THE PREPARATION AND MASS SPECTRA OF SUBSTITUTED 2-X-(4-CHLOROPHENYL)FURAN DERIVATIVES. RELATIVE REACTIVITY OF FURAN DERIVATIVES IN RADICAL AROMATIC SUBSTITUTION*

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The arylation of the substituted 2-X-furan derivatives, where X is H, CH_3, C_2H_5, $COCH_3$, $COOCH_3$, CHO, CN, and CH_2OH with 4-chlorophenyl radical generated by the aprotic diazotization of 4,4'-dichlorodiazoaminobenzene with isopentyl nitrite is described in this work. Competitive experiments were carried out to obtain the values of the relative reactivity of furan derivatives. The structure of prepared furan derivatives was proved by ^1H-NMR and mass spectrometry.

In our previous paper[1] we described the arylation of furan with aryl radical generated by the aprotic diazotization of diazoaminobenzene derivatives with isopentyl nitrite. The aim of this work is to generalize this arylation method to monosubstituted derivatives of furan and to determine their reactivity with respect to furan itself. From the above reason we studied the reaction of substituted 2-X-furan derivatives, where X is CH_3, C_2H_5, CH_3CO, CN, and CH_2OH with 4-chlorophenyl radical formed on the aprotic diazotization of 4,4'-dichlorodiazoaminobenzene with isopentyl nitrite. Only the preparation of 2-X-5-(4-chlorophenyl)furan derivatives by Meerwein arylation for X is CHO (63% yield)[2], CH_3CO (52% yield)[3], $COOCH_3$ (11% yield)[4,5], and by Gomberg arylation for X is CH_3 (30% yield)[6] have been reported earlier. The arylation of substituted 2-X-furan derivatives with X is CN, C_2H_5, and CH_2OH has yet not been described.

Substituted 5-(4-chlorophenyl)-2-X-furan derivatives *II*–*V* were prepared by the arylation of corresponding furan derivatives with 4,4'-dichlorodiazoaminobenzene and isopentyl nitrite in 44–66% yields. The fact, that this method is not restricted only to substituted furan derivatives bearing electron withdrawing substituents and is therefore of general purpose, favours it over other methods used until now. Except of 2-formyl- or 2-acetylfuran this method affords even higher yields than that of Meerwein, which is the most apparent for 2-methoxyfuran. Anomalous course of the

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arylation was observed for 2-hydroxymethylfuran when bis[5-(4-chlorophenyl)-2-furyl]methane was produced instead of the expected 5-(4-chlorophenyl)-2-hydroxymethylfuran.

From the ^{1}H-NMR and mass spectra it turns out that 4-chlorophenyl radical enters position 5 of all monosubstituted furan derivatives. The values of chemical shifts and coupling constants given in Table I are typical for substituted 2,5-furan derivatives[7]. The position of the center of aromatic proton multiplet δ(A,A',B,B',4 H) and also the position of furan proton δ(3 H) depend on the substituent attached to furan at position 2, both being increased by the electron withdrawing substituents and vice versa. Mass spectra (Fig. 1 and 2) of compounds studied (Table I) show very intensive peaks belonging to the molecular ions. These are dominant peaks in spectra of compounds *I*, *II*, *V*, *VI*. Common feature of fragmentation of all the compounds

