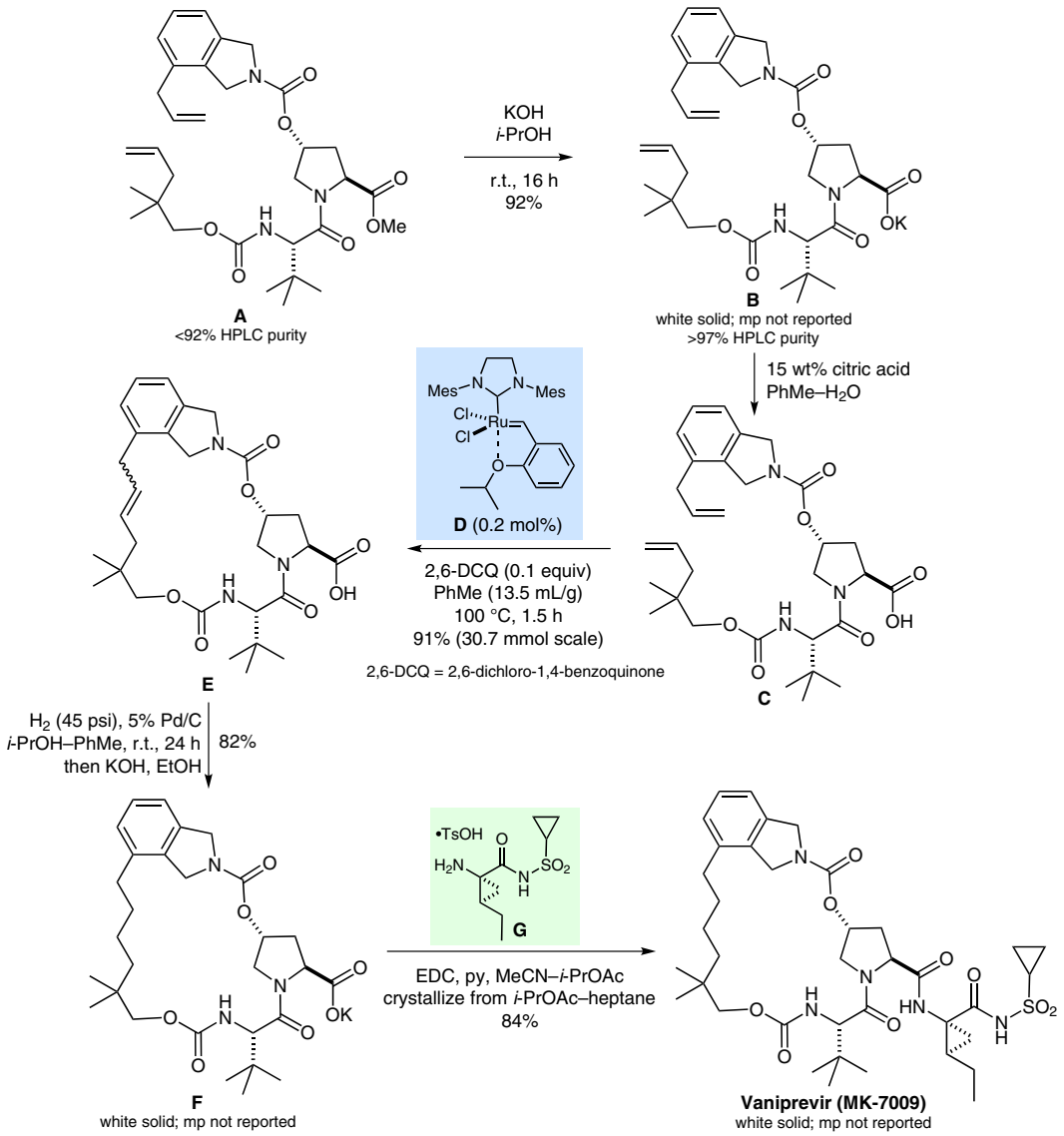
J. KONG,* C.-Y. CHEN,* J. BALSELLS-PADROS, Y. CAO, R. F. DUNN, S. J. DOLMAN, J. JANEY, H. LI, M. J. ZACUTO (MERCK RESEARCH LABORATORY, RAHWAY, USA)
Synthesis of the HCV Protease Inhibitor Vaniprevir (MK-7009) Using Ring-Closing Metathesis Strategy
J. Org. Chem. **2012**, *77*, 3820–3828.

Synthesis of Vaniprevir



Significance: The key step in this synthesis of vaniprevir is the construction of the macrocycle (91% yield) via ring-closing metathesis (RCM). By using simultaneous slow addition of the substrate and the catalyst **D** (0.2 mol%), the RCM reaction could be conducted at high concentration (0.13 M) on a 100 g scale.

Comment: 2,6-Dichloro-1,4-benzoquinone was added to suppress isomerization of the allyl alkene in the isoindoline unit in **C** and consequent competing formation of a 19-membered ring by-product. An important contributor to the success of the RCM reaction was the high purity of crystalline **B**.

SYNFACTS Contributors: Philip Kocienski
Synfacts 2012, 8(7), 0693 Published online: 19.06.2012
DOI: 10.1055/s-0031-1290413; **Reg-No.:** K03112SF

Category

Synthesis of Natural Products and Potential Drugs

Key words

vaniprevir

MK-7009

HCV protease inhibitors

ring-closing metathesis

macrocyclization

SYNFACT of the month