

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/229138182>

Conformational analysis of 1-piperidineacetic acid by X-ray, FTIR and ab initio calculations

ARTICLE *in* JOURNAL OF MOLECULAR STRUCTURE · AUGUST 2002

Impact Factor: 1.6 · DOI: 10.1016/S0022-2860(02)00127-8

CITATIONS

16

READS

10

5 AUTHORS, INCLUDING:



Zofia Dega-Szafran

Adam Mickiewicz University

236 PUBLICATIONS 2,475 CITATIONS

SEE PROFILE

Conformational analysis of 1-piperidineacetic acid by X-ray, FTIR and ab initio calculations

Z. Dega-Szafran*, Z. Kosturkiewicz, E. Nowak, M. Petryna, M. Szafran

Faculty of Chemistry, A. Mickiewicz University, 60-780 Poznań, Poland

Received 21 January 2002; accepted 6 February 2002

Abstract

The 1-piperidineacetic acid was synthesized as monohydrate and its structure has been determined by X-ray diffraction methods. The crystals are orthorhombic, space group $P2_12_12_1$, $a = 6.7693(7)$, $b = 10.816(1)$, $c = 11.452(1)$ Å, $Z = 4$, $R = 0.037$. The acid molecule appears in the zwitterionic form with two equivalent carboxylic oxygen atoms. The water molecules link carboxylic groups into infinite chains parallel to the z axis, by O–H...O hydrogen bonds of the lengths 2.85(2) and 2.75(2) Å. The $N^+(1)$ –H proton forms bifurcated hydrogen bond intramolecular with O(1) and intermolecular with O(2') of the length 2.795(2) and 2.775(3) Å, respectively. Five of the most stable conformers of 1-piperidineacetic acid and four of its monohydrate were analyzed by B3LYP/6-31G(d,p) calculations. For anhydrous acid, **NPA1** conformer with intramolecular N...H–O hydrogen bond is the most stable. The structure of conformer **NPA1** is similar to that of the most stable conformer of *N,N*-dimethylglycine. The zwitterionic form, **ZPA1**, is stabilized by the electrostatic interaction between the positively charged N^+H and negatively charged oxygen atoms of COO^- group. **ZPA1** is less stable than **NPA1** and the energy difference between them is 23.8 kcal/mol. In the case of monohydrate the difference is only 4.6 kcal/mol. This indicates that addition of water molecule increases the stability of the zwitterionic form of 1-piperidineacetic acid, **ZPAW3**. © 2002 Published by Elsevier Science B.V.

Keywords: Piperidineacetic acid; X-ray diffraction; Bifurcated hydrogen bonds; FTIR; B3LYP calculations

1. Introduction

Amino acids are known to exist as zwitterions in the crystalline state and in solution. However, in the gas phase they are present in their neutral forms, which was established both experimentally and theoretically [1]. The addition of successive water molecules stabilizes the zwitterionic form in the gas phase [2,3].

Glycine is a simple compound built of an amino group and a carboxy group connected by a methylene group. This structure has three internal rotational degrees of freedom: the rotation of the hydroxyl group about the C=O bond, the rotation about the C–C bond, and the rotation of the amino group about the C–N bond. The most stable conformers of glycine [1], its complexes with water molecules [2,3] and *N*-methylated derivatives [4] have been intensively studied by ab initio calculations.

In this article, we examine the structure of 1-piperidineacetic acid monohydrate crystal by X-ray diffraction and the potential energy surface for the

* Corresponding author. Tel.: +48-61-829-1216; fax: +48-61-865-8008.

E-mail address: degasz@amu.edu.pl (Z. Dega-Szafran).

Table 1

Crystal data and structure refinement for 1-piperidineacetic acid monohydrate (ZPAWX)

