Furan derivatives. LVIII.
Transfer of a substituent effect through the furan—benzene system
Alkaline hydrolysis of methyl esters of 4-(5-X-2-furyl)benzoic acids

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Some substituted 2-X-5-(4-methoxycarbonylphenyl)furans, where X = H, CH_3, C_2H_5, $HOCH_2$, CHO, Br, I, CH_3CO, NC, O_2N, and CH_3OOC, were prepared. The rate constants of alkaline hydrolysis of the prepared derivatives in 60% acetone at 25°C were determined and correlated with Hammett constants ($\varrho = 1.056$) and $\sigma_p(X\text{-}C_4H_2O)$ constants ($\varrho = 2.854$). The found values of the rate constants are discussed in connection with a transfer of the substituent effect through the furan—benzene system. Correlations of the shifts of the CO stretching frequencies of methyl esters in the i.r. spectra with the $\sigma_p(X\text{-}C_4H_2O)$ constants are also reported.

In our previous work [1] we studied the transfer of the substituent effect through the furan—benzene system in substituted 2-X-5-(4-carboxyphenyl)furans. From the calculated slope of a linear dependence of pK_a *vs.* σ ($\varrho = 0.555$) we found 2.74 much weaker transfer of the substituent effect than through the benzene ring itself.
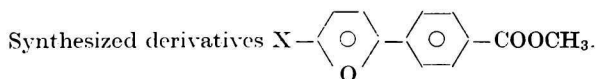
The purpose of this work was to compare previous results [1] with determined values of the rate constants of alkaline hydrolysis of the corresponding methyl esters. Therefore we prepared some derivatives not yet described in literature, *i.e.* substituted 2-X-5- -(4-methoxycarbonylphenyl)furans, where X = H, CH_3, C_2H_5, $HOCH_2$, CHO, Br, I, CH_3CO, NC, O_2N, and CH_3OOC. Their characteristics are summarized in Table 1.

The rate constants of alkaline hydrolysis (reactions of the second order) of the prepared methyl esters in 60% acetone at 25°C are listed in Table 2 together with the corresponding Hammett σ_p constants [2] and σ_p 2-X-5-furyl constants, denoted as $\sigma_p(X\text{-}C_4H_2O)$ [1]. The obtained ratio of the rate constants $k_I/k_0 = 0.849$ (k_0 is the rate constant of alkaline hydrolysis of unsubstituted methyl benzoate determined under the same conditions) indicates a weak electron-donor character of the furan ring as a substituent linked in *p*-position to the benzene ring. This conclusion is in conformity with the results of our previous work [1] ($\sigma_p(C_4H_3O) = -0.1$).

A relatively low value of the rate constant of compound *IV* ($k_{IV}/k_0 = 0.118$) is brought about by the formation of R-CH_2O^- anion under the conditions of hydrolysis. On the other hand, the considerably high value of the rate constant of compound *XII* ($k_{XII}/k_0 = 14.368$) is caused by the simultaneous hydrolysis of two methoxycarbonyl groups, one linked to the furan and the other to the benzene ring.

The correlation dependence ($r = 0.993$) of the rate constants of hydrolysis on the Hammett σ_p constants of the substituents linked to the furan ring ($\varrho_I = 1.056$) and on

Table 1

Synthesized derivatives $X-\langle\!\langle{}^{O}\!\rangle\!\rangle-\langle\!\langle{}O{}\rangle\!\rangle-COOCH_3$.

No.	X	Formula	M	Calculated/found			M.p.
				% C	% H	% (others)	[°C]
I	H	$C_{12}H_{10}O_3$	202.20	71.14	5.03		121
				71.20	5.00		
II	CH_3	$C_{13}H_{12}O_3$	216.22	72.03	5.62		77—78
				72.21	5.59		
III	C_2H_5	$C_{14}H_{14}O_3$	230.24	73.10	6.17		54—55
				73.00	6.12		
IV	$HOCH_2$	$C_{13}H_{12}O_4$	232.22	67.10	5.20		116—118
				67.11	5.12		
V	HONCH	$C_{13}H_{11}NO_4$	245.22	67.76	4.58	5.89 (N)	156—158
				67.67	4.52	5.71 (N)	
VI	OHC	$C_{13}H_{10}O_4$	230.21	67.58	4.49		152
				67.82	4.37		
VII	Br	$C_{12}H_9BrO_3$	281.10	51.49	3.48	28.16 (Br)	132—133
				51.27	3.22	28.42 (Br)	
VIII	I	$C_{12}H_9IO_3$	328.10	43.80	2.79		108—111
				43.90	2.76		
IX	CH_3CO	$C_{14}H_{12}O_4$	244.23	68.99	5.04		156
				68.90	4.97		
X	NC	$C_{13}H_9NO_4$	227.21	70.38	3.96	6.19 (N)	156—158
				70.58	4.10	6.33 (N)	
XI	O_2N	$C_{12}H_9NO_5$	247.20	57.91	3.79	5.69 (N)	163—165
				58.20	3.64	5.67 (N)	
XII	CH_3OOC	$C_{14}H_{12}O_5$	260.23	64.56	4.63		157—158
				64.55	4.65		

