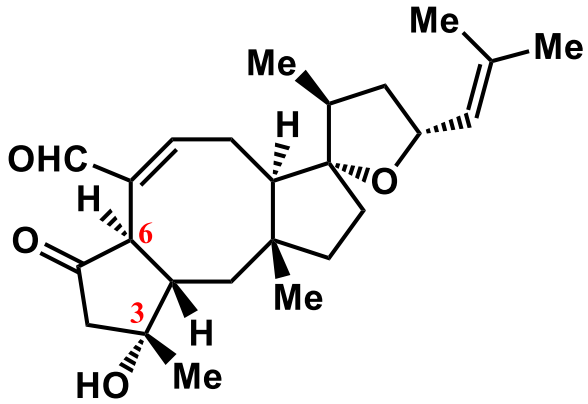
Natural Products Hot Paper

Total Synthesis of (+)-6-epi-Ophiobolin A

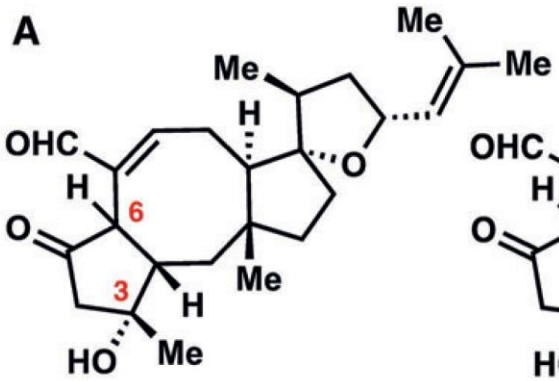


ophiobolin A (1)
(C6-H = β)

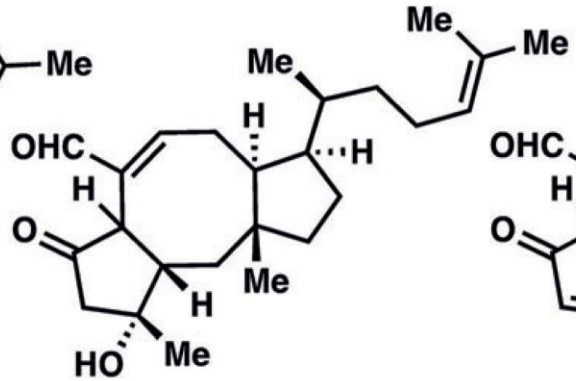
6-*epi*-ophiobolin A (2)
(C6-H = α)

DOI: 10.1002/anie.201913150.

