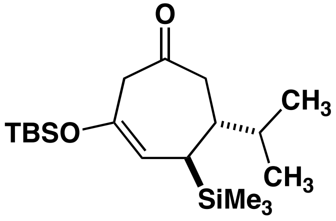
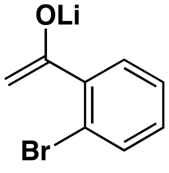
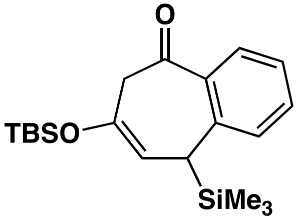
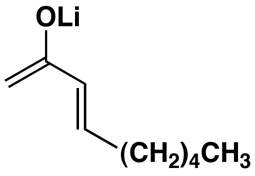
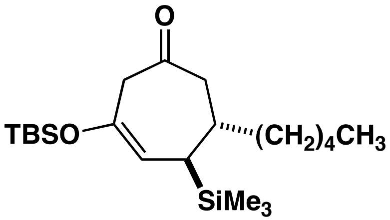
E → 5,6-*cis*
Z → 5,6-*trans*

Takeda, K.; Takeda, M.; Nakajima, A.; Yoshii, E. *J. Am. Chem. Soc.* **1995**, *117*, 6400-6401.

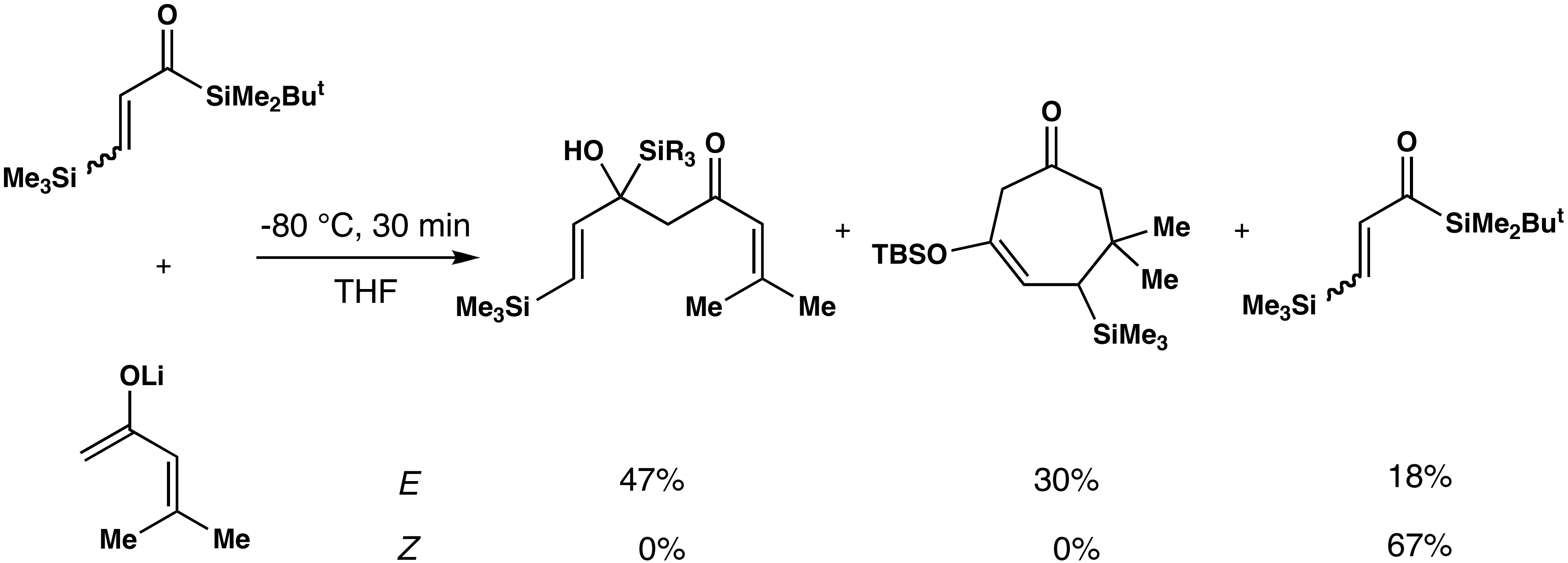


ketone enolate	product	yield	ketone enolate	product	yield
		73%			73%
		84%			82%
		84%			30%
		67%			



