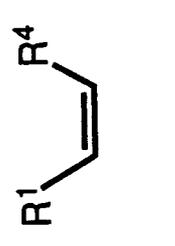
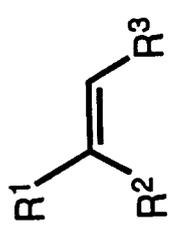


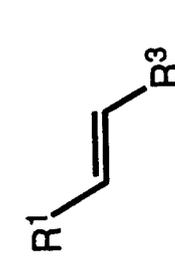
tetra-



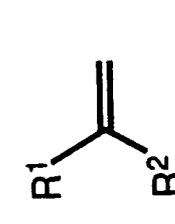
cis-di-



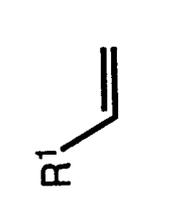
tri-



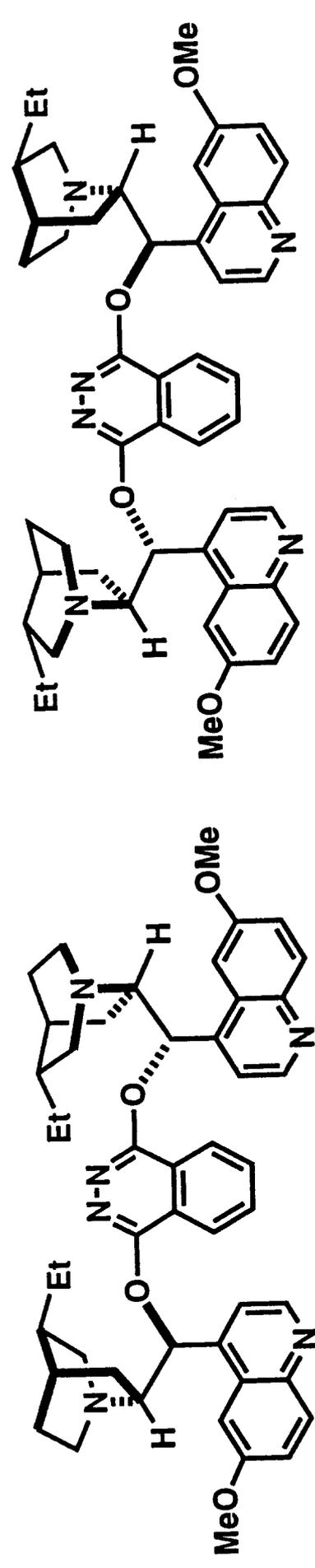
trans-di-



gem-di-



mono-



(DHQ)₂-PHAL,

Ligand used in AD-mix- α

(DHQD)₂-PHAL,

Ligand used in AD-mix- β

Substrate for

Olefin

AE

AD



>95% ee

NR



~80% ee

>95% ee



>95% ee

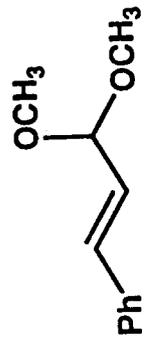
30-50% ee *



>95% ee

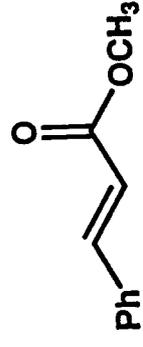
NR

X = OAc, OBn, N₃, Cl



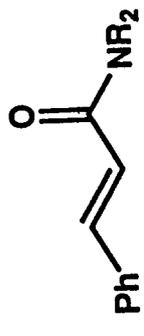
>95% ee

NR



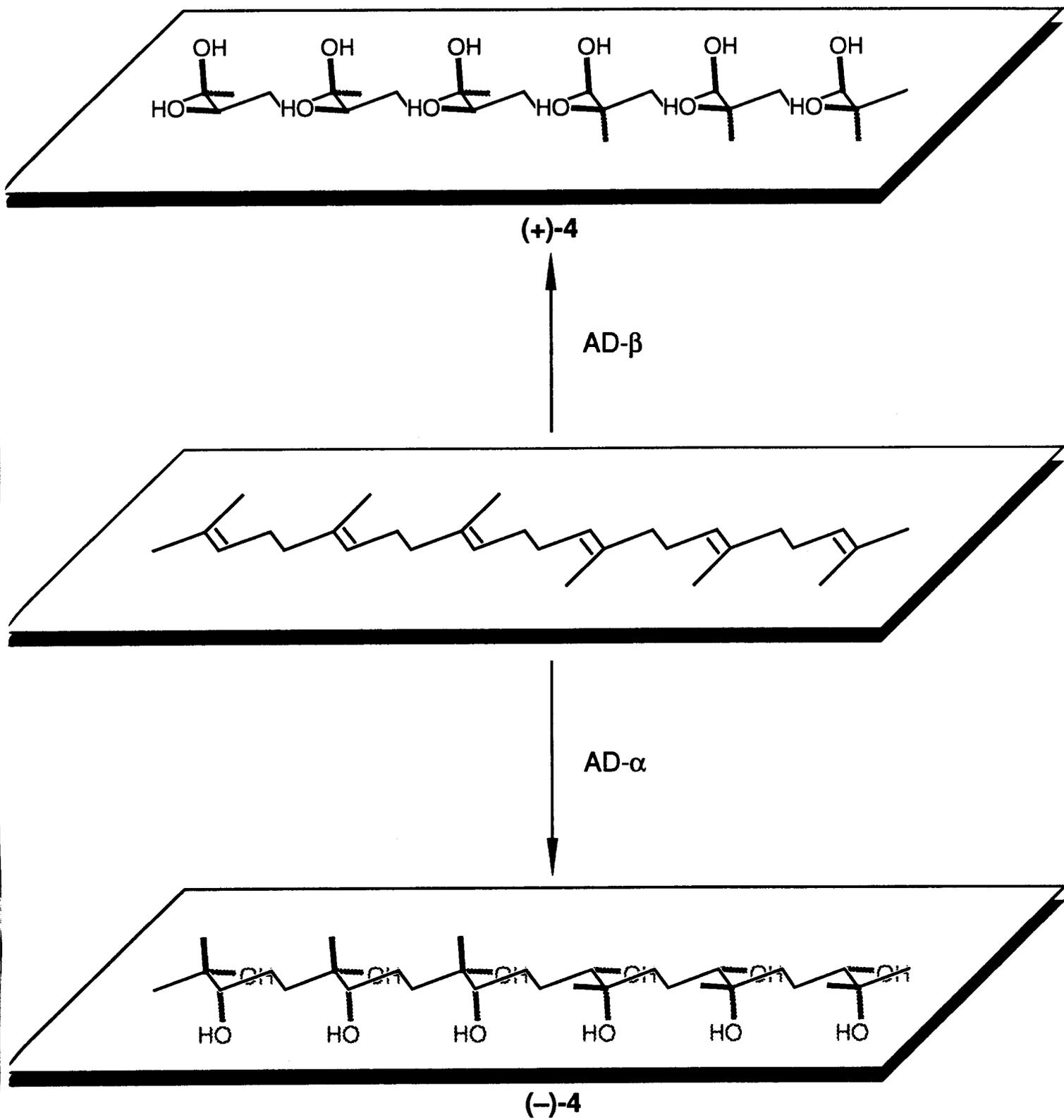
>95% ee

NR

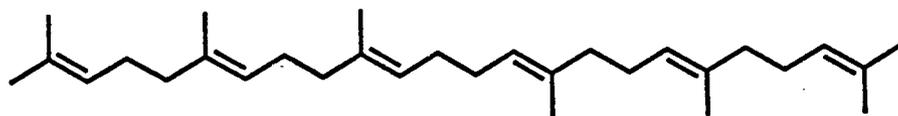


>95% ee

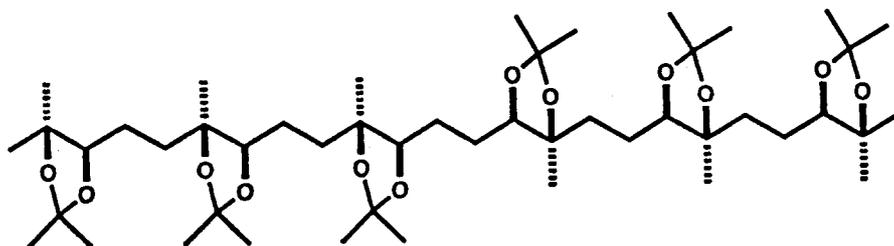
NR



Scheme 2: The asymmetric dihydroxylation (AD) of squalene using the dihydroquinidine based ligand (AD- β) and the dihydroquinine based ligand (AD- α).



