

SUBSTITUTED 3-(5-PHENYL-2-FURYL)ACRYLIC ACIDS AND THEIR METHYL ESTERS. TRANSMISSION OF POLAR EFFECTS ACROSS THE FURAN-ETHENE SYSTEM*

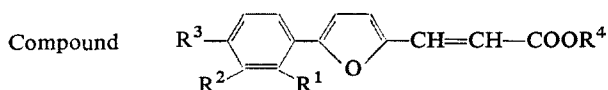
A. KRUTOŠÍKOVÁ, J. SURÁ, J. KOVÁČ and S. JUHÁS

*Department of Organic Chemistry,
Slovak Institute of Technology, 880 37 Bratislava*

Received July 29th, 1974

Thirteen mono and disubstituted 3-(5-phenyl-2-furyl)acrylic acids and their ten methyl esters have been prepared. The apparent pK_a values of these acids in 80% methyl cellosolve, as well as the rate constants of the alkaline hydrolysis of their methyl esters in 60% aqueous acetone, have been determined. The obtained values are correlated with the σ substituent constants and the transmission of the polar effects of substituents across the furan-ethene system is discussed.

In our previous papers^{1,2} we described the preparation of 5-aryl-2-furancarbaldehydes and their condensation with compounds containing a reactive methylene group³⁻⁵. In the present study we report the reaction of 5-aryl-2-furancarbaldehydes, under the conditions of Perkin synthesis, leading to 3-(5-aryl-2-furyl)acrylic acids.



	R ¹	R ²	R ³	R ⁴		R ¹	R ²	R ³	R ⁴
<i>I</i> ,	H	H	NO ₂	H	<i>XIII</i> ,	H	CF ₃	Cl	H
<i>II</i> ,	H	NO ₂	H	H	<i>XIV</i> ,	H	H	NO ₂	CH ₃
<i>III</i> ,	NO ₂	H	H	H	<i>XV</i> ,	H	NO ₂	H	CH ₃
<i>IV</i> ,	H	H	Cl	H	<i>XVI</i> ,	NO ₂	H	H	CH ₃
<i>V</i> ,	H	Cl	H	H	<i>XVII</i> ,	H	H	Cl	CH ₃
<i>VI</i> ,	Cl	H	H	H	<i>XVIII</i> ,	H	Cl	H	CH ₃
<i>VII</i> ,	H	H	Br	H	<i>XIX</i> ,	H	H	Br	CH ₃
<i>VIII</i> ,	Br	H	H	H	<i>XX</i> ,	H	H	H	CH ₃
<i>IX</i> ,	H	H	H	H	<i>XXI</i> ,	H	H	CH ₃	CH ₃
<i>X</i> ,	H	H	CH ₃	H	<i>XXII</i> ,	H	H	OCH ₃	CH ₃
<i>XI</i> ,	H	H	OCH ₃	H	<i>XXIII</i> ,	H	CF ₃	H	CH ₃
<i>XII</i> ,	H	CF ₃	H	H					

* Part LXIII in the series Furan Derivatives; Part LXII: This Journal 40, 3357 (1975).

We chose the Perkin synthesis of these acids rather than the direct arylation of 3-(2-furyl)acrylic acid because the arylation does not afford homogeneous products and the isolation of the desired acids from the reaction mixtures is difficult⁶. The double bond in the prepared 3-(5-aryl-2-furyl)acrylic acids has *trans*-configuration as evidenced by the presence of a strong band in the region of 980 cm^{-1} , corresponding to the bending vibration $\nu(\text{C—H})$ in *trans*-disubstituted derivatives⁷. The low yields (Table I) are probably due to the use of a practical grade (98.9)% acetic anhydride, since the presence of even a small amount of acetic acid is known to lower the yield of the α,β -unsaturated acid⁸. The methyl 3-(5-aryl-2-furyl)acrylates (XIV to XXIII) (Table II) were prepared from the acids either by esterification with methanol, catalysed by sulphuric acid, or by treatment with diazomethane, the latter procedure giving better yields.

