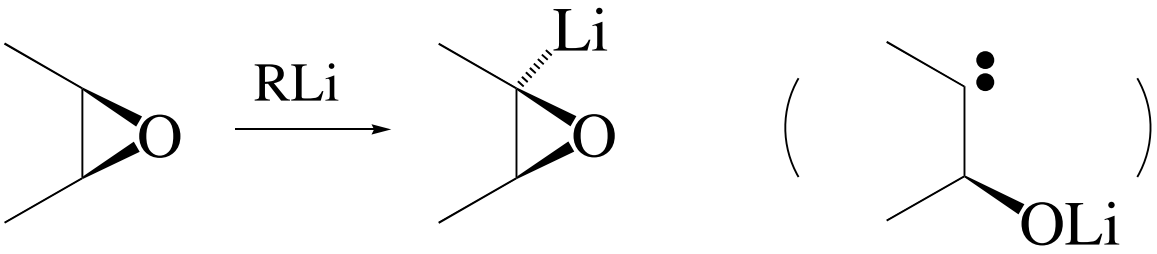
Expanding the Utility of Epoxides in Synthesis

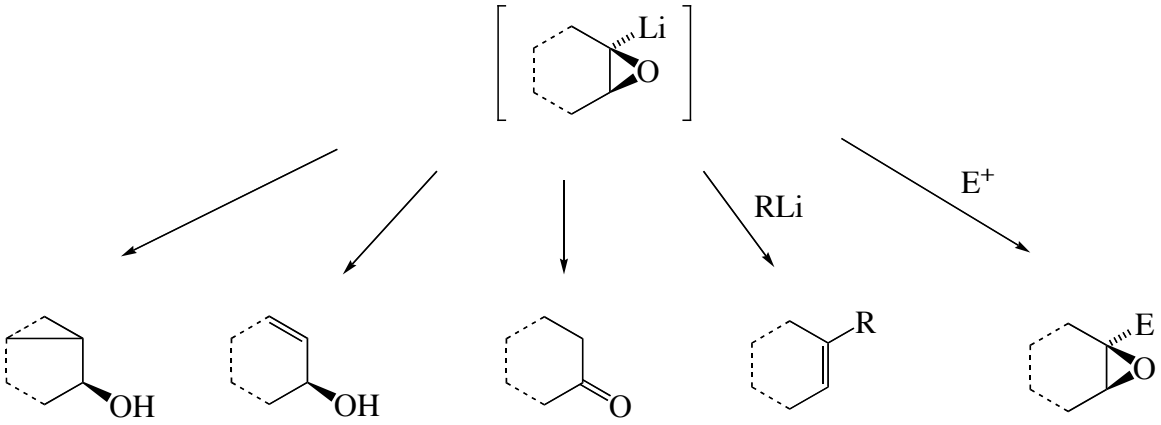
Dr David M Hodgson

Chemistry Research Laboratory
University of Oxford

21/9/04



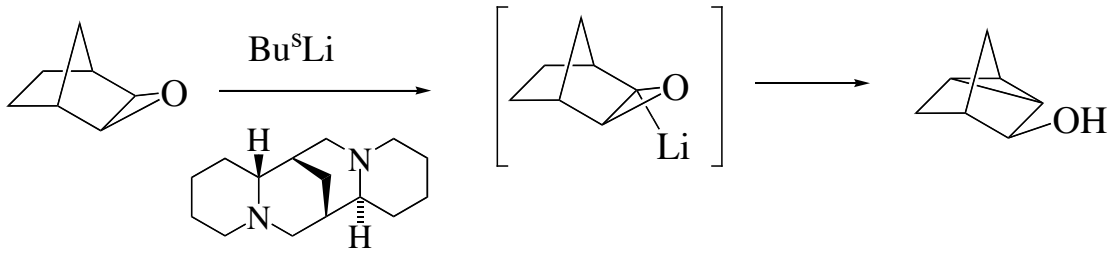
Reactivity of Lithiated Epoxides



selectivity depends upon: epoxide, base (+ ligand), solvent, temperature

Review: with Emmanuel Gras, *Synthesis*, 2002, 1625.

Exo-norbornene oxide rearrangement



–78 °C to rt

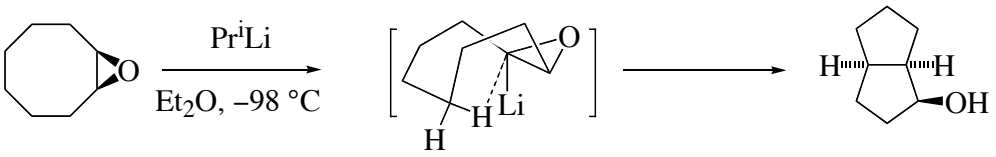
Et_2O 43% *y*, 49% *ee*

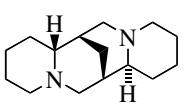
C_5H_{12} 73% *y*, 52% *ee*

Richard Wisedale

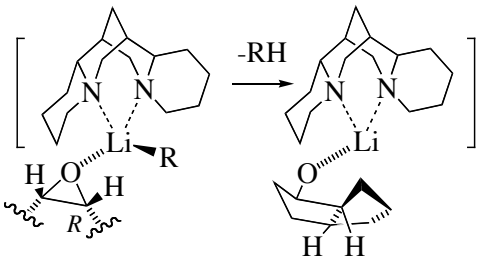
Organolithiums in Enantioselective Synthesis, ed. D. M. Hodgson, Springer, 2003.

Sparteine (SP) & α-Isosparteine (α-ISP)

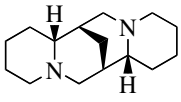




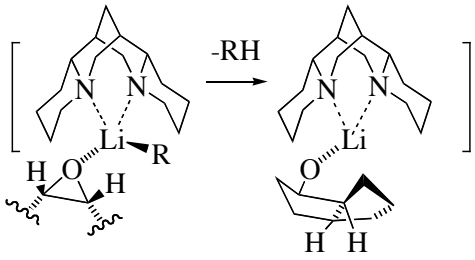
(–)-sparteine



1.4 eq 74% *y*, 83% *ee*
0.01 eq 65% *y*, 31% *ee*



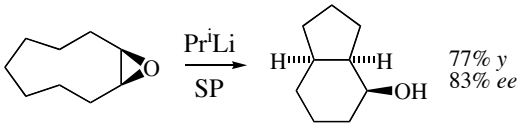
(–)-α-isosparteine



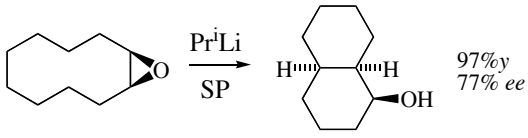
0.2 eq 86% *y*, 84% *ee*
0.01 eq 71% *y*, 69% *ee*

Gary Lee, *Chem Comm*, 1996, 1015; *JCSP1*, 1998, 2151.

