UNIVERSITÄT BERN

Total Synthesis of (−)-Haouamine B Pentaacetate and Structural Revision of Haouamine B

Yuichi Momoi,Kei-ichiro Okuyama, Hiroki Toya, Kenji Sugimoto, Kentaro Okano, Hidetoshi Tokuyama*, *Angew. Chem. Int. Ed.* **2014 Early View**
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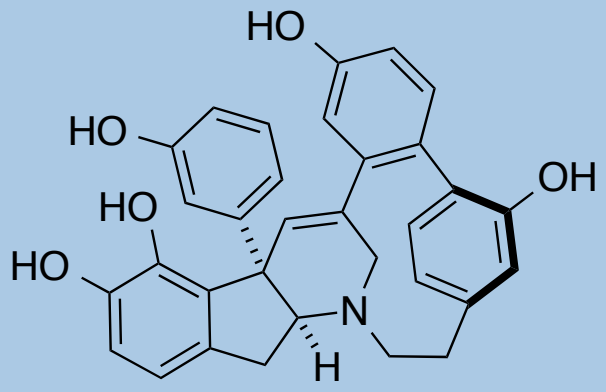
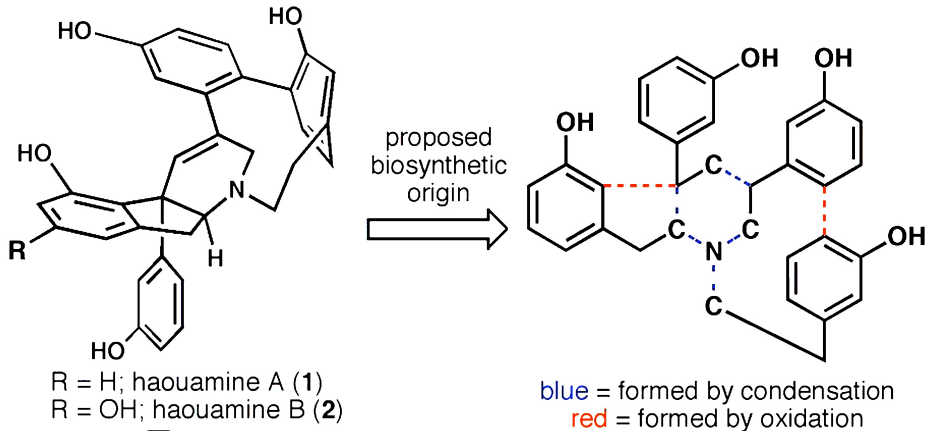


Nicolas Volkoff
16/10/2014

Introduction

- Extracted from a Tunicate *Aplidium haouarianum*
- Anticancer activity against colon carcinoma cells
- Position of the 2nd „OH“ in Haouamine B was uncertain

