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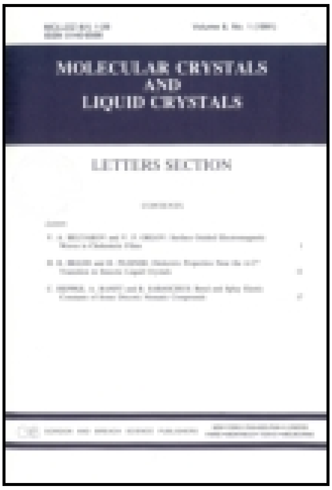

Molecular Crystals and Liquid Crystals
Publication details, including instructions for authors and subscription information:
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Synthesis, Crystal Structure and Characterization of (Z)-2-N′-hydroxyisonicotinamidine

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Published online: 27 May 2014.

To cite this article: M. Prabhuswamy, Dinesha, K. J. Pampa, S. Madan Kumar, G. K. Nagaraja & N. K. Lokanath (2014) Synthesis, Crystal Structure and Characterization of (Z)-2-N′-hydroxyisonicotinamidine, Molecular Crystals and Liquid Crystals, 593:1, 243-252, DOI: 10.1080/15421406.2013.875735

To link to this article: http://dx.doi.org/10.1080/15421406.2013.875735

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Mol. Cryst. Liq. Cryst., Vol. 593: pp. 243–252, 2014
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ISSN: 1542-1406 print/1563-5287 online
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Synthesis, Crystal Structure and Characterization of *(Z)*-2-*N′*-hydroxyisonicotinamidine

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The compound (Z)-2-N′-hydroxyisonicotinamidine, (2) was synthesized and characterized by ^{1}H NMR, FT-IR, FAB-Mass, UV-Visible Spectra, and elemental Analysis. Its molecular structure was solved by single crystal X-ray diffraction method. The title molecule, $C_6H_7N_3O$ is crystallized in the orthorhombic crystal system with the space group $Pna2_1$ and with unit cell parameters $a = 12.5664(8)$ Å, $b = 8.8622(6)$ Å, $c = 5.7953(4)$ Å, $\alpha = 90°$, $\beta = 90°$, $\gamma = 90°$, and $Z = 4$. The molecular and crystal structure of the title molecule is stabilized by an intramolecular interaction of the type N—H···O, and the intermolecular interactions of types N—H···N and O—H···N.

Keywords Amidoxime; characterization; crystal structure; inter-molecular interactions

Introduction

Versatile heterocyclic compounds were synthesized from carbonitrile. The reaction of carbonitrile with hydroxylamine hydrochloride gave amidoximes. Amidoximes are compounds bearing both a hydroxyimino and an amino group at the same carbon atom. Amidoximes are bifunctional molecules exhibiting a rich, diverse chemistry, and provides the intermediates for the preparation of heterocycles such as oxadiazoles. These are less basic because of the introduction of the oxygen atom. A number of amidoximes has already been used as drugs, or currently being in clinical trials. Amidoximes are absorbed from the gastrointestinal tract and then reduced to the activity of amidines. So, they act as prodrugs for the amidines [1, 2]. Their numerous pharmaceutical applications such as bactericidal and fungicidal [3], local anesthetics [4], antitumor and antimalarial agents [5], and their ability to release NO were clarified, giving a new insight to their mode of action and allowing the design of new therapeutic agents [6]. Prompted by these observations, it was contemplated to synthesis of the title compound *(Z)* -2-*N′*-hydroxyisonicotinamidine and it is well characterized by the single-crystal X-ray diffraction, ^{1}H NMR, FT-IR, FAB-Mass, UV-Visible Spectra, and elemental Analysis (Scheme 1).

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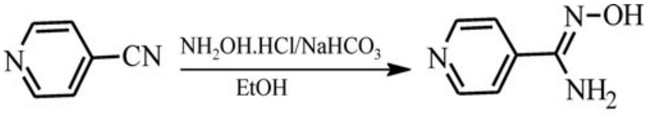

(1) **(2)**

Scheme 1. Synthesis of Compound (*Z*)-2-*N′*-hydroxyisonicotinamidine.

