P. ZHAO, C. M. BEAUDRY* (OREGON STATE UNIVERSITY, CORVALLIS, USA)

Enantioselective and Regioselective Pyrone Diels-Alder Reactions of Vinyl Sulfones: Total Synthesis of (+)-Cavicularin

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Total Synthesis of (+)-Cavicularin

Significance: (+)-Cavicularin, isolated from the liverwort *Cavicularia densa*, is a chiral cyclophane natural product. Because of its unusual molecular structure, several total syntheses have been reported to date. Zhao and Beaudry report a conceptionally different approach, which relies on an intramolecular enantioselective pyrone Diels–Alder reaction with subsequent CO₂ extrusion to generate the aromatic A ring of the natural product.

Comment: The synthesis commences with a remarkably selective one-pot three-component Suzuki cross-coupling between dibromide $\bf B$ and boronic esters $\bf A$ and $\bf C$. Coupling product $\bf D$ was further advanced to α -hydroxy pyrone $\bf E$. In the presence of cinchona alkaloid $\bf F$, this material underwent the desired Diels–Alder reaction to yield intermediate $\bf G$, which immediately eliminated ${\bf CO}_2$ and phenylsufinic acid to generate $\bf H$ as a single regioisomer. Finally, reduction and protecting group removal yielded (+)-cavicularin in 7.3% overall yield.

 SYNFACTS Contributors: Erick M. Carreira, Christian Ebner

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