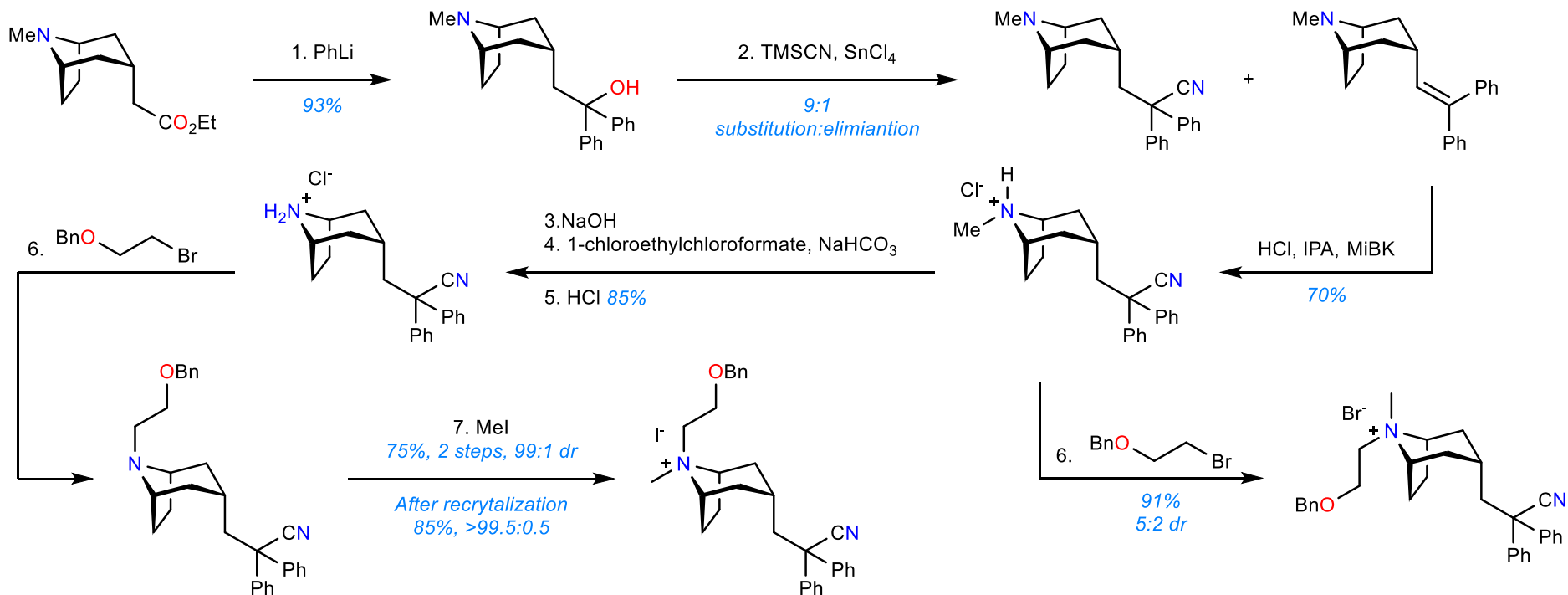
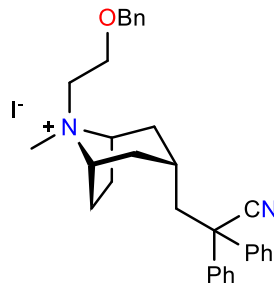


