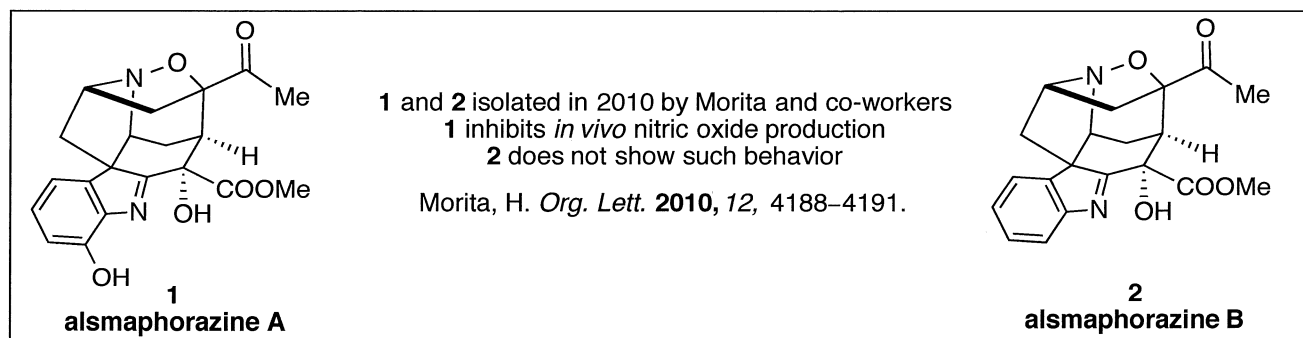


A Synthesis of Alsmaphorazine B Demonstrates the Chemical Feasibility of a New Biogenetic Hypothesis

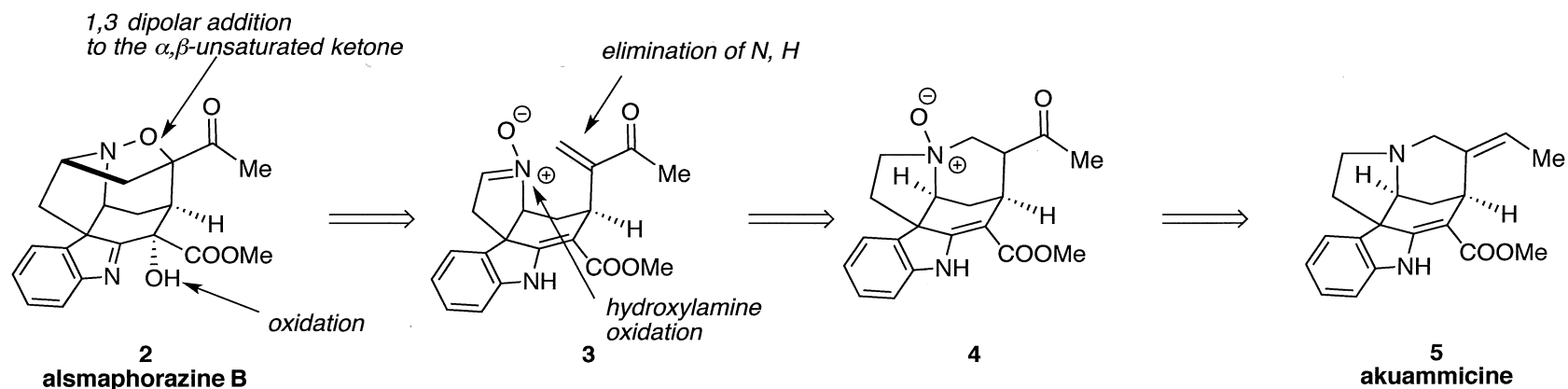
Allen Y. Hong and Christopher D. Vanderwal*

