

Resolution of a racemate

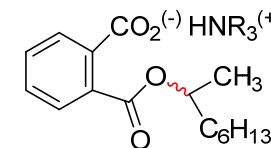
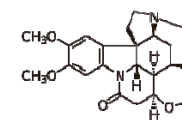
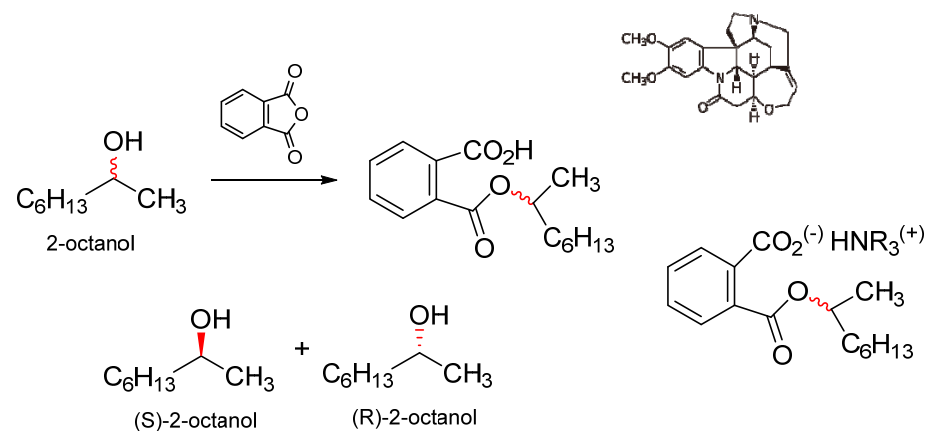
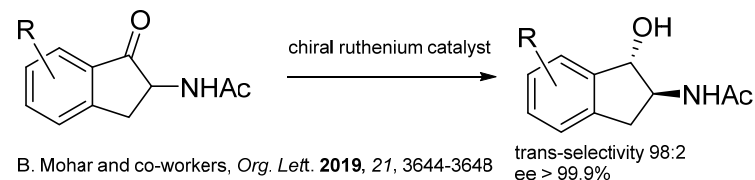
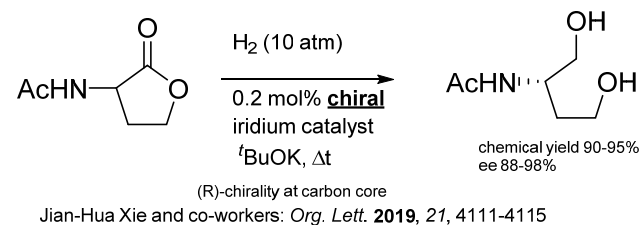
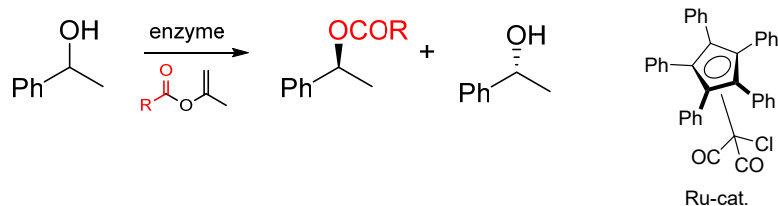
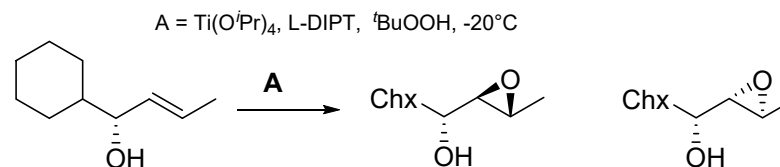
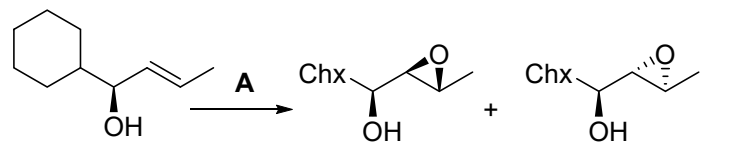
a. 'Classical': A (rac) 50% A(R) + 50% A(S)

b. Separation of enantiomers on CHIRAL column
(Y. Okamoto, T. Ikai, *Chem. Soc. Rev.*, 2008, 37, 2593-2608)

c. 'Kinetic': A (rac) 50% A(R) + 50% B(S)

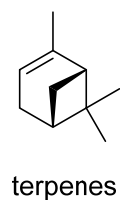
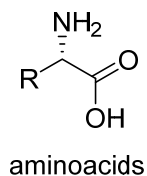
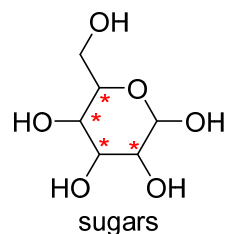
d. Dynamic: A (rac) 100% A(R) or 100% A(S)

A(S) (50%) + A(R)-X (50%)



