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)