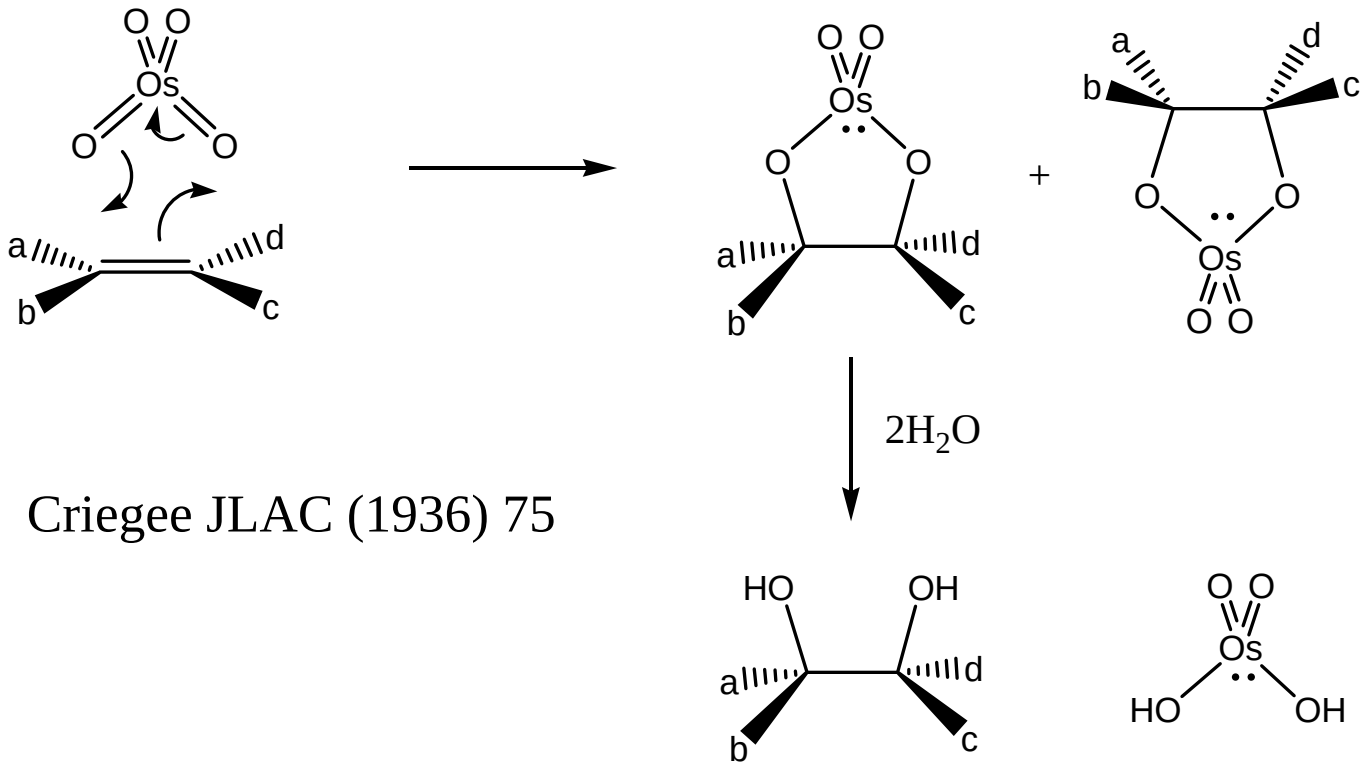
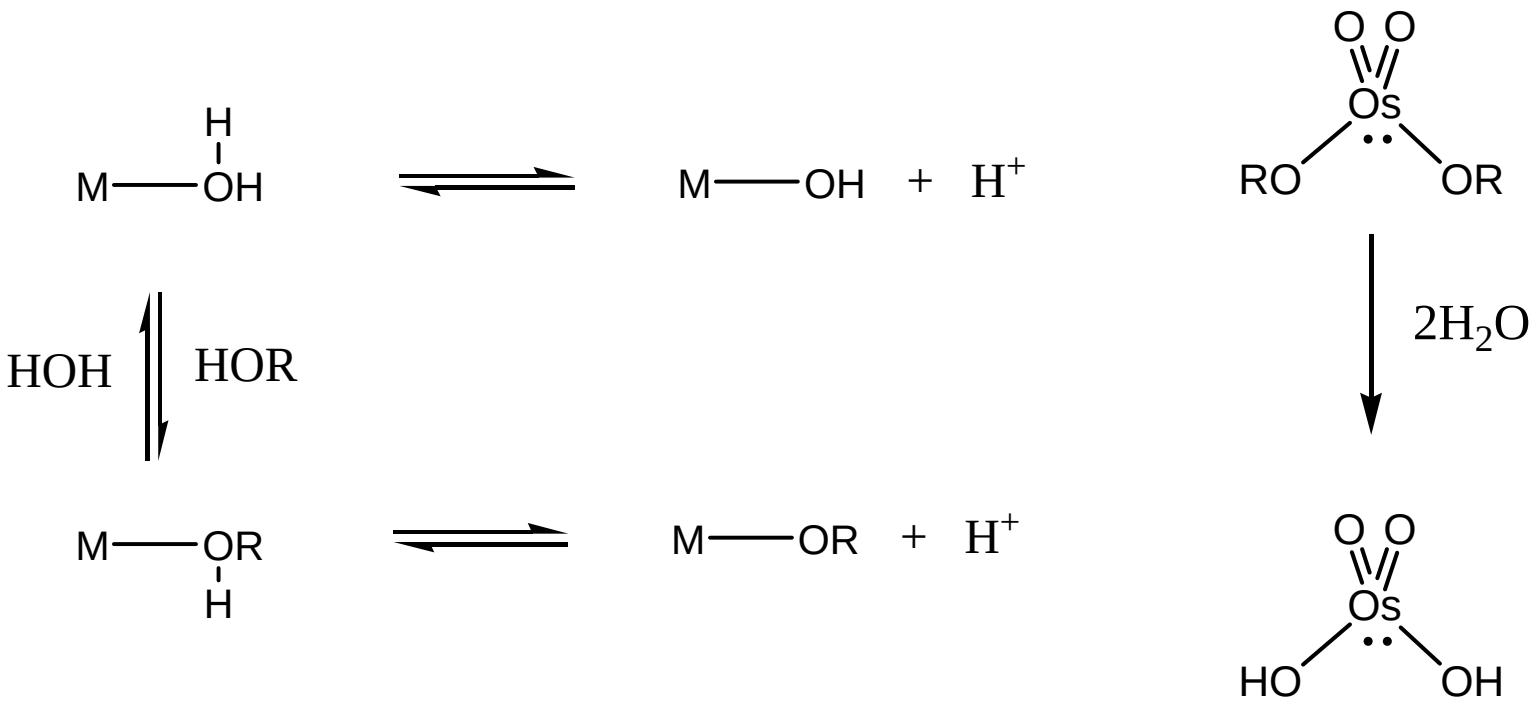
Sharpless Dihydroxylation



