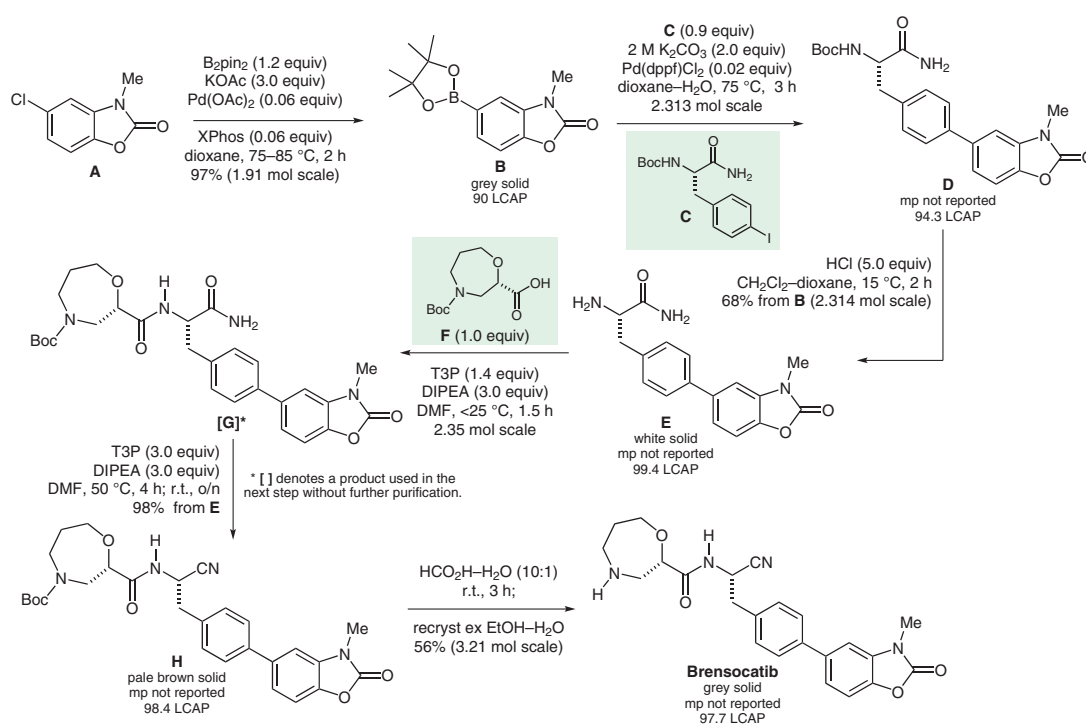
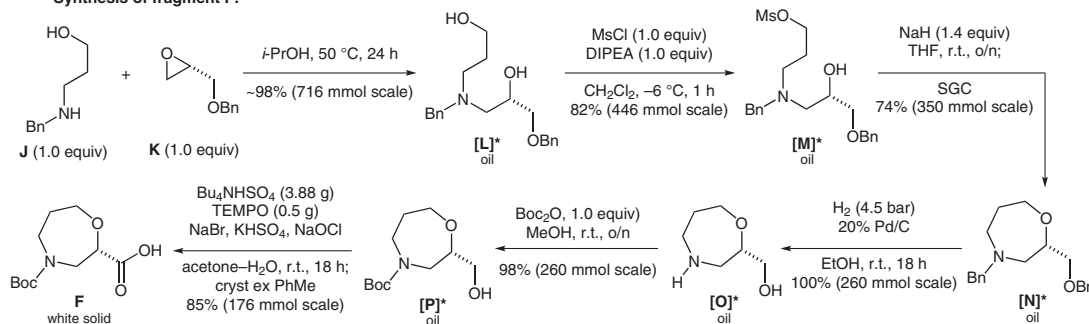


Synthesis of Brensocatib (AZD7986)



Synthesis of fragment F:



Significance: Cathepsin C (CatC) is a cysteine dipeptidyl amino-peptidase that activates most tissue-degrading elastase-related serine proteases. The highlighted paper describes the discovery of brensocatib (AZD7986), a CatC inhibitor. Brensocatib is now a clinical candidate to impair protease-driven tissue degradation in COVID-19 (B. Korkmaz, A. Lesner, S. Marchand-Adam, C. Moss, D. E. Jenne *J. Med. Chem.* **2020**, *63*, 13258).

Comment: While the paper includes some synthetic details, the potential manufacturing route depicted is taken from an earlier patent (WO 2015 110826 A1). The notable feature is the one-pot amidation (**E** → **G**) and amide dehydration reactions (**G** → **H**) used to construct the amidoacetonitrile moiety.