BROMINATION OF ARYLFURANS

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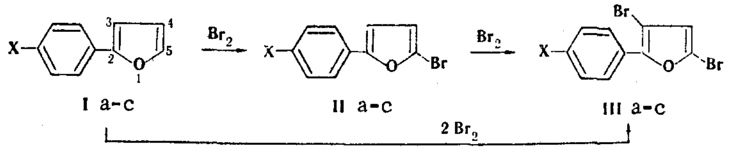
The bromination of 2-arylfurans has been studied. The structures of the compounds obtained have been determined with the aid of NMR spectra.

Continuing our investigations on the synthesis and transformations of arylfuran derivatives [1], we have studied the bromination of 2-arylfurans (Ia-c) by bromine in dichloroethane. Our investigations have shown that when an equimolar amount of bromine is used bromination takes place in the free α-position of the furan, and 2-aryl-5-bromofurans (IIa-c) are formed with yields of 75-84%. The further bromination of the 2-aryl-5-bromofurans, and also the bromination of 2-arylfurans with 2 moles of bromine leads to the formation of dibromo derivatives of 2-arylfurans (IIIa-c) with yields of 77-96%.

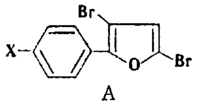


I–III a X=Br; b X=Cl; c X=NO₂

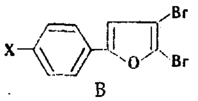
It was extremely important to determine the position of entry of the second bromine atom in the bromination of the 2-aryl-5-bromofurans, since there is a limited number of examples of electrophilic substitution reactions of 5-substituted 2-arylfurans in the literature [2].

The determination of the position of entry of the bromine atom into the furan ring in compounds (IIa-c) and (IIIa-c) was performed with the aid of ^{1}H and ^{13}C NMR spectra (Tables 1 and 4).

In the ^{1}H NMR spectra of compounds (IIa-c), the observed spin–spin coupling constants (SSCC) (J = 3.4-3.5 Hz) correspond to the interaction of the 3-H and 4-H protons of the furan ring; this leads to the conclusion that in the monobromo derivatives (IIa-c) the bromine atom has entered position 5 of the furan nucleus.



A



B

X=Cl, Br, NO₂

The choice between the two possible variants of the position of the bromine atom in the dibromo derivatives (IIIa-c) (structure A or B) was made on the basis of a comparison of the experimental chemical shifts of the furan proton (δH) in compounds (IIIa-c) and its calculated values for structures A and B. The calculation of the chemical shift δH was performed by an additive scheme:

$$\delta 3\text{-H}(4\text{-H}) = \delta H_0 \underset{R}{\bar{Z}} Z_{3(4)},$$

where δH_0 is the chemical shift of the 3-H or 4-H proton of unsubstituted furan, and $Z_{3(4)}$ is the change in the value of H_0 on the introduction into unsubstituted furan of a substituent R (R = Br, p-BrC_6H_4, p-ClC_6H_4, p-$NO_2C_6H_4$). We determined the increments $Z_{3(4)}$ from

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TABLE 1. Parameters of the ^{1}H NMR Spectra of Compounds (I-IV)

Compound	Chemical shifts, δ, ppm					Spin-spin coupling constants, Hz		
	5-H	4-H	3-H	m-H	o-H	$^3J_{45}$	$^4J_{35}$	$^3J_{34}$
Ia	7,40	6,41	6,58	7,30	7,55	1,8	0,75	3,45
Ib	7,42	6,42	6,58	7,52	7,52	1,8	0,75	3,45
Ic	7,56	6,54	6,87	8,25	7,77	~2,0	~1,0	~3,50
IIa	—	6,32	6,52	7,32	7,60	—	—	3,50
IIb	—	6,32	6,53	7,45	7,45	—	—	3,45
IIc	—	6,45	6,81	8,21	7,70	—	—	3,50
IIIa	—	6,39	—	7,34	7,84	—	—	—
IIIb	—	6,39	—	7,49	7,77	—	—	—
IIIc	—	6,47	—	8,06	8,04	—	—	—
IV	7,98	6,51	—	7,52	7,79	1,90		

TABLE 2. Values of the Increments Z for Substituted Furans*

R	Z_3, ppm	Z_4, ppm
2, p-BrC_6H_4	0,21	0,05
2, p-ClC_6H_4	0,21	0,04
2, p-$NO_2C_6H_4$	0,50	0,17
2-Br	−0,07	0,01
2,3-Br	—	0,09
2,4-Br	−0,05	—

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*Solvents, $CDCl_3$; for unsubstituted furans, δ3-H = δ4-H = 6.37 ppm.

the spectra of the bromofurans and of the p-substituted arylfurans (Ia-c). Their values are given in Table 2.

