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BOEHRINGER INGELHEIM PHARMA GMBH, BIBERACH/RISS AND INGELHEIM, GERMANY)
Facile Entry to an Efficient and Practical Enantioselective Synthesis of a Polycyclic Cholesteryl Ester Transfer
Protein Inhibitor
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Synthesis of a CETP Inhibitor

Category

Synthesis of Natural
Products and
Potential Drugs

Key words

CETP inhibitors

Hantzsch pyridine
synthesis

asymmetric ketone
reduction

diastereoselective
lactol
hydrogenation

SYNFACT
of the month

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 $\text{RuCl}_2(\text{MeO-BIBOP})\text{-(Ampy)}$ (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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