1. AD- β
2. Acetone,
PTSA } 3x



78%

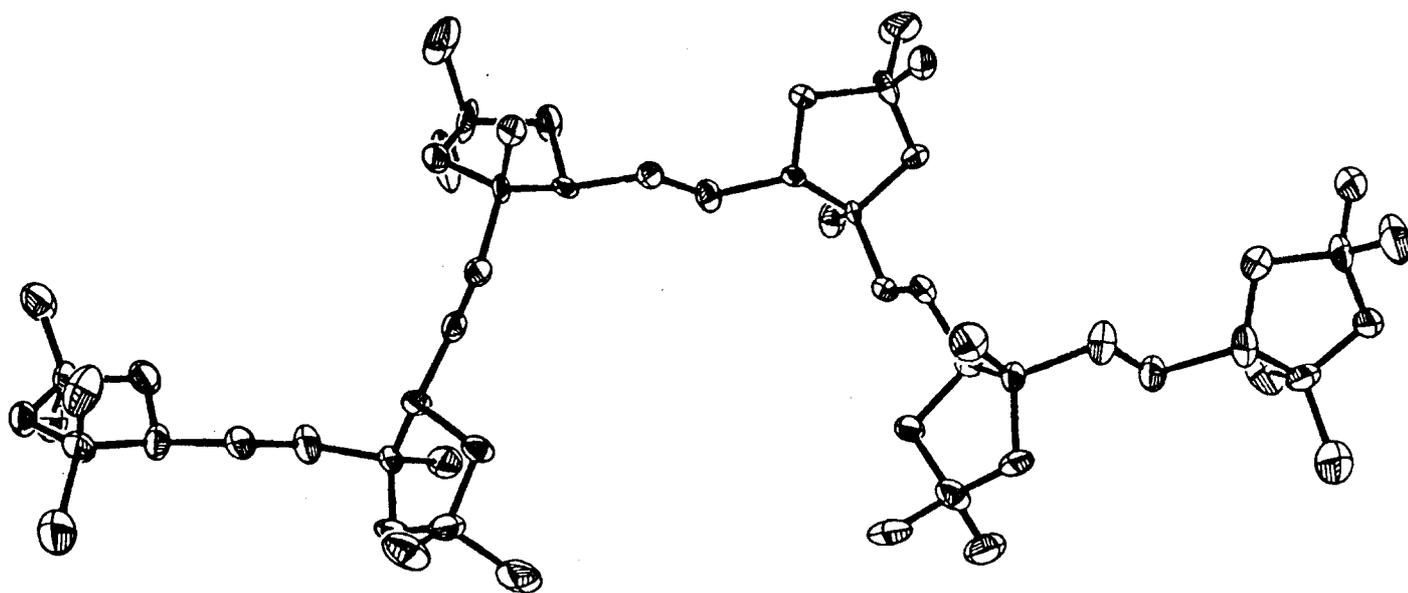


Figure 2: X-ray crystal structure of squalene dodecaol hexaacetonide, (-)-3.

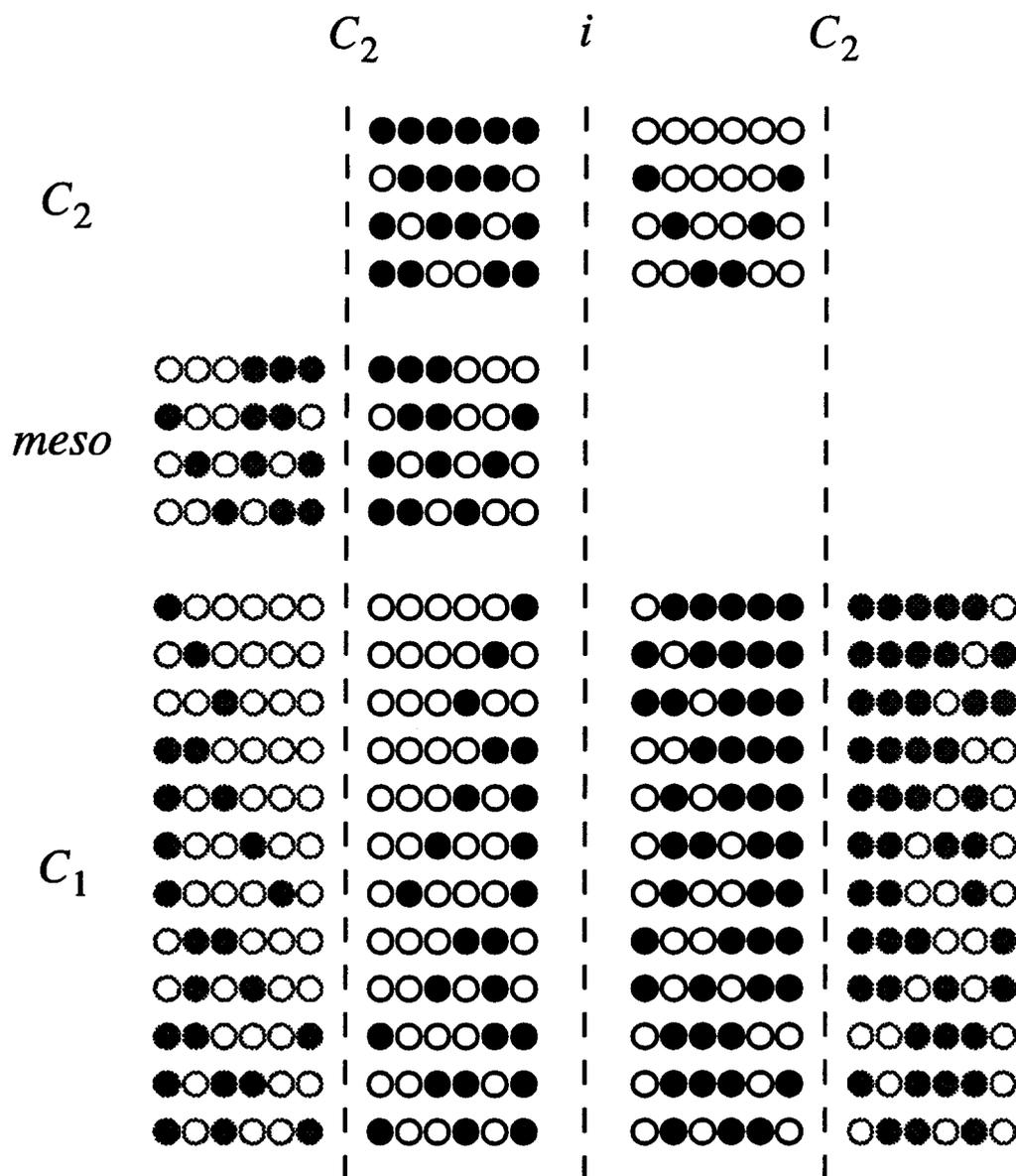
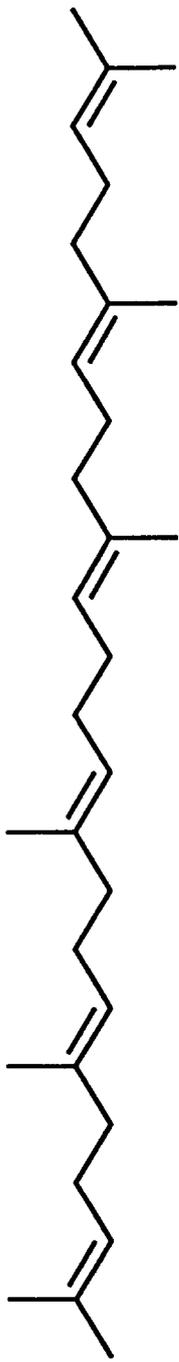
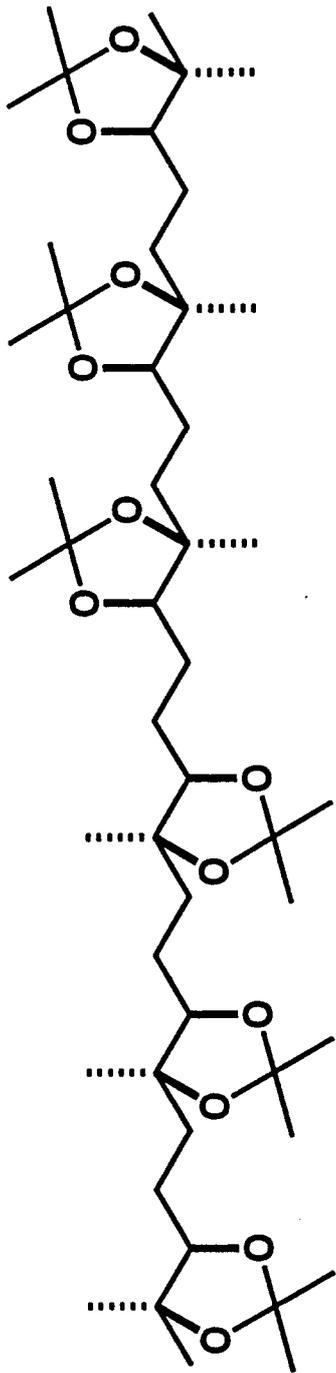


Figure 3. The relationships of the sixty-four (2^6) isomers. The symmetry operations listed at the top reduce the number of isomers to thirty-six: four C_2 symmetrical diastereomers and their enantiomers; four *meso* diastereomers that have no enantiomers; twelve diastereomers with no symmetry and their enantiomers. Each circle may be thought of as a disk that is white on one side and black on the other. The C_2 operation is a two-fold rotation axis normal to the plane of the page between the third and fourth circles. The i operator is an inversion center (center of symmetry) between the third and fourth circles. The 28 gray representations in the two outside columns are the isomers removed by symmetry considerations.



