Reaction of 5-phenyl-2,3-dihydrofuran-2,3-dione with 6,7-dimethoxy-3,4-dihydroisoquinoline. Crystal structure of 1-benzoyl-8,9-dimethoxy-2,3,5,6-tetrahydropyrrolo[2,1-*a*]isoquinoline-2,3-dione

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The reaction of 5-phenyl-2,3-dihydrofuran-2,3-dione with 6,7-dimethoxy-3,4-dihydroisoquinoline gave 1-benzoyl-2-hydroxy-8,9-dimethoxy-3,5,6,10b-tetrahydropyrrolo[2,1-*a*]isoquinolin-3-one and its oxidation product, *viz.*, 1-benzoyl-8,9-dimethoxy-2,3,5,6-tetrahydropyrrolo[2,1-*a*]isoquinoline-2,3-dione. The last-mentioned compound was studied by X-ray structural analysis.

Key words: 5-phenyl-2,3-dihydrofuran-2,3-dione; 1-benzoyl-2-hydroxy-8,9-dimethoxy-3,5,6,11-tetrahydropyrrolo[2,1-*a*]isoquinolin-3-one, oxidation; 1-benzoyl-8,9-dimethoxy-2,3,5,6-tetrahydropyrrolo[2,1-*a*]isoquinoline-2,3-dione, crystal and molecular structure.

Previously, it has been demonstrated that 5-aryl-2,3-dihydrofuran-2,3-diones react with 1,3,3-trimethyl-3,4-dihydroisoquinoline to form 2-aroylpyruvoyl-3,3-dimethyl-1-methylene-1,2,3,4-tetrahydroisoquinoline.[1] As part of continuing studies of the reactions of 5-aryl-2,3-dihydrofuran-2,3-diones with 3,4-dihydroisoquinolines, we studied the reaction of 5-phenyl-2,3-dihydrofuran-2,3-dione (**1**) with 6,7-dimethoxy-3,4-dihydroisoquinoline (**2**).

It was established that the reaction of equimolar amounts of compounds **1** and **2** in anhydrous dioxane in the cold yields two compounds, namely, yellow 1-benzoyl-2-hydroxy-8,9-dimethoxy-3,5,6,10b-tetrahydropyrrolo[2,1-*a*]isoquinolin-3-one (**3**) and dark-red 1-benzoyl-8,9-dimethoxy-2,3,5,6-tetrahydropyrrolo[2,1-*a*]isoquinoline-2,3-dione (**4**) (Scheme 1).

