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Communication

Enantioselective Synthesis of Euonyminol

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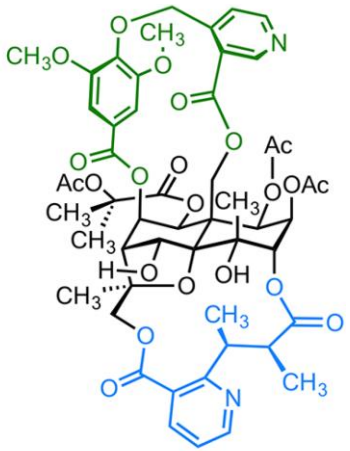
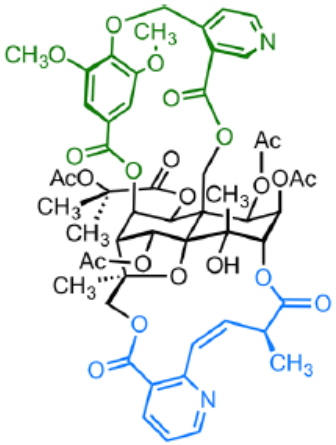
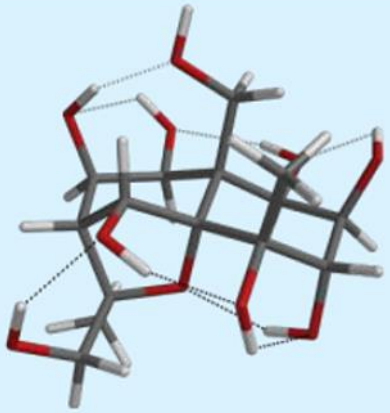


cathedulin E-4 (1)



cathedulin K-19 (2)



euonyminol (3)

