KINETICS OF CONDENSATION OF 5-NITROFURFURYL SULFONES WITH ALDEHYDES*

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The kinetics of the condensation of 5-nitrofurfuryl phenyl sulfone with 5-X-2-furaldehydes (X = H, CH_3, OCH_3, $NHCOCH_3$, Cl, Br, $COOC_2H_5$, COOH, NO_2) and 5-(4-X-phenyl)--2-furaldehydes (X = H, CH_3, OCH_3, $NHCOCH_3$, Cl, Br, $COOC_2H_5$, COOH, NO_2) to corresponding 1-(5-nitro-2-furyl)-1-phenylsulfonyl-2-(5-X-2-furyl)ethylenes or 1-(5-nitro-2-furyl)-1-phenylsulfonyl-2-[5(4-X-phenyl)-2-furyl]ethylenes were investigated. The measurements were carried out in the system acetic acid–ammonium acetate–piperidine at 118°C or methanol–piperidine at 41°C by spectrophotometry. The reaction is of the second order and its rate constant is correlative with the σ_p^+ constants of the substituents. For the comparison of the effect of the SO_2R residue on the condensation rate some measurements were also carried out with 5-nitrofurfuryl methyl sulfone. The pK_a values of both starting sulfones were also measured spectrophotometrically.

In preceding papers we described a suitable method of preparation of saturated sulfones of the 5-nitrofuran series[1] as well as the possiblities of their utilization in condensation reactions with aldehydes[2–4] (equation (A), where R^1 is alkyl or aryl and R^2 is the residue of the aromatic or heterocyclic aldehyde). In this paper we present the results of the study of the condensation kinetics of sulfones of this type $\left(R = C_6H_5 \text{ or } CH_3\right)$ with 5-substituted 2-furaldehydes and 5-(4-X-phenyl)-2-fural-dehydes.

In condensation reactions of the sulfones of the $R—SO_2—CH_2—Y$ type where R is alkyl or aryl and Y an electron-accepting group as CN(ref.[5]), COOM (ref.[6–11]), COOR $\left(\text{ref.}^7\right)$, NO_2 $\left(\text{ref.}^{12}\right)$, the possibility of delocalisation of the free electron pair in the temporarily formed carbanion exists only to the neighbouring electro-accepting group. Literature also contains data on pK values[13] of some types of these C—H acids, but the kinetics of condensation reactions of these substances has not been investigated so far either.

The structure of carbanions, the condensation rate of which is the subject of this study, is substantially different from the preceding in its ability of delocalisation of the free electron pair after the splitting off of the proton to the neighbouring furan

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nucleus. This delocalisation is effectively furthered by the electron-accepting NO_2 group bound in the position 5 of the furan ring (a), while in basic medium the limit structure (b) probably prevails.
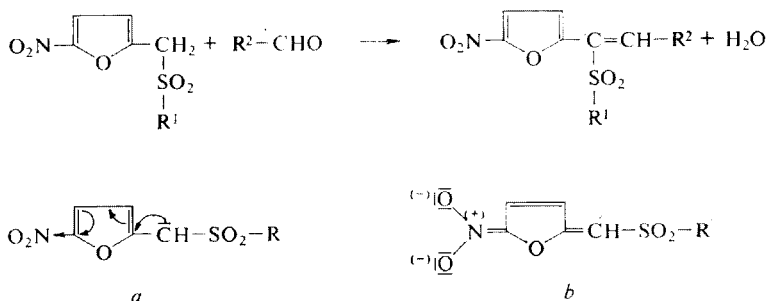
This idea is supported by the total disappearance of the absorption bands corresponding to the 5-nitro-2-furan residue (for SO_2—CH_3 at 308 nm, for $SO_2C_6H_5$ at 318 nm) and the appearance of intensively bathochromically shifted bands[3,4]. The tendency of such anions to pass to the limit structure (b) is not surprising in the case of furan derivatives because the furan nucleus easily changes its aromatic character, and in addition to this, in the case of the anion (b) an advantageous overlapping of the p-orbitals of the carbon atom takes place in consequence of its planar structure with the p-orbitals of the furan nucleus after the splitting off of the proton. The consequence is a general stabilisation of the system. In spite of the spreading of the negative charge over the whole molecule such anions enter the condensation reaction with aromatic and heterocyclic aldehydes under formation of corresponding unsaturated sulfones. From the study of UV spectra it follows that these sulfones are not planar[2] in consequence of steric compression on the ethylene carbon atoms and that they probably have the configuration[3] E.

