

X-ray Mapping in Heterocyclic Design.

I. Diffractometric Study of Crystalline 1,2-Dihydro-2-Imino-1-Carboxymethylpyridine Monohydrate: Structural Evidence for the Zwitterionic Character of the Molecule

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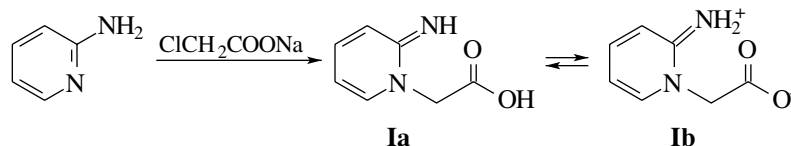
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Abstract—A single-crystal X-ray diffraction analysis of 1,2-dihydro-2-imino-1-carboxymethylpyridine is carried out. The transparent colorless crystals are orthorhombic, and the unit-cell parameters are as follows: $a = 5.026(1) \text{ \AA}$, $b = 12.320(7) \text{ \AA}$, $c = 25.551(1) \text{ \AA}$, space group $Pbca$. The structure is solved and refined to $R_1 = 0.0562$. In the six-membered heterocycle, the partially ordinary bonds alternate with the partially double bonds. The plane of the carboxylate group is almost perpendicular to the plane of the pyridine ring, and the existence of intramolecular hydrogen bonds becomes impossible. The crystal structure involves an extended system of intermolecular bonds, including those with the participation of water molecules.

This paper begins a series of structural studies on heterocyclic compounds that readily enter into the reactions of cyclization and ring transformation. It continues our earlier works in this field [1–4]. The X-ray mapping implies the determination of the crystal structures of the initial compound, resulting product, and possible intermediates of a reaction. In this work, we determined the crystal structure of 1,2-dihydro-2-imino-1-carboxymethylpyridine (**I**) by X-ray diffraction analysis. This compound is known as “pyridylglycine” and

serves as the initial substance for subsequent cyclizations. It was first obtained in 1924 by the reaction between 2-aminopyridine and chloroacetic acid [5]; however, its structure remained unknown. Later, Tschitschibabin [6] showed that the acetic residue of **I** is attached to the pyridine nitrogen atom. Data on the crystal structure of **I** are absent in the Cambridge Structural Database [7]. In the literature, it is often represented in the imino form **Ia** [8]. Compound **I** was obtained by the reaction [5]



and recrystallized as a monohydrate from a solution in the isopropanol : water (1 : 1) mixture. Transparent colorless crystals have a needlelike habit.

EXPERIMENTAL

Crystals **I** ($C_7H_8N_2O_2 \cdot H_2O$) are orthorhombic. The unit-cell parameters were determined and refined on a CAD-4 automated diffractometer using 25 reflections in the θ range 12° – 13° [9] (λMoK_α , graphite monochromator). The crystal data are as follows: $a = 5.026(1) \text{ \AA}$, $b = 12.320(7) \text{ \AA}$, $c = 25.551(1) \text{ \AA}$, $V = 1582(1) \text{ \AA}^3$, $d_{\text{calcd}} = 1.429 \text{ g/cm}^3$, $\mu(Mo) = 0.113 \text{ mm}^{-1}$, $Z = 8$, and space group $Pbca$. A total of 1257 unique reflections with $I \geq 2\sigma(I)$ were collected in the $\theta \leq 26^\circ$

range with the same diffractometer by the ω -scan technique. The experimental set of diffraction data was processed with the WinGX96 program package [10]. The non-hydrogen atoms were revealed by the direct method and refined in the anisotropic approximation by the least-squares procedure using the SHELX97 program package [11]. The hydrogen atoms were located from the difference synthesis of electron density and included in the refinement in the isotropic approximation. The final discrepancy factors are $R_1 = 0.0562$ and $wR_2 = 0.0925$. The atomic coordinates and thermal parameters are listed in Table 1. The residual electron density lies between $\Delta\rho_{\text{max}} = 0.190$ and $\Delta\rho_{\text{min}} = -0.188 \text{ e/\AA}^3$. The molecular drawing shown in the figure was obtained with the PLUTON96 program [12].