## Background

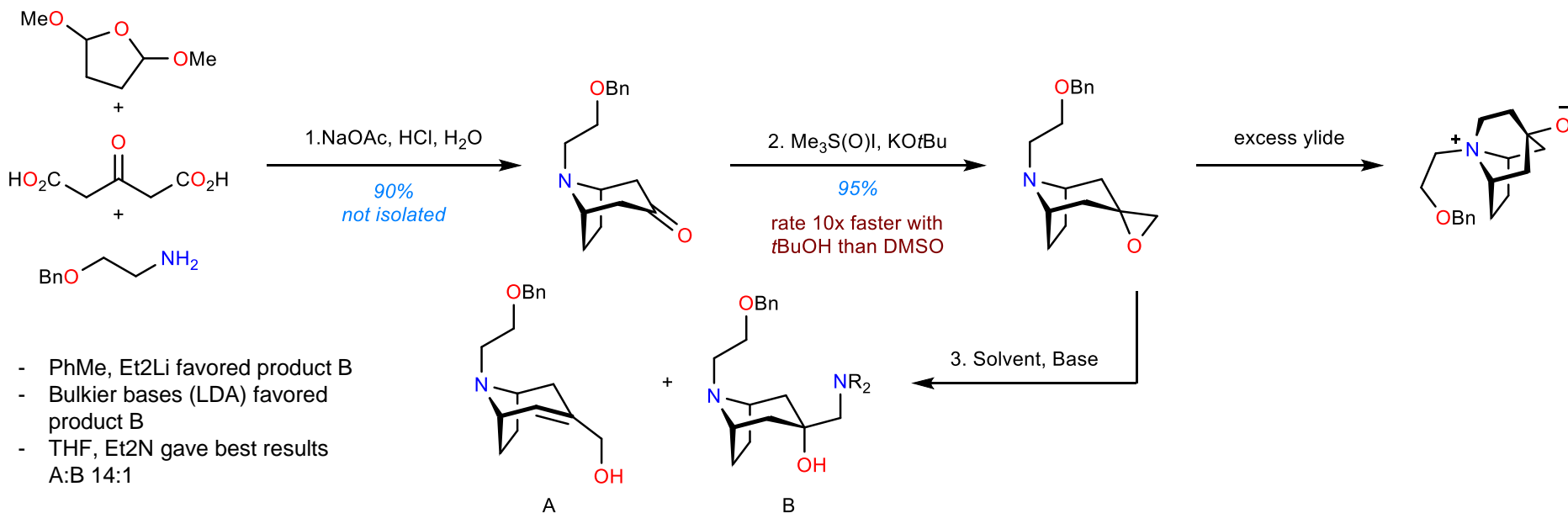
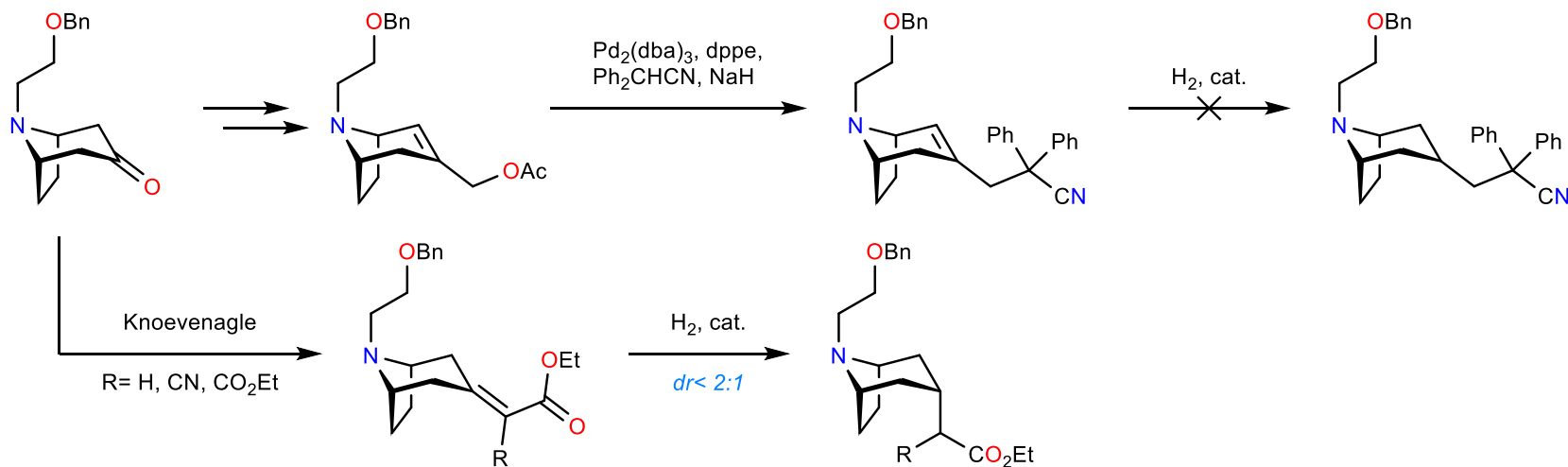
- 4<sup>th</sup> leading cause of death worldwide
- In 2012 3 million people died from COPD
- Adults diagnosed with asthma are 12x more at risk to develop COPD
- Persistent respiratory symptoms and limited airflow

