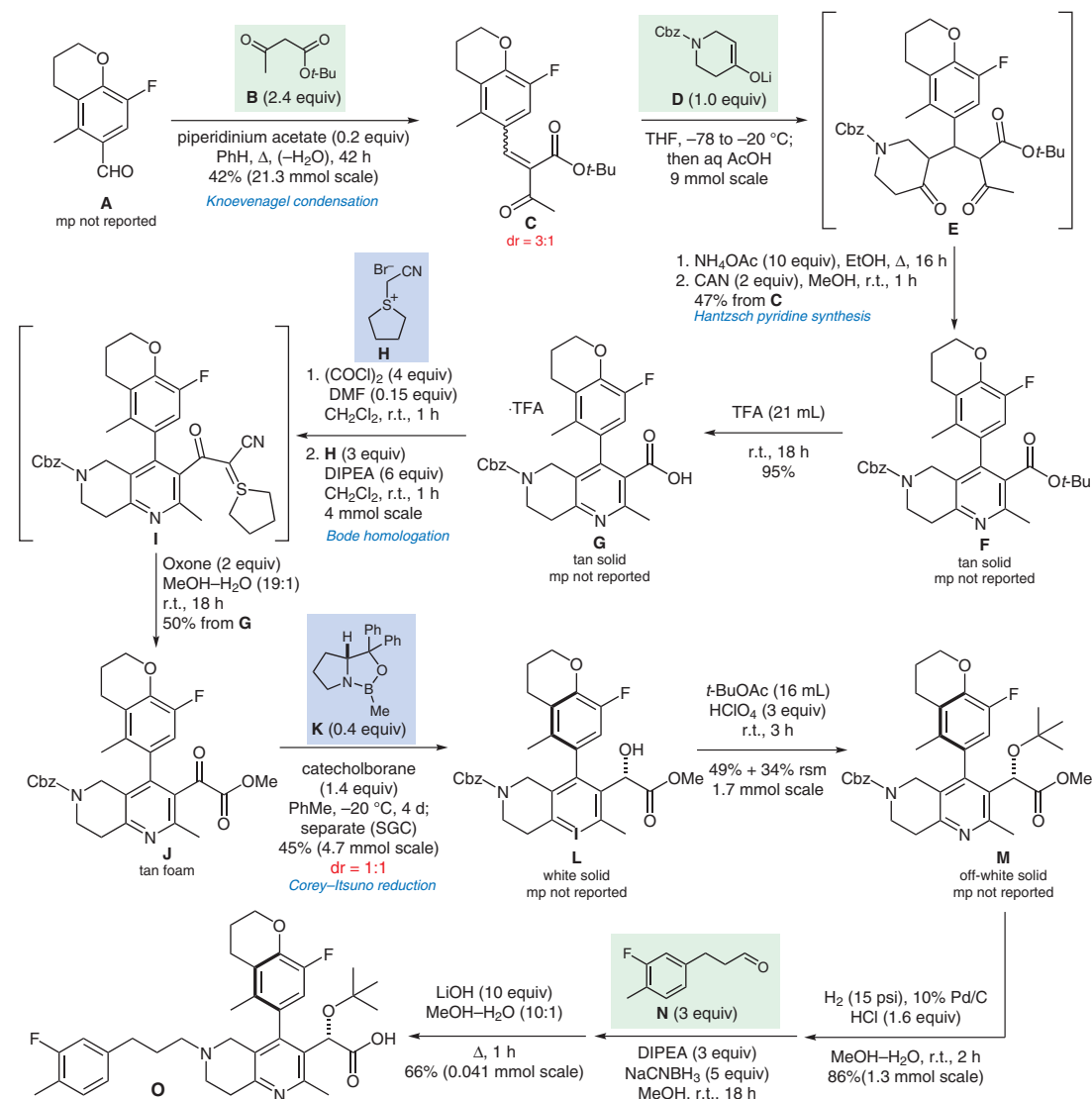


## Synthesis of an HIV-1 Integrase Allosteric Site Inhibitor



**Significance:** Tetrahydronaphthyridine **O** inhibits HIV-1 integrase, one of the three enzymes encoded in the HIV-1 genome required for viral replication. A noteworthy step in the small-scale synthesis depicted is the Bode homologation of carboxylic acid **G** to  $\alpha$ -keto ester **J** via sulfur ylide **I** (L. Ju, A. R. Lippert, J. W. Bode *J. Am. Chem. Soc.* **2008**, *130*, 4253).

**Comment:** Corey-Itsuno asymmetric reduction of  $\alpha$ -keto ester **J** gave a 1:1 mixture of diastereoisomers from which the desired atropisomer **L** was isolated in 45% yield by column chromatography and crystallization. Tetrahydronaphthyridine **F** was constructed in four steps in 20% overall yield using a Hantzsch pyridine synthesis.