Empirical formula	C ₇ H ₁₅ NO ₃
Formula weight	161.20
Temperature (K)	295(2)
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	<i>P</i> 2 ₁ 2 ₁ 2 ₁
Unit cell dimensions	<i>a</i> = 6.7693(7) Å <i>b</i> = 10.816(1) Å <i>c</i> = 11.452(1) Å
Volume	838.5(1) Å ³
<i>Z</i>	4
Density (calculated)	1.277 mg m ^{−3}
Absorption coefficient	0.099 mm ^{−1}
<i>F</i> (000)	352
Crystal size	0.6 × 0.1 × 0.1 mm ³
Theta range for data collection	5.14–25.01°
Index ranges	−4 ≤ <i>h</i> ≤ 8, −12 ≤ <i>k</i> ≤ 12, −13 ≤ <i>l</i> ≤ 13
Reflections collected	4385
Independent reflections	1463 [<i>R</i> (int) = 0.0312]
Completeness to $\theta = 25.01^\circ$	98.8%
Absorption correction	None
Refinement method	Full-matrix least-squares on <i>F</i> ²
Data/restraints/parameters	1463/0/160
Goodness-of-fit on <i>F</i> ²	1.019
Final <i>R</i> indices [<i>I</i> > 2σ(<i>I</i>)]	<i>R</i> 1 = 0.0370, <i>wR</i> 2 = 0.0670
<i>R</i> indices (all data)	<i>R</i> 1 = 0.0466, <i>wR</i> 2 = 0.0709
Absolute structure parameter	0.2(15)
Largest diff. peak and hole	0.122 and −0.146 eÅ ^{−3}

anhydrous form and monohydrate by B3LYP/6-31G(d,p) calculations.

2. Experimental

1-piperidineacetic acid was prepared according to the method reported previously [5]; m.p. 204–205 °C from acetonitrile (Ref. [6] 214–216 °C from chloroform). The deuterated compound was prepared by three-fold recrystallization from CH₃OD.

FTIR spectra were measured in Nujol and Fluorolube mulls at 2 cm^{−1} resolution using a Bruker IFS 113V instrument, which was evacuated to avoid water and CO₂. Each spectrum consists of 250 scans at 31 °C.

The crystals were obtained from the CH₃CN–CH₃OH (10:1) solution by slow evaporation. Diffraction measurements were carried out at ambient

temperature on KUMA KM4 diffractometer equipped with a CCD detector. The diffractometer was positioned at 60 mm from the crystal. Data reduction was performed using the KM4 CCD software [7]. Lorentz and polarization corrections were applied, but not absorption corrections. The structure was solved by direct methods using SHELXS-97 program [8], and refined on *F*² by full-matrix least-squares method with SHELXL-97 program [9]. The parameters of non-hydrogen atoms were refined with anisotropic displacement factors. The hydrogen atoms were located on a difference Fourier map; their positional and thermal parameters were refined with isotropic displacement factors. The final *R* = 0.0370 for 1272 reflections [*F*₀ > 2σ(*F*₀)], and 0.0466 for all 1463 data. The crystal data are given in Table 1. The fractional atomic coordinates and the list of anisotropic displacement parameters have been deposited in CCDC, No. CCDC 176394.

The ab initio calculations were performed with the GAUSSIAN-98 program package [10]. The conformers were optimized using Becke's three-parameter hybrid method with the Lee, Yang, and Parr correlation functional (B3LYP) [11–14]. The basis set, 6-31G(d,p), was used in the present calculations [15].

3. Results and discussion

3.1. X-ray diffraction study

The atomic numbering scheme and the conformation of 1-piperidineacetic acid monohydrate (ZPAWX) as observed in the crystal are shown in Fig. 1. The selected bond lengths, bond angles and torsion angles are collected in Table 2. The molecule appears in the zwitterionic form with two almost equivalent C–O bonds. The piperidine ring adopts a little deformed chair conformation, with the asymmetry parameter equal 5.1 [16]. The CH₂COO substituent is in the equatorial and N⁺–H hydrogen atom in the axial positions. The conformation of C(2)N⁺–CH₂COO is *gauche* (−74.7(2)°). The water molecules have the following geometry: O(W)–H(W1) and O(W)–H(W2) are equal 0.87(3) Å and the H–O(W)–H angle is 96(1)°. They link, as double donors, the 1-piperidineacetic acid molecules through the carboxylate oxygen atoms, O(1) and O(2), into

