Enantioselective Synthesis of Arcutinidine, Arcutinine, and Arcutine

Significance: Li and co-workers present the enantioselective total synthesis of arcutinidine, arcutinine, and arcutine, which are diterpenoid alkaloids bearing the highly complex arcutine core. In their concise synthetic route leading to the preparation of these natural products in 18 or 19 steps from enantioenriched alcohol A, the authors implemented a reaction cascade comprising a Prins cyclization followed by a cationic rearrangement, thereby reliably converting the hetidine skeleton in F into the desired arcutine core present in G. Furthermore, completion of the synthesis allowed the team to correct the absolute configuration reported for arcutine.

Comment: Silylation and formylation of enantioenriched alcohol A gave dienophile B, which was subsequently employed in a Diels–Alder reaction with diene C to give cyclohexene D. Following vinylation, protection of the hydroxyl group as a methoxymethyl ether, and formation of cyclic enone E, anionic Diels–Alder cycloaddition under careful exclusion of air afforded hetidine scaffold F. Upon treatment with acid, Prins cyclization and Wagner–Meerwein rearrangement resulted in the formation of cyclic ether G. Oxidation state adjustments led to H, which was converted into arcutidine. The esters arcutinine and arcutine each proved accessible in one synthetic operation from arcutinidine.