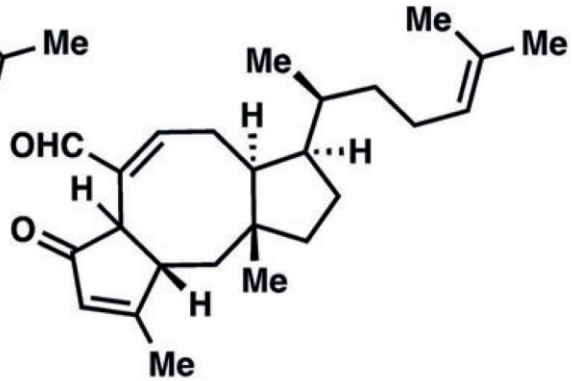
A



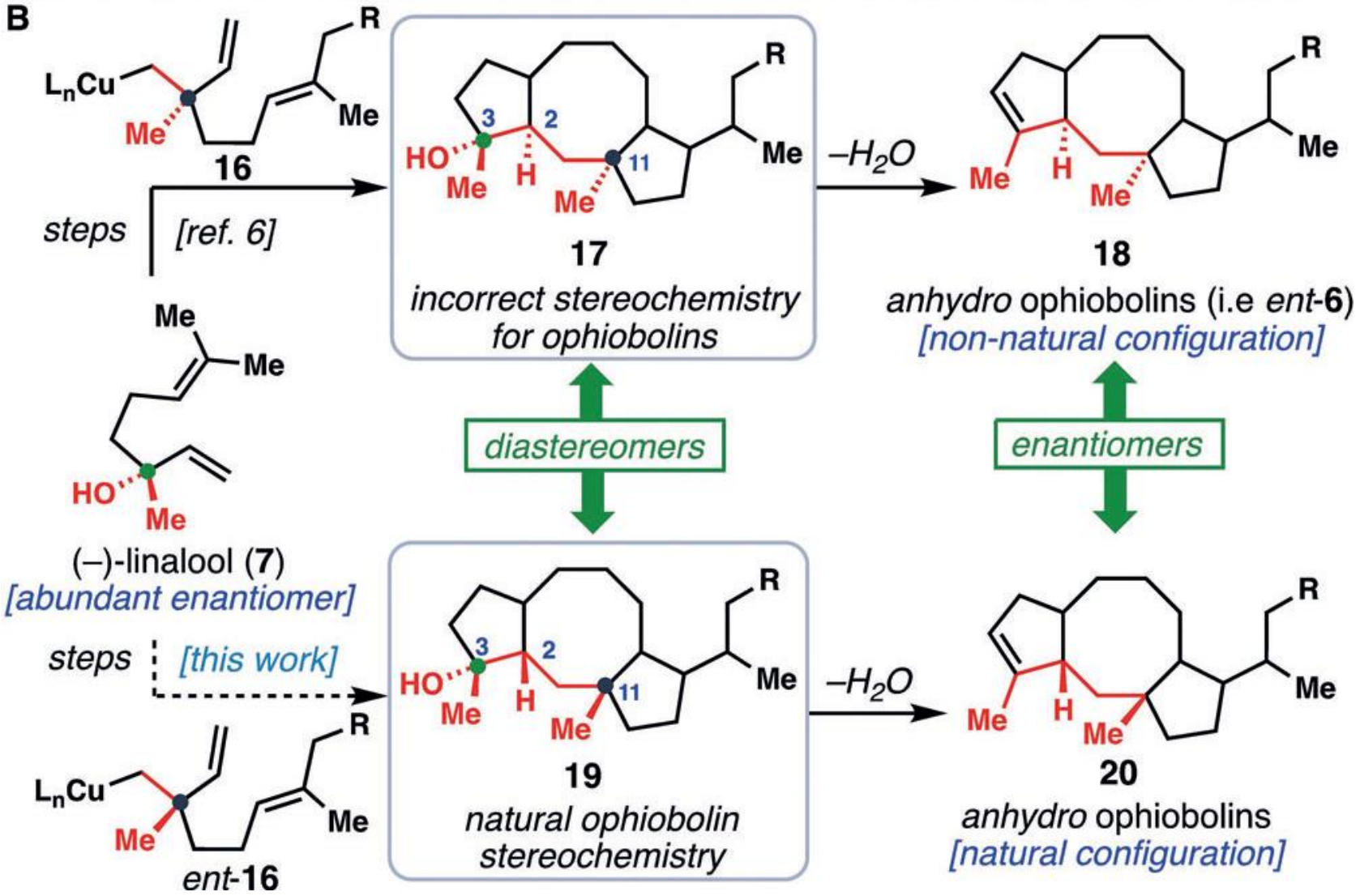
ophiobolin A (**1**)
(C6-H = β)
6-*epi*-ophiobolin A (**2**)
(C6-H = α)



ophiobolin C (**3**)
(C6-H = β)
6-*epi*-ophiobolin C (**4**)
(C6-H = α)

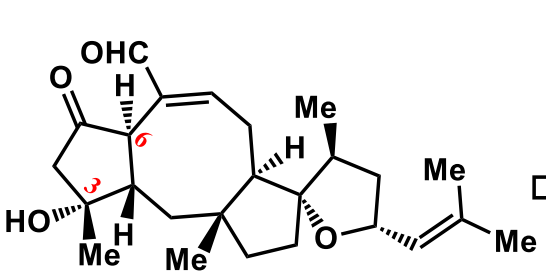


ophiobolin N (**5**)
(C6-H = β)
6-*epi*-ophiobolin N (**6**)
(C6-H = α)



