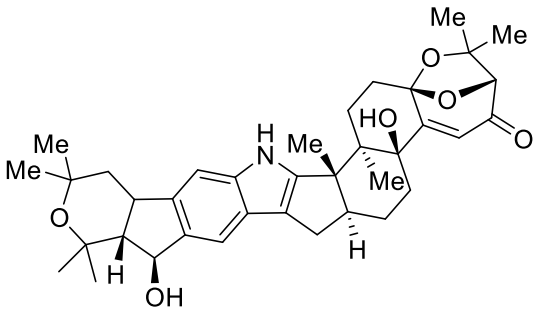
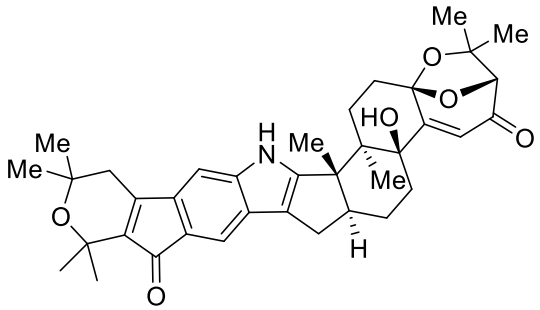
TOTAL SYNTHESIS OF SHEARININES D AND G: A CONVERGENT APPROACH TO INDOLE DITERPENOIDS

Hauser, N.; Imhof, M. A.; Eichenberger, S. S.; Kündig, T.; Carreira, E. M. *Angew. Chem. Int. Ed.* **2022**, *61*, e202112838