University of California, Irvine

J. Am. Chem. Soc. ASAP. DOI: 10.1021/jacs.5b04686



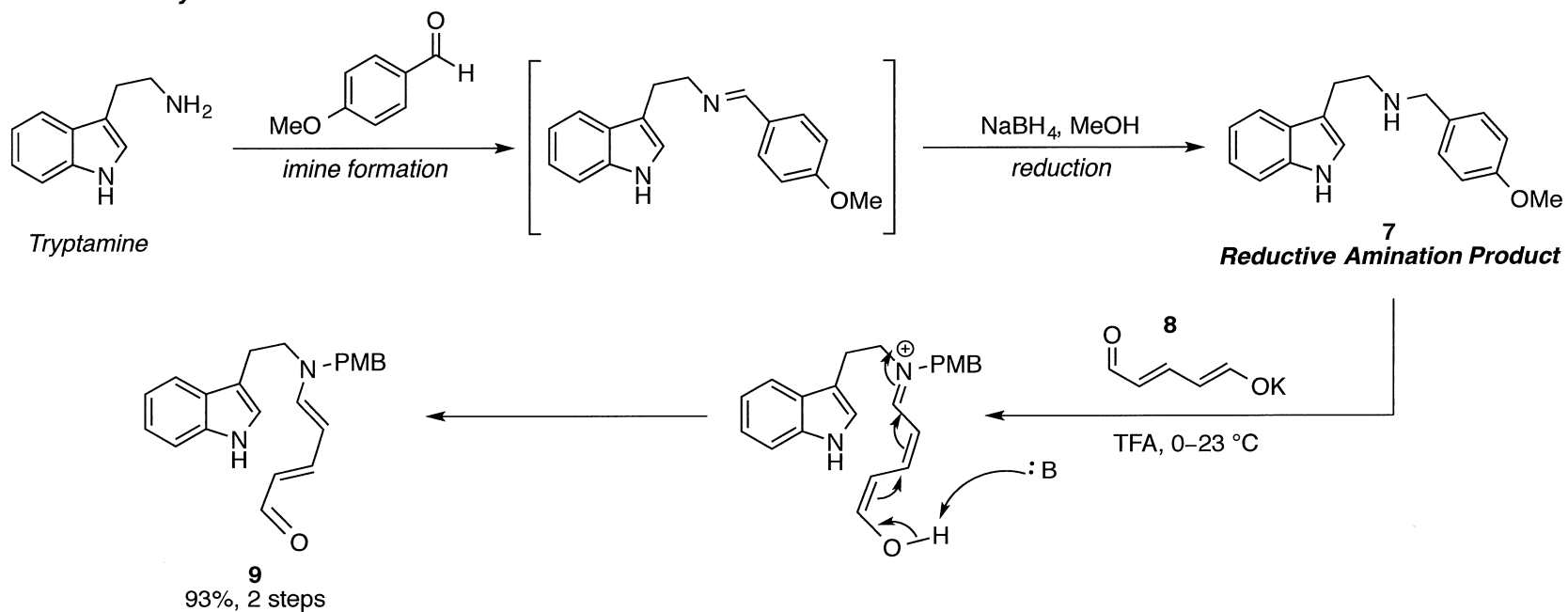
The Biogenesis Hypothesis/Retrosynthetic Analysis



