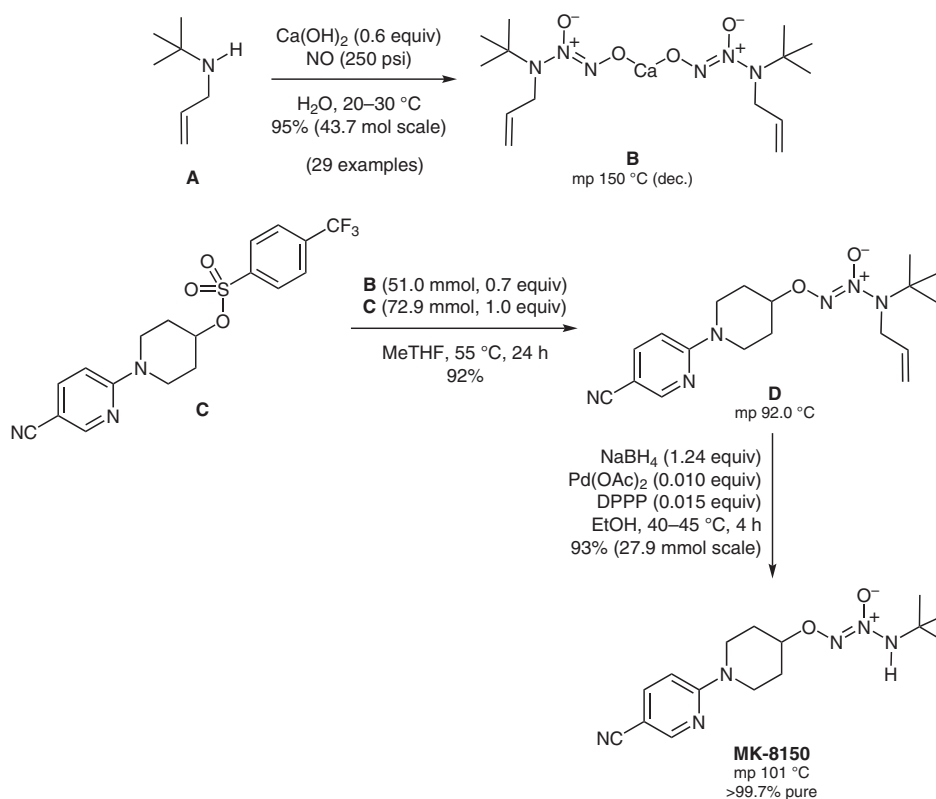


Synthesis of MK-8150



Significance: Nitric oxide (NO) plays a key role in the regulation of cardiovascular, immune, and nervous systems. Diazeniumdiolate (DAZD)-based NO donors release two equivalents of NO at pH 7.4 and 37 °C, thereby enabling modulation of NO concentration in cellular environments and control physiological processes. MK-8150 is a DAZD NO donor and a potent and significant blood-pressure-lowering drug candidate.

Comment: The synthesis of MK-8150 depicted is based on an efficient synthesis of stable diazeniumdiolate calcium salt **B** by reaction of secondary amine **A** with NO at high pressure (250 psi) in water containing calcium hydroxide. Under these conditions calcium salt **B** precipitated driving the reaction to completion. O-Alkylation of calcium diazeniumdiolate salt **B** followed by reductive deallylation afforded MK-8150 in 85% yield from **C**.

- Use of barium hydroxide or magnesium hydroxide in place of calcium hydroxide gave lower yields.
- 29 examples; yields typically >90% yield (four exceptions)