

Five-Membered 2,3-Dioxo Heterocycles: LXV.* Reaction of 1-Methyl-3,4-dihydroisoquinolines with Aroylketenes. Crystalline and Molecular Structure of (1Z,3Z)-4-Hydroxy-1-[6,7-dimethoxy-3,3-dimethyl-3,4-dihydroisoquinolin-1(2H)-ylidene]-4-phenylbut-3-en-2-one

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Abstract—Aroylketenes generated *in situ* by thermolysis of 6-aryl-2,2-dimethyl-4H-1,3-dioxin-4-ones reacted with 3,3-dialkyl-1-methyl-3,4-dihydroisoquinolines to give (1Z,3Z)-4-aryl-4-hydroxy-1-[3,3-dialkyl-3,4-dihydroisoquinolin-1(2H)-ylidene]but-3-en-4-ones. The crystalline and molecular structure of (1Z,3Z)-4-hydroxy-1-[6,7-dimethoxy-3,3-dimethyl-3,4-dihydroisoquinolin-1(2H)-ylidene]-4-phenylbut-3-en-2-one was studied by X-ray diffraction.

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5-Arylfuran-2,3-diones are known to undergo thermal decarbonylation to give aroylketenes which are capable of participating in cycloaddition reactions with active dienophiles [2, 3] and acylating weak nucleophiles with formation of aroylacetyl derivatives [2, 4]. On the other hand, furandiones can acylate nucleophilic reagents to produce aroylpyruvoyl derivatives at a temperature lower than that required for generation of aroylketenes [2, 5]. We previously described reactions of 5-arylfuran-2,3-diones with 1-methyl-3,4-dihydroisoquinolines, which led to the formation of β -acylation products of the corresponding enamino tautomers, (2Z,5Z)-1-aryl-3-hydroxy-5-[3,3-dialkyl-3,4-dihydroisoquinolin-1(2H)-ylidene]pent-2-ene-1,4-diones whose structure was proved by X-ray analysis [1]. It is known that 6-aryl-2,2-dimethyl-4H-1,3-dioxin-4-ones [6] ([4+2]-cycloaddition products of aroylketenes with acetone) undergo retro-Diels–Alder reaction with generation of aroylketenes [7].

In continuation of our studies on reactions of dioxo heterocycles and heterocumulenes derived therefrom

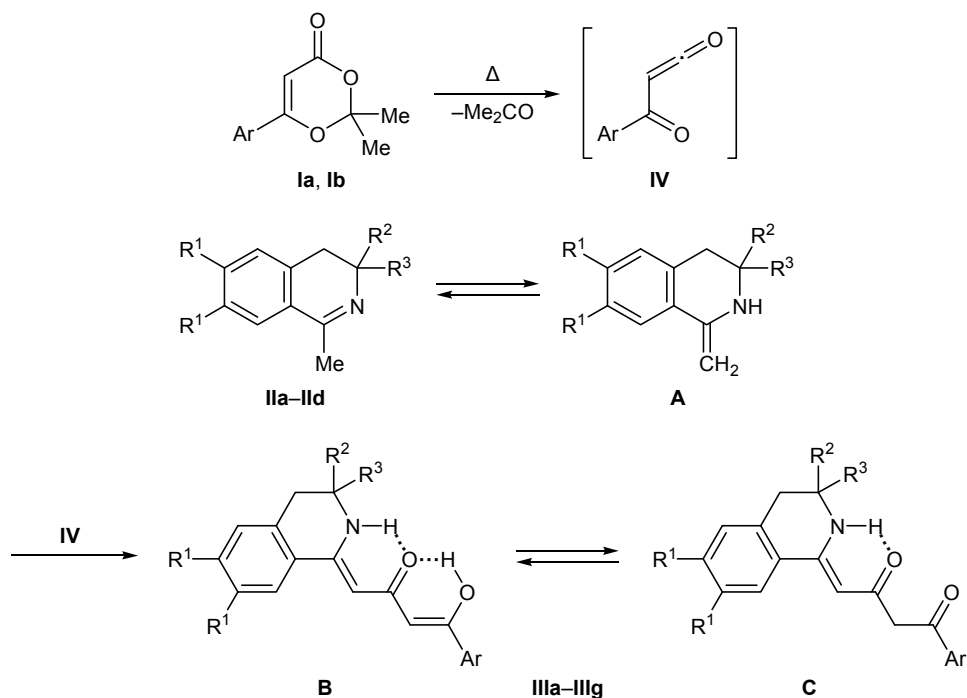
with enamines of the isoquinoline series, in the present communication we report on the reaction of 6-aryl-2,2-dimethyl-4H-1,3-dioxin-4-ones **Ia** and **Ib** with 1-methyl-3,4-dihydroisoquinolines **IIa–IIId**.

