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 (1R,2S)-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 RuCl₂(MeO-BIBOP)-(Ampy) (S. Rodríguez et al. Adv. Synth. Catal. 2014, 356, 301) in isopropanol under 300 psi H₂ 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.