Synthesis of MK-8831

**Significance:** A Merck team has devised a route to HCV NS3/4a protease inhibitors containing a spirocyclic proline core. Optimization of the structure–activity relationships resulted in the identification of the clinical candidate MK-8831 with excellent pan-genotypic activity and safety profile.

**Comment:** Ketone \( \text{F} \) was cyclized with the previously reported macrocyclic prolinone \( \text{G} \) employing benzoic acid and pyrrolidine. Initial conditions gave very poor yields, but the optimized methods gave spirocycle \( \text{H} \) in 50% yield and high levels of diastereoselectivity (dr = 99:1).