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SYNFACTS Highlights in Current Synthetic Organic Chemistry

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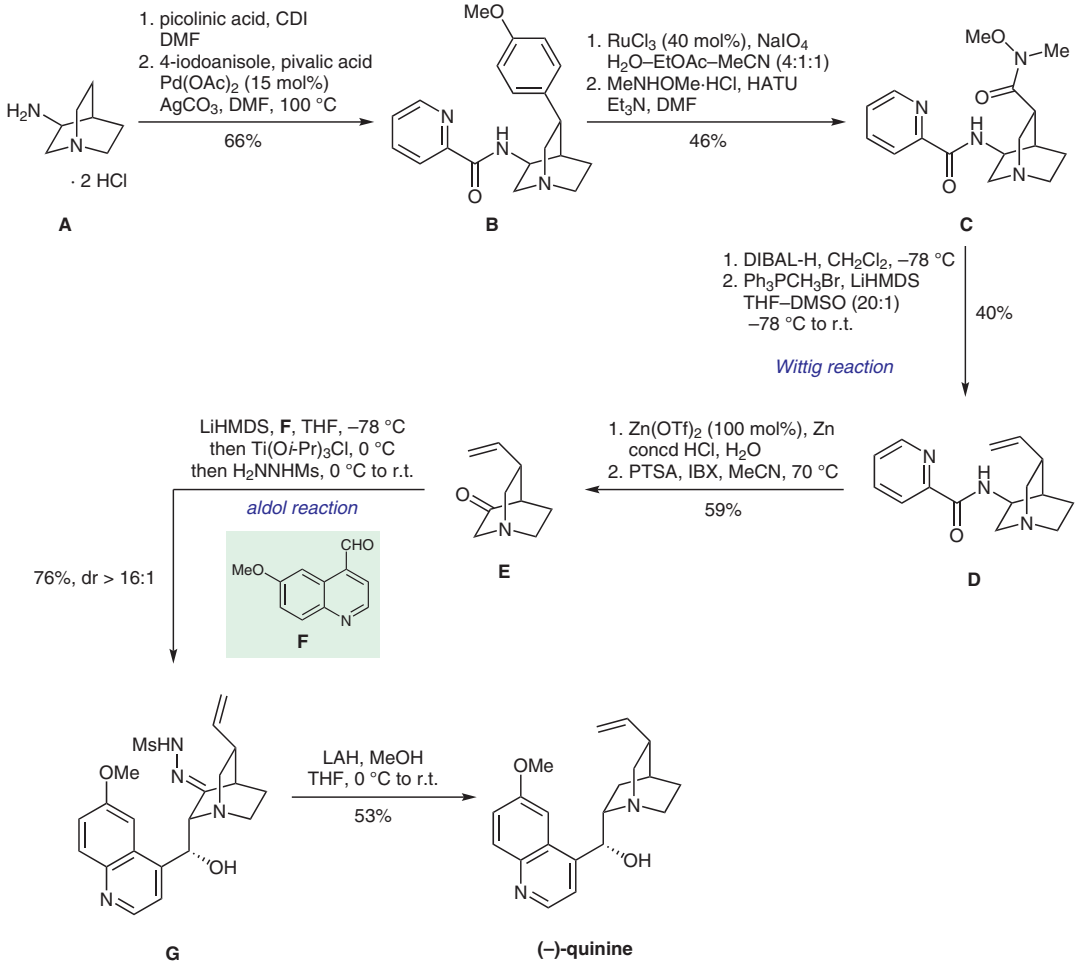
D. H. O'DONOVAN, P. AILLARD, M. BERGER, A. DE LA TORRE, D. PETKOVA, C. KNITTL-FRANK, D. GEERDINK, M. KAISER, N. MAULIDE* (UNIVERSITY OF VIENNA, AUSTRIA; UNIVERSITY OF BASEL AND SWISS TROPICAL AND PUBLIC HEALTH INSTITUTE, BASEL, SWITZERLAND; ASTRAZENECA, CAMBRIDGE, UK)

C–H Activation Enables a Concise Total Synthesis of Quinine and Analogues with Enhanced Antimalarial Activity
Angew. Chem. Int. Ed. **2018**, DOI: 10.1002/anie.201804551.

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.

SYNFACTS Contributors: Erick M. Carreira, Matthieu J. R. Richter
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Synthesis of Natural Products and Potential Drugs

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palladium catalysis
C–H activation