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Development of a Scalable Synthesis for an Inhaled pan-JAK Inhibitor
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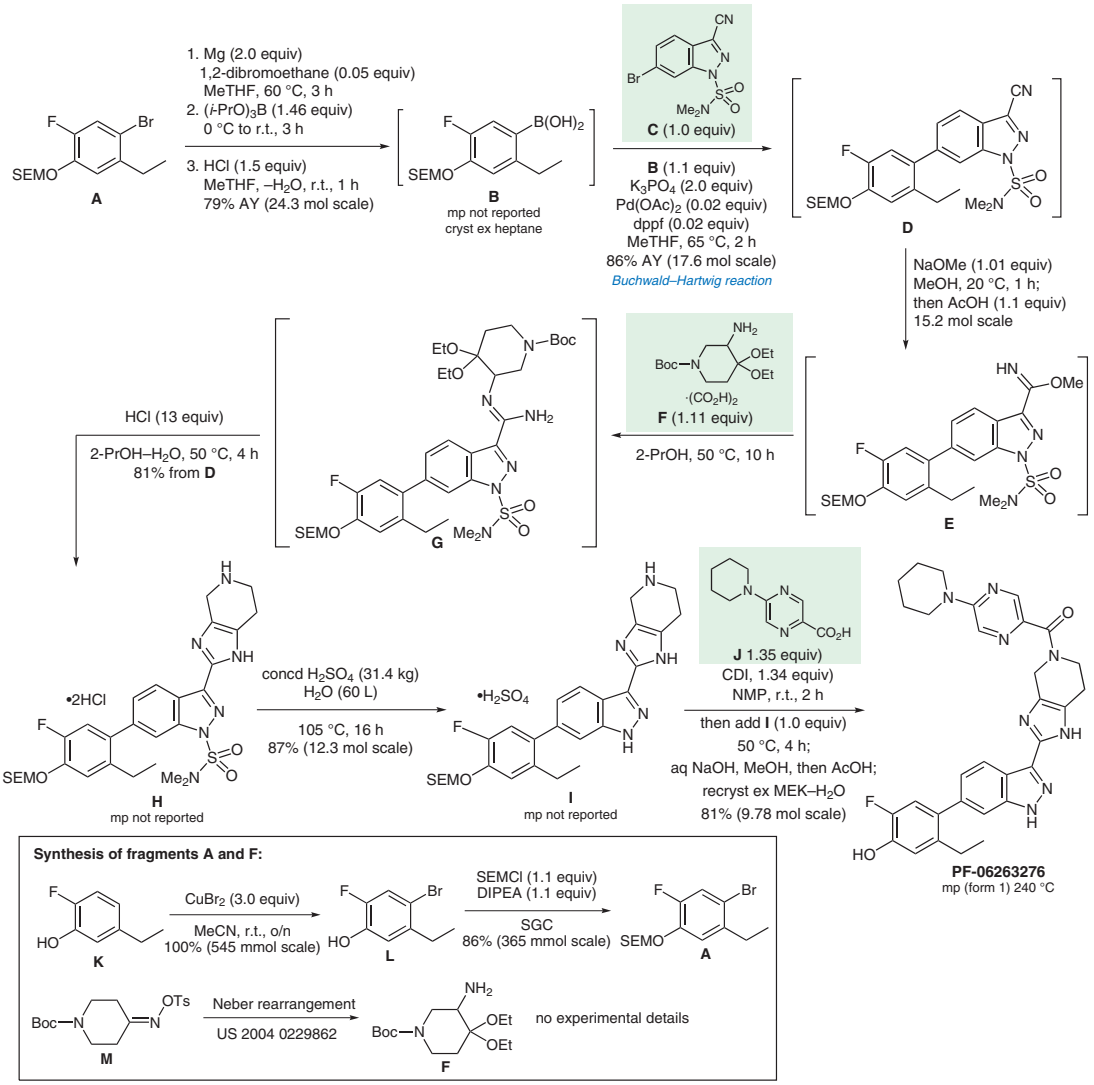
Synthesis of pan-JAK Inhibitor PF-06263276



Significance: PF-06263276 is a pan-Janus kinase inhibitor that is of interest for the treatment of inflammatory diseases. The synthesis depicted is a telescoped variant of the discovery synthesis (P. Jones et al. *J. Med. Chem.* **2017**, *60*, 767). A notable feature is the three-step conversion of nitrile **D** into crystalline imidazole dihydrochloride **H** in 81% yield.

Comment: The dimethylsulfamoyl protecting group on indazole **D** served two purposes. It enhanced the electrophilicity of the nitrile group, and it increased the stability of the imidate **E**. Unfortunately, hydrolysis of the dimethylsulfamoyl group required 35% aqueous sulfuric acid at 105 °C for sixteen hours.

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Category

Synthesis of Natural Products and Potential Drugs

Key words

PF-06263276

Suzuki–Miyaura cross-coupling

imidazole ring formation

amidation

dimethylsulfamoyl protecting group

Synfact of the Month