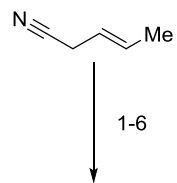


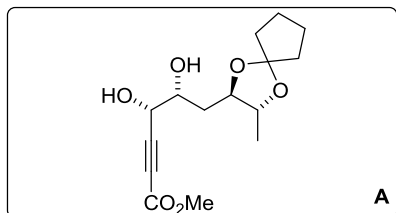
Total Synthesis of Bryostatin 3

Barry M. Trost, Youliang Wang, Andreas K. Buckl, Zhongxing Huang, Minh H. Nguyen, Olesya Kuzmina

Science. 2020, 368, 1007



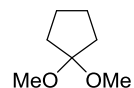
1-6



- 1) $K_2OsO_4(H_2O)_2$ (1 mol%), (DHQD)₂PHAL (2 mol%), $K_3Fe(CN)_6$, $MeSO_2NH_2$, K_2CO_3 , $NaHCO_3$
- 2) **1**, CSA, DCM
- 3) DIBAL-H, Et_2O
- 4) $[Ph_3PCH_2]I$, NaHMDS
- 5) methylpropiolate, LDA, *then* $ZnBr_2$, $PdCl_2dppf$ (10 mol%)
- 6) $K_2OsO_2(OH)_4$ (25 mol%), (DHQ)₂PHAL (60 mol%), $K_3Fe(CN)_6$, $MeSO_2NH_2$, K_2CO_3 , $NaHCO_3$

1) Name Reaction?
hint: (R,R) product obtained

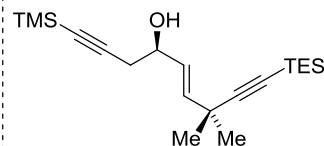
Sharpless asymmetric dihydrogenation



1

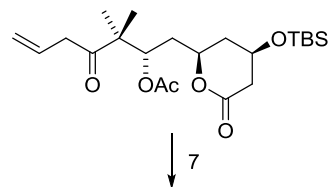
4) Name Reaction?

Stork-modified Wittig Reaction



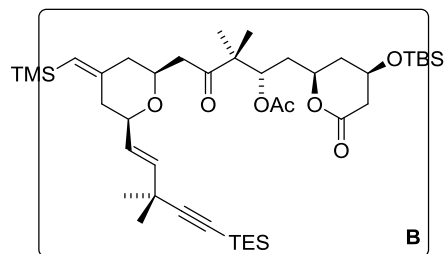
2

7) *hint: ring formation; syn addition favored*



7

- 7) **2**, $[CpRu(MeCN)_3]PF_6$ (10 mol%)

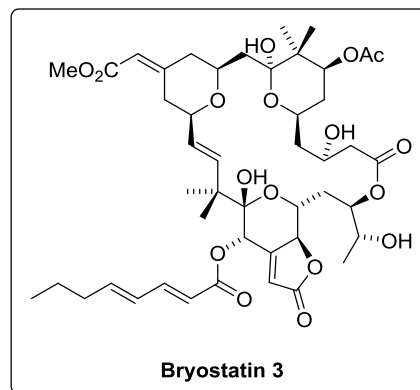


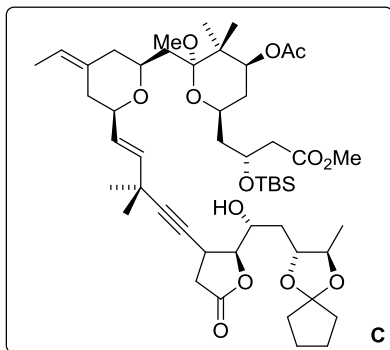
B

8-11

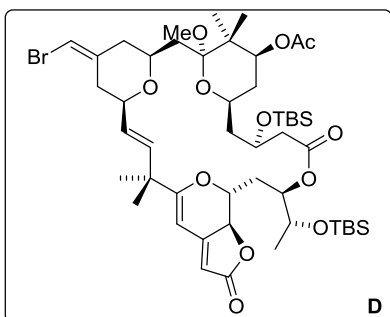
- 8) NBS, DMF
- 9) PPTS, MeOH
- 10) $AgNO_3$, THF/ H_2O
- 11) **A**, $Pd(OAc)_2$ (5 mol%), TDMPP (7.5 mol%), benzene, air free

9) Structure of PPTS?
Mechanism?
10) *hint: desilylation*
11) *hint: ring formation*

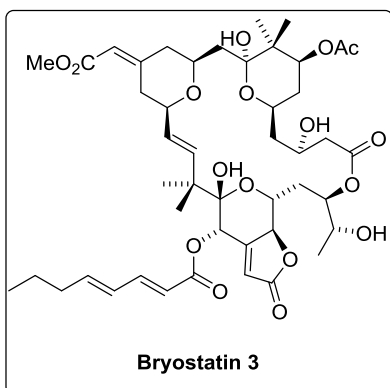




12-16

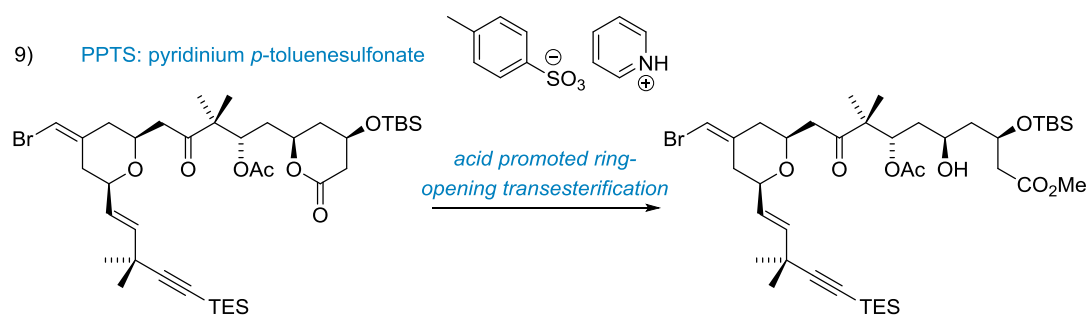


17-22



12) AuCl(IPr) (10 mol%),
AgSbF₆ (20 mol%), DCM, rt
13) ZrCl₄ (250 mol%), MeOH
14) TBSOTf, 2,6-lutidine, DCM,
-78 °C, 15 min
15) Me₃SnOH, DCE
16) 2,4,6-Cl₃PhCOCl, Et₃N, THF,
then slow addition into DMAP in
toluene

17) methylrhodium troxide, UHP,
1-methylimidazole, MeOH
18) ClCH₂CO₂H, MeOH
19) 2,4-octadienoic anhydride, DMAP
20) Pd₂(dba)₃CHCl₃ (20 mol%),
Xantphos (60 mol%), CO, DIPEA,
DMF/MeOH
21) HF (aq.)/MeCN
22) TFA/H₂O/DCM



12) Classify the cyclization
with Baldwin's rules

14) *hint: bis-silylated
product obtained*

15) who developed this
chemistry?

16) Name Reaction?

Yamaguchi macrolactonization

6-endo-dig cyclization

ring-closing
ketalization

K. C. Nicolaou

17) who developed this
chemistry?

Yamazaki conditions

18) *hint: anti product favored*