Total Syntheses of (–)-Kopsifoline D and (–)-Deoxoapodine: Divergent Total Synthesis via Late-Stage Key Strategic Bond Formation

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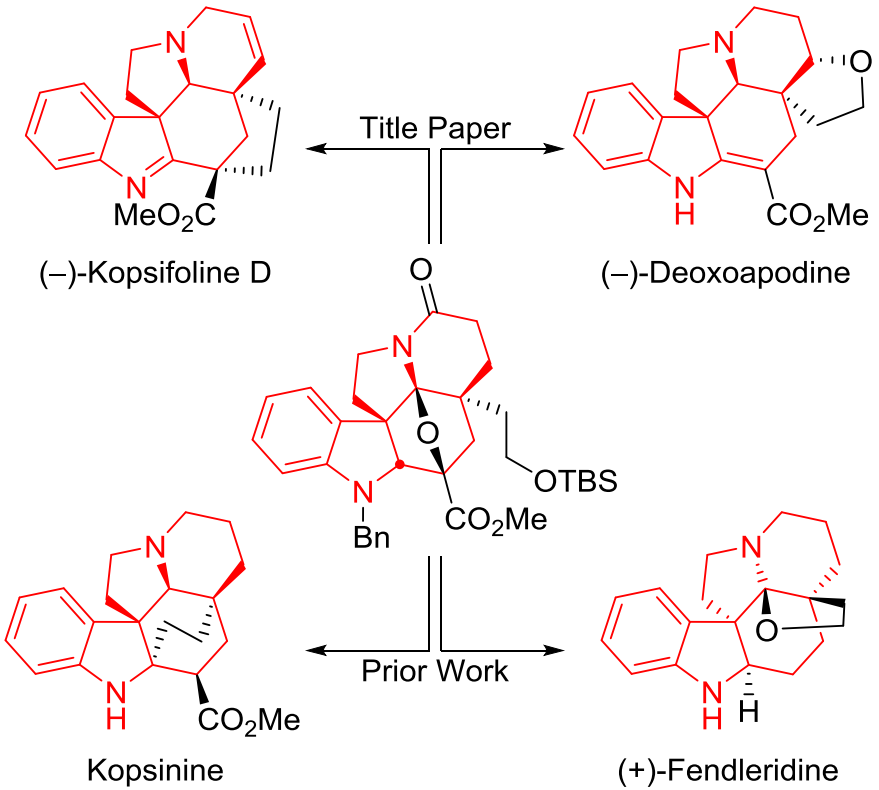
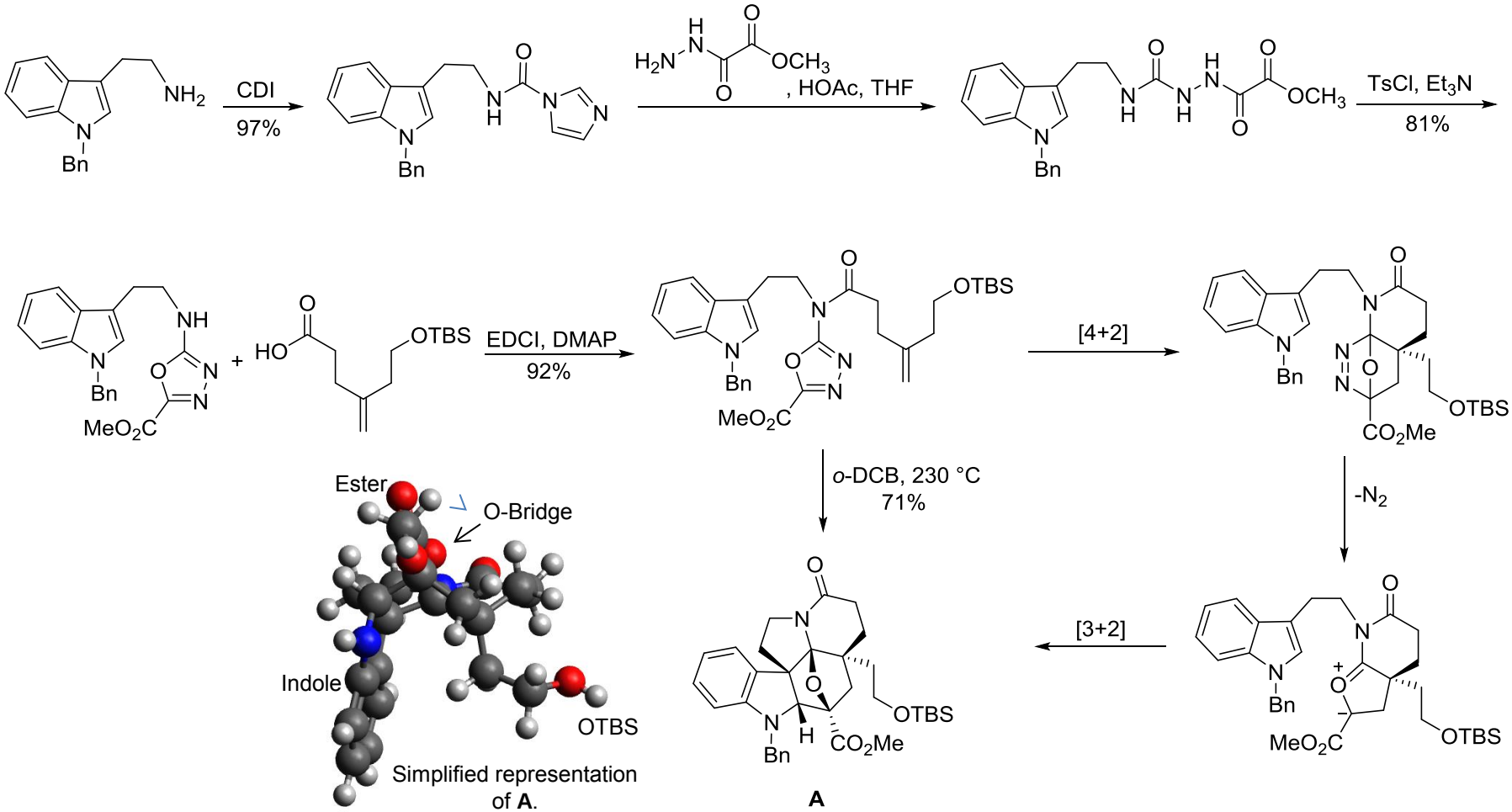
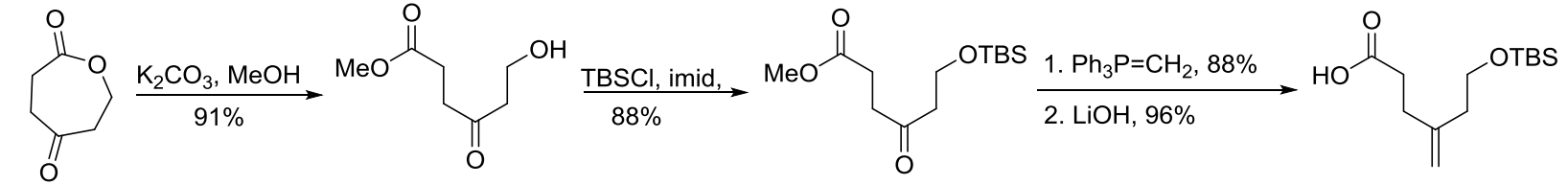
Kopsifolines and Related Compounds