$\sigma_p(\text{X-C}_4\text{H}_2\text{O})$ ($\varrho_I = 2.854$, $r = 0.986$) is seen in Fig. 1. Statistical parameters of these correlations are listed in Table 3.

The obtained ratio $\varrho_I/\varrho_{Bz} = 0.429$, where $\varrho_{Bz} = 2.46$ [3], is the slope of the linear correlation of rate constants of the alkaline hydrolysis of substituted methyl benzoates in 60% acetone at 25°C, demonstrates that the furan—benzene system transfers the substituent effect weaker than the benzene ring itself.

The calculated ratio $\varrho_I/\varrho_{Bz} = 0.429$ is higher than the ratio of slopes (0.364) obtained from measurements of pK_a values of substituted 2-X-5-(4-carboxyphenyl)furans in 50% ethanol at 25°C [1]. This difference may be explained by a different solvation ability of the used solvents (acetone, ethanol) as well as by a hydrogen bond formed between heteroatom of the furan ring and ethanolic hydrogen, in accordance with our recent works [4, 5].

The relationship between the $\sigma_p(\text{X-C}_4\text{H}_2\text{O})$ constants and the differences in wavenumbers of the carbonyl stretching vibrations of the prepared methyl esters and methyl benzoate itself ($r = 0.986$) is shown in Fig. 2. A comparison of the wavenumber values for the compounds *I* and *XII* (see Table 2) confirms the electron-donor character of the furan ring.
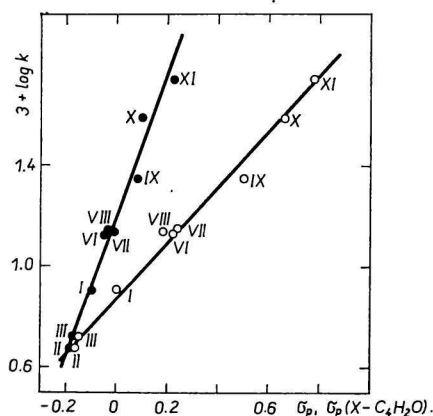
Fig. 1. Dependence of $\log k + 3$ on σ_p ($\circ$) and on σ_p X-furyl constants ($\bullet$).

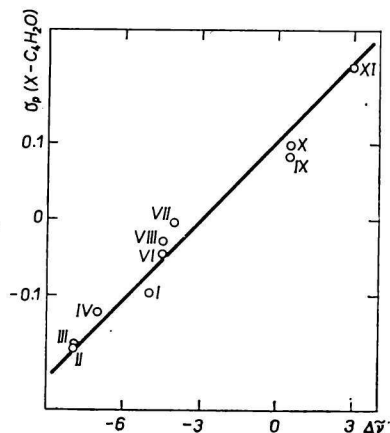$\circ$ $\varrho = 1.056$, $r = 0.993$; $\bullet$ $\varrho = 2.854$, $r = 0.986$.

Fig. 2. Dependence of σ_p 2-X-furyl constants on $\Delta\nu$ of the CO stretching vibrations of 2-X-5-(4-methoxycarbonylphenyl)furans and methyl benzoate.

$\varrho = 0.031$, $r = 0.986$.

Table 2

Values of the rate constants of alkaline hydrolysis in 60% acetone at 25°C and i.r. spectra of the synthesized derivatives in chloroform

No.	$k \cdot 10^2$	k/k_0 [a]	σ_p X Hammett	σ_p (X-C$_4$H$_2$O)	ν(C=O) [cm^{-1}]	$\Delta\nu$ [b] [cm^{-1}]
I	0.807	0.849	0	−0.098	1720	−5
II	0.476	0.501	−0.17	−0.171	1717	−8
III	0.522	0.549	−0.151	−0.164	1717	−8
IV	0.1125	0.118		−0.122	1718	−7
VI	1.34	1.410	0.22	−0.048	1721	−4.5
VII	1.365	1.436	0.232	−0.001	1720.5	−4.0
VIII	1.35	1.421	0.18	−0.03	1721	−4.5
IX	2.225	2.342	0.522	0.083	1725.5	+0.5
X	3.85	4.052	0.66	0.098	1725.5	+0.5
XI	5.48	5.768	0.778	0.203	1728	+3.5
XII	13.65	14.368				

a) $k_0 = 0.95 \times 10^2$ for methyl benzoate (*XIII*).

b) $\Delta\nu = \nu_1 - \nu$, where ν_1 is the wavenumber of 2-X-5-(4-methoxycarbonylphenyl)furans and ν the wavenumber of methyl benzoate (*XIII*) (1725 cm^{-1}).

