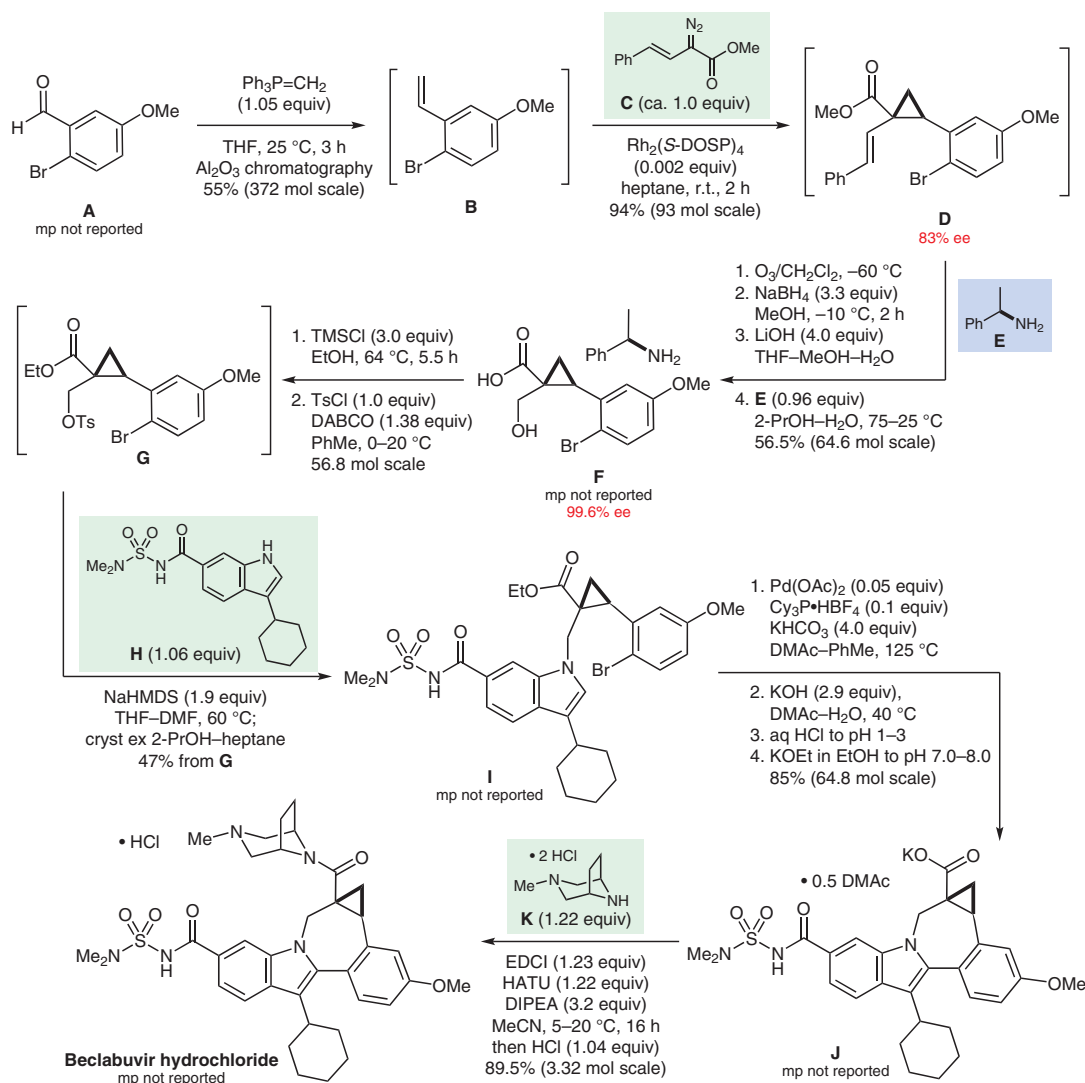


Synthesis of Beclabuvir



Significance: Beclabuvir (Ximency[®], BMS-791325) is a non-nucleoside, nonstructural protein 5B (NS5B) RNA polymerase inhibitor that was approved in Japan for use in combination with Asunaprevir and Daclatasvir for the treatment of hepatitis C virus infection.

Comment: Key steps in the large-scale synthesis depicted include (1) the rhodium-catalyzed asymmetric cyclopropanation of styrene **C** (94% yield, 83% ee) and (2) the construction of the seven-membered ring by an intramolecular Heck reaction. Beclabuvir was prepared in twelve linear steps with five isolations in 8% overall yield.