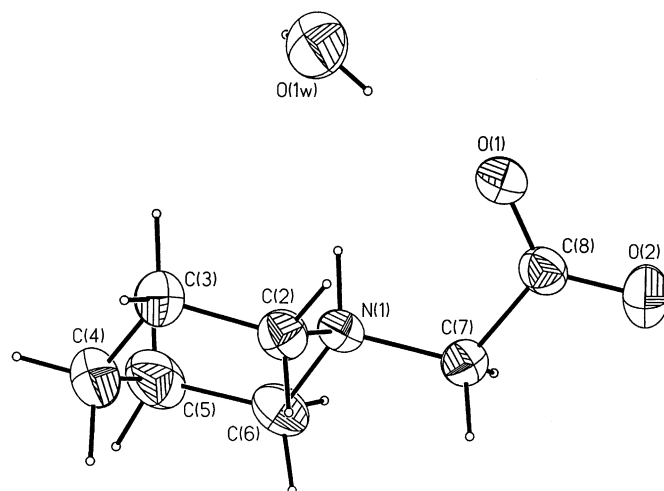


Fig. 1. Molecular structure and atom numbering scheme showing 50% probability displacement ellipsoid in 1-piperidineacetic acid monohydrate.

infinite hydrogen bonded chains parallel to the z -axis, assigned as $C_2^2(6)$ symbol in the graph theory [17]. The $N^+(1)$ –H hydrogen atom forms bifurcated hydrogen bonds [18] and is engaged both in the $N^+(1)$ –H \cdots O(1) intramolecular hydrogen bond, (2.795(2) Å), forming a five-membered ring, and in the $N^+(1)$ –H \cdots O(2') intermolecular hydrogen bond (2.775(3) Å) (Table 3). A similar bifurcated $N^+H\cdots O,O$ hydrogen bond is in α -glycine and β -glycine [19] and in 3-(1-pyrrolidynyl)propionic acid hemihydrate [20]. Both, intramolecular $N^+(1)\cdots O(1)$ and intermolecular $N^+(1)\cdots O(2')$ hydrogen bonds and water molecule form a six-membered hydrogen bond ring **R6** (Fig. 2). Some short C–H \cdots O contacts appear in the structure.

3.2. FTIR spectra

The FTIR spectra shown in Fig. 3 confirm the structure of the compound revealing frequencies typical of zwitterionic amino acids. The strong bands at 1620 and 1400 cm^{-1} are typical of the ν_{as} COO and ν_s COO modes. A broad band in the region 2800–2500 cm^{-1} , which shifts to the 2200–1900 cm^{-1} is assigned to the stretching vibration of the H-bonded N^+ –H or N^+ –D groups. Similar absorption was found in the spectrum of 1-piperidineacetic acid in CDCl_3 solution [21]. Two bands at

3481 and 3266 cm^{-1} are assigned to the stretching vibration of the water molecule.

3.3. B3LYP calculations

Figs. 4 and 5 show the B3LYP/6-31G(d,p) optimized conformers of 1-piperidineacetic acid and its monohydrate, respectively. The dipole moments, total and relative energies are given in Table 4. Tables 2, 3 and 5 show the B3LYP/6-31G(d,p) optimized geometrical parameters of the conformers of Figs. 4 and 5, respectively. In the optimized conformers the C(7)–C(8) bond can assume two different orientations. In **NPAW1**, **NPAW2**, **NPA1** and **NPA4** the torsion angle between the C(7)–C(8) bond and the C(2)–H or C(6)–H α -axial hydrogen is between 169 and 173° which indicates an almost anti arrangement. In the remaining compounds, it is between 2 and 6° (an almost *syn* arrangement).

3.3.1. Conformers of 1-piperidineacetic acid

It is obvious from Table 4, that the energy of conformer **NPA1** takes the global minimum. This type of conformer is also the most stable for *N,N*-dimethylglycine [4]. The intramolecular H-bond has profound significance for its stability. The conformer **NPA4** with the *trans* arrangement of the C=O/OH bond cannot form H-bond and is 4 kcal/mol less stable than the conformer **NPA1**.

Table 2
Selected bond lengths (Å), bond angles and selected torsion angles (°) for 1-piperidineacetic acid and its monohydrate

