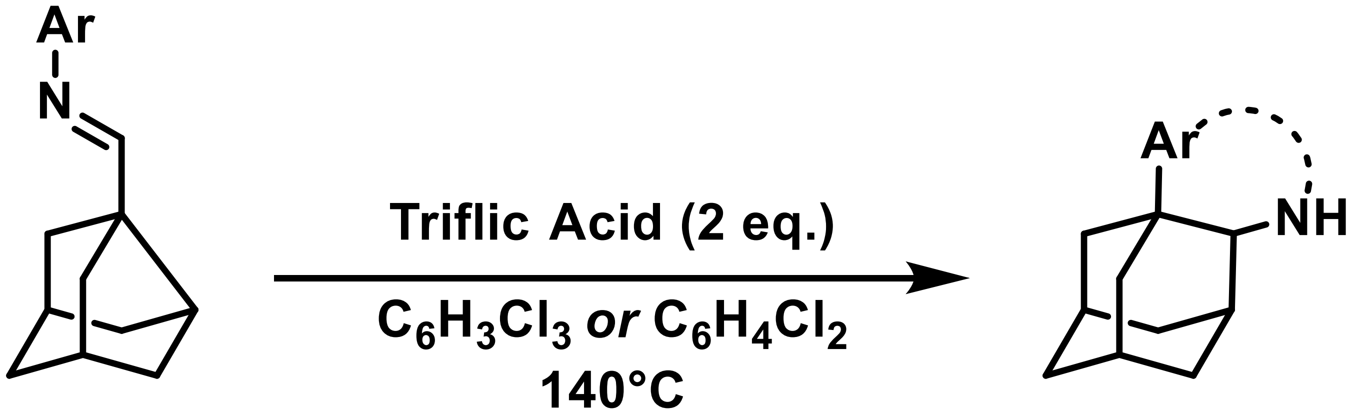
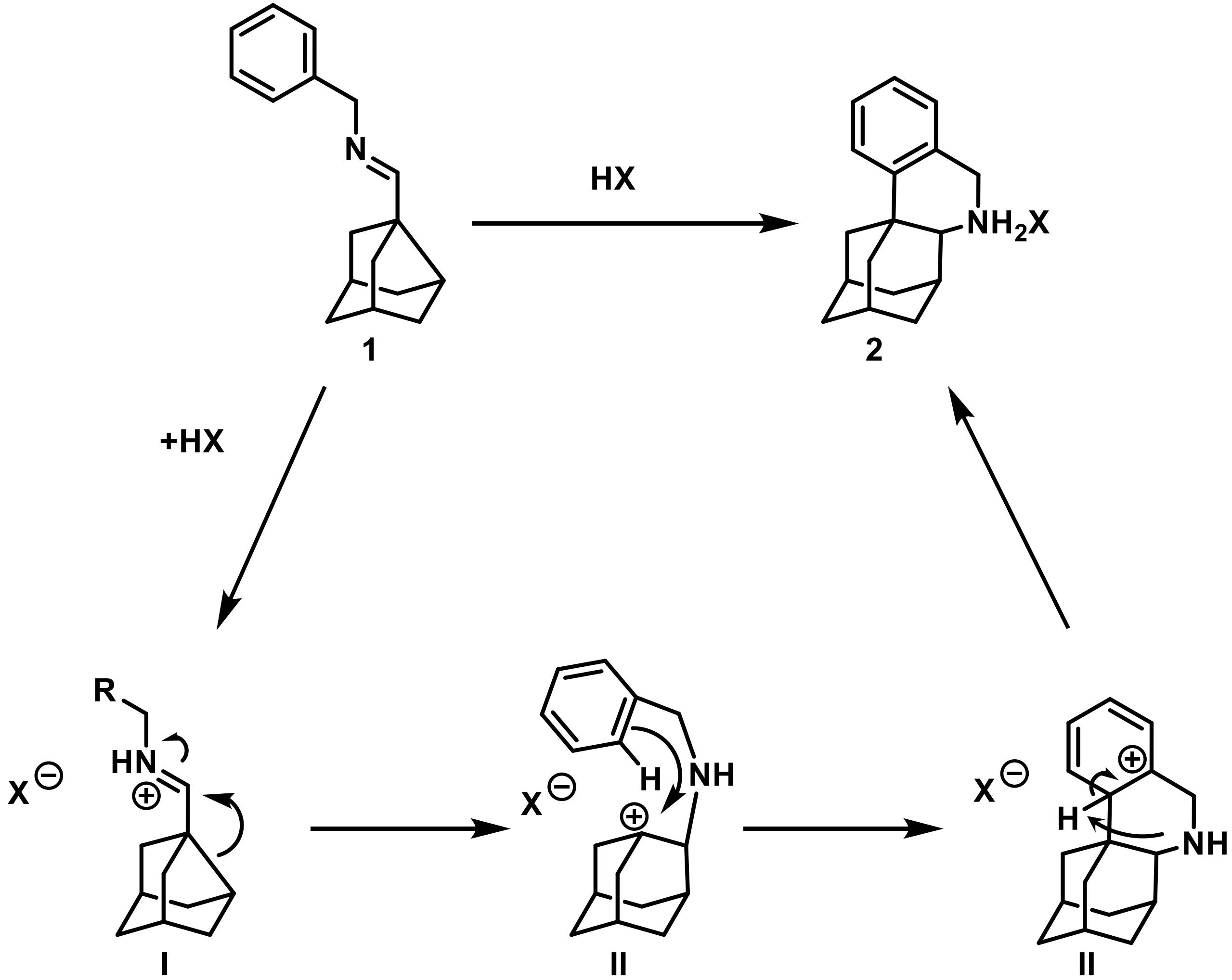
Brønsted acid induced rearrangement of noradamantane imines



