

Furan derivatives

176. Synthesis and properties of 4-[2-(5-X-2-furyl)vinylene]-benzoic acids and their methyl esters

*V. KNOPPOVÁ, ^bA. BEŇO, and *J. KOVÁČ

^aDepartment of Organic Chemistry, Slovak Technical University,
812 37 Bratislava

^bDepartment of Analytical Chemistry, Faculty of Natural Sciences,
Komenský University, 842 15 Bratislava

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By the Wittig reaction of 4-methoxycarbonylbenzyltriphenylphosphonium bromide with 5-X-2-furaldehydes, where X = H, CH₃, NO₂, Br, I, COOCH₃, the corresponding methyl 4-[2-(5-X-2-furyl)vinylene]benzoates were prepared. Alkali hydrolysis of these compounds gave the appropriate benzoic acids. Ultraviolet and infrared spectra are presented and discussed. The pK values were determined potentiometrically.

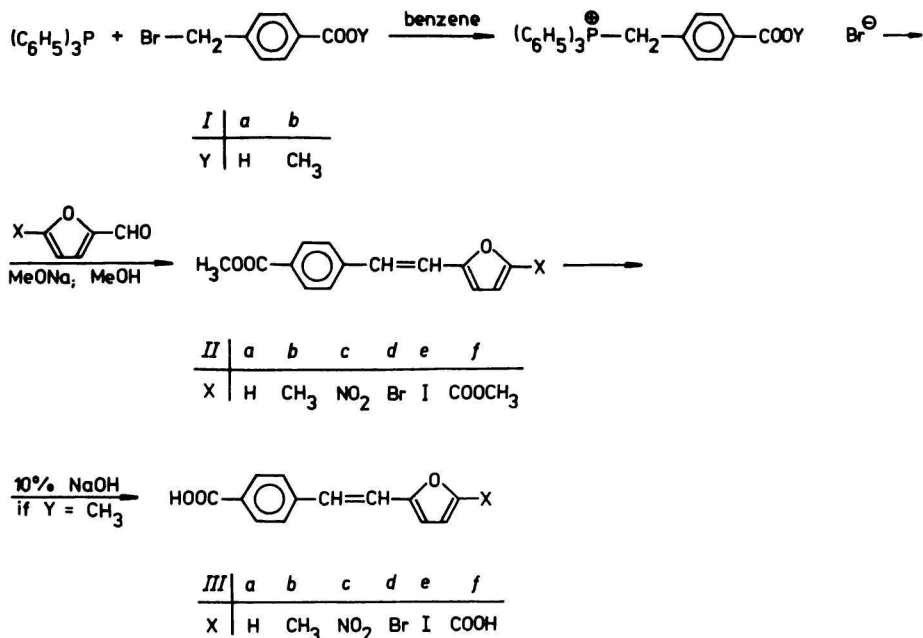
Реакцией Виттига 4-карбметоксибензилтрифенилфосфонийбромидом с 5-X-2-фураляльдегидами, где X = H, CH₃, NO₂, Br, I и COOCH₃ были приготовлены соответствующие метиловые эфиры 4-(5-X-фурил-2-винил)бензойной кислоты. Щелочной гидролиз указанных соединений дает соответствующие бензойные кислоты. Приводятся и обсуждаются УФ и ИК спектры. Значения pK были определены потенциометрически.

In the last few years, attention has been focused on investigation of the effects of substituents on the reaction centre through furan ring. A certain transfer of polar effects was found in systems where the substituent was bound directly to the furan ring [1], in compounds of the arylfuran type [2], and in bridge furan derivatives where the aromatic ring was separated from the furan ring by —SO₂ [3], —S— [3], —CO— [4], —O— [5, 6], and —CH=CH— [7, 8] groups. On the basis of this knowledge the effect of the substituent on the furan ring on acidity of the carboxyl group bound to benzene ring of 4-[2-(5-X-2-furyl)vinylene]benzoic acids was investigated and compared.

