

**MOLECULAR AND CRYSTAL
STRUCTURE OF 4,6,6-TRIMETHYL-
2-OXO-5,6-DIHYDRO-2H-PYRAN-
3-CARBONITRILE AND 4,6,6-TRIMETHYL-
2-OXO-1,2,5,6-TETRAHYDROPYRIDINE-
3-CARBONITRILE**

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Single crystals of 4,6,6-trimethyl-2-oxo-5,6-dihydro-2H-pyran-3-carbonitrile and 4,6,6-trimethyl-2-oxo-1,2,5,6-tetrahydropyridine-3-carbonitrile were prepared and submitted to X-ray diffraction analysis. Both compounds have a molecular structure belonging to the C_1 symmetry group. The heterocyclic rings are in a distorted envelope conformation. The crystals belong to the monoclinic system and each contain four molecules in the unit cell. In the crystal the pyridine derivative exists in the form of centrosymmetric dimers stabilized by intermolecular hydrogen bonds between the oxygen atoms of the carbonyl group and the hydrogen atom at the nitrogen atom of the ring.

Keywords: 4,6,6-trimethyl-2-oxo-5,6-dihydro-2H-pyran-3-carbonitrile, 4,6,6-trimethyl-2-oxo-1,2,5,6-tetrahydropyridine-3-carbonitrile, AM1 method, X-ray crystallographic analysis.

Six-membered heterocycles such as 4,6,6-trimethyl-2-oxo-5,6-dihydro-2H-pyran-3-carbonitrile (**1**) and 4,6,6-trimethyl-2-oxo-1,2,5,6-tetrahydropyridine-3-carbonitrile (**2**) and their derivatives have a broad spectrum of biological activity and are of interest as potential cardiovascular, anticancer, and neurotropic preparations [1-3]. We obtained compounds **1** and **2** earlier by the condensation of 4-hydroxy-4-methyl-2-pentanone with cyanoacetic ester in the presence of ammonium acetate. The synthesized compounds were identified on the basis of data from elemental analysis and ^1H NMR spectroscopy [4].

The geometric structure of the molecules is one of the basic characteristics of chemical compounds. It is directly related to both the physical and the chemical properties of the substances, including their reactivity, and in many cases their biological activity. X-ray crystallographic analysis of single crystals of these substances was performed in order to obtain objective detailed information about the spatial and geometric structure of compounds **1** and **2**.

Spatial models of compounds **1** and **2** were obtained by X-ray crystallographic analysis, and the ellipsoids of the thermal vibrations and the designations of the atoms are shown in Fig. 1. The most important geometric characteristics of the molecules are given in Tables 1 and 2.

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In the condensed phase both compounds have a molecular structure belonging to the C_1 symmetry point group. The heterocyclic ring is in a distorted *envelope* conformation. The dihedral angle between the O(1)–C(6)–C(5) and C(3)–C(4)–C(5) planes in the molecule **1** is $132.2(2)^\circ$, and the projection of the atom at the apex of the *envelope* C(6) from the plane of the other ring atoms amounts to $0.583(3)$ Å. In the molecule **2** the deflection of the C(6) atom from the basal plane of the heterocycle is $0.562(7)$ Å, and the corresponding bending angle is $134.4(2)^\circ$. In both molecules the oxygen atom of the carbonyl group, the cyano group, and the C(10) atom of the methyl group at the C(4) atom lie in the basal plane of the heterocycle. The methyl groups at the C(6) atom are arranged in such a way that the pseudoplane in which this atom and the C(7) and C(8) atoms lie is practically orthogonal with the basal plane of the heterocyclic ring ($92.9(2)^\circ$ for the molecule of compound **1** and $91.7(2)^\circ$ for the molecule of compound **2**).

Quantum-chemical calculations of the structures with full optimization of their geometry by the AM1 method [5] were undertaken in order to obtain an idea of the structure of the isolated molecules in the gas phase. The geometric parameters obtained experimentally (X-ray crystallographic analysis) and calculated theoretically (AM1) differ little (Tables 1 and 2). This indicates that the structure of the investigated compounds does not undergo any substantial changes during the crystallization process. The largest changes are in the shortening of the valence bond between the heteroatom and the carbonyl carbon atom and amount to only ~ 0.055 Å in each molecule.

The intermolecular distances in the crystal of compound **1** correspond to normal van der Waals contacts. The comparatively loose packing of the molecules conditions the relatively low density of the substance (1.208 g/cm³).

