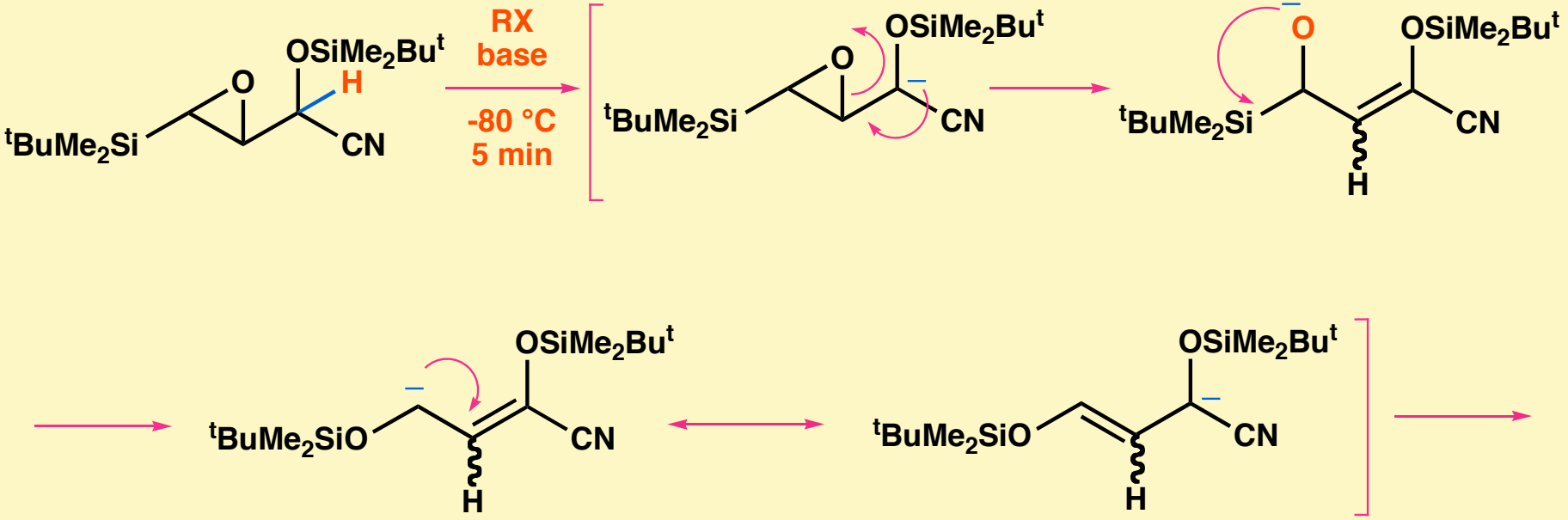
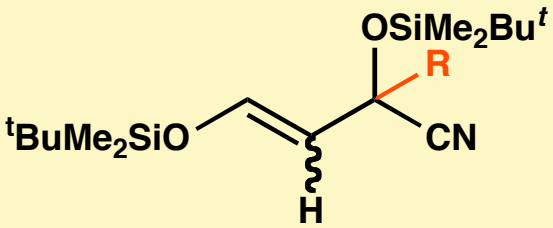
Alkylation of Metalated *O*-Silyl Cyanohydrins of β-Silyl-α,β-epoxyaldehydes



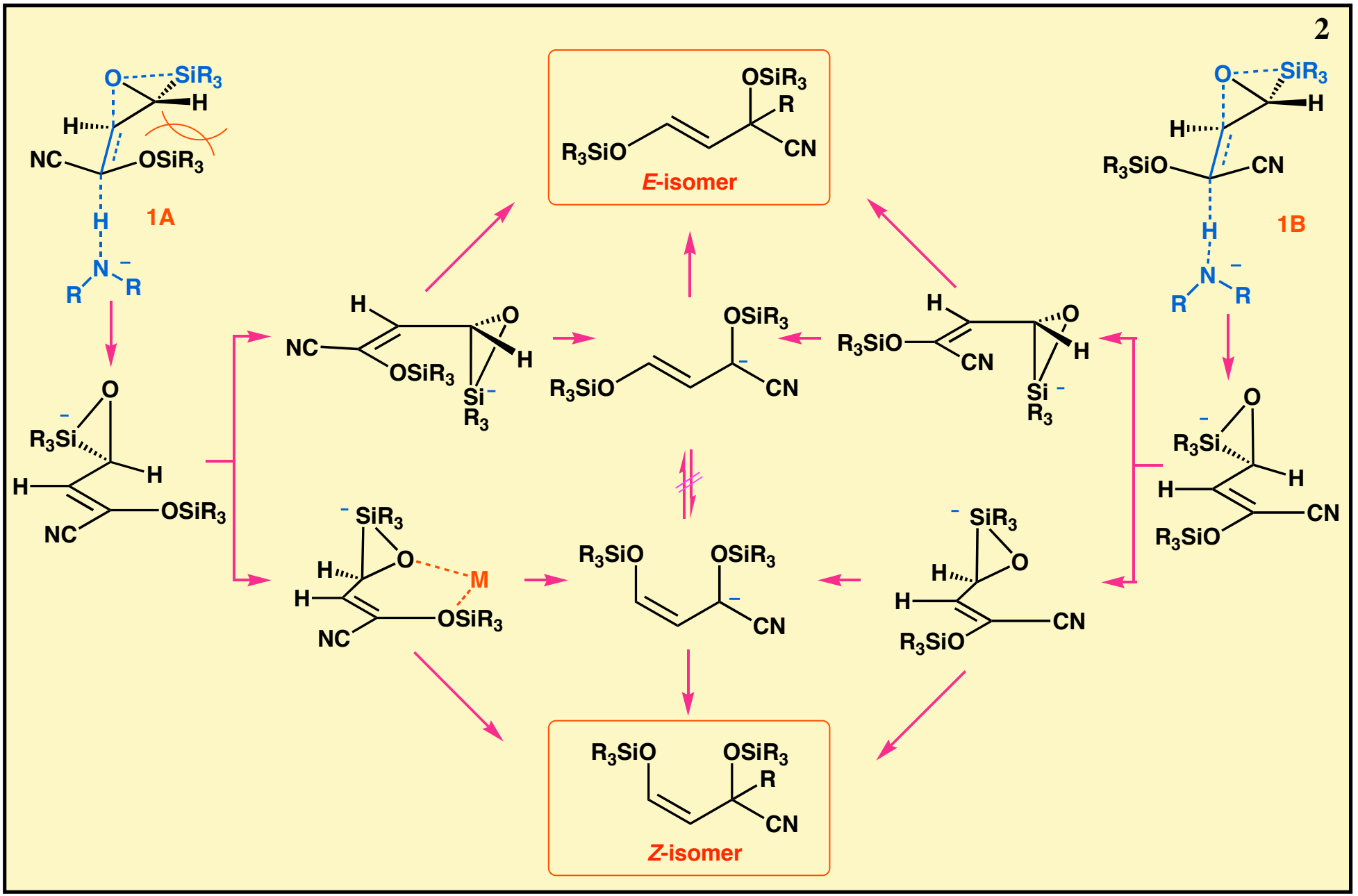


R = Me, Et, Pr^{i}, $CH_2CH{=}CH_2$, CH_2Ph

base	yield (%)
$LiN^{i}Pr_2$ (LDA)	58 - 98
$LiN(SiMe_3)_2$ (LHMDS)	15 - 90
$NaN(SiMe_3)_2$ (NHMDS)	80 - 98
$KN(SiMe_3)_2$ (KHMDS)	80 - 95

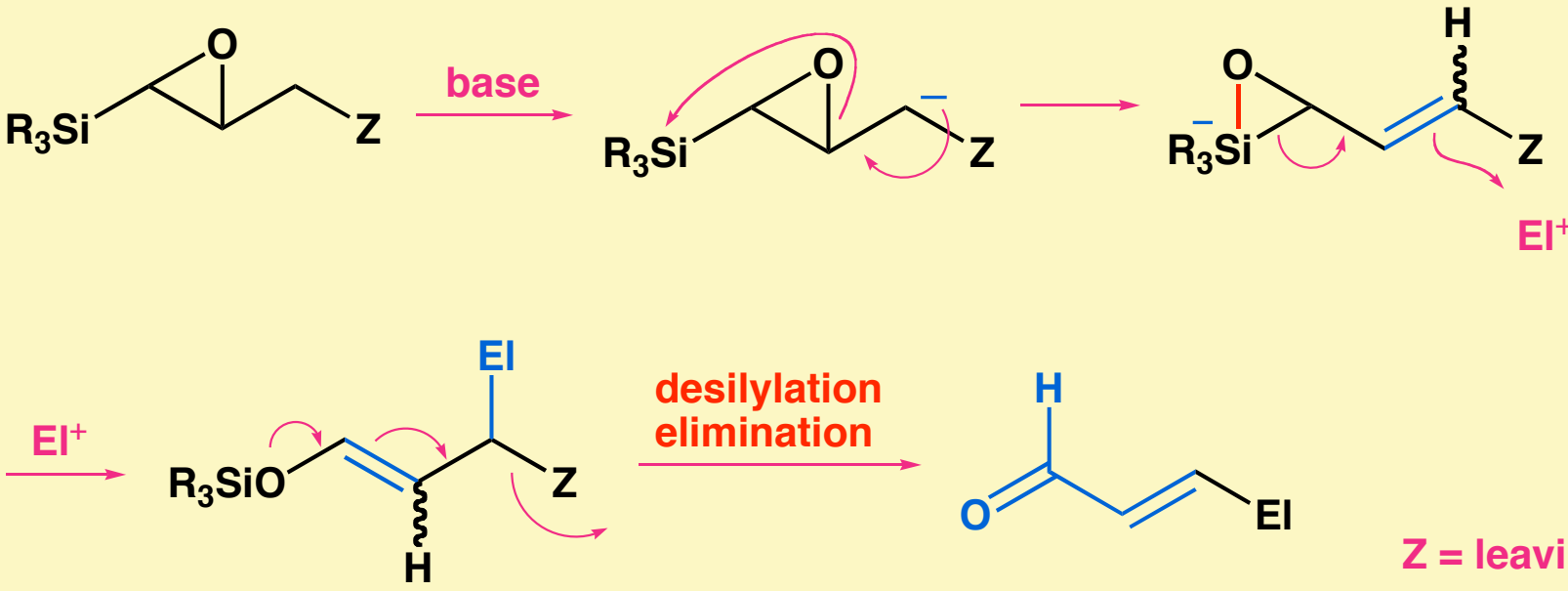
Takeda, K.;Kawanishi, E.;Sasaki, M.;Takahasi, Y.;Yamaguchi, K. *Org. Lett.* **2002**, *4*, 1511-1514.

