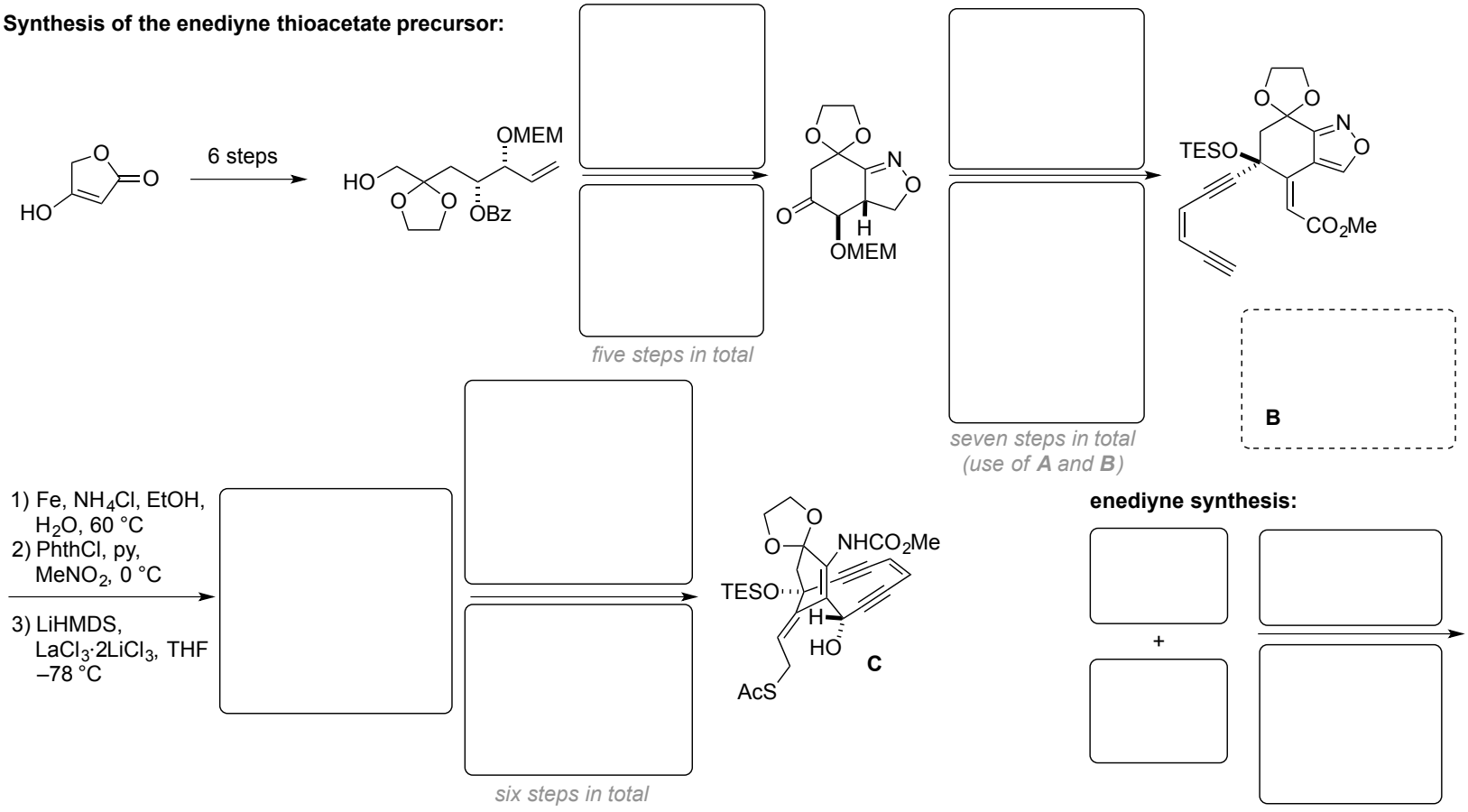
E17: Total Synthesis of Shishijimicin A[1-4]

Synthesis of the enediyne thioacetate precursor:



- Shishijimicin A is a rare marine natural product with extreme antitumor properties (IC_{50} = 0.48 pM against P388 leukemia cells)
- Similar to calicheamicin γ_1^I the mode of action involves a Bergmann-cycloaromatization, enabling cleavage of double-stranded DNA
- Total synthesis should yield enough material to investigate the compound in depth (e.g. for antibody-drug conjugate formation)

[1] K.C. Nicolaou, Z. Lu, R. Li, J. R. Woods, T. Sohn, *J. Am. Chem. Soc.* **2015**, *137*, 8716–8719.

