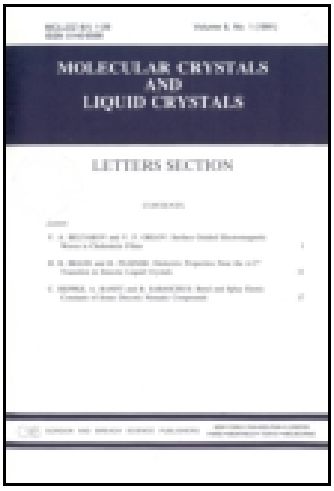

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Synthesis, Crystal Structure, and Characterization of 2-Phenyl-N-(pyrazin-2-yl)Acetamide

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Synthesis, Crystal Structure, and Characterization of 2-Phenyl-*N*-(pyrazin-2-yl)Acetamide

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The title compound, 2-Phenyl-N-(pyrazin-2-yl)acetamide, $C_{12}H_{11}N_3O$, was prepared by the coupling reaction and the product was crystallized by using toluene and methanol mixture(1:1) The structure of the compound was confirmed by elemental analysis, FTIR, ^1H NMR, thermogravimetric analysis, differential thermal analysis, UV-Visible spectroscopy, and single-crystal X-ray diffraction. The compound crystallizes in the monoclinic space group P $2_1/c$ with the following unit-cell parameters: $a = 8.1614(10)$, $b = 14.9430(13)$, $c = 9.3877(9)$ Å, $\beta = 103.653(12)^\circ$, and $Z = 4$. The crystal structure was solved by direct methods 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 0.0465 for 1486 observed reflections. An intramolecular C—H···O hydrogen bond generates an S(6) graph-set motif. In the crystal, molecules are linked by N—H···O and C—H···O hydrogen bonds, forming a two-dimensional network.

Keywords Acetamide; crystal structure; FTIR; ^{1}H NMR spectrum; inter-molecular interactions; pyrazine; thermo gram

Introduction

Pyrazines are a class of compounds that occur almost ubiquitously in nature. Pyrazine derivatives have been reported to possess diverse pharmacological activities including antimicrobial activity, fungicidal activity, herbicidal activity, antioxidant activity, and antialgal antituberculosis activity [1–8].

N-Substituted-2-arylacetamides are very interesting compounds because of their structural similarity to the lateral chain of natural benzylpenicillin [9,10]. Amide bonds play a major role in the elaboration and composition of biological systems, which are the main chemical bonds that link amino acid building blocks together to give proteins. Amide bonds are not limited to biological systems and are indeed present in a huge array of molecules, including major marketed drugs. Amide derivatives possessing anti-inflammatory [11–13], antimicrobial [14], and antitubercular [15] activities are reported in the literature.

Prompted by the above reports, we have attempted to synthesize new *N*-Substituted-2-arylacetamide derivatives and characterization was done by the elemental analysis, FTIR, ^{1}H

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NMR, thermogravimetric analysis (TGA), UV-Visible spectroscopy, and single-crystal X-ray diffraction. Crystal structure of some of the *N*-Substituted-2-arylacetamide derivatives are reported in the literature [16–19].

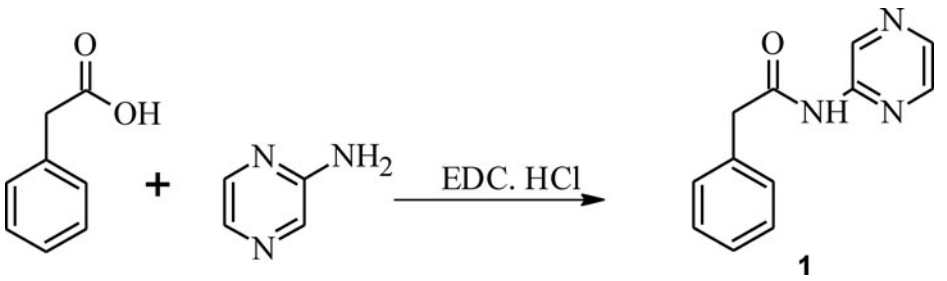
Experimental

Materials and Methods

All chemicals were purchased commercially and used without prior purification. Melting point was taken in 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}) and ^{1}H-NMR (400 MHz) spectrum was recorded on a Varian 400 spectrometer, with 5 mm PABBO BB-1H TUBES. A Shimadzu DTG-60 thermogravimetric analyzer was used to obtain TGA curve under nitrogen atmosphere with a heating rate of 10°C min^{-1}. The UV-Vis spectrum was recorded in Shimadzu UV-2550 UV-Visible spectrophotometer. Elemental analysis was carried out by using VARIO EL-III (Elementar 10 Analysensysteme GmBH).