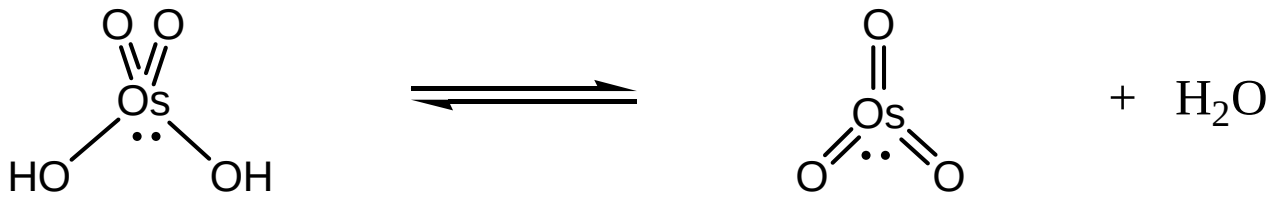
Criegee JLAC (1936) 75

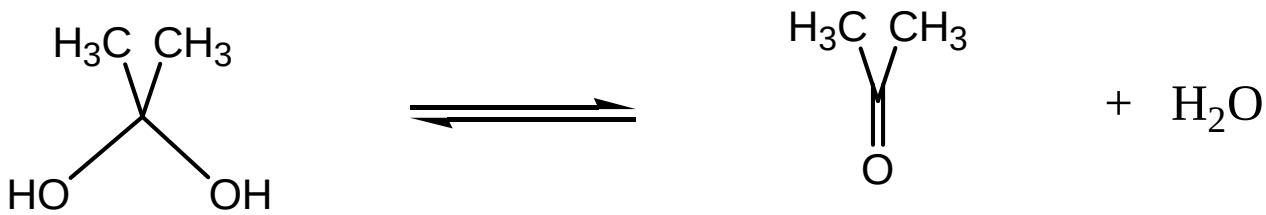
Jacobsen, Marko, France, Svendsen, Sharpless JACS (1989) 737

