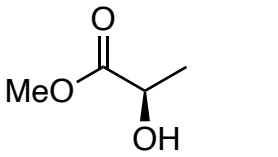
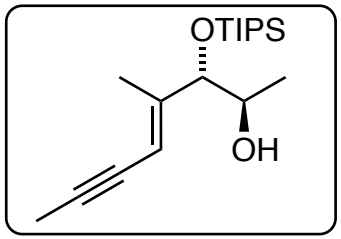
Total Synthesis of the Allenic Macrolide (+)-Archangiumide

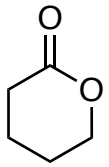
Sutro, J. L.; Fürstner, A. Total Synthesis of the Allenic Macrolide (+)-Archangiumide. *J. Am. Chem. Soc.* **2024**, *146*, 2345-2350.



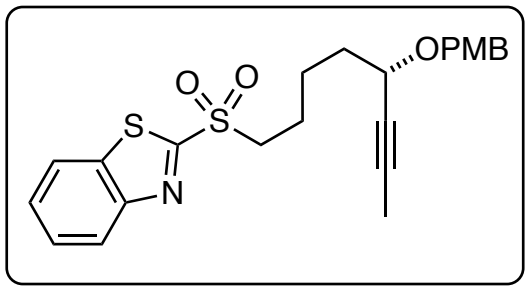
1-9



A



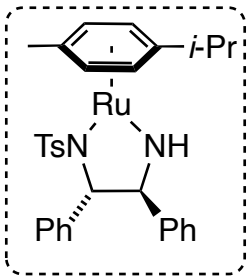
10-16



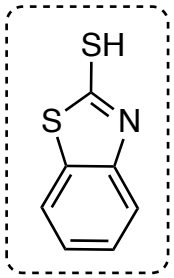
B

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_2CO_3, MeOH
6. $B_2(pin)_2$, NaO*t*-Bu, THF, CuCl (20 mol%), Xantphos (20 mol%) *then* MeI
7. I_2, NaOH, THF
8. propyne, CuI (20 mol%), $Pd(PPh_3)_2Cl_2$ (10 mol%), $HNEt_2$, THF, -20 ˚C to rt
9. TsOH•H_2O (25 mol%), MeOH

10. propynyllithium, THF, -78 ˚C to rt
11. TBSCl, imid., DCM
12. **1** (1 mol%), *i*-PrOH
13. PMBBr, KHMDS, NEt_3, THF, -78 ˚C to rt
14. TBAF, THF, 0 ˚C to rt
15. **2**, DEAD, PPh_3, THF, 0 ˚C to rt
16. $[(NH_4)_6Mo_7O_{23}]$•$4H_2O$ (30 mol%), H_2O_2, EtOH, THF



1

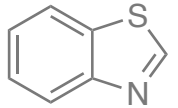


2

3) This reaction proceeds with 8:1 dr. What stereochemical model would you use to rationalize this? Felkin-Anh. See below for details.

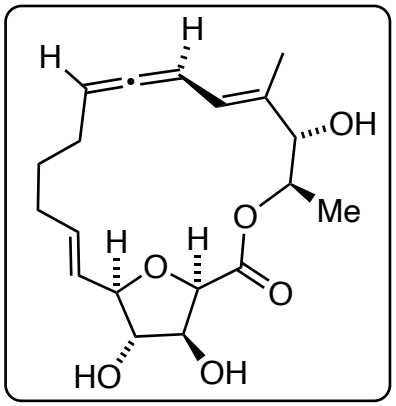
12) For whom is this type of catalyst named? Ryoji Noyori

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

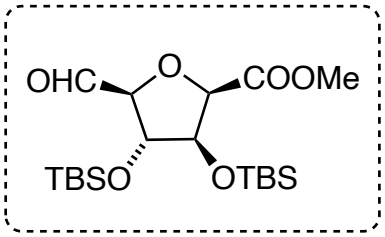


benzothiazole

17-22

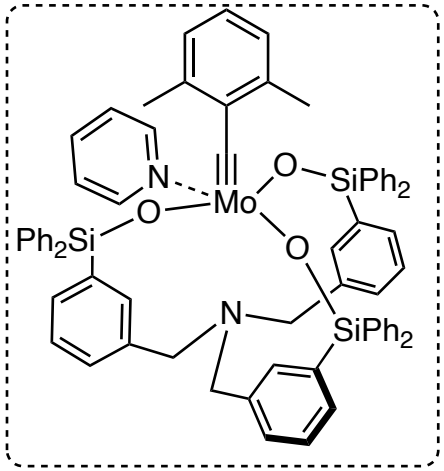


(+)-archangiumide

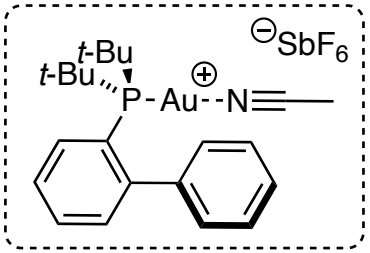


3

17. LDA, THF, -100 ˚C *then* **3**, DMF, -78 ˚C to rt
18. KOH (aq.), *i*-PrOH, THF, 0 ˚C
19. Yamaguchi's reagent, NEt_3, PhMe *then* **A**, DMAP
20. **4** (10 mol%), PhMe, 5 Å MS, 110 ˚C
21. TBAF, THF, 0 ˚C to rt
22. **5** (10 mol%), DCM, 40 ˚C