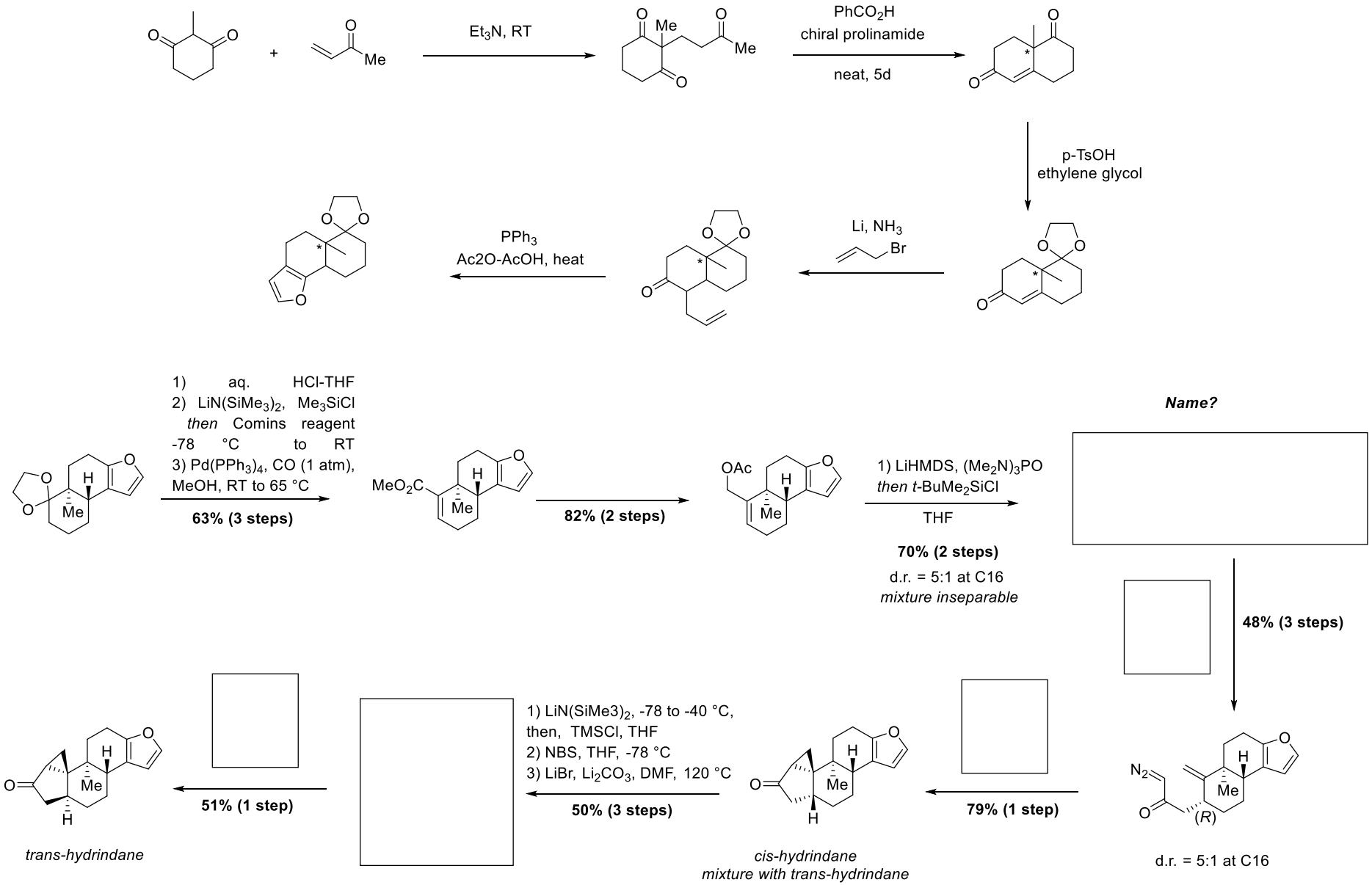


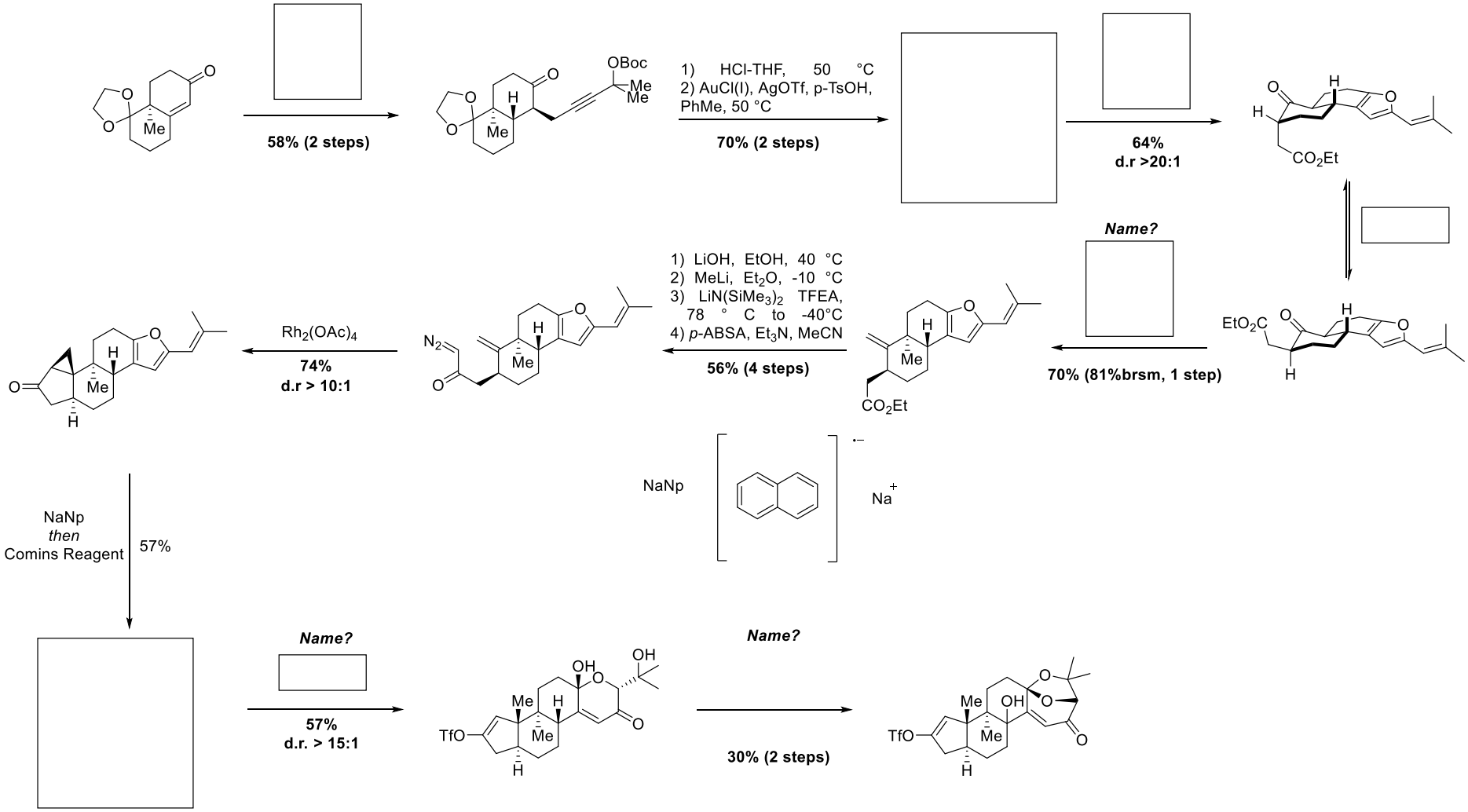
Shearinine D

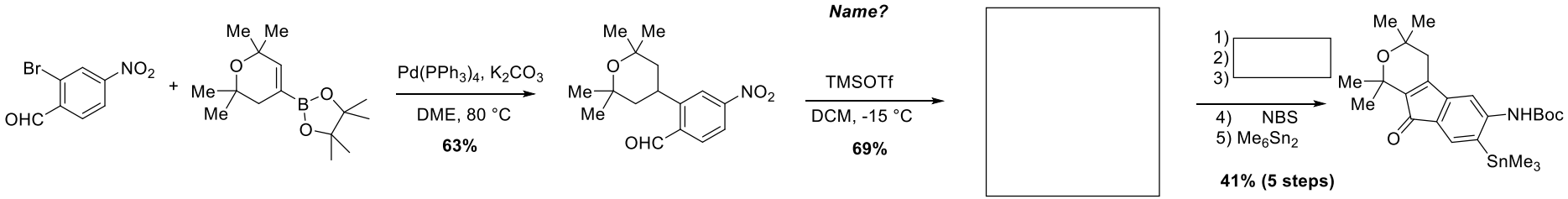


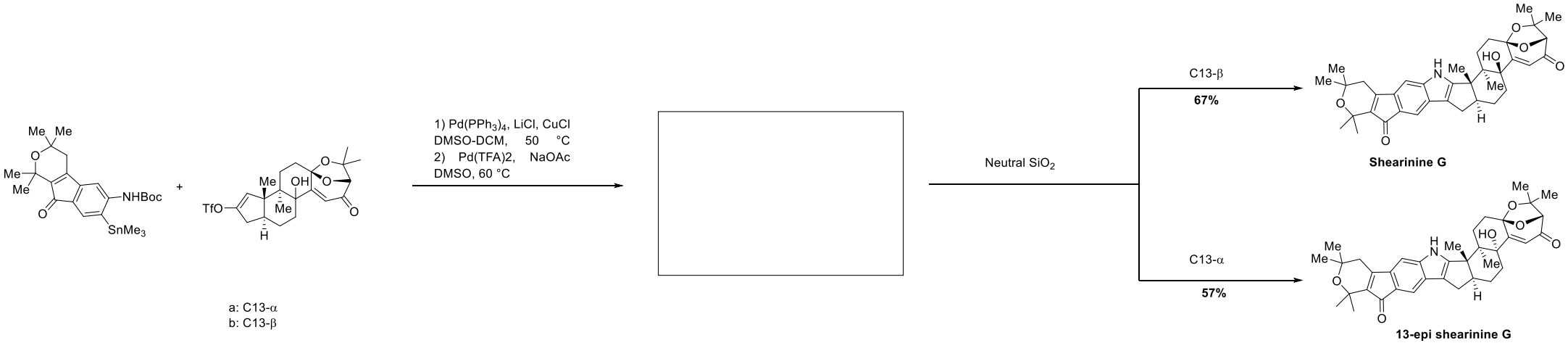
Shearinine G

- Complex indole diterpenoids
- Isolated from marine fungi Eupenicillium spp. and *Penicillium janthinellum* and *Escovopsis weberi*

