SYNTHESIS AND STRUCTURE OF ANILS OF 2-FORMYL-3-HYDROXYBENZOFURAN*

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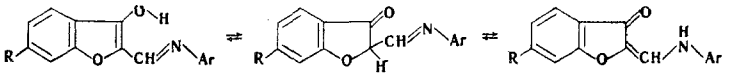
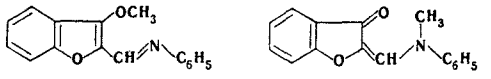
A number of anils of 2-formyl-3-hydroxybenzofuran (I) and their derivatives, which are models of the individual tautomeric forms II and III, were synthesized. A ketoamine structure (Ic) was assigned to compounds I as a result of a study of the electronic, vibrational, and PMR spectra.

The structure of anils of 2-formyl-3-hydroxybenzo[b]thiophene was discussed in communication [2]. In order to investigate the effect of the character of the heteroatom in the five-membered ring and other structural factors on the structure of the anils, we synthesized azomethines of the I type from 2-formyl-3-hydroxybenzofuran (R = H) and 2-formyl-3-hydroxy-6-methylbenzofuran (R = CH_3), for which Ia ⇌ Ic tautomeric equilibria are possible.



Ia Ib Ic



II III

We also obtained II and III, which are models of tautomeric forms Ia and Ic, respectively.

To determine the character of the Ia ⇌ Ic tautomeric equilibrium, we used data from the electronic, vibrational, and PMR spectra of I-III.

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TABLE 1. Spectral Characteristics of I-III

Comp.	R	Ar	Electronic spectra,* λ, nm (ε · 10^{-3})	IR spectra,† ν, cm^{-1}
I	H	C_6H_5	270(9,69), 330(9,29), 417(31,0)	1600, 1625, 1715
	H	p-$CH_3OC_6H_4$	275(11,3), 343(6,47), 426(26,8)	1610, 1710
	H	p-ClC_6H_4	270(14,6), 330(10,6), 418(32,0)	1610, 1710
	H	2,4,6-$(CH_3)_3C_6H_2$	265(9,3), 322(11,5), 397(25,9)	1625, 1690
	CH_3	C_6H_5	272(11,2), 338(11,3), 415(31,3)	1605, 1635, 1710
	CH_3	p-$CH_3OC_6H_4$	275(12,5), 337(10,6), 428(32,2)	1606, 1710
	CH_3	p-$NO_2C_6H_4$	284(6,8), 348(10,4), 416(38,5)	1620, 1718
II			325(22,7), 323(24,4)	1625
III			265(14,4), 325(11,1), 405(27,5)	1620, 1690

*In methanol.

†In mineral oil.

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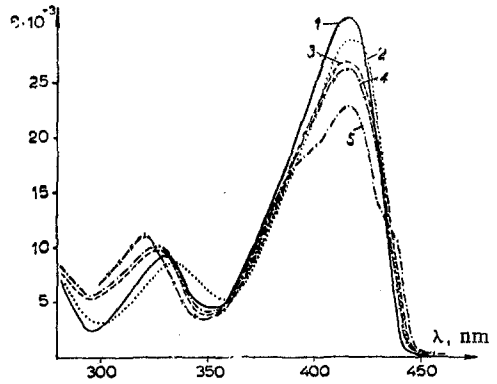

Fig. 1

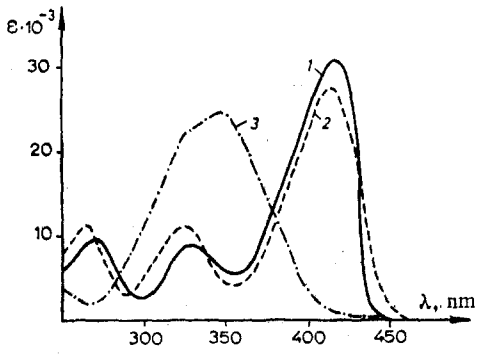

Fig. 2

Fig. 1. Electronic spectra of 2-(N-phenylaminomethylene)-3(2H)-benzofuranone (I, R = R' = H): 1) in methanol; 2) in acetic acid; 3) in pyridine; 4) in dimethyl sulfoxide; 5) in benzene.

