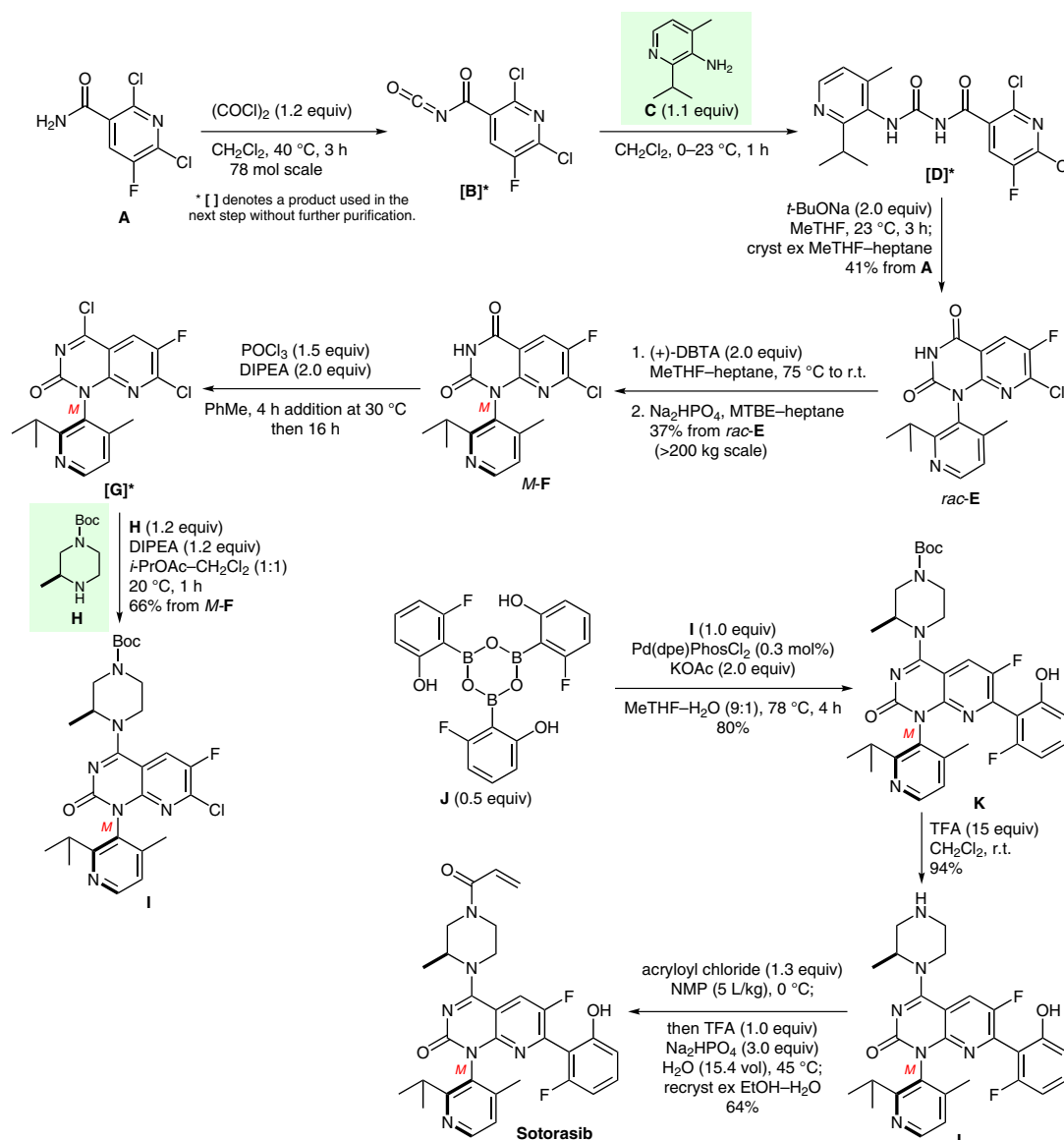


# Synthesis of Sotorasib



**Significance:** Sotorasib (AMG 510, Lumakras) is the first ever FDA-approved drug that inhibits KRAS, a cancer target that has been termed “undruggable” even after over 40 years of cancer research. It was approved for KRAS G12C-mutated non-small cell lung cancer (NSCLC).

**Comment:** Urea **D** cyclized to give *rac*-dione **E** as a mixture of atropisomers in 41% yield over three steps. Chiral separation via the (+)-2,3-dibenzoyl-D-tartrate salt of *rac*-dione **E** led to M-dione **M-F** in 37% yield over two steps. For experimental details, see: WO 2021 097207 A1 and WO 2020 232130 A1.