X-ray Structure Analysis Online

Synthesis and Structural Studies of 2-((3-Methyl-4-(2,2,2-trifluoroethoxy)pyridin-2-yl)methylthio)-1-(methylsulfonyl)-1*H*-benzo[d]imidazole

C. M. Shivaprasad,* S. Madan Kumar, B. C. Manjunath,** T. R. Swaroop,* K. S. Rangappa,*† and N. K. Lokanath****

**Department of Studies in Chemistry, University of Mysore, Mysore 570 006, India*
***Department of Studies in Physics, University of Mysore, Mysore 570 006, India*

The title compound is synthesized and characterized using spectral studies and an X-ray diffraction method. It belongs to the monoclinic crystal system with space group $P2_1/c$, and cell parameters a = 16.184(7)Å, b = 8.5876(13)Å, c = 15.0540(7)Å, β = 114.510(12)˚ and Z = 4. The molecules are connected by C–H···F and C–H···O hydrogen bonds. In addition, short contacts of the type C–F···π are observed.

(Received July 9, 2013; Accepted October 4, 2013; Published on web December 10, 2013)

The benzimidazole derivatives of heterocyclic compounds show important various biological activities.[1] They are used in the preparation of antimicrobial,[2] antioxidant[3] and anti-inflammatory[4] agents. Also, they are useful in the synthesis of Lansoprazole, which is an antiulcerative drug.[5] We present here the synthesis, characterization and crystal structure using the X-ray diffraction method of the title compound. A schematic diagram of the molecule is shown in Fig. 1.

To a solution of 2-(((3-methyl-4-(2,2,2-trifluoroethoxy)pyridin-2-yl)methyl)thio)-1*H*-benzo[d]imidazole (10 mmol) and tetrabutyl ammonium bromide (1 mmol) in toluene (20 mL), a solution of 50% KOH (25 mL) was added at 0˚C, followed by the addition of methane sulfonyl chloride (12 mmol). The reaction mixture was allowed to undergo vigorous stirring at room temperature for 6 – 10 h, and the reaction progress was monitored by TLC. After completion of the reaction, the organic phase was separated from the aqueous phase, and the organic phase was washed with water (20 mL) and brine (20 mL), dried over anhydrous sodium sulfate and concentrated to give crude products, which were purified by column chromatography over silica gel using a hexane-EtOAc (6:4) mixture as the eluent.

Spectral details: IR (KBr) cm^{-1}: 2920, 1674, 1580, 1522; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.21 (s, 3H, CH_3), 2.81 (s, 3H, CH_3), 4.42 (q, 2H, CH_2CF_3), 5.35 (s, 2H, CH_2), 7.23 (t, 2H, J = 8.0 Hz, Ar-H), 7.45 (d, 1H, 8.0 Hz, Ar-H), 7.74 (q, 2H, 8.0 Hz, Ar-H), 8.52 (d, 1H, 8.0 Hz, Ar-H)

MS (ESI): m/z 432 (M + 1); Analytic calculated: C 47.32, H 3.74 and N 9.74, Found C 47.40, H 3.99 and N 9.84. M. P. 104 – 106˚C.

A suitable plate-like single crystal of the title compound with dimensions of 0.16 × 0.20 × 0.21 mm was chosen for an X-ray diffraction study. X-ray intensity data were collected at 296 K on a Bruker CCD diffractometer equipped with Cu K_α radiation

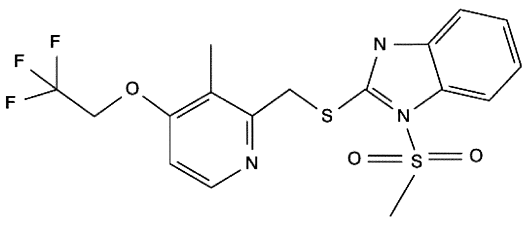

Fig. 1 Schematic diagram of the title compound.

Table 1 Crystal and experimental data

Empirical formula: $C_{17}H_{16}N_3F_3O_3S_2$	
Formula weight = 431.47	
T = 296 K	
Crystal system: monoclinic	Space group: $P2_1/c$
a = 16.184(7)Å	
b = 8.5876(13)Å	β = 114.510(12)˚
c = 15.0540(17)Å	
V = 1903.7(9)Å^3	
D_x = 1.505 g/cm^3	D_m (Floatation) = not measured
Radiation: Cu K_α (λ = 1.54178 Å)	
μ(Cu K_α) = 3.026 mm^{-1}	F(0 0 0) = 888
Crystal size = 0.12 × 0.16 × 0.18 mm^3	
No. of reflections collected = 14075	
No. of independent reflections = 2948	
θ range for data collection: 5.9 to 62.5˚	
Data/Restraints/Parameter = 2948/0/256	
Goodness-of-fit on F^2 = 1.03	
Final R indices [$I > 2\sigma(I)$]: R_1 = 0.0493, wR_2 = 0.1412	
$(\Delta/\sigma)_{max}$ = 0.000	
$(\Delta\rho)_{max}$ = 0.56 e. Å^{-3}	$(\Delta\rho)_{min}$ = –0.45 e. Å^{-3}
Measurement: Bruker X8 Proteum II CCD SYSTEM	
Program system: APEX2	
Structure solution: SHELXS-97[7]	
Structure refinement: SHELXL-97[7]	
CCDC deposition number: 9472889	

† To whom correspondence should be addressed.
E-mail: rangappaks@gmail.com

Table 2 Intermolecular hydrogen-bonding and weak interactions geometry (e.s.d's are given in parentheses)

