

## STUDY OF THE PRODUCTS OF ELECTROPHILIC ISOPROPYLATION OF FURFURAL AND 2-ACETYLFURAN

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It was found that the predominant products of isopropylation of furfural under catalysis with aluminum chloride are the following; 4-isopropylfurfural (40%), 4,5-diisopropylfurfural (31%), 3,4,5-triisopropylfurfural (26%). The products of analogous isopropylation of 2-acetylfuran are 5-isopropyl-2-acetylfuran (19%), 4-isopropyl-2-acetylfuran (47%), 4,5-diisopropyl-2-acetylfuran (34%).

It is known<sup>1</sup> that in furan and thiophene compounds substituted in  $\alpha$ -position with a group containing carbonyl group adjacent to the ring (*i.e.* —CHO, —COR, —COOR) the heteroatom and the carbonyl group compete during electrophilic substitution in that the first directs the substituent into the position 5, while the carbonyl group favours the position 4 by deactivating the position 5 by the —M effect. This effect — M can be still further enhanced by reaction conditions<sup>1,2</sup>. The reactions of this type have been studied more with thiophene derivatives and it has been demonstrated that the ratio of the 4- and 5- substituted isomers in the reaction products is also affected by the structure of the carbonyl-containing substituent<sup>1,3</sup>. In analogous furan derivatives it was supposed on the basis of the available data that for the direction of electrophilic substitution the effect of the heteroatom is decisive. Only a few cases were known where the substitution took place in the position  $\beta$  even when the position  $\alpha$  was free, but some of these cases are outside the scope of the problems<sup>4</sup> concerned. The reaction of the complex of furfural with aluminum chloride and isopropyl chloride in which 4-isopropylfurfural<sup>6,7</sup> is formed still remains of central importance<sup>5</sup>. Therefore this reaction was taken as the starting point of this study. The possibility of the isomerization of the supposed primarily formed 5-isopropylfurfural has already been experimentally investigated, but has not been confirmed<sup>5</sup>. In spite of this, with reference to another study<sup>8</sup>, this possibility was reconsidered<sup>1</sup>. Attention should also be drawn to the study of the acylation of methyl 2-furoate with caproic anhydride under catalysis with stannic chloride, leading to a mixture of methyl 4- and 5-caproyl-2-furoate in a 32 : 62 ratio, while a further substance, detected by gas chromatography, could not be identified<sup>9,10</sup>. In the present study we in-

investigated the product of electrophilic isopropylation of furfural and 2-acetylfuran by means of new identification methods.

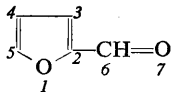
The isopropylation of furfural under catalysis with an excess of aluminum chloride was carried out by a method described earlier<sup>5</sup>. The reaction product distilled in the 86–109°C/9 Torr interval, which is broader than indicated in the original paper (101–103°C/22 Torr). When the products were analysed by gas chromatography it was found that the mixture consists of four substances. On the basis of the mass spectra taken with a mass spectrometer coupled with a gas chromatograph single components were identified. Substance *I* with the least retention time represented 3% rel. of the mixture (read from the gas chromatograph) and it was not identified. Substance *II* with a 40% relative representation ( $M^+ m/e$  138) was monoisopropylfurfural, substance *III* with a 31% relative representation ( $M^+ m/e$  180) was diisopropylfurfural, and substance *IV* with a 26% ( $M^+ m/e$  222) was triisopropylfurfural. Substance *II* was obtained by fractional distillation in a high concentration, and on the basis of <sup>1</sup>H-NMR spectra it was confirmed that it was 4-isopropylfurfural. In the <sup>1</sup>H-NMR spectrum of the mixture of di- and trialkylated product (1 : 1) obtained by fractional distillation the signal of the single proton of the furan nucleus was found, corresponding to the position 3 (7.17 p.p.m., singlet). Hence, the dialkylated product is 4,5-diisopropylfurfural. The unidentified substance has the same retention time in the gas chromatogram as 5-isopropylfurfural prepared by an independent reaction sequence<sup>11–13</sup>. In order to exclude the possibility that 4-isopropylfurfural is formed during the reaction as a product of isomerization of 5-isopropylfurfural only we reproduced the attempt at isomerization of pure 5-isopropylfurfural under the conditions of alkylation, but unchanged 5-isopropylfurfural only was recovered. Alkylation of furfural with n-propyl chloride was also carried out under the same conditions. The relative composition of the mixture of products after a more than double reaction time was the following: *I* (6%), *II* (48%), *III* (22%), *IV* (24%). The dialkylated product *II* was also identified as 4-isopropylfurfural according to <sup>1</sup>H-NMR. According to gas chromatography and comparison with standards other substances also agree with the product of alkylation with isopropyl chloride. A slower reaction course and the slightly shifted ratio of the products in favour of the monoalkylated one may be caused by isomerization of the propyl cation to the more stable isopropyl cation.