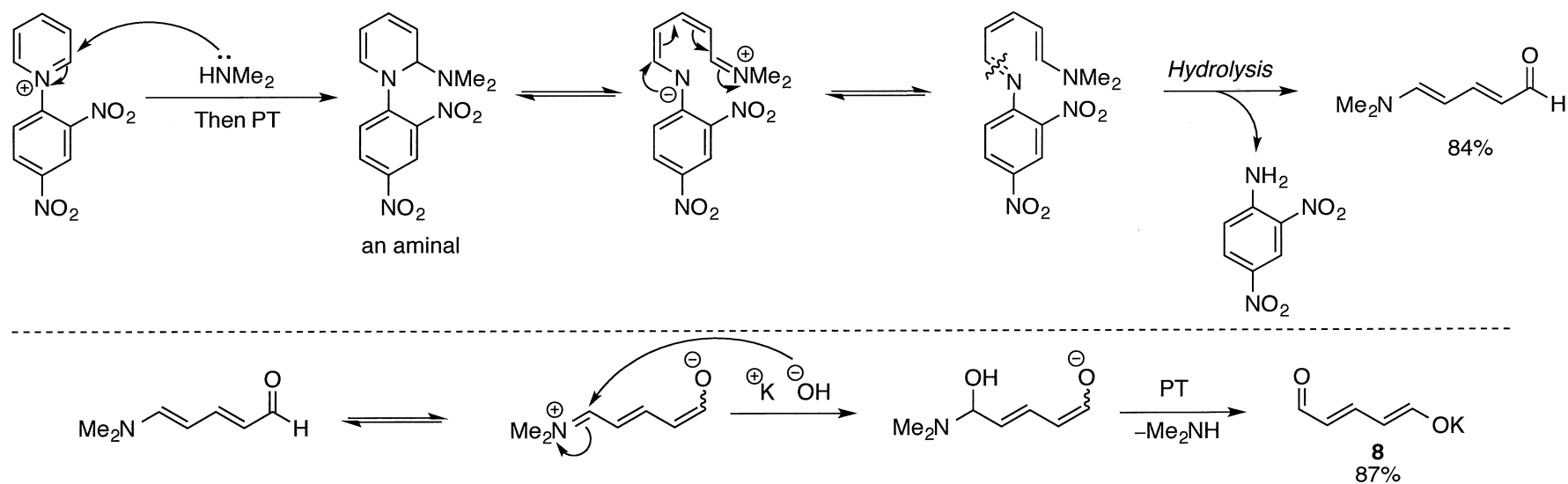
Is this proposed biosynthesis reasonable?

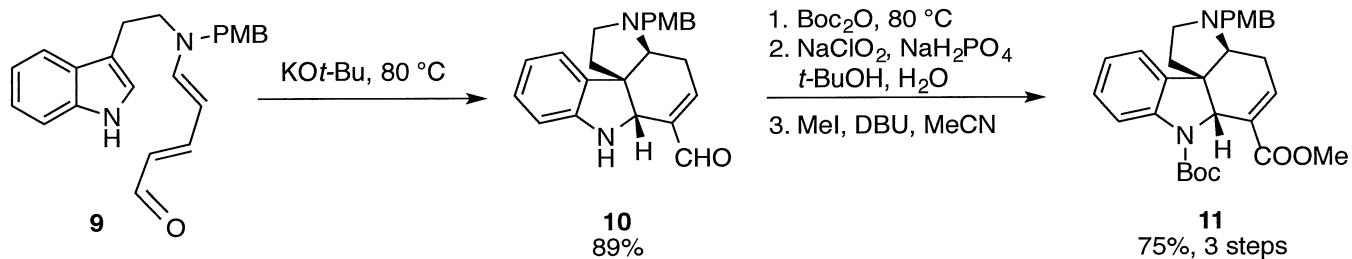
Need lots of akuammicine 5 for study!