The measurement of the reaction kinetics was carried out in the system acetic acid–ammonium acetate–piperidine (A), *i.e.* under conditions similar to the preparation of unsaturated sulfones[3,4], or in methanol–piperidine (B). In both cases the reaction was of the second order. The homogeneous solution necessary for kinetic measurements was achieved in the case of method A by using an eight-fold amount of acetic acid. However, under these conditions the reaction did not take place by spectrophotometric measurement criteria. It was found advantageous to use 0·08M piperidine and 0·16M ammonium acetate per 1M of the starting sulfone or aldehyde (8-fold excess in comparison with the amount used in the synthesis). For the checking of whether a side reaction did not take place we followed by UV spectrophotometry the behaviour of unsaturated sulfones under the reaction conditions under which condensation usually took place. As no change of the spectra could be observed, side reactions could be excluded. For the following of the kinetics the system methanol–piperidine was found suitable, in which spectrophotometric measurements could be carried out directly in the cells.

The comparison of the rate constants of the condensation of aldehydes of the furan and phenylfuran series showed that in some cases the aldehydes of the furan series enter the reaction with the corresponding saturated sulfone more willingly. In the case of 5-nitro-2-furaldehyde the rate constant could not be measured under the

TABLE I

Values of the Rate Constants k_2 (1 mol^{-1} min^{-1}) and the Half-Time $t_{1/2}$ (min) of the Reaction of 5-Nitrofurfuryl Phenyl Sulfone with 5-X-Substituted 2-Furaldehydes

No	X	Method A			Method B			σ_p^+
		$k_2 . 10^{-2}$	$t_{1/2}$	$\log k_2$	k_2	$t_{1/2}$	$1 + \log k_2$	
1	H	3·12	64·1	2·4941	4·90	816·3	1·6902	0·00
2	CH$_3$	0·86	232·6	1·9345	0·152	6 578·9	0·1818	−0·311
3	Br	7·80	25·6	2·8921	16·80	238·1	2·2253	+0·150
4	I	4·08	49·0	2·6106	10·00	400·0	2·000	+0·135
5	COOCH$_3$	1·66	120·5	2·2201	1·60	1 250·0	1·2041	+0·489
6	NO$_2$	—	—	—	40·40	99·0	2·6064	+0·790

conditions used. In the case of the aldehydes of the furan series the log k values can be correlated with the σ_p^+ constants of substituents (Table I and II, and Figs 1 and 2). If the value of log k of the derivative with the COOCH$_3$ group was also correlated, an appreciable decrease in the correlation coefficient took place with both methods, which has the value 0·97 for method A (without the derivative with the COOCH$_3$ group) and 0·95 for method B. If only 4 derivatives were taken for correlation (in method A) or 5 derivatives (in method B), these dependences may be considered as orientational only. The correlation of log k on σ_p^+ constants of substituents for the phenylfuran series is very good in both methods $(r = 0·98, \varrho = 0·345\ (A); r = 0·96, \varrho = 0·403\ (B))$. The largest deviations from a linear dependence in both systems was observed for 5-(4-carboxyphenyl)-2-furaldehyde. Evidently, the COOH group of this aldehyde is converted to the corresponding salt under the effect of basic reagents, which results in a decrease in its reactivity.

We checked this fact by measuring the UV spectra of this aldehyde in pure methanol and methanolic piperidine. The aldehyde displays absorption bands at 325 and 338 (sh) nm, while the anion at 300, 312 (sh) and 340 (sh) nm. The comparison of the aldehydes of phenylfuran series with substituents OCH$_3$ and NHCOCH$_3$ under the conditions of condensation A and B is interesting. In methanolic piperidine (B) these derivatives reacted as expected, while in acetic acid medium (A) they reacted very

rapidly, which prevented our obtaining the necessary kinetic data under these conditions. Their increased reactivity may be interpreted by protonation of the free electron pair on the oxygen or nitrogen atom in acid medium, and by this the proportional increase in reactivity of the CO grop.