For each molecule, there are:
 six sites for reaction,
 each with two possible facial selectivities.
 for a total of

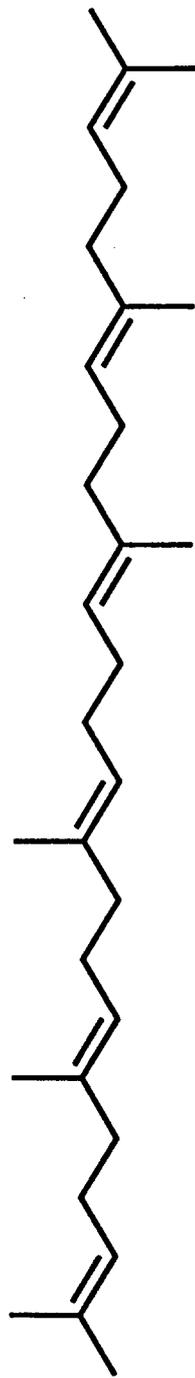
$$(2)^6 = 64 \text{ outcomes.}$$



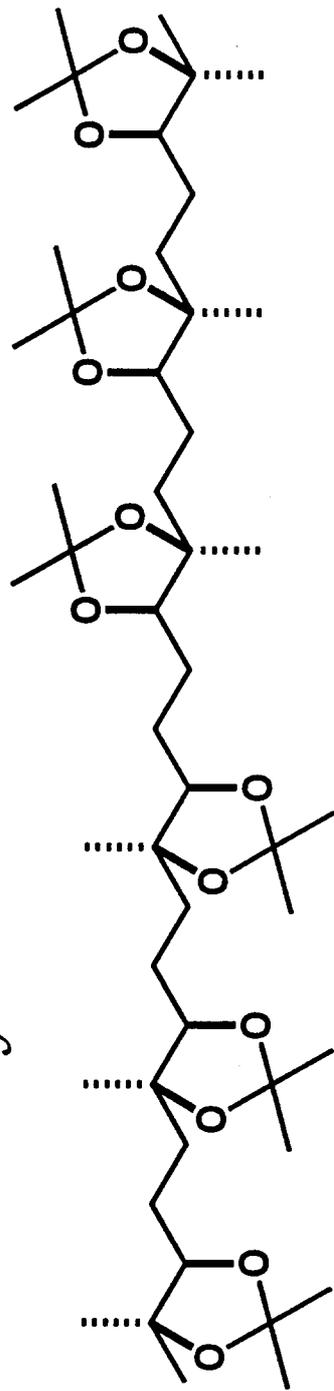
Statistically, this diastereomer's yield would be:

$$\frac{\text{both enantiomers}}{64 \text{ outcomes}} = 0.03125$$

Experimentally, the yield is 4.38%.

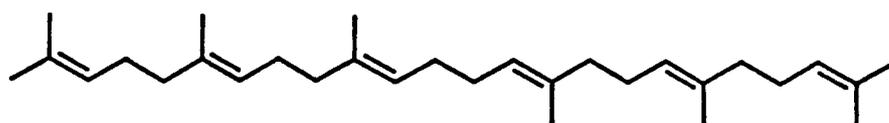


*For each molecule, there are:
six chemical reactions,
one which is enantioselective and
five which are diastereoselective
for a total of
twelve yields.*

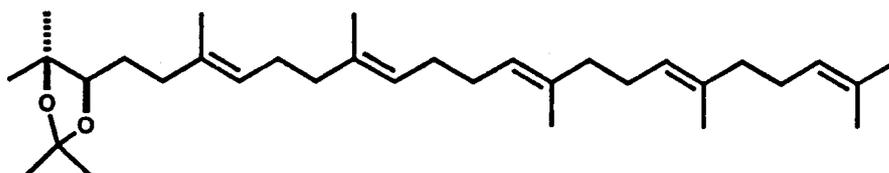


*A single diastereomer is formed in 78% overall yield.
Thus the average yield is:*

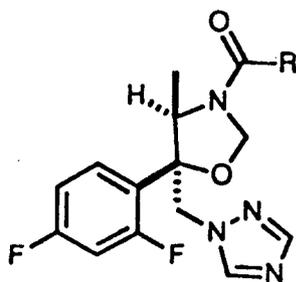
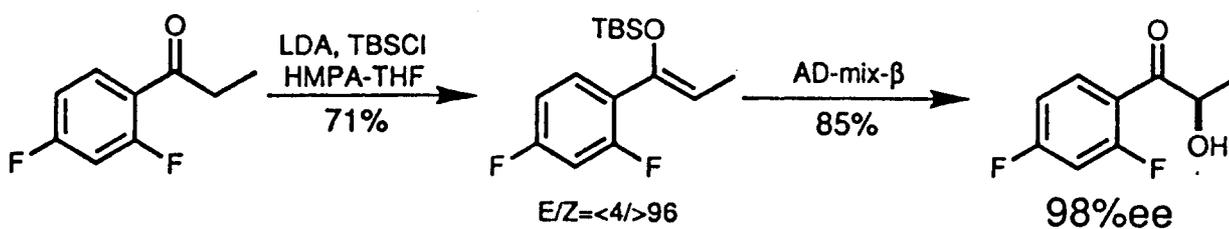
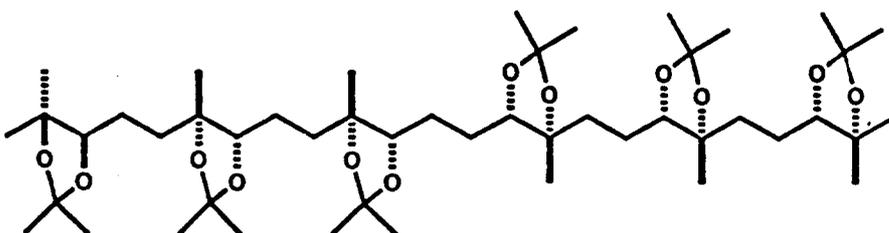
$$(0.78)^{1/12} = 0.98$$



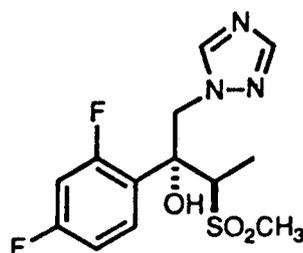
1. AD- β
2. Acetone, PTSA



1. AD- α
2. Acetone, PTSA
71%

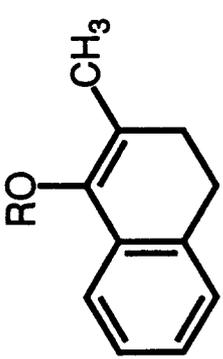
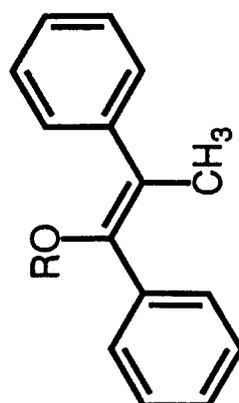
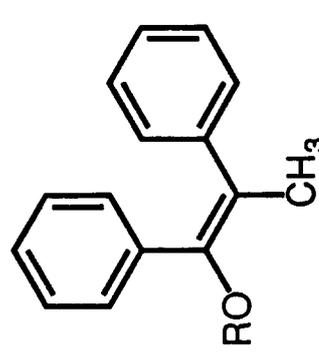


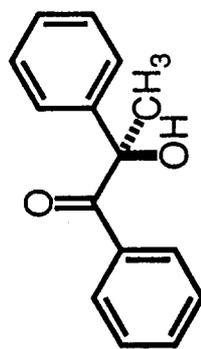
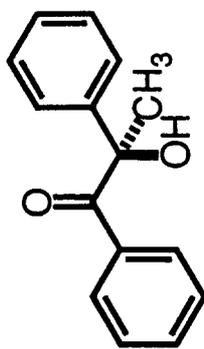
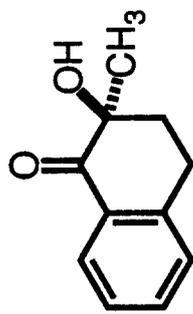
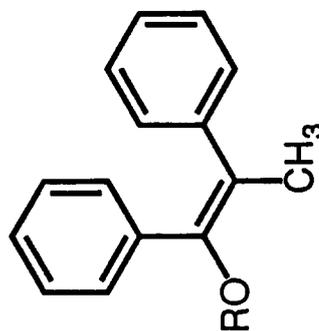
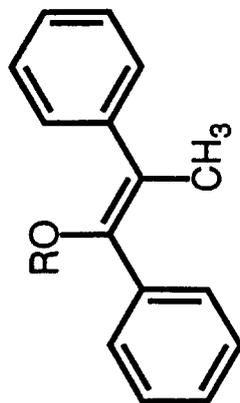
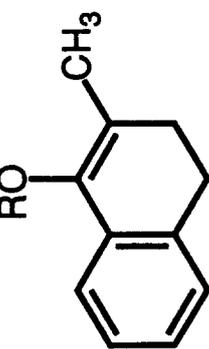
Sankyo