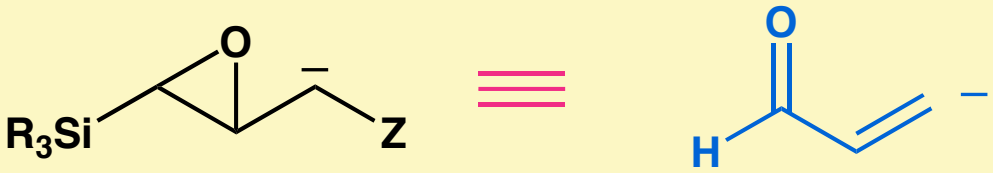
A Proposed Reaction Pathway



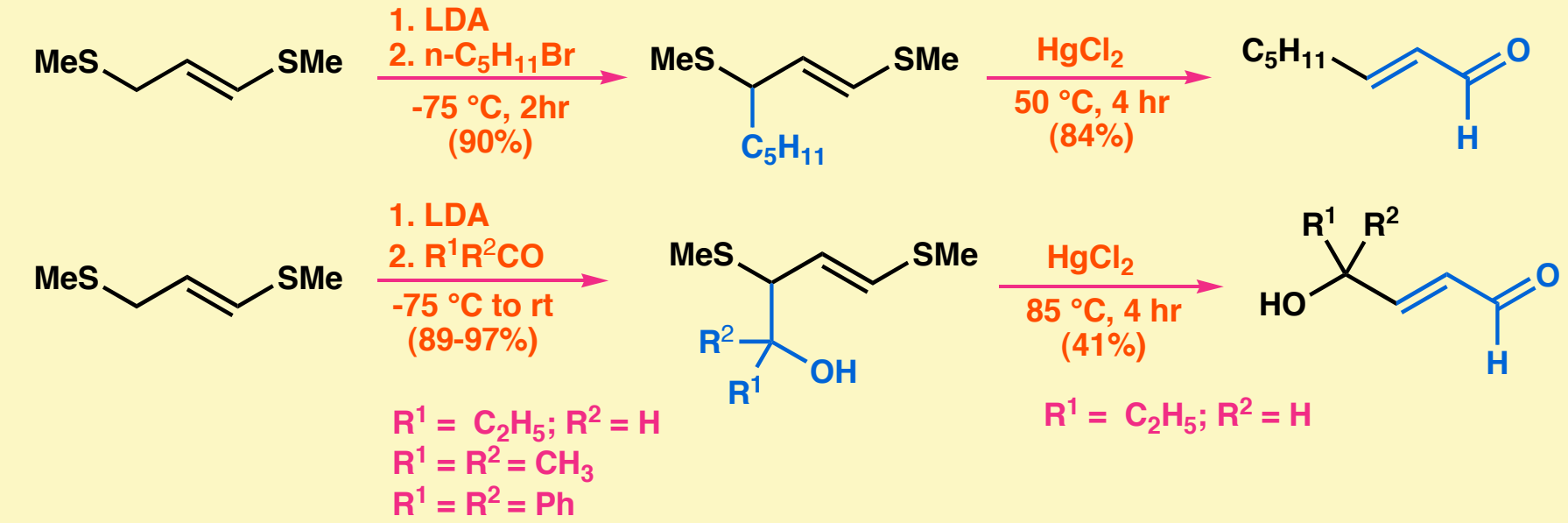
Sasaki, M.;Kawanishi, E;Nakai, Y.;Matsumoto, T.;Yamaguchi, K.;Takeda, K. *J. Org. Chem.* **2003**, *68*, 9330-9339.

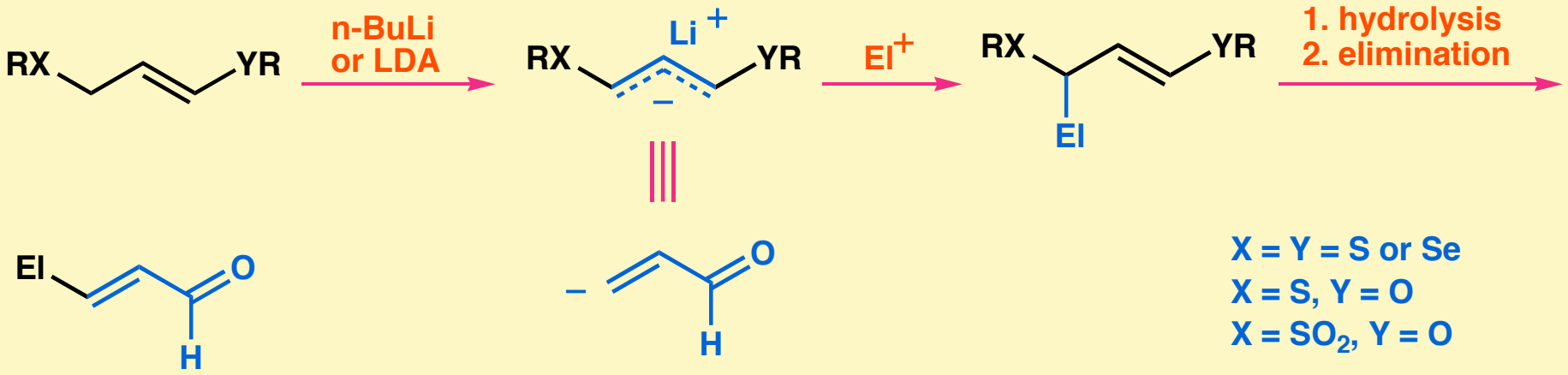
An Approach to New Acrolein β-Anion Equivalent





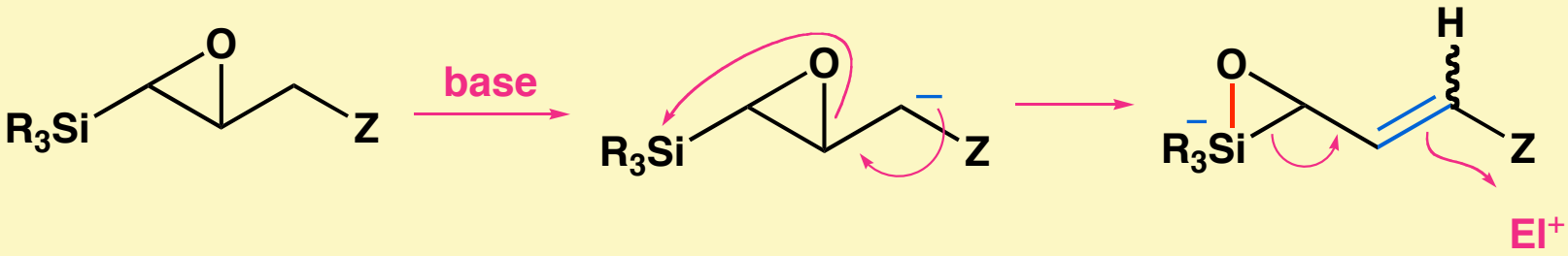
Equivalents of the Acrolein β-Anion Synthon

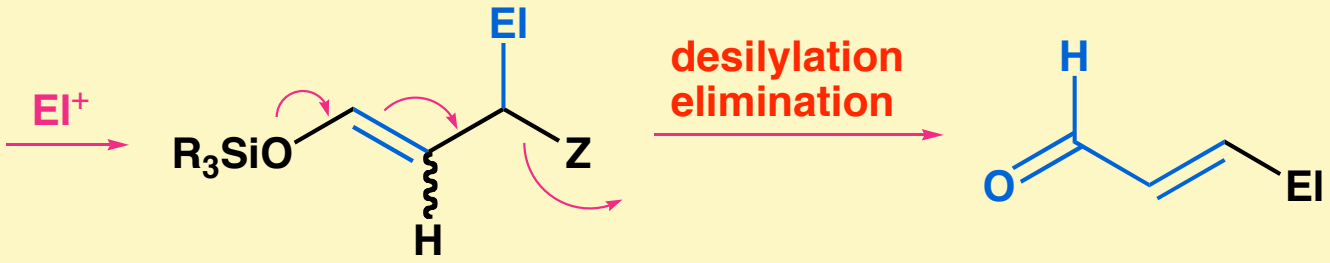




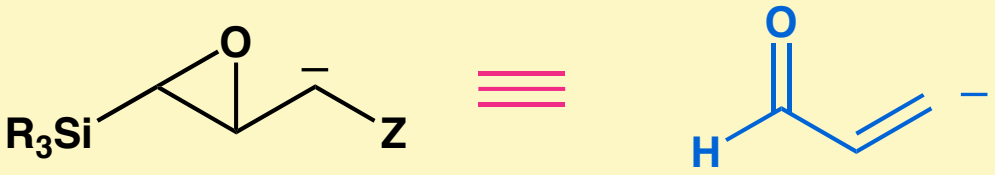
Corey, E. J.; Erickson, B. W.; Noyori, R. *J. Am. Chem, Soc*. **1971**, *93*, 1724-1729.
Chinchilla, R.; Nájera, C. *Chem. Rev*. **2000**, *100*, 1891-1928.