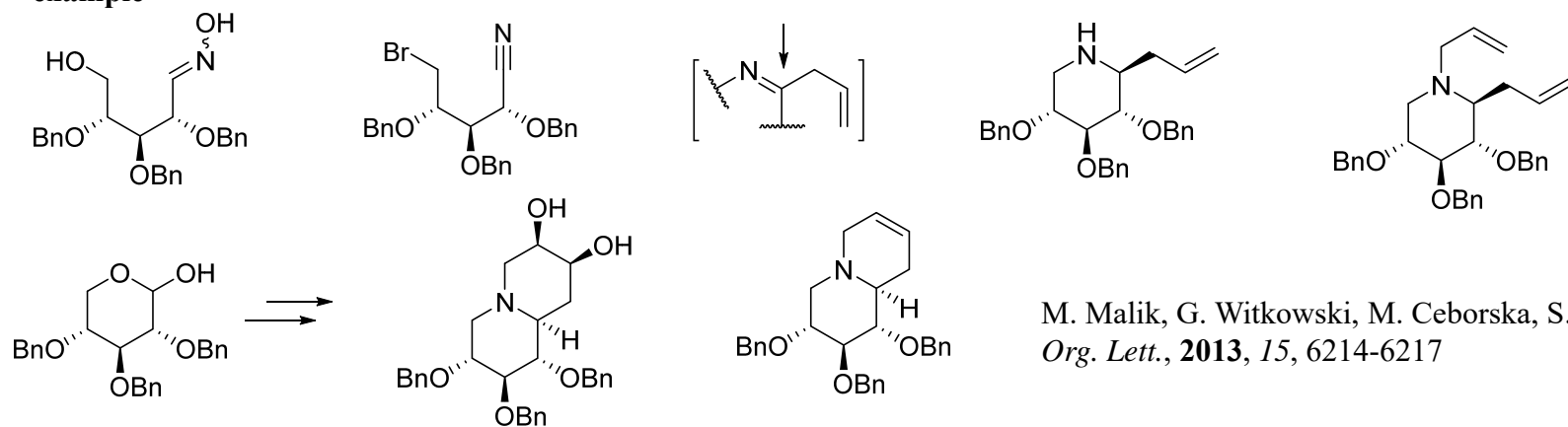
Enzymatic separation: Bäckvall and co-workers, *Chem. Eur. J.* **2006**, 12, 225-232; enzymes in biotransformations: K. Faber, .. *Angew.* **2008**, 47, 8782-8793 (minireview)

Chiron approach - Transfer of chirality from the easily available, optically pure starting materials onto optically pure targets

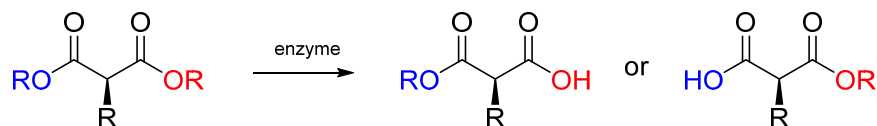
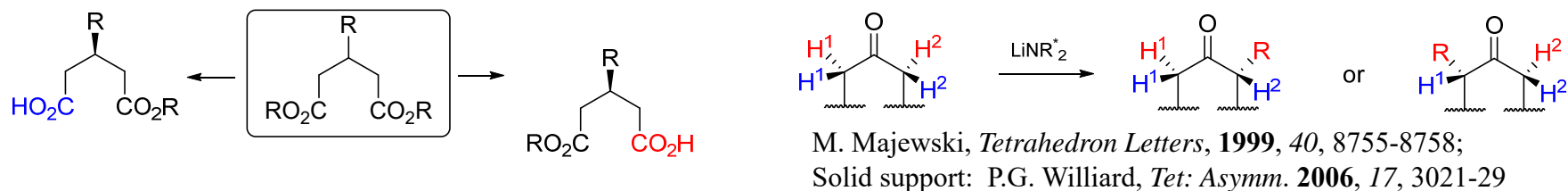


S. Hanessian, *Total Synthesis of Natural Products: The Chiron Approach*;
B. Fraser-Reid, *Acc. Chem. Res.* **1996**, 29(2), 57-66

example



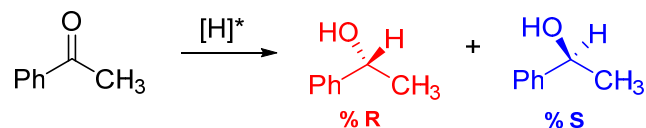
Desymmetrization of symmetrical derivatives



Planning the syntheses of optically active compounds

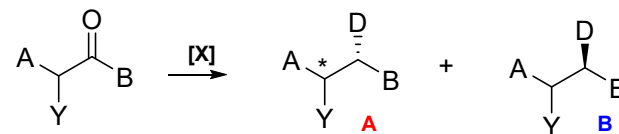
Optically active compounds can be obtained on several routes from achiral material (catalysis, desymmetrization) or chiral (resolution of a racemate, chiral pool etc.).

Enantiodifferentiating reactions

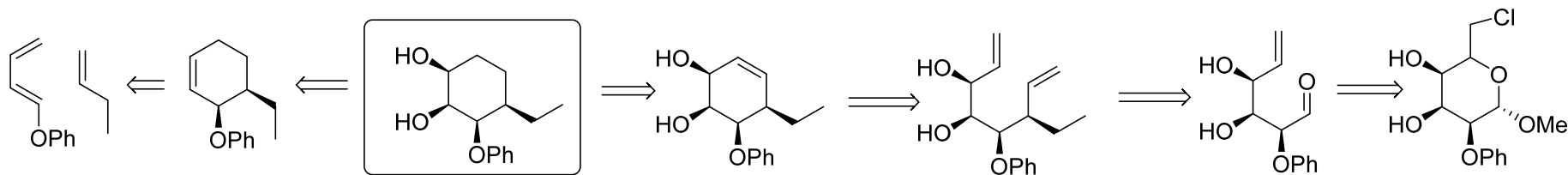


$$ee = \frac{R - S}{R + S} \times 100\% \quad R > S$$

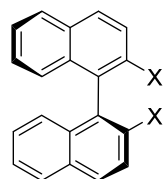
Diastereodifferentiating reactions



$$de = \frac{A - B}{A + B} \times 100\% \quad A > B$$

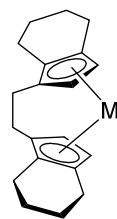


privileged catalysts *Small-Molecule C-H donors in Asymmetric Catalysis*; A.G. Doyle, E.N. Jacobsen, *Chem. Rev.* **2007**, 107 (12), 5713-5743



