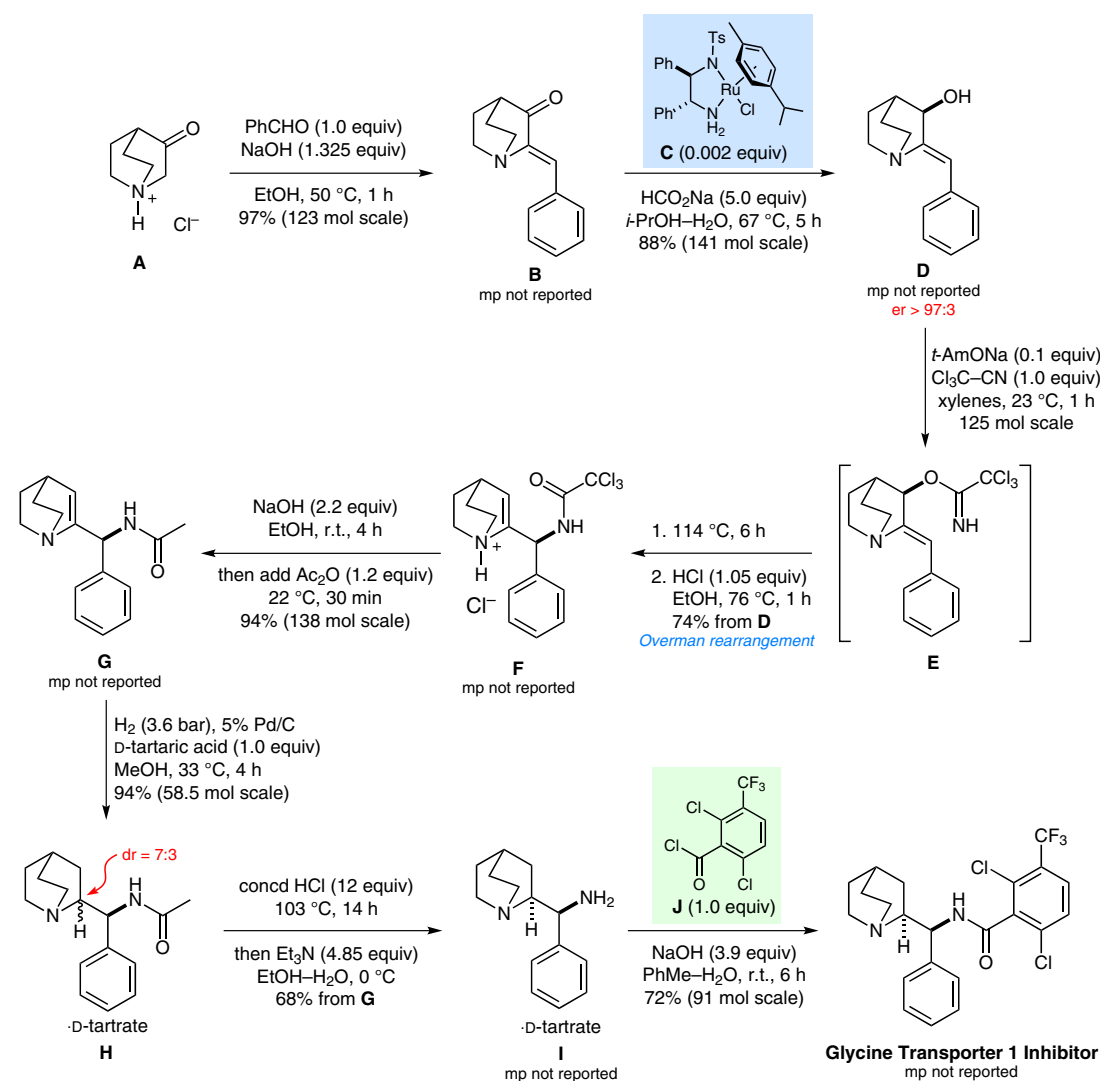


Synthesis of a Glycine Transporter 1 Inhibitor



Significance: The target glycine transporter 1 (GlyT1) inhibitor was of interest for the treatment of schizophrenia and acute manic disorders. Key steps in the synthesis were (1) a Noyori asymmetric transfer hydrogenation (**B** \rightarrow **D**), and (2) an Overman rearrangement by which allylic alcohol **D** was converted into the allylic amide **F**. This is the first example of a multikilogram scale-up of an Overman rearrangement.

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Comment: The eight-step synthesis depicted proceeded in 20% overall yield and delivered 24.2 kg of API. The initial isolated material was an undesired polymorph, but simply suspending the solid in water and heating to 55 $^{\circ}\text{C}$ for two hours resulted in smooth conversion into the desired polymorph.