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.

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.