- Common pentacyclic core structure.
- Allows for a common intermediate.
- Same synthetic strategy provides access to a number of natural products.



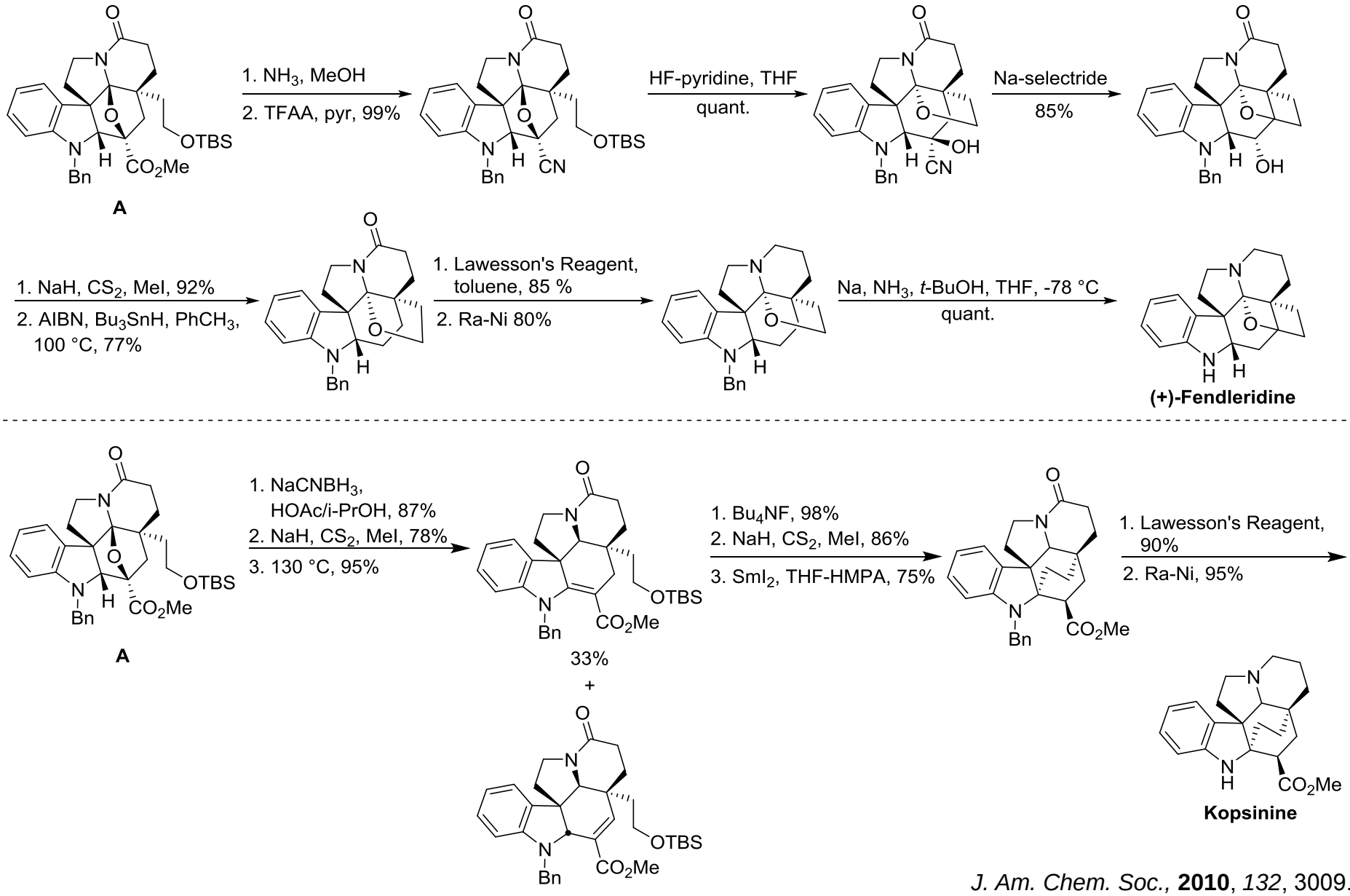
Synthesis of the Common Intermediate





