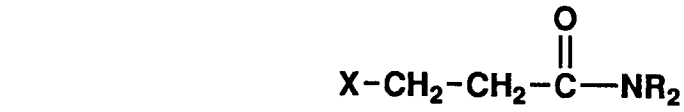
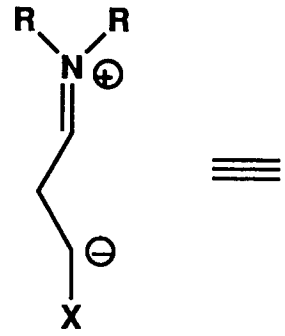
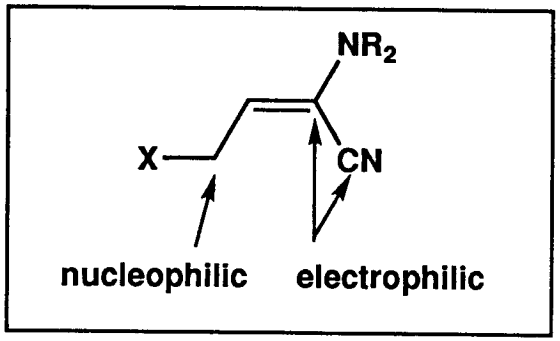
BACKGROUND





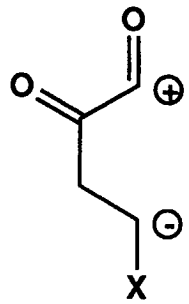
1,3 dipolar reagent

≡



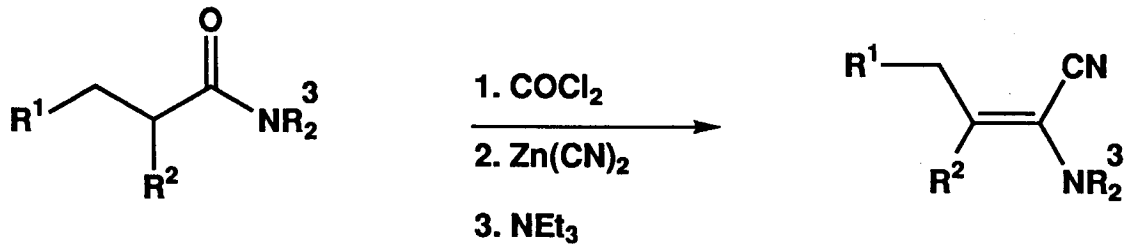
X = H, SPh,SO_2Ph, $SiMe_3$

≡

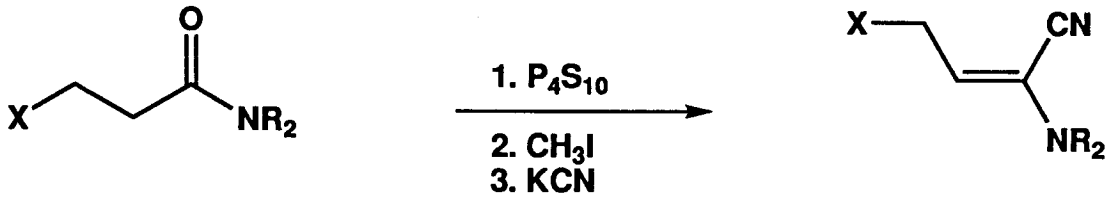


1,4 dipolar reagent

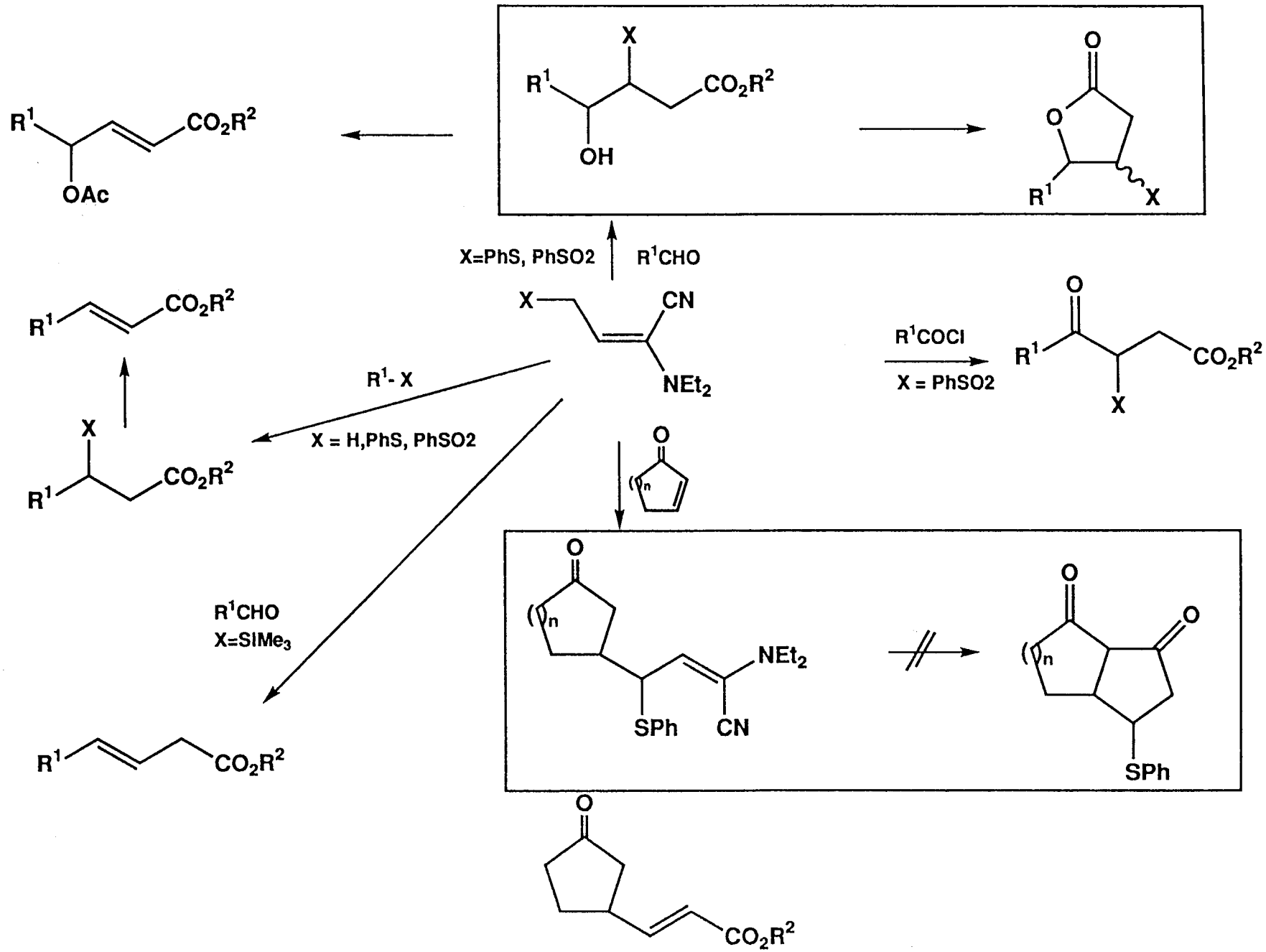
SYNTHESIS OF α - CYANOENAMINES

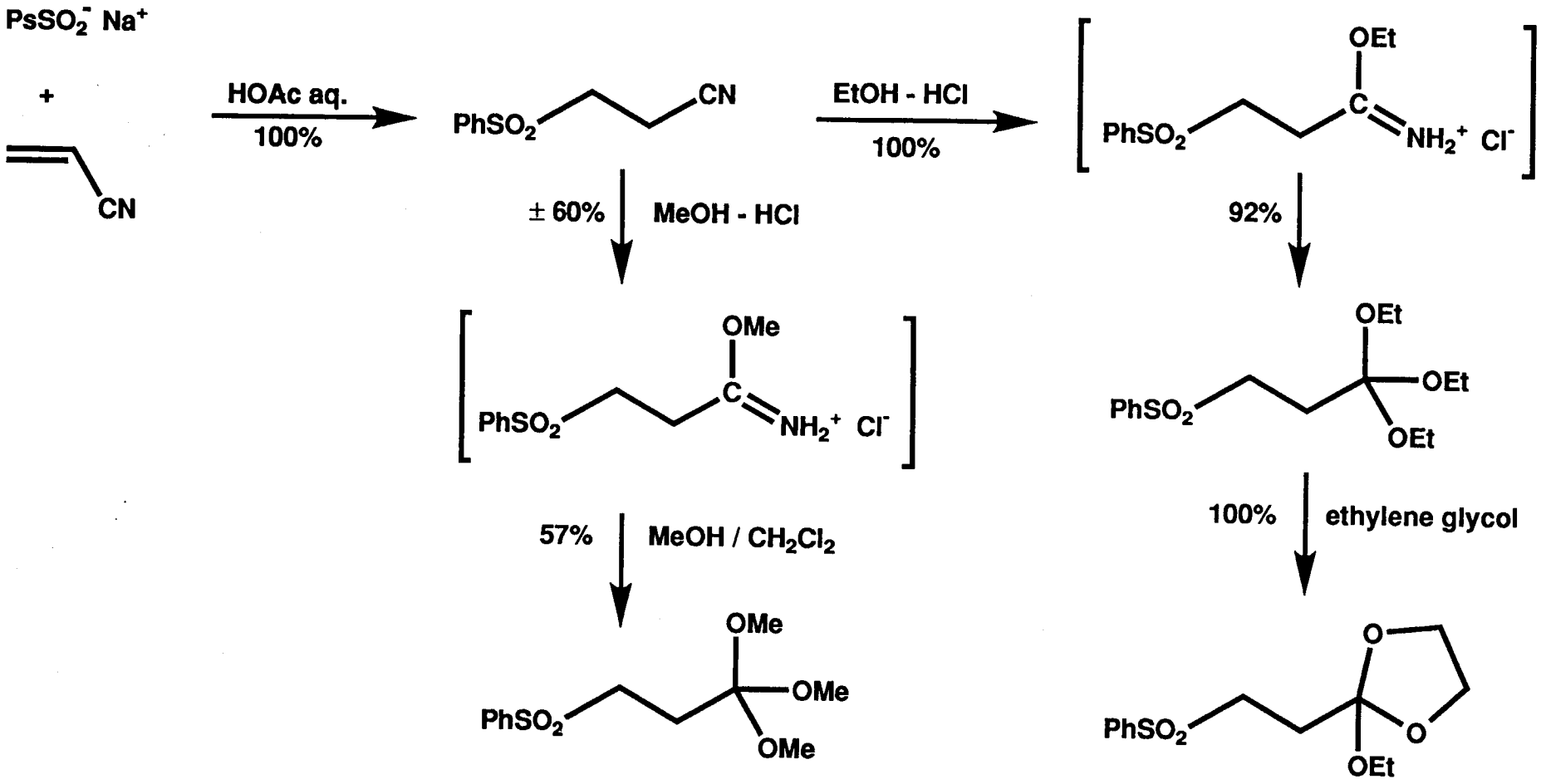


R^1, R^2 = H, alkyl, aryl

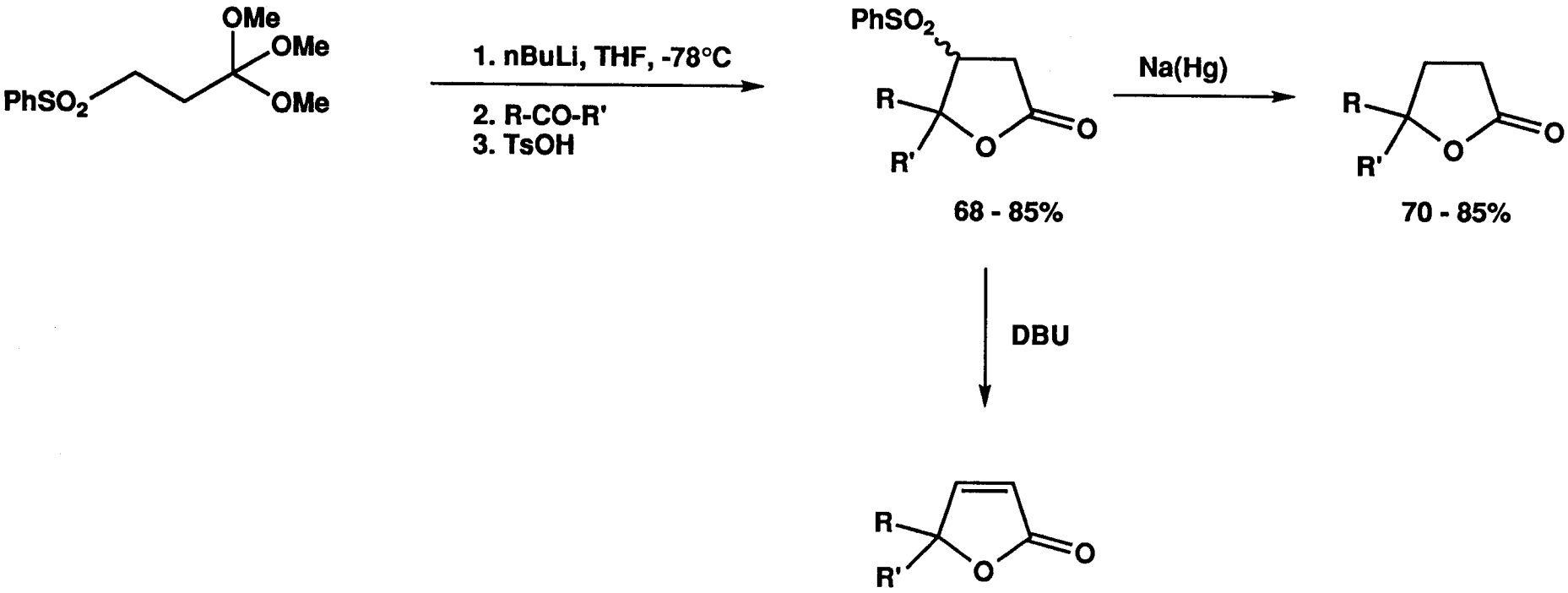


X = PhS, $PhSO_2$

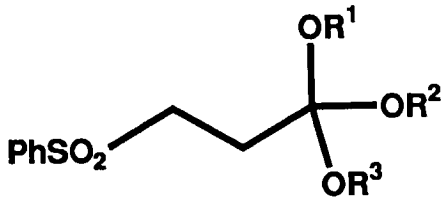

X
R1
CO2R2
OH
O
O
R1
X
R1
CO2R2
OAc
X=PhS, PhSO2
R1CHO
X
CN
NEt2
R1COCl
X = PhSO2
R1
O
CO2R2
X
R1- X
X = H,PhS, PhSO2
X
R1
CO2R2
O
n
R1CHO
X=SiMe3
O
n
NEt2
SPh
CN
O
n
O
SPh
R1
CO2R2
O
CO2R2


PsSO2- Na+
+
CN
HOAc aq.
100%
PhSO2
CN
EtOH - HCl
100%
OEt
C
PhSO2
NH2+ Cl-
± 60%
MeOH - HCl
92%
OMe
C
PhSO2
NH2+ Cl-
OEt
OEt
PhSO2
OEt
57%
MeOH / CH2Cl2
100%
ethylene glycol
OMe
OMe
PhSO2
OMe
O
O
PhSO2
O
OEt

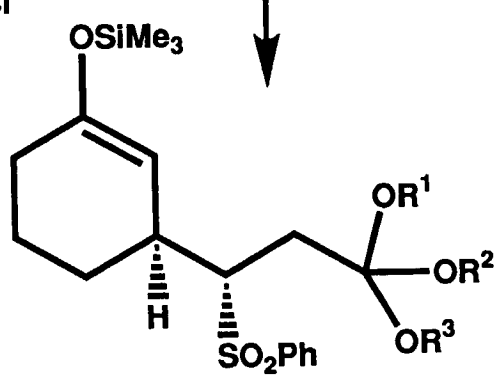
[3 + 2] ANNULATIONS : γ - LACTONES and BUTENOLIDES



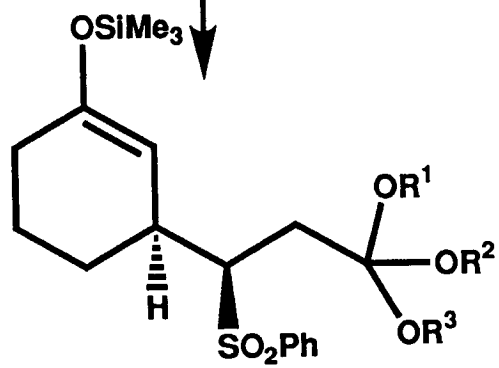
JAN09



1. nBuLi, HMPA.THF, -78°C
2. Cyclohexenone
