Asymmetric Total Synthesis of (+)-Mannolide C

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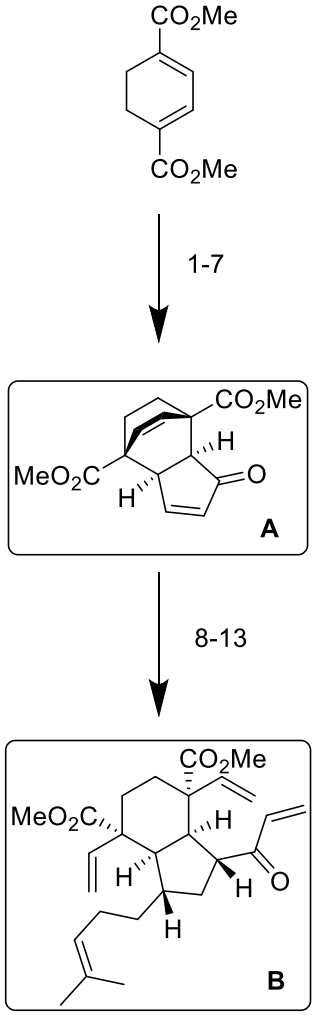
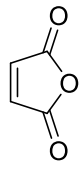


1. **1**, 170 °C
2. MeMgBr, CuI, -20 °C *then* Ac_2O, NaOAc, 60 °C
3. $LiAlH(O\textit{t}\text{-}Bu)_3$, -78 °C to -20 °C
4. MsCl, Et_3N, DMAP, 0 °C
5. $NaBH_4$, $CeCl_3$, 0 °C
6. vinyl acetate, Lipozyme TL IM, 40 °C, 4d
7. DMP, $NaHCO_3$, 0 °C



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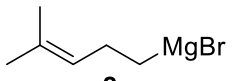

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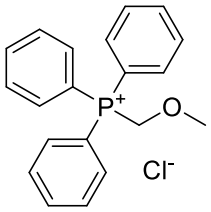

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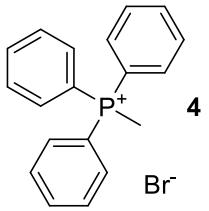

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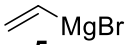

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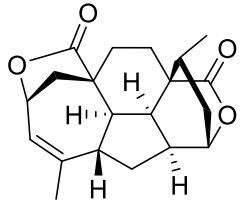
8. **2**, CuBr•DMS, HMPA, -78 °C *then* **A**, TMSCl, -20 °C
9. **3**, KHMDS, 0 °C *then* product of step 8, 60 °C *then* 2 M HCl, 40 °C
10. TMSOTf, $(TMSOCH_2)_2$ 0 °C *then* *m*-CPBA, $NaHCO_3$ 0 °C
11. O_3, -78 °C *then* DMS *then* **4**, KHMDS, -40 °C
12. Zn, AcOH, NaOAc, NaI, r.t. *then* conc. HCl, r.t.
13. **5**, $CeCl_3$, -78 °C *then* DMP, 0 °C

Step 1: Name the reaction

Hint: Steps 5-6 are for resolution

Step 5: Name the reaction
Step 6: How does the resolution with Lipozyme TL IM work?

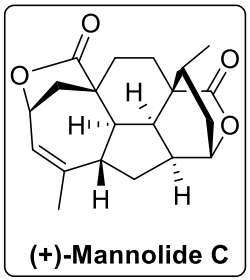


(+)-Mannolide C

Hint: Two equivalents of **4** are used in step 11

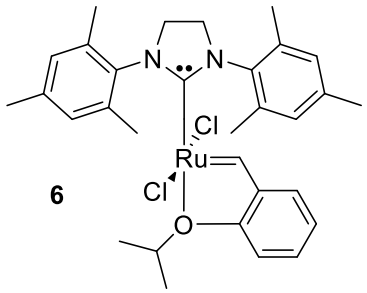
B

14-22



(+)-Mannolide C

14. **6**, MW, toluene, 150 °C
15. DBU, toluene, reflux
16. $AlMe_3$, $Ni(acac)_2$, LiBr, -5 °C
17. $NaBH_4$, r.t. *then* K_2CO_3
18. $Mn(OAc)_3 \cdot 2H_2O$, TBHP, 3Å MS, 55 °C
19. KHMDS, MeI -78 °C to 50 °C
20. $TsNHNH_2$, toluene, 60 °C *then* silica gel, **7**, 0 °C *then* NaOAc, reflux
21. OsO_4, NMO, TsOH, r.t.
22. **8**, toluene, reflux



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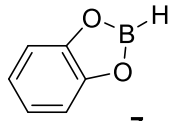

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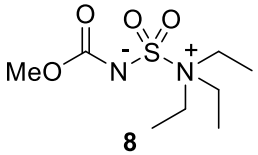

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Step 14: Please name the reagent

Step 22: Please name the reagent