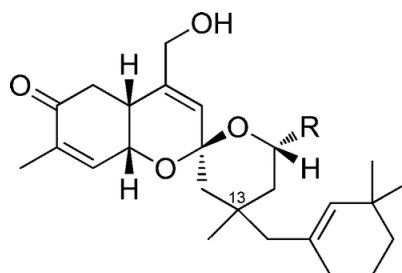


## Synthetic Challenge #7

### August 28, 2014

#### Total Synthesis of Gombaspiroketal A-C



- 1 (R = OMe, 13R)  
2 (R = OMe, 13S)  
3 (R = OH, 13R)

#### Gombaspiroketal A-C (1-3)

The goal of this Challenge is to develop and defend a synthetic strategy for the total synthesis of the gombaspiroketal. These sesterterpenes were isolated from the sponge *Clathria gombawuiensis* (Shin *et al. Org. Lett.* **2014**, *16*, 2826-2829). Their structure and relative configuration was determined from HRMS, as well as 1D and 2D NMR analysis. The absolute configuration was established by comparison between experimental and calculated CD spectra. Bizarrely, the authors proposed that gombaspiroketal A and B are epimers at C-13 based on tenuous evidence. DFT calculations show that these structures are much more likely to be epimers at C-11 and/or C-16 (M. Gravel, unpublished results). You can either target the originally proposed structures or a revised one, so long as your strategy allows to clear up the controversy.

Your presentation should consist of a brief retrosynthetic analysis explaining the reasons behind important disconnections, followed by a synthetic plan which details the reagents used and possible protecting groups. As would be the case for a real research proposal, issues of chemo- and diastereoselectivity must be addressed. Your route doesn't have to be enantioselective, but it would be useful to confirm the absolute configuration. Your synthesis should possess a good balance between originality and feasibility. In this regard, it would be beneficial to briefly show some precedent for the most difficult/uncertain steps in the sequence. Each team's synthesis should take ~30 minutes to present.

Please provide the name of your team and a list of team members to Dr. Gravel at your earliest convenience.