CRYSTAL STRUCTURE OF (2-METHYLPHENOXY)-ACETOHYDRAZIDE

Naresh Sharma[a]†, P. Naveen[b], Shaukath Ara Khanum[b], Rajni Kant[a] and Vivek K. Gupta[a]*

Keywords: Crystal structure, Direct methods, Hydrogen bond

The title compound, (2-methyl-phenoxy)-acetohydrazide, was synthesized by refluxing compounds *o*-cresol, ethyl chloroacetate and anhydrous potassium carbonate in the presence of dry acetone. The compound crystallizes in the monoclinic crystal system with space group $P2_1/n$ having unit cell parameters: a = 11.5460(2), b = 6.86700(10), c = 12.7506(3)Å, β = 110.022(2)º and Z = 4 . The crystal structure was solved by direct method using single crystal x-ray diffraction data collected at room temperature and refined by full-matrix least-squares procedures to a final R- value of 0.0377 for 1619 observed reflections. In the crystal structure, molecules are linked into infinite two-dimensional networks by the N–H···N and N–H···O, C−H…O and C−H…π type of hydrogen bonds.

Corresponding Authors*
Mob: +91 9419102467
E-Mail: vivek_gupta2k2@hotmail.com
[a] X-ray Crystallography Laboratory, Post-Graduate Department of Physics & Electronics, University of Jammu, Jammu Tawi -180 006, India. Presently posted at GDC (Boys), Kathua
[b] Department of Chemistry, Yuvaraja's College, University of Mysore, Mysore-570 005, Karnataka, India.

Introduction

Hydrazides have been found to have many commercial and scientific applications.[1-2] It is also used as a raw material in the manufacture of agricultural chemicals, a powerful reducing agent in fuel cells,[3] plant growth regulators in extractive fields[4] and antimicrobial drugs in pharmaceutical applications,[5] precursors for synthesis of heterocycles.[6-7] The vast interest in hydrazine structures is enthused by their value to understand structure–activity relationships and the ongoing search for in vivo active drug lead compound. Careful literature survey for functional groups which could be considered as pharmacophores for the antitubercular activities revealed that the hydrazide moiety is common among most of the antitubercular agents such as salinazid and verazide.[8-9] The structure of the title compound was elucidated by spectral methods and XRD studies.

Experimental

Synthesis

A mixture of *o*-cresol (1.00 g, 0.009 mol), ethyl chloroacetate (1.69 g, 0.01385mol) and anhydrous potassium carbonate (2.86 g, 0.027 mol) was refluxed for 8 hours in the presence of dry acetone. The reaction mixture was cooled and solvent was removed by distillation. The residual mass was diluted with water and extracted with ether. The organic layer was washed with 10 % sodium hydroxide solution, brine and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and the resultant liquid was purified by column chromatography to achieve 2-methylphenoxyacetic acid ethyl ester. Finally, (2-methylphenoxy)acetohydrazide as white solid was furnished from stirring 2-methylphenoxy-acetic acid ethyl ester (0.5 g, 0.0025mol) and hydrazine hydrate (0.128 g, 0.0025mol) in the presence of ethanol. The product so obtained was filtered, washed with water and recrystallized from ethanol with 75 % yield, m.p. 128-130 ºC. ^{1}H NMR ($CDCl_3$): 2.2 (s, 3H, CH_3), 4.2 (s, 2H,CH_2) 7.0-7.65 (m, 4H, Ar-H), 9.3 (1H, NH), 4.6 (2H NH_2). IR (Nujol): 1673 (C=O), 3700–3640 cm^{-1} (NH), 3500-3300 cm^{-1} (NH_2). Structure of the title compound is given in Figure 1.

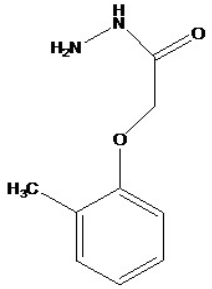

Figure 1. Chemical structure of (2-methylphenoxy)acetohydrazide

X-Ray Structure determination

X-ray intensity data of 46905 reflections (of which 1869 were unique) were collected at 293K on Oxford Diffraction Xcalibur Sapphire3 diffractometer, equipped with graphite-monochromated MoKα radiation (λ=0.71073 Å). The intensities were measured by ω scan mode for θ ranges 3.51 to 26.00° with hkl values $-14 < h < 14$, $-8 < k < 8$, $-15 < l < 15$. 1619 reflections were treated as observed using ($I > 2\sigma(I)$) as criterion. Data were corrected for Lorentz, polarization and absorption factors. The structure was solved by direct methods using SHELXS97.[10] All non-hydrogen atoms of the molecule were located in the best E-

map. Full-matrix least-squares refinement was carried out using SHELXL97.[10] All the hydrogen atoms were geometrically fixed and allowed to ride on their parent C atoms with C-H = 0.93-0.97 Å, and U_{iso}(H) = 1.2-1.5 U_{eq}(C). The final refinement cycles converged to an R = 0.0377 for the observed data. Atomic scattering factors were taken from International Tables for X-ray Crystallography (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4). The crystallographic data are summarized in Table 1.

