H. LI,* J. P. SCOTT* ET AL. (MERCK RESEARCH LABORATORIES, RAHWAY, USA AND MERCK SHARP & DOHME RESEARCH LABORATORIES, HODDESDON, UK)
Synthesis of Bis-Macrocyclic HCV Protease Inhibitor MK-6325 via Intramolecular sp^2–sp^3 Suzuki–Miyaura Coupling and Ring Closing Metathesis
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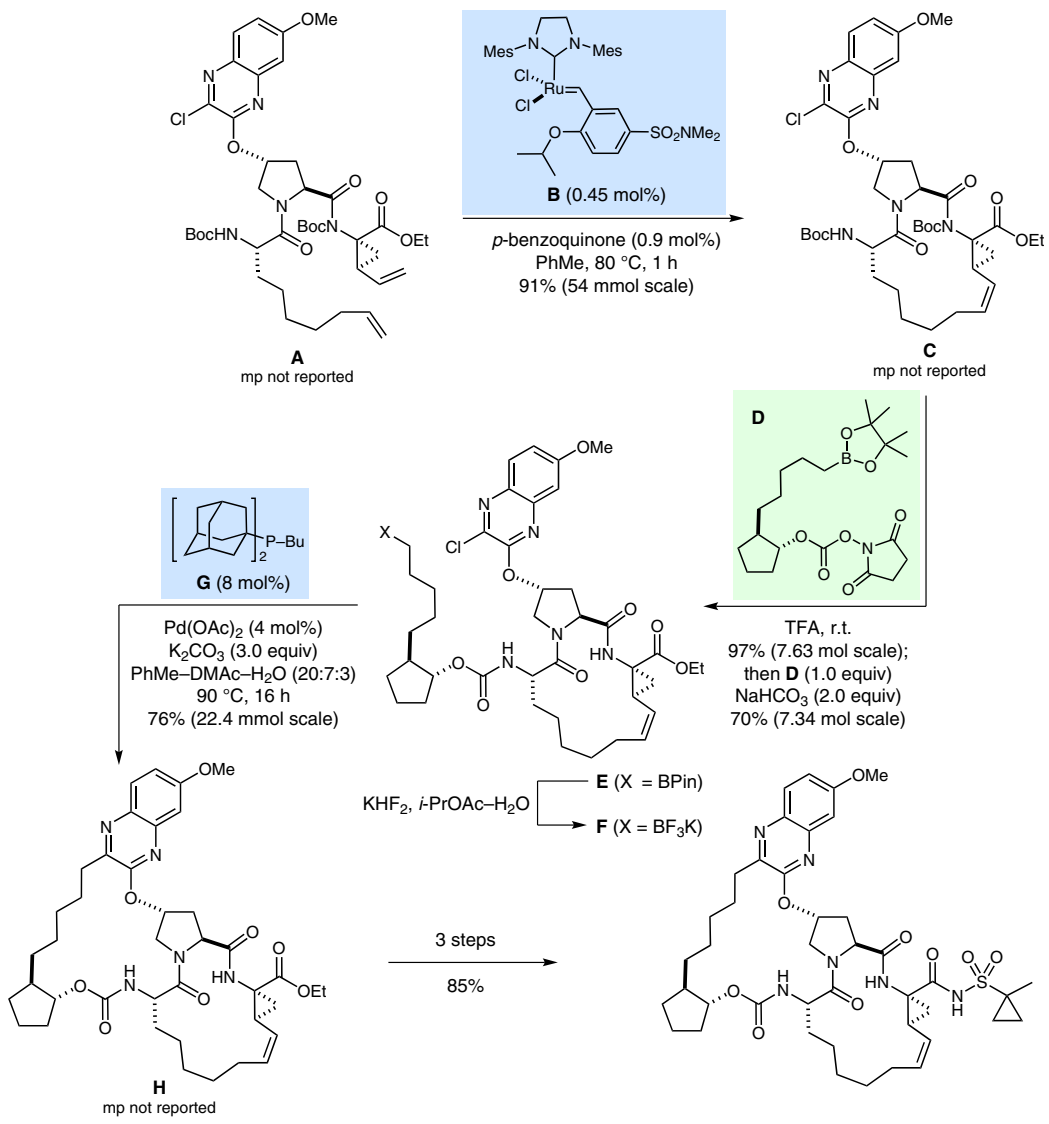
Synthesis of HCV Protease Inhibitor MK-6325



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.

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Category
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Key words
MK-6325
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macrocyclization

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