FURAN DERIVATIVES—III

SYNTHESIS AND PROPERTIES OF β-KETOSULPHIDES AND SULPHUR DERIVATIVES OF CHALCONES OF 5-NITROFURAN SERIES

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Abstract—A series of 2-(5-nitro-2-furyl)-2-oxoethylarylsulphides 3a-3h has been prepared by the reaction of 5-nitro-2-furylbromomethylketone 1 with 4-substituted thiophenols 2a-2h. The determined rates of carbanion formation (log k'), pK values as well as 'H NMR data show that in these compounds transmission of polar effects by the substituents through the -S- group occurs. Compounds 3a-3h react with aromatic aldehydes affording sulphur chalcone derivatives of the 5-nitrofuran series 4a-4h. 'H NMR, IR and UV spectra of prepared compounds are discussed.

With respect to controversial data about the transmission of polar effects by the substituents through the SO₂¹⁻⁷ group we studied this problem on the 5-nitrofurfurylarylsulphides and sulphones⁸ as well as on β -ketosulphones⁹ of the 5-nitrofuran series. A linear correlation of Hammett's substituent constants with studied characteristics of hydrogen atoms of the methylene group shows that the transmission of polar effects by the substituents through the SO₂ group is possible.^{8,9} In consequence of the acidity of hydrogen atoms of the methylene group directly attached to the 5-nitrofuran ring these compounds can be used in the synthesis of α,β -unsaturated sulphones.^{10,11}

This paper deals with a synthesis and transmission of polar effects by the substituents in 2 - (5 - nitro - 2 - furyl) - 2 - oxoethyl sulphides containing the CH₂ group

situated between the 5-nitro-2-furoyl- and 4-Xphenylthiol residues. Sulphides 3a-3h were prepared by the reaction of 4-substituted thiophenols 2a-2h with 1 in ethanol in 64-81% yield (Table 1). Of these compounds only the preparation of 3a has been described.¹² Attempts to prepare sulphides from sodium thiophenolates in ethanol or in dry acetone catalysed by K₂CO₃ were unsuccessful; only resinous compounds were obtained.⁸ Since β -ketosulphides give the corresponding carbanions readily, we used them in the synthesis of sulphur chalcone derivatives of the 5-nitrofuran series 4a-4h (Table 2) using a one-stage condensation of 3a-3h with benzaldehyde in glacial acetic acid catalysed by piperidine and ammonium acetate (Scheme 1).

The UV spectra of 3a-3h display 3 bands in the



Compound No.	х	Formula	m.p. °C	%C	Calc. %H	Found %N	%S	Yield %
3a	н	C ₁₂ H ₉ NO ₄ S	68-69					79
3b	CH ₃	C ₁₃ H ₁₁ NO ₄ S	77-78	56.21	3.99	5.05	11.56	75
				55.99	4.04	5.19	11.94	
3c	CH ₃ O	CDHDNO ₅ S	78-79	53.23	3.77	4.77	10.94	78
				53.16	3.82	4.76	10.99	
3d	CH3CONH	$C_{14}H_{12}N_2O_5S$	172	52.51	3.77	8.74	10.00	81
				52.23	3.87	8.76	10.21	
3e	CI	C12H8NO4SCI	80-82	48.41	2.71	4.70	10.77	64
				48.42	2.73	4.65	11.00	
3f	NO ₂	$C_{12}H_8N_2O_6S$	141-143	46.75	2.61	9.08	10.40	80
				46.70	2.58	8.99	10.64	
3g	CH3OOC	$C_{14}H_{11}NO_6S$	125-127	52.34	3.45	4.36	9.98	74
				52.07	3.40	4.28	10.21	
3h	HOOC	C13H9NO6S	193-195	50.80	2.95	4.56	10.42	70
				50.61	3.11	4.48	10.26	

Table 1. Physical and chemical properties of 2-(5-nitro-2-furyl)-2-oxoethyl-4-X-phenylsulphides

Table 2. Physical and chemical properties of 1-(5-nitro-2-furoyl)-1-4-X-phenyltio-2-phenylethylenes

