

Outline

1. Introduction
 - Extraction
 - Biology
2. Biosynthesis
3. Degradation
4. 3-Tropinone and (+)-2-Tropinone
5. Cocaine from 3-Tropinone
 - Willstätter (1901)
 - Cha (2000)
6. RCM
 - Hu (2011)
7. [3+2]
 - Tufariello (1979)
 - Davis (2010) and Córdova (2012)
 - Shing (2011)
8. Condensation
 - Rapoport (1998)
 - Pearson (2000)

Reviews and books

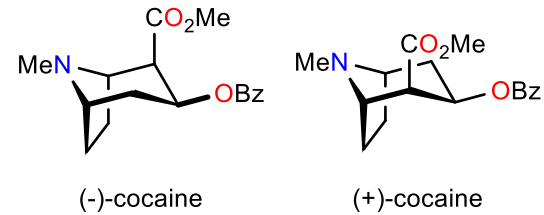
1. Synthesis of tropane alkaloids
 - <https://doi.org/10.1016/bs.alkal.2018.06.001>
 - <https://doi.org/10.1021/cr050995>
2. Biosynthesis of tropanes
 - <https://doi.org/10.1007/3-540-48146-X>
 - <https://doi.org/10.1039/B001713M>
3. Overview of cocaine
 - <https://doi.org/10.1021/acchemneuro.8b00117>

WARNING

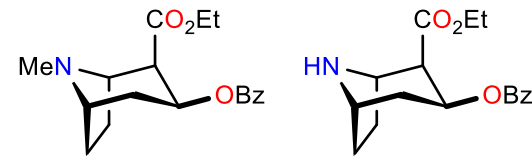




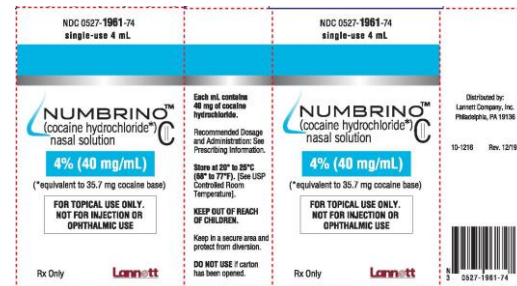
- The leaves from the coca plant have been chewed on by the Peruvian Indians for religious rituals and its ability to suppress hunger
- Officially isolated in 1855 by Niemann from *Erythroxylum coca*
- While there are many species of coca plants *Erythroxylum coca* and *Erythroxylum novogranatense* are harvested for their high cocaine contents
- To extract cocaine the leaves are first treated with basic water
- Then kerosene is added to dissolve the coca alkaloids, after extracting the coca alkaloids, they are precipitated with acid
- The dried precipitate is treated with permanganate to decompose unwanted coca alkaloids
- This solution is treated with ammonium hydroxide, forming a precipitate “cocaine base”
- This “cocaine base” is dissolved in acetone, filtered, and HCl is added to precipitate cocaine hydrochloride



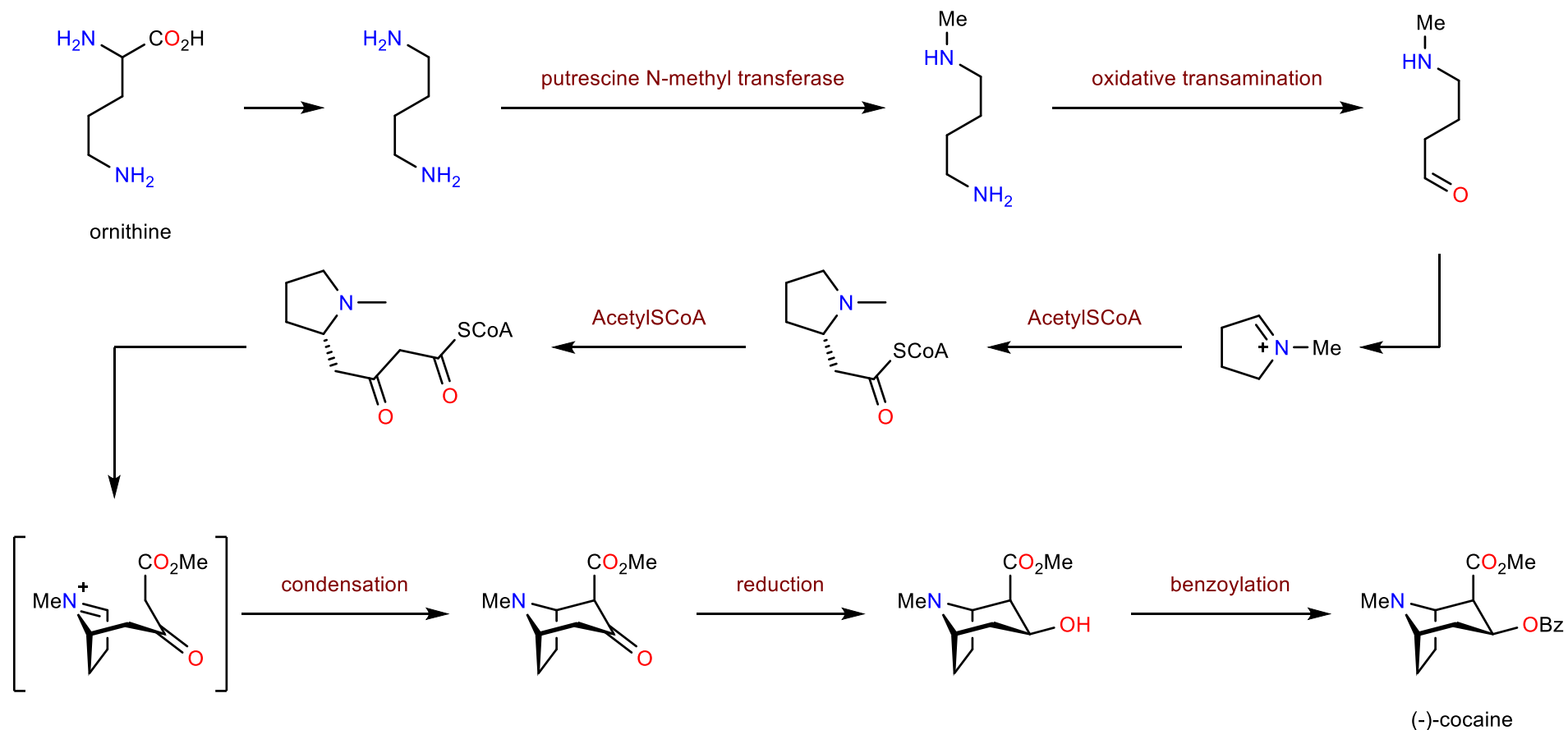
- Only R-(-)-cocaine is addictive
- S-(+)-cocaine is metabolized faster, and does not bind as strongly to the [³H]mazindol binding site of the dopamine transporter



