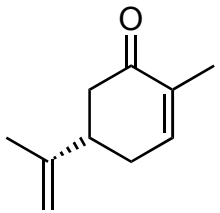
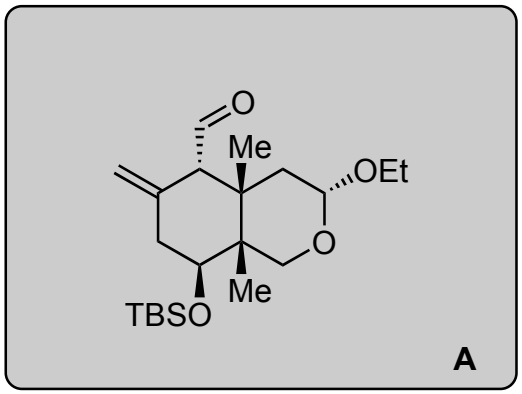
Asymmetric Total Synthesis of Norzoanthamine

Zhengyuan Xin, Hui Wang, Haibing He, Xiaoli Zhao, Shuanhu Gao

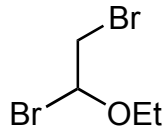
Angew. Chem. Int. Ed. **2021**, *60*, 12807-12812.



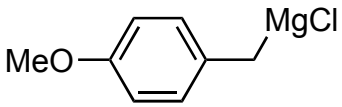
1-16



17-23



1



2

1. NaOH, H_2O_2, MeOH *then* *N*-acetyl-*L*-cysteine, $(PhSe)_2$, NaOH, MeOH
2. imH, DMAP, TBSCl, DMF
3. DBU, HCHO (aq.), THF
4. O_3, -78 °C, MeOH *then* $Cu(BF_4)_2$, $Fe(BF_4)_2$, -20 °C
5. TESCl, imH, DMAP, DMF
6. P(*n*-Bu)$_3$, HCHO (aq.), $CHCl_3$
7. TIPSCl, imH, DMAP, DCM
8. MeLi, Et_2O, -78 °C
9. PDC, 4Å MS, MeCN/PhMe, 65 °C
10. PPTS, MeOH
11. $PhNMe_2$, DCM, **1**
12. AIBN, Bu_3SnH, PhMe, reflux
13. Ph_3PCH_3Br, *t*-BuOK, 0 °C
14. TBAF, THF
15. *p*-TSA, EtOH, $CHCl_3$
16. DMP, DCM

17. **2**, THF, -78 °C to r.t.
18. Ac_2O, Et_3N, DMAP, DCM
19. **3**, $PhSiH_3$, acetone, 38 °C *then* TBAF, NaOH (aq.)
20. Na, NH_3, -78 °C
21. Ac_2O, DMAP, THF *then* (CO_2H) (aq.)
22. $Mn(dpm)_3$, $PhSiH_3$, *t*-BuOOH, *i*-PrOH *then* IBX
23. Et_3N, TMSOTf, DCM, -78 °C to -20 °C *then* IBX, **4**

Step 1: Name of the SM?
(*S*)-+-carvone

Step 6: Name of the reaction?
Baylis-Hillman

Step 9: Name of the reaction?
Babler oxidation

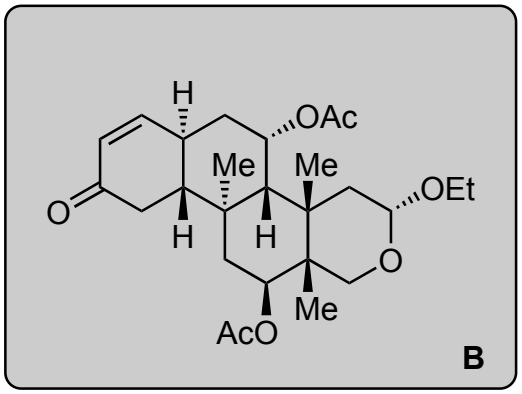
Hint: Step 10 is a mono deprotection

Step 12: Name of the reaction?
Ueno-Stork cyclization

Hint: Step 14 is a mono deprotection

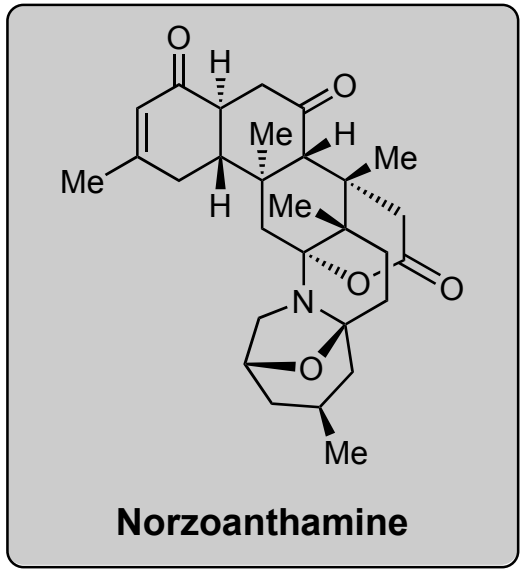
Hint: Step 15 is an epimerization

Step 20: Name of the reaction?
Birch reduction

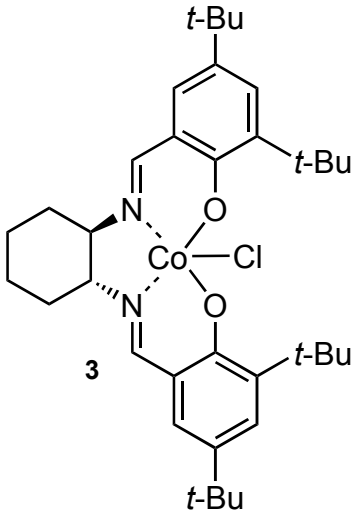


B

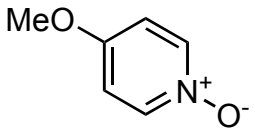
24-34



Norzoanthamine

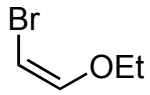


3

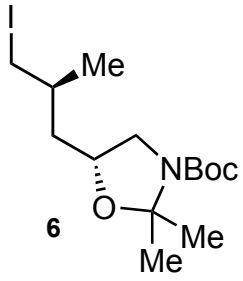


4

24. CSA, H_2O, MeCN
25. MeLi, THF *then* $LiAlH_4$ *then* TIPSOTf, imH, THF/MeCN
26. TEMPO, PIDA, DCM
27. *t*-BuLi, **5**, THF *then* SM *then* $(CO_2H)_2$
28. *t*-BuLi, **6**, THF/Et_2O, -78 °C *then* SM
29. TPAP, NMO, 4Å MS, DCM
30. $Pd(PPh_3)_4$, Bu_3SnH, THF
31. TBAF, THF, 55 °C
32. PCC, NaOAc, 4Å MS, DCM
33. 2-methyl-2-butene, $NaClO_2$, NaH_2PO_4, *t*-BuOH, THF, H_2O
34. AcOH, H_2O, 100 °C



5



6

What is the general name of the ligand in complex **3**, how are these ligands made?

Salen. Condensation of salicylaldehyde derivatives + ethylenediamine derivatives

Hint: Step 25 mono deprotection happens

Step 29: Name of the reaction?
Hint: Three reactions take place

Ley-Griffith oxidation

Hint: Two transformations occur in step 32

Step 33: Name of the reaction?
Why is 2-methyl-2-butene added?

Pinnick oxidation. Scavenging hypochlorous acid byproduct