## ORIGINAL PAPER

# Synthesis, Characterization and Crystal Structures of N'-(5-Bromo-2-hydroxybenzylidene)-2-fluorobenzohydrazide in Unsolvated and Monohydrate Forms

Ling-Wei Xue · Yong-Jun Han · Gan-Qing Zhao · Yun-Xiao Feng

Received: 16 March 2011/Accepted: 31 May 2011/Published online: 10 June 2011 © Springer Science+Business Media, LLC 2011

Abstract A new hydrazone derivative, N'-(5-bromo-2hydroxybenzylidene)-2-fluorobenzohydrazide (BFBH), has been prepared and crystallized from absolute methanol and 95% ethanol, respectively, yielding unsolvated and monohydrate forms of the compound, viz. BFBH (1) and BFBH·H<sub>2</sub>O (2). The two forms of the compound were characterized by elemental analysis, IR spectra, <sup>1</sup>HNMR spectra, and X-ray single crystal structural determination. The unsolvated form of the compound crystallizes in the monoclinic space group  $P2_1/c$  with unit cell dimensions a = 6.879(1) Å, b = 28.911(2) Å, c = 8.724(1) Å,  $\beta = 127.685(2)^{\circ}, V = 1373.1(3) \text{ Å}^3, Z = 4, R_1 = 0.0569,$ and  $wR_2 = 0.1352$ . The monohydrate forms of the compound crystallizes in the monoclinic space group  $P2_1/$ c with unit cell dimensions a = 14.873(3) Å, b = 7.265(1)Å, c = 13.043(2) Å,  $\beta = 96.281(2)^{\circ}$ , V = 1400.9(4) Å<sup>3</sup>, Z = 4,  $R_1 = 0.0402$ , and  $wR_2 = 0.0890$ . The two structures are similar to each other, except for the presence of a water molecule in (2).

**Keywords** Synthesis · Crystal structure · X-ray diffraction · Hydrazone · Solvent effect

## Introduction

Hydrazone derivatives are readily prepared by the reaction of aldehydes with hydrazine compounds, with quantitive yields and high purity. In the last few decades, hydrazone derivatives

e-mail: pdsuchemistry@163.com

have been proved to have interesting biological activities such as antibacterial, antifungal, and antitumor [1–5]. In recent years, hydrazone derivatives have also been introduced to coordination chemistry, since they have versatile O, N, or S donor atoms [6–8]. Detailed study on the preparation and structures of such compounds seems important to understand their biological activities and coordination capabilities. In this paper, a new hydrazone derivative, N'-(5-bromo-2-hydroxybenzylidene)-2-fluorobenzohydrazide (BFBH), has been prepared and crystallized from absolute methanol and 95% ethanol, respectively, yielding unsolvated and monohydrate forms of the compound, viz. BFBH (1) and BFBH·H<sub>2</sub>O (2) (Chart 1).

#### Experimental

#### Materials and Methods

5-Bromosalicylaldehyde and 2-fluorobenzohydrazide with AR grade were purchased from Fluka. Other reagents and solvents were used without further purification. Elemental (C, H and N) analyses were made on a Perkin-Elmer Model 240B automatic analyser. IR spectra were recorded on an IR-408 Shimadzu 568 spectrophotometer. The <sup>1</sup>HNMR spectra were recorded on Bruker AVANCE 400 MHz spectrometer with tetramethylsilane as the internal reference. X-ray diffraction was carried out on a Bruker SMART 1000 CCD area diffractometer.

#### Preparation of BFBH (1)

The compound was prepared by the condensation reaction of equimolar quantities of 5-bromosalicylaldehyde (0.20 g, 1 mmol) with 2-fluorobenzohydrazide (0.15 g, 1 mmol) in

L.-W. Xue ( $\boxtimes$ ) · Y.-J. Han · G.-Q. Zhao · Y.-X. Feng College of Chemistry and Chemical Engineering, Pingdingshan University, Pingdingshan 467000, Henan, People's Republic of China



Chart 1 The unsolvated and monohydrate forms of BFBH

absolute methanol (30 ml). The mixture was stirred at ambient temperature for 1 h to give a colorless solution. After keeping the solution in air for a week to slow evaporate, colorless block-like single crystals were formed. The crystals were isolated by filtration, and were washed three times with methanol, and dried in air. Yield 0.18 g (53%). Analysis calculated for C<sub>14</sub>H<sub>10</sub>BrFN<sub>2</sub>O<sub>2</sub>: C, 49.9; H, 3.0; N, 8.3%; found: C, 49.7; H, 3.0; N, 8.2%. IR data (KBr, cm<sup>-1</sup>): 3237 (m), 1642 (s), 1605 (s), 1540 (s), 1509 (s), 1472 (s), 1383 (w), 1345 (s), 1313 (m), 1265 (s), 1188 (m), 1122 (w), 1018 (m), 917 (m), 837 (m), 810 (m), 693 (w), 621 (m), 556 (w), 473 (w). <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  (ppm) 6.82 (d, 1H), 7.40–7.43 (m, 3H), 7.79 (s, 1H), 8.01 (m, 2H), 8.76 (s, 1H), 10.08 (b, 1H).