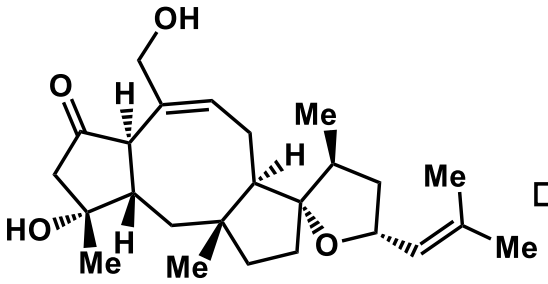
Stereochemical considerations in past and present routes to ophiobolin members.

Retrosynthetic analysis of the (+)-6-epi-Ophiobolin A



6-*epi*-ophiobolin A (2)
(C6-H = α)

swern oxidation



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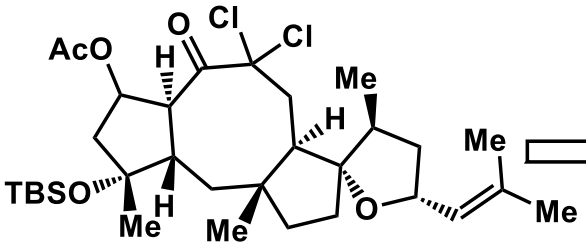
Corey-Chaykovsky epoxidation



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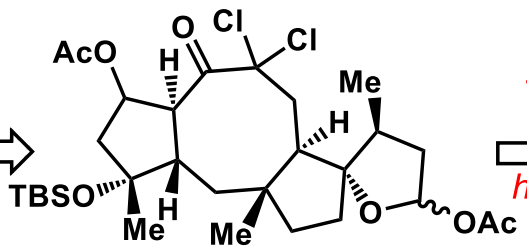

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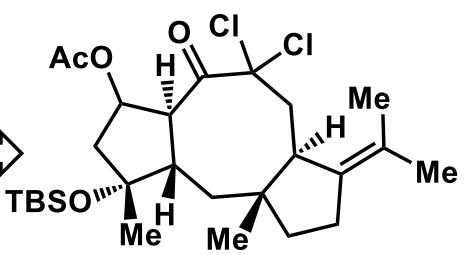
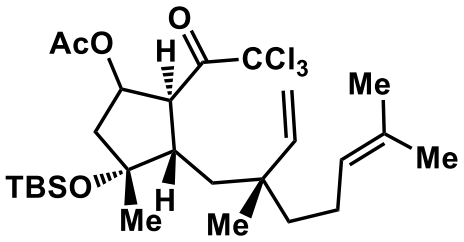
singlet oxygen ene reaction

hydroformylation reaction

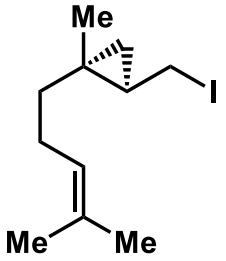


25

8-endo/5-exo radical cascade cyclization



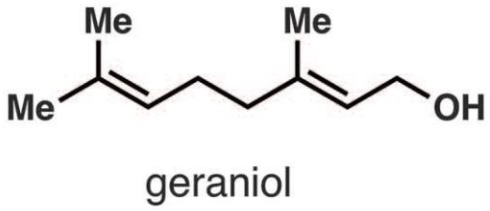
24



21
(from geraniol)

+

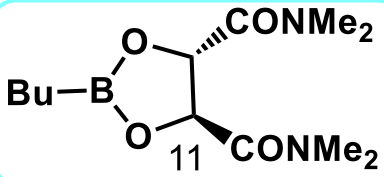
22
(from (-)-linalool (7))

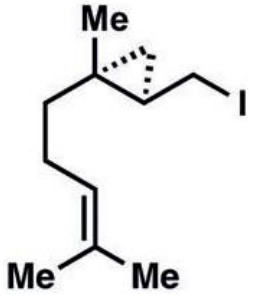


geraniol

C Et_2Zn, CH_2I_2, **11**
D I_2, PPh_3

67% (2 steps)