Experimental

Materials and Methods

Melting point was taken in an open capillary tube and was uncorrected. The purity of the compound was confirmed by thin-layer chromatography using Merck silica gel 60 F_{254} coated aluminum plates. IR spectrum was recorded on Shimadzu-FTIR Infrared spectrometer in KBr (ν_{max} in cm^{-1}). ^1H NMR (400 MHz) spectrum was recorded on a Bruker Avance II 400 spectrometer, with 5 mm PABBO BB-1H TUBES, using $CDCl_3$ as a solvent and TMS as internal standard (chemical shift in δ ppm). The FAB mass spectra were recorded on a JEOL SX 102/DA-6000 spectrophotometer/Data system using Argon/Xenon (6 kV, 10 mA) FAB gas, at 70 eV. The UV-Vis spectrum was recorded in Shimadzu UV-2550 UV-Visible spectrophotometer. Elemental analysis was carried out by using VARIO EL-III (Elementar Analysensysteme GmBH).

Procedure for the Preparation of (Z)-2-N′-hydroxyisonicotinamidine(2)

Sodium bicarbonate (70 mmol, 5.88 g) was added in portions to a solution of hydroxylamine hydrochloride (70 mmol, 4.79 g) in 18 mL of water. A solution of 4-cyanopyridine (35 mmol, 3.64 g) in 34 mL of ethanol was then added, and the mixture stirred under reflux for 6 hr. The precipitate formed was filtered off and recrystallized from ethanol. Yield 71%; m.p. 207–209°C.

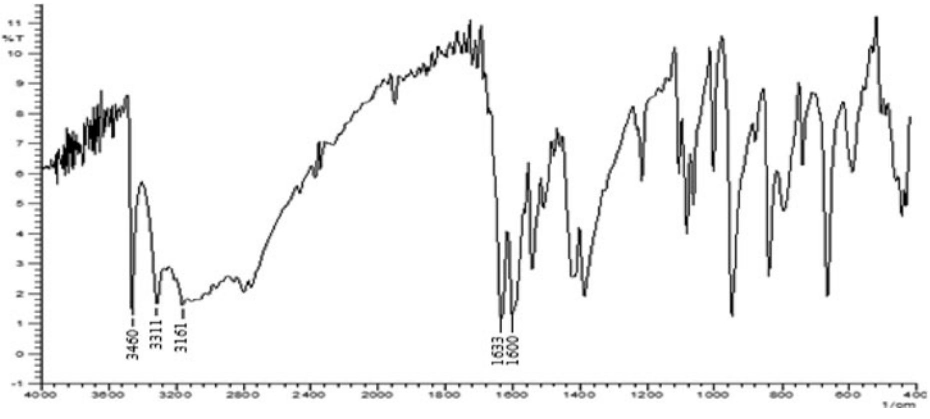

Figure 1. FT-IR spectrum.

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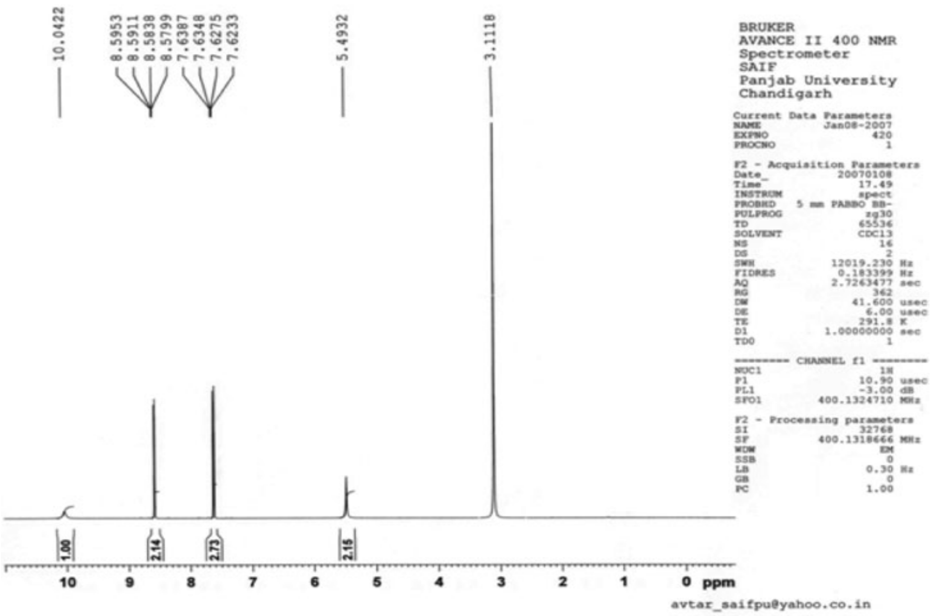

