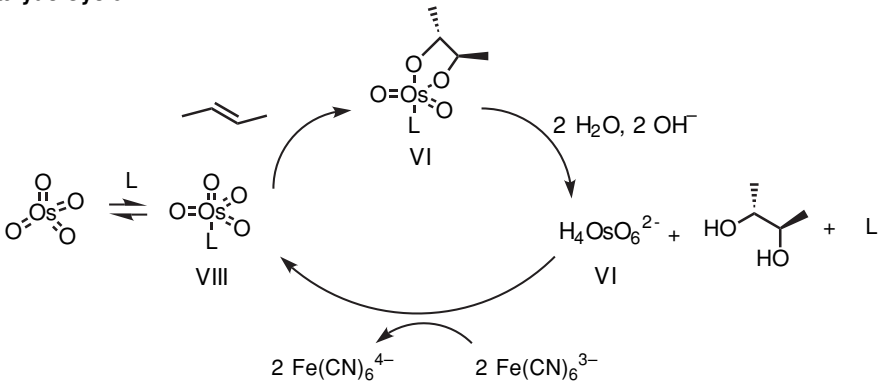
Review:

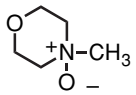
Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483-2547.

Ligands such as pyridine accelerate the osmylation of olefins (Criegee, R.; Marchand, B.; Wannowius, H. *Liebigs Ann. Chem.* **1942**, *550*, 99-133.)

Catalytic Cycle:



Turnover is achieved by re-oxidation with stoichiometric oxidants:



UpJohn Process: VanRheenen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, 1973-1976.

$K_3Fe(CN)_6$ Minato, M.; Yamamoto, K.; Tsuji, J. *J. Org. Chem.* **1990**, *55*, 766-768.

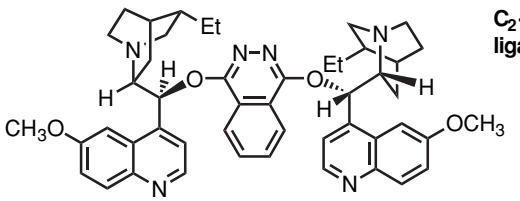
In the original Sharpless procedure, using NMO, reoxidation was believed to compete with hydrolysis, leading to a competing 2nd-cycle oxidation that was less enantioselective:

Ogino, Y.; Chen, H.; Kwong, H.-L.; Sharpless, K. B. *Tetrahedron Lett.* **1991**, *32*, 3965-3968.

Balance of evidence appears to favor 3 + 2 Mechanism (vs. 2 + 2 pathway).

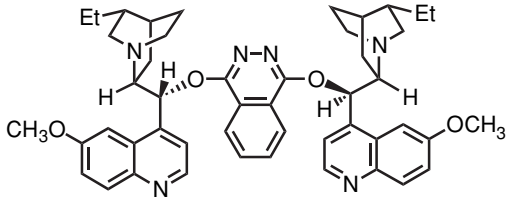
See, e.g., Corey, E.J.; Noe, M. C.; Grogan, M. J. *Tetrahedron Lett.* **1996**, *37*, 4899-4902.

DelMonte, A. J.; Haller, J.; Houk, K. N.; Sharpless, K. B.; Singleton, D. A.; Strassner, T.; Thomas, A. A. *J. Am. Chem. Soc.* **1997**, *119*, 9907-9908.



$(DHQD)_2$-PHAL
Ligand for AD-mix-β

C_2-symmetric, pseudo-enantiomeric ligands:



$(DHQ)_2$-PHAL
Ligand for AD-mix-α,
(slightly less enantioselective)

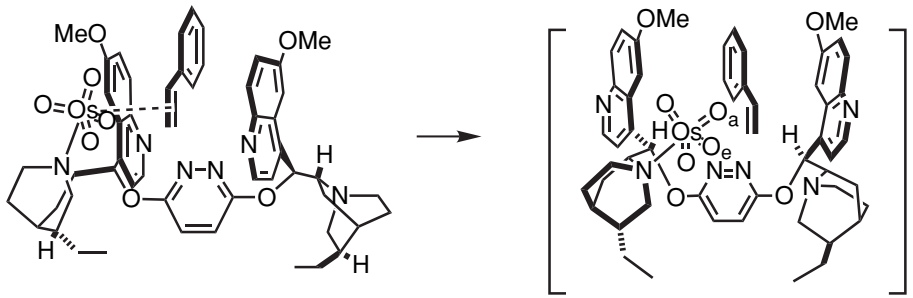
AD-mix reagents are commercially available:

1.4 g AD-mix-β will oxidize 1 mmol olefin, contains:
0.98 g $K_3Fe(CN)_6$ (3 mmol)
0.41 g K_2CO_3 (3 mmol)
0.0078 g $(DHQD)_2$-PHAL (0.01 mmol)
0.00074 g $K_2OsO_2(OH)_4$ (0.002 mmol)

Conditions: *t*-BuOH, H_2O (1:1), 0 °C, 6-24 h

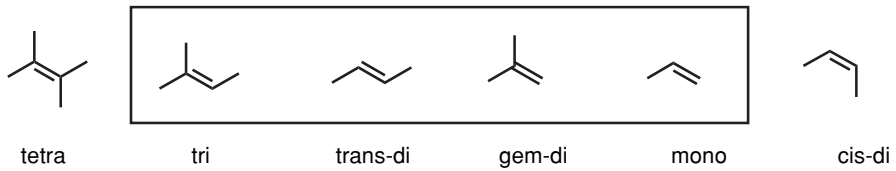
Sharpless, K. B., et al. *J. Org. Chem.* **1992**, *57*, 2768-2771.

Corey proposes a U-shaped binding pocket:

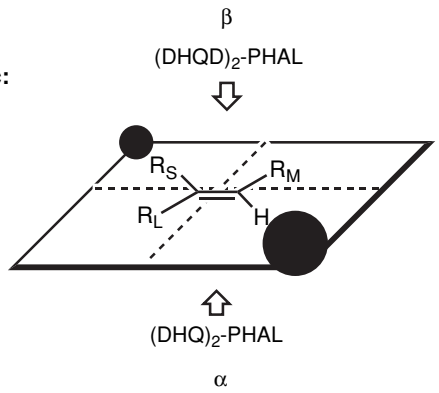


Corey, E. J.; Guzman-Perez, A.; Noe, M. C. *Tetrahedron Lett.* **1995**, *36*, 3481-3484.

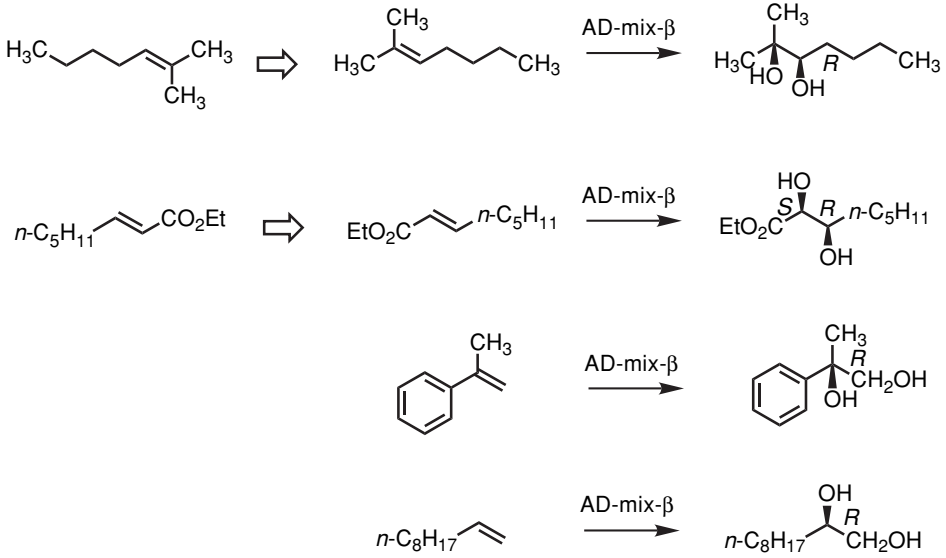
4 of 6 Olefin substitution classes are successfully dihydroxylated:

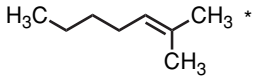
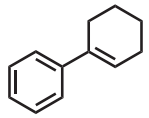
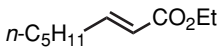
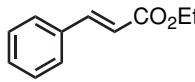
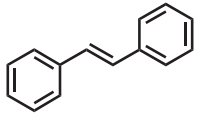
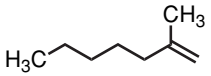
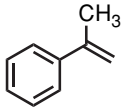
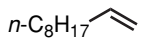
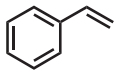


Mnemonic:



Application of Mnemonic:



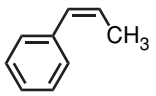
	AD-mix-β [$(DHQD)_2$-PHAL]	AD-mix-α [$(DHQ)_2$-PHAL]
	% ee, config.	% ee, config.
 *	98, *R*	95, *S*
 *	99, *R,R*	97, *S, S*
 *	97, *R,R*	93, *S, S*
 *	99, 2*S*, 3*R*	96, 2*R*, 3*S*
 *	97, 2*S*, 3*R*	95, 2*R*, 3*S*
 *	>99.5, *R,R*	>99.5, *S, S*
	78, *R*	76, *S*
	94, *R*	93, *S*
	84, *R*	80, *S*
	97, *R*	97, *S*

* addition of $CH_3SO_2NH_2$ leads to faster reaction

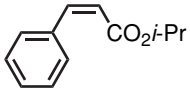
from: Sharpless, K. B., et al. *J. Org. Chem.* **1992**, *57*, 2768-2771.

Cis-Disubstituted Olefins are generally poor substrates. With a modified catalyst, DHQD-IND, fair to good enantioselectivities can be obtained:

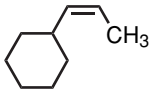
ee at 0 °C



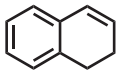
72 (1*R*, 2*S*)



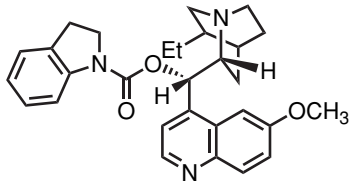
80, (2*S*, 3*R*)



56, (1*R*, 2*S*), 44% ee of enantiomer with DHQ-IND



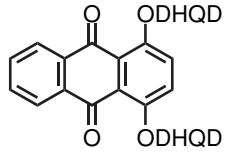
16, (1*R*, 2*S*)



DHQD-IND

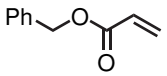
Wang, L.; Sharpless, K. B. *J. Am. Chem. Soc.* **1992**, *114*, 7568-7570.

$(DHQD)_2AQN$ is often a superior ligand:

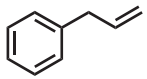


$(DHQD)_2AQN$

90% ee vs. 63% ee, $(DHQD)_2PHAL$



88% ee vs. 77% ee, $(DHQD)_2PHAL$



78% ee vs. 44% ee, $(DHQD)_2PHAL$

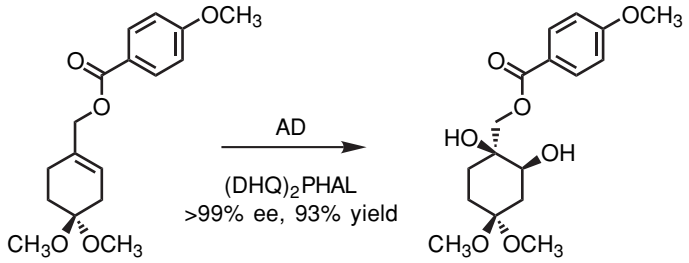
Becker, H.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 448-451.

a few tetra-substituted olefins work well, see:
Sharpless, K. B., et al. *J. Am. Chem. Soc.* **1993**, *115,* 8463-8464.

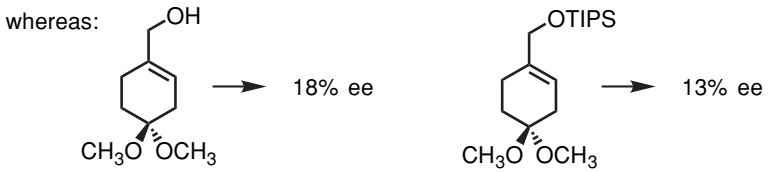
93% ee, 94% yield

a best case, ee's and yields are not yet generally high

Allylic 4-methoxybenzoates are particularly good substrates:

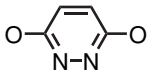


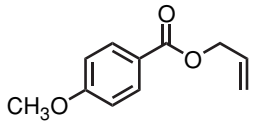
whereas:



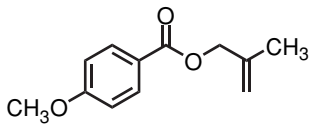
AD, $(DHQD)_2PYDZ$

PYDZ =

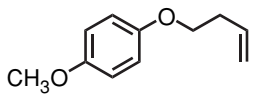




>99% yield, 98% ee



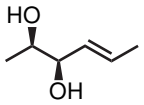
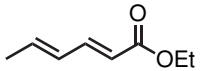
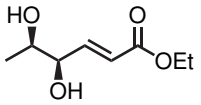
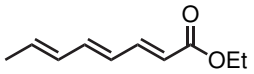
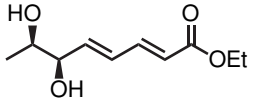
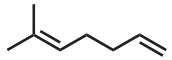
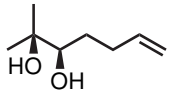
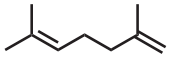
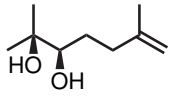
98% yield, 97% ee



