Synthesis of HCV Protease Inhibitor MK-6325

Significance: MK-6325 is a potent HCV NS3/4A protease inhibitor. The construction of the daunting bis-macrocyclic structure was accomplished by a ring-closing metathesis (RCM) to forge the 15-membered macrocycle followed by an intramolecular Suzuki–Miyaura cross-coupling to append the 18-membered macrocycle.

Comment: The route depicted delivered multikilogram quantities of the MK-6325. Construction of fragment D was achieved using (1) a Novozyme 435 resolution with succinic anhydride and (2) an iridium-catalyzed hydroboration. CataCXium A (G) was superior to all other ligands evaluated for the Suzuki–Miyaura reaction.