S. KALIDINDI, A. S. GANGU, S. KUPPUSAMY, S. SATHASIVAM, V. SHEKARAPPA, S. MURUGAN, S. BONDIGELA, M. KANDASAMY, K. GHANTA, A. VINODINI, A. SHRIKANT, R. RAMACHANDRAN, W. P. GALLAGHER, N. KOPP, F. GONZÁLEZ-BOBES*, M. D. EASTGATE, R. VAIDYANATHAN* (BRISTOL-MYERS SQUIBB, NEW BRUNSWICK, USA AND BRISTOL-MYERS SQUIBB RESEARCH AND DEVELOPMENT CENTER, BANGALORE, INDIA)

Development of a Scalable Synthetic Route to BMS-986251, Part 2: Synthesis of the Tricyclic Core and the API

Org. Process Res. Dev. 2021, 25, 1556–1572, DOI: 10.1021/acs.oprd.1c00125.

Synthesis of the Tricyclic Core of BMS-986251

Significance: ROR γ t is a nuclear receptor that regulates the production of proinflammatory cytokines, such as IL-17 and IL-22. BMS-986251 is a ROR γ t inverse agonist that is of interest for the treatment of immunological disorders. For syntheses of related analogues, see: D. Marcoux et al. *J. Med. Chem.* 2019, 62, 9931; A. Karmakar et al. *Org. Process Res. Dev.* 2021, 25, 1001.

Comment: Highlights of the synthesis of BMS-986251 depicted are (1) a high-yielding four-step aza-Michael addition/mesylation/annulation sequence to form the tricyclic core, and (2) installation of the heptafluoroisopropyl moiety through a three-step carboxylation–bistrifluoromethylation–deoxyfluorination sequence.

SYNFACTS Contributors: Philip Kocienski
Synfacts 2021, 17(11), 1177 Published online: 19.10.2021
DOI: 10.1055/s-0040-1720909; Reg-No.: K05621SF

© 2021, Thieme. All rights reserved.
Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

Category

Synthesis of Natural Products and Potential Drugs

Key words

BMS-986251

halogen–metal exchange

deoxyfluorination

annulation

Synfact
of the
Month

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