Synthesis of (±)-Alopecuridine

Significance: (±)-Alopecuridine A is a Lycopodium alkaloid that is a biological precursor for the significantly cytotoxic (±)-sieboline A. The first total synthesis is achieved here in 13 steps, followed by the conversion into (±)-sieboline A that validates the biogenetic pathway.

Comment: Compounds E and F were obtained as an inseparable mixture of diastereoisomers that were subjected to semipinacol rearrangement conditions. This generated a mixture of diastereomers that could then be separated by chromatography to give the desired intermediate G in 45% yield. The tricyclic core J was synthesized with a samarium iodide mediated coupling.