Compound			m.p.	Calc. found				Yield
No.	Х	Formula	°Ċ	%C	%H	%N	%S	C.
4a	Н	C ₁₉ H ₁₃ NO ₄ S	156	64.96	3.71	3.99	9.13	49
				64.63	3.40	4.09	9.28	
4b	CH ₃	C ₂₀ H ₁₅ NO ₄ S	129	65.75	4.11	3.83	8.78	42
				64.96	3.99	3.73	8.85	
4c	CH ₃ O	C20H15NO5S	138-139	62.97	3.93	3.67	8.42	45
				62.99	4.08	3.73	8.59	
4d	CH ₃ CONH	$C_{21}H_{16}N_2O_5S$	149	61.76	3.92	6.86	7.86	51
				61.50	4.11	7.01	7.81	
4e	Cl	C19H12NO4SCI	151-152	59.16	3.11	3.63	8.31	45
				59.12	3.33	3.70	8.49	
4f	NO ₂	C19H12N2O6S	120-122	57.58	3.03	7.07	8.09	58
				57.30	3.01	7.00	8.35	
4g	CH ₃ OOC	C21H1SNO6S	136-137	61.62	3.66	3.43	7.84	55
3				61.48	3.70	3.60	7.94	
4h	HOOC	C ₂₀ H ₁₃ NO ₆ S	203-205	60.75	3.29	3.54	8.10	48
				60.62	3.12	3.53	8.14	

208-227 nm, 246-268 nm and 286-315 nm regions. The UV spectra of 3a-3f measured in alkaline soln show absorption in the 424-492 nm region, resulting from the presence of carbanion (Table 3). Comparison of the pK values reveals that the acidity of hydrogens of the CH₂ group is about the same in both types of sulphides having the same substituent X (see canonical structures for the two types of carbanion at II and III). Although acidifying groups in I and 3a-3h are strongly electronwithdrawing 5-nitrofuryl and 5-nitro-2-furoyl remainders, respectively. This fact can be explained by various structures of carbanions II and III.

These compounds are strong C-acids comparable with disulphones of the aromatic series.⁵ It is evident that carbanion II can predominantly delocalise its negative charge on the directly bonded 5-nitrofuran ring whilst carbanion III does so on the -COCH-S- grouping. It might be assumed that both types of carbanions have a tendency of adopting a planar arrangement which in the case of III facilitates overlapping between the p-orbitals of the carbon and oxygen atoms. A good linear correlation of Hammett's substituent constants σ_p , with log k' (r = 0.90; $\rho = 0.53$) and pK values (r = 0.97; $\rho = 1.39$) and chemical shifts of CH₂ protons (r = 0.97; $\rho =$

Table 3. Chemical shifts, pK values of compounds prepared and rate constants k'/s^{-1} of carbanion formation

Compound No.	CH2	pK	k'. 10 ⁵	Compound No.	δ _{C=C-H}	
3a	4.45	10.03	9.58	4a	7.71	
3b	4.35	10.16	8.16	4b	7.62	
3c	4.23	10.26	7.76	4c	7.55	
3d	4.33	9.76	10.81	4d	7.64	
3e	4.49	9.63	10.36	4 e	7.78	
3f	4.79	8.81		4f	8.15	
3g	4.65		19.91	4g	7.97	
3h	4.65		6.01	4h		



I: pK = 10.15 - 8.89

3a-3f: pK = 10.26 - 8.81



0.53) points out that the acidity of hydrogens of the CH_2 group of **3a-3h** is influenced by the 5-nitro-2-furoyl residue as well as by the nature of the substituent attached to the *p*-position of the benzene ring.

