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FURAN DERIVATIVES—LXXVII

SYNTHESIS AND STUDY OF SULPHIDES AND SULPHONES OF 5-NITROFURAN SERIES

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Abstract—Two series of 5-nitro-2-furfurylarylsulphides **4a–4f** and 5-nitro-2-furfurylarylsulphones **5a–5g** were prepared by the reaction of 5-nitrofurfurylbromide[1] with 4-substituted thiophenols **2a–2f** and with 4-substituted benzenesulphinic acids **3a–3g**, respectively. In these compounds the transmission of polar effects of the substituents by the –S– and SO_2 groups, respectively, was found to take place. p*K* Values of compounds studied has been determined spectroscopically.

Transmission of polar effects by various atoms or groups has been studied by several authors. However, no systematic work has been done on the SO_2 group. Some authors[1-3] report that conjugation does not appear to have any marked effect on the vibration of the SO_2 group, while Koch[4] supposes, on the basis of UV spectra, that interaction between the SO_2 group and the double bond should be expected. Transmission of polar effects by the SO_2 group was reported by Nepluev[5] and by Amell.[6] All sulphones in which transmission of polar effects by the SO_2 group has been studied, so far contain the CH_2SO_2 group situated between a substituted aromatic nucleus and an electron withdrawing group, e.g. CN, COOR, SO_2, COR.

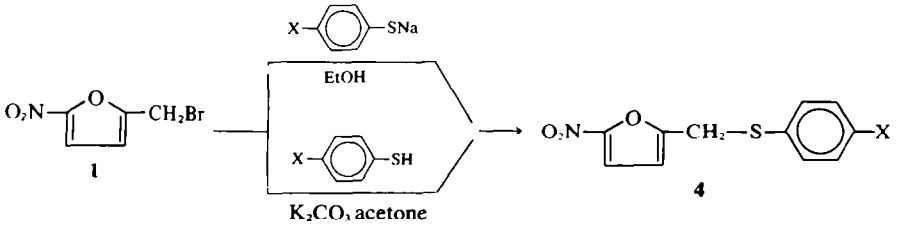
This paper deals with the synthesis and transmission of polar effects of 5-nitrofurfurylaryl sulphides and 5-nitrofurfurylaryl sulphones. The sulphides **4a–4f** were prepared by the reaction of 4-substituted thiophenol sodium salts with **1** in methanol (method A) or by the reaction of 4-substituted thiophenols with **1** in anhydr. acetone in the presence of anhydr. K_2CO_3 (method B).

In both methods the reactions were carried out under N_2 to prevent the formation of by-products, diaryldisulphides. In both cases high yields of all sulphides were obtained, with the exception of compound **4a** (41%) where resinous compounds were formed. If 5-nitrofurfurylnitrate was used, the sulphide yields were substantially lower (30–50%). Attempts to prepare 4-dimethylaminophenyl- and 4-methoxyphenyl-5-nitrofurfuryl-sulphides were not successful even under various reaction conditions (using temperatures from −20°C to 20°C and reaction times from 0.5 to 5 h). Only diaryldisulphides could be isolated from the reaction mixture.

The sulphones **5a–5g** were synthesised from furfurylalcohol (Scheme 2). Product **1** was not isolated but reacted directly with the sulphinic acid salts **3a–3g** to give the corresponding sulphones.

In both types of compounds the CH_2SO_2 and CH_2S groups are directly attached to the 5-nitrofuran nucleus. These structures enable a more effective delocalization of the free electron pair of the carbanion increasing its stability and its acidity. The stability of the carbanion can be explained as illustrated in Scheme 3. While in structure **6** d-orbitals of the sulphur atom take part in the stabilization of the carbanion, in structure **7** delocalization of the electron pair through the 5-nitrofuran nucleus occurs.[7] Which of these structures prevails in the stabilization of the anion depends on the nature of the group bonded on the SO_2 group. By analogy, in the sulphides, the stabilization effect will depend on the nature of group attached to the S atom.

The influence of transmission of polar effects on the acidity of the methylene hydrogens in the sulphones and sulphides investigated was studied by measuring p*K* values and the rate constants for carbanion formation.



