

Five-Membered 2,3-Dioxo Heterocycles: LXVI.* Reactions of (2Z,5Z)-1-Aryl-3-hydroxy-5-[3,3-dimethyl-3,4-dihydroisoquinolin-1(2H)-ylidene]pent-2-ene-1,4-diones with *o*-Phenylenediamine and Hydrazine. Crystalline and Molecular Structure of 2-{(Z)-8,8-Dimethyl-2,3,8,9-tetrahydro[1,4]dioxino[2,3-g]isoquinolin-6(7H)-ylidene}-1-(3-phenyl-1H-pyrazol-5-yl)ethanone

V. V. Khalturina^a, Yu. V. Shklyayev^a, Z. G. Aliev^b, and A. N. Maslivets^c

^a Institute of Technical Chemistry, Ural Division, Russian Academy of Sciences, Perm, Russia

^b Institute of Chemical Physics Problems, Russian Academy of Sciences, Chernogolovka, Moscow oblast, Russia

^c Perm State University, ul. Bukireva 15, Perm, 614990 Russia
e-mail: koh2@psu.ru

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Abstract—(2Z,5Z)-1-Aryl-3-hydroxy-5-[3,3-dimethyl-3,4-dihydroisoquinolin-1(2H)-ylidene]pent-2-ene-1,4-diones reacted with *o*-phenylenediamine and hydrazine to give 3-[(Z)-2-aryl-2-oxoethylidene]-1,2,3,4-tetrahydroquinoxalin-2-ones and 1-(3-aryl-1H-pyrazol-5-yl)-2-[(Z)-3,3-dimethyl-3,4-dihydroisoquinolin-1(2H)-ylidene]ethanones, respectively. The crystalline and molecular structure of 2-{(Z)-8,8-dimethyl-2,3,8,9-tetrahydro[1,4]dioxino[2,3-g]isoquinolin-6(7H)-ylidene}-1-(3-phenyl-1H-pyrazol-5-yl)ethanone was determined by X-ray analysis.

