Synthesis of Prostaglandin D<sub>2</sub> Receptor Antagonist

**Significance:** An efficient kilogram-scale synthesis of the target prostaglandin D<sub>2</sub> 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 (<sup>99</sup>% ee) and (2) a mild sulfenylation using the shelf-stable S-aryltiodoimidate I.

**Comment:** The high <i>er</i> of the hydrogenation was surprisingly insensitive to solvent, but it was sensitive to the <i>E/Z</i> 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 <i>E/Z</i> ratio of the Horner–Wadsworth–Emmons reaction (14:1) could be upgraded to 1000:1 by crystallizing the phosphate salt of G.

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**Synfacts** 2010, 10, 1095-1095  Published online: 22.09.2010  DOI: 10.1055/s-0030-1258073; Reg-No.: K06810SF

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**Key words**
- prostaglandin D<sub>2</sub> receptor antagonists
- pyridine annulation
- azaindoles
- sulfenylation
- asymmetric hydrogenation