96% yield, 91%ee

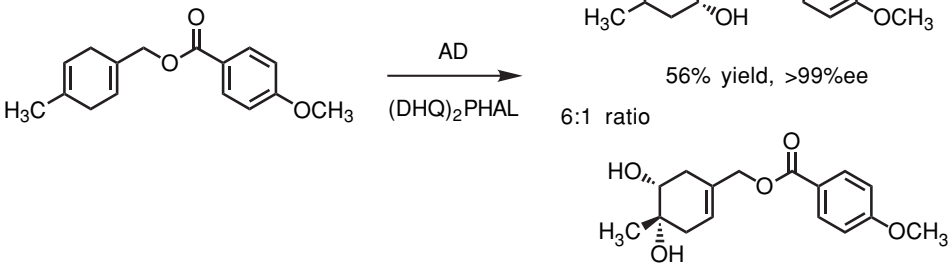
Corey, E. J.; Guzman-Perez, A.; Noe, M. C. *J. Am. Chem. Soc.* **1995**, *117*, 10805-10816.

Regioselectivity of AD with Diene Substrates ($(DHQD)_2$-PHAL as Ligand):

Substrate	Product	% yield, % ee
		78, 93
		78, 92
		93, 95
		73, 98
		70, 98

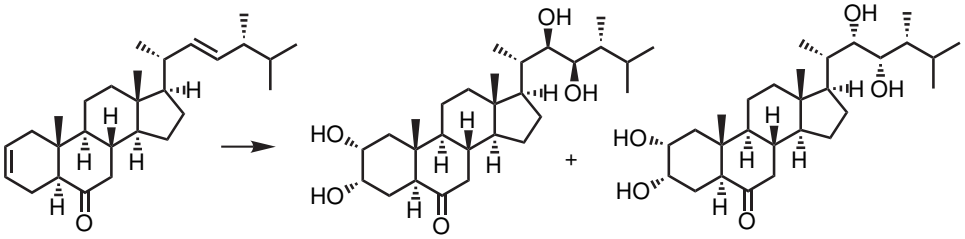
in general, AD is selective for more electron-rich double bond

Xu, D.; Crispino, G. A.; Sharpless, K. B. *J. Am. Chem. Soc.* **1992**, *114*, 7570-7571.



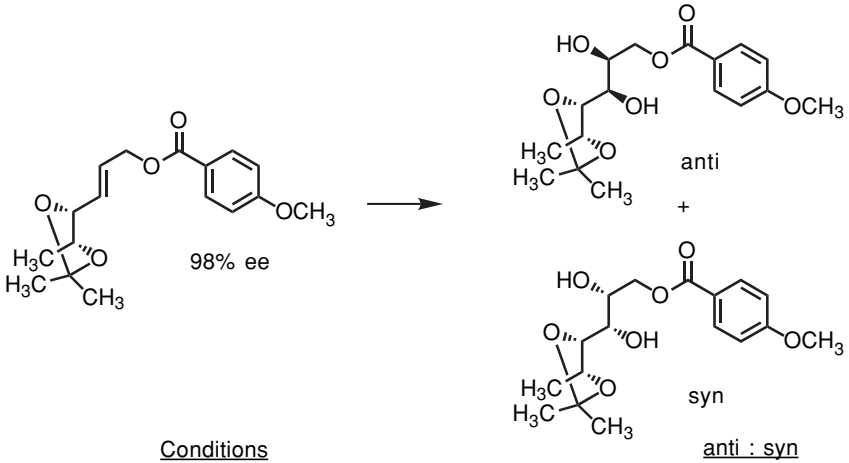
Corey, E. J.; Guzman-Perez, A.; Noe, M. C. *J. Am. Chem. Soc.* **1995**, *117*, 10805-10816.

Use of AD with Chiral Olefins:



OsO_4 alone	1 : 1.6
$(DHQD)_2$-PHAL	10 : 1

Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483-2547, and refs. therein.



Conditions		anti : syn
OsO_4, NMO	88% yield (mixture)	1.9 : 1
$(DHQ)_2$PHAL (matched)	86% yield (anti)	54 : 1
$(DHQD)_2$PYDZ (mismatched)	86% yield (syn)	1 : 35

Guzman-Perez, A.; Corey, E. J. *Tetrahedron Lett.* **1997**, *38*, 5941-5944.