3. Me_3SiCl



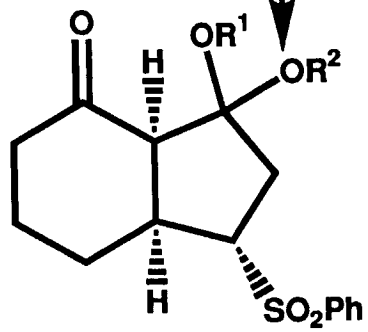
+



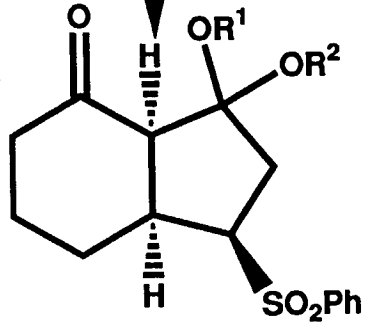
$R^1 = R^2 = R^3 = OMe$	4	1
$R^1 = R^2 = R^3 = OEt$	10	1
$R^1,R^2 = -(CH_2)_2$, $R^3 = OEt$	6.7	1

10% Me_3SiOTf, CH_2Cl_2, -78°C

ANTI

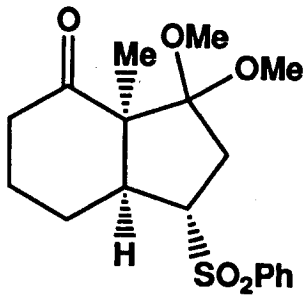


+

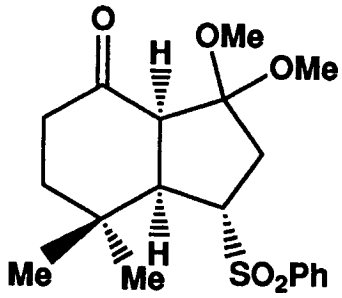


SYN

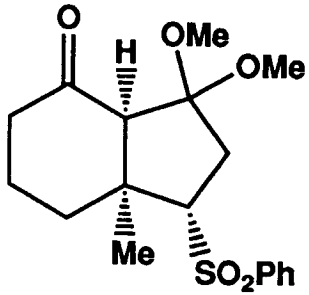
$R^1 = R^2 = R^3 = OMe$	48%	12%
$R^1 = R^2 = R^3 = OEt$	75%	-
$R^1,R^2 = -(CH_2)_2$, $R^3 = OEt$	73%	-



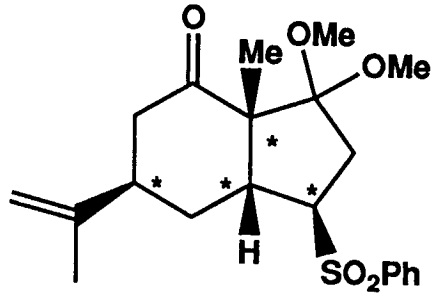
54%



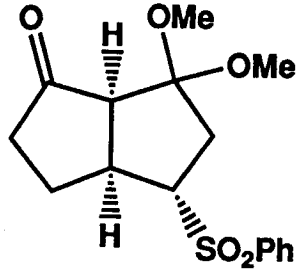
60%



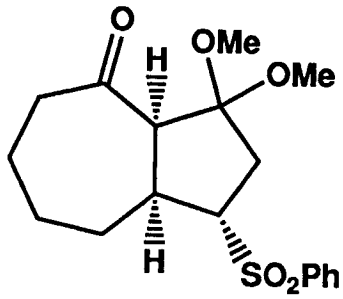
0%



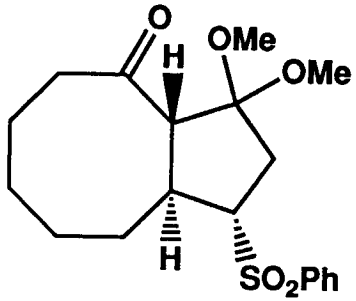
50%



50%



65%

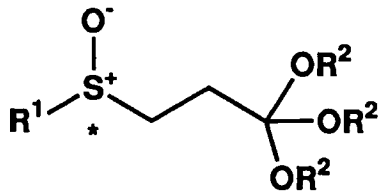


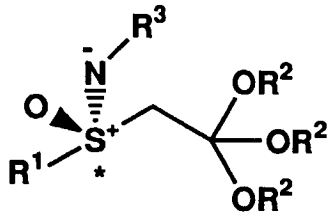
46%

CHIRAL CYCLOPENTANNULATION REAGENTS

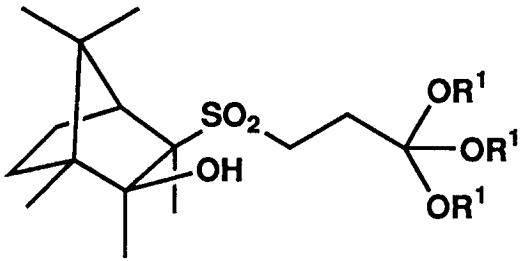
DESIGN

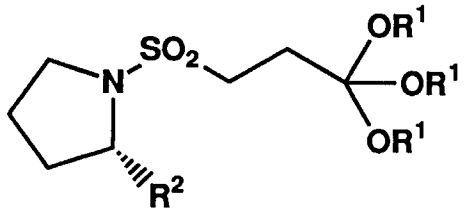
1. Chirality on Sulfur



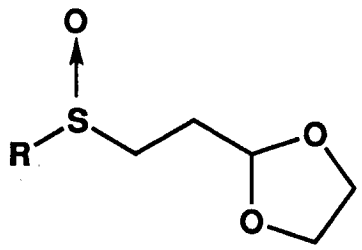


2. Chirality on Substituent





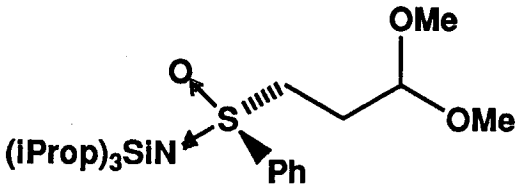
1. Chiral Sulfoxides :



R = pTolyl, tBu

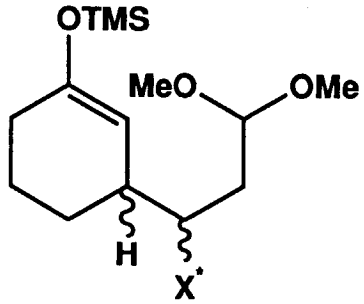
gives predominantly <u>1,2 addition</u> under various conditions