The reactions were carried out by heating equimolar amounts of compounds **I** and **II** in boiling anhydrous toluene for 60–90 min, the progress of the reactions being monitored by chromatography. As a result, we isolated in good yields the corresponding (1Z,3Z)-4-aryl-4-hydroxy-1-[3,3-dialkyl-3,4-dihydroisoquinolin-1(2H)-ylidene]but-3-en-2-ones **IIIa–IIIg**. Presumably, the reaction involves acylation of the β -CH group in enamino tautomer **A** of isoquinolines **IIa–IIId** with aroylketene **IV** generated by thermal decomposition of 6-aryl-2,2-dimethyl-4H-1,3-dioxin-4-ones (via elimination of acetone molecule). The structure of compound **IIIe** was proved by X-ray analysis.

Compounds **IIIa–IIIg** are yellow crystalline or oily substances, which are readily soluble in dimethyl sulfoxide and dimethylformamide, poorly soluble in common organic solvents, and insoluble in water and alkanes; the products gave a positive color test (cherry

* For communication LXIV, see [1].

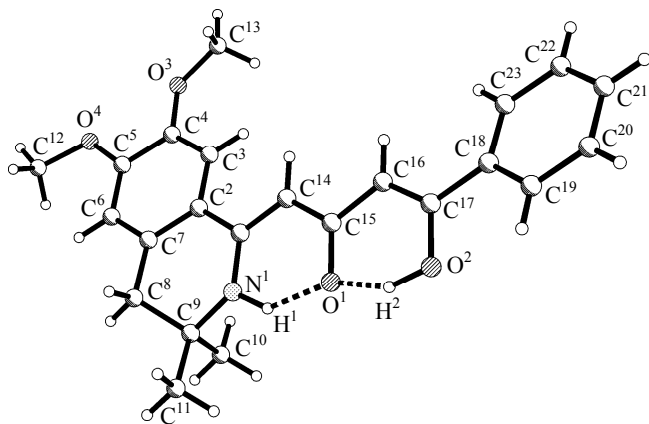
Scheme 1.



I, Ar = Ph (**a**), 4-MeC₆H₄ (**b**); **II**, R¹ = H, R² = R³ = Me (**a**); R² = Me, R³ = Bu (**b**); R¹ = MeO, R² = R³ = Me (**c**); R¹ = EtO, R² = R³ = Me (**d**); **III**, R¹ = H, R² = R³ = Me, Ar = Ph (**a**), 4-MeC₆H₄ (**b**); R² = Me, R³ = Bu, Ar = Ph (**c**), 4-MeC₆H₄ (**d**); R¹ = MeO, R² = R³ = Me, Ar = Ph (**e**), 4-MeC₆H₄ (**f**); R¹ = EtO, R² = R³ = Me, Ar = Ph (**g**).

color) for enolic hydroxy group with an alcoholic solution of iron(III) chloride.

