Total Synthesis of ‘Aliskiren’: The First Renin Inhibitor in Clinical Practice for Hypertension


**Synthesis of Aliskiren**

**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 → D probably involves the initial generation of a benzylic carbocation stabilized by the 4-methoxyphenyl group.

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