Figure 2. ^{1}H NMR spectra.

Results and Discussion

FT-IR Spectral Analysis

The FT-IR spectrum of the crystal structure was shown in Fig. 1. IR spectra showed strong absorption bands at 3311 and 3460 cm^{-1} due to primary amine group and vibration band at 3161 cm^{-1} due to the hydroxyl group. The absorption peaks at 1600 and 1633 cm^{-1} were due to the stretching vibration corresponds to —C=C and —C=N groups.

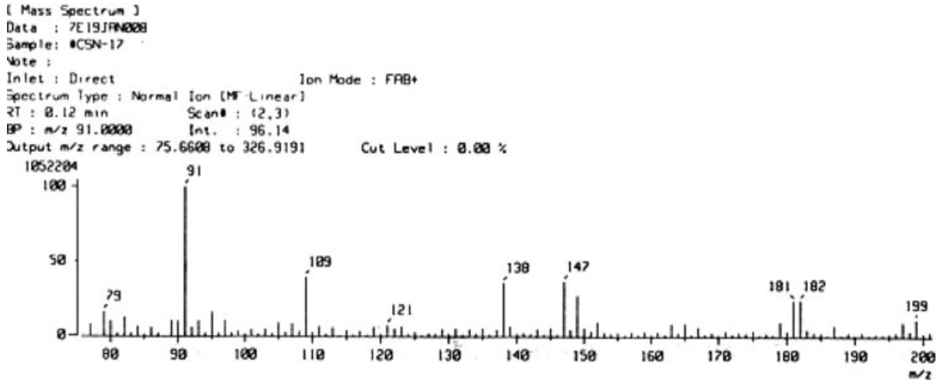

Figure 3. FAB mass spectrum.

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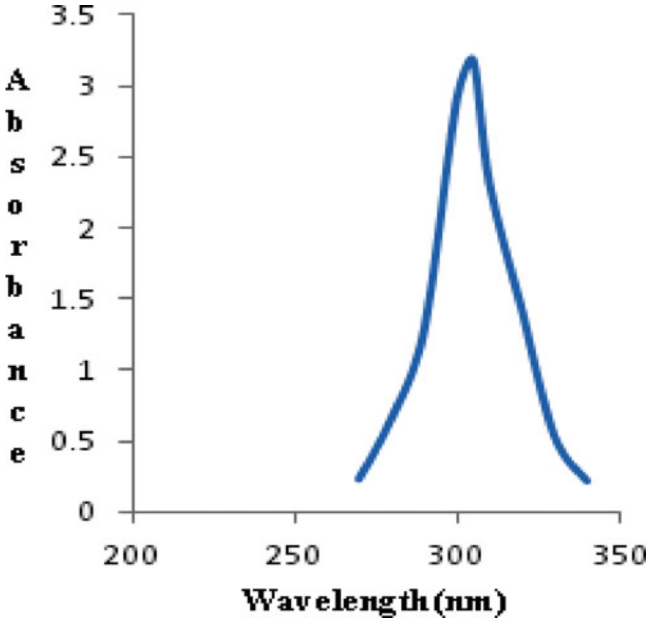

Figure 4. UV-visible spectrum.

