X-RAY CRYSTALLOGRAPHY OF HYDRAZONE DERIVATIVES – A COMPARATIVE STUDY

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Abstract

There has been considerable interest in the development of novel compounds with anticonvulsant, analgestic, anti-inflammatory, antiplatelet, antimalarial, antimicrobial, antitumoral and antiviral activities. Hydrazones an azometine-NHN=CH- proton constitute an important class of compounds for new drug development. Therefore, many researchers have synthesized these compounds as target structures and evaluated their biological activities.Using X-ray diffraction the crystal and molecular structures of hydrazones, (E)-N'-(4-Methoxybenzylidene)pyridine-3-carbohydrazide dihydrate (compound 1) and (E)-N'-(3,4-Dimethoxybenzylidene)nicotinohydrazide monohydrate (compound 2), have been determined.

Introduction

Hydrazone moiety plays an important key role in heterocyclic chemistry. Hydrazones are a class of organic compounds which possess the structure $R_1R_2C=NNH_2$. They are related to ketone and aldehyde in which oxygen has been replaced with NNH_2 functional group. These azometine-NHN=CH- proton constitute an important class of compounds for new drug development.They are formed usually by the action of hydrazine on ketones or aldehydes. Hydrazone nucleus is found in natural and synthetic products of biological interest. Literature studies revealed that hydrazones and various substituted hydrazones are associated with abroad spectrum of biological activities such as antioxidant, antibacterial, antiviral, analgesic, antiplatelet,antimicrobial, and anticancer activities.The C=N double bond in hydrazones are important compounds in drug design as they act as ligands for metal complexes, organocatalysis and synthesis of organic compounds. The C=N bond of hydrazone and terminal nitrogen atom containing a lone pair of electron is responsible for the physical and chemical properties. Metal complexes with hydrazones also have potential applications as catalysts, luminescent probes and molecular sensors.In this study, we describe the structure-activity effects of two hydrazone derivatives and are comparison.

Result and discussion

The compound1 comprises one benzohydrazide molecule and two water molecules (Fig 1). The hydrazone molecule adopts *trans* conformation with respect to the C═N bond with the torsion angle of -177.41 (16)° (C8—N1—N2—C9). Phenyl and pyridine rings (C2—C7 and N3/C10—C14, respectively) are each planner with a dihedral angle 8.55 (10)° between their mean-planes. The methylidenehydrazide fragment O2/C9/N2/N1/C8 in the compound 1 is essentially planar with maximum deviation being -0.0375 (13) A for the N1 atom. The mean-planes of the benzene andpyridine rings make dihedral angles of 2.71 (14)° and 11.25 (13)°, respectively, with mean–plane of the methylidenehydrazide fragment. The C8═N1 and C9═O2 bond lengths are 1.270 (2) and 1.2199 (18) A, respectively, which isvery close to the values found in related structures listed in Table 2. The angles of N2—C9—O2, O2—C9—C10 and N2—C9—C10 are 122.46(14)°, 120.50(14)° and 117.04(13)° respectively which indicate that the position of C9 atom is in nearly trigonal planar geometry. The methoxy group is co–planar with the benzene ring to which it is bound with the C1—O1—C2—C3 torsion angle = -0.26 (27)°.

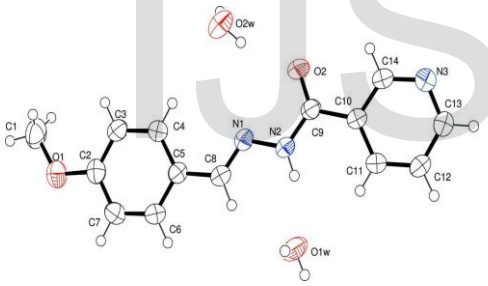

Fig. 1

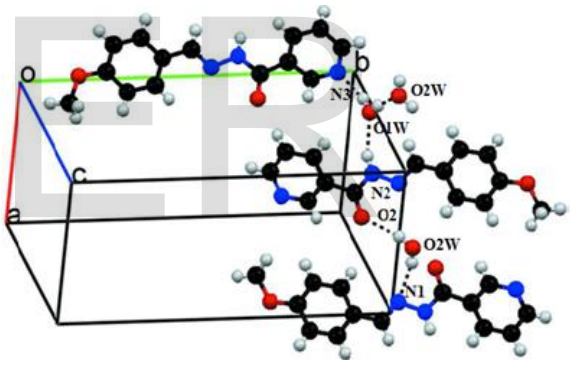

Fig. 2

In the crystal packing (Fig. 2), the molecules of benzohydrazide and water are linked by N2—H2N2...O1W, O1W—H2O1...O2W, O2W—H2O2...O2, O1W—H1O1...N3 and O2W—H1O2...N1 hydrogen bonds into a three–dimensional network.

