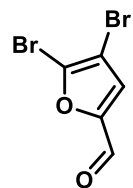


Total Synthesis of Daphgraciline



1) DIBAL, DCM,
then TBSCl, Im

A

2) *n*BuLi, BOMCl,
THF, -78°C

then *n*BuLi, HCHO(g),
THF, -78°C

B

3) PPh₃, DIAD,
TsHN-CH₂-CH=CH₂

THF, TBAF

C

4) *m*CPBA, DCM
↓
then Ac₂O, NEt₃,
DMAP, DCM

G

7) PhMe, BHT, 140°C

dr = 2.3:1

F

6)

DCM, 0°C

E

5) DHQD, MeCN,
55°C

D

8) K₂OsO₄ • 2 H₂O,
NMO, MeSO₂NH₂,
THF/*t*BuOH/H₂O

↓

9) IBX,
DMSO

H

10) KOH, *t*BuOH,
H₂O, 90°C

11) TMSCHN₂,
PhMe, MeOH

I

12) NaH, CS₂, MeI,
THF, 0°C to 25°C

13) PhCl, 148°C

J

14) Sml₂, THF

15) DIBAL, DCM,
TIPSCI, Im

K

16) Li / EtNH₂,
-78°C,
MeI, EtOH, 25°C

↓

17) KHMDS,
Ts-Im,
THF, 0°C

O

23) TPP, O₂, hv,
CDCl₃, -55°C, P(OEt)₃

N

19) EtMgBr, -78°C,
Et₂O

20) *p*-TsOH, MeOH

21) DMP, DCM

22) I₂, KOH, MeOH,
0°C

M

18)

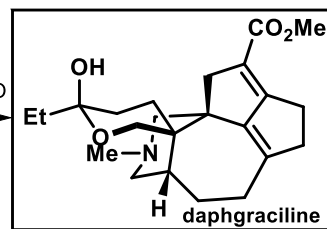
Cp₂TiCl₂, Zn, THF,
70°C, H₂O

L

24) MgSO₄, 140°C,
1,2-dichlorobenzene

P

25) *p*-TsOH, THF/H₂O



Hints:

- **D** has one six-membered heterocycle
- conditions 5) initiate a type II [5+2]
- **M** contains a spiro-lactone