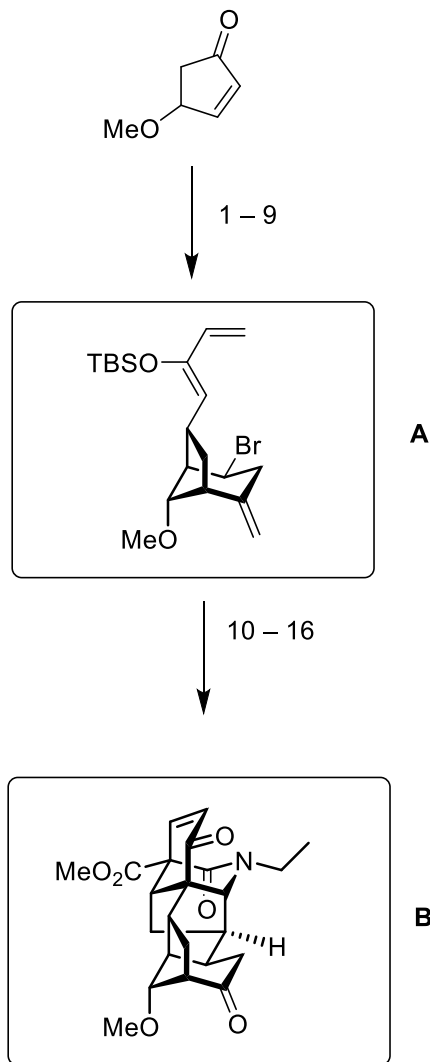
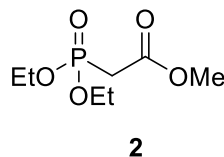
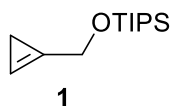


# Total Synthesis, Relay Synthesis, and Structural Confirmation of the C18-Norditerpenoid Alkaloid Neofinaconitine

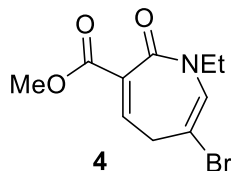
Y. Shi, J. T. Wilmot, L. U. Nordstrøm, D.S. Tan, D. Y. Gin  
*J. Am. Chem. Soc.* **2013**, *135*, 14313–14320.



1. TBSOTf, Et<sub>3</sub>N, **1**, CH<sub>2</sub>Cl<sub>2</sub> 0 °C
2. NaOH, THF/H<sub>2</sub>O, r.t.
3. **2**, KHMDS, THF, 0 °C
4. H<sub>2</sub>, Pd/C, EtOAc, r.t.
5. MeONHMe•HCl, AlMe<sub>3</sub>, 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**, SnCl<sub>4</sub>, MeCN, 4Å MS, r.t.
11. OsO<sub>4</sub>, NMO, THF, H<sub>2</sub>O then Pb(OAc)<sub>4</sub>
12. DBU, PhMe, 0 °C
13. Tf<sub>2</sub>NH, CH<sub>2</sub>Cl<sub>2</sub>, r.t.
14. CAN, MeCN/H<sub>2</sub>O, 60 °C
15. MsCl, Et<sub>3</sub>N, CH<sub>2</sub>Cl<sub>2</sub>, 50 °C
16. AIBN, Bu<sub>3</sub>SnH, PhH, 80 °C



Step 1: Ideas for synthesis of cyclopropene **1**?

Hint Step 10: Desilylation occurs.

Step 11: Please name the reaction.

**Lemieux-Johnson type**

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<sub>a</sub> would you place Tf<sub>2</sub>NH on the following list of acids:

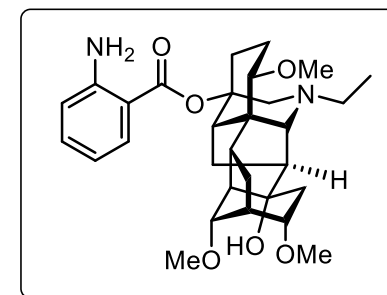
TfOH < HCl < MeSO<sub>3</sub>H < TFA < AcOH

**Tf<sub>2</sub>NH < TfOH < HCl < MeSO<sub>3</sub>H < TFA < AcOH**

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

**E = 1.6 V, one of the strongest shelf-stable oxidants**

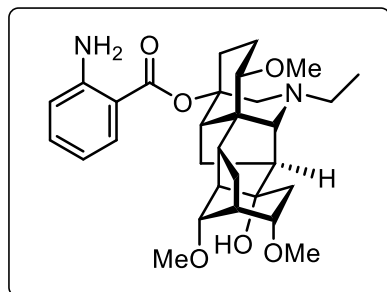
Hint Step 15: Heterocycle opening.



Neofinaconitine

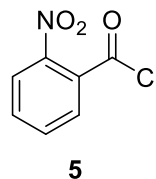
B

17 – 27



Neofinaconitine

17. TMSOTf, Et<sub>3</sub>N, CH<sub>2</sub>Cl<sub>2</sub>, 0 °C
18. PhSeCl, CH<sub>2</sub>Cl<sub>2</sub>, 0 °C
19. NaIO<sub>4</sub>, THF, r.t. *then* NaHCO<sub>3</sub>, H<sub>2</sub>O
20. H<sub>2</sub>, Pd/C, EtOAc, r.t.
21. NaBH<sub>4</sub>, MeOH, 0 °C
22. MeI, *t*-BuOK, THF, 0 °C
23. LiBH<sub>4</sub>, THF, r.t.
24. CrO<sub>3</sub>, H<sub>2</sub>SO<sub>4</sub>, r.t.
25. LiAlH<sub>4</sub>, THF, 80 °C
26. **5**, Et<sub>3</sub>N, PhH, 80 °C
27. Zn, 3M HCl, MeOH, r.t.



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Hint step 21 and 22: Double reaction.

Hint step 24: Formal -CH<sub>2</sub>- deletion.

Step 24: Please name the reagent.

Jones reagent

Step 1:

