Y.-L. ZHONG*, M. WEISEL, G. R. HUMPHREY, D. J. MUZZIO, L. ZHANG, M. A. HUFFMAN, W. ZHONG, K. M. MALONEY, K. R. CAMPOS (MERCK & CO., INC., RAHWAY, USA) Scalable Synthesis of Diazenium diolates: Application to the Preparation of MK-8150 Org. Lett. 2019, 21, 4210-4214.

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-pressurelowering 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)

SYNFACTS Contributors: Philip Kocienski Synfacts 2019, 15(09), 0967 Published online: 20.08.2019 DOI: 10.1055/s-0039-1690491; Reg-No.: K04819SF

Synthesis of Natural Products and **Potential Drugs**

Key words

MK-8150 diazeniumdiolates nitric oxide

