ISSN 1070-4280, Russian Journal of Organic Chemistry, 2011, Vol. 47, No. 7, pp. 1062–1065. © Pleiades Publishing, Ltd., 2011.
Original Russian Text © V.V. Konovalova, Yu.V. Shklyaev, P.A. Slepukhin, A.N. Maslivets, 2011, published in Zhurnal Organicheskoi Khimii, 2011, Vol. 47, No. 7, pp. 1045–1048.

Five-Membered 2,3-Dioxo Heterocycles: LXXVIII.* Acylation of Fischer's Base with Aroylketenes. Crystalline and Molecular Structure of (1*E*, 3*Z*)-4-(4-Chlorophenyl)-4-hydroxy-1-(1,3,3-trimethyl-2,3-dihydro-1*H*-indol-2-ylidene)but-3-en-2-one

V. V. Konovalova[a], Yu. V. Shklyaev[a], P. A. Slepukhin[b], and A. N. Maslivets[c]

[a] *Institute of Technical Chemistry, Ural Division, Russian Academy of Sciences, Perm, Russia*

[b] *Postovskii Institute of Organic Synthesis, Ural Division, Russian Academy of Sciences, ul. S. Kovalevskoi 20, Yekaterinburg, 620219 Russia*

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

Received October 16, 2010

Abstract— Aroylketenes generated by thermolysis of 6-aryl-2,2-dimethyl-4*H*-1,3-dioxin-4-ones reacted with 1,3,3-trimethyl-2-methylidene-1,3-dihydro-2*H*-indole (Fischer's base) to produce (1*E*,3*Z*)-4-aryl-4-hydroxy-1-(1,3,3-trimethyl-1,3-dihydro-2*H*-indol-2-ylidene)but-3-en-2-ones. The crystalline and molecular structures of (1*E*,3*Z*)-4-(4-chlorophenyl)-4-hydroxy-1-(1,3,3-trimethyl-2,3-dihydro-1*H*-indol-2-ylidene)but-3-en-2-one were determined by X-ray analysis.

DOI: 10.1134/S1070428011070153

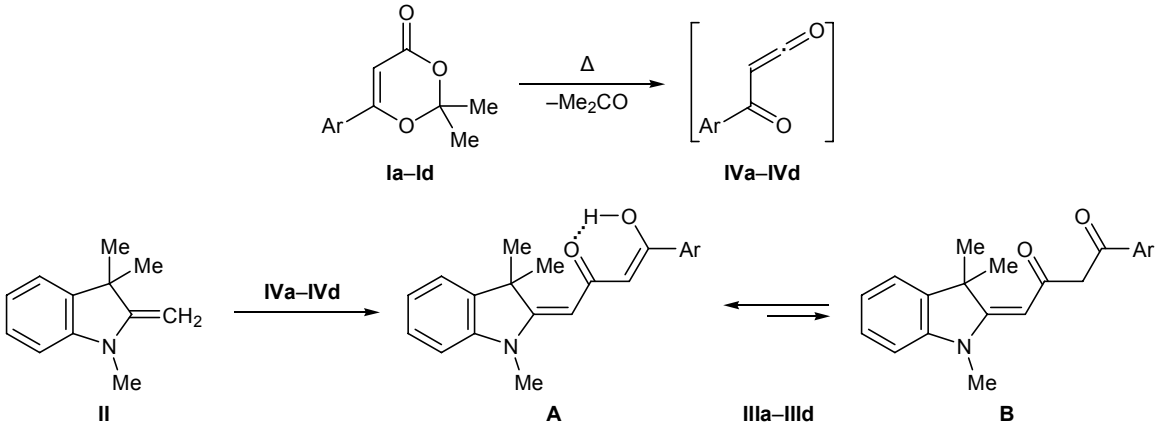
5-Arylfuran-2,3-diones are known to undergo thermal decarbonylation with formation of aroylketenes that are capable of reacting with active dienophiles according to the cycloaddition pattern [2, 3] and acylating weak nucleophiles yielding aroylacetyl derivatives [2, 4]. On the other hand, furandiones themselves can acylate nucleophiles at a temperature below that necessary for generation of aroylketenes, leading to aroylpyruvoyl derivatives [2, 5]. We previously reported on the reaction of 5-arylfuran-2,3-diones with 1-methyl-3,4-dihydroisoquinolines, which gave β-CH-acylation products of their enamino tautomers, (2*Z*,5*Z*)-1-aryl-3-hydroxy-5-[3,3-dialkyl-3,4-dihydroisoquinolin-1(2*H*)-ylidene]pent-2-ene-1,4-diones; the product structure was confirmed by X-ray analysis [6]. It is known that 6-aryl-2,2-dimethyl-4*H*-1,3-dioxin-4-ones [7], [4+2]-cycloaddition products of aroylketenes at the C=O bond of acetone, undergo thermal retro-Diels–Alder reaction thus acting as a source of aroylketenes [8].

