S. CHANG, S. HUR, R. BRITTON* (SIMON FRASER UNIVERSITY, BURNABY, CANADA) Total Synthesis of Ascospiroketal A Through a Ag^I-Promoted Cyclization Cascade *Angew. Chem. Int. Ed.* **2015**, *54*, 211–214.

Total Synthesis of Ascospiroketal A

Significance: Ascospiroketal A was isolated in 2007 from the marine fungus *Ascochyta salicorniae*. This natural product is characterized by a spiroketal that is part of a fused tricyclic system. While the relative configuration of the spirocyclic core could be elucidated by NOESY spectroscopy, no sterochemical information for the side chain could be obtained. Britton and co-workers present a synthetic strategy, which allowed not only for the efficient construction of the core fragment but also for a late-stage introduction of the contested side chain. Their efforts culminated not only in the first total synthesis of ascospiroketal A but also in the establishment of the C15-C2'-C3' stereochemistry.

Comment: The synthesis commenced with the preparation of enantioenriched aldehyde **D** from hydroxyoxetane A. A diastereoselective aldol reaction with ketone F gave cyclization precursor G. Extending a method developed in their laboratory (Org. Lett. 2012, 14, 5844), Britton and co-workers exposed G to a combination of Ag₂O and AgBF₄. Ketal **H** is presumed to be formed first, followed by nucleophilc opening of the oxetane, yielding a 1:1 mixture of I and J. The complete diastereoselective oxetane opening might be attributed to the chelation of silver(I). Notably, the undesired isomer I could be epimerized to J. After several isomeric side chains were attached, the authors found that ascospiroketal A possesses the configuration as depicted above.

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Category

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