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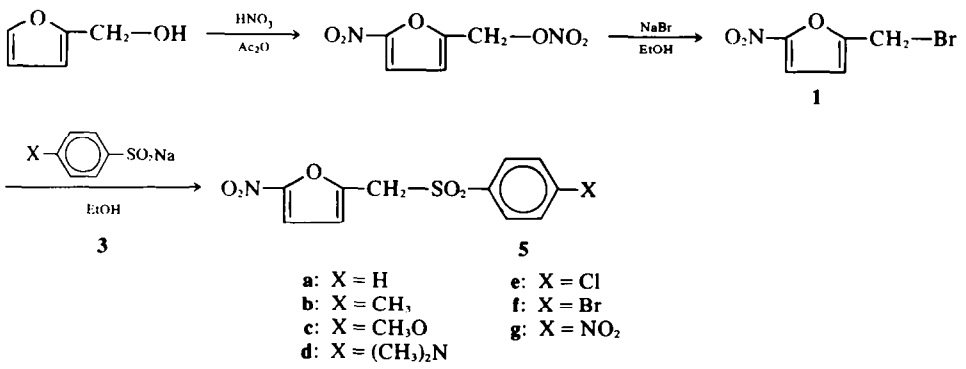
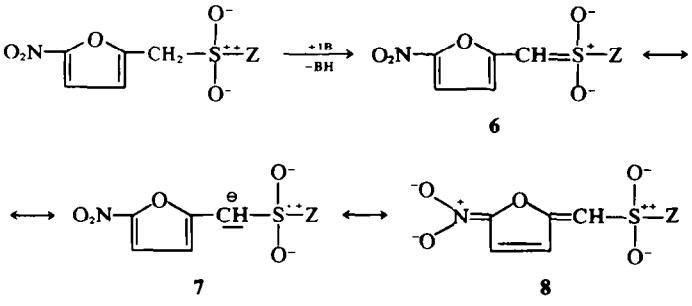
a: X = H **d**: X = Cl
b: X = CH_3 **e**: X = Br
c: X = CH_3CONH **f**: X = NO_2

Scheme 1.



a: X = H
b: X = CH_3
c: X = CH_3O
d: X = $(CH_3)_2N$
e: X = Cl
f: X = Br
g: X = NO_2

Scheme 2.



Scheme 3.

The pK values were determined spectroscopically. In alkaline media the carbonions studied showed strong absorption in the visible region. From the pK values of the sulphides and sulphones it follows that these compounds are strong C-acids, comparable only with the disulphones of the aromatic series.[5] The pK values of the sulphides were found to be between 8.89 (**4f**) and 10.15 (**4b**). In this case, the acidity of the methylene hydrogens may be ascribed not only to the influence of the 5-nitrofuryl residue, but mainly to the interaction of the free electron pair of the sulphur atom with the *p*-substituent. This is also supported by good correlation of pK values of this series with the substituent Hammett σ_p constants (r = 0.97, ρ = +1.59). The value indicates the rather strong transmission of polar effects by the sulphur atom. It is interesting to note that the pK values of the sulphones **5a–5g** (Table 3) did not differ substantially from those of the corresponding sulphides **4a–4f**. In the sulphides the acidity of the methylene group was influenced by the interaction of the free electron pair of sulphur with the substituted aromatic nucleus, whereas in the sulphones the main acidifying effect was due to the SO_2 group.

These results indicate that transmission of polar effects by the SO_2 group does occur and is also supported by the pK values of the extreme derivatives **5d** (pK = 10.34) and **5g** (pK = 9.33). The dependence of $\log K/K_0$ on σ_p constants in sulphones **5c–5g** is linear with ρ = +0.68 and r = 0.90 (Fig. 1). This is in accord with the data reported by Amel and Marek[6] who found good correlation in 4-substituted phenylphenylacylsulphones with the Hammett σ_p constants (ρ = +2.01). A rather low ρ value showed that electron withdrawing substituents increase the acidity of the methylene hydrogens of the sulphones. However, in this case the influence of the substituents is not so marked as that in other types of sulphones,[6] i.e. carbanion structure **6** is less in evidence. In the stabilization of carbanions structure **8** probably predominates in compounds with either electrondonating or electron withdrawing substituents.

Carbanion formation rate in the aromatic 5-nitrofurfuryl-sulphides series **4a–4b** is linearly dependent on OH-ion concentration in the pH region under consideration (9–11)(Fig. 2). Similar linear dependence of

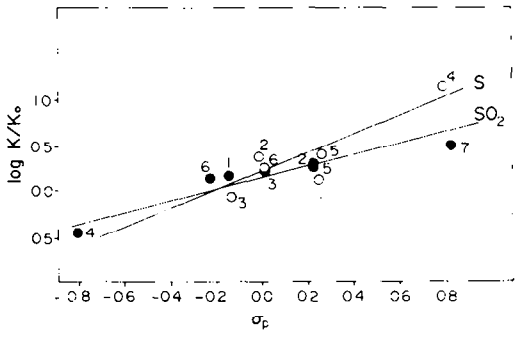


Fig. 1. A plot of $\log K/K_0$ vs Hammett σ_p constants of 5-nitrofurfuryl-(4-X-phenyl)sulphides (S) and appropriate sulphones (SO_2).