*Synthesis of Compound 2-Phenyl-*N*-(pyrazin-2-yl)acetamide (1)*

Phenylacetic acid (1 mmol), 2-aminopyrazine (1 mmol), and 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride (0.01 mol) were dissolved in dichloromethane (20 mL). To this mixture triethylamine was added and stirred at room temperature for about 3 hr. The contents were poured into 100 mL of ice-cold aqueous hydrochloric acid with stirring and extracted thrice with dichloromethane. The organic layer was washed with saturated $NaHCO_3$ solution and brine solution, dried and concentrated under reduced pressure to yield the title compound. Single crystals were grown from methanol and toluene (1:1) mixture by the slow evaporation method. (1.30g, 87%) [m.p.: 148–150°C].



Scheme 1.

Results and Discussion

Elemental Analysis

In order to confirm the chemical composition of the synthesized compound CHN analysis was carried out. The experimental and calculated percentages of C, H, and N were given

Table 1. Elemental analysis for $C_{12}H_{11}N_3O$

Element	Experimental (%)	Calculated (%)
Carbon	67.57	67.59
Nitrogen	19.69	19.71
Hydrogen	5.22	5.20

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.

UV-Vis Spectral Analysis

Like IR spectroscopy, UV-Vis spectroscopy also useful in the evaluation of compounds. In the UV electronic spectrum, compounds are analyzed based on the characteristic frequencies (or λ_{max}) corresponding to definite groups. In unsaturated compounds like **1**, π to π^* transition is common with λ_{max} 305 nm (Fig. 1). There was no absorption peak between 360 nm and 900 nm in the entire visible region. Hence, the material may be useful for optoelectronic applications.

Thermal Gravimetric Analysis

In the present thermal study of compound **1**, weight loss was measured from the ambient temperature to 600°C. In Fig. 2 thermal gravimetric analysis (TGA) curve shows that compound is stable up to 232°C indicating the absence of moisture in the crystal. A weight loss of around 87% occurs between 232°C and 254°C which is due to the loss of one molecule of phenyl ring and pyrazine ring. Above 500°C, 13% of the residue was left out

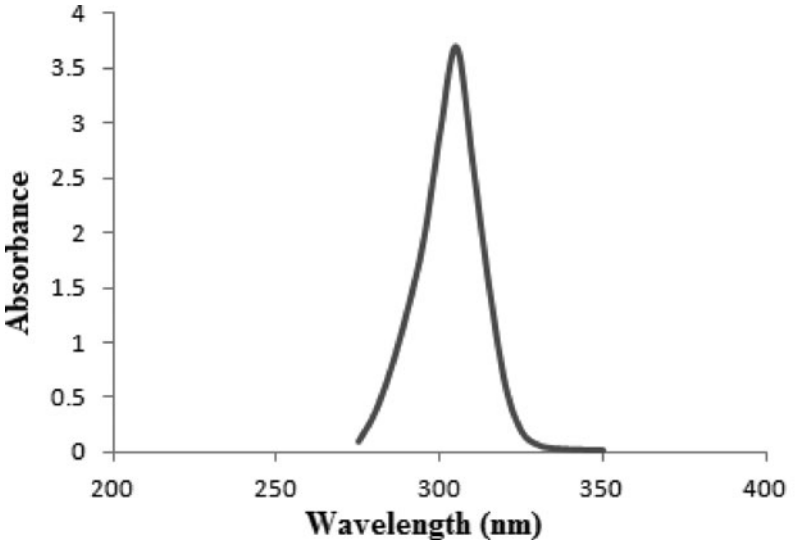


Figure 1. UV-visible spectrum of the 2-phenyl-*N*-(pyrazin-2-yl)acetamide **(1)**.