Experimental

The i.r. spectra were measured with a UR-20 (Zeiss, Jena) spectrophotometer using 1.0-mm NaCl cells and chloroform solutions (concentration 2×10^{-2} M) in the range 1600—1800 cm^{-1}. The reading accuracy of wavenumbers was ± 0.5 cm^{-1}.

Table 3

Statistical parameters of correlations of substituted 2-(4-methoxycarbonylphenyl)furans

Correlation	n	r	q	s_ϱ	q	s_q	s
$\log k + 3$ *vs.* $\sigma_p(X\text{-}C_4H_2O)$	9	0.986	2.854	0.184	1.192	−0.001	0.065
$\log k + 3$ *vs.* σ_p	9	0.993	1.056	0.045	0.885	0.034	0.043
$\sigma_p(X\text{-}C_4H_2O)$ *vs.* $\Delta\nu(C{=}O)$	10	0.986	0.031	0.001	0.092	−0.021	0.021

n is the number of compounds in the correlation, r correlation coefficient, ϱ slope, s_ϱ its standard deviation, q calculated value for unsubstituted compound, s_q its error, s standard deviation.

5-(4-Methoxycarbonylphenyl)-2-furancarbaldehyde (*VI*) was prepared as described in [6], 2-hydroxymethyl-5-(4-methoxycarbonylphenyl)furan (*IV*) was prepared by reaction of *VI* with NaBH₄ [7], 5-(4-methoxycarbonylphenyl)-2-furonitrile (*X*) was obtained from oxime *V* according to [8].

2-(4-Methoxycarbonylphenyl)furan (I)

The reaction mixture of methyl 4-aminobenzoate (4.15 g; 0.0275 mole), isopentylnitrite (6.5 ml; 0.058 mole), and furan (100 ml) was allowed to stand at 30°C for 48 hrs. The mixture was then filtered, furan distilled off, and the product distilled with water steam. Yield 1.8 g, 32.3%.

5-(4-Methoxycarbonylphenyl)-2-acetylfuran (IX)

Diazonium salt of methyl 4-aminobenzoate (prepared from 0.21 mole of amine) was added to a solution of 2-acetylfuran (0.2 mole) in acetone (16 ml); then the solution of $CuCl_2 \cdot 2H_2O$ (0.055 mole) in water (8 ml) was added to the reaction mixture. When the reaction was finished (4 hrs), water was added (500 ml), the formed precipitate sucked off, washed with water, and recrystallized from ethyl acetate. Yield 45%.

2-Methoxycarbonyl-5-(4-methoxycarbonylphenyl)furan (XII)

A mixture of *X* (0.0056 mole), methanol (35 ml), and conc. H_2SO_4 (2 ml) was refluxed for 4 hrs and then poured on ice (100 g). The formed precipitate was washed with water and purified by chromatography (silica gel, eluent toluene). Yield 27.5%.

2-X-5-(4-Methoxycarbonylphenyl)furans (II, III, VII—IX)

An excess of etheric solution of diazomethane was added to etheric solution of the corresponding acid, prepared as described in [1]. After filtration, the solution was evaporated in vacuum and the corresponding ester was obtained by crystallization from alcohol in nearly quantitative yield.

Hydrolysis

Reaction mixtures for the investigation of the alkaline hydrolysis were prepared by mixing the 10^{-3} M solution (25 ml) of the corresponding ester in 60% (weight) acetone with 0.01 M-KOH (25 ml) in 60% acetone, both the solutions being tempered to 25°C. In appropriate time intervals, samples (5 ml) were withdrawn from the reaction mixture and poured into 0.01 N-HCl (5 ml). After addition of 60% acetone (15 ml) the excess acid was titrated with 0.01 N-KOH. The equivalence point (pH 8) was identified by a pH-meter with the combined glass calomel electrode.

The rate constants were calculated from the equation for the second-order reaction, applying the method of least squares. A calculator Hewlett—Packard, type 9810 A, was used.

The Hammett correlations were made with σ_p [2] and $\sigma_p(X\text{-}C_4H_2O)$ [1] constants. Parameters of the linear correlations were calculated with a Regnezentralen Gier computer.

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