4



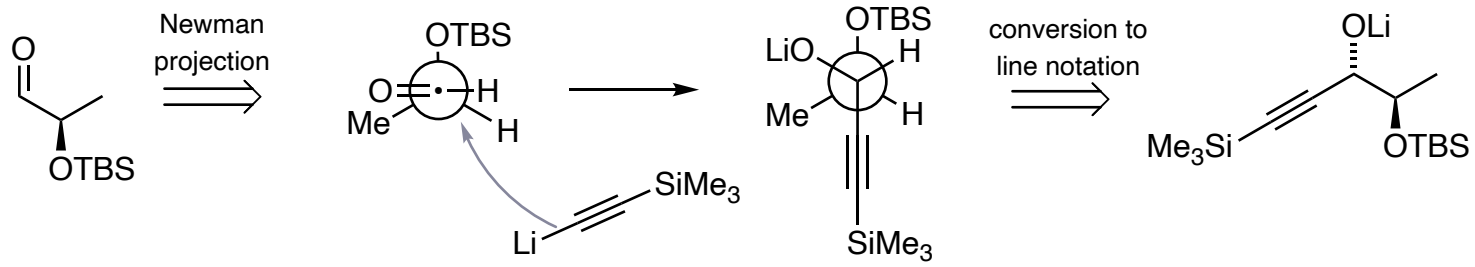
5

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

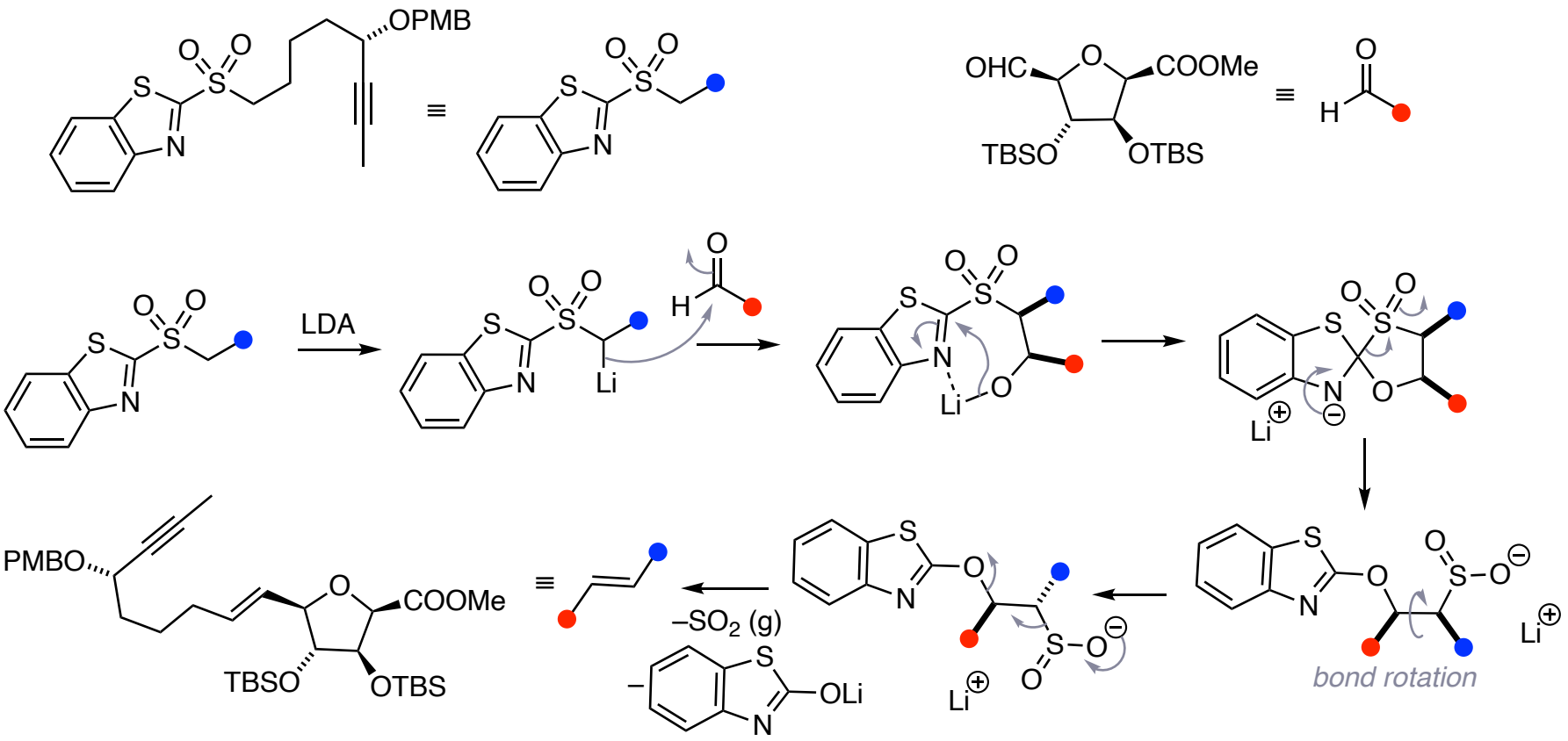
20) What is this type of catalyst referred to as? "Canopy" catalyst. See *J. Am. Chem. Soc.* **2021**, *143*, 15538-15555.