The IR spectra of **IIIa-IIIg** contained broadened absorption bands due to stretching vibrations of OH and NH groups involved in intramolecular hydrogen bond (3384–3417 cm⁻¹) and H-bonded carbonyl group (1582–1591 cm⁻¹). Compounds **IIIa-IIIg** displayed in the ¹H NMR spectra signals from protons in aromatic



Structure of the molecule of (1*Z*,3*Z*)-1-[6,7-dimethoxy-3,3-dimethyl-3,4-dihydroisoquinolin-1(2*H*)-ylidene]-4-hydroxy-4-phenylbut-3-en-2-one (**IIIe**) according to the X-ray diffraction data.

rings and substituents therein, a six-proton singlet at δ 1.27–1.28 ppm from two methyl groups in position 3 of the isoquinoline ring (**IIIa**, **IIIb**, **IIIe-IIIg**) or a three-proton singlet at δ 1.27 ppm and signals at δ 0.96–1.22 ppm from nine protons in the 3-methyl and 3-butyl groups (**IIIc**, **IIIId**), a two-proton singlet at δ 2.82–2.91 ppm from the methylene protons on C⁴ in the isoquinoline ring, and singlets at δ 5.67–5.77 (1-H), 6.18–6.28 (3-H), 10.42–10.57 (NH), and 16.04–16.07 ppm (OH, enol tautomer **B**). In addition, minor signals assignable to diketone tautomer **C** were present, the most characteristic of which were those located at δ 4.00–4.10 (2H, 3-H) and 10.95–11.08 ppm (1H, NH). In keeping with the signal intensity ratios, compounds **IIIa-IIIg** in DMSO-*d*₆ exist as mixtures of enol and ketone tautomers **B** and **C** at a ratio of ~9:1.

Figure shows the structure of molecule **IIIe** determined by X-ray analysis. Compound **IIIe** crystallizes as a 2:1 solvate with toluene, which includes two independent molecules. All bond lengths and bond angles in the two crystallographically independent molecules are equal within experimental error, and they coincide with the corresponding parameters of structurally related (2*Z*,5*Z*)-3-hydroxy-5-{8,8-dimethyl-2,3,8,9-tetrahydro[1,4]dioxino[2,3-*g*]isoquinolin-

6(*7H*)-ylidene}-1-phenylpent-2-ene-1,4-dione [1]. Molecules **IIIe** in crystal are stabilized by two strong intramolecular hydrogen bonds $O^2-H^2 \cdots O^1$ and $N-H \cdots O^1$. Their parameters are given below.

D-H...A	d(D-H)	d(H...A)	\angle DHA	d(D...A)
$O^2-H^2 \cdots O^1$	1.089	1.458	153.99	2.483
	1.208	1.368	148.40	2.478
$N-H \cdots O^1$	1.043	1.720	140.86	2.613
	0.992	1.786	140.93	2.632

It is seen that both intramolecular hydrogen bonds are characterized by similar parameters. The $C^{15}=O^1$ bond length is 1.292 Å in both molecules, i.e., it is appreciably extended. Thus compound **IIIe** in crystal has the structure of enol tautomer **B**.

EXPERIMENTAL

The IR spectra were recorded on an FSM-1201 spectrometer from samples dispersed in mineral oil. The 1H and ^{13}C NMR spectra were measured on a Bruker AM-400 instrument (400 MHz for 1H) from solutions in DMSO- d_6 using tetramethylsilane as internal reference. The purity of the isolated compounds was checked by thin-layer chromatography on Silufol plates using ethyl acetate–benzene (1:5) or ethyl acetate as eluent; development with iodine vapor.

