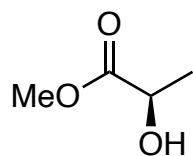


## Total Synthesis of the Allenic Macrolide (+)-Archangiumide

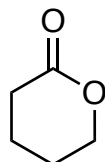
Sutro, J. L.; Fürstner, A. Total Synthesis of the Allenic Macrolide (+)-Archangiumide. *J. Am. Chem. Soc.* **2024**, *146*, 2345-2350.



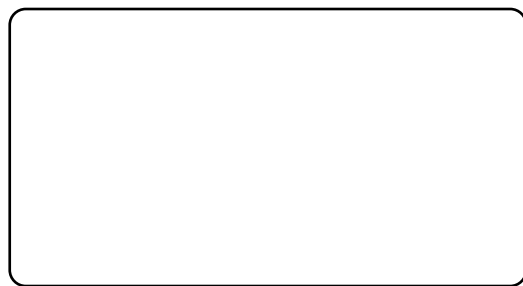
1-9



**A**



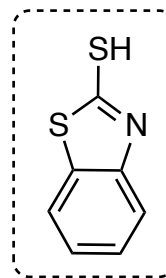
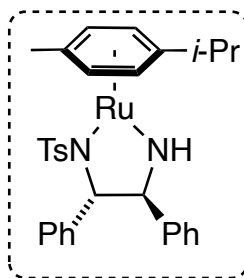
10-16



**B**

1. TBSCl, imid., DCM
2. DIBAL-H, DCM, -78 °C
3. *n*-BuLi, TMS acetylene, THF, -78 °C
4. TIPSOTf, 2,6-lut., DCM, 0 °C to rt
5. K<sub>2</sub>CO<sub>3</sub>, MeOH
6. B<sub>2</sub>(pin)<sub>2</sub>, NaOt-Bu, THF, CuCl (20 mol%), Xantphos (20 mol%) *then* Mel
7. I<sub>2</sub>, NaOH, THF
8. propyne, CuI (20 mol%), Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (10 mol%), HNET<sub>2</sub>, THF, -20 °C to rt
9. TsOH·H<sub>2</sub>O (25 mol%), MeOH

10. propynyllithium, THF, -78 °C to rt
11. TBSCl, imid., DCM
12. **1** (1 mol%), *i*-PrOH
13. PMBBBr, KHMDS, NEt<sub>3</sub>, THF, -78 °C to rt
14. TBAF, THF, 0 °C to rt
15. **2**, DEAD, PPh<sub>3</sub>, THF, 0 °C to rt
16. [(NH<sub>4</sub>)<sub>6</sub>Mo<sub>7</sub>O<sub>23</sub>]·4H<sub>2</sub>O (30 mol%), H<sub>2</sub>O<sub>2</sub>, EtOH, THF

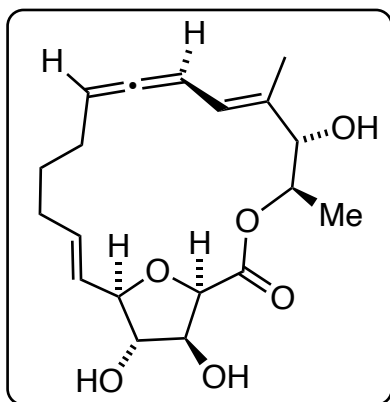


3) This reaction proceeds with 8:1 dr. What stereochemical model would you use to rationalize this?

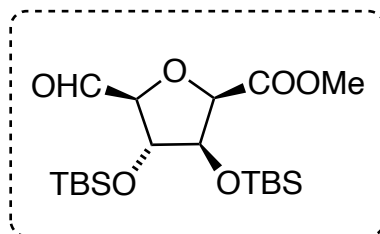
12) For whom is this type of catalyst named?

15) What is the name of the heterocyclic scaffold in **2**?

17-22

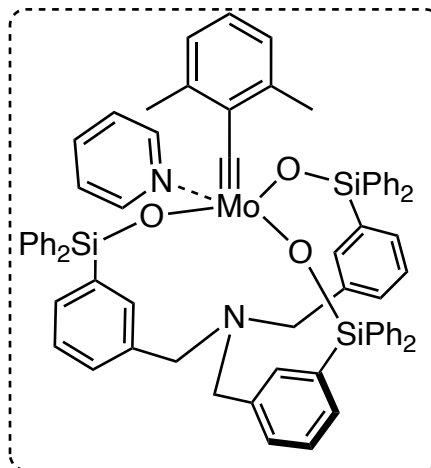


**(+)-archangiumide**

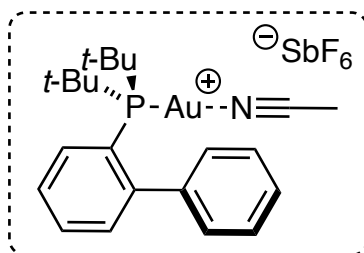


**3**

17. LDA, THF,  $-100\text{ }^{\circ}\text{C}$  then **3**, DMF,  $-78\text{ }^{\circ}\text{C}$  to rt
18. KOH (aq.), *i*-PrOH, THF,  $0\text{ }^{\circ}\text{C}$
19. Yamaguchi's reagent,  $\text{NEt}_3$ , PhMe then **A**, DMAP
20. **4** (10 mol%), PhMe, 5 Å MS,  $110\text{ }^{\circ}\text{C}$
21. TBAF, THF,  $0\text{ }^{\circ}\text{C}$  to rt
22. **5** (10 mol%), DCM,  $40\text{ }^{\circ}\text{C}$



**4**



**5**

17) What is the name of this reaction? Provide a mechanism. **3** was made in six steps from D-mannono-1,4-lactone.

20) What is this type of catalyst referred to as?

22) Propose a mechanism. Where would you expect the central carbon of the allene to appear in a  $^{13}\text{C}$  NMR spectrum?