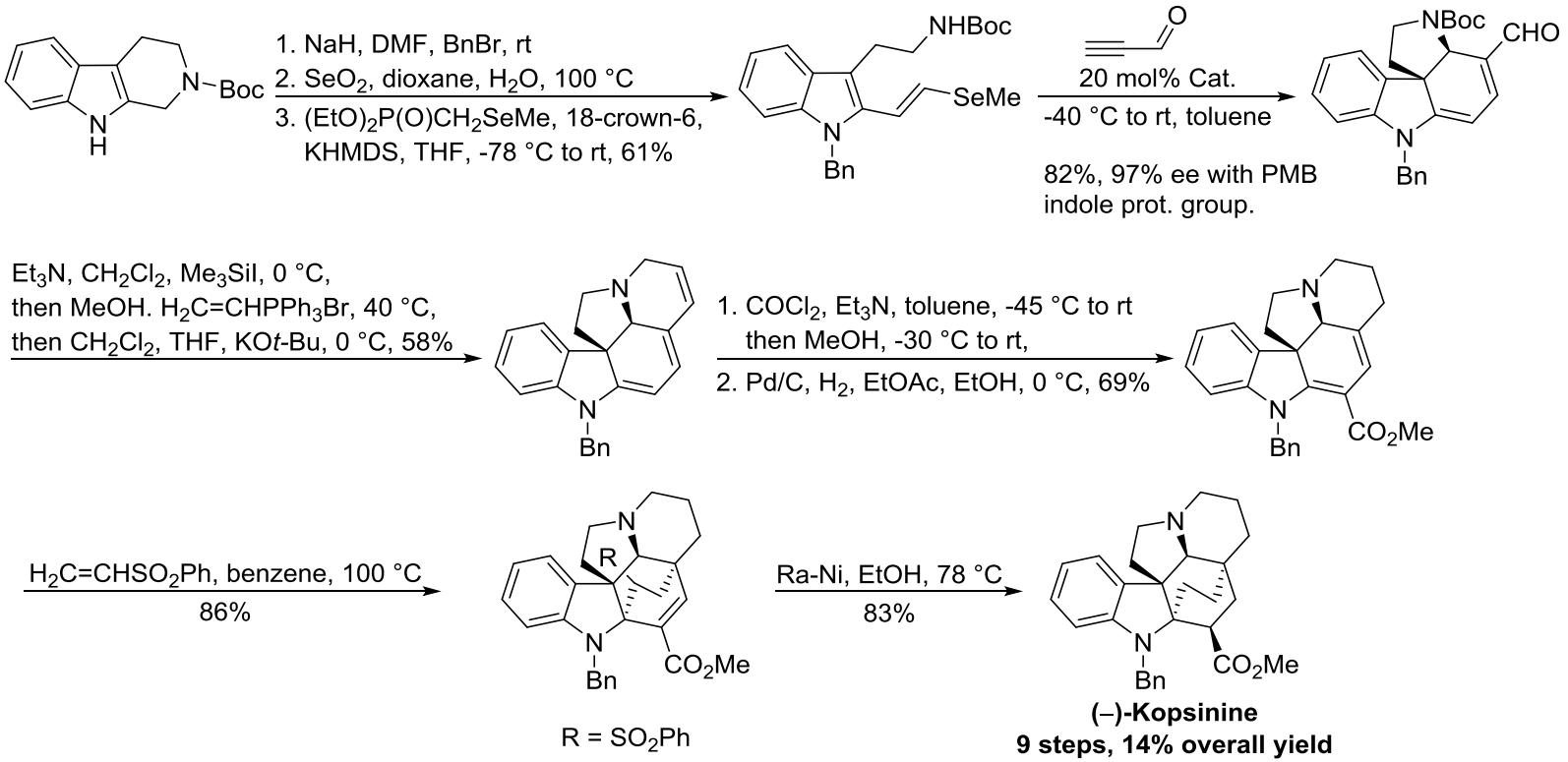
J. Am. Chem. Soc., **2010**, *132*, 3009.

Synthesis of (+)-Fendleridine and Kopsinine



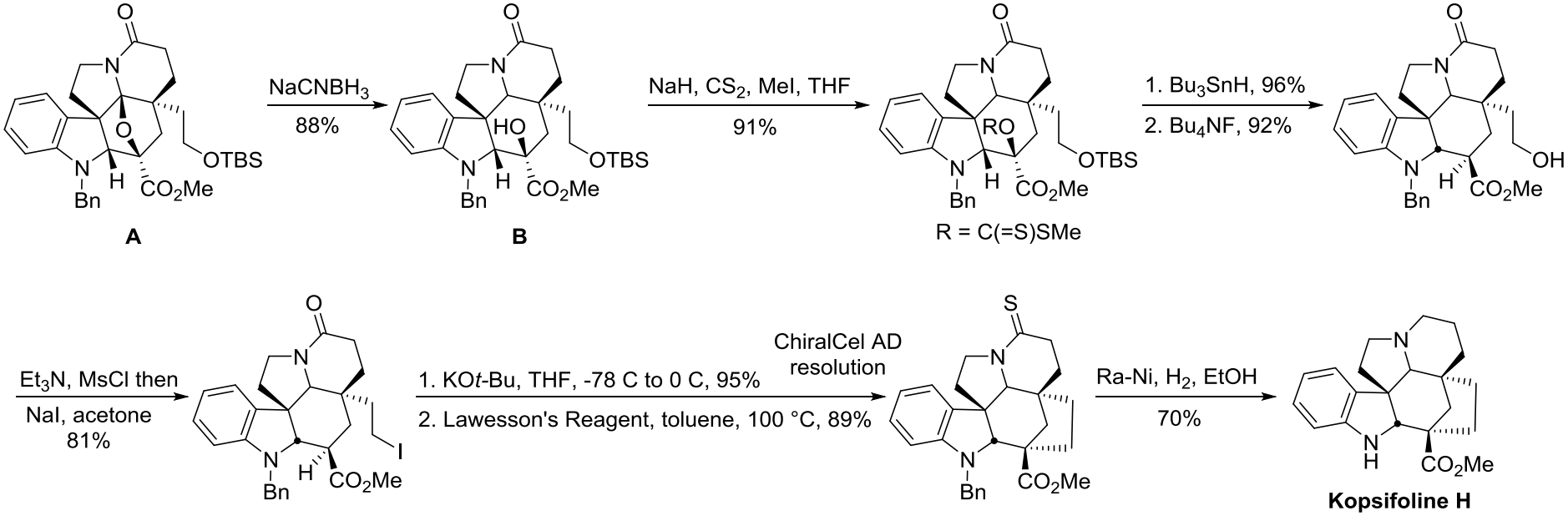
J. Am. Chem. Soc., **2010**, *132*, 3009.
Org. Lett., **2013**, *15*, 868.

