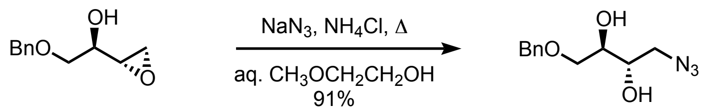
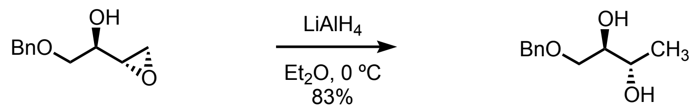
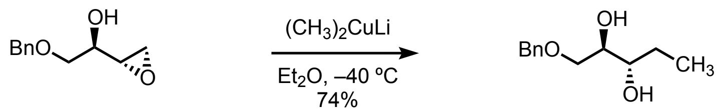
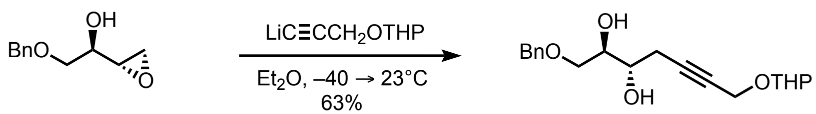
Opening of Terminal Epoxides:

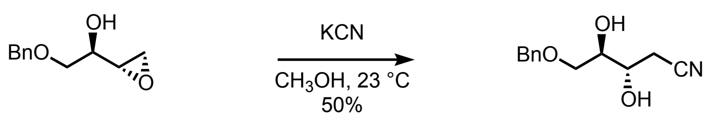
• Nucleophilic opening of terminal epoxides is often highly regioselective





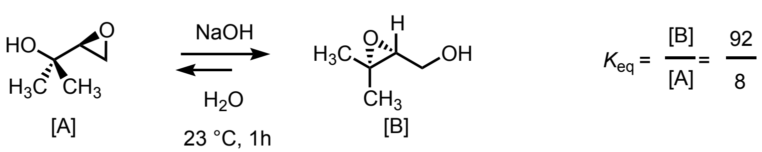






Behrens, C. H.; Sharpless, K. B.; *Aldrichimica Acta,* **1983**, *16*, 67–80.

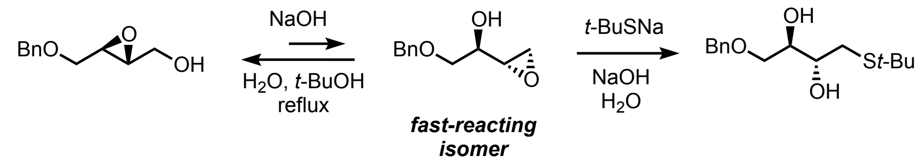
Payne Rearrangement



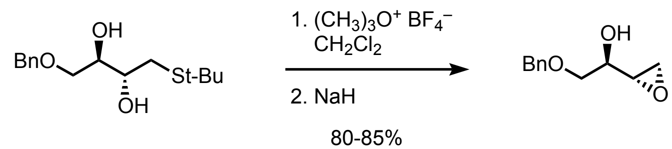
• Steric factors permitting, equilibrium generally favors the more substituted epoxide.

Payne, G. B. *J. Org. Chem.* **1962**, *27*, 3819–3822

Payne Rearrangement-Opening Sequence:



• β-Hydroxy sulfides are readily converted into terminal epoxides.

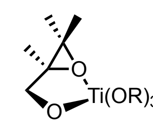


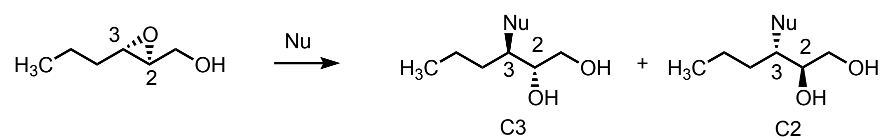
Behrens, C. H.; Sharpless, K. B.; *Aldrichimica Acta,* **1983**, *16*, 67–80.

