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Crystallographic and conformational analyses of zwitterionic form of (*E*)-2-methoxy-6-[(2-morpholinoethylimino)methyl]phenolate

Hande Petek,[(1)]* Çiğdem Albayrak,[(2)] Nazan Ocak İskeleli,[(3)] Erbil Ağar,[(2)] and İsmet Şenel[(1)]

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The single crystal X-ray diffraction analysis of the title compound, $C_{14}H_{20}N_2O_3$, reveals that the structure is adapted to its zwitterionic form and $R_2^2(12)$ centrosymmetric dimers are formed by N^+–H$\cdots O^-$ type ionic weak hydrogen bonds in the crystal structure. The title compound crystallizes in the triclinic space group $P-1$ with $a = 5.9255(13)$ Å, $b = 9.853(3)$ Å, $c = 12.248(3)$ Å, $\alpha = 101.793(19)^\circ$, $\beta = 94.941(17)^\circ$, $\gamma = 104.36(2)^\circ$, $Z = 2$, $D_x = 1.308$ g/cm^3, μ (Mo-K$_\alpha$) $= 0.092$ mm^{-1}. The structure was solved by direct methods and refined to a final $R = 0.0371$ for 2183 reflections with $I > 2\sigma$ (I). The crystal structure is stabilized by N^+–H$\cdots O^-$ type intra-molecular hydrogen bonds and N^+–H$\cdots O^-$ type packing interactions referred to as weak hydrogen bonds. To elucidate conformational flexibility of the title molecule, the selected torsion angle is varied from -180° to $+180^\circ$ in every 10° separately and then molecular energy profile is calculated and construed. In addition, charge-population analysis of the crystallographically observed structure confirms its zwitterionic form.

KEY WORDS: crystal structure; schiff base; morpholine; zwitterion; PM3; conformational analysis.

Introduction

Schiff bases are widely used as ligands in the field of coordination chemistry[1] and they play an important role in various field of chemistry due to their biological activities.[2–5] N-substituted *o*-hydroxyimines have been reported to display thermochromism and photochromism in the solid state by H-atom transfer from the hydroxy O atom to the N atom.[6]

In general, *O*-hydroxy Schiff bases exhibit two possible tautomeric forms, the phenol-imine (or benzenoid) and keto–amine (or quinoid) forms. Depending on the tautomers, two types of intra-molecular hydrogen bonds are possible: O–H$\cdots$N in benzenoid and N–H$\cdots$O in quinoid tautomers. *O*-hydroxy Schiff bases have been previously observed in the keto form, in the enol form or in enol/keto mixtures[7,8] by means of the H-atom transfer.

Another form of the Schiff base compounds is also their zwitterionic form.[9] Zwitterions of Schiff bases have an ionic intra-molecular hydrogen bond (N^+–H$\cdots O^-$) and their N^+–H

[(1)] Department of Physics, Faculty of Arts and Sciences, Ondokuz Mayıs University, Kurupelit 55139, Samsun, Turkey.
[(2)] Department of Chemistry, Faculty of Arts and Sciences, Ondokuz Mayıs University, Kurupelit 55139, Samsun, Turkey.
[(3)] Department of Science Education, Sinop Faculty of Education, Ondokuz Mayıs University, 57000 Sinop, Turkey.
* To whom correspondence should be addressed; e-mail: hpetek@omu.edu.tr.

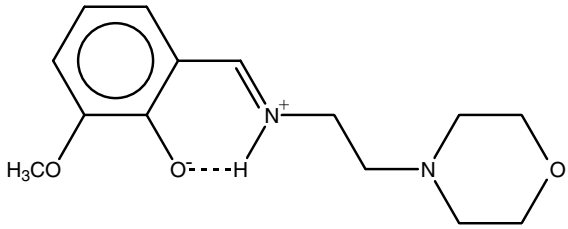

Fig. 1. Chemical diagram of the zwitterionic form for the title compound.

bond lengths are longer than the standard interatomic separations observed in neutral N–H bonds (0.87 Å). The other ionic bonds in the zwitterions, C–O^-, is not a key indicator as distinctive as N^+–H bond, because NH forms of Schiff bases in solid state can be regarded as a resonance hybrid of two canonical structures, the quinoidal and zwitterionic forms.[10]

Here we report the molecular and crystal structure of (*E*)-2-methoxy-6-[(2-morpholinoethylimino)methyl]phenolate (Fig. 1), determined by single crystal X-ray diffraction study, and the conformational analysis of the title molecule with respect to the selected torsion angle is achieved by PM3 semi-empirical quantum mechanical model. In order to computationally verify zwitterionic character of the crystallographically observed geometry of the title compound, the calculated excess charges located on the non-H atoms are incorporated into the discussion.