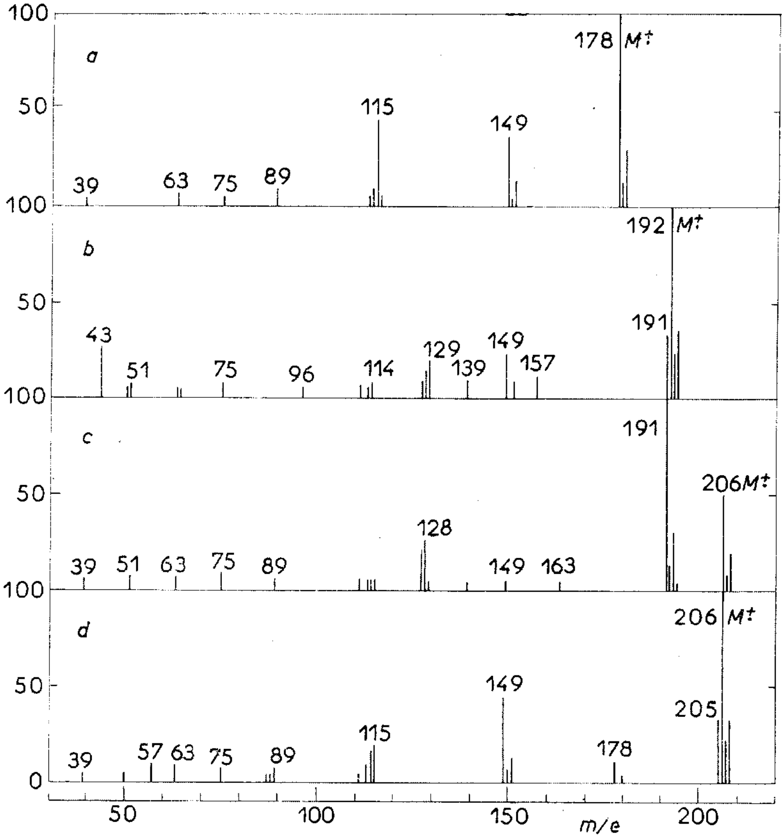


FIG. 1

Mass Spectra of Compounds *I* (*a*), *II* (*b*), *III* (*c*), *VI* (*d*)

TABLE I

^{1}H-NMR and Mass Spectra of the Substituted 2-X-5-(4-Chlorophenyl)furan Derivatives

Number	X	δ3 H^a	δ4 H	$J_{3,4}$^{b}	δ^c	δX	M^d
I	H	6·53(d,d)	6·35(d,d)	3·5	7·36(m)	7·34(d,d) $J_{4,5}$ = 1·54 $J_{3,5}$ = 0·5	178
II	CH_3	5·93(d)	6·40(d)	3·3	7·31(m)	1·27(s)	192
III	C_2H_5	5·96	6·43(d)	3·3	7·32(m)	CH_3 = 1·17(t) CH_2 = 2·62(q) J_{CH_2,CH_3} = 7	206
IV	$COCH_3$	7·15(d)	6·68(d)	3·6	7·48(m)	2·43(s)	220
V	$COOCH_3$	7·13(d)	6·61(d)	3·6	7·43(m)	3·82(s)	236
VI	CHO	7·21(d)	6·73(d)	3·7	7·45(m)	9·54(s)	206
VII	CN	7·05(d)	6·61(d)	3·6	7·43(m)		203

^{a} s Singlet, d doublet, t triplet, q quadruplet, m multiplet, chemical shifts in p.p.m. units; ^{b} coupling constants in Hz; ^{c} center of aromatic multiplet; ^{d} molecular ion.

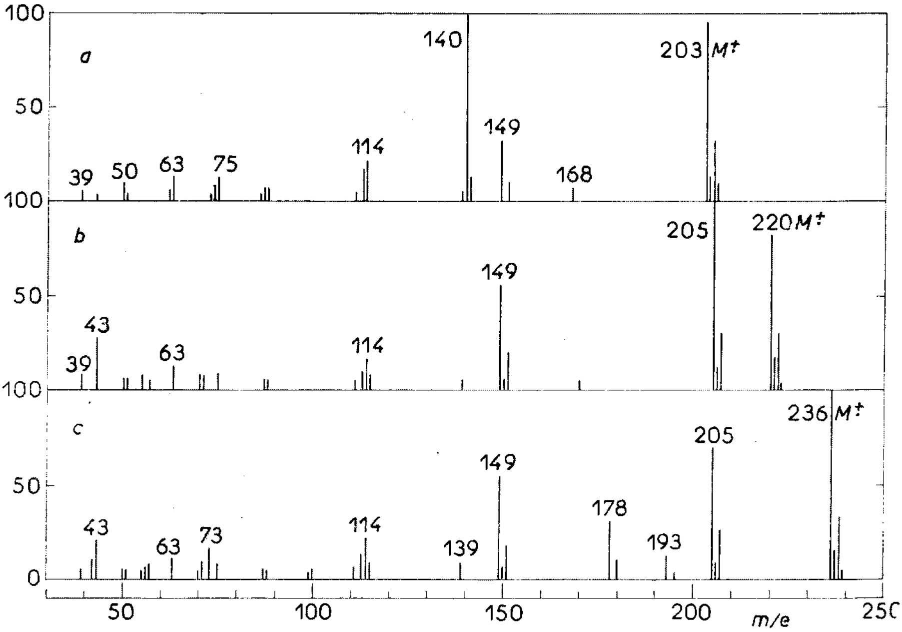
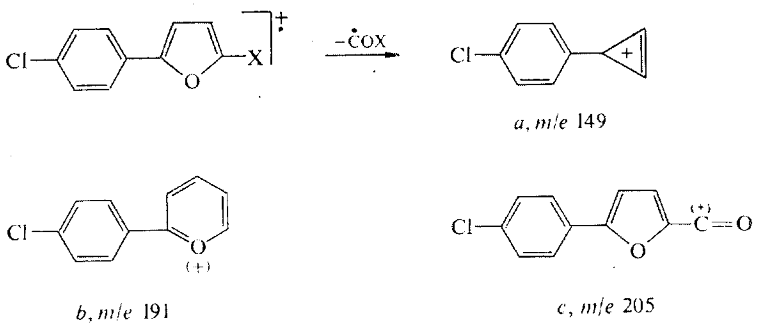
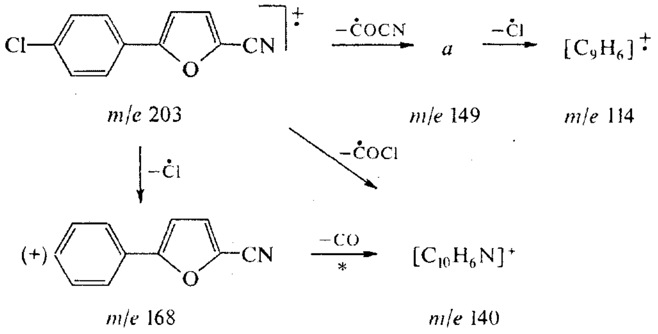


