Total Synthesis of (±)-Lycopodine

Significance: In 1968, Stork and co-workers reported the total synthesis of the alkaloid natural product (±)-lycopodine. This natural product, isolated over 130 years ago, is part of a family of compounds that have long attracted attention for the bioactivity and structural complexity.

Comment: Cyclization followed by conjugate addition furnishes ketone C, which is then elaborated to amide E. After Friedel–Crafts alkylation and functional group modulation, enol ether H is subjected to ozonolysis and selenium dioxide-mediated oxidation. Keto ester I then rapidly gave access to the natural product.