Table 1. Atomic coordinates ($\times 10^4$) and equivalent (isotropic for H atoms) thermal parameters U_{eq}/U_{iso} ($\text{\AA}^2 \times 10^3$)

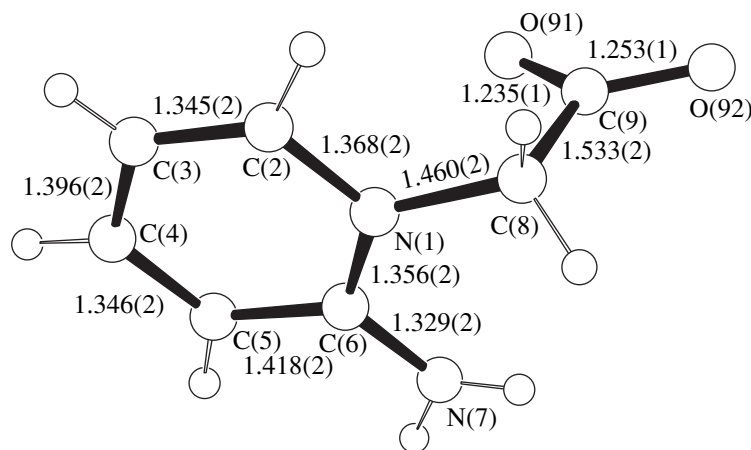
Atom	<i>x</i>	<i>y</i>	<i>z</i>	U_{eq}/U_{iso}
N(1)	-2438(2)	3690(1)	3977(1)	28(1)
C(2)	-4121(3)	3719(1)	3557(1)	35(1)
C(3)	-3941(3)	2987(1)	3168(1)	42(1)
C(4)	-1940(3)	2202(1)	3188(1)	39(1)
C(5)	-260(3)	2163(1)	3598(1)	34(1)
C(6)	-508(3)	2924(1)	4011(1)	29(1)
N(7)	1134(2)	2899(1)	4419(1)	37(1)
C(8)	-2549(3)	4587(1)	4350(1)	31(1)
C(9)	-402(3)	5439(1)	4236(1)	30(1)
O(91)	961(2)	5326(1)	3838(1)	41(1)
O(92)	-243(2)	6195(1)	4563(1)	43(1)
O(10)*	1176(2)	5036(1)	2754(1)	62(1)
H(2)	-5413(24)	4356(9)	3584(4)	39(3)
H(3)	-5075(24)	2973(9)	2906(4)	43(4)
H(4)	-1833(23)	1721(9)	2914(4)	44(4)
H(5)	1148(23)	1620(9)	3655(4)	38(3)
H(71)	2537(29)	2329(11)	4430(5)	70(4)
H(72)	920(27)	3254(10)	4702(5)	59(4)
H(81)	-2405(23)	4339(8)	4711(4)	29(3)
H(82)	-4143(23)	4881(8)	4313(4)	27(3)
H(101)*	1179(31)	5105(12)	3086(5)	90(5)
H(102)*	-231(30)	4976(11)	2616(5)	72(5)

* Atoms of the water molecule.

RESULTS AND DISCUSSION

Two tautomeric forms are possible for molecule **I**: imino form **Ia** and zwitterionic form **Ib**. In the crystal, the molecule exists as an inner salt, that is, in the zwitterionic form **Ib** containing NH_2 rather than the NH

group. The geometry of the positively charged 2-aminopyridinium fragment distinctly resembles the skeleton of 2-iminopyridine. Indeed, the formally ordinary and double bonds alternate in the six-membered heterocycle (figure), as it is often observed in the imino structure. Moreover, the endocyclic C–N bonds are signifi-



Atomic numbering and the structure of the molecule studied.