2. Chiral Sulfoximines : poor diastereoselectivity



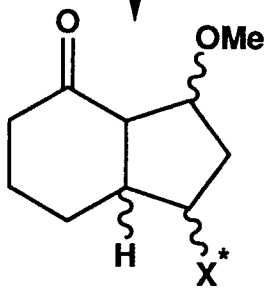
1. nBuLi, HMPA
THF, -78°C

2. cyclohexenone
-30°C, 1hr
3. TMSCl, Et_3N



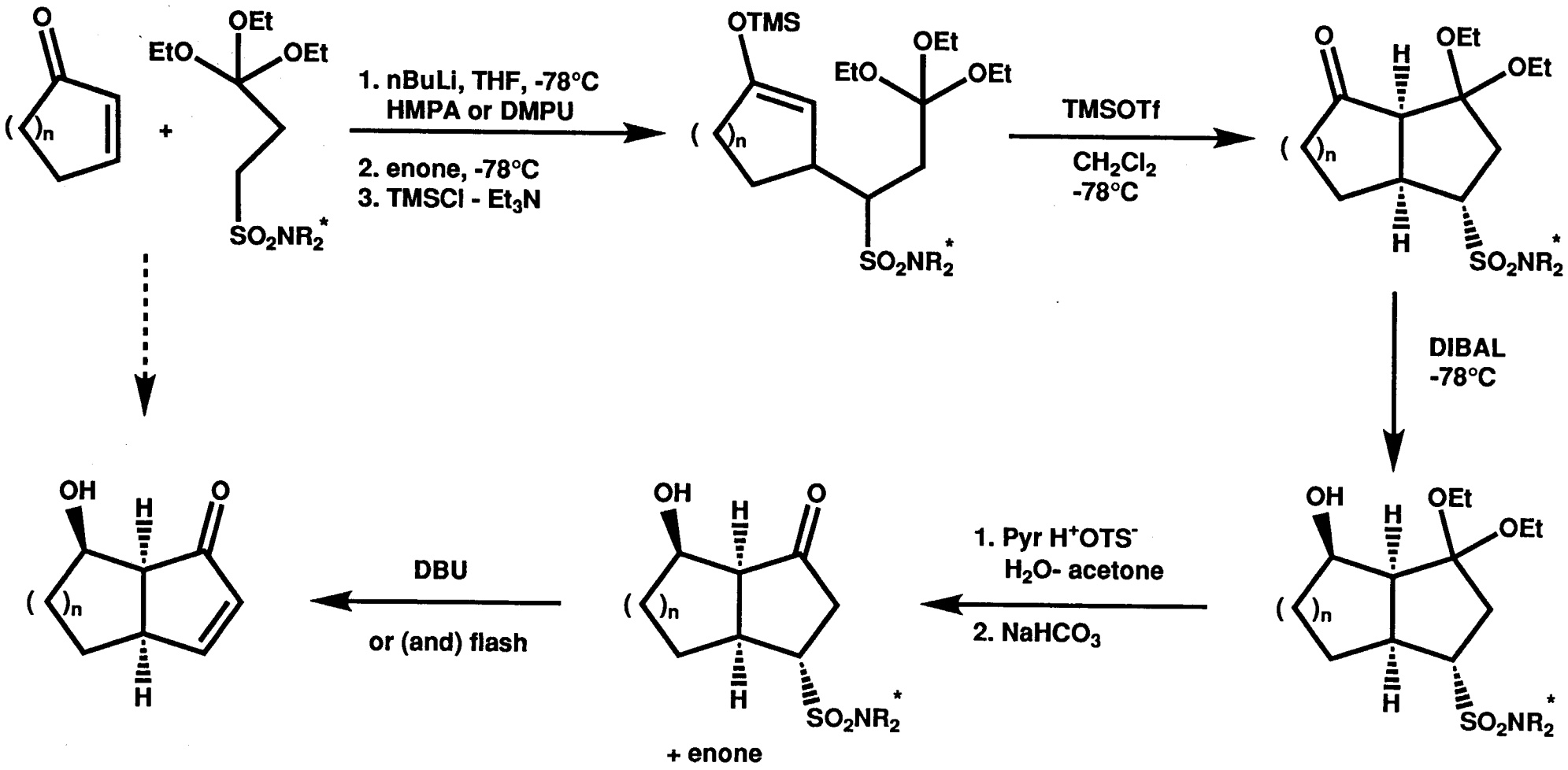
95% (33:3:55:9)

$TiCl_4$

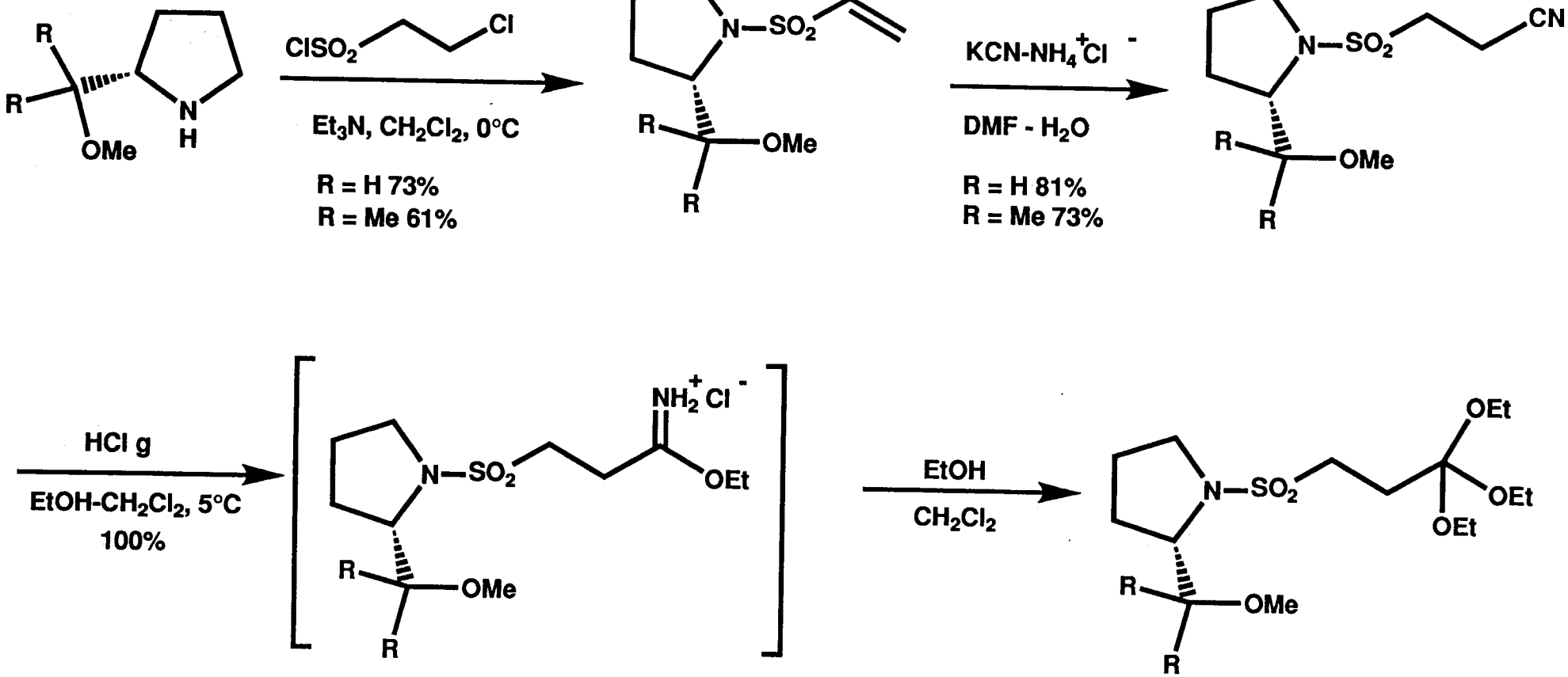


61% (39:33:6:10:9:3)

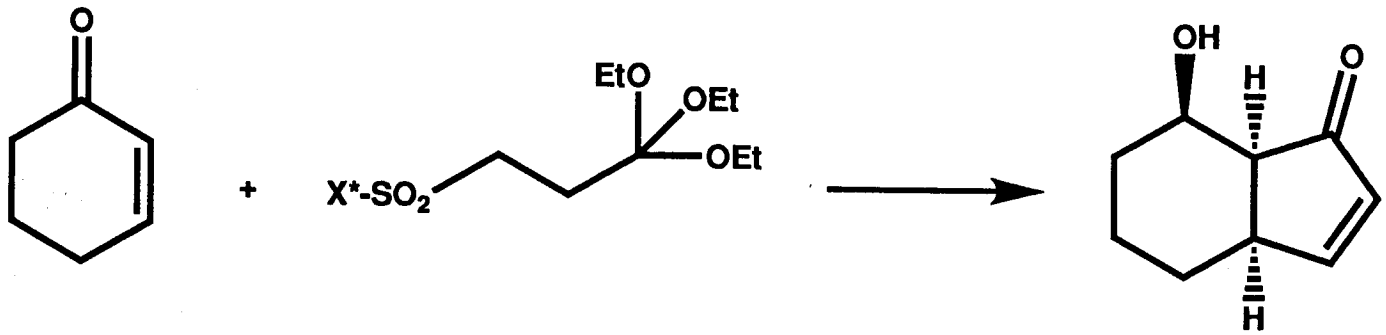
Asymmetric Cyclopentannulation

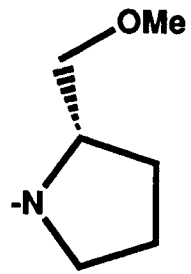
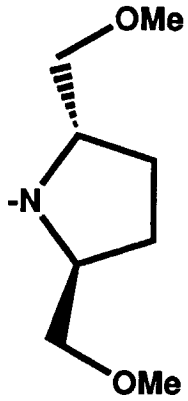
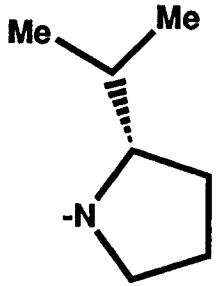
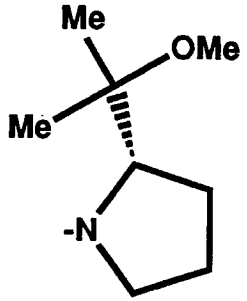


JAN01

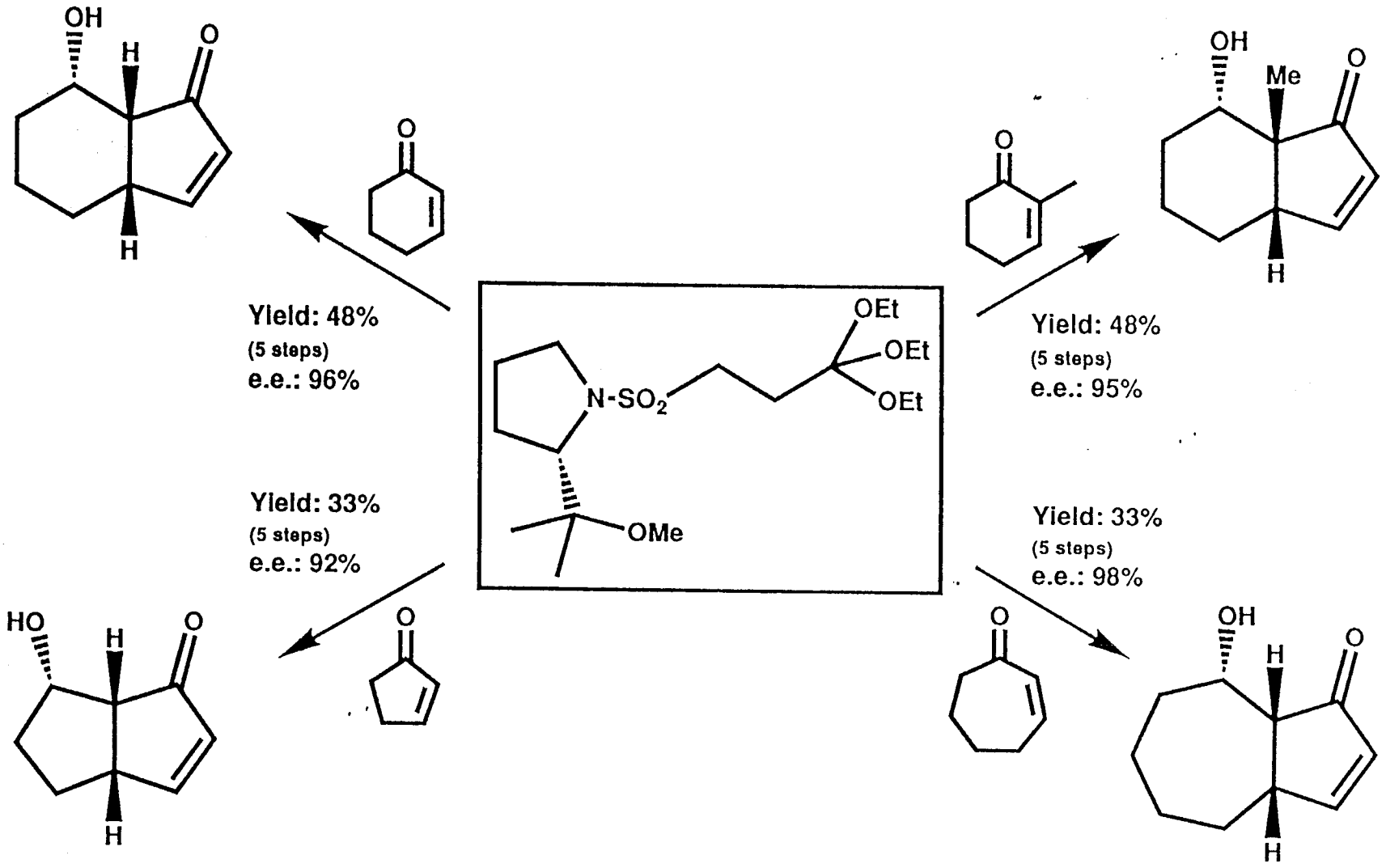

R
R
OMe
N
H
ClSO2
Cl
Et3N, CH2Cl2, 0°C
R = H 73%
R = Me 61%
N—SO2
R
OMe
R
KCN-NH4+Cl -
DMF - H2O
R = H 81%
R = Me 73%
CN
HCl g
EtOH-CH2Cl2, 5°C
100%
NH2+ Cl -
OEt
EtOH
CH2Cl2
OEt
OEt
R = H 85%
R = Me 82%