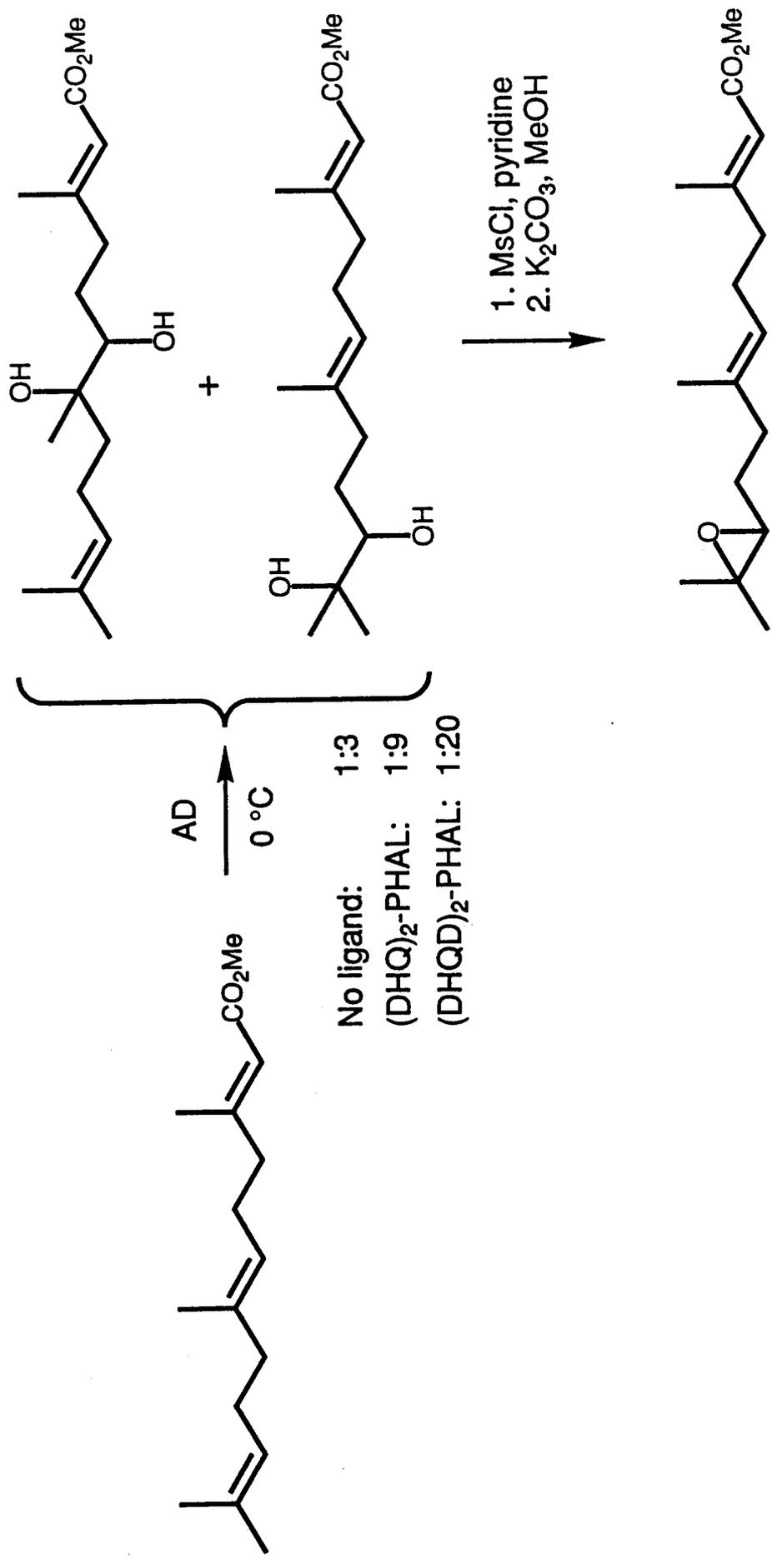


Schering-Plough

AD of Tetra-substituted Enol Ethers with Super-AD-mix- β

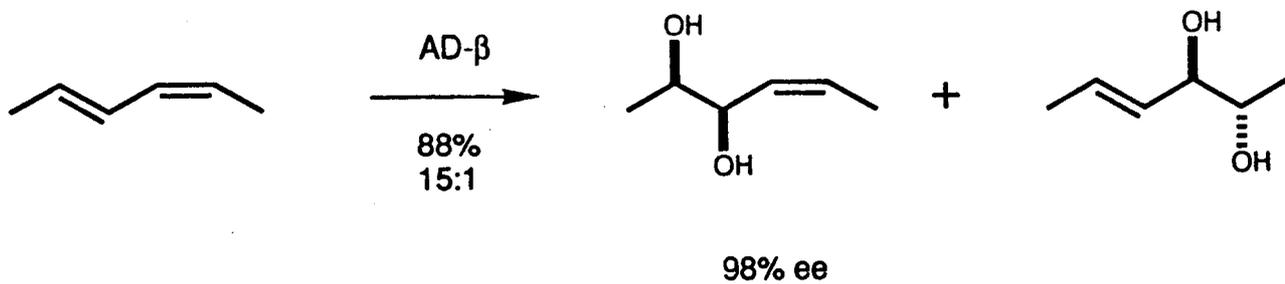
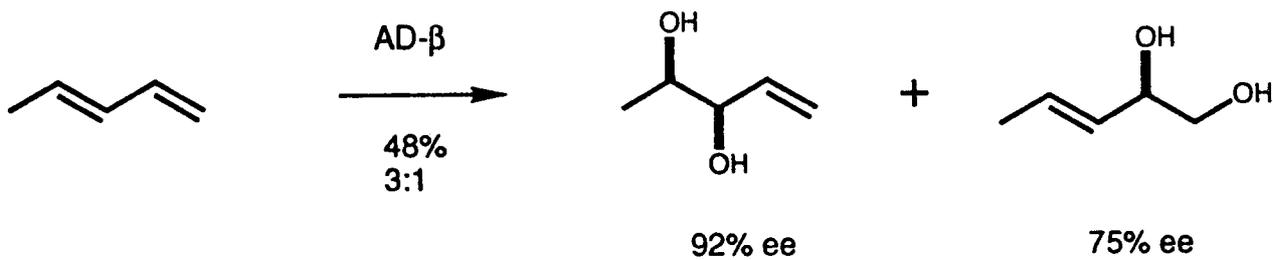
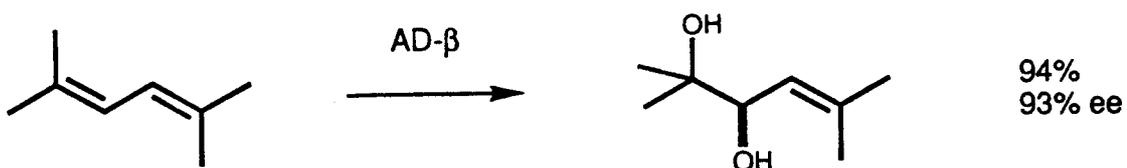
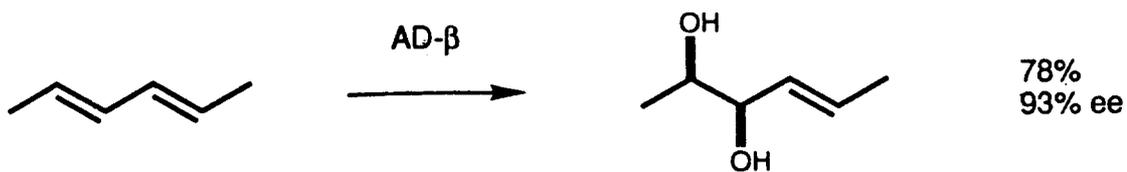
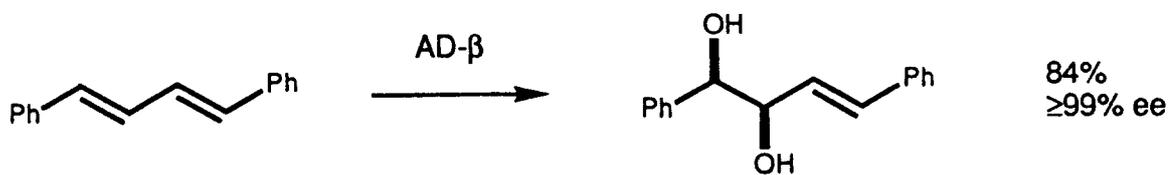
enol ether	R = CH ₃	R = TBS	R = SiPh ₂ Bu ^t	confign
	64 %ee (94%)	67 %ee (89%)	68 %ee (90%)	S
		75 %ee (22%)		R
		53 %ee (48%)		R

