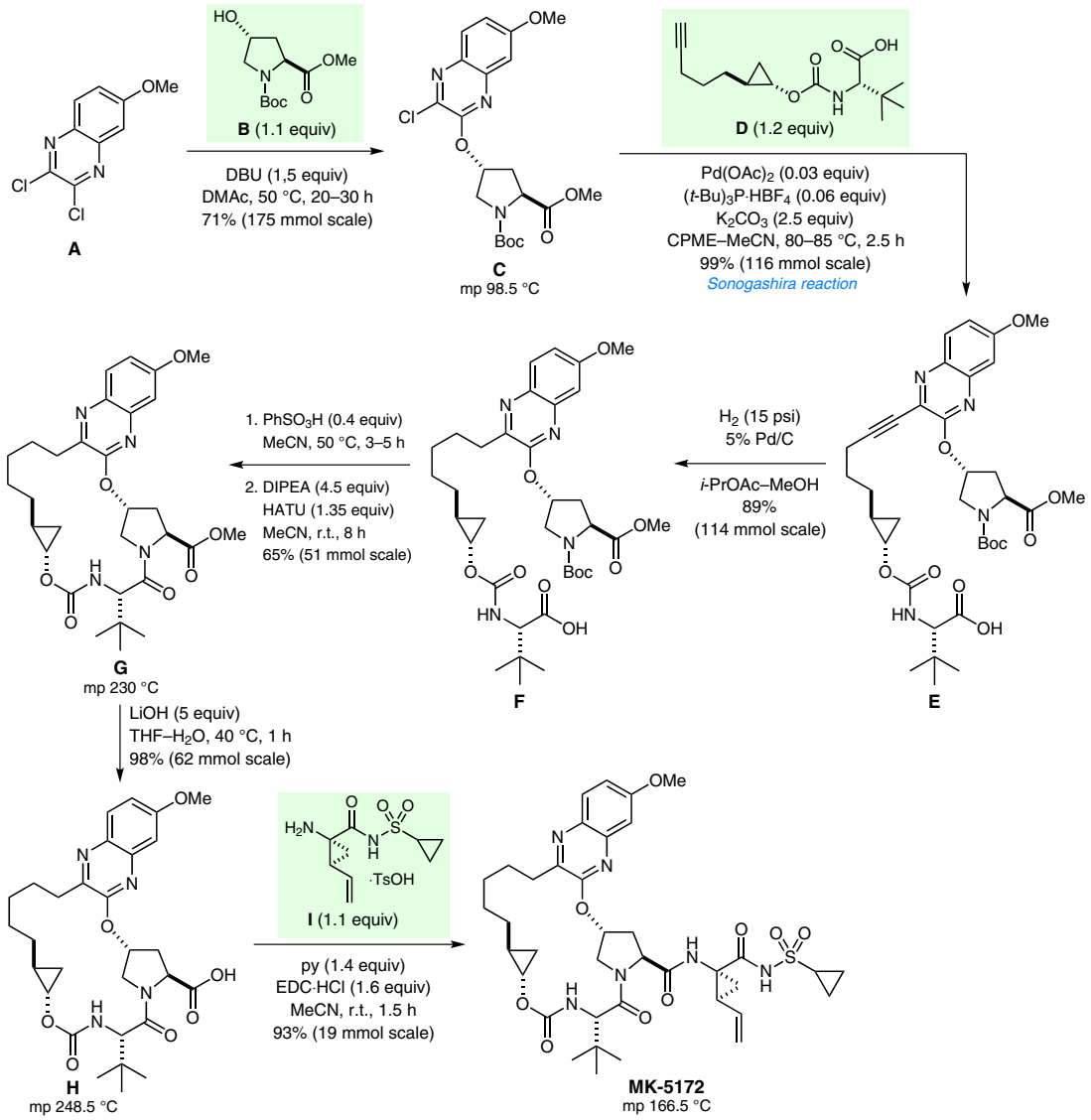
J. KUETHE,* Y.-L. ZHONG,* N. YASUDA,* G. BEUTNER, K. LINN, M. KIM, B. MARCUNE, S. D. DREHER, G. HUMPHREY, T. PEI (MERCK RESEARCH LABORATORIES, RAHWAY, USA)
Development of a Practical, Asymmetric Synthesis of the Hepatitis C Virus Protease Inhibitor MK-5172
Org. Lett. **2013**, *15*, 4174–4177.

Synthesis of MK-5172



Significance: MK-5172 is a hepatitis C virus protease inhibitor. Key steps in the synthesis depicted are (1) the regioselective S_NAr reaction of dichloroquinoxaline **A** with prolinol derivative **B** and (2) construction of the 18-membered macrocycle using a macrolactamization (**F** → **G**).

Comment: The medicinal chemistry route to MK-5172 is based on a ring-closing metathesis strategy (S. Harper et al. *ACS Med. Chem. Lett.* **2012**, *3*, 332). The best regioselectivity (20:1) and minimization of double substitution in the S_NAr reaction of **A** with **B** was achieved using 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as the base in polar solvents such as DMSO, NMP, or DMAc.

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