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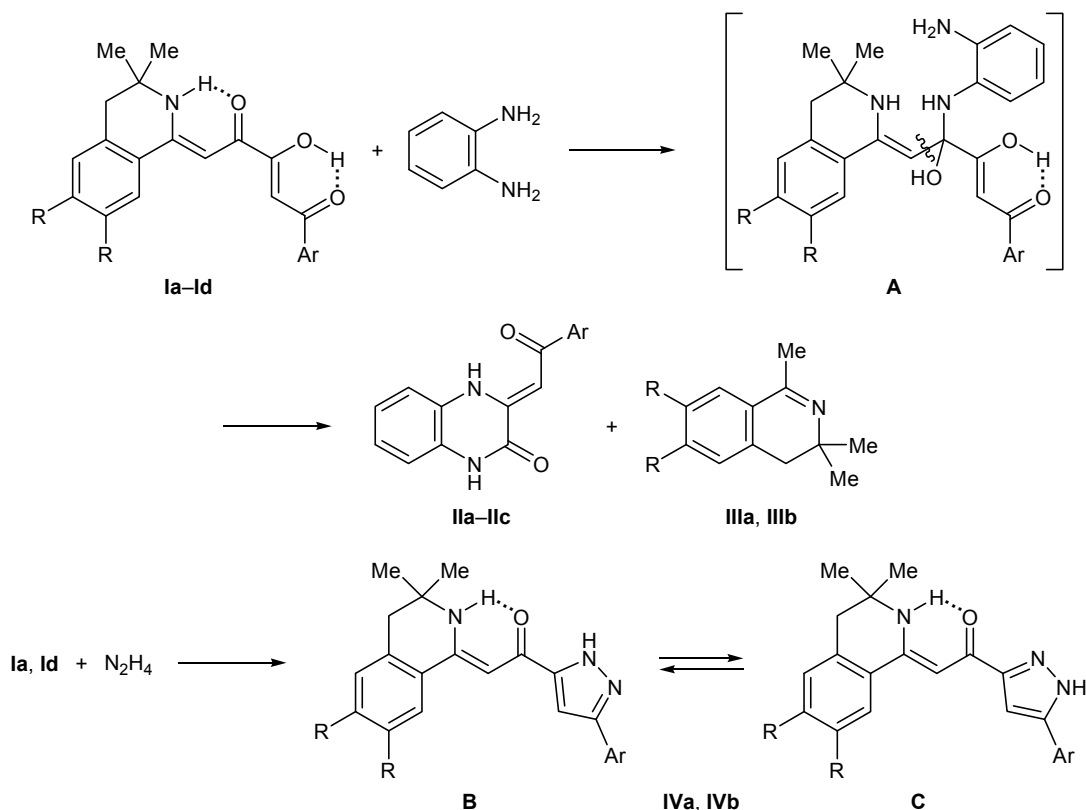
We previously reported on the reaction of 5-arylfuran-2,3-diones with 3,3-dialkyl-1-methyl-3,4-dihydroisoquinolines, which occurred as β -CH-acylation of enamino tautomer of isoquinolines with carbonyl group in position 2 of 5-arylfuran-2,3-diones and was accompanied by opening of the furan ring. The products were the corresponding (2Z,5Z)-1-aryl-3-hydroxy-5-[3,3-dialkyl-3,4-dihydroisoquinolin-1(2H)-ylidene]pent-2-ene-1,4-diones **I** whose structure was proved by X-ray analysis [2]. These compounds were formerly assigned the structure of NH-acylation products of tautomeric *N*-aroylpyruvoyl-3,3-dimethyl-1,2,3,4-tetrahydro-2-methylideneisoquinolines [3], taking into account mainly easy elimination of isoquinoline by the action of *o*-phenylenediamine, which is typical of *N*-aroylpyruvoylamines [4]. With a view to rationalize the observed pattern we examined reactions of com-

pounds **I** with difunctional nitrogen-centered nucleophiles, *o*-phenylenediamine and hydrazine.

The reactions of compounds **Ia–Ic** with *o*-phenylenediamine were carried out by heating equimolar amounts of the reactants in boiling ethanol or acetic acid over a period of 1–1.5 h (the progress of the reactions was monitored by chromatography). As a result, we isolated the corresponding 3-[(Z)-2-oxo-2-phenylethylidene]-1,2,3,4-tetrahydroquinoxalin-2-ones **IIa–IIc** (Scheme 1) which were identified by comparing with samples obtained independently from aroylpyruvic acid esters and *o*-phenylenediamine [5]. Presumably, in the first step amino group in *o*-phenylenediamine attacks side-chain carbonyl carbon atom (C⁴) in compounds **I** to form cyclic hemiaminal **A**; next follows rupture of the C⁴–C⁵ bond with hydrolytic elimination of isoquinoline molecule. This scheme is analogous to the reaction of 1,6-diarylhexane-1,3,4,6-tetraones with difunctional nucleophiles (*o*-aminoben-

* For communication LXV, see [1].

Scheme 1.



I, RR = OCH₂CH₂O, Ar = Ph (**a**); R = H, Ar = 4-MeC₆H₄ (**b**), 4-ClC₆H₄ (**c**), 4-BrC₆H₄ (**d**); **II**, Ar = Ph (**a**), 4-MeC₆H₄ (**b**), 4-ClC₆H₄ (**c**); **III**, RR = OCH₂CH₂O (**a**); R = H (**b**); **IV**, RR = OCH₂CH₂O, Ar = Ph (**a**); R = H, Ar = 4-BrC₆H₄ (**b**).

zenethiol [6] and pyridine-2,3-diamine [7]), which also involves cleavage of the C²–C³ bond and hydrolytic elimination of aryl methyl ketones.