Table 1. Crystal data and other experimental details

CCDC Number	**974706**
Crystal description	Block
Crystal size	0.30 x 0.20 x 0.20 mm
Empirical formula	$C_9H_{12}N_2O_2$
Formula weight	180.21
Radiation, Wavelength	MoK_α, 0.71073 Å
Unit cell dimensions	a= 11.5460(2)Å
	b= 6.86700(10) Å
	c= 12.7506(3) Å
	α= 90.0º
	β = 110.022(2)º
	γ= 90.0º
Crystal system, Space group	monoclinic , P2/n
Unit cell volume	949.85(3) Å^3
No. of molecules per unit cell, Z	4
Absorption coefficient	0.091 mm^{-1}
F(000)	384
θ range for entire data collection	3.50 <θ< 29.06
Reflections collected / unique	46905/ 1869
Reflections observed $I > 2\sigma(I)$)	1619
Range of indices	h= -14 to 14
	k=-8 to 8
	l= -51 to 51
No. of parameters refined	131
Final R-factor	0.0377
$w_R(F2)$	0.0955
R_{int}	0.0293
R_σ	0.0477
Goodness-of-fit	1.042
Final residual electron density	-0.164 < Δρ < 0.133 eÅ^{-3}

Results and discussions

There is only one molecule present in an asymmetric unit cell. The bond lengths and bond angles of the title compound are in agreement with the corresponding values obtained in case of related structures.[11] The six C-C bond lengths in the phenyl ring lie in the range 1.366(3)-1.395(2) Å (the average being 1.380(3) Å and the range of these values agree well with the literature value.[12] The C10=O10 distance [1.226(2)Å] confirms the double bond character. The bond angles in the benzene ring vary from 117.6(2) to 121.8(2)º with an average of 119.7(2)º. In the title compound, $C_9H_{12}N_2O_2$, the dihedral angle between the mean planes of the benzene ring (C1–C6) and acetohydrazide group (O10/C10/N11/N12) is 3.1(1)° (Fig. 2). In the molecule, the benzene ring is nearly planar with a maximum deviation of 0.0072 Å observed for the atom C5. In the acetohydrazide group, the N—N bond length is relatively short [1.414(1) Å], suggesting some degree of electronic delocalization in the molecule. An ORTEP[13] view of the title compound with atomic labeling is shown in Fig. 2. The geometry of the molecule was calculated using the PLATON [14] and PARST [15] softwares.

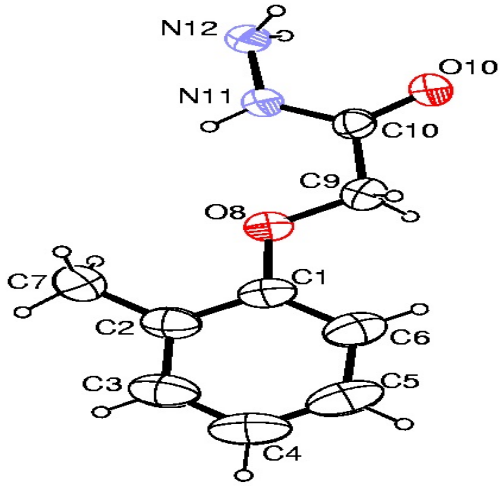

Figure 2. ORTEP view of the molecule of title compound

Table 2. Selected bond lengths (Å) and bond angles (º) for non hydrogen atoms (e.s.d.'s are given in parentheses)

Bond distances(Å)		**Bond angles(°)**	
C(1) - C(2)	1.395(2)	C(2)-C(1)-C(6)	121.3(2)
C(1) - O(8)	1.376(2)	C(6)-C(1)-O(8)	123.6(2)
C(2) - C(7)	1.502(3)	C(1)-C(2)-C(7)	120.8(2)
C(3) - C(4)	1.379(3)	C(3)-C(4)-C(5)	119.6(2)
C(4) - C(5)	1.366(3)	C(1)-O(8)-C(9)	117.4(2)
C(10)-N(11)	1.321(2)	C(9)-C(10)-N(11)	117.7(2)
C(1) - C(6)	1.385(2)	C(2)-C(1)-O(8)	115.1(2)
C(9) - C(10)	1.507(2)	C(1)-C(2)-C(3)	117.6(2)
C(5) - C(6)	1.393(3)	C(3)-C(2)-C(7)	121.5(2)
C(2) - C(3)	1.387(3)	C(2)-C(3)-C(4)	121.8(2)
O(8) - C(9)	1.412(2)	C(4)-C(5)-C(6)	120.7(2)
C(10) -O(10)	1.226(2)	C(1)-C(6)-C(5)	119.0(2)

