

TRANSMISSION OF POLAR EFFECTS  
IN 4-SUBSTITUTED 5-PHENYL-2-FURANCARBOXYLIC ACIDS\*

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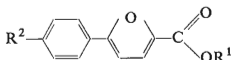
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A series of 4-substituted 5-phenyl-2-furancarboxylic acids and of their methyl esters was prepared, the  $pK_a$  values of the acids were determined and found to correlate with Hammett  $\sigma_p$  constants of the substituents. The reaction constant  $\rho$  was used to calculate Jaffé transmission coefficient for furane ring  $\pi(\text{Fu}) = 0.316$ .

During preparation of some 4-substituted 5-phenyl-2-furancarboxylic acids the phenyl group is introduced to the 5 position of the furane ring<sup>1</sup>. The synthesis of these compounds was reported also by other authors<sup>2-6</sup>. The physical constants recorded in these communications are not however in mutual agreement. Meerwein arylation of ester of pyromucic acid has not yet been accomplished<sup>3</sup>.

In connexion with our previous studies devoted to the arylation of 2-furaldehyde and to determination of the transmission coefficient through benzene and furane rings<sup>7,8</sup> in the present work we prepared a series of 4-substituted 5-phenyl-2-furancarboxylic acids I–VIII (Table I) with the aim to verify their physical constants and to determine their  $pK_a$  values.



	R <sup>1</sup>	R <sup>2</sup>		R <sup>1</sup>	R <sup>2</sup>
I	H	NO <sub>2</sub>	IX	CH <sub>3</sub>	NO <sub>2</sub>
II	H	CN	X	CH <sub>3</sub>	CH <sub>3</sub> CO
III	H	CH <sub>3</sub> CO	XI	CH <sub>3</sub>	Cl
IV	H	Cl	XII	CH <sub>3</sub>	Br
V	H	Br	XIII	CH <sub>3</sub>	H
VI	H	H	XIV	CH <sub>3</sub>	CH <sub>3</sub>
VII	H	CH <sub>3</sub>	XV	CH <sub>3</sub>	CH <sub>3</sub>
VIII	H	CH <sub>3</sub> O	XVI	CH <sub>3</sub>	NH <sub>2</sub>

\* Part II in the series Furane Derivatives; Part XLVIII: Chem. zvesti, in press.

At the same time we employed Meerwein arylation to prepare methyl ester of pyromucic acid in the case of the derivative substituted at benzene ring by an electron-withdrawing group. The other methyl esters (Table II) were prepared by the reaction of appropriate acids with diazomethane. As follows from Table I substances *II–VIII* melted within broad temperature range. In addition to elemental analysis, thin-layer chromatography on siluphol has proved that we are dealing with pure compounds. Substance *IV* was prepared also by hydrolysis of 5-(4-chlorophenyl)-2-furonitrile<sup>9</sup>. The acid so prepared was identical with the compound prepared by procedure *A* (see Experimental). Due to aromatic character of methyl ester of pyromucic acid, its arylation proceeds with lower yields than the arylation of the parent acid.

Table III presents IR and UV characteristics of prepared compounds. The  $\nu(\text{CO})$  band for compounds *IX–XVI* occurs in the  $1739–1725\text{ cm}^{-1}$  region and its position is dependent on the character of substituent. In correlating  $\text{pK}_a$  constants of the 5-phenyl-2-furancarboxylic acids (Table III) with Hammett  $\sigma$  constants we utilized

