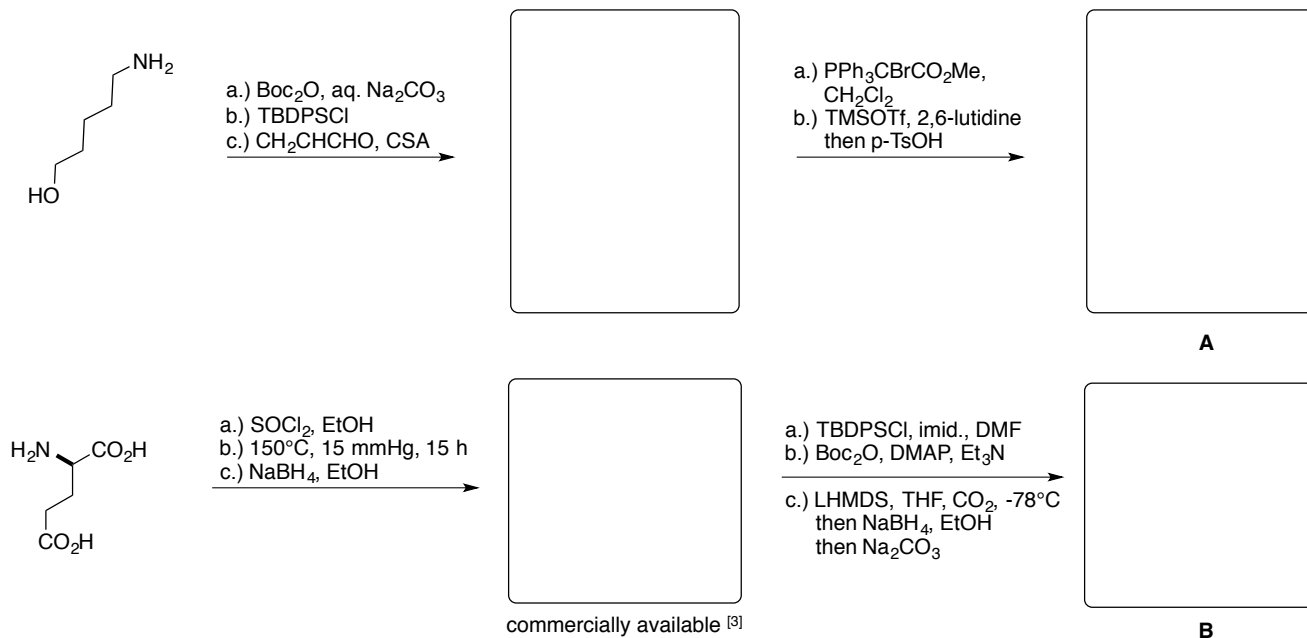
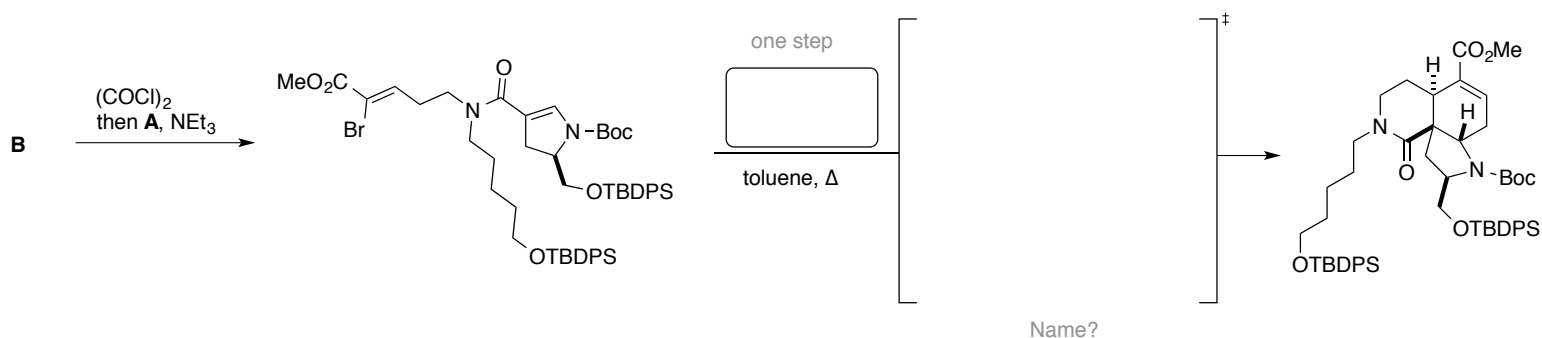