Water-Alcohol Exchange



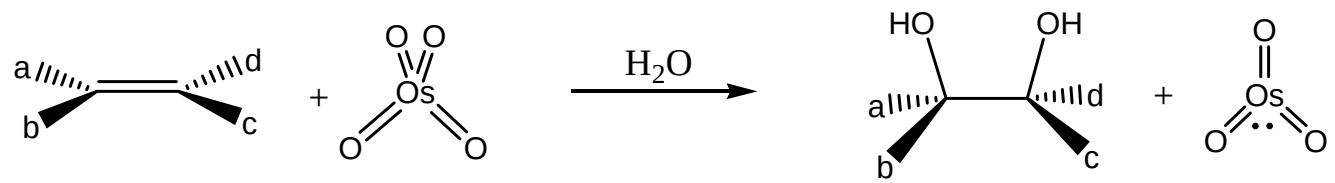
Hydration

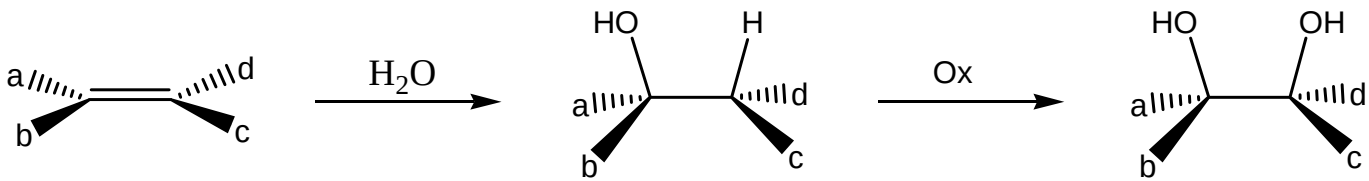




No Redox

Oxidation/Reduction

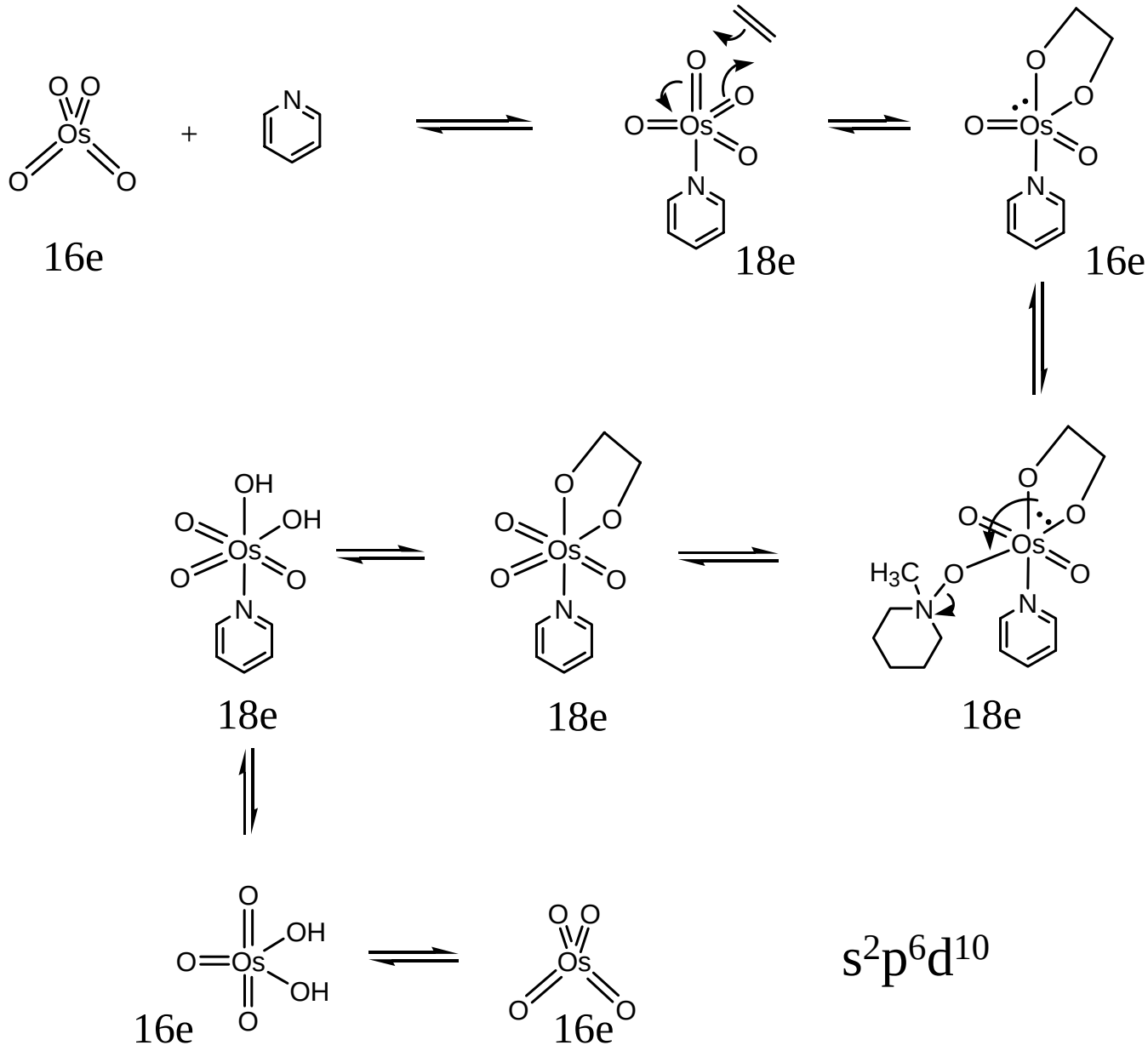




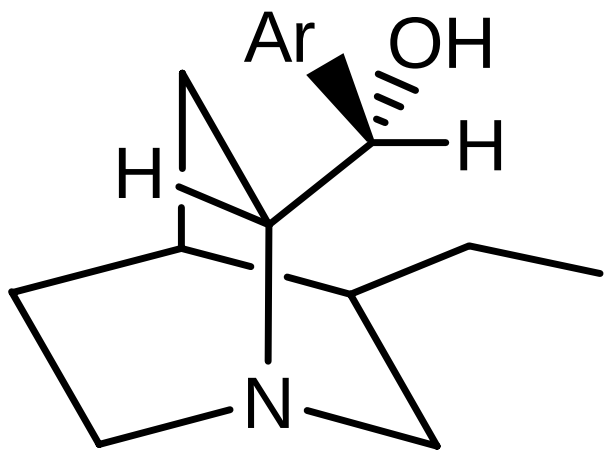
CH_4 —Ox→ CH_3OH

OsO_4 Os(VIII) O^{2-}

OsO_3 Os(VI)

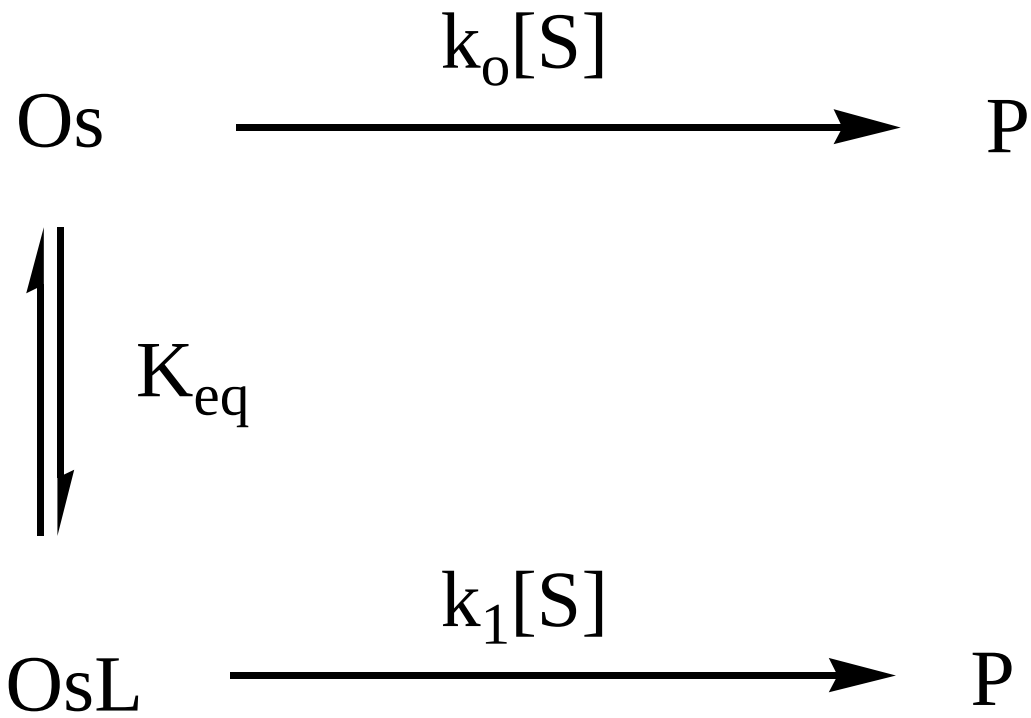

16e
18e
16e
18e
18e
18e
16e
16e
$s^2p^6d^{10}$

Asymmetric Dihydroxylation (AD)



DHQD: Dihydroquinidine

Kinetics



$$dP/dt = k_o[Os][S] + k_1[OsL][S] \ldots\ldots(1)$$

$$K_{EQ} = [OsL]/([Os][L]) \ldots\ldots\ldots\ldots\ldots(2)$$

$$[Os] + [OsL] = [Os]_T \ldots\ldots\ldots\ldots\ldots\ldots(3)$$

From (2) and (3),

$[Os] + K_{EQ}[Os][L] = [Os]_T$

$[Os] = [Os]_T/(K_{EQ}[L]+1)$……(4)

Similarly from (2) and (3)

$[OsL]/(K_{EQ}[L]) + [OsL] = [Os]_T$

$[OsL] = K_{EQ}[L][Os]_T/(K_{EQ}[L]+1)$……(5)

Substituting (4) and (5) into (1)

$dP/dt = (k_o + k_1K_{EQ}[L])[Os]_T[S]/(K_{EQ}[L]+1)$

$k_{obs} = (k_o + k_1K_{EQ}[L])/(K_{EQ}[L]+1)$……..(6a)

$k_{obs} = k_o + (K_{EQ}[L](k_1-k_o))/(K_{EQ}[L]+1)$……..(6)

$k_1 = k_f + k_s$

$ee\% = (k_f - k_s)/(k_f + k_s)$

$ee\% = (\%R - \%S)$absolute value

From equation (6a),

$k^f_{obs} = (k_o/2 + k_f K_{EQ}[L])/(K_{EQ}[L]+1)$

$k^s_{obs} = (k_o/2 + k_s K_{EQ}[L])/(K_{EQ}[L]+1)$

$(ee\%)obs = (k_f - k_s)\, K_{EQ}[L]/(k_o + k_1 K_{EQ}[L])$

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Kinetic Role of the Alkaloid Ligands in Asymmetric Catalytic Dihydroxylation

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Received August 25, 1988

$$\Delta k = k_2 - k_0 = \frac{(k_1 - k_0)K_{eq}[\text{amine}]}{K_{eq}[\text{amine}] + 1} \qquad (1)$$

$$\text{ee} = \frac{(k_f - k_s)K_{eq}[\text{amine}]}{k_1 K_{eq}[\text{amine}] + k_0} \qquad (2)$$