Fig. 2. Electronic spectra (in methanol): 1) 2-(N-phenylaminomethylene)-3(2H)-benzofuranone; 2) 2-(N,N'-methylphenylaminomethylene)-3(2H)-benzofuranone (III); 3) 2-formyl-3-methoxybenzofuran anil (II).

TABLE 2. Azomethines Ic

R	Ar	mp, °C	Empirical formula	Found, %		Calc., %		Synthetic method (yield, %)
				C	H	C	H	
H	C_6H_5	170	$C_{15}H_{11}NO_2$	75,4	4,9	75,7	4,6	A(70), B(53), C(88)
H	p-$CH_3C_6H_4$	213	$C_{16}H_{13}NO_2$	76,3	5,0	76,5	5,2	A(75), B(49), C(80)
H	m-$CH_3C_6H_4$	180	$C_{16}H_{13}NO_2$	76,8	5,4	76,5	5,2	A(78), B(51)
H	p-$CH_3OC_6H_4$	165	$C_{16}H_{13}NO_3$	72,3	4,7	71,9	4,9	A(82), B(50)
H	p-ClC_6H_4	244	$C_{15}H_{10}ClNO_2$*	66,1	3,7	66,3	3,7	A(87), B(66)
H	p-$NO_2C_6H_4$	290	$C_{15}H_{10}N_2O_4$	63,9	3,7	63,6	3,6	B(80)
H	m-$NO_2C_6H_4$	238	$C_{15}H_{10}N_2O_4$	63,3	3,4	63,6	3,6	B(84)
H	2,4,6-$(CH_3)_3C_6H_2$	62—63	$C_{18}H_{17}NO_2 \cdot C_3H_8O$ †	74,4 76,7	7,4 5,0	74,4 76,5	7,4 5,2	B(52) A(53)
CH_3	C_6H_5	201	$C_{16}H_{13}NO_2$					
CH_3	p-$CH_3OC_6H_4$	184	$C_{17}H_{15}NO_3$	72,9	5,4	72,6	5,4	A(45)
CH_3	p-$NO_2C_6H_4$	295	$C_{16}H_{12}N_2O_4$	65,1	4,2	64,9	4,1	A(40)
CH_3	p-ClC_6H_4	245	$C_{16}H_{12}ClNO_2$‡	67,4	4,3	67,3	4,2	A(48)

*Found, %: Cl 12.7. Calculated, %: Cl 13.0.

† The solvated compound ($C_{18}H_{17}NO_2 \cdot$ iso-C_3H_7OH).

‡ Found, %: Cl 12.7. Calculated, %: Cl 12.4.

As in the case of the previously described [2] azomethines of 2-formyl-3-hydroxybenzo[b]thiophene, the electronic spectra of anils I contain the absorption band at 400-430 nm (Table 1 and Figs. 1 and 2) that is characteristic for o-quinoid structures of hydroxyaldimines [3]. This band is only slightly sensitive to the effect of the solvent, temperature, and variation in the structure of aryl substituent Ar (Table 1).

Azomethines I consequently exist as one of three possible tautomeric forms in solution. Structure Ib can be excluded because of the absence in the PMR spectrum (Fig. 3) of the characteristic splitting pattern of the AB protons of the CH—CH=N group, and a comparison of the electronic absorption spectra of azomethines I, II, and III (methyl derivatives of tautomers Ia and Ic) makes it possible to make an obvious choice in favor of Ic (Fig. 2).