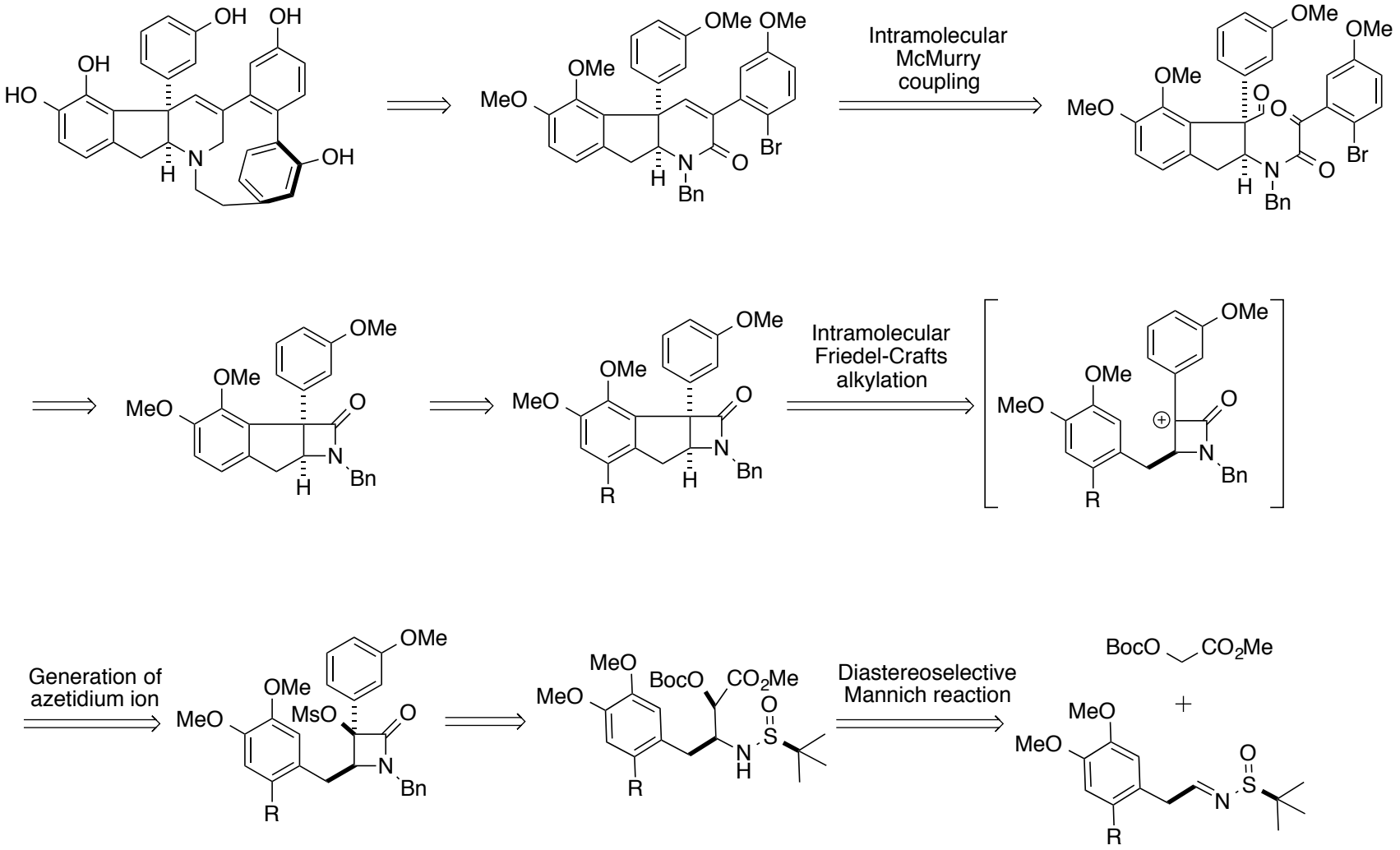


R = H; haouamine A (**1**)
R = OH; haouamine B (**2**)

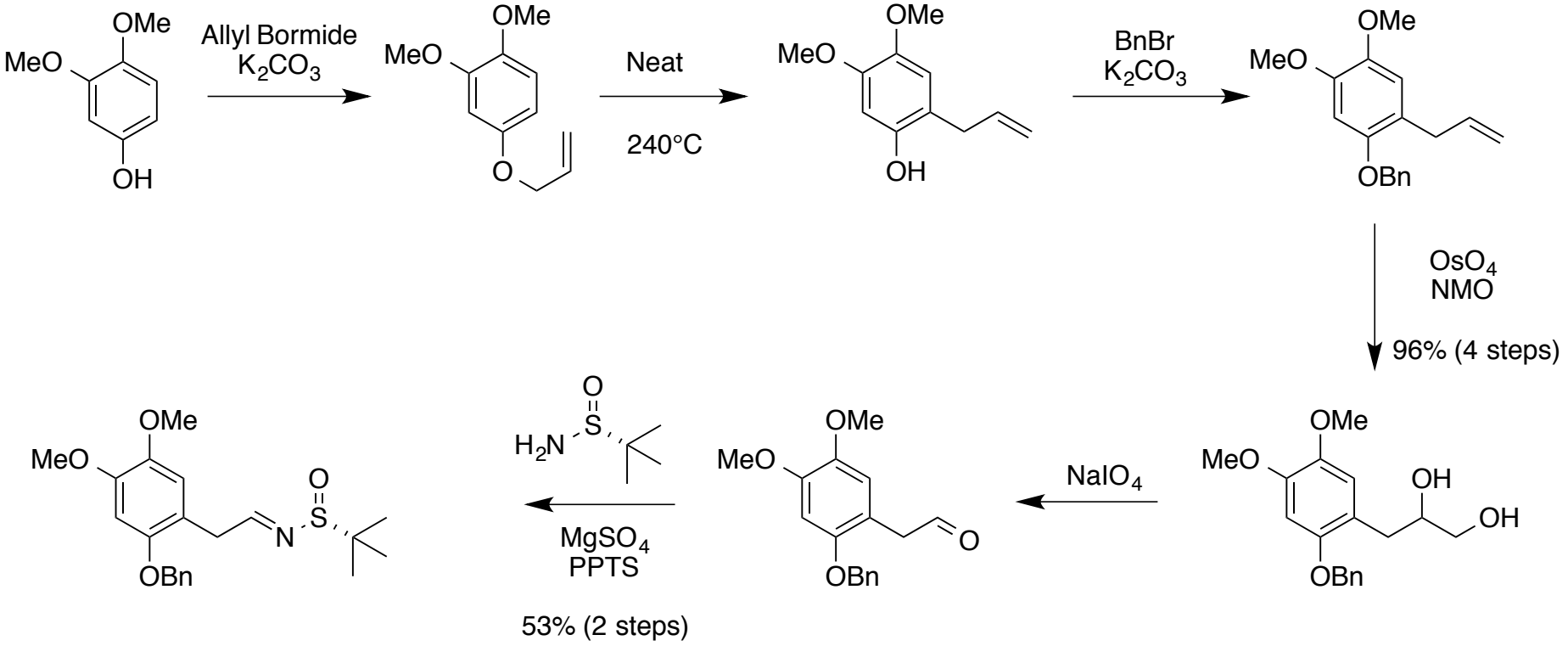
blue = formed by condensation
red = formed by oxidation

