

washed successively with water, 20% HCl, and water and dried successively with K_2CO_3 and sodium metal. The ether was removed by distillation, and the product was vacuum distilled. In the preparation of low-boiling 2-furylcyclopropane derivatives the latter were removed together with the water and excess hydrazine hydrate by distillation and were then extracted from the distillate by means of ether and obtained from the extracts as in the method described above.

2-Furylcyclopropane (IV). A 42-g (0.2 mole) sample of 1-(2-furyl)-3-dimethylamino-1-propanone was added with shaking to a mixture of 150 ml of diethylene glycol, 11.2 g (0.2 mole) of KOH, and 33 ml (0.6 mole) of hydrazine hydrate, after which periodic shaking was continued for another 30-40 min. The mixture was then heated on an oil bath at 140° for 4 h, after which it was allowed to stand for 1 h without heating. Another 11.2 g of KOH was added, and the mixture was heated to 230° (bath temperature) after the condenser was adjusted for distillation, during which nitrogen was evolved, and the 2-furylcyclopropane distilled from the mixture along with the water and excess hydrazine hydrate. The organic layer was separated from the aqueous layer and washed successively with water, rapidly with 2.5% HCl and 20% KOH, and water, after which it was dried successively with K_2CO_3 and sodium metal. Distillation over Na in a stream of nitrogen gave 11.2 g (50%) of 2-furylcyclopropane.

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SYNTHESIS OF 2-PHENYL-4-HYDROXYBENZOFURAN

DERIVATIVES

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2-Phenyl-4-hydroxybenzofuran was obtained by dehydrogenation of 2-phenyl-4-oxo-4,5,6,7-tetrahydrobenzofuran under the influence of sulfur. The transformations of 2-phenyl-4-hydroxybenzofuran and its derivatives were studied.

In contrast to 5- and 6-hydroxybenzofuran derivatives, 4-hydroxybenzofuran derivatives are relatively inaccessible and have not been studied in detail. However, they are of particular interest as heteroanalogs of biologically active 4-hydroxyindole derivatives [1].

The present research is a continuation of our studies of 4-hydroxybenzofuran derivatives [2]. We found that 2-phenyl-4-hydroxybenzofuran (Ia) is formed in high yield in the dehydrogenation of 2-phenyl-4-oxo-4,5,6,7-tetrahydrobenzofuran [3] with sulfur. Compound Ia was previously isolated in very low yield in the reaction of resorcinol and ω -diazoacetophenone [4].

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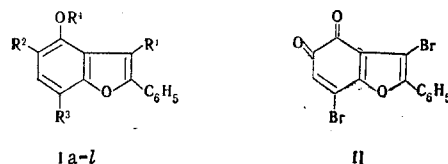
The PMR spectrum of Ia contains two multiplets — a three-proton multiplet centered at 7.41 ppm and a two-proton multiplet centered at 7.87 ppm — which, with respect to the character of their splitting, remain practically unchanged also in the spectra of derivatives Ib,c,g-j (see below). Both of these multiplets were therefore assigned to the protons of a phenyl substituent. In addition, the spectrum of Ia contains a singlet at 7.30 ppm, which in this system can belong only to the 3-H quartet, a quartet at 6.66 ppm with $J_1 = 8.5$ Hz and $J_2 = 1.5$ Hz, which, according to the splitting and the chemical shift, was assigned to the 5-H proton, and signals of two protons at 7.05 ppm. The latter signals are related to the protons in the 6 and 7 positions. The assignment of the signal at 6.66 ppm to the 5-H proton rather than to the 7-H proton was made on the basis of their chemical shifts. Although both protons are in the ortho position relative to the oxygen-containing substituent, the donor effect of the furan oxygen atom is considerably weakened due to inclusion of its unshared pair of electrons in the system of aromatic conjugation. Owing to this and to the effect of the ring currents of the furan ring, the signal of the 7-H proton should be found at weaker field as compared with 5-H.

