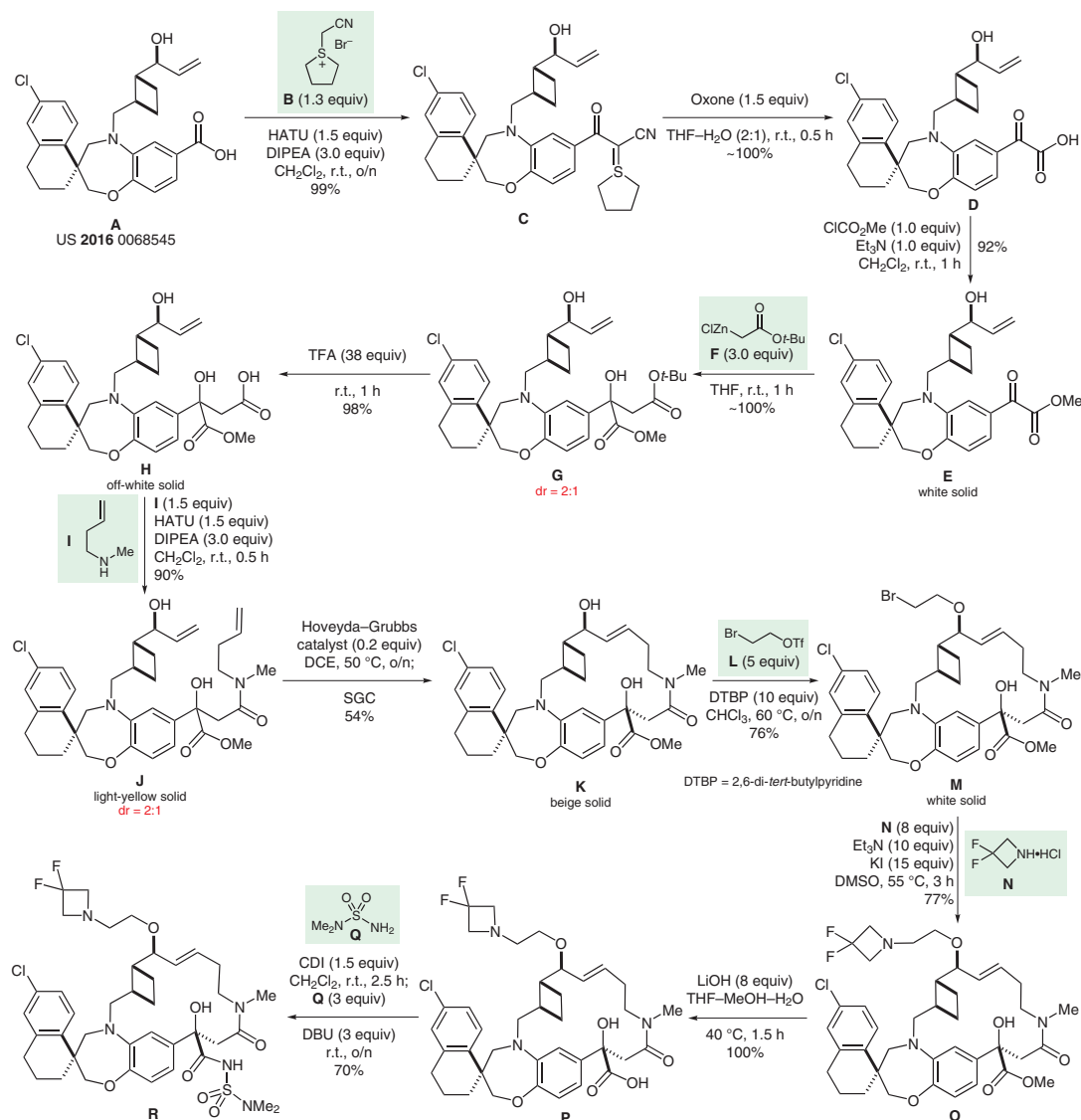


Synthesis of a Macrocyclic Mcl-1 Inhibitor



Significance: Overexpression of the antiapoptotic protein Mcl-1 benefits survival of some cancer cells. The target molecule **R** is an inhibitor of Mcl-1. A key step in the synthesis depicted is the macrocyclization of diene **J** by ring-closing metathesis.

Comment: The addition of Reformatsky reagent **F** to the keto group in **E** generated a mixture of diastereoisomers **G** (dr = 2:1) that was later separated by column chromatography to give the desired diastereoisomer **K**.