Selection of the Chiral Auxiliary

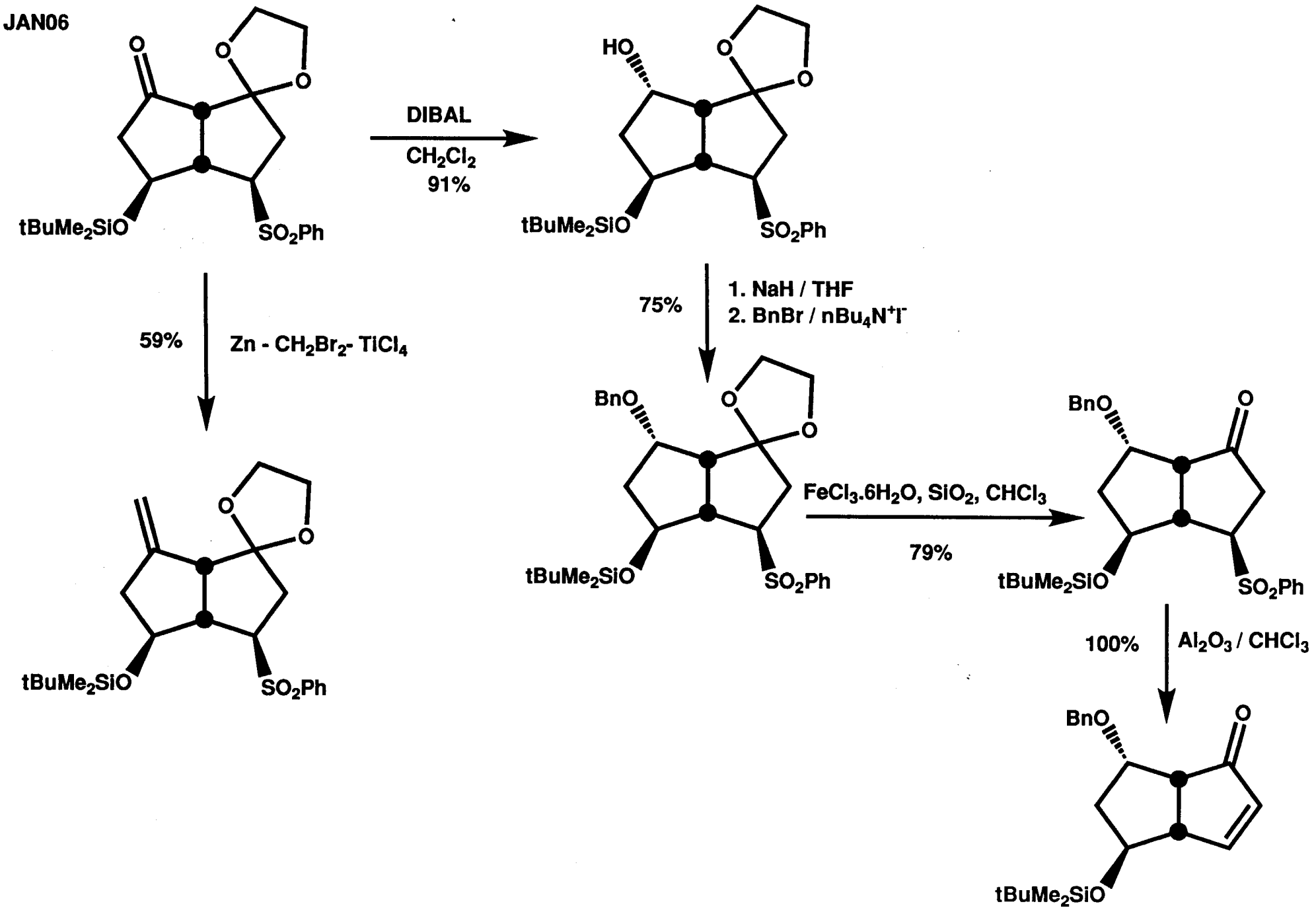


X*				
Yield % (5 steps)	52	40	29	48
e.e. %	62	40	53	**96**

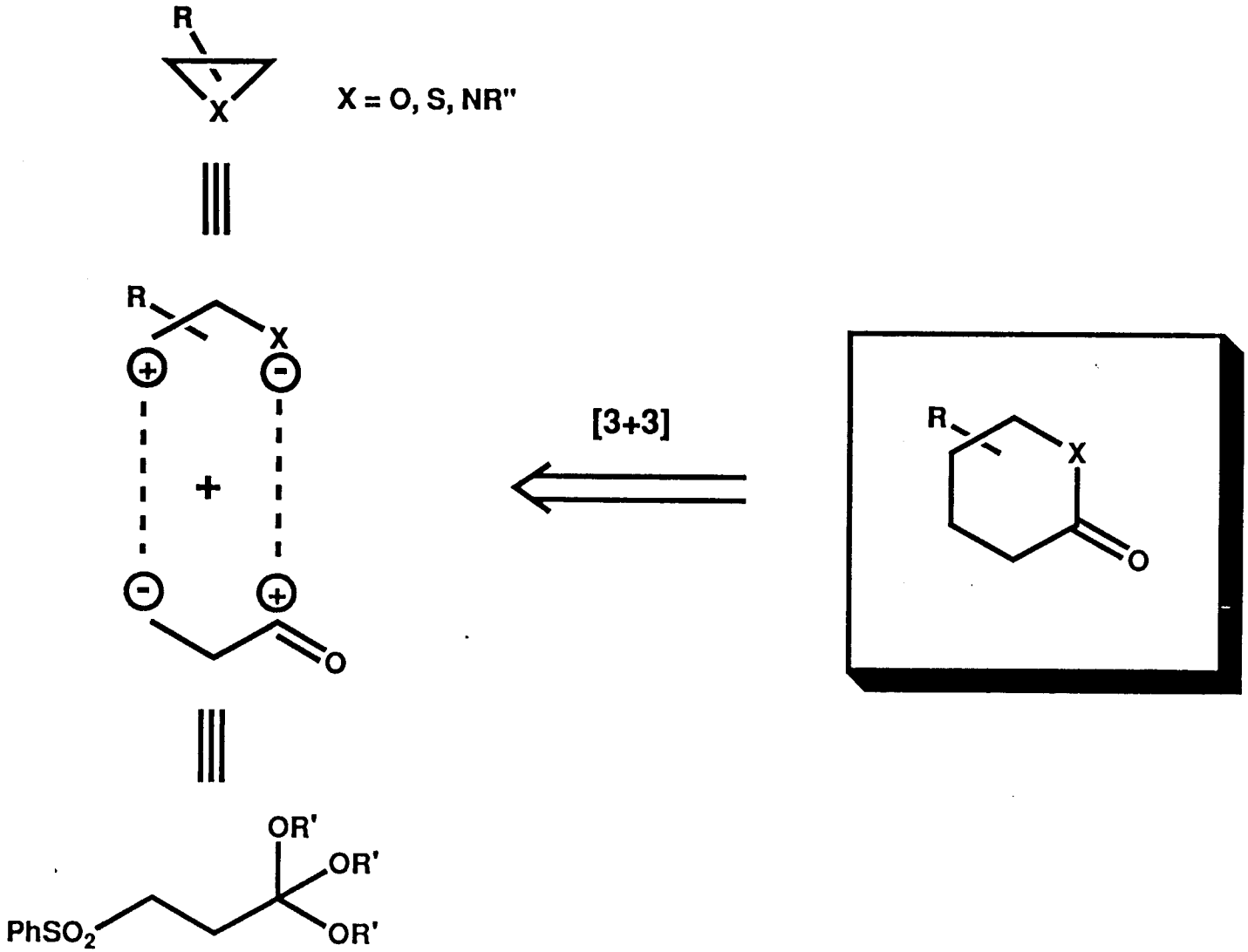
JAN05


OH
H
O
H
O
Yield: 48%
(5 steps)
e.e.: 96%
OEt
OEt
OEt
N-SO2
OMe
Yield: 33%
(5 steps)
e.e.: 92%
HO
H
O
H
O
O
Me
O
H
Yield: 48%
(5 steps)
e.e.: 95%
Yield: 33%
(5 steps)
e.e.: 98%
OH
H
O
H

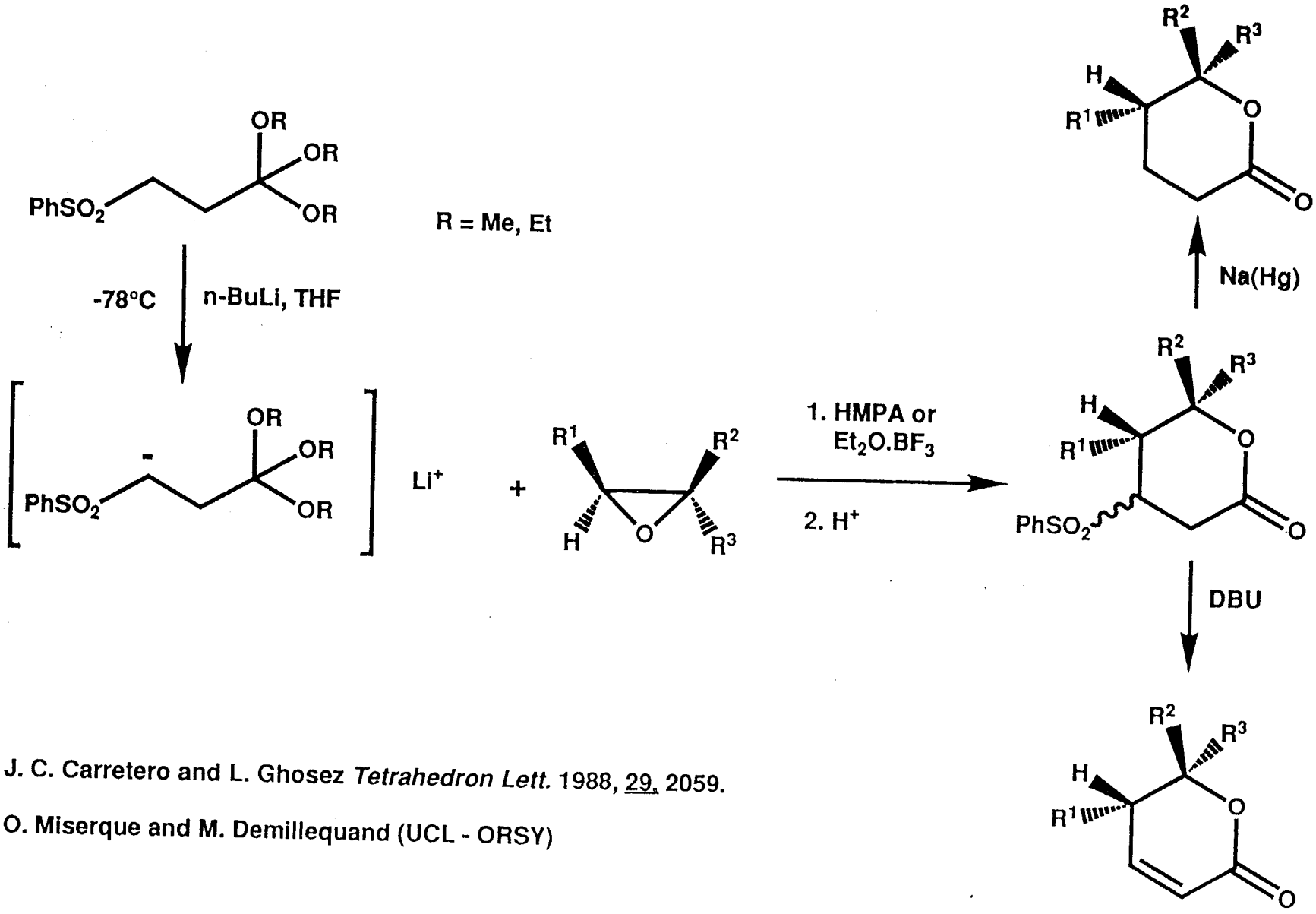
JAN06


DIBAL
CH_2Cl_2
91%
HO
$tBuMe_2SiO$
SO_2Ph
75%
1. NaH / THF
2. BnBr / $nBu_4N^+I^-$
BnO
59%
Zn - CH_2Br_2- $TiCl_4$
$FeCl_3.6H_2O$, SiO_2, $CHCl_3$
79%
100%
Al_2O_3 / $CHCl_3$
O