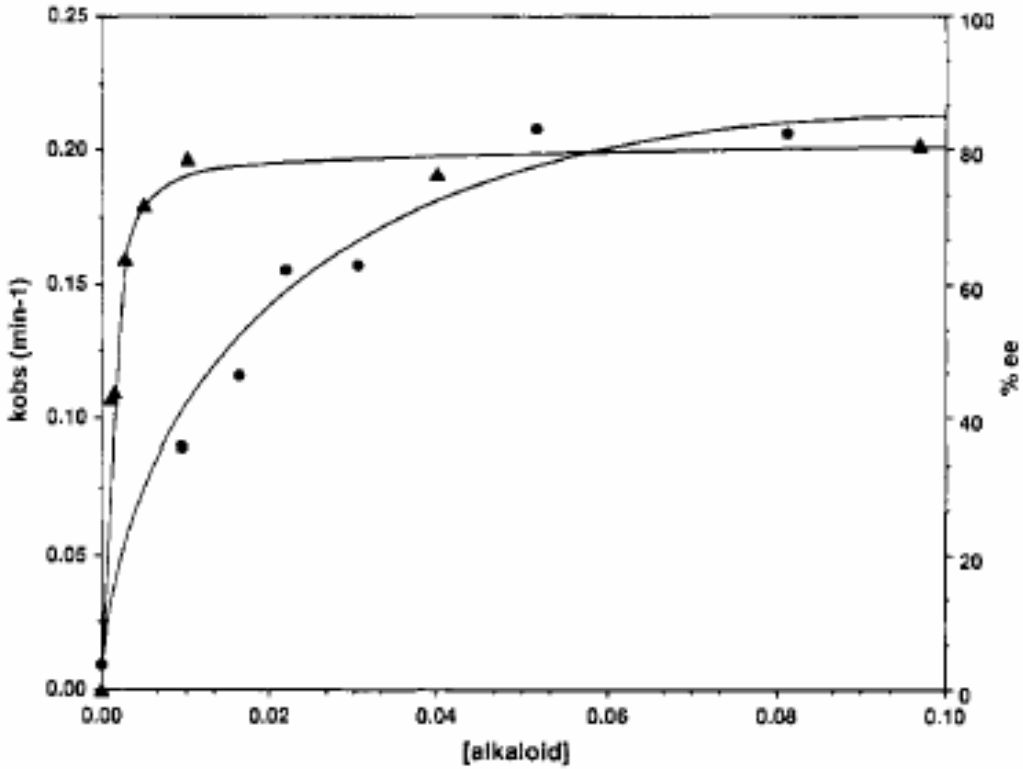
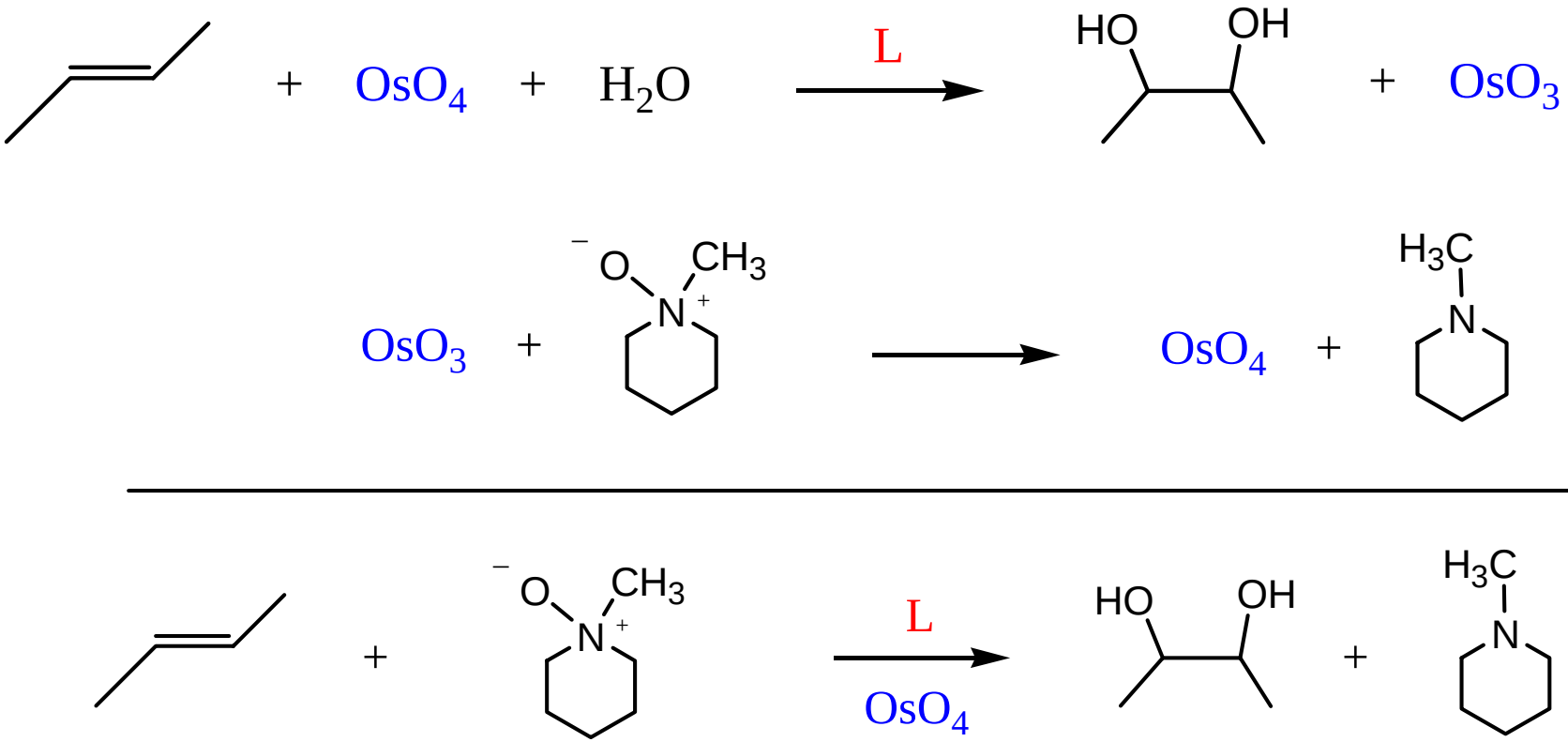
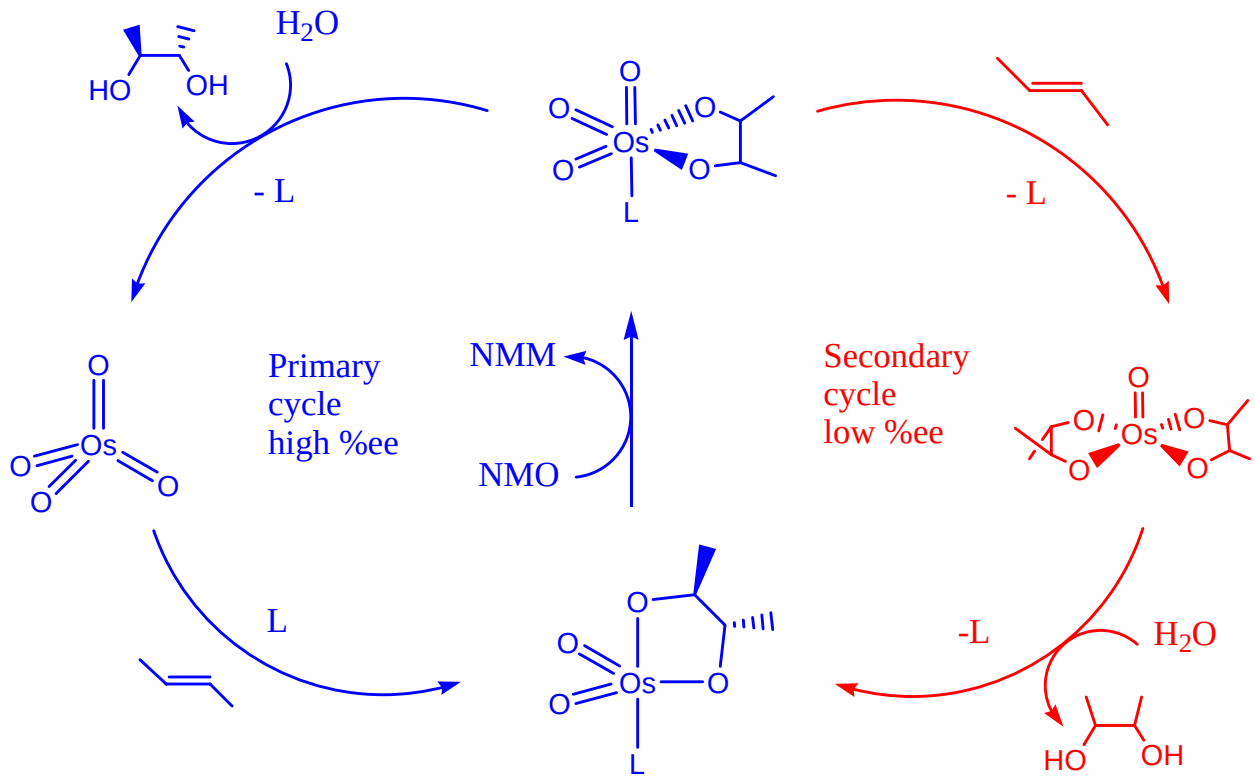


