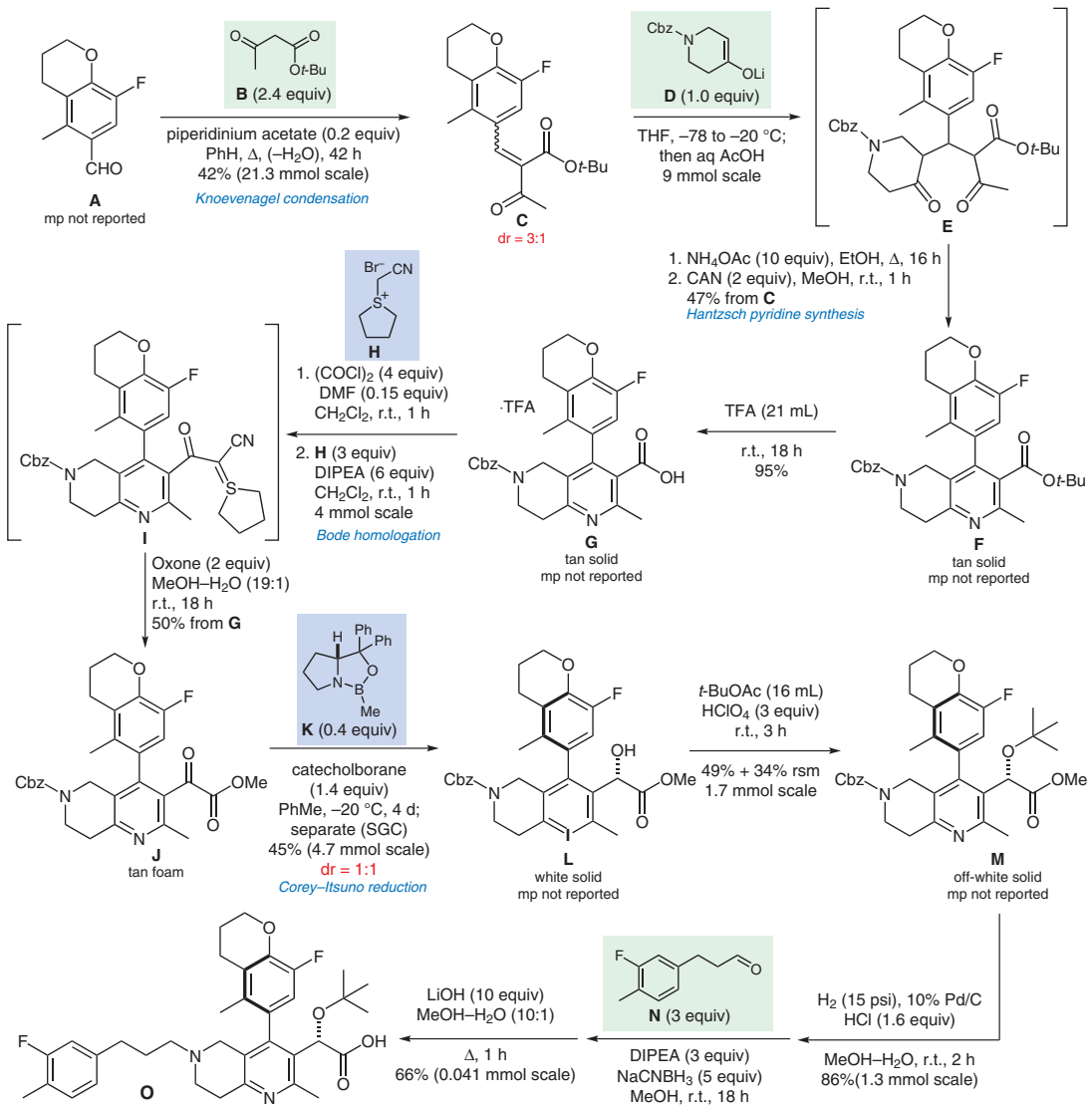
K. M. PEESE* ET AL. (BRISTOL-MYERS SQUIBB RESEARCH & DEVELOPMENT, WALLINGFORD AND GLAXOSMITHKLINE, COLLEGEVILLE, USA)

5,6,7,8-Tetrahydro-1,6-naphthyridine Derivatives as Potent HIV-1-Integrase-Allosteric-Site Inhibitors
J. Med. Chem. **2019**, *62*, 1348–1361.

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 markworthy step in the small-scale synthesis depicted is the Bode homologation of carboxylic acid **G** to α-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 α-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.

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Synfacts 2019, 15(04), 0333 Published online: 19.03.2019
DOI: 10.1055/s-0037-1612292; **Reg-No.:** K00419SF