Synthesis and crystal structure of ethyl 1-benzyl-2-hydroxy-5-methyl-3-oxo-2-phenacyl-2,3-dihydropyrrole-4-carboxylate

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Reaction of 5-phenyl-2,3-dihydro-2,3-furandione with ethyl 3-benzylamino-2-butenoate, resulting in ethyl 1-benzyl-2-hydroxy-5-methyl-3-oxo-2-phenacyl-2,3-dihydropyrrole-4-carboxylate and benzylamide of *N*-benzoylpyruvic acid, was studied. The structure of the pyrrole derivative was confirmed by X-ray analysis.

Key words: 5-phenyl-2,3-dihydro-2,3-furandione, ethyl 3-benzylamino-2-butenoate, ethyl 1-benzyl-2-hydroxy-5-methyl-3-oxo-2-phenacyl-2,3-dihydropyrrole-4-carboxylate, crystal and molecular structure.

It is known that amines and alcohols under mild conditions provoke scission of the 5-aryl-2,3-dihydro-2,3-furandione ring, attacking carbon atom C(2) of the heterocycle with the formation of aroylpyruvic carbamides[1] and esters[2], respectively. Weaker nucleophilic agents, for example, phenols, are unable to cause scission of the furandione ring and react only with aroylketenes, which are generated by thermolysis of the latter, to give phenyl aroylacetates.[3,4]

We studied the interaction of 5-phenyl-2,3-dihydro-2,3-furandione (**1**) with ethyl 3-benzylamino-2-butenoate (**2**), containing two nucleophilic centers: the nitrogen atom of a secondary amino group and a carbon atom C(2). Nucleophilicity of nitrogen atom in compound **2** is lower as compared with that in amines due to the conjugation of its unshared electron pair with C(2)=C(3) bond. Because of this, the more probable result of the reaction may be formation of ethyl *N*-benzyl-*N*-benzoylacetyl-2-butenoate (**3**), the product of a reaction of benzoyl ketene (**4**) at nitrogen atom of compound **2** (Scheme 1).

However, it was found that boiling equimolar amounts of compounds **1** and **2** in benzene results in formation of two substances: light colored benzoylpyruvic *N*-benzylamide (**5**) which was identified by the comparison with the known sample[5] and colorless ethyl 1-benzyl-2-hydroxy-5-methyl-3-oxo-2-phenacyl-2,3-dihydropyrrole-4-carboxylate (**6**), whose structure was established by X-ray analysis since IR and ^{1}H NMR spectroscopy do not allow one to make an unambiguous choice between structure **6** and possible regioisomer **7**.

The general appearance of molecule **6** (with indication of the position of only one hydrogen atom H(30)) is shown in Fig. 1. Bond length and valence angle values are given in Table 1.

The dihydropyrrole ring, being sterically overloaded, is planar. Steric factors must be responsible for the considerable lengthening of intracyclic bonds. Thus, double bond C(8)=C(9) is 1.403 Å long. The bonds C(6)—C(7) and C(6)—C(10) are considerably lengthened, their lengths are 1.533 and 1.473 Å, respectively. As to the rest, bond lengths and valence angles have values close to common ones, that does not need any comments.

Benzene fragment plane forms an angle of 66.1° with heterocyclic plane, and a torsion angle C(6)—N(11)—C(11)—C(12) is equal to 90.4°. The conformation of the O(1)—C(6) bond is twisted (the H(30)—O(1)—C(6)—C(7) angle is equal to −69°, *i.e.*, it is in *gauche*-conformation). A plane traced through atoms C(6), C(21), C(22) has bisector orientation with respect to dihydropyrrole ring. The orientation of planar benzene fragment is characterized by a torsion angle C(6)—C(21)—C(22)—C(20) equal to 158.1°. Carbethoxy group, with the exception of methyl carbon atom C(29), is planar and coplanar with the heterocyclic plane.