P. S. Baran, N. Z. Burns, *J. Am. Chem. Soc.* **2006**, 128, 3908

Retrosynthetic Approach



Preparation of the sulfinimine



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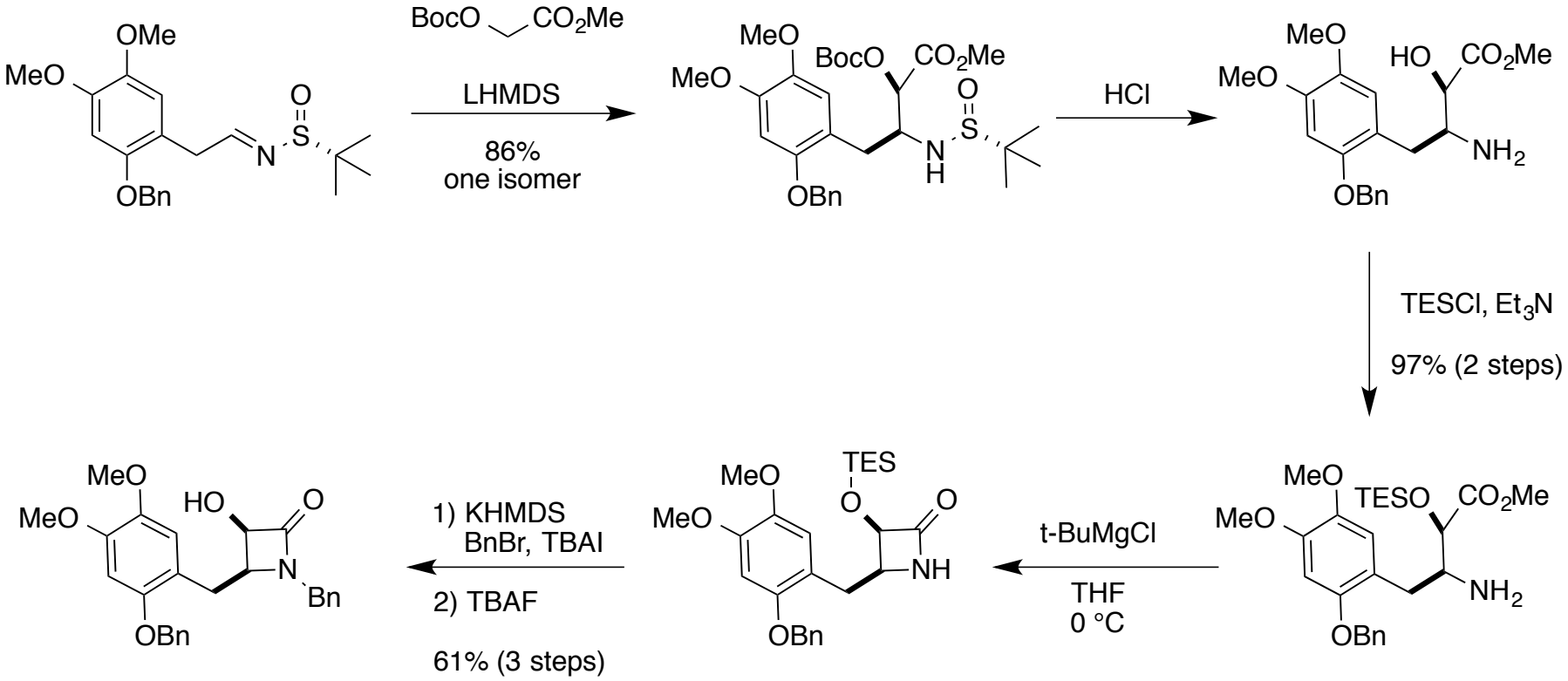
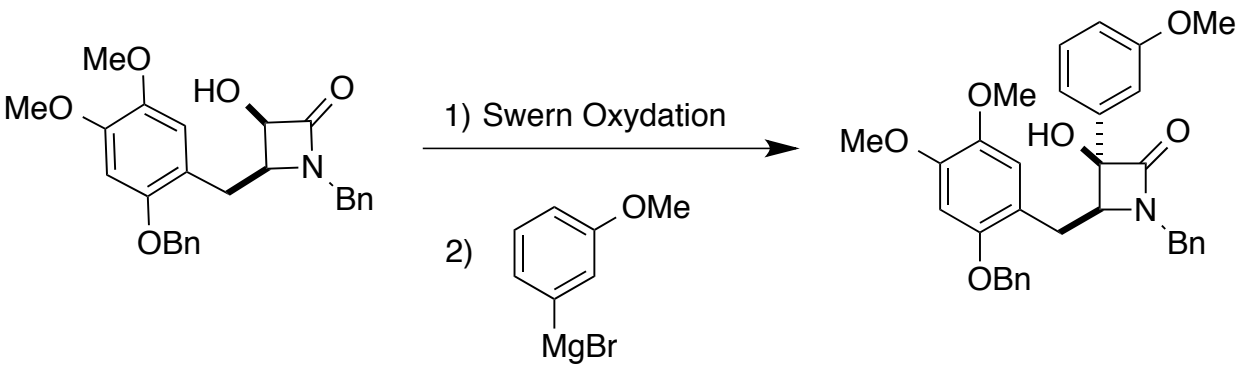
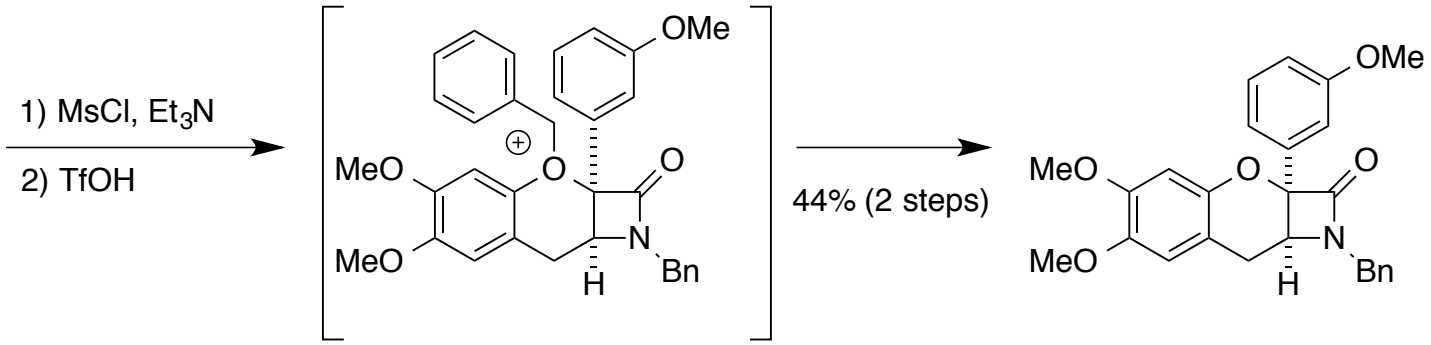
Formation of the β-Lactame