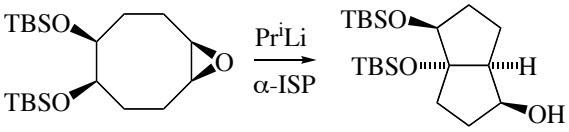
Rearrangements of Medium-sized Cycloalkene Oxides



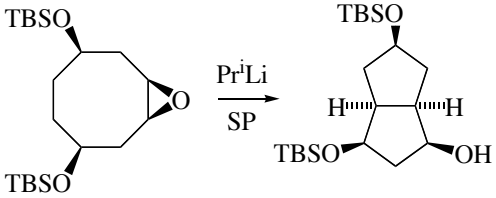
77% *y*
83% *ee*



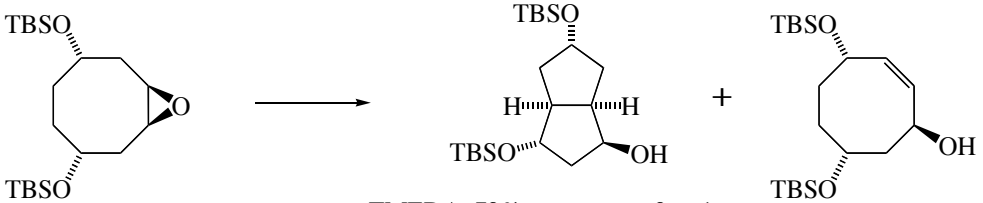
97%*y*
77% *ee*



72% *y*, 89% *ee*

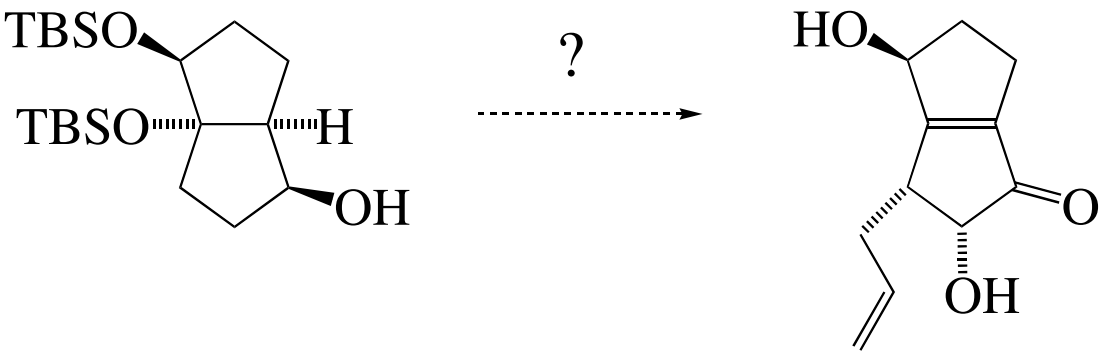


70% *y*, 84% *ee*



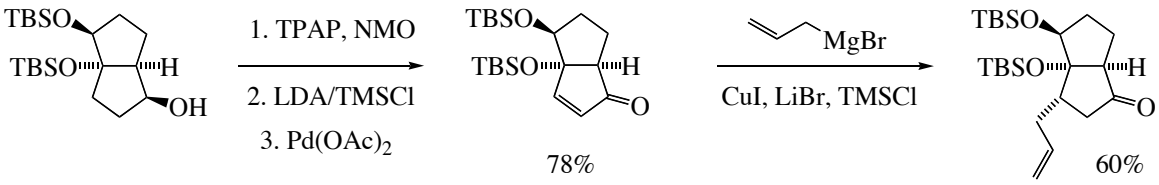
TMEDA	70% *y*		0 : 1	
SP	60% *y*	73% *ee*	1 : 1.25	70% *ee*
α-ISP	75% *y*	83% *ee*	1 : 0.2	61% *ee*

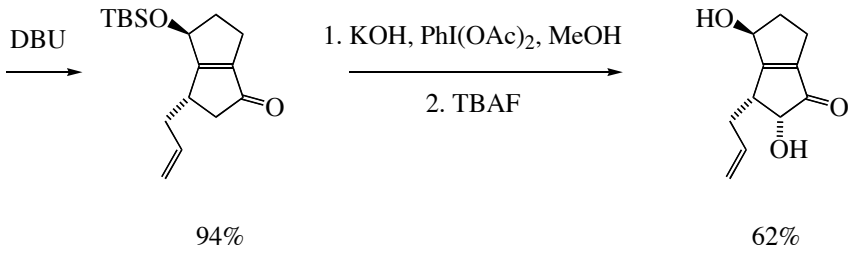
Iain Cameron, *OL*, 2001, 441; *JCSP1*, 2001, 2161.



(–)-xialenon A

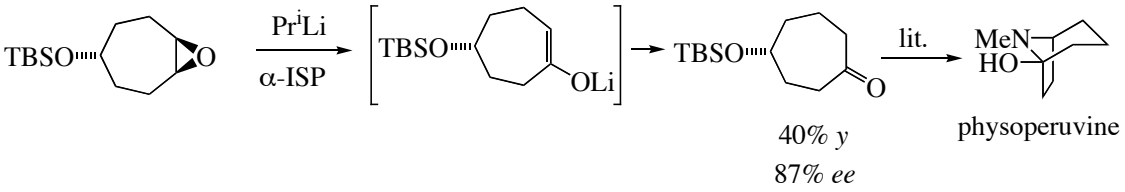
(–)-xialenon A synthesis





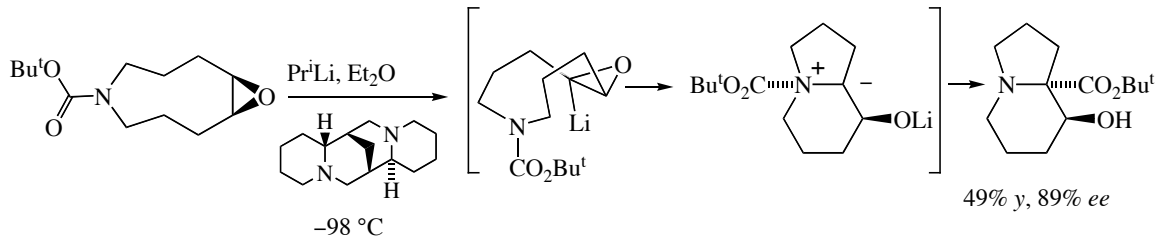
Jean-Marie Galano, *Chem Comm*, 2002, 2436; *Tetrahedron,* 2003, 9719.