^{1}H NMR Spectral Analysis

The ^{1}H NMR spectrum of the crystal structure was shown in Fig. 2. ^{1}H NMR spectrum showed sharp singlet at δ 5.49 and δ 10.0 ppm due to NH_2 and O-H protons, respectively. The four aromatic protons displayed two signals; a doublet of doublet at δ 7.63 ppm and δ 8.59 ppm with coupling constants of nearly 1.62 Hz and 4.54 Hz.

Fast Atom Bombardment Analysis

The formation of compound (*Z*)-2-*N'*-hydroxyisonicotinamidine was confirmed by recording its fast atom bombardment (FAB)-Mass spectrum and shown in Fig. 3. The compound showed a molecular ion peak at m/z 138 $(M+H)^+$ in agreement with the molecular formula $C_6H_7N_3O$. The base peak was seen at m/z 91 due to the formation of molecular ion radical of 4-methylpyridine during fragmentation.

Table 1. Elemental analysis for $C_6H_7N_3O$

Element	Experimental (%)	Calculated (%)
Carbon	52.47	52.55
Nitrogen	30.55	30.64
Hydrogen	5.09	5.14

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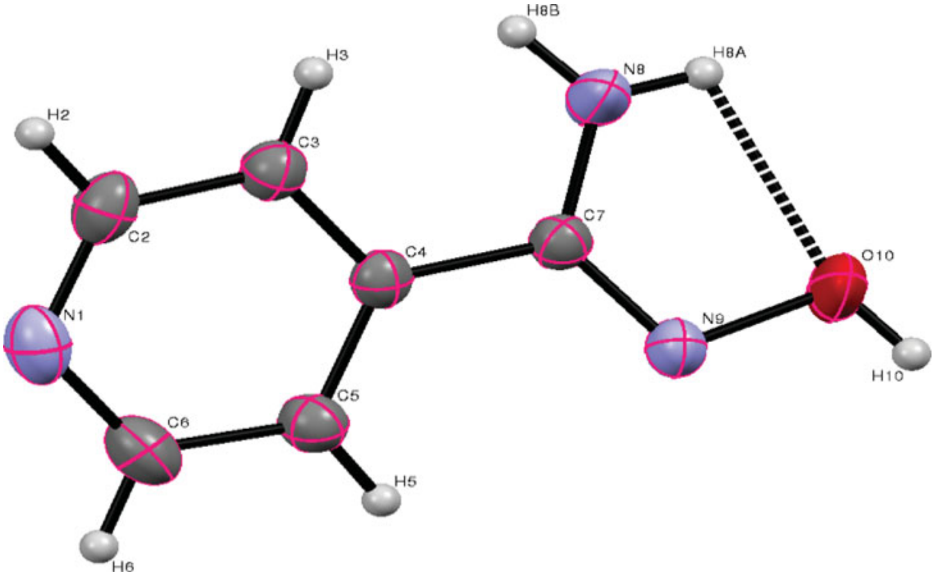

Figure 5. *ORTEP* view of the title molecule with atom numbering scheme. The displacement ellipsoids for nonhydrogen atoms are drawn at 50% probability level. Dashed line indicates intramolecular hydrogen bond of the type N—H···O.

UV-Vis Spectral Analysis

Like FT-IR spectroscopy, UV spectroscopy also useful in the evaluation of the compounds. On UV electronic spectrum compounds are analyzed based on the characteristic frequencies corresponding to define groups and it is shown in Fig. 4. The UV-Vis spectrum was recorded by using methanol as a solvent. From the graph, it was observed that the compound shows an absorption peak at 305 nm. The transmittance of the compound is due to the π-π^*