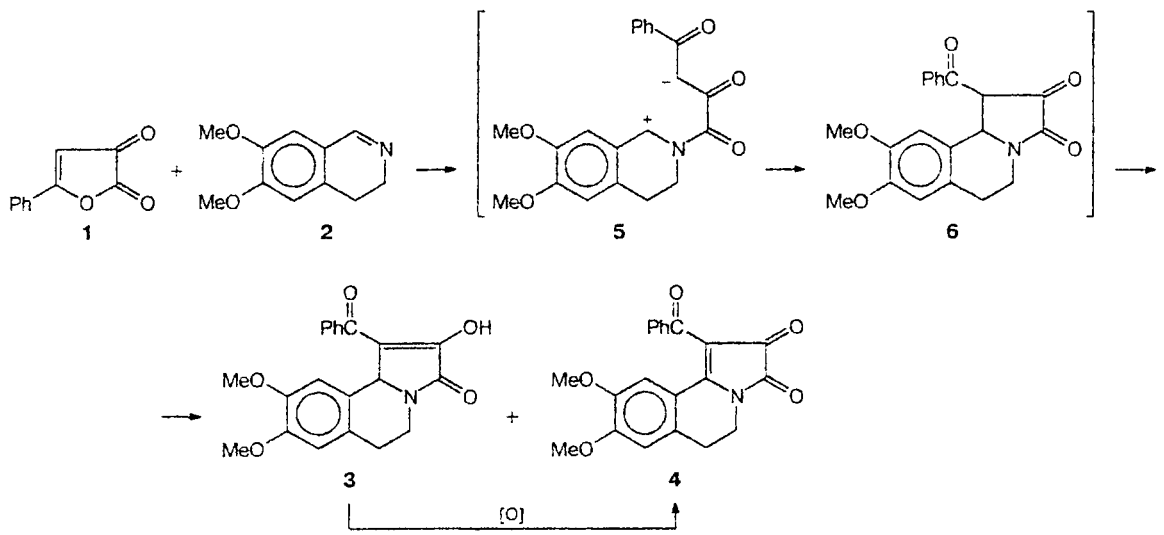
A possible scheme of the reaction involves the ring opening of compound **1** by the nucleophilic attack of the trigonal N atom of isoquinoline **2** and cyclization of intermediate **5** to hexahydropyrroloisoquinoline **6**. The migration of the proton from the C atom to the O atom of the carbonyl group in compound **6** yields one of the reaction products, *viz.*, compound **3**. Product **4** forms, apparently, by oxidation of compound **3** under the reaction conditions. Unexpectedly, this oxidation proceeds readily, whereas monocyclic 3-hydroxy-2-pyrrolones related to compounds **3** (see Ref. 2) are stable to oxidation. Unlike pyrrolediones reported previously,[3] compound **4** does not react with alcohols, and therefore, it can be recrystallized from ethanol. To confirm the structure of compound **4**, we studied it by X-ray structural analysis. The overall view of molecule **4** is shown in Fig. 1.* The bond lengths and bond angles are given in Tables 1 and 2. The six-membered heterocycle adopts a distorted boat conformation. The N, C(4), C(5), and C(12) atoms are in a single plane (within 0.006 Å). The C(6) and C(7) atoms deviate from this plane in one direction by 0.88 and 0.47 Å, respectively. Both MeO groups are coplanar with the plane of the benzene ring and are arranged symmetrically with respect to each other. The orientation of the benzoyl fragment with respect to the dihydropyrrole ring is characterized by the C(2)—C(3)—C(15)—O(3) and C(3)—C(15)—C(16)—C(17) torsion angles of 37.1° and 27.5°, respectively. The angle between the planes of the benzene ring of the benzoyl fragment and the dihydropyrrole ring is 58.2°. The dihydropyrrole ring is noncoplanar with the dimethoxyphenyl substituent. The angle between the

* The atomic numbering scheme, which is used in the discussion of the molecular structure of compound **4**, is given in Fig. 1.

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 10, pp. 1845—1848, October, 1997.

1066-5285/97/4610-1751 $18.00

Scheme 1



planes of these fragments is 22.3°. The C(3)—C(4)—C(12)—C(11) torsion angle is 20.1°. The noncoplanarity of the pyrrole ring and its substituents at positions 4 and 5 decreases the probability of formation of the common π-conjugated system. However, the double C(3)=C(4) bond is noticeably elongated [1.387(3) Å]. The C(4)—C(12) bond [1.444(3) Å] is substantially shortened compared to the standard bond length between sp^2 hybridized C atoms (1.46 Å).[4,5] However, the C(2)—C(3) and C(3)—C(15) bonds [1.457(3) and 1.458(3) Å, respectively] are not shortened. The N—C(1) and N—C(4) bonds [1.370(3) Å and 1.394(2) Å, respectively] are substantially longer than the bond between the planar N atom and the sp^2 hybridized C atom (1.34 Å).[5] The lengths of these bonds are in the range of the values observed in the nitrogen-containing heterocycles. Therefore, the elongation of the C(3)=C(4) bond due to its participation in the π-conjugation, if this is the case, has no significant effect on the lengths of the adjacent bonds. However, the deeper (red) color of the crystals of compound **4** compared to the yellow color of compound **3** is indicative of the presence of a more extended conjugation system in the former compound. The analogous elongation of the double C=C bond was also observed in other pyrrole derivatives. For example, these bonds are 1.357(8) Å and 1.403(5) Å in the molecules of Z-2-ethoxycarbonylmethylene-4,5-diphenyl-2,3-dihydropyrrol-3-one[6] and 1-benzyl-2-hydroxy-5-methyl-3-oxo-2-phenacyl-2,3-dihydropyrrole-4-carboxylic acid,[7] respectively. The substantially elongated bond between the C atoms of the carbonyl groups of the pyrrole ring [1.543(3) Å] suggests that not the entire pyrrole ring,