4th PRS-Group seminar
20th of September 2019

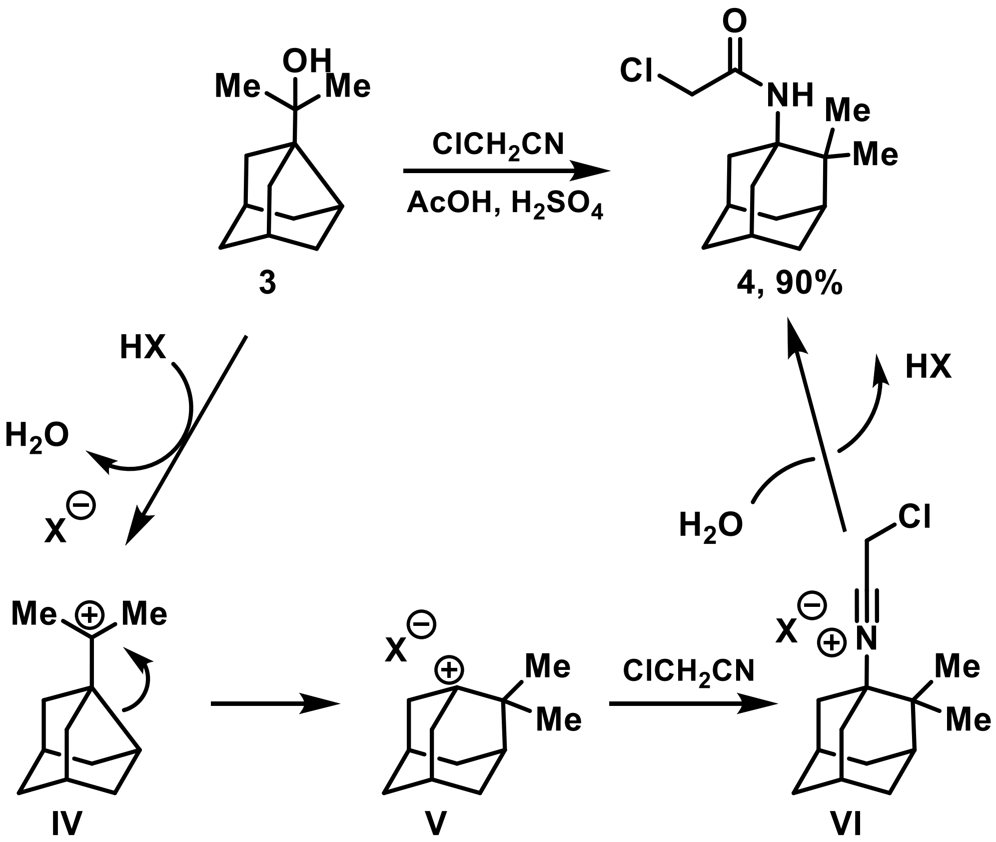
Benjamin Zonker

Recapitulation: Working hypothesis



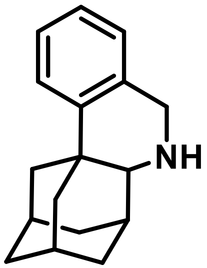
Meerwein, H.; *Liebigs. Ann. Chem*. **1914**, *405*, 129-175;
Torres, E.; Fernández, R.; Miquet, S.; Font-Bardia, M.; Vanderlinden, E.; Naesens, L.; Vázquez, S., *ACS Med. Chem. Let*. **2012**, *3*, 1065-1069

Recapitulation: Known rearrangement

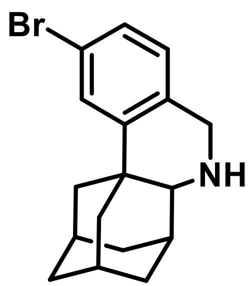


Torres, E.; Fernández, R.; Miquet, S.; Font-Bardia, M.; Vanderlinden, E.; Naesens, L.; Vázquez, S., *ACS Med. Chem. Let*. **2012**, *3*, 1065-1069.