The bromination of Ia with 1 mole of bromine proceeds ambiguously, and only 2-phenyl-4-hydroxy-7-bromobenzofuran (Ib) was isolated from the mixture of substances. The structure of the latter is confirmed by the PMR spectrum in which, in addition to the signals of a phenyl group (7.40 and 7.84 ppm), a singlet at 7.32 ppm (3-H) and two doublets with $J = 8.5$ Hz are observed. The doublet at 6.53 ppm was assigned to the 5-H proton on the basis of its chemical shift; the other doublet (7.14 ppm) is the 6-H signal. The bromine in Ib is consequently in the 7 position. Bromination of benzofuran Ia with excess bromine leads exclusively to 2-phenyl-3,5,7-tribromo-4-hydroxybenzofuran (Ic). The PMR spectrum of the latter contains a signal at 7.52 ppm, which, considering orienting effect of the hydroxyl group in the phenyl ring, can be confidently assigned to the 6-H proton.

As in the case of other 4-, 5-, and 6-acetoxymethylfurans [2, 5], the bromination and nitration of 2-phenyl-4-acetoxymethylbenzofuran (Id) lead only to the 3-bromo (Ie) and 3-nitro (If) derivatives. 2-Phenyl-3-bromo- (Ig) and 2-phenyl-3-nitro-4-hydroxybenzofuran (Ih), respectively, were obtained by hydrolysis of Ie and If.

The presence of substituents in the 3 position in Ig and Ih is confirmed by the PMR spectra. The PMR spectrum of Ig is very close with respect to the position and multiplicity of the signals to the spectrum of starting Ia and differs from it with respect to the absence of the singlet assigned to the 3-H proton in the spectrum of Ia. Compound Ig is consequently 2-phenyl-3-bromo-4-hydroxybenzofuran. The pronounced overlapping of the signals in the PMR spectrum of Ih (three- and five-proton multiplets at 7.46 and 7.92 ppm, respectively) hinders the determination of the position of the nitro group. However, considering the effect of the nitro group on the chemical shifts and the multiplicity of the protons in various positions of the molecule, as well as the absence of a singlet that would be unambiguously identified on the background of markedly split multiplets, it can be concluded that the substituent is in the 3 position.

The nitration of benzofuran Ia proceeded ambiguously, and only 2-phenyl-4-hydroxy-5,7-dinitrobenzofuran (II) was isolated from the mixture of reaction products. Two singlets (7.80 and 8.75 ppm) are observed distinctly in addition to the multiplets of the phenyl ring in the PMR spectrum of II; this indicates incorporation of both nitro groups in the benzene ring of the molecule. Moreover, according to the additive effect of substituents [6], the weak-field value of 8.75 ppm is possible only for the 6-H proton, which is under the influence of two o-nitro groups. The second signal (7.8 ppm) consequently belongs to the 3-H proton.



I a-l
I a. $R^1=R^2=R^3=R^4=H$; b. $R^1=R^2=R^4=H$, $R^3=Br$; c. $R^1=R^2=R^3=Br$, $R^4=H$; d. $R^1=R^2=R^3=H$, $R^4=COCH_3$; e. $R^1=Br$, $R^2=R^3=H$, $R^4=COCH_3$; f. $R^1=NO_2$, $R^2=R^3=H$, $R^4=COCH_3$; g. $R^1=Br$, $R^2=R^3=COCH_3$; h. $R^1=NO_2$, $R^2=R^3=COCH_3$; i. $R^1=R^4=H$, $R^2=R^3=NO_2$; j. $R^1=R^4=H$, $R^2=NO_2$, $R^3=Br$; k. $R^1=COCH_3$, $R^2=R^3=NO_2$, $R^4=H$; l. $R^1=R^3=Br$, $R^2=OH$, $R^4=H$.
II

It is known that quinones are formed in the reaction of halogen derivatives of hydroxybenzofuran with nitric acid [2, 7]. In connection with the interest in quinones of the benzofuran series, we studied the reaction of bromo derivatives Ib and Ic, obtained in the present research, with nitric acid. However, a quinone is not formed in the reaction of nitric acid with Ib, and the reaction gives two substances — 2-phenyl-4-hydroxy-5-nitro-7-bromobenzofuran (Ij) and 5,7-dinitro derivative II. The latter is formed by replacement of the bromine in the 7 position by a nitro group. Replacement of bromine by a nitro group in the benzofuran series has been previously observed [7]. The PMR spectrum of Ij is similar with respect to its multiplicity to the PMR spec-