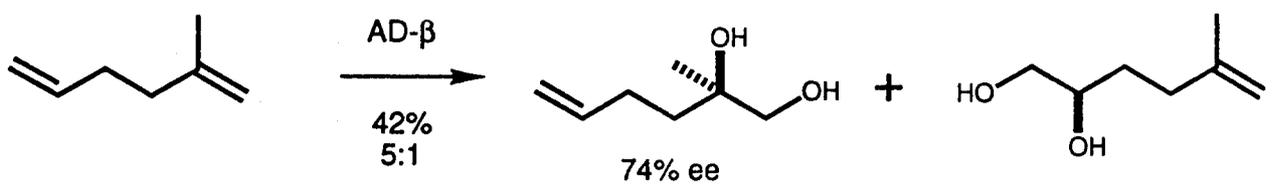
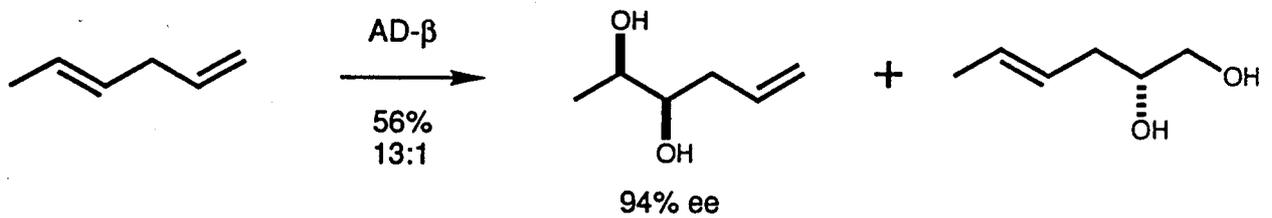
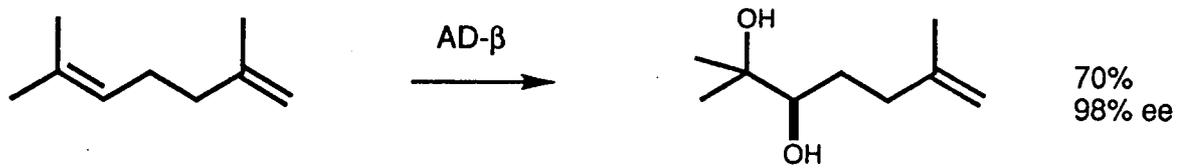
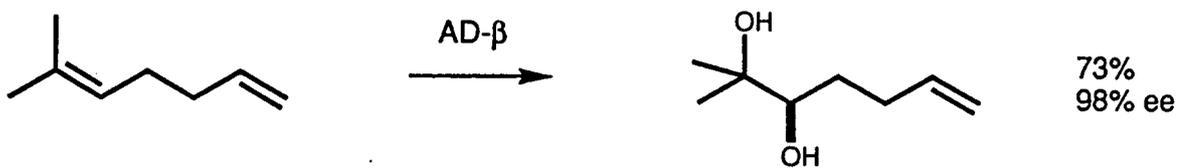
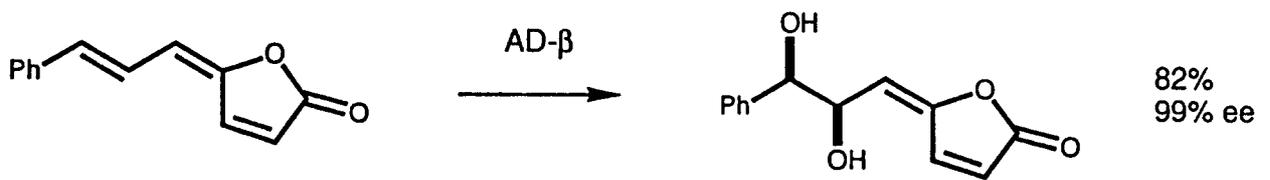
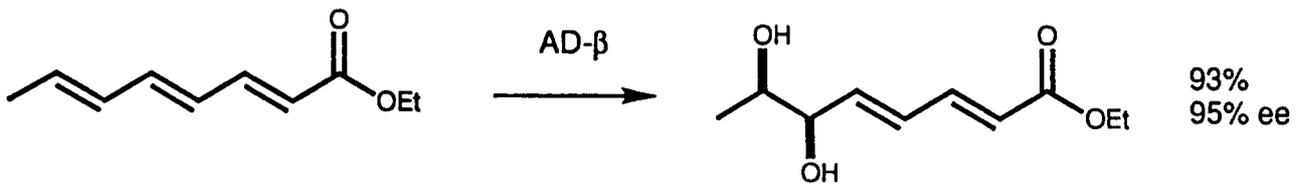
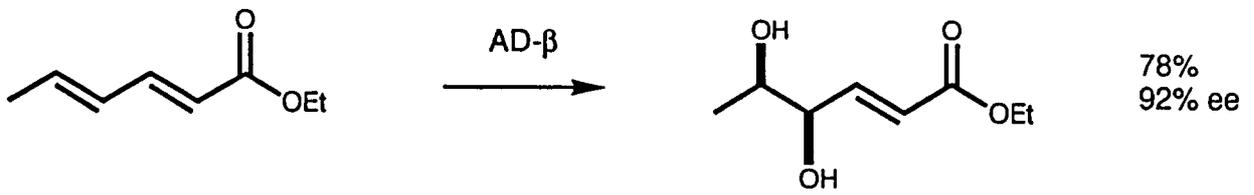


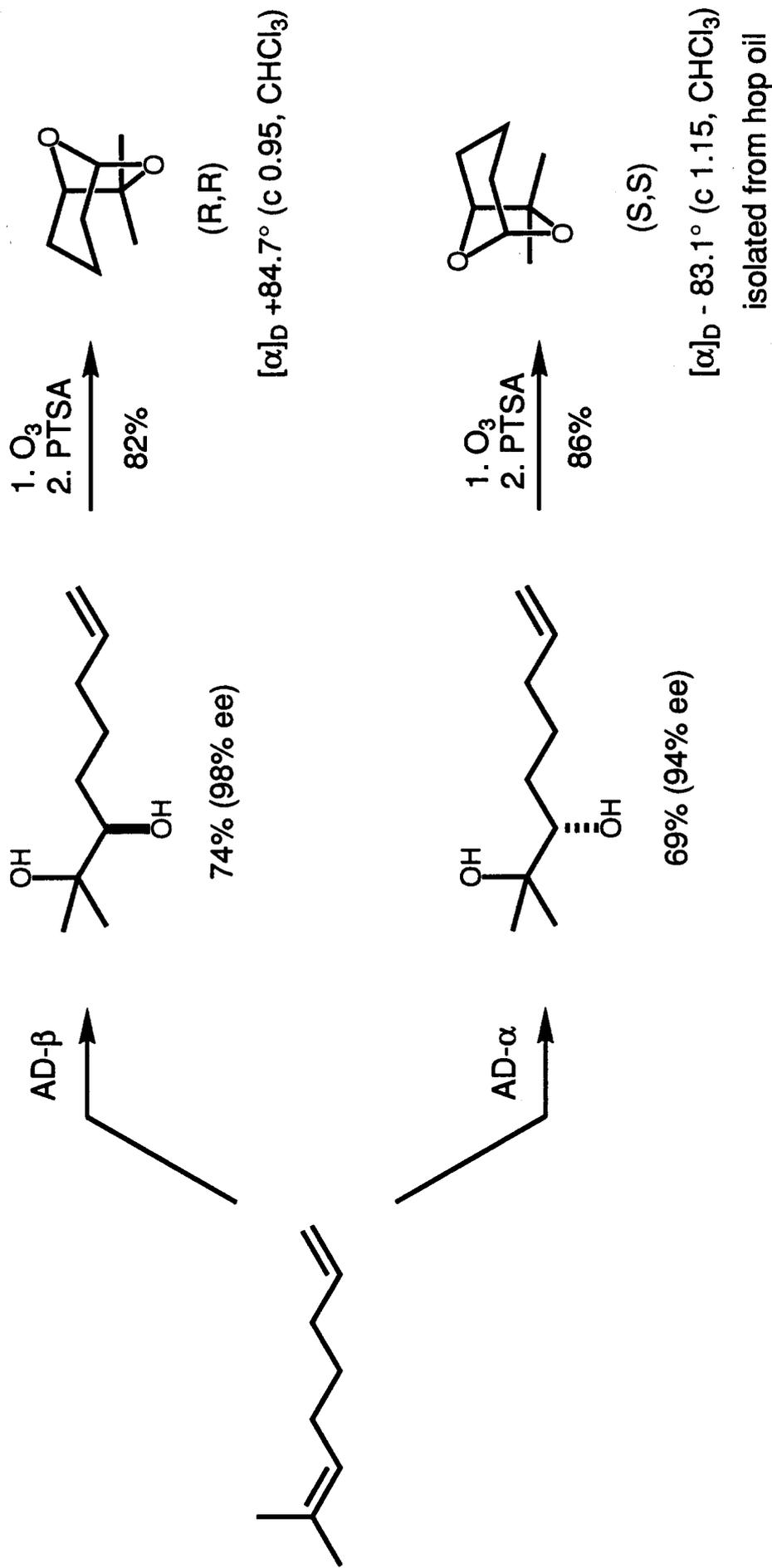


(DHQ)₂-PHAL: 92% ee *R*

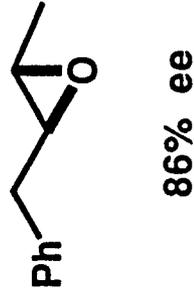
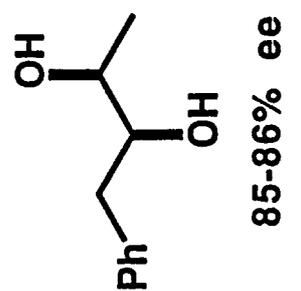
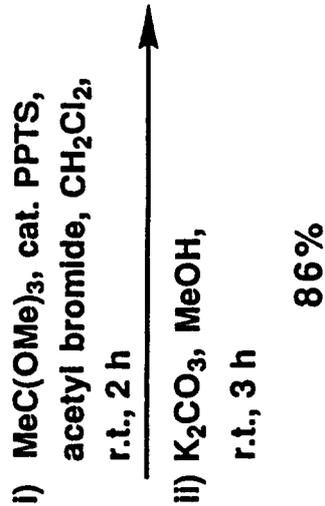
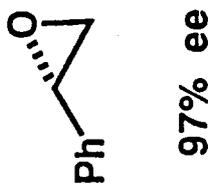
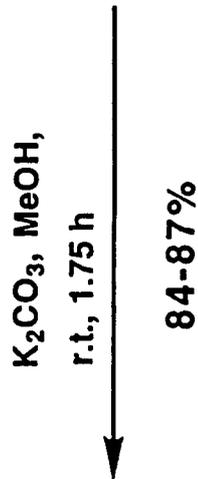
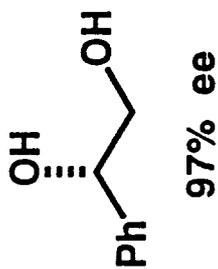
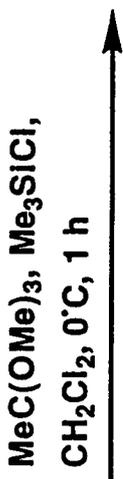
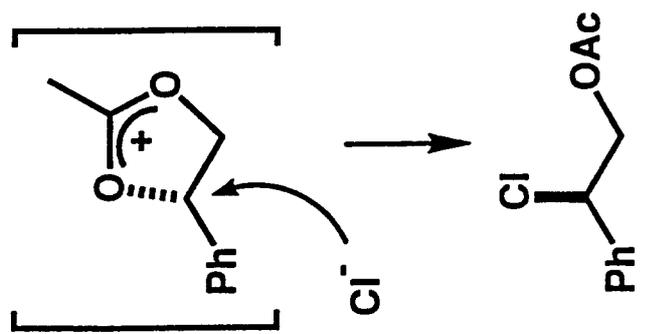
(DHQD)₂-PHAL: 97% ee *S*