Experimental

Synthesis of the title compound

The compound was prepared by reflux a mixture of a solution containing salicylaldehyde (0.5 g 4.1 mmol) in ethanol (20 ml) and a solution containing 4-(2-aminoethyl)morpholine (0.53 g 4.1 mmol) in 20 ml ethanol. The reaction mixture was stirred for 1 h under reflux. The crystals of title compound suitable for X-ray analysis were obtained from methyl alcohol by slow evaporation (yield % 95; m.p. 355–357 K).

X-ray crystallography

A suitable sample of size 0.420 × 0.317 × 0.130 mm was selected for the crystallographic study. All diffraction measurements were performed at room temperature (296 K) using graphite monochromated MoK_α radiation and an STOE IPDS 2 diffractometer. The systematic absences and intensity symmetries indicated the monoclinic $P-1$ space group. A total of 11629 reflections with $[1.71^\circ < \theta < 27.88^\circ]$ were collected in the rotation mode and cell parameters were determined by using X-AREA software.[11] Absorption correction ($\mu = 0.092$ mm^{-1}) was achieved by the integration method via X-RED software.[11]

Table 1. Crystallographic Data for the Title Compound

CCDC deposit No.	CCDC 288736*
Color/shape	Yellow/Prism
Chemical formula	$C_{14}H_{20}N_2O_3$
Formula weight	264.32
Temperature	296 K
Crystal system	Triclinic
Space group	*P –1*
Unit cell parameters	$a = 5.9255(13)$ Å
	$b = 9.853(3)$Å
	$c = 12.248(3)$ Å
	$\alpha = 101.793(19)^\circ$
	$\beta = 94.941(17)^\circ$
	$\gamma = 104.36(2)^\circ$
Volume	671.0(3)Å^3
Z	2
Density	1.308 g/cm^3
Absorption coefficient	0.092 mm^{-1}
T_{min}, T_{max}	0.9765, 0.9937
Diffractometer/meas. meth.	STOE IPDS 2/ϖ -scan
θ range for data collection	1.71° to 27.88°
Unique reflections measured	3172
Independent/observed reflections	3172/2183
Data/restraints/parameters	2183/0/253
Extinction Coefficient	0.073(10)
Goodness of fit on F^2	1.003
Final *R* indices [$I > 2\sigma(I)$]	$R_1 = 0.0371$, $wR_1 = 0.1048$
R indices (all data)	$R_2 = 0.0602$, $wR_2 = 0.1146$

*CCDC 288736 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

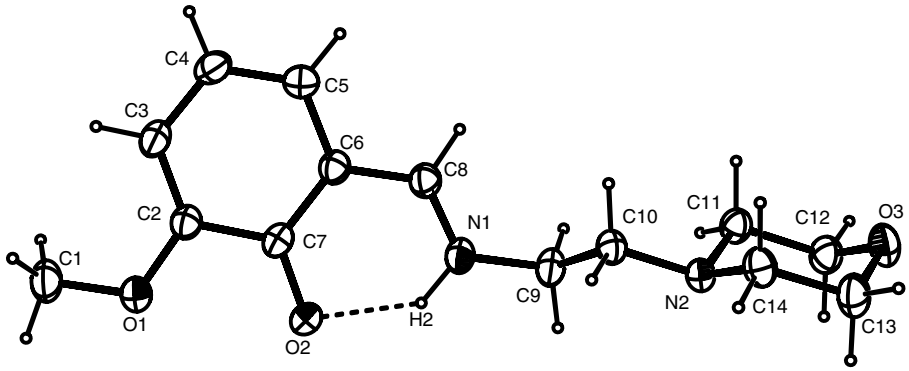

Fig. 2. An ORTEP view of the title molecule with the atomic numbering scheme showing intramolecular ionic hydrogen bond, which is depicted by dashed lines. Displacement ellipsoids are shown at the 30 % probability level.