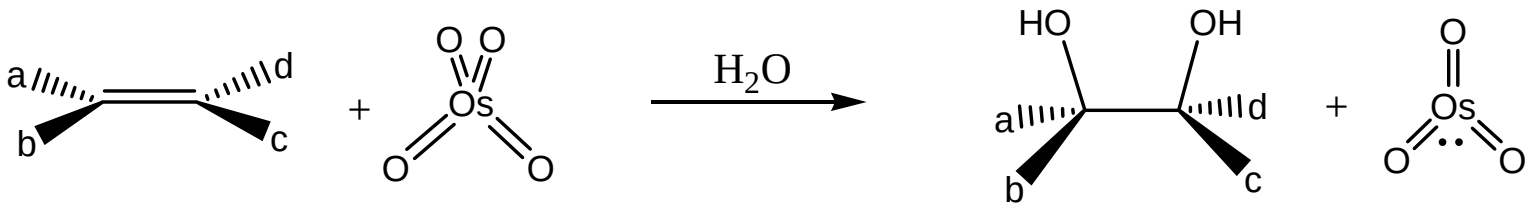
Figure 1. Plot of the concentration of alkaloid ligand **1** vs observed rate constant k_{obsd} (●) and % ee (▲) for the catalytic dihydroxylation of *trans*-stilbene. Conditions: 25 °C, $[OsO_4]_0 = 3.8 \times 10^{-4}$ M, $[NMO]_0 = 0.2$ M, $[\text{stilbene}]_0 = 0.1$ M.


+ OsO4 + H2O
L
HO
OH
+ OsO3
OsO3 +
O
CH3
N
+
OsO4 +
H3C
N
+
O
CH3
N
+
L
OsO4
HO
OH
+
H3C
N

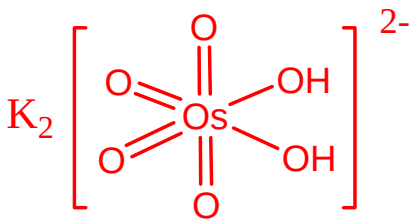
Catalytic Cycle

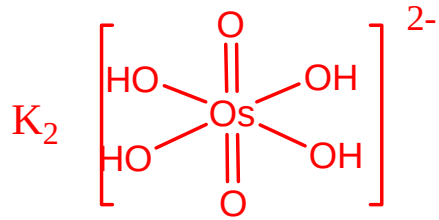


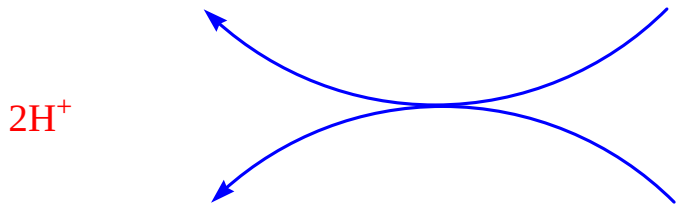
Aqueous condition



Os(VIII) Os(VI)