Compounds **Ia** and **Id** reacted with an equimolar amount of hydrazine in boiling ethanol (reaction time 30 min) to produce the corresponding 1-(3-aryl-1*H*-pyrazol-5-yl)-2-[(1*Z*)-3,3-dimethyl-3,4-dihydroiso-

quinolin-1(2*H*)-ylidene]ethanones **IVa** and **IVb** (Scheme 1) via successive attack by amino groups in hydrazine molecule on carbon atoms in the enolized β-diketone fragment of **Ia** and **Id**. The structure of compound **IVa** was proved by X-ray analysis.

Compounds **IVa** and **IVb** are colorless crystalline substances with high melting points (they melt with decomposition), which are readily soluble in DMSO and DMF, poorly soluble in other organic solvents, and insoluble in water and saturated hydrocarbons. Their IR spectra contained absorption bands due to stretching vibrations of the NH groups and carbonyl group involved in intramolecular hydrogen bond at 3100–3120 and 1605–1608 cm⁻¹, respectively (broad bands). Compounds **IVa** and **IVb** displayed in the ¹H NMR spectra signals from protons in the aromatic rings and substituents therein, a six-proton singlet from two methyl groups in position 3 of the isoquinoline fragment (δ 1.28 and 1.34 ppm for **IVa** and **IVb**, respectively), a two-proton singlet from the endocyclic methylene group (δ 2.81 and 2.99 ppm for **IVa** and **IVb**), singlets from the side-chain 2-H proton (δ 6.28–

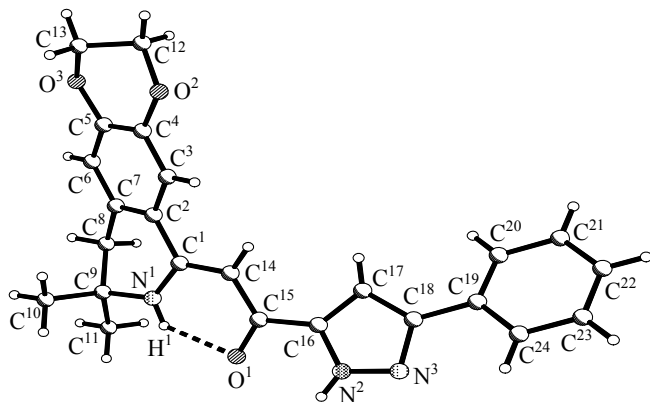


Fig. 1. Structure of the molecule of 2-[(6*Z*)-8,8-dimethyl-2,3,8,9-tetrahydro[1,4]dioxino[2,3-*g*]isoquinolin-6(7*H*)-ylidene]-1-(3-phenyl-1*H*-pyrazol-5-yl)ethanone (**IVa**).

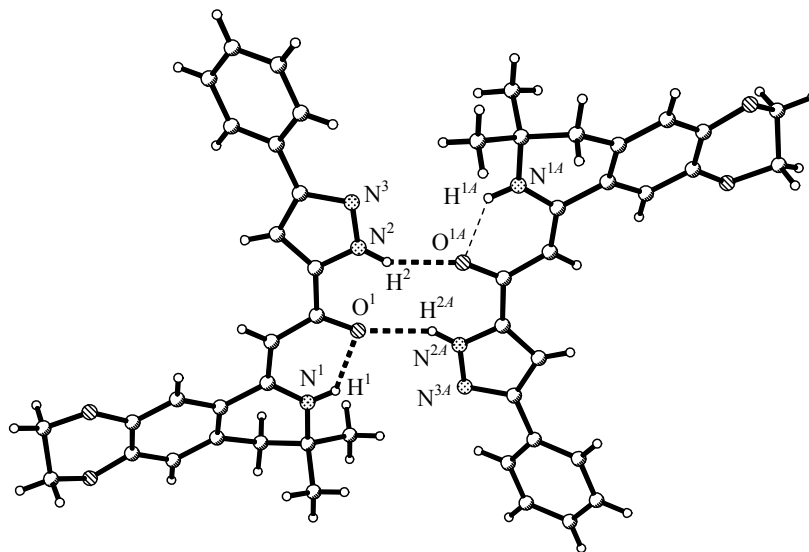


Fig. 2. Centrosymmetric dimer formed by molecules **IVa** in crystal.

