Synthesis of PF-03463275

**Significance:** PF-03463275 is a glycine transporter type 1 (GlyT1) inhibitor that has potential for the treatment of schizophrenia. The synthesis depicted features the first kilogram-scale application of iridium-catalyzed hydrogen borrowing to achieve the operational equivalent of reductive amination in the union of C and D to give E. The only byproduct of the reaction is water.

**Comment:** An extensive optimization study achieved a S/C of ≥2000 (i.e. lower than 0.05 mol% of catalyst), but the reaction tended to stall thereby requiring a second charge of catalyst. After this work was complete the authors discovered that water and a tertiary amine are essential for high catalyst activity resulting in high rates and complete conversion on a single charge.