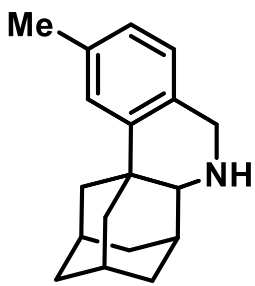
Results: Updated scope



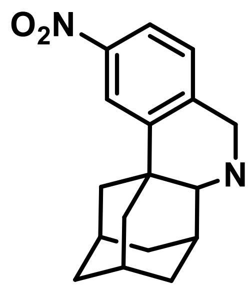
2a, 94%



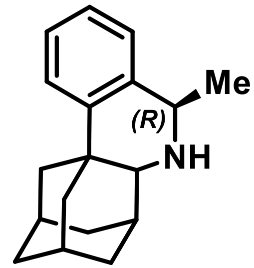
2b, 93%



2b, 88%

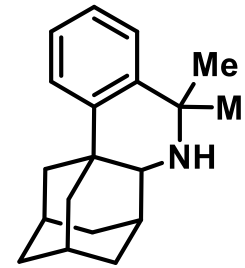


2d, 74%

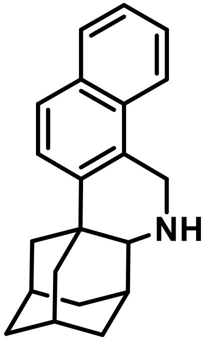


2e, 83%,

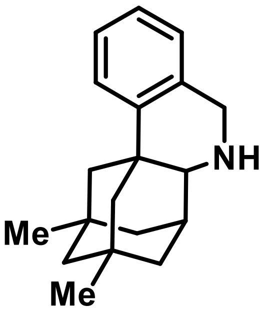
dr = 1:1



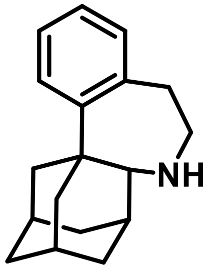
2f, 85%



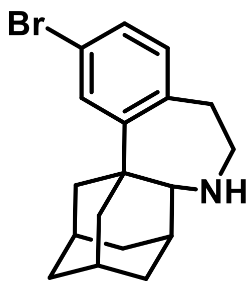
2g, 60%



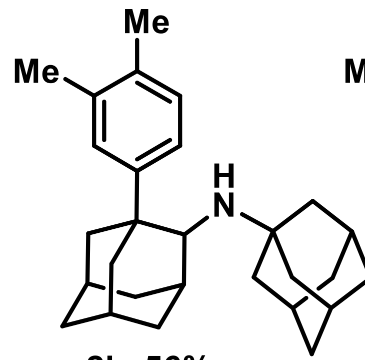
2h, 88%



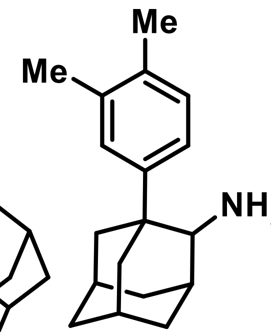
2i, 58%



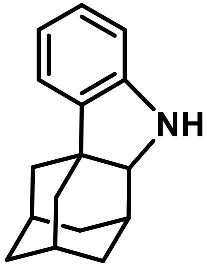
2j, 84%



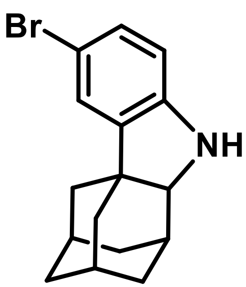
2k, 56%



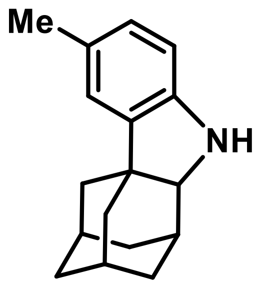
2l, 40%



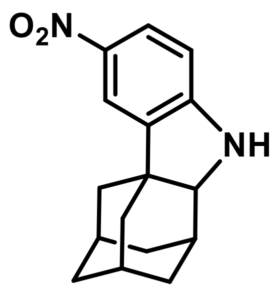
2m, 87%



2n, 73%



2o, 68%



2p, 15%

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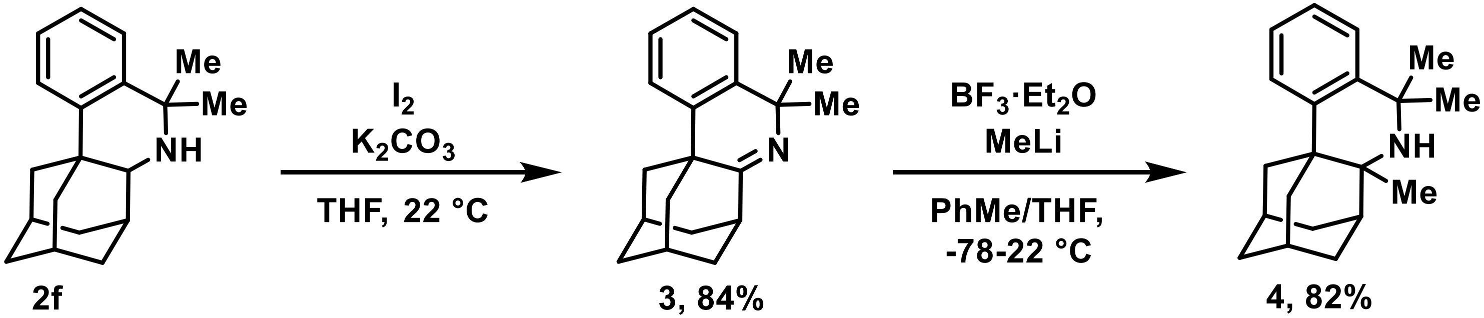
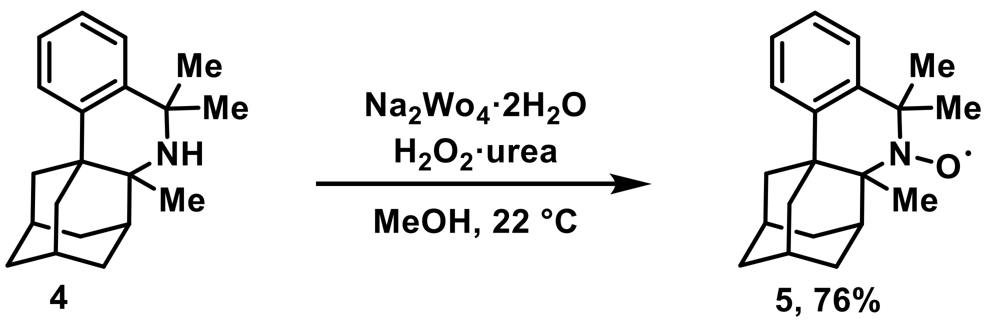
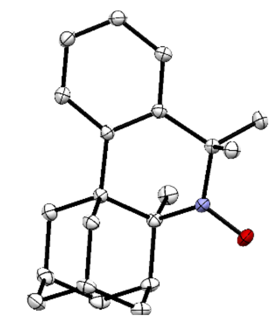
Postfunktionalization: Synthesis of nitroxide

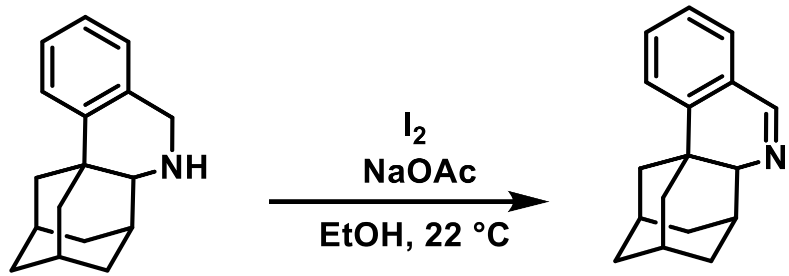




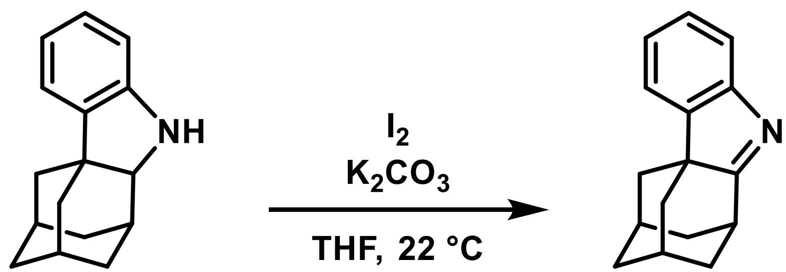


B. Zonker, E. Duman, H. Hausmann, J. Becker, R. Hrdina, *manuscript in preparation*, **2019.**

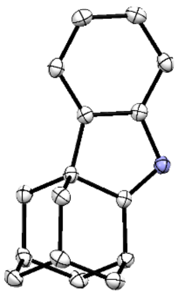
Postfunctionalization: Strained cyclic imines