Parameter	Monohydrate					Anhydrous				
	X-ray	B3LYP/6-31G(d,p)				B3LYP/6-31G(d,p)				
		ZPAWX	ZPAW1	ZPAW2	ZPAW3	ZPAW4	NPA1	NPA2	NPA3	NPA4
<i>Bond lengths</i>										
N(1)–C(7)	1.492(2)	1.464	1.464	1.524	1.506	1.464	1.441	1.441	1.463	1.528
N(1)–C(2)	1.501(2)	1.477	1.480	1.518	1.515	1.476	1.467	1.467	1.468	1.516
N(1)–C(6)	1.505(2)	1.474	1.473	1.518	1.522	1.473	1.467	1.467	1.468	1.516
C(7)–C(8)	1.523(3)	1.534	1.537	1.573	1.604	1.538	1.531	1.531	1.523	1.588
C(8)–O(1)	1.249(2)	1.339	1.352	1.261	1.259	1.344	1.357	1.357	1.356	1.258
C(8)–O(2)	1.242(2)	1.211	1.205	1.238	1.231	1.207	1.211	1.211	1.210	1.234
<i>Bond angles</i>										
C(7)–N(1)–C(2)	112.6(1)	111.82	112.00	111.98	110.54	111.60	114.70	114.70	112.07	111.51
C(7)–N(1)–C(6)	110.0(1)	113.74	114.01	111.98	110.47	113.63	114.70	114.70	112.92	111.51
C(2)–N(1)–C(6)	109.8(1)	111.79	111.77	111.78	110.65	111.72	113.04	113.04	111.36	111.76
N(1)–C(7)–C(8)	115.7(1)	110.56	110.56	115.04	113.16	111.13	117.16	117.16	112.37	114.99
O(2)–C(8)–O(1)	126.7(1)	123.44	123.52	131.99	126.95	123.56	122.46	122.46	122.20	132.96
O(2)–C(8)–C(7)	113.9(2)	123.41	124.28	111.47	116.25	123.34	126.79	110.74	124.91	110.87
O(1)–C(8)–C(7)	119.4(2)	113.12	112.17	116.54	116.79	113.05	110.74	126.79	112.90	116.16
<i>Torsion angles</i>										
C(2)–N(1)–C(7)–C(8)	–74.7(2)	–88.05	–88.41	–62.24	–61.24	84.30	–66.62	–66.62	145.04	–62.86
C(6)–N(1)–C(7)–C(8)	162.6(2)	144.15	143.44	63.22	61.56	–148.28	66.67	66.67	–88.22	62.86
N(1)–C(7)–C(8)–O(2)	–174.4(2)	165.70	165.16	–179.98	–148.03	–163.24	–0.06	179.95	–116.38	180.00
N(1)–C(7)–C(8)–O(1)	4.1(2)	–16.20	–16.67	0.02	31.74	18.75	179.95	–0.06	64.16	0.003

Table 3
Hydrogen bond parameters (Å, deg) for 1-piperidineacetic acid monohydrate

Parameter	X-ray	B3LYP/6-31G(d,p)			
	ZPAWX	NPAW1	NPAW2	ZPAW3	ZPAW4
N(1)–H	0.95(3)	–	–	1.024	1.017
N(1)H...O(1)	2.55(3)	–	–	3.798	–
N(1)H...O(2')	2.19(4) ^a	–	–	–	–
N(1)...O(1)	2.795(2)	2.604	2.592	2.793	2.859
N(1)...O(2')	2.775(3) ^a	–	–	3.681	3.639
N(1)H...O(W)	3.44	–	–	–	1.819
N(1)...O(W)	3.94	5.689	3.850	5.656	2.835
O(1)–H	–	0.992	0.996	–	–
N(1)...HO(1)	–	1.888	1.857	–	–
O(1)...H(W)	1.98(3)	2.539	2.034	2.108	–
O(2)...H(W)	1.88(4) ^b	2.085	–	2.160	–
O(1)...O(W)	2.85(3)	3.173	2.862	2.948	–
O(2)...O(W)	2.75(4) ^b	2.993	–	2.966	–
C(8)–O(1)–H	–	104.01	103.36	–	–
N(1)–H...O(W)	115(4)	–	–	–	174.44
O(1)...H–O(W)	171(3)	123.31	142.17	143.81	–
O(2)...H–O(W)	174(4) ^b	155.10	–	139.54	–
N(1)–H...O(1)	95(3)	–	–	–	–
N(1)–H...O(2)	119(4) ^a	–	–	–	–
N(1)...H–O(1)	–	126.58	128.04	–	–
H–N(1)–C(2)	108.3(4)	–	–	106.80	108.54
H–N(1)–C(7)	106.8(4)	–	–	107.11	109.25
O(2)–C(8)–O(1)–H	–	–179.45	–178.04	–	–
C(7)–C(8)–O(1)–H	–	2.44	3.78	–	–
H–N(1)–C(7)–C(8)	44.1(4)	–	–	179.99	179.39
H–N(1)–C(2)–C(3)	60.3(4)	–	–	–60.56	–63.46

^a Symmetry codes: $x - 0.5, 1.5 - y, z$.

