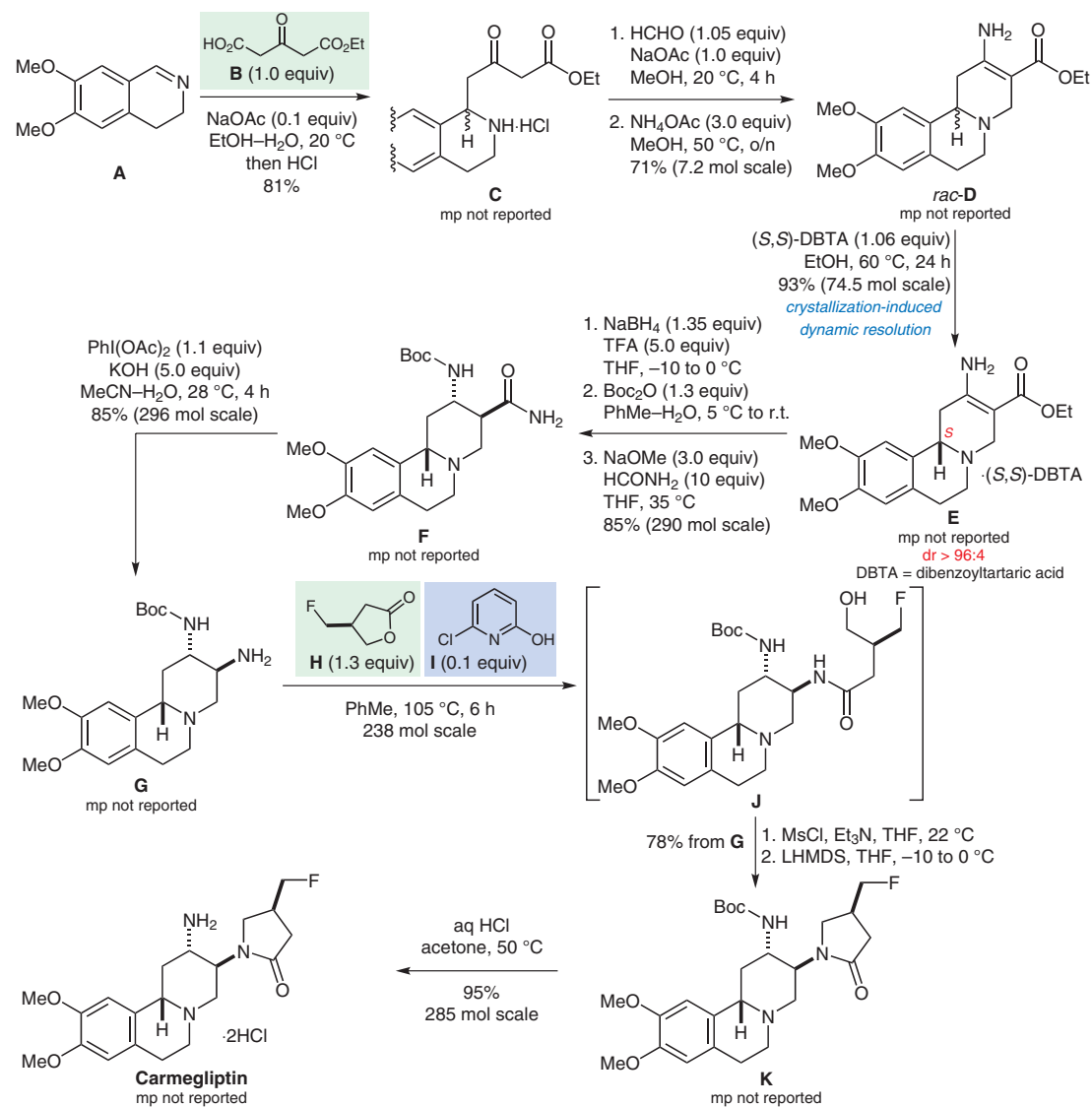


S. ABRECHT, J.-M. ADAM, U. BROMBERGER, R. DIODONE, A. FETTES,* R. FISCHER, V. GOECKEL, S. HILDBRAND, G. MOINE, M. WEBER (F. HOFFMANN-LA ROCHE LTD., BASEL, SWITZERLAND)

An Efficient Process for the Manufacture of Carmegliptin

Org. Process Res. Dev. **2011**, *15*, 503-514.

Synthesis of Carmegliptin



Significance: Carmegliptin is a dipeptidyl dipeptidase-IV inhibitor under development for the treatment of type-2 diabetes. Over 1000 kg was synthesized by the route depicted featuring an efficient crystallization-induced dynamic resolution of *rac-D* and a large-scale Hofmann rearrangement of the amide **F**.

SYNFACTS Contributors: Philip Kocienski
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Comment: J.-M. Adam et al. (*Org. Process Res. Dev.* **2011**, *15*, 515) describe the synthesis of lactone **H** by asymmetric hydrogenation (10 kg scale), but a route starting from commercial (*S*)-*tert*-butyl glycidyl ether (derived from a Jacobsen hydrolytic kinetic resolution) delivered >500 kg of **H**.

Category

Synthesis of Natural Products and Potential Drugs

Key words

carmegliptin
DPP-4 inhibitors
Mannich reaction
crystallization-induced dynamic resolution
Hofmann rearrangement

SYNFACTS
of the month