2a **6, 62%**

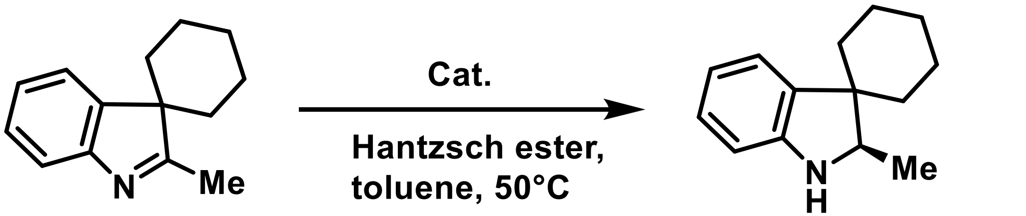


2m **7, 91%**

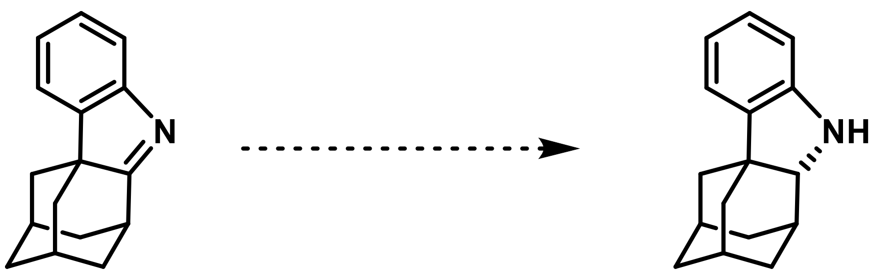


B. Zonker, E. Duman, H. Hausmann, J. Becker, R. Hrdina, *manuscript in preparation*, **2019.**

Postfunctionalization: Enantioselective reduction

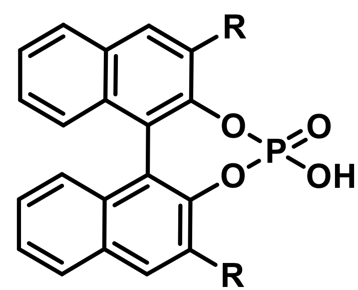


8 **(*R*)-9, 86%, 75% ee**



7 **(*R*)-2m**

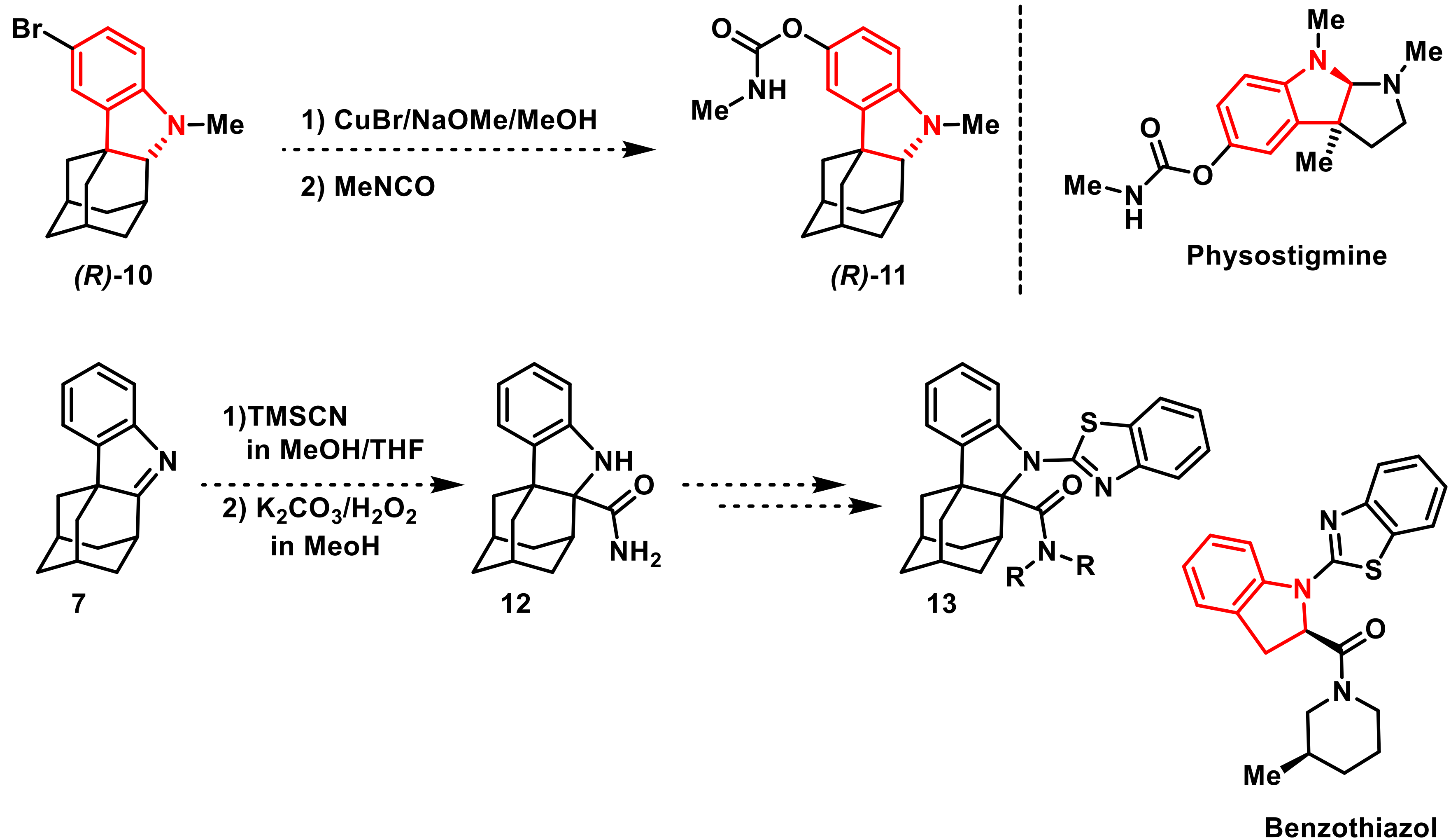
Cat.



R= 9-Anthracenyl

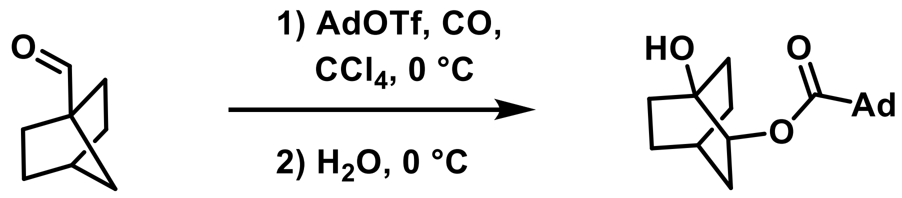
M. Rueping, C. Brinkmann, A. P. Antonchick, I. Atodiresei, *Org. Lett.* **2010**, *12*, 4604-4607.

Postfunctionalization: Indoline derivatives



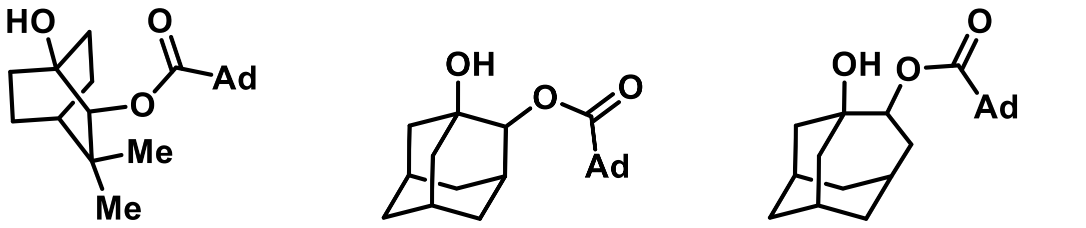
M. Mao, M. G. Ren, Q. H. Song, *Chem. Eur. J.* **2012**, *18*, 15512-15522;
Y. Wei, D. Zhao, D. Ma, *Angew. Chem.* **2013**, *125*, 13226-13229.