- Drinking alcohol while using (-)-cocaine forms a more toxic metabolite
- A mixture of cocaine, adrenaline, and carbonate has been used as a local anesthetic for ear, nose, and throat surgeries since the 1940's
- Cocaine has been approved by the FDA as local anesthetic for nasal mucus membranes



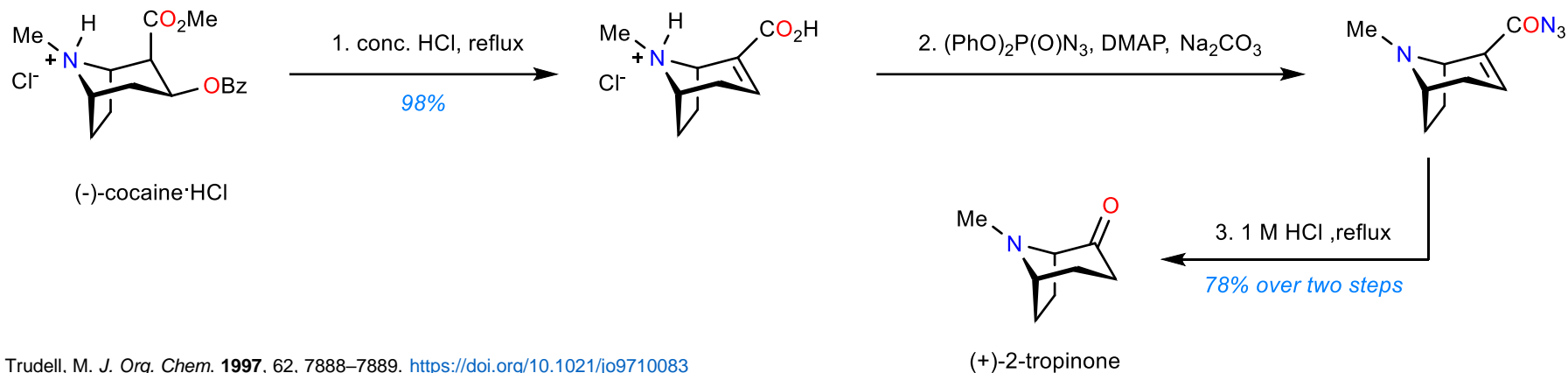
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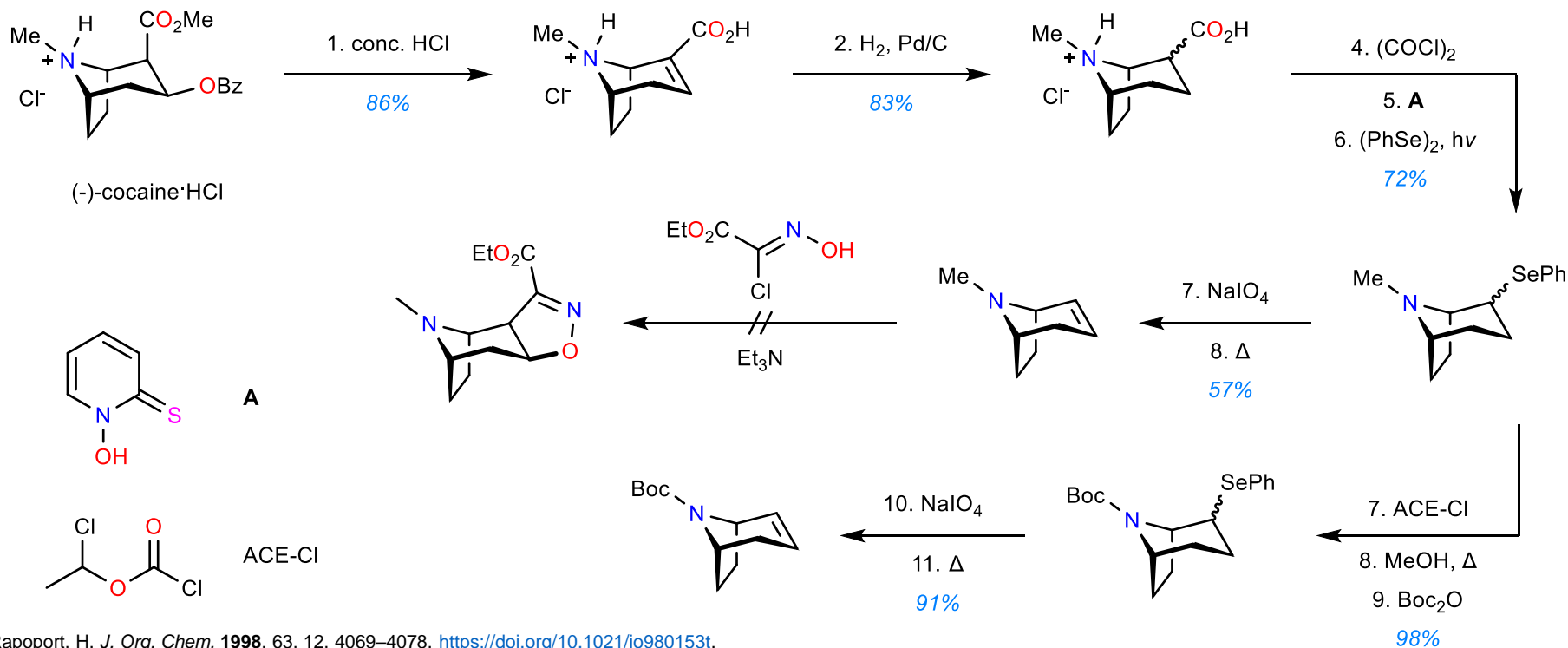
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O' Hagan, D. *Nat. Prod. Rep.* **2001**, 18, 494–502. <https://doi.org/10.1039/B001713M>