An Approach to New Acrolein β-Anion Equivalent



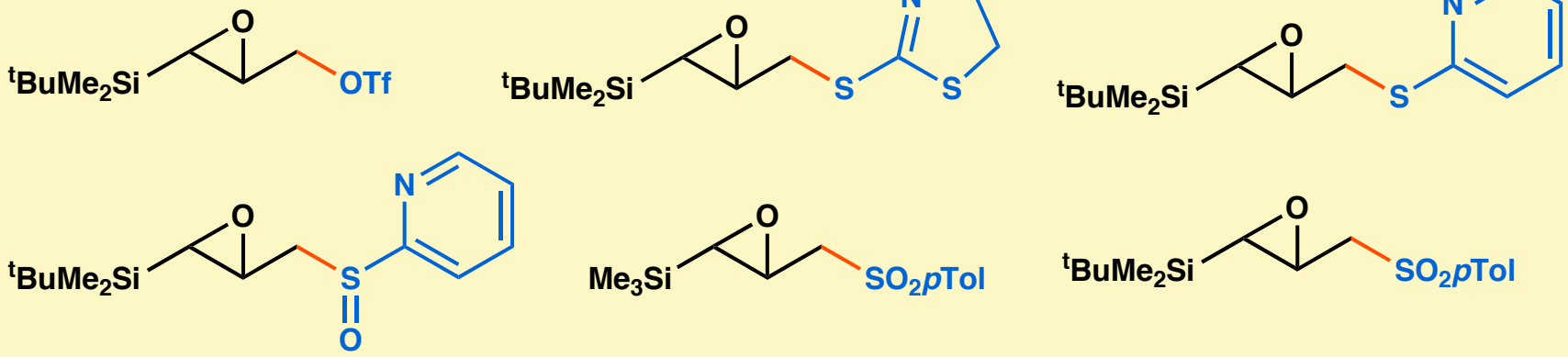


Z = leaving group

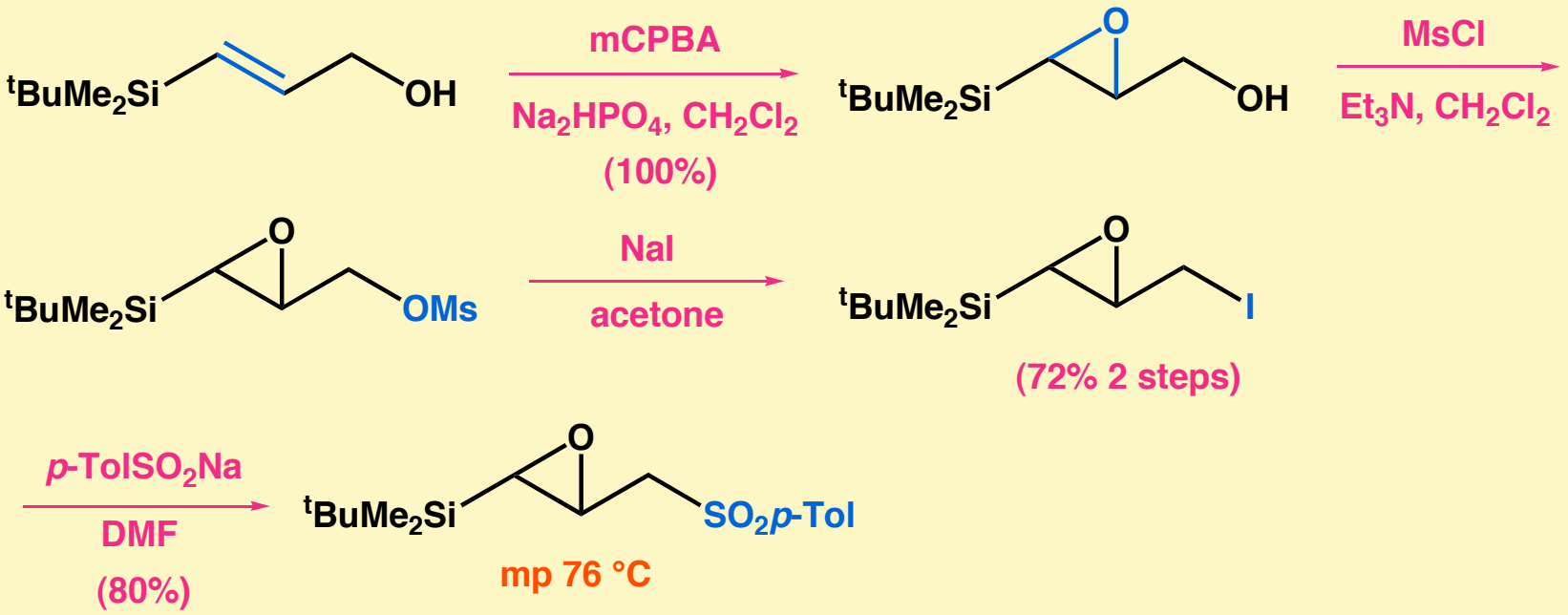


Acrolein β-Anion Equivalent

New Acrolein β-Anion Equivalents

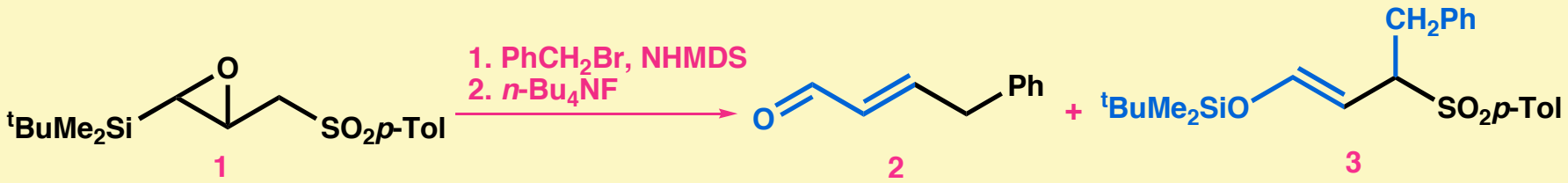


Preparation of γ-(*p*-Toluenesulfonyl)-α,β-epoxysilane



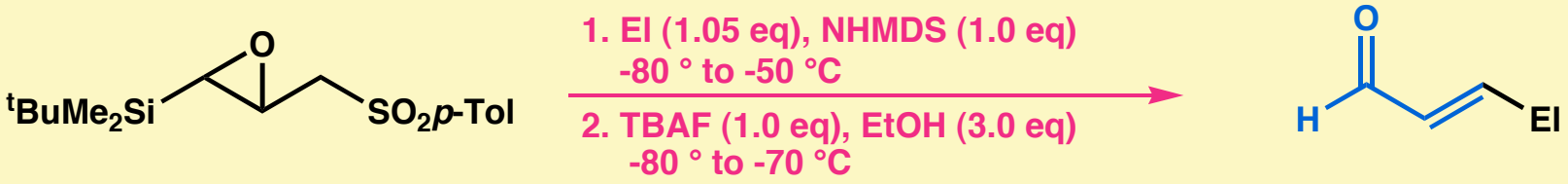
Reaction of γ-Methalated γ-Sulfonyl-α,β-epoxysilane with Electrophile Followed by Desilylation with Concomitant Elimination of the Sulfonyl Group (I)

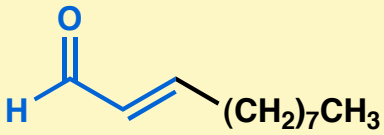
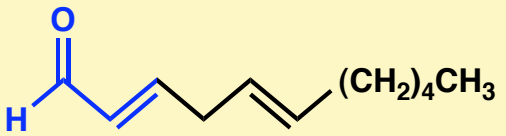
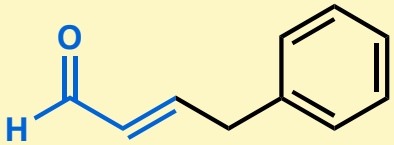
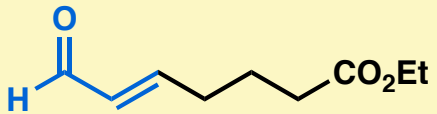
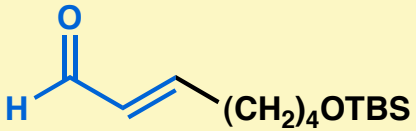
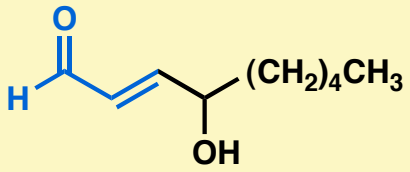
7



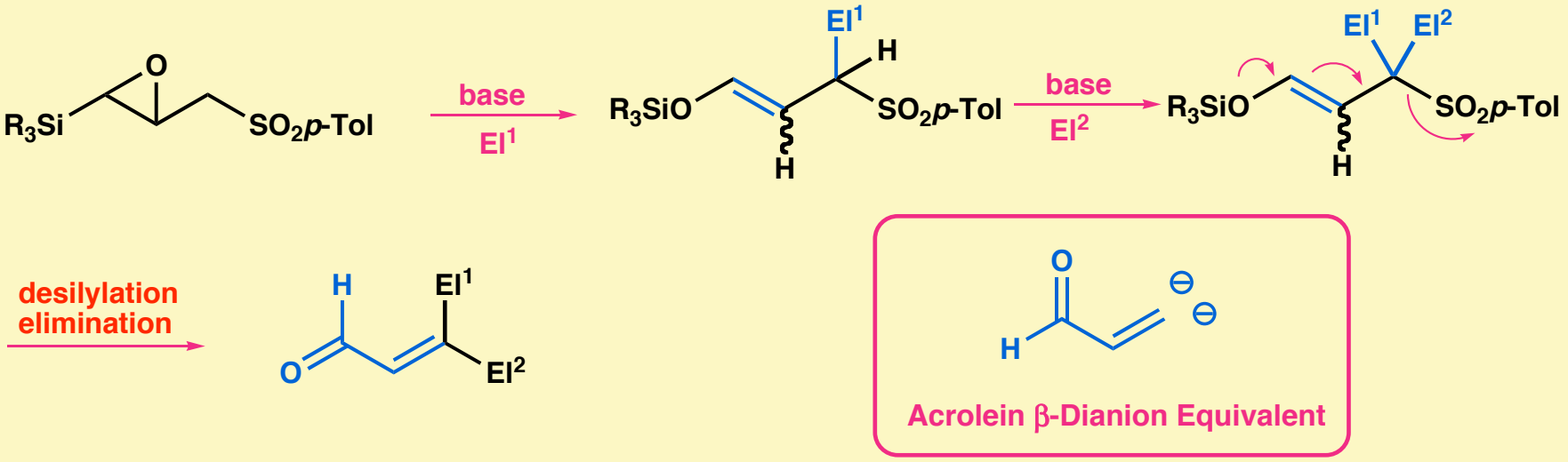
conditions	yield (%)	
	2	3
1. BnBr (1.0 eq), NHMDS (1.0 eq), -80 ° to -60 °C, 40 min 2. TBAF (1.1 eq), THF (0.1 M), -80 ° to -60 °C, 30 min	29	41
1. BnBr (1.0 eq), NHMDS (1.0 eq), -80 ° to -60 °C, 30 min 2. EtOH (1.0eq), TBAF (1.1 eq), THF (0.08 M), -85 ° to -80 °C, 10 min	61	9
1. BnBr (1.05 eq), NHMDS (1.0 eq), -80 ° to -60 °C, 30 min 2. EtOH (3.0eq), TBAF (1.1 eq), THF (0.08 M), -85 ° to -70 °C, 15 min	85	-