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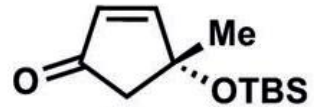
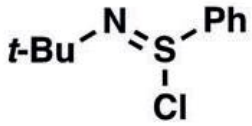
a. *t*-BuLi, CuI•DMS



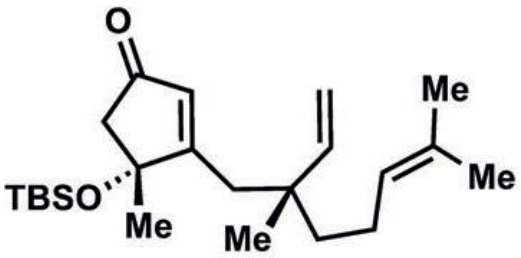
22

then add



HMPA

57%

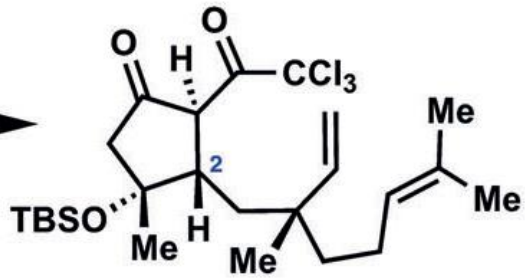


23

b. $PhMe_2SiLi$
CuI, DIBAL
HMPA, MeLi

then add
Cl_3CCOCl

61%



