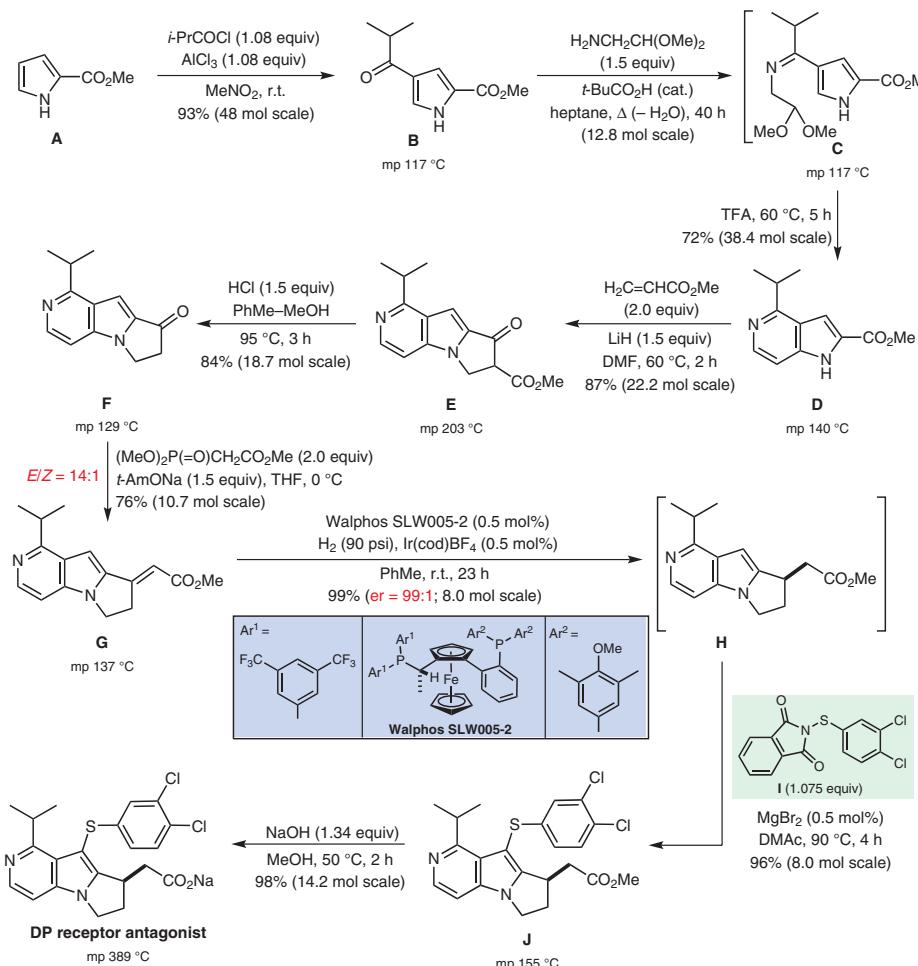


Category
Synthesis of Natural Products and Potential Drugs

Synthesis of Prostaglandin D₂ Receptor Antagonist



Significance: An efficient kilogram-scale synthesis of the target prostaglandin D₂ receptor antagonist features a Friedel–Crafts cyclization of an iminopyrrole to generate the azaindole core in **D**. Key steps are (1) a very efficient asymmetric hydrogenation to install the single stereogenic center (**G** → **H**) and (2) a mild sulfenylation using the shelf-stable *N*-arylthiophthalimide **I**.

Comment: The higher of the hydrogenation was surprisingly insensitive to solvent, but it was sensitive to the *E/Z* ratio. Thus, batches of **G** that contained 9% of the *Z*-isomer afforded **H** in only 81% ee, whereas batches of **G** containing 1% of the *Z*-isomer gave **H** in 96% ee. The *E/Z* ratio of the Horner–Wadsworth–Emmons reaction (14:1) could be upgraded to 1000:1 by crystallizing the phosphate salt of **G**.