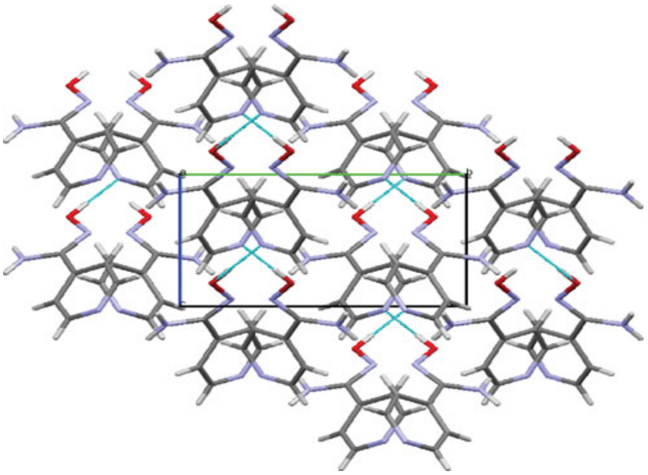

Figure 6. Packing of molecules when viewed down *a*-axis.

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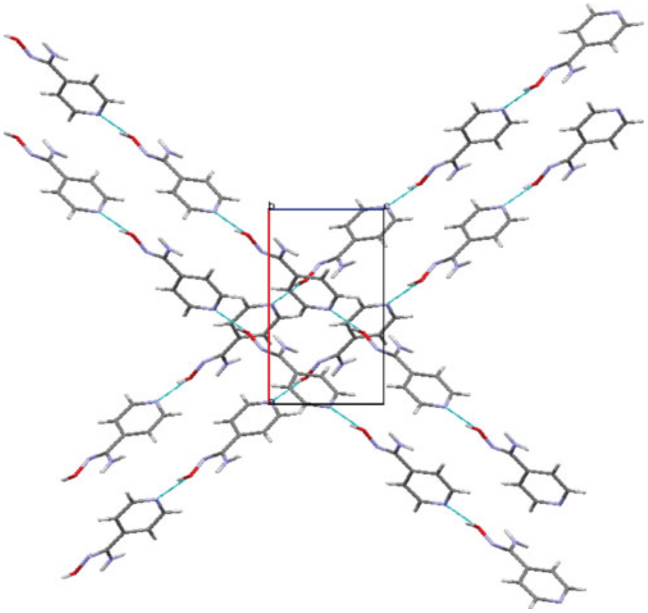

Figure 7. Packing of molecules when viewed down *b*-axis.

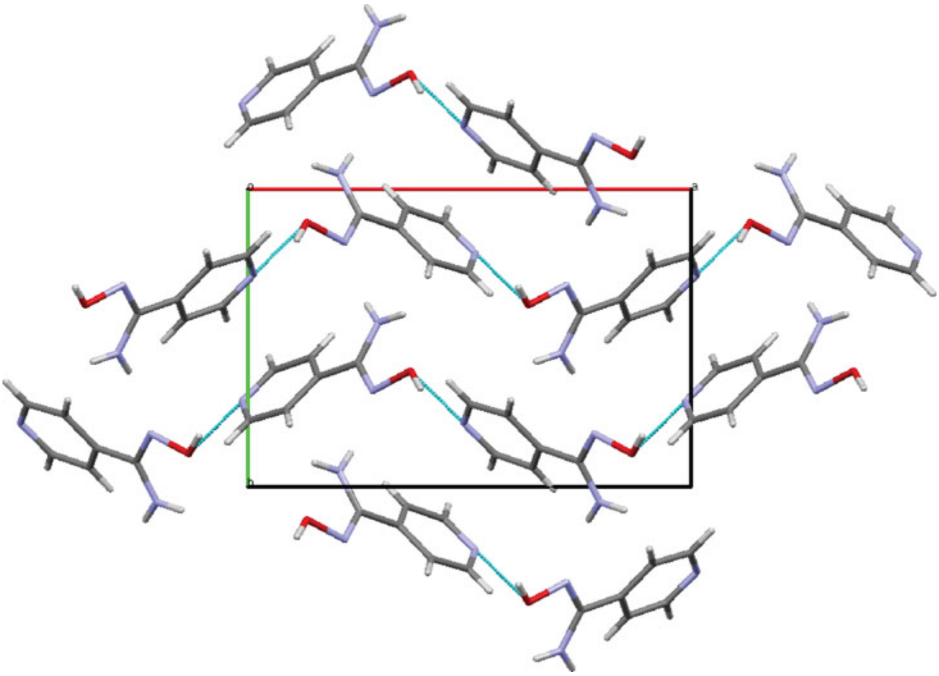

Figure 8. Packing of molecules when viewed down *the c*-axis.

