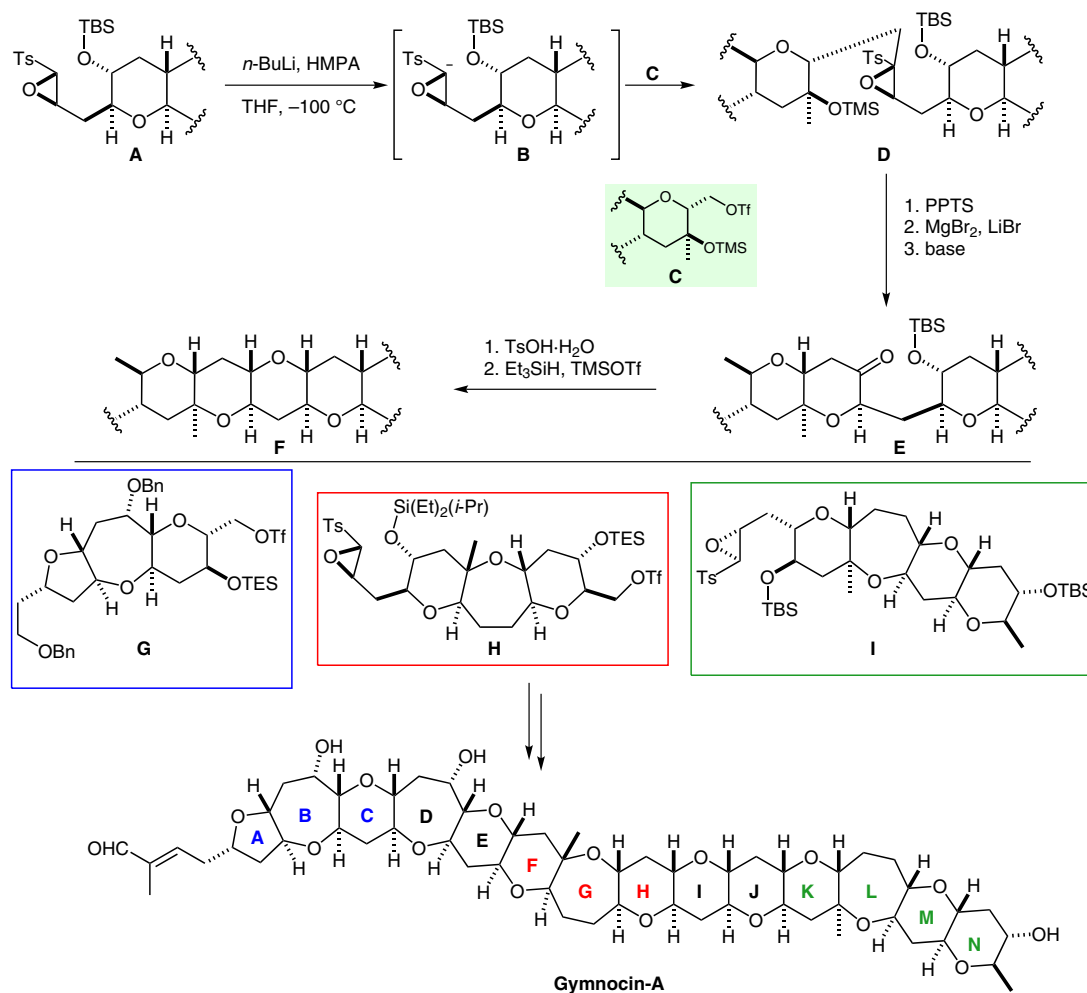


## Synthesis of Gymnocin-A



**Significance:** Gymnocin-A, a polycyclic ether isolated from *Karenia mikimotoi* in 2002, exhibits strong cytotoxicity ( $\text{IC}_{50} = 1.3\text{ }\mu\text{g/mL}$ ) against mouse leukemia cells. Structurally, this natural product is characterized by 14 consecutive ether rings. Thus far, only one total synthesis has been reported (C. Tsukano, M. Sasaki *J. Am. Chem. Soc.* **2003**, *125*, 14294). Herein, Mori and co-workers present a strategically different approach, relying on the union of the three fragments **G**, **H**, and **I** by an oxiranyl anion coupling.

**Comment:** The presented synthesis is centered around a multi-step coupling protocol uniting two fragments and concomitantly forming two new cyclic ethers in between. Thereby, a tosyl epoxide of type **A** was deprotonated and reacted with triflate **C**, generating **D**. Acid-mediated TMS deprotection, epoxide opening, and ether formation then yielded ketone **E**. The second ether ring was ultimately formed by acid-mediated hemiacetalization and reduction with  $\text{Et}_3\text{SiH}$ .