There is a shortened intermolecular contact, whose length is 2.71 Å, in the crystal between atom O(1) of the

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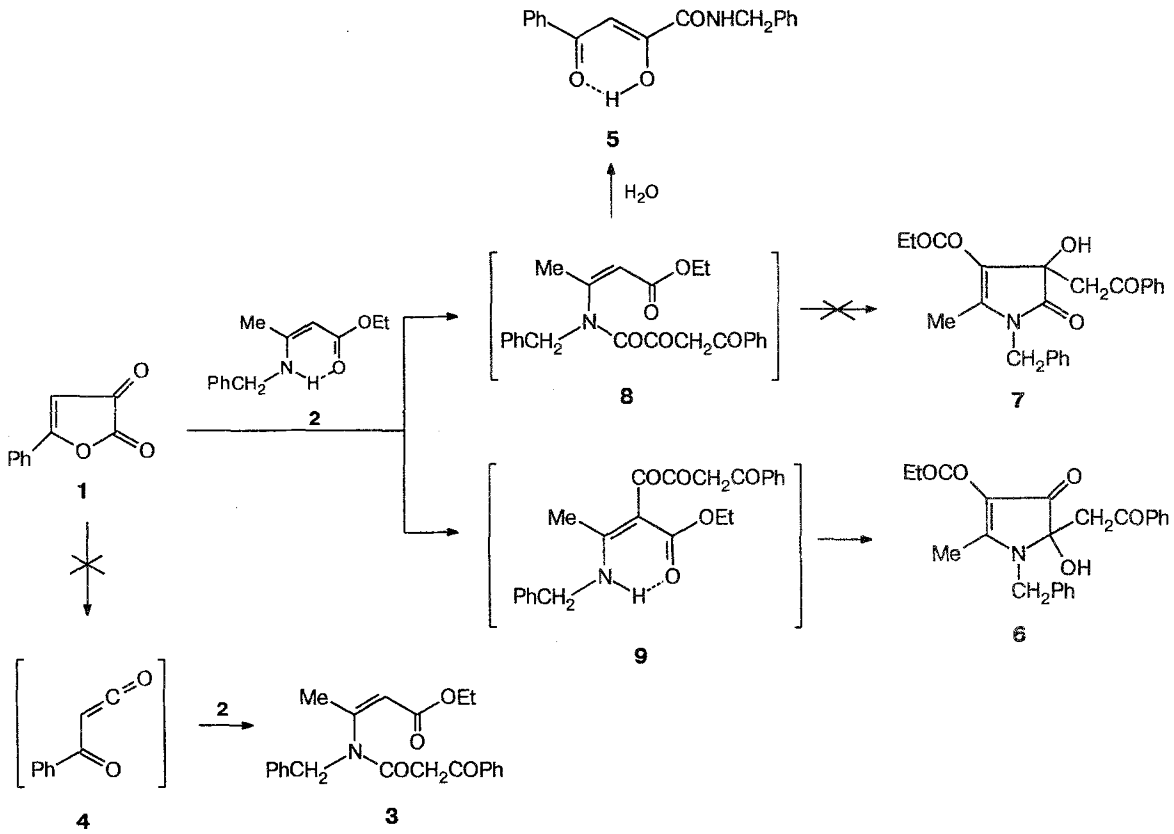
Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 8, pp. 1552—1555, August, 1995.