^b Symmetry codes: $x - 0.5, 1.5 - y, 1 - z$.

Table 4
Energy (a.u.), relative energy (kcal/mol) and dipole moments (μ , Debye) for 1-piperidineacetic acid

Structure	Energy	μ	E_{rel}
<i>Monohydrate</i>			
NPAW1	–556.235812	8.8	0
NPAW2	–556.235504	4.3	0.2
ZPAW3	–556.207087	14.5	4.6
ZPAW4	–556.203108	12.3	20.5
<i>Anhydrous</i>			
NPA1	–479.804690	5.6	0
NPA2	–479.802785	0.9	1.2
NPA3	–479.802785	0.9	1.2
NPA4	–479.798281	1.9	4.0
ZPA1	–479.766813	10.9	23.8

Conformers **NPA2** and **NPA3** are less stable than **NPA1** and the energy difference is only 1.2 kcal/mol. Both **NPA2** and **NPA3** have similar conformation (Table 2) except the conformation of the COOH group (Table 5). In both conformers, a formation of H-bond is not possible. The question arises why the relative energy, E_{rel} , of **NPA1** and **NPA3** is lower than that of **NPA4**. Probably, the main factor that contributes to the energy difference between these conformers is the non-bonding electron–electron pair repulsion between the nitrogen and oxygen atoms. From Fig. 4 and Table 4, it is obvious that this type interaction is greater for **NPA4** than for **NPA2** and **NPA3**.

As mentioned in Section 1, the zwitterionic form of glycine and *N,N*-dimethylglycine does not exist in the gas phase. Jensen and Gordon [2] have shown that two water molecules stabilized the glycine zwitterion. The

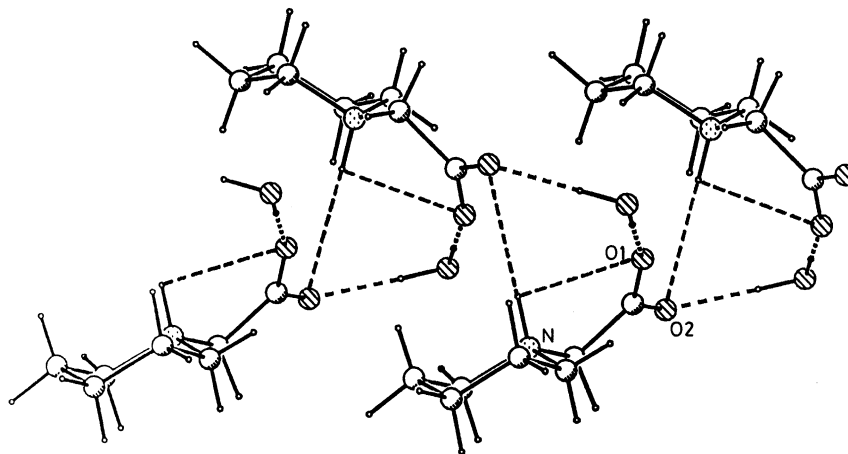


Fig. 2. Hydrogen bonds system in the crystal of 1-piperidineacetic acid monohydrate.

zwitterionic form of glycine dihydrate is 11.6 kcal/mol higher in energy than the neutral form.

It was surprising to find that the anhydrous 1-piperidineacetic acid can exist in the zwitterionic form, **ZPA1** in the gas phase. The structure of **ZPA1** is 23.8 kcal/mol higher in energy than that of **NPA1**. The structure of **ZPA1** is stabilized by the electrostatic interactions between the positively charged N^+H atom and the negatively charged oxygen atoms of the COO^- group.

The electrostatic interactions increase the barrier of rotation about the C(7)–C(8) bond. In the case of equatorial *N*-methylpiperidine betaine, the rotation barrier is ca. 6 kcal/mol [22]. The barrier of rotation

of the CO_2 group is also ca. 6 kcal/mol [23]. The relatively high rotation barriers are probably responsible for the stability of **ZPA1** structure.

