T. SAKAI, S. MATSUSHITA, S. ARAKAWA, K. MORI, M. TANIMOTO, A. TOKUMASU,
T. YOSHIDA, Y. MORI* (MEIJO UNIVERSITY, NAGOYA, JAPAN)
Total Synthesis of Gymnocin-A
J. Am. Chem. Soc. **2015**, *137*, 14513–14516.

Synthesis of Gymnocin-A

Significance: Gymnocin-A, a polycyclic ether isolated from *Karenia mikimotoi* in 2002, exhibits strong cytotoxicity ($\text{IC}_{50} = 1.3 \mu\text{g/mL}$) 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 Et_3SiH .

SYNFACTS Contributors: Erick M. Carreira, Christian Ebner
Synfacts 2016, 12(2), 0111 Published online: 16.01.2016
DOI: 10.1055/s-0035-1561120; Reg-No.: C08415SF