Scheme 1



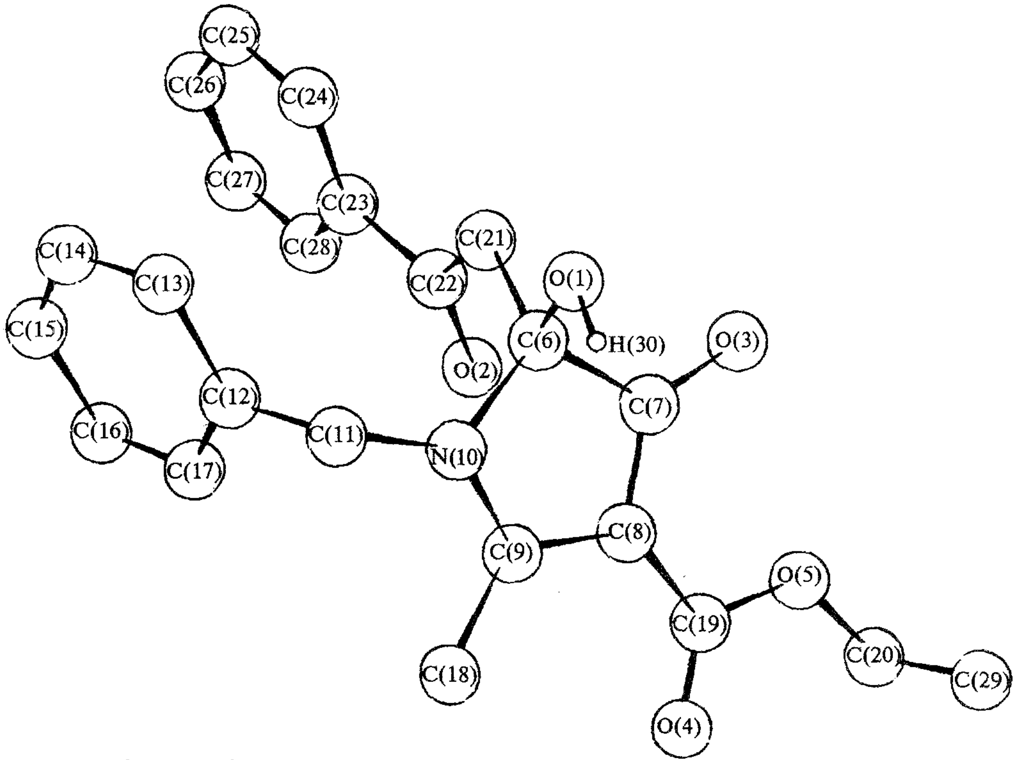


Fig. 1. Structure **6**.

Table 1. Main geometric parameters of molecule **6**

Bond	*d*/Å	Bond	*d*/Å
O(1)—C(6)	1.409(3)	O(1)—H(30)	0.92(5)
O(2)—C(22)	1.215(4)	O(3)—C(7)	1.238(4)
O(4)—C(19)	1.213(5)	O(5)—C(20)	1.443(6)
O(5)—C(19)	1.334(5)	C(6)—N(10)	1.473(4)
C(6)—C(21)	1.521(5)	C(6)—C(7)	1.533(5)
C(7)—C(8)	1.417(5)	C(8)—C(9)	1.403(5)
C(8)—C(19)	1.434(5)	C(9)—N(10)	1.337(4)
C(9)—C(18)	1.490(5)	N(10)—C(11)	1.480(4)
C(11)—C(12)	1.511(5)	C(12)—C(13)	1.390(6)
C(12)—C(17)	1.370(6)	C(13)—C(14)	1.397(8)
C(14)—C(15)	1.356(8)	C(15)—C(16)	1.364(9)
C(16)—C(17)	1.391(7)	C(20)—C(29)	1.353(9)
C(21)—C(22)	1.517(4)	C(22)—C(23)	1.492(5)
C(23)—C(24)	1.380(5)	C(24)—C(25)	1.396(6)
C(25)—C(26)	1.379(6)	C(26)—C(27)	1.368(8)
C(27)—C(28)	1.385(6)		