Synthesis of 6-membered ring heterocycles based on a [3+3] strategy

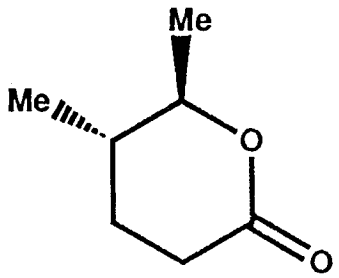


[3+3] Annulations : δ-Lactones and Pentenolides

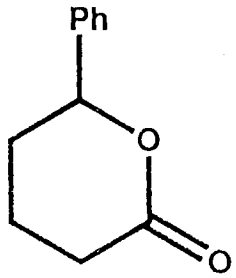


J. C. Carretero and L. Ghosez *Tetrahedron Lett.* 1988, 29, 2059.

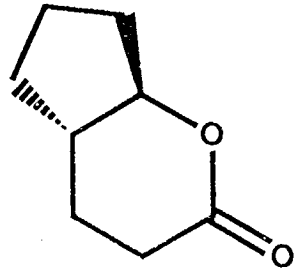
O. Miserque and M. Demillequand (UCL - ORSY)



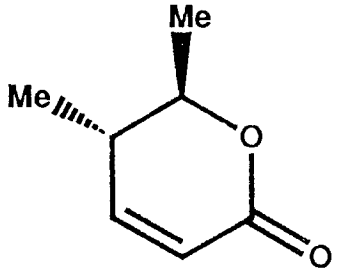
48%



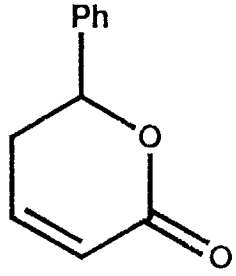
48%



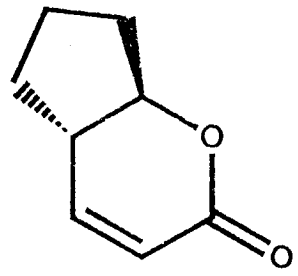
62%



68%



62%

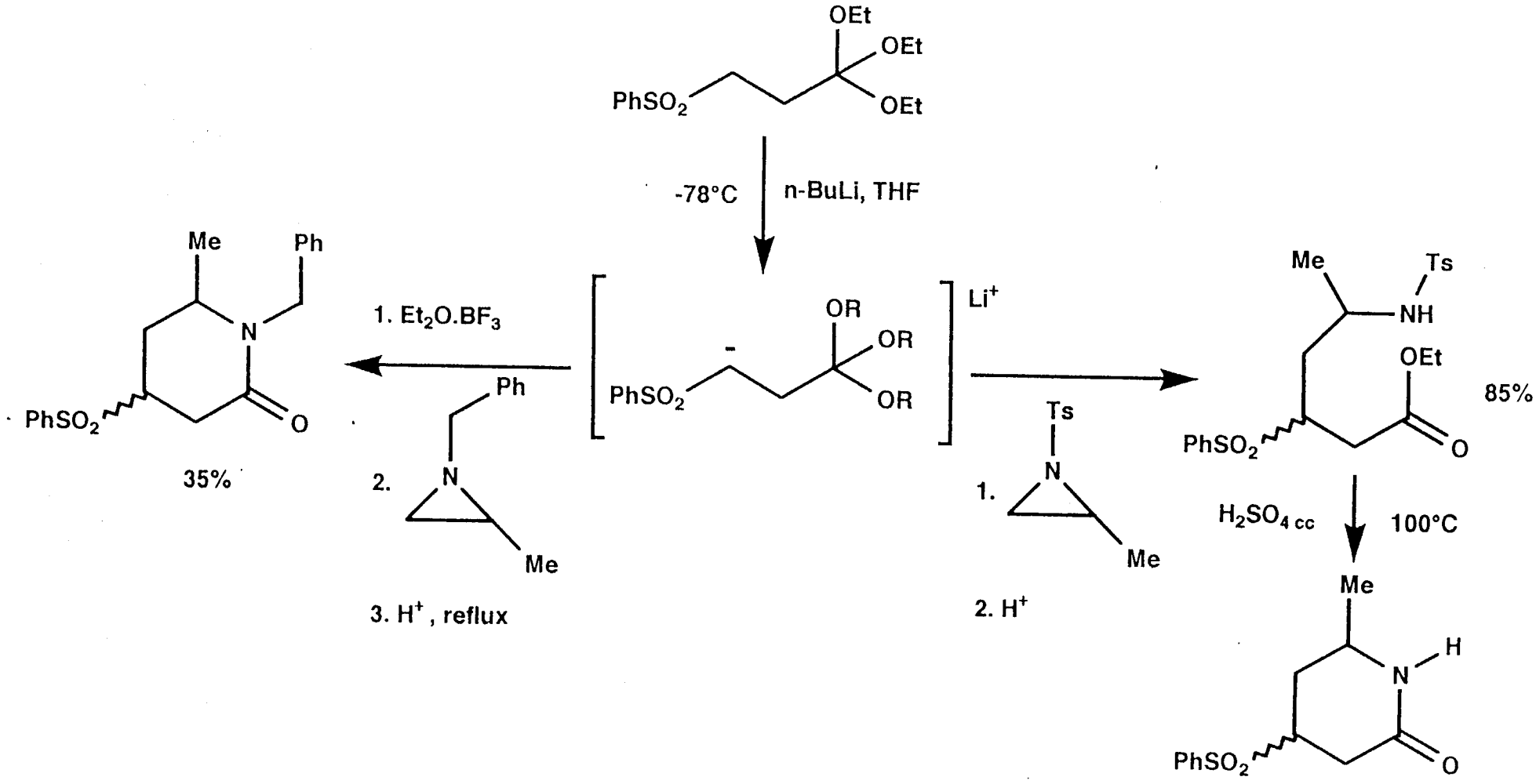


69%

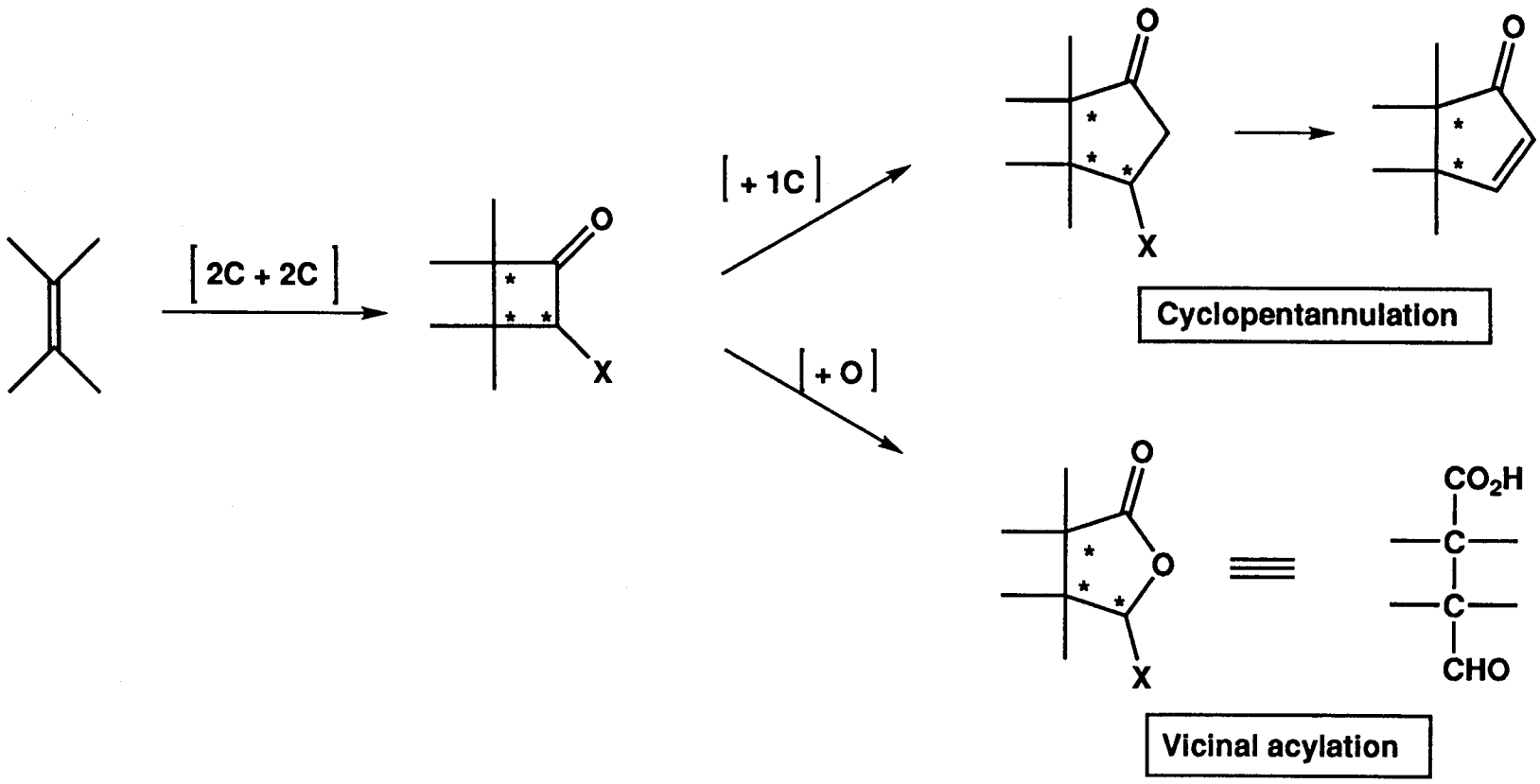
J.C. Carretero and L. Ghosez *Tetrahedron Lett.* 1988, 29, 2059.