In continuation of our studies on reactions of dioxo heterocycles and heterocumulenes based thereon with enamines of the isoquinoline series, in the present work we examined reactions of 6-aryl-2,2-dimethyl-4*H*-1,3-dioxin-4-ones with another heterocyclic enamine, 1,3,3-trimethyl-2-methylidene-2,3-dihydro-1*H*-indole (**II**, Fischer's base).

6-Aryl-2,2-dimethyl-4*H*-1,3-dioxin-4-ones **Ia**–**Id** reacted with compound **II** at a ratio of 1:1 on heating in boiling anhydrous toluene over a period of 10–30 min (TLC) to produce in good yield the corresponding (1*E*,3*Z*)-4-aryl-4-hydroxy-1-(1,3,3-trimethyl-2,3-dihydro-2*H*-indol-2-ylidene)but-3-en-2-ones **IIIa**–**IIId** (Scheme 1). Presumably, thermally induced elimination of acetone molecule from 6-aryl-2,2-dimethyl-4*H*-1,3-dioxin-4-one **Ia**–**Id** generates aroylketene **IVa**–**IVd** which acylates the exocyclic methylene carbon atom in Fischer's base **II**, as was reported previously for the reaction of dioxinones **I** with 1-methyl-3,4-dihydroisoquinolines [9]. The structure of compound **IIIc** was proved by X-ray analysis (see figure).

* For communication LXXVII, see [1].

Scheme 1.

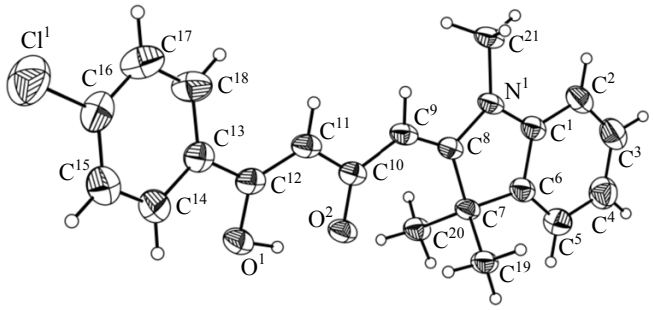


Ar = Ph (**a**), 4-MeC_6H_4 (**b**), 4-ClC_6H_4 (**c**), 4-$EtOC_6H_4$ (**d**).

Compounds **IIIa**–**IIId** were isolated as orange crystalline substances, which were readily soluble in dimethyl sulfoxide and dimethylformamide, poorly soluble in other common organic solvents, and insoluble in water and saturated hydrocarbons; they showed a positive color test (cherry color) for enolic hydroxy group with an alcoholic solution of iron(III) chloride.