The wavenumbers of the $\nu(\text{C=O})$ bands range between $1711\text{--}1689\text{ cm}^{-1}$. The electronic spectra of the compounds I–XXIII exhibit two bands in the regions $228\text{--}260\text{ nm}$ and $329\text{--}375\text{ nm}$. Comparison of the values of the longer wavelength maxima for the compounds I–XXIII with that of 5-aryl-2-furancarboxylic acids and their methyl esters^{9,10} shows that the incorporation of one double bond into the conjugated system results in a bathochrome shift of the band, $\Delta\lambda_{\text{max}} = 10\text{--}30\text{ nm}$ (Table III). The effect of the position and nature of substituent on the benzene ring of the phenylfuran system was analogous to that already discussed^{1,5,11}. The apparent $\text{p}K_{\text{a}}$ values for 3-(5-aryl-2-furyl)acrylic acids were determined potentiometrically in 80% methyl cellosolve at 25°C . Due to the low solubility in water of the studied compounds, it was not possible to determine the thermodynamic dissociation constants. The rate constants of the alkaline hydrolysis of the methyl 3-(5-aryl-2-furyl)acrylates, measured in 60% aqueous acetone at 25°C , are listed in Table III. Plots of the $\text{p}K_{\text{a}}$ values or logarithms of the hydrolysis rate constants against the substituent constants σ ¹² show linear correlations (Table IV). It is interesting that, similarly as found in our previous paper⁵, the *ortho* derivatives fit the cor-

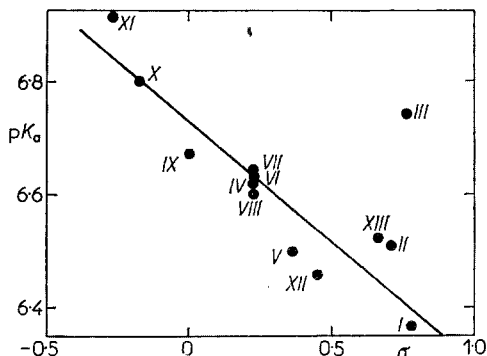


FIG. 1
Hammett Dependence of $\text{p}K_{\text{a}}$ on the Values of σ Substituent Constants for 3-(5-Aryl-2-furyl)acrylic Acids

relation, when the σ_p constants are used. This fact was found for compounds in which the centers are apart from each other, also by other authors^{13,14}. In the measured series of derivatives we observed a statistically significant deviation in the case of the compounds *III* and *XVI* (which were not included in the correlation, cf. Fig. 1). However, compounds of this type with a nitro group in the position 2 of the

TABLE I
3-(5-Aryl-2-furyl)acrylic Acids

Compound ^a	Formula (mol.wt.)	Calculated/Found			M.p., °C (yield, %)
		% C	% H	% N	
<i>I</i>	C ₁₃ H ₉ NO ₅ (259·2)	60·23	3·50	5·40	262—264 (30)
		60·58	3·52	5·62	
<i>II</i>	C ₁₃ H ₉ NO ₅ (259·2)	60·23	3·50	5·40	241 (23)
		60·52	3·48	5·71	
<i>III</i>	C ₁₃ H ₉ NO ₅ (259·2)	60·23	3·50	5·40	182 (18)
		60·41	3·58	5·61	
<i>IV</i>	C ₁₃ H ₉ ClO ₃ (248·7)	62·79	3·64	14·25 ^b	196—198 (17)
		63·00	3·74	14·21 ^b	
<i>V</i>	C ₁₃ H ₉ ClO ₃ (248·7)	62·79	3·64	14·25 ^b	187—190 (29)
		62·84	3·69	14·27	
<i>VI</i>	C ₁₃ H ₉ ClO ₃ (248·7)	62·79	3·64	14·25 ^b	192—196 (24)
		62·86	3·70	14·29	
<i>VII</i>	C ₁₃ H ₉ BrO ₃ (293·1)	53·26	3·09	27·25 ^b	198—201 (22)
		53·28	3·08	27·31	
<i>VIII</i>	C ₁₃ H ₉ BrO ₃ (293·1)	53·27	3·09	27·25 ^b	184—186 (21, 5)
		53·09	3·01	27·30	
<i>IX</i>	C ₁₃ H ₁₀ O ₃ (214·2)	72·88	4·74	—	175—179 (33)
		72·62	4·91	—	
<i>X</i>	C ₁₄ H ₁₂ O ₃ (228·2)	73·67	5·29	—	172—175 (26)
		73·62	5·21	—	
<i>XI</i>	C ₁₄ H ₁₂ O ₄ (244·2)	68·84	4·95	—	173—176 (31)
		69·14	5·14	—	
<i>XII</i>	C ₁₄ H ₉ F ₃ O ₃ (228·2)	59·58	3·21	—	207—210 (21)
		59·58	3·36	—	
<i>XIII</i>	C ₁₄ H ₈ F ₃ ClO ₃ (316·7)	53·10	2·54	—	208—212 (24)
		53·10	2·61	—	

^a Compounds *I*—*XIII* were crystallized from 96% ethanol. ^b Halogen content.