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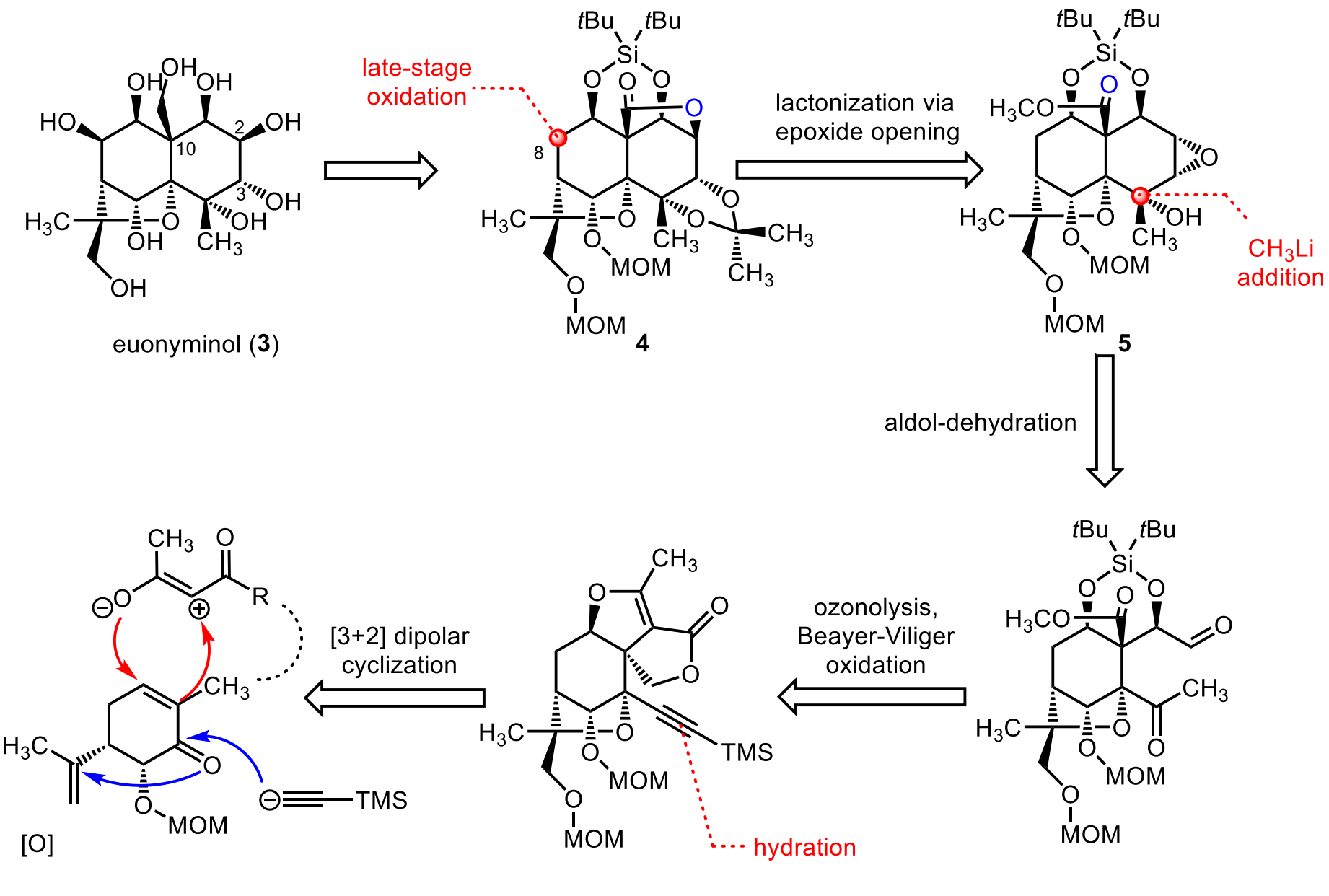
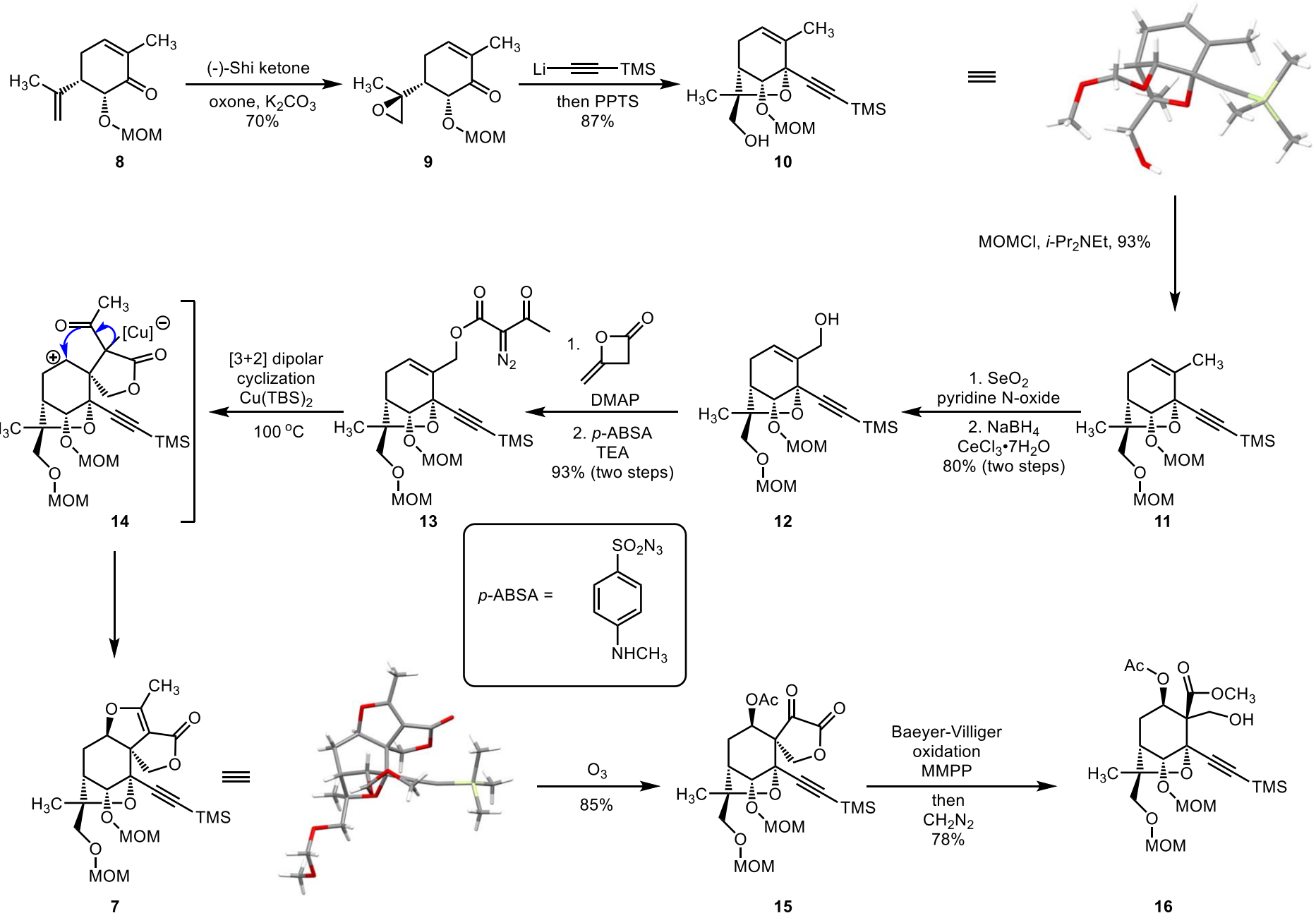
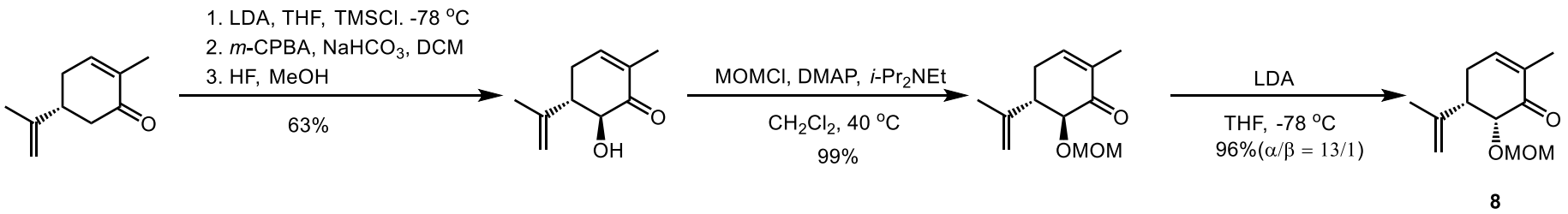
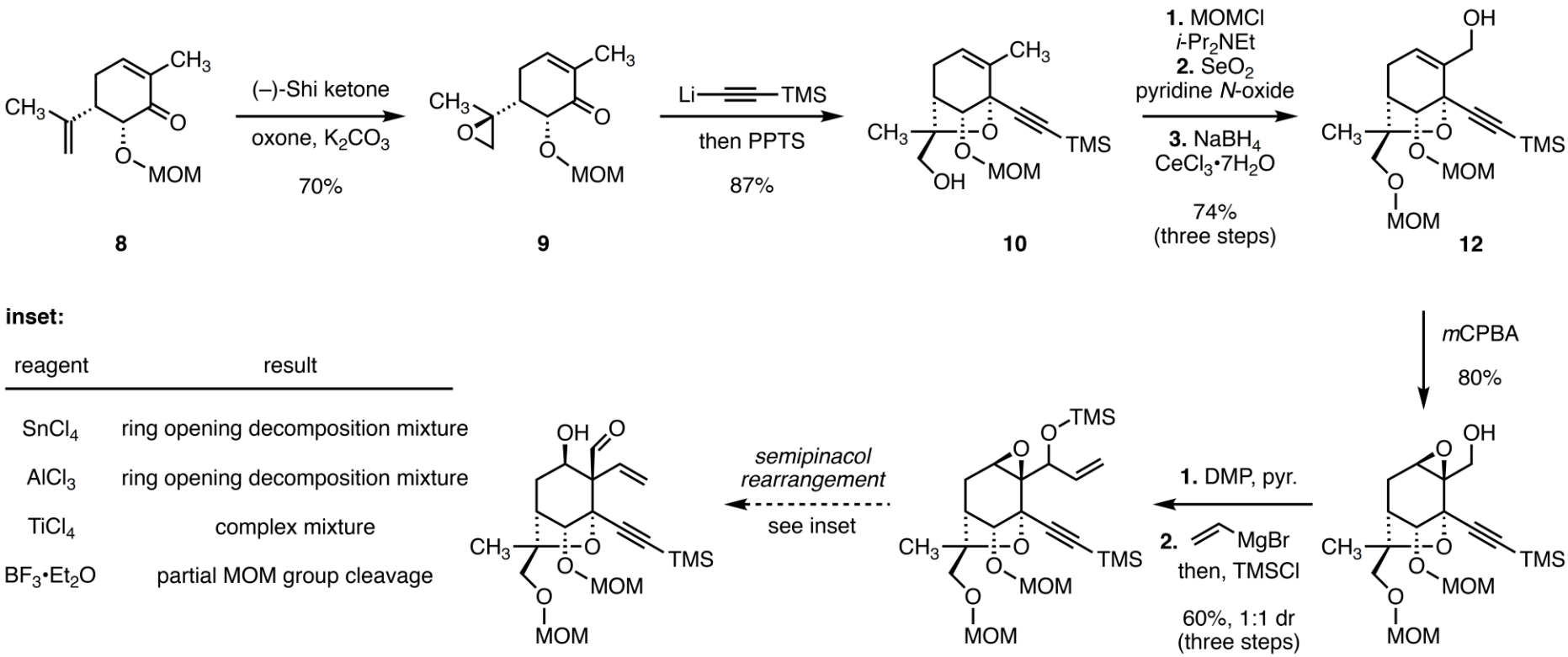

euonyminol (3)
late-stage oxidation
4
lactonization via epoxide opening
5
CH3Li addition
aldol-dehydration
6
ozonolysis, Beayer-Viliger oxidation
7
hydration
[3+2] dipolar cyclization
8
[O]