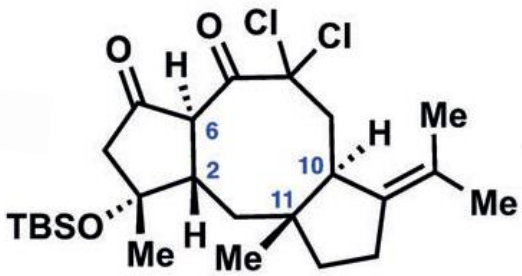
24

c. CuBr/**L1**
DTBP

DMF
70 °C

55%

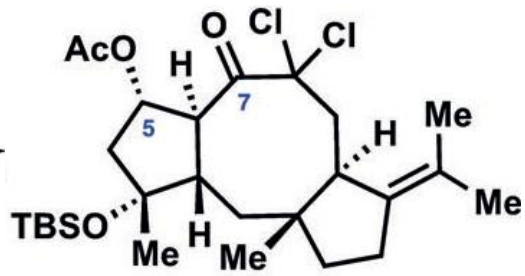
L1 = 4,4'-di-*t*-Bu-bipy



25

d. $NaBH_4$
MeOH/THF
70%

e. Et_3N, DMAP
DCM, Ac_2O
then DMP
70%



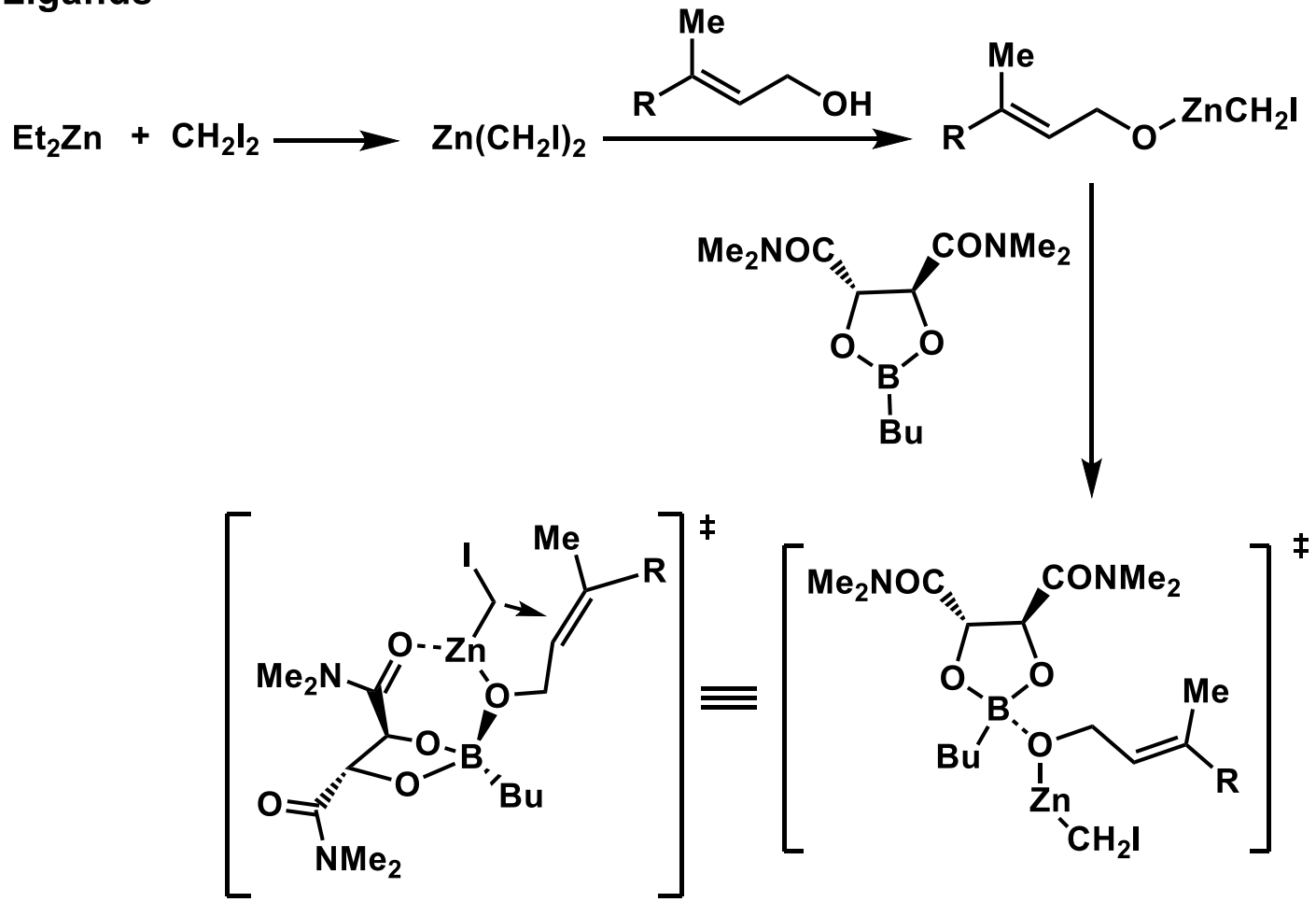
26

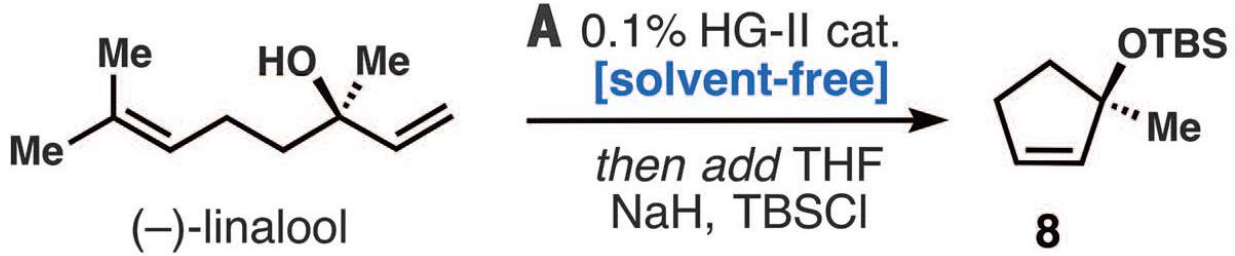
f. O_2
methylene
blue

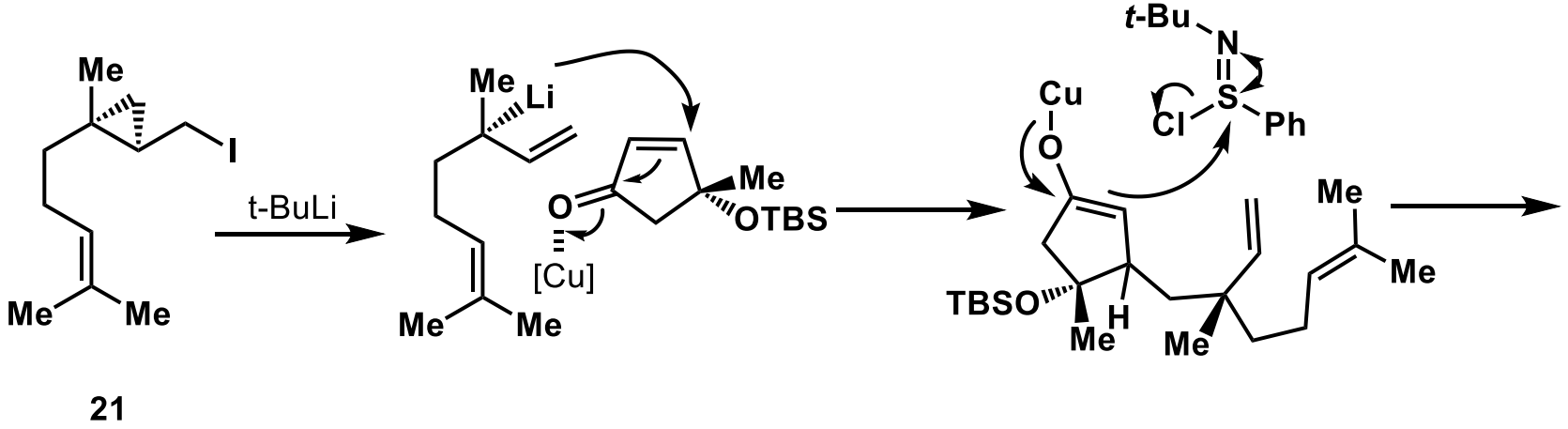