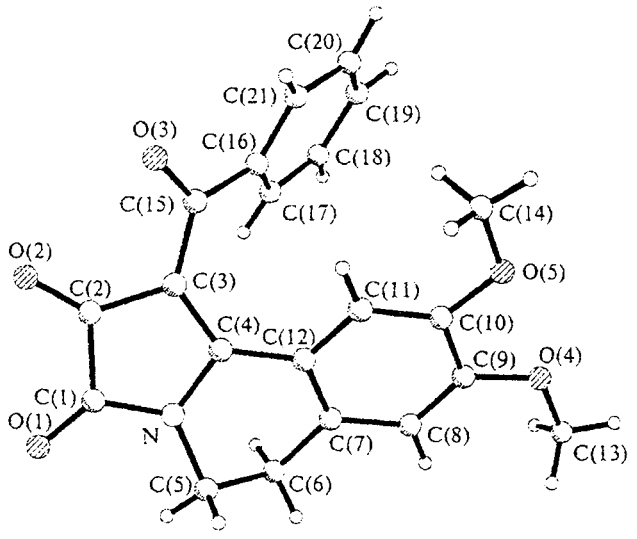


Fig. 1. Overall view of molecule **4**.

Table 1. Bond lengths (*d*) in molecule **4**

Bond	*d*/Å	Bond	*d*/Å
O(1)—C(1)	1.210(3)	C(5)—C(6)	1.513(4)
O(2)—C(2)	1.210(3)	C(6)—C(7)	1.514(3)
O(3)—C(15)	1.225(2)	C(7)—C(8)	1.393(3)
O(4)—C(9)	1.356(2)	C(7)—C(12)	1.402(3)
O(4)—C(13)	1.431(3)	C(8)—C(9)	1.380(3)
O(5)—C(10)	1.358(2)	C(9)—C(10)	1.415(3)
O(5)—C(14)	1.415(3)	C(10)—C(11)	1.371(3)
N—C(1)	1.370(3)	C(11)—C(12)	1.398(3)
N—C(4)	1.394(2)	C(15)—C(16)	1.490(3)
N—C(5)	1.463(3)	C(16)—C(17)	1.385(3)
C(1)—C(2)	1.543(3)	C(16)—C(21)	1.394(3)
C(2)—C(3)	1.457(3)	C(17)—C(18)	1.390(3)
C(3)—C(4)	1.387(3)	C(18)—C(19)	1.386(5)
C(3)—C(15)	1.458(3)	C(19)—C(20)	1.374(5)
C(4)—C(12)	1.444(3)	C(20)—C(21)	1.384(4)

Table 2. Bond angles (ω) in molecule **4**

Angle	ω/deg	Angle	ω/deg	Angle	ω/deg
C(1)—N—C(4)	110.6(2)	N—C(5)—C(6)	108.5(2)	C(11)—C(12)—C(7)	119.7(2)
C(1)—N—C(5)	126.1(2)	C(5)—C(6)—C(7)	109.9(2)	C(11)—C(12)—C(4)	121.2(2)
C(4)—N—C(5)	122.6(2)	C(8)—C(7)—C(12)	118.7(2)	C(7)—C(12)—C(4)	119.1(2)
O(1)—C(1)—N	127.0(2)	C(8)—C(7)—C(6)	121.9(2)	O(3)—C(15)—C(3)	119.4(2)
O(1)—C(1)—C(2)	127.5(2)	C(12)—C(7)—C(6)	119.3(2)	O(3)—C(15)—C(16)	119.5(2)
C(2)—C(1)—N	105.6(2)	C(9)—C(8)—C(7)	121.1(2)	C(3)—C(15)—C(16)	120.9(2)
O(2)—C(2)—C(3)	132.1(2)	C(8)—C(9)—C(10)	120.0(2)	C(17)—C(16)—C(21)	119.8(2)
O(2)—C(2)—C(1)	122.5(2)	C(8)—C(9)—O(4)	125.3(2)	C(17)—C(16)—C(15)	122.1(2)
C(3)—C(2)—C(1)	105.4(2)	C(9)—O(4)—C(13)	116.9(2)	C(21)—C(16)—C(15)	118.1(2)
C(4)—C(3)—C(2)	106.8(2)	C(10)—C(9)—O(4)	114.6(2)	C(16)—C(17)—C(18)	120.0(2)
C(4)—C(3)—C(15)	132.4(2)	C(10)—O(5)—C(14)	116.3(2)	C(19)—C(18)—C(17)	119.3(3)
C(2)—C(3)—C(15)	120.7(2)	O(5)—C(10)—C(11)	125.5(2)	C(20)—C(19)—C(18)	121.2(3)
C(3)—C(4)—N	111.5(2)	O(5)—C(10)—C(9)	115.7(2)	C(19)—C(20)—C(21)	119.5(3)
C(3)—C(4)—C(12)	131.6(2)	C(11)—C(10)—C(9)	118.8(2)	C(20)—C(21)—C(16)	120.2(3)
N—C(4)—C(12)	116.9(2)	C(10)—C(11)—C(12)	121.4(2)		