Enantioselective Epoxide to Ketone Rearrangement



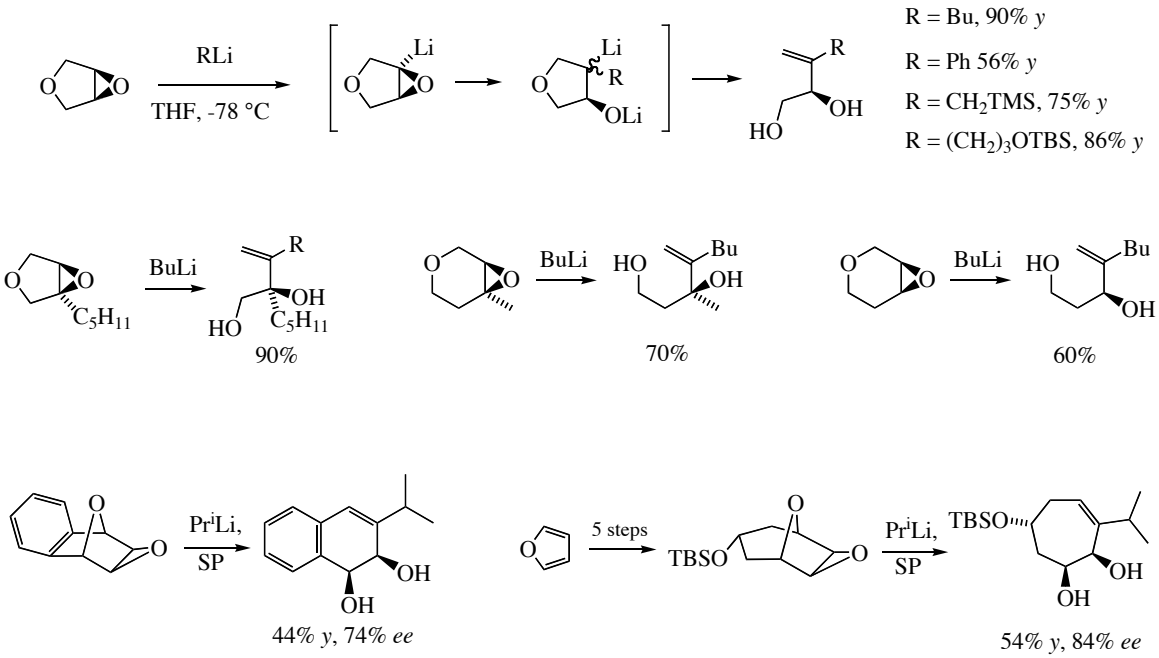
Matthew Jones, Lesley Robinson, *TL*, 1999, 8637.

Rearrangements of Aza substrates



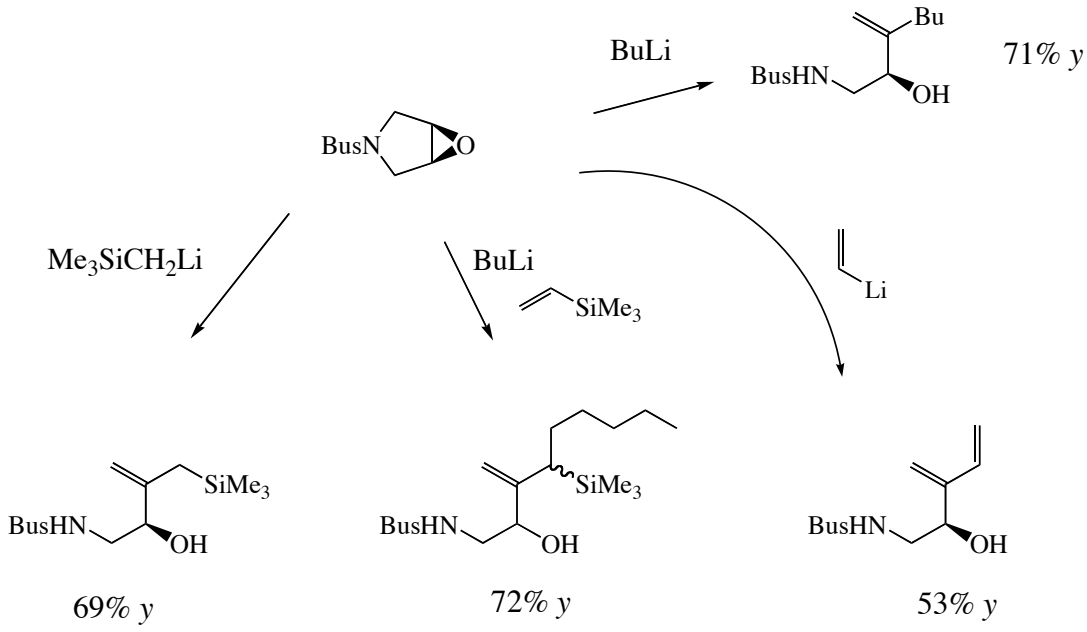
Lesley Robinson,
Chem Comm, 1999, 309; *JCSP1*, 2001, 2161.

Alkylative Route to Unsaturated Diols



Matthew Stent, *OL*, 2001, **3**, 3401; *Synthesis*, 2002, 1445 (Feature Article); *Org. Biomol. Chem.*, 2003, 1139 (Cover Article)

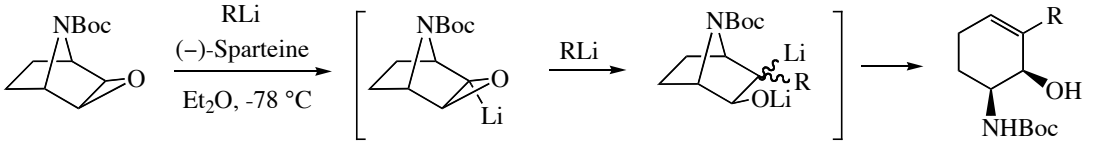
Acyclic Amino alcohols



Tim Miles, *Synlett*, 2002, 310; *Tetrahedron*, 2003, 9729.

Enantioselective Alkylative Desymmetrisation

amino alcohols



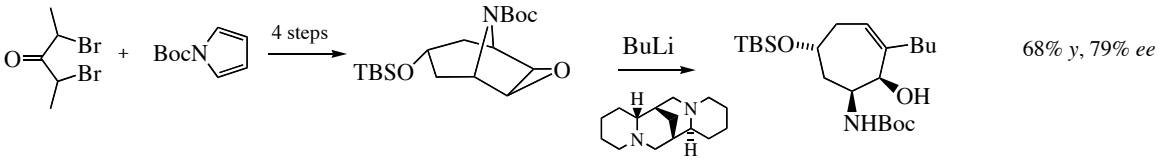
R = Bu^s, 74% *y*

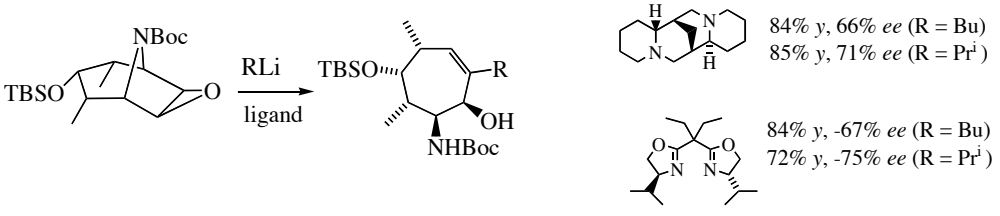
R = Pr^i, 78% *y*, 87% *ee*

R = Bu^n, 55% *y*, 67% *ee*

Chris Maxwell, *Ang. Chem.*, 2002, 4313; *Tetrahedron*, 2004, 3611.