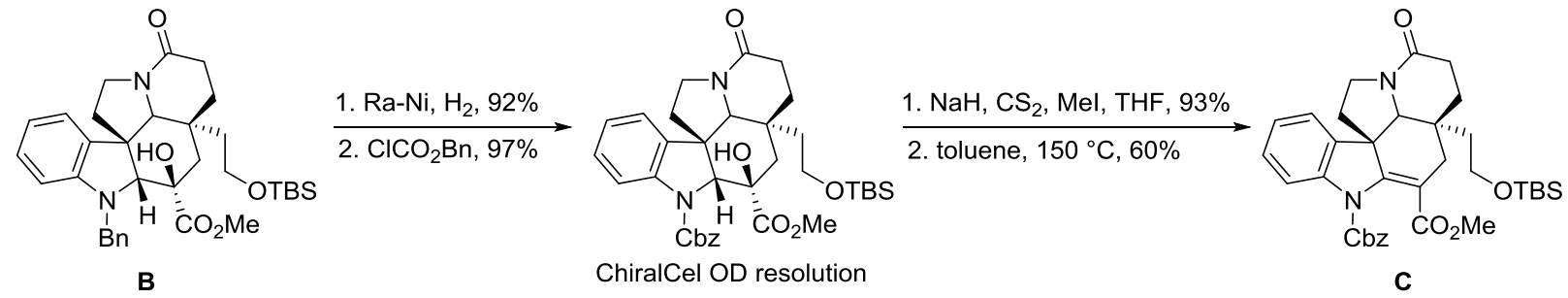
MacMillan's Enantioselective Synthesis of (–)-Kopsinine

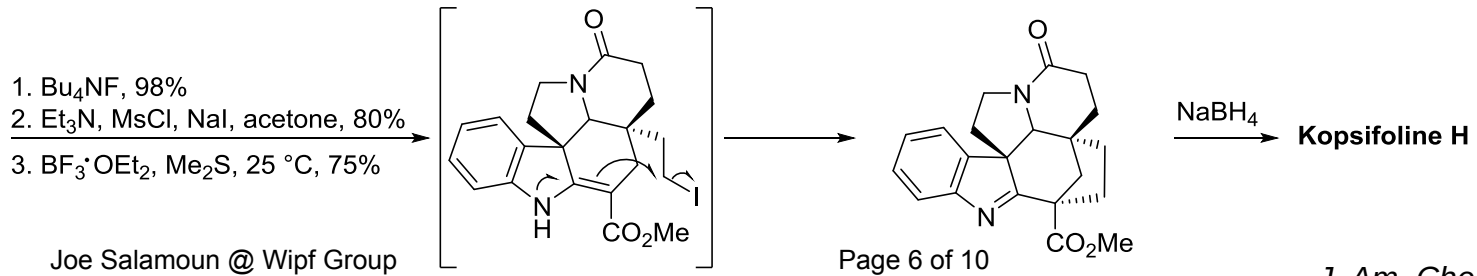


Nature, **2011**, *475*, 183.