O. Miserque and M. Demillequand (UCL - ORSY)

[3+3] Annulations : δ-Lactams



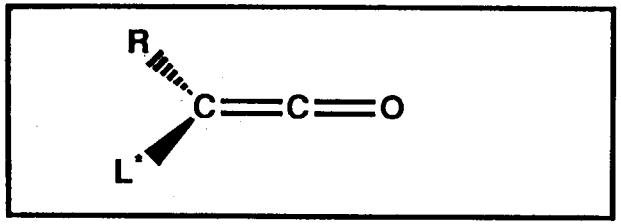
T. Delplanche, O. Miserque and M. Demillequand (UCL - ORSY)

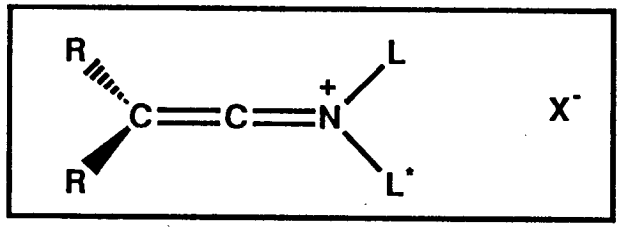


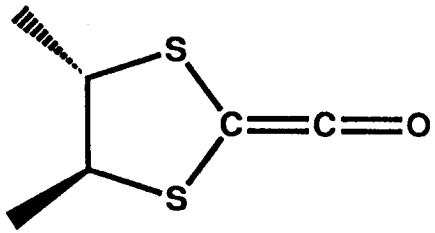
1st step : [2 + 2] cycloaddition with a chiral reagent

2nd step : strain - assisted insertion of CH_2 or O

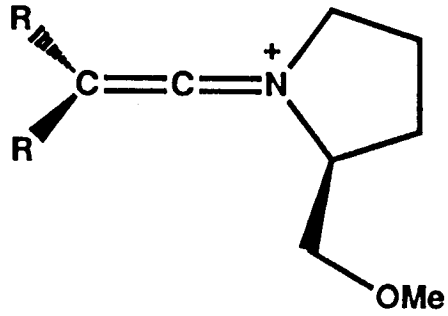
CHIRAL REAGENTS FOR [2 + 2] CYCLOADDITIONS



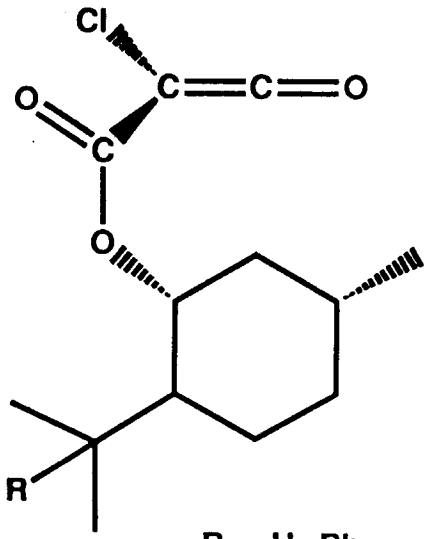




poor de (±10%)

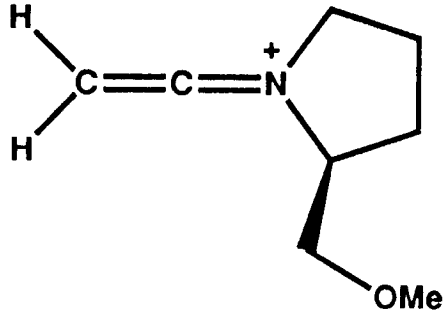


70-98 %de



poor de (< 20%)

R = H, Ph

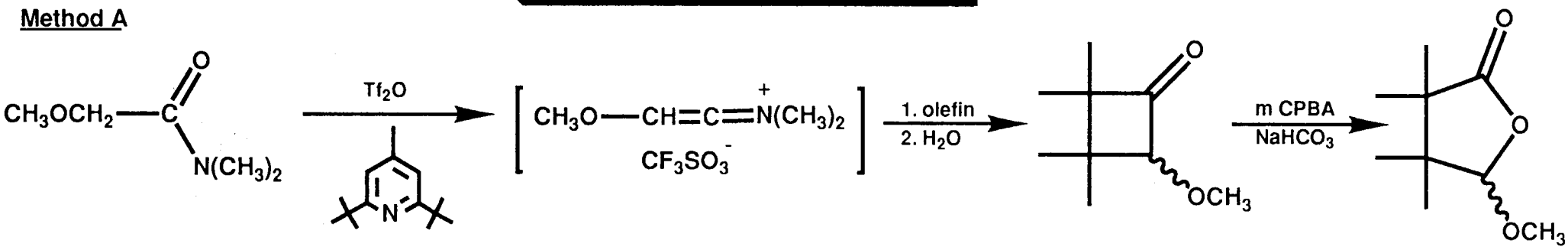


± 55% de

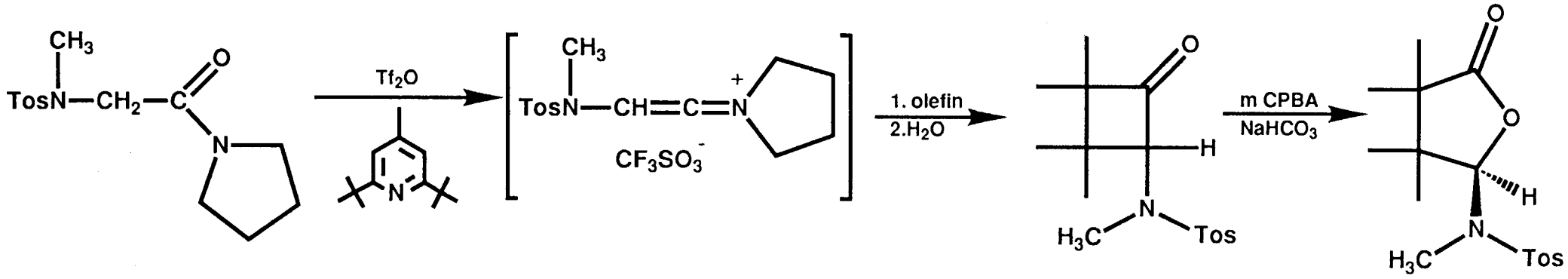
E2

Vicinal Acylation of Olefins

Method A



Method B

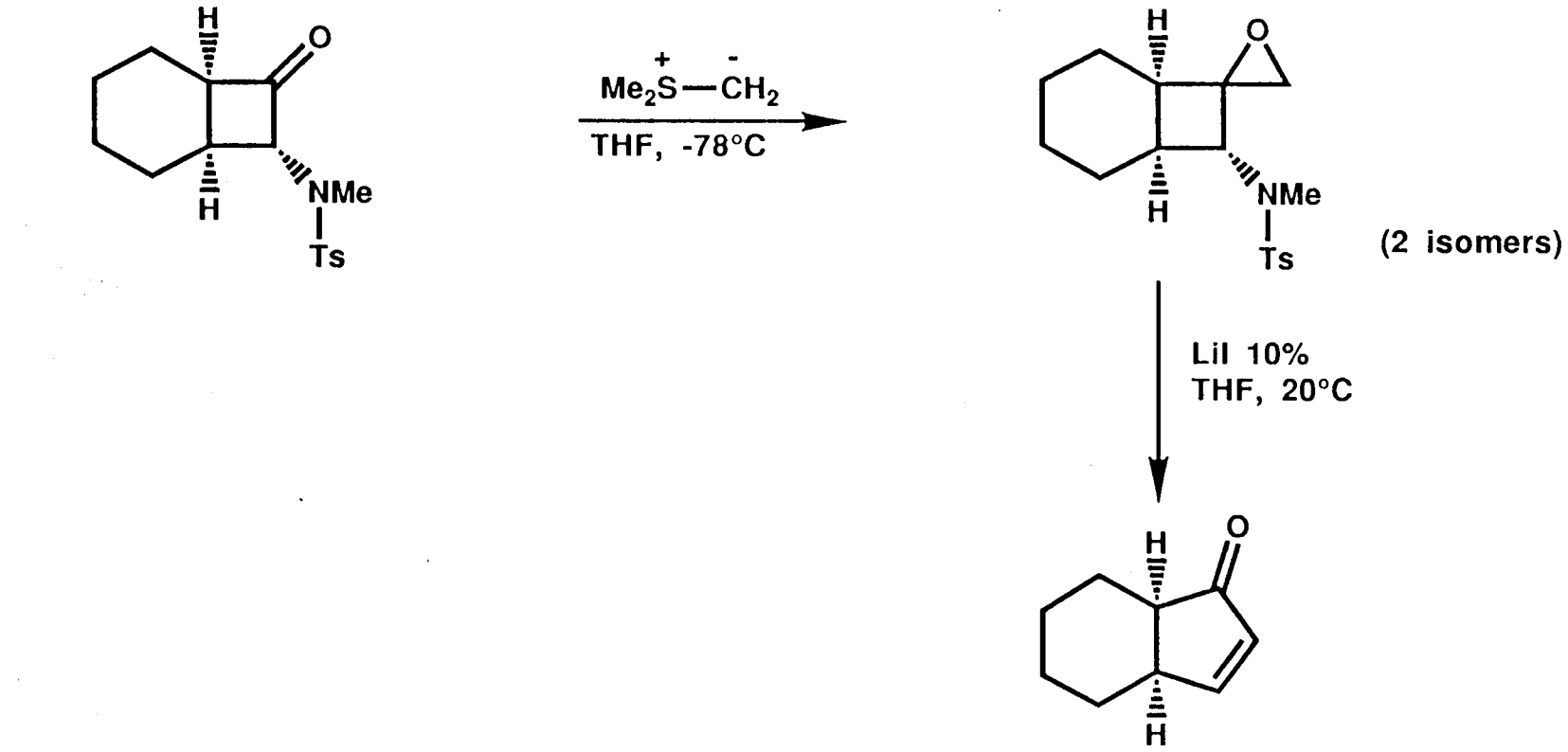


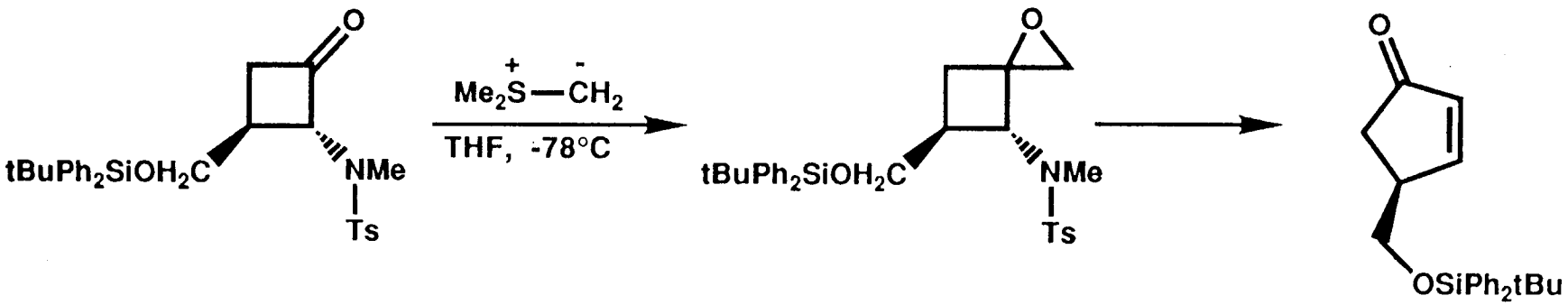
Yields : A 62 - 85% for cycloaddition ; 75 - 90% for oxidation