6.45 ppm) and 4-H in the pyrazole ring (δ 6.83–6.89 ppm), and NH protons in the isoquinoline (δ 11.50–11.57 ppm) and pyrazole rings (δ 13.39–13.61 ppm).

The structure of molecule **IVa** is shown in Fig. 1. The N^1-H^1 and $C^{15}=O^1$ groups are involved in fairly strong intramolecular hydrogen bond with the following parameters: ($N^1 \cdots O^1$ 2.64, $H^1 \cdots O^1$ 2.01 Å, $\angle N^1 H^1 O^1$ 131.9°). The phenyl ring in position 3 of the pyrazole ring deviates from the pyrazole ring plane as a result of steric repulsion between hydrogen atoms on C^{17} , C^{14} , and C^{20} . The torsion angles $O^1 C^{15} C^{16} N^2$ and $N^3 C^{18} C^{19} C^{24}$ are 17.8 and 20.9°, respectively. All bond lengths in molecule **IVa** are consistent with the corresponding standard values within the experimental error (0.005–0.007 Å). Difference syntheses of electron density localized hydrogen atom on the N^2 atom, indicating that molecules of **IVa** in crystal have tautomeric structure **B**. However, bond length distribution over the pyrazole ring is not unambiguous. The N^2-C^{16} bond (1.340 Å) is shorter than N^3-C^{18} (1.360 Å). Nevertheless, analysis of crystal packing shows that compound **IVa** exists as tautomer **B**. The only shortened intermolecular contact was revealed between the O^1 and N^2 atoms (2.77 Å). It may be interpreted as fairly strong hydrogen bond $N^2-H^2 \cdots O^1$, giving rise to centrosymmetric dimers (Fig. 2).

EXPERIMENTAL

The IR spectra were recorded from samples dispersed in mineral oil on an FSM-1201 spectrophotometer. The 1H NMR spectra were measured from solu-

tions in $DMSO-d_6$ on a Bruker AM-400 spectrometer operating at 400 MHz; the chemical shifts were determined relative to tetramethylsilane as internal reference. The purity of the products was checked by thin-layer chromatography on Silufol plates using ethyl acetate–benzene (1:5) or ethyl acetate as eluent; spots were visualized by treatment with iodine vapor.

3-[(Z)-2-Oxo-2-phenylethylidene]-1,2,3,4-tetrahydroquinoxalin-2-one (IIa). A solution of 0.6 mmol of compound **Ia** and 0.6 mmol of *o*-phenylenediamine in 20 ml of ethanol was heated for 1 h under reflux. The mixture was cooled, and the precipitate was filtered off. Yield 90%, mp 267–268°C (decomp.; from ethyl acetate); published data [5]: mp 266–267°C. IR spectrum, cm^{-1} : 3058 br (NH), 1691 (C=O, amide), 1617 br (COPh). 1H NMR spectrum, δ , ppm: 6.83 s (1H, CH), 7.14–8.00 m (9H, H_{arom}), 12.04 s and 13.67 s (1H each, NH).

Compounds **IIb** and **IIc** were synthesized in a similar way.

3-[(Z)-2-(4-Methylphenyl)-2-oxoethylidene]-1,2,3,4-tetrahydroquinoxalin-2-one (IIb). Yield 88%, mp 229–230°C (decomp.; from ethyl acetate); published data [5]: mp 229–230°C.