(1Z,3Z)-1-[3,3-Dimethyl-3,4-dihydroisoquinolin-1(2H)-ylidene]-4-hydroxy-4-phenylbut-3-en-2-one (IIIa). A solution of 2.0 mmol of 2,2-dimethyl-6-phenyl-4*H*-1,3-dioxin-4-one (**Ia**) and 2.0 mmol of isoquinoline (**IIa**) in 20 ml of anhydrous toluene was heated for 60 min under reflux. The mixture was cooled, and the precipitate was filtered off. Yield 0.60 g (85%), oily substance. IR spectrum, ν , cm^{-1} : 3385 br (NH, OH), 1587 br (CO). 1H NMR spectrum, δ , ppm: **B**: 1.28 s (6H, Me), 2.91 s (2H, 4'-H), 5.77 s (1H, 1-H), 6.28 s (1H, 3-H), 7.31–8.04 m (9H, H_{arom}), 10.53 s (1H, NH), 16.07 s (1H, OH); **C**: 1.20 s (6H, Me), 2.86 s (2H, 4'-H), 4.10 s (2H, 3-H), 5.87 s (1H, 1-H), 7.28–7.98 m (9H, H_{arom}), 11.02 s (1H, NH). Found, %: C 78.82; H 6.75; N 4.20. $C_{21}H_{21}NO_2$. Calculated, %: C 78.97; H 6.63; N 4.39.

Compounds **IIIb–IIIg** were synthesized in a similar way.

(1Z,3Z)-1-[3,3-Dimethyl-3,4-dihydroisoquinolin-1(2H)-ylidene]-4-hydroxy-4-(4-methylphenyl)but-3-en-2-one (IIIb). Yield 86%, oily substance. IR spectrum, ν , cm^{-1} : 3386 br (NH, OH), 1585 br (CO). 1H NMR spectrum, δ , ppm: **B**: 1.27 s (6H, Me), 2.35 s

(3H, MeC_6H_4), 2.91 s (2H, 4'-H), 5.74 s (1H, 1-H), 6.22 s (1H, 3-H), 7.27–7.85 m (8H, C_6H_4), 10.47 s (1H, NH), 16.05 s (1H, OH); **C**: 1.20 s (6H, Me), 2.37 s (3H, MeC_6H_4), 2.86 s (2H, 4'-H), 4.04 s (2H, 3-H), 5.84 s (1H, 1-H), 7.22–7.93 m (8H, C_6H_4), 11.01 s (1H, NH). Found, %: C 79.24; H 7.15; N 4.02. $C_{22}H_{23}NO_2$. Calculated, %: C 79.25; H 6.95; N 4.20.

(1Z,3Z)-1-[3-Butyl-3-methyl-3,4-dihydroisoquinolin-1(2H)-ylidene]-4-hydroxy-4-phenylbut-3-en-2-one (IIIc). Yield 84%, oily substance. IR spectrum, ν , cm^{-1} : 3385 br (NH, OH), 1584 br (CO). 1H NMR spectrum, δ , ppm: **B**: 0.98 t (3H, CH_3CH_2 , $J = 7.0$ Hz), 1.14–1.22 m (6H, $CH_2CH_2CH_2$), 1.27 s (3H, 3- CH_3), 2.84 s (2H, 4'-H), 5.70 s (1H, 1-H), 6.24 s (1H, 3-H), 7.45–8.03 m (9H, H_{arom}), 10.57 s (1H, NH), 16.06 s (1H, OH); **C**: 0.91 t (3H, CH_3CH_2 , $J = 7.0$ Hz), 1.08–1.16 m (6H, $CH_2CH_2CH_2$), 1.24 s (3H, 3- CH_3), 2.78 s (2H, 4'-H), 4.06 s (2H, 3-H), 5.79 s (1H, 1-H), 7.39–7.97 m (9H, H_{arom}), 11.08 s (1H, NH). Found, %: C 79.68; H 7.53; N 3.70. $C_{24}H_{27}NO_2$. Calculated, %: C 79.74; H 7.53; N 3.87.