Forward Synthesis

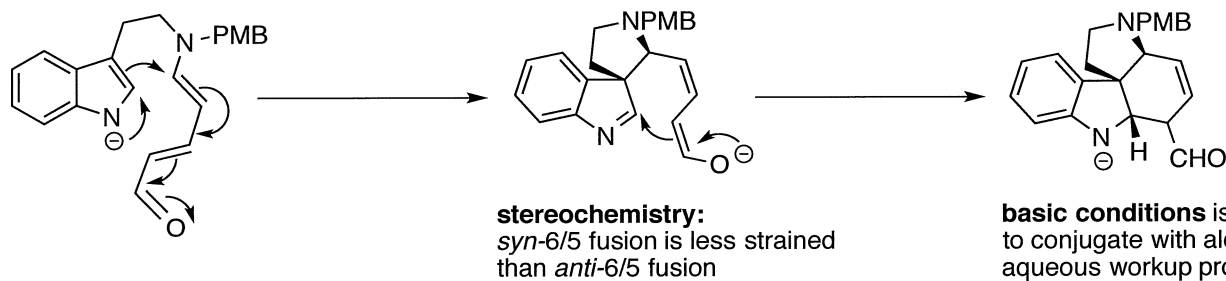


Preparation of compound 8: Zincke Reaction



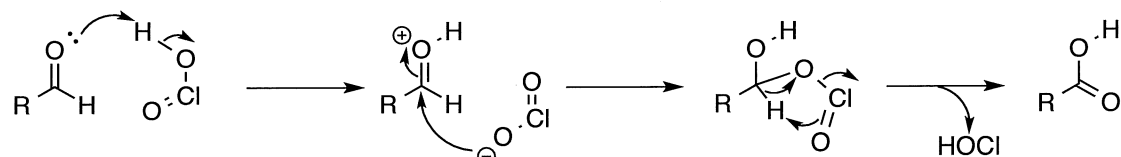


Anionic Cyclizations: in the style of Markó (9 to 10)

