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MOLECULAR STRUCTURE OF (4*Z*)-{[(1*R*,6*S*)-7,7-DIMETHYL-2-OXO-3-OXABICYCLO [4.1.0]HEPT-4-EN-4-YL]METHYLENE}-2-PHENYL-1,3-OXAZOL-5(4H)-ONE

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The (4*Z*)-{[(1*R*,6*S*)-7,7-dimethyl-2-oxo-3-oxabicyclo[4.1.0]hept-4-en-4-yl]methylene}-2-phenyl-1,3-oxazol-5(4H)-one compound is synthesized and its molecular structure is determined.

Keywords: oxazolone, formyl enol lactone derivative of ketocaronic acid, Erlenmeyer reaction, single crystal X-ray diffraction analysis.

Aldehyde condensation with N-acyl glycines under the action of acetic anhydrides (Erlenmeyer reaction) leads to the formation of 5(4H)-oxazolones (azlactones) that are convenient synthons for the synthesis of amino acid derivatives. Aromatic, heterocyclic, and α,β-unsaturated aldehydes readily enter into the Erlenmeyer reaction and afford oxazolone with good yield. However, fatty aldehydes hardly react with acyl glycines, while this reaction with terpene aldehydes has been poorly studied [1].

We have determined that 4-formyl enol lactone derivative of ketocaronic acid **II** obtained by successive oxidative transformations of monoterpene (+)-3-carene **I** (Fig. 1) can be easily condensed with the hippuric acid in the acetic anhydride medium [2, 3]. The structure of obtained 5(4H)-oxazolone **III** was determined by NMR spectroscopy and single crystal X-ray diffraction analysis.

Experimental. (4*Z*)-{[(1*R*,6*S*)-7,7-Dimethyl-2-oxo-3-oxabicyclo[4.1.0]hept-4-en-4-yl]methylene}-2-phenyl-1,3-oxazol-5(4H)-one **III**. To the solution of 0.8 g (4.8 mmol) of compound **II** in 25.8 ml of acetic anhydride we added 0.86 g (4.8 mmol) of hippuric acid and 0.66 g (4.8 mmol) of potassium carbonate. The reaction mixture was stirred for 5 h, left for the night, and then it was evaporated. The residue was dissolved in methylene chloride, washed with water, dried with Na_2SO_4, evaporated, and chromatographed (SiO_2, ethyl acetate: petroleum ether eluent, 4:1). We obtained 1.07 g (72%) of compound **III** in the form of light-yellow crystalline substance. T_{melt} 162°C, $[\alpha]_D^{20}$ 31.2° (s 0.2, $CHCl_3$). ^1H NMR spectrum* (δ/ppm, *J*/Hz): 1.09 s and 1.35 s (3H, hem-CH_3), 2.04 dd (1H, H^7, *J* 7.2, 6.0), 2.10 d (1H, H^8, *J* 7.2), 6.54 s (1H, H^4), 7.0 d (1H, 6H, *J* 6.0 Hz), 7.45-7.63 m (3H, H_{arom}), 8.12 d (2H, $H_{\text{arom,}}$ *J* 8.5 Hz). ^{13}C NMR spectrum (δ/ppm): 15.97 and 27.03 (hem-CH_3), 25.74 (C^{10}), 30.80 and 31.08 (C^8, C^7), 115.53 (C^6), 122.15 (C^4), 125.25 (C^5), 128.83, 128.83, 129.18, 129.18, 130.31, 134.06 ($C_{\text{arom.}}$), 146.12 (C^3), 165.05, 165.59, 166.54 (C^2, C^1, C^9). Found, %: C 69.23, H 4.83, N 4.21. $C_{18}H_{15}NO_4$.

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*Numbering of carbon atoms in the NMR spectra corresponds to numbering in the molecular structure shown in Fig. 2.

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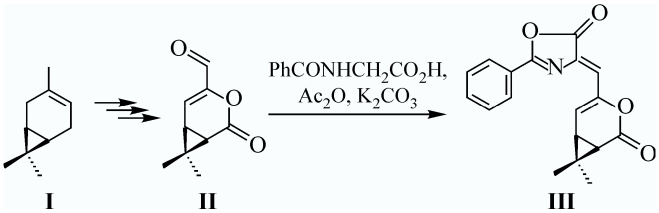

Fig. 1. Scheme of the synthesis of (4Z)-{[(1*R*,6*S*)-7,7-dimethyl-2-oxo-3-oxabicyclo[4.1.0]hept-4-en-4-yl]methylene}-2-phenyl-1,3-oxazol-5(4H)-one **III**.

