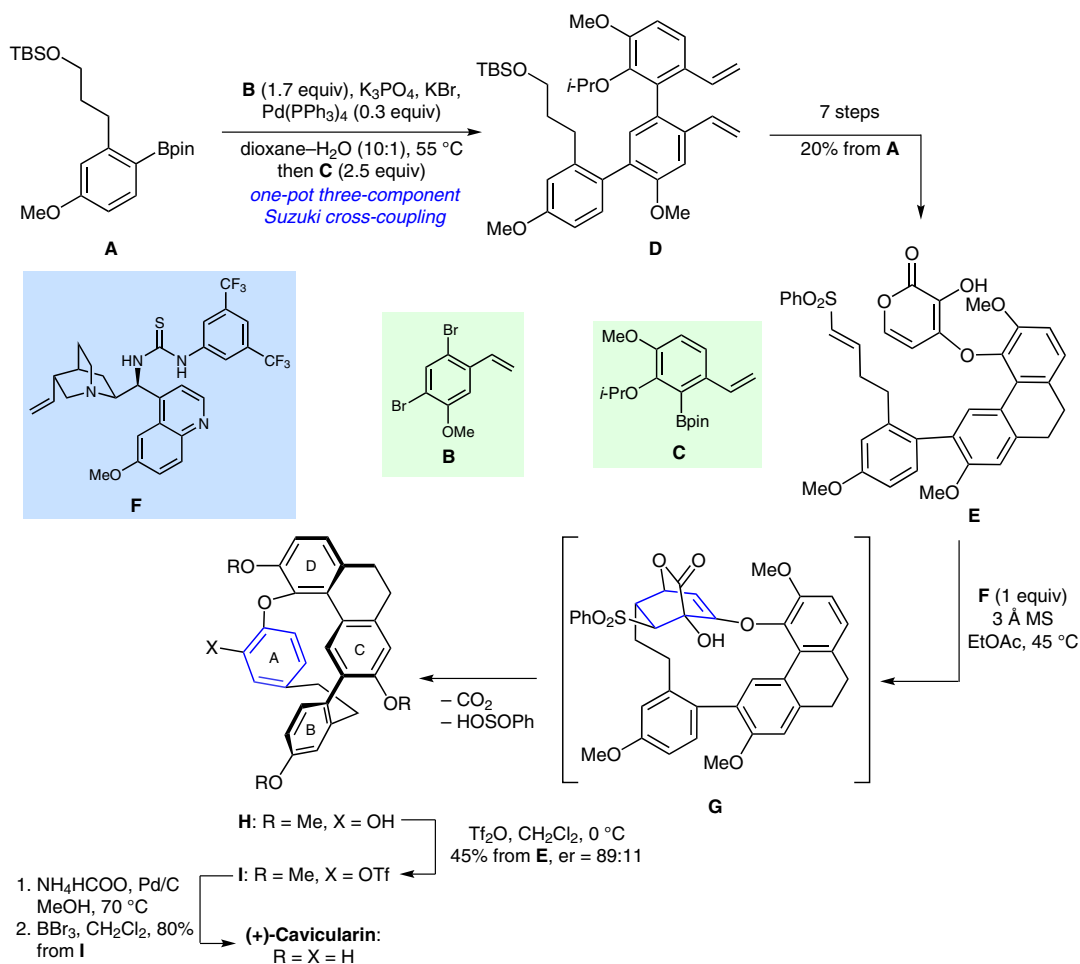


Total Synthesis of (+)-Cavicularin



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 **B** and boronic esters **A** and **C**. Coupling product **D** was further advanced to α -hydroxy pyrone **E**. In the presence of cinchona alkaloid **F**, this material underwent the desired Diels–Alder reaction to yield intermediate **G**, which immediately eliminated CO₂ and phenylsulfonic acid to generate **H** as a single regioisomer. Finally, reduction and protecting group removal yielded (+)-cavicularin in 7.3% overall yield.