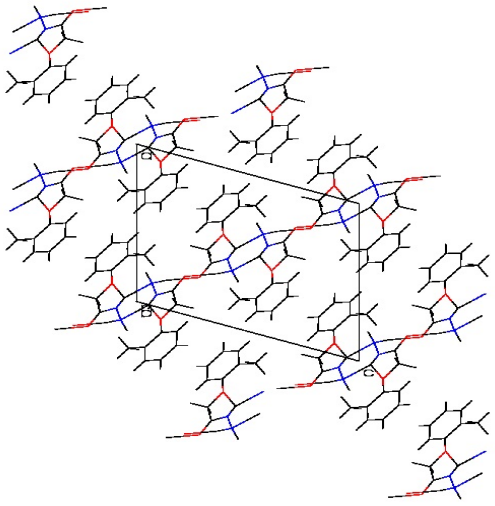

Figure 3. The crystal packing viewed down by the b-axis

Table 3. Geometry of intermolecular hydrogen bonds

D-H…A	D-H (Å)	H…A (Å)	D…A (Å)	θ[D-H…A (°)]
N11−H11…O8	0.86(1)	2.29(1)	2.646(1)	104(1)
C9−H9A...O10^{i}	0.97	2.55	3.277(2)	131.3
N11− H11…N12^{ii}	0.86(1)	2.20(1)	2.918(1)	139(1)
N12− H122…O10^{iii}	0.88(1)	2.06(1)	2.941(1)	170
N12− H121…Cg1^{iv}	0.93(1)	2.58	3.405(1)	147

Symmetry codes: (i) –*x*+1/2, *y*-1/2, -*z*+1/2; (ii) –*x*+1, -*y*+1, -*z*+1; (iii) –*x*+1/2, *y*+1/2, -*z*+1/2; (iv) –*x*+1, -*y*, -*z*+1

A packing view of the molecules in the unit cell viewed down the b-axis is shown in Fig.3. In the crystal structure (Fig. 3), molecules are linked into infinite two-dimensional networks by the N–H···N and N–H···O, C−H…O and C−H…π type of hydrogen bonds. Molecules are packed in layers. The benzene moiety is involved C-H…π contact in the crystal structure. Details of N−H…N, N−H…O, C−H…O and C−H…π interactions are given in Table 2.

Acknowledgments

RK acknowledges the Department of Science & Technology for the single-crystal X-ray diffractometer sanctioned as a National Facility under project No. SR/S2/CMP-47/2003. SAK gratefully acknowledged the financial support provided by the UGC, New Delhi, under the Major research project-scheme [UGC MRP No.F.39-737/2010 (SR) dated 06/01/2010].

References

[1]Rothgery, E. F., *Kirk-Othmer Encyclopedia of Chemical Technology,* 5th ed.; Wiley: Hoboken, NJ, **2005**), *13,* 562.

[2]Schmidt, E. W., *Hydrazine and its Derivatives: Preparation, Properties, Applications*, 2nd ed.; Wiley: Hoboken, NJ, **2001**.

[3]Yamada, K., Yasuda, K., Fujiwara, N., Siroma, Z., Tanaka, H., Miyazaki, Y., and Kobayashi, T., *Electrochem. Commun.*, **2003**, *5*, 892.

[4]Huffman, C. W., Godar, E. M., Ohki, K., Torgeson, D. C., *J. Agric. Food Chem.*, **1968**, *16*, 1041.

[5]Balsamo, A., Macchia, B., Macchia, F., Rossello, A., Giani, R., Pifferi, M. Pinza, G. and Broccali, G., *Chem J. Med.,* **1983**, *26*, 1648.

[6]Hafez, E. A. A., Abed, N. M., Elmoghayer, M. R. H. and El-Agamey, A. G., *Heterocycles*, **1984**, *22*, 1821.

[7]Khanum, S. A., Shashikanth, S., Umesha, S. and Kavitha, R., *Eur. J. Med. Chem.,* **2005**, *40*, 1156.

[8]Bijev, A., *Arzneim.-Forsch/Drug Res.,* **2006**, *56***,** 96e103.

[9]Sbardella, G., Mai, A., Artico, M., Loddo, R., Setzuc, M. G. and Collac, P. L., *Bioorg. Med. Chem. Lett.*, **2004,** *14*, 1537e1541.

[10]Sheldrick, G.M., *Acta Cryst.,* **2008,** *A64*, 112.

[11]Fun, H. K., Quah, C. K., Malladi, S. M. V. A. and Isloor, A. M., *Acta Cryst.***, 2011,** *E67*, o165.

[12]Allen, F. H., Kennard, O., Watson,D. G., Brammer, L., Orpen, A. G., and Taylor, R., *J. Chem.Soc., Perkin Trans-II.*, **1987**, S1.

[13]Farrugia, L. J. *J Appl Cryst.,* **1997,** *30*, 565.

[14]Spek, A. L., *Acta Cryst*., **2009,** *D65*, 148.

[15]Nardelli, M., *J Appl Cryst*., **1995,** *28*, 659.

Received: 04.07.2015.
Accepted: 22.07.2015