Friedel-Crafts Alkylation

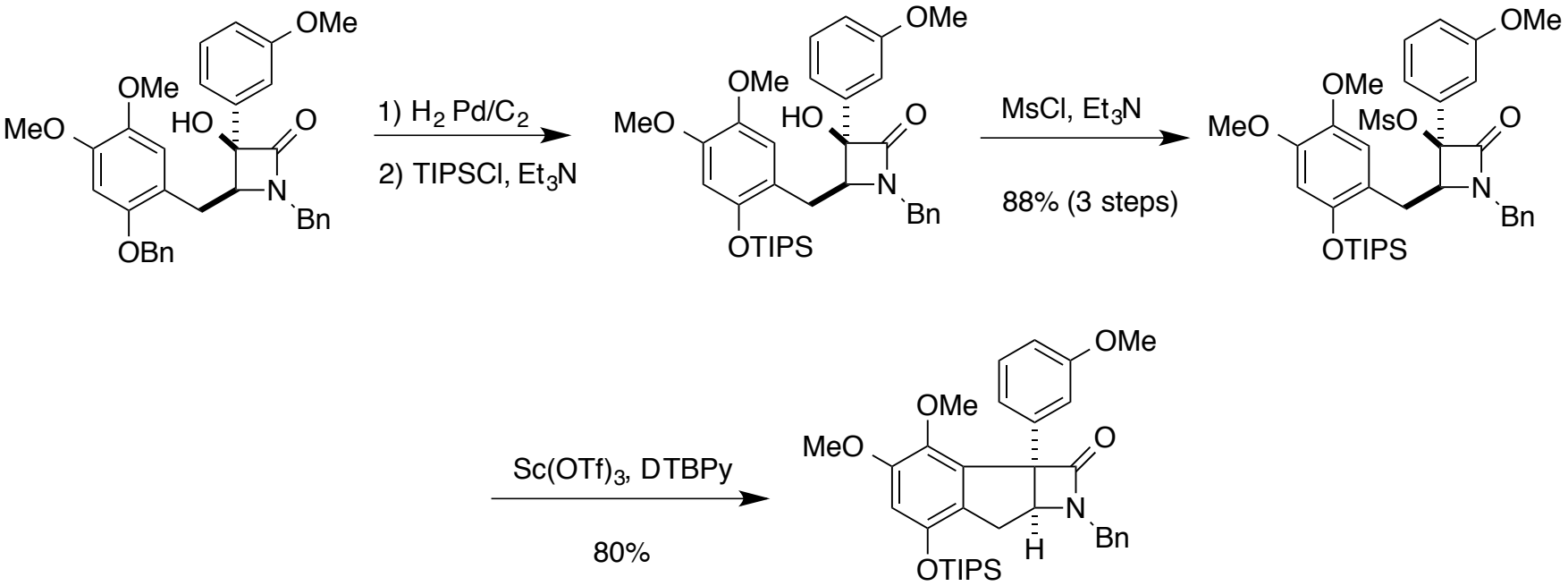


76% (2 steps)