Degradation

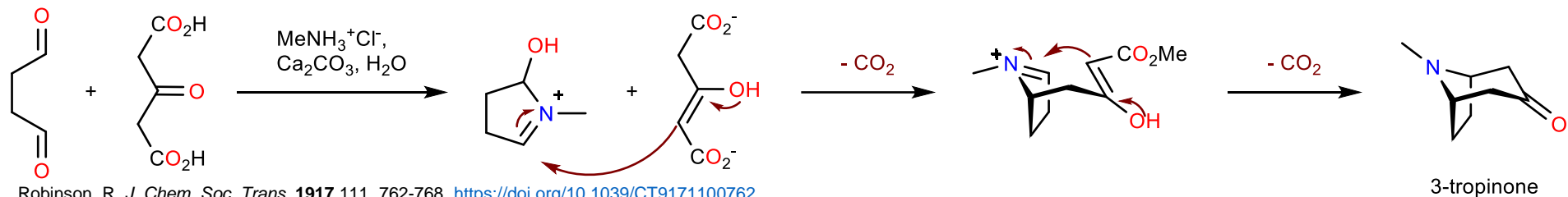


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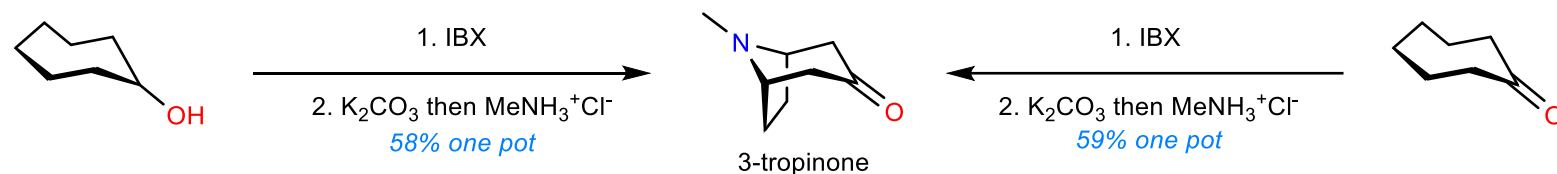


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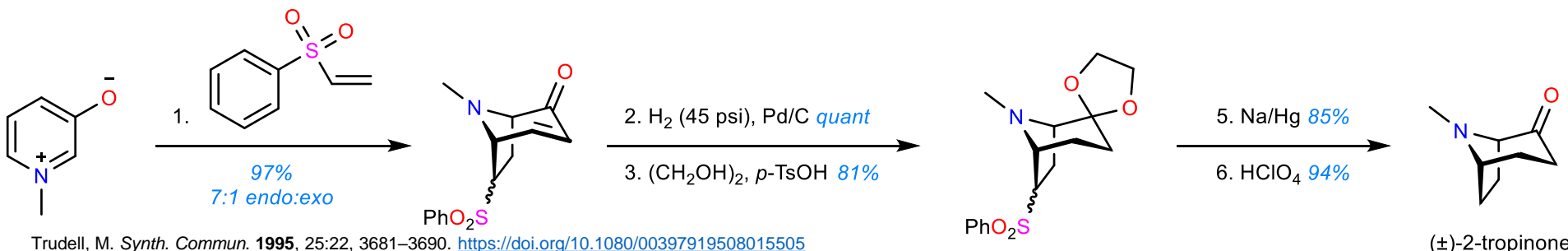
3-Tropinone and (+)-2-Tropinone



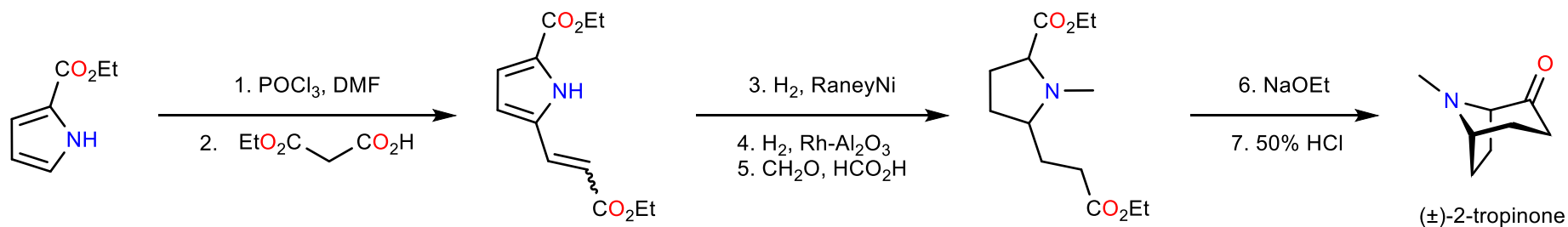
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Movassaghi, M. *Chem. Commun.* **2013**, 49, 10775-10777 <https://doi.org/10.1039/C3CC44461A>



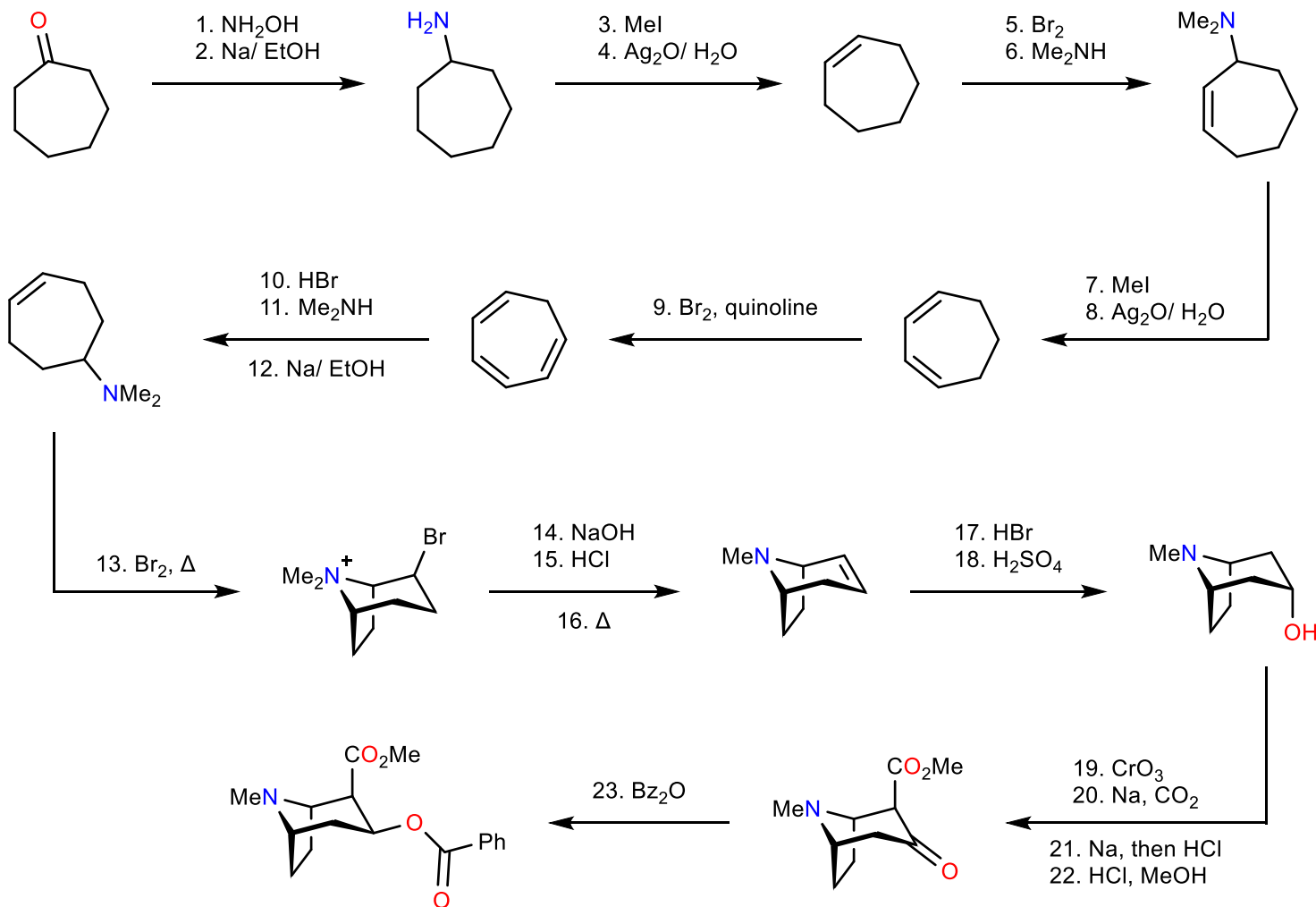
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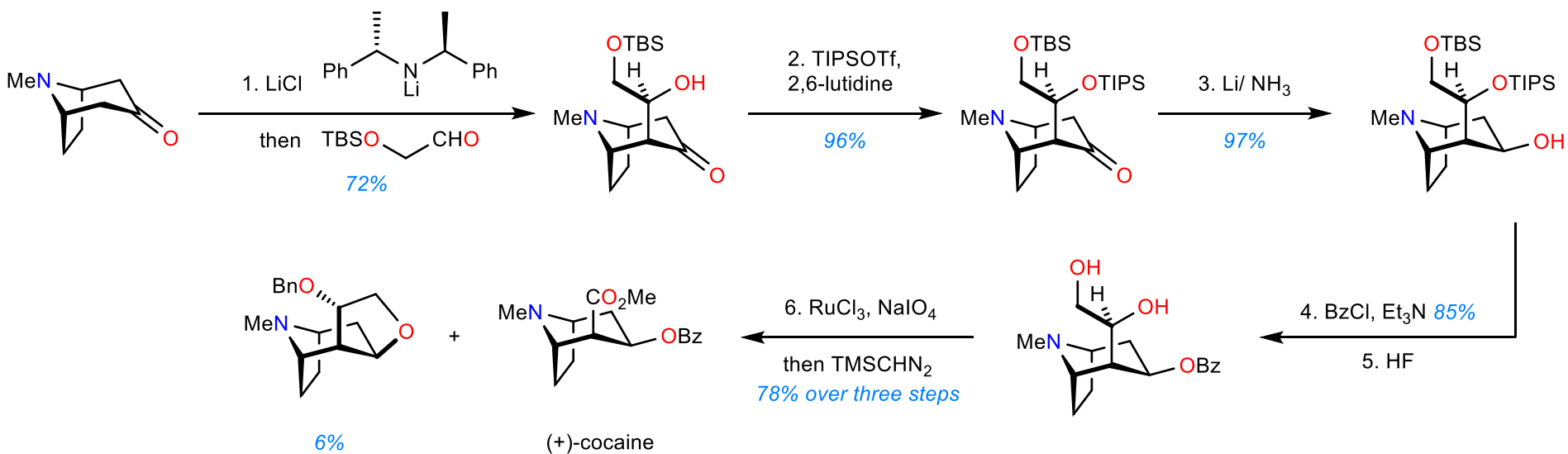