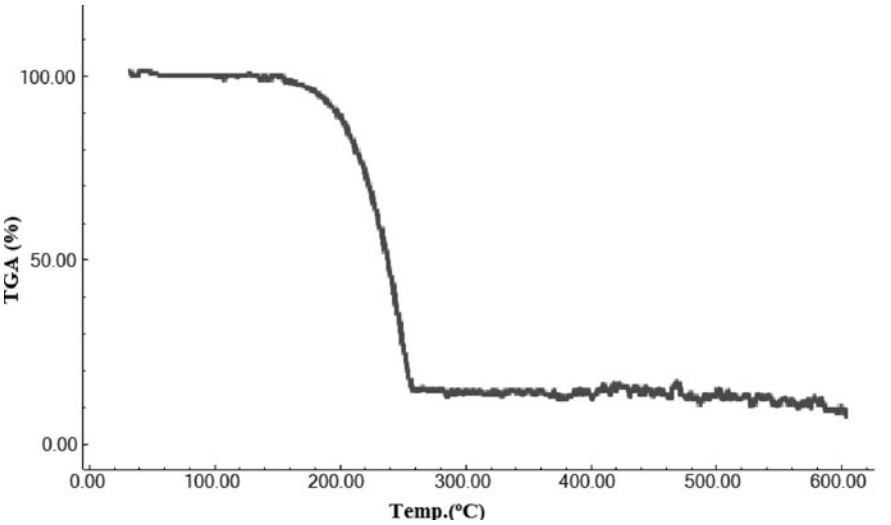


Figure 2. TGA curve of 2-phenyl-*N*-(pyrazin-2-yl)acetamide **(1)**.

which was due to the charring of carbon. Thus, the TG study confirms the formation of the compound in the stoichiometric ratio.

FTIR and 1H NMR Spectral Analysis

The IR bands at 3211 cm^{-1} for NH and 1662 cm^{-1} C═O are characteristic of stretching vibration of amide bonds as shown in Fig. 3. The absorption band observed at 3051 cm^{-1}

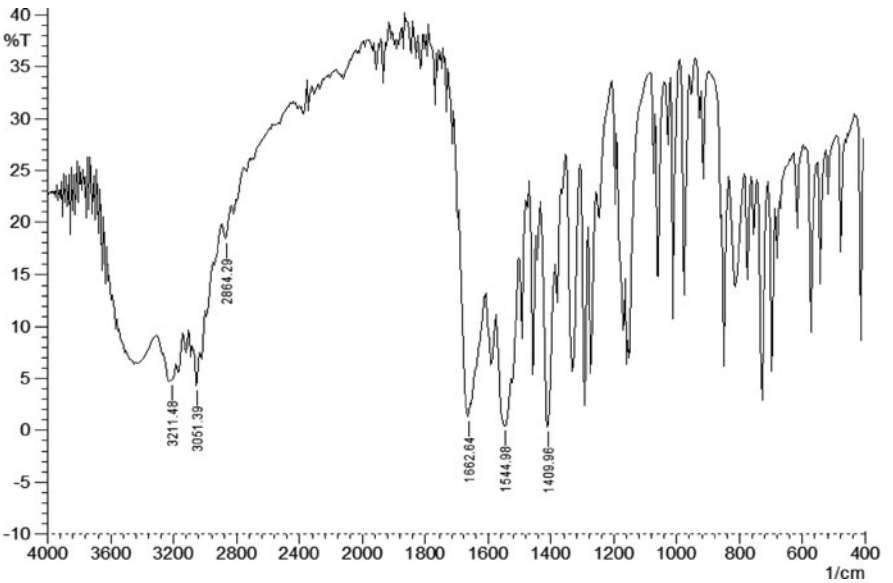


Figure 3. FTIR spectrum of the 2-phenyl-*N*-(pyrazin-2-yl)acetamide **(1)**.

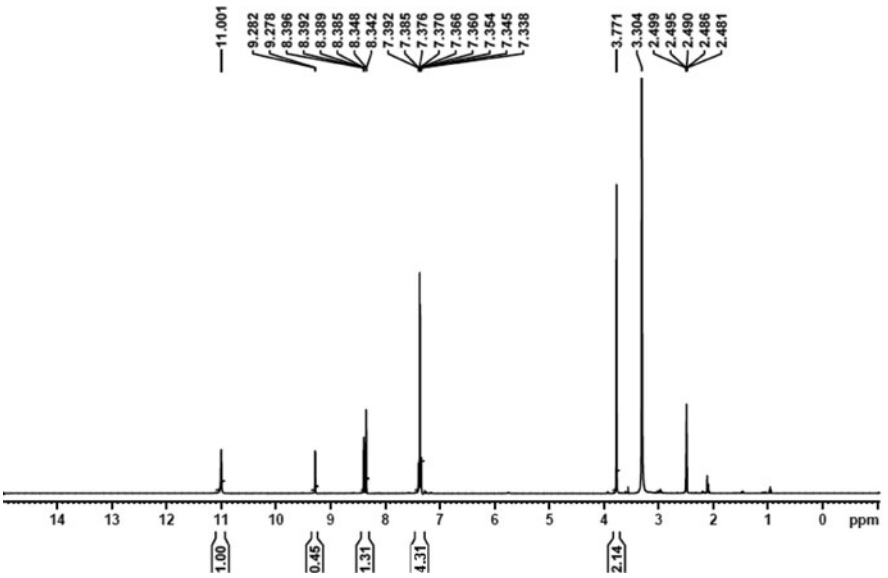


Figure 4. ^{1}H NMR spectrum of the 2-phenyl-*N*-(pyrazin-2-yl)acetamide (**1**).

