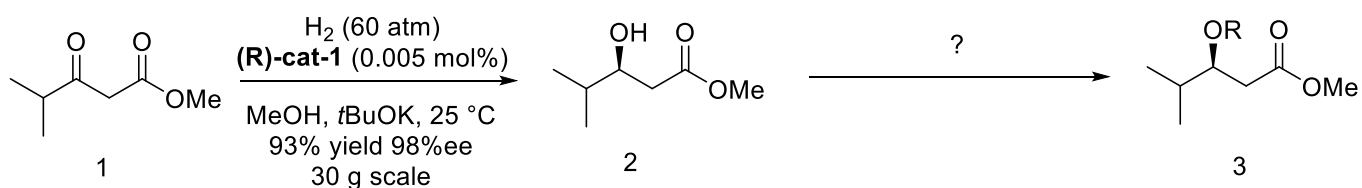
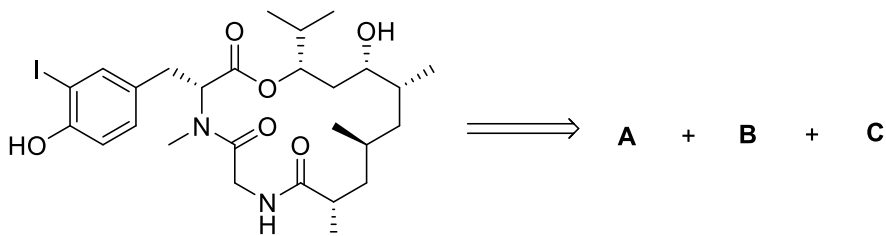
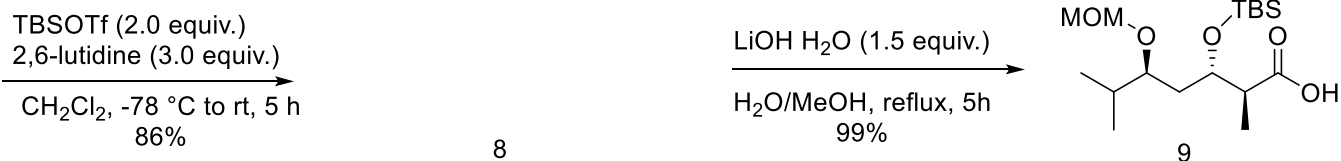
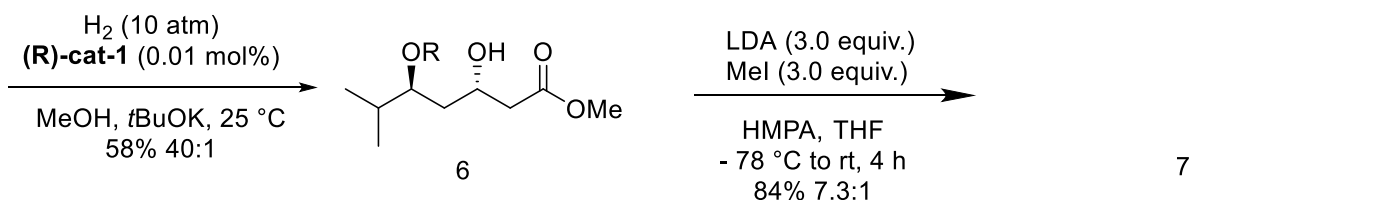
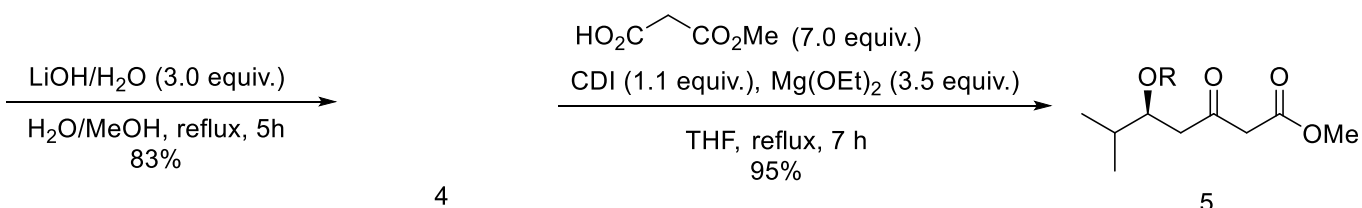


Total Synthesis of (-)-Doliculide

W. Che, D. C. Wen, S.-F. Zhu, Q.-L. Zhou, *Helv. Chim. Acta* **2019**, *102*, e19000



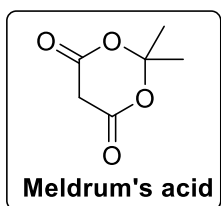
mechanism?



