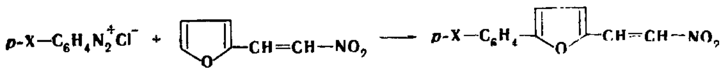
ARYLATION OF FURAN DERIVATIVES VIA THE MEERWEIN REACTION

A. F. Oleinik, G. A. Modnikova, T. I. Vozyakova,
E. N. Burgova, and K. Yu. Novitskii

UDC 724.2

Meerwein arylation of 2-arylfurans and 2-furylnitroethylene gave 2,5-diarylfurans and 5-aryl-2-furylnitroethylenes. Meerwein arylation of 2-acylfurans gives 2,5-diarylfurans and substituted azobenzenes in addition to 2-acyl-5-arylfurans.

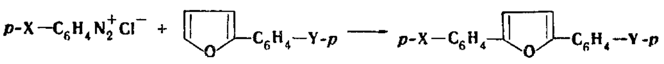
Continuing our research on Meerwein arylation of furan derivatives [1], we have studied the behavior of furan derivatives with electron-acceptor substituents in the 2 position in this reaction. It was found that 2-furylnitroethylene is arylated under the conditions of the Meerwein reaction to give 5-aryl-2-furylnitroethylenes. The entry of the aryl residue into the 5 position of the furan ring of furylnitroethylene was confirmed by conversion of the 5-arylfurylnitroethylenes to the corresponding furylethylamines.



I a-c

a $X=Br$; b $X=Cl$; c $X=NO_2$

We have shown that 2-arylfurans undergo arylation under the conditions of the Meerwein reaction only in those cases in which there are electron-acceptor substituents in the benzene ring of these compounds. Arylation does not take place when the benzene ring of the starting arylfuran is unsubstituted or when an electron-donor substituent is present in the benzene ring.



II a-d

II a $X=Br$, $Y=Cl$; b $X=Br$, $Y=NO_2$; c $X=Cl$, $Y=NO_2$; d $X=NO_2$, $Y=NO_2$

The use of the method for the arylation of 2-arylfurans examined here makes it possible to also obtain unsymmetrical 2,5-diarylfurans with different residues in the benzene rings in addition to the symmetrical 2,5-diarylfuran, which have already been synthesized by other methods [2, 3].

As in the case of 2-acetylfuran [1], 2,5-diarylfurans (IV) and substituted chlorobenzenes V are formed in addition to the chief reaction products — 5-aryl-2-acylfurans (III) — in the acylation of 2-propionyl- and 2-n-butyrylfuran. The substituted chlorobenzenes (V) are the usual side products of the Meerwein reaction. The formation of substituted azobenzenes VI was a novel result for the reaction under consideration.

The side formation of azobenzenes in the Meerwein reaction was not observed in the arylation of furan derivatives but has been described in the case of arylation of unsaturated compounds [4].

S. Ordzhonikidze All-Union Scientific-Research Pharmaceutical-Chemistry Institute, Moscow. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 452-456, April, 1975. Original article submitted August 8, 1973.

TABLE 1. 2,5-Diarylfurans

Compound	X	Y	mp, °C	Empirical formula	Found, %			Calc., %			PMR, δ, ppm^f		Yield, %
					C	H	N	C	H	N	3-*H*	4-*H*	
IIa	Br	Cl	181—183^a	$C_{16}H_{10}BrClO$	57,4	3,2		57,6	3,0		7,08s	7,08s	15
IIb	Br	NO_2	180—182^b	$C_{16}H_{10}BrNO_3$	55,6	2,9	4,1	55,8	2,9	4,1			31
IIc	Cl	NO_2	175,5—177^{b,c}	$C_{16}H_{10}ClNO_3$	63,8	3,4		64,1	3,4		7,15d	7,36d^e	32
IId^3	NO_2	NO_2	266—267^d	$C_{16}H_{10}N_2O_5$	61,6	3,3	9,1	61,9	3,2	9,0	7,48s	7,48s	19

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[a] From ethanol. [b] From dimethylformamide, R_f 0.70 (yellow spot).
[c] Found: Cl 11.6%. Calculated: Cl 11.8%. [d] From acetone. [e] $J_{3,4}$ = 3.5.
[f] In deuterodimethyl sulfoxide; s is singlet and d is doublet.