Angle	ω/deg	Angle	ω/deg
C(19)—O(5)—C(20)	118.2(3)	C(6)—O(1)—H(30)	111.0(2.8)
O(1)—C(6)—C(7)	111.6(8)	O(1)—C(6)—N(10)	110.7(4)
O(1)—C(6)—C(21)	104.6(4)	C(7)—C(6)—N(10)	101.9(3)
C(7)—C(6)—C(21)	114.1(4)	N(10)—C(6)—C(21)	114.1(8)
O(3)—C(7)—C(6)	119.5(3)	O(3)—C(7)—C(8)	132.5(6)
C(6)—C(7)—C(8)	107.9(3)	C(9)—C(8)—C(9)	124.2(3)
C(7)—C(8)—C(9)	107.2(5)	C(7)—C(8)—C(19)	128.5(4)
C(8)—C(9)—N(10)	112.4(3)	C(8)—C(9)—C(18)	125.7(5)
N(10)—C(9)—C(18)	121.9(5)	C(6)—N(10)—C(9)	110.4(4)
C(6)—N(10)—C(11)	120.5(3)	C(9)—N(10)—C(11)	127.8(3)
N(10)—C(11)—C(12)	113.2(6)	C(13)—C(12)—C(17)	119.2(1.2)
C(11)—C(12)—C(13)	119.1(7)	C(11)—C(12)—C(17)	121.8(8)
C(12)—C(13)—C(14)	118.9(7)	C(13)—C(14)—C(15)	121.2(1.0)
C(14)—C(15)—C(16)	119.9(1.5)	C(15)—C(16)—C(17)	119.9(8)
C(12)—C(17)—C(16)	120.9(8)	O(4)—C(19)—O(5)	121.1(6)
O(4)—C(19)—C(8)	126.2(5)	O(5)—C(19)—C(8)	112.7(3)
O(5)—C(20)—C(29)	112.5(8)	C(6)—C(21)—C(22)	115.1(4)
O(2)—C(22)—C(21)	119.4(1.1)	O(2)—C(22)—C(23)	121.4(9)
C(21)—C(22)—C(23)	119.2(4)	C(22)—C(23)—C(24)	123.0(8)
C(22)—C(23)—C(28)	117.8(5)	C(24)—C(23)—C(28)	119.2(1.1)
C(23)—C(24)—C(25)	120.1(9)	C(24)—C(25)—C(26)	120.2(7)
C(25)—C(26)—C(27)	119.8(1.5)	C(26)—C(27)—C(28)	120.6(1.0)
C(23)—C(28)—C(27)	120.1(5)		

carboxy group and atom O(3) of the carbonyl group of a neighboring molecule connected with the former by a screw axis, which may be attributed to a H-bond of the O—H...O type. The geometric parameters of this bond (O(1)—H(30) = 0.92 Å, H(30)···O(3) = 1.79 Å, angle O(1)—H(30)—O(3) = 175°) suggest that it is sufficiently strong.

The scheme of obtaining compound **5** includes an attack of nitrogen atom of enamino ether **2** to atom C(2) of furandione **1** and the hydrolysis of intermediate **8** under the experiment conditions. Pyrrolone **6** represents a ring form of ethyl 2-[1-(benzylamino)ethylidene]-3,4,6-trioxo-6-phenylhexanoate (**9**), formed upon the scission of furandione cycle **1** as a result of an attack of atom C(2) of compound **2**. The synthesis of compound **6** is the first example of initial scission of 5-aryl-2,3-dihydro-2,3-furandione ring upon the action of CH nucleophilic agent.

Compound **3** was not detected in the reaction mixture, that suggests the scission of furandione ring **1** under the action of enaminoether **2** to be completed at a temperature below the temperature of decarbonylation.

Experimental

The IR spectrum is recorded on an UR-20 instrument. The ^{1}H NMR spectrum is recorded on an RYa-2310 (60 MHz) spectrometer in DMSO-d_6, internal standard HMDS. The course of the reaction and the purity of the products obtained were monitored by TLC using Silufol plates in a benzene—ethyl acetate (1:1) system, development with iodine vapor.

Interaction of 5-phenyl-2,3-dihydro-2,3-furandione with ethyl 3-benzylamino-2-butenoate. A mixture of 1.00 g (6 mmol)

Table 2. Atomic coordinates ($\times10^4$, for H atoms — $\times10^3$) in molecule **6**