TABLE I  
Substituted 5-Phenyl-2-furancarboxylic Acids

Compound	Formula m. w.	Calc./Found		M. p., °C <sup>a</sup> yield, %
		% C	% H	
<i>I</i>	$\text{C}_{11}\text{H}_7\text{NO}_5$ <sup>b</sup>	56.66	3.03	251–252
	233.2	56.69	3.10	40
<i>II</i>	$\text{C}_{12}\text{H}_7\text{NO}_3$ <sup>c</sup>	67.61	3.31	257–260
	213.21	67.63	3.48	40
<i>III</i>	$\text{C}_{13}\text{H}_{10}\text{O}_4$	67.82	4.38	233–235
	230.2	67.92	4.44	38
<i>IV</i>	$\text{C}_{11}\text{H}_7\text{ClO}_3$ <sup>d</sup>	59.35	3.17	198–201
	222.6	59.50	3.40	20
<i>V</i>	$\text{C}_{11}\text{H}_7\text{BrO}_3$ <sup>e</sup>	49.41	2.64	198–200
	267.1	49.32	2.74	18
<i>VI</i>	$\text{C}_{11}\text{H}_8\text{O}_3$	70.21	4.29	152–155
	188.2	70.08	4.30	12
<i>VII</i>	$\text{C}_{12}\text{H}_{10}\text{O}_3$	71.28	4.98	188–190
	202.2	71.30	5.02	15
<i>VIII</i>	$\text{C}_{12}\text{H}_{10}\text{O}_4$	66.05	4.62	190–192
	218.2	66.01	4.61	12

<sup>a</sup> Compound *I* was crystallized from acetic acid, compounds *II–V* from 50% ethanol, *VI* from water, and compounds *VII* and *VIII* from benzene. <sup>b</sup> Calculated: 6.01% N; found: 5.99% N. <sup>c</sup> Calculated: 6.57% N; found: 6.55% N. <sup>d</sup> Calculated: 15.92% Cl; found: 16.01% Cl. <sup>e</sup> Calculated: 29.92% Br; found: 29.99% Br.

the applicability of these constants to the furane ring which was established in many cases, for instance, in solvolysis of furfurylcarbinol derivatives<sup>10</sup>, in correlations of  $pK_a$  values of 2-furancarboxylic acids<sup>11</sup>, of rate constants of the rearrangement of thiocyanates of 5-phenyl-2-furfuryl type to corresponding isothiocyanates<sup>7</sup>, and of symmetrical and asymmetrical C=O stretching vibrations of substituted 2-(5-phenyl)-2-furfurylidene-1,3-indandiones<sup>8</sup>. By the least square method we obtained in our case  $\rho = 0.481$  ( $r = 0.981$ ). The value of Jaffé transmission coefficient  $\pi$  (Fu) = 0.316. The results of our study on alkaline solvolysis of the methyl esters will be reported in a subsequent paper.

### EXPERIMENTAL

5-Phenyl-2-furancarboxylic acids I, III—VIII. A) Appropriate 4-substituted aniline (0.1 mol. was dissolved in 60 ml of 15% HCl. The solution was cooled to 0°C and diazotated at the tempe-

TABLE II  
Methyl Esters of Substituted 5-Phenyl-2-furancarboxylic Acids

Compound	Formula m. w.	Calc./Found		M. p., °C <sup>a</sup> yield, %
		% C	% H	
IX	C <sub>12</sub> H <sub>9</sub> NO <sub>5</sub> <sup>b</sup> 247.2	58.30	3.67	172—173
		58.25	3.60	18
X	C <sub>14</sub> H <sub>12</sub> O <sub>4</sub> 244.2	68.85	4.95	140—141
		68.77	5.00	96
XI	C <sub>12</sub> H <sub>9</sub> ClO <sub>3</sub> <sup>c</sup> 236.6	60.90	3.83	133—134
		60.70	3.75	11
XII	C <sub>12</sub> H <sub>9</sub> BrO <sub>3</sub> <sup>d</sup> 281.1	51.27	3.23	128—129
		51.23	3.38	19
XIII	C <sub>12</sub> H <sub>10</sub> O <sub>3</sub> 202.2	71.28	4.98	65—66
		71.28	5.06	94
XIV	C <sub>13</sub> H <sub>12</sub> O <sub>3</sub> 216.2	72.21	5.59	63—64
		72.20	5.43	95
XV	C <sub>13</sub> H <sub>12</sub> O <sub>4</sub> 232.2	67.23	5.21	69—70
		67.21	5.28	95
XVI	C <sub>12</sub> H <sub>11</sub> NO <sub>3</sub> <sup>e</sup> 217.2	66.35	5.10	127—128
		66.32	5.02	87

<sup>a</sup> Compounds IX—XII, and XVI were crystallized from 50% ethanol, compounds XIII—XV from n-hexane. <sup>b</sup> Calculated: 5.67% N, found: 5.67% N. <sup>c</sup> Calculated: 14.98% Cl; found: 15.12% Cl. <sup>d</sup> Calculated: 28.43% Br; found: 28.52 Br. <sup>e</sup> Calculated: 6.48% N; found: 6.48% N.