TABLE 2. 5-Aryl-2-acylfurans

Compound	X	R	bp, °C	mp, °C (from petroleum ether)	R_f	Empirical formula	Found, %			Calculated, %			IR spectrum (CO, cm-1)	UV spectrum^b		Yield, %^{c}
							C	H	halogen	C	H	halogen		λ_{max}, nm	lg ε	
IIIa	Br	C_2H_5	160—162 (10 mm)	85—86	0,55 [chloroform—petroleum ether (2:1)]	$C_{13}H_{11}BrO_2$	55,9	4,0	28,7	55,9	4,0	28,6	1665	323; 225	4,49; 4,14	34
IIIb	Cl	C_2H_5	157—160 (2 mm)	67—69		$C_{13}H_{11}ClO_2$	66,6	4,7	15,0	66,5	4,7	15,1	1675	323; 225	4,45; 4,15	44
IIIc	NO_2	C_2H_5		135—136^a	0,56 (chloroform)	$C_{13}H_{11}NO_4$	63,3	4,5		63,6	4,5		1680	324; 226	4,48; 4,19	27
IIId	Br	C_3H_7	175—180 (6 mm)	102—103,5	0,66 [chloroform—petroleum ether (1:1)]	$C_{14}H_{13}BrO_2$	57,3	4,4	27,3	57,3	4,5	27,3	1660	324; 225	4,47; 4,13	23
IIIe	Cl	C_3H_7	147—150 (6 mm)	90,5—91,5		$C_{14}H_{13}ClO_2$	67,6	5,3	14,3	67,6	5,3	14,3	1660	324; 226	4,48; 4,19	28

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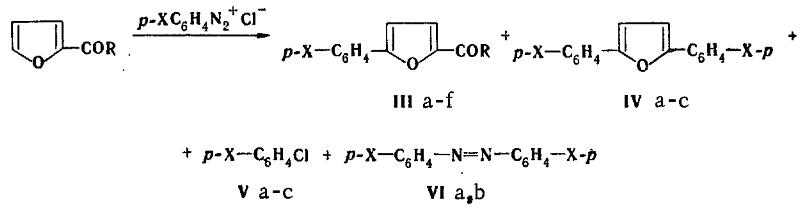
[a] From ethyl acetate. [b] In ethanol. [c] Based on the converted 2-acylfuran.

It is interesting to note that the yields of 5-aryl-2-acylfurans decrease as the alkyl chain of the acyl residues is lengthened; replacement of the halogen in the benzene ring of the diazonium salt by a nitro group has the same effect (see Table 2). 2-Butyryl-5-(p-nitrophenyl)furan (IIIf) was not obtained at all under our conditions, whereas 2,5-diarylfurans (IVa-c) were formed in all cases of arylation of acylfurans. Substituted azobenzenes VI were isolated in the halogenation of acylfurans, but their formation was not observed during nitrophenylation of these compounds. The separation of mixtures of diarylfurans IV and azobenzenes VI presented certain difficulties in view of the closeness of their physical properties (melting points, solubilities, and chromatographic mobilities). The composition of these mixtures was established by means of their mass spectra.