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Table 2. Crystal data and structure refinement

Parameter	Value
CCDC deposit No.	945510
Empirical formula	$C_6 H_7 N_3 O$
Formula weight	137.15
Temperature	293(2) K
Wavelength	1.54178 Å
Crystal system, space group	Orthorhombic, $Pna2_1$
Unit cell dimensions	$a = 12.5664(8)$ Å $\alpha = 90°$
	$b = 8.8622(6)$ Å $\beta = 90°$
	$c = 5.7953(4)$ Å $\gamma = 90°$
Volume	645.4(7) $Å^3$
Z, Calculated density	4, 1.411 Mg/m^3
Absorption coefficient	0.847 mm^{-1}
$F_{(000)}$	288
Crystal size	0.21 × 0.19 × 0.18 mm
Theta ranges for data collection	6.11–64.59°
Limiting indices	$-12 \leq h \leq 14, -10 \leq k \leq 10, -6 \leq l \leq 2$
Reflections collected/unique	3875/786 [R (int) = 0.0313]
Completeness to theta = 64.59°	98.5%
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	786/1/92
Goodness-of-fit on F^2	1.092
Final R indices [I > 2sigma(I)]	$R1 = 0.0279$, $wR2 = 0.0737$
R indices (all data)	$R1 = 0.0279$, $wR2 = 0.0737$
Absolute structure parameter	0.3(4)
Extinction coefficient	0.168(8)
Largest diff. peak and hole	0.153 and −0.137 e. $Å^{-3}$

transition of the constituent group. Hence, the material may be useful for optoelectronic applications.

Elemental Analysis

In order to confirm the chemical composition of the synthesized compound Carbon (C), Hydrogen (H), and Nitrogen (N) analysis was carried out. The experimental and calculated percentages of C, H, and N were given in Table 1.The differences between experimental and calculated percentages of C, H, and N were very close to each other and within the experimental errors. This confirms the formation of the product in the stoichiometric proportion.

Single Crystal X-Ray Diffraction Method

A colorless block-shaped single crystal of the suitable size of the title compound was selected for data collection. X-ray intensity data were collected for the title compound at temperature 293 K, on Bruker AXS Proteum2 CCD diffractometer with X-ray generator

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Table 3. Selected bond lengths and angles (Å,°)

O(10)-N(9)	1.4183(19)
C(2)-N(1)	1.337(3)
N(9)-C(7)	1.293(2)
C(4)-C(7)	1.476(2)
N(1)-C(6)	1.342(3)
C(7)-N(8)	1.356(2)
N(1)-C(2)-C(3)	123.66(19)
C(7)-N(9)-O(10)	108.29(13)
C(2)-N(1)-C(6)	116.73(16)
N(9)-C(7)-N(8)	123.60(16)
N(9)-C(7)-C(4)	117.91(13)
N(8)-C(7)-C(4)	118.41(16)
N(1)-C(6)-C(5)	123.66(18)

operating at 45 kV and 10 mA, using CuKα radiation ($\lambda = 1.54178$ Å). Data were collected with different settings of ϕ (0° and 90°), keeping the scan width of 0.5°, exposure time of 5 s, the sample to detector distance was 45.10 mm [7]. A complete data set is processed using the software SAINT PLUS [8]. The structure was solved by direct methods and refined by full-matrix least squares method on F^2 using SHELXS and SHELXL programs [9]. All nonhydrogen atoms were revealed in the first difference Fourier map itself. All hydrogen atoms were positioned geometrically (C–H = 0.93 Å, N–H = 0.86 Å, O–H = 0.82 Å) and refined using a riding model with $U_{iso}(H) = 1.2\ U_{eq}$ (C,N) and $U_{iso}(H) = 1.5\ U_{eq}$ (O). After several cycles of refinement, the final difference Fourier map showed peaks of no chemical significance and the residual is saturated to 0.0279. The geometrical calculations were carried out using the program PLATON [10]. The molecular and packing diagrams were generated using the software MERCURY [11].

