

## SYNTHESIS AND PROPERTIES OF SUBSTITUTED 5-BENZOYL-2-FURANCARBOXYLIC ACIDS AND THEIR METHYL ESTERS\*

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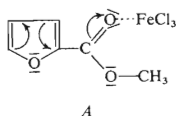
Acylation of methyl 2-furancarboxylate with 4-X- and 3-X-substituted benzoyl chlorides (X = H, 4-CH<sub>3</sub>, 4-Cl, 4-CH<sub>3</sub>O, 4-(CH<sub>3</sub>)<sub>2</sub>N, 4-NO<sub>2</sub> and 3-NO<sub>2</sub>) yielded the appropriate methyl esters of substituted benzoylfurancarboxylic acids which were converted by alkaline hydrolysis to the corresponding carboxylic acids. On the basis of pK measurements, a discussion is presented on the transmission effect of the particular substituent across the —CO— bridge upon the reaction centre.

The effect of substituents across the —S— or —SO<sub>2</sub>— group upon the reaction centre in several sulfur derivatives of furan has been examined in some earlier papers of this series<sup>1-3</sup>. The present paper reports on the synthesis and the transmission of polar effects across the —CO— group in some *para* and *meta* substituted 5-benzoyl-2-furancarboxylic acids VIII–XIV and their methyl esters I–VII.

Compounds I–VII were prepared by the Friedel–Crafts acylation of methyl 2-furancarboxylate (pyromucic acid methyl ester) with the appropriate 3- and 4-substituted benzoyl chlorides in benzene under catalysis of ferric chloride. Methyl 5-benzoyl-2-furancarboxylate was prepared<sup>4</sup> in tetrachloromethane; when this solvent was used in acylations with substituted benzoyl chlorides, the isolation of the required product was difficult because of a considerable amount of tars. Low yields were also obtained in dichloromethane (18% of compound I). Satisfactory yields of compounds I–V (Table I) were obtained with the use of a catalytic amount (0.1 g) of ferric chloride while the preparation of derivatives (VI and VII) substituted by methoxy and dimethylamino groups required an equimolar amount of the catalyst. The need of a greater amount of the catalyst can be explained by its interaction with the unshared electron pair on the oxygen or nitrogen atom of substituents. In this manner, a certain amount of ferric chloride cannot act as catalyst. A special catalytic effect on the reaction course has been observed in the case of *meta* and *para* nitrobenzoyl chlorides as acylation agents. With the use of a catalytic amount of ferric chloride, methyl 2-furancarboxylate was acylated at position 5 while the corresponding 3- or 4-nitrobenzophenones were obtained when an equimolar amount of the catalyst was used. The

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formation of benzophenones can be explained as follows. In the presence of a sufficient amount of the catalyst, the unshared electron pair on the oxygen atom of the ester group is first attacked with the formation of a  $nv$ -complex<sup>5</sup> (A). In view of the lowered electron density on the furan ring, benzene is more readily acylated by the very reactive nitrobenzoyl cation than the position 4 of the furan ring in the resulting complex. The acylation of the benzene ring is thus preferred to that of the furan ring substituted by an electron-accepting group.



The hydrolysis of methyl esters *I–VI* to the free carboxylic acids *VIII–XIV* was accomplished in 10% aqueous sodium hydroxide. The reaction time varied with the

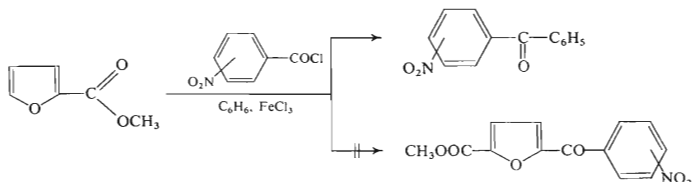
TABLE I

Methyl 5-(3-X- and 4-X-Benzoyl)-2-furancarboxylates

Compound X	Formula (M.w.)	M.p., °C yield, %	Calculated/Found			$\lambda_{max}$ , nm log $\epsilon$			$\nu(\text{C}=\text{O})$ I, $\text{cm}^{-1}$	$\nu(\text{C}=\text{O})$ II, $\text{cm}^{-1}$
			% C	% H	% N					
<i>I</i> 4-H	$\text{C}_{13}\text{H}_{10}\text{O}_4$ (230.2)	78–78.5 41	67.82 67.75	4.35 4.22	—	208 3.97	219 3.97	292 4.26	1 658 1 734, 1 749	
<i>II</i> 4-NO <sub>2</sub>	$\text{C}_{13}\text{H}_9\text{NO}_6$ (275.2)	154 49	56.62 56.49	3.27 3.06	5.09 4.89	204 4.24	269 4.25	299 4.37	1 662 1 740 r	
<i>III</i> 3-NO <sub>2</sub>	$\text{C}_{13}\text{H}_9\text{NO}_6$ (275.2)	167 46	56.62 56.10	3.27 2.99	5.09 5.31	222 4.32	246 4.20	294 4.20	1 662 1 740	
<i>IV</i> 4-CH <sub>3</sub>	$\text{C}_{14}\text{H}_{12}\text{O}_4$ (244.2)	103 42	68.85 69.13	4.92 4.98	—	206 4.15	219 4.06	294 4.31	1 654 1 735, 1 748	
<i>V</i> 4-Cl	$\text{C}_{13}\text{H}_9\text{ClO}_4^a$ (264.7)	122 47	58.97 58.53	3.40 3.51	—	207 4.10	211 4.11	294 4.37	1 658 1 738, 1 749	
<i>VI</i> 4-CH <sub>3</sub> O	$\text{C}_{14}\text{H}_{12}\text{O}_5$ (260.2)	46 44	64.61 64.24	4.61 4.73	—	206 4.29	225 4.09	293 4.23	1 610 1 730 r	
<i>VII</i> 4-(CH <sub>3</sub> ) <sub>2</sub> N	$\text{C}_{15}\text{H}_{15}\text{NO}_4$ (273.3)	129–130 35	65.93 65.59	5.49 5.25	5.13 5.37	206 4.26	227 4.11	307 4.62	1 610 1 720, 1 775	

