Synthesis of Ileabethoxazole, Pseudopteroxazole, and seco-Pseudopteroxazole

Significance: The oxazole diterpenoids ileabethoxazole, pseudopteroxazole, and seco-pseudopteroxazole, isolated from Pseudopterogorgia elisabethae, possess potent inhibitory activity against Mycobacterium tuberculosis. Structurally, these natural products are characterized by a hexasubstituted benzene connected to an oxazole. Li and co-workers achieved the total syntheses of these targets relying on a palladium-catalyzed cascade reaction followed by a 6π-electrocyclization.

Comment: Alkyne A, available in six steps from (+)-isopulegol, undergoes a palladium-catalyzed cascade reaction to give C in 55% yield. Upon heating in the presence of air, the desired 6π-electrocyclization occurred, providing key intermediate D. Later, alkyne F was obtained, which underwent a radical cyclization ultimately leading to (+)-ileabethoxazole. Furthermore, both (+)-pseudopteroxazole and (+)-seco-pseudopteroxazole could be accessed from D.