The proposed system of calculating the chemical shift of the furan proton was first checked on the 2-aryl-5-bromofurans (IIIa-c) as a result of which it was found that the experimental and calculated values obtained agreed to within ±0.06 ppm.

For the aryldibromofurans (IIIa-c), calculation by the additive scheme showed that the chemical shift of the proton of the furan ring agreed well with the value of δH calculated for structure A (Table 3).

On this basis, it was concluded that the second bromine atom in the 2-aryldibromofurans (III) had entered position 3 of the furan ring. In favor of this idea also is the width of the signal of the proton of the furan ring, which is 0.3 Hz and coincides with the natural width of the standard line of the substance in the spectrum (CH_2Cl_2, 0.3 Hz), since the 4-H proton scarcely interacts with the other protons in (IIIa-c). In contrast to the 4-H proton, the 3-H proton of the furan ring is characterized by an interaction with the protons of the 2-p-substituted aryl ring, which leads to a broadening of the 3-H signal (0.48 Hz).

The results of ^{13}C NMR spectroscopy also agree with the structure shown for the dibromo derivatives (IIIa-c). We used the 2,3- and 2,4-dibromofurans as model compounds for the assignment of the signals in the ^{13}C NMR spectra of the 2-aryl-3,5-dibromofurans and to estimate the influence of a bromine atom on the parameters of the ^{13}C spectra.

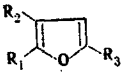
Table 4 gives the chemical shifts of the ^{13}C atoms of the furan nucleus and the direct spin-spin coupling constants $J_{^{13}CH}$ for unsubstituted furan, 2,3- and 2,4-dibromofurans, and 2-arylfurans.

An analysis of the figures in Table 4 relating to the model compounds shows that when two bromine atoms are present in the furan nucleus the signal of an α-C atom directly bound

TABLE 3. Calculated and Experimental Values of the Chemical Shifts of the Protons of the Furan Rings in the 2-Aryl-3,5-dibromofurans (IIIa-c)

Compound	Structure	Calculated chemical shifts, δ, ppm		Experimentally determined chemical shift of the proton, δ, ppm
		3-H	4-H	
IIIa	A	—	6,36	6,39
	B	6,65	—	
IIIb	A	—	6,37	6,39
	B	6,67	—	
IIIc	A	—	6,49	6,47
	B	6,96	—	

TABLE 4. ^{13}C Chemical Shifts and SSCCs in Furan, the Dibromofurans, and 2-Arylfurans



R_1	R_2	R_3	δ, ppm				$^1J_{\beta\text{-CH}}$, Hz
			2-C	3-C	4-C	5-C	
H	H	H	142,6	109,6	109,6	142,6	174,7
Br	Br	H	123,3	101,8	115,7	144,6	181,6
H	Br	Br	123,0	114,2	101,2	142,5	186,8
p-BrC_6H_4	H	H	153,2	105,7	111,8	142,4	*
p-BrC_6H_4	H	Br	155,1	107,9	113,6	122,1	181,6
p-ClC_6H_4	Br	Br	150,6	97,7	117,4	122,5	186,8
p-BrC_6H_4	Br	H	147,7	96,4	116,2	141,7	180,9

*$J_{3\text{-CH}}$ = 173.8 Hz; $J_{4\text{-CH}}$ = 175.5 Hz.

to a bromine atom shifts upfield by 20 ppm relative to the α-C signal in unsubstituted furan. In these circumstances, the signal of a substituted β-carbon atom shifts upfield by ~8 ppm and that of an unsubstituted β-carbon atom downfield by 5-6 ppm. The effect of substituents (bromine atoms) on $J_{\beta\text{-CH}}$ is shown in an increase of this constant when a bromine atom is present in a position adjacent to the given carbon atom. The presence of bromine atoms in both neighboring positions causes a further rise in the constant $J_{\beta\text{-CH}}$.