3.3.2. Conformers of 1-piperidineacetic acid monohydrate

A geometry optimization initiated from the X-ray geometry (**ZPAWX**) leads to a neutral structure, **NPAW2**, (Fig. 5), which has comparable energy with **NPAW1**, but smaller dipole moment (Table 4). Both structures are stabilized by intramolecular $O-H \cdots N$ hydrogen bond. From Table 4, **ZPAW3** is less stable than **ZPAW1** by 4.6 kcal/mol but **ZPAW4** by 20.5 kcal/mol. The difference in stability of **ZPAW3**

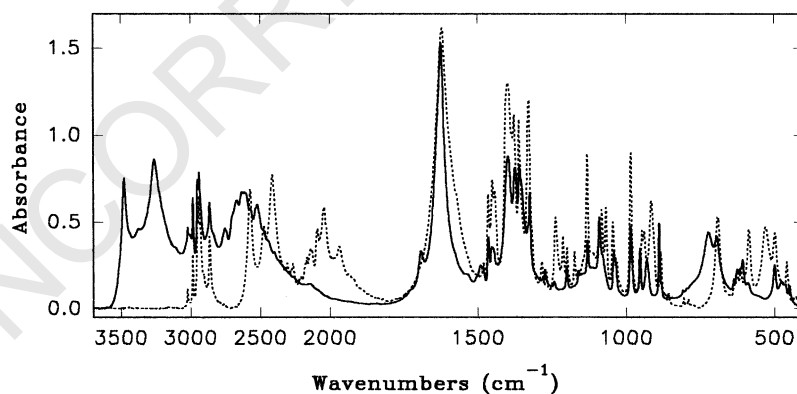


Fig. 3. FTIR spectrum (emulsion in Nujol and Fluorolube) of 1-piperidineacetic acid monohydrate (solid line); dotted line represents the spectrum of deuterated sample.

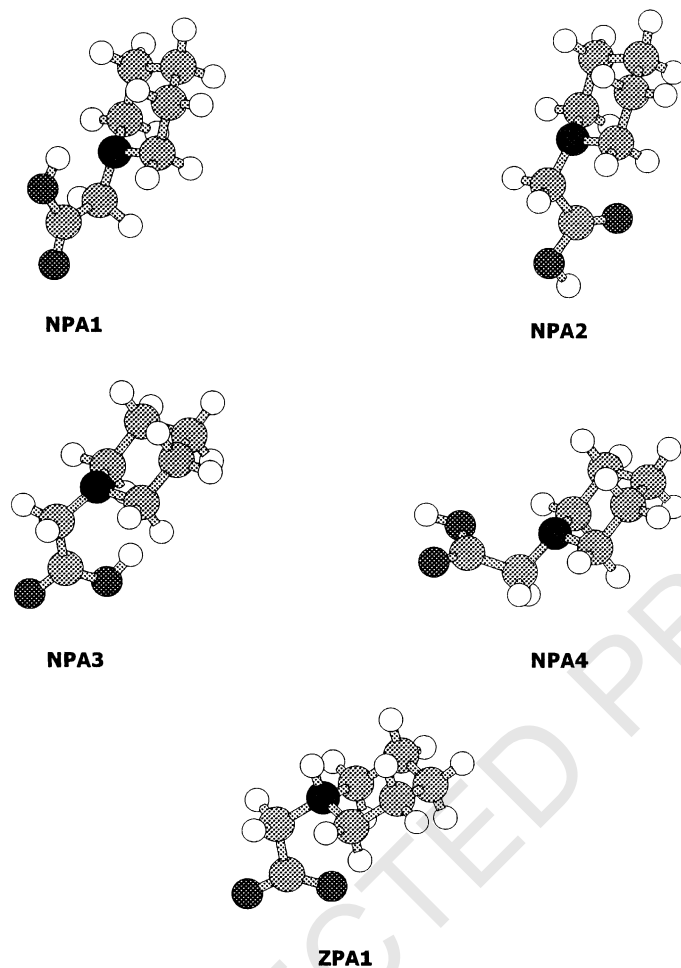


Fig. 4. Optimized B3LYP/6-31G(d,p) structures for the five most stable conformers of 1-piperidineacetic acid.

and **ZPAW4** can be explained by the water solvation effect. Water molecules interact more strongly with the carboxylate functionality than with the $\text{N}^+ - \text{H}$ one [24,25].

4. Conclusions

1-Piperidineacetic acid crystallizes as monohydrate in the zwitterionic form and its structure was determined by X-ray diffraction. The piperidine ring adopts a little deformed chair conformation with CH_2COO^- group at the equatorial and the $\text{N}^+ - \text{H}$ hydrogen atom at the axial positions. The $\text{N}^+ \text{H}$

hydrogen atom forms a bifurcated hydrogen bond, intramolecular with the O(1) atom and intermolecular with the O(2') atom. Water molecules link 1-piperidineacetic acid molecules through carboxylic oxygen atoms into infinite hydrogen bonded chain, parallel to the z axis.

