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X-RAY DIFFRACTION AND QUANTUM-CHEMICAL ANALYSIS OF A SINGLE CRYSTAL OF 2,5-DIMETHYL-3,4-DIHYDRO-2H-PYRAN-2-CARBOXYLIC ACID

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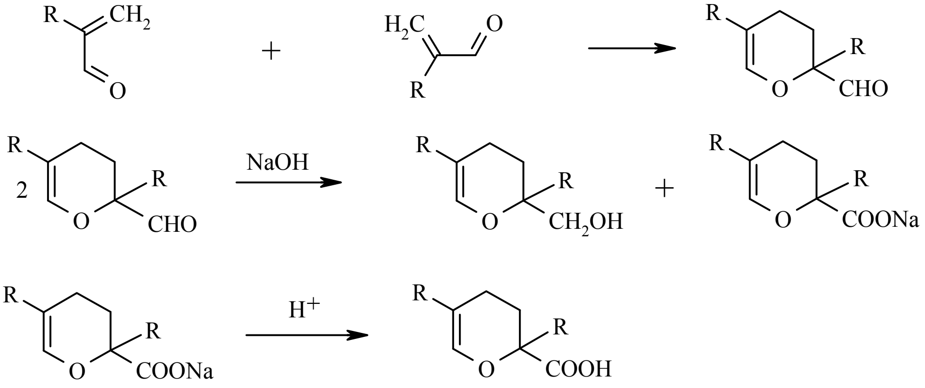
The structure of synthesized 2,5-dimethyl-3,4-dihydro-2H-pyran-2-carboxylic acid was investigated by the single crystal X-ray diffraction analysis method. It was established that the molecule of the acid exists in the form of the endo isomer while the single crystal exists as a racemate of the two enantiomeric endo stereomers. Quantum-chemical calculations of a model of the macrocell of the acid by means of the semiempirical MOPAC2009 program agree well with the X-ray diffraction data.

Keywords: 2,5-dimethyl-3,4-dihydro-2H-pyran-2-carboxylic acid, quantum-chemical calculations, MOPAC2009, RM1, single crystal X-ray diffraction analysis, Winmostar.

Pyran derivatives and the dimers of acrolein and its homologs in particular are valuable starting substances for the synthesis of dyes, plasticizers, surface-active substances, fungicides, insecticides, and drugs [1]. The dimers of α-alkylacroleins are synthesized by the Diels–Alder reaction, and their subsequent disproportionation in an alkaline medium by the Cannizzaro reaction leads to the formation of oxidation products (the salts of pyrancarboxylic acids) and reduction products (pyran alcohols) [2].



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The 2,5-dialkyl-3,4-dihydro-2H-pyran-2-carboxylic acids can have different internal molecular structures on account of stereoisomerism.

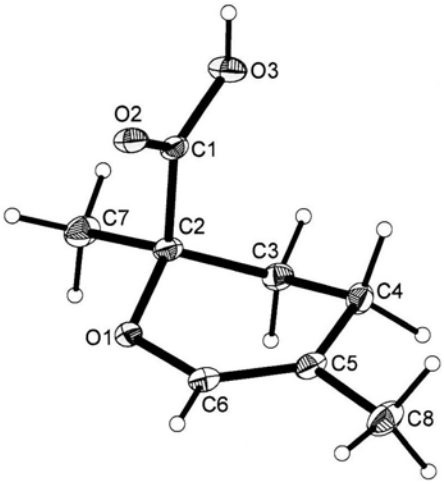

Fig. 1. An independent part of the unit cell of a single crystal of compound **1** and the numbering of the atoms. The thermal ellipsoids are represented with 30% probability.

Consequently, they can be formed as stereoisomers with dual spatial arrangement of the carboxyl group in relation to the dihydropyran ring (axial (*endo*) or equatorial (*exo*)) and as enantiomers (optical isomers) resulting from the presence of an asymmetric (chiral) carbon atom in the molecule of the acid. Accordingly the