In the second part of our study we carried out isopropylation of 2-acetylfuran<sup>14</sup> under approximately identical conditions. In the mixture of alkylation products obtained by distillation (b.p. 103–125°C/14 Torr) gas chromatography indicated three predominant substances with relative percentage read from the gas chromatogram. By recording mass spectra on a gas chromatograph-mass spectrometer an additional three substances were also found in trace amounts. The alkylation products were identified as follows: Substance *V* (19% rel.) with  $M^+ m/e$  182 as monoisopropyl-2-acetylfuran, substance *VI* (47%) with  $M^+ m/e$  152 as monoisopropyl-2-acetylfuran,

two substances indicated as *VII* and *VIII* then followed which according to their  $M^+ m/e$  194 were identified as isomers of diisopropyl-2-acetylfuran. Further, the mixture contained substance *IX* (34%) with  $M^+ m/e$  194 which again indicates an isomer of diisopropyl-2-acetylfuran, and finally traces of a substance indicated as *X* ( $M^+ m/e$  236), a triisopropyl-2-acetylfuran. On the basis of  $^1H$ -NMR spectrum of the mixture of substances *V* and *VI* (in a 1 : 2 ratio) obtained by fractional distillation it may be said that substance *V* is 5-isopropyl-2-acetylfuran and substance *VI* 4-isopropyl-2-acetylfuran. For substance *IX* the structure of 4,5-diisopropyl-2-acetylfuran may be proposed. It is formed evidently by isopropylation of the primarily formed 4- and 5-isopropyl derivative. For electrophilic isopropylation the position 3 is much less reactive. For substances *VII* – *VIII* the structures of 3,5-diisopropyl-2-acetylfuran and 3,4-diisopropyl-2-acetylfuran remain as probable and for substance *X* the structure of 3,4,5-triisopropyl-2-acetylfuran is most probable. The possibility of the substitution in the side chain may be excluded in view of the fact that 2-acetylfuran was alkylated in the form of a complex of the carbonyl group with the catalyst.

On the basis of the results obtained and in view of the mentioned literature data (especially<sup>9</sup>) it may be stated that the reactivity of the positions 4 and 5 in furan derivatives containing in the  $\alpha$ -position the groups —CHO, —COR, —COOR is comparable in electrophilic substitutions. The —M effect of the  $\alpha$ -substituent should be also taken into consideration (—CHO > —COCH<sub>3</sub> > —COOCH<sub>3</sub>). In agreement with this is the fact that the formation of a single monoalkylated derivative in the position 4 was observed during alkylation of furfural, that in the alkylation of 2-acetylfuran two monoalkylated derivatives substituted in the position 4 and 5 in a 5 : 2 ratio are formed, and that in the alkylation of the methyl 2-furoate<sup>9</sup> two monoacylated derivatives substituted in the position 4 and 5 in an approximate 1 : 2 ratio are formed. The isopropylation of 2-acetylfuran may be further used to demonstrate the greater effect of the oxygen heteroatom than of the sulfur heteroatom in 2-acetyl-

TABLE I  
Indices of Chemical Reactivity of Furfural

	Position	$q$	$S_e$	$S_n$	$S_r$
	1	1.795	0.838	0.328	0.583
	2	1.050	1.054	0.728	0.891
	3	0.938	0.771	1.465	1.118
	4	1.080	0.965	0.639	0.802
	5	0.875	0.940	1.643	1.287
	6	0.700	0.416	2.090	1.253
	7	1.561	1.252	0.926	1.089

thiophene during the isopropylation of which 5-isopropyl derivative is formed in traces only<sup>15</sup>.

The results of our work were confronted with the indices of chemical reactivity for furfural and 2-acetylfuran, calculated by means of Hückel's approximation of the quantum chemical method of molecular orbitals (MO-LCAO) (see Table I and Table II). The value of electrophilic superdelocalizability  $S_e$  of furfural, corresponding to the position 4, is higher than the value corresponding to the position 5. For 2-acetylfuran the  $S_e$  values of positions 4 and 5 are equal and at the same time slightly higher than for furfural. The difference of the  $\pi$ -electron densities  $q$  values of the positions 4 and 5 are still more pronounced in both substances, *i.e.* higher for the position 4. Hence, it may be stated that the calculated values are in agreement with the obtained results and the conclusions drawn from our work.