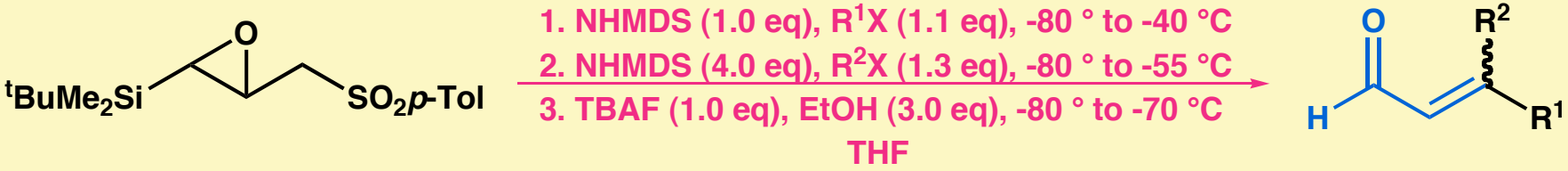
Reaction of γ-Methalated γ-Sulfonyl-α,β-epoxysilane with Electrophile Followed by Desilylation with Concomitant Elimination of the Sulfonyl Group (II)

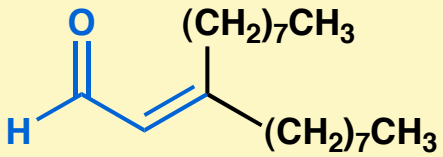
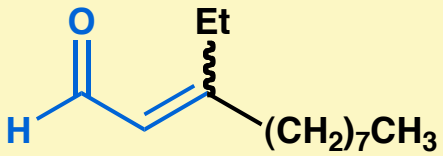


El	product	yield (%)	El	product	yield (%)
$I(CH_2)_7CH_3$		84	Br, $(CH_2)_4CH_3$		82
Br		85	I, CO_2Et		74
$I(CH_2)_4OTBS$		68	$OHC(CH_2)_4CH_3$		77

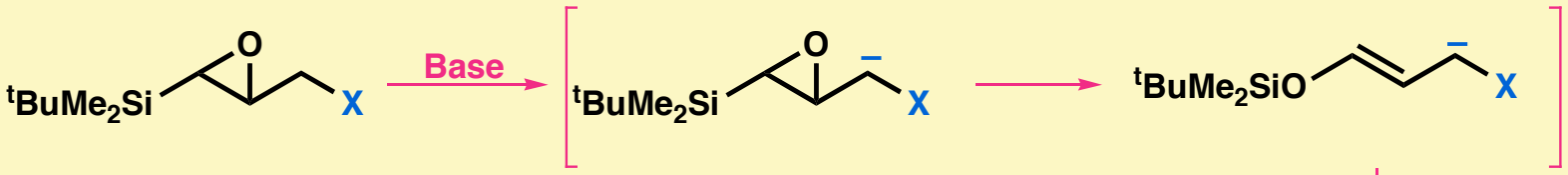
An Approach to New Acrolein β-Dianion Equivalent

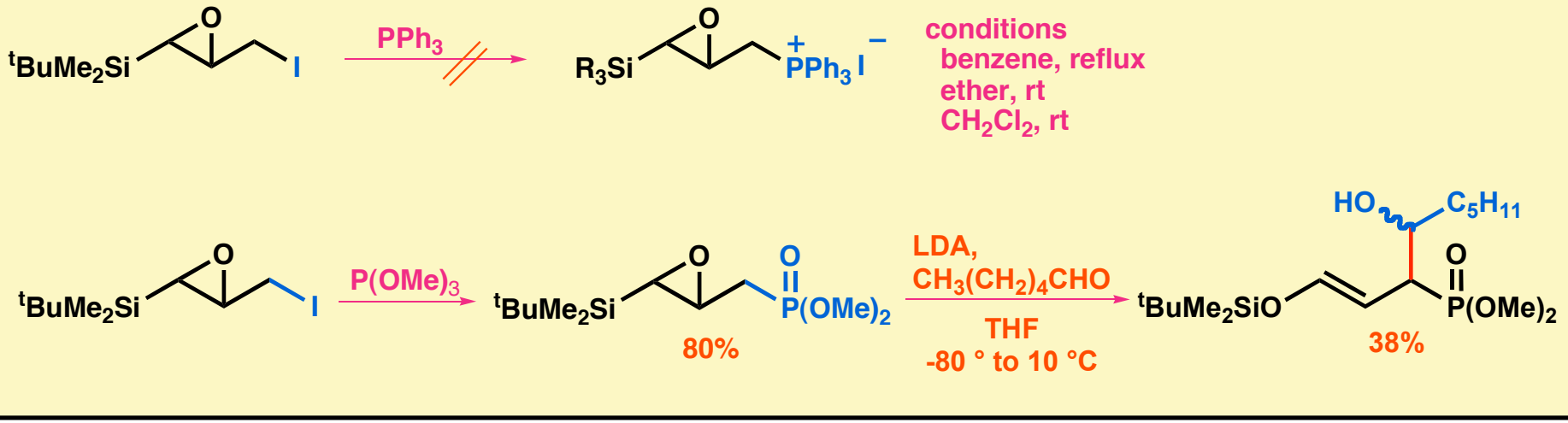




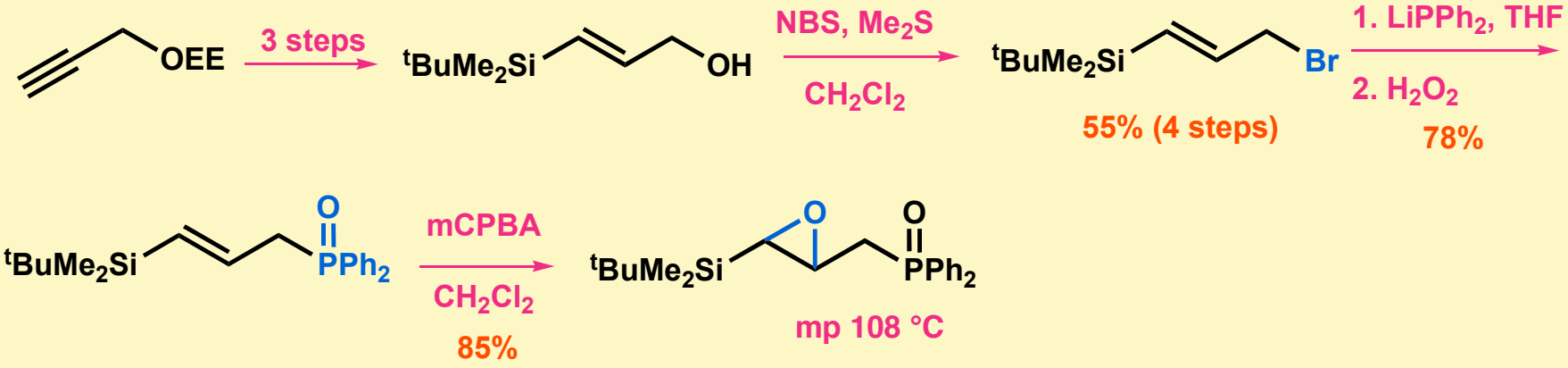
R^1X	R^2X	product	yield (%)
$I(CH_2)_7CH_3$	$I(CH_2)_7CH_3$		76
$I(CH_2)_7CH_3$	IEt		52