New substrates: Similar cage expansion



14

15, 64%



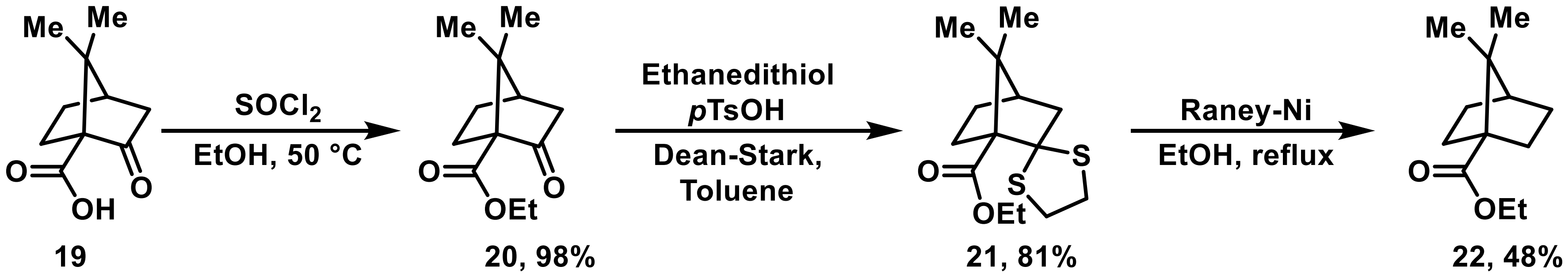
16, 89%

17, 43%

18, 94%

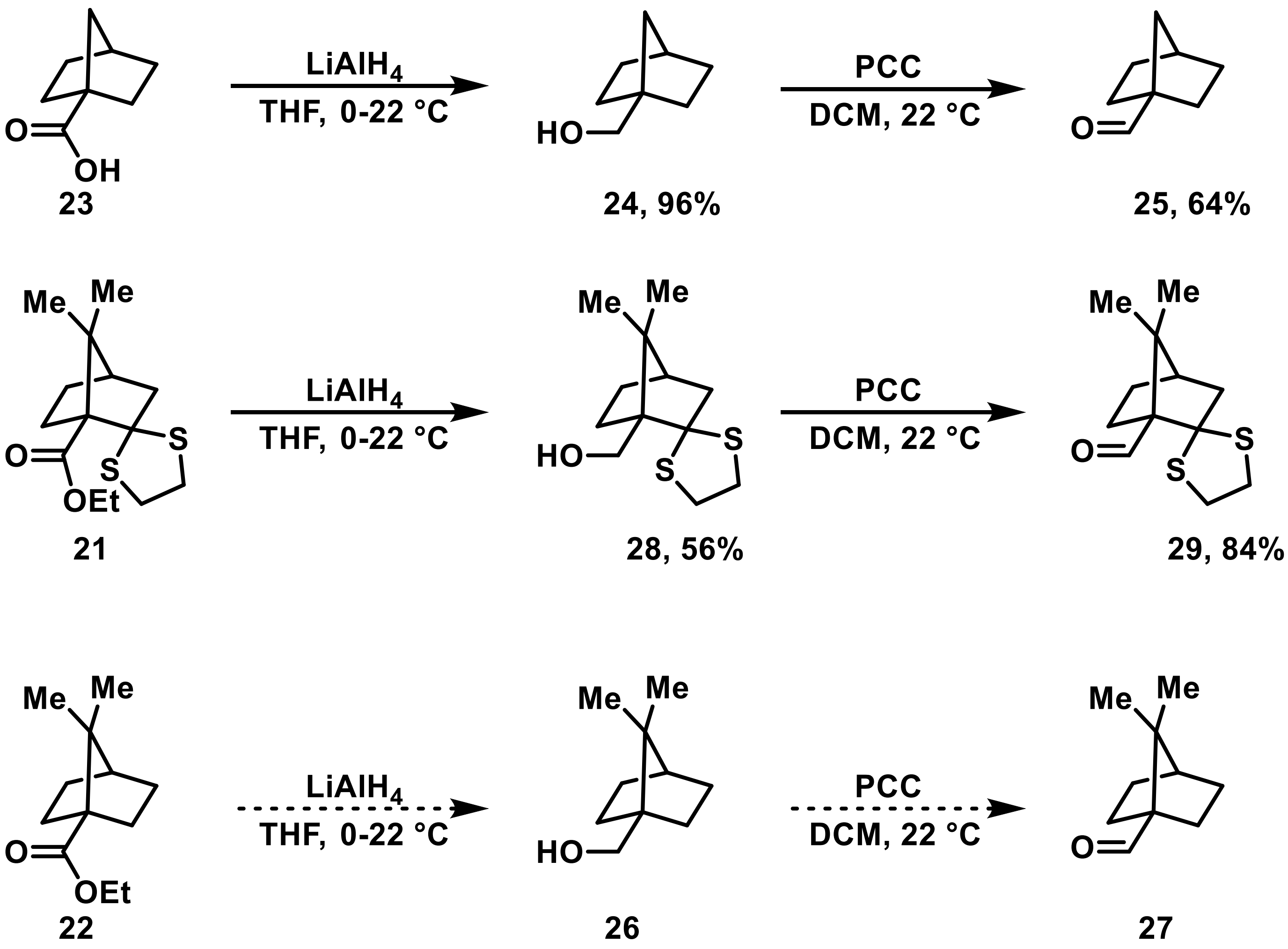
Takeuchi, K. i.; Kitagawa, I.; Akiyama, F.; Shibata, T.; Kato, M.; Okamoto, K., *Synthesis* **1987,** *07*, 612-615.