TABLE II
Methyl 3-(5-Phenyl-2-furyl)acrylates

Compound	Formula (mol.wt.)	Calculated/Found			M.p., °C (yield, %)
		% C	% H	% N	
<i>XIV</i>	C ₁₄ H ₁₁ NO ₅ (273·2)	61·53	4·05	5·12	158–162 (82)
		61·83	4·22	5·30	
<i>XV</i>	C ₁₄ H ₁₁ NO ₅ (273·2)	61·53	4·05	5·12	144–147 (85)
		61·84	4·28	5·29	
<i>XVI</i>	C ₁₄ H ₁₁ NO ₅ (273·2)	61·53	4·05	5·12	72 (62)
		61·59	4·09	5·33	
<i>XVII</i>	C ₁₄ H ₁₁ ClO ₃ (262·7)	64·14	4·22	13·49 ^a	95–98 (75)
		64·44	4·49	13·25	
<i>XVIII</i>	C ₁₄ H ₁₁ ClO ₃ (262·7)	64·14	4·22	13·49 ^a	123–124 (68)
		64·42	4·39	13·25	
<i>XIX</i>	C ₁₄ H ₁₁ BrO ₃ (307·1)	54·74	3·61	26·01 ^a	98–100 (91)
		55·04	3·82	25·75	
<i>XX</i>	C ₁₄ H ₁₂ O ₃ (228·2)	73·67	5·29	—	106–108 (69)
		73·90	5·40		
<i>XXI</i>	C ₁₅ H ₁₄ O ₃ (242·3)	74·36	5·81	—	110–112 (71)
		74·02	5·60		
<i>XXII</i>	C ₁₅ H ₁₄ O ₄ (258·3)	69·37	5·46	—	117–120 (85)
		69·21	5·43		
<i>XXIII</i>	C ₁₅ H ₁₁ F ₃ O ₃ (296·2)	60·81	3·74	—	94·5–96 (87)
		61·09	3·84		

^a Halogen content.

benzene ring often show deviations from other derivatives of the studied series; we discussed this fact already elsewhere^{1,5}.

The comparison of p*K*_a value of the compound *IX* with the value published for 3-(2-furyl)acrylic acid¹⁵ shows that the introduction of a phenyl ring into the position 5 results in a decrease in the acidity of the carboxyl in the position 2 of the furan nucleus. We found a similar fact in the study of transmission effects across the phenylfuran system¹⁶. The transmission factor of the polar effects across the furan–ethene system was calculated using the relation $\pi = \varrho_{(\text{FuA})} / \varrho_{\text{Bz}} = 0.246$, where $\varrho_{(\text{FuA})}$ is the slope of the plot p*K*_a against σ for 3-(5-aryl-2-furyl)acrylic acids and ϱ_{Bz} is the slope for benzoic acids taken from the literature¹⁷ ($\varrho_{\text{Bz}} = 1.68$). Ana-

TABLE III

Ultraviolet (λ_{\max} , nm) and Infrared ($\nu(\text{C}=\text{O})$, cm^{-1}) Absorption Spectra of the Compounds I—XXIII, pK_a Values of the Acids and Rate Constants for the Hydrolysis of the Esters (k_h , $1 \text{ mol}^{-1} \text{ min}^{-1}$)