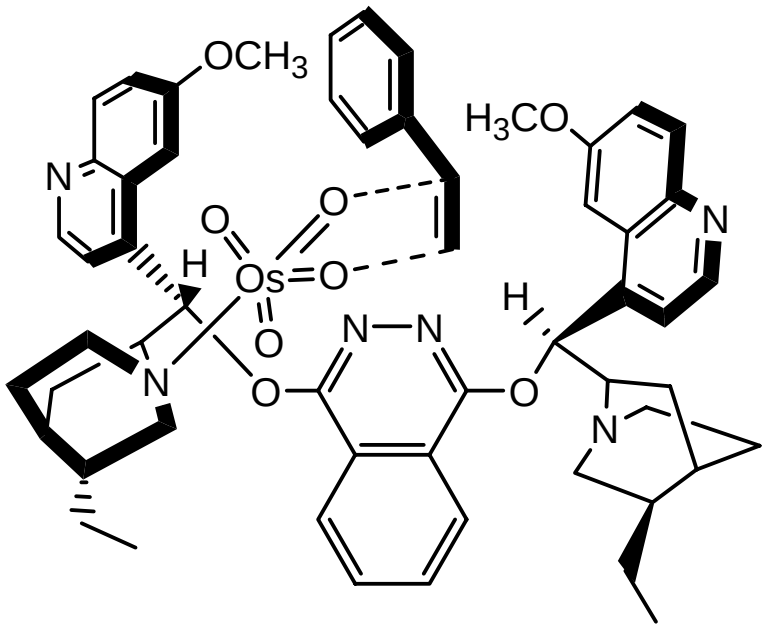


$2H^+$ $2K^+$

$2K_4Fe(CN)_6$ $2K_3Fe(CN)_6$

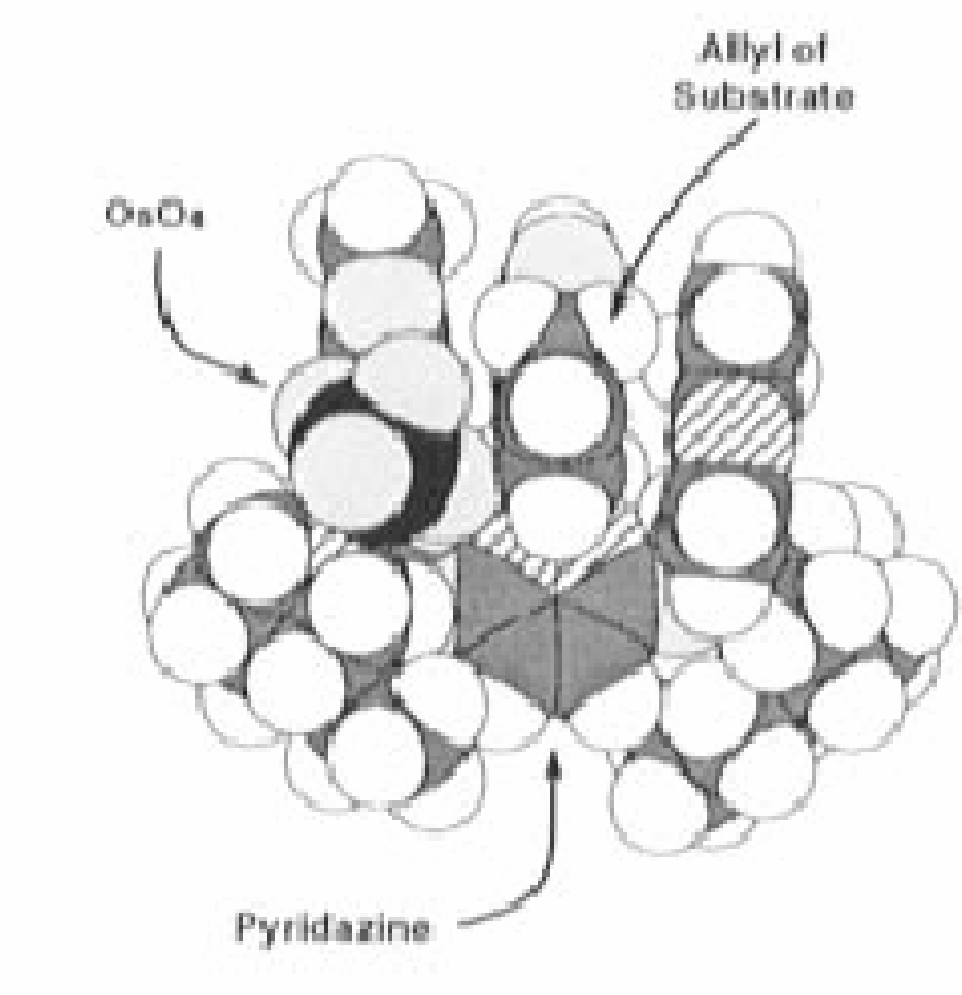
2Fe(II) 2Fe(III)