TABLE 1. Recording Parameters and Crystallographic Data of Compound **1**

Empirical formula	$C_8H_{12}O_3$
M, g/mol	156.18
Temperature, K	100(2)
Wave length, Å	0.71073
System	Triclinic
Space group	$P\bar{1}$
Unit cell parameters:	
a, Å	6.206(2)
b, Å	8.431(3)
c, Å	8.611(3)
α, deg	86.60(3)
β, deg	85.23(3)
γ, deg	69.40(3)
Volume of cell, *V*, Å^3	420.1(2)
Number of molecules in cell, *Z*	2
Density, ρ, g/cm^3	1.24
Absorption coefficient, μ, mm^{-1}	0.09
F(000)	168
θ_{max}	33.76
Crystal size, mm^3	0.50 × 0.31 × 0.18
Color	Colorless
Measured reflections	6631
Unique reflections	2840
Number of refined parameters	106
S, *GOOF*	1.00
Divergence factors [$I > 2\sigma(I)$]	$R_1 = 0.0585$, $wR_2 = 0.1429$
Divergence factors (all reflections)	$R_1 = 0.0901$, $wR_2 = 0.1538$

internal structure of such substances will affect their physical and chemical characteristics. One of the effective methods for determination of the structure of these substances is the X-ray diffraction analysis that we used for a single crystal of synthesized 2,5-dimethyl-3,4-dihydro-2H-pyran-2-carboxylic acid (**1**). In addition quantum-chemical calculations of a model of the crystal of compound **1** were made by means of the semiempirical MOPAC2009 program.

As seen from the results of X-ray diffraction analysis of compound **1** (Table 1), the unit cell contains two enantiomeric (*R*)- and (*S*)-molecules of compound **1**, which are stereoisomers with the *endo* arrangement of the carboxyl group in relation to the dihydropyran ring (Fig. 1). Consequently compound **1** exists in the form of the racemate (*r*-**1**) – an equimolar mixture of the pair of enantiomers of **1**.

One molecule of *endo*-2,5-dimethyl-3,4-dihydro-2H-pyran-2-carboxylic acid ((*R*-**1**) or (*S*-**1**) respectively) is regarded as an independent crystallographic part of the unit cell. In this molecule the dihydropyran ring has a *half-chair* conformation, while the C(2) and (3) atoms deviate from the average plane of the other four atoms of the ring by 0.336(1) and -0.382(1) Å respectively. Such a structure for compound **1** is explained by the antara surface mechanism of formation of the dihydropyran ring during the [4+2] cyclization of two molecules of methacrolein by the Diels–Alder reaction, where one acts as heterodiene and the other as dienophile [3]. The experimental bond lengths and valence angles between the atoms of the molecule of **1** are presented in Table 2.

On account of the formation of average in strength (mainly electrostatic) hydrogen bonds O(3)–H(3)···O(2)^{i} [4] between the carboxyl groups (Table 3) the two enantiomeric (*R*)- and (*S*)-molecules of **1** in the crystalline state merge into centrosymmetric dimers *r*-**1**. In turn each of these molecules of the carboxyl dimer *r*-**1** is linked by means of weak (electrostatic/dispersion) hydrogen contacts in the [011] and [01$\bar{1}$] directions with the opposite enantiomeric molecules of other *r*-**1** dimers and also form centrosymmetric dimers. Compound **1** therefore crystallizes in the centrosymmetric space group $P\bar{1}$ (Table 1). Thus, during crystallization the *r*-**1** dimers form a network of chains both in the [011] direction on account of weak hydrogen contacts C(6)–H(6)···O(2)^{ii} and C(8)–H(8A)···O(2)^{ii} and in the [01$\bar{1}$] direction by means of C(3)–H(3A)···O(1)^{iii} contacts. The lengths of the formed hydrogen bonds and contacts are given in Table 3. A projection of the crystal structure along the *a* axis of packing of the chains of the dimers of the racemate *r*-**1** during the formation of the network (monolayer) is shown in Fig. 2. The accumulation of the monolayers on account of other electrostatic and dispersion contacts leads to growth of the crystal.

TABLE 2. The Experimental (X-ray Diffraction) and Calculated (RM1) Intramolecular Interatomic Bond Lengths (*d*) and Valence Angles (ω) in the Crystal of Compound **1**

Bond	$d_{A–B}$, Å		Angle A–B–C	$\omega_{A–B–C}$, deg	
	PCA	RM1		PCA	RM1
O(1)–C(2)	1.429(2)	1.406	C(2)–O(1)–C(6)	115.6(1)	116.1
O(1)–C(6)	1.390(2)	1.366	O(1)–C(2)–C(3)	110.7(1)	111.6
O(2)–C(1)	1.213(2)	1.231	O(1)–C(2)–C(7)	106.2(1)	105.7
O(3)–C(1)	1.320(2)	1.330	C(3)–C(2)–C(7)	112.4(1)	112.1
C(2)–C(3)	1.530(2)	1.532	O(1)–C(2)–C(1)	108.0(1)	107.7
C(2)–C(7)	1.527(2)	1.528	C(1)–C(2)–C(3)	111.2(1)	109.8
C(2)–C(1)	1.539(2)	1.524	C(1)–C(2)–C(7)	108.0(1)	109.6
C(3)–C(4)	1.528(2)	1.524	O(2)–C(1)–O(3)	124.0(1)	120.7
C(4)–C(5)	1.497(2)	1.488	O(2)–C(1)–C(2)	123.1(1)	125.2
C(5)–C(6)	1.333(2)	1.337	O(3)–C(1)–C(2)	112.9(1)	113.9
C(5)–C(8)	1.509(2)	1.483	C(2)–C(3)–C(4)	110.5(1)	109.3
			C(3)–C(4)–C(5)	111.1(1)	110.1
			C(4)–C(5)–C(6)	120.9(1)	121.5
			C(4)–C(5)–C(8)	118.2(1)	117.0
			C(6)–C(5)–C(8)	120.9(1)	121.6
			C(5)–C(6)–O(1)	125.3(1)	124.5