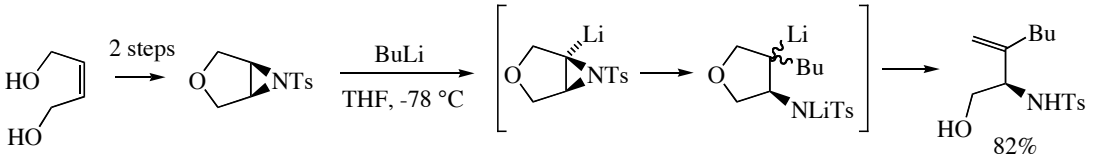
Aminocycloheptenols

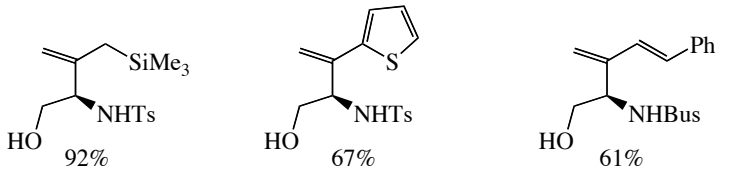


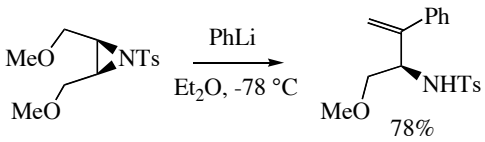


Edyta Paruch, *Ang. Chem.*, 2002, 4313; *Tetrahedron*, 2004, 5185.

Alkylative Desymmetrisation of *Aziridines*

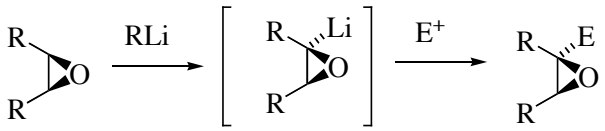




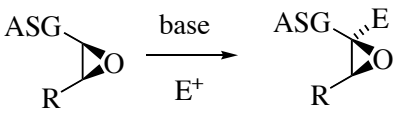


Tim Miles, Bogdan Stefane, *Chem Comm*, 2004, in press.

Direct Deprotonation-Electrophilic Substitution of Simple Epoxides ?

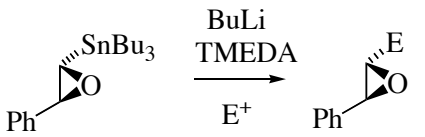


'activated' epoxides:

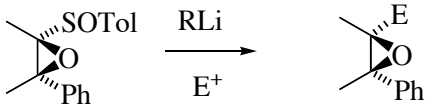


Eisch, 1976

'indirect' deprotonations:



Pfaltz, 1991

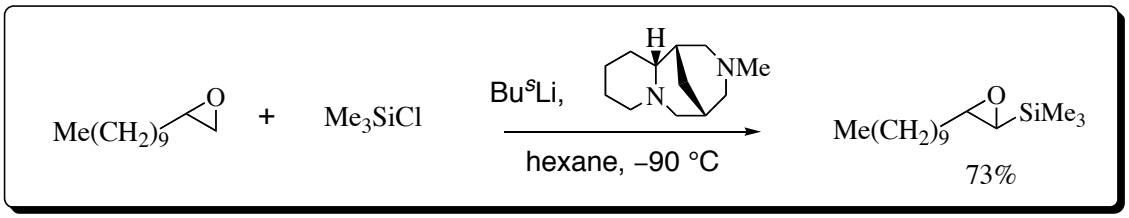


Satoh, 1999

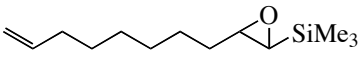
"metal-hydrogen exchange reaction is obviously *not* useful for generation of nonstabilised (H substituent) oxiranyl anions and destabilised (alkyl substituent) oxiranyl anions."

Satoh, *Chem. Rev.*, 1996, 3303.

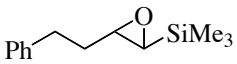
α,β-Epoxysilanes by *direct* silylation of terminal epoxides



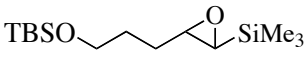
73%



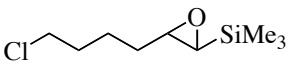
71%



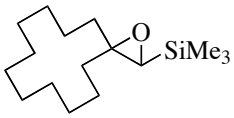
61%



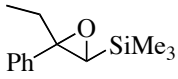
74%



65%



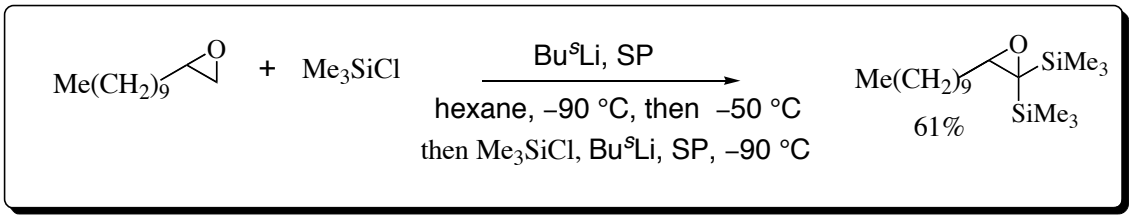
67%



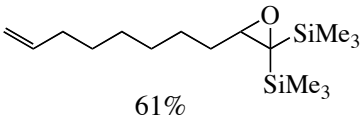
71% (97 : 3, *E* : *Z*)

Stephanie Norsikian, *OL*, 2001, 461.

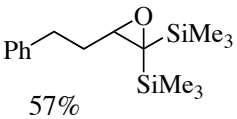
α,β-Epoxy*di*silanes by direct double silylation of terminal epoxides



