SYNTHESIS AND ELECTROPHILIC SUBSTITUTION REACTIONS OF 2-ARYL-3,4-BIS(CARBOMETHOXY)FURANS

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The thermal decomposition of the products of hydrogenation of the adducts obtained from arylfurans and dimethyl acetylenedicarboxylate leads to the formation of 2-aryl-3,4-bis(carbomethoxy)furans. The bromination of these compounds takes place in the 5 position of the furan ring; depending on the concentration of the nitric acid used, nitration leads to the formation of products of nitration in both the furan and the benzene rings.

β-Substituted furans are difficult to obtain, and relatively little study has been devoted to them. The introduction of substituents in the 3 and 4 positions when the 2 or 5 position of the furan ring is free cannot be accomplished by a direct method. Such compounds are obtained only by indirect methods, one of which is the diene synthesis, which makes it possible to pass from a furan through an adduct with dimethyl acetylenedicarboxylate to 3,4-disubstituted furans [1, 2].

Continuing our research on the synthesis and transformations of arylfurans [3] we investigated the possibility of the use of the latter as starting compounds in the synthesis of 2-aryl-3,4-bis(carboxymethoxy)furans. We have previously shown that 2-arylfurans with electron-donor substituents in the benzene ring readily undergo the diene synthesis with dimethyl acetylenedicarboxylate to give the corresponding adducts [3]. In the present research adducts of arylfurans with dimethyl acetylenedicarboxylate were subjected to hydrogenation in the presence of Pd/C, and dimethyl 3-aryl-3,6-endoxotetrahydro-4,5-phthalates (Ia-c) in quantitative yields.

Thermal decomposition of hydrogenation products I led to splitting out of ethylene and the formation of the previously undescribed 2-aryl-3,4-bis(carbomethoxy)furans (II). The structures of I and II were confirmed by data from the PMR spectra.

We studied the electrophilic substitution reactions of 2-aryl-3,4-bis(carbomethoxy)furans II in the case of nitration and bromination. The nitration and bromination of 2-arylfurans with free 3, 4, and 5 positions in the furan ring and electron-acceptor groups as substituents in the benzene ring were described in [4, 5]. In the examples described electrophilic monosubstitution took place in the 5 position of the furan ring.

In the present research 2-arylfurans (IIa-c) with electron-donor substituents in the benzene ring and with carbomethoxy groups in the 3 and 4 positions of the furan ring were subjected to nitration and bromination. It was established that the bromination of arylfurans IIa-c takes place in the 5 position of the furan ring to give 5-bromofurans IIIa-c.

The nitration of 2-aryl-3,4-bis(carbomethoxy)furans II with nitric acid in acetic anhydride proceeded via different pathways, depending on the nitric acid concentration. When a solution containing 18% nitric acid in acetic acid was used as the reagent for nitration, one nitro group was incorporated in the furan ring (IVa-c). In one case Va, which was formed as a result of incorporation of a nitro group in the ortho position relative to the acetamido group, was also obtained as a side product. (See top, following page.)

The use of a more concentrated solution of nitric acid in acetic anhydride (38% HNO_3) as the nitrating agent led to the incorporation of two nitro groups in the arylfuran molecule — one in the free α position of the furan ring and one in the benzene ring in the ortho position relative to the electron-donor substituent (VIa,b).

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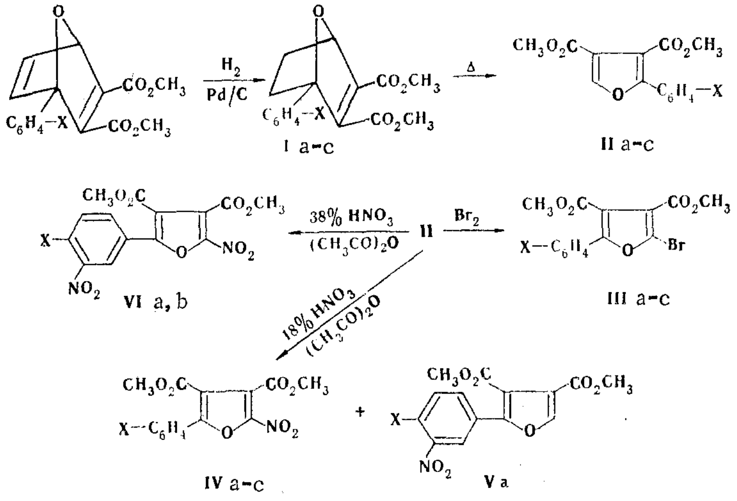

I–VI a X=NHCOCH$_3$-*p*; b X=OCH$_3$-*p*; c X=CH$_3$-*p*

The structures of bromination products III and nitration products IV-VI were proved by means of the PMR spectra.

EXPERIMENTAL

The PMR spectra of the compounds were recorded with a Varian XL-100 spectrometer with tetramethylsilane as the internal standard. Thin-layer chromatography (TLC) was carried out on Silufol UV-254 with development in UV light.