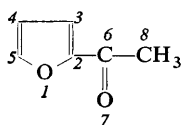
## EXPERIMENTAL

The boiling point temperatures were not corrected. Before analysis the solid substances were dried at 0.5 Torr vacuum for 6 hours. Gas chromatography was carried out on a Chrom II apparatus, provided with a flame ionization detector. The IR spectra were recorded with a Zeiss UR-10 spectrophotometer in tetrachloromethane. The <sup>1</sup>H-NMR spectra were measured on a BS-477, 60 MHz instrument, using deuteriochloroform as solvent and tetramethylsilane as internal standard. The mass spectra were taken on a Gas Chromatograph-Mass Spectrometer LKB 9000, AB Stockholm.

### Friedel Crafts Reaction of Isopropyl Chloride with Furfural

96.1 g (1 mol) of furfural were added dropwise to a suspension of 160 g (1.2 mol) of aluminum chloride in 500 ml of carbon disulfide under occasional shaking. The reaction was strongly exothermic. Isopropyl chloride (87.4 g; 1 mol) was then added at room temperature and after a few minutes the reaction started under evolution of hydrogen chloride, but without an observable

TABLE II  
Indices of Chemical Reactivity of 2-Acetylfuran Position

	Position	$q$	$S_e$	$S_n$	$S_r$
	1	1.793	0.837	0.310	0.573
	2	1.056	1.085	0.748	0.917
	3	0.951	0.789	1.299	1.044
	4	1.082	0.973	0.635	0.804
	5	0.891	0.973	1.482	1.227
	6	0.690	0.379	1.768	1.074
	7	1.609	1.301	0.690	0.995
	8	1.924	0.954	0.124	0.539



evolution of heat. Hydrogen chloride ceased to escape approximately after 16 hours. The mixture was poured onto 500 g of crushed ice, the carbon disulfide phase was washed with water and sodium acetate solution, and after addition of 500 ml of the same solution it was steam-distilled. The alkylation product distilled with water, it dissolved in carbon disulfide and gave it a pink coloration. The carbon disulfide solution of the product was washed with sodium hydrogen carbonate, dried over anhydrous sodium sulfate and concentrated. The residue was rectified to give 6.2 g of liquid of b.p. 55.5°C/9 Torr (furfural) and 12 g of a pink liquid of b.p. 86–109°C/9 Torr. Gas chromatography (polypropylene sebacate on Chromosorb W, 133°C, 0.20 atp N<sub>2</sub>) indicated that it is a mixture of substances *I–IV*. The crystalline dinitrophenylhydrazone mixture gave on thin layer of alumina (Reanal; chloroform solution of the sample, n-hexane–benzene mixture 1 : 1 as eluting solvent) three spots:  $R_{F1} = 0.33$ ,  $R_{F2} = 0.45$ ,  $R_{F3} = 0.59$ .

Mass spectra (obtained with a mass spectrometer coupled with a gas chromatograph): *II*:  $M^+ m/e$  138 (55%), 123 (100%), 41 (53%), 39 (42%), 67 (36%), 27 (19%), 29 (16%), 65 (15%), 28 (13%), 53 (12%). *III*:  $M^+ m/e$  180 (38%), 165 (100%), 123 (36%), 41 (28%), 28 (26%), 43 (24%), 39 (19%), 27 (15%), 109 (13%), 55 (12%), 67 (12%), 77 (12%), 91 (12%), 53 (10%). *IV*:  $M^+ m/e$  222 (48%), 207 (100%), 43 (94%), 41 (30%), 71 (20%), 55 (18%), 28 (16%), 27 (16%), 208 (14%), 91 (13%), 39 (11%), 95 (10%).

Substance *II* was obtained by fractional distillation (b.p. 86–88°C/10 Torr) in a high concentration and its <sup>1</sup>H-NMR spectrum indicated the following values: 1.20 p.p.m. (6 H, doublet,  $J = 7$  Hz, CH<sub>3</sub>); 2.80 p.p.m. (1 H, quartet,  $J = 7$  Hz, CH); 7.15 p.p.m. (1 H, singlet, C<sub>(3)</sub>H); 7.45 p.p.m. (1 H, singlet, C<sub>(5)</sub>H); 9.57 p.p.m. (1 H, singlet, —CHO). IR spectrum: 3360 w, 2970 s, 2930 m, 2875 m, 2835 m, 2800 m, 2750 w, 2705 w, 1700 s, 1600 m, 1515 s, 1470 m, 1390 m, 1380 m, 1315 m, 1275 m, 1205 w, 175 m, 1100 w, 1080 w, 1025 w, 980 m, 970 m, 945 m, 875 w, 850 m, 825 w.