perature 0–5°C by 25 ml of 30% sodium nitrite. The solution was stirred for another 10 min and then 11.5 g (0.1 mol) of 2-furancarboxylic acid dissolved in 65 ml of acetone were added, along with a solution of 3 g of  $\text{CuCl}_2 \cdot 2 \text{H}_2\text{O}$  in 20 ml of water. The reaction mixture was set aside for one day at room temperature. The precipitate was removed by filtration with suction, washed with water and dissolved in 5% aqueous sodium hydrogen carbonate solution. After filtration 5-aryl-2-furancarboxylic acid was released by hydrochloric acid and purified by crystallization. B) When arylation according to procedure A yields an oil product, the product is extracted with chloroform. The extract is concentrated under vacuum, and then it is purified converting it to the sodium salt, as mentioned in the preceding paragraph, and then crystallized.

5-(4'-Cyanophenyl)-2-furancarboxylic acid (II). *p*-Aminobenzonitrile (23.6 g, 0.2 mol) was dissolved in 180 ml of 1% HCl. The solution was diazotated at 0–5°C with 50 ml of 30% sodium nitrite. The solution of the diazonium salt so prepared was then added to a solution containing 23 g (0.2 mol) of pyromucic acid, 64 g of sodium acetate, and 8 g of  $\text{CuCl}_2 \cdot 2 \text{H}_2\text{O}$  in 240 ml of water cooled to 5°C. The reaction mixture was then slowly warmed up to 30°C and stirred at

TABLE III  
IR and UV Characteristics of Compounds I–XVI and  $pK_a$  Constants of Acids I–VIII  
 $\lambda_{\text{max}}$  in nm,  $\nu(\text{CO})$  in  $\text{cm}^{-1}$ .

Compound	$\lambda_{\text{max}}$	$\log \epsilon$	$\lambda_{\text{max}}$	$\log \epsilon$	$\lambda_{\text{max}}$	$\log \epsilon$	$\nu(\text{C=O})$	$pK_a$
I	216	4.24	339	4.59	—	—	1 678 1 704	4.11
II	224	4.12	317	4.53	330	4.43	1 715	4.13
III	230	4.02	320	4.52	337	4.42	1 690 1 704	4.19
IV	218	4.02	302	4.42	317	4.26	1 675	
V	219	4.14	305	4.51	316	4.36	1 680	4.41
VI	218	4.10	303	4.44	314	3.27	1 690	4.45
VII	218	4.03	308	4.37	320	4.16	1 688	4.55
VIII	220	4.03	315	4.45	—	—	1 690	4.58
IX	218	3.98	339	4.32	339	4.15	1 739	—
X	230	4.15	322	4.66	340	4.53	1 690 1 735	—
XI	220	4.02	308	4.44	317	4.26	1 732	—
XII	221	4.17	307	4.59	320	4.44	1 730	—
XIII	217	4.10	304	4.42	312	4.25	1 727	—
XIV	220	4.06	310	4.42	320	4.30	1 727	—
XV	221	4.00	316	4.45	327	4.22	1 725	—
XVI	215	4.15	319	4.60	332	4.51	1 722	—

this temperature for 3 h. The light green precipitate formed was separated by filtration with suction, washed with water and crystallized.

*Hydrolysis of 5-(4'-chlorophenyl)-2-furonitrile.* The crude nitrile (5 g, 0.025 mol) was dissolved in 100 ml of ethanol, 5 g of KOH were added and the mixture was refluxed for 12 h. Then it was concentrated by evaporation of the solvent to 1/4 of the initial volume and acidified with hydrochloric acid (1 : 1). The precipitate, 5-(4-chlorophenyl)-2-furancarboxylic acid, was filtered off and purified by crystallization. Its physical constants agreed well with the data for compound V prepared by procedure B (Table I).