Compound	λ_{\max} (log ϵ)	λ_{\max} (log ϵ)	λ_{\max} (log ϵ)	$\nu(\text{C}=\text{O})$	pK_a	$k_h \cdot 10^2$
I	228 (4.17)	310 sh (4.00)	374 (4.46)	1 702	6.37	—
II	234 (4.23)	276 sh (3.90)	341 (4.47)	1 717	6.51	—
III	230 (4.22)	—	327 (4.34)	1 704	6.74	—
IV	242 (4.17)	237 sh (4.16)	247 (4.46)	1 700	6.62	—
V	236 (4.24)	—	344 (4.50)	1 698	6.50	—
VI	238 (4.20)	—	344 (4.43)	1 697	6.65	—
VII	229 (4.17)	255 sh (4.02)	348 (4.51)	1 695	6.63	—
VIII	236 (4.20)	—	341 (4.43)	1 694	6.60	—
IX	235 (4.26)	—	348 (4.48)	1 691	6.67	—
X	238 (4.24)	—	350 (4.50)	1 690	6.80	—
XI	259 (4.15)	227 sh (4.03)	358 (4.45)	1 689	6.92	—
XII	235 (4.22)	—	342 (4.49)	1 693	6.46	—
XIII	240 (4.26)	—	348 (4.60)	1 709	6.52	—
XIV	229 (4.16)	312 sh (4.00)	375 (4.44)	1 710	—	3.36
XV	235 (4.34)	274 (4.00)	341	1 710	—	2.14
XVI	230 (4.27)	—	329 (4.37)	1 710	—	1.39
XVII	239 (4.18)	—	348 (4.49)	1 708	—	1.88

TABLE III
(Continued)

Compound	λ_{\max} (log ϵ)	λ_{\max} (log ϵ)	λ_{\max} (log ϵ)	$\nu(\text{C}=\text{O})$	$\text{p}K_a$	$k_h \cdot 10^2$
<i>XVIII</i>	237 (4.28)	—	345 (4.56)	1 708	—	1.98
<i>XIX</i>	236 (4.15)	254 sh (4.15)	345 (4.46)	1 707	—	1.53
<i>XX</i>	234 (4.21)	240 sh (4.18)	347 (4.45)	1 707	—	1.10
<i>XXI</i>	233 (4.17)	309 sh (4.05)	347 (4.36)	1 707	—	1.09
<i>XXII</i>	260 (4.15)	246 sh (4.00)	360 (4.37)	1 705	—	0.81
<i>XXIII</i>	236 (4.30)	—	345 (4.56)	1 711	—	1.67

logously, the transmission factor was calculated also from the rates of hydrolysis of 3-(5-aryl-2-furyl)acrylates, $\pi = 0.215$ (taking ρ_{Bz} as 2.23 (ref.⁸).

EXPERIMENTAL

3-(5-Aryl-2-furyl)acrylic Acids (*I—XIII*)

A mixture of 5-aryl-2-furancarbaldehyde (0.1 mol), anhydrous sodium acetate (8.2 g; 0.1 mol) and acetic anhydride (150 ml) was heated under reflux. The reaction mixture was poured into cold water (400 ml) and allowed to stand for 12 hours. The aqueous layer was decanted and neutralized with a saturated sodium carbonate solution. The sodium salt of the resulting acid partly precipitated. The organic layer was boiled briefly with a 10% sodium carbonate solution, the solution was filtered, cooled and the separated sodium salt filtered off. The sodium salts were combined, dissolved in water, acidified with 10% hydrochloric acid and the precipitated acid was purified by crystallisation.

Methyl 3-(5-Aryl-2-furyl)acrylates

A (*XVI*, *XVIII*, *XX*, *XXI*): Concentrated sulphuric acid (1 ml) was added to a solution of 3-(5-aryl-2-furyl)acrylic acid (0.01 mol) in methanol (40 ml) and the mixture was refluxed. The methanol (30 ml) was distilled off and the separated ester was purified by crystallisation.

B (*XIV*, *XV*, *XVII*, *XIX*, *XXII*, *XXIII*): An ethereal solution of 3-(5-aryl-2-furyl)acrylic

TABLE IV

Statistical Parameters of the Hammett Correlation between σ Substituent Constants and pK_a Values for 3-(5-Phenyl-2-furyl)acrylic Acids or the Logarithms of the Rate Constants of Their Methyl Esters Hydrolysis, k_h

Correlation	n^a	r^b	ρ^c	s_{ρ}^d	q^e	s_q^f	s^g
$pK_a-\sigma$	12	0.924	0.4165	0.054	6.726	0.023	0.060
$\log k_h-\sigma$	9	0.937	0.479	0.068	1.077	0.029	0.067

^a Number of derivatives; ^b correlation coefficient; ^c slope; ^d slope error; ^e calculated value for the unsubstituted derivative; ^f error q ; ^g standard deviation.

acid was treated with an ethereal diazomethane solution till the solution remained yellow. After 4 hours' standing at room temperature the solvent was distilled off and the remaining crude ester was crystallized from methanol.