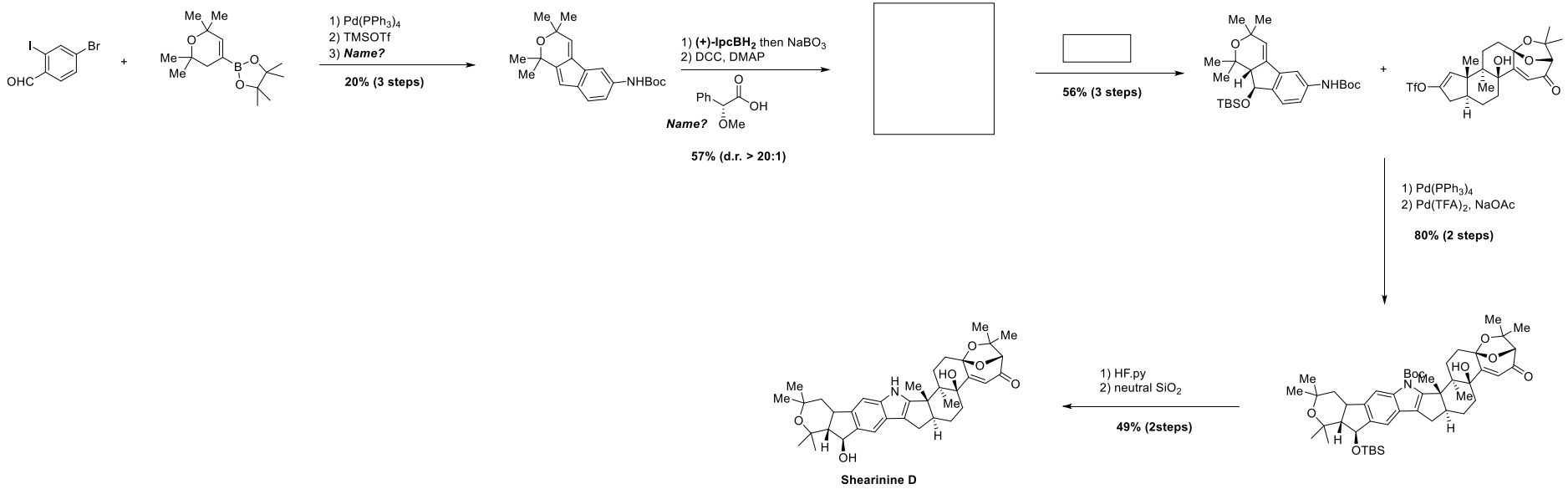

Et3N, RT
PhCO2H
chiral prolinamide
neat, 5d
p-TsOH
ethylene glycol
Li, NH3
Br
PPh3
Ac2O-AcOH, heat
1) aq. HCl-THF
2) LiN(SiMe3)2, Me3SiCl
then Comins reagent
-78 °C to RT
3) Pd(PPh3)4, CO (1 atm),
MeOH, RT to 65 °C
63% (3 steps)
82% (2 steps)
1) LiHMDS, (Me2N)3PO
then t-BuMe2SiCl
THF
70% (2 steps)
d.r. = 5:1 at C16
mixture inseparable
Name?
48% (3 steps)
d.r. = 5:1 at C16
79% (1 step)
1) LiN(SiMe3)2, -78 to -40 °C,
then, TMSCl, THF
2) NBS, THF, -78 °C
3) LiBr, Li2CO3, DMF, 120 °C
50% (3 steps)
cis-hydrindane
mixture with trans-hydrindane
51% (1 step)
trans-hydrindane

