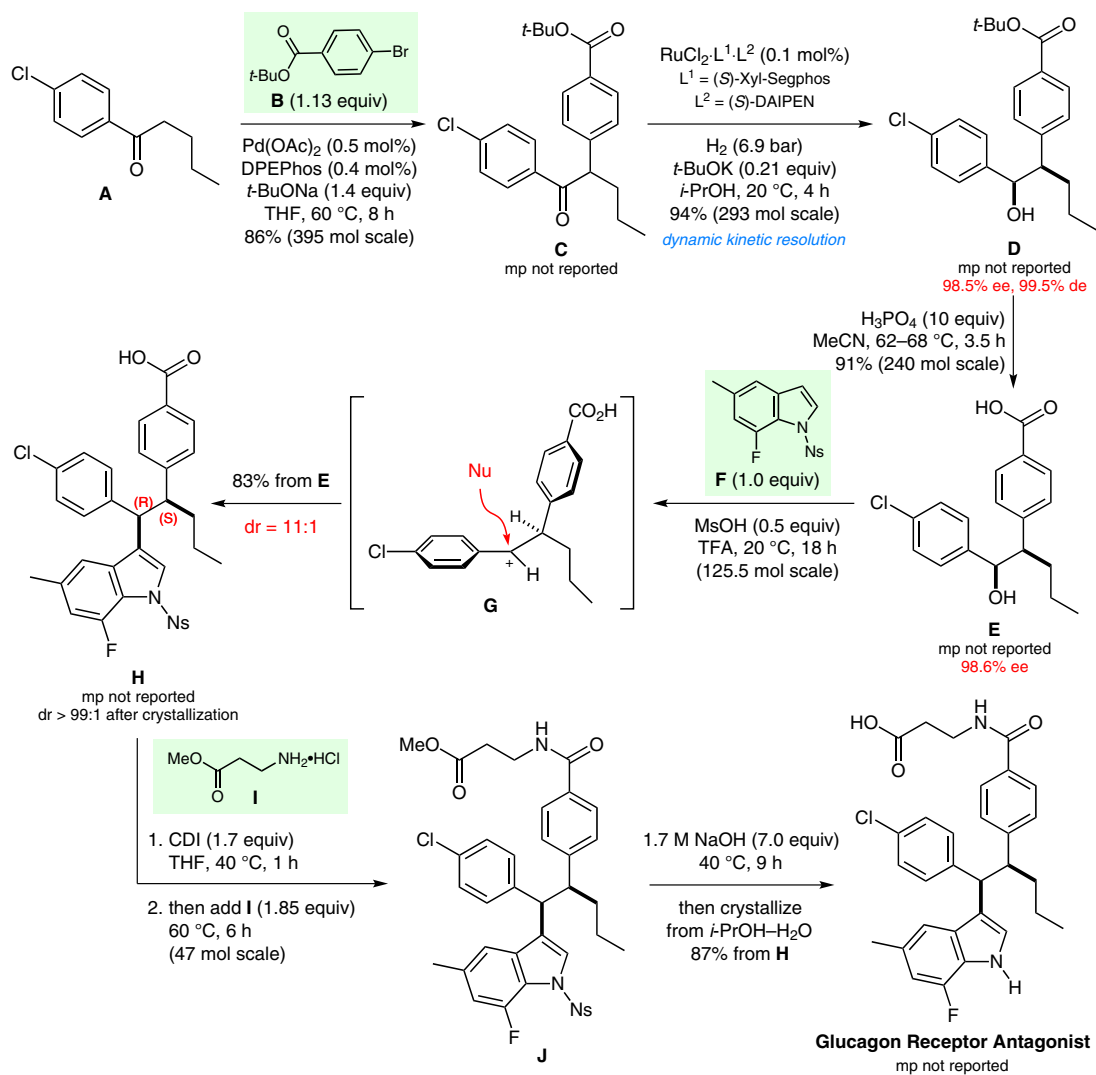


## Synthesis of a Glucagon Receptor Antagonist



**Significance:** The target glucagon receptor antagonist is a candidate for the treatment of type 2 diabetes. Key steps in the synthesis of the sterically congested 1,1,2-triarylalkane core are (1) the asymmetric Noyori hydrogenation of ketone **C** involving a dynamic kinetic resolution and (2) the *anti*-selective Friedel–Crafts alkylation of the fluoroindole **F** by chiral benzylic carbocation **G**.

**Comment:** Optimal Friedel–Crafts diastereoselectivity and yield were achieved with nosyl-protected indole **F** using TFA as solvent and catalytic MsOH. A highly efficient, large-scale Larock-type synthesis of fluoroindole **F** from 2-bromoaniline was also developed. For the stereochemistry of the *anti*-selective Friedel–Crafts alkylation, see: J. Y. L. Chung et al. *Org. Lett.* 2008, 10, 3037.