E3: Synthesis of Manzamine A and Related Alkaloids [1,3]

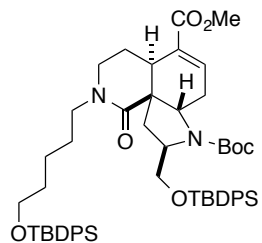


Manzamine A and related alkaloids have been isolated from marine sponges of the genera *Haliclona* and *Pellina* found in the Okinawa Sea in 1986, which exhibit a broad biological activity (anti-bacterial, antimalarial, anti-tumor, anti-inflammatory and anti-HIV).^[2] The combination of the complex and unusual structure of Manazamine A (pentacyclic core, two tertiary amides, two *Z*-olefins and five stereocenters) and its promising biological activity have inspired numerous synthetic investigations.^[1,2] Four total syntheses by Winkler (1999), Martin (1998), Fukuyama (2010) and Dixon (2012) have been reported.^[2]

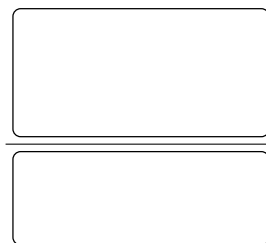
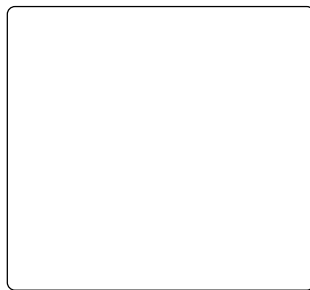


- [1] J. M. Humphrey, Y. Liao, A. Ali, T. Rein, Y.-L. Wong, H.-L. Chen, A. K. Country, S. F. Martin, *J. Am. Chem. Soc.* **2002**, *124*, 8584-8592.
 [2] P. Jakubec, A. Hawkins, W. Felzmann, D. J. Dixon, *J. Am. Chem. Soc.* **2012**, *134*, 17482-17485.
 [3] Y. Hamada, O. Hara, A. Kawai, Y. Kohno, T. Shioiri, *Tetrahedron* **1991**, *47*, 8635-8652.

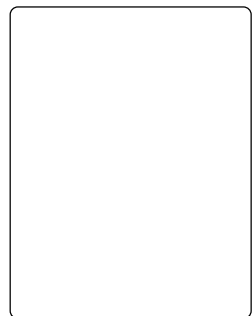
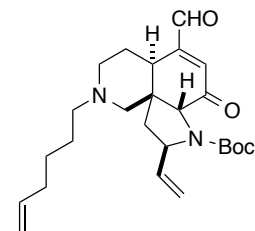




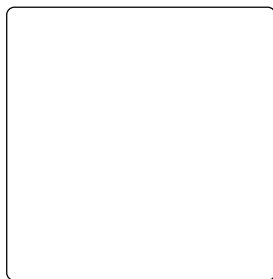
CrO₃, 3,5-dimethylpyrazole,
CH₂Cl₂, -18°C



5 steps



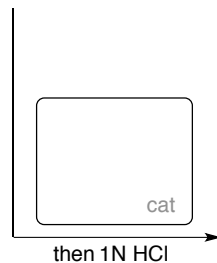
a.) KOH, MeOH, Δ
b.) CH₂CH(CH₂)₃COCl,
Et₃N, CH₂Cl₂



cat



a.) HC(OMe)₃ MeOH, HCl
b.) CH₂CHCH₂CH₂Li,
-78 °C to -20°C then H₂O
(+ formation of a carbamate)



then 1N HCl



DIBAL-H



Ircinol A

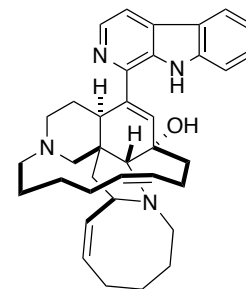
DMP



Ircinal A

a.) tryptamine,
CF₃CO₂H
b.) DDQ, Et₃N

Name?



Manzamine A