#### Preparation of BFBH·H<sub>2</sub>O (2)

The monohydrate form of BFBH was prepared by the same method as that for (1), with 95% ethanol as solvent instead of absolute methanol. Colorless needle-like single crystals of the compound were formed after evaporating the solvent for a week. Yiled 0.21 g (59%). Analysis calculated for C<sub>14</sub>H<sub>12</sub>BrFN<sub>2</sub>O<sub>3</sub>: C, 47.3; H, 3.4; N, 7.9%; found: C, 47.5; H, 3.5; N, 7.8%. IR data (KBr, cm<sup>-1</sup>): 3450 (w), 3229 (m), 1642 (s), 1605 (s), 1540 (s), 1509 (s), 1471 (s), 1382 (w), 1345 (s), 1312 (m), 1265 (s), 1183 (m), 1121 (w), 1018 (m), 917 (m), 837 (m), 811 (m), 693 (w), 623 (m), 556 (w), 475 (w). <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  (ppm) 6.82 (d, 1H), 7.40–7.43 (m, 3H), 7.79 (s, 1H), 8.01 (m, 2H), 8.76 (s, 1H), 10.08 (b, 1H).

#### X-ray Diffraction

Data were collected from selected crystals mounted on glass fibres. The data for the two compounds were processed with SAINT [9] and corrected for absorption using SADABS [10]. The structures were solved by direct method using the program SHELXS-97, and were refined by full-matrix least-squares technique on  $F^2$  using anisotropic displacement parameters [11]. The amino and water H atoms in both compounds were located from difference Fourier maps and refined isotropically, with N–H, O–H, and H…H distances restrained to 0.90(1), 0.85(1), and 1.37(2) Å, respectively. The remaining H atoms were

placed at the calculated positions. Idealized H atoms were refined with isotropic displacement parameters set to 1.2 (1.5 for O) times the equivalent isotropic U values of the parent carbon and oxygen atoms. The F atom in (1) is disordered over two sites with occupancies of 0.629(3) and 0.371(3). The crystallographic data for the compounds are listed in Table 1. Selected bond lengths and angles are in listed in Table 2. Hydrogen bonding interactions are summarized in Table 3.

#### **Results and Discussion**

We have first prepared and crystallized the block-liked monohydrate form of the compound in 95% ethanol. Considering the presence of a lattice water molecule in the compound, the absolute methanol was used to repeat the

Table 1 Crystal and structure refinement data for (1) and (2)

Compound:	(1)	(2)
CCDC	817500	817501
Molecular formula	$C_{14}H_{10}BrFN_2O_2$	C14H12BrFN2O3
Molecular weight	337.2	355.2
Crystal system	Monoclinic	Monoclinic
Space group	$P2_{1}/c$	$P2_{1}/c$
a/Å	6.879(1)	14.873(3)
b/Å	28.911(2)	7.265(1)
c/Å	8.724(1)	13.043(2)
β/°	127.685(2)	96.281(2)
V/Å <sup>3</sup>	1373.1(3)	1400.9(4)
Ζ	4	4
$D_{\text{calc}} \text{ (g cm}^{-3})$	1.631	1.684
Crystal dimensions (mm)	$0.23 \times 0.21 \times 0.20$	$0.27 \times 0.23 \times 0.22$
$\mu (\text{mm}^{-1})$	3.007	2.957
Radiation $\lambda$	Mo Kα (0.71073 Å)	Mo Kα (0.71073 Å)
$T_{\min}/T_{\max}$	0.5447/0.5846	0.5023/0.5623
Reflections measured	10752	8686
Range/indices (h, k, l)	-8, 8; -36, 36; -11, 11	-18, 18; -8, 9; -16, 14
$\theta$ limit (°)	1.41-27.00	2.76-27.00
Unique reflections	2933 $[R_{\rm int} = 0.0665]$	3038 [ $R_{\rm int} = 0.0409$ ]
Observed reflections $(I > 2\sigma(I))$	1358	1934
Parameters	195	200
Restraints	2	4
Goodness of fit on $F^2$	1.019	1.027
$R_1, wR_2 [I \ge 2\sigma(I)]^a$	0.0569, 0.1352	0.0402, 0.0890
$R_1$ , $wR_2$ (all data) <sup>a</sup>	0.1340, 0.1693	0.0822, 0.1048
$a P = \Sigma    E    -  E    / \Sigma   $	$E \downarrow \dots B = [\Sigma_{\text{even}} (E^2)]$	$z^2 \frac{2}{2} \frac{2}{2} \frac{1}{2}$