III a-f IV a-c

V a-c VI a,b

III-VI a $R=C_2H_5$, X=Br; b $R=C_2H_5$, X=Cl; c $R=C_2H_5$, $X=NO_2$; d $R=C_3H_7$, X=Br; e $R=C_3H_7$, X=Cl; f $R=C_3H_7$, $X=NO_2$

EXPERIMENTAL METHOD

The PMR spectra were recorded with a C-60 JEOL spectrometer with tetramethylsilane as the internal standard. The IR spectra of mineral-oil suspensions of the compounds were recorded with a Perkin-Elmer 457 spectrometer. The UV spectra were obtained with a Hitachi spectrophotometer. The mass spectra were obtained with an LKV-9000 mass spectrometer. Thin-layer chromatography (TLC) was carried out on Silufol UV-254 silica gel with development in UV light.

1-[α'-(p-Bromophenyl)-α-furyl]-2-nitroethylene (Ia). A solution of 34.7 g (250 mmole) of 1-(α-furyl)-2-nitroethylene in 150 ml of acetone and a solution of 5 g of cupric chloride in 10 ml of water were added to a solution of 250 mmoles of p-bromobenzenediazonium chloride in 125 ml of water, after which the mixture was stirred at 40° for 30 min and at 20-25° for 4 h. It was then diluted with 500 ml of water, and the resulting precipitate was removed by filtration and washed with ethanol to give 28 g (38%) of Ia with mp 181.5-182.5° (from acetone). Found: C 49.1; H 2.7; N 5.0%. $C_{12}H_8BrNO_3$. Calculated: C 49.0; H 2.7; N 4.8%. PMR spectrum (in deuteropyridine): 6.91 (3H, d*), 7.03 (4H, d), and 7.84 ppm (CH=CH, q).

1-[α'-(p-Chlorophenyl)-α-furyl]-2-nitroethylene (Ib). This compound, with mp 164-164.5° (from acetone), was obtained similarly in 38% yield. Found: C 57.8; H 3.2; Cl 14.0; N 5,7%. $C_{12}H_8ClNO_3$. Calculated: C 57.7; H 3.2; Cl 14.2; N 5.6%. PMR spectrum in deuteropyridine: 6.91 (3H, d), 7.00 (4H, d), and 7.81-7.91 ppm (CH=CH, q).

1-[α'-(p-Nitrophenyl)-α-furyl]-2-nitroethylene (Ic). This compound, with mp 234-236° (from acetone), was similarly obtained in 32% yield. Found: C 55.5; H 3.0; N 10.2. $C_{12}H_8N_2O_5$. Calculated: C 55.4; H 3.1; N 10.7%. PMR spectrum (in deuterodimethylformamide), 7.34 (3,4H, q) and 8.22 ppm (CH=CH, q).

1-Amino-2[α'-(bromophenyl)-α-furyl]ethane Picrate. A solution of 1.4 g (5 mmole) of Ia in 20 ml of absolute ether was added to 10 ml of 1 M lithium aluminum hydride solution, and the mixture was refluxed and stirred for 8 h. The resulting complex was decomposed with 2.7 g of potassium sodium tartrate in 13 ml of water, the mixture was stirred for 1.5 h, the ether layer was separated, and the aqueous layer was extracted with ether. The extract was dried and vacuum evaporated, and the residual oil was treated with an ether solution of picric acid to give 1.5 g (65%) of 1-amino-2-[α-(p-bromophenyl)-α-furyl]ethane picrate with mp 192.5-193.5° (from alcohol). Found: C 43.7; H 3.0; N 11.5%. $C_{18}H_{15}BrN_4O_8$. Calculated: C 43.7; H 3.0; N 11.3%. PMR spectrum (in deuterodimethylformamide): 6.41 (3H, d), 6.91 (4H, d), 3.10

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*The following abbreviations are used here and subsequently; s is singlet, d is doublet, t is triplet, and q is quartet.

(CH_2, t), and 3.60 ppm (CH_2, t).

1-Amino-2-[α'-(p-chlorophenyl)-α-furyl]ethane Picrate. This compound, with mp 193-195° (from alcohol), was similarly obtained. Found: C 47.9; H 3.4; N 12.4%. $C_{18}H_{15}ClN_4O_8$. Calculated: C 47.9; H 3.3; N 12.4%.