The structure was solved by direct methods using SHELXS-97.[12] The refinement was carried out by full-matrix least-squares method on the positional and anisotropic temperature parameters of the non-hydrogen atoms, or equivalently corresponding to 253 crystallographic parameters. All non-hydrogen atoms were refined anisotropically and the positions of H atoms were obtained from difference Fourier map of electron density in the unit cell. The structure was refined to $R_1 = 0.0371$ for observed reflections which obeyed to the condition of 2183 $I > 2\sigma\ (I)$ and to $R_1 = 0.0602$ for all 3172 data used in refinement process. The maximum peaks and deepest hole observed in the final $\Delta\rho$ map were 0.20 and -0.13 eÅ^{-3}, respectively. The scattering factors were taken from SHELXL-97.[12] The data collection conditions

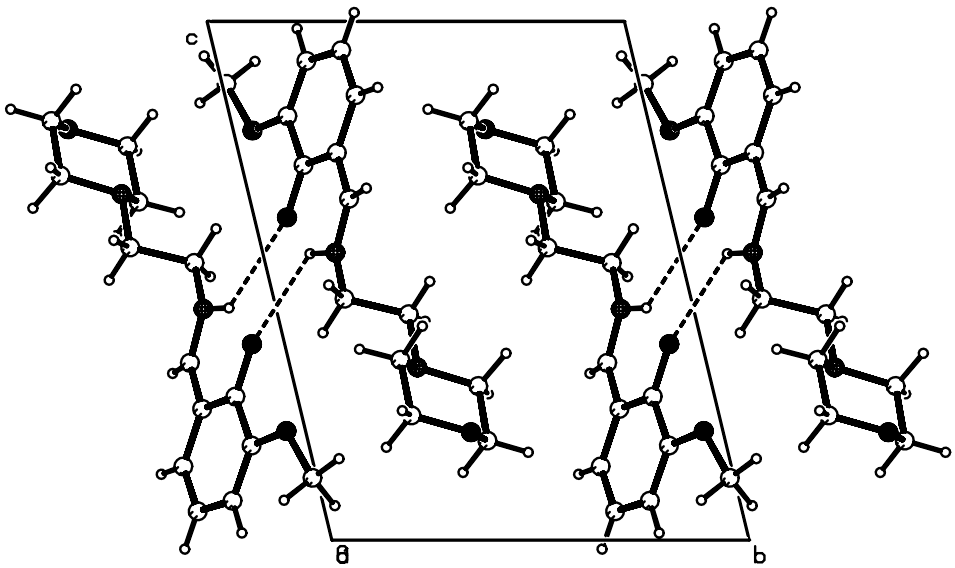

Fig. 3. Crystal packing diagram of the title compound showing two $R_2^2(12)$ centrosymmetric dimers formed by N^+–H$\cdots O^-$ type crystal packing interactions viewed down the *a*-axis.

and parameters of refinement process are listed in Table 1.

Computational procedure

The geometry optimization of the zwitterionic form of the molecule leading to energy minima was achieved by using PM3 self-consistent field molecular orbital method[13] at the restricted Hartree-Fock (RHF) level[14] with the aid of WinMopac 7.21 package.[15] Non-Linear Least Squares (NLLSQ) gradient minimization routine was used in the optimization procedure with very precise GNorm of 0.01 by allowing arbitrary valance of N1 and O2 atoms. To elucidate conformational flexibility of the title molecule, the selected torsion angle [T(N1–C9–C10–N2)] is varied from −180° to −180° in every 10° and thus molecular energy profile is obtained by performing single point calculations on the calculated potential energy surface. In addition, residual charges located on each of non-H atom for the structure were calculated in order to reveal zwitterionic character of the crystallographically observe structure.

Results and discussion

An ORTEP-3 plot[16] with the atom-numbering scheme and molecular packing drawing[17] with intramolecular hydrogen bond and crystal packing interactions (weak H-bonds) in the crystal structure of the title compound are shown in Figs. 2 and 3, respectively. Comparative results obtained from the X-ray crystallographic and computational studies are presented in Table 2.