<sup>a</sup> Calculated: 13.42% Cl; found: 13.78% Cl.

substituent type. Surprisingly, the most difficult hydrolysis and the lowest yields were encountered in the case of the nitro derivatives *IX* and *X*; most probably, the OH ions attack not only the carbon atom of the ester grouping but also the keto group. The latter attack is accompanied by cleavage of the molecule.



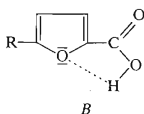
SCHEME 1

TABLE II  
5-(3-X- and 4-X-Benzoyl)-2-furancarboxylic Acids

Compound X	Formula (M.w.)	M.p., °C yield, %	Calculated/Found			$\lambda_{\max}$ nm log $\epsilon$	pK	$\nu(\text{C}=\text{O})$ , $\text{cm}^{-1}$		
			% C	% H	% N			I,	II,	
<i>VIII</i> 4-H	$\text{C}_{12}\text{H}_8\text{O}_4$ (216.2)	179 97	66.67 66.84	3.70 3.82	—	208 4.02	219 4.02	297 4.29	3.64 1 655	1 700, 1 730 r
<i>IX</i> 4-NO <sub>2</sub>	$\text{C}_{12}\text{H}_7\text{NO}_6$ (261.2)	273–274 72	55.17 55.52	2.68 2.54	5.36 5.48	205 4.00	242 3.87	362 4.25	3.30 1 640	1 700 i
<i>X</i> 3-NO <sub>2</sub>	$\text{C}_{12}\text{H}_7\text{NO}_6$ (261.2)	293–295 81	55.17 55.43	2.68 2.85	5.36 5.56	208 4.12	221 4.38	320 4.09	— 1 645	1 700
<i>XI</i> 4-CH <sub>3</sub>	$\text{C}_{13}\text{H}_{10}\text{O}_4$ (230.2)	194–195 97	67.82 68.10	4.35 4.25	—	207 4.14	221 4.12	301 4.36	3.80 1 654	1 700, 1 690 r
<i>XIII</i> <sup>a</sup> 4-Cl	$\text{C}_{12}\text{H}_7\text{ClO}_4$ (250.6)	244–245 95	57.48 57.12	2.79 2.55	—	206 4.24	237 4.26	309 3.81	3.50 1 650	1 700, 1 690 r
<i>XIII</i> 4-CH <sub>3</sub> O	$\text{C}_{13}\text{H}_{10}\text{O}_5$ (246.2)	198–199 97	63.41 63.57	4.06 4.05	—	204 4.26	224 4.19	316 4.41	3.85 1 610	1 716, 1 700 r
<i>XIV</i> 4-(CH <sub>3</sub> ) <sub>2</sub> N	$\text{C}_{14}\text{H}_{13}\text{NO}_4$ (259.2)	229–230 98	64.90 64.72	5.01 4.95	5.41 5.58	206 4.37	238 4.12	340 4.56	— 1 615	1 680 i


<sup>a</sup> Calculated: 14.17% Cl; found: 14.61% Cl.

The IR spectra of derivatives *I–XIV* exhibit characteristic  $\nu(\text{C}=\text{O})\text{I}$  bands of the ketonic carbonyl group and the  $\nu(\text{C}=\text{O})\text{II}$  bands of the ester of carboxylic carbonyl group. The first band at about  $1650\text{ cm}^{-1}$  (Table I and II) can be ascribed to the ketonic group on the basis of the IR spectrum of 5-benzyl-2-furancarboxylic acid. In the case of derivatives with electron-donating substituents, the  $\nu(\text{C}=\text{O})\text{I}$  band is shifted to lower wavenumbers while the electron-accepting groups shift the band to higher wavenumbers. On the other hand, the position of the  $\nu(\text{C}=\text{O})\text{II}$  band (at about  $1740\text{ cm}^{-1}$ ) is not affected by substituents. However, the band corresponding to  $\nu(\text{CO})\text{II}$  stretching vibrations is split due to the existence of the *s-cis* and *s-trans* isomers. The splitting of the carbonyl group has also been observed with methyl esters of substituted 5-aryl-2-furancarboxylic acids, see ref.<sup>6</sup>. The  $\nu(\text{C}=\text{O})\text{II}$  stretching vibrations band of the acids *VIII–XIV* occurs in the  $1680–1730\text{ cm}^{-1}$  region, i.e., at lower wavenumbers when compared with the corresponding esters *I–VII*. In the case of acids, the band is not split, probably due to fixation of a certain amount of one (*s-cis*) of the two isomers by a hydrogen bond extending to the oxygen atom of the furan ring (*B*).



