

DISSOCIATION CONSTANTS OF 5-ARYL-2-FURANCARBOXYLIC ACIDS AND ALKALINE HYDROLYSIS RATES OF THEIR METHYL ESTERS*

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Dissociation constants (pK_a) of twenty one 5-aryl-2-furancarboxylic acids in 50% ethanol, and rate constants (k_h) of alkaline hydrolysis of their methyl esters in 60% aqueous acetone, were determined. A linear correlation between σ -substituent constants and pK_a or k_h was observed and the transmission factor for the furan nucleus was calculated.

Dissociation constants of *m*- and *p*-furylbenzoic acids were already measured by two groups of authors^{1,2} and on the basis of these measurements the electronic effects of the 2-furyl group were determined. The effect of a fused benzene nucleus on the acidity of a carboxyl group in the position 2 of the furan nucleus was also already studied³. In our previous papers^{4,5} we described the preparation of 5-aryl-2-furancarboxylic acids and their methyl esters. In the present study we report pK_a values of 5-aryl-2-furancarboxylic acids and rate constants of the alkaline hydrolysis of their methyl esters; the aim of these studies was to determine the transmission factor for the furan nucleus and to compare the found value with the already published data^{6,7}.

The apparent dissociation constants of 5-aryl-2-furancarboxylic acids, measured potentiometrically in 50% (v/v) ethanol, are listed in Table I. A comparison of pK_a values of 5-aryl-2-furancarboxylic acids with that of 2-furancarboxylic acid³ (pK_a 4.54) shows that benzene nucleus in the position 5 of the furan ring enhances the acidity of the carboxyl in the position 2. The extraordinarily high value of the dissociation constant of 5-(2-nitrophenyl)-2-furancarboxylic acid (IV),¹ pK_a 4.76, can be explained by a wider dihedral angle between benzene and furan nuclei. This widening is caused by the presence of a nitro group in the position 2 of the benzene ring; consequently, the $-M$ effect of the nitro group cannot exhibit. Such anomalous behaviour of thus-substituted derivative has been already discussed^{8,9}.

A plot of the found values of the dissociation constants (excluding *ortho*-substituted

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and disubstituted derivatives) against Hammett σ substituent constants¹⁰ is linear (Fig. 1). A comparison of the substituent effects on the acid strength in the benzene series ($\rho = 1.522$, ref.¹⁰), in the furan series ($\rho = 2.12$, ref.³), and in the studied 5-aryl-2-furancarboxylic acids ($\rho = 0.502$) shows that the smallest transmission of the substituent effect is in the latter series. This finding is in accord with the previous papers^{4,6,7}.

FIG. 1
Hammett Dependence of the pK_a Values of 5-Aryl-2-furancarboxylic Acids on σ -Constants ($\rho = 0.502$, $r = 0.981$); For numbering of the derivatives see Table I.

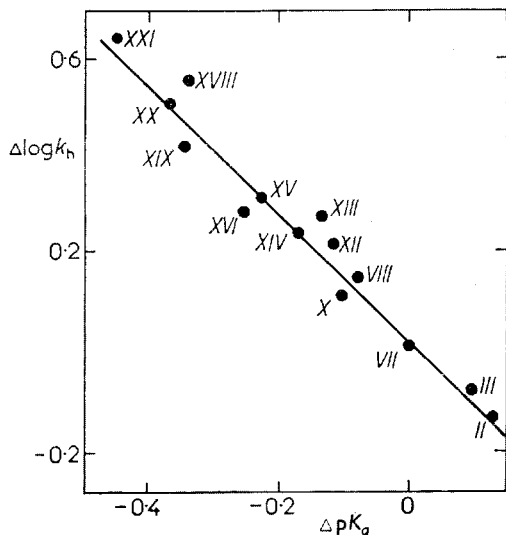
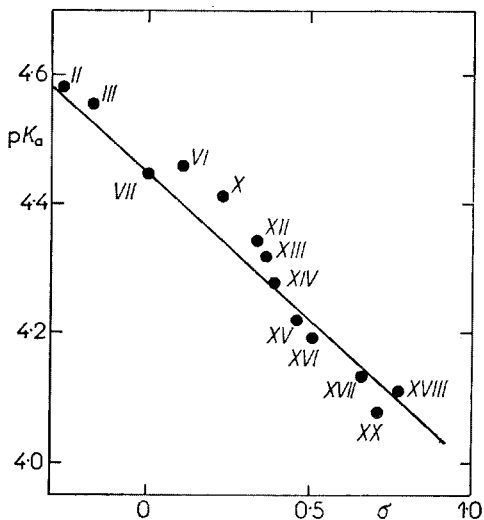


FIG. 2
Plot of pK_a Values of 5-Aryl-2-furancarboxylic Acids against the Hydrolysis Rate Constants of Their Methyl Esters ($\rho = 1.314$, $r = 0.964$)

The rate constants of the alkaline hydrolysis of methyl 5-aryl-2-furancarboxylates, measured in 60% acetone at 25°C, are shown in Table II. The comparison with the data for methyl benzoates¹¹ leads to the same conclusions as in the case of the dissociation constants: methyl 5-aryl-2-furancarboxylates are hydrolysed faster than

TABLE I

Apparent Dissociation Constants of 5-(X-Phenyl)-2-furancarboxylic Acids in 50% Ethanol at 25°C