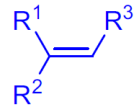

(-)-Shi ketone
oxone, K2CO3
70%
Li—≡—TMS
then PPTS
87%
MOMCl, i-Pr2NEt, 93%
1. SeO2
pyridine N-oxide
2. NaBH4
CeCl3•7H2O
80% (two steps)
1.
DMAP
2. p-ABSA
TEA
93% (two steps)
[3+2] dipolar
cyclization
Cu(TBS)2
100 °C
p-ABSA =
SO2N3
NHCH3
O3
85%
Baeyer-Villiger
oxidation
MMPP
then
CH2N2
78%
8
9
10
11
12
13
14
7
15
16


1. LDA, THF, TMSCl. -78 °C
2. m-CPBA, NaHCO3, DCM
3. HF, MeOH
63%
MOMCl, DMAP, i-Pr2NEt
CH2Cl2, 40 °C
99%
LDA
THF, -78 °C
96%(α/β = 13/1)
OH
OMOM
OMOM
8


(–)-Shi ketone
oxone, K2CO3
70%
Li—≡—TMS
then PPTS
87%
1. MOMCl
i-Pr2NEt
2. SeO2
pyridine N-oxide
3. NaBH4
CeCl3•7H2O
74%
(three steps)
mCPBA
80%
1. DMP, pyr.
2. MgBr
then, TMSCl
60%, 1:1 dr
(three steps)
semipinacol
rearrangement
see inset
8
9
10
12
inset:
reagent
result
SnCl4
ring opening decomposition mixture
AlCl3
ring opening decomposition mixture
TiCl4
complex mixture
BF3•Et2O
partial MOM group cleavage

SHI ASYMMETRIC EPOXIDATION

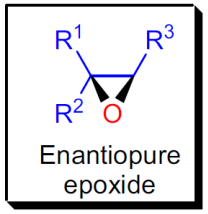
(References are on page 676)



R^{1-3} = H, alkyl, aryl, substituted alkyl, substituted aryl, alkenyl, alkynyl

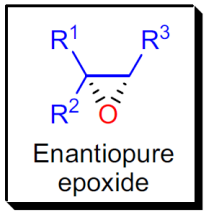
Shi's catalyst

$KHSO_5$
or 30% H_2O_2 (3.0 equiv)
H_2O / CH_3CN; pH ~7-10
50-90% yield, > 90% ee

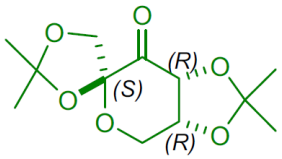


Enantiopure epoxide

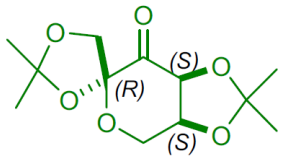
or



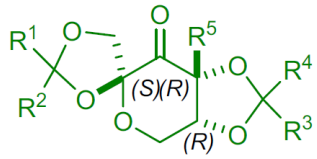
Enantiopure epoxide



Shi's catalyst derived from D-fructose

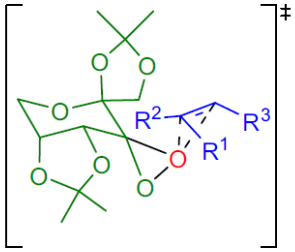


Shi's catalyst derived from L-fructose

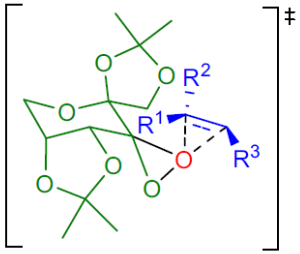


Shi's generalized catalysts (derived from D-fructose)

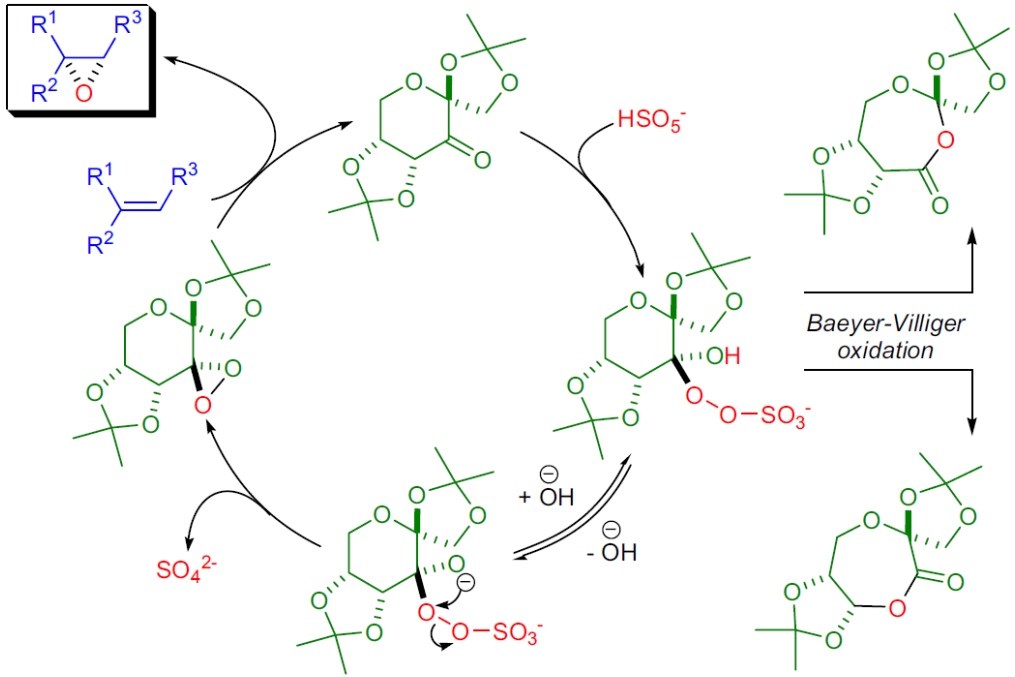
R^{1-2} = Me, Et, $-(CH_2)_4-$, $-(CH_2)_5-$, $-(CH_2)_6-$
R^{3-4} = Me, Et, i-Pr, H, F, Bn, $-(CH_2)_4-$, $-(CH_2)_5-$, $-(CH_2)_6-$
R^5 = H, F