New substrates: Old synthesis – new purpose

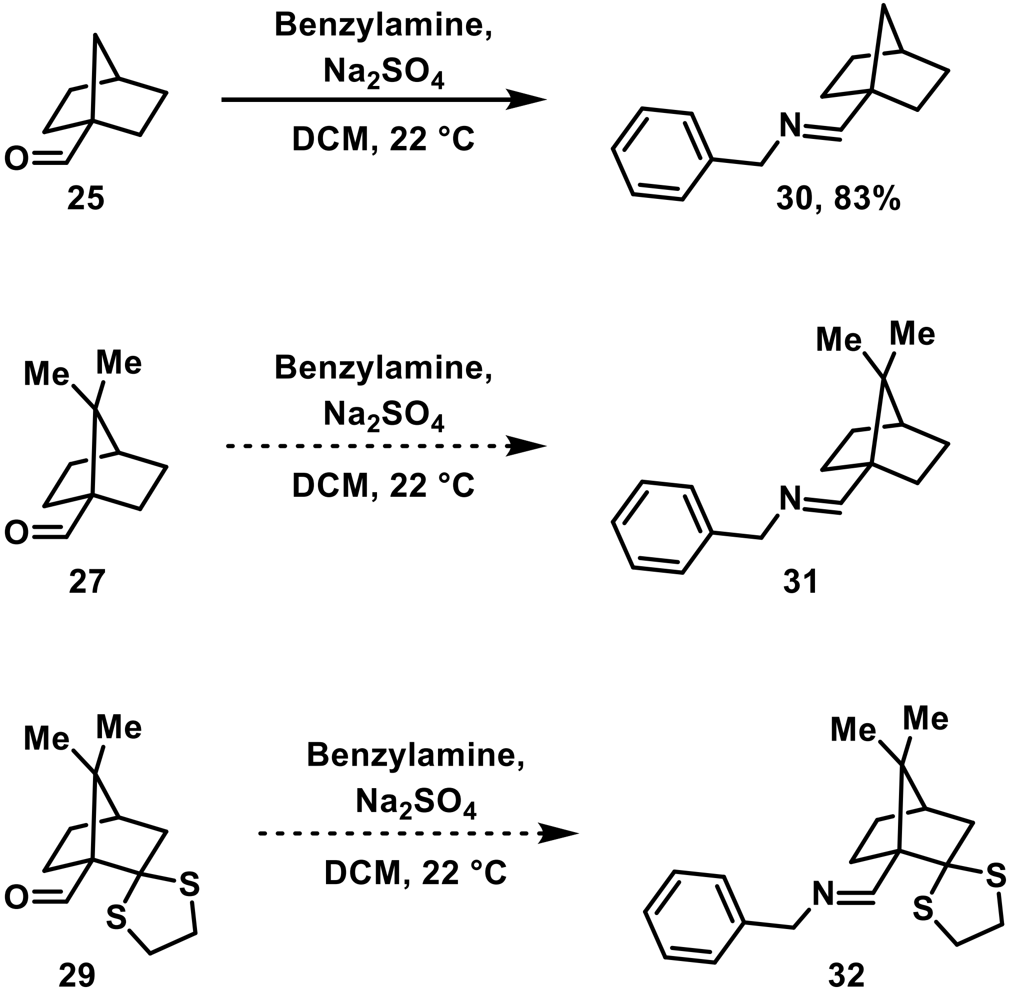


B. Zonker, *PRS-group anniversary conference*, Hornberg, August **2018**.

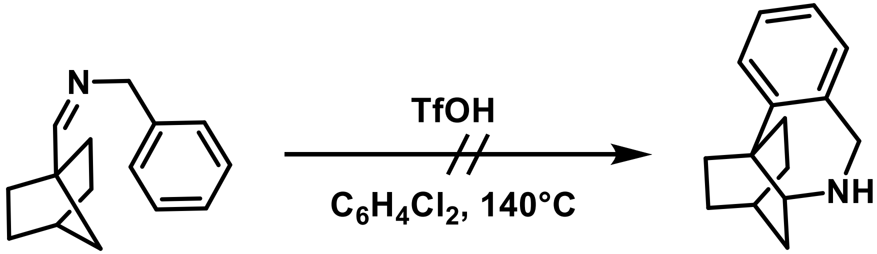
New substrates: Precursor synthesis



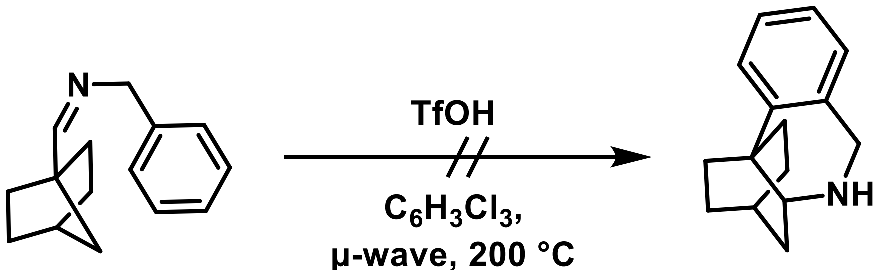
New substrates: Precursor synthesis



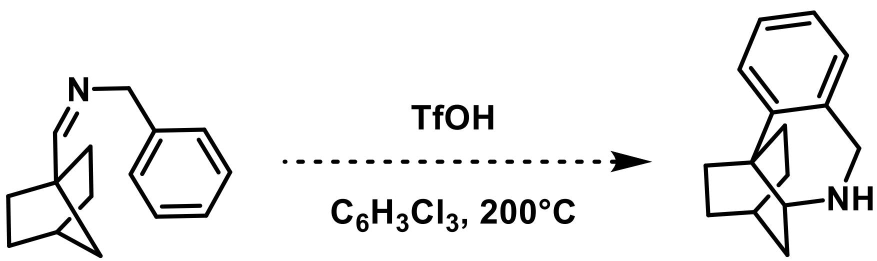
New substrates: Rearrangement reactions



30 33

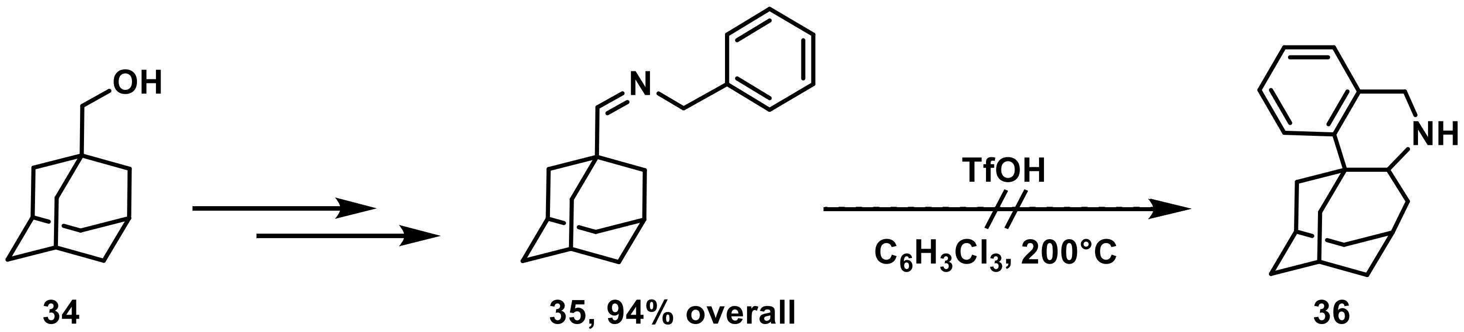