2,3-Epoxy alcohols:

• $Ti(O\text{-}i\text{-}Pr)_4$ can catalyze the addition of nucleophiles to C3 of 2,3-epoxy alcohols:

Proposed:



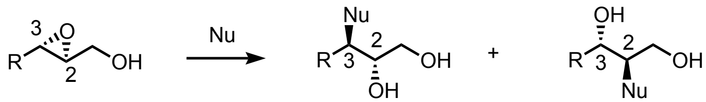


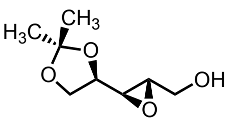
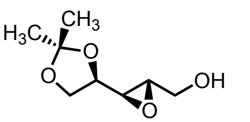
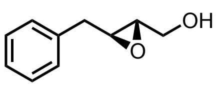
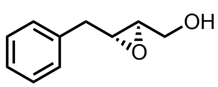
Nucleophile	$Ti(Oi\text{-}Pr)_4$ (equiv)	C3 : C2	yield
Et_2NH	0	3.7 : 1	4
Et_2NH	1.5	20 : 1	90
i-PrOH	0	-	0
i-PrOH	1.5	100 : 1	88
$(allyl)_2NH$	1.5	100 : 1	96
allyl alcohol	1.5	100 : 1	90
NH_4OBz	1.5	100 : 1	74
NH_4OAc	1.5	65 : 1	73
KCN	1.7	2.4 : 1	76

Caron, M.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 1557–1560.

M. Movassaghi

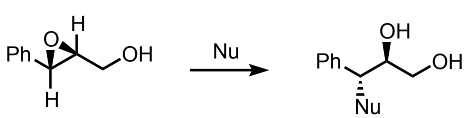
• Regioselectivity of uncatalyzed nucleophilic opening of 2,3-epoxy alcohols varies with the substrate and reaction conditions.



substrate	nucleophile	regioselectivity C3 : C2	combined yield (%)
	NaN_3	1 : 10	90
	NaSPh	1 : >10	76
	NaN_3	1.4 : 1	71
	NaSPh	1 : 1.4	72

Behrens, C. H.; Sharpless, K. B.; *J. Org. Chem.* **1985**, *50*, 5696–5704.

• Phenyl substitution at C3 of 2,3-epoxy alcohols can lead to high C3-regioselectivity.

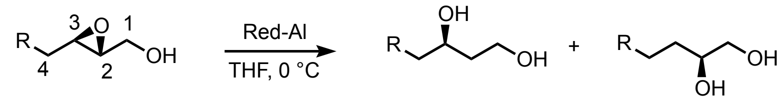


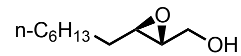
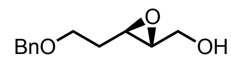
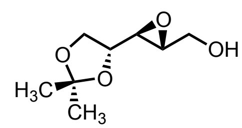
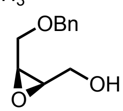
reagent	Nu	yield
allyl magnesium bromide	allyl	96
R_2CuLi or $R_2(CN)CuLi_2$	R	76-88
NaN_3/NH_4Cl	N_3	>95
R_2NH/KOH	R_2N	84
ArONa	ArO	83
PhSH/NaOH	PhS	82

Hanson, R. M. *Chem. Rev.* **1991**, *91,* 437–575, and references therein.

• C2 reduction of 2,3-epoxy alcohols using Red-Al is highly selective when C4 is oxygenated.

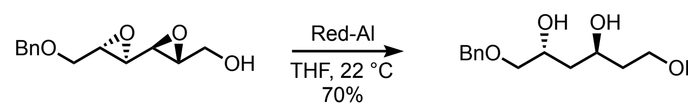
Red-Al = $[(CH_3OCH_2CH_2O)_2AlH_2]^{-}Na^{+}$



epoxy alcohol	C2 reduction C2 : C3	C3 reduction yield (%)
	1 : 1	94
	5 : 1	89
	40 : 1	98
	>100 : 1	78
	100 : 1	95

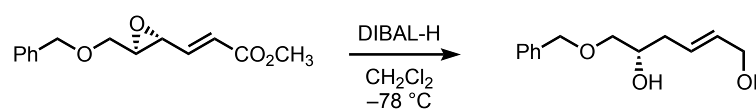
Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Viti, S. M. *J. Org. Chem.* **1982**, *47*, 1378–1380.
Finan, J.; Kishi Y. *Tetrahedron Lett.* **1982**, 23, 2719–2722.

• 1,3-Bis-epoxides:



Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Viti, S. M. *J. Org. Chem.* **1982**, *47*, 1378–1380.

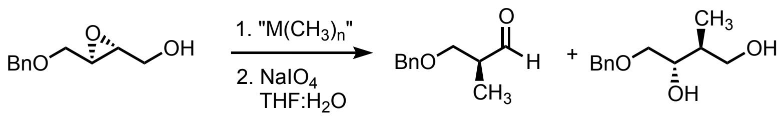
• Allylic epoxides:



Nicolaou, K. C.; Uenishi, J. *J. Chem. Soc., Chem. Commun.* **1982**, 1292–1293.

