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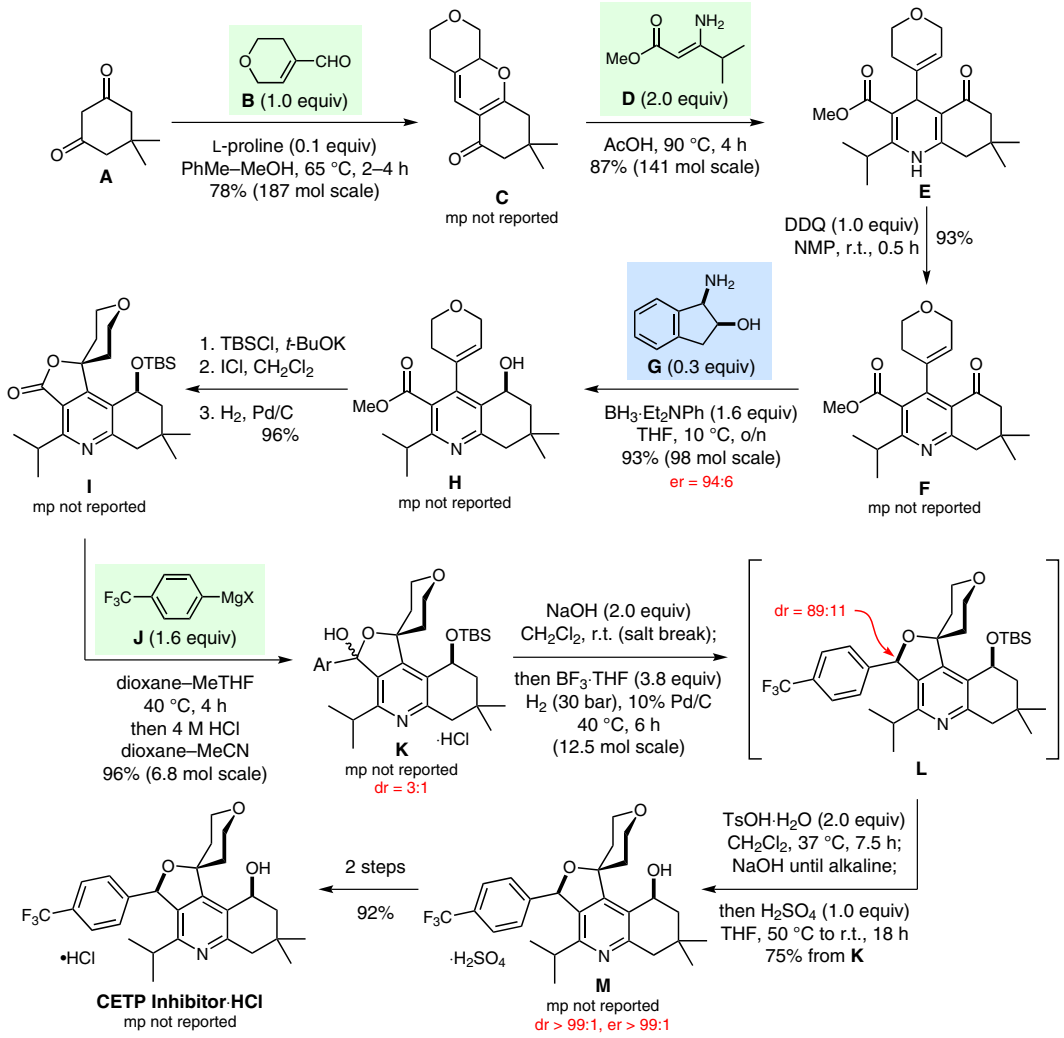
Facile Entry to an Efficient and Practical Enantioselective Synthesis of a Polycyclic Cholesteryl Ester Transfer Protein Inhibitor

Org. Lett. **2014**, *16*, 4142–4145.

Synthesis of a CETP Inhibitor



Significance: The target molecule is a cholesteryl ester transfer protein (CETP) inhibitor that is of interest for the treatment of atherosclerosis. Key steps in the synthesis depicted are (1) a highly efficient Hantzsch reaction leading to pyridine **I**, (2) an enantioselective reduction of the highly hindered ketone **F** using (1*R*,2*S*)-1-amino-2-indanol as a chiral chaperone and (3) a diastereoselective hydrogenation of the lactol **K**.

Comment: The asymmetric hydrogenation of ketone **F** using 0.01 mol% of the proprietary catalyst $RuCl_2$(MeO-BIBOP)–(Ampy) (S. Rodríguez et al. *Adv. Synth. Catal.* **2014**, *356*, 301) in isopropanol under 300 psi H_2 afforded **H** in 90% yield and with er > 99:1. The scale of the reaction is not specified nor is a detailed experimental procedure provided, whereas scale and experimental details are provided for the borane reduction depicted.

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SYNFACT of the month

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