<https://goldcopd.org/gold-reports/>



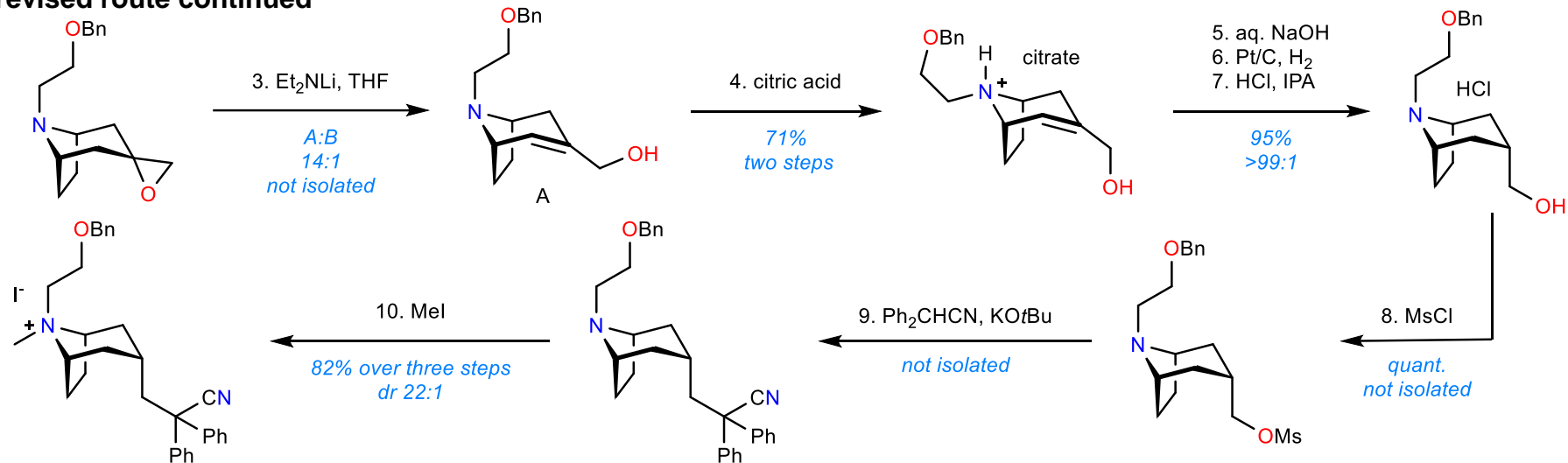
- The tropane ester is an expensive starting material
- Recrystallization after hydroxy group substitution on process scale could only achieve yields of 49%
- Dealkylation/ realkylation adds two additional steps

Bream, R. *Org. Process. Res. Dev.* **2013**, *17*, 641-650. <https://doi.org/10.1021/op3002933>



- PhMe,  $\text{Et}_2\text{Li}$  favored product B
- Bulkier bases (LDA) favored product B
- THF,  $\text{Et}_2\text{N}$  gave best results
- A:B 14:1

## 1<sup>st</sup> revised route continued



## 2<sup>nd</sup> revised route