Compounds **IIIa**–**IIId** displayed in the IR spectra absorption bands due to stretching vibrations of the enolic hydroxy group involved in intramolecular hydrogen bond (broad band at 3060–3085 cm^{-1}) and H-bonded carbonyl group in the side chain (broad band at 1605–1610 cm^{-1}). The ^1H NMR spectra of **IIIa**–**IIId** contained signals from protons in the aromatic rings and substituents therein, a six-proton singlet from methyl groups in position *3* of the indole ring (δ 1.72–1.76 ppm), a singlet from the *N*-methyl group (δ 3.29–3.32 ppm), a singlet from 1-H (δ 5.40–5.42 ppm), a singlet from 3-H (δ 6.39–6.45 ppm), and a broadened singlet from the enol OH proton (δ 17.39–17.45 ppm); these signals correspond to enol tautomer **A**. In addition, minor signals assignable to diketone tautomer **B** were present, δ, ppm: 1.56–1.57 (6H, 3-CH_3), 3.13–3.32 (3H, 1-CH_3), 4.09–4.16 (C^3H_2), 5.27–5.30 (1-H). These findings indicate that compounds **IIIa**–**IIId** in DMSO-d_6 exist as mixtures of enol (**A**) and diketone (**B**) tautomers at a ratio of ~5 : 1.

According to the X-ray diffraction data, compound **IIIc** crystallizes in space group $P2_1/c$ belonging to monoclinic crystal system. Molecules **III** in crystal exist in the keto enol rather than diketone form, where the carbonyl group in the *p*-chlorobenzoyl fragment is enolized. The hydroxy proton is involved in intramolecular hydrogen bond: O^1–H^1 1.00(2), $H^1\cdots O^2$ 1.51(2), $O^1\cdots O^2$ 2.449(2) Å, $\angle O^1H^1O^2$ 155(1)°. The bond lengths in the side chain (see table) indicate their strong conjugation. Despite obvious lack of conjugation in the indole system, the benzene ring therein turned out to be conjugated with the keto enol fragment through the enamino moiety. This is reflected, e.g., in leveling of the C–N bond lengths in the indole fragment and redistribution of bond lengths in the ylidene fragment. The C^8–C^9 bond is somewhat longer than standard isolated double C=C bond (1.34 Å), whereas the C^9–C^{10} bond is considerably shorter than standard single C–C bond (1.54 Å). Molecules **III** in crystal extend along the 0*a* axis and are packed in layers parallel to the Miller plane (100) so that chlorine atoms in molecules located in neighboring layers appear maximally close to each other. No shortened intermolecular contacts were found in the crystalline structure of compound **III**, except for several contacts with methyl hydrogen atoms, which are likely to be related to general geometric requirements for packing of molecular layers.



Structure of the molecule of (1*E*,3*Z*)-4-(4-chlorophenyl)-4-hydroxy-1-(1,3,3-trimethyl-2,3-dihydro-1*H*-indol-2-ylidene)-but-3-en-2-one (**IIIc**) according to the X-ray diffraction data; non-hydrogen atoms are shown as thermal vibration ellipsoids with a probability of 50%.

Selected bond lengths in the molecule of (1*E*,3*Z*)-4-(4-chlorophenyl)-4-hydroxy-1-(1,3,3-trimethyl-2,3-dihydro-1*H*-indol-2-ylidene)but-3-en-2-one (**IIIc**)

Bond	*d*, Å	Bond	*d*, Å
Cl^1–C^{16}	1.7327(17)	C^7–C^8	1.5303(17)
O^1–C^{12}	1.3280(15)	C^8–C^9	1.3662(18)
O^2–C^{10}	1.2832(14)	C^9–C^{10}	1.4252(17)
N^1–C^8	1.3669(15)	C^{10}–C^{11}	1.4373(18)
N^1–C^1	1.3945(17)	C^{11}–C^{12}	1.3598(18)
N^1–C^{21}	1.4506(15)	C^{12}–C^{13}	1.4740(19)
C^6–C^7	1.5086(19)		

EXPERIMENTAL

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

(1*E*,3*Z*)-4-Hydroxy-4-phenyl-1-(1,3,3-trimethyl-2,3-dihydro-1*H*-indol-2-ylidene)but-3-en-2-one (IIIa). A solution of 1.5 mmol of compound **Ia** and 1.5 mmol of Fischer's base (**II**) in 20 ml of anhydrous toluene was heated for 30 min under reflux. The mixture was cooled, and the precipitate was filtered off. Yield 92%, mp 184–186°C (decomp., from ethanol). IR spectrum, ν, cm^{-1}: 3080 br (OH), 1610 br (C=O). ^{1}H NMR spectrum, δ, ppm: tautomer **A**: 1.73 s (6H, Me), 3.30 s (3H, NMe), 5.42 s (1H, 1-H), 6.43 s (1H, 3-H), 7.00–7.87 m (9H, H_{arom}), 17.39 s (1H, OH); tautomer **B**: 1.57 s (6H, Me), 3.21 s (3H, NMe), 4.14 s (2H, 3-H), 5.30 s (1H, 1-H), 6.97–8.00 m (9H, H_{arom}). 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**–**IIId** were synthesized in a similar way.