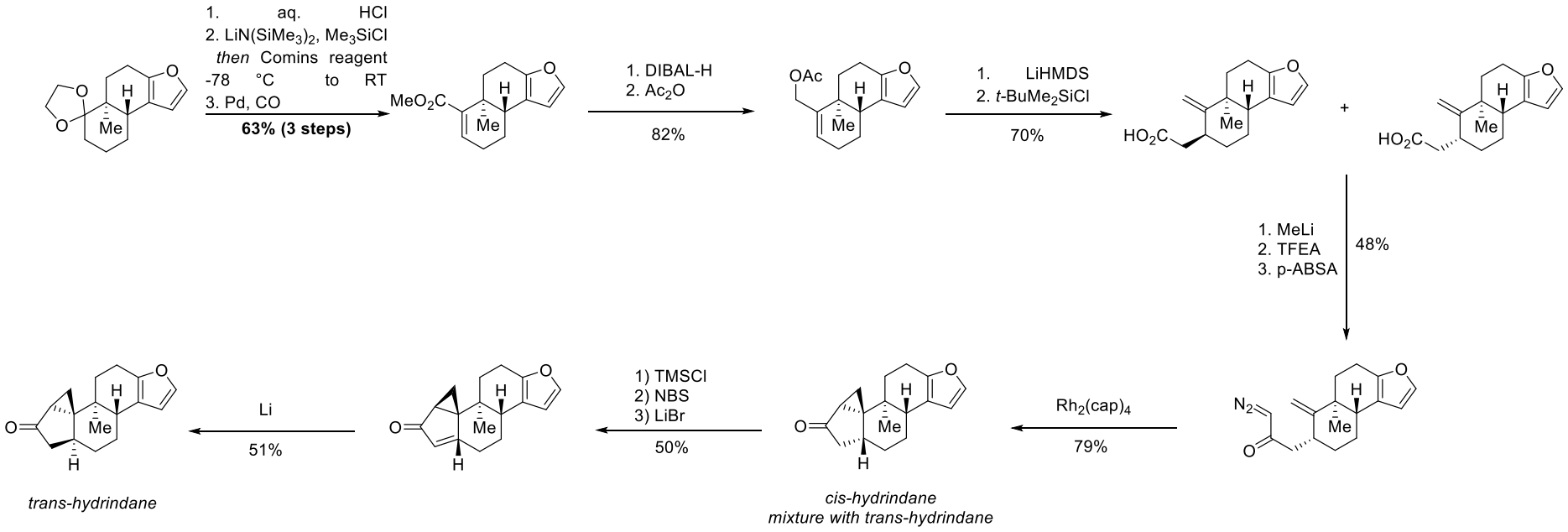

58% (2 steps)
1) HCl-THF, 50 °C
2) AuCl(I), AgOTf, p-TsOH, PhMe, 50 °C
70% (2 steps)
64%
d.r >20:1
Name?
70% (81%brsm, 1 step)
1) LiOH, EtOH, 40 °C
2) MeLi, Et2O, -10 °C
3) LiN(SiMe3)2 TFEA, 78 ° C to -40°C
4) p-ABSA, Et3N, MeCN
56% (4 steps)
Rh2(OAc)4
74%
d.r > 10:1
NaNp
Na+
NaNp
then
Comins Reagent
57%
Name?
57%
d.r. > 15:1
Name?
30% (2 steps)