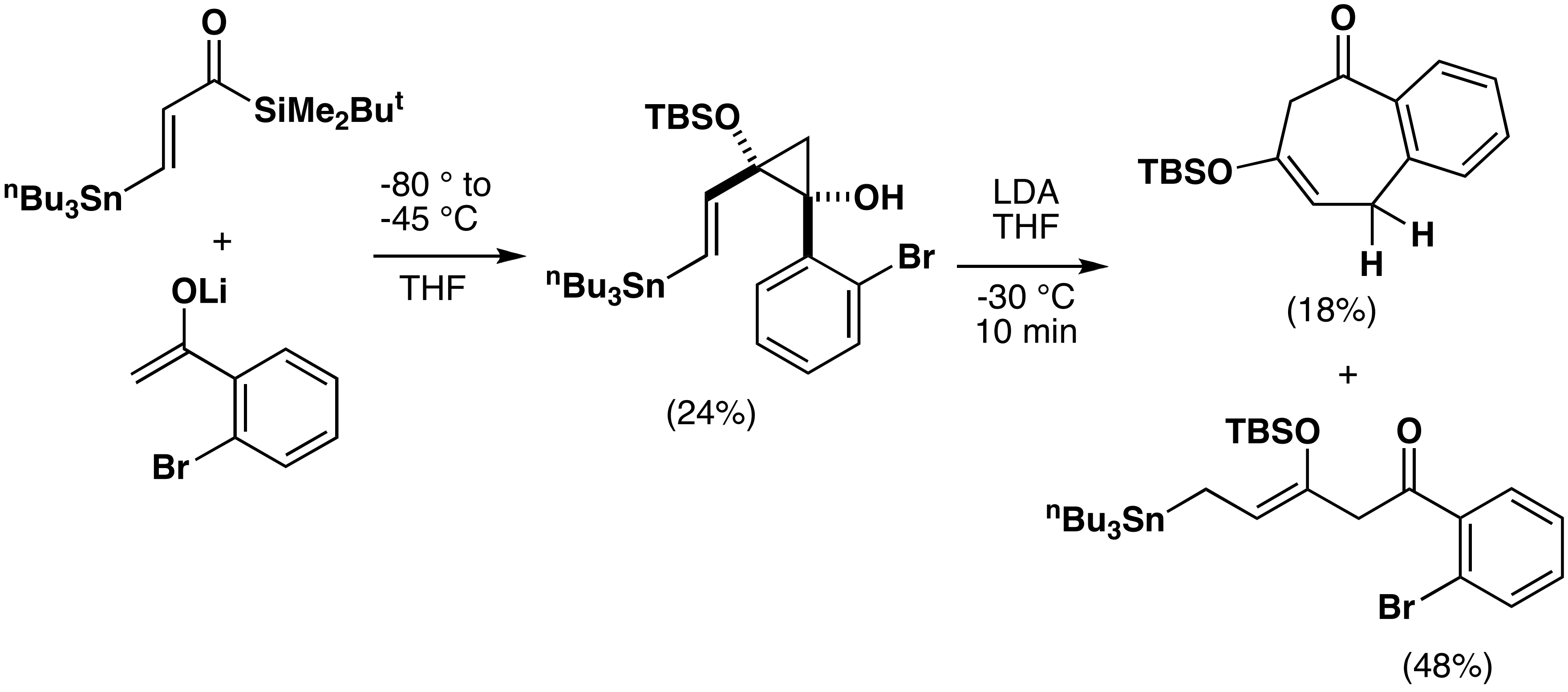
ketone enolate	product	yield (recovery of acylsilane)	ketone enolate	product	yield (recovery of acylsilane)
		31% (56%)			18% (31%)
		11% (59%)			0% (77%)
		29% (55%)			