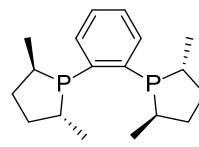
X = OH BINOL
X = PPh₂ BINAP

Diels-Alder
Mykaiyama aldol
aldehyde allylation
hydrogenation
alkene isomerization
Heck reaction



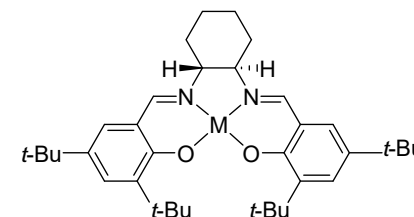
Brintzinger's
ligand

Alkene reduction
imine reduction
alkene carbometallation
Ziegler-Natta
polymerization



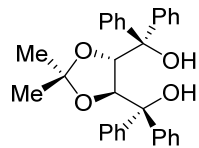
MeDuPhos

hydrogenation
hydrophosphination
hydroacylation
hydrosilylation
Bayer-Villiger oxidation



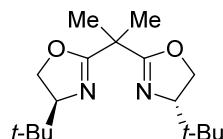
salen complexes

epoxidation
epoxide ring-opening
Diels-Alder
imine cyanation
conjugate addition



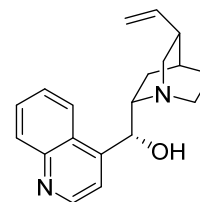
TADDOLate
ligand

Diels-Alder
aldehyde alkylation
ester alcoholysis
iodolactonization



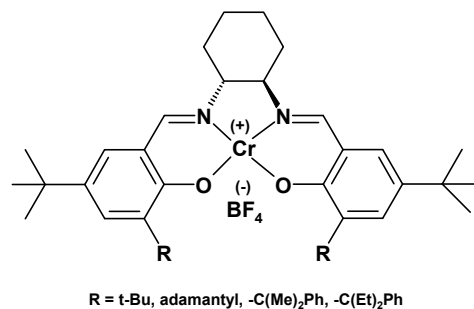
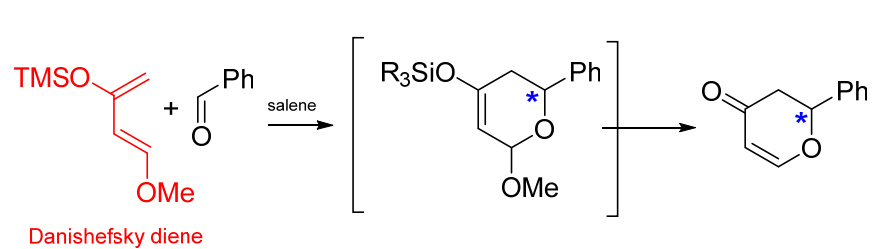
Bis(oxazoline)

Diels-Alder
Makaiyama aldol
conjugate addition
cyclopropanation
aziridination

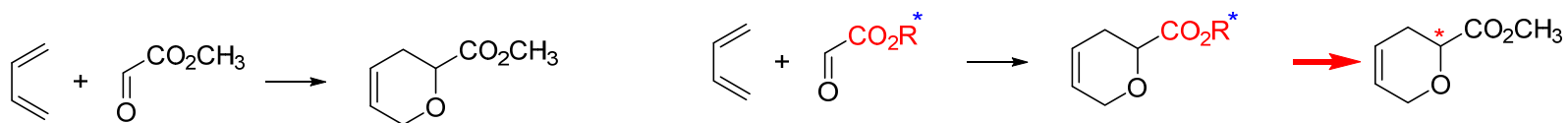


Cinchona alkaloid
derivatives

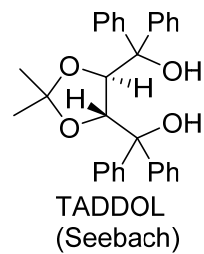
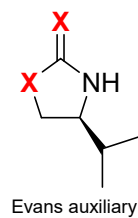
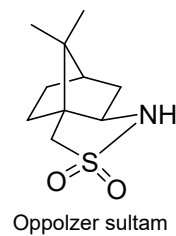
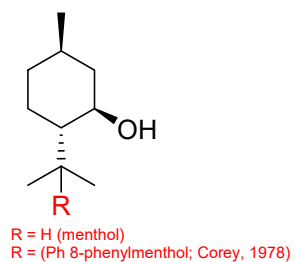
dihydroxylation
acylation
heterogeneous hydrogenation
phase transfer catalysis



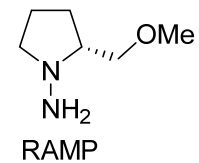
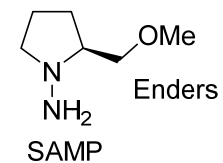
ee > 90% Jurczak,
TL, 2008, 6810