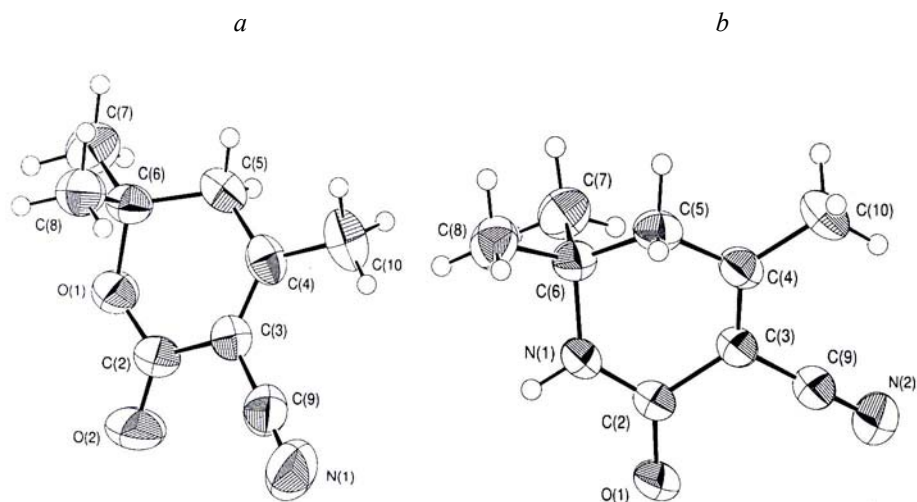


Fig. 1. Spatial models of the molecule of compound **1** (a) and the molecule of compound **2** (b) according to X-ray crystallographic analysis.

In the crystallization state compound **2** exists in the form of centrosymmetric dimers linked by intermolecular hydrogen bonds between the carbonyl oxygen atom and the hydrogen atom at the nitrogen atom of the ring, and this is rather specific for 2(1H)-pyridone structures (Fig. 2). The geometry of the molecules in the dimer agree with each other within the experimental accuracy limits. The length of the hydrogen bonds is $2.894(2)$ Å ($N(1)–H = 0.89(3)$, $H\cdots O(1) = 2.02(3)$ Å, $N(1)–H\cdots O(1) = 178(2)^\circ$), which corresponds to standard values for such bonds [6].

TABLE 1. The Principal Bond Lengths (l) in the Molecules of Compounds **1** and **2**, Determined by XCA and Calculated by the AM1 Method

1			2		
Bond	$l, \text{\AA}$		Bond	$l, \text{\AA}$	
	XCA	AM1		XCA	AM1
O(1)–C(2)	1.323(3)	1.378	N(1)–C(2)	1.330(2)	1.384
C(6)–O(1)	1.478(3)	1.443	C(6)–N(1)	1.475(2)	1.454
C(2)–O(2)	1.206(3)	1.230	C(2)–O(1)	1.238(2)	1.245
C(2)–C(3)	1.478(4)	1.476	C(2)–C(3)	1.490(2)	1.492
C(3)–C(4)	1.345(4)	1.353	C(3)–C(4)	1.344(2)	1.352
C(4)–C(5)	1.490(4)	1.488	C(4)–C(5)	1.500(3)	1.488
C(5)–C(6)	1.518(3)	1.530	C(5)–C(6)	1.522(3)	1.546
C(4)–C(10)	1.484(4)	1.477	C(4)–C(10)	1.494(2)	1.480
C(3)–C(9)	1.429(3)	1.418	C(3)–C(9)	1.434(3)	1.419
C(9)–N(1)	1.143(4)	1.163	C(9)–N(2)	1.144(3)	1.163

TABLE 2. The Principal Bond Angles (ω) in the Molecules of **1** and **2**, Determined by X-ray Crystallographic Analysis and Calculated by the AM1 Method

1			2		
Angle	$\omega, \text{deg.}$		Angle	$\omega, \text{deg.}$	
	XCA	AM1		XCA	AM1
C(2)–O(1)–C(6)	120.5(2)	118.6	C(2)–N(1)–C(6)	124.0(1)	122.2
O(1)–C(2)–C(3)	118.5(2)	119.8	N(1)–C(2)–C(3)	116.1(2)	117.4
C(2)–C(3)–C(4)	121.6(3)	120.3	C(2)–C(3)–C(4)	121.7(2)	121.2
C(3)–C(4)–C(5)	117.7(2)	119.3	C(3)–C(4)–C(5)	118.6(1)	120.7
C(4)–C(5)–C(6)	113.6(2)	112.4	C(4)–C(5)–C(6)	113.3(2)	113.7
O(1)–C(6)–C(5)	108.6(2)	111.7	N(1)–C(6)–C(5)	107.6(1)	111.1
C(8)–C(6)–C(7)	111.3(3)	110.4	C(4)–C(5)–C(6)	110.0(1)	107.0