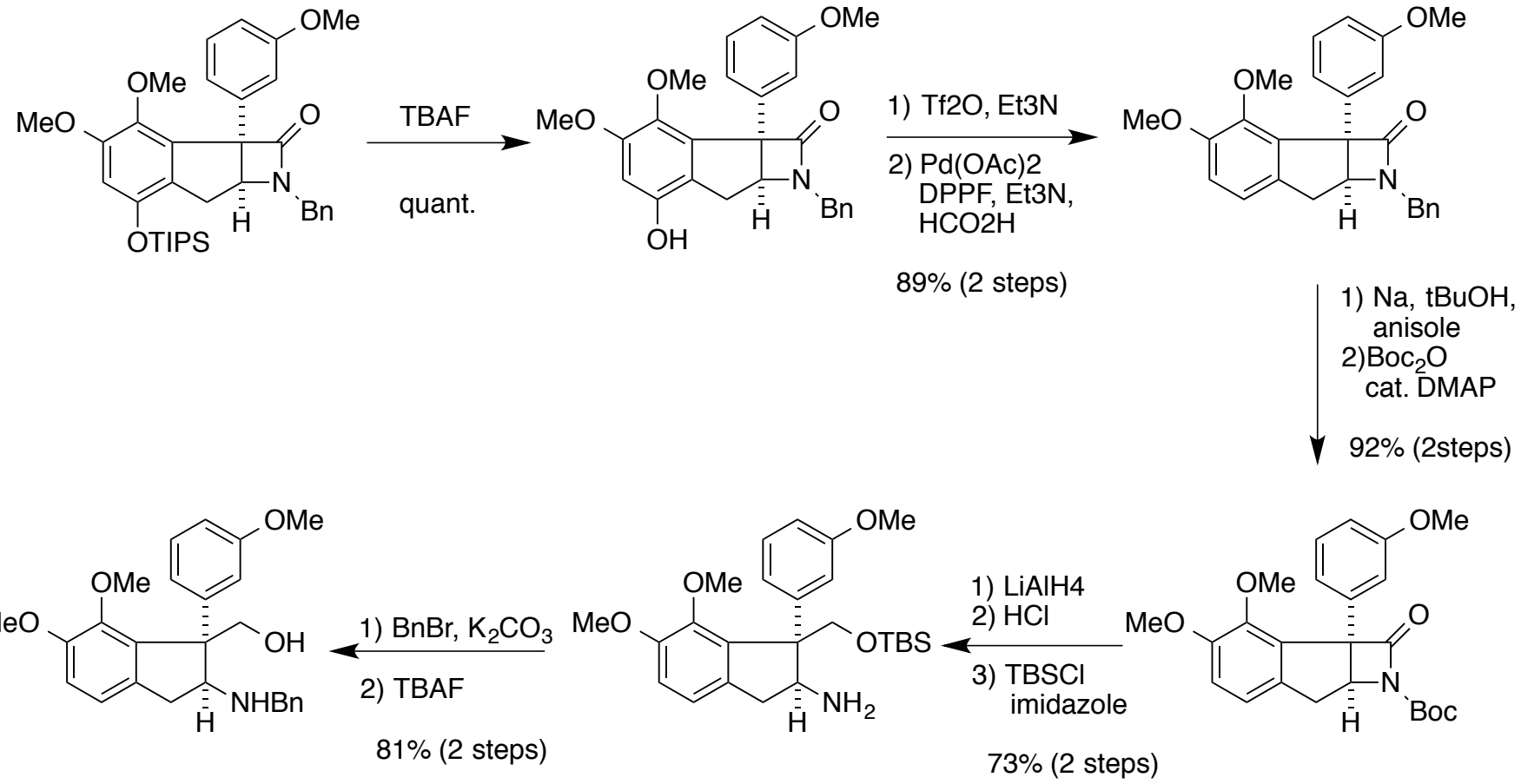


> Wrong product obtained

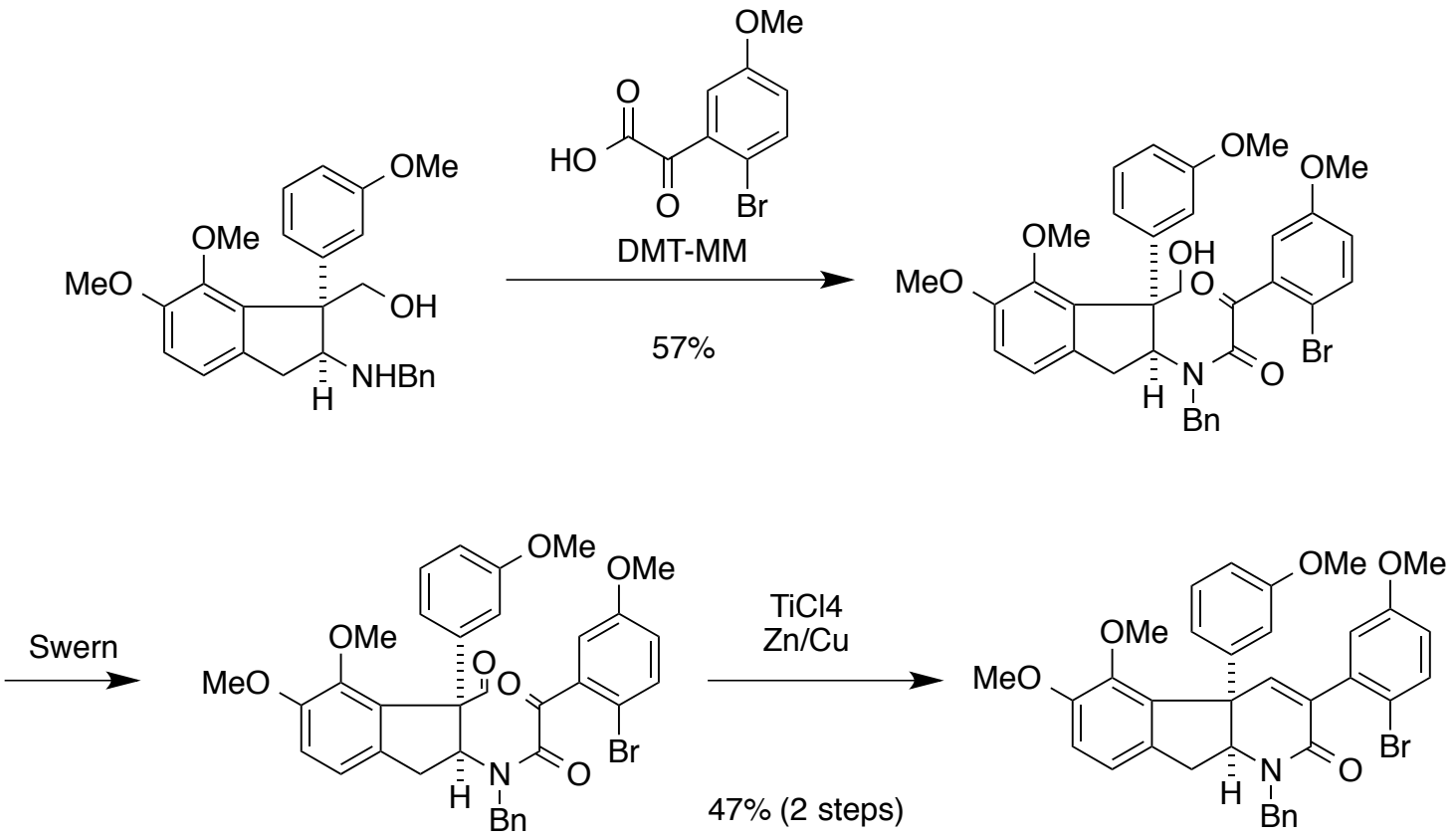
Friedel-Crafts Alkylation



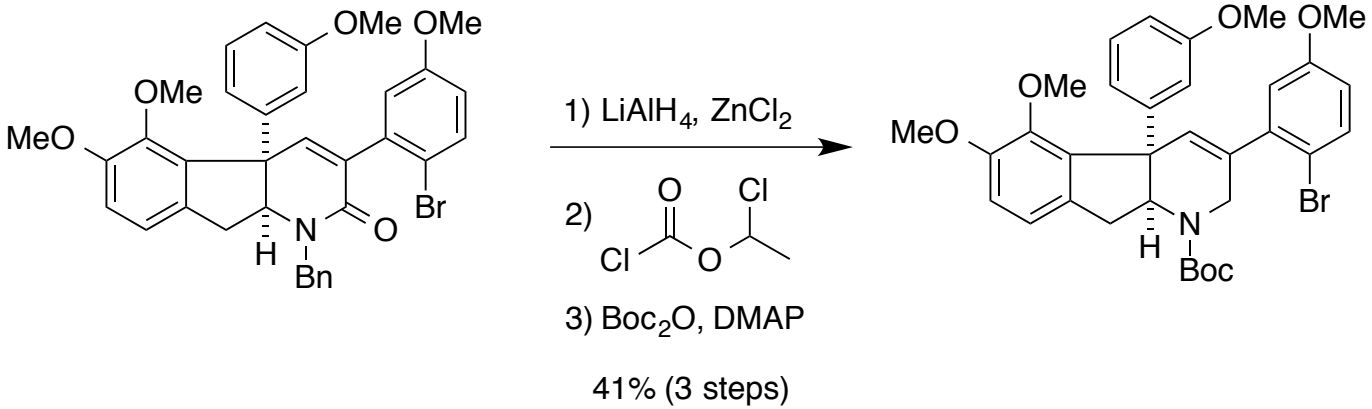