X-ray diffraction analysis revealed that the title compound is crystallized in the orthorhombic crystal system with the space group $Pna2_1$. The unit cell parameters are $a = 12.5664(8)$ Å, $b = 8.8622(6)$ Å, $c = 5.7953(4)$ Å, $\alpha = 90°$, $\beta = 90°$, $\gamma = 90°$, and $V = 645.4(7)$ Å^3. The *ORTEP* view of the title molecule with displacement ellipsoids drawn at 50% probability level is shown in Fig. 5.

Table 4. Selected torsion angles (°)

N(1)-C(2)-C(3)-C(4)	0.0(3)
C(3)-C(2)-N(1)-C(6)	0.4(3)
O(10)-N(9)-C(7)-N(8)	−3.4(3)
O(10)-N(9)-C(7)-C(4)	179.83(14)
C(3)-C(4)-C(7)-N(9)	156.65(16)
C(5)-C(4)-C(7)-N(9)	−23.7(2)
C(3)-C(4)-C(7)-N(8)	−20.3(2)
C(5)-C(4)-C(7)-N(8)	159.40(17)
C(4)-C(5)-C(6)-N(1)	−0.6(3)

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Table 5. Hydrogen bond geometry (Å,°)

D—H···A	d(D—H)	d(H···A)	d(D···A)	<(DHA)
N8—H8*A*···O10*	0.86	2.18	2.4990(2)	102
N8—H8*B*···N9^{i}	0.86	2.29	3.1247(2)	162
O10—H10···N1^{ii}	0.82	1.97	2.7578(2)	162

Symmetry codes: (i) $1/2-x$, $-1/2+y$, $1/2+z$; (ii) $-1/2+x$, $1/2-y$, $-1+z$; (*) Intramolecular interaction.

The packing of molecules when viewed down *a*-axis, *b*-axis, and *c*-axis are given in Figs. 6–8, respectively. The crystal data and structure refinement details are given in Table 2. Bond lengths and bond angles are given in Table 3. Torsion angles and Hydrogen-bond geometry are given in Tables 4 and 5, respectively.

The pyridine ring, N1/C2/C3/C4/C5/C6 lies in the axial position with respect to the plane described by the amidxoime chain N8—C7—N9—O10, confirmed by the dihedral angle 21.83(9)°. A torsion angle of 156.65(16)° about C3—C4—C7—N9 confirms that the pyridine ring attached at C7 reflects *Anti-Periplanar* conformation. The overall geometry of the title compound is similar to the molecule *N*'-Hydroxynicotinamidine [12].

An intramolecular interaction N8–H8A···O10 forms a five-membered planar ring C7/N8/H8A/O10/N9 with amidoxime chain. The crystal structure exhibits N8–H8A···π interaction (N8–H8A···*Cg1* [where *Cg1* is the centroid of the ring N1/C2/C3/C4/C5/C6 with a symmetry code *1/2–x,* –1/2+*y,* –1/2+*z*] with a N—*Cg* distance of 3.2956(17) Å, N—H···*Cg* angle of 138°) and the structure is stabilized by the intermolecular interactions of types N—H···O, N—H···N, and O—H···N in the crystal lattice.

Conclusion

The compound *(Z)*-2-*N*′-hydroxyisonicotinamidine, (2) was synthesized and characterized by means of ^{1}H NMR, FAB-Mass, FT-IR, and UV–visible spectroscopy data. The molecular structure of this compound was determined by single crystal XRD method. The crystal structure of the title compound reveals a potentially tautomeric amidoximes to be the amino-oxime form and it adopts a nonplanar *cis-syn* configuration. Spectral data show that the material may be useful for optoelectronic applications.

Acknowledgments

The authors thank the IOE X-ray diffraction facility, University of Mysore, Mysore for collecting the data.

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