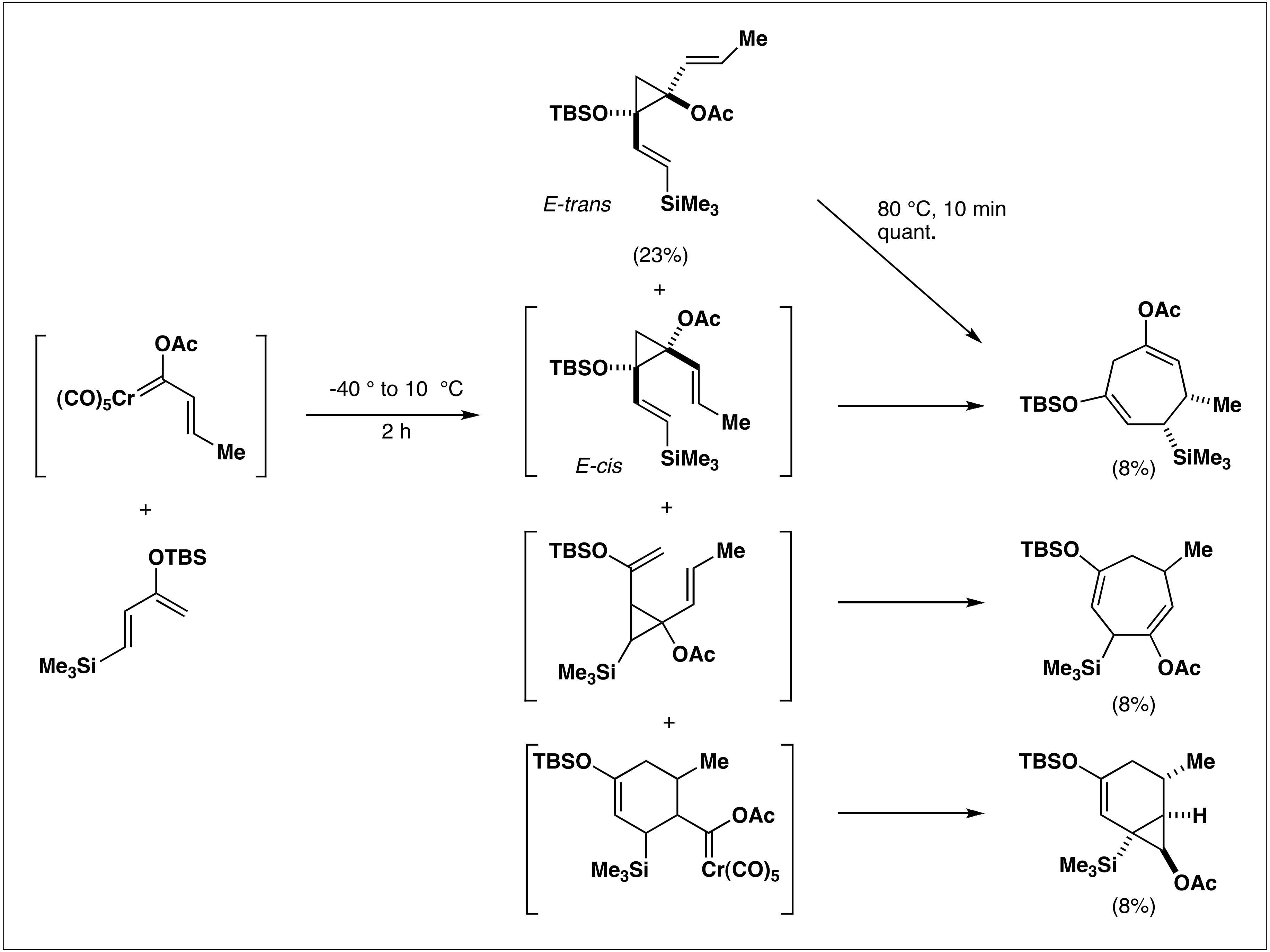
Low-temperature Quenching of the [3 + 4] Annulation