Origin of Stereoselectivity

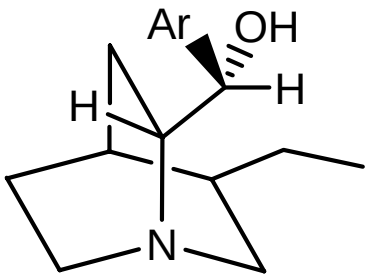


$(DHQD)_2PHAL$

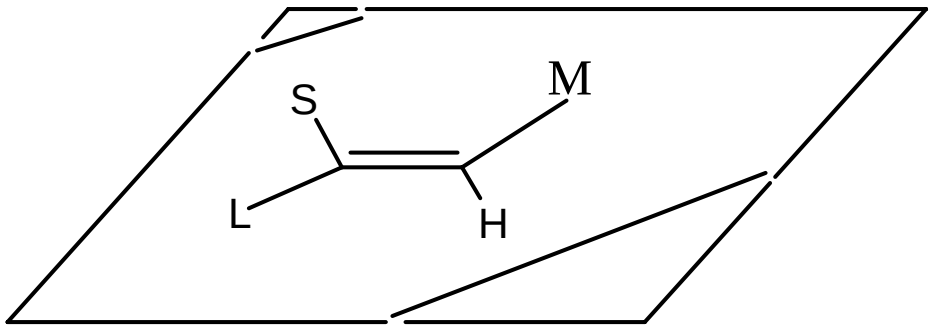
Corey, JACS (1996) p319

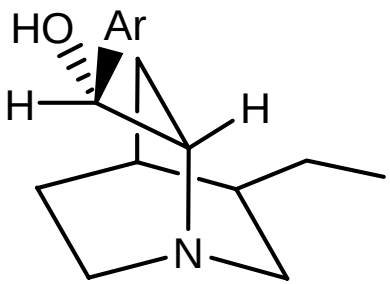

Allyl of
Substrate
OsO4
Pyridazine

Mnemonic



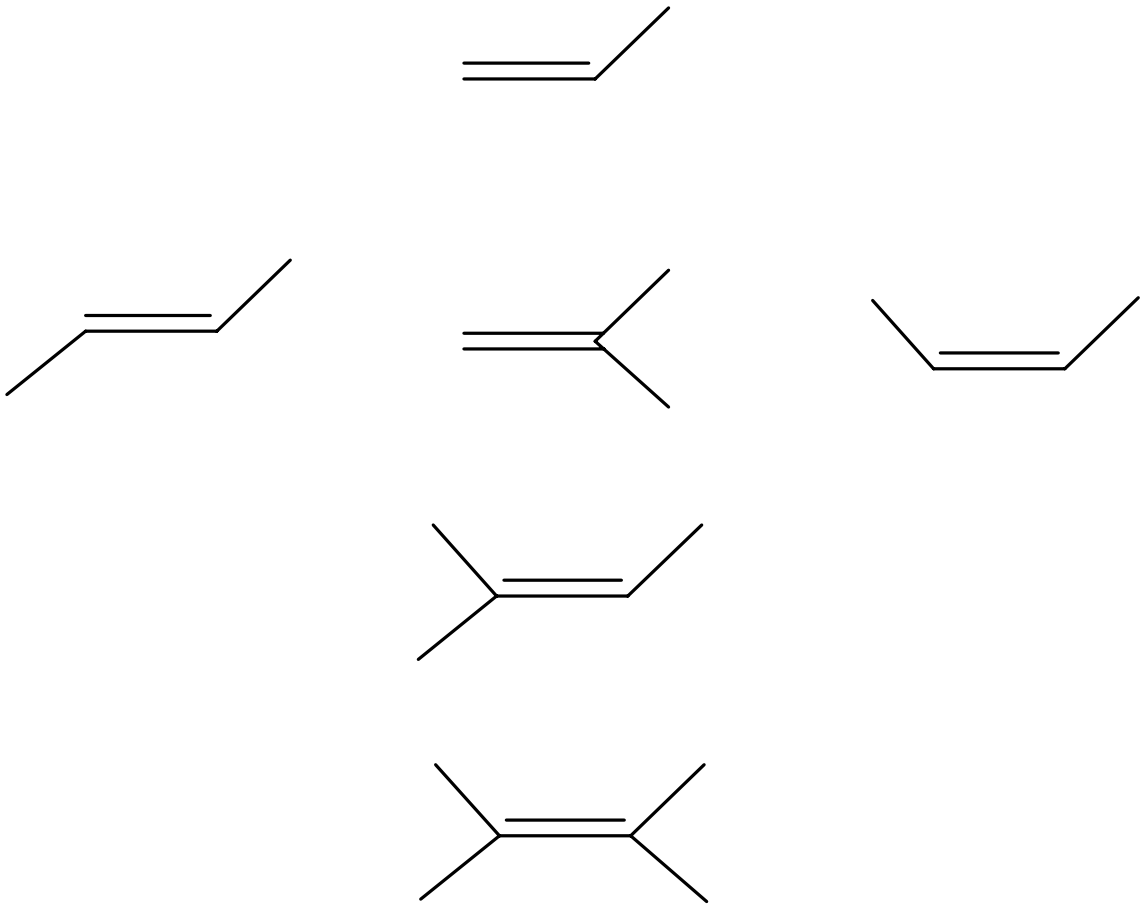
DHQD: Dihydroquinidine



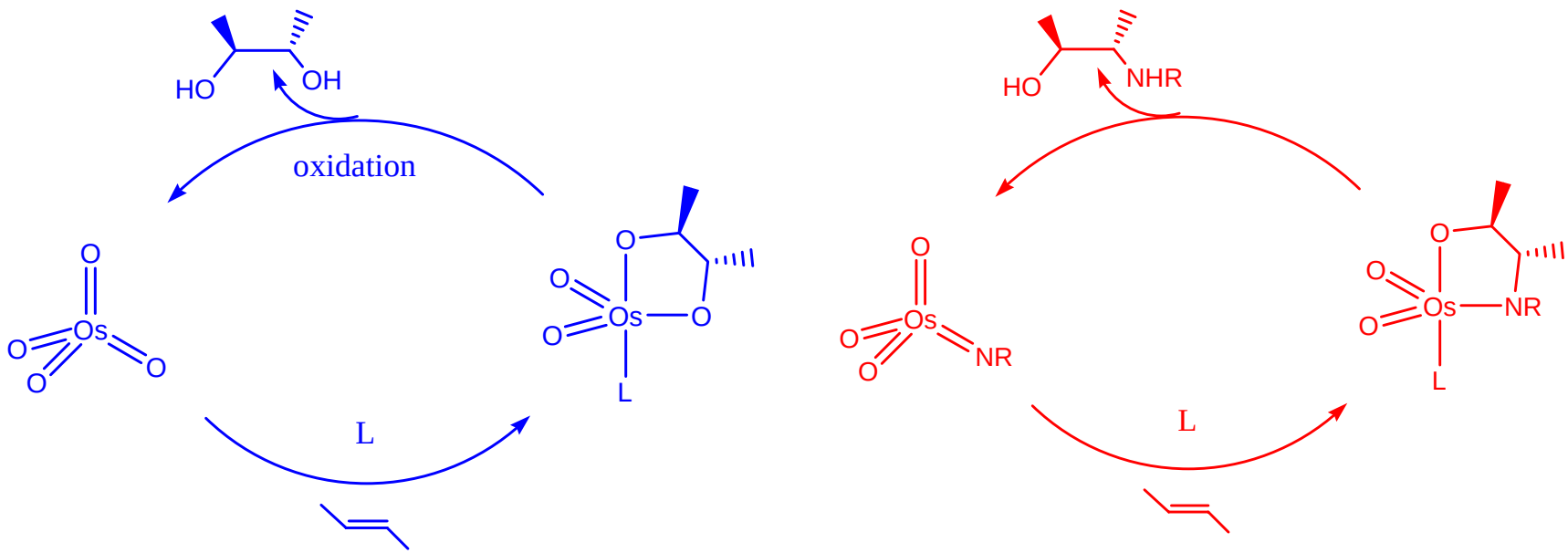


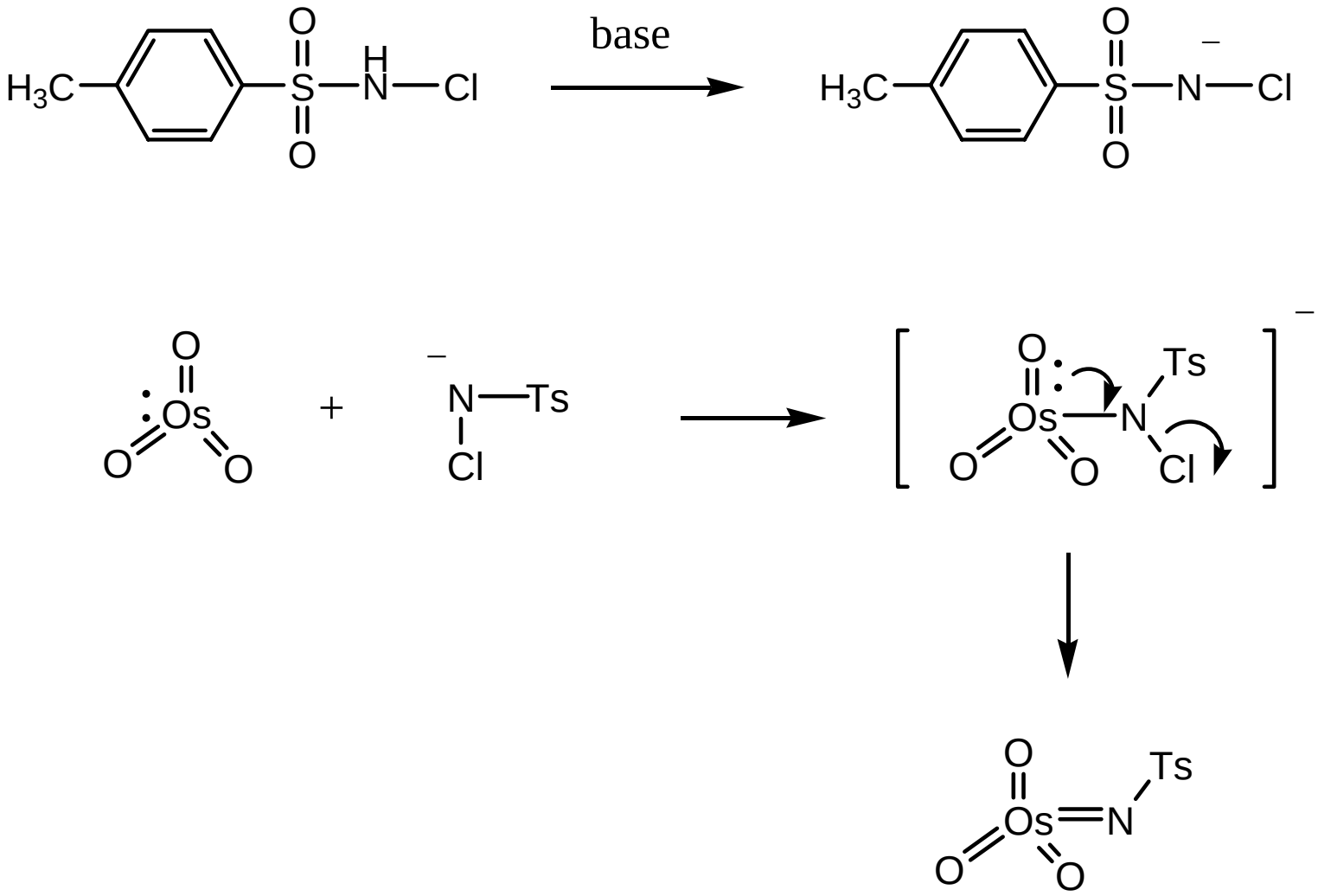
DHQ: Dihydroquinine

Alkenes

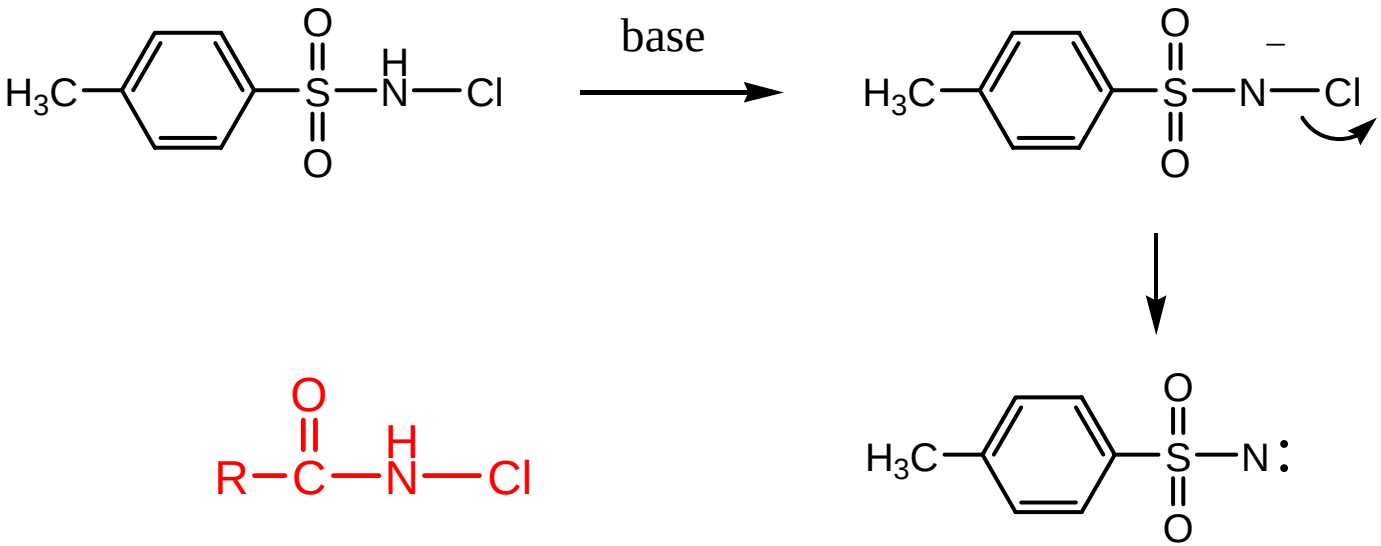


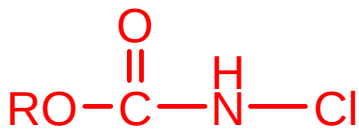
