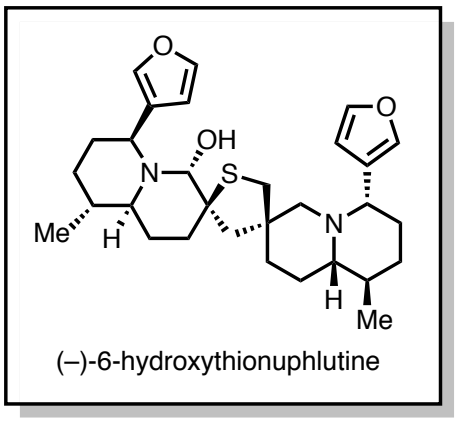
Engle Lab Short Problem Set

11/16/2017

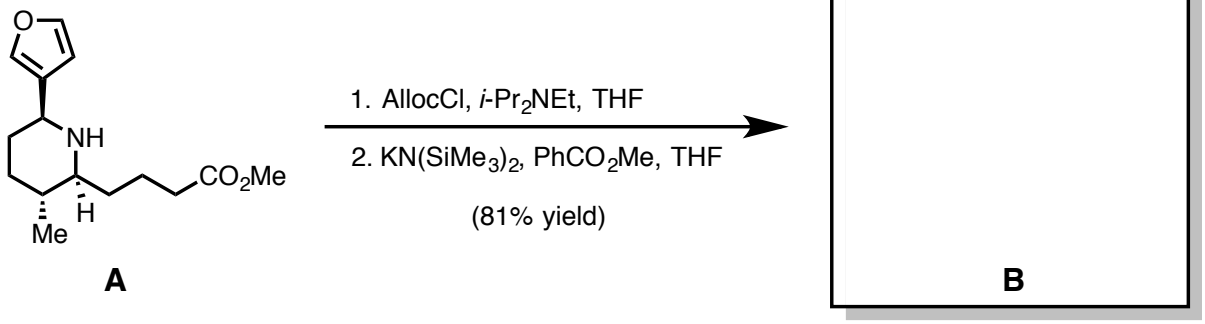


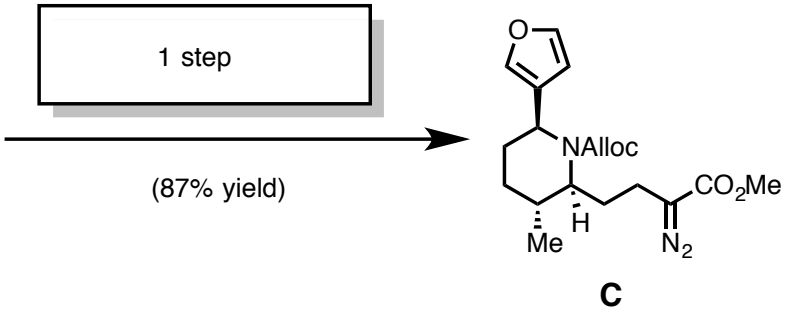
(–)-6-hydroxythionuphlutine

J. Am. Chem. Soc. **2017**, *139*, 13272.

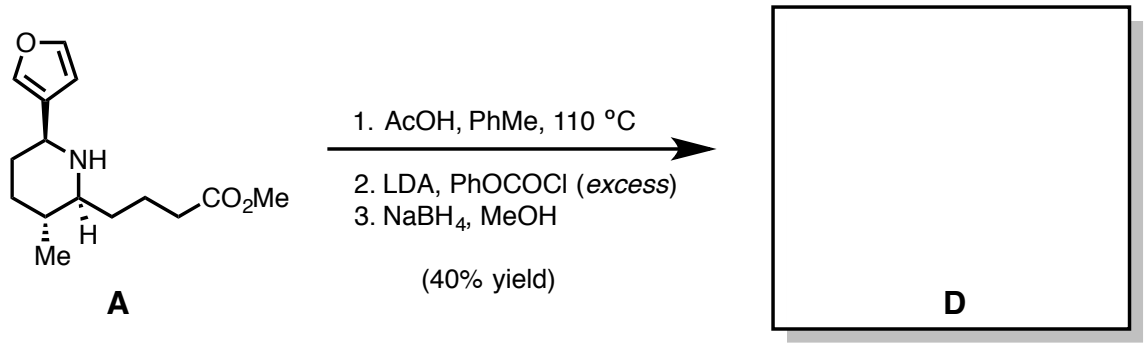
Due to their unique structures and potent biological activity, *Nuphar* alkaloids have recently become popular targets for total synthesis. Despite being known since the 1960's, the first total synthesis of a *Nuphar* alkaloid was not reported until Shenvi,Äôs synthesis of (–)-neothiobinupharidine in 2013. Wu and coworkers later expanded upon this work and completed syntheses of five hydroxylated *Nuphar* alkaloids and showed that all compounds exhibited potent bioactivity. The elegant work carried out by Shenvi and Wu paved the way for future biological studies. Yet, a critical challenge that has remained unmet is the selective synthesis of unsymmetrically oxidized congeners. This problem set revolves around Zakarians solution to this challenge.

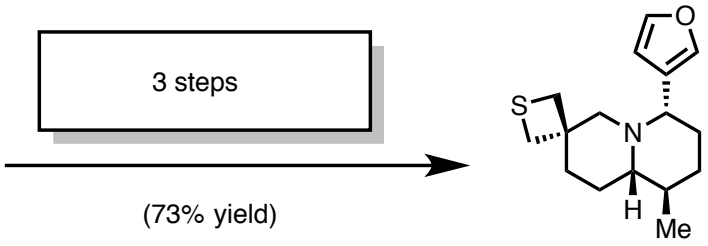
1. Zakarian's strategy involves the synthesis of a late stage intermediate **A** that is then used to access compounds **C** and **E**. Provide structure **B** and the reagent(s) necessary for the synthesis of compound **C**.





2. The synthesis of compound **E** is a little more involved, but you can do it. I believe in you.





E

3. The key step of the synthesis gives a 1:1 mixture of diastereomers. These are then separated and only the ‚Äúcorrect‚Äù diastereomer is carried through the final 2 steps leading to (–)-6-hydroxythionuphlutine. Bonus: What is the name of the rearrangement leading to intermediate **F**.