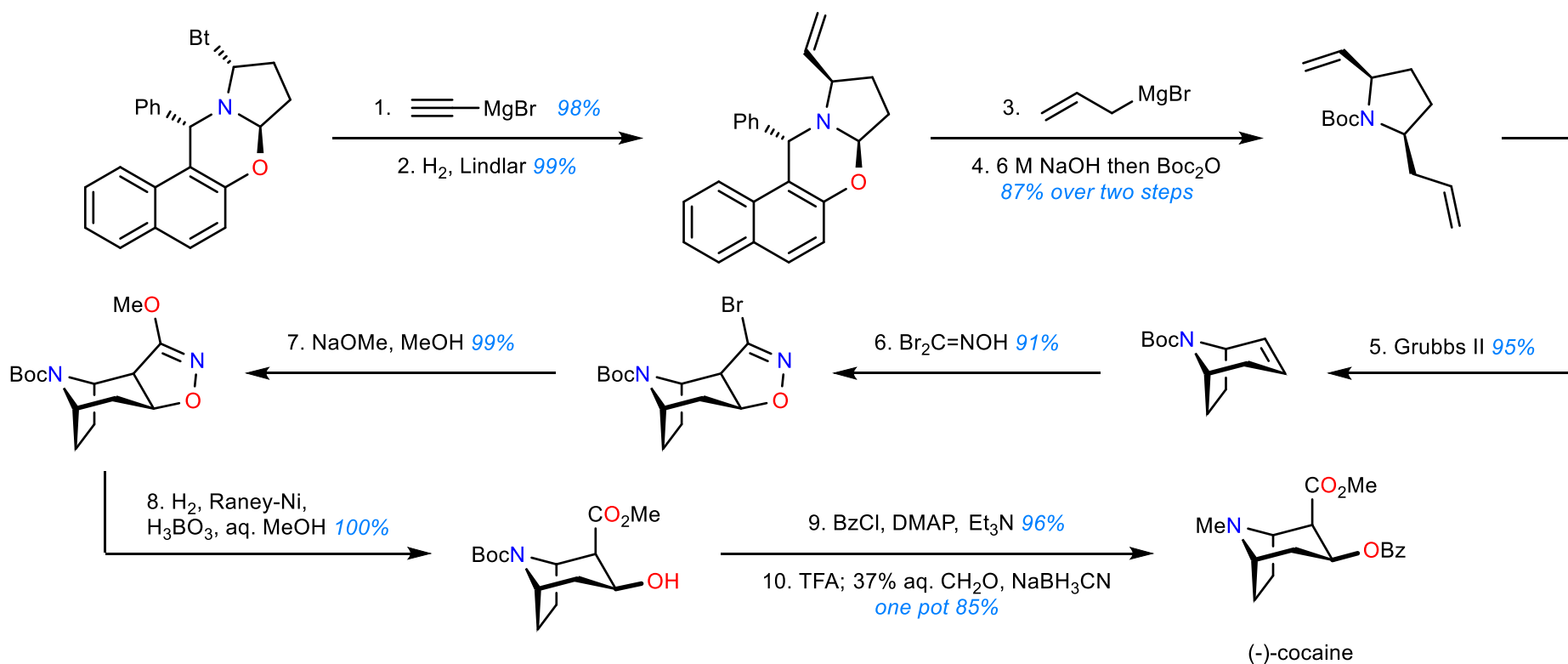
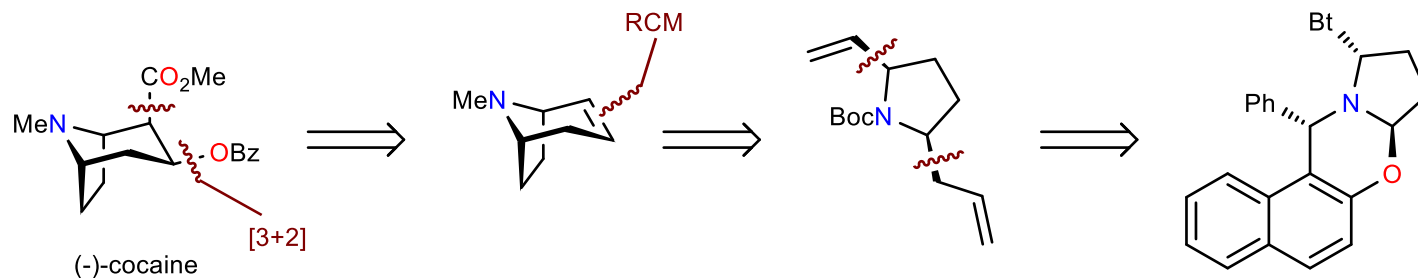
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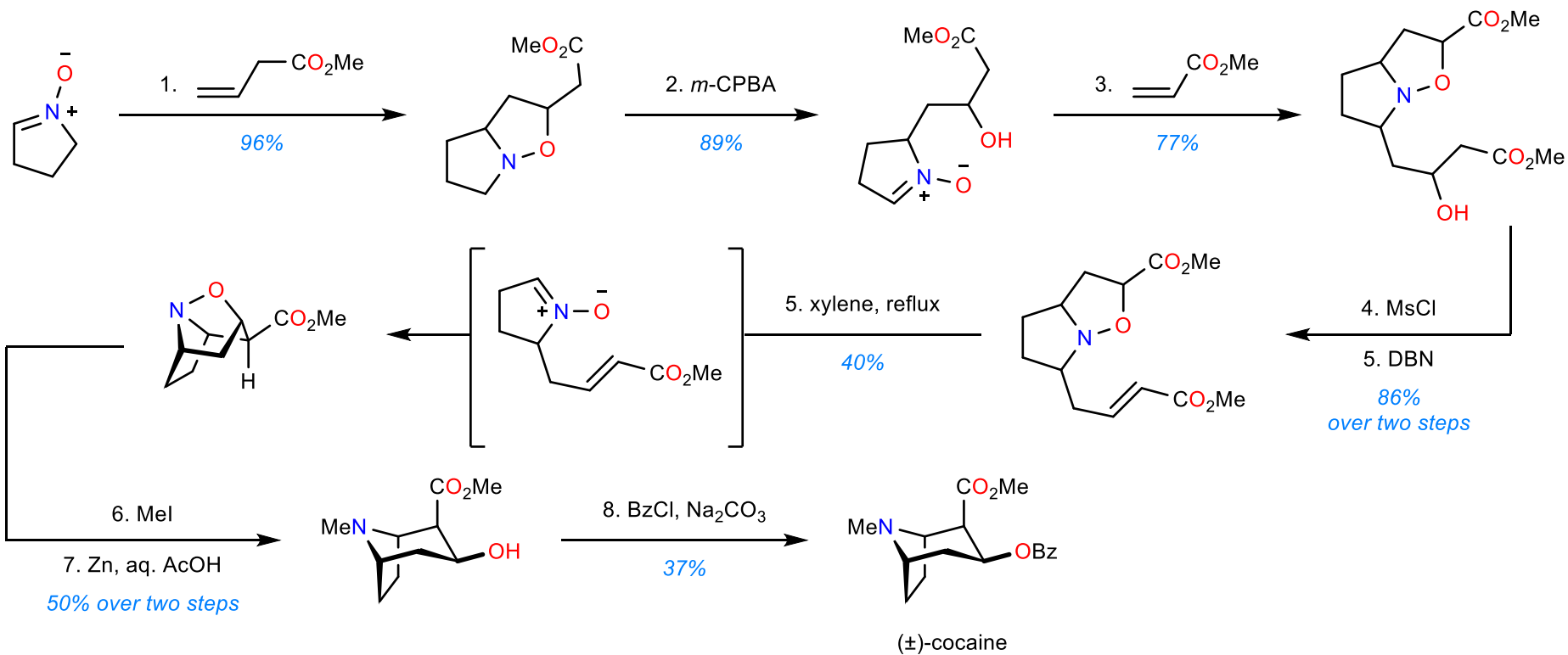
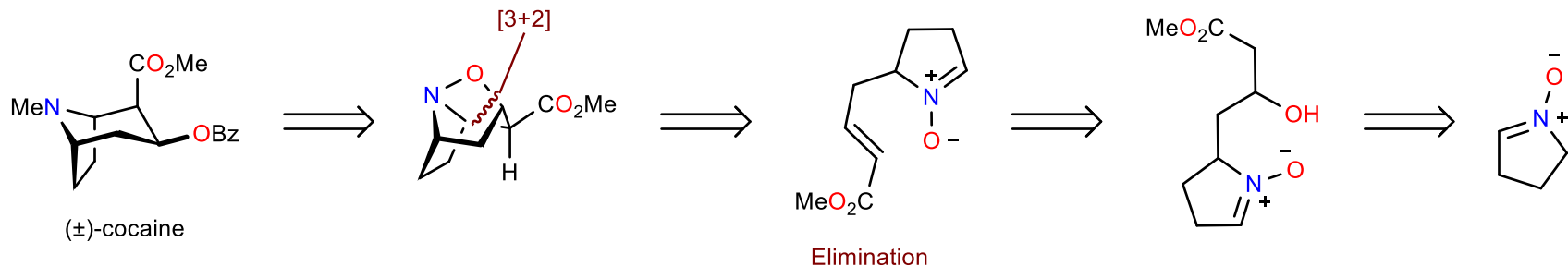