On assigning the signals to 3-C and 4-C in the 2-arylfurans, we made use of an analogy with benzene, in which an aryl substituent shifts upfield the signal of a carbon atom present in the ortho position to the substituent and downfield that of a carbon atom in the meta position to the substituent [3]. Accordingly, the signal at δ 105.7 ppm in a 2-arylfuran, shifted upfield relative to the signal at δ 109.6 ppm in unsubstituted furan, was assigned to the 3-C atom, and the signal at δ 111.8 ppm was assigned to the 4-C atom. The subsequent introduction of two bromine atoms in the α- and β-positions of the furan ring of a 2-arylfuran caused an upfield shift of the 5-C signal by ~20 ppm relative to the initial 2-arylfuran. As follows from Table 4, the signals of substituted and unsubstituted β-carbon atoms shift upfield and downfield, respectively, and the assignment of these signals to 3-C and 4-C corresponds to the structure of the 3,5-dibromo derivative and leads to complete correspondence between the change in the ^{13}C chemical shifts caused by the introduction of these bromine atoms into furan (Δδ = −8 and ~ +6 ppm) and into a 2-arylfuran (Δδ = −8 and +5.6 ppm). The opposite assignment of the two signals mentioned, corresponding to the structure of a 4,5-dibromo derivative, would lead to far greater discrepancy in the corresponding changes of the chemical shifts, which would amount to ~ −14 and +11.7 ppm for 2-arylfuran derivatives. It follows from this that the dibromo derivatives (IIIa-c) formed are, in accordance with what has been said above, 2-aryl-3,5-dibromofurans.

In harmony with this conclusion are the SSCC values $^1J_{\beta\text{-CH}}$ in the 2-aryl-3,5-dibromofurans (IIIa-c) and in 2,4-dibromofuran, which may be considered as a consequence of the similar mutual arrangement of the CH group and the bromine atoms in these compounds.

TABLE 5. Brominated 2-Arylfurans

Compound	mp, °C[a]	R_f	UV spectrum		Found, %			Empirical formula	Calculated, %			Yield, %
			λ_{max}	log ε	C	H	Br		C	H	Br	
IIa	83—85	0,79[b]	223 295	3,92 4,44	39,3	2,0		$C_{10}H_6Br_2O$	39,8	2,0		75
IIb	68,5—69	0.80[c]	222 293	3,93 4,46	46,5	2,3		$C_{10}H_6BrClO$	46,6	2,3		84
IIc	118,5—119,5	0,72[d]	242 352	3,95 4,26	44,7	2,3	30,2	$C_{10}H_6BrNO_3$	44,8	2,3	29,8	75
IIIa	94—95	0,90[d]			31,4	1,7	62,9	$C_{10}H_5Br_3O$	31,5	1,7	62,9	96
IIIb	73—74				35,6	1,6		$C_{10}H_5Br_2ClO$	35,7	1,5		77
IIIc	122—124	0,78[d]	238 345	4,00 4,27	34,3	1,4	46,3	$C_{10}H_5Br_2NO_3$[e]	34,6	1,4	46,1	77

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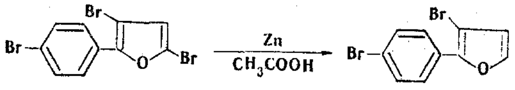
[a] Compounds (IIa) and (IIIa and b) were crystallized from methanol, and (IIb and c) and (IIIc) from ethanol. [b] In chloroform. [c] In a mixture of chloroform and hexane (1:1). [d] In benzene, [e] Found: N 3.6%. Calculated: N 4.0%.

We have effected the reduction of 3,5-dibromo-2-(p-bromophenyl)furan (IIIa) with zinc in acetic acid.



IIIa IV

The structure of the 3-bromo-2-(p-bromophenyl)furan (IV) so formed was shown with the aid of ^{1}H and ^{13}C NMR spectra (Tables 1-4). The fact that in compound (IV) the bromine atom is present in position 3 of the furan nucleus is an additional proof of the entry of the second bromine atom into position 3 of the furan ring in the bromination of a 2-aryl-5-bromofuran. This direction of electrophilic substitution is probably explained by the greater stability of the intermediate σ-complex because of better conditions of the delocalization of the charge on attack in position 3 than in position 4.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were taken on C-60HL (Jeol), XL-100 (Varian), and WH-90 (Bruker) instruments with $CDCl_3$ as solvent and TMS as internal standard.