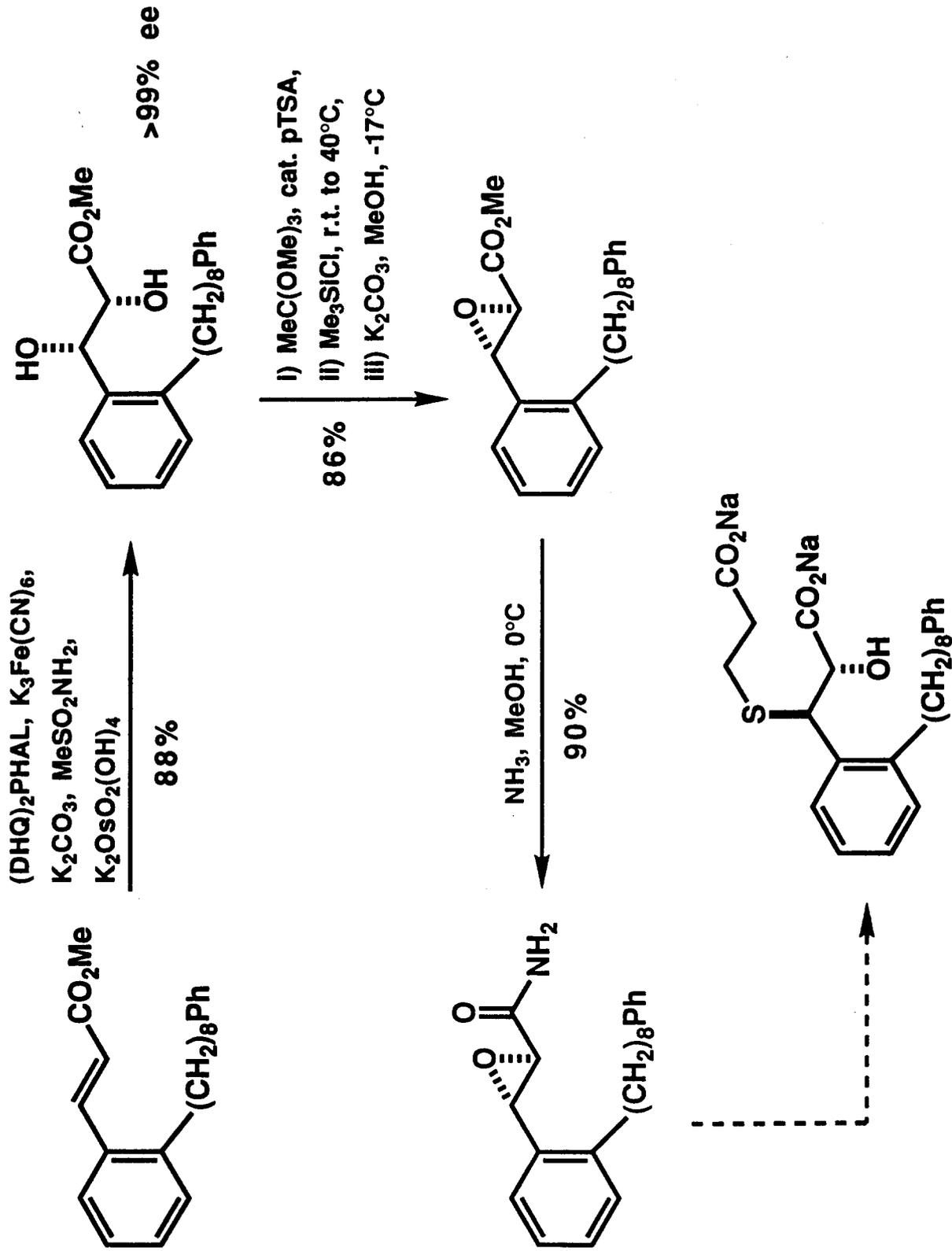




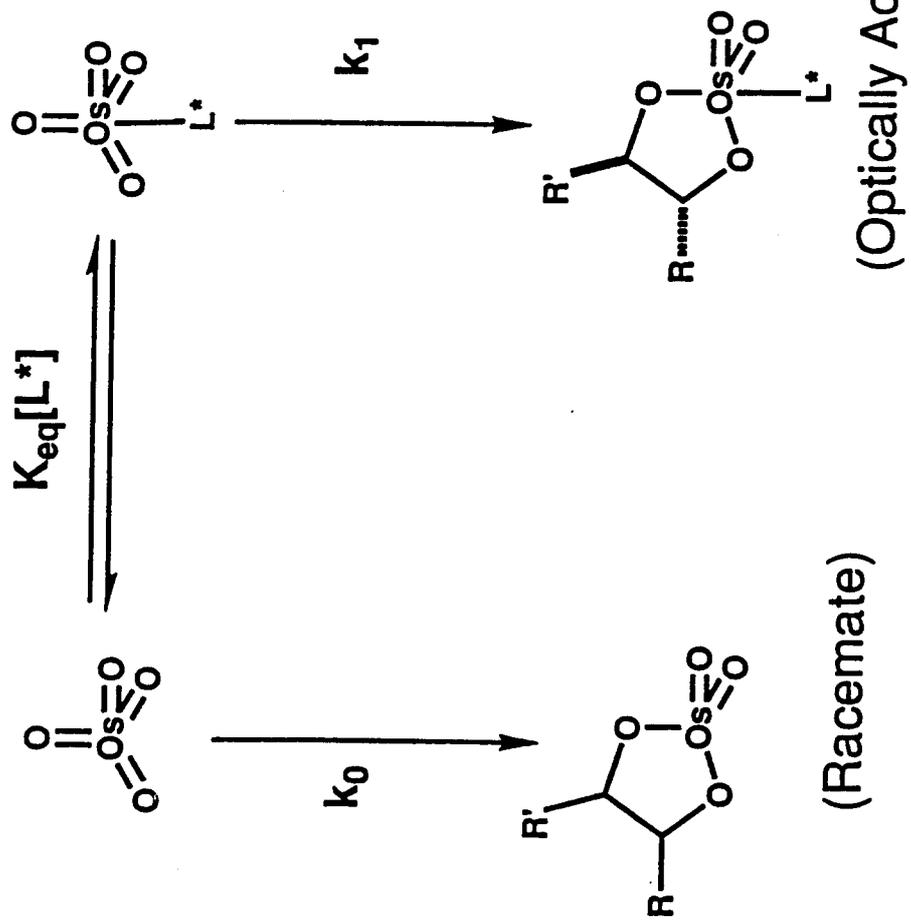
Preparation of Chiral Acetoxy Halides and Epoxides



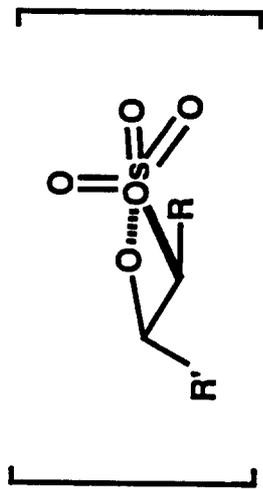
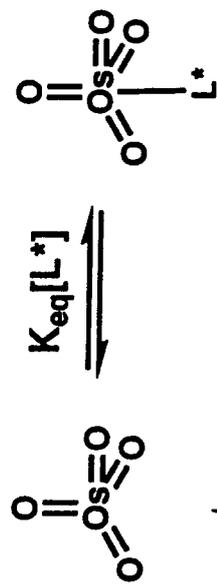
Formal Synthesis of SKF 104353



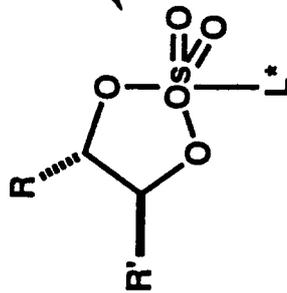
Concerted [3+2] Mechanism



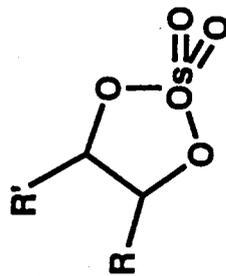
Stepwise [2+2] Mechanism



Common Intermediate,
Metallaioxetane

 $k_2[\text{L}^*]$ 

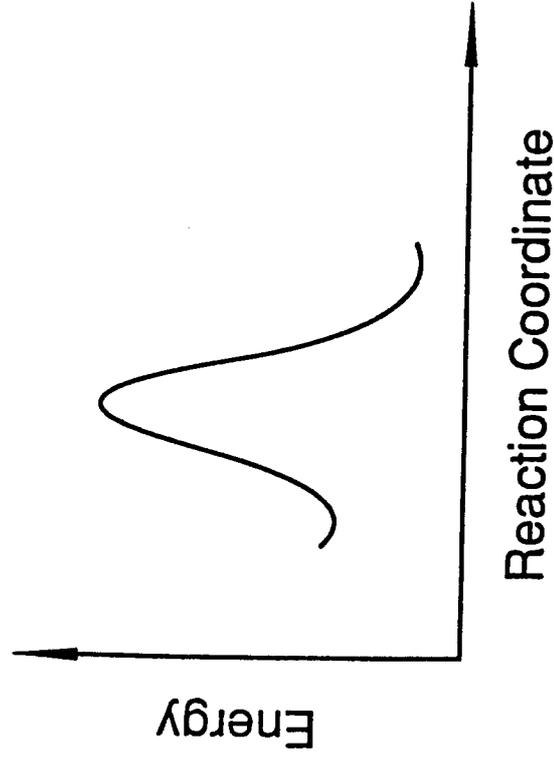
(Optically Active)

 k'_0 

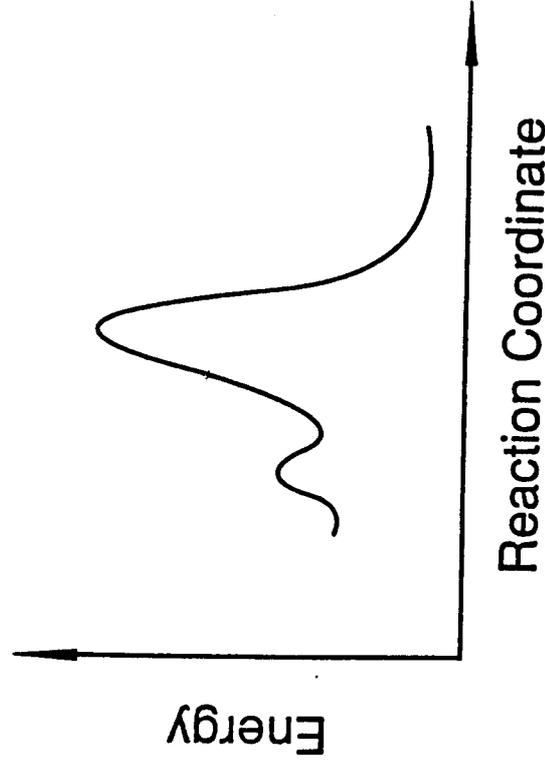
(Racemate)

Possible Energy Diagrams for the Osmylation Reaction

Concerted [3+2] Mechanism



Stepwise [2+2] Mechanism



Concerted [3+2] Mechanism

$$\text{rate} = \frac{(k_0 + k_1 K_{\text{eq}}[\text{L}])}{(1 + K_{\text{eq}}[\text{L}])} [\text{OsO}_4]_{\text{T}} [\text{olefin}]$$

Stepwise [2+2] Mechanism

$$\text{rate} = \frac{(k'_0 + k_2[\text{L}])k_a/k_a}{(1 + K_{\text{eq}}[\text{L}])} [\text{OsO}_4]_{\text{T}} [\text{olefin}]$$

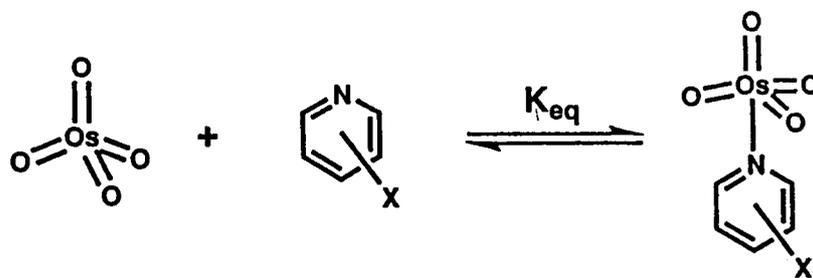
Both show saturation kinetics
Kinetically indistinguishable

$$\text{Define LAE} = \frac{\text{Observed Rate of Reaction with Ligand Saturation}}{\text{Observed Rate of Reaction without Ligand}}$$

$$\text{LAE} = \frac{k_1}{k_0}$$

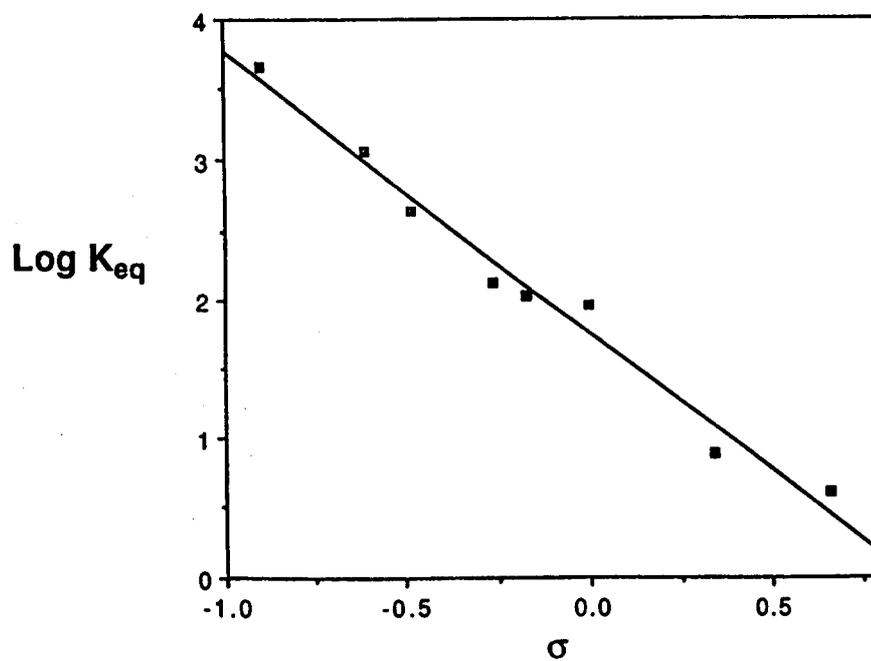
$$\text{LAE} = \frac{k_2}{k'_0 K_{\text{eq}}}$$

Binding Constants of Different Substituted Pyridines with Osmium Tetroxide

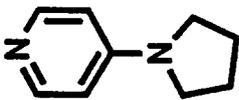
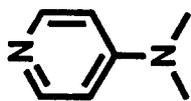
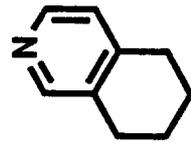
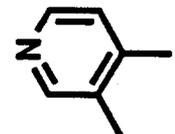
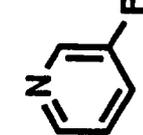


$K_{eq} (M^{-1})$	4460	1139	429	135	110	93	7.5	4.0

Correlation of Pyridine-OsO₄ Binding with σ in Toluene

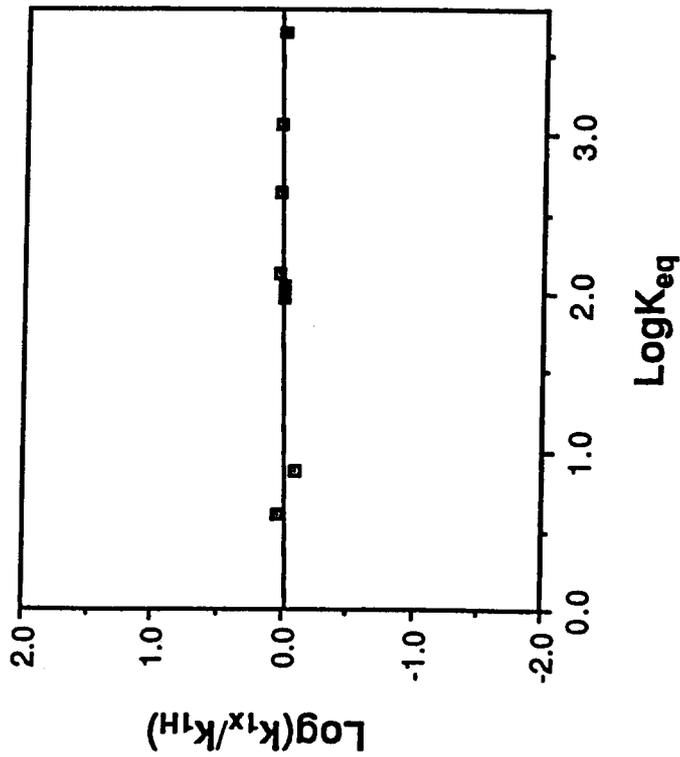


Observed LAE Values for Cyclohexene with Different Substituted Pyridines

Ligand	12.1	12.9	12.6	12.8	12.0	11.8	9.4	12.6
								
								
								
								
								
								
								
LAE	12.1	12.9	12.6	12.8	12.0	11.8	9.4	12.6

$$\text{LAE} = \frac{\text{Observed Rate of Reaction with Ligand Saturation}}{\text{Observed Rate of Reaction without Ligand}}$$

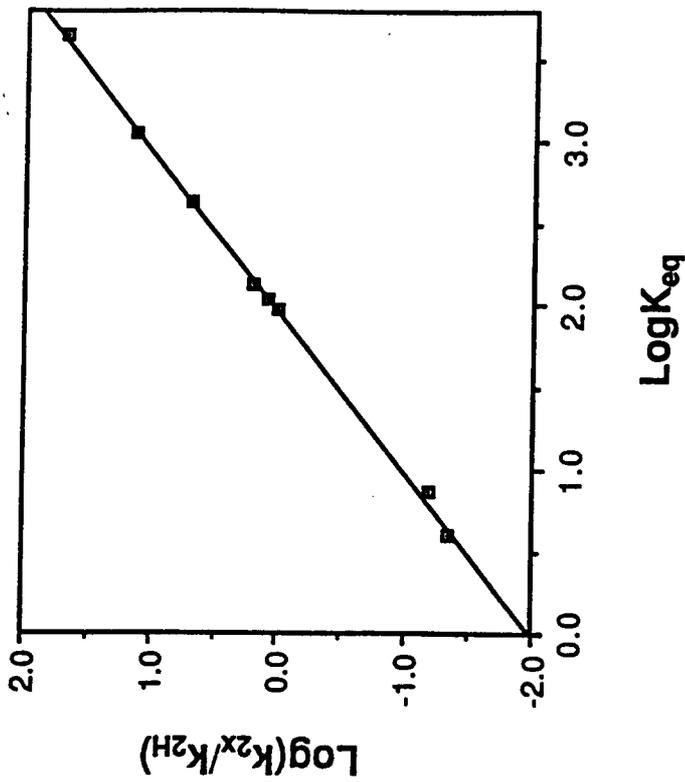
Concerted [3+2] Mechanism



$$\rho = 0$$

The rate constant k_1 does not change with the binding constant K_{eq} .