The present work deals with synthesis of these acids and their methyl esters.

The compounds mentioned above were prepared by the Wittig reaction in two ways. In the first case the starting compound was *p*-methoxycarbonylbenzyltriphenylphosphonium bromide (*Ib*), prepared by the reaction of *p*-methoxycarbonylbenzyl bromide with triphenylphosphine in benzene, which was

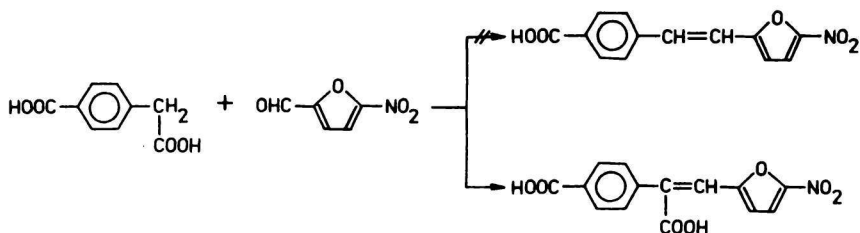
used for condensation with 5-X-2-furaldehydes in methanol under the catalysis of sodium methoxide as base. Methyl ester *IIC* was prepared by the Wittig method in 1976 after [9] (Scheme 1). The obtained methyl esters *IIa—IIf* were hydrolyzed in



Scheme 1

10% NaOH to give the appropriate acids *IIIa—IIIf*. The acids *IIIa—IIIc* were prepared also directly from 4-carboxybenzyltriphenylphosphonium bromide with 2-furaldehyde and its 5-methyl and 5-nitro derivatives, respectively. All methyl esters and acids were separated and purified on a silica gel column giving pure isomers (*E*), the structures of which were proved by ¹H-n.m.r. spectrometry. The protons *H_A* and *H_B* on the double bond appeared in the spectrum as two doublets of the interaction constant 16.3 Hz, which is characteristic of the arrangement of protons in *E* isomers.

To prepare 4-[2-(5-nitro-2-furyl)vinylene]benzoic acid also the condensation reaction of 4-carboxyphenylacetic acid with 5-nitro-2-furaldehyde [10, 11] was carried out at boiling with subsequent decarboxylation. Though different catalysts (pyridine, piperidine) and solvents (ethanol, pyridine, acetic anhydride) were used in this reaction, instead of the expected acid, only the condensation product without subsequent decarboxylation was obtained. Its structure was verified by



Scheme 2

general analytical methods (Scheme 2). The synthesized 4-[2-(5-X-2-furyl)vinylene]benzoic acids and their methyl esters are presented in Tables 1 and 2.

With the 4-[2-(5-X-2-furyl)vinylene]benzoic acids and their methyl esters, which represent a conjugated system of benzene and furan rings connected through the —CH=CH— group, the last absorption band was shifted to 341–402 nm (with acids) and 340–382 nm (with methyl esters) and was of high intensity. This phenomenon was observed also with other furan derivatives containing a further chromophore [12]. The other two bands at 204–227 and 244–287 nm can be assigned to $\pi \rightarrow \pi^*$ electron transfer in the furan part of the molecule. With the synthesized 2-(4-carboxyphenyl)-3-(5-nitro-2-furyl)acrylic acid the last absorption maximum appeared at 380 nm, *i.e.* it was shifted hypsochromically by 22 nm, when compared to the *IIIc* derivative, due to deplanation of the system by the bulky COOH group bound on ethylene bond.