The UV spectra were obtained in ethanol on a EP-3 spectrophotometer. TLC was performed on Silufol UV-254, and the spots were detected in UV light.

2-(p-Bromophenyl)furan (Ia). At 0-2°C, a solution of 13.8 g (200 mmole) of sodium nitrite in 20 ml of water cooled to 0°C was added to a solution of 34.4 g (154 mmole) of p-bromoaniline in 350 ml of 5% hydrochloric acid cooled to 0°C. The reaction mixture was stirred at 0°C for 30 min, and then a solution of 27.2 g (200 mmole) of zinc chloride in 100 ml of water cooled to 10°C was added and stirring was continued at 2-5°C for another 10 min. The precipitate that had deposited was combined with the distillate isolated from the mother liquor on salting out with sodium chloride. The combined precipitates were dried on the filter with suction at a water-jet pump for 2 h, and were added to 300 ml of furan. Then 2 g of caustic soda ground to a powder and 20 g of anhydrous sodium acetate were added to the reaction mixture. It was stirred at room temperature for 9 h, the furan was driven off, and then the 2-(p-bromophenyl)furan was distilled in a current of nitrogen. Yield 23.3 g (52%), mp 82-84°C (see [5]).

2-Bromo-5-(p-bromophenyl)furan (IIa). Over 2 h, 1.5 ml (29.2 mmole) of dry bromine in 11 ml of dry dichloroethane was added to a boiling solution of 5 g (22.4 mmole) of 2-(p-bromophenyl)furan in 14 ml of dry dichloroethane. The reaction mixture was boiled for 4 h, cooled, washed with saturated sodium bicarbonate solution, dried with calcined sodium sulfate, boiled with activated carbon, and evaporated in vacuum. The precipitate that deposited was filtered off and washed with petroleum ether. The bromofurans (IIb and c) (Table 5) were obtained similarly.

3,5-Dibromo-2-(p-bromophenyl)furan (IIIa). Over 2 h, 3.7 ml (73 mmole) of dry bromine in 29 ml of dry dichloroethane was added to a boiling solution of 8 g (35.9 mmole) of compound (Ia) in 27 ml of dry dichloroethane. The reaction mixture was boiled for 7 h cooled, washed with saturated sodium bicarbonate solution, dried with calcined sodium sulfate, and evaporated in vacuum, and the precipitate that had deposited was filtered off. The dibromofurans (IIIb and c) (Table 5) were obtained similarly. The same dibromofuran (IIIa) was obtained by brominating 4 g (13.2 mmole) of (IIa) in 7 ml of dry dichloroethane with 0.7 ml (13.2 mmole) of dry bromine in 6 ml of dry dichloroethane, mp 94-95°C. A mixture with the dibromo derivative obtained by the bromination of (Ia) showed no depression of the melting point.

3-Bromo-2-(p-bromophenyl)furan (IV). At 85°C, 4 g (10.4 mmole) of (IIIa) was added in portions to a mixture of 2.0 g (30.7 mmole) of zinc, 1.8 ml of acetic acid, and 5 ml of water. The reaction mixture was heated at 100-104°C for 4 h, cooled, treated with 20 ml of water, and extracted with ether; the ethereal extracts were washed with water, dried with sodium sulfate, and evaporated in vacuum. This gave 2 g (63%) of compound (IV); mp 53.5-54°C (from petroleum ether). Found: C 39.4; H 2.0; Br 52.9%. $C_{10}H_6Br_2O$. Calculated: C 39.8; H 2.0; Br 52.9%.

LITERATURE CITED

1. A. F. Oleinik, E. V. Adamskaya, K. Yu. Novitskii, N. P. Solov'eva, and E. M. Peresleni, Khim. Geterotsikl. Soedin., No. 1, 17 (1979).
2. G. Dana, P. Scribe, and J.-P. Girault, C. R., Ser. C, 275, No. 1, 49 (1972).
3. G. Levy and G. Nelson, Carbon-13 in Nuclear Magnetic Resonance for Organic Chemists, Wiley-Interscience, New York (1972).
4. F. W. Wehrli and T. Wirthlin, Interpretation of Carbon-13 NMR Spectra, Heyden, London (1965).
5. A. Johnson, J. Chem. Soc., No. 10, 895 (1946).