

Synthesis of Aliskiren

Category

Synthesis of Natural Products and Potential Drugs

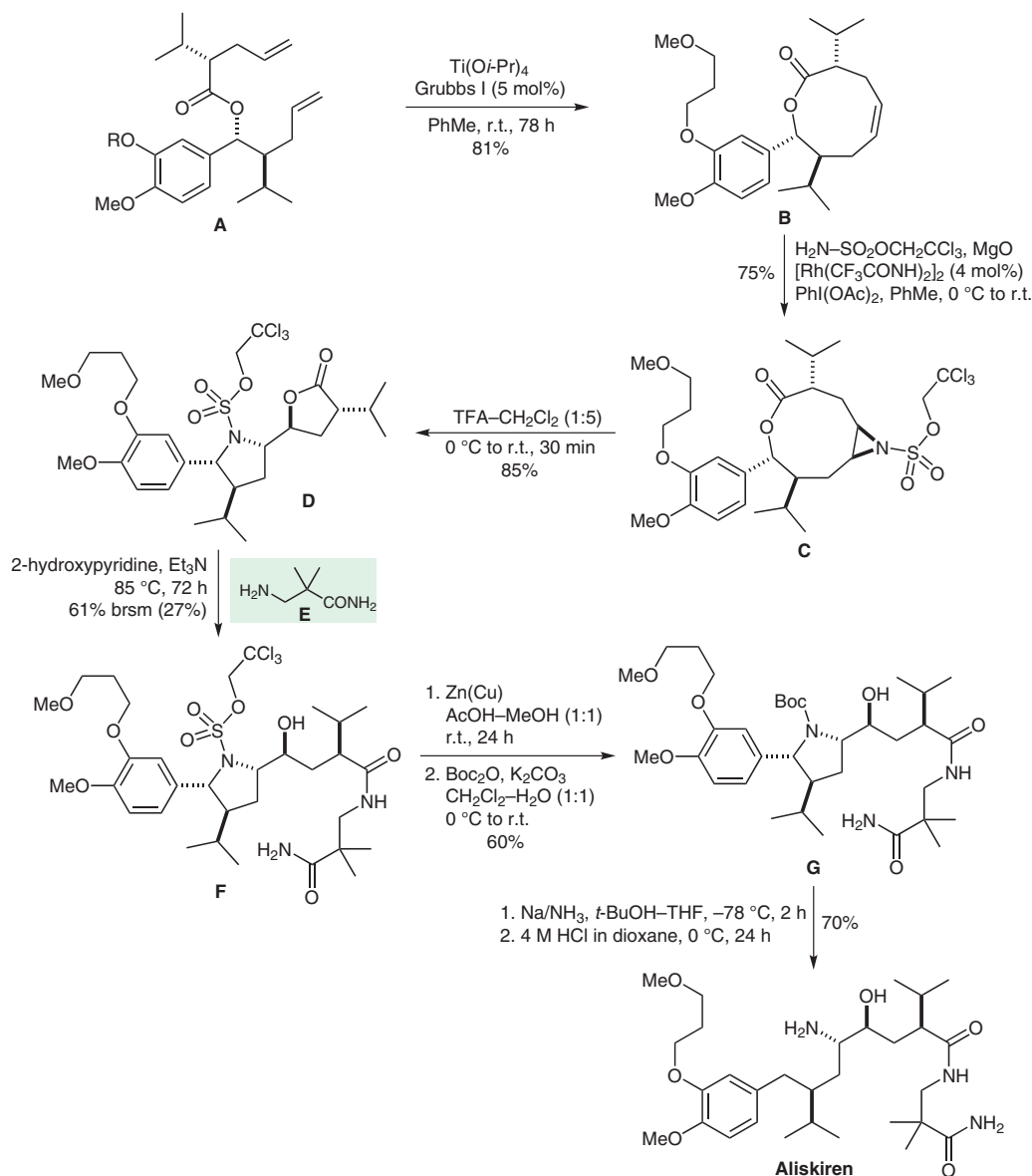
Key words

aliskiren

ring-closing metathesis

macrocyclization

Du Bois aziridination



Significance: Aliskiren is a novel renin inhibitor that is prescribed for the treatment of hypertension. This short and elegant synthesis features the construction of a nine-membered ring by ring-closing metathesis to give **B** followed by an acid-catalyzed rearrangement of the aziridine **C** to give pyrrolidine **D** in 81% yield.

Comment: The diene **A** was an 8:1 mixture of diastereoisomers. The minor (*syn*) isomer failed to undergo ring-closing metathesis. The rearrangement **C** \rightarrow **D** probably involves the initial generation of a benzylic carbocation stabilized by the 4-methoxyphenyl group.

SYNFACTS Contributors: Philip Kocienski
Synfacts 2010, 7, 0735-0735 Published online: 22.06.2010
DOI: 10.1055/s-0029-1220014; Reg-No.: K03110SF