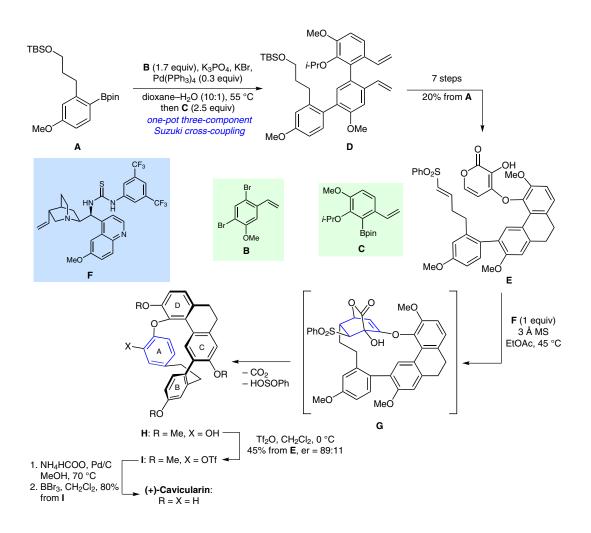
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Enantioselective and Regioselective Pyrone Diels-Alder Reactions of Vinyl Sulfones: Total Synthesis of (+)-Cavicularin

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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 CO<sub>2</sub> 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  $\alpha$ -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.

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Category

Synthesis of Natural Products and Potential Drugs

**Key words** 

(+)-cavicularin

Suzuki crosscoupling

pyrone Diels-Alder reaction



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