Total Synthesis of (-)-6-epi-Ophiobolin N

Significance: The ophiobolin family of sesterpenes is characterized by a fused 5-8-5 ring system. Brill, Grover, and Maimone developed a radical cascade cyclization to assemble this ring system, culminating in the total synthesis of (-)-6-epi-ophiobolin N. The complete synthesis is remarkably short for a sesterterpene, merely requiring nine linear steps.

Comment: Commencing from farnesol, cyclization precursor 5 could be accessed in four steps. The central radical cascade gave the fused carbon skeleton of the target molecule in 56% yield. TADDOL-derived thiol 6 was found to be crucial to favor the correct stereochemistry at C15. The natural product was obtained after four additional steps.