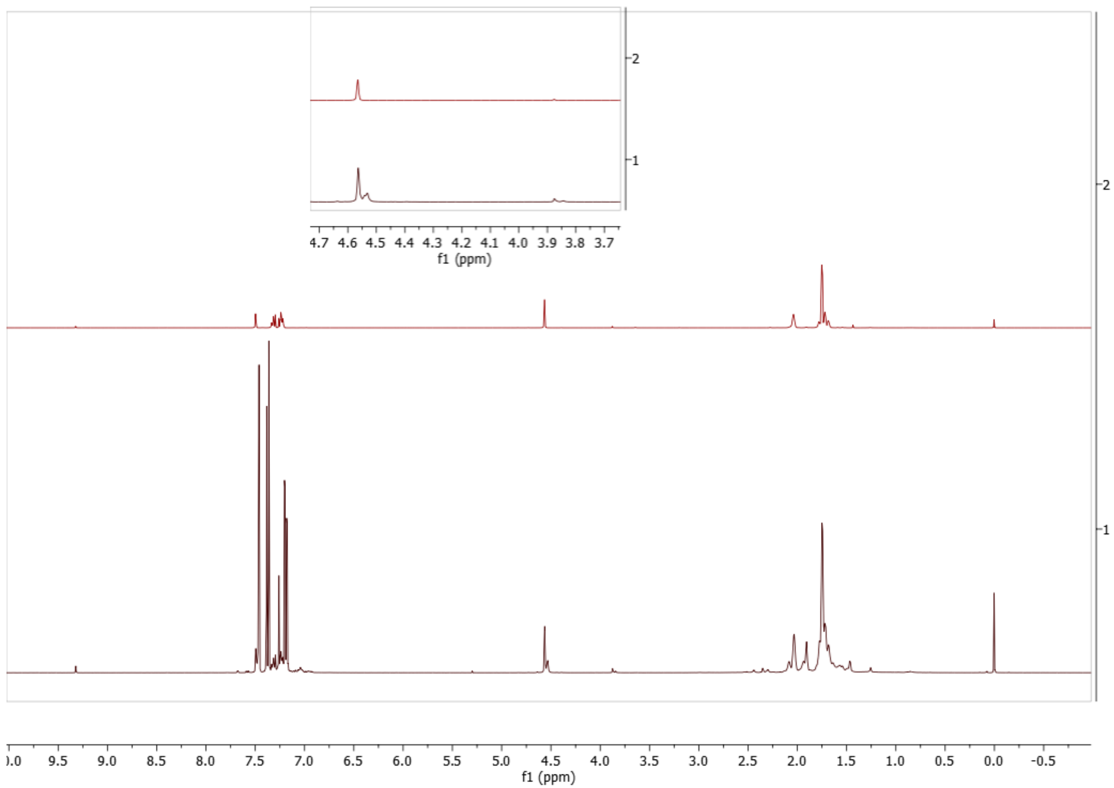
30 33



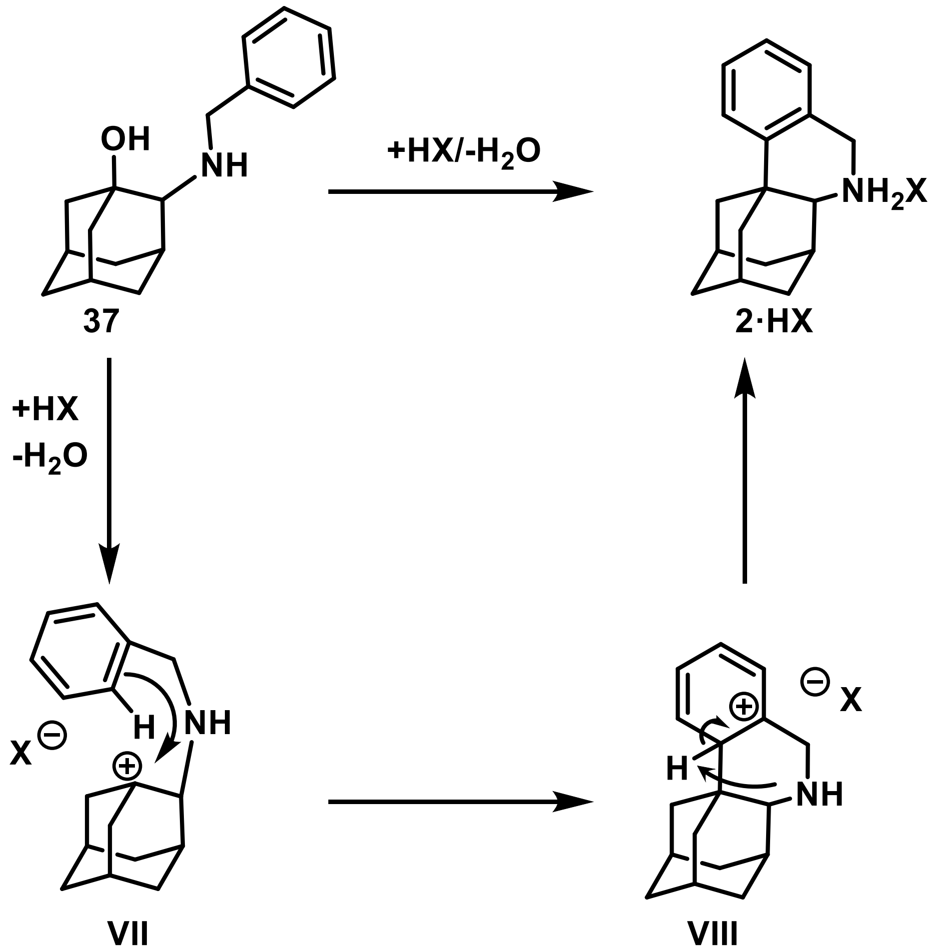
30 33

New substrates: Next try





Mechanistic inquiries: Friedel-Crafts barrier



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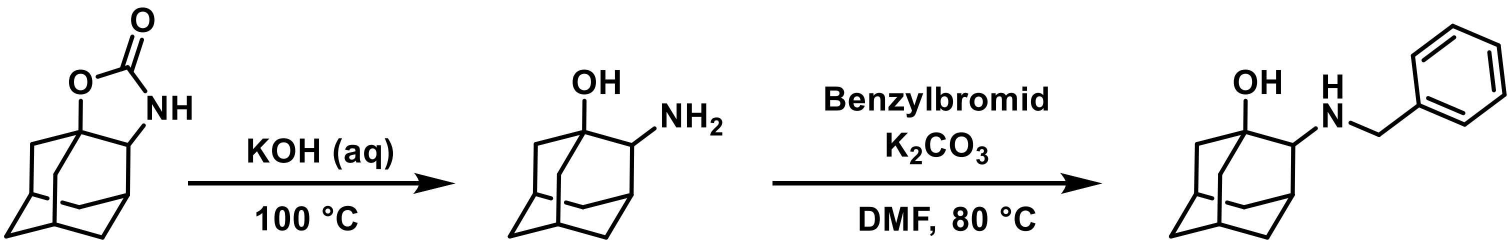
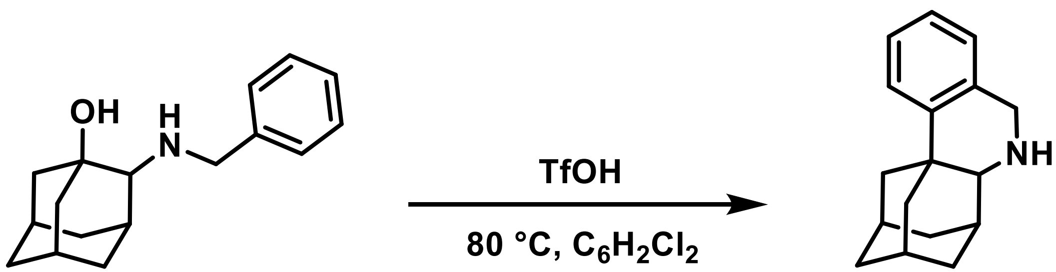
Mechanistic inquiries: Friedel-Crafts barrier



38 — 39, 98% — 40, 51%



40 — 2a
66% after 17h

