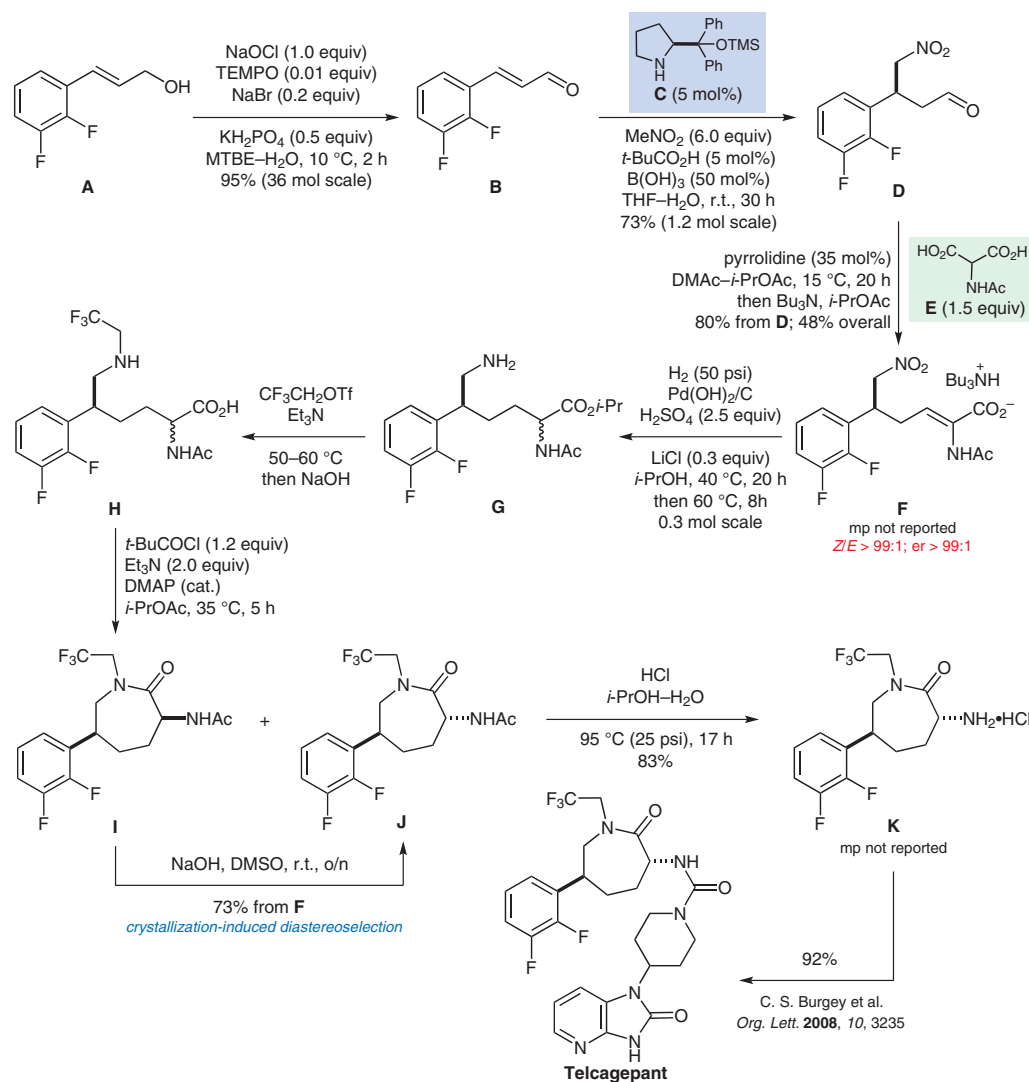


# Synthesis of Telcagepant



**Significance:** Telcagepant is a selective antagonist of calcitonin gene related peptide (CGRP) that is in phase clinical trials for the treatment of migraine. The synthesis featured an enantioselective 1,4-addition of nitromethane, which is the first application of iminium organocatalysis (**B** → **D**) on an industrial scale and a highly stereoselective Doebner–Knoevenagel condensation that created the enamide **F**.

**Comment:** The formation of desfluoro impurities that accompanied the hydrogenation of **F** was minimized by conducting the reaction in the presence of LiCl. The mixture of caprolactams **I** and **J** (2:1) was converted into pure **J** by crystallization-induced diastereoselection. The synthesis was accomplished in 27% overall yield and involved only three isolated crystalline intermediates (**F**, **J** and **K**).