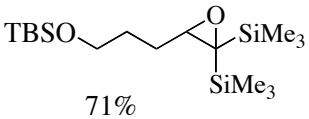
61%



61%



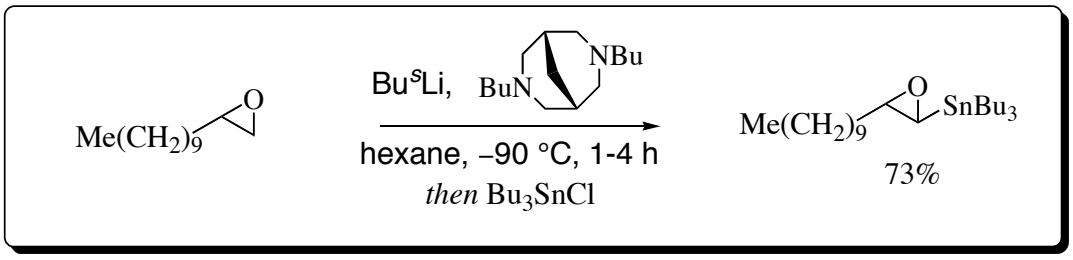
57%



71%

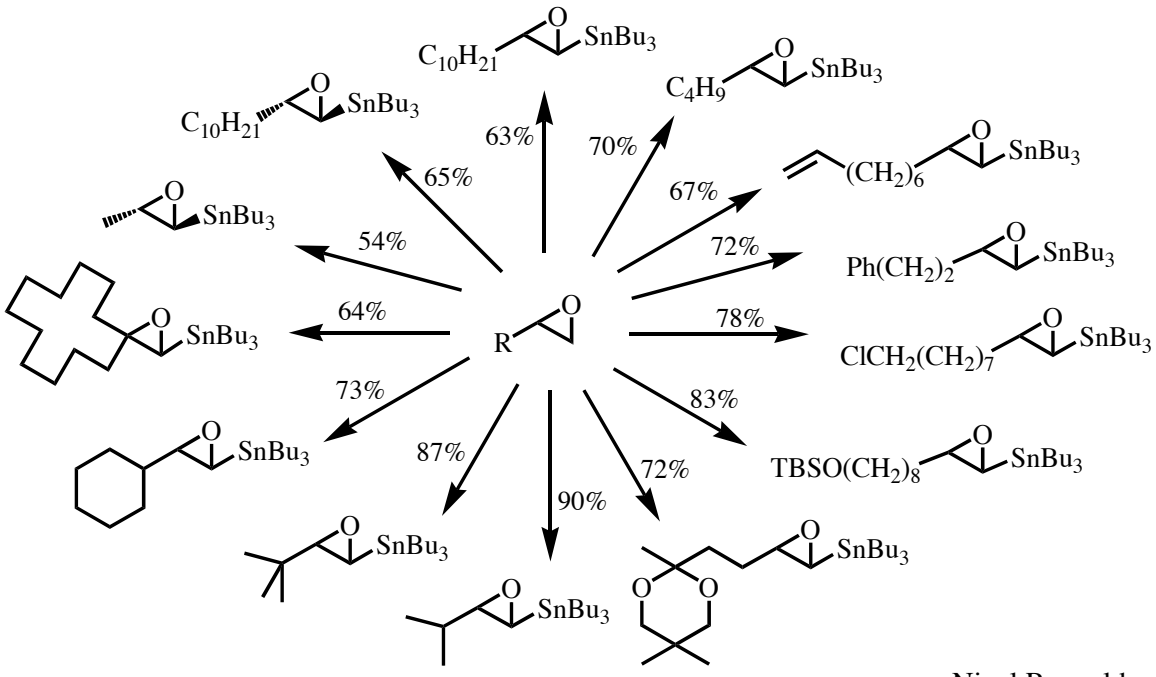
Eirene Kirton, *Synlett*, 2004, 1610

α,β-Epoxystananes by stannylation of terminal epoxides



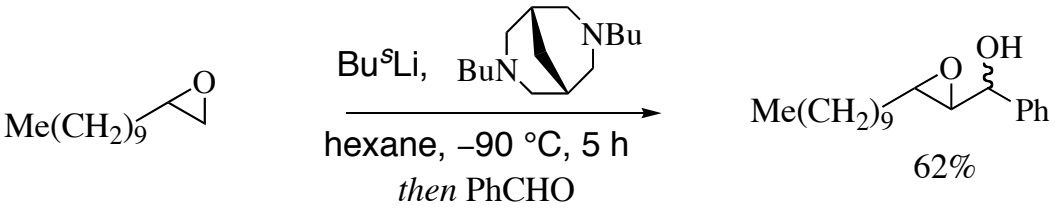
Nigel Reynolds

α,β-Epoxystananes by stannylation of terminal epoxides

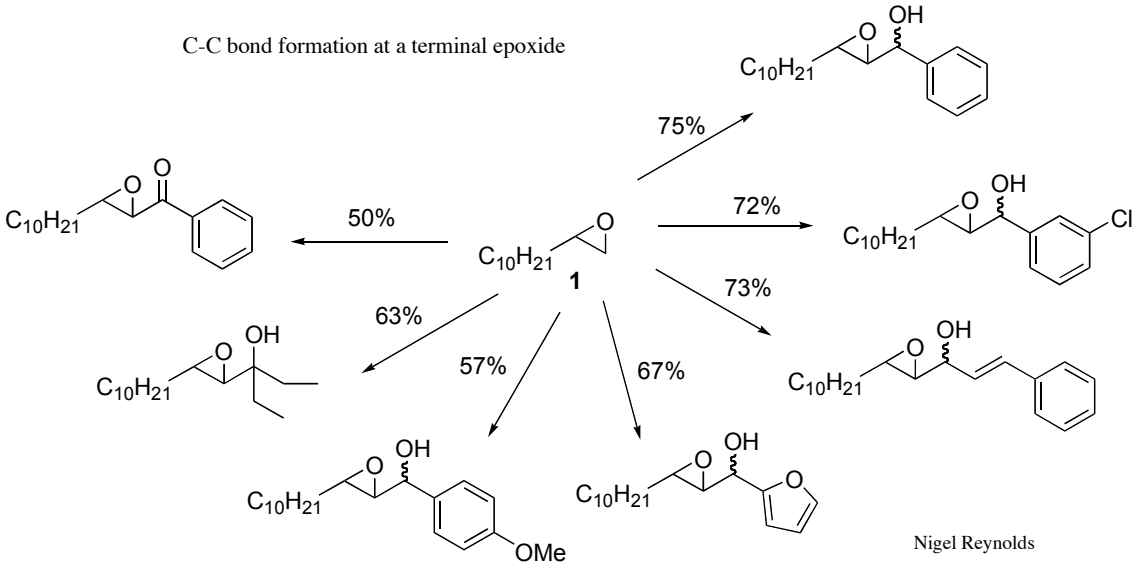


Nigel Reynolds

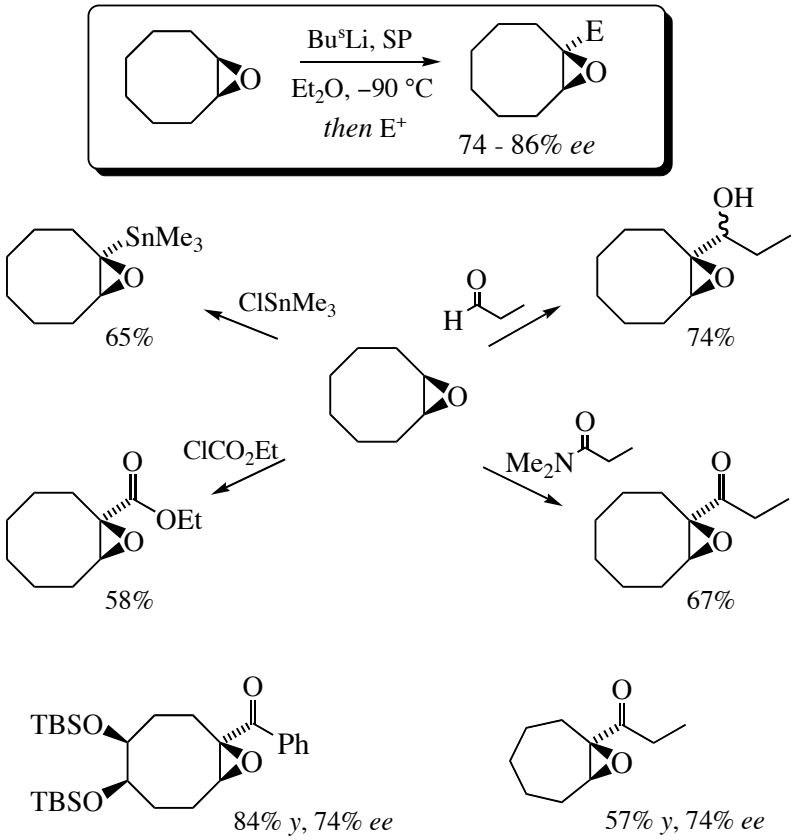
C-C bond formation at a terminal epoxide