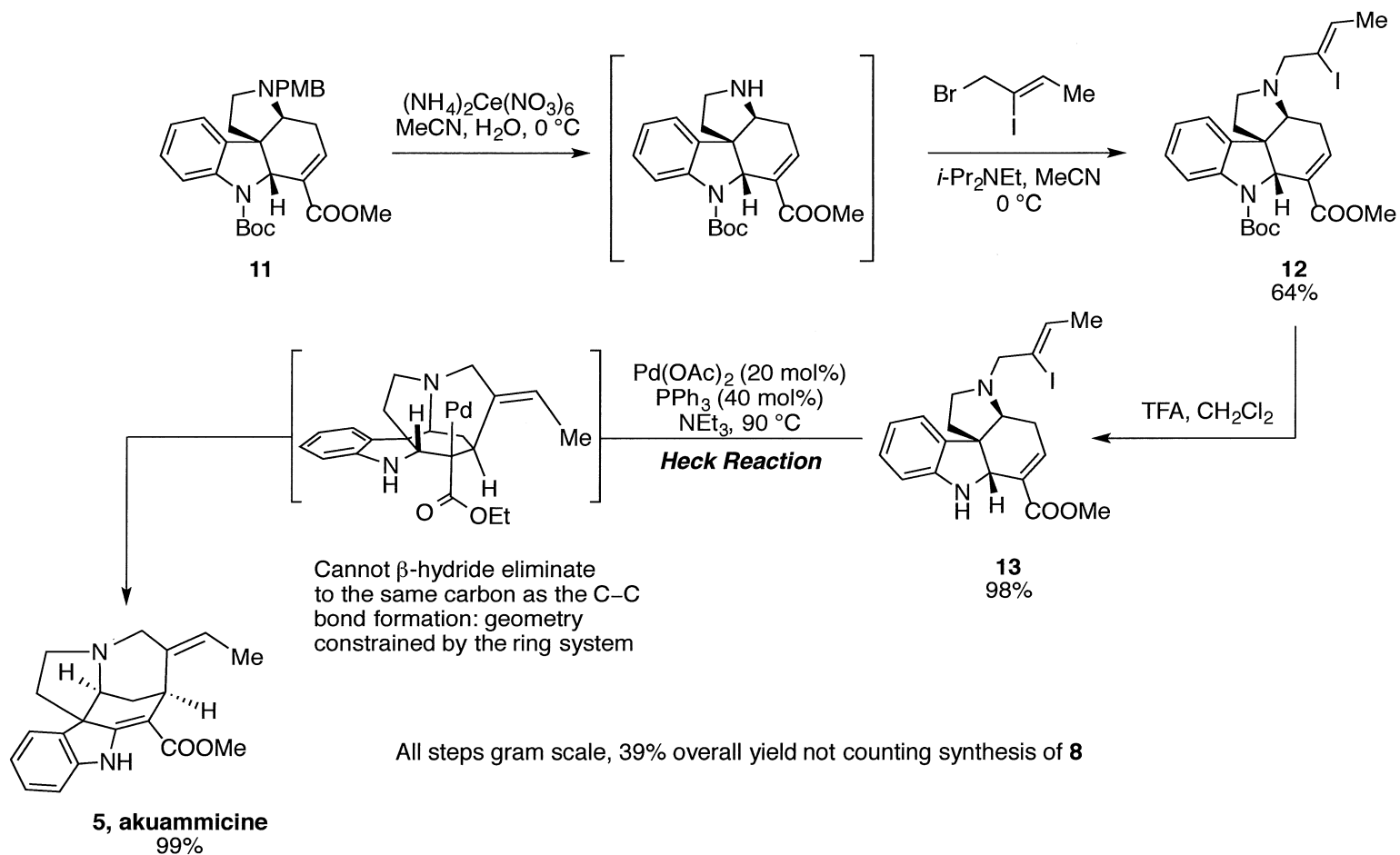


Turet, L.; Marko, I. E.; Tinant, B.; Declercq, J. P.; Touillaux, R. *Tetrahedron Lett.* **2002**, *43*, 6591–6595.
 Martin, D. B. C.; Vanderwal, C. D. *J. Am. Chem. Soc.* **2009**, *131*, 3472–3473.

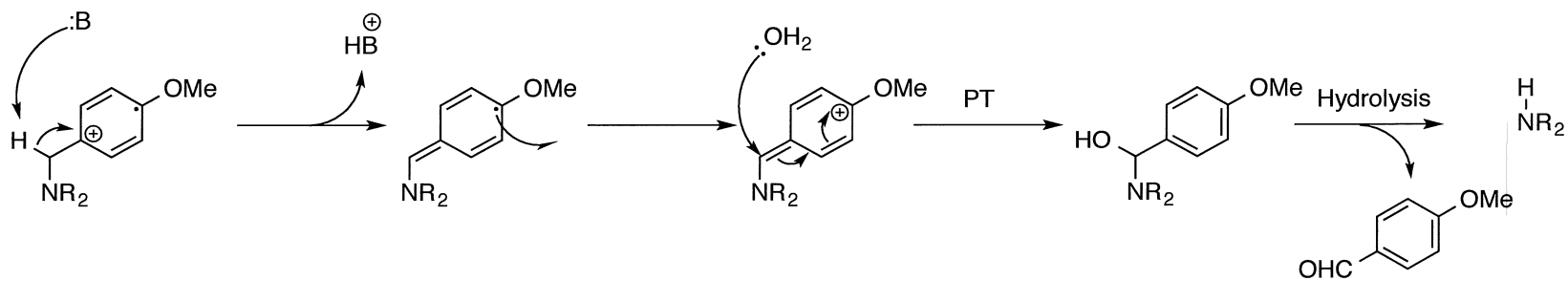
Pinnick Oxidation (10 to 11)

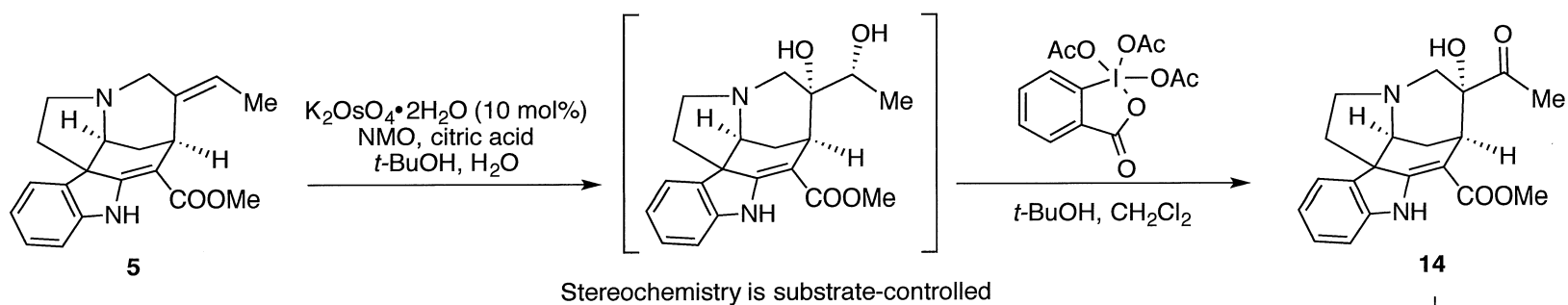


In the present case, sodium phosphate monobasic acts both as a proton source to initiate the reaction and a proton sink for the acidic byproduct.