and 2864 cm^{-1} were due to the aromatic and aliphatic C—H stretching, respectively. Appearance of absorption band at 1662 cm^{-1}, 1554 cm^{-1}, and 1409 cm^{-1} were due to the C=O, C=N, and C=C stretching, respectively.

The ^{1}H NMR spectrum (Fig. 4) of compound (**1**), showed singlet at δ 3.77 ppm indicated the two protons of O=C—CH_2 of amide moiety. Two doublets appeared at δ 8.34 ppm (J = 2.4 Hz) and δ 9.27 ppm (J = 1.6 Hz) were due to pyrazine 6H and 3H protons. In addition to this, a doublet of doublet was observed in the region δ 8.40 ppm (J = 1.6 Hz and 2.8Hz) representing pyrazine 5H proton and hence confirming the presence of pyrazine moiety. Amide NH proton observed at δ 11.00 ppm confirms the formation of amide link.

Single Crystal X-Ray Diffraction Method

Single crystal of suitable size of the title compound **1** was selected for data collection. X-ray intensity data of 4352 reflections (of which 2177 unique) were collected on *X'calibur* CCD area-detector diffractometer equipped with graphite monochromated MoKα radiation (λ = 0.71073 Å). The crystal used for data collection was of dimensions 0.30 × 0.20 × 0.20 mm. The cell dimensions were determined by least-squares fit of angular settings of 1165 reflections in the θ range 4.02–26.59°. The intensities were measured by ω scan mode for θ ranges 3.52–25.99°. 1486 reflections were treated as observed ($I > 2\sigma$ (I)). Data were corrected for Lorentz, polarization and absorption factors. The structure was solved by direct methods using SHELXS97 [20]. All nonhydrogen atoms of the molecule were located in the best E-map. All the hydrogen atoms were geometrically fixed and allowed to ride on their parent C/N atoms with C-H = 0.93–0.97 Å and N-H distance of 0.86 Å, with U_{iso}(H) = 1.2U_{eq}(C). Full-matrix least-squares refinement was carried out using SHELXL97 [20].

Table 2. Crystal data and structure refinement

CCDC No	949576
Crystal description	Block-shaped
Crystal color	Light-green
Crystal size	0.3 × 0.2 × 0.2 mm
Empirical formula	C_{12} H_{11} N_3 O
Formula weight	213.24
Radiation, Wavelength	Mo $K\alpha$, 0.71073 Å
Unit cell dimensions	$a = 8.1614(10)$, $b = 14.9430(13)$, $c = 9.3877(9)$ Å $\beta = 103.653(12)^\circ$
Crystal system	Monoclinic
Space group	P 2_1/c
Unit cell volume	1112.5(2) Å^3
No. of molecules per unit cell, Z	4
Temperature	293(2)
Absorption coefficient	0.085 mm^{-1}
F(000)	448
Scan mode	ω scan
θ range for entire data collection	$3.52 < \theta < 25.99^\circ$
Range of indices	$h = -10$ to 9, $k = -11$ to 18, $l = -11$ to 6
Reflections collected/unique	4352/2177
Reflections observed ($I > 2s(I)$)	1486
R_{int}	0.0266
R_{sigma}	0.0452
Structure determination	Direct methods
Refinement	Full-matrix least-squares on F^2
No. of parameters refined	146
Final R	0.0465
$wR(F^2)$	0.0997
Weight	$1/[\sigma^2 (F_o^2)+(0.0456P)^2+ 0.0608P]$ where $P = [F_o^2 + 2F_c^2]/3$
Goodness-of-fit	1.023
$(\Delta/\sigma)_{max}$	0.001 (for U12 C7)
Final residual electron density	$-0.129 < \Delta\rho < 0.117$ Å^{-3}
Measurement	*X'calibur system–-Oxford diffraction make U.K.*
Software for structure solution:	SHELXS97 (Sheldrick, 2008)
Software for refinement:	SHELXL97 (Sheldrick, 2008)
Software for molecular plotting:	ORTEP-3 (Farrugia,2012) PLATON (Spek, 2009)
Software for geometrical calculation	PLATON (Spek, 2009) PARST (Nardelli, 1995)

The crystal data and structure refinement details are reported in Table 2.