Measurements

Spectra: The electronic absorption spectra in the region 200–480 nm were taken on a recording spectrophotometer Specord UV VIS (Zeiss). Measurements were made at room temperature in $2-4 \cdot 10^{-5} M$ solutions in dioxane in a 1 cm cell. The infrared spectra were recorded on a double-beam UR 20 (Zeiss) spectrophotometer, in $1 \cdot 10^{-2} M$ chloroform solutions in 1 mm NaCl cells. The instrument was calibrated using polystyrene.

Determination of the dissociation constants: The apparent pK_a constants were determined by potentiometric titration of $5 \cdot 10^{-3} M$ solutions of the acids with a 0.1M tetramethylammonium hydroxide solution under nitrogen at $25 \pm 0.2^\circ C$. The apparatus used was Radiometer pHM 4c equipped with glass and calomel electrodes (Radiometer G 200 B and Radiometer K 100, respectively), the titration was performed using an automatic burette Radiometer ABU 1c, maximum volume 0.25 ml. The accuracy was 0.02 pH unit. The value found for benzoic acid, $pK_a = 6.63$, was in accord with the value published by Simon¹⁹.

Kinetic measurements: A thermostated $10^{-3} M$ solution (50 ml) of the ester in 60% (vol/vol) aqueous acetone and 0.01M-KOH in 60% aqueous acetone (50 ml) was mixed at $25^\circ C$. Samples (10 ml) were withdrawn from the mixture at appropriate time intervals, poured into 0.01M-HCl (10 ml) the excess of which was titrated with 0.01M-KOH, using a TTT 1c titrator (Radiometer). The hydrolysis rate constants were calculated according to the equation for a second order reaction and evaluated by the method of least squares, using a Hewlett Packard 9810A computer. The statistical parameters of the correlations are shown in Table IV.

REFERENCES

1. Krutošiková A.: *Thesis*. Slovak Institute of Technology, Bratislava 1970.
2. Frimm R., Kováč J., Krutošiková A.: *Chem. Zvesti* 27, 101 (1973).
3. Krutošiková A., Frimm R., Kováč J.: *Sb. Ved. Pr. Vys. Šk. Tech.* p. 55, Bratislava 1969 to 1970.

4. Krutošiková A., Kováč J., Frimm R., Kováč Š., Sticzay T.: *Chem. Zvesti* 25, 142 (1971).
5. Krutošiková A., Kováč J., Frimm R., Kováč Š., Sticzay T.: *Chem. Zvesti* 25, 147 (1971).
6. Freund W. J.: *J. Chem. Soc.* 1952, 3068.
7. Cleverly B.: *Anal. Chem.* 32, 128 (1960).
8. Kalnin P.: *Helv. Chim. Acta* 11, 977 (1928).
9. Krutošiková A., Kováč J., Sýkora V.: *This Journal* 39, 1892 (1974).
10. Krutošiková A., Kováč J., Rentka J., Čakrt M.: *This Journal* 39, 767 (1974).
11. Frimm R., Kováč J., Benze K.: *Chem. Zvesti* 22, 477 (1968).
12. McDaniel D. M., Brown H. C.: *J. Org. Chem.* 23, 425 (1958).
13. Krutošiková A., Kováč J., Perjessy A., Olejnik A. F., Novickij K. Yu.: *This Journal*, 40, 1550 (1975).
14. Silver N. S., Boykin D. W. jr: *J. Org. Chem.* 35, 759 (1970).
15. Hopff H., Krieger A.: *Helv. Chim. Acta* 44, 1058 (1961).
16. Krutošiková A., Surá J., Kováč J., Kalfus K.: *This Journal*, in press.
17. Exner O., Jonáš J.: *This Journal* 27, 2296 (1962).
18. Tommilla E.: *Ann. Acad. Sci. Fenn.* 459, No 3 (1942).
19. Simon W., Kováts E., Chopard-dit-Jean L. M., Heilbronner E.: *Helv. Chim. Acta* 37, 1872 (1954).

Translated by M. Tichý.