TABLE 3. The Experimental (X-Ray Diffraction) and Calculated (RM1) Geometrical Parameters of the Hydrogen Bonds D–H···A (Length *d*, Angle, ω) in the Crystal of Compound **1**

Hydrogen bond D–H···A	$d_{D–H}$, Å		$d_{H\cdots A}$, Å		$d_{D\cdots A}$, Å		$\omega_{D–H\cdots A}$, deg	
	PCA	RM1	PCA	RM1	PCA	RM1	PCA	RM1
O(3)–H(3)···O(2)^{i}	0.90(2)	0.996	1.75(2)	1.615	2.649(2)	2.605	176(2)	173
C(6)–H(6)···O(2)^{ii}	0.95	1.096	2.53	2.662	3.450(2)	3.650	164	150
C(8)–H(8A)···O(2)^{ii}	0.98	1.101	2.73	2.861	3.655(2)	3.870	157	151
C(3)–H(3A)···O(1)^{iii}	0.99	1.112	2.70	2.659	3.688(2)	3.760	175	175

Symmetry operation: *i*-*x*, -*y*, 2-*z*; *ii*-*x*, 1-*y*, 2-*z*; *iii*-*x*, 1-*y*, 1-*z*.

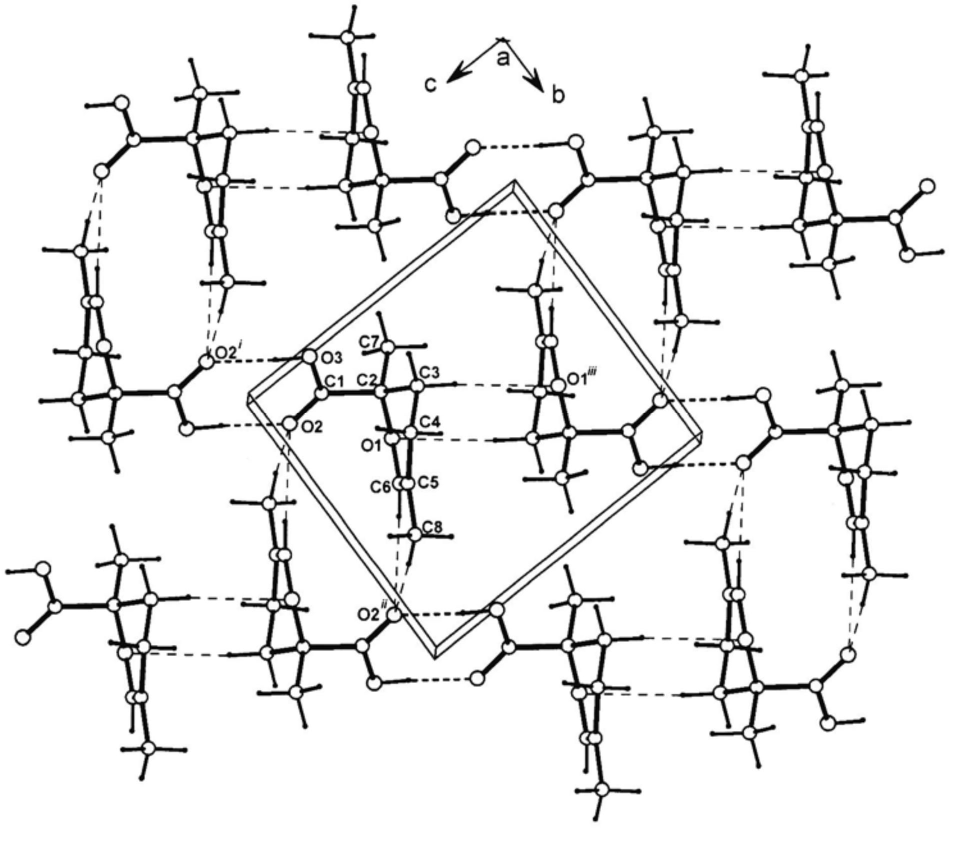

Fig. 2. Projection of the crystal structure along the *a* axis of packing of the dimers *r*-**1** during the formation of the monolayer. Hydrogen bonds: medium O–H···O (—) and weak C–H···O (----).