FIG. 2

Mass Spectra of Compounds *VII* (*a*), *IV* (*b*), *V* (*c*)



SCHEME 1



SCHEME 2

I; X = H
II; X = CH$_3$
III; X = C$_2$H$_5$
IV; X = COCH$_3$

V; X = COOCH$_3$
VI; X = CHO
VII; X = CN

is the formation of the ion *a* with *m/e* 149 (Scheme 1). Formation of other charged fragments depends on the nature of the substituent X. Intensive fragments arise from the cleavage of single bond in β-position to furan ring. Ion *b* with *m/e* 191, formed in the case of compounds *II* and *III* by the fission of H$^\bullet$, resp. CH$_3^\bullet$ fragments, may have structure of the substituted pyrilium ion. Similar situation was encountered in the case of fragmentation of alkylfuranes[8]. Formation of fragment *c* (one of the possible structures) with *m/e* 205 in the case of compounds *IV*–*VI* we ascribe to the splitting of H$^\bullet$, CH$_3^\bullet$, or OCH$_3^\bullet$ fragments from the molecular ions. Cleavage of fragments CO and Cl$^\bullet$ from the molecular ion of compound *VII* (Scheme 2) leading to fragment with m/e 140 was confirmed by both the presence of the metastabile ion (m = 96·5) and technique described by Jennings[9]. Analogous splitting occurs also with compound *I*, in which case cleavage of CO + Cl$^\bullet$ fragments leads to ion $(C_9H_7)^+$ with m/e 115.

Our further interest was concentrated in the effect of the substituents at position 2 on radical aromatic substitution of the substituted 2-X-furan derivatives by 4-chlorophenyl radical. Relative reactivity k_{rel} was determined by the method of competitive reactions[10]. The arylation of large excess of equimolar amounts of furan substituted 2-X-furan derivative was carried out and k_{rel} was calculated from the equation

$$k_{rel} = \text{mol}[I]/\text{mol}[X] .$$

In order to determine the amounts of the products of the arylation, the reaction mixture was analysed by gas chromatography. As it follows from the results given in Table II, the most reactive of all the derivatives is 2-formylfuran.

EXPERIMENTAL

Mass spectra of all the compounds were recorded with MS 902 S spectrometer using direct inlet system, 70 eV ionizing source energy, trap current 100 A, and temperature of the ion source 110°C. ^{1}H-NMR spectra were recorded with Tesla BS 487 C spectrometer (80 MHz) using hexamethyldisiloxane as internal standard. Concentration of all samples in $CDCl_3$ was 0·2 M. Gas–liquid chromatography measurement was carried out on Hewlett-Packard 7620 A instrument equipped with two 2432 × 2 mm columns filled with 10% UCW-98 on Chromosorb P, and FID detector working at 270°C. The Hewlett–Packard system of integrator-calculator directly

TABLE II

Relative Reactivity k_{rel} of the Substituted 2-X-Furan Derivatives Based on Reactivity of Furan