(1Z,3Z)-1-[3-Butyl-3-methyl-3,4-dihydroisoquinolin-1(2H)-ylidene]-4-hydroxy-4-(4-methylphenyl)but-3-en-2-one (IIIId). Yield 85%, mp 164–166°C (decomp., from petroleum ether). IR spectrum, ν , cm^{-1} : 3384 br (NH, OH), 1582 br (CO). 1H NMR spectrum, δ , ppm: **B**: 0.96 t (3H, CH_3CH_2 , $J = 7.0$ Hz), 1.15–1.21 m (6H, $CH_2CH_2CH_2$), 1.27 s (3H, 3- CH_3), 2.35 s (3H, MeC_6H_4), 2.84 s (2H, 4'-H), 5.67 s (1H, 1-H), 6.18 s (1H, 3-H), 7.26–7.77 m (8H, C_6H_4), 10.51 s (1H, NH), 16.04 s (1H, OH); **C**: 0.90 t (3H, CH_3CH_2 , $J = 7.0$ Hz), 1.09–1.15 m (6H, $CH_2CH_2CH_2$), 1.24 s (3H, 3- CH_3), 2.37 s (3H, MeC_6H_4), 2.79 s (2H, 4'-H), 4.00 s (2H, 3-H), 5.76 s (1H, 1-H), 7.23–7.91 m (8H, C_6H_4), 11.07 s (1H, NH). Found, %: C 79.85; H 7.83; N 3.59. $C_{25}H_{29}NO_2$. Calculated, %: C 79.96; H 7.78; N 3.73.

(1Z,3Z)-1-[6,7-Dimethoxy-3,3-dimethyl-3,4-dihydroisoquinolin-1(2H)-ylidene]-4-hydroxy-4-phenylbut-3-en-2-one (IIIe). Yield 87%, mp 142–143°C (decomp., from ethyl acetate). IR spectrum, ν , cm^{-1} : 3385 br (NH, OH), 1589 br (CO). 1H NMR spectrum, δ , ppm: **B**: 1.28 s (6H, Me), 2.84 s (2H, 4'-H), 3.84 s and 3.86 s (3H each, OMe), 5.74 s (1H, 1-H), 6.23 s (1H, 3-H), 6.91 s and 7.33 s (1H each, 5'-H, 8'-H), 7.46–7.48 m (3H, H_{arom}), 7.79–7.81 m (2H, H_{arom}), 10.47 s (1H, NH), 16.06 s (1H, OH); **C**: 1.20 s (6H, Me), 2.78 s (2H, 4'-H), 3.82 s and 3.83 s (3H each, OMe), 4.07 s (2H, 3-H), 5.82 s (1H, 1-H), 6.89 s and 7.27 s (1H each, 5'-H, 8'-H), 7.61–7.63 m (3H, H_{arom}), 8.01–8.03 m (2H, H_{arom}), 10.97 s (1H, NH). Found, %:

C 72.68; H 6.84; N 3.67. $C_{23}H_{25}NO_4$. Calculated, %: C 72.80; H 6.64; N 3.69.

X-Ray diffraction study of compound IIIe. Compound IIIe crystallized as a 2:1 solvate with toluene. Yellow crystals, $C_{23}H_{25}NO_4 \cdot 0.5 C_6H_5CH_3$, triclinic crystal system, space group $P-1$. Unit cell parameters: $a = 11.444(2)$, $b = 12.919(2)$, $c = 17.669(2)$ Å; $\alpha = 76.56(1)$, $\beta = 87.32(1)$, $\gamma = 70.62(1)^\circ$; $V = 2395.5(6)$ Å³; $M = 425.51$; $d_{calc} = 1.180$ g/cm³; $Z = 4$. A set of experimental reflection intensities was acquired on a KM-4 automatic four-circle diffractometer with χ geometry (monochromatized MoK_α irradiation, $\omega/2\theta$ scanning, $2\theta_{max} = 50^\circ$, 89.6% of possible reflection number). Total of 7578 independent reflections were measured ($R_{int} = 0.0192$), 3695 of which were with $I \geq 2\sigma(I)$. No correction for absorption was introduced ($\mu = 0.079$ mm⁻¹). The structure was solved by the direct method using SIR92 program [8], followed by a series of calculation of electron density maps. The positions of all hydrogen atoms, except for H¹ and H², were set on the basis of geometry considerations. The H¹ and H² atoms were localized objectively from the difference synthesis of electron density. The molecule of toluene was refined with fixed geometry because of large dispersion of bond lengths. The refinement by the least-squares procedure in full-matrix anisotropic approximation (SHELXL-97 [9]) was terminated at $R_1 = 0.0671$, $wR_2 = 0.1804$ [3695 reflections with $I \geq 2\sigma(I)$] and at $R_1 = 0.1455$, $wR_2 = 0.2314$ (all reflections); goodness of fit 1.022.