Asymmetric Aminohydroxylation (AA)



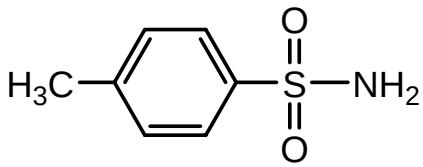

base

Nitrene Sources





pKa



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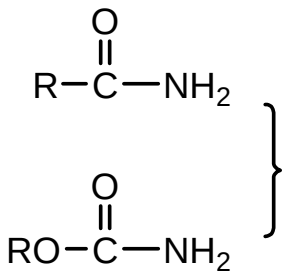
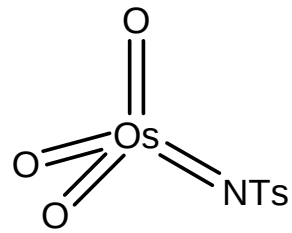
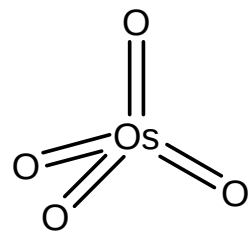


17

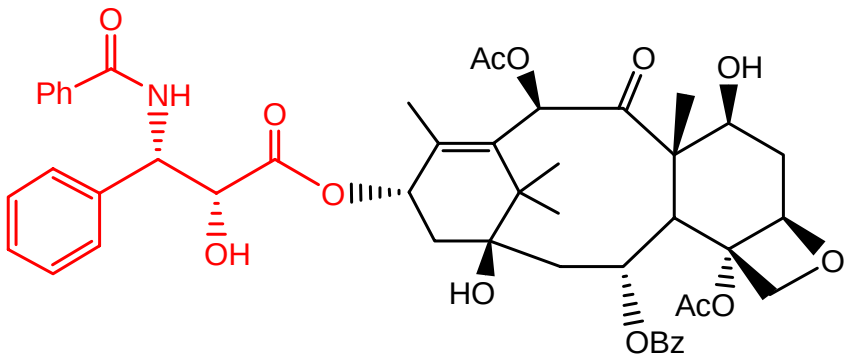


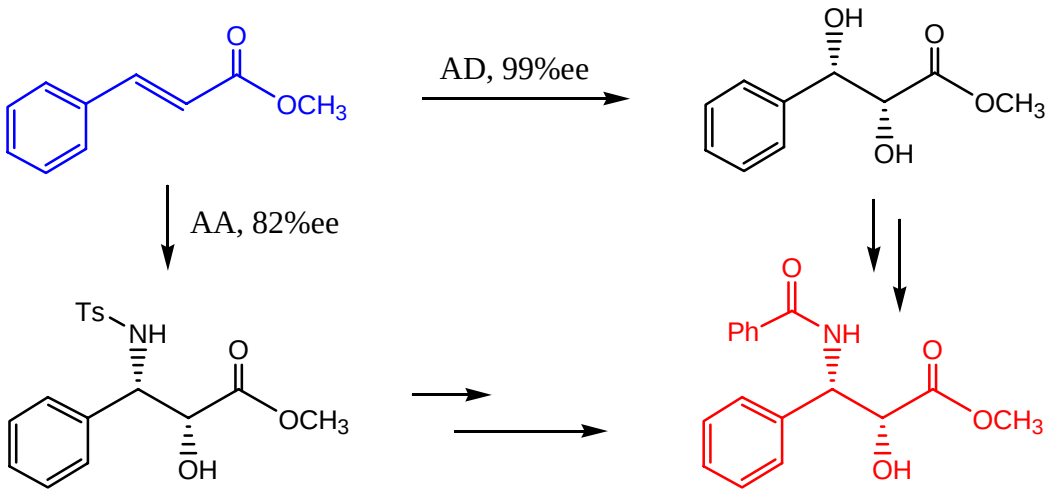
H_2O 16



NH_3 35

Paclitaxel (Taxol)





AD: *JOC* (1994) p5104
AA: *Acta Chem. Scand.* (1996) *50*, p649