2-(p-Chlorophenyl)-5-(p-bromophenyl)furan (IIa). A 5-g (28 mmole) sample of 2-(p-chlorophenyl)furan [5] in 40 ml of acetone and a solution of 0.6 g of cupric chloride in 2 ml of water were added to a solution of 28 mmole of p-bromobenzenediazonium chloride in 15 ml of water, after which the mixture was stirred at 20-25° for 4 h. Water (100 ml) was added, and the resulting precipitate was removed by filtration and washed with water and petroleum ether. Diarylfurans IIb-d were similarly obtained (see Table 1).

2-(p-Chlorophenyl)-5-(p-anilino)furan. Hydrazine hydrate (8 ml) and 1 g of Raney nickel were added to a solution of 1 g (3.3 mmole) of IIc in 100 ml of butanol, and the solution was heated at 90° for 3 h. It was then cooled, the catalyst was removed by filtration, and the solvent was removed by vacuum distillation. The residue was recyrstallized from ethanol to give 0.7 g (78%) of 2-(p-chlorophenyl)-5-(p-anilino)furan with mp 180-182°. Found: C 71.1; H 4.5; Cl 13.1%. $C_{16}H_{12}ClNO$. Calculated: C 71.2; H 4.5; Cl 13.1%.

Reaction of p-Bromobenzenediazonium Chloride with 2-Propionylfuran. A solution of 18 g (140 mmole) of 2-propionylfuran [6] in 15 ml of acetone and a solution of 3.2 g of cupric chloride in 6.5 ml of water were added to a solution of 140 mmole of p-bromobenzenediazonium chloride in 73 ml of water, after which the mixture was stirred at 20-25° for 4 h. Water (500 ml) was added, and the resulting precipitate was removed by filtration. The filtrate was extracted with ether, and the extract was dried with sodium sulfate and distilled to give 4.7 g of unchanged 2-propionylfuran, 13.3 g of 1-bromo-4-chlorobenzene (Va) (mp 65-66°), and 10.2 g of 5-(p-bromophenyl)-2-propionylfuran (IIIa) (see Table 2). The precipitate that formed after water was added to the reaction mixture was washed with water and petroleum ether to give 9.6 g of a mixture of 2,5-di(p-bromophenyl)furan (IVa) and 4,4'-dibromoazobenzene (VIa); R_{fIVa}* 0.677 (fluorescence) and R_{fVIa} 0.673 (absorption) [chloroform–petroleum ether (1:1)]. Mass spectrum of a mixture of IVa and VIa: M_{IVa}^{+} with m/e 376/378/380 (the distribution of the peak intensities indicates the presence of two bromine atoms in the compound), ion peak with m/e 155/157 ($M-C_4H_2OC_6H_6Br$), M_{VIa}^{+} with m/e 338/340/342 (the splitting of the peak intensities indicates the presence of two bromine atoms in the compound), ion peaks with m/e 155/157 ($M-N_2C_6H_4Br$), and ion peaks with m/e 183-185 ($M-C_6H_4Br$).

Reaction of p-Chlorobenzenediazonium Chloride with 2-Propionylfuran. This reaction was carried out as described above. A total of 23.5 g of unchanged 2-propionylfuran was isolated from the reaction with 40 g (320 mmole) of 2-propionylfuran. Workup also gave 12.5 g of 1,4-dichlorobenzene (Vb) with mp 53-54°, 14.62 g of 5-(p-chlorophenyl)-2-propionylfuran (IIIb) (see Table 2), and 0.43 g of a mixture of IVb and VI; R_{fIVb} 0.81 (fluorescence) and R_{fVIb} 0.80 (absorption) [chloroform–petroleum ether (2:1)]. Repeated crystallization of the mixture of IVb and VIb from ethanol gave 0.19 g of 4,4'-dichloroazobenzene (VIb) with mp 183-185° (mp 183-184° [7]). Mass spectrum of azobenzene VIb: M^{+} 250/252/254 (the distribution of the peak intensities indicates the presence of two chlorine atoms in the compound). Ion peaks with m/e 111/113 ($M-N_2C_6H_4Cl$), and ion peaks with m/e 139/141 ($M-C_6H_4Cl$).