D-H···A	D-H(Å)	H···A(Å)	D···A(Å)	D-H···A(°)
C28-H28A...F2$^{(i)}$	0.96	2.52	3.414(4)	155
C5-H22B...O6$^{(ii)}$	0.97	2.43	3.225(4)	139

Symmetry codes: (i) 1–*x*, 1/2–*y*, 1/2–*z* (ii) 1–*x*, 1/ 2–*y*, 1/2–*z*
Centroids: *Cg*(1): N17/C16/N24/C23/C18,
Cg(3): C18/C19/C20/C21/C22/C23

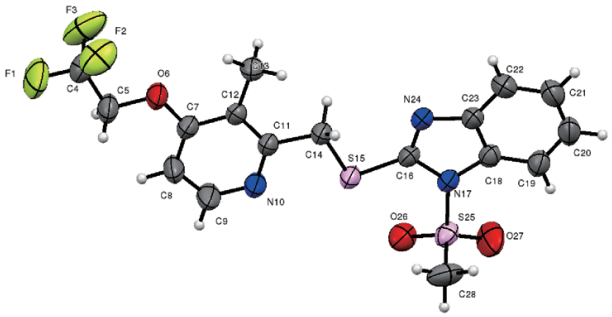

Fig. 2 ORTEP drawing of the title molecule with thermal ellipsoids drawn at 50% probability.

(λ = 1.54178 Å). Data reduction of all the collected reflections and absorption correction were carried out using the *APEX 2* package,[6] which resulted in 2704 observed reflections ($I > 2\sigma(I)$). The structure was solved by direct methods using *SHELXS*.[7] The structure was then refined by a full-matrix least-squares method with anisotropic temperature factors for non-hydrogen atoms using *SHELXL*.[7] All non-hydrogen atoms were revealed in the first Fourier map, itself. After several cycles of refinement with the anisotropic parameter for the non-hydrogen atoms, the residual was saturated to 0.0493. The details of the crystal data and refinement are given in Table 1. Figure 2 represents an *ORTEP*[8] drawing of the molecule with thermal ellipsoids drawn at 50% probability. The crystallographic data is deposited in Cambridge Crystallographic Data Center (Ref. No. CCDC 947289).

The molecules are linked by inter-molecular hydrogen bonds C28–H28A···F2 and C5–H5A···O26 (Table 2 anf Fig. 3). The C28–H11A–F3 intermolecular hydrogen bond exists between the methylsulfonyl (atom C28) and trifluoroethoxy (atom F2) moiety. Also, atom C5 of the trifluroethoxy group forms a hydrogen bond with atom O26 group of methylsulfonyl. Further, short contacts C4–F1···*Cg*(3) and a C4–F3···*Cg*(1) are observed with distance of 4.146(4)Å [angle 106.0(2)˚] and 3.925(3)^{0} Å [angle 126.74(18)˚], respectively. The packing

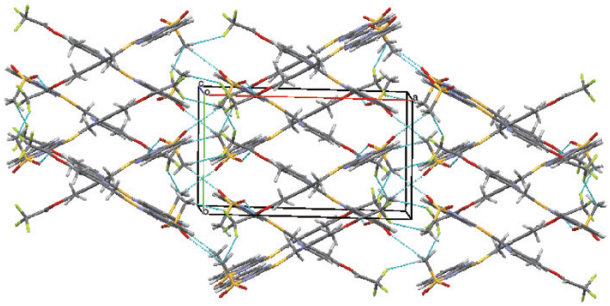

Fig. 3 Packing diagram of the title compound, viewed along the crystallographic *c*-axis. Dotted lines represents inter molecular hydrogen bonds.

diagram of the molecule along *c*-axis is shown in figure 3. However, the bond lengths and angles of this title compound are comparable to the similar structure of 2-[3-methyl-4-(2,2,2-trifluoroethoxy)-pyridin-2-yl]methylsulfanyl-1*H*-benzimidazole monohydrate.[9]

Acknowledgements

The authors thank IOE, University of Mysore for providing Single crystal X-ray diffractometer facility for data collection.

References

1. Y. Bansal and Silakari, *Bioorg. Med. Chem.*, **2012**, *20*, 6208.
2. S. Ozden, D. Atabey, S. Yildiz, and H. Goker, *Bioorg. Med. Chem.* **2005**, *13*, 1587.
3. Z. Ates-Alagoz, B. Can-Eke, T. Coban, M. Iscan, and E. Buyukbingol, *Arch. Der. Pharm.* **2004**, *337*, 188.
4. M. Sabat, J. C. Vanrens, M. J. Lauferweiler, T. A. Brugel, J. Maier, A. Golebiowski, B. De. V. Easwaran, L. C. Hsieh, R. L. Walter, M. J. Mekel, A. Evdokimov, and M. J. Januz, *Bioorg. Med. Chem.*, **2006**, *16(23)*, 5973.
5. G. M. Reddy, K. Mukkanti, T. L. Kumar, J. M. Babu, and P. P. Reddy, *Synth. Commun.*, **2008**, *38*, 3477.
6. Bruker, *APEX2, SAINT and SADABS*. **2009** Bruker AXS Inc., Madison, Wisconsin, USA.
7. G. M. Sheldrick, *Acta Cryst.*, **2008**, *A64*, 112.
8. C. F. Macrae, P. R. Edigington, P. McCabe, E. Pidcock, G. P. Sheilds, R. Taylor, M. Towler, and J. Van de Streek, *J. Appl. Cryst.*, **2006**, *39*, 453.
9. G. B. Ren, M. H. Hong, J. L. Zhong, J. L. Zhong, D. X. Yi, and L. H. Xu, *Acta Cryst.*, **2011**, *E67*, o270.