Application of the Epoxysilane Rearrangement to Wittig-Type Olefination Reaction

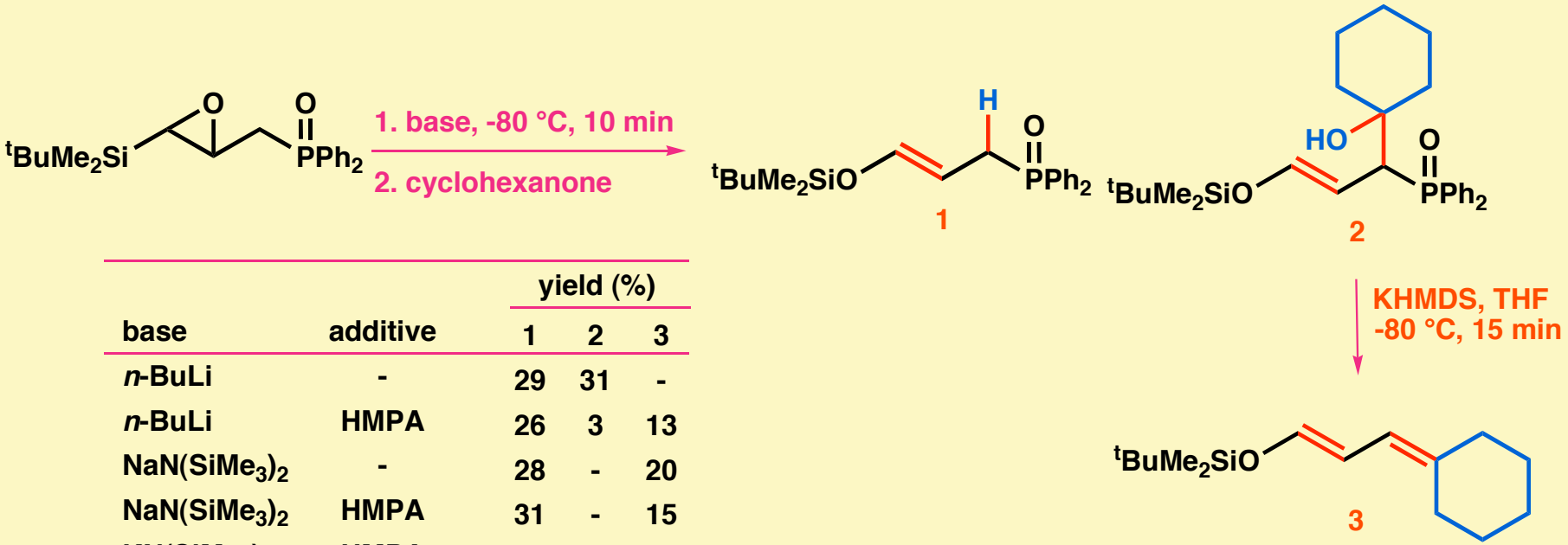




Preparation of γ-Phosphinoyl-α,β-epoxysilane

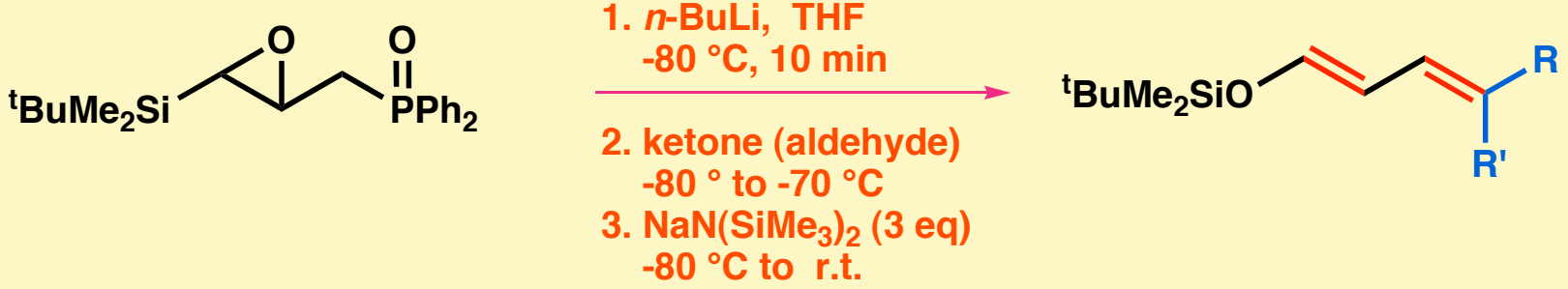


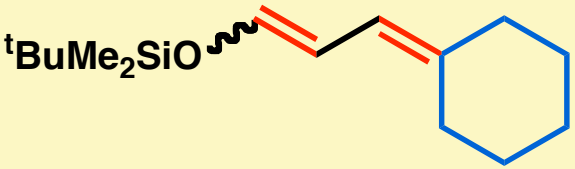
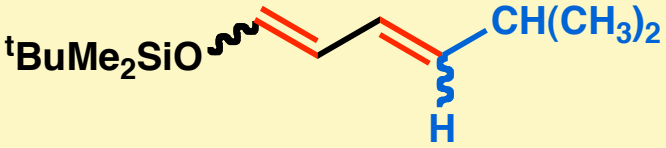
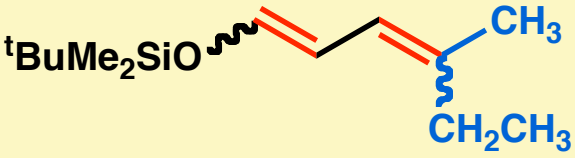
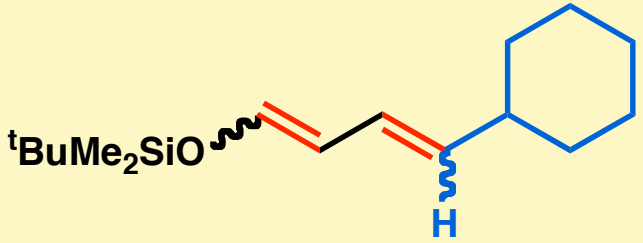
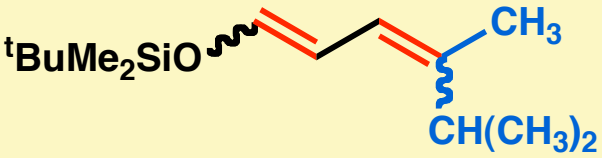
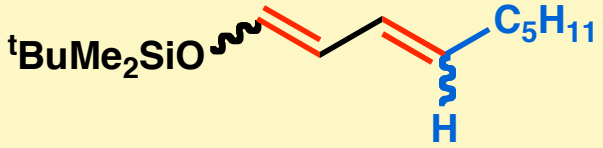
Reactions of γ-Phosphinoyl-α,β-epoxysilane with Cyclohexanone



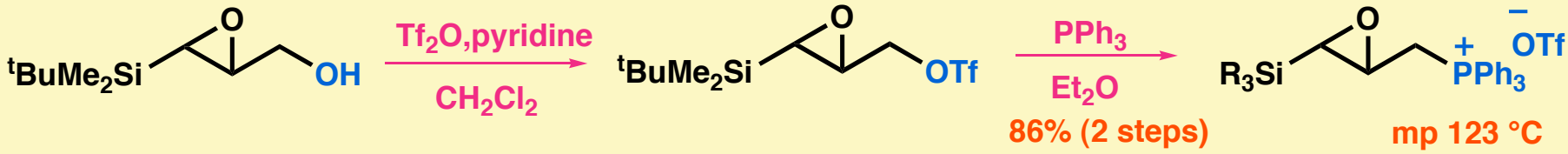
		yield (%)		
base	additive	1	2	3
n-BuLi	-	29	31	-
n-BuLi	HMPA	26	3	13
$NaN(SiMe_3)_2$	-	28	-	20
$NaN(SiMe_3)_2$	HMPA	31	-	15
$KN(SiMe_3)_2$	HMPA	53	-	-

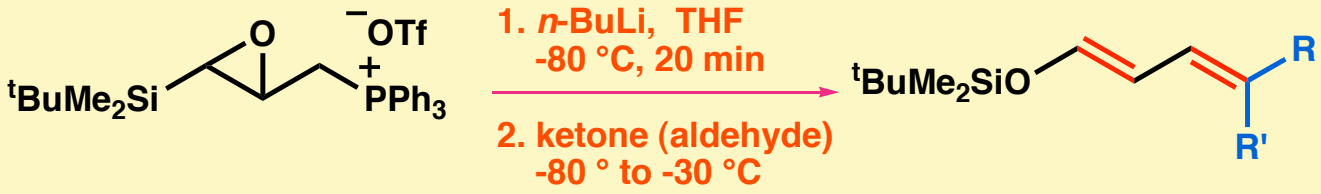
Reactions of γ-Phosphinoyl-α,β-epoxysilane with Ketones and Aldehydes

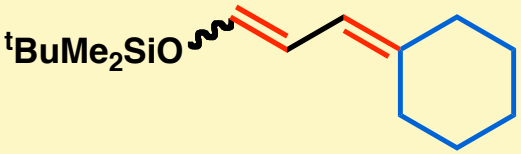
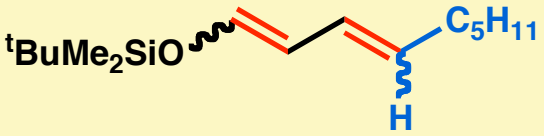
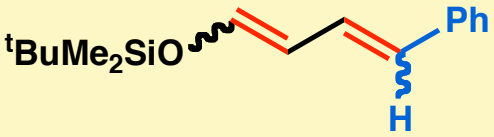
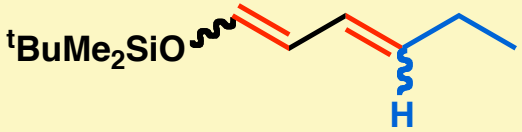
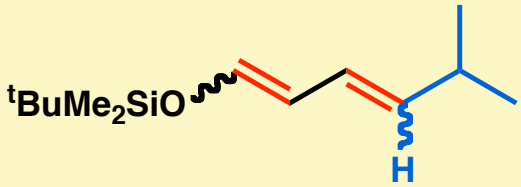


	yield (%)		yield (%)
	80		54
	52		60
	57		24

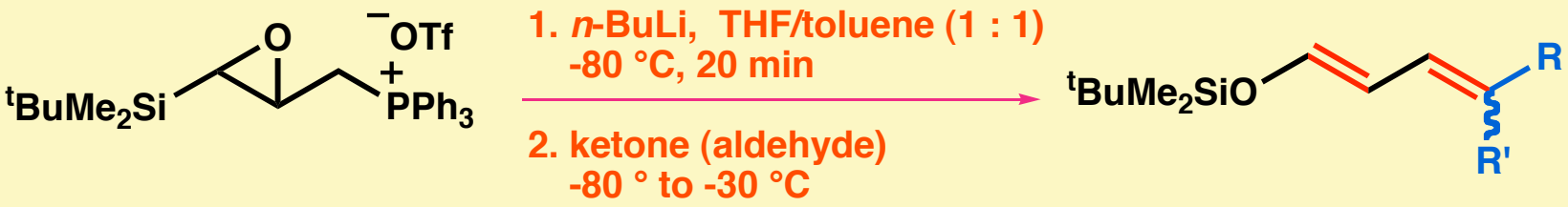
Preparation and Reactions of γ-Phosphonio-α,β-epoxysilane