(1*E*,3*Z*)-4-Hydroxy-4-(4-methylphenyl)-1-(1,3,3-trimethyl-2,3-dihydro-1*H*-indol-2-ylidene)but-3-en-2-one (IIIb). Yield 89%, mp 180–182°C (decomp., from ethanol). IR spectrum, ν, cm^{-1}: 3085 br (OH), 1605 br (C=O). ^{1}H NMR spectrum, δ, ppm: **A**: 1.72 s (6H, Me), 2.37 s (3H, **Me**C_6H_4), 3.29 s (3H, NMe), 5.40 s (1H, 1-H), 6.39 s (1H, 3-H), 6.99–7.77 m (8H, H_{arom}), 17.42 s (1H, OH); **B**: 1.56 s (6H, Me), 2.21 s (3H, **Me**C_6H_4), 3.13 s (3H, NMe), 4.09 s (2H, 3-H), 5.27 s (1H, 1-H), 6.96–7.90 m (8H, H_{arom}). Found, %: C 79.19; H 6.95; N 4.03. $C_{22}H_{23}NO_2$. Calculated, %: C 79.25; H 6.95; N 4.20.

(1*E*,3*Z*)-4-(4-Chlorophenyl)-4-hydroxy-1-(1,3,3-trimethyl-2,3-dihydro-1*H*-indol-2-ylidene)but-3-en-2-one (IIIc). Yield 90%, mp 172–173°C (decomp., from CCl_4). IR spectrum, ν cm^{-1}: 3060 br (OH), 1610 br (C=O). ^{1}H NMR spectrum, δ, ppm: **A**: 1.73 s (6H, Me), 3.31 s (3H, NMe), 5.42 s (1H, 1-H), 6.45 s (1H, 3-H), 7.00–7.88 m (8H, H_{arom}), 17.45 s (1H, OH); **B**: 1.57 s (6H, Me), 3.22 s (3H, NMe), 4.15 s (2H, 3-H), 5.29 s (1H, 1-H), 6.96–8.00 m (8H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 23.18 (3′-CH_3), 47.66 (CH_3N), 93.04 ($C^{3'}$), 98.68 (C^3), 108.54 (C^1), 121.65–142.94 (C_{arom}), 171.00 ($C^{2'}$), 172.60 (C^4), 187.28 (C^2). Found, %: C 71.17; H 5.75; N 3.82. $C_{21}H_{20}ClNO_2$. Calculated, %: C 71.28; H 5.70; N 3.96.

X-Ray analysis of compound IIIc. The X-ray diffraction data were acquired from a 0.25×0.22×0.19-mm fragment of a red prismatic crystal of **III** at 150(2) K on an Xcalibur-3 automatic diffractometer with a CCD detector (Oxford Diffraction) according to standard procedure [ω-scanning, scan step 1°, λ = 0.71073 Å (MoK_α)]; CrysAlis program [10]. Monoclinic crystal system, space group $P2_1/c$; unit cell parameters: a = 17.0539(14), b = 10.1234(6), c = 10.8388(4) Å; β = 104.258(6)°; V = 1813.6(2) Å^3; $C_{21}H_{20}ClNO_2$; Z = 4; d = 1.296 g/cm^3. Total of 11442 reflection intensities were measured in the range $-23 < h < 24$, $-7 < k < 14$, $-15 < l < 6$; 5408 reflections were independent (R_{int} = 0.0220), and 3003 reflections were characterized by $I > 2\sigma(I)$; completeness 97.5% for $2.79 < \Theta < 30.51$. The structure was solved by the direct method using SHELXS-97 program and was refined with respect to F^2 in anisotropic approximation for non-hydrogen atoms (SHELXL-97 [11]); hydrogen atoms were included in the refinement procedure according to the riding model in isotropic approximation with dependent thermal parameters. The enol OH hydrogen atom was refined independently in isotropic approximation. No correction for absorption was introduced because of its smallness (μ = 0.224 mm^{-1}). The final divergence factors were R_1 = 0.0408, wR_2 = 0.1075 [for reflections with $I > 2\sigma(I)$] and R_1 = 0.0817, wR_2 = 0.1150 (all reflections); S = 1.012. The maximal and minimal residual electron density peaks were 0.368 and –0.354 $\bar{e}$/Å^3, respectively.