The PMR spectrum of I (R = H, Ar = C_6H_5) presented in Fig. 3, like the spectra of all of the other anils, confirms structure Ic. In fact, the signal of the NH proton of Ic, which is split as a result of spin-spin coupling with the vicinal CH proton and vanishes on deuteration (repeated recrystallization from deuteroethanol), appears distinctly at weak field at 10 and 15 ppm. The J value of 13 Hz indicates practically complete shifting of the tautomeric equilibrium to favor the formation of Ic [4]. Judging from the δ_{NH} values, the intramolecular hydrogen bond in the Ic molecules and in the analogous benzothiophene derivatives [2] is the weakest among all of the previously studied compounds with an arylamino-3-propenone fragment [4-6]. It should be noted that while the chemical shift of the NH protons is practically independent of the nature of the heteroatom in the five-membered ring (for the same Ar group), the signal of the CH protons of Ic is shifted to strong field as compared with the analogous benzothiophene anils and enters the region of

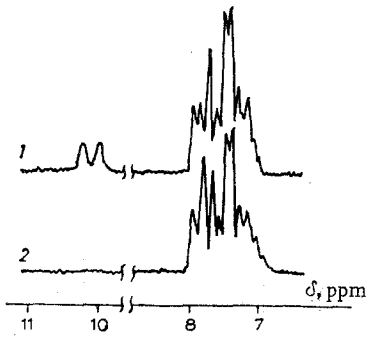

Fig. 3. PMR spectra of 2-(N-phenylaminomethylene)-3-(2H)-benzofuranone (in dimethyl sulfoxide): 1) undeuterated; 2) N-deuterated.

aromatic proton signals. This is probably due to the large anisotropic contribution of sulfur as compared with oxygen. A certain reorganization of the pattern of the proton signal in the 7.8 ppm region, where the signal of the methylidyne proton possibly lies, is observed in the PMR spectrum of deuterated compound Ic (Fig. 3).

The IR spectroscopic data (Table 1) confirm the conclusion that the 2-formyl-3-hydroxybenzofuran anils (I) have a quinoid ketoamine structure. The spectra of compounds of the I type have an intense band of the ring carbonyl group (at ~1700 cm^{-1}), which appears at 1690 cm^{-1} in the spectrum of III, and a band at 1600-1620 cm^{-1}, which corresponds to vibrations localized primarily on the exocyclic conjugated C=C bond. The band at ~1700 cm^{-1} is absent in the spectrum of azomethine II, which has an imine structure, and absorption appears in the 1625 cm^{-1} region, which is characteristic for the C=N bond [2].

The data obtained demonstrate that neither replacement of the sulfur heteroatom by oxygen in I, nor variation of the structure of I on the part of the amine component (in particular, decreasing the basicity of the imine nitrogen in p-nitroanils), nor introduction of a weak donor CH_3 group into the benzofuran ring, nor creation of steric hindrance for the hydrogen on the imine nitrogen in the mesidine derivative affect the position of the tautomeric equilibrium of anils I: they exist in o-quinoid form Ic.

EXPERIMENTAL

2-Ethoxymethylene-3(2H)-benzofuranone (V). A mixture of 6.7 g (0.05 mole) of coumaranone (IV) [7], 15 ml (0.1 mole) of ethyl orthoformate, and 15 ml (0.15 mole) of acetic anhydride was heated on an oil bath at 130-140° for 4-5 h. The reaction product was vacuum fractionated to give a fraction with bp 155-157° (2 mm). The yellow oil crystallized on cooling to give 4.1 g (44%) of product. IR spectrum: $\nu_{C=O}$ 1710 cm^{-1}, 1650, 1600 cm^{-1}. Found,%: C 69.8; H 5.6. $C_{11}H_{10}O_3$. Calculated,%: C 69.5; H 5.3.