<sup>a</sup>  $R_1 = \Sigma ||F_o| - |F_c|| / \Sigma |F_o|, wR_2 = [\Sigma w (F_o^2 - F_c^2)^2 / \Sigma w (F_o^2)^2]^{1/2}$ 

Table 2 Selected bond lengths (Å) and angles (°) for (1) and (2)

	(1)	(2)
Bond lengths		
C1–C7	1.447(6)	1.453(5)
C2-O1	1.340(5)	1.359(4)
C7-N1	1.275(5)	1.278(4)
N1-N2	1.381(5)	1.378(4)
N2-C8	1.350(5)	1.349(4)
C8–O2	1.229(5)	1.227(4)
C8–C9	1.485(6)	1.498(5)
C10–F1	1.314(5)	1.327(4)
Bond angles		
C1C2O1	122.5(4)	122.7(3)
C2C1C7	122.6(4)	122.5(3)
C1C7N1	120.1(4)	120.9(3)
C7-N1-N2	117.2(4)	117.8(3)
N1-N2-C8	119.3(4)	118.6(3)
N2-C8-O2	121.4(4)	122.5(3)
N2-C8-C9	116.0(4)	117.8(3)
O2–C8–C9	122.6(4)	119.6(3)

Table 3 Hydrogen geometries for (1) and (2)

D–H···A	<i>d</i> ( <i>D</i> –H) (Å)	$d(\mathbf{H}\cdots A)$ (Å)	$d(D\cdots A)$ (Å)	Angle( $D$ -H···A) (°)
(1)				
01-H1N1	0.82	1.92	2.624(5)	144
$N2-H2\cdots O2^{i}$	0.90(1)	2.01(2)	2.861(5)	157(4)
N2-H2F1'	0.90(1)	2.35(4)	2.856(8)	115(3)
$C7-H7\cdots O2^{i}$	0.93	2.47	3.187(5)	134
(2)				
O3–H3A…O2	0.847(10)	1.860(11)	2.703(4)	174(4)
N2-H2…F1	0.896(10)	2.36(4)	2.796(4)	110(3)
$N2-H2\cdots O3^{i}$	0.896(10)	1.987(19)	2.832(4)	157(4)
01-H1…N1	0.82	1.93	2.646(4)	145
G . 1	(1) 1/0	2.10	1/2	

Symmetry code: (i) -1/2 + x, 3/2 - y, -1/2 + z

preparation. Fortunately, needle-like single crystals of the unsolvated form of the compound were obtained. Both the monohydrate and the unsolvated forms of the compound were crystallizing in air-stable colorless crystals. The elemental analyses are in agreement with the formulae proposed by the X-ray determination. The crystals of (1) and (2) are soluble in methanol, ethanol, acetonitrile, and chloroform, and insoluble in water.

# Crystal Structure Description

The molecular structures of (1) and (2) are depicted in Figs. 1 and 2, respectively. Both compounds crystallize in



**Fig. 1** Perspective view of (1) with 30% probability thermal ellipsoids. Hydrogen bond is drawn as a *dashed line*. Only the major component of the disordered F atom is shown



Fig. 2 Perspective view of (2) with 30% probability thermal ellipsoids. Hydrogen bonds are drawn as *dashed lines* 

the monoclinic space group  $P2_1/c$ . The major difference between the complexes is in the components of the molecules: compound (1), synthesized and crystallized in absolute methanol, has no water molecule in the structure, while compound (2), synthesized and crystallized in 95% ethanol, has solvent water molecules in the crystal. The water molecule in (2) is linked to the hydrazone compound via N–H…O and O–H…O hydrogen bonds.

In both compounds, the hydrazone molecules display *trans* configuration about the C=N double bonds. The bond lengths are within normal ranges [12–14], and are comparable to each other. The C7=N1 bond lengths in both compounds are 1.28(1) Å, confirming them as double bonds. The C8–N2 bond lengths of 1.35(1) Å and the N1–N2 bond lengths of 1.38(1) Å in the compounds are relatively short, suggesting some degree of delocalization in each of the acetohydrazide systems. The dihedral angles between the two benzene rings in the compounds are 14.9(2)° in (1) and 48.8(2)° in (2). It can be seen that molecule of (2) is much more distorted than (1), which might be caused by the intermolecular hydrogen bonds formed among the hydrazone molecules with the water molecules in (2).