Atom	*x*	*y*	*z*
O(1)	6420(1)	2031(0)	2453(3)
O(2)	8978(2)	736(1)	1200(5)
O(3)	8100(2)	2060(1)	−494(3)
O(4)	1081(2)	2351(2)	2792(5)
O(5)	339(2)	2421(1)	21(4)
C(6)	7434(2)	1666(1)	2274(5)
C(7)	8321(3)	1939(1)	1112(4)
C(8)	9264(3)	2031(1)	2241(5)
C(9)	9037(3)	1812(1)	3963(5)
N(10)	8027(2)	1593(1)	4033(3)
C(11)	7415(3)	1412(1)	5662(5)
C(12)	7495(3)	771(1)	5904(5)
C(13)	6496(3)	497(2)	5956(6)
C(14)	6572(5)	−96(2)	6197(7)
C(15)	7598(6)	−404(2)	6407(6)
C(16)	8579(4)	−136(2)	6364(7)
C(17)	8525(3)	453(2)	6112(6)
C(18)	9811(3)	1806(1)	5567(5)
C(19)	299(3)	2276(1)	1771(5)
C(20)	1365(4)	2642(2)	−648(8)
C(21)	7052(3)	1116(1)	1489(5)
C(22)	7988(3)	629(1)	1298(5)
C(23)	7669(3)	29(1)	1196(5)
C(24)	6551(3)	−107(1)	1218(6)
C(25)	6313(4)	−677(2)	1113(7)
C(26)	7192(5)	−1107(1)	973(7)
C(27)	8301(4)	−973(1)	945(6)
C(28)	8549(3)	−408(1)	1048(6)
C(29)	1209(4)	3207(2)	−1035(16)
H(30)	654(4)	235(2)	316(6)
H(31)	772(3)	161(2)	671(5)
H(32)	659(3)	159(2)	556(6)
H(33)	573(4)	76(2)	588(7)
H(34)	579(4)	−26(2)	628(7)
H(35)	766(4)	−84(2)	646(7)
H(36)	934(4)	−35(2)	647(7)
H(37)	922(3)	65(2)	603(6)
H(38)	947(4)	165(2)	670(7)
H(39)	12(5)	222(2)	578(7)
H(40)	46(4)	158(2)	531(7)
H(41)	141(6)	269(3)	−250(10)
H(42)	209(5)	247(3)	4(8)
H(43)	676(4)	122(2)	21(6)
H(44)	642(3)	100(2)	219(5)
H(45)	590(4)	20(2)	130(6)
H(46)	546(4)	−75(2)	114(6)
H(47)	695(4)	−152(2)	94(6)
H(48)	895(4)	−127(2)	86(7)
H(49)	932(4)	−29(2)	104(6)
H(50)	193(5)	335(3)	−138(9)
H(51)	99(7)	328(3)	4(12)
H(52)	49(5)	335(3)	−156(9)

of compound **1** and 1.26 g (6 mmol) of ether **2** was refluxed in 30 mL of benzene for 80 min. The precipitate of pyrrolone **4** formed in hot solution was filtered off and recrystallized from EtOH. Yield 0.45 g (21 %), m.p. 161—162 °C. IR (Vaseline oil), ν/cm^{-1}: 3150 (OH); 1690, 1682, 1650 (C=O); 1642 (C=C). ^{1}H NMR (δ): 1.18 (t, 3 H, $\underline{Me}CH_2O$); 2.43 (s, 3 H, Me); 3.58 (s, 3 H, Me); 4.07 (q, 2 H, $Me\underline{CH_2}O$); 4.75 (s, 2 H, $\underline{CH_2}Ph$); 7.35 (m, 10 H, 2 Ph). Found (%): N, 3.78. $C_{23}H_{23}NO_5$. Calculated (%): N, 3.55. The filtrate was evaporated; the residue was recrystallized twice from EtOH. 0.29 g (17 %) of amide **5** was obtained, m.p. 92—93 °C (*cf.* Ref. 5: m.p. 93 °C).

The crystals of compound **6** are monoclinic, a = 11.751(4), b = 23.475(7), c = 7.361(3) Å, γ = 84.7(1)°, V = 2021.9 Å^3, mol. weight 393.43, d_{calc} = 1.292 g cm^{-3}, Z = 4, space group $P2_1/n$. The experiment was carried out with a DAR-UM automatic diffractometer (monochromatic Cu-Kα radiation). 1398 independent nonzero reflections were registered below maximum magnitude $\sin\theta/\lambda$ = 0.61 Å^{-1}. Absorption was not taken into account. The structure was solved by the direct method. Hydrogen atoms were localized from a difference electron density synthesis. The least-squares refinement in full-matrix anisotropic (for H atoms — in isotropic) approximation was completed at R = 0.046. The atomic coordinates are given in Table 2. All calculations were performed on a PC/AT using an AREN software package.[6]

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Received December 22, 1994