Concise Total Synthesis of (±)-Verrubenzospirolactone

Significance: Isolated from Sinularia verruca, verrubenzospirolactone possesses a unique pentacyclic structure featuring a spirocyclic butenolide and five contiguous stereocenters. The target was synthesized in five steps, including a biomimetic intramolecular Diels–Alder cycloaddition.

Comment: Readily available methylhydroquinone (A) was condensed with citral (B) in a Knoevenagel condensation–electrocyclization sequence. Oxidation, olefination, and isomerization of the resulting 2H-chromene C yielded the Z and E isomers of E, both of which underwent an intramolecular Diels–Alder cycloaddition to form (±)-verrubenzospirolactone and its diastereoisomer G, respectively.