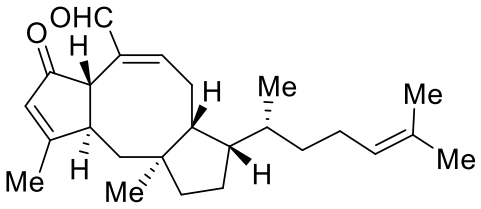
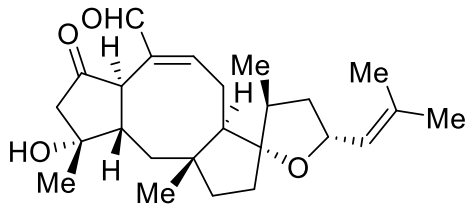
Enantioselective synthesis of Ophiobolin sesterpene via a programmed radical cascade

Brill, Z. G.; Grover, H. K.; Maimone, T. J. *Science* **2016**, *352*, 1078–1082.
Thach, D.; Brill, Z.; Grover, H.; Esguerra, K.; Thompson, J.; Maimone, T. *Angew. Chem. Int. Ed.* **2020**, *59*, 1532-1536.



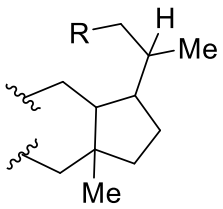
previous work
(-)-6-*epi*-ophiobolin N



this work
(+)-6-*epi*-ophiobolin A

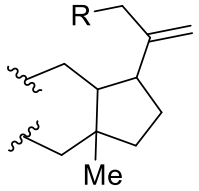
termination modes of the 8-*endo*-5-*exo* cyclization cascade

a. DIBAL/ *n*-BuLi
b. TMS_3SiH Thiol Et_3B/air

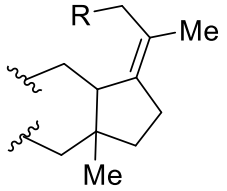


(-)-6-*epi*-ophiobolin N

a. DIBAL/ *n*-BuLi
b. $Ir(ppy)_3$, Et_3N DMSO, hυ

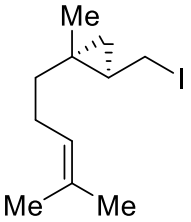


a. CuCl/bipy EtOH



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

Starting from geraniol and (-)-linalool



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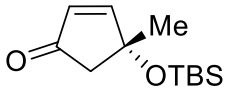
2 steps from geraniol



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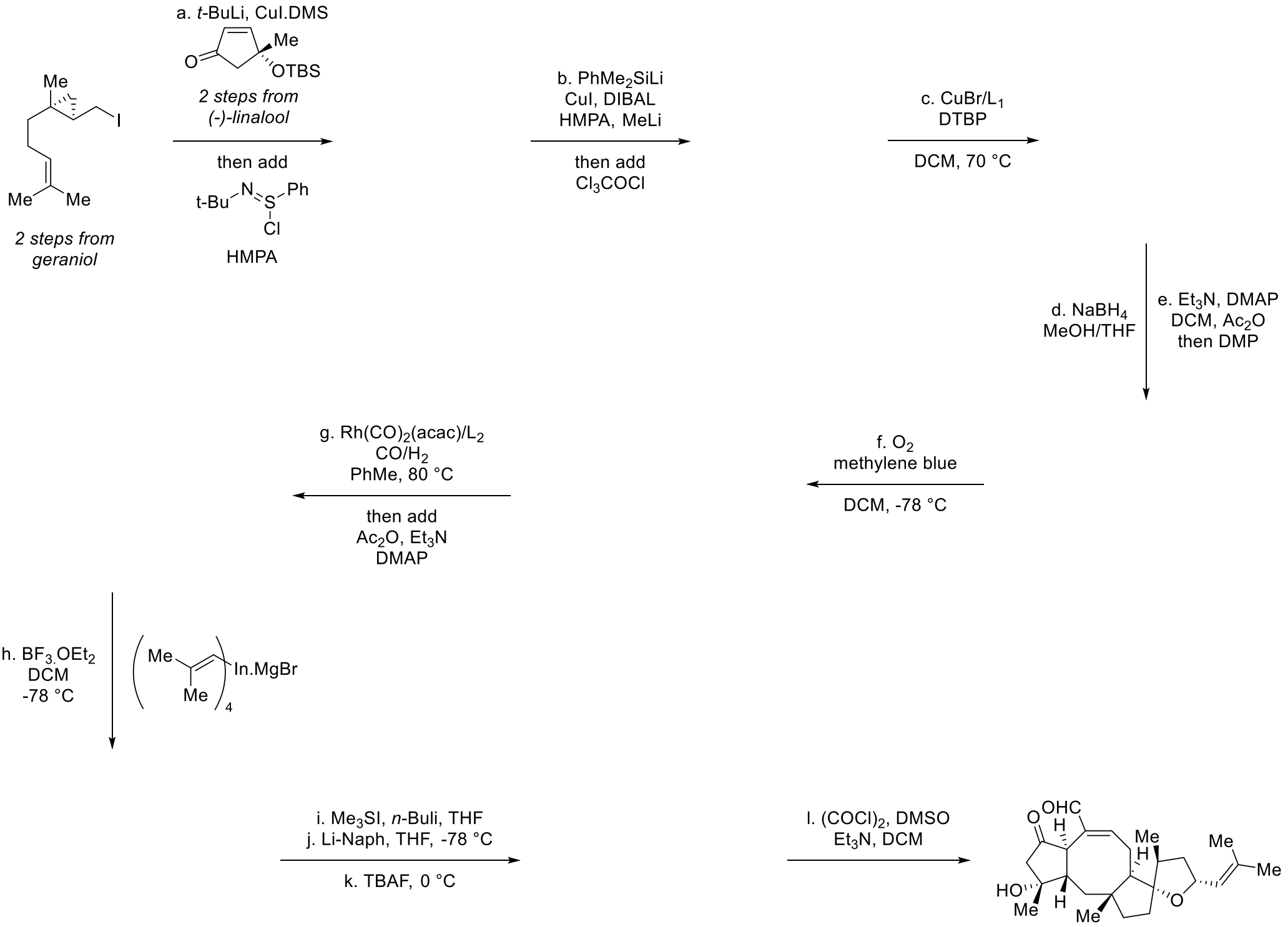
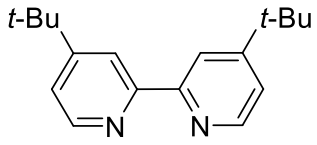
2 steps from (-)-linalool


a. t-BuLi, CuI.DMS
Me
O
OTBS
2 steps from
(-)-linalool
then add
t-Bu
N
S
Ph
Cl
HMPA
Me
I
Me
Me
2 steps from
geraniol
b. PhMe2SiLi
CuI, DIBAL
HMPA, MeLi
then add
Cl3COCl
c. CuBr/L1
DTBP
DCM, 70 °C
d. NaBH4
MeOH/THF
e. Et3N, DMAP
DCM, Ac2O
then DMP
f. O2
methylene blue
DCM, -78 °C
g. Rh(CO)2(acac)/L2
CO/H2
PhMe, 80 °C
then add
Ac2O, Et3N
DMAP
h. BF3.OEt2
DCM
-78 °C
Me
In.MgBr
Me
4
i. Me3SI, n-Buli, THF
j. Li-Naph, THF, -78 °C
k. TBAF, 0 °C
l. (COCl)2, DMSO
Et3N, DCM
OHC
O
H
Me
H
Me
Me
HO
Me
H
Me
O

L_1 = 

L_2 =