Dimethyl 3-(p-Acetamidophenyl)-3,6-endoxotetrahydro-4,5-phthalate (Ia). An 11.3-g (33 mmole) sample of the adduct obtained from the diene synthesis with p-acetamidophenylfuran and dimethyl acetylenedicarboxylate [3] was dissolved in 30 ml of acetone and hydrogenated at 20°C and atmospheric pressure in the presence of 9.1 g of 2% Pd/C until 740 ml (33 mmole) of hydrogen had been absorbed. The catalyst was removed by filtration, and the acetone was removed by distillation *in vacuo* to give 11.4 g (99%) of Ia with mp 124-126°C (dec., from benzene) and R_f 0.75 (ethyl acetate). PMR spectrum ($CDCl_3$), δ: $CH_2^{4,5}$ 1.40-2.40 m, $COCH_3$ 2.13 s, $COOCH_3^{1,2}$ 3.63 s, 3.81 s, CH 5.38, $J_{6,5} + J_{6,4}$ = 4.0 Hz, aromatic protons 7.36-7.62 ppm, NH 8.09 ppm. Found: C 62.6; H 5.4; N 4.0%. $C_{18}H_{19}NO_6$. Calculated: C 62.6; H 5.5; N 4.0%.

Dimethyl 3-(p-Anisyl)-3,6-endoxotetrahydro-4,5-phthalate (Ib). This compound, with mp 108-110°C [benzene–petroleum ether (1:1)] and R_f 0.6 (chloroform), was similarly obtained in 99% yield. PMR spectrum ($CDCl_3$), δ: CH_2 1.56-2.30 m, $COOCH_3^{1,2}$ 3.61 s, 3.79 s, OCH_3 3.80, CH 5.35, $J_{6,5} + J_{6,4}$ = 4.2 Hz, aromatic protons 6.80-7.50 m ppm. Found: C 64.2; H 5.7%. $C_{17}H_{18}O_6$. Calculated: C 64.2; H 5.7%.

Dimethyl 3-(p-Tolyl)-3,6-endoxotetrahydro-4,5-phthalate (Ic). This compound, with mp 63-64°C (from alcohol) and R_f 0.75 (chloroform), was obtained in 99% yield. Found: C 67.8; H 5.7%. $C_{17}H_{16}O_5$. Calculated: C 68.0; H 5.4%.

2-(p-Acetamidophenyl)-3,4-bis(carbomethoxy)furan (IIa). An 11.3-g sample of Ia was heated at 190-200°C *in vacuo* [26 mm (mercury column)] for 30 min, after which the residue was recrystallized. Furans IIb,c (Table 1) were similarly obtained.

2-(p-Acetamidophenyl)-3,4-bis(carboxymethoxy)-3,4-bis(carbomethoxy)-5-bromofuran (IIIa). A solution of 0.8 g (5 mmole) of bromine in 10 ml of dry dichloroethane was added dropwise in the course of an hour to a refluxing solution of 1.4 g (4.5 mmole) of IIa in 15 ml of dry dichloroethane, and the reaction mixture was heated in a boiling water bath for 4 h. It was then cooled, and the resulting precipitate was removed by filtration. Bromofurans IIIb,c (Table 1) were similarly obtained.

2-(p-Acetamidophenyl)-3,4-bis(carbomethoxy)-5-nitrofuran (IVa) and 2-(3-Nitro-4-acetamidophenyl)-3,4-bis(carbomethoxy)furan (Va). A solution of 1.9 ml of nitric acid (sp. gr. 1.4) in 17 ml of acetic anhydride was added dropwise to a cooled (to −2°C) solution of 1.9 g (6.2 mmole) of IIa in 11 ml of acetic anhydride, and the reaction mixture was stirred at 0°C for 2 h and then at 12°C for 1.5 h. The precipitated Va was removed by filtration (Table 1). The mother liquor was poured into 100 ml of ice water, and the aqueous mixture was neutralized