Spiro transition state



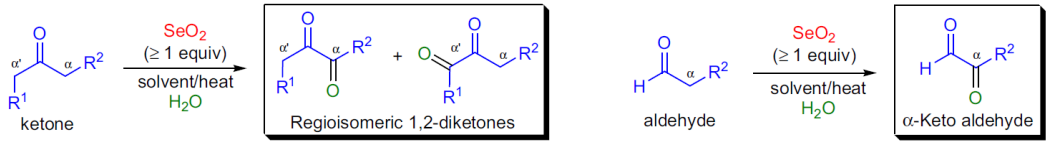
Planar transition state



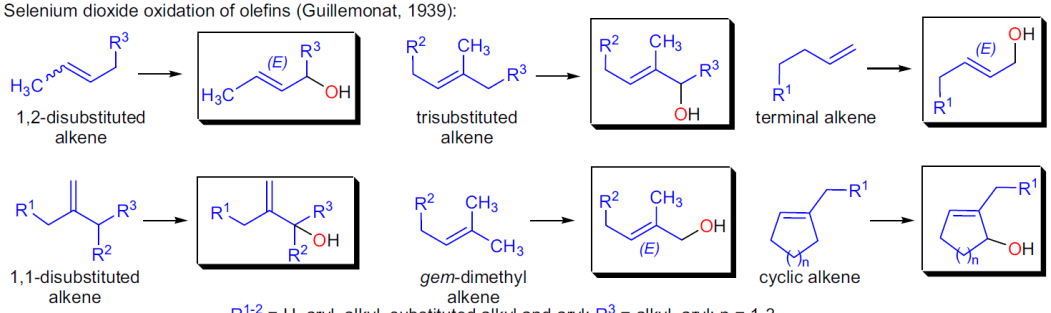
RILEY SELENIUM DIOXIDE OXIDATION

(References are on page 663)

Selenium dioxide oxidation of ketones and aldehydes (Riley, 1932):



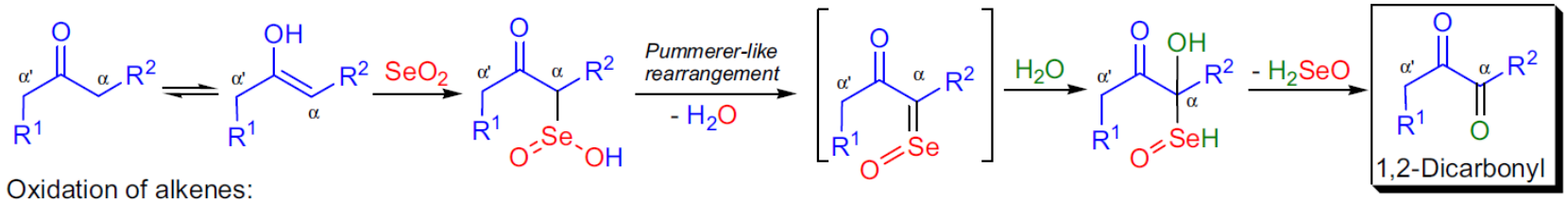
Selenium dioxide oxidation of olefins (Guillemonat, 1939):



R^{1-2} = H, aryl, alkyl, substituted alkyl and aryl; R^3 = alkyl, aryl; n = 1-3

Mechanism: [24-41]

Oxidation of carbonyl compounds:



Oxidation of alkenes:

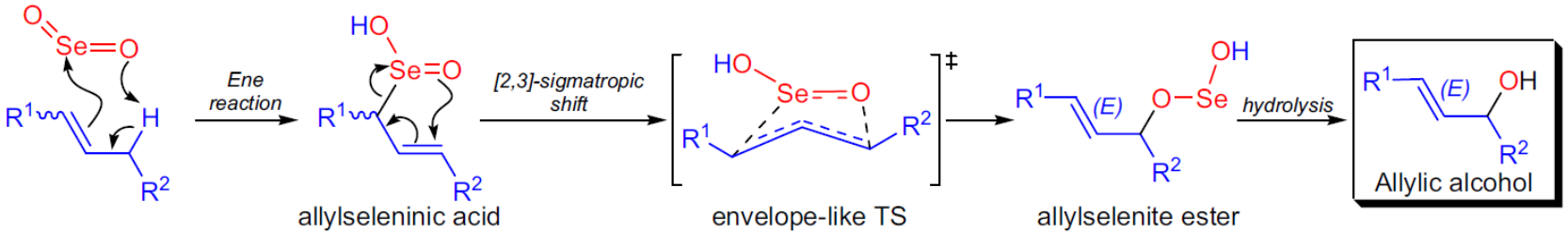
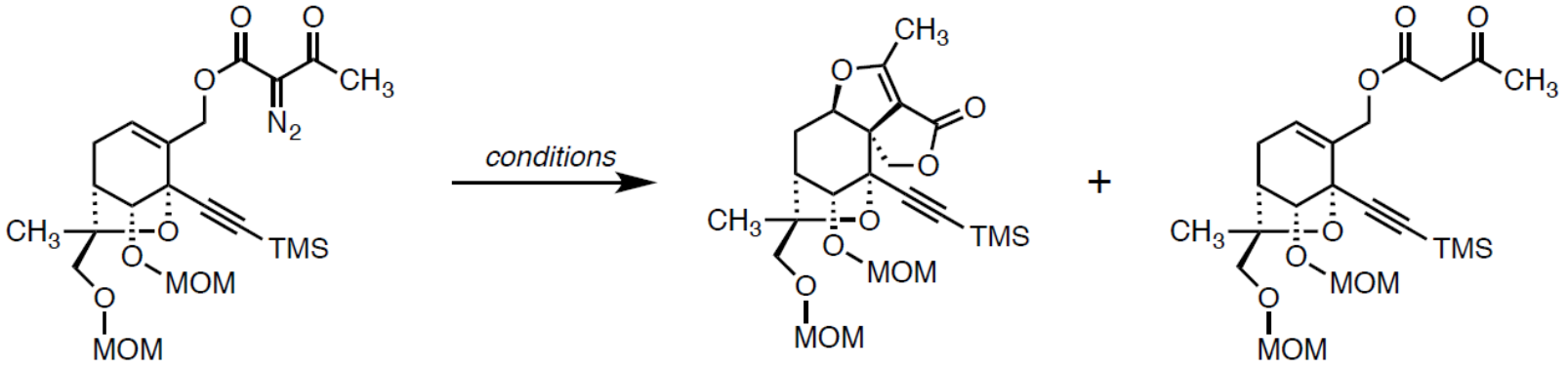
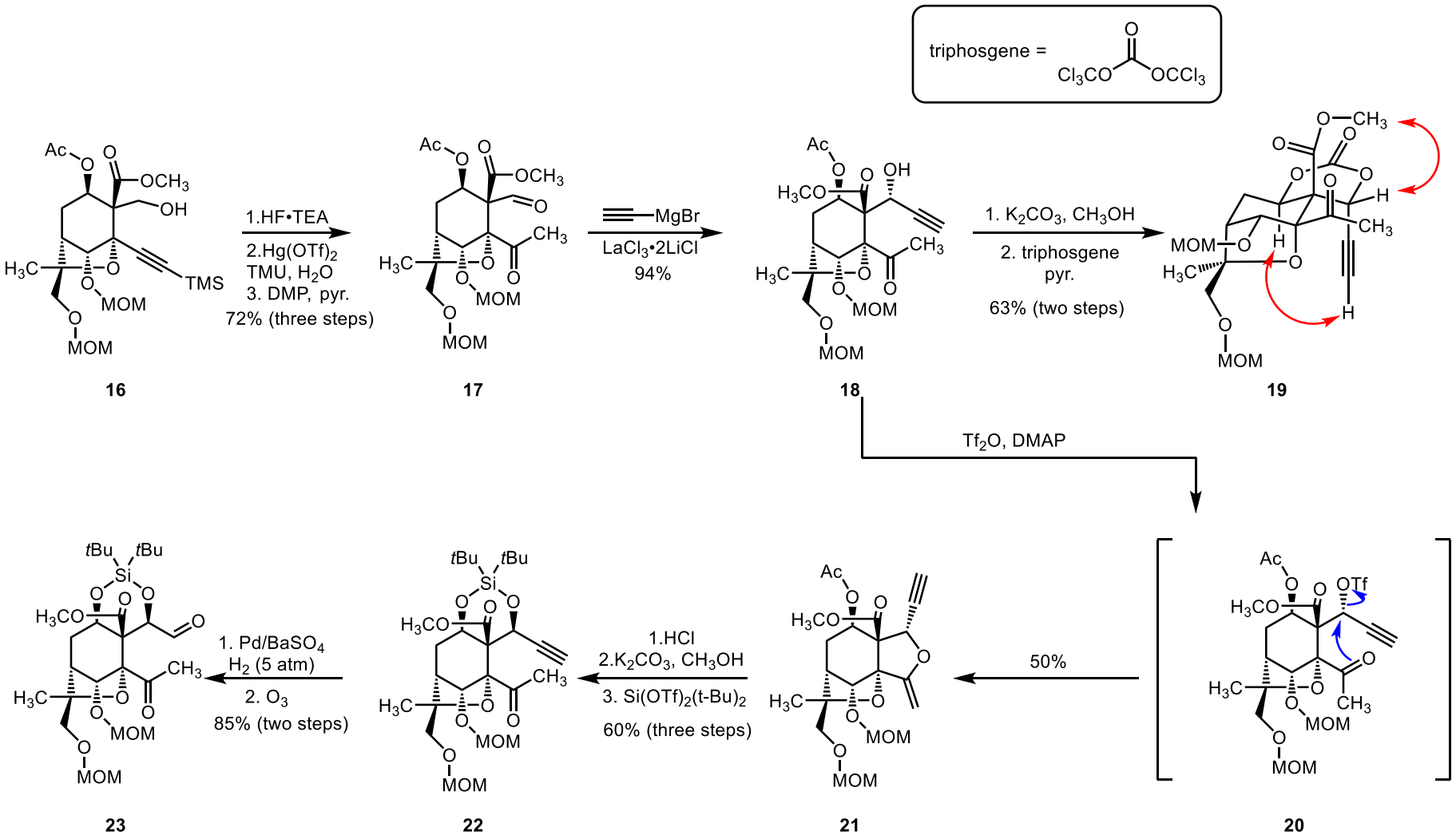