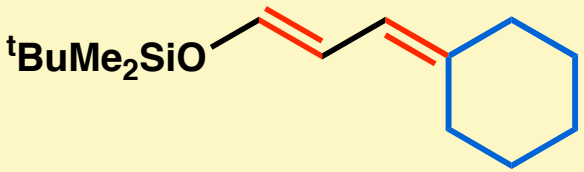
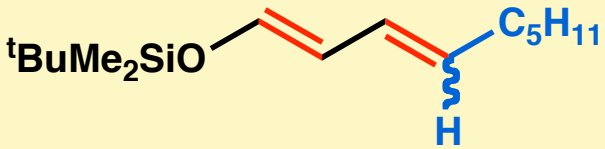
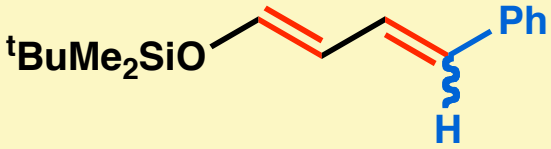
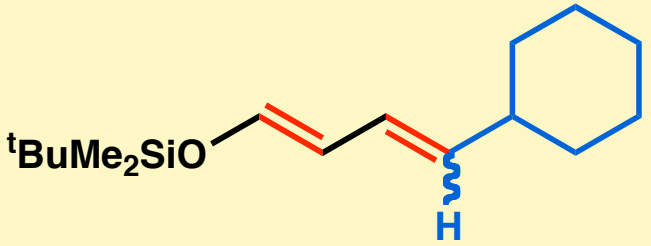
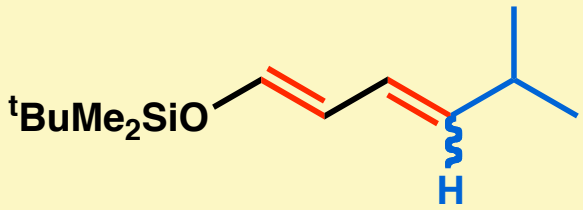




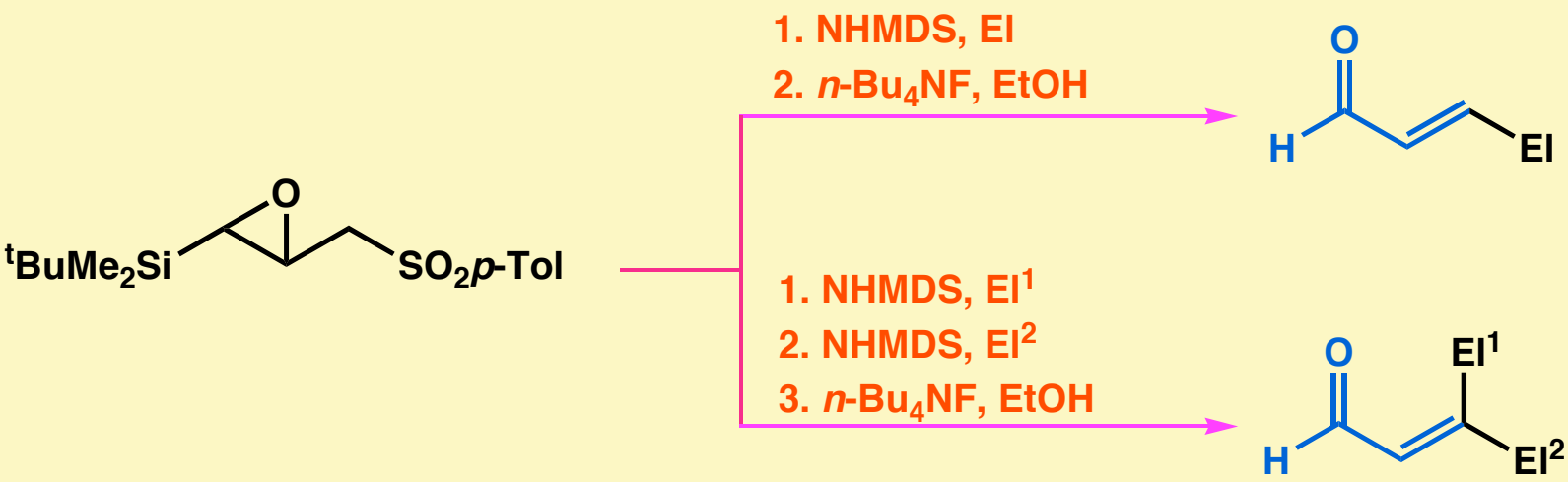
	yield (%)		yield (%)
	36		59
	74		51
	63		

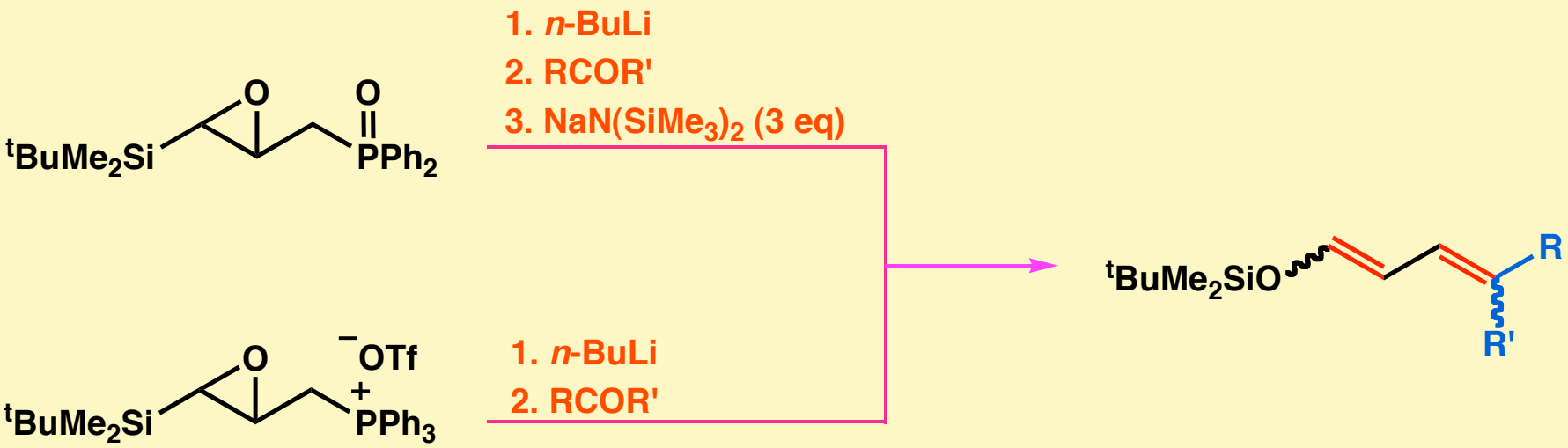
Reactions of γ-Phosphonio-α,β-epoxysilane with Ketones and Aldehydes



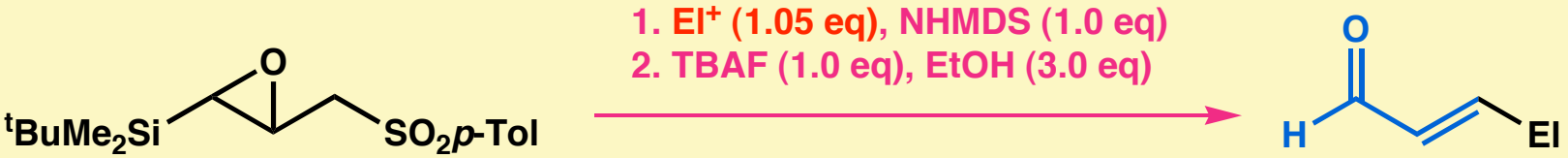
	yield (%)		yield (%)
	54 (-80 °C to rt)		73
	76		77
	69		

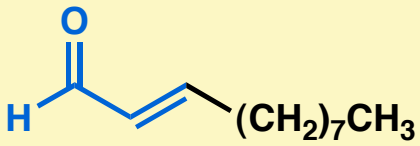
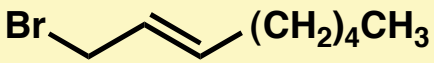
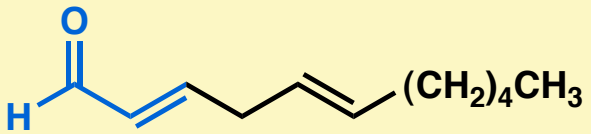
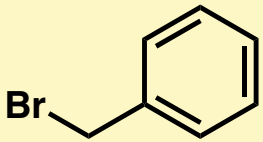
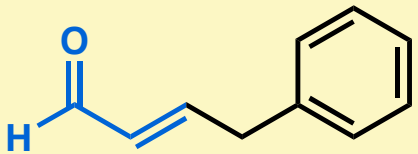
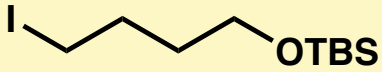
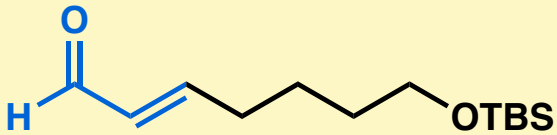
Summary


