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Total Synthesis of (±)-Alopecuridine and Its Biomimetic Transformation into (±)-Sieboldine A

Synthesis of (±)-Alopecuridine

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