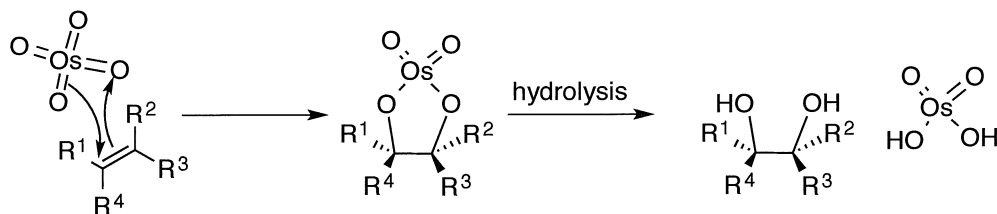


Oxidative Cleavage of PMB protecting group (11 to 12)

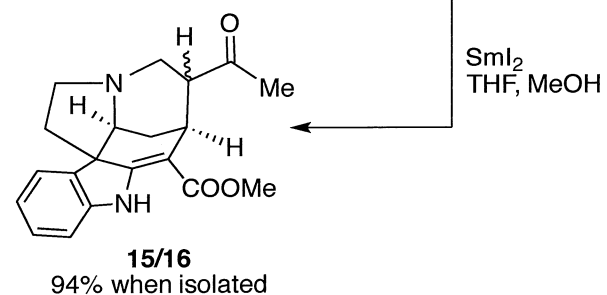




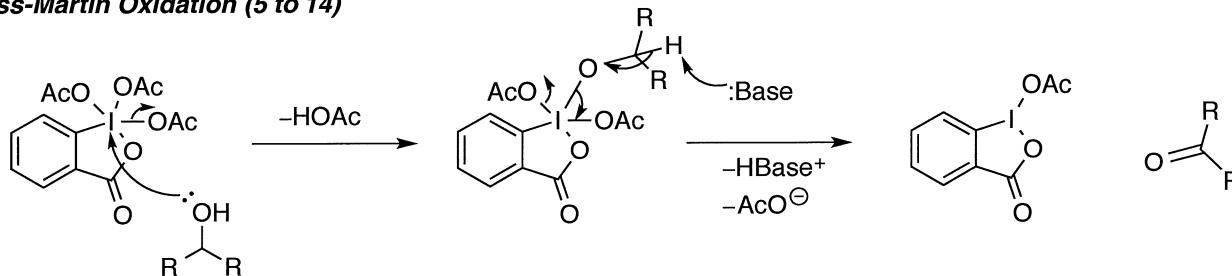
Dihydroxylation Reaction (5 to 14)



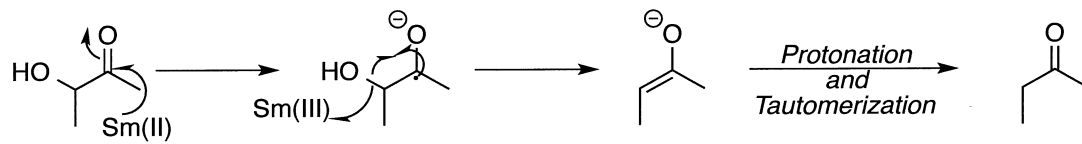
Osmium is re-oxidized by *N*-methylmorpholine-*N*-oxide
Citric acid is a ligand for osmium, which accelerates the reaction