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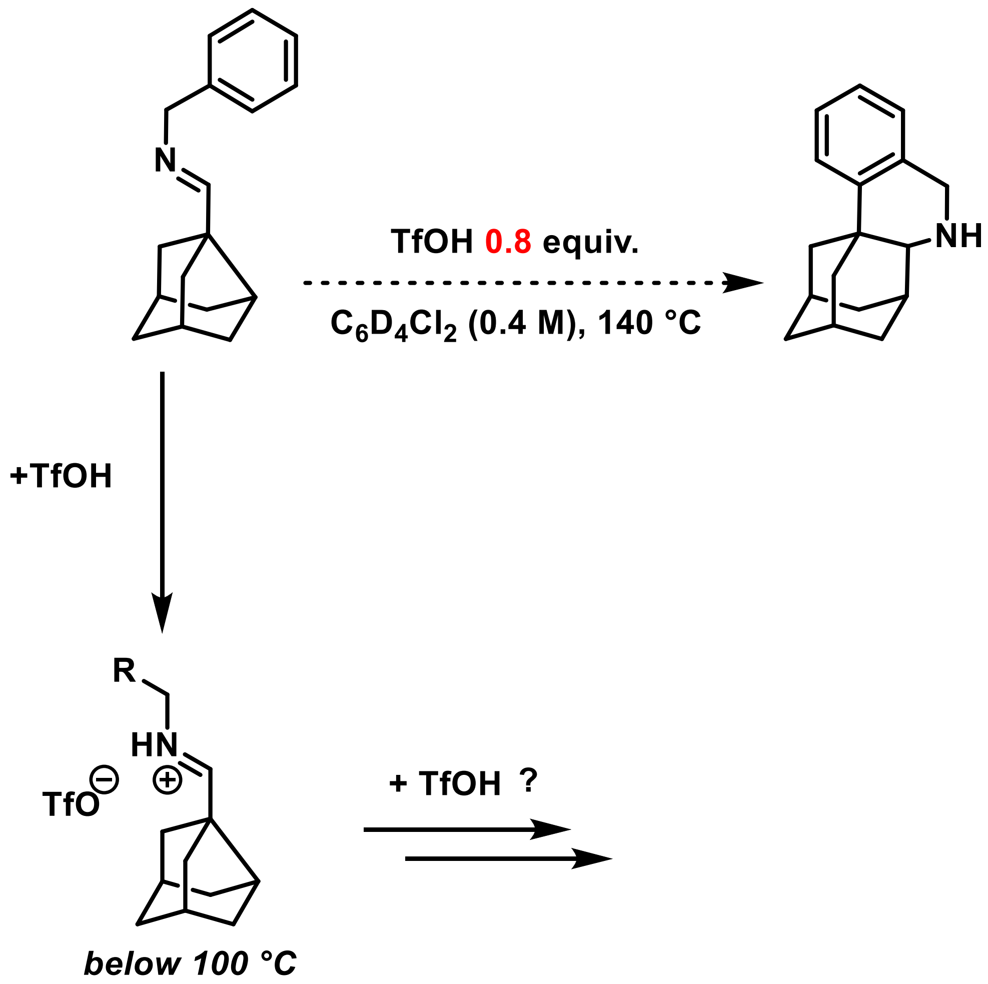
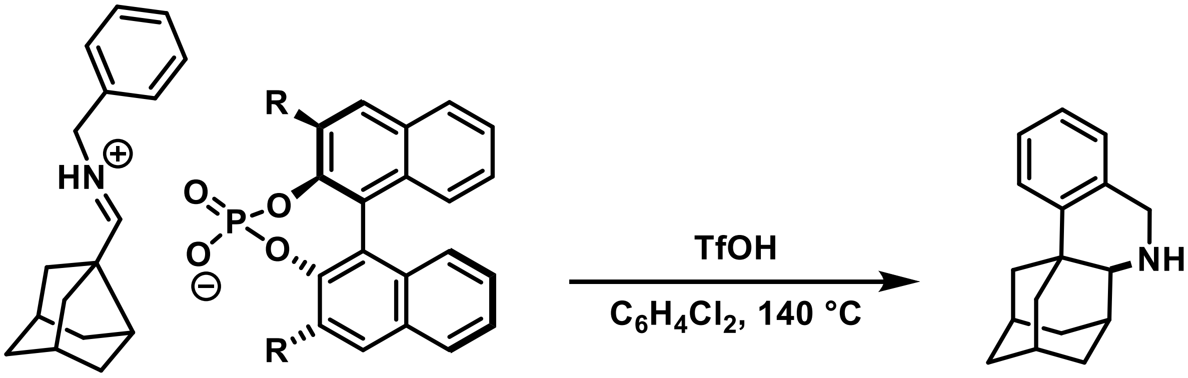
Mechanistic inquiries: Substoichiometric TfOH



Follow-up & Outlook



writing, writing, and more writing…

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Acknowledgement

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Ediz Duman

PRS-Group

Analytical department

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