(1*E*,3*Z*)-4-(4-Ethoxyphenyl)-4-hydroxy-1-(1,3,3-trimethyl-2,3-dihydro-1*H*-indol-2-ylidene)but-3-en-

2-one (IIId). Yield 88%, mp 142–144°C (decomp., from CCl_4). IR spectrum, ν, cm^{-1}: 3080 br (OH), 1610 br (C=O). ^1H NMR spectrum, δ, ppm: **A**: 1.39 t (3H, CH_2CH_3), 1.76 s (6H, Me), 3.32 s (3H, NMe), 4.11–4.18 m (2H, OCH_2), 5.42 s (1H, 1-H), 6.39 s (1H, 3-H), 7.04–7.87 m (8H, H_{arom}), 17.40 s (1H, OH); **B**: 1.26 t (3H, CH_2CH_3), 1.57 s (6H, Me), 3.20 s (3H, NMe), 4.05–4.08 m (2H, OCH_2), 4.16 s (2H, 3-H), 5.29 s (1H, 1-H), 6.95–7.96 m (8H, H_{arom}). Found, %: C 76.00; H 7.13; N 3.67. $C_{23}H_{25}NO_3$. Calculated, %: C 76.01; H 6.93; N 3.85.

This study was performed under financial support by the Presidium of the Russian Academy of Sciences (program no. 18), by the Russian Foundation for Basic Research (project no. 08-03-01032), and by the President of the Russian Federation (project no. MK-2998.2011.13).

REFERENCES

1. Stepanova, E.E., Babenysheva, A.V., and Maslivets, A.N., *Russ. J. Org. Chem*., 2011, vol. 47, p. 937.
2. Andreichikov, Yu.S., Gein, V.L., Zalesov, V.V., Kozlov, A.P., Kollents, G., Maslivets, A.N., Pimenova, E.V., and Shurov, S.N., *Khimiya pyatichlennykh 2,3-dioksogeterotsiklov* (Chemistry of Five-Membered 2,3-Dioxo Heterocycles), Perm: Perm. Gos. Univ., 1994, p. 5.
3. Nekrasov, D.D. and Shurov, S.N., *Khim. Geterotsikl. Soedin*., 2005, p. 1245.
4. Novikov, A.A., Vostrov, E.S., and Maslivets, A.N., *Russ. J. Org. Chem*., 2005, vol. 41, p. 1234.
5. Andreichikov, Yu.S., Voronova, L.A., and Milyutin, A.V., *Zh. Org. Khim*., 1979, vol. 15, p. 847.
6. Khalturina, V.V., Shklyaev, Yu.V., Aliev, Z.G., and Maslivets, A.N., *Russ. J. Org. Chem*., 2009, vol. 45, p. 728.
7. Andreichikov, Yu.S., Gein, L.F., and Plakhina, G.D., *Zh. Org. Khim*., 1980, vol. 16, p. 2336.
8. Vostrov, E.S., Novikov, A.A., Maslivets, A.N., and Aliev, Z.G., *Russ. J. Org. Chem*., 2007, vol. 43, p. 224.
9. Khalturina, V.V., Shklyaev, Yu.V., Aliev, Z.G., and Maslivets, A.N., *Russ. J. Org. Chem*., 2009, vol. 45, p. 1515.
10. *CrysAlis CCD, Version 1.171.29.9* (release 23-03-2006 CrysAlis171.NET), Oxford Diffraction.
11. Sheldrick, G.M., *Acta Crystallogr., Sect. A*, 2008, vol. 64, p. 112.