Five of the most stable conformers of 1-piperidineacetic acid and four of its monohydrate were analyzed by B3LYP/6-31G(d,p) calculations. Both for anhydrous acid and its monohydrate the lowest energy conformers are neutral with intramolecular O(1)–H...N hydrogen bonds (**NPA1** and **NPAW1**). The zwitterionic forms (**ZPA1** and **ZPAW3**) are higher in energy by 23.8 and 4.6 kcal/mol,

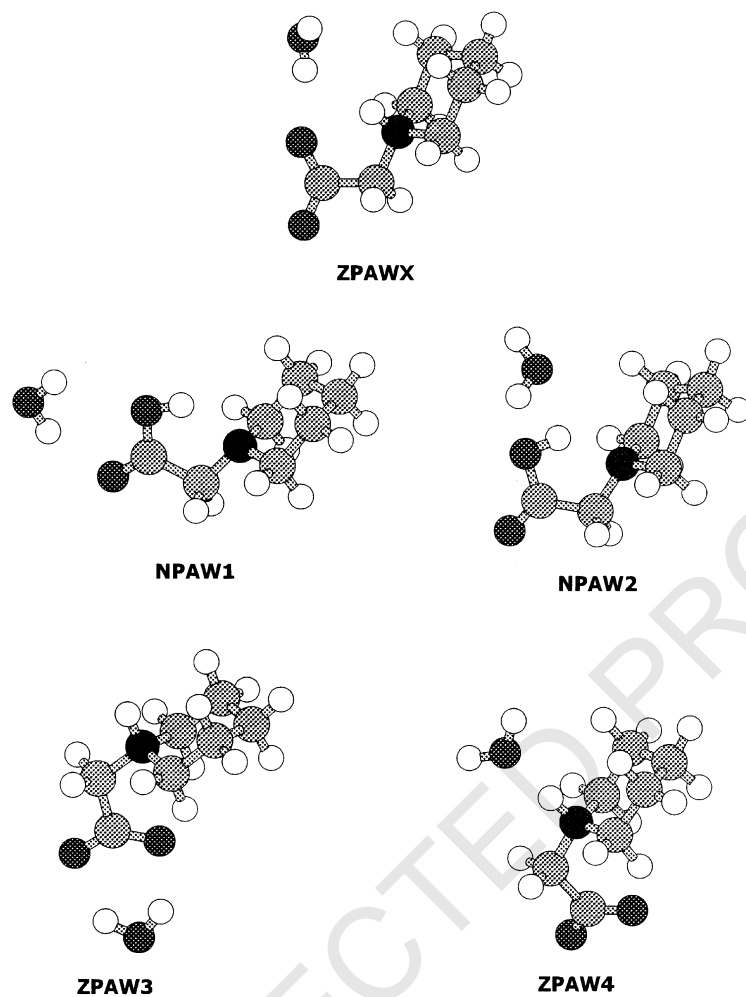


Fig. 5. Optimized B3LYP/6-31G(d,p) structures for the four most stable conformers of 1-piperidineacetic acid monohydrate.

Table 5

Hydrogen bond parameters (Å, deg) for 1-piperidineacetic acid optimized by B3LYP/6-31G(d,p) level of theory

Parameter	NPA1	NPA2	NPA3	NPA4	ZPA1
N(1)–H	–	–	–	–	1.024
O(1)–H	0.987	0.973	0.973	0.973	–
N···HO(1)	1.930	4.401	2.485	3.802	–
N···O(1)	2.629	3.693	3.001	2.952	2.800
N···(2)	3.601	2.931	3.561	3.420	3.686
C(8)–O(1)–H	104.40	106.20	106.20	105.93	–
N(1)···H–O(1)	125.55	–	113.48	–	–
H–N(1)–C(2)	–	–	–	–	107.04
H–N(1)–C(7)	–	–	–	–	107.67
O(2)–C(8)–O(1)–H	179.31	–0.007	–179.01	2.53	–
C(7)–C(8)–O(1)–H	–2.67	179.99	1.0	–177.99	–
H–N(1)–C(7)–C(8)	–	–	–	–	180.00
H–N(1)–C(2)–C(3)	–	–	–	–	–61.31

respectively, than their neutral forms. The zwitter-ionic form is stabilized by the electrostatic interaction between the positively charged N^+H and negatively charged oxygen atoms of the COO group and by water molecule. The electrostatic interaction increases the rotation barrier about $\text{C}(7)–\text{C}(8)$ bond.

