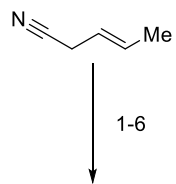


Total Synthesis of Bryostatin 3

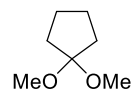
Barry M. Trost, Youliang Wang, Andreas K. Buckl, Zhongxing Huang, Minh H. Nguyen, Olesya Kuzmina

Science. 2020, 368, 1007



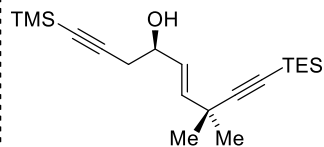
- 1) $K_2OsO_4(H_2O)_2$ (1 mol%), (DHQD)₂PHAL (2 mol%), $K_3Fe(CN)_6$, $MeSO_2NH_2$, K_2CO_3 , $NaHCO_3$
- 2) **1**, CSA, DCM
- 3) DIBAL-H, Et_2O
- 4) $[Ph_3PCH_2]I$, NaHMDS
- 5) methylpropiolate, LDA, then $ZnBr_2$, $PdCl_2dppf$ (10 mol%)
- 6) $K_2OsO_2(OH)_4$ (25 mol%), (DHQ)₂PHAL (60 mol%), $K_3Fe(CN)_6$,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

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



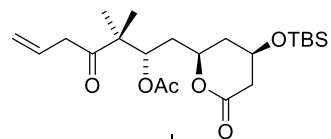
1

4) Name Reaction?



2

7) hint: ring formation;
syn addition favored



Reaction 7

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

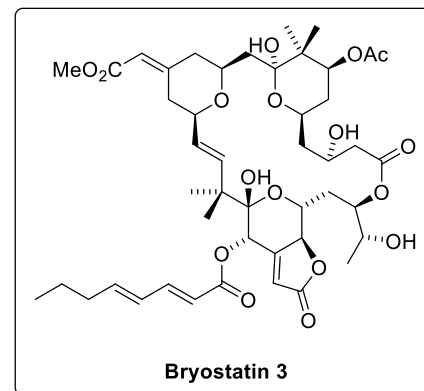
9) Structure of PPTS?
Mechanism?

10) hint: desilylation
11) hint: ring formation



Reaction 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





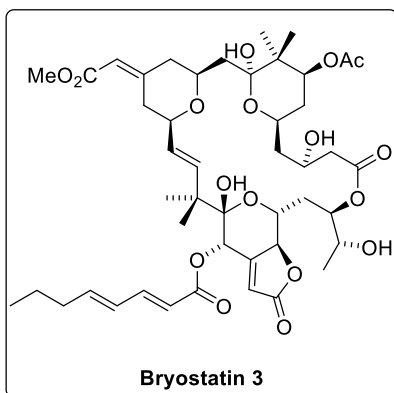
C

12-16



D

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) methylrhenium trioxide, 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?

- 17) who developed this chemistry?
- 18) *hint: anti product favored*