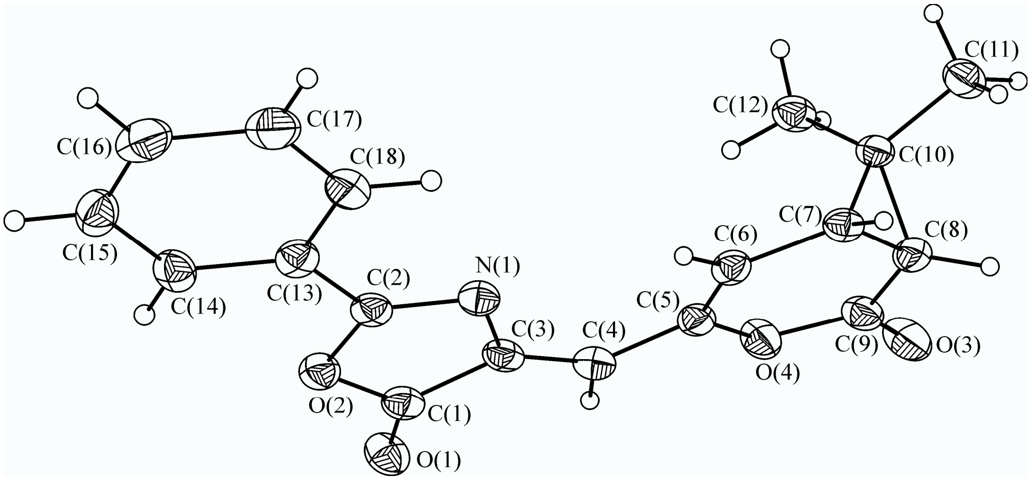

Fig. 2. Molecular structure of **III** (thermal ellipsoides are shown with 50% probability).

Calculated, %: C 69.89, H 4.89, N 4.53. ^{13}C and ^1H NMR spectra were measured on a Bruker AM-300 spectrometer (75.5 MHz and 300 MHz respectively), the internal standard was TMS. The melting temperature was determined on a Boetius warm stage.

Single crystal X-ray diffraction analysis. Yellow orthorhombic crystals, $C_{18}H_{15}NO_4$, ($M = 309.31$), at 120 K $a = 6.0246(7)$ Å, $b = 13.3890(16)$ Å, $c = 18.543(2)$ Å, $V = 1495.8(3)$ Å^3, space group $P2_12_12_1$, $Z = 4$, $d_x = 1.374$ g/cm^3. An experimental set of 15314 reflections was obtained on Bruker SMART 1000 CCD area detector [4] at 120 K (λM_0K_α radiation, $\theta_{max} = 28.00°$) from a single crystal of 0.55×0.40×0.25 mm. After the equivalent reflections were averaged, 3587 independent reflections were obtained ($R_{int} = 0.0381$), which were used to interpret and refine the structure. Absorption ($\mu = 0{,}098$ mm^{-1}) was not taken into account.

The structure was solved using the direct method; all non-hydrogen atoms were localized in electron density difference syntheses and were refined in the in anisotropic approximation against F^2_{hkl} ; all hydrogen atoms were located into geometrically calculated positions. The final value of uncertainty factors is as follows: $R1 = 0.0435$ (calculated against F^2_{hkl} for 3315 reflections with $I > 2\sigma(I)$), $wR2 = 0.0958$ (calculated against F^2_{hkl} for 3587 reflections), $GOOF = 1.004$, 208 refined parameters.

All calculations were performed using the SHELXTL PLUS5 software complex [5].

Atom coordinates, torsion angles, and temperature parameters have been deposited with the Cambridge Crystallographic Data Centre (CCDC No. 711886), and one can get them for free at www.ccdc.cam.uk/conts/retrieving.html (or from CCDC, 12 Union Road, Cambridge CB2 1EZ; fax: +44 1223 335 033; or deposit@ccdc.cam.ac.uk).

Results and discussion. Single crystal X-ray diffraction analysis of the obtained crystal showed that azlactone **III** is formed as an independent isomer with Z-configuration of the exocyclic double bond (Fig. 2). Bond lengths and bond angles are shown in Tables 1 and 2.

TABLE 1. Bond Lengths *d*, Å in the structure of **III**

Bond	*d*	Bond	*d*	Bond	*d*	Bond	*d*
O(1)–C(1)	1.197(2)	N(1)–C(2)	1.292(2)	C(6)–C(7)	1.465(3)	C(13)–C(14)	1.397(3)
O(2)–C(2)	1.387(2)	N(1)–C(3)	1.402(2)	C(7)–C(10)	1.521(2)	C(13)–C(18)	1.405(3)
O(2)–C(1)	1.397(2)	C(1)–C(3)	1.484(3)	C(7)–C(8)	1.532(3)	C(14)–C(15)	1.391(3)
O(3)–C(9)	1.203(2)	C(2)–C(13)	1.453(3)	C(8)–C(9)	1.475(3)	C(15)–C(16)	1.384(3)
O(4)–C(9)	1.370(2)	C(3)–C(4)	1.344(3)	C(8)–C(10)	1.529(2)	C(16)–C(17)	1.392(3)
O(4)–C(5)	1.406(2)	C(4)–C(5)	1.444(3)	C(10)–C(12)	1.500(3)	C(17)–C(18)	1.382(3)
		C(5)–C(6)	1.335(3)	C(10)–C(11)	1.510(3)		