The quantum-chemical modeling of the single crystal of compound **1** was realized with the semiempirical MOPAC2009 program [5] and the Winmostar graphical interface [6] using the reparametrized RM1 method. This method of calculation was used because it makes it possible to optimize the geometry of molecules consisting of the atoms of the elements C, N, H, and O with least error for the lengths of the bonds and the angles between them in comparison with other methods with neglect of diatomic differential overlap [7, 8]. During quantum-chemical calculations of the macrocell of compound **1**, consisting of (2×2×2) unit cells, with the translational vectors (Tv) and the MERS(2,2,2) function for the solid state, the interatomic distances and valence angles (Table 2), the geometric parameters of the hydrogen bonds D–H···A (Table 3), and the parameters of the unit cell in the single crystal (a = 6.308, b = 8.540, c = 8.878 Å, α = 84.33, β = 84.86, γ = 70.26°; V = 447.13 $Å^3$, ρ = 1.160 g/cm^3) were obtained.

As seen from the data in Table 2, the experimental intramolecular parameters of compound **1** and the values calculated by the RM1 method agree fully with each other. At the same time, the calculated intermolecular interactions at the carboxyl groups in the dimer *r*-**1** (average hydrogen bond O(3)–H(3)···$O(2)^i$) are slightly reduced, while the intermolecular interactions on account of the weak hydrogen contacts C–H···O of the different nature are increased (by not more than 5%) in comparison with the experimental values (Table 3). The increase in the calculated sizes of the unit cell of compound **1** compared with the experimental values (Table 1) is explained by the fact that for the molecule of **1** there are three different increased hydrogen contacts C–H···O, the total contribution of which to the volume of the unit cell increases its dimensions, to one hydrogen bond O(3)–H(3)···$O(2)^i$.

Thus, it was established by X-ray diffraction that 2,5-dimethyl-3,4-dihydro-2H-pyran-2-carboxylic acid crystallizes in the centrosymmetric $P\bar{1}$ space group; the unit cell contains two enantiomeric molecules, which are in the form of the *endo* stereomer on account of the axial position of the carboxyl group in relation to the dihydropyran ring. The semiempirical MOPAC2009 quantum-chemical calculations of the model of the macrocell of the acid agree well with the obtained X-ray crystallographic data.

EXPERIMENTAL

2,5-Dimethyl-3,4-dihydro-2H-pyran-2-carboxylic Acid (1). Sodium 2,5-dimethyl-3,4-2H-pyran-2-carboxylate (5 g, 28.1 mmol) was dissolved in water (20 ml) and cooled to 0°C. To the obtained solution of the salt, diethyl ether (15 ml) was added, and 15% aqueous solution of H_2SO_4 (9 ml) was then added drop by drop with vigorous stirring. The acid **1** was extracted from the water with diethyl ether, thereby preventing its lactonization in the aqueous phase. After evaporation of the ether at room temperature compound **1** (3.9 g, 25 mmol) was obtained in the form of transparent crystals.

X-Ray Diffraction Analysis. The crystal structure of compound **1** was investigated on a KUMA KM4CCD four-circle diffractometer. The structure was solved by the direct method with the *SHELX* software package [9]. Full-matrix least-squares refinement of the coordinates and anisotropic temperature parameters (for the non-hydrogen atoms) was done on the F^2 basis. The hydrogen atoms were found from geometric considerations and were refined (except for H-3) in the "rider" model. The H-3 hydrogen atom was refined in isotropic approximation. The bond lengths and the angles between the atoms in the molecule of compound **1**, the numbering of which is shown in Fig. 1, are given in Table 2. The geometric parameters of the hydrogen bonds are given in Table 3. The crystallographic data (apart from the structure factors) for the investigated structure have been deposited in the Cambridge Crystallographic Structural Database as supplementary materials (deponent CCDC 779250).

Quantum-Chemical Calculations. By means of the semiempirical MOPAC2009 program [5] and the Winmostar graphical interface [6], quantum-chemical calculations by the RM1 method were performed on a model of the macrocell consisting of (2×2×2) unit cells of the crystal of compound **1** using the translational vectors of the unit cell Tv and the MERS(2,2,2) function for the solid state with energy normalization coefficient GNORM = 10.

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