B 65 - 80% for cycloaddition ; 80 - 93% for oxidation

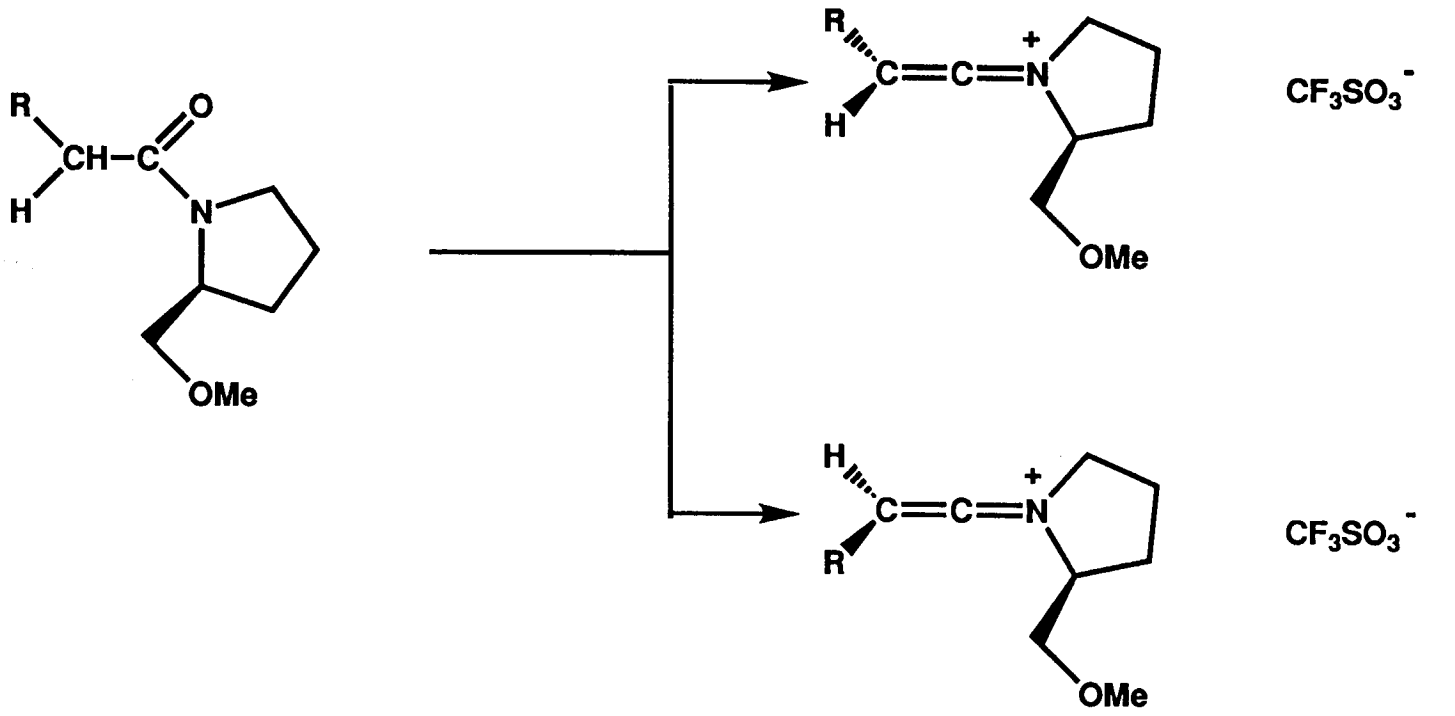
Scope : Broad

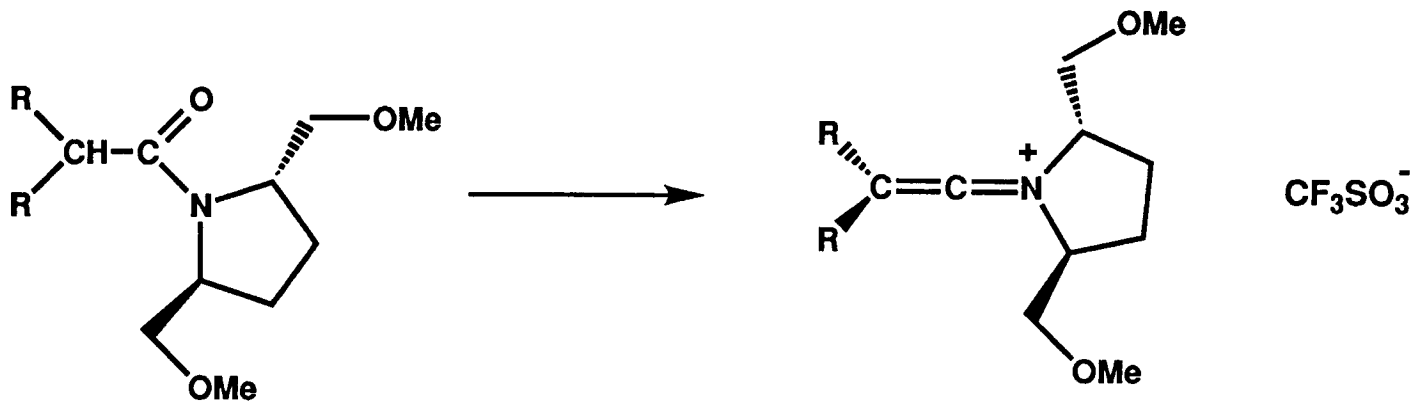
C. Génicot, B. Gobeaux (UCL - ORSY)