Table S1. Optimization of the [3+2] cycloaddition.



13 **7** **S4**

entry	conditions	results
1	$Cu(OTf)_2$, DCE, 50 °C	complex mixture
2	$Rh_2(OAc)_4$, CH_2Cl_2, 23 °C	formation of S4
3	$Rh_2(esp)_4$, CH_2Cl_2, 23 °C	complex mixture
4	$Cu(TBS)_2$, toluene, 110 °C (0.1 M)	40% of **7**; 25% of **S4**
5	$Cu(TBS)_2$, toluene, 100 °C (0.02 M)	67% of **7**
6	$Cu(TBS)_2$, deoxygenated toluene, 100 °C (0.02 M)	83% of **7**


triphosgene =
1.HF•TEA
2.Hg(OTf)2
TMU, H2O
3. DMP, pyr.
72% (three steps)
MgBr
LaCl3•2LiCl
94%
1. K2CO3, CH3OH
2. triphosgene
pyr.
63% (two steps)
Tf2O, DMAP
50%
1.HCl
2.K2CO3, CH3OH
3. Si(OTf)2(t-Bu)2
60% (three steps)
1. Pd/BaSO4
H2 (5 atm)
2. O3
85% (two steps)
16
17
18
19
20
21
22
23

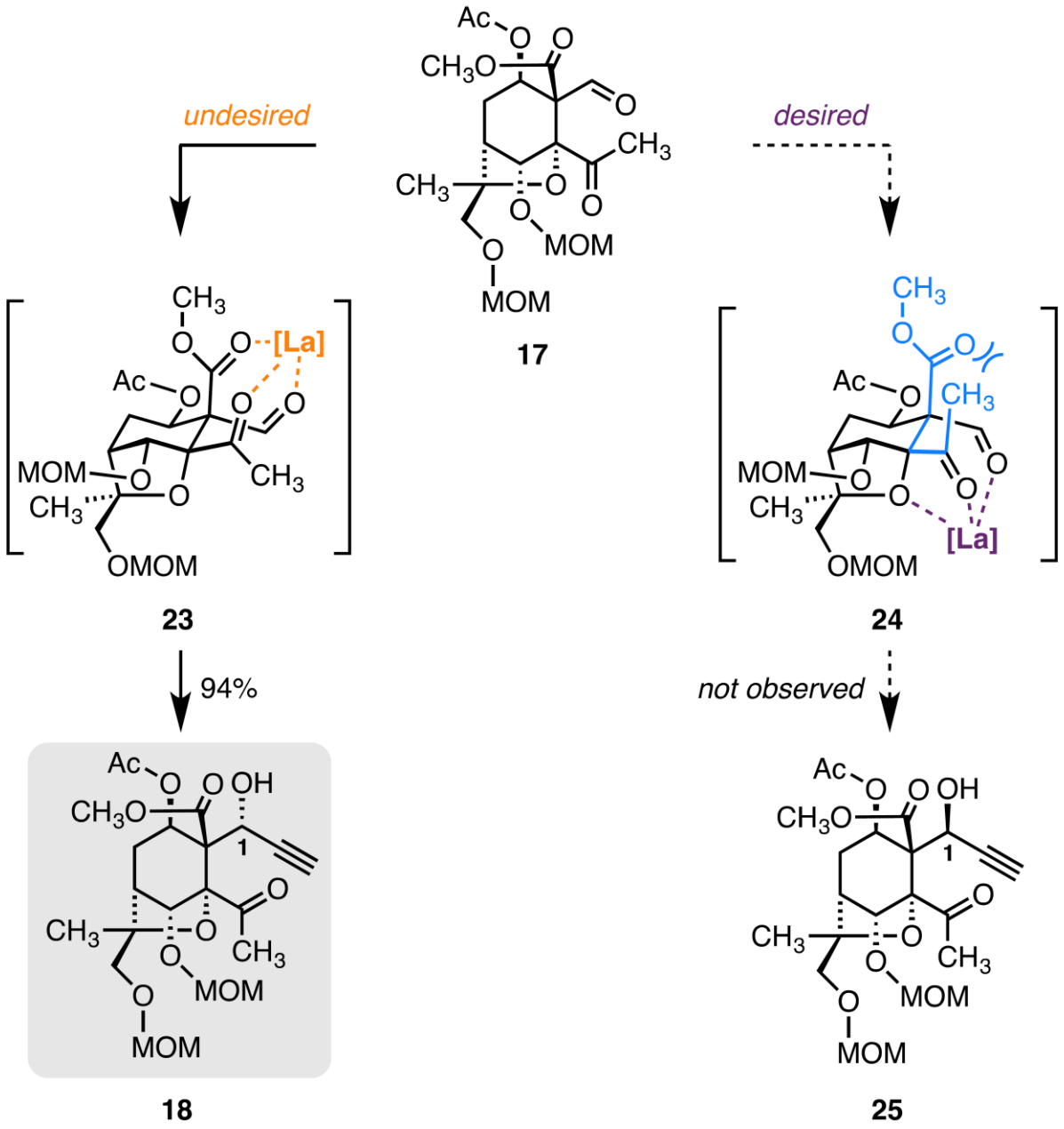
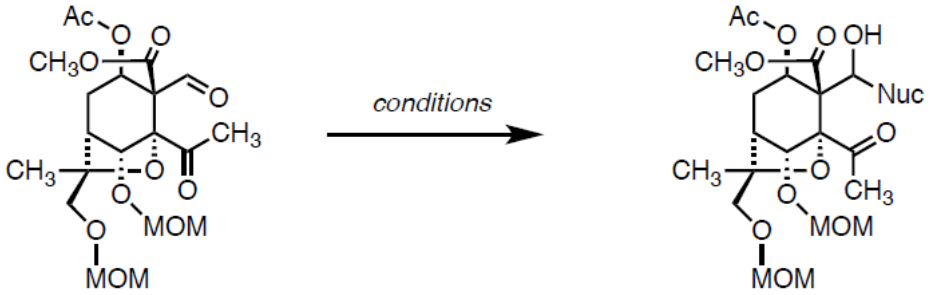
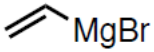
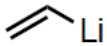