DCM
–78 °C

56%
(~3:1 dr)

Enantioselective Cyclopropanation of Allylic Alcohols with Dioxaborolane Ligands







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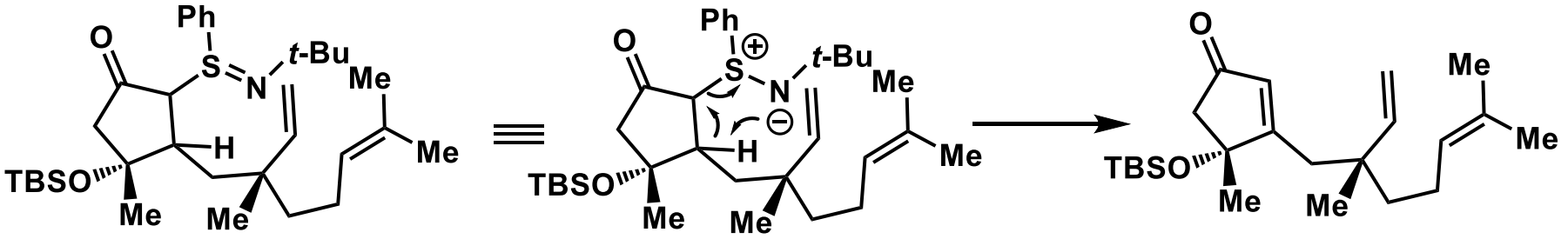
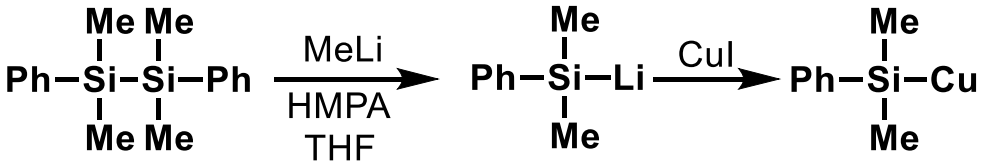
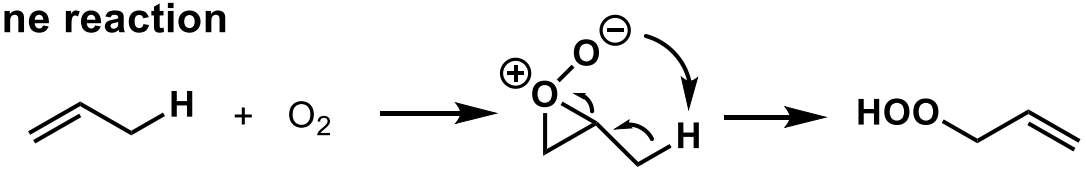
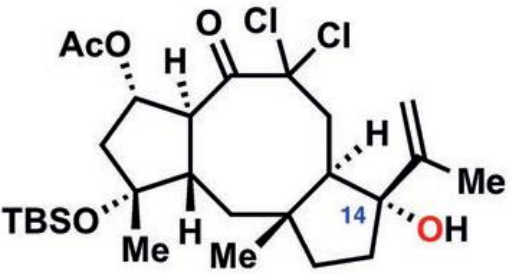