Synthesis of Kopsifoline H and Dihydrokopsifoline D







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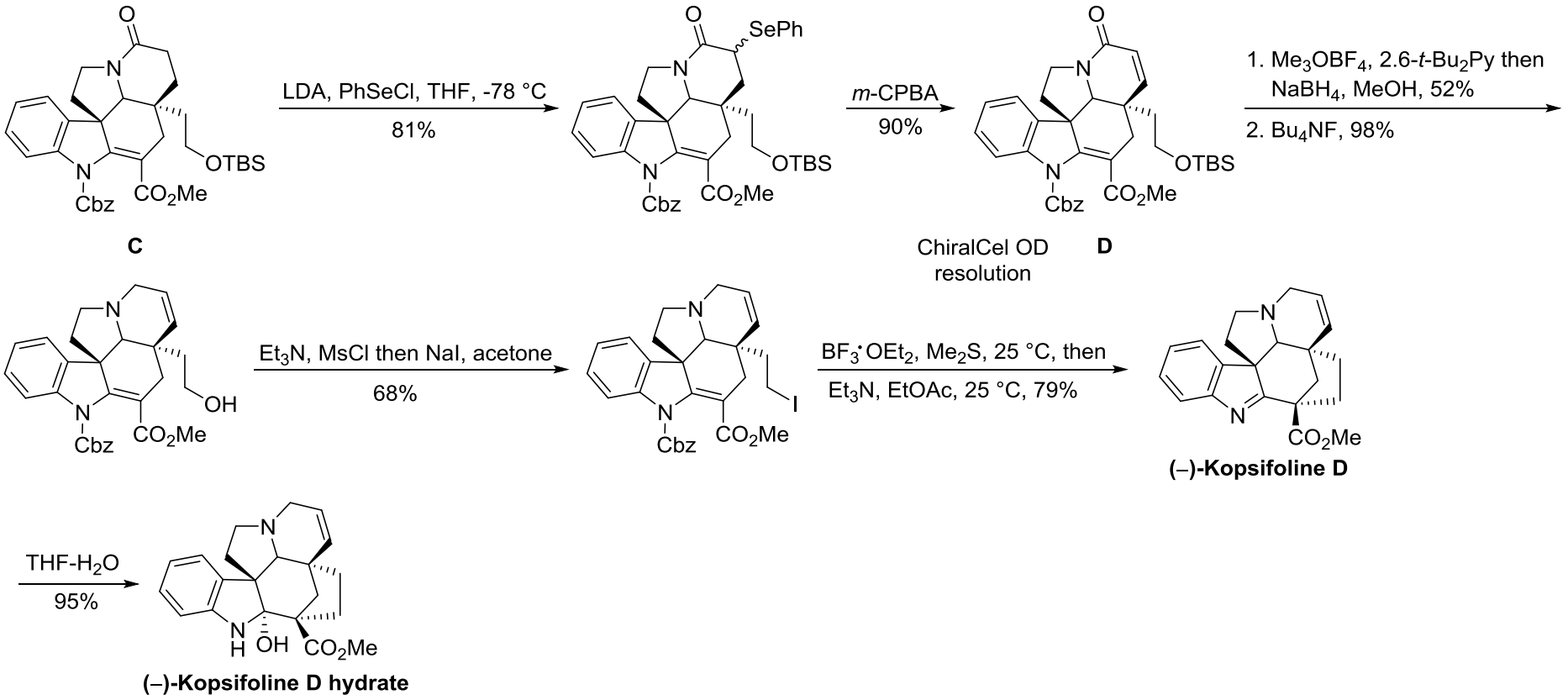
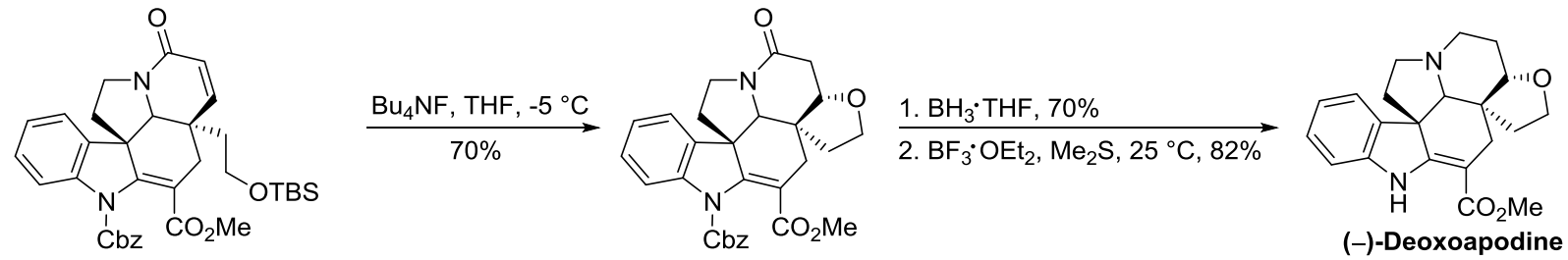
Synthesis of Kopsifoline D and Deoxoapodine