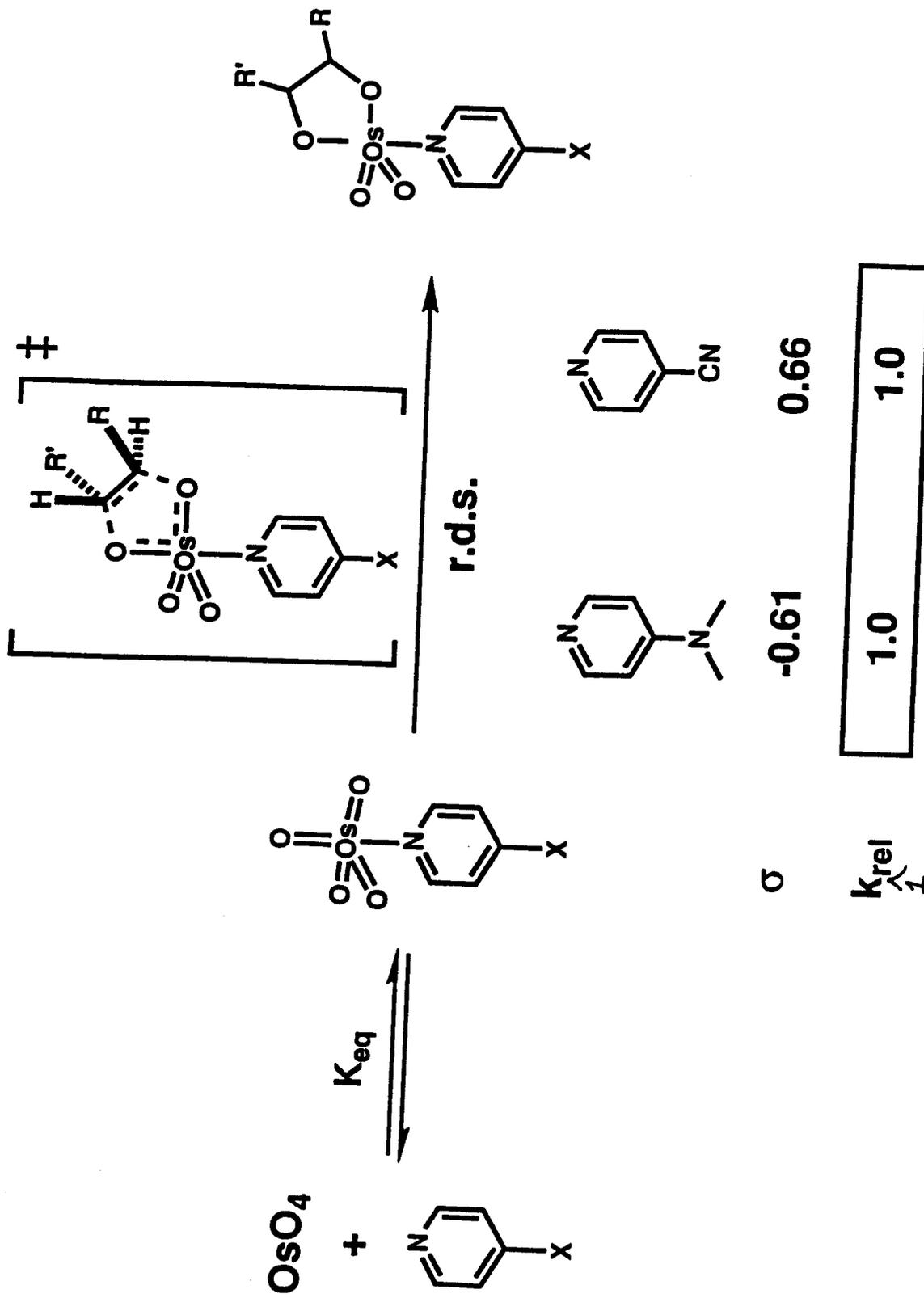
Stepwise [2+2] Mechanism



$$\rho = -2.0$$

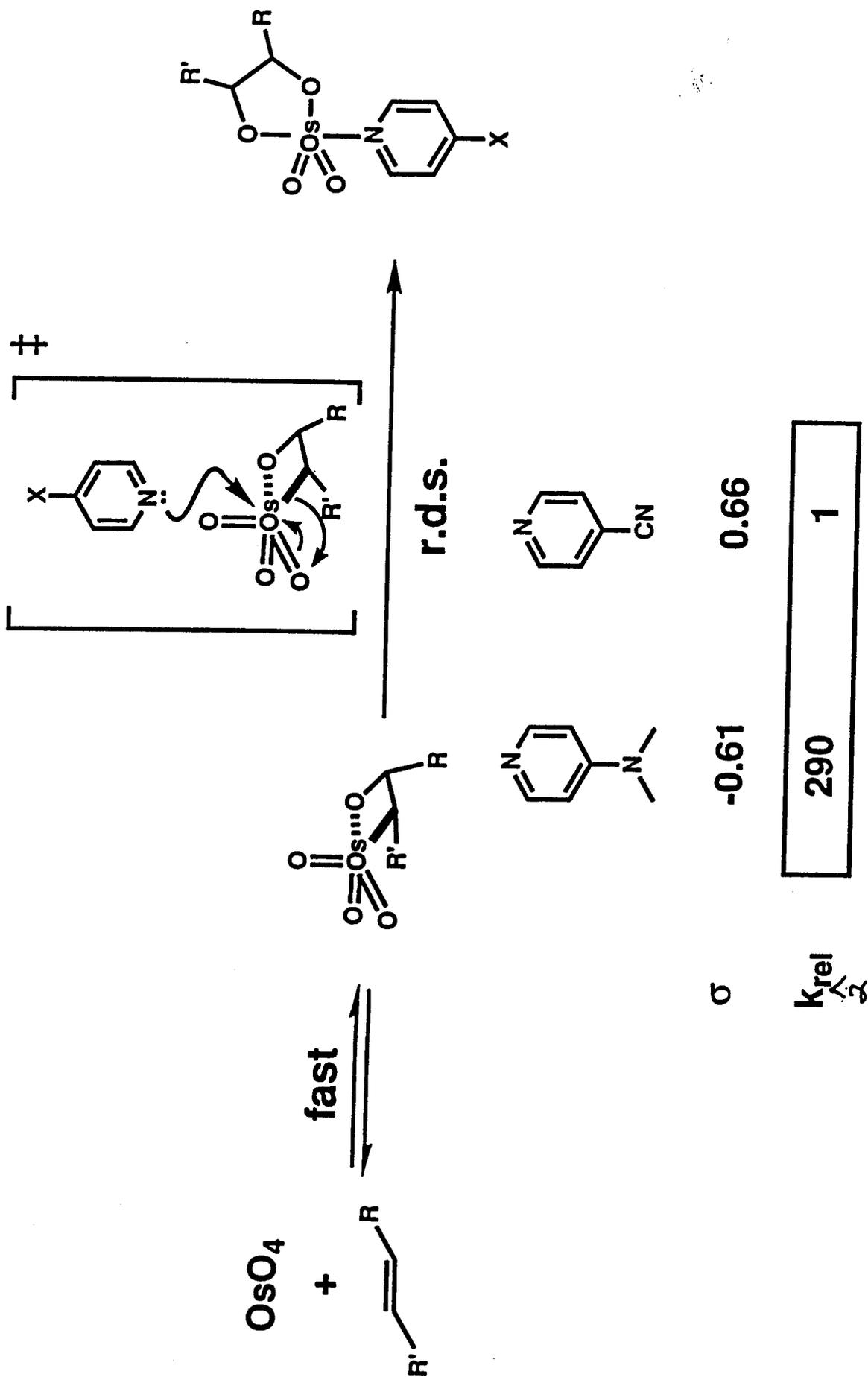
The rate constant k_2 depends on the binding constant K_{eq} . It increase with the nucleophilicity of the pyridine.

Concerted [3+2] Mechanism

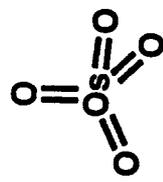


Stepwise [2+2] Mechanism

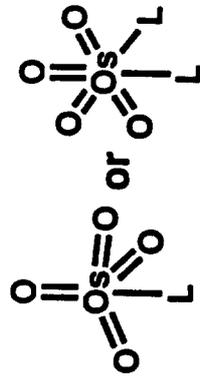
32



Extended Hückel Calculations on Concerted [3+2] Mechanism



LUMO ———



LUMO ———



LUMO ———

HOMO ———

HOMO ———

HOMO ———

Upon coordination of ligand, the osmium complex is a better donor and a better acceptor toward the LUMO and HOMO of an approaching alkene.

Jørgensen and Hoffmann

Stepwise [2+2] Mechanism