It is seen that this structure reported here adopts a zwitterion form, because its N^+–H bond distance [1.18(3) Å] is comparable with the similar zwitterions in the literature [1.11(3) Å; 1.10(3) Å].[18,19] The C7–O2 bond length [1.296(2) Å] is intermediate between single and double carbon to oxygen bond legths (1.362 Å, 1.222 Å),[20] whereas the C2–O1 is 1.362(2) Å. In addition to this, the shortening of C2–C3, C4–C5 and the elongation of C2–C7, C3–C4, C5–C6 and C6–C7 bonds can be explained by a quinoid resonance contribution to the ring containing O^- in the *ortho* position. The bonds of C6–C8, C8–N1 and N1–C9 with their respective bond distances of 1.430(3), 1.285(3) and 1.457(3) Å indicate the zwitterionic character of the title compound.[19]

The existence of N1–C9, C9–C10 and C10–N2 single bonds allowing for three torsional degrees of freedom has a significant effect on the

Table 2. Comparative Results of the Selected Bond Lengths (Å), Bond and Torsion Angles (°)

	X-ray	PM3
Bond Lengths		
C8–N1	1.287(2)	1.38
N1–C9	1.464(2)	1.47
O1–C1	1.424(2)	1.40
C6–C8	1.425(2)	1.37
C9–C10	1.516(2)	1.53
C10–N2	1.456(2)	1.48
O1–C2	1.362(2)	1.37
O2–C7	1.296(2)	1.23
Bond Angles		
C8–N1–C9	122.7(1)	119.84
N1–C8–C6	123.4(1)	122.36
N2–C10–C9	111.7(1)	109.49
C1–O1–C2	117.2(1)	117.35
N1–C9–C10	111.1(1)	112.69
O2–C7–C6	122.8(1)	121.52
Torsion Angles		
C8–N1–C9–C10	73.9(2)	85.12
C9–N1–C8–C6	175.4(1)	− 161.71
N1–C9–C10–N2	168.5(1)	− 174.88
C1–O1–C2–C3	10.3(2)	1.55
O2–C7–C6–C8	5.0(2)	− 3.27
O1–C2–C7–O2	− 2.4(2)	1.17

Table 3. Hydrogen Bonding Geometry and Crystal Packing Interaction (Å, °) for the Title Compound

D–H···A	D···H	H···A	D···A	D–H···A
N1–H2···O2	1.18(3)	1.52(3)	2.578(2)	145(2)
N1–H2···O2†	1.18(3)	2.52(3)	3.238 (2)	118(2)

Note. D: donor, A: acceptor. Symmetry transformations used to generate equivalent atoms: † $-x, -y+2, -z+1$.

conformational flexibility in gas-phase. According to the results given in Table 2, the protonated N1 atom exhibits planar sp^2 hybridization, while the other nitrogen atom (N2), C9 and C10 display tetrahedral sp^3 hybridization. The morpholine ring in the title compound adopts an almost perfect chair conformation, with a total puckering amplitude of $Q_T = 0.993(4)$ Å.[21] The plane through the C atoms of the morpholine ring makes a dihedral angle of 81.60(5)° with the C2–C7 ring. The bond distances and angles in morpholine rings are in good agreement with the literature values.[22,23]

There is a strong N^+–H···O^- type intramolecular hydrogen bond. The crystal structure is stabilized by N^+–H···O^- type packing interactions similar to weak H-bonds. Due to small D–H···A angle and long D···A distance, this interaction can not be classified as a conventional hydrogen bond. Geometrical parameters of the intramolecular H-bond and the packing interaction referred to as intermolecular weak H-bond are listed in Table 3. Both interactions are charge-assisted, since the title compound is in zwitterionic form. The interactions referred to as N^+–H···O^- type intermolecular weak H-bonds lead to $R_2^2(12)$centrosymmetric dimer formations in the crystal structure (Fig. 3).[24]