Reduction of the β-Lactame



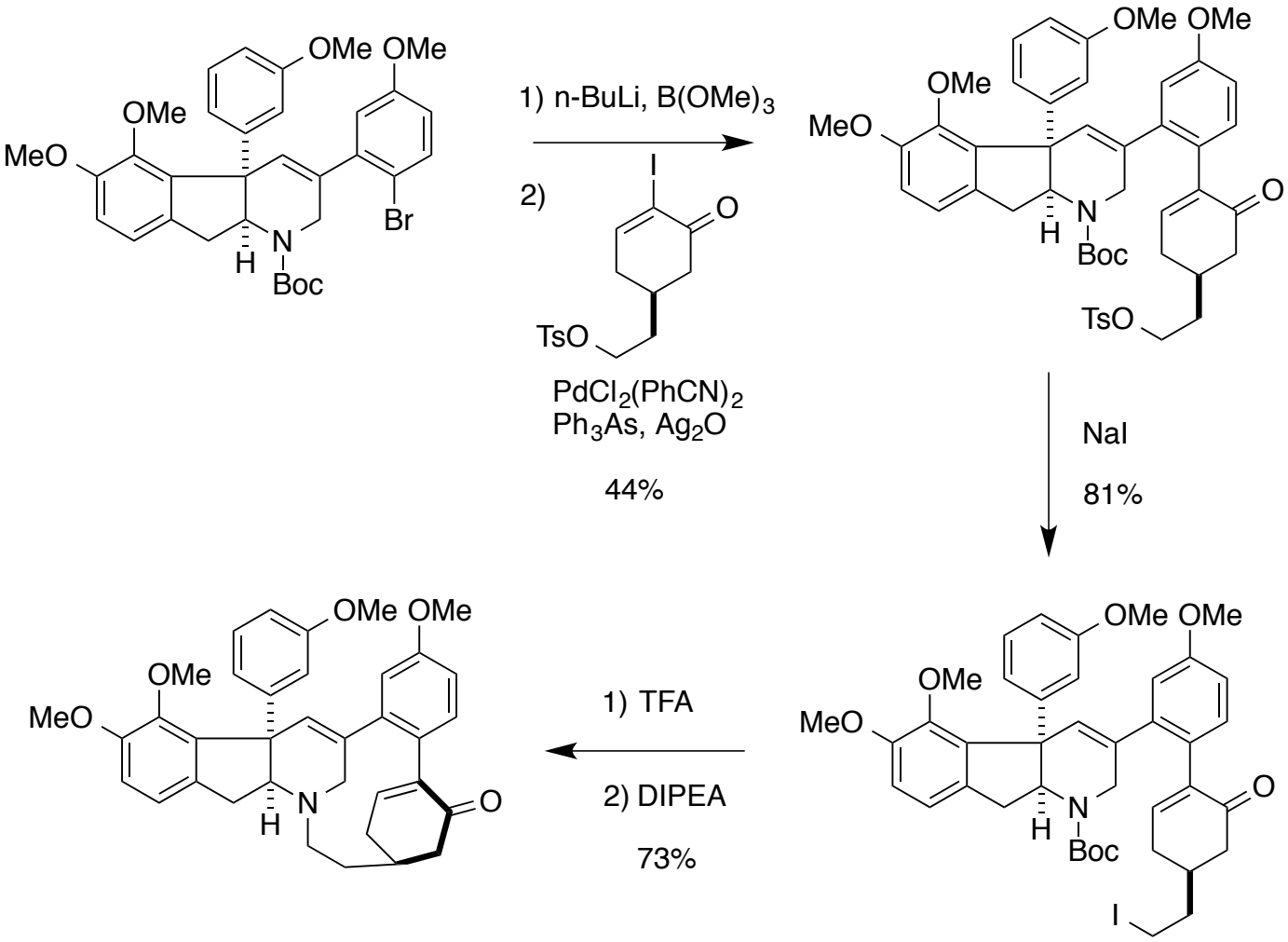
Intramolecular McMurry coupling



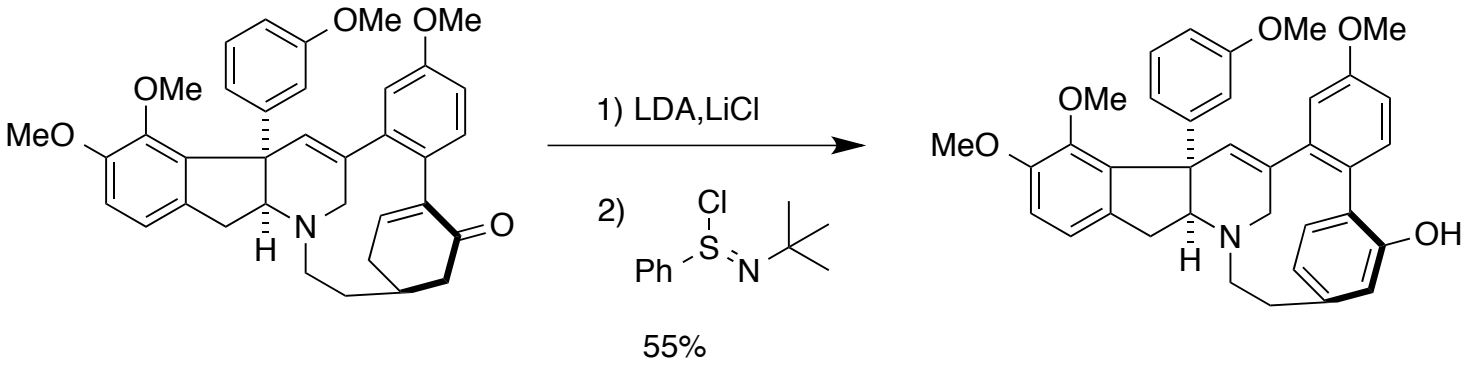
Reduction of the amide