Table 2. Parameters of hydrogen bonds*

<i>D</i> – <i>H</i>	<i>d</i> (<i>D</i> – <i>H</i>)	<i>d</i> (<i>H</i> ··· <i>A</i>)	ω DHA	<i>d</i> (<i>D</i> ··· <i>A</i>)	<i>A</i> (symmetry operation)
N(7)–H(71)	0.999	1.976	171.3	2.967	O(92) (1/2 – <i>x</i> ; <i>y</i> – 1/2; <i>z</i>)
N(7)–H(72)	0.850	2.029	168.4	2.866	O(92) (– <i>x</i> ; 1 – <i>y</i> ; 1 – <i>z</i>)
O(10)–H(101)	0.861	1.936	176.2	2.795	O(91) (<i>x</i> ; <i>y</i> ; <i>z</i>)
O(10)–H(102)	0.788	2.045	172.4	2.828	O(10) (<i>x</i> – 1/2; <i>y</i> ; 1/2 – <i>z</i>)

* *D* is a donor atom, *A* is an acceptor atom, and *H* is a hydrogen atom (distances *d* and angles ω are expressed in Å and deg, respectively).

cantly longer than the exocyclic C–N bond. Hence, the NH₂ group should be considered as a part of the *immobium* group C = NH₂⁺.

The angle between the planes of the carboxylate group and the pyridinium ring is 80.81(5)°; therefore, the intramolecular contact H(2)···O(91) is impossible. The crystal structure is characterized by an extensive system of intermolecular hydrogen bonds. The H(71) and H(72) atoms of the NH₂ group contact carboxylate atoms O(92) of different molecules to form the three-dimensional framework of hydrogen bonds. The water molecule also takes an active part in hydrogen bonding. It is involved in two types of contacts: one is the contact with the O(91) atom of the carboxylate group, and the other is the contact with a symmetrically related water molecule. The geometric parameters of the hydrogen bonds are given in Table 2.

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REFERENCES

- Babaev, E.V., Efimov, A.V., Zhukov, S.G., and Rybakov, V.B., *Khim. Geterotsikl. Soedin.*, 1998, no. 7, p. 983.
- Babaev, E.V., Bozhenko, S.V., Maiboroda, D.A., Rybakov, V.B., and Zhukov, S.G., *Bull. Soc. Chim. Belg.*, 1997, vol. 106, no. 11, p. 631.
- Zhukov, S.G., Rybakov, V.B., Babaev, E.V., Paseshnichenko, K.A., and Schenk, H., *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.*, 1997, vol. 53, p. 1909.
- Babaev, E.V., Bozhenko, S.V., Zhukov, S.G., and Rybakov, V.B., *Khim. Geterotsikl. Soedin.*, 1997, no. 8, p. 1105.
- Reindel, F., *Chem. Ber.*, 1924, vol. 57, p. 1381.
- Tschitschibabin, A.E., *Chem. Ber.*, 1925, vol. 57, p. 2092.
- Allen, F.H. and Kennard, O., *Chem. Des. Autom. News*, 1993, vol. 8, p. 31.
- Sych, E.D. and Gorb, L.T., *Ukr. Khim. Zh.*, 1976, no. 9, p. 961.
- CAD-4 Software, Version 5.0*, Delft: Enraf–Nonius, 1989.
- Farrugia, L.J., *WinGX-96: An Integrated System of Publicly Available Windows Programs for the Solution, Refinement, and Analysis of Single-Crystal X-ray Diffraction Data*, Glasgow: Univ. of Glasgow, 1996.
- Sheldrick, G.M., *SHELX97: Programs for the Solution and Refinement of Crystal Structures*, Göttingen: Univ. of Göttingen, 1997.
- Spek, A.L., *PLUTON96: Molecular Graphics Program*, Utrecht: Univ. of Utrecht Press, 1996.

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