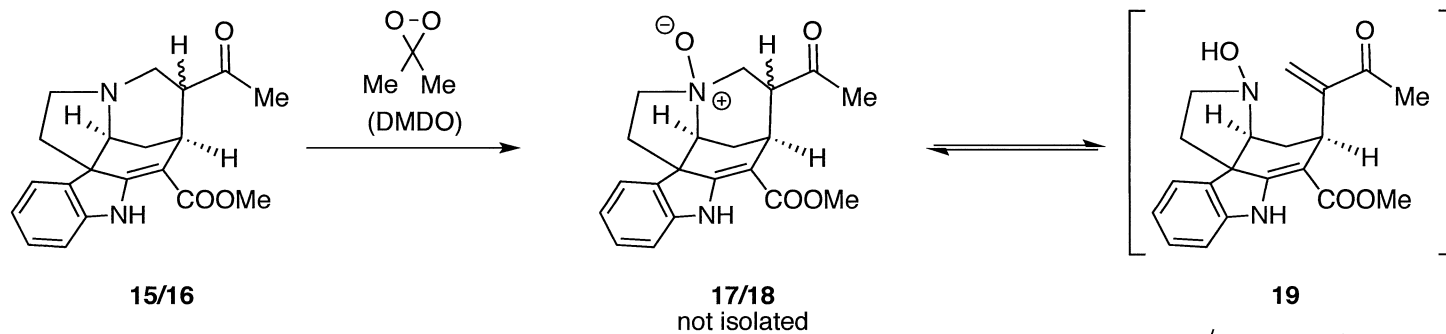


Dess-Martin Oxidation (5 to 14)

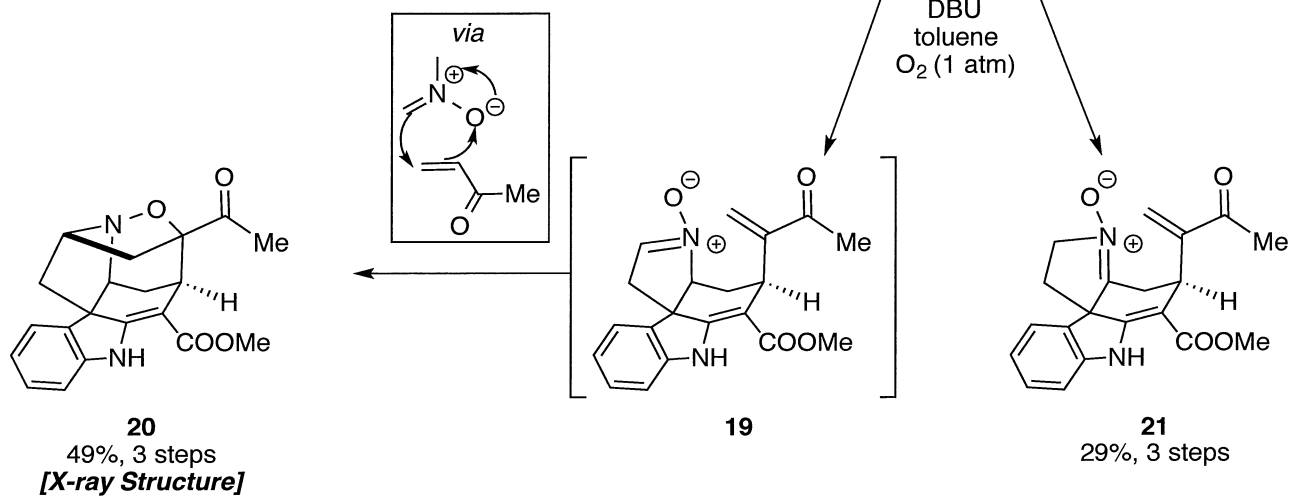


Reduction with samarium diiodide (14 to 15/16)