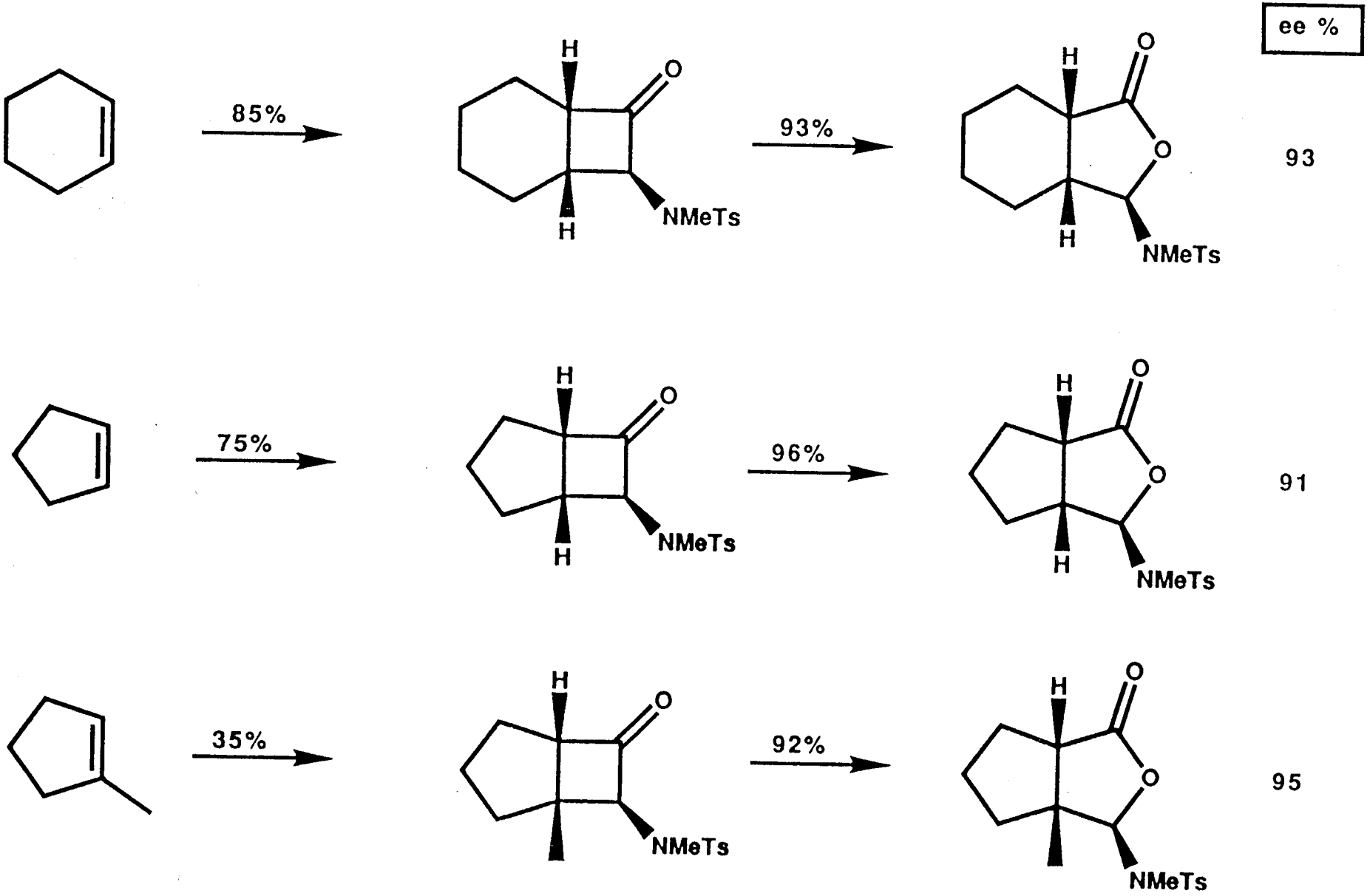




S. Vanwetswinkel (UCL - ORSY)

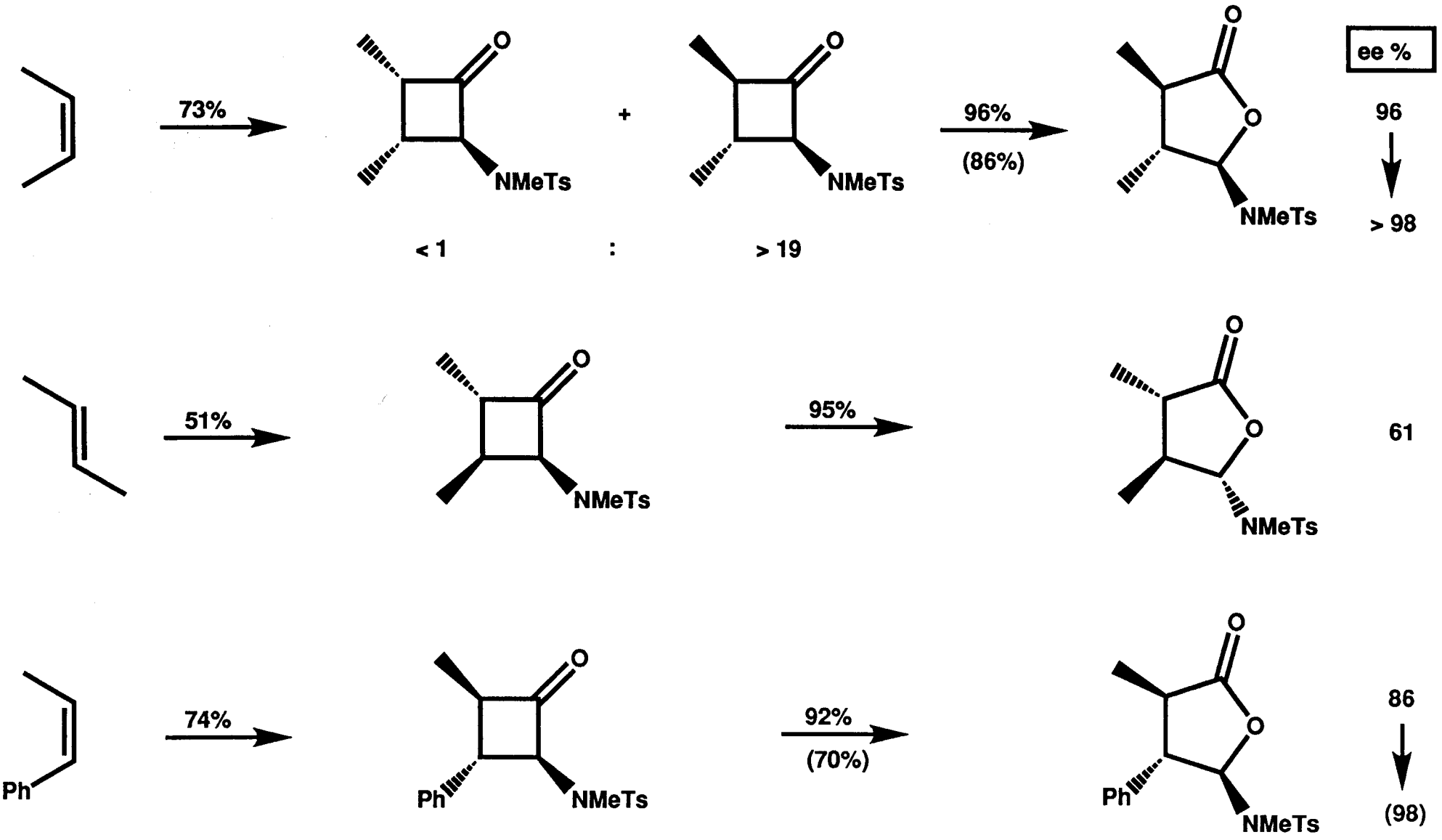

R
CH
C
O
H
N
OMe
R
C
C
N
H
OMe
CF3SO3-
H
C
C
N
R
OMe
CF3SO3-

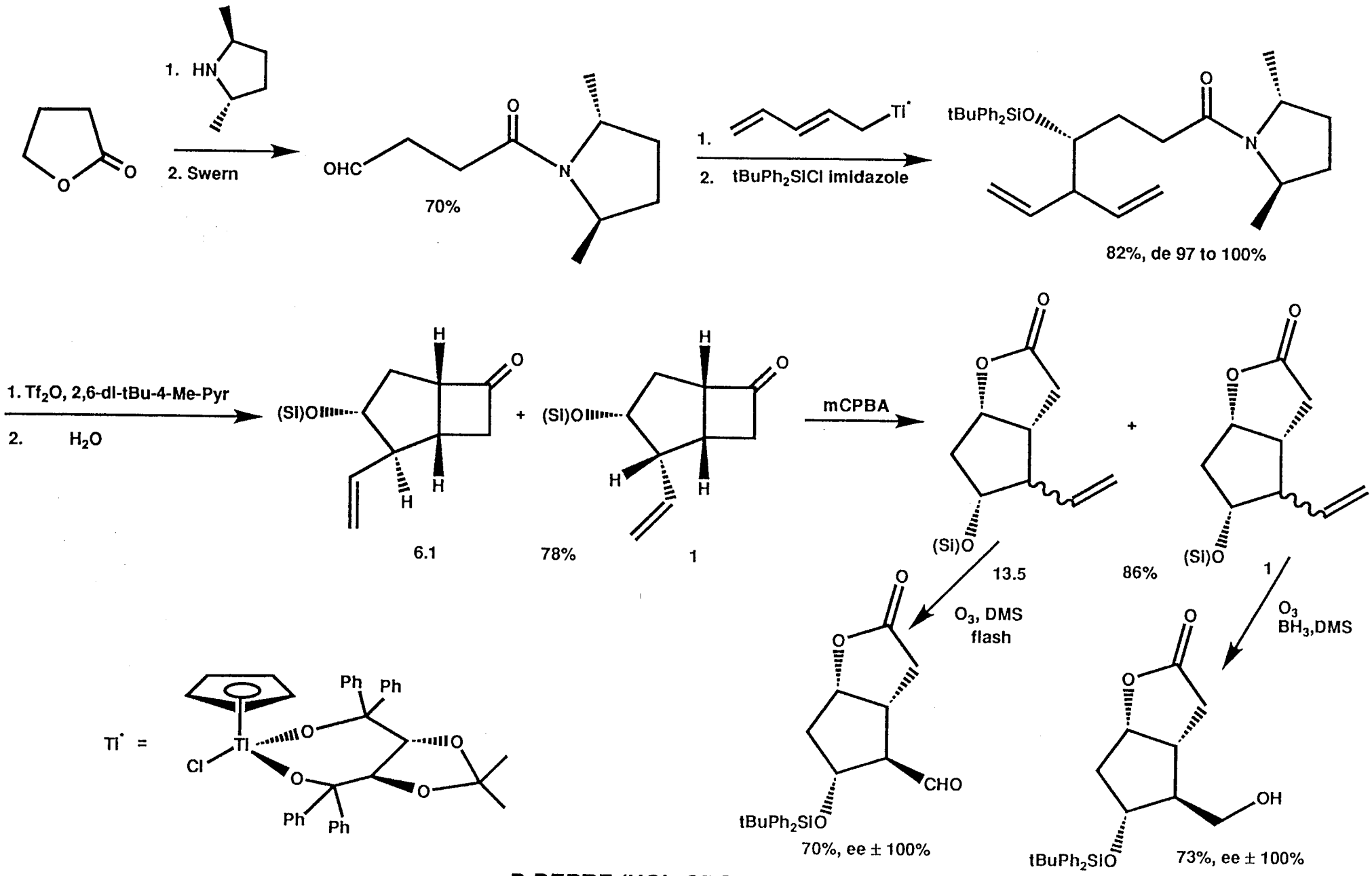

R
CH
C
O
R
N
OMe
OMe
R
C
C
N
R
OMe
CF3SO3-


ee %
85%
93%
NMeTs
93
75%
96%
NMeTs
91
35%
92%
NMeTs
95

JAN21

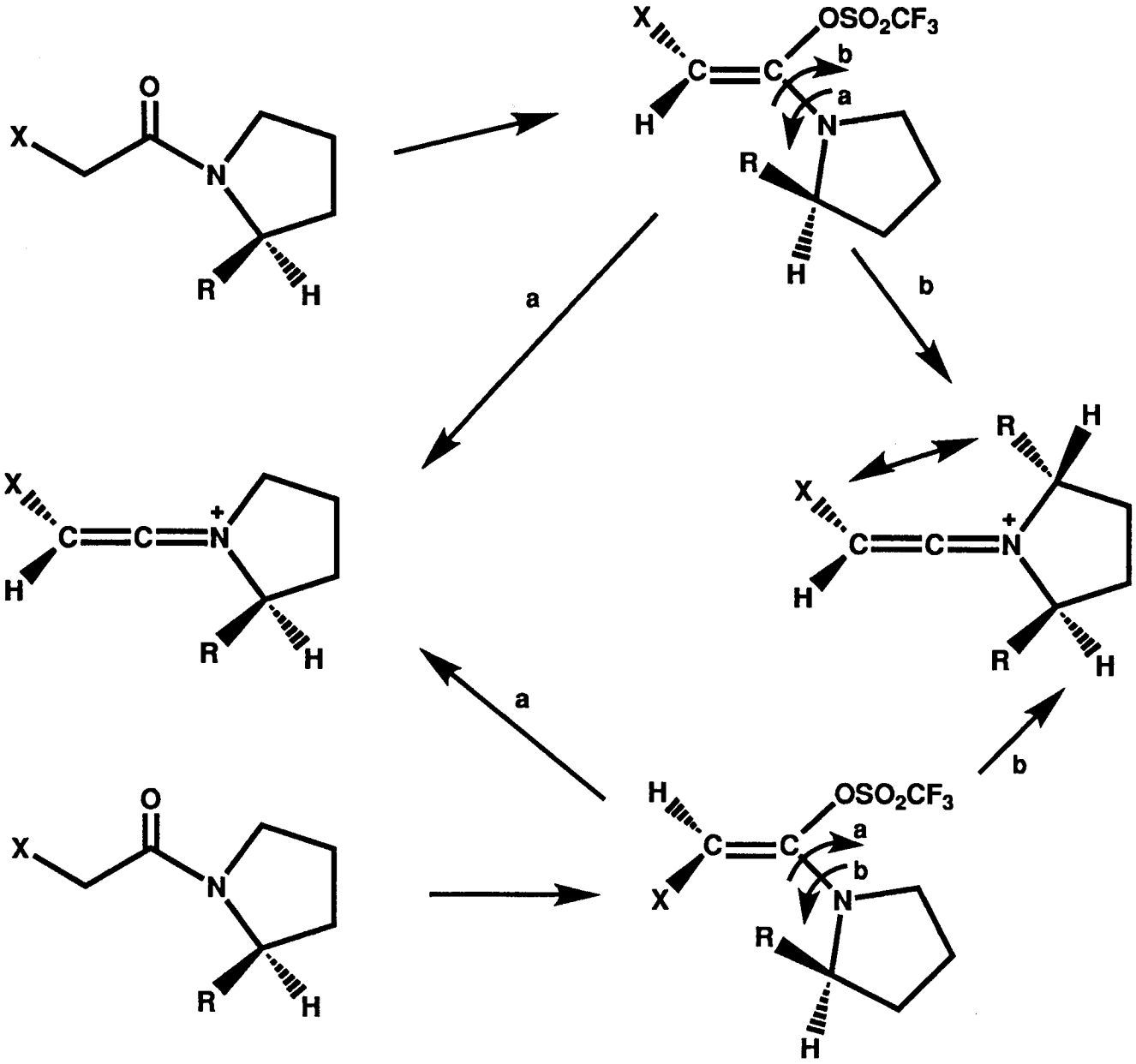
1,2 - DISUBSTITUTED OLEFINS



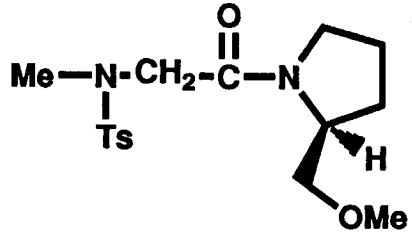


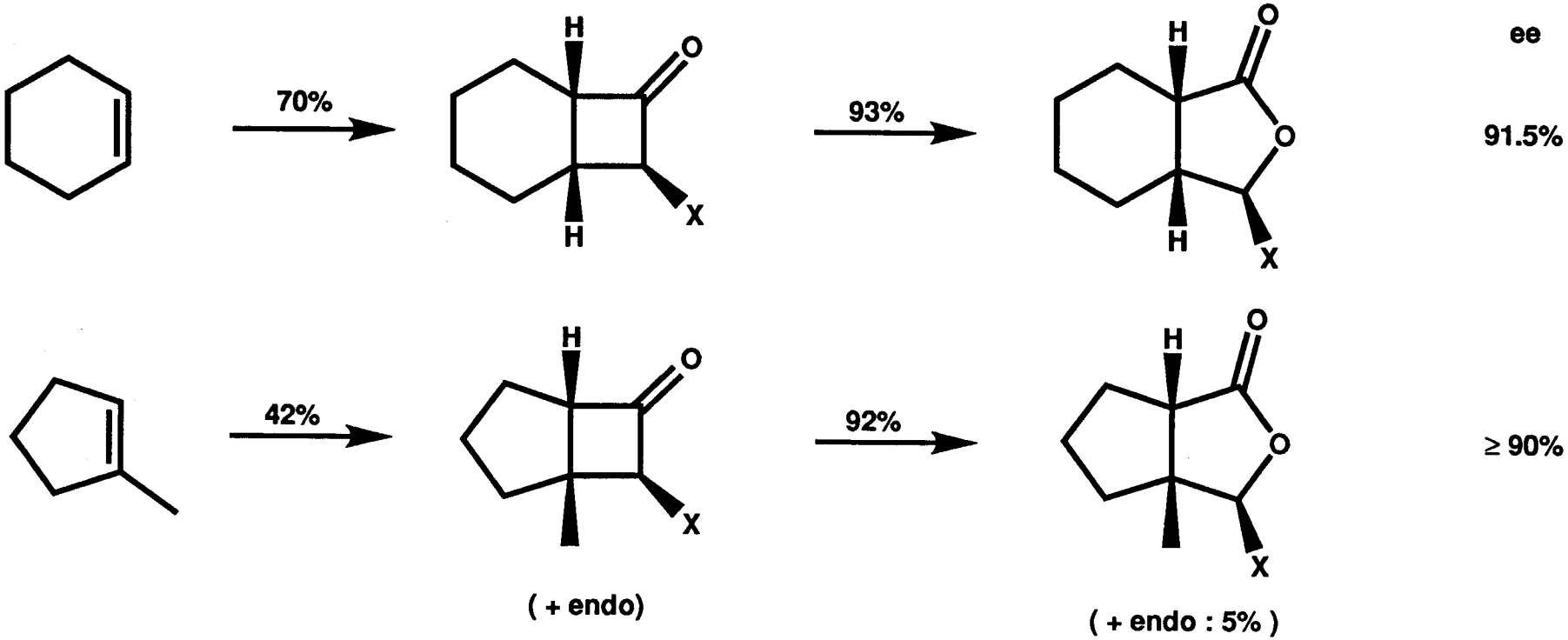
D.DEPRE (UCL-ORSY)

TORQUOSELECTIVITY

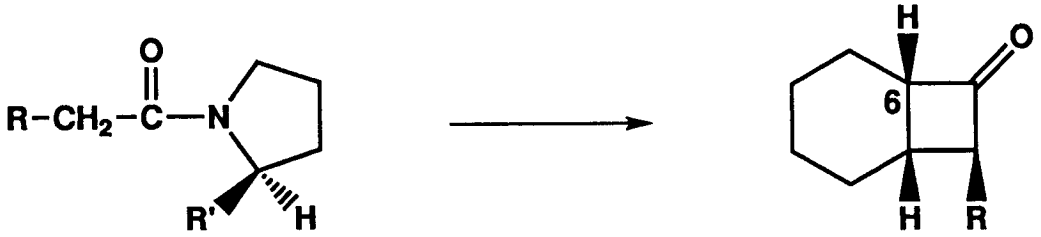


Vicinal Acylation of Olefins with





	ee
	91.5%
	≥ 90%



R	R'	ee%	Conf. C_6
NTsMe	Me	90	S
NTsMe	CH_2OMe	92	S
$HCMe_2$	CH_2OMe	98	S
Me	CH_2OMe	82	S

High ee's result from two sequencial asymmetric reactions :

Torquoselective formation of keteniminium salt
Facial selective cycloaddition