Nigel Reynolds

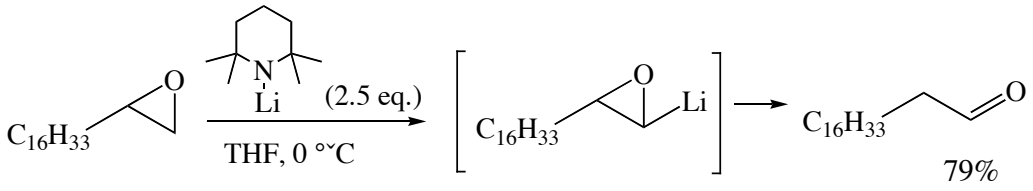


Direct *enantioselective* epoxide functionalisation

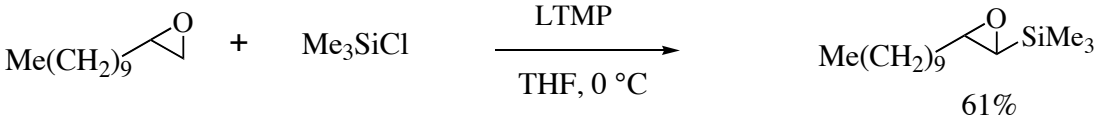


Emmanuel Gras, *Ang. Chem.*, 2002, 2376; *Org. Biomol. Chem.*, 2003, 4293.

LTMP and terminal epoxides

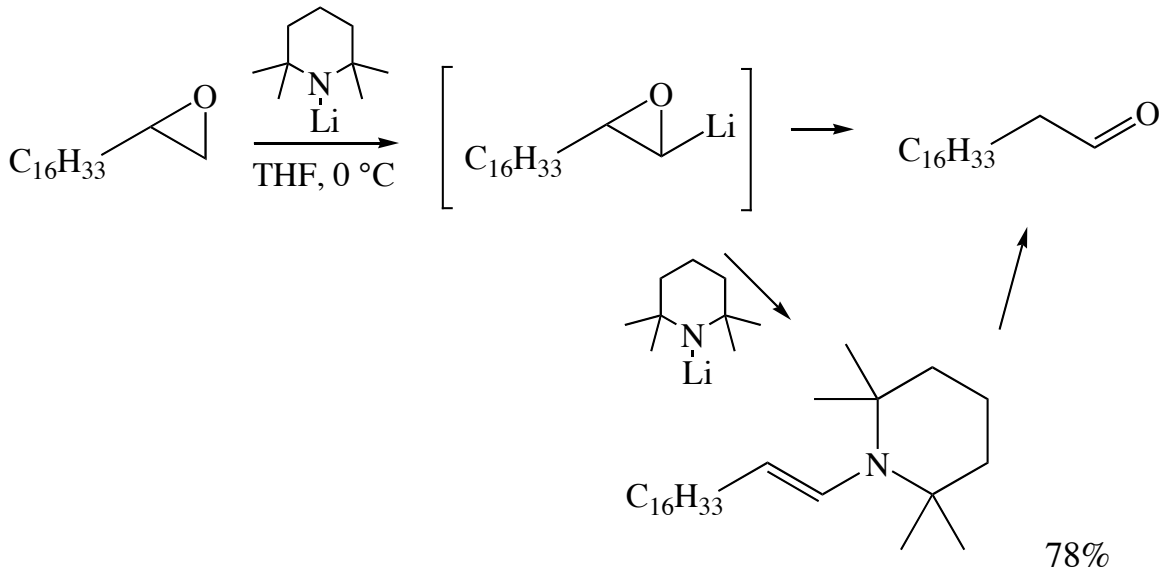


Yamamoto, *Chem. Commun.* 1994, 2103.



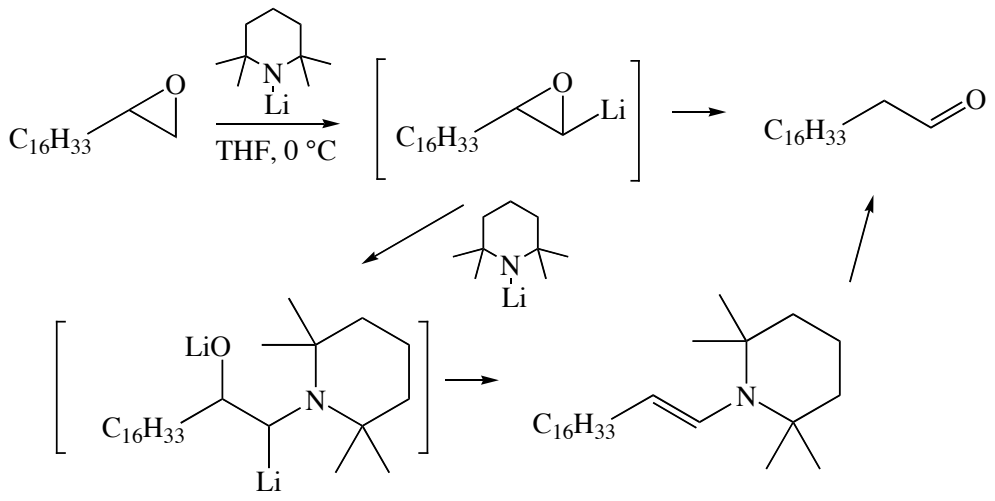
Nigel Reynolds, *TL,* 2002, 7895

LTMP and terminal epoxides



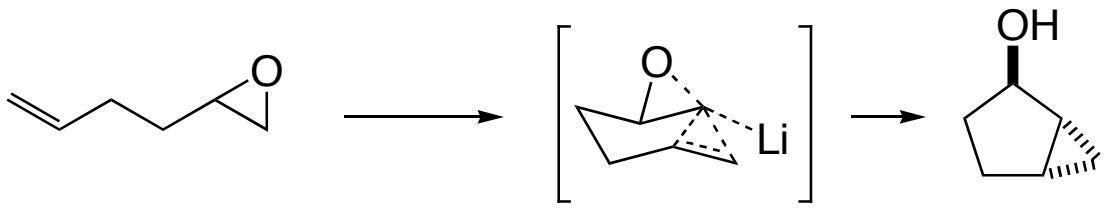
Chris Bray

LTMP and terminal epoxides



Chris Bray, *J. Am. Chem. Soc*., 2004, 6870.

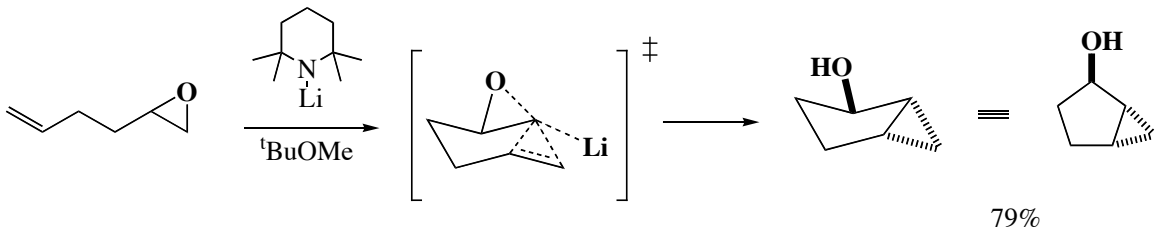
Unsaturated terminal epoxides



with *t*-BuLi 9%

LTMP ?