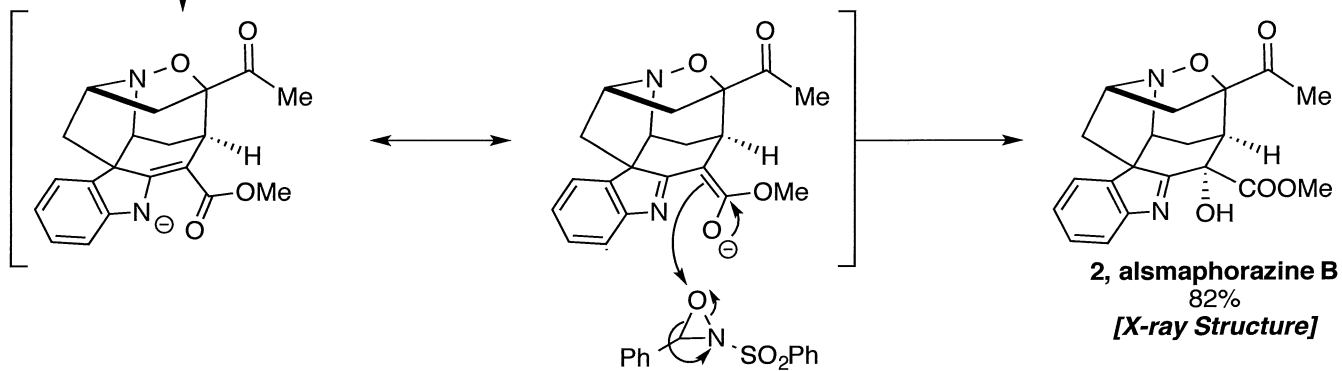




Conditions tried from 20 to 2:
m-CPBA, DMDO



LiHMDS
 -78 °C to RT

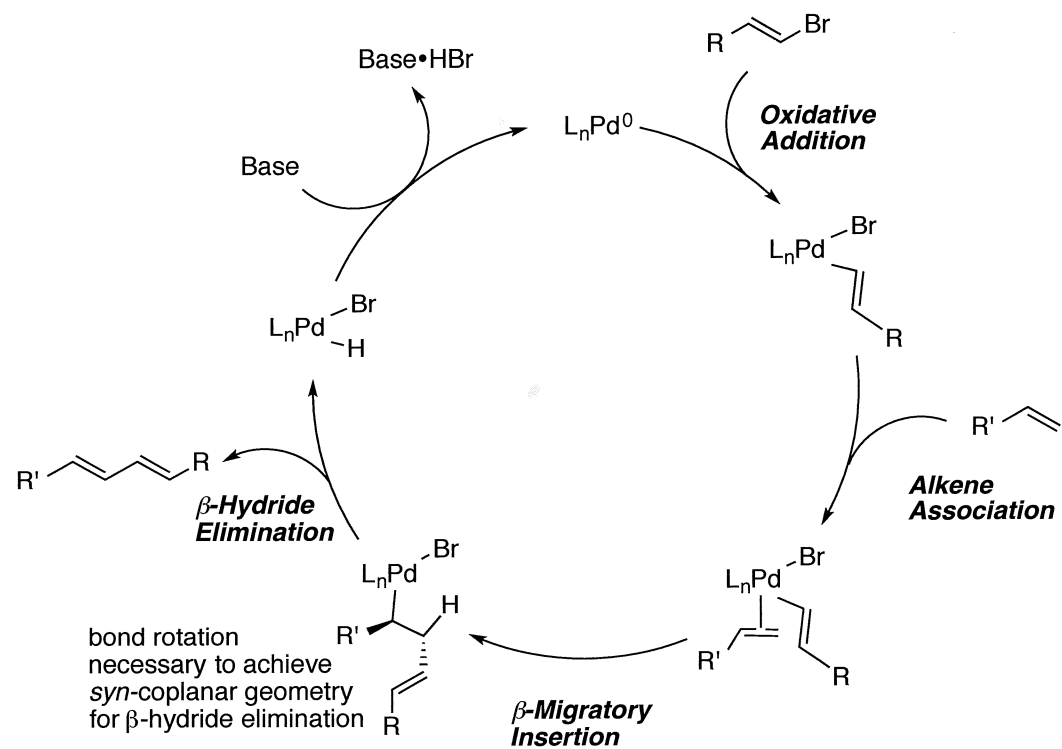


"15 steps"
 not counting synthesis
 of Zincke aldehyde

10.6% overall yield

Heck Reaction (13 to 5)

Classic Heck Reaction



In Hong and Vanderwal's example, the only *syn*-coplanar hydrogen is **not** on the carbon to which the coupling partner has bonded.