Compound	Substituent X	pK_a	Compound	Substituent X	pK_a
<i>I</i>	2-methoxy	4.76	<i>XII</i>	3-fluoro	4.34
<i>II</i>	4-methoxy	4.58	<i>XIII</i>	3-chloro	4.32
<i>III</i>	4-methyl	4.55	<i>XIV</i>	3-bromo	4.28
<i>IV</i>	2-nitro	4.55	<i>XV</i>	3-trifluoromethyl	4.22
<i>V</i>	3,5-dichloro	4.49	<i>XVI</i>	4-acetyl	4.19
<i>VI</i>	3-methoxy	4.46	<i>XVII</i>	4-cyano	4.13
<i>VII</i>	H	4.45	<i>XVIII</i>	4-nitro	4.11
<i>VIII</i>	3,4-dichloro	4.45	<i>XIX</i>	3-trifluoromethyl- 4-chloro	4.10
<i>IX</i>	2-chloro	4.33	<i>XX</i>	3-nitro	4.08
<i>X</i>	4-bromo	4.41	<i>XXI</i>	3-nitro-4-chloro	3.90
<i>XI</i>	2-bromo	4.39			

TABLE II

Rate Constants, k_h ($1 \text{ mol}^{-1} \text{ min}^{-1}$), for the Alkaline Hydrolysis of Methyl 5-(X-Phenyl)-2-furancarboxylates in 60% Acetone at 25°C

Compound	X	$k_h \cdot 10^2$	Compound	X	$k_h \cdot 10^2$
<i>XXII</i>	2-methoxy	1.64	<i>XXXIII</i>	3,5-dichloro	4.58
<i>XXIII</i>	4-methoxy	1.83	<i>XXXIV</i>	3-chloro	4.61
<i>XXIV</i>	3-amino	2.03	<i>XXXV</i>	4-acetyl	4.63
<i>XXV</i>	2-amino	2.16	<i>XXXVI</i>	2-bromo	5.12
<i>XXVI</i>	4-methyl	2.16	<i>XXXVII</i>	3-trifluoromethyl	5.14
<i>XXVII</i>	H	2.59	<i>XXXVIII</i>	2-nitro	6.10
<i>XXVIII</i>	4-bromo	3.26	<i>XXXIX</i>	3-trifluoromethyl- 4-chloro	6.50
<i>XXIX</i>	3,4-dichloro	3.67	<i>XL</i>	3-nitro	8.05
<i>XXX</i>	3-fluoro	4.16	<i>XLI</i>	4-nitro	9.35
<i>XXXI</i>	2-chloro	4.35	<i>XLII</i>	3-nitro-4-chloro	11.20
<i>XXXII</i>	3-bromo	4.40			

TABLE III

Statistical Parameters of the Hammett Correlation between σ Substituent Constants and pK_a Values of 5-Aryl-2-furancarboxylic Acids, or Logarithms of the Hydrolysis Rate Constants of Their Methyl Esters (k_h), and the Transmission Factor, $\pi_{(Fu)}$

Correlation	n^a	r^b	ρ^c	s_ρ^d	q^e	s_q^f	s^g	$\pi_{(Fu)}^h$
$pK_a - \sigma$	13	0.981	0.502	0.024	4.476	0.096	0.033	0.329
$\log k_h - \sigma$	13	0.983	0.648	0.033	0.418	0.014	0.042	0.291

^a Number of compounds; ^b correlation coefficient; ^c slope; ^d slope error; ^e calculated value for the unsubstituted derivative; ^f error q ; ^g standard deviation; ^h transmission factor for the furan ring.

the corresponding methyl benzoates, but the substituent effects are smaller in the former than in the latter series. The same magnitude of the substituent effect is indicated by the linear relationship between pK_a and k_h values for the particular derivatives (Fig. 2).

The transmission factor of the polar substituent effects for the furan ring (2,5-furylene bridge) was calculated from the slopes of the linear relationships between dissociation constants, or hydrolysis rates, and the Hammett constants (Table III), using the equation $\pi_{(Fu)} = \rho/\rho_{Bz}$, where ρ is the slope of the studied dependence for the 5-aryl-2-furan derivatives and ρ_{Bz} is the slope of the same dependence for benzene analogues^{10,11}. The fact that the transmission factors, $\pi_{(Fu)}$ calculated from the dissociation constants, differ from that obtained from the ester hydrolyses, can be ascribed to a different solvation of the furan nucleus in different solvent systems^{7,12}. We assume that the increased polarity of the solvent is also responsible for the fact that the value of the transmission factor is lower than the value determined previously^{6,7}.

EXPERIMENTAL

The preparation of 5-aryl-2-furancarboxylic acids was described previously^{4,5}.

Measurement of the dissociation constants. The apparent pK_a values were determined by potentiometric titration of $5 \cdot 10^{-3} M$ solutions of the acids in 50% (v/v) ethanol with 0.01M tetramethylammonium hydroxide under nitrogen at $25 \pm 0.2^\circ C$. The values were calculated using the Henderson equation¹³. The measurements were carried out on a Research pH Meter Beckman GB instrument equipped with a glass (Radiometer G 222 CGU) and calomel (Radiometer K 4112) electrodes, using a Radiometer ABU 1c automatic burette (maximum volume 0.25 ml). The accuracy was 0.02 pH units.

Kinetics measurements. A thermostated $10^{-3} M$ solution of the ester (50 ml) in 60% (v/v) acetone was mixed with a thermostated 0.01M-KOH solution (50 ml) in 60% acetone at $25^\circ C$.

Samples (10 ml) were withdrawn at appropriate time intervals, poured into 0.01M-HCl (10 ml) and the excess acid was then titrated with 0.01M-KOH using a TTT 1c Radiometer Titrator. The hydrolysis rate constants were calculated from the equation for a second-order reaction and were evaluated by the least squares method on a Hewlett Packard 9810A computer. The statistical parameters of the correlations are listed in Table III.

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