(1Z,3Z)-1-[6,7-Dimethoxy-3,3-dimethyl-3,4-dihydroisoquinolin-1(2H)-ylidene]-4-hydroxy-4-(4-methylphenyl)but-3-en-2-one (III f). Yield 88%, mp 139–141°C (decomp., from ethyl acetate). IR spectrum, ν , cm⁻¹: 3417 br (NH, OH), 1591 br (CO). ¹H NMR spectrum, δ , ppm: **B**: 1.27 s (6H, Me), 2.35 s (3H, MeC₆H₄), 2.83 s (2H, 4'-H), 3.83 s and 3.85 s (3H each, OMe), 5.72 s (1H, 1-H), 6.18 s (1H, 3-H), 6.91 s (1H, 5'-H or 8'-H), 7.26–7.28 m (2H, C₆H₄), 7.32 s (1H, 8'-H or 5'-H), 7.68–7.70 m (2H, C₆H₄), 10.42 s (1H, NH), 16.06 s (1H, OH); **C**: 1.20 s (6H, Me), 2.37 s (3H, MeC₆H₄), 2.78 s (2H, 4'-H), 3.82 s and 3.83 s (3H each, OMe), 4.02 s (2H, 3-H), 5.81 s (1H, 1-H), 6.89 s (1H, 5'-H or 8'-H), 7.23–7.26 m (2H, C₆H₄), 7.28 s (1H, 8'-H or 5'-H), 7.90–7.92 m (2H, C₆H₄), 10.97 s (1H, NH). Found, %: C 73.25; H 6.94; N 3.53. $C_{24}H_{27}NO_4$. Calculated, %: C 73.26; H 6.92; N 3.56.

(1Z,3Z)-1-[6,7-Diethoxy-3,3-dimethyl-3,4-dihydroisoquinolin-1(2H)-ylidene]-4-hydroxy-4-phenylbut-3-en-2-one (III g). Yield 89%, mp 133–135°C (decomp., from ethanol). IR spectrum, ν , cm⁻¹: 3385 br (NH, OH), 1584 br (CO). ¹H NMR spectrum, δ , ppm: **B**: 1.27 s (6H, Me), 1.34–1.38 m (6H, CH₃CH₂O), 2.82 s (2H, 4'-H), 4.08–4.14 m (4H, CH₂O), 5.71 s (1H, 1-H), 6.23 s (1H, 3-H), 6.89 s and 7.32 s (1H each, 5'-H, 8'-H), 7.46–7.48 m (3H, H_{arom}), 7.79–7.81 m (2H, H_{arom}), 10.45 s (1H, NH), 16.05 s (1H, OH); **C**: 1.19 s (6H, Me), 1.41–1.44 (6H, CH₃CH₂O), 2.76 s (2H, 4'-H), 4.07 s (2H, 3-H), 4.16–4.18 m (4H, CH₂O), 5.79 s (1H, 1-H), 6.87 s and 7.23 s (1H each, 5'-H, 8'-H), 7.61–7.63 m (3H, H_{arom}), 8.01–8.03 m (2H, H_{arom}), 10.95 s (1H, NH). ¹³C NMR spectrum, δ_C , ppm: 14.60 and 14.73 (CH₃CH₂), 27.74 (3-CH₃), 49.57 (C⁴), 63.85 and 64.18 (CH₂O), 88.87 (C³), 98.00 (C³), 110.40 (C¹), 112.88–151.38 (C_{arom}), 156.08 (C¹), 167.78 (C⁴), 189.21 (C²). Found, %: C 73.61; H 7.25; N 3.43. $C_{25}H_{29}NO_4$. Calculated, %: C 73.69; H 7.17; N 3.44.

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