

Studies Toward the Total Synthesis of the Marine Tetraterpenoid (–)-Gukulenin A

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In 2010, the marine tetraterpenoid (–)-gukulenin A (**1**) was isolated by Rho and coworkers from the sponge *Phorbas gukhulensis*.¹ (–)-Gukulenin A is constitutionally characterized by a structurally unique heterodimeric scaffold and besides the synthetically challenging molecular architecture, (–)-gukulenin A exerts antiproliferative activity on different human cancer cell lines in the nanomolar range.¹

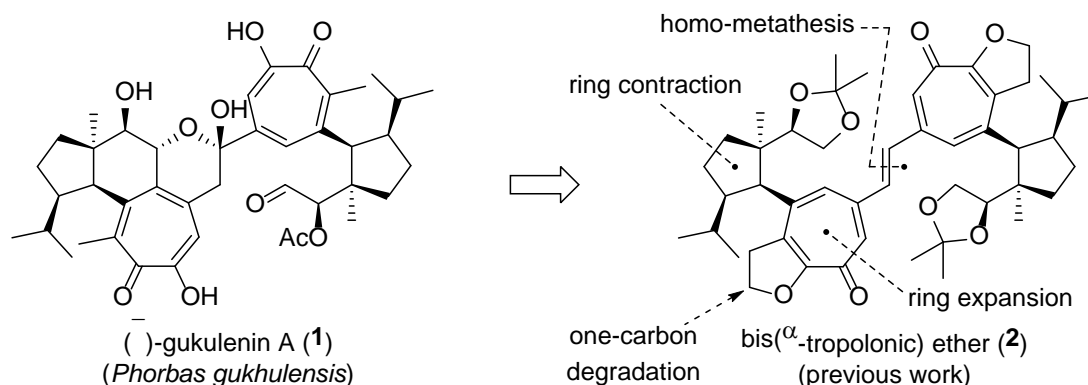


Figure 1: (–)-Gukulenin A (1**) and previous work on the bis(α -tropolonic) ether (**2**).**

In 2018, we presented the symmetry-driven synthesis of the bis(α -tropolonic) ether (**2**) as an advanced gukulenin A precursor.² The formation of the seven-membered α -tropolonic ether unit was realized by a novel photochemically triggered two-carbon ring expansion (alkyne-de Mayo reaction) which was developed in our research group.³ However, cleavage of the dihydrofuran moiety in order to initiate one-carbon atom degradation proved to be unexpectedly challenging. This circumstance forced us to take a synthetic detour and thus we present our latest results toward the total synthesis of the marine tetraterpenoid (–)-gukulenin A.

¹ Park, S. Y.; Choi, H.; Hwang, H.; Kang, H.; Rho, J.-R. *J. Nat. Prod.* **2010**, *73*, 734–737.

² Tymann, D.; Bednarzick, U.; Iovkova-Berends, L.; Hiersemann, M. *Org. Lett.* **2018**, *20*, 4072–4076.

³ Tymann, D.; Tymann, D. C.; Bednarzick, U.; Iovkova-Berends, L.; Rehbein, J.; Hiersemann, M. *Angew. Chem.* **2018**, *130*, 15779–15783.