TABLE 1. Characteristics of the Compounds Obtained

Compound	mp, °C	Found, %				Empirical formula	Calculated, %				Yield, %
		C	H	Br	N		C	H	Br	N	
Ia	161–162 ^{a,b}	80.0	5.2	—	—	C ₁₄ H ₁₀ O ₂	80.0	4.8	—	—	72
Ib	124–125 ^a	58.3	3.1	27.6	—	C ₁₄ H ₈ BrO ₂	58.2	3.1	27.6	—	29
Ic	202–203 ^c	37.2	1.8	54.0	—	C ₁₄ H ₇ Br ₂ O ₂	37.6	1.6	53.6	—	96
Id	64–65 ^d	76.2	5.0	—	—	C ₁₆ H ₁₂ O ₃	76.2	4.8	—	—	64
Ie	97–99 ^e	58.0	3.4	24.0	—	C ₁₆ H ₁₁ BrO ₃	58.0	3.4	24.1	—	90
If	168–169 ^e	64.7	3.6	—	4.7	C ₁₆ H ₁₁ NO ₅	64.7	3.7	—	4.7	78
Ig	144–145 ^d	58.0	3.2	27.6	—	C ₁₄ H ₈ BrO ₂	58.2	3.1	27.6	—	98
Ih	183–185 ^f	66.0	3.4	—	4.9	C ₁₄ H ₉ NO ₄	65.9	3.5	—	5.4	96
Ii	223–224 ^g	56.2	2.7	—	9.3	C ₁₄ H ₈ N ₂ O ₆	56.0	2.7	—	9.3	20
Ij	182–183 ^h	50.2	2.5	24.1	3.8	C ₁₄ H ₈ BrNO ₄	50.3	2.4	23.9	4.2	16
Ik	211–213 ^g	44.3	2.0	21.1	7.3	C ₁₄ H ₇ BrNO ₆	44.3	1.9	21.1	7.4	45
Il	155 ^{f,h}	43.8	2.1	—	—	C ₁₄ H ₈ Br ₂ O ₃	43.8	2.1	—	—	100
II	180–182 ^{g,h}	43.7	1.7	41.5	—	C ₁₄ H ₆ Br ₂ O ₃	44.0	1.6	41.8	—	21

^aFrom CCl₄.

^bThe melting points and analytical data for Ia are not presented in [4].

^cFrom CHCl₃.

^dFrom hexane.

^eFrom alcohol.

^fFrom benzene.

^gFrom acetone.

^hWith decomposition.

TABLE 2. Data from the PMR spectra (δ , ppm) of Ia-c,g-j

Compound	3-H	5-H	6-H	7-H	C ₆ H ₅	OH
Ia	7.30	6.66	7.05;	7.07	7.44, 7.92	8.89
Ib	7.32	6.53	7.14	—	7.40, 7.84	9.82
Ic	—	—	7.52	—	7.44, 8.09	9.70
Ig	—	6.68	7.07;	7.11	7.47, 8.10	9.04
Ih	—	—	7.46;	7.92	—	—
Ii	7.80	—	8.75	—	7.49, 7.97	8.75
Ij	7.62	—	8.18	—	7.46, 7.95	—

trum of II. The 7 position in the molecule is known to be occupied, and of the two observed singlets, one (7.62 ppm) belongs to 3-H, and the other (8.18 ppm), according to the chemical shift [6], belongs to 6-H.

An o-quinone – 2-phenyl-3,7-dibromo-4,5-dioxobenzofuran (II) – and 2-phenyl-3-bromo-4-hydroxy-5,7-dinitrobenzofuran (Ik) are formed in the reaction of nitric acid with 2-phenyl-3,5,7-tribromo-4-hydroxybenzofuran (Ic). The structure of Ik is confirmed by the fact that we obtained it by nitration of Ig.

The o-quinoid structure of II is proposed on the basis of a comparison of its UV spectrum with the UV spectra of o- and p-benzofuranquinones, which we have previously obtained [2]. A bathochromic shift of the absorption maximum to the visible region of the spectrum (460 nm) is observed in the UV spectra of o-quinones, particularly in the spectra of II; this is confirmed by the data obtained during a study of the UV spectra of o- and p-benzoquinones [8]. Quinone II was reduced with sodium hydrosulfite to 4,5-dihydroxy derivative II. An absorption band appears at 3400 cm⁻¹ (OH) in the IR spectrum of the latter; this band is absent in the spectrum of starting II.

EXPERIMENTAL

The PMR spectra of deuteroacetone solutions of the compounds were recorded with a JNM-4H-100 spectrometer with tetramethylsilane as the internal standard. The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-10 spectrometer.