X	Product ratio[a]	Retention time[b]	k_{rel}
CH_3	2·02	3·87	1·87
C_2H_5	2·21	5·11	1·90
$COCH_3$	1·40	9·98	1·13
$COOCH_3$	3·55	11·39	2·67
CHO	3·63	8·04	3·14
CN	1·05	6·82	0·92

[a] Ratio of weight amounts of products of the arylation of furan derivative and furan; it represents the average of at least three measurements. [b] Retention time of the product corresponding to the substituted furan, (retention time of the product corresponding to furan amounts to 2·83 min).

connected with GC instrument was used for quantitative measurement. The content of the individual products in the reaction mixture was determined by the method of external standard and the values of retention time are given based on that of compound *I*. Furan, 2-methylfuran, 2-formylfuran, and 2-hydroxymethylfuran were commercial chemicals, distilled before use. 2-Acetylfuran was prepared by the acetylation of furan[11], 2-ethylfuran was obtained by Kizner--Wolf reduction of 2-acetylfuran[12]. 2-Carbmethoxyfuran was prepared by the esterification of 2-furancarboxylic acid[13] and synthesis of 2-cyanofuran was performed according to ref.[14].

5-(4-Chlorophenyl)-2-furan Derivatives

Mixture of 4,4'-dichlorodiazoaminobenzene (2·65 g, 0·01 mol), isopentyl nitrite (2 ml, 0·017 mol) and a substituted 2-X-furan derivative (50 ml) was kept at 30°C for 48 h, and then either distilled in steam to remove excess of a substituted 2-X-furan derivative or concentrated through the vacuum distillation in the case of 2-methyl- or 2-ethylfuran. Afterwards the residue was chromatographed on the column filled with silica gel. In such a way the following compounds were obtained: 5-(4-*Chlorophenyl*)-2-*methylfuran* (II), eluent heptane-benzene 1 : 1, 66% yield, m.p. 59—61°C (light petroleum), ref.[6] and ref.[7] record m.p. 59—61°C and 51—52°C respectively.

5-(4-*Chlorophenyl*)-2-*ethylfuran* (III), eluent CCl_4, 65·1% yield, b.p. 85°C/1 Torr. For $C_{12}H_{11}$.ClO (206·7) calculated: 69·74% C, 36% H, 17·15% Cl; found: 70·01% C, 5·36% H, 17·03% Cl. 5-(4-*Chlorophenyl*)-2-*acetylfuran* (IV) eluent benzene, 58·4% yield, b.p. 65°C/1 Torr, m.p. 62 to 64°C (light petroleum), ref.[3] m.p. 60·5—61·5°C.

5-(4-*Chlorophenyl*)-2-*carbmethoxyfuran* (V), eluent benzene, 57% yield, m.p. 132—133°C (heptane), ref.[4] m.p. 133—134°C.

5-(4-*Chlorophenyl*)-2-*formylfuran* (VI), eluent benzene, 61·7% yield, m.p. 131—132° (heptane), ref.[2] m.p. 131°C.

5-(4-*Chlorophenyl*)-2-*cyanofuran* (VII), eluent CCl_4, 44·6% yield, m.p. 75—76°C matches with that reported earlier[14].

Bis(5-(4-*chlorophenyl*)-2-*furyl*)*methane* (VIII), eluent benzene–heptane 1 : 1, 0·2 g, m.p. 111 to 114°C (heptane) was obtained by the reaction of 4,4'-dichlorodiazoaminobenzene (0·01 mol) and isopentyl nitrite (2 ml, 0·017 mol) with 2-hydroxymethylfuran (50 ml) and by the work up of the reaction mixture as in previous cases. ^{1}H-NMR spectrum: δ 7·41 (m, center of AA'BB', 4 H), 6·62 (d, 4 H), 6·19 (d, 3 H); $J_{3,4} = 3{\cdot}5$ Hz, $J_{3H,CH_2} = 1$ Hz, $J_{4H,CH_2} = 0$ Hz. Mass spectrum: $M^+ = 368$ m/e.

Relative Reactivities of Furan Derivatives

K_{rel} were determined through the reaction of 4,4'-dichlorodiazoaminobenzene (1·32 g, 0·005 mol) and isopentyl nitrite (2 ml, 0·017 mol) with furan (0·25 mol) and a substituted 2-X-furan derivative (0·025 mol), carried out at 30°C for 24 h.

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