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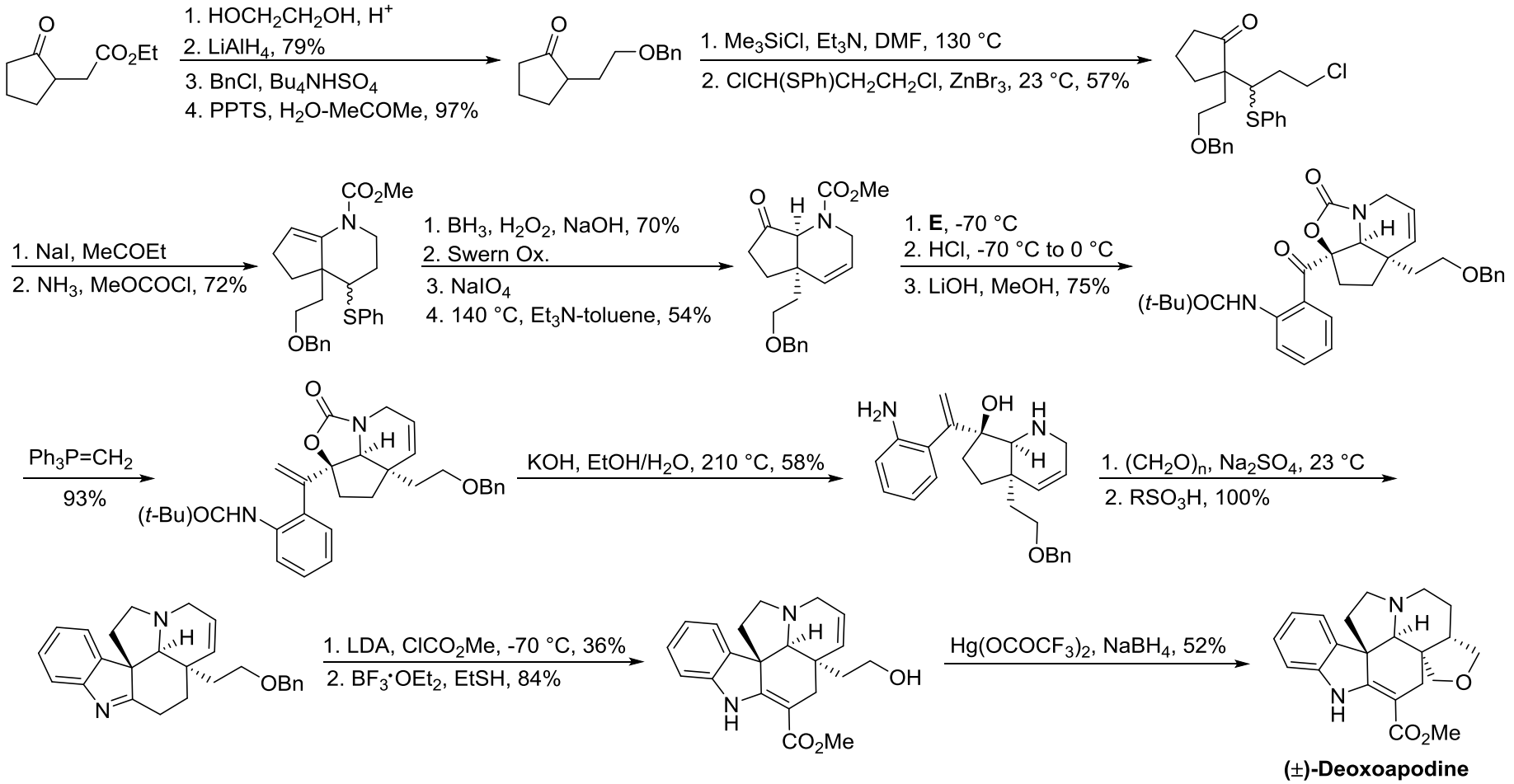
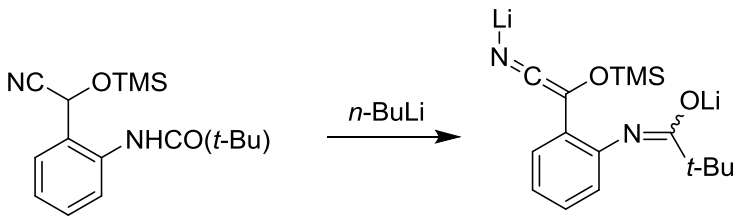
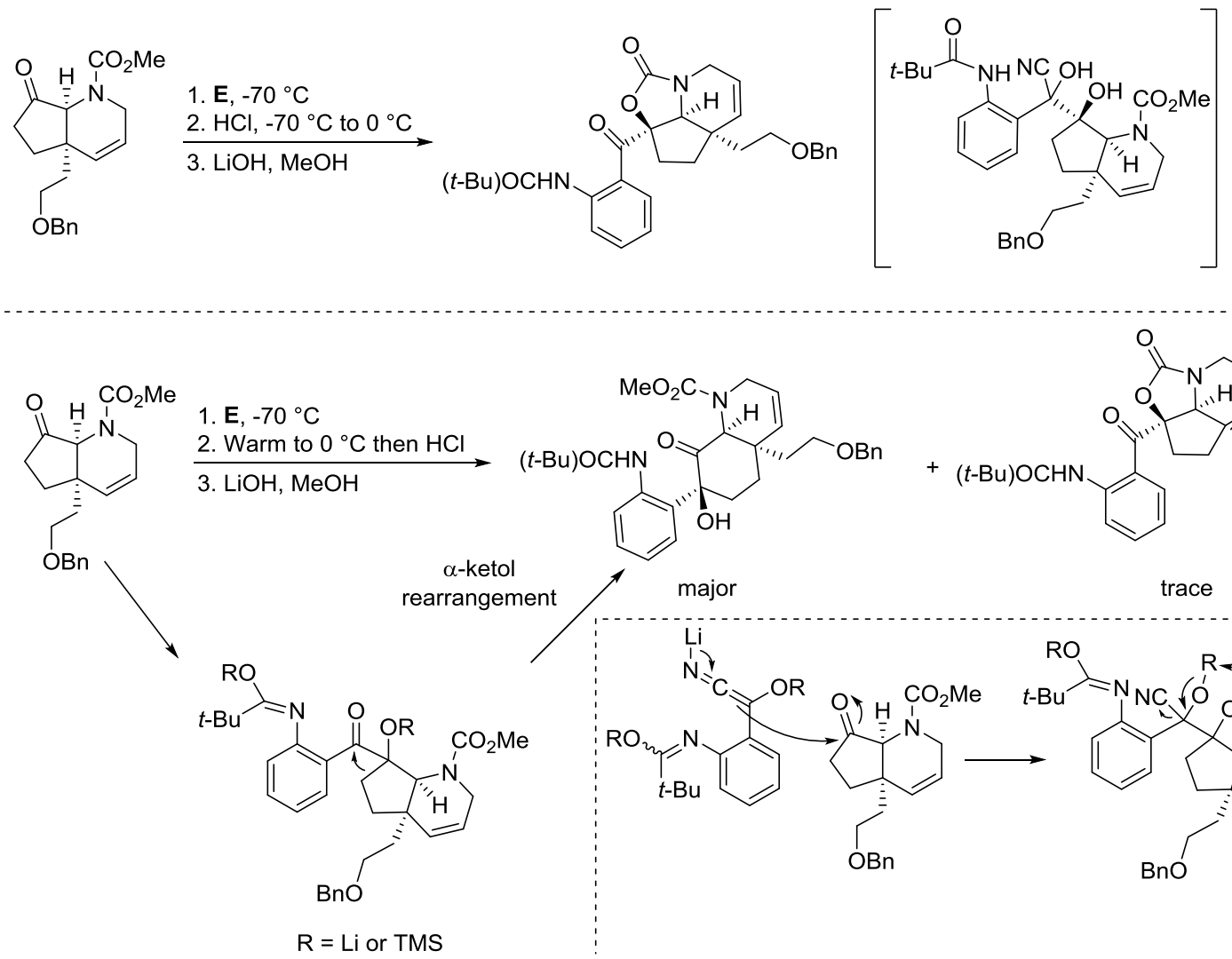
Overman Racemic Synthesis of Deoxoapodine





J. Am. Chem. Soc., **1991**, *113*, 2598.

Key Step from Overman Synthesis



J. Am. Chem. Soc., **1991**, *113*, 2598.

Conclusions

- Practical use of the same intermediate for the synthesis of a variety of natural products with the same core structure.

- The synthetic routes utilize similar chemistry displaying reproducibility/usefulness of the reactions.

- Key steps are diastereoselective but not enantioselective. It is a racemic synthesis with chiral separation of key intermediates. This invites questions about the true yields of the reactions when accounting for enantiomers.