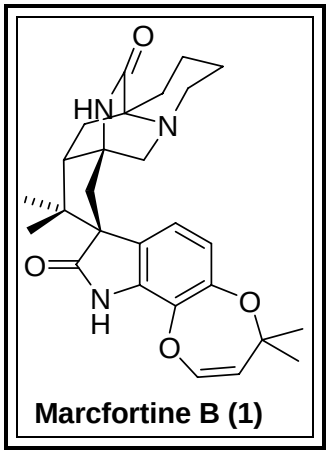
Synthesis of (±)-Marcfortine B



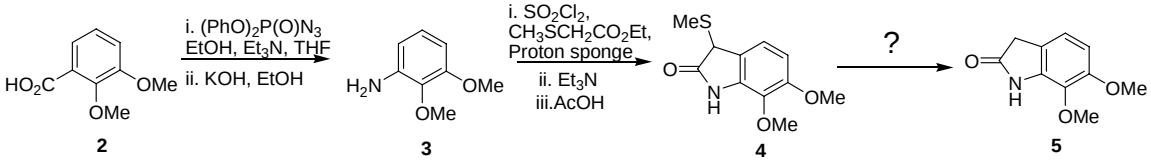
Marcfortine B (1)

Marcfortine B is a secondary metabolite isolated from a *Penicillium* species. Like other Marcfotine alkaloids and the closely related paraherquamide class of compounds, it displays potent anthelmintic activity.

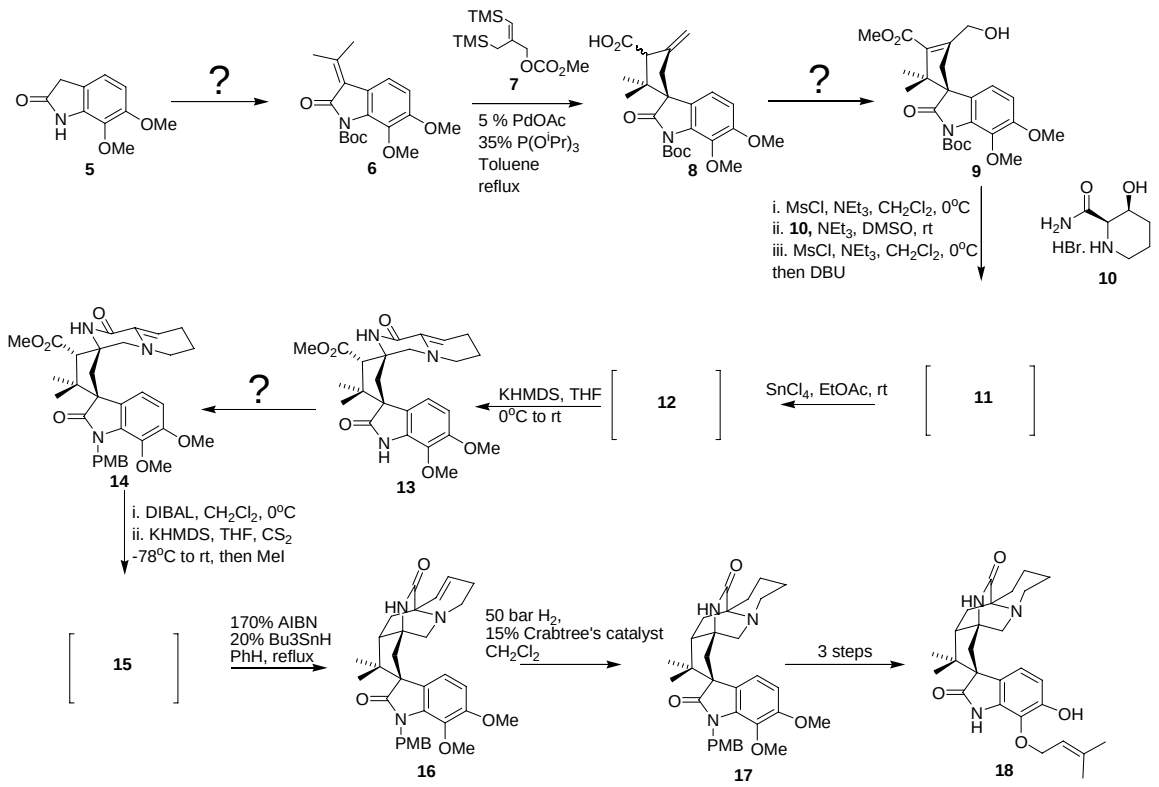
The first total synthesis of Marcfortine B has been reported recently by B. Trost and co-workers. The heavily substituted spirocyclic cyclopentane ring is a motif present in a number of related compounds and this synthesis serves to showcase a method developed by Trost for its installation.

Questions

1. The synthesis begins with the 'known' oxindole **5**. Its synthesis is not worthy of discussion in Trost's paper but here it most certainly is. Look at the scheme below and rationalize the formation of **4** from **2**.



2. What conditions might you use for the desulfurization of **4** to give oxindole **5**?



3. How would you perform the two transformations necessary to go from **5** to **6**? Is the order of these transformations important?

4. A palladium catalysed carboxylative [3+2] cycloaddition gives access to the cyclopentane **8**. How might the palladium (0) source interact with substrate **7**? Could you suggest a feasible mechanism for the cycloaddition based upon this?

5. Suggest a way of converting **8** to **9** (3 steps).

6. Propose a structure for **11**.

7. What happens when **11** is treated with $SnCl_4$? Give an appropriate structure for **12**.

8. A ring-closing conjugate addition gives rise to a single isomer of **13**. Can you account for the selectivity of the reaction given that with the analogous N-methyl amide, the selectivity is completely reversed?

9. As luck would have it, compound **13** is about as soluble as brick dust. How would you add the PMB protecting group to improve solubility?

10. Propose a structure for **15**. What is the name of the new functional group formed?

11. Suggest a mechanism for the radical cyclization to **16**.

12. Alkene **16** is then hydrogenated to give **17** which is only a few steps away from Marcfortine B. How would you finish the synthesis? The published synthesis happens to go via compound **18**.