chiral auxiliaries

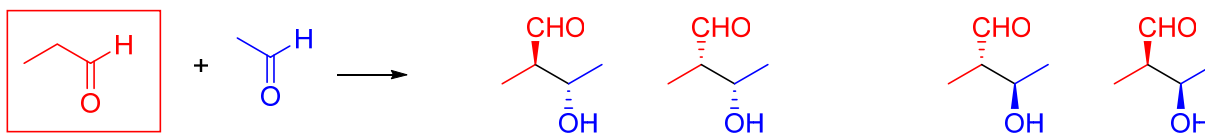
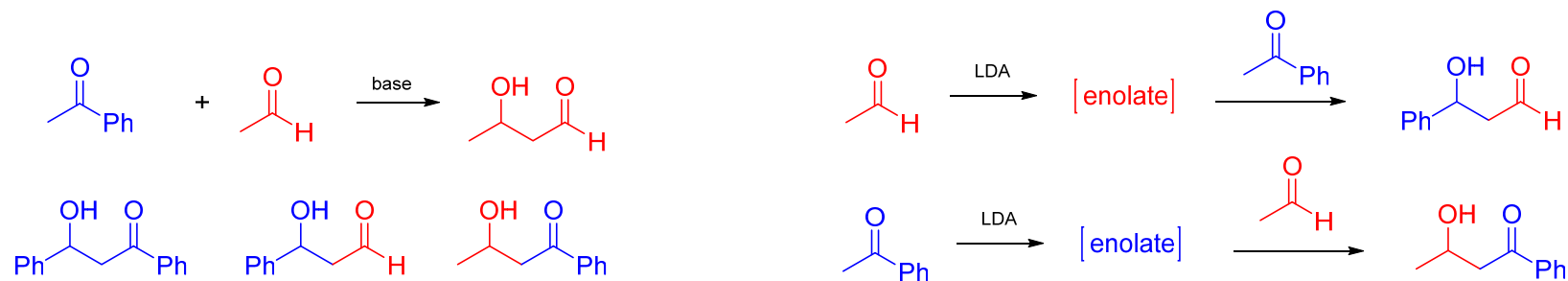


From L-
or
D-tartaric acid

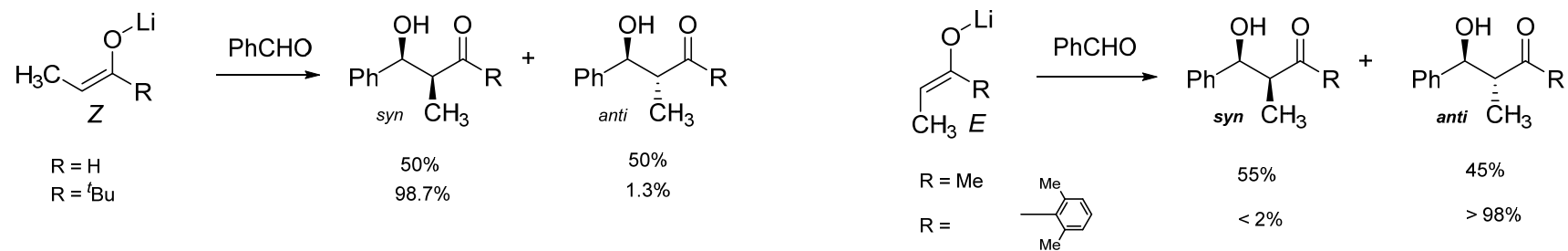
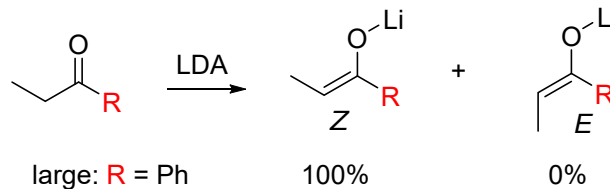


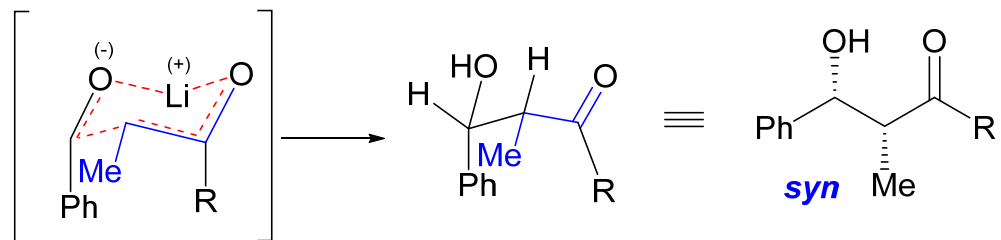
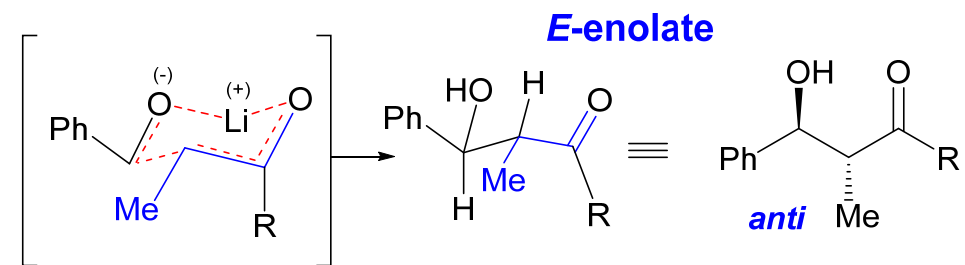
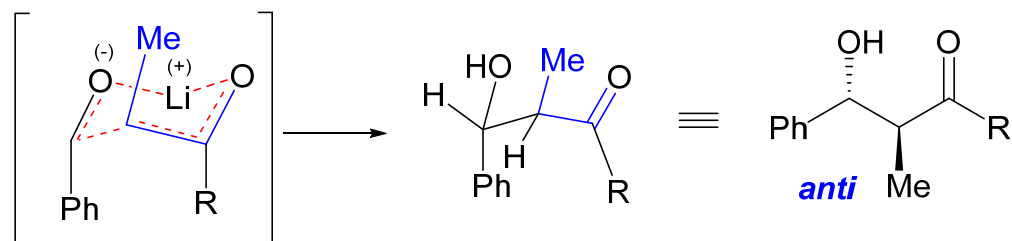
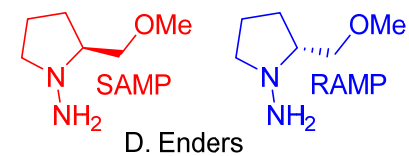
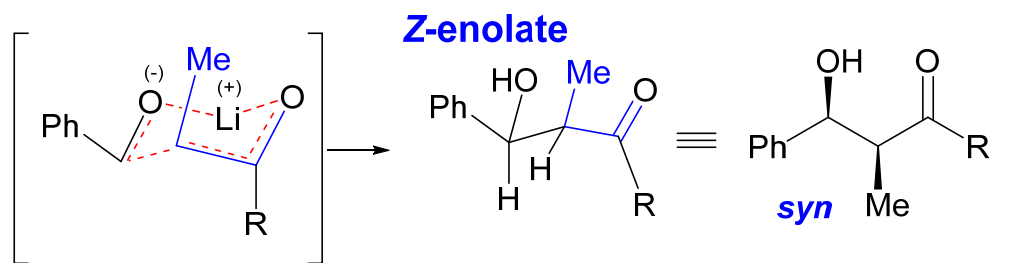
Enders

Aldol reaction

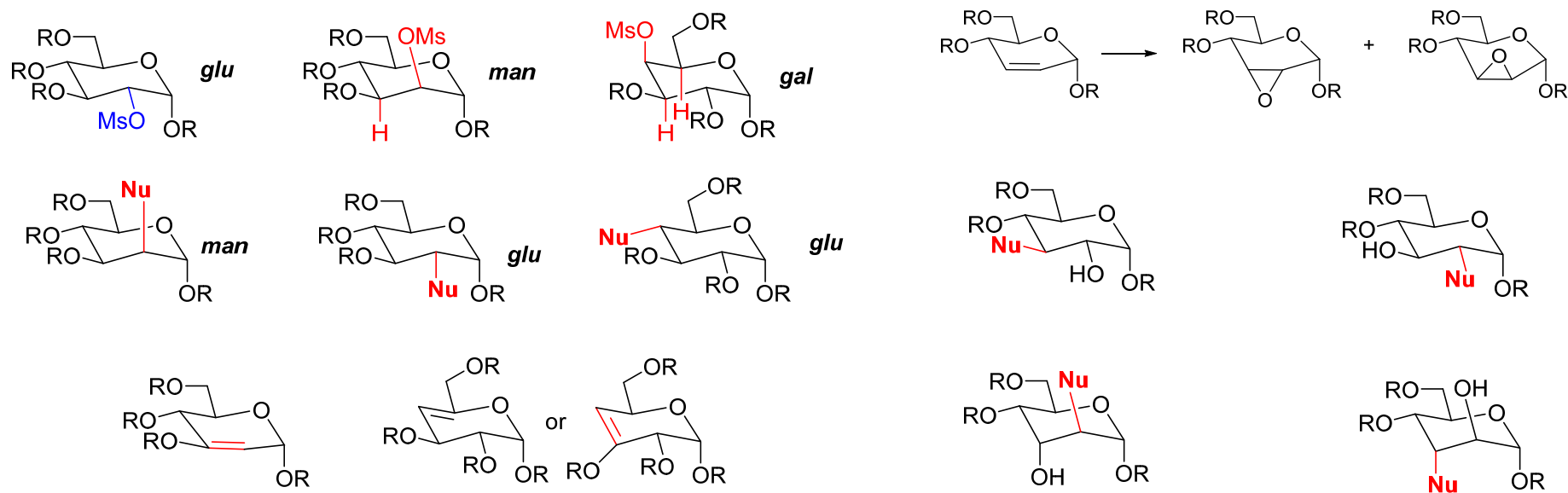


kinetic control: the Z-enolates are formed preferably especially when large substituents (R) are present