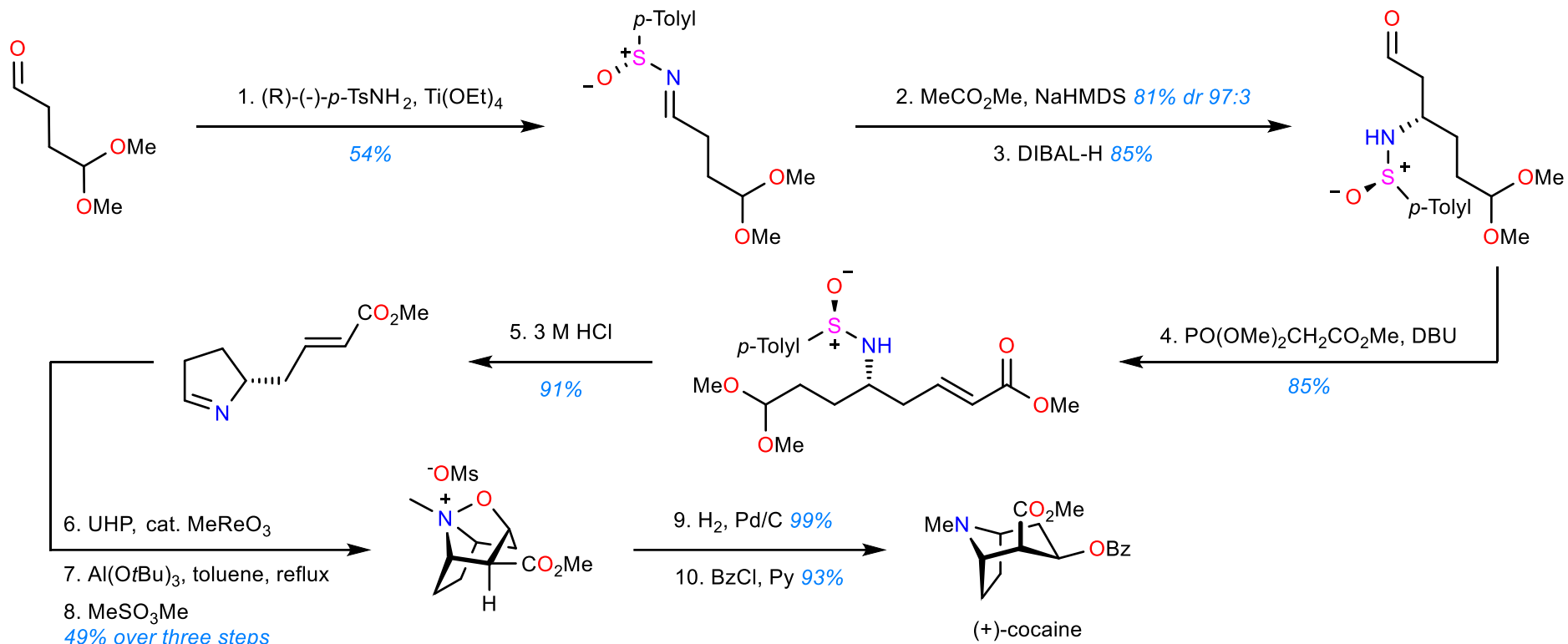
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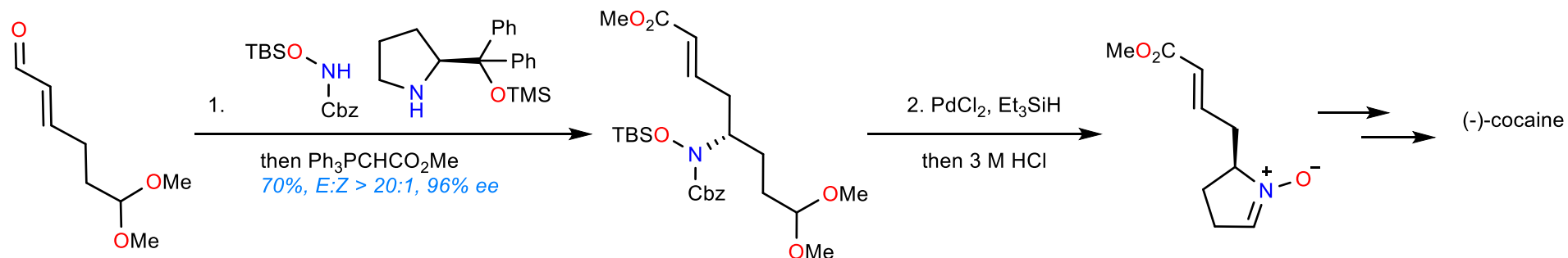




