Significance: Gymnocin-A, a polycyclic ether isolated from *Karenia mikimotoi* in 2002, exhibits strong cytotoxicity (IC₅₀ = 1.3 μg/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 Et₃SiH.