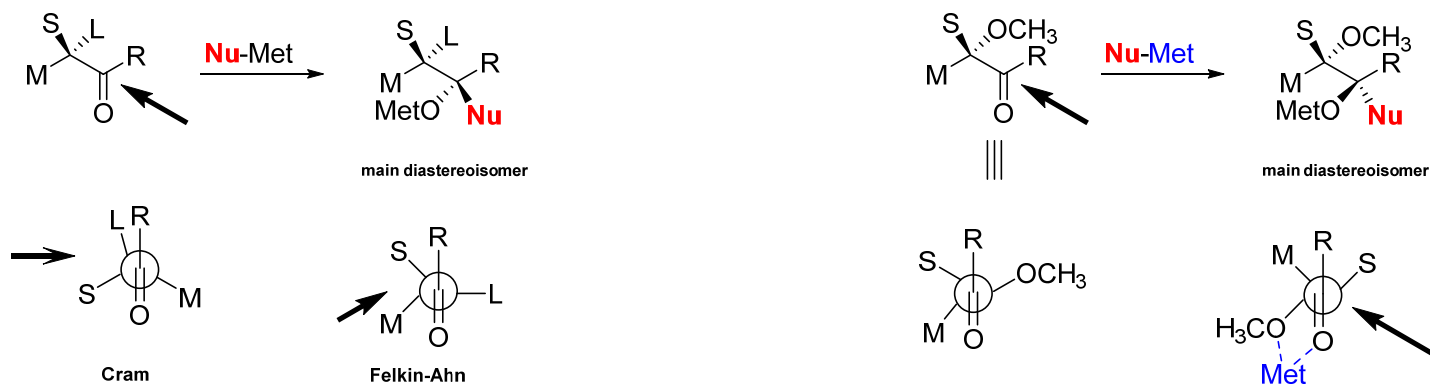




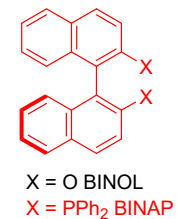
Substitution / elimination reactions



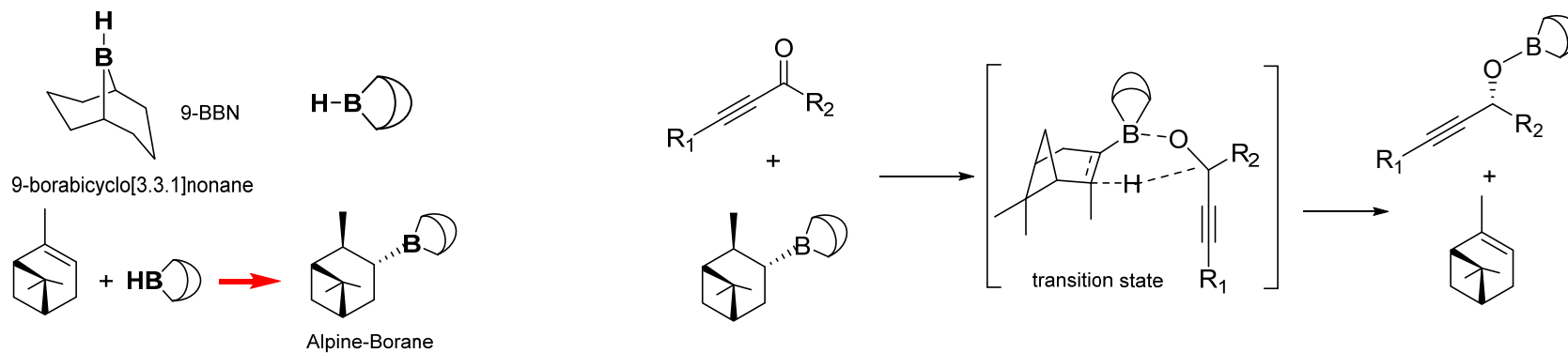
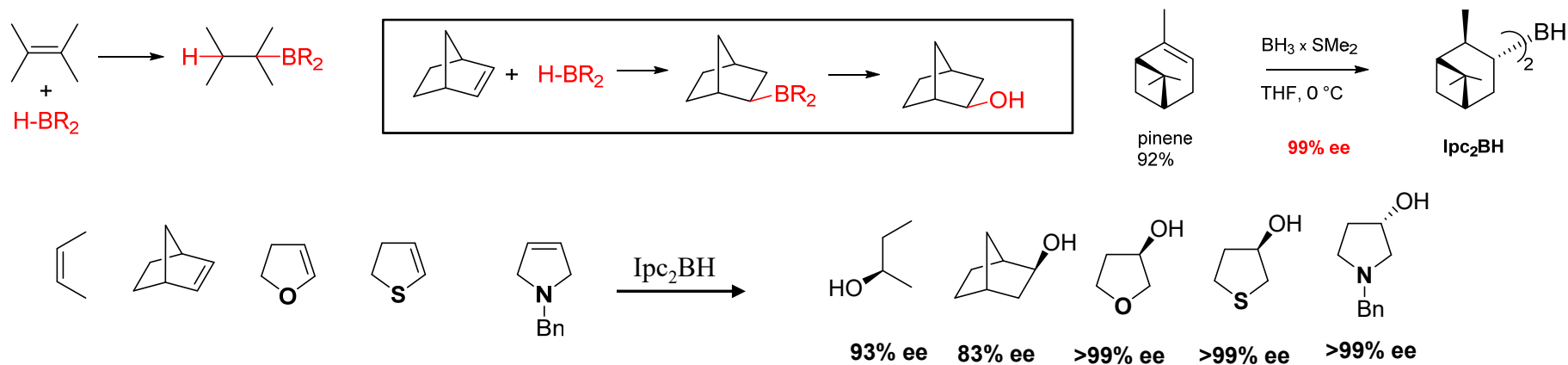
Addition to carbonyl group



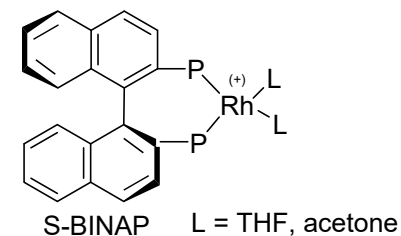
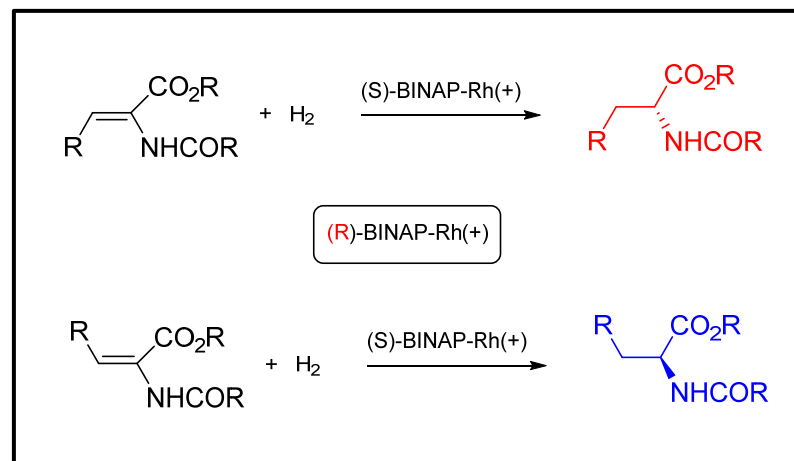
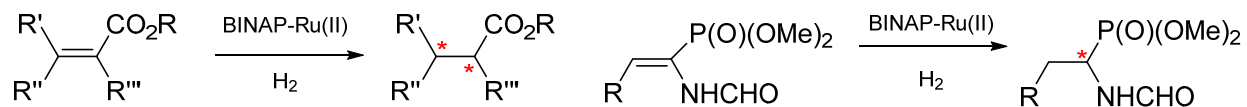
How to realize the asymmetric reduction of the carbonyl group????