1. NHMDS, EI
2. n-Bu4NF, EtOH
tBuMe2Si
SO2p-Tol
O
H
EI
1. NHMDS, EI1
2. NHMDS, EI2
3. n-Bu4NF, EtOH
EI1
EI2

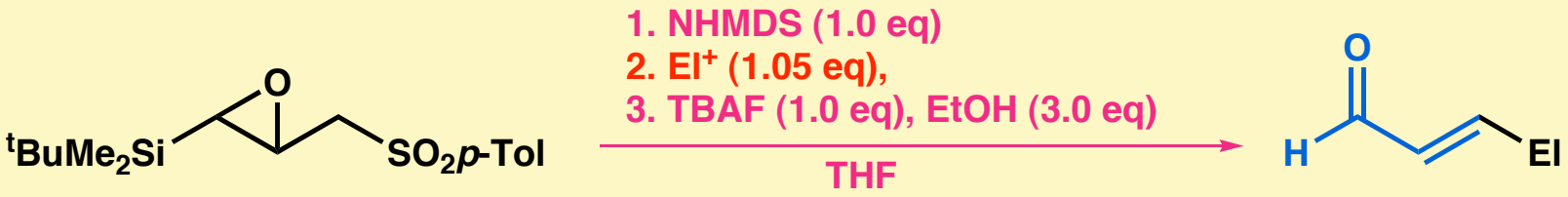

1. n-BuLi
2. RCOR'
3. NaN(SiMe3)2 (3 eq)
tBuMe2Si
PPh2
1. n-BuLi
2. RCOR'
OTf
PPh3
tBuMe2SiO
R
R'

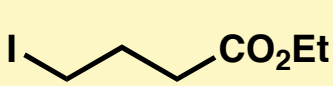
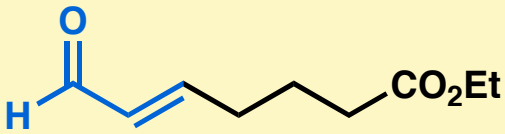
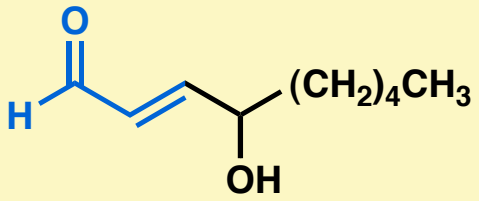
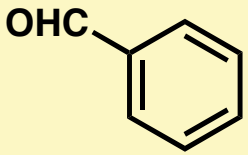
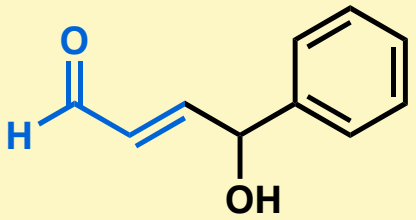
Reaction of γ-Methalated γ-Sulfonyl-α,β-epoxysilane with Electrophile Followed by Desilylation with Concomitant Elimination of the Sulfonyl Group (II)



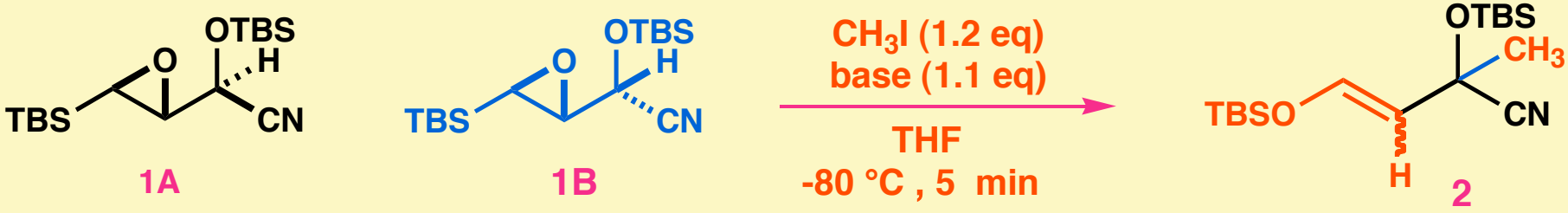
El+	conditions	product	yield (%)
$I(CH_2)_7CH_3$	1. -80 ° to -50 °C, 40 min 2. -80 ° to -70 °C, 20 min		84
	1. -80 ° to -50 °C, 30 min 2. -80 ° to -70 °C, 15 min		82
	1. -80 ° to -60 °C, 30 min 2. -80 ° to -70 °C, 15 min		85
	1. -80 to -40 °C, 45 min 2. -80 ° to -70 °C, 15 min		68

Reaction of γ-Methalated γ-Sulfonyl-α,β-epoxysilane with Electrophile Followed by Desilylation with Concomitant Elimination of the Sulfonyl Group

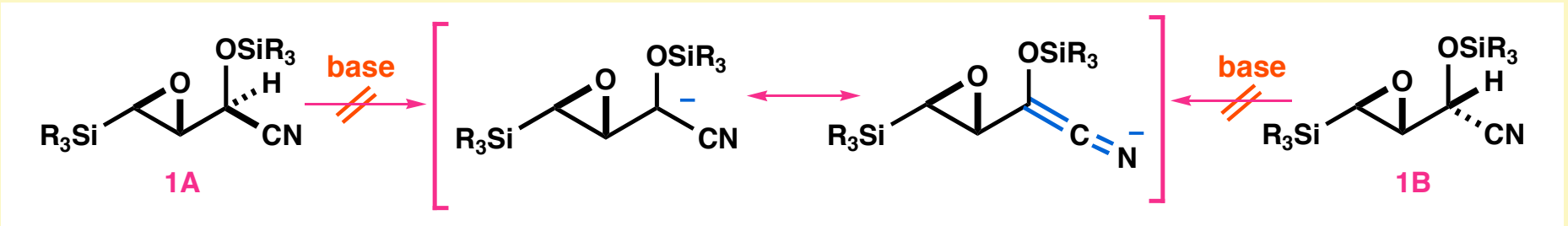


El^+	conditions	product	yield (%)
	1. -80 °C, 5 min 2. -80 ° to -40 °C, 40 min 3. -80 ° to -70 °C, 20 min		74
$OHC(CH_2)_4CH_3$	1. -80 °C, 5 min 2. -80 ° to -60 °C, 20 min then CH_3COOH (1.0 eq) 3. -80 ° to -70 °C, 15 min		77
	1. -80 °C, 5 min 2. -80 ° to -60 °C, 20 min then CH_3COOH (1.0 eq) 3. -80 ° to -70 °C, 15 min		49

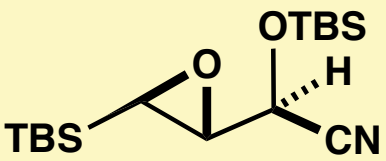
Methylation of Metalated *O*-Silyl Cyanohydrins of *trans*-β-Silyl-α,β-epoxyaldehydes



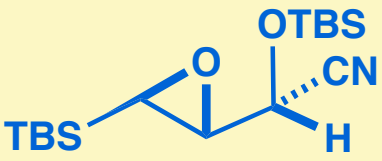
base	diastereomer	yield (%)	*E/Z*	SM
LDA (in hexane/THF)	1A	82	2.5	
	1B	84	22.0	
$LiN(SiMe_3)_2$ (1.0M in THF)	1A	44	23.0	40
	1B	83	31.0	
$NaN(SiMe_3)_2$ (1.0M in THF)	1A	91	40.0	
	1B	92	47.0	
$KN(SiMe_3)_2$ (0.5M in toluene)	1A	84	0.9	
	1B	87	9.7	



Solvent Effect on *E*/*Z* Selectivity

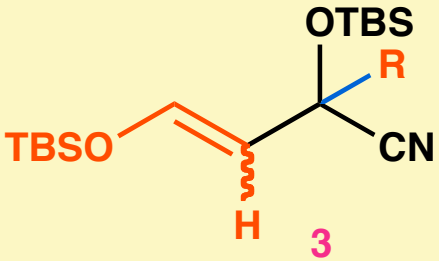


1A



1B

RX (1.2 eq)
Base (1.1 eq)
solvent/HMPA
-80 °C, 5 min



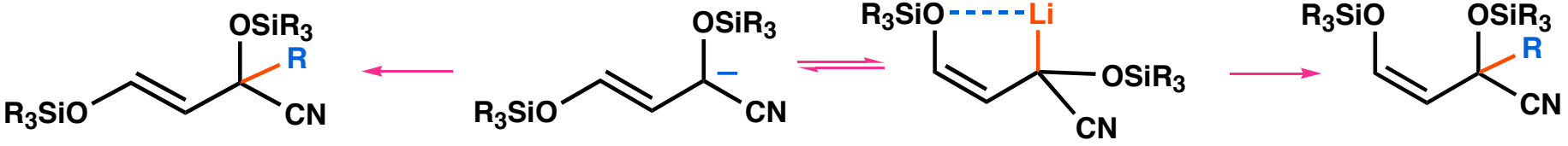
3

solvent	SM	yield (%)	E/Z
hexane	1A	93	1.5
	1B	78	6.0
ether	1A	84	1.9
	1B	77	28.0
toluene	1A	86	1.0
	1B	83	24.0
THF	1A	85	28.0
	1B	84	52.0

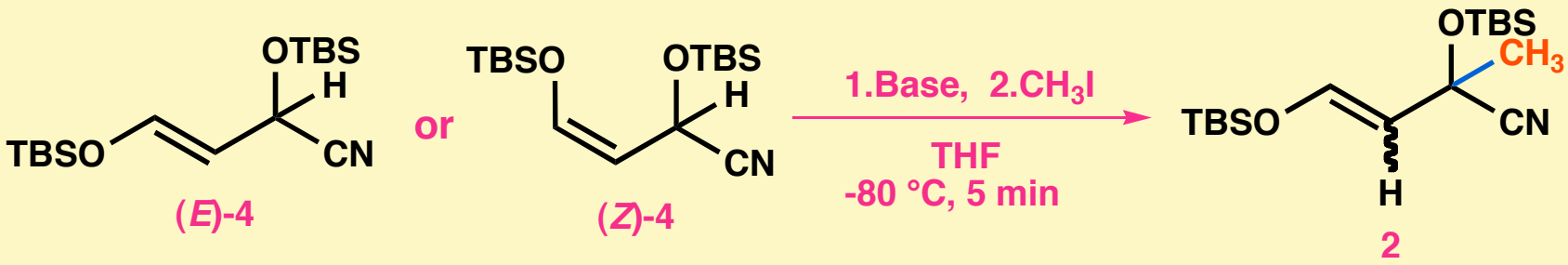
Base: NHMDS, RX: BnBr

base	SM	HMPA	yield (%)	E/Z	SM (%)
LDA	1A	(–)	82	2.5	-
	1A	(+)	61	28.0	26
	1B	(–)	84	22.0	-
	1B	(+)	85	*E*	8
KHMDS	1A	(–)	84	0.9	-
	1A	(+)	92	15.0	-
	1B	(–)	87	9.7	-
	1B	(+)	84	*E*	-

