Synthesis of an Inhibitor of Histone Lysine Demethylases KDM2/7

**Significance:** The target molecule **M** is a first-in-class highly selective cell-active inhibitor of the histone lysine demethylases KDM2/7 that are involved in epigenetic gene expression. In total 45 racemic N-acyl indoline derivatives were prepared, from which the enantiomers of **M** were selected for further evaluation.

**Comment:** Synthesis of the indoline (S,S)-**H** entails treatment of the N-aryl imine **F** with cesium hydroxide under phase-transfer conditions in the presence of the quinine-derived salt **G** (0.1 equiv). A delocalized 2-aza-pentadienyl anion is generated that undergoes 6π electrocyclization in 89% yield (dr = 10:1, er = 88:12). Preparative chiral HPLC then delivered **H** with dr > 20:1 and er > 99:1. For details on the asymmetric electrocyclization, see: E. E. Maciver, S. Thompson, M. D. Smith Angew. Chem. Int. Ed. 2009, 48, 9979.)