Total Synthesis of Bryostatin 3
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Science 2020, 368, 1007–1011.

1. Name Reaction and reagent mixture
   hint: \((R,R)\) product obtained
   Sharpless asymmetric dihydrogenation
   AD-mix \(\beta\)

2. Name Reaction?
   Stork-modified Wittig Reaction

3. Name reagent mixture
   AD-mix \(\alpha\)

4. Name reaction: ring formation; syn-addition favored
8. NBS, DMF
9. PPTS, MeOH
10. AgNO₃, THF/H₂O
11. A, Pd(OAc)₂ (5 mol%), TDMPP (7.5 mol%) benzene, inert conditions

TDMPP = tris(2,6-dimethoxyphenyl)phosphine

12. AuCl(IPr) (10 mol%), AgSbF₆ (20 mol%), CH₂Cl₂, r.t.
13. ZrCl₄ (2.50 equiv), MeOH
14. TBSOTf, 2,6-lutidine, CH₂Cl₂, –78 °C, 15 min
15. Me₃SnOH, DCE
16. 2,4,6-Cl₃PhCOCl, Et₃N, THF, then slow addition into DMAP, toluene

12. Classify the cyclization with Baldwin’s rules 6-endo-dig cyclization

9. Structure of PPTS? (intermediates of step 9 shown on page 3)

10. hint: desilylation

11. hint: ring formation

PPTS: pyridinium p-toluenesulfonate

14. hint: bis-silylated product obtained

15. Who developed this chemistry?
   K. C. Nicolaou

16. Name Reaction?
   Yamaguchi macrolactonization

bryostatin 3
17. methylrhenium tetroxide, UHP, 1-methylimidazole, MeOH
18. \( \text{ClCH}_2\text{CO}_2\text{H}, \text{MeOH} \)
19. 2,4-octadienoic anhydride, DMAP
20. \( \text{Pd}_2(\text{dba})_3\text{CHCl}_3 \) (20 mol%), Xantphos (60 mol%), CO, \( \text{i-Pr}_2\text{NEt} \)
   DMF, MeOH
21. HF (aq.), MeCN
22. TFA, \( \text{H}_2\text{O}, \text{DCM} \)

17. Name the conditions?  
   *Yamazaki conditions*

18) hint: anti-product favored

*Intermediates in step 9:*

- Acid promoted ring-opening transesterification
- Ring-closing ketalization