An ORTEP view of the title compound with atomic labeling is shown in Fig. 5 [21]. The geometry of the molecule was calculated using the PLATON [22] and PARST [23] softwares. The title molecule, comprises of two 6-membered rings, vis a phenyl ring and a pyrazole ring (Fig. 5).

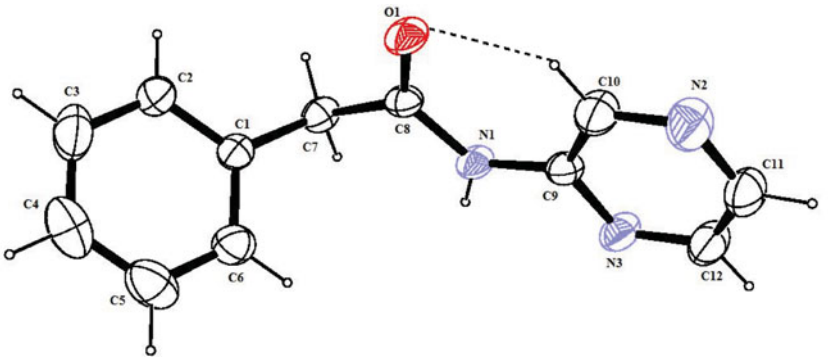


Figure 5. *ORTEP* view of the molecule with displacement ellipsoids drawn at 40%. H atoms are shown as small spheres of arbitrary radii.

The packing of molecules when viewed down from different axis are given in Fig. 6 and Fig. 7, respectively.

Bond lengths and angles of the title molecules are within normal ranges [24] and correspond to those observed in related structures [25].

The dihedral angle between the mean planes of the phenyl ring and pyrazine rings is 81.37(6)°. The double bonds C8 = O1 is confirmed by its respective distance of 1.230(2) Å. The length of the double bond C8 = O1 is larger than the standard value for carbonyl group (1.192 Å) and lengthening of the C8 = O1 double bond is due to strong intramolecular hydrogen bond between C10 and O1. This intramolecular interaction leads to the formation of a virtual six-membered ring comprising atoms O1, C8, N1, C9, C10, and H10. Bond distances and bond angles for non- hydrogen atoms are listed in Table 3. Packing view of the molecules in the unit cell viewed down the a and b axis is shown in (Fig. 5 and 6, respectively). In the crystal, molecules are held together by strong C—H···O and N—H···O intermolecular interactions. Details of intra and intermolecular hydrogen bonding are given in Table 4.

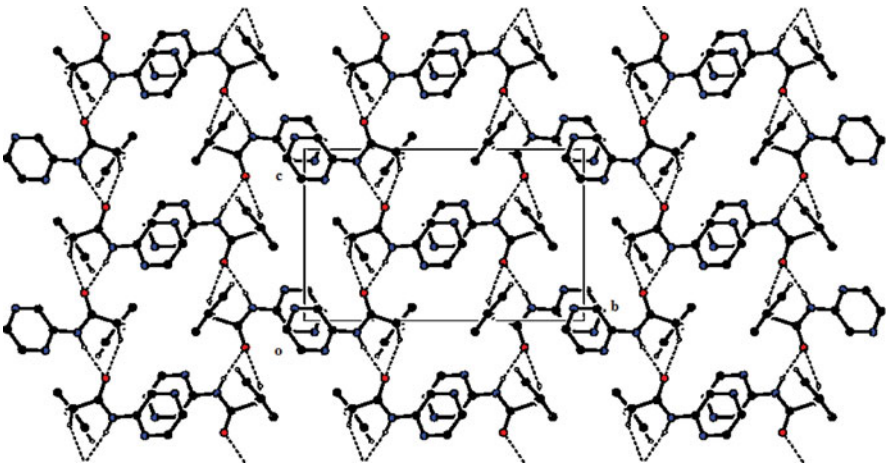


Figure 6. The packing arrangement of molecules viewed down the *a*-axis.

