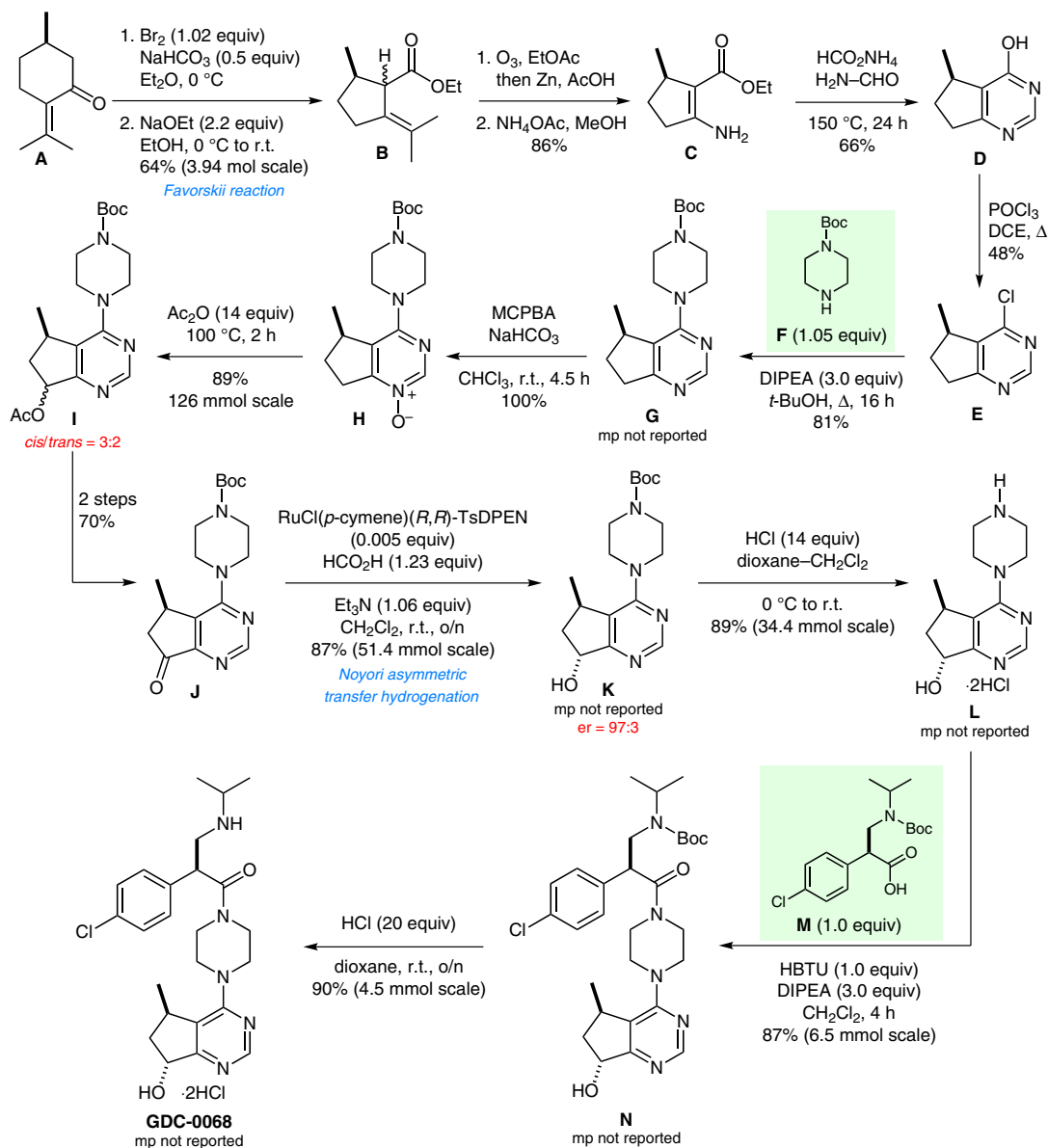


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Discovery and Preclinical Pharmacology of a Selective ATP-Competitive Akt Inhibitor (GDC-0068) for the Treatment of Human Tumors

J. Med. Chem. **2012**, *55*, 8110–8127.

Synthesis of Akt Inhibitor GDC-0068



Significance: Akt is a kinase that controls cellular processes by phosphorylating substrates involved in apoptosis, transcription, cell cycle progression and translation. GDC-0068 is an Akt inhibitor that is in clinical trials for the treatment of cancer.

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 Synfacts 2013, 9(1), 0014 Published online: 17.12.2012
 DOI: 10.1055/s-0032-1317718; Reg-No.: K09112SF

Comment: Key steps in the synthesis depicted are (1) the use of a Favorskii ring contraction in the conversion of (*R*)-pulegone (**A**) to the ester **B** and (2) the Noyori asymmetric transfer hydrogenation of ketone **J**.