General Strategy for Synthesis of C-19 Methyl-Substituted Sarpagine/Macroline/Ajmaline Indole Alkaloids Including Total Synthesis of 19(S),20(R)-Dihydroperaksine, 19(S),20(R)-Dihydroperaksine-17-al, and Peraksine


Total Synthesis of (+)-Dihydroperaksine-17-al, (+)-Dihydroperaksine, and (+)-Peraksine

Significance: The sarpagine alkaloids (+)-19(S),20(R)-dihydroperaksine-17-al, (+)-19(S),20(R)-dihydropraksine (both isolated from Rauwolfia serpentina) and (+)-peraksine (isolated from Rauwolfia perakensis) have in common the structural feature of a β-methyl group at C-19. Cook and co-workers report the first enantio- and stereospecific synthesis of all three alkaloids.

Comment: After introduction of the chiral methyl group by N-alkylation, the pentacyclic core was formed by haloboration followed by a palladium-catalyzed intramolecular α-vinylation of the ketone. Common intermediate F was then converted into (+)-peraksine, (+)-dihydroperaksine-17-al, and (+)-dihydropraksine by a specific acetal protection and hydroboration–oxidation sequence.