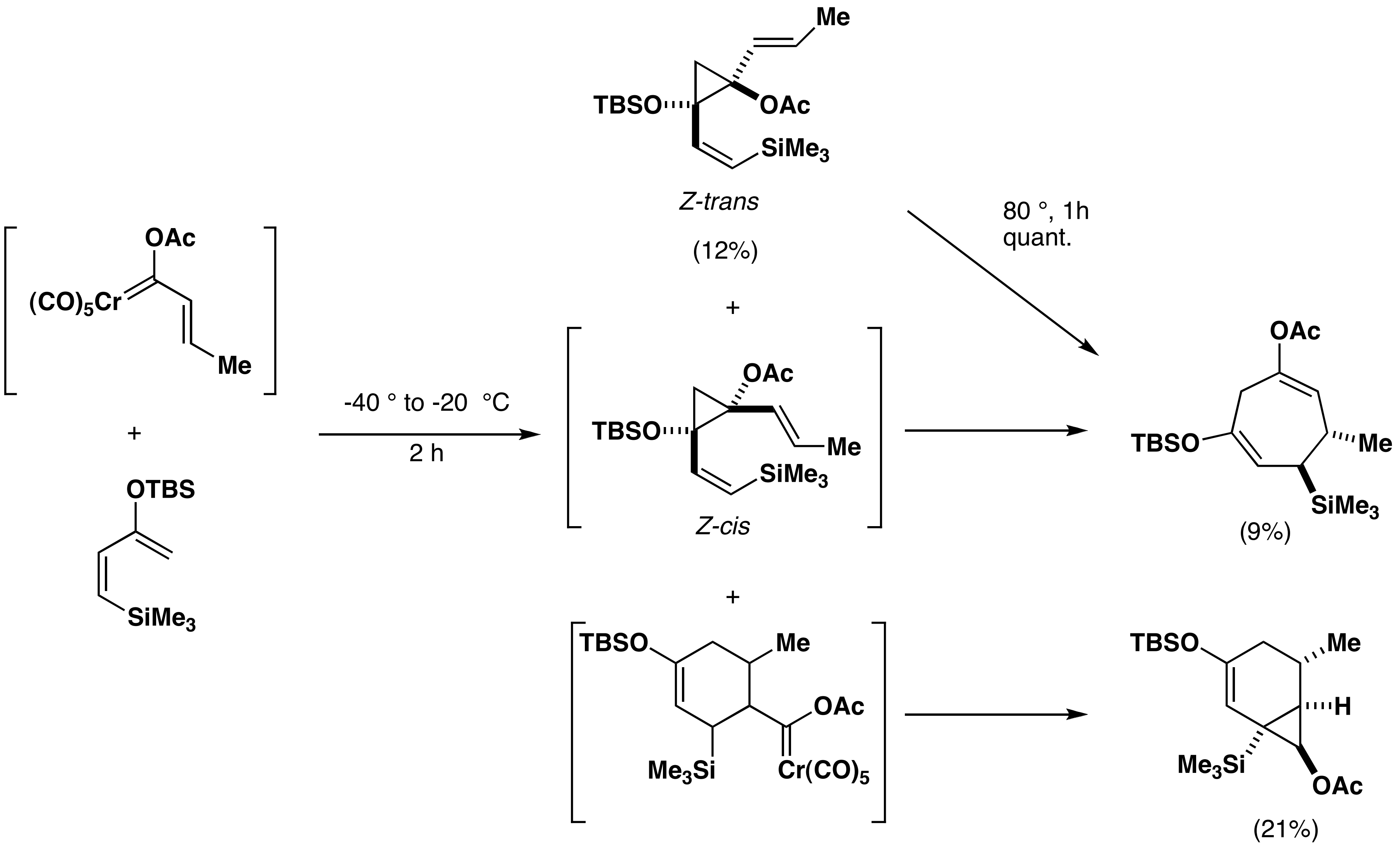


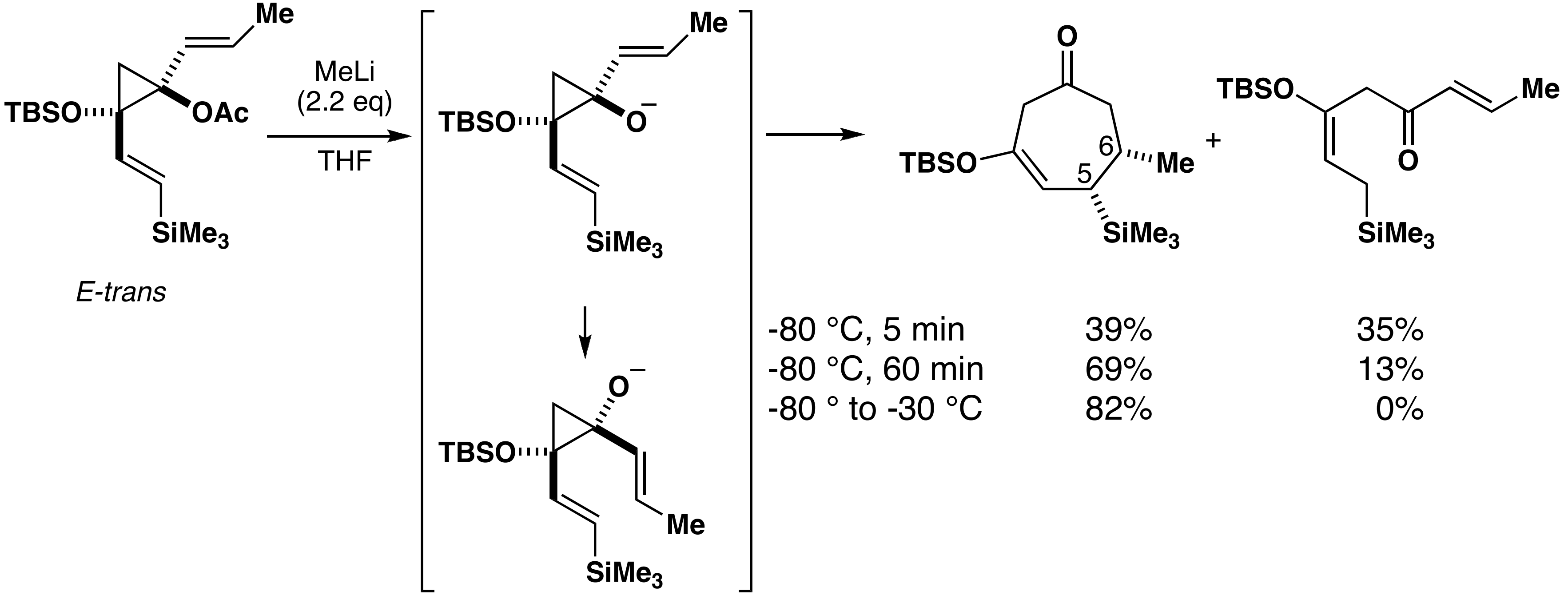
E	47%	30%	18%
Z	0%	0%	67%

Trapping of a Cyclopropanolate Intermediate



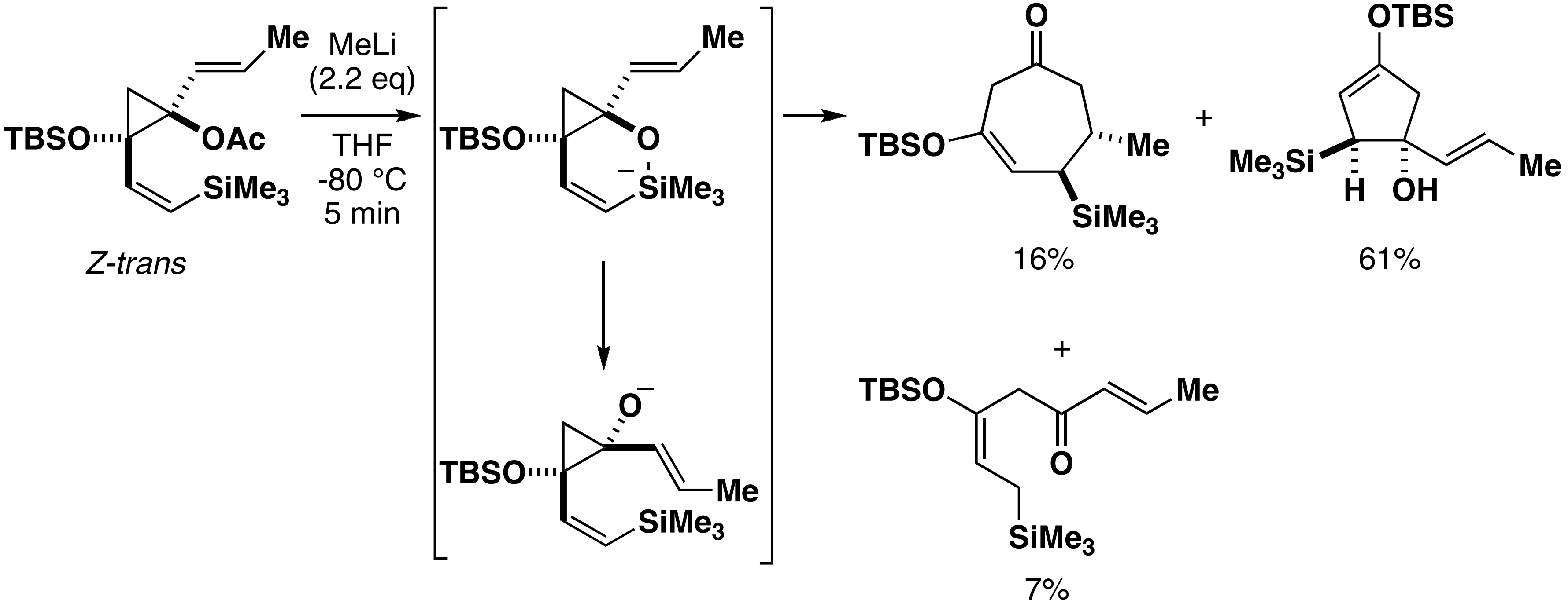

OAc
(CO)5Cr
Me
+
OTBS
Me3Si
-40 ° to 10 °C
2 h
Me
TBSO
OAc
E-trans
SiMe3
(23%)
+
OAc
TBSO
Me
E-cis
SiMe3
+
TBSO
Me
OAc
Me3Si
+
TBSO
Me
OAc
Me3Si
Cr(CO)5
80 °C, 10 min
quant.
OAc
TBSO
Me
SiMe3
(8%)
TBSO
Me
Me3Si
OAc
(8%)
TBSO
Me
H
Me3Si
OAc
(8%)


(CO)$_5$Cr
OAc
Me
+
OTBS
SiMe$_3$
-40 ° to -20 °C
2 h
TBSO
OAc
Me
SiMe$_3$
Z-trans
(12%)
+
OAc
TBSO
Me
SiMe$_3$
Z-cis
+
TBSO
Me
OAc
Me$_3$Si
Cr(CO)$_5$
80 °, 1h
quant.
OAc
TBSO
Me
SiMe$_3$
(9%)
TBSO
Me
H
Me$_3$Si
OAc
(21%)



