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 C by condensation of the 5-amino-1*H*-pyrazole-3-carboxylate **A** with the aldehyde **B** and (2) construction of the pyrimidine-4,5,6-triamine derivative **H** through reaction of [(E)-phenyldiazenyl]malononitrile (G) 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 **B** from commercially available 2,2,3,3tetrafluoro-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.

 $\textbf{SYNFACTS Contributors:} \ Philip \ Kocienski$

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

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)-pheynldiazenylmalononitrile

pyrimidine-4,5,6triamine ring formation

1H-pyrazolo[3,4b]pyridine ring formation



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