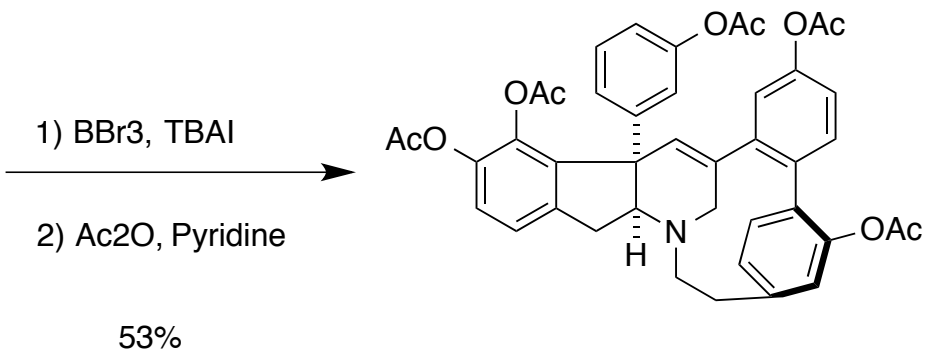


Macrocyclisation



Rearomatisation





Conclusion

- Confirmation of the structure of Haouamine B pentaacetate
- 40 steps and 0.055% Yield (83% average) starting from comercially available 3,4-dimethoxyphenol
- Diastereoselective Mannich reaction
- Intramolecular Friedel-Crafts alkylation
- McMurry coupling

Thank you for your attention