In the compound 2, molecule contains one more methoxy group in the 3rd position of the benzene ring and only one water molecule is present (Fig 3). The molecule of compound 2 exists in a *trans* conformation with respect tothe C8═N1 double bond [1.277 (2) A] with the torsion angle N2—N1—C8—C5 = -177.58 (14)°. It also adopts theamido form with the C9═O3 bond length of 1.2322 (19) A which is very close to the reported C═O bond length of asimilar structure (Wang *et al.*, 2010). The benzene and pyridine rings (C2—C7 and N3/C10—C14, respectively) are eachplanar with a dihedral angle of 5.10 (14)° between their mean-planes. The angles of N2—C9—O3, O3—C9—C10 and N2—C9—C10 are

122.34(16)°, 121.05(15)° and 116.61(14)° respectively which indicate that the position of C9 atom is in nearly trigonal planar geometry. One of the methoxy group is almost coplanar with the C2—C7 benzenering whereas the other one deviates somewhat from the benzene ring plane [torsion angles: C1—O1—C2—C7 = -3.9 (3),C15—O2—C3—C4 = 16.5 (3)°].

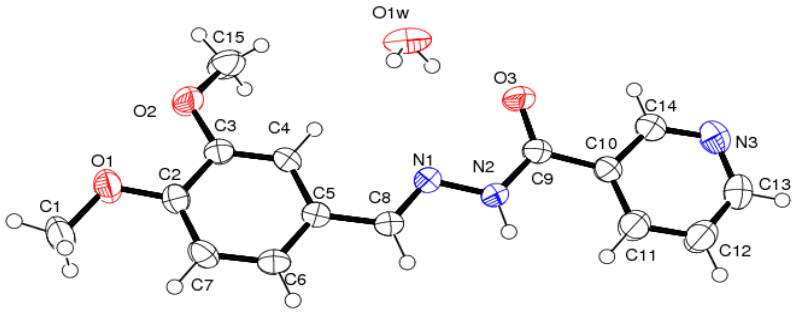

Fig. 3

The water molecule forms six H–bonds with three different nicotinohydrazone molecules. N—H..O, O—H...O, O—H...N and C—H...O hydrogen bonds are present in the crystal system. One of the H atoms of the watermolecule forms bifurcated hydrogen bonds to the azomethine nitrogen and the carbonyl oxygen atoms of one neighboring molecule. The water molecule acts as a hydrogen bond acceptor towards another nicotinohydrazone molecule through N–H...O and C—H...O hydrogen bonds. The molecular pattern is characterized by three different graph-set motifs (Bernstein et al., 1995) *viz*. $R^2_2(5)$, $R^2_2(6)$ and a $R^2_2(7)$ type. The $R^2_2(5)$ motif occurs between water and one nicotinohydrazone molecule and $R^2_2(6)$ and a $R^2_2(7)$ motifs are formed between the same water molecule and other nicotinohydrazone molecule (Fig. 4).

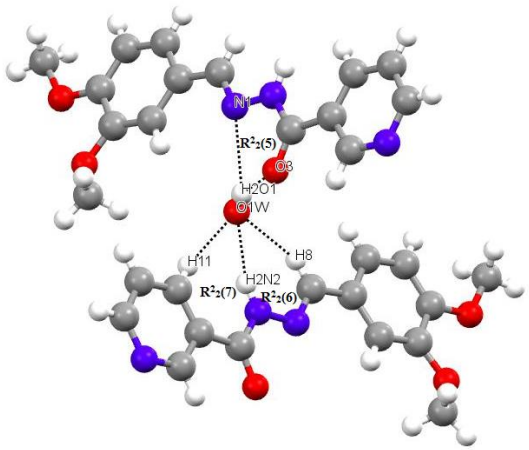

Fig. 4

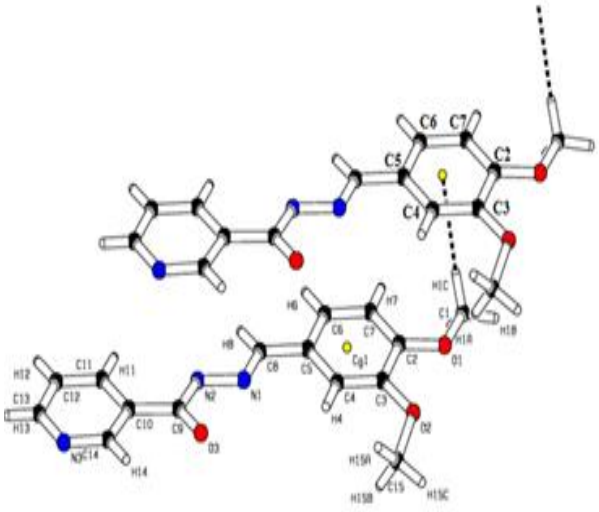

Fig. 5

Furthermore, The C1—H1C...π interactions involving the phenyl (C2—C7) ring with minimum C...Cg^i (x+1, y, z) separation of 3.729(3) Å is observed (Fig.5).