In the crystal structure of (1), the hydrazone molecules are linked through intermolecular N–H $\cdots$ O and C–H $\cdots$ O hydrogen bonds, forming chains along the *c* axis (Fig. 3).



Fig. 3 Molecular packing of (1), viewed along the *a* axis. Hydrogen bonds are drawn as *dashed lines* 



Fig. 4 Molecular packing of (2), viewed along the *b* axis. Hydrogen bonds are drawn as *dashed lines* 

In the crystal structure of (2), the hydrazone molecules are linked by the water molecules through intermolecular N–H…O and O–H…O hydrogen bonds, forming chains along the *c* axis (Fig. 4). In addition, there are  $\pi \cdots \pi$  stacking interactions (Table 4), O–H… $\pi$ , and C–F… $\pi$  interactions among the adjacent benzene rings in both compounds [15].

# **Supplementary Material**

CCDC-817500 and 817501 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at http://www.ccdccam.ac.uk/

Cg	Distance between ring centroids (Å)	Dihedral angle (°)	Perpendicular distance of $Cg(I)$ on $Cg(J)$ (Å)	Beta angle (°)	Gamma angle (°)	Perpendicular distance of Cg(J) on $Cg(I)$ (Å)
0						
(1)						
$Cg(1)-Cg(2)^{a}$	4.099	5.47	3.546	31.53	30.10	3.493
$Cg(1)$ – $Cg(2)^{b}$	3.816	5.47	3.499	24.24	23.51	3.480
$Cg(2)-Cg(1)^{c}$	3.816	5.47	3.480	23.51	24.24	3.499
$Cg(2)-Cg(1)^{d}$	4.099	5.47	3.493	30.10	31.53	3.546
(2)						
$Cg(3)-Cg(3)^{\rm e}$	4.360	0.02	3.529	35.96	35.96	3.529
$Cg(4)$ – $Cg(4)^{f}$	3.775	0.02	3.333	28.02	28.02	3.333

Table 4 Parameters between the planes for (1) and (2)

Cg(1) and Cg(2) are the centroids of C1–C2–C3–C4–C5–C6 and C9–C10–C11–C12–C13–C14 in (1), respectively. Cg(3) and Cg(4) are the centroids of C1–C2–C3–C4–C5–C6 and C9–C10–C11–C12–C13–C14 in (2), respectively. Symmetry codes: (a) -1/2 + x, 1/2 - y, -1/2 + z; (b) -1/2 + x, 1/2 - y, 1/2 + z; (c) 1/2 + x, 1/2 - y, -1/2 + z; (d) 1/2 + x, 1/2 - y, 1/2 + z; (e) -x, 2 - y, -z; (f) 1 - x, 1 - y, -z

const/retrieving.html or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0)1223-336033 or e-mail: deposit @ccdc.cam.ac.uk.

**Acknowledgments** This research was supported by the National Sciences Foundation of China (No. 20676057 and 20877036) and Top-class foundation of Pingdingshan University (No. 2008010).

# References

- 1. Adibi H, Khodaei MM, Pakravan P, Abiri R (2010) Pharm Chem J 44:219–227
- Ajani OO, Obafemi CA, Nwinyi OC, Akinpelu DA (2010) Bioorg Med Chem 18:214–221
- Rasras AJM, Al-Tel TH, Al-Aboudi AF, Al-Qawasmeh RA (2010) Eur J Med Chem 45:2307–2313
- 4. Ozkay Y, Tunali Y, Karaca H, Isikdag I (2010) Eur J Med Chem 45:3293–3298

- 5. Adibi H, Khodaei MM, Pakravan P, Abiri R (2010) Pharm Chem J 44:219–227
- 6. Liu F, Zhang WP, He SY (2010) Russ J Coord Chem 36:105-112
- Wang J-X, Li X-Z, Zhu L-N, Wang J-Y, Qu H (2010) J Chem Crystallogr 40:726–730
- Naskar S, Naskar S, Butcher RJ, Chattopadhyay SK (2010) Inorg Chim Acta 363:3641–3646
- Bruker, SMART and SAINT. Area Detector Control and Integration Software, Bruker Analytical X-ray Instruments Inc., Madison, WI, USA, 1997
- Sheldrick GM (1996) SADABS. Program for empirical absorption correction of area detector. University of Göttingen, Göttingen
- Sheldrick GM (1997) SHELXL-97. Program for the refinement of crystal structures. University of Göttingen, Göttingen
- Allen FH, Kennard O, Watson DG, Brammer L, Orpen AG, Taylor R (1987) J Chem Soc Perkin Trans 2:S1–S19
- 13. Yang D-S (2007) J Chem Crystallogr 37:343–348
- 14. Li W-H (2009) J Chem Crystallogr 39:449-452
- 15. Spek AL (2009) Acta Crystallogr D65:148-155