$^1O_2$ ene reaction

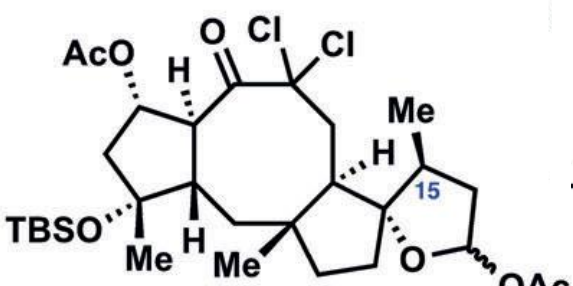




27

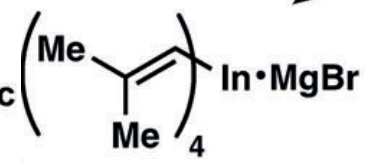
g. $Rh(CO)_2(acac)$/**L2**
CO/H_2 (1:1)
PhMe
80 °C

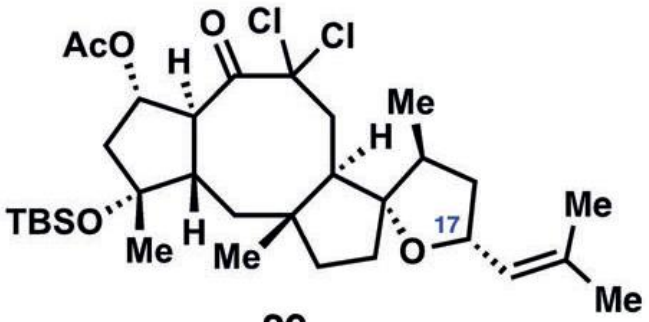
then add
Ac_2O, Et_3N
DMAP
44%



28

h. $BF_3 \cdot OEt_2$
DCM
–78 °C
64% [>20:1 dr]

