Total Synthesis of (−)-Quinine

Significance: Quinine is a cinchona alkaloid with potent antimalarial activity, which has drawn the attention of the synthetic community for decades. Employing a C–H activation strategy, Maulide and co-workers report an enantioselective total synthesis of quinine in ten steps and 5% overall yield.

Comment: A picolinamide directing group enabled introduction of an aryl group on the quinuclidine scaffold to afford B. Oxidative degradation of the anisole unit gave the corresponding carboxylic acid, which was further transformed into olefin D. An aldol reaction of E with aldehyde F followed by a two-step reduction of the ketone ultimately gave (−)-quinine.