

Synthesis of the Indole Core of MK-3281

Category

Synthesis of Natural Products and Potential Drugs

Key words

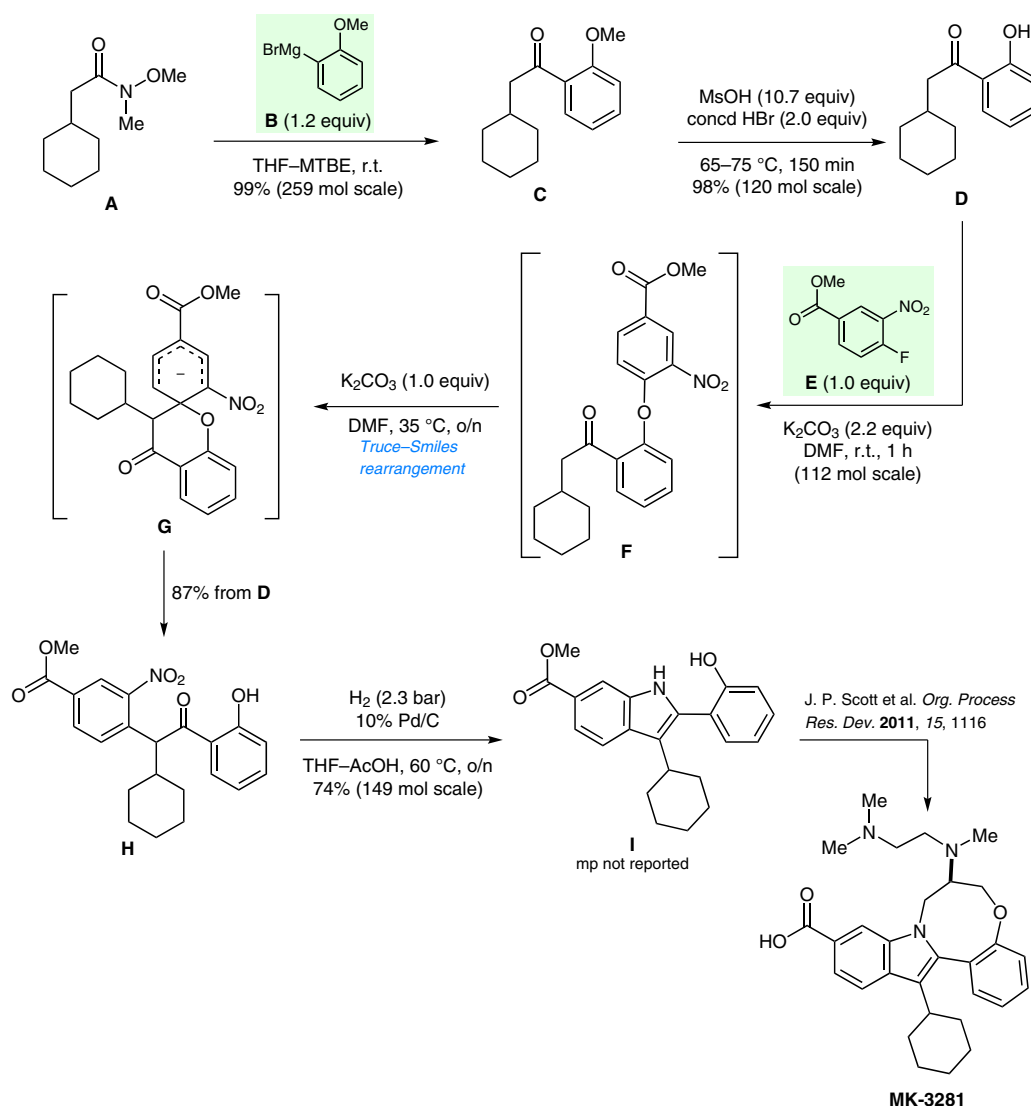
MK-3281

RNA polymerase NS5B inhibitor

indole ring synthesis

Truce–Smiles rearrangement

SYNFACT
of the month



Significance: MK-3281 inhibits hepatitis C RNA polymerase NS5B. A synthesis starting from the indole fragment **I** was recently described: J. P. Scott et al. *Org. Process Res. Dev.* **2011**, *15*, 1116. In this paper a large scale synthesis of the MK-3281 fragment **I** is described that features a Truce–Smiles rearrangement.

Comment: The highly telescoped synthesis of the indole fragment **I** depicted was accomplished on a >50 kg scale and delivered the target indole in 55% overall yield in five steps. All of the yields are assay yields. For the discovery synthesis of MK-3281, see: F. Narjes et al. *J. Med. Chem.* **2011**, *54*, 289.