[2] A. L. Smith, E. N. Pitsinos, C. K. Hwang, Y. Mizuno, H: Saimoto, G. R. Scarlato, T. Suzuki, K. C. Nicolaou, *J. Am. Chem. Soc.* **1993**, *115*, 7612–7624.

[3] Y.-F. Lu, C. W. Harwig, A. G. Fallis, *Can. J. Chem.* **1995**, *73*, 2253–2262.

[4] Y. Schott, M. Decker, H. Rommelspacher, J. Lehmann, *Bioorg. Chem. Lett.* **2006**, *16*, 5840

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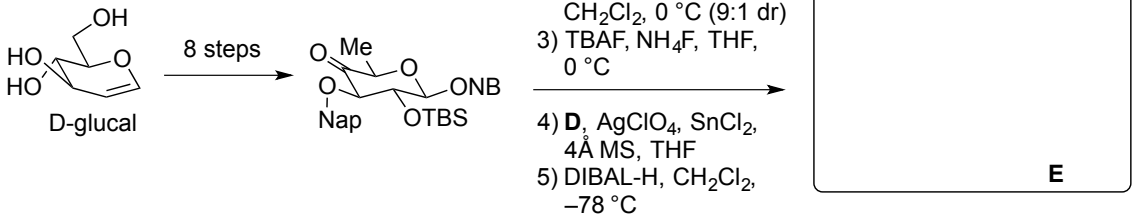
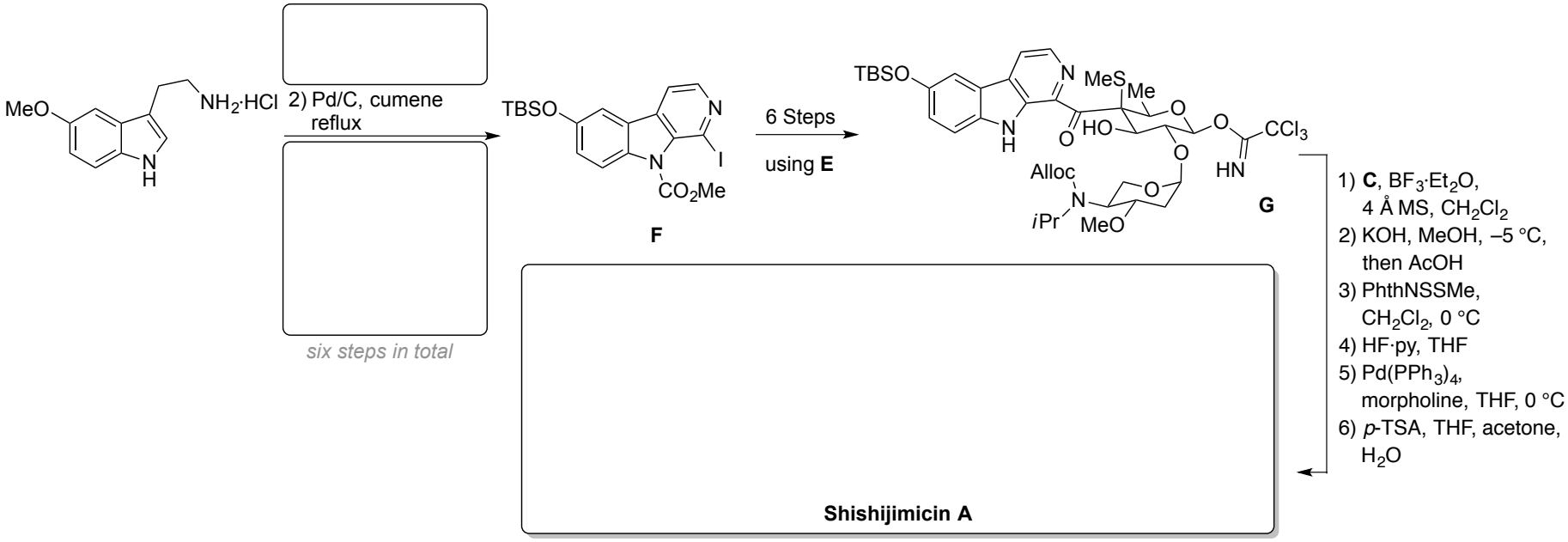
E17: Total Synthesis of Shishijimicin A[1-4]

Disaccharide construction:



Assembly of the natural product:



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