Reaction of p-Nitrobenzenediazonium Chloride with 2-Propionylfuran. This reaction was carried out as described above. A total of 10.5 g of unchanged 2-propionylfuran was isolated from the reaction of 20 g (160 mmole) of 2-propionylfuran, and workup gave 6.7 g of 1-nitro-4-chlorobenzene (Vc, mp 75-77°), 4.98 g of 5-(p-nitrophenyl)-2-propionylfuran (IIIc) (see Table 2), and 0.66 g (2.8%) of 2,5-di(p-nitrophenyl)furan (IVc) with mp 264-266° (from acetone) (mp 275-277° [3]) and R_f 0.59 (chloroform, fluorescence). Mass spectrum of diarylfuran IVc: M^{+} with m/e 310, 280 ($M-NO$), 264 ($M-NO_2$), 234 ($M-NO_2-NO$), 218 ($M-2NO_2$), and 189 ($M-C_6H_4NO_2$).

Reaction of p-Bromobenzenediazonium Chloride with 2-n-Butyrylfuran. This reaction was carried out as described above. Workup of the reaction mixture obtained from 40 g (290 mmole) of 2-n-butyrylfuran [6] gave 10.4 g of unchanged 2-n-butyrylfuran, 20.9 g of 1-chloro-4-bromobenzene (Va), 14.3 g of 5-(p-bromophenyl)-2-n-butyrylfuran (IIIb) (see Table 2), and 1.2 g of a mixture of 2,5-di(p-bromophenyl)furan (IVa) and 4,4'-dibromoazobenzene (VIa) with

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*Compound IVa, which has a known structure, served as the reference spot.

$R_{f\,IVa}$ 0.677 (fluorescence) and $R_{f\,VIa}$ 0.673 (absorption)[chloroform — petroleum ether (1:1)].

Reaction of p-Chlorobenzenediazonium Chloride with 2-n-Butyrylfuran. This reaction was carried out as described above. Workup of the reaction mixture obtained from 40 g (290 mmole) of 2-n-butyrylfuran gave 11.2 g of unchanged 2-n-butyrylfuran, 22.2 g of 1,4-dichlorobenzene (Vb), 14.3 g of 5-(p-chlorophenyl)-2-n-butyrylfuran (IIIe) (see Table 2), and 0.3 g of a mixture of IVb and VIb with $R_{f\,IVb}$ 0.81 (fluorescence) and $R_{f\,VIb}$ 0.80 [absorption, chloroform—petroleum ether (2:1)]. Repeated cyrstallization of the mixture from acetone gave 0.2 g of 4,4'-dichloroazobenzene (VIb), with mp 185-186°.

Reaction of p-Nitrobenzenediazonium Chloride with 2-n-Butyrylfuran. This reaction was carried out as described above. Workup of the reaction mixture obtained from 20 g (145 mmole) of 2-n-butyrylfuran gave 11.2 g of unchanged 2-n-butyrylfuran, 11.7 g of 1-nitro-4-chlorobenzene (Vc), and 0.6 g (3%) of 2,5-di(p-nitrophenyl)furan (IVc) with mp 264-266°. No melting-point depression was observed for a mixture of diarylfuran IVc with a genuine sample. The product had R_f 0.59 (chloroform, fluorescence). A change in the reaction conditions (temperatures up to 40° and pH values from 1 to 3) did not change the yields of reaction products (the reaction was accompanied by resinification).

The authors thank N. P. Solov'eva, O. S. Anisimova, and A. I. Ermakov for recording the PMR and mass spectra and for the interest they displayed with respect to the present research.

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