2-Formyl-3-hydroxybenzofuran (VI). A 1.0-g (0.05 mole) sample of V was dissolved in 3 ml of acetic acid, 2 ml of water was added, and the mixture was cooled. The solution began to darken, and a precipitate formed. The precipitate was removed rapidly by filtration, washed with cold 50% acetic acid, and dried in a vacuum desiccator. The dry substance was purified by vacuum sublimation to give 0.57 g (67%) of colorless needles with mp 114-115° (dec.). IR spectrum: $\nu_{C=O}$ 1663 cm^{-1}. PMR spectrum (in CH_2Cl_2): δ 9.75 (CHO) and 8.02 ppm (OH). Found,%: C 66.5; H 4.0. $C_9H_6O_3$. Calculated,%: C 66.6; H 3.7.

3-Chloro-2-formylbenzofuran. A 10-ml sample of phosphorus oxychloride was added by drops with stirring to a cooled (to 0°) solution of 3.7 g (0.03 mole) of IV in 10 ml of dimethylformamide, and the mixture was heated to 60° for 2 h. The resulting viscous mass was poured over ice, and the brown precipitate was steam distilled to give 3 g (61%) of colorless crystals of 3-chloro-2-formylbenzofuran with mp 78°. IR spectrum: $\nu_{C=O}$ 1680 cm^{-1}. PMR spectrum: δ 9.95 ppm (singlet, CHO). Found,%: C 60.2; H 2.8; Cl 19.3. $C_9H_5ClO_2$. Calculated,%: C 59.9; H 2.8; Cl 19.6.

2-Formyl-3-methoxybenzofuran (VII). A 0.42-g (0.02 g-atom) sample of sodium was dissolved in 30 ml of methanol, 3.0 g (0.016 mole) of 3-chloro-2-formylbenzofuran and a small crystal of potassium iodide (as a catalyst) were added, and the mixture was refluxed on a water bath for 4 h. The hot solution was filtered to remove the precipitated sodium chloride, and the filtrate was cooled to give 2.4 g (82%) of crystals of aldehyde VII. Two recrystallizations from alcohol gave a product with mp 79-80°. IR spectrum: $\nu_{C=O}$ 1643 cm^{-1}. Found,%: C 68.2; H 4.9. $C_{10}H_8O_3$. Calculated,%: C 68.2; H 4.6.

Azomethines I (Table 1). A. Compound IV or its 6-methyl derivative [8] was heated in alcohol with the corresponding N,N'-diarylformamidine, obtained according to the methods in [9-11]. The azomethines were yellow-green crystals (from ethanol or isobutyl alcohol).

B. Equimolecular amounts of V and the appropriate substituted aniline were dissolved in ethanol or benzene, and the product was recrystallized from a suitable solvent. This method was used to obtain III from N-methylaniline and V. The yellow-green crystals (from butanol) had mp 133-134°. IR spectrum: $\nu_{C=O}$ 1690 cm^{-1}. PMR spectrum (in deuterodimethyl sulfoxide): δ 3.72 ppm (singlet, CH_3). Found,%: C 76.5; H 5.4. $C_{16}H_{13}NO_2$. Calculated,%: C 76.2; H 5.2.

C. Equimolecular amounts of VI and the appropriate aniline were condensed in ethanol and the product was recrystallized.

Azomethines II. These compounds were obtained by heating equimolecular amounts of aldehyde VII with aniline to 100° without a solvent. The product was recrystallized twice from isopropyl alcohol to give yellow crystals with mp 68-69°. IR spectrum: $\nu_{C=N}$ 1625 cm^{-1}. Found,%: C 76.6; H 5.0. $C_{16}H_{13}NO_2$. Calculated,%: C 76.5; H 5.2.

The absorption spectra in the UV and visible regions (Table 1) were recorded with a Specord (German Democratic Republic) spectrophotometer. The IR spectra (Table 1) were obtained with a UR-20 spectrometer. The PMR spectra of about 15% solutions of the compounds were recorded with an RYa-2305 spectrometer (60 MHz) at 25° with hexamethyldisiloxane as the internal standard.

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