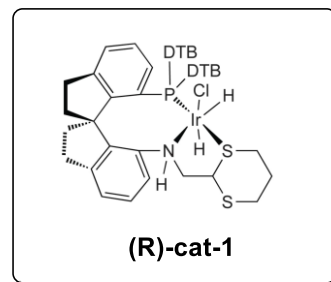
1/ **Meldrum's acid** (2.0 equiv.)
 DMAP (1.6 equiv.), DCC (1.2 equiv.)
 CH₂Cl₂, 0 °C to rt, 6h

2/ NaBH₄ (3.5 equiv.)
 AcOH (36 equiv.)
 CH₂Cl₂, -10 °C, 12 h
 99%

Propose mechanism?



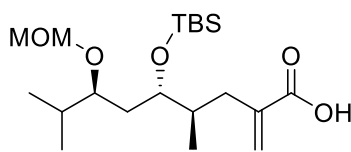
10



Propose mechanism?

1/ $\text{Me}_2\text{N}^+=\text{I}^-$ (2.5 equiv.)
MeOH, 60 °C, 12 h

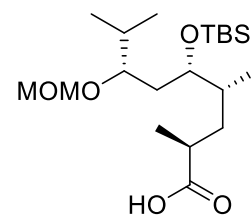
2/ LiOH H₂O (3.0 equiv.)
H₂O, reflux, 16 h
66%



11

H₂ (6 atm)
(R)-cat-2
Et₃N (5.0 equiv.)

MeOH, 45 °C
99% yield
dr 95.4:4.6



12

1/ Meldrum's acid (1.5 equiv.)
DMAP (2.5 equiv.), DCC (3.0 equiv.)
CH₂Cl₂, 0 °C to rt, 6h

2/ NaBH₄ (3.5 equiv.)
AcOH (30 equiv.)
CH₂Cl₂, -10 °C, 12 h
83%

13

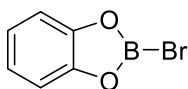
1/ $\text{Me}_2\text{N}^+=\text{I}^-$ (2.5 equiv.)
MeOH, 60 °C, 12 h

2/ LiOH H₂O (3.0 equiv.)
H₂O, reflux, 12 h
71%

14

H₂ (6 atm)
(R)-cat-2
Et₃N (5.0 equiv.)

MeOH, 45 °C, 12 h
99% yield
dr 97.3:2.7



(2.5 equiv.)

CH₂Cl₂, -78 °C, 30min
83%

15

B (1.3 equiv.)

DEPC (2.3 equiv.)
Et₂N (2.5 equiv.)

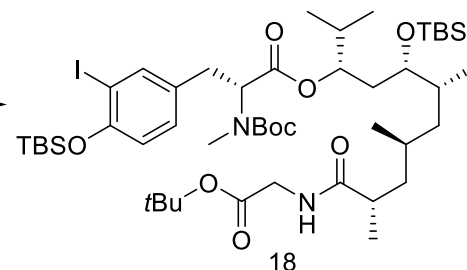
DMF, 0 °C, 5 h
96%

16

C

DMAP (1.2 equiv.)
DCC (4.5 equiv.)
CH₂Cl₂, -20 °C, 1.5 h
85%

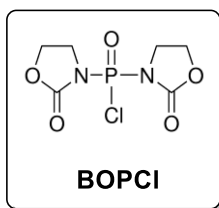
17



18

1/ TFA, CH₂Cl₂
0 °C to rt, 3 h

2/ BOPCl (5.0 equiv.)
DMAP (8.5 equiv.)
CH₂Cl₂, 0 °C to rt, 20h
20% + 70%



19

1/ NH₃ aq, MeOH, rt, 1 h
89%

2/ TBAF (1.5 equiv.)
THF, 0 °C, 10 min
83%

(-)-doliculide