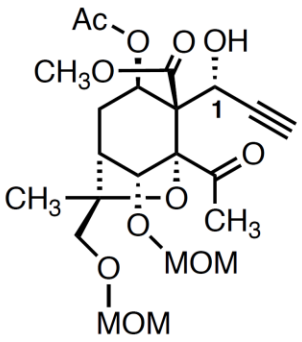
Figure 2. Stereochemical model for the addition of ethynylmagnesium bromide to the neopentyl aldehyde **17**.

Table S2. Evaluation of nucleophiles in the addition to the neopentyl aldehyde **17**.



17

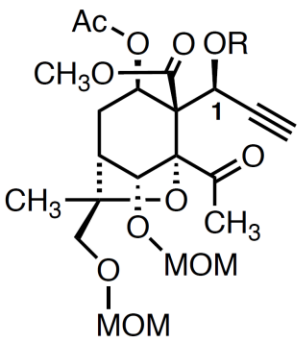
entry	conditions	results
1		no reaction, **17** was recovered
2	 , $LaCl_3 \cdot 2LiCl$	no reaction, **17** was recovered
3		no reaction, **17** was recovered
4	 , $CeCl_3$	no reaction, **17** was recovered
5		no reaction, **17** was recovered
6	 , $LaCl_3 \cdot 2LiCl$	94%, >20:1 dr
7	$TMSCN, Et_3N$	60%, 3:1 dr, not separable[1]



18

Mitsunobu reaction

see inset 1

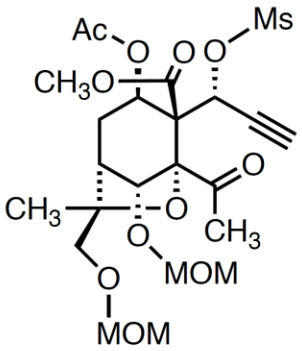


inset 1:

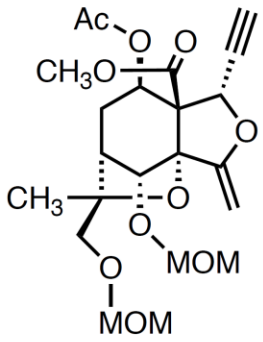
conditions	result
DEAD, PPh_3, 4-nitrobenzoic acid	no reaction
DEAD, $(CH_3)_3P$, chloroacetic acid	no reaction

MsCl, Et_3N

50%



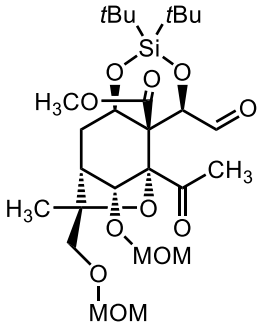
see inset 2



21

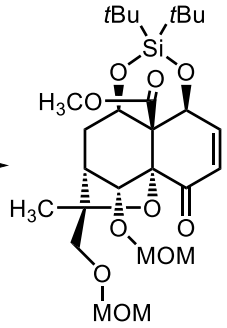
inset 2:

conditions	result
LDA	no reaction
KHMDS	decomposition
DBU	loss of Ms group



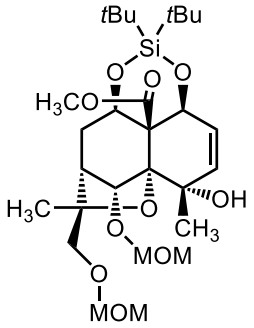
6

aldol-dehydration
1. NaOEt, EtOH
2. MsCl, Et_3N



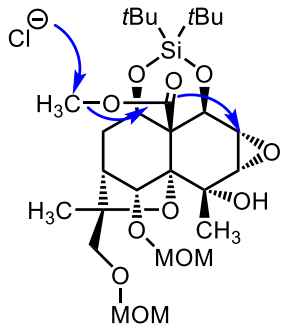
26

CH_3Li•LiBr
90%



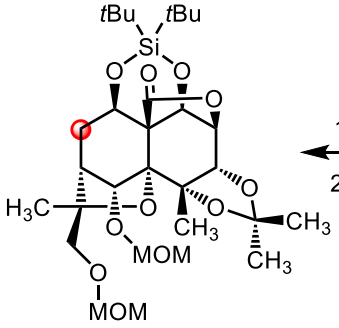
27

DMDO, 99%



5

1. LiCl, 130 °C
2. PTSA, 2,2-DMP
68% (two steps)



4

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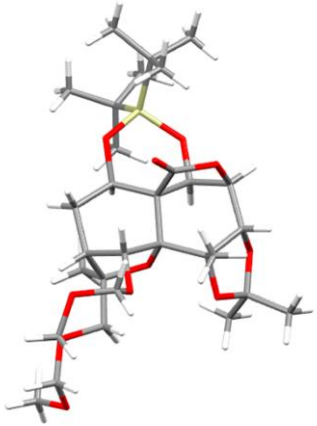
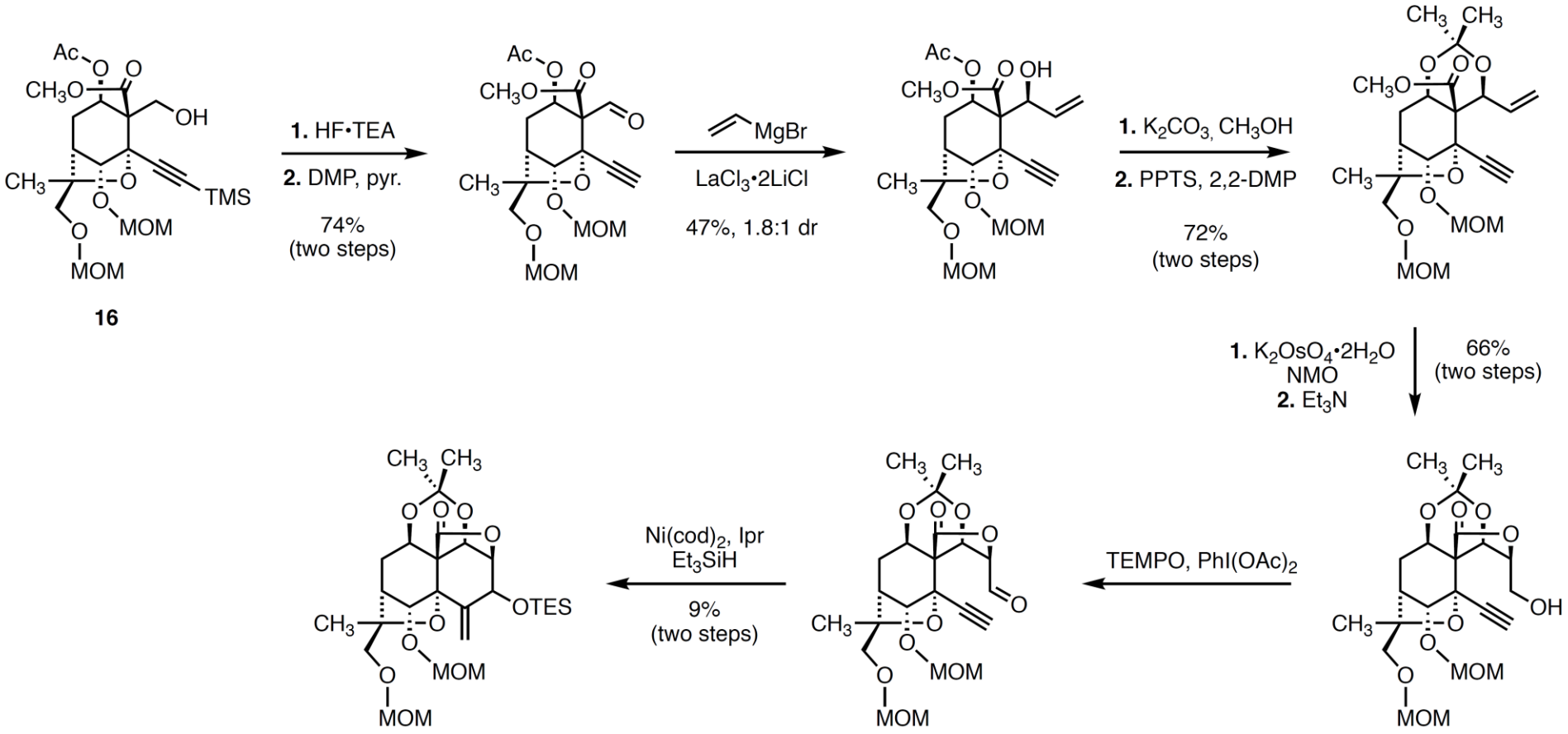
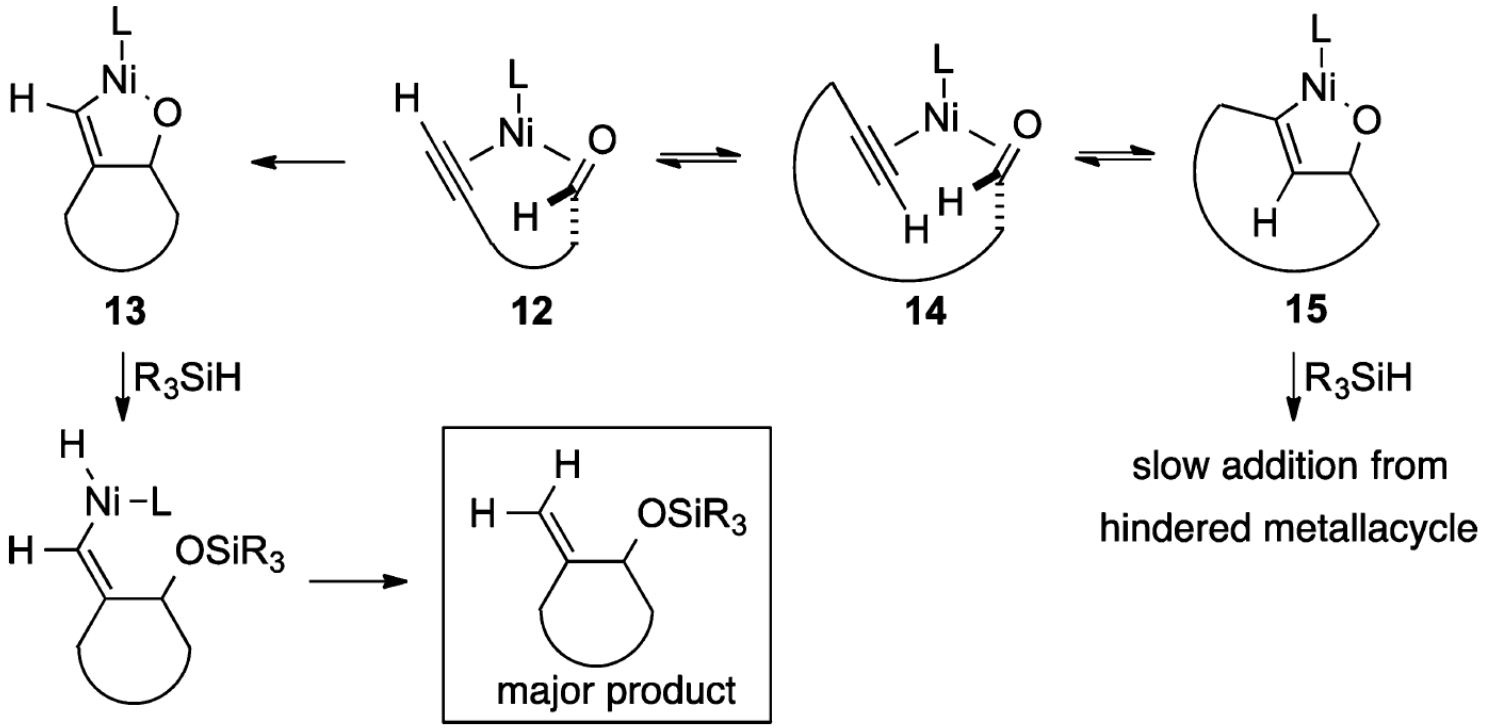