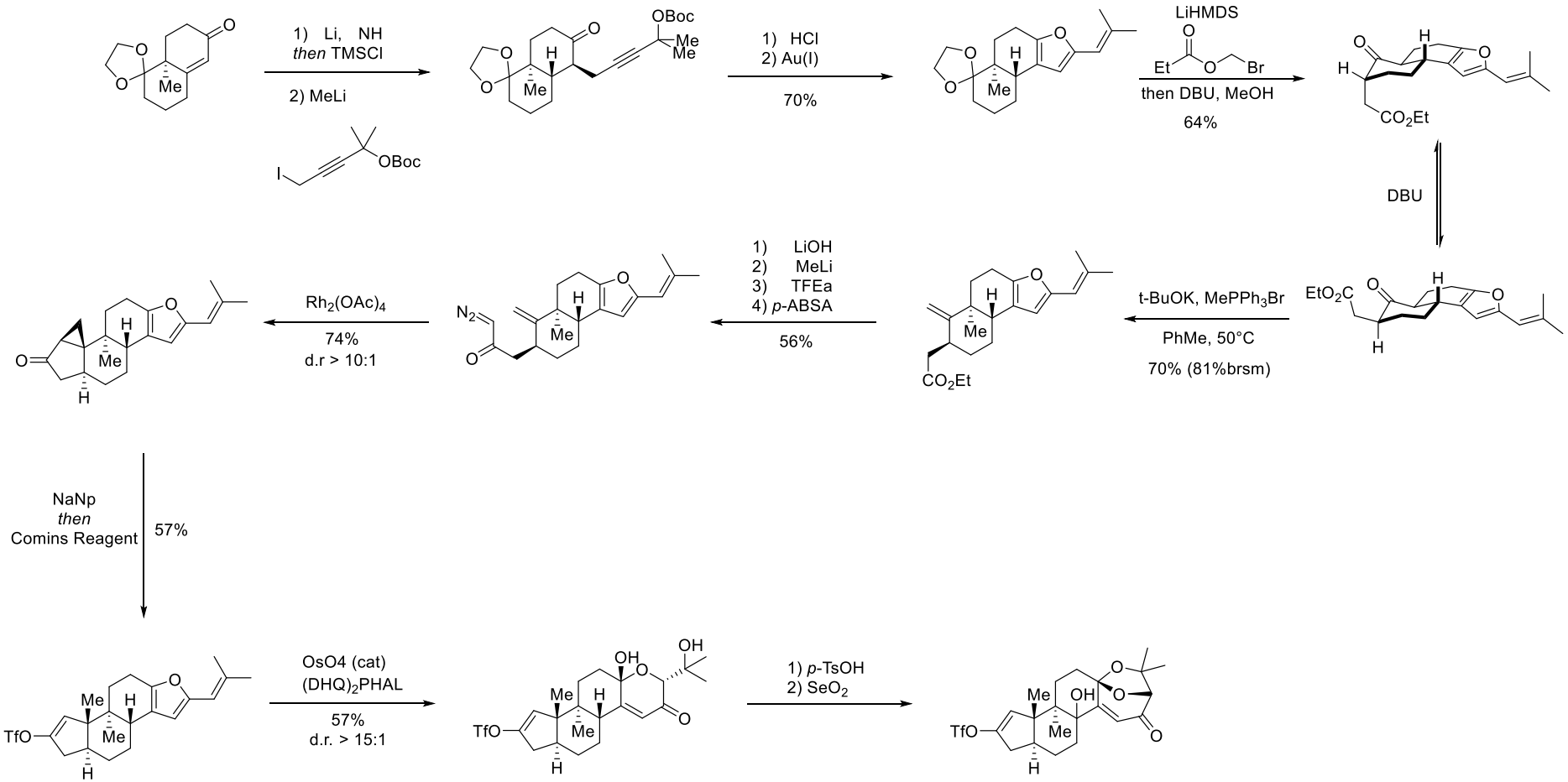

Br
NO2
OHC
Me Me
Me
Me
B
O
O
Pd(PPh3)4, K2CO3
DME, 80 °C
63%
Name?
TMSOTf
DCM, -15 °C
69%
1)
2)
3)
4) NBS
5) Me6Sn2
41% (5 steps)
NHBoc
SnMe3