Sulphides 3a-3h react with benzaldehyde to give appropriate 1 - (5 - nitro - 2 - furoyl) - 1 - arylthio - 2 phenylethylenes 4a-4h in 42-58% yield. In the IR spectra the newly synthesised compounds display common characteristic bands: **3a–3h** $\nu_{as}(NO_2) = 1546-1552 \text{ cm}^ \nu_s(NO_2) = 1346-1353 \text{ cm}^{-1}; \quad \nu(C=O) = 1693-1697 \text{ cm}^ \nu$ (C=O) = 1693–1697 cm⁻¹ and 4a-4h: ν (C=O) = 1663-1669 cm⁻¹, i.e. in the region of absorption of α,β -unsaturated ketones.¹³ All these bands are intense and only slightly influenced by the character of the substituents. The ν (C=C) bands of 4a-4h overlapped by the bands belonging to the skeletal vibrations of the benzene and furan rings, respectively, are observed in the range of 1585-1596 cm⁻¹. All these compounds display a band in the 877-893 region assigned to the vibration of the furan ring.¹⁴ In the UV spectra of 4a-4h, four bands are observed in the regions: 206-232, 262-277, 300-320 and 385-403 nm. The sharp m.p. chromatograms on silufol plates and 'H NMR spectra confirm that chalcones 4a-4h are pure geometrical isomers which can theoretically exist in Z and E forms. Comparison of the measured chemical shift of the ethylene proton ($\delta =$ 7.71 ppm) of 4a and the chemical shift calculated on the basis of additive increments¹⁵ for $E(\delta = 7.13 \text{ ppm})$ and $Z(\delta = 7.44 \text{ ppm})$ isomers reveals that compounds studied exist in the Z configuration.

This conclusion is also confirmed by the results obtained with the shift reagent Eu(FOD)₃. From the dependence of inductive chemical shifts on the molar ratio of substrate and shift reagent it was found that the largest inductive shift is observed for the ethylenic proton, i.e. it is situated most closely to the europium ion, and a small shift is observed for H₃ protons of the furan ring. The chemical shifts of *o*-protons of the unsubstituted phenyl ring attached to the ethylene carbon are only slightly affected by the shift reagent. A good linear Hammett correlation of the σ_p substituent constants with chemical shifts of the ethylene proton was observed (r = 0.98; $\rho = 0.58$) indicating that the configuration of 4a-4h is the same.

EXPERIMENTAL

UV spectra were recorded with a Zeiss Specord UV VIS instrument. The determination of pK values and rate constants k' of the carbanion formation was carried out in 10.0 mm cells thermostated at 25°±0.02°C. Kinetic measurements were performed by gradually decreasing the band which appeared at around 424-492 nm. The determination of pK values of 3a-31 was carried out using the same method and conditions as in the case of sulphides (I) reported previously.⁸ For kinetic measurements the reaction mixture consisted of a methanol soln of sulphide (0.5 ml; c = 0.0004 M) and a methanol soln of piperidine (9.5 ml;c = 0.04 M). ¹H NMR spectra were recorded with a Tesla BS 487 spectrometer (80 MHz) in CDCl₃ using TMS as internal standard. IR spectra were recorded with a Zeiss UR-20 spectrophotometer for chloroform soln (c = 0.02 M) in 0.609 mm cells. The starting compound 1 was prepared by brominating 2 - acetyl - 5 nitrofuran¹² in benzene.¹⁶ Compounds 2a-2e were obtained by the reduction of the corresponding arylsulphochlorides with zinc in conc. HCI'^2 and 2f by the reduction of 4-nitrochlorobenzene with Na₂S₂.¹⁸ Compound 2 g was prepared by the diazotation of 4-aminobenzoic acid followed by a reaction with Na2S2. Compound 2 h was obtained by esterificating compound 2 g.

2 - (5 - Nitro - 2 - furyl) - 2 - oxoethyl - p - substitutedphenyl sulphides (3a-3b)

To a soln of 1 (4.7 g, 0.02 mole) in ethanol (50 ml), 4-substituted thiophenol 2a-2h (0.02 mole) was added at 50°C and the reaction





mixture was stirred for 2 h. After cooling yellow crystals were filtered off and recrystallized from ethanol. If an oily product separated then alcohol was decanted and the residue was recrystallized.

Benzylidene derivatives of 3a-3h; compounds 4a-4h

To a soln of sulphide 3a-3h (0.01 mole) dissolved in glacial acetic acid (40 ml), benzaldehyde (1.6 g, 0.15 mole) and piperidine (0.5 ml) and ammonium acetate (1.5 g) was added. The reaction mixture was heated on a water bath under reflux with stirring for 2.5 h at 100°C and after cooling was poured with vigorous stirring on to crushed ice (100 g). The crude yellow product was filtered off and recrystallized from ethanol and acetic acid, respectively (4a-4c).

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