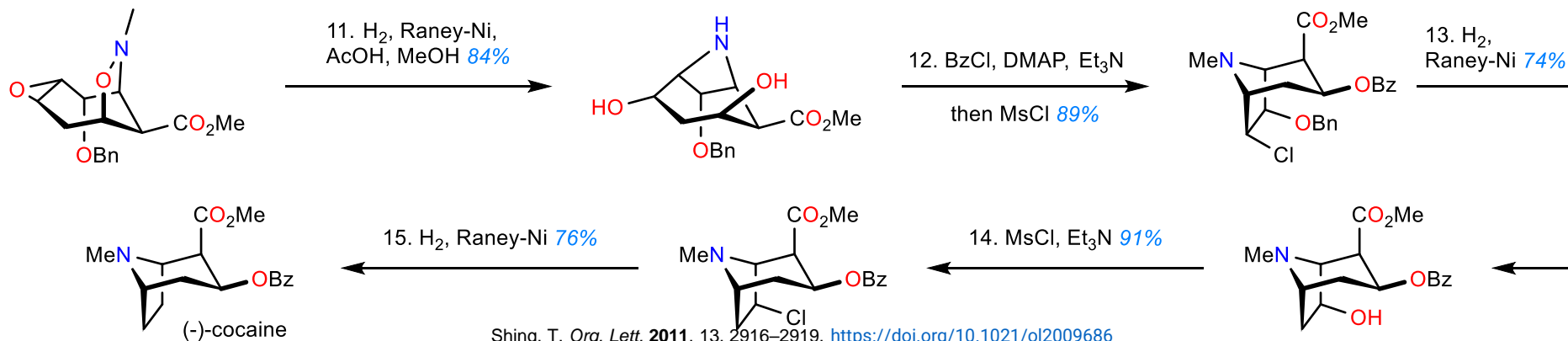
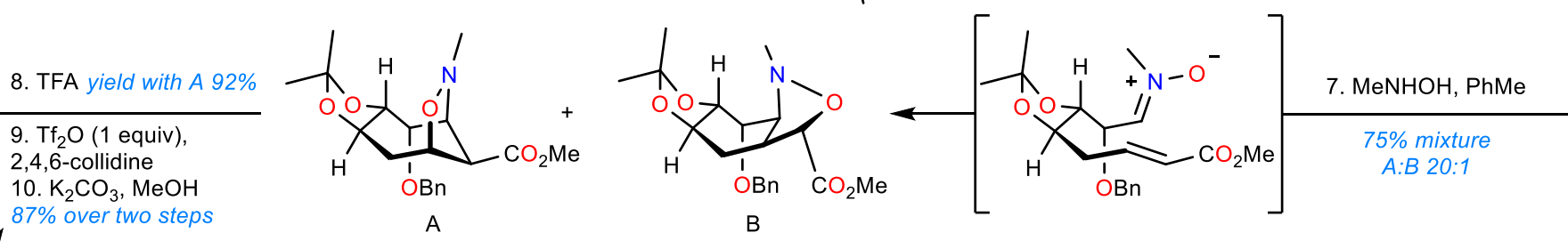
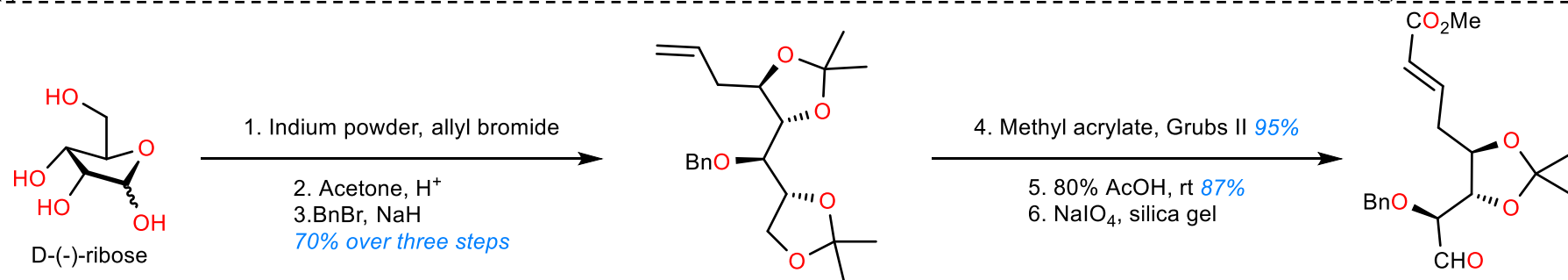
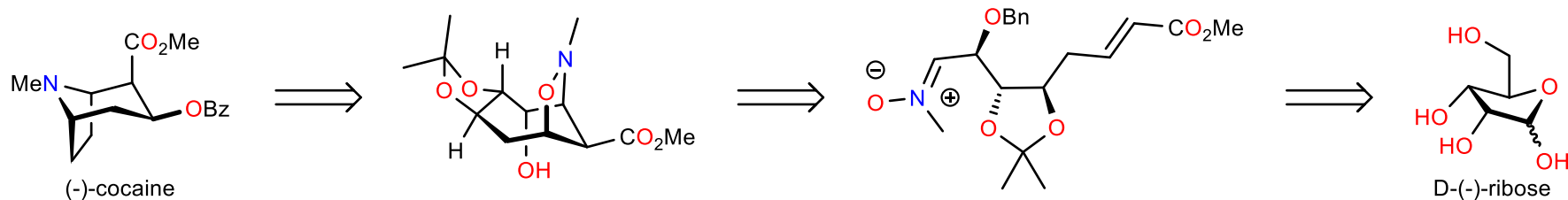