In the i.r. spectra of both series of compounds similar bands occurred: $\tilde{\nu}(\text{C}=\text{O})$, $\tilde{\nu}(\text{C}=\text{C})$, and bands characteristic of furan ring. The vibrations $\tilde{\nu}(\text{C}=\text{O})$ of free acids were observed in the region of 1680–1695 cm^{-1} , while those of methyl esters were shifted to higher wavenumbers 1715–1726 cm^{-1} . For the absorption bands $\tilde{\nu}(\text{C}=\text{O})$ of esters, band splitting was characteristic which vanished and appeared only as a small shoulder in the case of acids. These bands were of strong intensity and only little affected by the nature of the substituent. The vibrations of the ethylene bond $\tilde{\nu}(\text{C}=\text{C})$ in both series were overlapped by vibrations of the benzene and furan rings and appeared in the region of 1603–1617 cm^{-1} as complex bands. With all synthesized compounds a narrow band was observed in the region of 840–870 cm^{-1} (with acids) and 870–885 cm^{-1} (with esters) which belongs to deformation vibrations of furan C—H.

The measured pK values of acids *IIIa*–*IIIe* varied in the range 5.70–5.42 indicating acids of lower acidity than the isomeric 5-styryl-2-furancarboxylic acids [8] (pK 4.18–4.83). Some difference in the transfer of polar effects was also observed: the ρ value of the compounds *IIIa*–*IIIe* was 0.392 while that of 5-styryl-2-furancarboxylic acids was 0.507.

Table 1

Methyl 4-[2-(5-X-2-furyl)vinylene]benzoates (*IIa—IIf*)

Compound	Formula	<i>M</i>	Calculated/found		Yield %	M.p. °C	λ_{\max}/nm log ϵ		$\tilde{\nu}(\text{C}=\text{O})$ cm^{-1}	
			% C	% H						
<i>IIa</i>	$\text{C}_{14}\text{H}_{12}\text{O}_3$	228.1	73.64	5.26	46.7	141—142	206	227	341	1716
			73.90	5.63			4.45	4.27		
<i>IIb</i>	$\text{C}_{13}\text{H}_{14}\text{O}_3$	242.1	74.30	5.78	42.5	125—128	207	226	351	1724
			75.00	5.91			4.41	4.25		
<i>IIc</i> ^a	$\text{C}_{14}\text{H}_{11}\text{O}_3\text{N}$	273.1	61.50	4.02	49.2	190—191	203	224, 283	382	1726
			61.24	4.30			4.00	3.99, 3.90		
<i>II d</i> ^b	$\text{C}_{14}\text{H}_{11}\text{O}_3\text{Br}$	307.1	54.07	3.58	51.5	107—108	204	225	340	1721
			54.80	3.81			4.12	3.84		
<i>IIe</i>	$\text{C}_{14}\text{H}_{11}\text{O}_3\text{I}$	354.2	47.45	3.10	53.4	103—104	205	224, 299	343	1715
			48.00	3.37			4.47	4.25, 4.07		
<i>II f</i>	$\text{C}_{16}\text{H}_{14}\text{O}_3$	286.1	67.10	4.89	51.7	139—140	204	224, 255	343	1726
			67.80	5.02			4.48	4.28, 3.82		

a) % N: calculated 5.58, found 5.23; b) % Br: calculated 26.05, found 26.19.

Table 2
4-[2-(5-X-2-Furyl)vinylene]benzoic acids (IIIa—IIIf)

