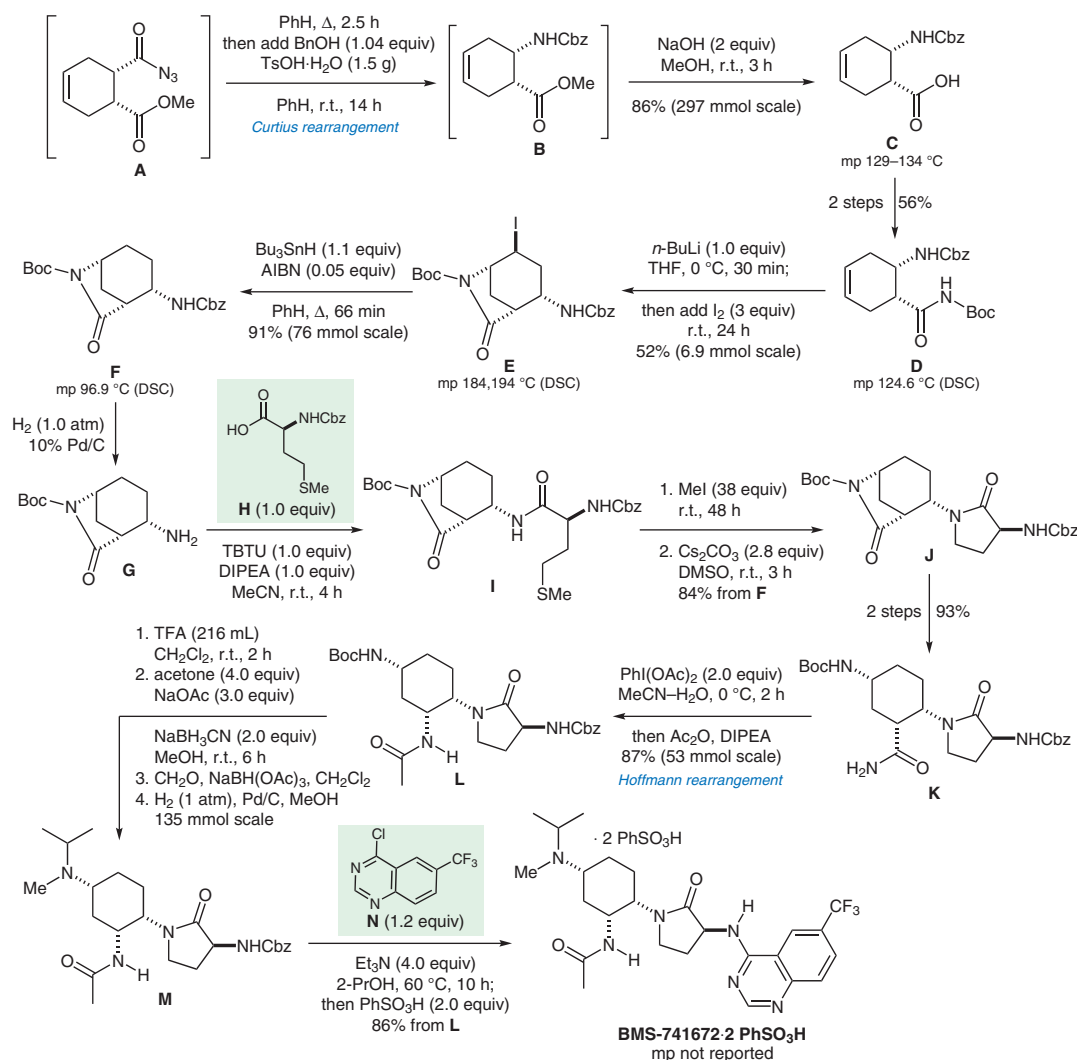


Synthesis of BMS-741672



Significance: BMS-741672 is a chemotactic chemokine receptor 2 (CCR2) antagonist that is of interest for the treatment of inflammatory, cardiovascular, and metabolic diseases. The discovery synthesis depicted (>20 steps) is based on construction of the all-*cis* 1,2,4-triaminocyclohexane core using a Curtius rearrangement (**A** \rightarrow **B**), an iodolactamization (**D** \rightarrow **E**), and a Hoffman rearrangement (**K** \rightarrow **L**).

Comment: The synthesis of lactam **G** was previously developed by Bristol-Myers Squibb (C. L. Campbell et al. *J. Org. Chem.* **2009**, *74*, 6368), and a shorter large-scale route to BMS-741672 was subsequently reported that delivered 50 kg of API for clinical evaluation (J. Deerberg et al. *Org. Process Res. Dev.* **2016**, *20*, 1949).