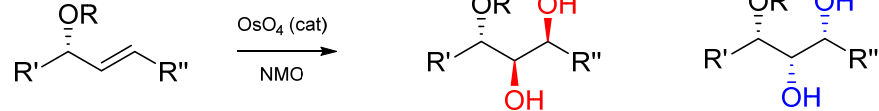
Asymmetric hydroboration of the C=C bonds H.C. Brown, P.V. Ramachandran, *Pure Appl. Chem.*, 1994, 66, 201-212



Catalytic enantioselective reduction of the C=C bonds BINAP complexes used for *ENANTIOSELECTIVE* reduction of C=C

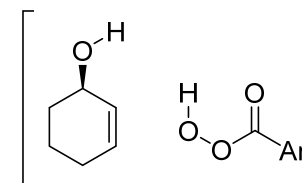
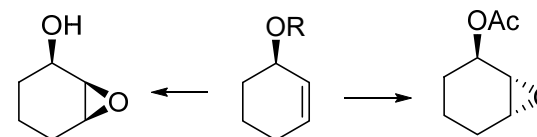


osmylation

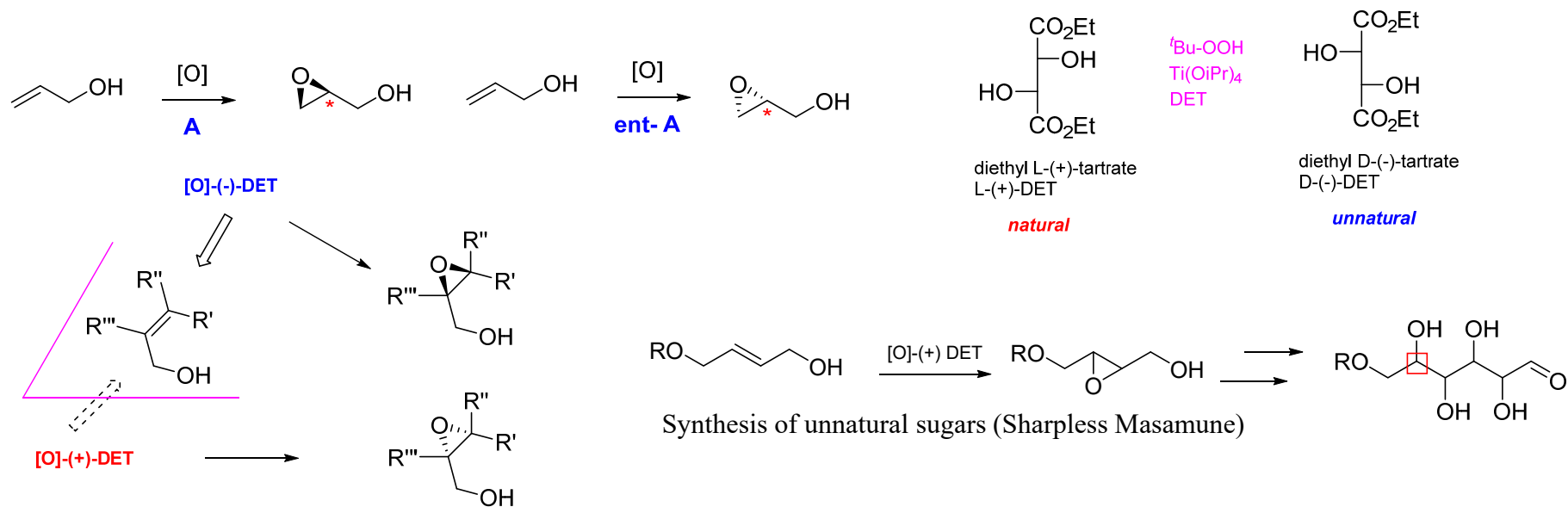


Kishi, et. al. Tetrahedron Lett. 1983, 3943; Tetrahedron, 1984, 2247

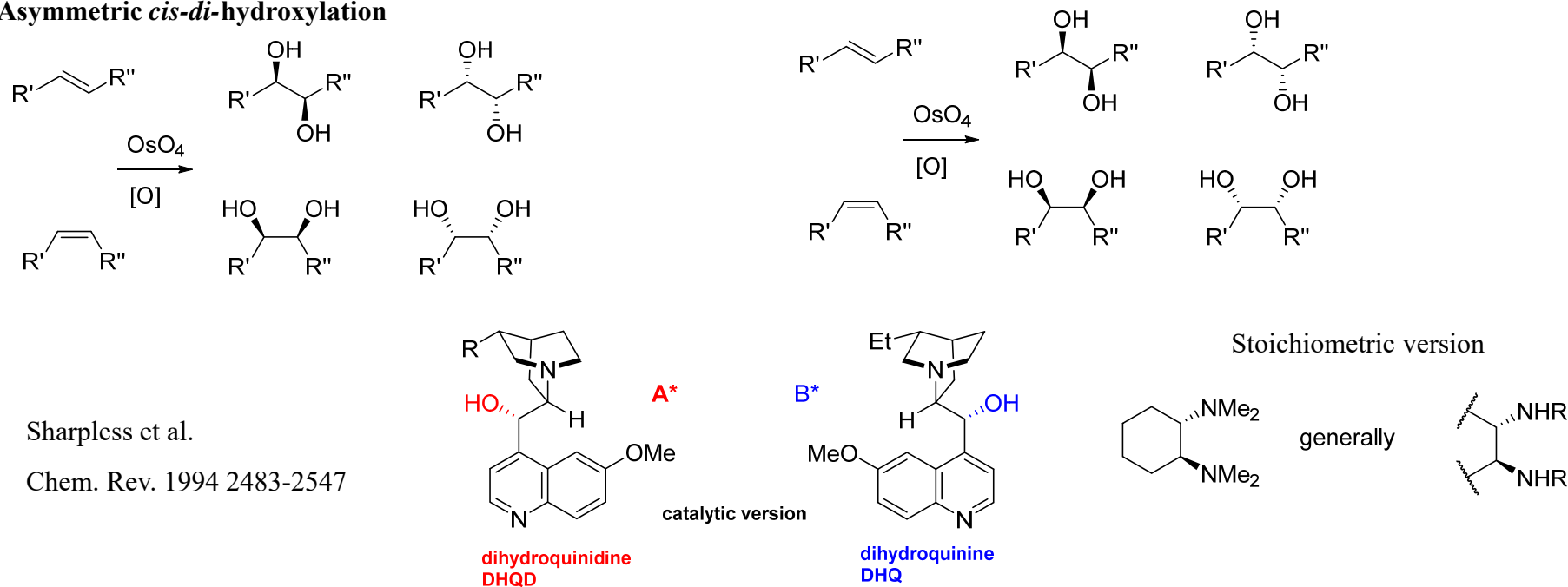
epoxidation

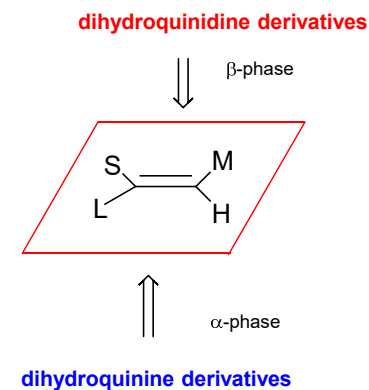
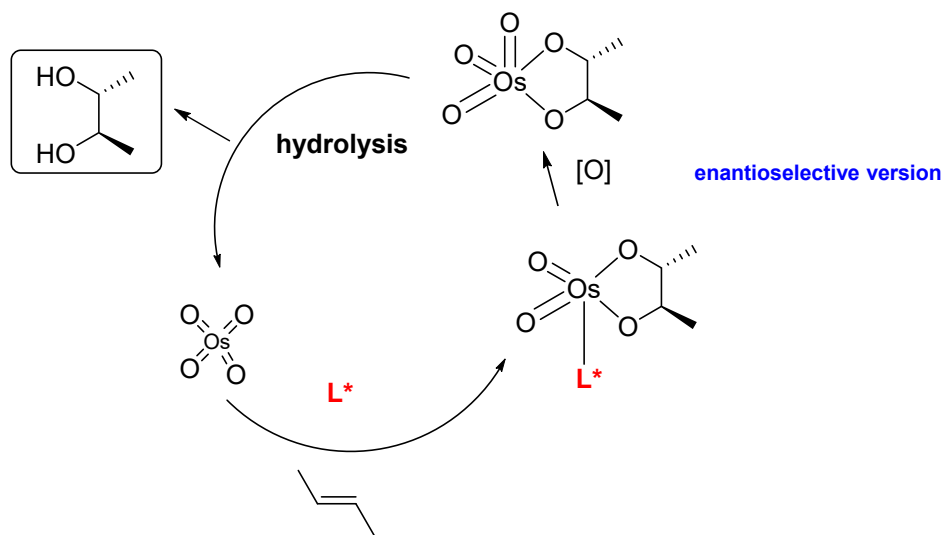