The calculated molecular energy profile of the title molecule against the selected torsional degree of freedom is shown in Fig. 4. Some discrepancies between the molecular conformations of the PM3 optimized structure (its heat of formation is −72.56 kcal/mol) and the X-ray structure are observed, furthermore both structure prefer non-planar geometry. According to X-ray crystallographic study N1–C9–C10–N2 torsion angle is −168.5(1)°, this torsion angle is obtained as −174.86° in the optimized geometry of the title compound. The most important difference between the X-ray and PM3 optimized structures is observed in relative orientation of the plane through the C atoms of the morpholine ring and the ring carrying O^-. While the dihedral angle between the mean plane through C11, C12, C13 and C14 atoms and the ring carrying O^- is 81.60(5)°,

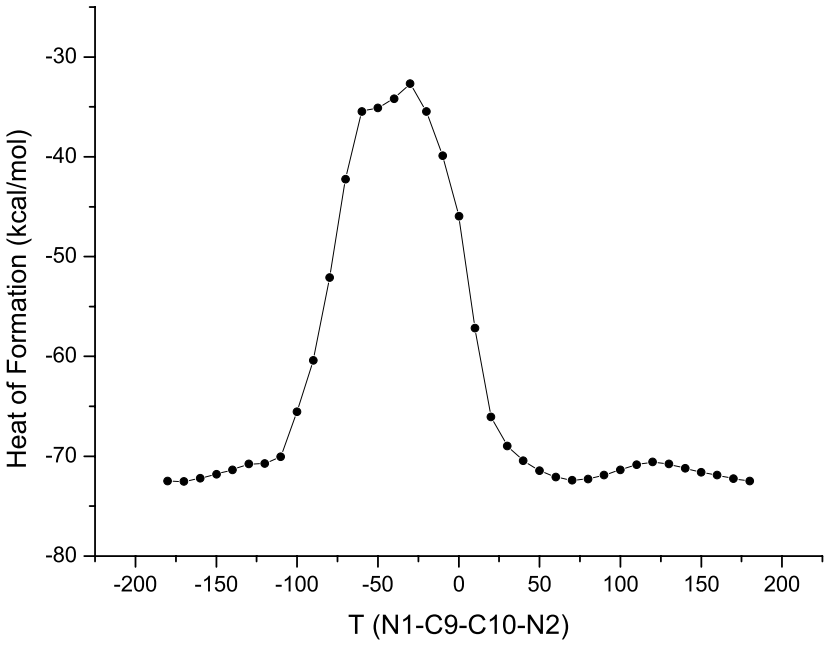

Fig. 4. Molecular energy profile against the selected torsional degree of freedom.

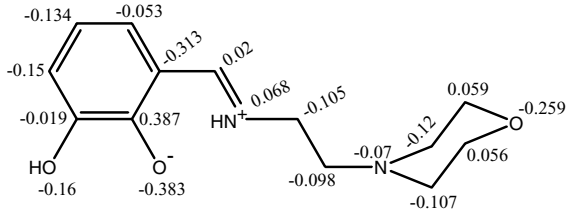

Fig. 5. Calculated excess charges on the non-H atoms of the title zwitterion.

this angle is 56.98° in the optimized geometry of the title zwitterion. The energy profile as function of T(N1–C9–C10–N2) shows evident maximum in the interval from −60° to 0° of the selected torsional degree of freedom. This augmentative effect in heat of formation value is due to short H–H contact between protonated N^+–H and hydrogens attached to C11. There is a considerable energy difference (approximately 26.66 kcal/mol) between heat of formation values of the most favorable and unfavorable conformer of the title compound. The observed conformational difference in the optimized structure is presumably due to strong intramolecular H-bond and weak intermolecular hydrogen bonding beside the contributions from packing of the molecules obeyed space group symmetry operations.

To verify the existence of charge-assisted hydrogen bond and weak hydrogen bond, excess charge located on each of non-H atom is calculated (Fig. 5). While residual charge on N1 atom is relatively positive in spite of lone pairs on N1, that of the other nitrogen atom is negative and the excess charge O^- in *ortho* position is of more negative character than the other oxygen atoms in the molecule. As a result of this charge distribution, it can be stated that the structure is adapted to zwitterionic form despite of the fact that the crystallographically observed structure is totally neutral. In the optimized geometry, N^+–H and C–O^- distance are obtained as 1.02 Å and 1.23 Å respectively. These results obviously verify the zwitterionic character of the crystallographically observed geometry of the title compound.

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