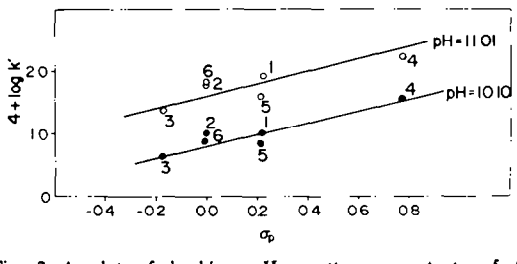


Fig. 2. A plot of $\log k'$ vs Hammett σ_p constants of 5-nitrofurfuryl-(4-X-phenyl)sulphides.

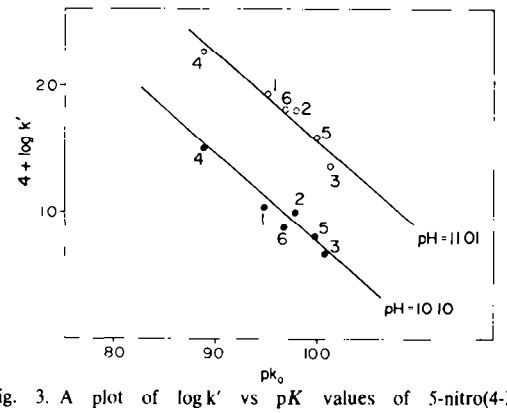


Fig. 3. A plot of log k′ vs pK values of 5-nitro(4-X-phenyl)sulphides.

log k′ on σ_p constants at given pH values was observed (ρ pH 10.10 = 0.79, r = 0.91, ρ pH 11.01 = 0.74, r = 0.93), (Fig. 3). Carbanion formation rates in sulphones **5a–5g** were not measurable under similar conditions, the reaction having taken place immediately owing to the strong acidifying effect of the SO_2 group.

EXPERIMENTAL

UV and visible spectra were recorded with a Specord UV VIS Zeiss instrument. To obtain kinetic data and pK values, measurements were carried out at various temps. in 10.0 mm cells. Heating was by water from an ultrathermostat.

Substituted thiophenols (**2b–2e**) were prepared by the reduction of the corresponding 4-substituted benzenesulphochlorides with zinc in concentrated HCl.[8] The sodium salt of **2f** was prepared by the reaction of 4-nitrochlorbenzene with Na_2S_2.[9] Compound **1** was prepared by the reaction of 5-nitrofurfurylnitrate with NaBr in ethanol.[10] 4-chloro-, 4-bromo- and 4-methoxybenzenesulphinic acids (**3c, 3e, 3f**) were prepared by the reaction of the corresponding diazo salts with SO_2 in the presence of powdered cuprum or Cu_2O.[11] 4-Nitrobenzenesulphinic acid **3g** was prepared by the reduction of 4-nitrobenzenesulphochloride with Na_2SO_3 in alkaline medium.[12]

Preparation of **3d**. A solution of 4-bromo-dimethylaniline (21g, 0.109 mole) in ether (45 ml) was gradually added, under N_2, to a stirred refluxing solution of lithium (2g) in ether (45 ml). After 15 min the solution was cooled and an ethereal solution of SO_2 (10–12 g) was carefully added. The white precipitate (**3d**) was filtered off and used without further purification in the synthesis of **5d**.

Preparation of **4a–4f**.

Method A. A solution of the Na-salts **2a–2f** (0.01 mole) in ethanol (15–20 ml) was, under N_2, to a stirred solution of **1** and the temp. kept at 20°C. After 3–5 h at room temp. the reaction mixture was poured into cold water (50 ml) and stirred for an additional 30 min. The precipitated sulphide was filtered off, washed with water, air dried and crystallized from ethanol. If, after pouring the reaction mixture into water, an oily product formed, then extraction with ether was found to be convenient for isolating the appropriate sulphide.