M. Movassaghi

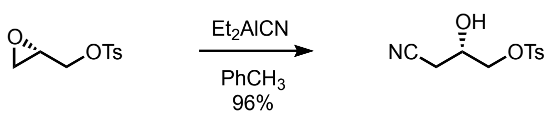
• The regioselectivity of epoxide opening can vary with the organometallic reagent.

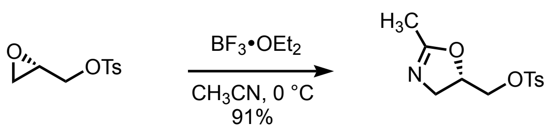


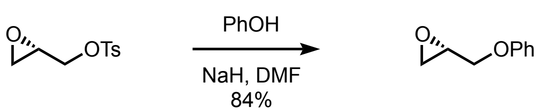
$(CH_3)_2CuLi$ Et_2O, –20 ºC	10-12%	74-79%
$(CH_3)_3Al$, CH_2Cl_2 0 → 23 ºC	69-73%	13-14%

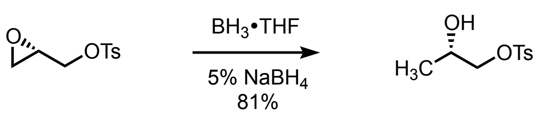
Johnson, M. R.; Nakata, T.; Kishi, Y. *Tetrahedron Lett.* **1979**, 4343–4346.
Roush, W. R.; Adam, M. H.; Peseckis, S. M. *Tetrahedron Lett.* **1983**, 1377–1380.

• AE of allyl alcohol followed by *in situ* derivatization affords versatile chiral building blocks, such as glycidol tosylate (now commercially available).
• Reactions of glycidol tosylate:



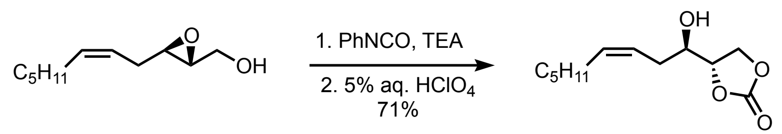




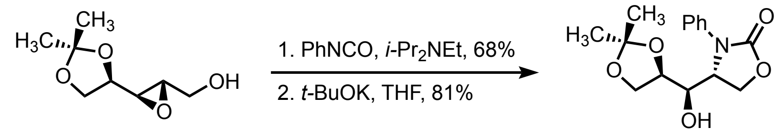


Klunder, J. M.; Onami, T.; Sharpless, K. B. *J. Org. Chem.* **1989**, *54*, 1295–1304.
Hanson, R. M. *Chem. Rev.* **1991**, *91*, 437–475.

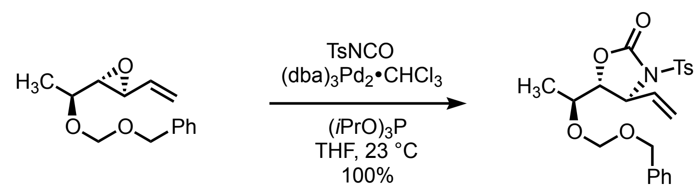
• Internal nucleophiles may be used to open 2,3-epoxy alcohols:



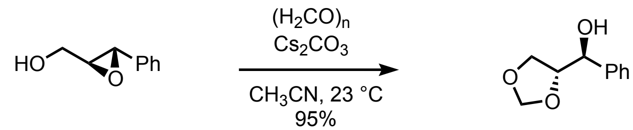
Corey, E. J.; Hopkins, P. B.; Munroe, J. E.; Marfat, A.; Hashimoto, S.-I. *J. Am. Chem. Soc.* **1980**, *102*, 7986–7987



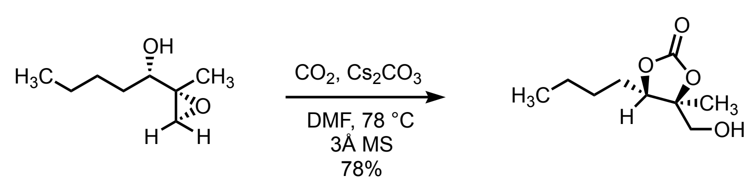
Minami, N.; Ko, S. S.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 1109–1111.



Trost, B. M.; Sudhakar, A. R. *J. Am. Chem. Soc.* **1987**, *109*, 3792–3794.



McCombie, S. W.; Metz, W. A. *Tetrahedron Lett.* **1987**, *28*, 383–386.



Myers, A. G.; Widdowson, K. L. *Tetrahedron Lett.* **1988**, *29*, 6389–6392.

M. Movassaghi