22) Propose a mechanism. Where would you expect the central carbon of the allene to appear in a ^{13}C NMR spectrum? Around 210 ppm. See below for mechanism.

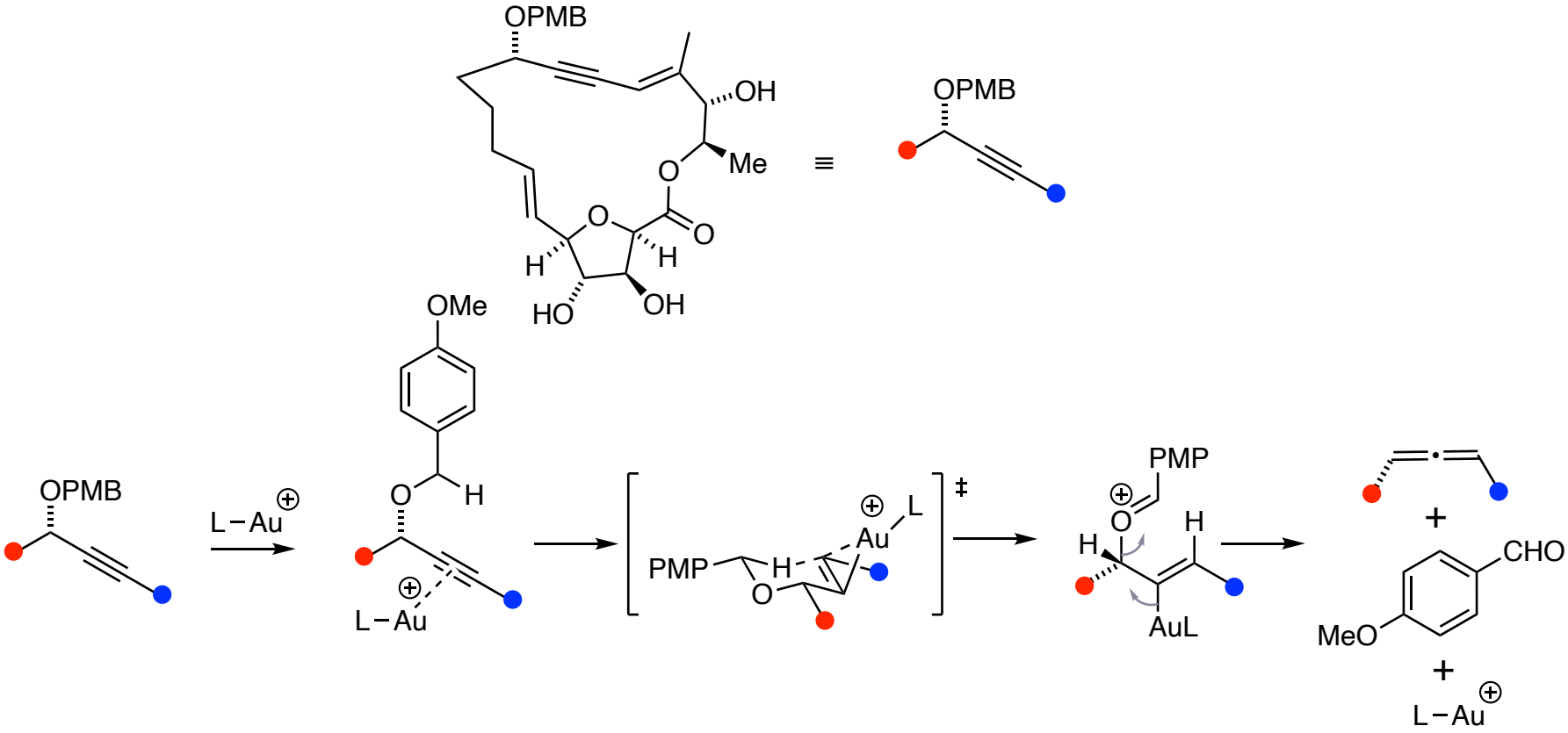
Step 3



Step 17



Step 22


OPMB
OH
Me
O
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HO
OH
≡
OPMB
OMe
OPMB
L−Au
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L−Au
PMP
H
O
Au
L
‡
PMP
O
H
H
AuL
+
CHO
MeO
+
L−Au