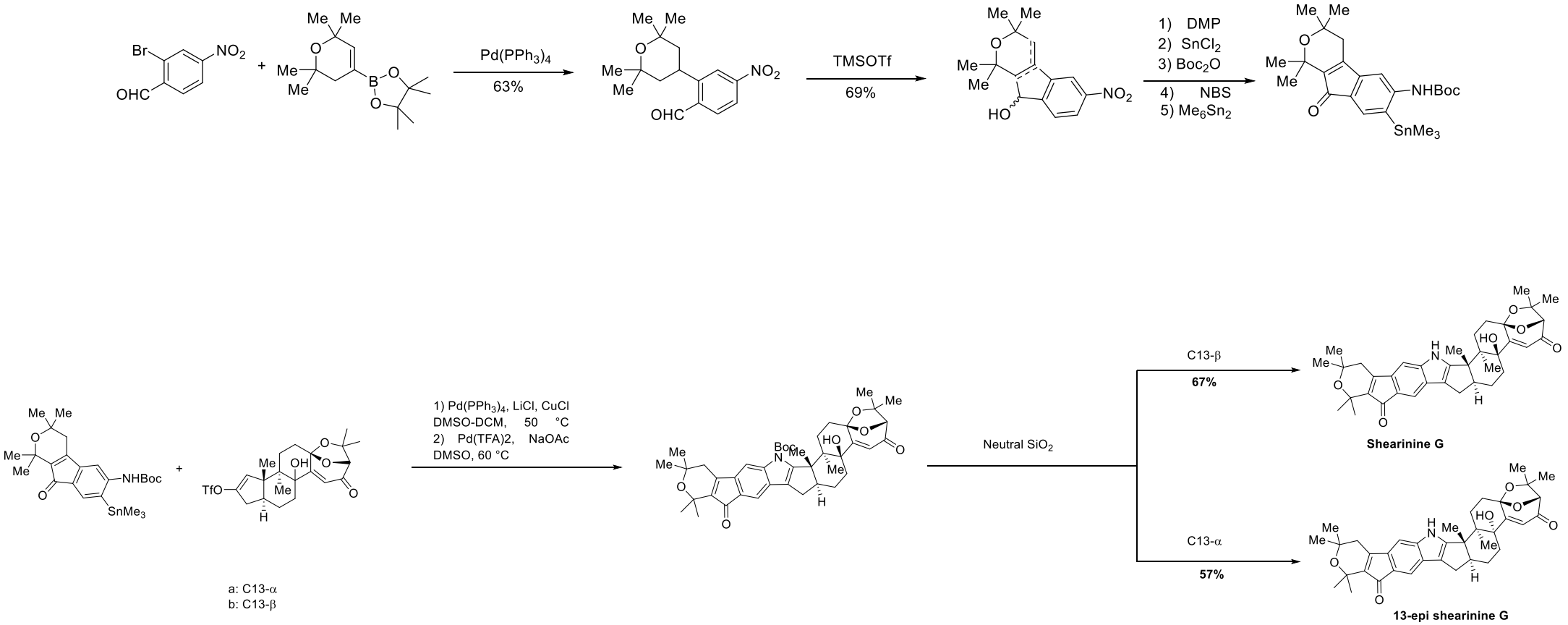

NHBoc
SnMe3
TfO
OH
1) Pd(PPh3)4, LiCl, CuCl
DMSO-DCM, 50 °C
2) Pd(TFA)2, NaOAc
DMSO, 60 °C
Neutral SiO2
C13-β
67%
C13-α
57%
Shearinine G
13-epi shearinine G