2-Phenyl-4-hydroxybenzofuran (Ia). A mixture of 21.2 g (0.1 mole) of 2-phenyl-4-oxo-4,5,6,7-tetrahydrobenzofuran and 4.8 g (0.15 mole) of sulfur was heated at 245° for 1.5 h, after which it was cooled to 20° and recrystallized from carbon tetrachloride to give 15.0 g of Ia. IR spectrum: 3200–3300 cm⁻¹ (OH).*

* The characteristics of the compounds obtained are presented in Tables 1 and 2.

2-Phenyl-4-hydroxy-7-bromobenzofuran (Ib). A solution of 2.9 g (0.018 mole) of bromine in 10 ml of acetic acid was added dropwise with stirring at 20° in the course of 30 min to a suspension of 3.8 g (0.018 mole) of Ia in 30 ml of acetic acid, and the resulting solution was stirred for 1 h. It was then diluted with water, and dried. Chromatography with a column filled with silica gel (elution with benzene) gave 1.5 g of 7-bromo derivative Ib.

2-Phenyl-3,5,7-tribromo-4-hydroxybenzofuran (Ic). A solution of 6.4 g (0.04 mole) of bromine in 3 ml of acetic acid was added dropwise with stirring at 20° in the course of 30 min to a suspension of 2.1 g (0.01 mole) of Ia in 25 ml of acetic acid, and the mixture was then stirred for 1 h. The resulting precipitate was removed by filtration, washed with water, and dried. The yield of tribromo derivative Ic was 4.3 g.

2-Phenyl-4-acetoxybenzofuran (Id). A mixture of 5.5 g (0.026 mole) of Ia, 2.6 ml (0.026 mole) of acetic anhydride, and 2.4 g (0.03 mole) of dry pyridine was heated at 100° for 6 h, after which it was poured into water, and the resulting precipitate was removed by filtration, washed with water, and dried. The yield of acetoxy derivative Id was 4.2 g.

2-Phenyl-3-bromo-4-acetoxybenzofuran (Ie). A solution of 0.8 g (0.005 mole) of bromine in 5 ml of chloroform was added dropwise with stirring at 20° in the course of 30 min to a solution of 1.26 g (0.005 mole) of acetoxy derivative Id in 25 ml of chloroform, and the mixture was stirred for 1 h. The resulting solution was washed with water and dried over magnesium sulfate, and the chloroform was removed by distillation to give 1.5 g of Ie.

2-Phenyl-3-nitro-4-acetoxybenzofuran (If). A solution of 3.5 g (0.05 mole) of nitric acid (sp. gr. 1.35) in 5 ml of acetic acid was added dropwise with stirring at 20° in the course of 30 min to a solution of 2.52 g (0.01 mole) of Id in 10 ml of acetic acid, and the mixture was stirred for 4 h. The resulting precipitate was removed by filtration, washed with water, and dried. The yield of If was 2.3 g.

2-Phenyl-3-bromo-4-hydroxybenzofuran (Ig). A 0.83-g (0.0025 mole) sample of Ie was added to a solution of 0.28 g (0.005 mole) of potassium hydroxide in 28 ml of alcohol, and the mixture was refluxed for 1 h. The resulting solution was diluted with water, and the precipitate was removed by filtration, washed with water, and dried to give 0.72 g of Ig.

2-Phenyl-3-nitro-4-hydroxybenzofuran (Ih). This compound was obtained by the method used to prepare Ig. The reaction of 0.2 g (0.0007 mole) of If and 0.073 g of potassium hydroxide in 6 ml of alcohol gave 0.165 g of 3-nitro derivative Ih.

2-Phenyl-4-hydroxy-5,7-dinitrobenzofuran (Ii). A solution of 10.5 ml of nitric acid (sp. gr. 1.35) in 10 ml of acetic acid was added dropwise with stirring in the course of 1 h to a suspension of 6.3 g (0.03 mole) of Ia in 50 ml of acetic acid, and the mixture was stirred for 1.5 h. The resulting precipitate was removed by filtration, washed with water, and dried. Chromatography with a column filled with silica gel (elution with benzene) gave 1.8 g (20%) of Ii.

