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An Efficient Process for the Large-Scale Synthesis of a 2,3,6-Trisubstituted Indole


Synthesis of the Indole Core of MK-3281

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.