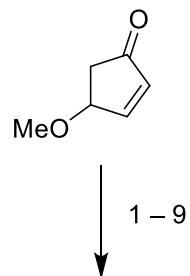


Total Synthesis, Relay Synthesis, and Structural Confirmation of the C18-Norditerpenoid Alkaloid Neofinaconitine

Y. Shi, J. T. Wilmot, L. U. Nordstrøm, D.S. Tan, D. Y. Gin
J. Am. Chem. Soc. **2013**, *135*, 14313–14320.



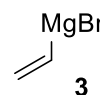
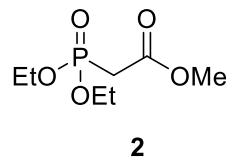
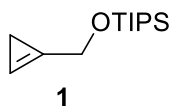
1 – 9



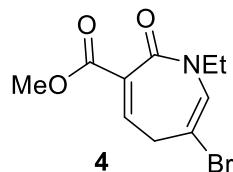
10 – 16



1. TBSOTf, Et₃N, **1**, CH₂Cl₂ 0 °C
2. NaOH, THF/H₂O, r.t.
3. **2**, KHMDS, THF, 0 °C
4. H₂, Pd/C, EtOAc, r.t.
5. MeONHMe•HCl, AlMe₃, PhMe
6. TBAF, THF, 0 °C
7. HBr, AcOH, PhF, 0 °C
8. **3**, THF, 0 °C
9. TBSOTf, KHMDS, THF, –78 °C



10. **4**, SnCl₄, MeCN, 4Å MS, r.t.
11. OsO₄, NMO, THF, H₂O then Pb(OAc)₄
12. DBU, PhMe, 0 °C
13. Tf₂NH, CH₂Cl₂, r.t.
14. CAN, MeCN/H₂O, 60 °C
15. MsCl, Et₃N, CH₂Cl₂, 50 °C
16. AIBN, Bu₃SnH, PhH, 80 °C



Step 1: Ideas for synthesis of cyclopropene 1?

Hint Step 10: Desilylation occurs.

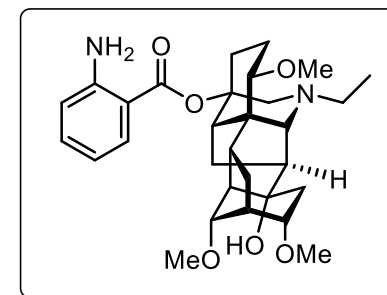
Step 11: Please name the reaction.

Hint Step 13: Two cyclizations occur. Think in terms of tautomers of given functional groups. One of the cyclizations was undesired.

Step 13: Where in terms of pK_a would you place Tf₂NH on the following list of acids:
 TfOH < HCl < MeSO₃H < TFA < AcOH

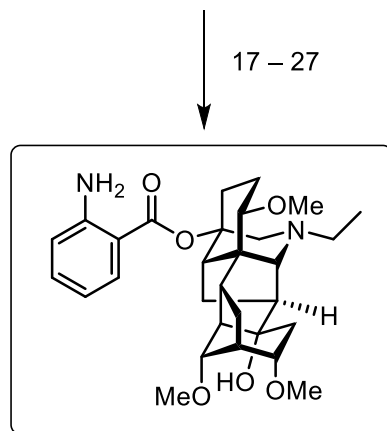
Step 14: Oxidation potential of CAN (vs SHE)? Is this a relatively small or large number?

Hint Step 15: Heterocycle opening.

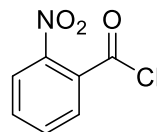


Neofinaconitine

B



17. TMSOTf, Et₃N, CH₂Cl₂, 0 °C
18. PhSeCl, CH₂Cl₂, 0 °C
19. NaIO₄, THF, r.t. *then* NaHCO₃, H₂O
20. H₂, Pd/C, EtOAc, r.t.
21. NaBH₄, MeOH, 0 °C
22. MeI, *t*-BuOK, THF, 0 °C
23. LiBH₄, THF, r.t.
24. CrO₃, H₂SO₄, r.t.
25. LiAlH₄, THF, 80 °C
26. **5**, Et₃N, PhH, 80 °C
27. Zn, 3M HCl, MeOH, r.t.



5

Hint step 21 and 22: Double reaction.

Hint step 24: Formal -CH₂- deletion.

Step 24: Please name the reagent.