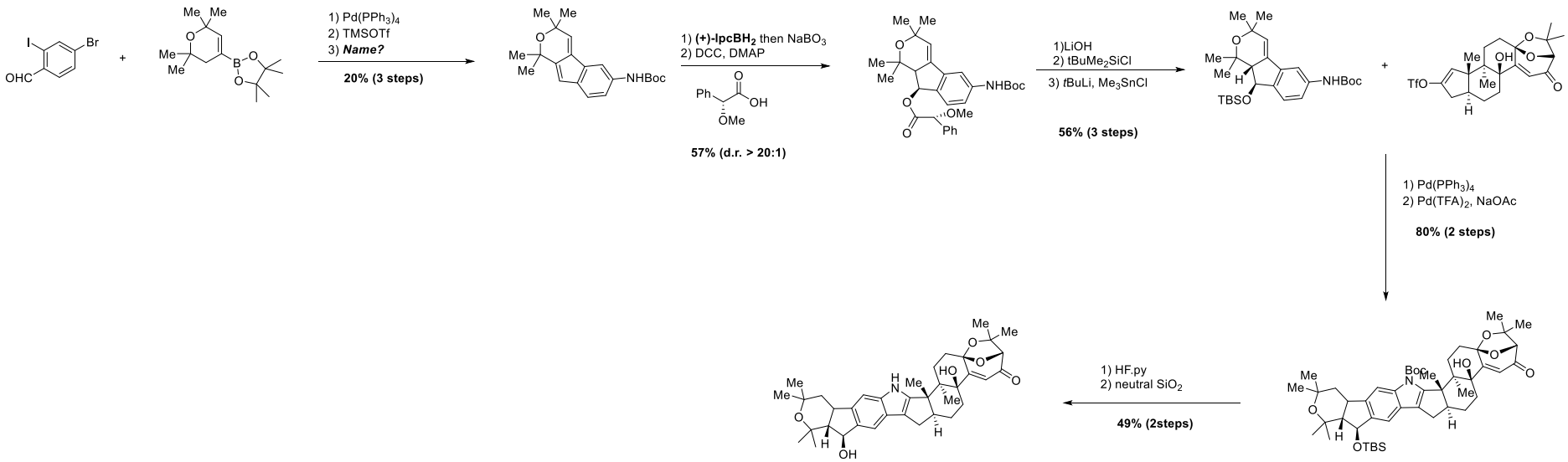
a: C13-α
b: C13-β


1) Pd(PPh3)4
2) TMSOTf
3) Name?
20% (3 steps)
1) (+)-IpcBH2 then NaBO3
2) DCC, DMAP
Name?
57% (d.r. > 20:1)
56% (3 steps)
1) Pd(PPh3)4
2) Pd(TFA)2, NaOAc
80% (2 steps)
1) HF.py
2) neutral SiO2
49% (2steps)
Shearinine D


1. aq. HCl
2. LiN(SiMe3)2, Me3SiCl
then Comins reagent
-78 °C to RT
3. Pd, CO
63% (3 steps)
1. DIBAL-H
2. Ac2O
82%
1. LiHMDS
2. t-BuMe2SiCl
70%
1. MeLi
2. TFEA
3. p-ABSA
48%
Rh2(cap)4
79%
1) TMSCl
2) NBS
3) LiBr
50%
Li
51%
trans-hydrindane
cis-hydrindane
mixture with trans-hydrindane


1) Li, NH
then TMSCl
2) MeLi
OBoc
1) HCl
2) Au(I)
70%
LiHMDS
then DBU, MeOH
64%
DBU
t-BuOK, MePPh3Br
PhMe, 50°C
70% (81%brsm)
1) LiOH
2) MeLi
3) TFEa
4) p-ABSA
56%
Rh2(OAc)4
74%
d.r > 10:1
NaNp
then
Comins Reagent
57%
OsO4 (cat)
(DHQ)2PHAL
57%
d.r. > 15:1
1) p-TsOH
2) SeO2


Pd(PPh3)4
63%
TMSOTf
69%
1) DMP
2) SnCl2
3) Boc2O
4) NBS
5) Me6Sn2
1) Pd(PPh3)4, LiCl, CuCl
DMSO-DCM, 50 °C
2) Pd(TFA)2, NaOAc
DMSO, 60 °C
Neutral SiO2
C13-β
67%
C13-α
57%
Shearinine G
13-epi shearinine G
a: C13-α
b: C13-β



Shearinine D