2-Phenyl-4-hydroxy-5-nitro-7-bromobenzofuran (Ij) and 2-Phenyl-4-hydroxy-5,7-dinitrobenzofuran (Ii). A solution of 0.25 ml of nitric acid (sp. gr. 1.35) in 5 ml of acetic acid was added dropwise with stirring at 20° in the course of 30 min to a solution of 0.35 g (0.0012 mole) of Ib in 5 ml of acetic acid, and the resulting precipitate was removed by filtration, washed with water, and dried to give 0.3 g of Ii. No melting-point depression was observed for a mixture of a sample of this product with a sample of the product obtained in the preceding experiment. The acetic acid mother liquor was diluted with water, and the precipitate was removed by filtration, washed with water, and dried. Chromatography with a column filled with silica gel (elution with benzene) gave 0.05 g of Ij.

2-Phenyl-3-bromo-4-hydroxy-5,7-dinitrobenzofuran (Ik) and 2-Phenyl-3,7-dibromo-4,5-dioxobenzofuran (II). A solution of 0.9 ml of nitric acid (sp. gr. 1.35) in 5 ml of acetic acid was added dropwise with stirring at 20° in the course of 30 min to a suspension of 2.5 g (0.0056 mole) of tribromobenzofuran Ic in 25 ml of acetic acid, and the mixture was stirred for 1 h. The resulting precipitate was removed by filtration, washed with water, and dried to give 0.95 g of Ik. The filtrate was diluted with water, and the precipitate was removed by filtration and dried. Chromatography with a column filled with silica gel (elution with benzene) gave 0.45 g of II. UV spectrum: λ_{\max} 460 nm ($\log \epsilon$ 3.47).

2-Phenyl-3,7-dibromo-4,5-dihydroxybenzofuran (IL). A solution of 0.5 g (0.0012 mole) of quinone II in 120 ml of ethyl acetate was shaken with a solution of 0.6 g of sodium hydrosulfite in 15 ml of water, after which the ethyl acetate solution was washed with water, dried with magnesium sulfate, and evaporated to give 0.5 g (quantitative yield) of IL. IR spectrum: 3400 cm^{-1} (OH).

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RESEARCH ON 2-ACYL-3-AMINO BENZOFURANS

III.* SCHMIDT REARRANGEMENT IN A SERIES OF 2- AND 3-ACYLBENZOFURAN DERIVATIVES

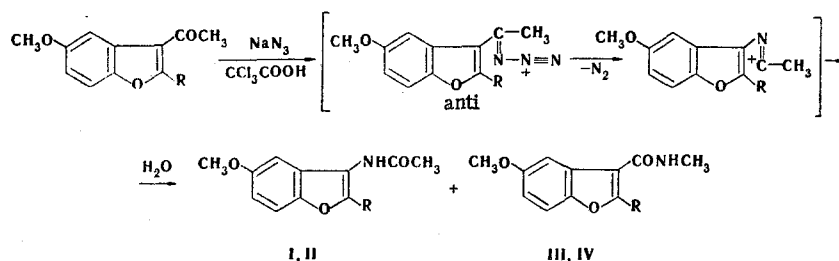
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It is demonstrated that, depending on the position of the acetyl substituent in the furan ring of benzofuran, the Schmidt rearrangement leads to benzofuran-2-carboxylic acid methylamide or to 3-acetamidobenzofuran derivatives.

It is known that 3-acetylbenzofuran oximes behave "anomalously" under the conditions of the Beckmann rearrangement and that the formation of the usual rearrangement products — amides — is not observed in this case [2, 3]. We have studied the possibility of the synthesis of 3-acetamidobenzofurans by means of the Schmidt rearrangement. It was established that the direction of the rearrangement depends on the position of the acyl substituent in the benzofuran system. Thus 3-acetamidobenzofuran derivatives (I and II, respectively) are formed in good yields in the reaction of sodium azide in trichloroacetic acid with 3-acetyl-5-methoxybenzofuran and 2-methyl-3-acetyl-5-methoxybenzofuran. The structures of I and II were proved by means of spectral methods and by alternative synthesis [4]. The formation of small amounts of the isomeric 5-methoxybenzofuran-3-carboxylic acid methylamide (III) was established by thin-layer chromatography (TLC).

A different direction of Schmidt rearrangement is observed when the reaction is carried out with 2-acetylbenzofuran under the same conditions, and benzofuran-2-carboxylic acid methylamide (V) is formed in 80% yield.



* See [1] for communication II.