3-[(Z)-2-(4-Chlorophenyl)-2-oxoethylidene]-1,2,3,4-tetrahydroquinoxalin-2-one (IIc). Yield 87%, mp 270–271°C (decomp.; from ethyl acetate); published data [5]: mp 270–271°C.

2-[(6Z)-8,8-Dimethyl-2,3,8,9-tetrahydro[1,4]dioxino[2,3-g]isoquinolin-6(7H)-ylidene]-1-(3-phenyl-1H-pyrazol-5-yl)ethanone (IVa). A solution of

0.1 mmol of compound **Ia** and 0.1 mmol of hydrazine hydrate in 10 ml of ethanol was heated for 30 min under reflux. The mixture was cooled, and the precipitate was filtered off. Yield 86%, mp >244°C (decomp.; from ethanol). IR spectrum, ν , cm^{-1} : 3100 br (NH), 1605 br (CO). ^1H NMR spectrum, δ , ppm: 1.28 s (6H, CH_3), 2.81 s (2H, 9-H), 4.33 m (4H, CH_2CH_2), 6.28 s (1H, 2-H), 6.83 s (1H, 4'-H), 7.29–7.87 m (7H, H_{arom}), 11.50 s (1H, NH), 13.39 s (1H, NH). Found, %: C 71.78; H 5.83; N 10.34. $\text{C}_{24}\text{H}_{23}\text{N}_3\text{O}_3$. Calculated, %: C 71.80; H 5.77; N 10.47.

X-Ray diffraction data for compound (IVa).

Colorless well-faceted elongated prism-like crystals, monoclinic crystal system; unit cell parameters: $a = 14.559(3)$, $b = 9.941(2)$, $c = 15.064(3)$ Å; $\beta = 110.13(3)^\circ$; $V = 2047.0(7)$ Å³; $M = 401.45$, $d_{\text{calc}} = 1.303$ g/cm³; $Z = 4$; space group $P2(1)/n$. Experimental reflection intensities were measured on a KM-4 automatic four-circle diffractometer with χ -geometry [monochromatized MoK_α irradiation, $\omega/2\theta$ scanning. $2\theta_{\text{max}} = 50.16^\circ$ (98.9%)]. Total of 3598 independent reflections ($R_{\text{int}} = 0.0436$) were measured, 1263 of which were characterized by $I \geq 2\sigma(I)$. No correction for absorption was introduced ($\mu = 0.087$ mm⁻¹). The structure was solved by the direct method using SIR92 program [8], followed by a series of calculations of electron density maps. Hydrogen atoms on N^1 , N^2 , C^{14} , and C^{17} were localized objectively by difference syntheses of electron density, while the positions of the other hydrogen atoms were set on the basis of geometry considerations. The structure was refined by the least-squares procedure in full-matrix anisotropic approximation (for non-hydrogen atoms) using SHELXL-97 software [9]. The final divergence factors were $R_1 = 0.0532$ and $wR_2 = 0.1466$ [for 1263 reflections with $I \geq 2\sigma(I)$]; goodness of fit 0.924.

Compound **IVb** was synthesized in a similar way.

1-[3-(4-Bromophenyl)-1H-pyrazol-5-yl]-2-[(1Z)-3,3-dimethyl-3,4-dihydroisoquinolin-1(2H)-ylidene]ethanone (IVb). Yield 89%, mp 237–239°C (decomp.; from ethanol). IR spectrum, ν , cm^{-1} : 3120 br (NH), 1608 br (CO). ^1H NMR spectrum, δ , ppm: 1.34 s (6H, CH_3), 2.99 s (2H, 4-H), 6.45 s (1H, 2-H), 6.89 s (1H, 4'-H), 7.37–8.12 m (8H, H_{arom}), 11.57 s (1H, NH), 13.61 s (1H, NH). Found, %: C 62.46; H 4.84; N 9.77. $\text{C}_{22}\text{H}_{20}\text{BrN}_3\text{O}$. Calculated, %: C 62.57; H 4.77; N 9.95.

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