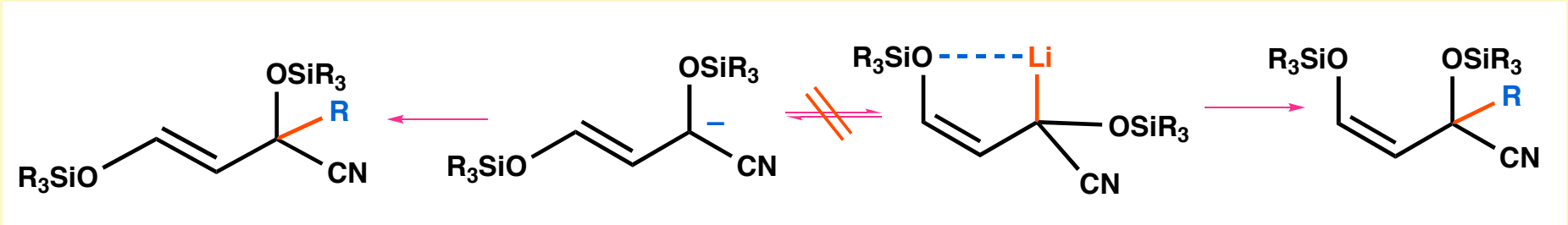
solvent: THF, RX: CH_3I



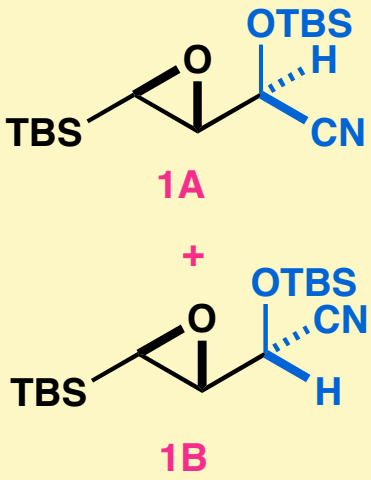
Alkylation of *O*-Silyl Cyanohydrins of β-Siloxyacrolein



	2			SM
Base	SM	yield (%)	*E/Z*	yield (%)
LDA	*E*	76	58.0	-
LHMDS	*E*	46	*E*	47
NHMDS	*E*	81	*E*	6
KHMDS	*E*	75	*E*	8
LDA	*Z*	41	0.01	18
LHMDS	*Z*	0	-	87
NHMDS	*Z*	30	0.02	59
KHMDS	*Z*	76	0.01	8

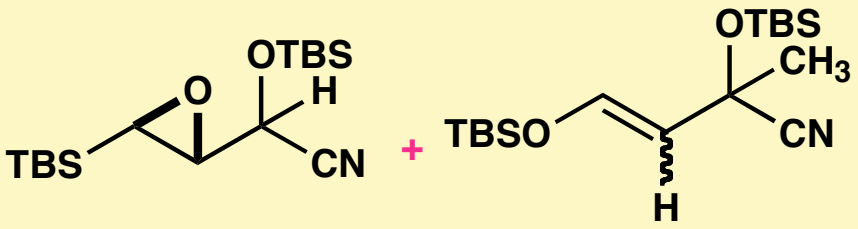


Base-Promoted Ring-Opening of Cyanohydrins of β-Silyl α,β-Epoxyaldehyde



CH_3I (0.5 eq)
LDA (0.5 eq)

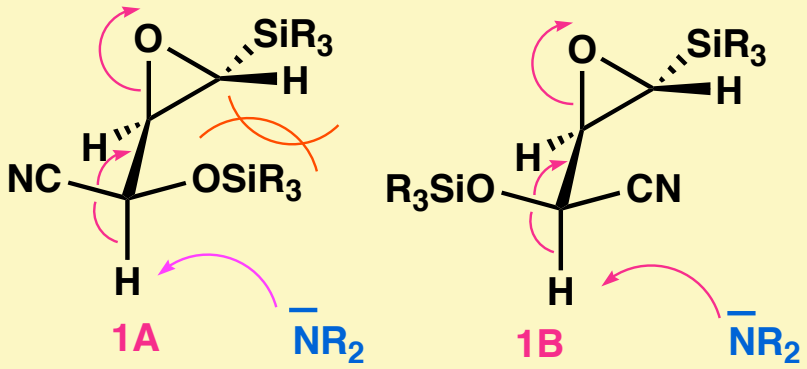
THF
-80 °C, 5 min



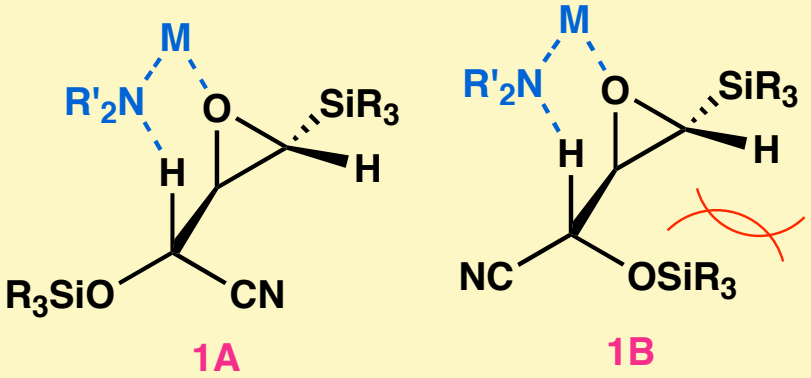
1A:1B = 1.00:1.04

	yield (%)		yield (%)	
HMPA	1	A:B	2	*E/Z*
(–)	40	1.00:0.70	35	6.6
(+)	67	1.00:0.76	26	25.0

***anti*-elimination**

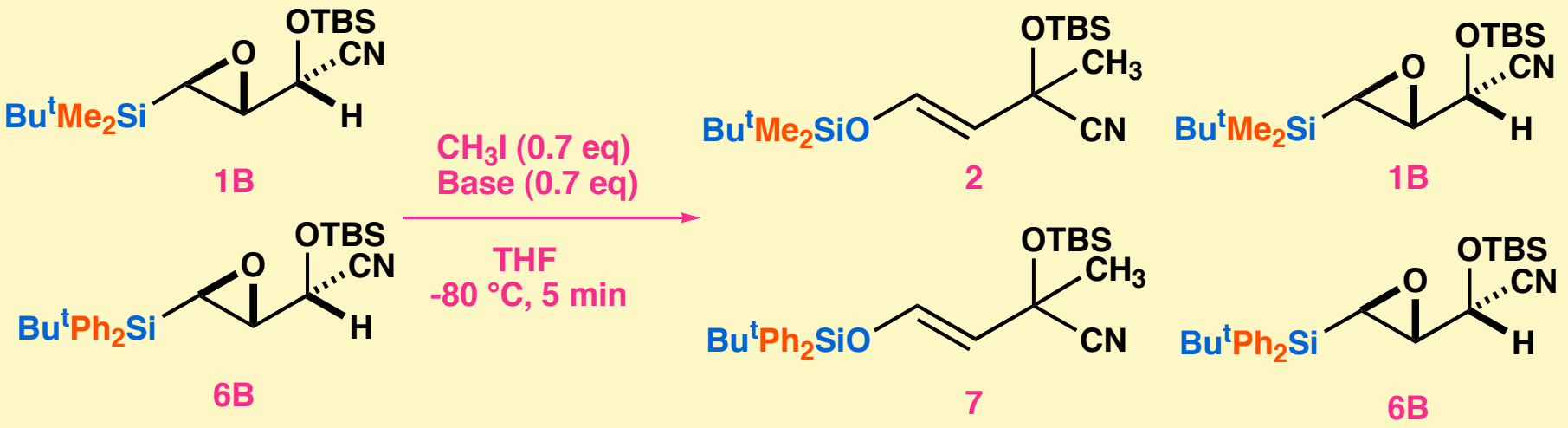


***syn*-elimination**

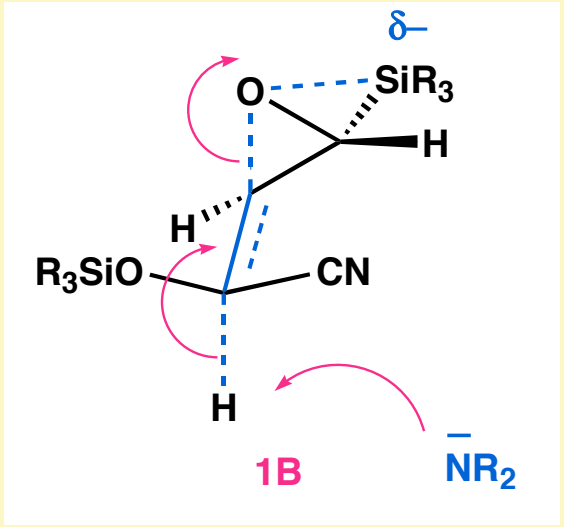


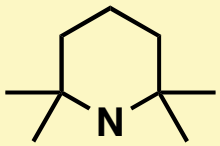
A-value: OTMS = 0.7
CN = 0.2

Substituent Effect of the Silyl Group on Rates of Ring Opening



	yield (%)			yield (%)	
base	2	7	7 (TBDPS)/2 (TBS)	1B	6B
$LiNEt_2$	18.8	6.0	0.32	24.4	39.1
LDA	21.5	6.7	0.31	18.1	39.8
LTMP	22.1	14.8	0.67	19.4	29.8



LTMP = 

TBS = Bu^tMe_2Si
TBDPS = Bu^tPh_2Si