Compound	Formula	M	Calculated/found		Yield %	M.p. °C	λ_{\max}/nm log ϵ			$\tilde{\nu}(\text{C}=\text{O})$ cm^{-1}	pK
			% C	% H							
IIIa	C ₁₃ H ₁₀ O ₃	214.1	72.86	4.67	80.5 ^b , 50.2 ^a	160—162	210	245	345	1690	5.62
			72.75	4.58			4.30	4.10	4.40		
IIIb	C ₁₄ H ₁₂ O ₃	228.1	73.63	5.25	52.5 ^a , 93.5 ^b	148—150	204, 227	244	345	1680	5.70
			73.46	5.28			4.40, 4.12	4.01	4.44		
IIIc	C ₁₃ H ₉ NO ₃	259.1	60.20	3.47	58.8 ^a , 82.9 ^b	290—293	205, 223	287	402	1710	5.42
			59.99	3.71			4.14, 4.01	3.57	3.72		
III d	C ₁₃ H ₉ O ₃ Br	293.0	53.23	3.07	90.7 ^b	218—219	204	244	341	1710	5.50
			52.97	3.18			4.42	4.29	4.54		
IIIe	C ₁₃ H ₉ O ₃ I	340.0	45.87	2.64	90.2 ^b	207—208	204	244	345	1681	5.58
			45.37	2.79			4.24	3.90	4.53		
III f	C ₁₄ H ₁₀ O ₃	258.1	65.08	3.87	95.8 ^b	257—260	205	251	347	1688	—
			64.58	4.01			4.30	4.14	4.37		

a) Prepared by the procedure A; b) prepared by the procedure B.

Experimental

Electronic absorption spectra of the compounds investigated were measured on a recording Specord UV VIS spectrophotometer in the region of 200—460 nm at $3\text{--}5 \times 10^{-5}$ M in ethanol. Infrared spectra were obtained on a double-beam UR-20 (Zeiss, Jena) spectrophotometer in the region of $700\text{--}3800\text{ cm}^{-1}$ using KBr technique (2 mg of compound).

The pK values were determined by potentiometric titration of 5×10^{-3} M solutions of the studied acids (20 ml) in 50% ethanol (v/v) with 0.1 M-NaOH solution at 25°C after [6].

p-Methoxycarbonylbenzyltriphenylphosphonium bromide (Ib)

In a round-bottomed flask *p*-methoxycarbonylbenzyl bromide (6 g; 0.026 mol), triphenylphosphine (7.3 g; 0.03 mol), and dry benzene (25 ml) were stirred and refluxed in nitrogen atmosphere for 3 h. After about 10 min a white crystalline phosphonium salt precipitated. After cooling it was sucked, washed with ether on the filter, and dried. Yield 71.9%, m.p. $255\text{--}256^\circ\text{C}$.

Methyl 4-[2-(5-X-2-furyl)vinylene]benzoates (II)

p-Methoxycarbonylbenzyltriphenylphosphonium bromide (5.4 g; 0.011 mol) was dissolved in methanol (20 ml) and the solution of 5-X-2-furaldehyde (0.011 mol) in methanol (20 ml) was added. The mixture was cooled to room temperature (with X = NO_2 to -10 to -20°C) and sodium methoxide (0.01 mol) was added under stirring and the mixture was allowed to stay for 1 h. After this time it was poured into water (1 l) under stirring and was allowed to stay overnight. The precipitate was sucked and washed with water. The aqueous layer was extracted thrice with ether. The ether layers were combined, dried with anhydrous Na_2SO_4 and the solution was evaporated to dryness. The crude product was crystallized from aqueous ethanol. Isolation of the final products was achieved on a silica gel column using chloroform as solvent. The purity of the prepared methyl esters was checked chromatographically on thin layers of SiO_2 in chloroform.

4-[2-(5-X-2-Furyl)vinylene]benzoic acids (III)

Procedure A

The procedure was similar to that used for the preparation of methyl esters. The starting compound was 4-carboxybenzyltriphenylphosphonium bromide (0.011 mol) and 5-X-2-furaldehyde (0.011 mol), where X = H, CH_3 , NO_2 .

Procedure B

Methyl 4-[2-(5-X-2-furyl)vinylene]benzoate (0.01 mol) was heated on a boiling water bath in 10% NaOH (30 ml) until all ester was converted to sodium salt of acid in the

solution. Hydrolysis proceeded more rapidly after addition of methanol (20 ml). Time of hydrolysis ca. 4 h. After hydrolysis was over, alcohol was distilled off and the solution was acidified with HCl (1 : 1) precipitating the appropriate acid. The acids were purified through their sodium salts.

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