Table 3. Coordinates of nonhydrogen atoms ($\times 10^4$) and hydrogen atoms ($\times 10^3$) and isotropic thermal parameters ($\times 10^3$) of molecule **4**

Atom	*x*	*y*	*z*	U/Å^2	Atom	*x*	*y*	*z*	U/Å^2
N	2528(1)	5398(2)	4121(1)	60(1)	C(17)	4224(1)	4870(3)	5702(1)	58(1)
O(1)	1810(1)	6590(3)	4429(1)	86(1)	C(18)	4781(1)	5020(4)	5838(2)	75(1)
O(2)	2416(1)	5195(2)	5954(1)	75(1)	C(19)	5127(1)	3739(5)	6247(2)	86(1)
O(3)	3300(1)	2599(3)	6420(1)	88(1)	C(20)	4929(1)	2332(5)	6524(2)	85(1)
O(4)	4249(1)	1801(2)	2819(1)	66(1)	C(21)	4377(1)	2219(4)	6417(1)	70(1)
O(5)	4240(1)	166(2)	4034(1)	70(1)	H(5a)	214(1)	481(4)	301(2)	82(8)
C(1)	2231(1)	5782(3)	4596(1)	64(1)	H(5b)	215(1)	677(4)	320(2)	89(9)
C(2)	2550(1)	4992(3)	5386(1)	59(1)	H(6a)	280(1)	623(3)	254(2)	70(7)
C(3)	3015(1)	4123(3)	5270(1)	51(1)	H(6b)	309(1)	715(3)	335(2)	76(7)
C(4)	2970(1)	4352(2)	4501(1)	49(1)	H(8)	358(1)	451(3)	247(1)	62(6)
C(5)	2371(1)	5770(4)	3295(1)	68(1)	H(11)	361(1)	161(3)	472(1)	50(5)
C(6)	2883(1)	6028(3)	3084(1)	66(1)	H(13a)	392(1)	270(3)	175(2)	66(7)
C(7)	3260(1)	4504(3)	3355(1)	51(1)	H(13b)	437(1)	385(4)	224(2)	85(9)
C(8)	3585(1)	3895(3)	2938(1)	54(1)	H(13c)	453(1)	204(4)	198(2)	94(9)
C(9)	3918(1)	2481(3)	3185(1)	51(1)	H(14a)	447(1)	−168(4)	475(2)	97(9)
C(10)	3920(1)	1592(2)	3860(1)	50(1)	H(14b)	388(2)	−108(5)	466(2)	124(14)
C(11)	3607(1)	2207(2)	4277(1)	48(1)	H(14c)	436(2)	11(6)	515(2)	137(14)
C(12)	3285(1)	3677(2)	4046(1)	47(1)	H(17)	399(1)	575(3)	545(2)	73(8)
C(13)	4269(1)	2672(4)	2141(2)	70(1)	H(18)	492(1)	617(5)	562(2)	114(11)
C(14)	4236(2)	−760(5)	4697(2)	99(1)	H(19)	551(1)	377(4)	634(2)	93(9)
C(15)	3433(1)	3325(3)	5916(1)	55(1)	H(20)	517(1)	145(4)	683(2)	99(10)
C(16)	4022(1)	3482(3)	5998(1)	52(1)	H(21)	420(1)	120(4)	660(2)	82(8)

but rather only the C(3)=C(4) bond, is involved in the possible π-conjugated system.