Method B. A solution of **1** (0.01 mole) in dry acetone (10 ml) was added under N_2, to the stirred mixture of compound **2**(a–b)

Table 1. Melting points, yields and elemental analyses of 5-nitrofurfuryl-(4-X-phenyl)sulphides

Compound No.	X	Formula	m.p.(°C)† b.p.	Analytical data Cald./found %C	%H	%N	%S	Yield %
4a	H	$C_{11}H_9NO_3S$	160°/3torr	56.17	3.86	5.95	13.63	
				55.88	3.56	5.78	13.45	41.2
4b	CH_3	$C_{12}H_{11}NO_3S$	65–66°	–	–	–	–	89.6
4c	CH_3CONH	$C_{13}H_{12}N_2O_4S$	124–126°	53.42	4.14	9.58	10.97	
				53.38	4.04	9.61	11.07	92.0
4d	Cl	$C_{11}H_8ClNO_3S$	48–49°	48.99	2.99	5.19	11.89	
				48.77	2.74	5.02	11.68	62.0
4e	Br	$C_{11}H_8BrNO_3S$	90–91°	42.06	2.57	4.46	10.21	
				41.84	2.46	4.38	10.32	71.5
4f	NO_2	$C_{11}H_8N_2O_5S$	157–160°	–	–	–	–	72.8

†Crystalized from ethanol.

Table 2. Melting points, yields and elemental analyses of 5-nitrofurfuryl-(4-X-phenyl)sulphones

Compound No.	X	Formula	m.p. (°C)	Analytical data Cald./found %C	%H	%N	%S	Re-cryst. solv.†	Yield %
5a	H	$C_{11}H_9NO_4S$	190–191°	–	–	–	–	A	72.5
5b	CH_3	$C_{12}H_{11}NO_4S$	198–200°	–	–	–	–	A	75.4
5c	CH_3O	$C_{12}H_{11}NO_5S$	218–221°	48.50	3.74	4.71	10.79		
				48.37	3.51	4.58	10.68	B	52.7
5d	$(CH_3)_2N$	$C_{13}H_{14}N_2O_4S$	220–222°	50.32	4.55	9.03	10.33		
				50.16	4.57	8.89	10.34	A	54.5
5e	Cl	$C_{11}H_8ClNO_4S$	210–211°	43.79	2.67	4.64	10.63		
				43.67	2.54	4.51	10.55	A	62.57
5f	Br	$C_{11}H_8BrNO_4S$	219–220°	38.17	2.33	4.05	9.26		
				38.06	2.22	3.94	9.11	C	65.0
5g	NO_2	$C_{11}H_8N_2O_7S$	188–189°	42.32	2.58	8.97	10.27		
				42.27	2.41	8.88	10.11	B	47.5

†A: acetic acid, B: ethanol, C: acetone.

Table 3. UV spectra and pK values of the synthesised sulphides and sulphones

Compound No.	λ_{max} [nm](log ϵ)	pK
4a	218(4.02), 244(3.84), 323(3.91)	9.83
3b	219(4.11), 254(3.85), 325(4.05)	10.15
4c	214(4.16), 268(4.27), 321(4.01)	9.72
4d	214(4.04), 258(3.84), 322(3.92)	10.01
4e	212(4.22), 230(4.13), 258(4.04), 322(3.98)	9.55
4f	214(4.22), 231 sh (4.09), 327(4.39)	8.89
5a	221(4.07), 260(3.34), 268(3.45), 274(3.56), 314(4.03)	9.71
5b	228(4.30), 274 sh (3.64), 314(4.15)	9.78
5c	211(3.94), 242(4.22), 269 sh (3.56), 315(3.97)	9.81
5d	217(4.19), 290(4.46)	10.34
5e	209i (4.03), 230(4.25), 309(4.00)	9.64
5f	209(4.06), 237(4.23), 312(3.98)	9.62
5g	214(4.06), 248(4.20), 309(4.15)	9.33

(0.01 mole) and anhydrous K_2CO_3 in dry acetone (20 ml), and the stirring continued for 3 h at room temp. The precipitates KBr was filtered off and the filtrate poured into cold water (50 ml). The sulphides **4a–4f** were isolated as described in Method A. (For m.ps, yields and analyses see Table 1).

Preparation of **5a–5g**. A mixture of 5-nitrofurfurylnitrate (18.8 g, 0.1 mole) and NaBr (10.7 g, 0.1 mole) in ethanol (150 ml) was refluxed for 1.5 h. The alkaline salt of compounds **3a–3g** (0.1 mole) was added and the mixture refluxed for an additional 2–3 h. The reaction mixture was poured into cold water and the precipitated sulphone filteres off, washed with water, air dried and recrystallized from the appropriate solvent (see Table 2).

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