LTMP and *unsaturated* terminal epoxides

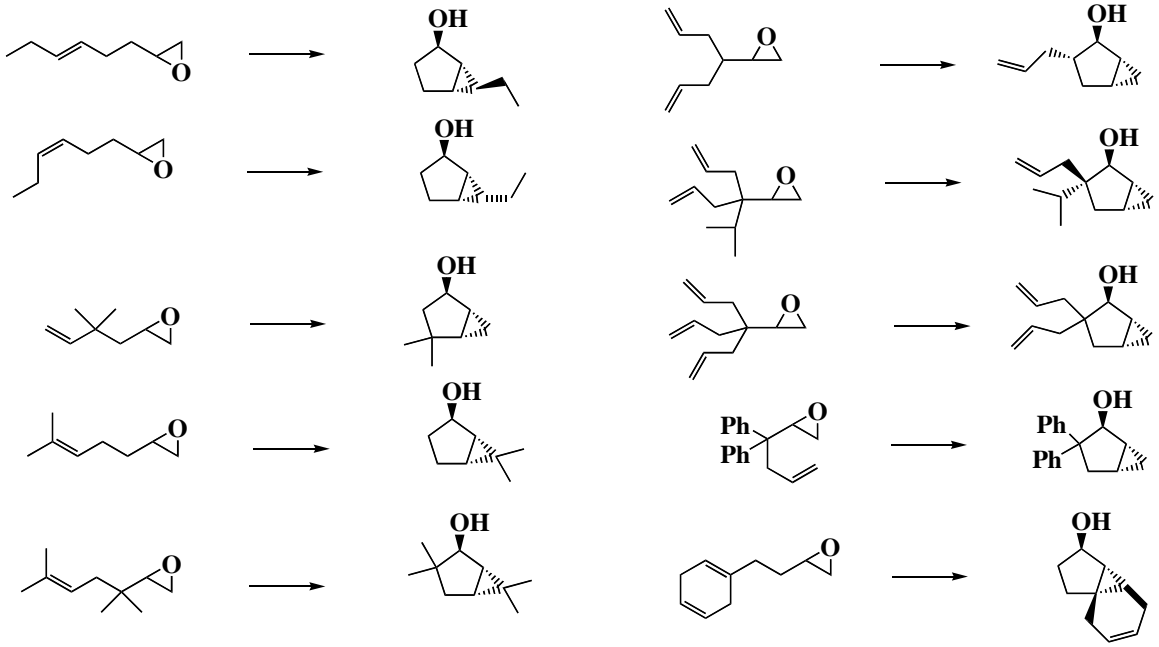


79%

J Chung

LTMP and *unsaturated* terminal epoxides

65 - 84% yields



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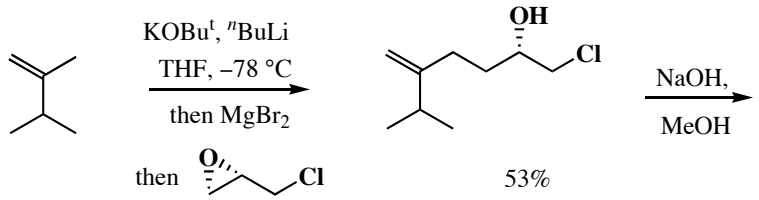
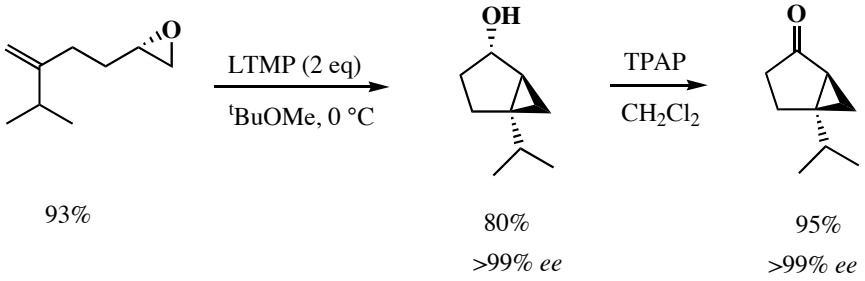
LTMP and *unsaturated* terminal epoxides

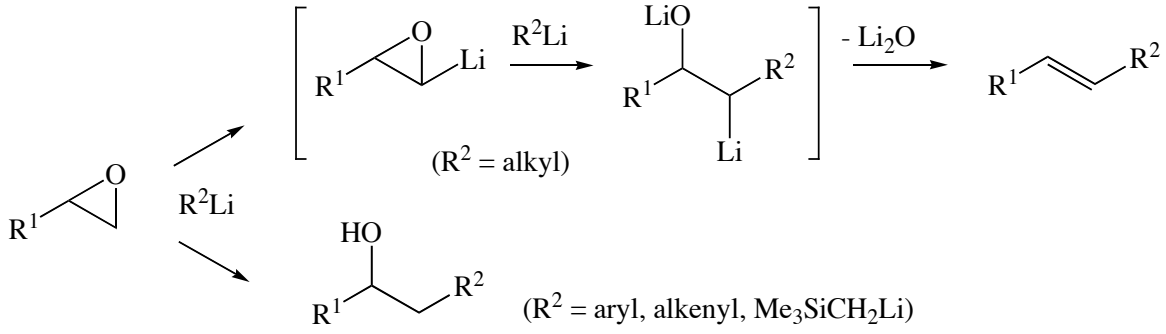
sabina ketone





Jack Chung, *J. Am. Chem. Soc.*, 2004, 8664.

Alkenes from terminal epoxides



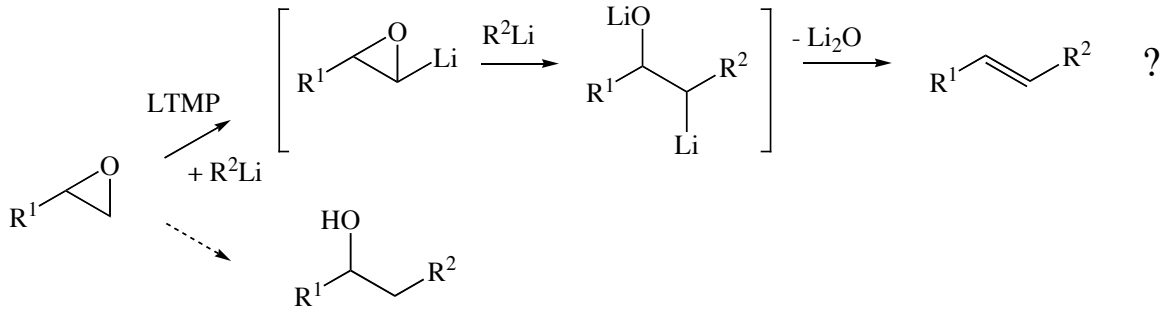
limitations:

(1) only simple *alkyl*lithiums are effective partners in the chemistry

(2) high *E*-selectivity is only observed with 2° and 3° alkyllithiums

(3) at least 2 equiv of R^2Li required

Alkenes from terminal epoxides



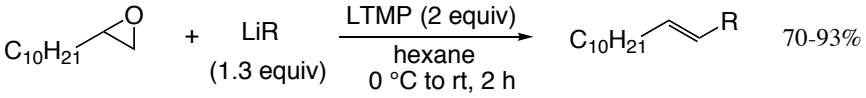
provided:

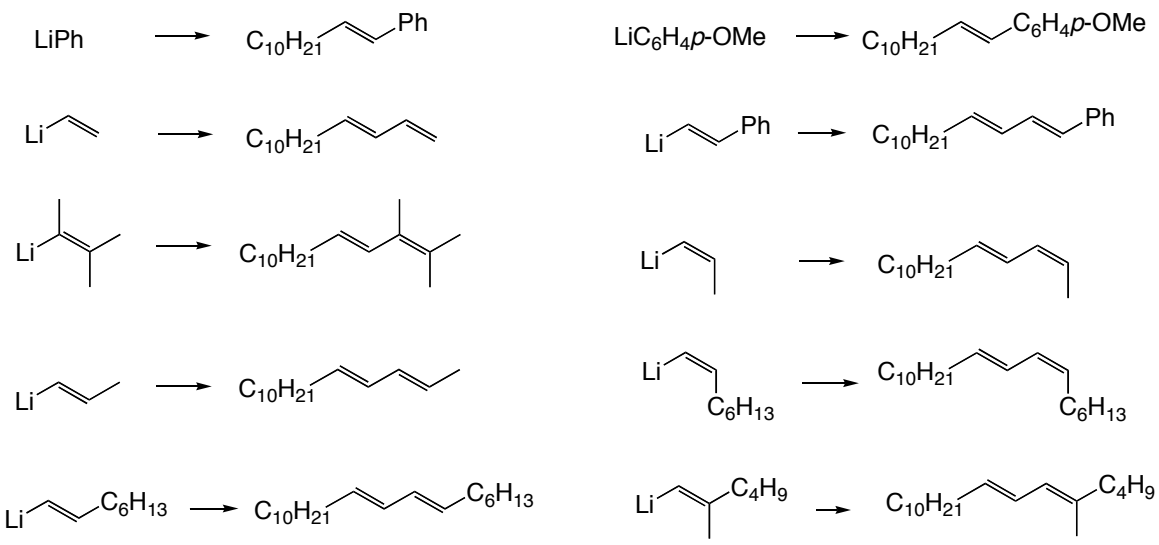
(i) LTMP reacts faster than R^2Li with epoxide

(ii) α-lithiated epoxide is preferentially trapped by R^2Li, rather than by LTMP

(iii) R^2Li is not consumed in deprotonating the generated tetramethylpiperidine

Alkenes from terminal epoxides





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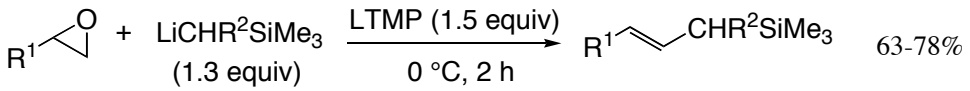
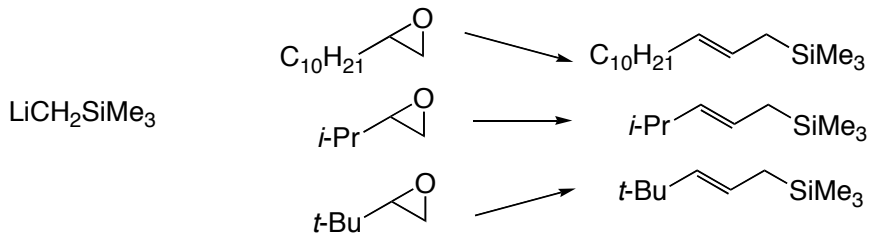
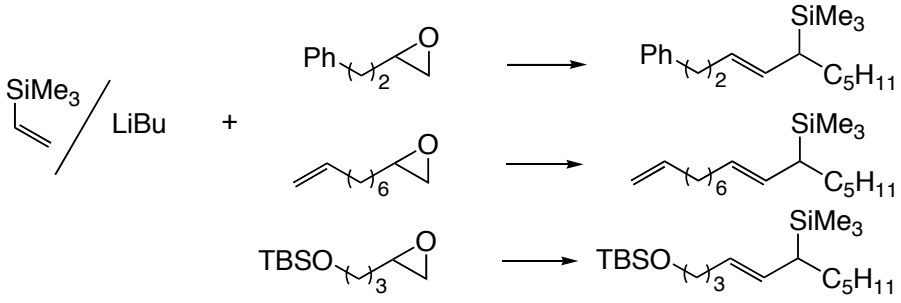
Allylsilanes from terminal epoxides







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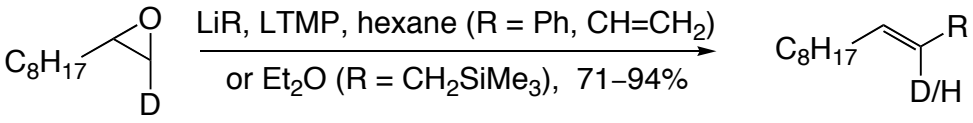
Deuterated terminal epoxides

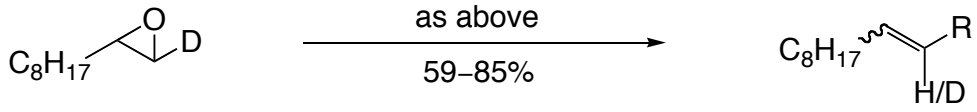


cis-**D**

R = Ph, *E*:*Z*, 98(94%D):2(96%D)

R = $CH{=}CH_2$, *E*:*Z*, 98(100%D):2(100%D)

R = CH_2SiMe_3, *E*:*Z*, 96(94%D):4(96%D)



trans-**D**

R = Ph, *E*:*Z*, 85(1%D):15(92%D)

R = $CH{=}CH_2$, *E*:*Z*, 86(0%D):14(100%D)

R = CH_2SiMe_3, *E*:*Z*, 81(8%D):19(94%D)

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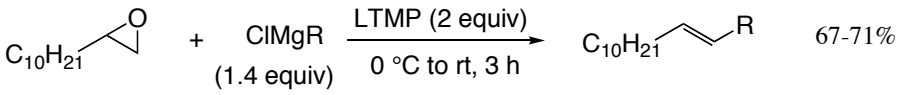
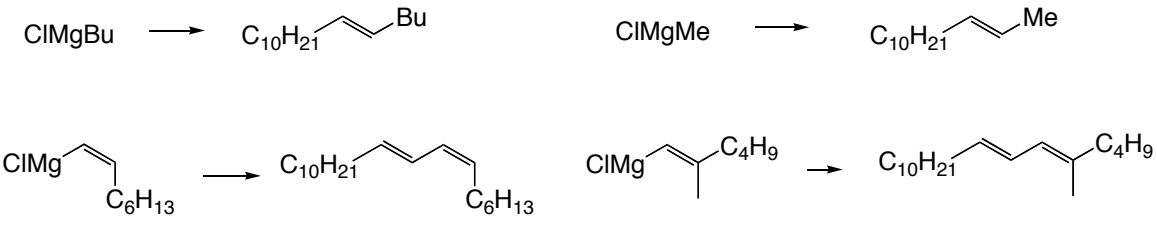
Alkenes from Epoxide using LTMP and Grignard Reagents





Matthew Fleming, *J. Am. Chem. Soc*., in press

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