TABLE 2. Bond Angles ω, deg in the Structure of **III**

Angle	ω	Angle	ω	Angle	ω
C(2)–O(2)–C(1)	105.31(14)	C(6)–C(5)–O(4)	122.65(17)	C(12)–C(10)–C(11)	114.45(16)
C(9)–O(4)–C(5)	122.14(15)	C(6)–C(5)–C(4)	127.99(17)	C(12)–C(10)–C(7)	121.15(17)
C(2)–N(1)–C(3)	105.38(15)	O(4)–C(5)–C(4)	109.34(15)	C(11)–C(10)–C(7)	115.85(16)
O(1)–C(1)–O(2)	122.93(18)	C(5)–C(6)–C(7)	122.21(17)	C(12)–C(10)–C(8)	119.64(16)
O(1)–C(1)–C(3)	132.32(19)	C(6)–C(7)–C(10)	120.95(16)	C(11)–C(10)–C(8)	119.64(16)
O(2)–C(1)–C(3)	104.74(15)	C(6)–C(7)–C(8)	115.21(16)	C(7)–C(10)–C(8)	60.32(12)
N(1)–C(2)–O(2)	116.35(16)	C(10)–C(7)–C(8)	60.08(12)	C(14)–C(13)–C(18)	119.97(17)
N(1)–C(2)–C(13)	127.01(16)	C(9)–C(8)–C(10)	120.17(16)	C(14)–C(13)–C(2)	121.20(17)
O(2)–C(2)–C(13)	116.58(15)	C(9)–C(8)–C(7)	118.29(16)	C(18)–C(13)–C(2)	118.78(17)
C(4)–C(3)–N(1)	129.93(17)	C(10)–C(8)–C(7)	59.60(11)	C(15)–C(14)–C(13)	119.42(18)
C(4)–C(3)–C(1)	121.83(17)	O(3)–C(9)–O(4)	116.62(18)	C(16)–C(15)–C(14)	120.44(19)
N(1)–C(3)–C(1)	108.16(16)	O(3)–C(9)–C(8)	124.17(18)	C(15)–C(16)–C(17)	120.29(19)
C(3)–C(4)–C(5)	127.80(17)	O(4)–C(9)–C(8)	119.21(16)	C(18)–C(17)–C(16)	120.03(19)
				C(17)–C(18)–C(13)	119.85(18)

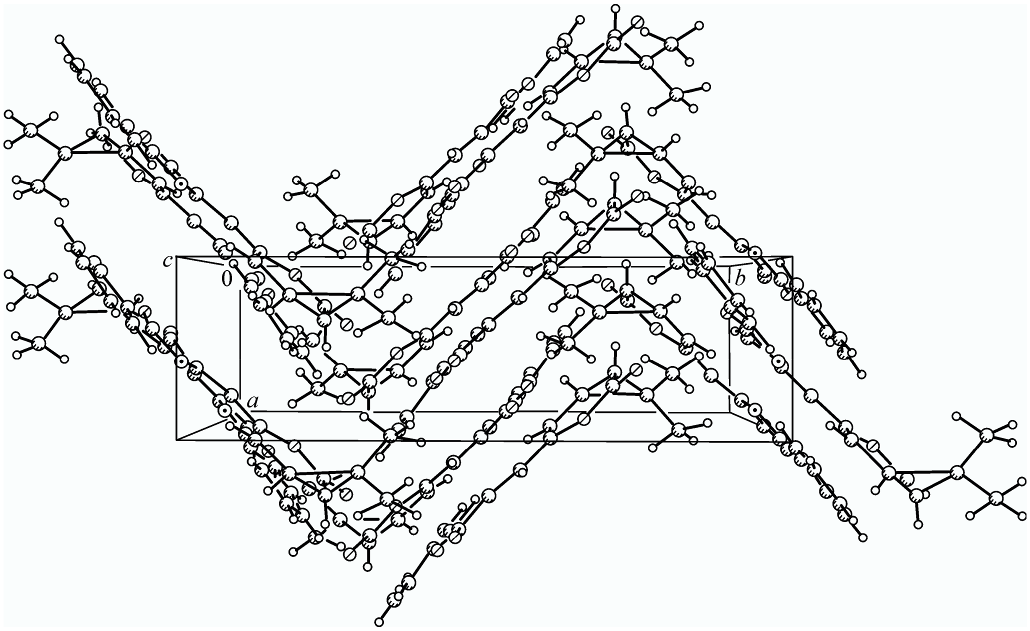

Fig. 3. Molecular packing in the crystal of **III**.

Phenyl, lactone, and azlactone cycles are located in one plane (deviation of atoms from the average plane is ±0.13 Å); cyclopropane ring is at an angle of 69.7° to this plane. The double bond formed as a result of the condensation reaction is in *cis* coplanar position to the double bond of the terpenoid part of the molecule (C(3)–C(4)–C(5)–C(6) torsion angle is 7.9(3)°).

Geometrical parameters of molecules have standard values.

Molecular packing in the crystal (Fig. 3) was determined by the van der Waals interactions.

For the first time we have obtained and characterized (4Z)-{[(1R,6S)-7,7-dimethyl-2-oxo-3-oxabicyclo[4.1.0]hept-4-en-4-yl]methylene}-2-phenyl-1,3-oxazol-5(4H)-one **III** using NMR and single crystal X-ray diffraction analyses**.**

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