16
1. HF•TEA
2. DMP, pyr.
74%
(two steps)
MgBr
LaCl3•2LiCl
47%, 1.8:1 dr
1. K2CO3, CH3OH
2. PPTS, 2,2-DMP
72%
(two steps)
1. K2OsO4•2H2O
NMO
2. Et3N
66%
(two steps)
TEMPO, PhI(OAc)2
Ni(cod)2, Ipr
Et3SiH
9%
(two steps)

Scheme 5. Mechanistic Rationale



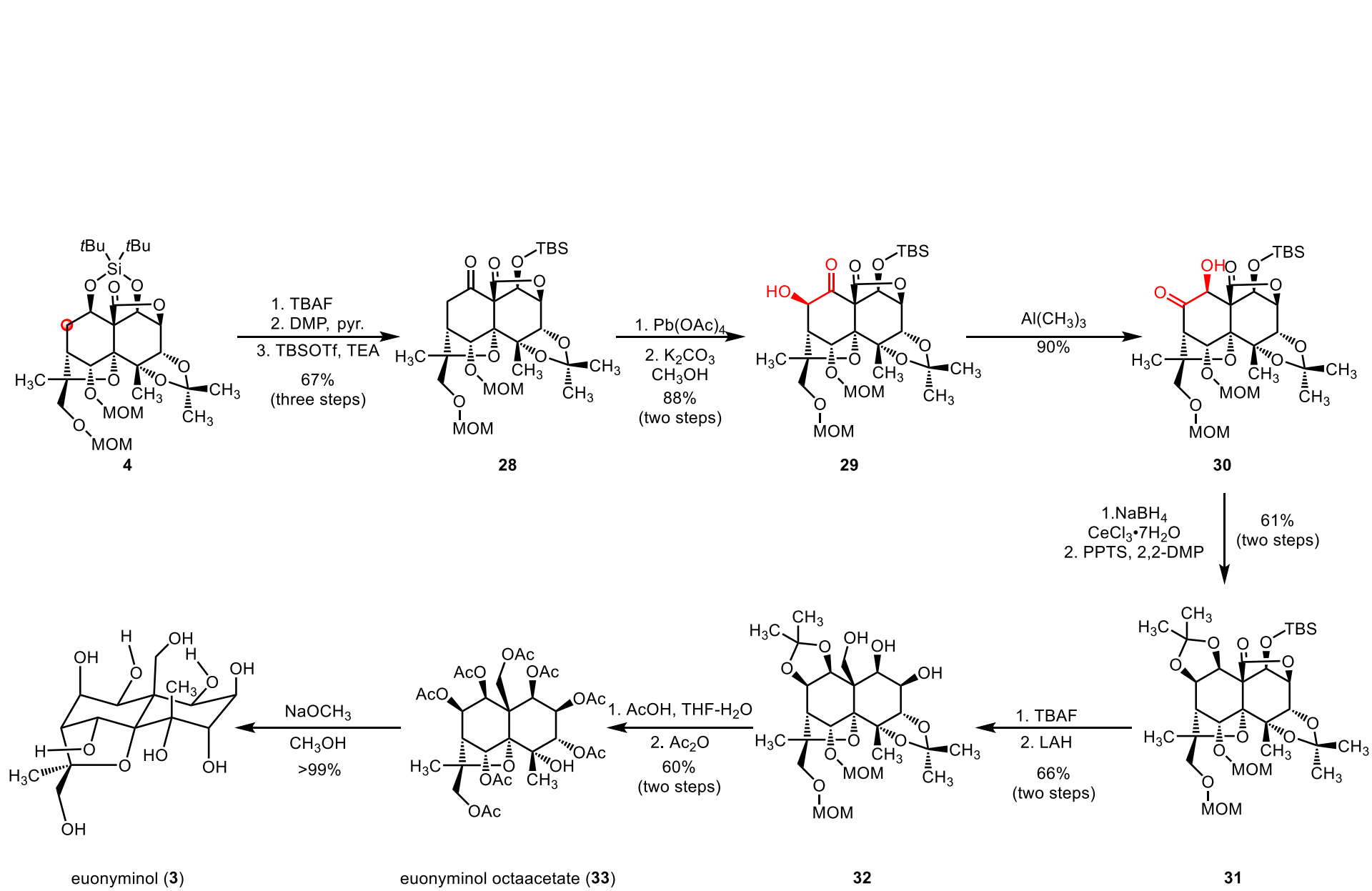
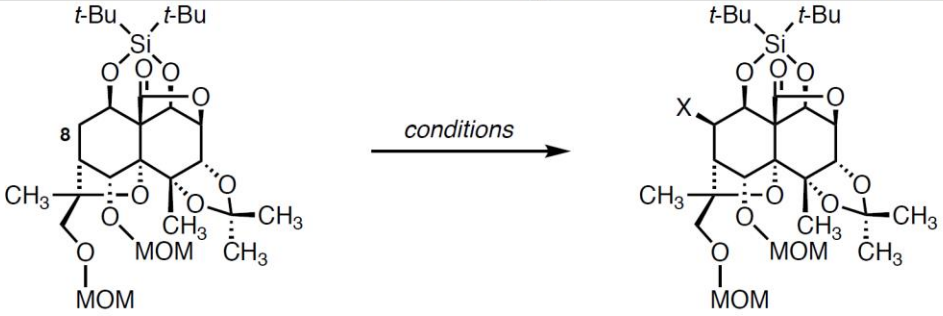
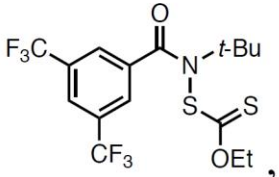
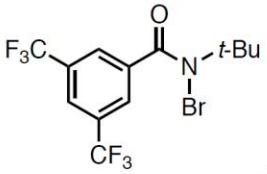

4
1. TBAF
2. DMP, pyr.
3. TBSOTf, TEA
67%
(three steps)
28
1. Pb(OAc)4
2. K2CO3
CH3OH
88%
(two steps)
29
Al(CH3)3
90%
30
1.NaBH4
CeCl3•7H2O
2. PPTS, 2,2-DMP
61%
(two steps)
31
1. TBAF
2. LAH
66%
(two steps)
32
1. AcOH, THF-H2O
2. Ac2O
60%
(two steps)
euonyminol octaacetate (33)
NaOCH3
CH3OH
>99%
euonyminol (3)

Table S4. Evaluation of conditions for the late-stage C8 oxidation of lactone **4**.



4

entry	conditions	results
1	Fe(*S,S*-PDP), H_2O_2	oxidation of the 1° MOM group resulted in decomposition
2	Fe(*R,R*-PDP), H_2O_2	oxidation of the 1° MOM group resulted in decomposition
3	TFDO	complex mixture
4	DMDO	no reaction, **4** was recovered
5	 , blue LED	no reaction, **4** was recovered
6	 , visible light	no reaction, **4** was recovered