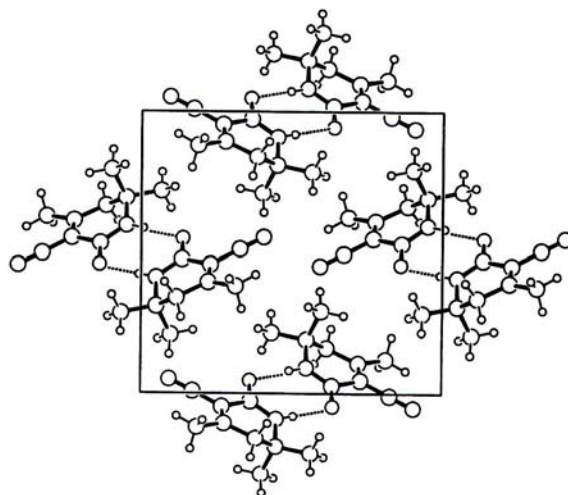


Fig. 2. Projection of the crystal structure of compound **2** along the [100] direction. (The dotted lines show the intermolecular hydrogen bonds.)

TABLE 3. The Crystallographic Characteristics of Compounds **1** and **2** and the Refinement Parameters of the Crystal Structures

Parameter	1	2
Empirical formula	C ₉ H ₁₁ NO ₂	C ₉ H ₁₂ N ₂ O
<i>M</i>	165.19	164.21
Crystal habit	Prism	Prism
Crystal size, mm	0.11×0.13×0.17	0.10×0.11×0.25
Crystal system	Monoclinic	Monoclinic
Unit cell parameters		
<i>a</i> , Å	7.2100(3)	6.3147(2)
<i>b</i> , Å	12.5279(7)	12.4171(4)
<i>c</i> , Å	10.2380(5)	13.1063(5)
β, deg	100.878(3)	116.422(2)
Unit cell volume <i>V</i> , Å ³	908.14(8)	920.32(5)
Space group	<i>P</i> 2 ₁ / <i>n</i>	<i>P</i> 2 ₁ / <i>c</i>
Molecular multiplicity, <i>Z</i>	4	4
<i>F</i> (000)	352	352
Density of substance ρ _{calc} , g/cm ³	1.208	1.185
Maximum angle 2θ _{max} , deg	55.0	55.0
Miller index ranges	-9 ≤ <i>h</i> ≤ 9 -16 ≤ <i>k</i> ≤ 14 -13 ≤ <i>l</i> ≤ 13	-7 ≤ <i>h</i> ≤ 8 -16 ≤ <i>k</i> ≤ 16 -16 ≤ <i>l</i> ≤ 17
Absorption coefficient μ, mm ⁻¹	0.09	0.08
Total number of reflections	3631	3875
Number of unique reflections	2275	2317
Number of reflections with <i>I</i> > 3σ(<i>I</i>)	1317	1404
<i>R</i> -factor [<i>I</i> > 3σ(<i>I</i>)]	0.049	0.044
<i>wR</i> ₂ index for all reflections	0.166	0.118
Number of refined parameters	121	157
<i>GOOF</i>	0.885	1.025
(Δ/σ) _{max}	0.003	0.003

EXPERIMENTAL

X-ray Crystallographic Analysis. The crystals of compounds **1** and **2** for X-ray crystallographic analysis were obtained by crystallization from ethanol.

The quantum-chemical calculations were performed by the AM1 method [5] with MOPAC 2007 software [7]. The optimized structures corresponded to minima on the potential energy surface of the molecular systems.

The diffraction data for single crystals of compounds **1** and **2** were collected on a Bruker-Nonius Kappa CCD automatic diffractometer. The crystal structure was solved by the method developed previously at the Latvian Institute of Organic Synthesis [8]. The initial *R* factor of the structures obtained after solution of the models was 25-30%. Further refinement was achieved by full-matrix least-squares treatment in anisotropic approximation for all non-hydrogen atoms with maXus software [9]. The positions of the hydrogen atoms were localized on the basis of Fourier difference syntheses of the electron density and were refined in isotropic approximation. The crystallographic characteristics of compounds **1** and **2** and the refinement parameters of the structures are given in Table 3.

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