As indicated by  $pK$  values (Table II), the 5-(4-X-benzoyl)-2-furancarboxylic acids are relatively strong organic acids; the acidity of the hydrogen of the carboxylic acid is affected by the nature of the substituent at position 4 of the benzene ring. The calculated values  $r = 0.98$  and  $\rho = 0.52$  ( $n = 5$ ) suggest a potential transmission of the polar effect of the particular substituent across the carbonyl group bridgehead. The  $pK$  value of 5-benzoyl-2-furancarboxylic acid is comparable with that of 5-phenylsulfonyl-2-furancarboxylic acid (Table III).

TABLE III

The  $pK$  Values of the  $\text{C}_6\text{H}_5\text{—Y—}$    $\text{—COOH}$  Type Acids

Y	CO	SO <sub>2</sub>	S	O	CH <sub>2</sub>
$pK$	3.64	3.77	4.61	4.45	4.85
Ref.	<sup>a</sup>	3	3	7	<sup>a</sup>

<sup>a</sup> This paper.

## EXPERIMENTAL

Methyl Esters *I—VII*

A mixture of methyl 2-furancarboxylate (0.03 mol), the substituted benzoyl chloride (0.03 mol), and ferric chloride (0.1 g in the preparation of compounds *I—V*; 0.03 mol with *VI* and *VII*) in benzene (100 ml) is heated at 85–95°C for 5 h (*I—V*) or 8–10 h (*VI* and *VII*), cooled down, and washed with aqueous sodium carbonate. The washing is extracted with benzene, the extract combined with the benzene solution of the product, and the whole evaporated. The residue is crystallised from 50% aqueous ethanol. Compound *I* may be isolated by distillation at 205 to 209°C/2 kPa.

Acids *VIII—XIV*

The title acids were prepared by hydrolysis of esters *I—VII* with 10% aqueous sodium hydroxide on a steam bath<sup>4</sup> and acidification with dilute (1 : 1) hydrochloric acid. Pure acids were obtained by crystallisation from 50% aqueous ethanol. For purposes of physico-chemical measurements, 5-benzyl-2-furancarboxylic acid was also prepared<sup>4</sup>.

## Methods

The IR absorption spectra were taken on a double-beam UR-20 (Carl Zeiss, Jena) spectrophotometer by the potassium bromide technique (2 mg of the substance per 1 g of KBr) in the case of the acids *VIII—XIV*; the corresponding methyl esters *I—VII* were measured in tetrachloromethane as solvent (concentration,  $2 \cdot 10^{-2}$  M/l) in 0.89 mm cells; the apparatus was calibrated by a 25  $\mu$ m polystyrene foil. The electron absorption spectra were measured on a recording Specord UV VIS (Carl Zeiss, Jena) spectrophotometer in the 200–800 nm region in ethanol as solvent (concentration, 2 to  $4 \cdot 10^{-5}$  M/l) at  $25 \pm 0.2^\circ\text{C}$ . The pK values of acids *VIII*, *IX*, *XI—XIII* were determined by potentiometric titration in 1 : 1 (v/v) ethanol–water with the use of a glass and calomel reference electrode<sup>8</sup>). Data calculated from the half neutralisation point were taken as the pK values (Table II and III).

## REFERENCES

1. Kada R., Knoppová V., Jurášek A., Kováč J.: *Tetrahedron* **32**, 1411 (1976).
2. Kada R., Knoppová V., Kováč J.: *This Journal* **40**, 1563 (1975).
3. Kada R., Surá J., Kováč J., Jurášek A., Arvay A.: *This Journal* **41**, 2571 (1976).
4. Galustjan G. G., Cukervanik I. P.: *Zh. Obshch. Khim.* **34**, 1478 (1964).
5. Belenkii L. I., Karmanova I. B., Vol'kenstein Yu. B., Petrovskii P. V., Fedorov L. A., Gol'd-farb Ya. L.: *Izv. Akad. Nauk SSSR Ser. Khim.* **1974**, 1725.
6. Černayová M., Kováč J., Foltýnová P., Ebringer L.: *Chem. Zvesti*, in press.
7. Krutošíková A., Surá J., Kováč J., Kalfus K.: *This Journal* **40**, 3357 (1975).
8. Dewar M. J. S., Grisdale P.: *J. Amer. Chem. Soc.* **84**, 3546 (1962).

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