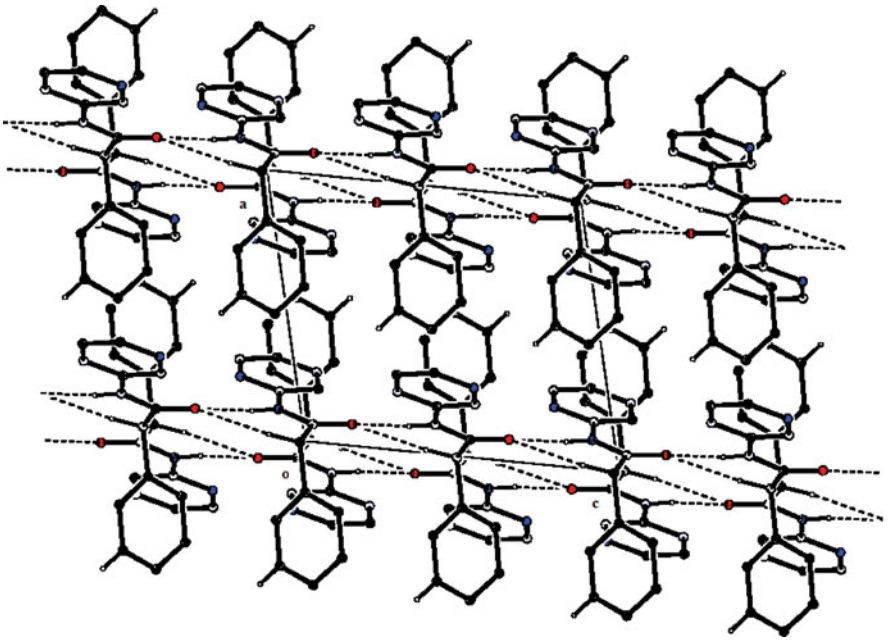


Figure 7. The packing arrangement of molecules viewed down the *b*-axis.

Table 3. Bond lengths (Å) and bond angles (°) for nonhydrogen atoms (e.s.d.'s are given in Parentheses)

Bond lengths (Å)			
O1-C8	1.230(2)	N1-C8	1.350(2)
N1-C9	1.401(2)	N2-C11	1.327(2)
N2-C10	1.332(2)	N3-C9	1.326(2)
N3-C12	1.334(2)	C1-C2	1.376(2)
C1-C6	1.382(2)	C1-C7	1.508(2)
C2-C3	1.379(3)	C3-C4	1.362(3)
C4-C5	1.375(3)	C5-C6	1.370(3)
C7-C8	1.511(2)	C9-C10	1.387(2)
C11-C12	1.361(3)		
Bond angles (°)			
C8-N1-C9	128.4(1)	C11-N2-C10	116.5(2)
C9-N3-C12	116.1(2)	C2-C1-C6	118.5(2)
C2-C1-C7	121.3(2)	C6-C1-C7	120.2(2)
C1-C2-C3	120.2(2)	C4-C3-C2	120.7(2)
C3-C4-C5	119.6(2)	C6-C5-C4	119.8(2)
C5-C6-C1	121.1(2)	C1-C7-C8	111.6(1)
O1-C8-N1	123.1(2)	O1-C8-C7	121.2(2)
N1-C8-C7	115.7(1)	N3-C9-C10	121.5(2)
N3-C9-N1	113.3(2)	C10-C9-N1	125.2(2)
N2-C10-C9	121.5(2)	N2-C11-C12	121.8(2)
N3-C12-C11	122.5(2)		

Table 4. Hydrogen–bonding geometry (e.s.d.'s in parentheses)

D–H . . . A	D–H(Å)	H . . . A(Å)	D . . . A(Å)	D–H . . . A(°)
C10-H10 . . . O1	0.930	2.266	2.867(2)	121
C7-H7B . . . O1^{i}	0.970	2.460	3.332(2)	149
N1-H1 . . . O1^{i}	0.860	2.053	2.902(2)	169

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

Conclusions

In summary, a new 2-phenyl-*N*-(pyrazin-2-yl)acetamide (**1**) was synthesized and characterized by spectral data. The structure of the compound was determined by single crystal X-ray diffraction method. The geometrical configuration of the compound was confirmed as Z. The crystal structure analysis shows that the compound forms a block shaped structure with the monoclinic crystal system. The elemental analysis confirms the formation of the compound in a stoichiometric ratio. TGA were carried out to study the thermal behavior of the crystal.

Acknowledgments

BN thanks the UGC for financial assistance through BSR one time grant for the purchase of chemicals. PSN thanks Mangalore University for research facilities and DST-PURSE for financial assistance. 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.

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