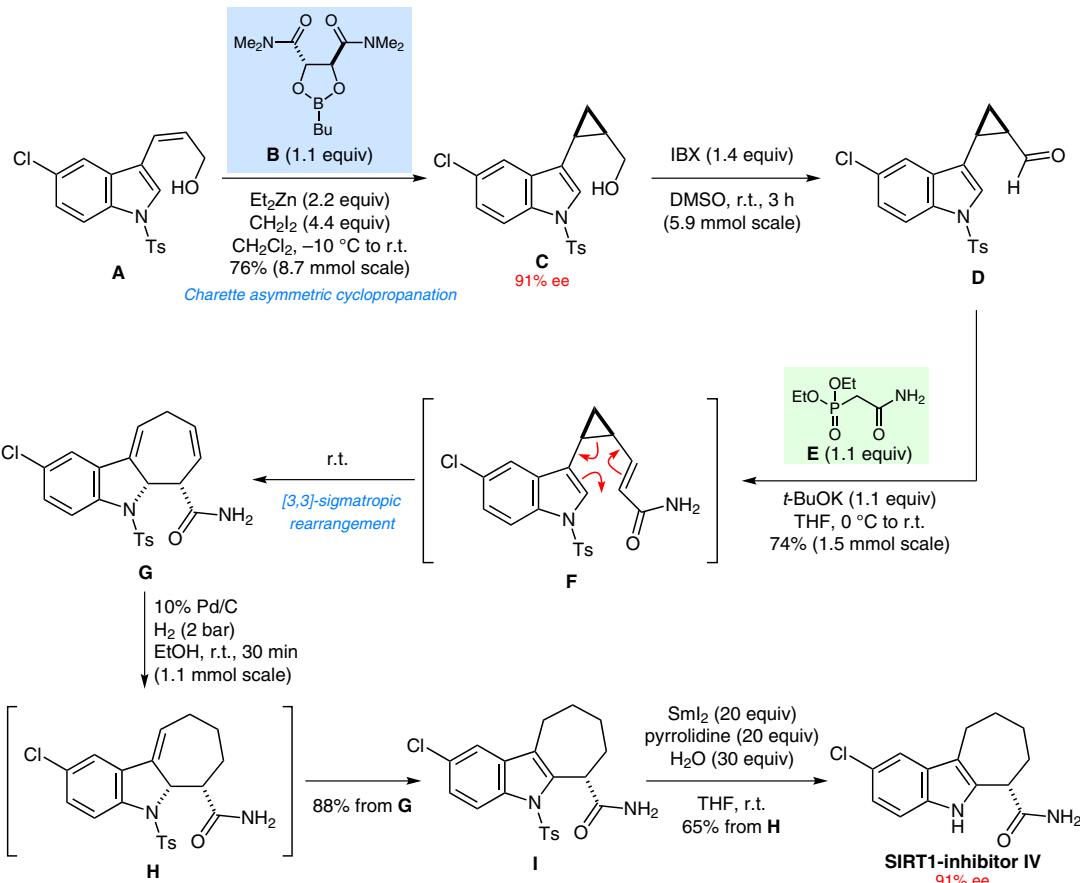


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Enantioselective Synthesis of Cyclohepta[b]indoles: Gram-Scale Synthesis of (S)-SIRT1-Inhibitor IV
Org. Lett. **2013**, *15*, 5472–5475.

Synthesis of a SIRT1 Inhibitor



Significance: SIRT1 deacetylates the p53 tumor suppressor protein, a key transcriptional regulator of genes involved in cell cycle regulation, apoptosis, and DNA repair. The target molecule is a potent SIRT1 inhibitor. The key step in the synthesis of the (S)-enantiomer depicted is the stereospecific [3,3]-sigmatropic rearrangement of the divinylcyclopropane intermediate **F** derived from aldehyde **D** via a Horner–Wadsworth–Emmons (HWE) reaction.

Comment: Twelve examples of the HWE-[3,3]-sigmatropic rearrangement cascade leading to cyclohepta[b]indoles are described. The temperature required for the [3,3]-sigmatropic rearrangement varies from room temperature to 140 °C, depending on the structure of the indole divinylcyclopropane. For an earlier synthesis of the racemic target and its chiral HPLC resolution, see: A. D. Napper et al. *J. Med. Chem.* **2005**, *48*, 8045.