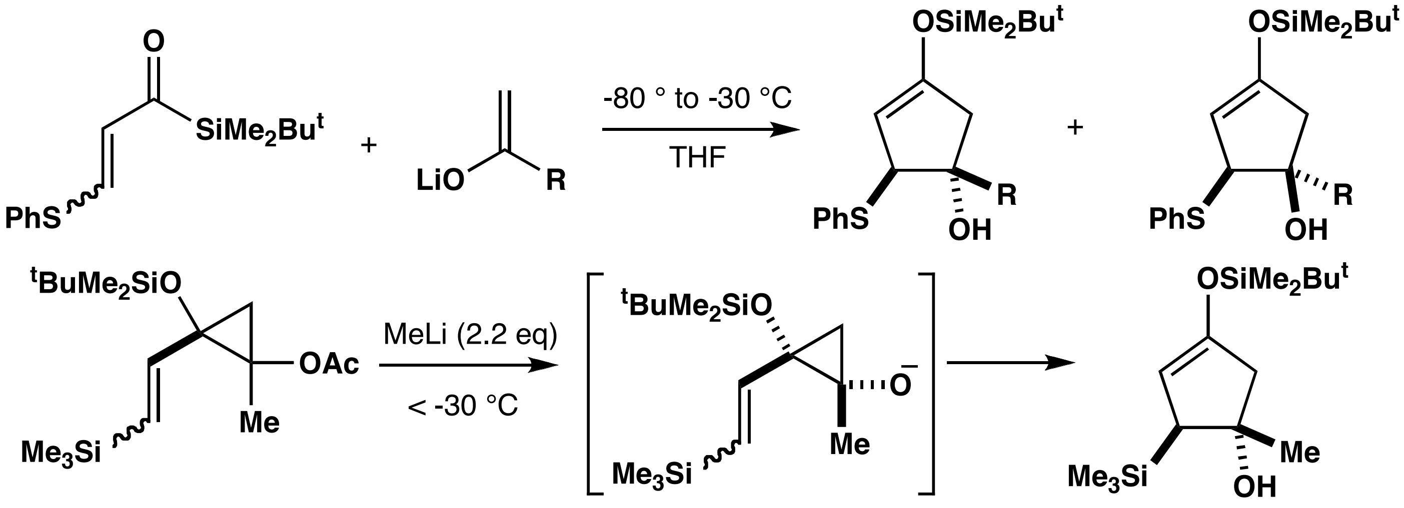
E-trans

-80 °C, 5 min	39%	35%
-80 °C, 60 min	69%	13%
-80 ° to -30 °C	82%	0%

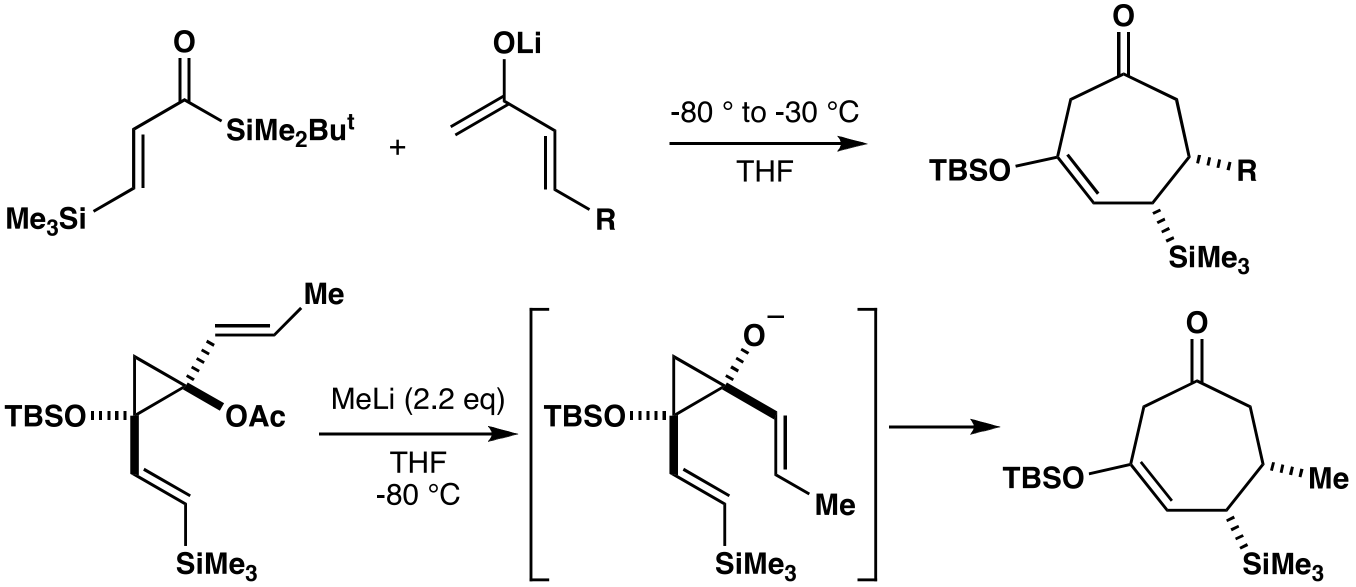

TBSO
OAc
Me
SiMe$_3$
Z-trans
MeLi
(2.2 eq)
THF
-80 °C
5 min
TBSO
O
SiMe$_3$
Me
TBSO
O$^-$
Me
SiMe$_3$
O
TBSO
Me
SiMe$_3$
16%
+
OTBS
Me$_3$Si
H
OH
Me
61%
+
TBSO
Me
O
SiMe$_3$
7%

Summary

[3 + 2] Annulation



[3 + 4] Annulation



Professor Emeritus Eiichi Yoshii

Professor Toru Koizumi

Professor Kentaro Yamaguchi (X-ray)

Formation of Cyclopropanediols

Koichi Sako
Hitoshi Nakamura
Junko Nakatani

[3 + 4] Annulation

Mika Takeda
Akemi Nakajima

[3 + 2] Annulation

Tomoko Makino
Masato Fujisawa
Keiki Sakurama
Ayako Sano

Synthesis of Natural Products

Ichiro Nakayama
Kanji Kitagawa

Grant-in-Aid for Encouragement of Young Scientists
The Reserch Foundation for Pharmaceutical Sciences