Table 1 Crystal data and refinement details for compound 1 and 2

Empirical formula	$C_{14}H_{13}N_3O_2 \cdot 2H_2O$	$C_{15}H_{15}N_3O_3 \cdot H_2O$
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/n$	$P2_1/n$
Temperature (K)	296	296
Unit cell dimensions		
a (Å)	7.6534 (6)	4.9128 (6)
b (Å)	16.3503 (11)	25.137 (4)
c (Å)	11.4887 (6)	12.2950 (16)
α (°) & γ (°)	90	90
β (°)	96.889 (2)	96.513 (4)
Volume ($Å^3$)	1427.26 (17)	1508.6 (4)
Z	4	4
R_{int}	0.028	0.036
Final R indices	R1 = 0.046	R1 = 0.048
(for I > 2σ(I))	wR2 = 0.155	wR2 = 0.141

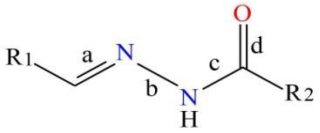

Table 2 Comparison of the bond lengths:

Compound	a (Å)	b (Å)	c (Å)	d (Å)	Reference
1	1.270(2)	1.3890(17)	1.3451(19)	1.2199(18)	Compound 1
2	1.277(2)	1.3806(19)	1.344(2)	1.2322(19)	Compound 2
3	1.278(2)	1.390(2)	1.344(2)	1.228(2)	Almeida et al., (2016)
4	1.274(3)	1.378(2)	1.345(3)	1.229(2)	Sravya et al., (2015)
5	1.275(2)	1.380(2)	1.350(3)	1.221(2)	Sreeja et al., (2014a)
6	1.2748(13)	1.3818(15)	1.3483(18)	1.2208(16)	Sreeja et al., (2014b)
7	1.269(4)	1.381(4)	1.341(4)	1.218(4)	Prasanna et al., (2013)
8	1.2721(18)	1.3736(18)	1.3582(18)	1.2258(17)	Nair et al., (2012)
9	1.272(4)	1.364(3)	1.356(4)	1.222(3)	Prabhu et al., (2011)
10	1.285(4)	1.378(3)	1.348(4)	1.223(4)	Husssian et al., (2010)
11	1.276(3)	1.388(3)	1.356(3)	1.236(3)	Ding & Ni, (2010)
12	1.279(5)	1.384(4)	1.3431(4)	1.230(4)	Kargar et al., (2010)
13	1.279(3)	1.383(2)	1.343(3)	1.231(2)	Wang et al., (2010)
14	1.264(3)	1.396(2)	1.334(3)	1.227(3)	Shafiq et al., (2009)
15	1.2841(8)	1.3764(7)	1.3559(8)	1.2274(8)	Cheng et al., (2008)

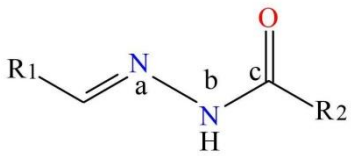

Table 3 Comparison of the bond angles:

Compound	a (°)	b (°)	c (°)	Reference
1	115.97(13)	117.85(12)	122.46(14)	Compound 1
2	115.72(14)	118.29(13)	122.34(16)	Compound 2
3	115.04(15)	117.89(15)	124.07(18)	Almeida et al., (2016)
4	117.49(18)	117.59(18)	122.4(2)	Sravya et al., (2015)
5	118.26(15)	117.22(15)	123.50(17)	Sreeja et al., (2014a)
6	118.60(9)	117.10(10)	123.57(12)	Sreeja et al., (2014b)
7	116.7(3)	118.5(3)	123.8(3)	Prasanna et al., (2013)
8	116.90(12)	117.28(12)	122.14(13)	Nair et al., (2012)
9	119.1(3)	116.5(2)	122.0(3)	Prabhu et al., (2011)
10	120.6(3)	116.3(3)	122.8(3)	Husssian et al., (2010)
11	114.8(2)	118.8(2)	121.4(3)	Ding & Ni, (2010)
12	115.9(3)	119.0(3)	123.0(3)	Kargar et al., (2010)
13	112.81(13)	119.77(13)	123.99(15)	Wang et al., (2010)
14	114.42(17)	119.46(17)	123.23(19)	Shafiq et al., (2009)
15	113.6(2)	118.82(17)	123.0(2)	Cheng et al., (2008)

Conclusion

The detailed conformational analysis on these two hydrazone derivatives indicates that, the hydrazone moiety adopts *trans* conformation in the compound1 and 2. The various substituents at different position in the hydrazone moiety produce the conformational changes. The bond lengths and bond angles in the two related compounds are in good agreement with the expected values and are largely comparable with the corresponding values reported in the related structures.

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