*Arylation of methyl ester of pyromucic acid.* A suspension of 80.6 g (0.64 mol) of methyl ester of pyromucic acid in 200 ml of water was added in one portion to a solution of 0.64 mol of 4-substituted benzenediazonium chloride prepared by procedure A. While stirring, 23.2 g of  $\text{CuCl}_2 \cdot 2 \text{H}_2\text{O}$  in 100 ml of water were then added. The reaction mixture was stirred at 50°C for another 4 h and set aside for 12 h at room temperature. The oil formed was separated, washed with water, and volatile components were removed by steam distillation. The residue was then crystallized. This procedure was used to prepare compounds IX, XI, and XII.

*Methylation of 5-aryl-2-furancarboxylic acids by diazomethane.* Substituted 5-phenyl-2-furancarboxylic acid was dissolved in required amount of ether (50–200 ml) and then ether solution of diazomethane was added until permanent colouration of the solution. The reaction mixture was allowed to stand for 1 h at ambient temperature. After solvent removal, the product was purified by crystallization.

*Methyl ester of 5-(4-aminophenyl)2-furancarboxylic acid.* A three-necked flask equipped with reflux condenser, stirrer, and separating funnel was charged with 50 ml of water and 0.4 g of iron powder. The mixture was heated on hot water bath and after removal of the bath 0.2 g of concentrated acetic acid was added, followed by slow addition of 0.6 g of methyl ester of 5-(4-nitrophenyl)-2-furancarboxylic acid. The reaction mixture was then heated for 1 h, the iron was precipitated by aqueous sodium carbonate solution and the amine was taken up to ether. After solvent removal, the residue was crystallized from 50% ethanol.

IR spectra were recorded with double-beam UR 20 Zeiss spectrophotometer in the 3600 to 800  $\text{cm}^{-1}$  region. The instrument was calibrated by polystyrene film. Acids I–VIII were measured in KBr pellets (2 mg compound/1 g KBr) and esters IX–XVI were measured in chloroform ( $2.5 \cdot 10^{-3}$  mol/l; NaCl cells were 1.02 mm thick).

Electronic absorption spectra of compounds I–XVI in the 200–480 nm region were taken on Specord UV VIS instrument (Zeiss, Jena). Measurements were carried out at room temperature using cells 1 cm thick ( $3 \cdot 10^{-5}$  M solutions of the compounds in spectrograde dioxane).

$pK_a$  constants of substituted 5-phenyl-2-furancarboxylic acids I–VIII were determined at  $25 \pm 0.02^\circ\text{C}$  by potentiometric titration of 0.001 M solution of the compounds in vol. 50% ethanol with 0.02 M sodium hydroxide. The solutions were prepared and titration was carried out under argon (for lamps), to exclude  $\text{CO}_2$  contamination. The instrument used was calibrated pH-meter OK-205 (Radelkis, Hungary), equipped with glass electrode combined with saturated silver chloride electrode, EA 121 U Type (Metrohm AG., Switzerland). The initial volume of the titrated solution was 30 ml. The solution of sodium hydroxide was added with the aid of piston burette E-274 (Metrohm AG., Switzerland). The glass electrode was calibrated by standard NBS buffers.

## REFERENCES

1. Marthur K. B. L., Mehra H. S.: *J. Chem. Soc.* 1961, 2576.
2. Freund W.: *J. Chem. Soc.* 1952, 3068.
3. Hahn W. E., Krajzewicz F., Nowaczyk M.: *Lódz. Towarz. Nauk, Wydział III, No 6, 15* (1960); *Chem. Abstr.* 55, 19 890 (1961).
4. Akashi H., Oda R.: *Repts. Inst. Chem. Research* 19, 93 (1949); *Chem. Abstr.* 45, 7519 (1951).
5. Akashi H., Oda R.: *J. Chem. Soc. Japan* 53, 202 (1950).
6. Malinowski S.: *Roczniki Chim.* 27, 84 (1953).
7. Krutošíková A.: *Thesis*. Slovak Technical University, Bratislava 1970.
8. Perjéssy A., Hrnčiar P., Krutošíková A.: *Tetrahedron* 28, 1035 (1972).
9. Považanec F., Kováč J., Krutošíková A.: *Chem. zvesti*, in press.
10. Noyce D. S., Kaiser V. V.: *J. Org. Chem.* 54, 1008 (1957).
11. Freeman F.: *J. Chem. Educ.* 47, 140 (1970).

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