**Discovery of the Soluble Guanylate Cyclase Stimulator Vericiguat (BAY 1021189) for the Treatment of Chronic Heart Failure**

**J. Med. Chem. 2017, 60, 5146–5161.**

**Synthesis of Vericiguat**

**Significance:** Vericiguat (BAY 1021189) is an orally available soluble guanylate cyclase (sGC) stimulator that has entered phase-three trials for the once-daily treatment of chronic heart failure. Key steps in the synthesis depicted are (1) construction of the 5-fluoro-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-carboxylate by condensation of the 5-amino-1H-pyrazole-3-carboxylate with the aldehyde and (2) construction of the pyrimidine-4,5,6-triamine derivative through reaction of [E]-phenyldiazenyl]malononitrile with amidine F.

**Comment:** Experimental details are provided for the noteworthy four-step synthesis (not shown) of the crystalline 2-fluoro-(3-morpholin-4-yl)acrylaldehyde from commercially available 2,2,3,3-tetrafluoro-1-propanol. The synthesis of pyrazole A is described in a patent (A. Straub et al. WO 2000/006569 A1). The [E]-phenyldiazenyl]malononitrile (G) was generated in situ by reaction of phenyldiazonium chloride with malononitrile.

**SYNFACTS Contributors:** Philip Kocienski

Synfacts 2017, 13(09), 0897 Published online: 18.08.2017

DOI: 10.1055/s-0036-1590758; Reg-No.: K03717SF

**Category**

**Synthesis of Natural Products and Potential Drugs**

**Key words**

vericiguat
soluble guanylate cyclase stimulator
(E)-phenyldiazenyl]malononitrile
pyrimidine-4,5,6-triamine ring formation
1H-pyrazolo[3,4-b]pyridine ring formation

This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.