Experimental

The IR spectra were recorded on a UR-20 spectrophotometer as Nujol mulls. The ^{1}H NMR spectra were measured on a Tesla BS 467 instrument (80 MHz) in chloroform-d with HMDS as the internal standard. The mass spectrum of compound **3** was recorded on a Varian MAT 311 spectrometer with direct introduction of the sample into the ion source (the energy of ionizing electrons was 70 eV). The course of the reaction and the purities of the resulting compounds were monitored by TLC on Silufol plates using a 3 : 2 benzene—ether mixture as the solvent.

The reaction of 5-phenyl-2,3-dihydrofuran-2,3-dione (1) with 6,7-dimethoxy-3,4-dihydroisoquinoline (2). A mixture of compound **1** (0.87 g, 5 mmol) and compound **2** (0.96 g, 5 mmol) was kept in anhydrous dioxane (25 mL) at 20—22 °C for 12 h. The solvent was evaporated. The residue was triturated with hot acetonitrile. After cooling of the solution, crystals of compound **3** that precipitated were filtered off. The yield of **3** was 0.98 g (54%), m.p. 183—185 °C (MeCN). IR, ν/cm^{-1}: 3150 (OH); 1683 (C=O); 1622 (C=C). ^{1}H NMR, δ: 3.44 (s, 3 H, MeOH); 3.71 (s, 3 H, MeOH); 2.81 (q, 2 H, CH_2); 4.09 (q, 2 H, CH_2); 5.74 (s, 1 H, CH); 7.21 (m, 7 H, H arom.); 9.00 (br.s, 1 H, OH). MS, *m/z* (I_{rel} (%)): 365 $[M]^+$ (14), 260 $[M-PhCO]^+$ (15), 106

$[PhCHO]^+$ (100). Found: N, 3.97%. $C_{21}H_{19}NO_5$. Calculated: N, 3.84%.

The mother liquor was concentrated. The residue was treated with hot ethanol and cooled. 1-Benzoyl-8,9-dimethoxy-2,3,5,6-tetrahydropyrrolo[2,1-*a*]isoquinoline-2,3-dione (**4**) that precipitated was filtered off and recrystallized from ethanol. The yield was 0.43 g (24%), m.p. 211—213 °C (decomp.). IR, ν/cm^{-1}: 1730 (C=O); 1700 (C=O). ^1H NMR, δ: 3.55 (s, 3 H, MeOH); 3.00 (t, 2 H, CH_2); 3.80 (t, 2 H, CH_2); 7.25 (m, 7 H, H arom.). Found: N, 4.01%. $C_{21}H_{17}NO_5$. Calculated: N, 3.85%.

Elongated quadrangular-prismatic dark-red crystals of compound **4** belong to the monoclinic system. The principal crystallographic data are as follows: a = 25.949(5) Å, b = 7.774(2) Å, c = 18.325(4) Å, β = 109.0(1)°, V = 3495.3 Å^3, M = 363.36, d_{calc} = 1.381 g cm^{-3}, Z = 8, space group $C2/c$.

The unit cell parameters and the experimental intensity data were measured on an automated four-circle KM-4 diffractometer (Kuma diffraction, Poland) with the χ-geometry using the θ/θ scanning technique in the angle range of 4° < θ < 80° (Cu-Kα radiation, graphite monochromator). A total of 3783 independent reflections were collected. The structure was solved by the direct method using the AREN program.[8] All other calculations were carried out on a PC/AT computer using the SHELXL program package.[9] The positions of the hydrogen atoms were located from the difference electron density syntheses. The structure was refined anisotropically (isotropically for H atoms) by the full-matrix least-squares method. The final value of the R factor was 0.042 using 2363 reflections with $I > 2\sigma(I)$, and R = 0.072 using a total set of reflections. The atomic coordinates are given in Table 3. The anisotropic thermal parameters can be obtained from the authors.

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Received November 13, 1996;
in revised form April 4, 1997