The fraction boiling at 106–108°C/10 Torr, which contained substances *III* and *IV* in a 1 : 1 ratio, was submitted to <sup>1</sup>H-NMR spectrometry in order to determine its structure. It contains the signal of the only proton of the furan nucleus, at 7.17 p.p.m. (singlet, C<sub>(3)</sub>H). For the mixture of crystalline dinitrophenylhydrazones elemental composition was calculated on the basis of the percentual composition of the mixture, read from the gas chromatogram under the supposition that compound *I* has the same composition as *II*. Calculated: 55.91% C, 5.39% H, 16.02% N; found: 55.12% C, 5.15% H, 16.29% N.

#### Friedel–Crafts Reaction of 2-Acetylfuran with Isopropyl Chloride

A solution of 22 g (200 mmol) of 2-acetylfuran in 100 ml of carbon disulfide was added dropwise at –10°C to a suspension of 32.1 g (220 mmol) of aluminum chloride in 120 ml of carbon disulfide. The addition was accompanied by evolution of heat and eventual formation of two phases. Isopropyl chloride (15.7 g; 200 mmol) was then added to the mixture at room temperature and the mixture allowed to stand for 12 hours, when the liberation of hydrogen chloride ceased. Hydrolysis was carried out similarly as after alkylation of furfural. The carbon disulfide solution of the product was washed with water, a sodium carbonate solution and a saturated sodium chloride solution. After drying over anhydrous sodium sulfate and evaporation of the solvents 3.9 g of a liquid boiling at 65–65.5°C/13 Torr (2-acetylfuran) and 12.9 g of a liquid with b.p. 103–125°C/14 Torr, containing the alkylation products, were obtained. Their mass spectra, recorded with a gas chromatograph-mass spectrometer, were the following: *V*:  $M^+ m/e$  152 (39%), 137 (100%), 43 (66%), 109 (32%), 39 (19%), 95 (17%), 28 (17%), 81 (16%), 41 (14%), 27 (12%). *VI*:  $M^+ m/e$  152 (31%), 137 (100%), 43 (99%), 39 (21%), 41 (13%), 53 (11%). *IIV*:  $M^+ m/e$  194 (33%), 43 (100%), 179 (63%), 28 (20%), 55 (14%), 137 (14%), 41 (13%), 27 (10%). *VIII*:  $M^+ m/e$  194 (25%), 179 (100%), 43 (83%), 28 (40%), 65 (28%), 41 (17%), 180 (14%), 151 (12%),

32 (11%), 39 (10%), 27 (10%), 91 (10%), IX:  $M^+$   $m/e$  194 (31%), 179 (100%), 43 (88%), 41 (18%), 137 (16%), 180 (13%), 39 (12%), 27 (11%), 77 (10%), 151 (10%). X:  $M^+$   $m/e$  236 (19%), 43 (100%), 28 (96%), 221 (59%), 41 (16%), 179 (15%), 32 (14%), 27 (11%), 193 (11%), 137 (10%), 222 (10%).

Fraction with b.p. 91–94°C/10 Torr, containing compounds V and VI in a 1 : 2 ratio, was submitted to  $^1\text{H-NMR}$  measurements. On the basis of its  $^1\text{H-NMR}$  spectrum these components were identified: 1.0–1.35 p.p.m. (two overlapping doublets, 1 : 2,  $J = 7$  Hz,  $\text{CH}_3$ ), 2.4 p.p.m. (two overlapping singlets, 1 : 2,  $\text{COCH}_3$ ), 2.75 p.p.m. (multiplet, CH), 6.1 p.p.m. (doublet, corresponds to  $\text{C}_{(4)}\text{H}$  of compound V, integration value is equal to one half of that of  $\text{C}_{(5)}\text{H}$  in compound VI), 7.1 p.p.m. (singlet, corresponds to  $\text{C}_{(3)}\text{H}$  of both isomers, integration value is 1.5 times higher than that of  $\text{C}_{(5)}$  of compound VI), 7.34 p.p.m. (singlet, corresponds to  $\text{C}_{(5)}\text{H}$  of compound VI). The mass spectrum, from which the relative composition of the mixture of the products was read, was obtained under the following conditions: neopentyl glycol sebacate on Chromosorb W, 180°C, 0.26 atp  $\text{N}_2$ .

#### Attempt at the Isomerization of 5-Isopropylfurfural

(3.6 g; 27 mmol) was suspended in 10 ml of carbon disulfide and a solution of 5-isopropylfurfural (3.1 g; 22.5 mmol) in carbon disulfide was added to it dropwise. The solution obtained was stirred for 12 hours at room temperature. After hydrolysis and isolation, which were carried out in the same manner as after isopropylation of furfural, 2.4 g of isopropylfurfural were recovered, b.p. 80–83°C/8 Torr.

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