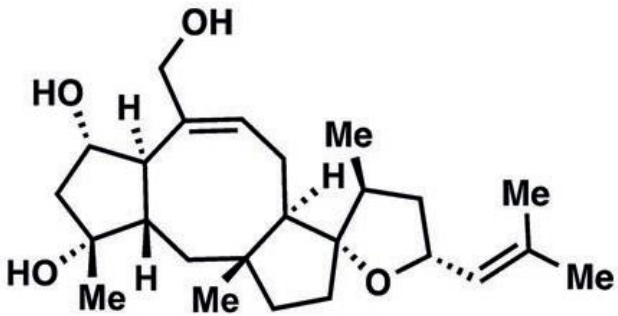




29

i. Me_3SI, *n*-BuLi
THF, 62%
j. Li-Naph, THF
–78 °C, 54%

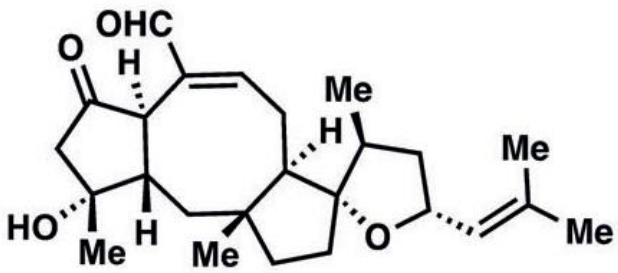
k. TBAF, 0 °C
96%



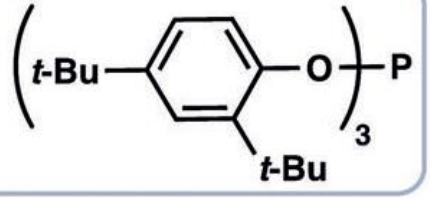
30

l. $(COCl)_2$, DMSO
Et_3N, DCM

85%

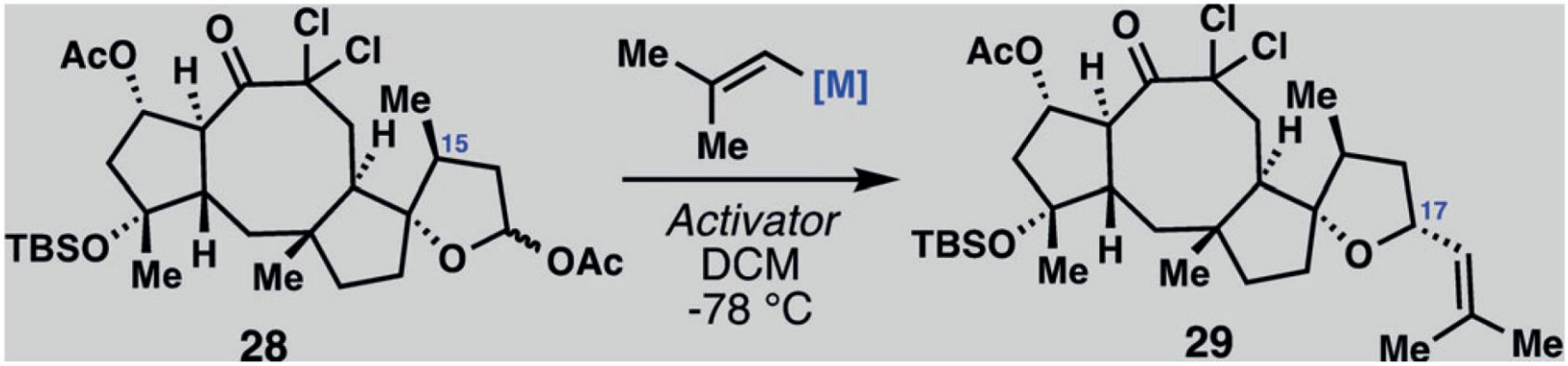


L2 =



(+)-6-*epi*-ophiobolin A (**2**)

Table 1: Synthesis of the tetracycle **29**: Selected results for the optimization of the reaction.



Entry[a]	Activator	Nucleophile	Yield [%] (**29**:17-*epi*-**29**)[b]
1	$BF_3{\cdot}OEt_2$	$MgBr(C_4H_7)$	36 (3:1)
2	$BF_3{\cdot}OEt_2$	$ZnBr(C_4H_7)$	11 (2:1)
3	$BF_3{\cdot}OEt_2$	$CeCl_2(C_4H_7)$	10 (1:1.5)
4	TMSBr	$CuTC(CN)(C_4H_7)$	17 (1:1)
5	$BF_3{\cdot}OEt_2$	$InCl_2(C_4H_7)$	<5
6	$BF_3{\cdot}OEt_2$	$In(C_4H_7)_3$	54 (1:1)
7	$BF_3{\cdot}OEt_2$	$In(C_4H_7)_4{\cdot}MgBr$	64 (>20:1)

[a] Yields and selectivities determined by ^{1}H NMR analysis. [b] Yields based on amount of correct C15 diastereomer in starting **28**. TC = thiophene 2-carboxylate, TMS = trimethylsilyl.

谢谢