Acknowledgments

The ab initio calculations were performed at the Poznan Supercomputing and Networking Centre.

References

- [1] A.G. Császár, *J. Mol. Struct.* 346 (1995) 141 and references cited therein.
- [2] J.H. Jensen, M.S. Gordon, *J. Am. Chem. Soc.* 117 (1995) 8159.
- [3] Y. Ding, K. Krogh-Jespersen, *J. Comput. Chem.* 17 (1996) 338.
- [4] A.D. Headley, S.D. Starnes, *J. Mol. Struct. (Theochem.)* 370 (1996) 147.
- [5] P. Barczyński, Z. Dega-Szafran, E. Dulewicz, M. Petryna, M. Szafran, *Pol. J. Chem.* 74 (2000) 1149.
- [6] W. Kliegel, *J. Graumann, Liebigs Ann. Chem.* (1983) 950.
- [7] KUMA KM4CCD Software, Version 161, KUMA Diffraction, Wrocław, Poland, 1999.
- [8] M.G. Sheldrick, *SHELXS-97*, Program for the Solution of Crystal Structures, University of Göttingen, Germany, 1997.
- [9] M.G. Sheldrick, *SHELXS-97*, Program for the Solution of Crystal Structures refinement, University of Göttingen, Germany, 1997.
- [10] M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, V.G. Zakrzewski, A.J. Montgomery Jr., R.E. Stratmann, J.C. Burant, S. Dapprich, J.M. Millam, A.D. Daniels, K.N. Kudin, M.C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G.A. Petersson, P.Y. Ayala, Q. Cui, K. Morokuma, D.K. Malick, A.D. Rabuck, K. Raghavachari, J.B. Foresman, J. Cioslowski, J.V. Ortiz, B.B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R.L. Martin, D.J. Fox, T. Keith, M.A. Al-Laham, C.Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P.M.W. Gill, B. Johnson, W. Chen, M.W. Wong, J.L. Andres, C. Gonzalez, M. Head-Gordon, E.S. Replogle, J.A. Pople, *GAUSSIAN98*, Revision A6, Gaussian, Inc., Pittsburgh, PA, 1998.
- [11] A.D. Becke, *Phys. Rev. A* 38 (1988) 3098.
- [12] A.D. Becke, *J. Chem. Phys.* 98 (1993) 5648.
- [13] C. Lee, W. Yang, R.G. Parr, *Phys. Rev. B* 37 (1988) 785.
- [14] B. Miehlich, A. Savin, H. Stoll, H. Preuss, *Chem. Phys. Lett.* 157 (1989) 200.
- [15] W.J. Hehre, L. Radom, P.v.R. Schleyer, J.A. Pople, *Ab Initio Molecular Orbital Theory*, Wiley, New York, 1986.
- [16] W.L. Duax, D.A. Norton, *Atlas of Steroid Structures*, Plenum Press, New York, 1975.
- [17] M.C. Etter, J.C. MacDonald, J. Bernstein, *Acta Crystallogr.* B46 (1990) 256.
- [18] G.R. Desiraju, T. Steiner, *The Weak Hydrogen Bond*, Oxford University Press, Oxford, 1999.
- [19] J. Donohue, in: A. Rich, N. Davison (Eds.), *Structural Chemistry and Molecular Biology*, Freeman, San Francisco, 1968, pp. 443–465.
- [20] M.A. Peterson, H. Hope, C.P. Nash, *Acta Crystallogr.* B38 (1982) 2490.
- [21] B. Brzezinski, G. Zundel, *Chem. Phys. Lett.* 44 (1976) 521.
- [22] M. Szafran, Z. Dega-Szafran, *J. Mol. Struct.* 598 (2001) 251.
- [23] O. Kikuchi, T. Watanabe, Y. Ogawa, H. Takase, O. Takahashi, *J. Phys. Org. Chem.* 10 (1997) 145.
- [24] A.D. Headley, B. Patel, E.T. Cheung, *Tetrahedron Lett.* 37 (1996) 6673.
- [25] A.D. Headley, R.E. Corone, E.T. Cheung, *J. Phys. Org. Chem.* 10 (1997) 898.