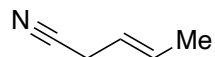


## Total Synthesis of Bryostatin 3

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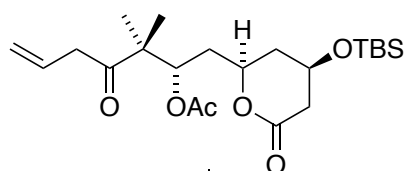
*Science* **2020**, *368*, 1007–1011.



1-6



**A**

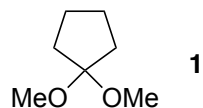


7



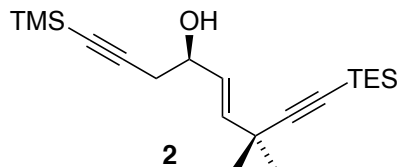
**B**

1.  $\text{K}_2\text{OsO}_4(\text{H}_2\text{O})_2$  (1 mol%),  $(\text{DHQD})_2\text{PHAL}$  (2 mol%),  $\text{K}_3\text{Fe}(\text{CN})_6$ ,  $\text{MeSO}_2\text{NH}_2$ ,  $\text{K}_2\text{CO}_3$ ,  $\text{NaHCO}_3$
2. **1**, CSA, DCM
3. DIBAL-H,  $\text{Et}_2\text{O}$
4.  $[\text{Ph}_3\text{PCH}_2\text{I}]$ , NaHMDS
5. methylpropiolate, LDA, then  $\text{ZnBr}_2$ ,  $\text{PdCl}_2\text{dppf}$  (10 mol%)
6.  $\text{K}_2\text{OsO}_2(\text{OH})_4$  (25 mol%),  $(\text{DHQ})_2\text{PHAL}$  (60 mol%),  $\text{K}_3\text{Fe}(\text{CN})_6$ ,  $\text{MeSO}_2\text{NH}_2$ ,  $\text{K}_2\text{CO}_3$ ,  $\text{NaHCO}_3$



**1**

7. **2**,  $[\text{CpRu}(\text{MeCN})_3]\text{PF}_6$  (10 mol%)



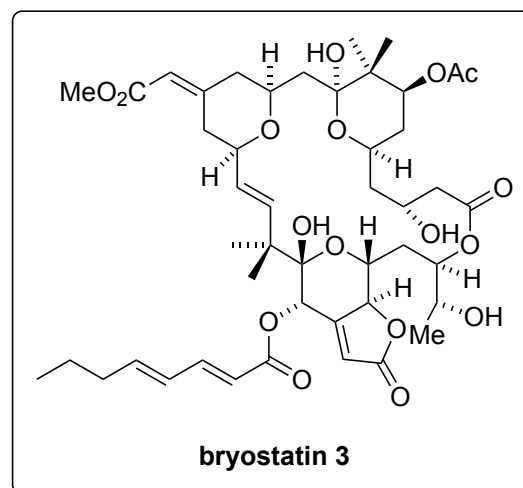
**2**

1. Name Reaction and reagent mixture  
*hint: (R,R) product obtained*

4. Name Reaction?

6. Name reagent mixture

7. *hint: ring formation; syn-addition favored*



8-11



12-16



8. NBS, DMF
9. PPTS, MeOH
10. AgNO<sub>3</sub>, THF/H<sub>2</sub>O
11. **A**, Pd(OAc)<sub>2</sub> (5 mol%), TDMPP (7.5 mol%)  
benzene, inert conditions

TDMPP = tris(2,6-dimethoxyphenyl)phosphine

12. AuCl(IPr) (10 mol%),  
AgSbF<sub>6</sub> (20 mol%), CH<sub>2</sub>Cl<sub>2</sub>, r.t.
13. ZrCl<sub>4</sub> (2.50 equiv), MeOH
14. TBSOTf, 2,6-lutidine, CH<sub>2</sub>Cl<sub>2</sub>,  
-78 °C, 15 min
15. Me<sub>3</sub>SnOH, DCE
16. 2,4,6-Cl<sub>3</sub>PhCOCl, Et<sub>3</sub>N, THF,  
*then* slow addition into DMAP, toluene

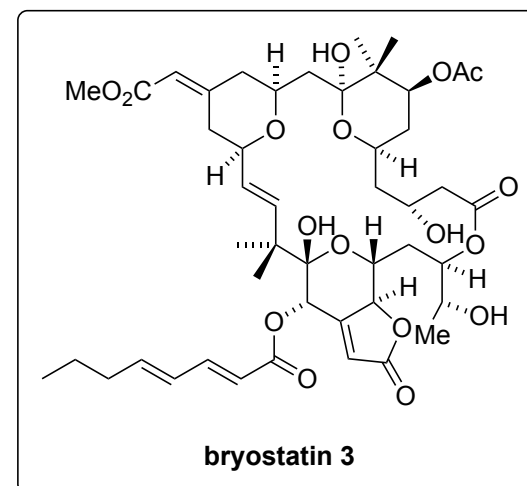
9. Structure of PPTS?
10. *hint: desilylation*
11. *hint: ring formation*

12. Classify the cyclization with Baldwin's rules

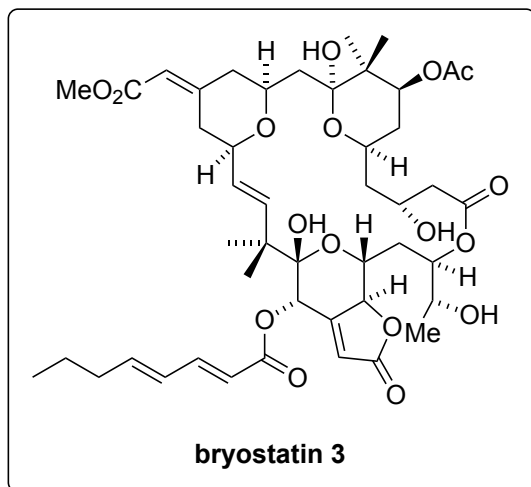
14. *hint: bis-silylated product obtained*

15. Who developed this chemistry?

16. Name Reaction?



17-22



17. methylrhodium trisoxane, UHP,  
1-methylimidazole, MeOH
18.  $\text{ClCH}_2\text{CO}_2\text{H}$ , MeOH
19. 2,4-octadienoic anhydride, DMAP
20.  $\text{Pd}_2(\text{dba})_3\text{CHCl}_3$  (20 mol%),  
Xantphos (60 mol%), CO, *i*-Pr<sub>2</sub>NEt  
DMF, MeOH
21. HF (aq.), MeCN
22. TFA, H<sub>2</sub>O, DCM

17. Name the conditions?

18) *hint: anti-product favored*