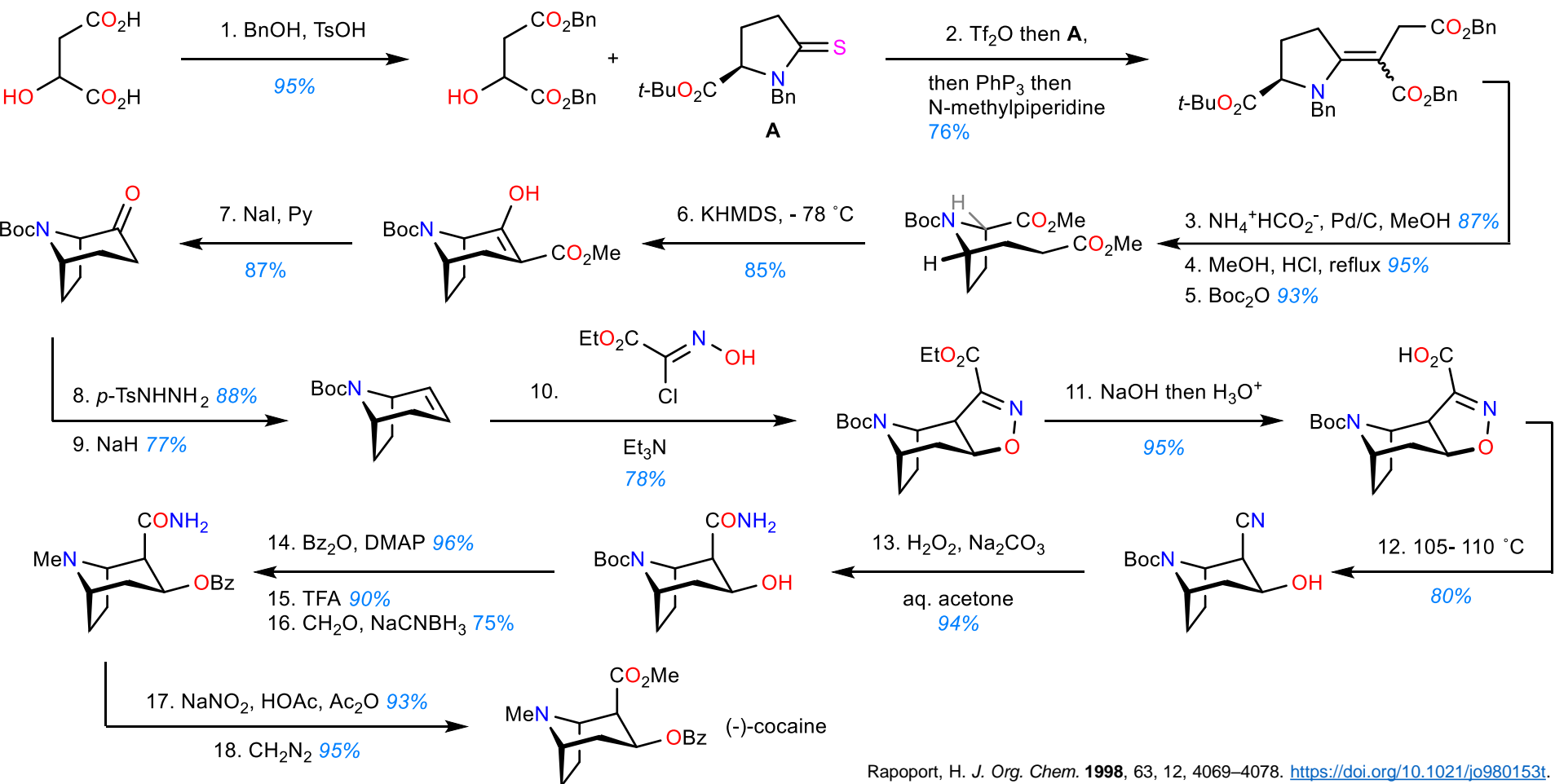
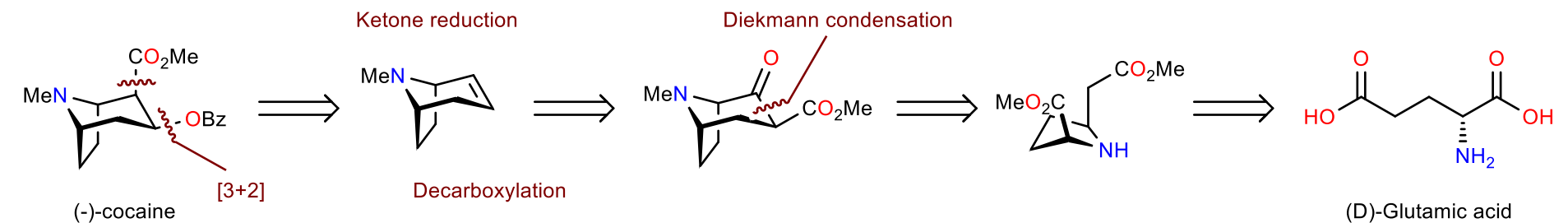
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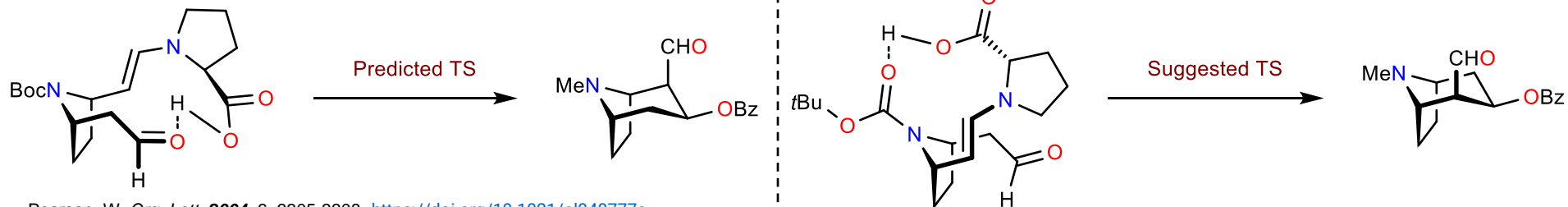
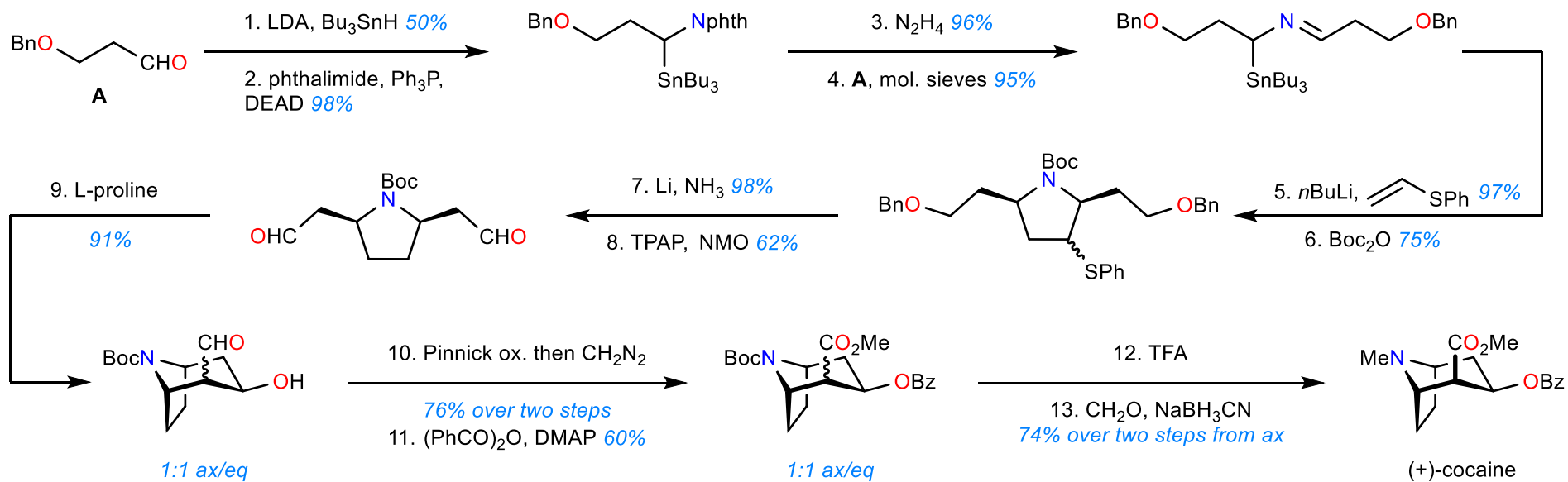
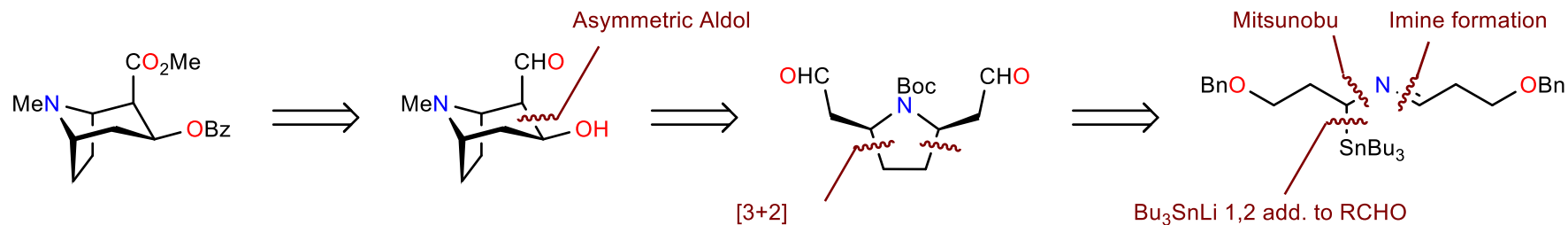
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