TABLE 1. 3,4-Bis(carbomethoxy)furans II-VI

Compound	mp,* °K	R_f†	PMR spectra,‡ δ, ppm						Found, %				Empirical formula	Calculated, %				Yield, %
			H^5	$COOCH_3$	OCH_3 (CH_3)	$COCH_3$	NH	aromatic protons	C	H	Br	N		C	H	Br	N	
IIa	178—180	0,50	8,40	3,85, 3,91		2,14	10,20	7,60—7,88	60,8	4,7	—	4,7	$C_{16}H_{15}NO_6$	60,6	4,7	—	4,4	66
IIb	72—75	0,63	7,89	3,81, 3,83	3,88	—	—	6,80—7,70	62,0	4,8	—	—	$C_{15}H_{14}O_6$	62,0	4,8	—	—	60
IIc	101—103	0,68	—	—	—	—	—	—	65,6	5,2	—	—	$C_{15}H_{14}O_5$	65,7	5,2	—	—	63
IIIa	206—208	0,55	—	3,89, 3,90	—	2,13	10,25	7,60—7,90	48,1	3,5	20,2	3,5	$C_{16}H_{14}BrNO_6$	48,5	3,5	20,2	3,5	67
IIIb	108—111	0,99	—	3,83, 3,86	3,88	—	—	6,80—7,70	49,3	3,6	—	—	$C_{15}H_{13}BrO_6$	48,8	3,5	—	—	70
IIIc	84—86	0,87	—	—	—	—	—	—	50,7	3,7	22,2	—	$C_{15}H_{13}BrO_5$	51,0	3,7	22,6	—	64
IVa	202—204	0,55	—	3,82, 4,02	—	2,16	10,41	7,80—8,10	53,5	4,0	—	7,6	$C_{16}H_{14}N_2O_8$	53,0	3,9	—	7,7	47
IVb	139—141	0,25	—	3,86, 3,89	4,02	—	—	6,95—8,06	53,9	4,1	—	4,2	$C_{15}H_{13}NO_8$	53,8	3,9	—	4,2	58
IVc	117—118	0,95	—	3,88, 4,02	2,44	—	—	7,39—7,99	56,5	4,2	—	4,4	$C_{15}H_{13}NO_7$	56,5	4,1	—	4,4	18
Va	176—179	0,84	8,54	3,86, 3,94	—	2,23	10,51	7,98—8,40	53,3	4,1	—	7,7	$C_{16}H_{14}N_2O_8$	53,0	3,9	—	7,7	10
VIa	174—176	0,72	—	3,89, 4,01	—	2,24	10,58	8,31—8,83	47,4	3,5	—	10,2	$C_{16}H_{13}N_3O_{10}$	47,2	3,2	—	10,3	72
VIb	147—149	0,10	—	3,90, 4,03	4,1	—	—	7,61—8,71	47,7	3,3	—	7,2	$C_{15}H_{12}N_2O_{10}$	47,4	3,2	—	7,4	69

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*The compounds were crystallized: IIb,c, IIIa-c, and IVb,c from alcohol, IIa and VIb from ethyl acetate, IVa from dichloroethane, and Va and VIa from benzene.

†The following solvents were used: ethyl acetate for IIa, IIIa,b, and Va, chloroform for IIb, and benzene for IIc, IIIc, IVa-c, and VIa,b.

‡The following solvents were used: d_6-DMF for IIb and $CDCl_3$ for IIb and IIIb.

with sodium bicarbonate and extracted with ethyl acetate. The extract was washed successively with a saturated solution of sodium bicarbonate and water until the wash water was neutral, after which it was dried with magnesium sulfate. The ethyl acetate was removed by distillation *in vacuo*, and the residue was recrystallized to give IVa. Nitrofurans IVb,c (Table 1) were similarly obtained.

2-(3-Nitro-4-acetamidophenyl)-3,4-bis(carbomethoxy)-5-nitrofuran (VIa). A 1.3-ml sample of nitric acid (sp. gr. 1.4) was added dropwise with stirring to 5 ml of cooled (to −5°C) acetic anhydride, 1.4 g (4.5 mmole) of IIa was added in portions at 0°C to the resulting solution, and the reaction mixture was stirred at this temperature for 3 h. The resulting precipitate was removed by filtration. Dinitrofuran VIb (Table 1) was similarly obtained.

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REACTIONS OF HETEROCYCLIC CATIONS WITH NITROGEN-CONTAINING NUCLEOPHILES.

10.[*] SYNTHESIS OF 3,5,7-TRIARYL-1,2-OXAZEPINIUM PERCHLORATES BY THE REACTION OF 2,4,6-TRIARYLPYRYLIUM SALTS WITH NITRONES AND SUBSTITUTED HYDROXYLAMINES

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2-Substituted 3,5,7-triaryl-1,2-oxazepinium perchlorates were obtained by the reaction of 2,4,6-triarylpyrylium salts in dimethylformamide with nitrones and N-arylhydroxylamines. The products are the first representatives of seven-membered cations with eight π electrons.

We have studied the reaction of 2,4,6-triarylpyrylium salts (I) in dimethylformamide (DMF) with nitrones II, which are 1,3-bipolar compounds [2], as a result of which we obtained 2-substituted 3,5,7-triaryl-1,2-oxazepinium salts (III) – the first representatives of seven-membered cations with eight π electrons.

The mechanism of the reaction of pyrylium salts with various nucleophiles has been thoroughly studied [3-5]. On the basis of this mechanism it may be assumed that the oxide center of the nitrone molecules with its increased electron density [6] attacks the 2 position of the pyrylium ring. The positively charged carbon atom probably reacts with the electronegative oxygen atom in intermediates IV and V, which may exist in equilibrium. This is confirmed by the formation of benzaldehyde in the reaction. The subsequent cyclization of V should proceed via scheme A or B. Alternative pathway B is not realized, since bands that are characteristic for the $C\equiv C$ bond and the NH group of expected perchlorate VI are absent in the IR spectra of the products. However, the structure of VII (which could have been obtained from salts VI by splitting out of phenylacetylene) must be excluded from the results of elementary analysis.

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[*] See [1] for Communication 9.

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