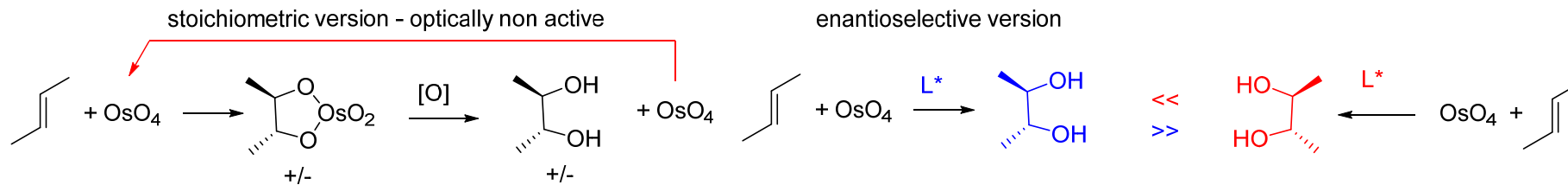


Asymmetric epoxidation of allylic alcohols

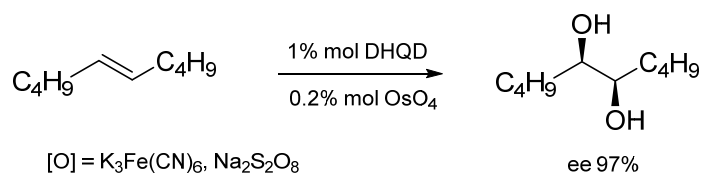


Asymmetric *cis-di*-hydroxylation





Instead of toxic and volatile OsO_4 , $\text{K}_2\text{OsO}_2(\text{OH})_4$ is used (*non-volatile*)



AD-mix commercially available mixture of osmate (catalytic amounts), oxidant $[\text{K}_3\text{Fe}(\text{CN})_6]$ excess], and chiral ligand (catalytic amount)

M.M. Heravi et al: *Tetrahedron: Asymmetry report number 176; TA*, 2017, 28, 987-1043

Asymmetric Sharpless dihydroxylation in natural products synthesis