For the estimation of the reactivity of saturated sulfones in the reaction with carbonyl compounds we determined the pK_a values of 5-nitrofurfuryl methyl sulfone (S_m) and 5-nitrofurfuryl phenyl sulfone (S_f). The pK_a values of sulfone S_m is slightly higher than that of S_f (by 0·20 pK units), which may be ascribed to the $+I$ effect of the CH_3 group bound to the SO_2 group. The determination of the condensation rate of both these sulfones with the most reactive aldehyde of the phenylfuran series, 5-(4-nitrophenyl)-2-furaldehyde, showed that in both systems (A, B) $k_{sm} > k_{sf}$ (Table II), which, though not in agreement with the pK_a values, may probably be interpreted by the larger steric requirements of the carbanion of the sulfone S_f in comparison with S_m.

EXPERIMENTAL

The aldehydes of the phenylfuran series used in the reaction were prepared by arylation of 2-furaldehyde of the correspondingly substituted diazonium salts under the conditions of the Meerwein reaction[14]. 5-Substituted 2-furaldehydes were synthetized according to literature in the following manner: 5-methyl-[15], 5-bromo-[16], 5-iodo- and 5-methoxycarbonyl-[17], 5-nitro-[18]. 5-Nitrofurfuryl phenyl and 5-nitrofurfuryl methyl sulfones were prepared from 5-nitrofurfuryl nitrate which reacted with sodium benzensulfinate and NaBr to the corresponding sulfone[1]. 1-(5-Nitro-2-furyl-
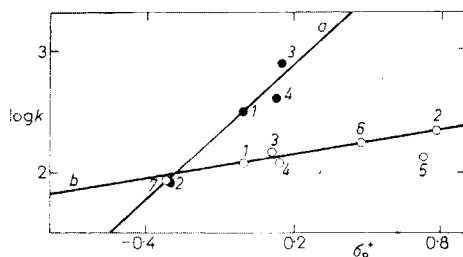

FIG. 1

Correlation of log k_2 and σ_p^+ of the Reaction of 5-Nitrofurfuryl Phenyl Sulfone with Aldehydes of the Furan (a) and Phenylfuran Series (b) According to Method A

Indications in Tables I and II. Values $r = 0.97$, $\varrho = 1.815$ (a); $r = 0.98$, $\varrho = 0.346$ (b).
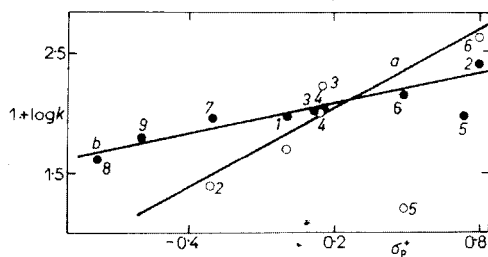
FIG. 2

Correlation of log k_2 and σ_p^+ of the Reaction of 5-Nitrofurfuryl Phenyl Sulfone with Aldehydes of the Furan (a) and Phenylfuran Series (b) According to Method B

Indications in Tables I and II. Values $r = 0.95$, $\varrho = 1.102$ (a); $r = 0.96$, $\varrho = 0.403$ (b).

TABLE II

Values of the Rate Constants k_2 (l mol^{-1} min^{-1}) and the Half-Times $t_{1/2}$ (min) of the Reaction of 5-Nitrofurfuryl Phenyl Sulfone with 5-(4-X-Phenyl-Substituted) 2-Furaldehydes

No	X	Method A			Method B			σ_p^+
		$k_2 . 10^{-2}$	$t_{1/2}$	$\log k_2$	k_2	$t_{1/2}$	$1 + \log k_2$	
1	H	1·24	161·3	2·0934	9·36	427·3	1·9712	0·000
2	NO_2	2·25	88·9	2·3522	24·50	163·3	2·3892	+0·790
3	Cl	1·48	135·1	2·1702	10·48	381·7	2·0203	+0·115
4	Br	1·28	156·2	2·1072	10·00	400·0	2·0000	+0·150
5	COOH	1·40	142·9	2·1461	9·00	444·4	1·9542	+0·728
6	$COOC_2H_5$	1·80	111·1	2·2553	12·80	312·5	2·1072	+0·482
7	CH_3	0·92	217·4	1·9638	8·92	448·5	1·9504	−0·311
8	OCH_3	—	—	—	4·24	943·4	1·6274	−0·778
9	$NHCOCH_3$	—	—	—	6·24	641·0	1·7952	−0·600
10	[a]	3·48	57·5	2·5416	58·4	285·4	2·7664	+0·790

[a] Values of rate constants for the reaction of 5-nitrofurfuryl methyl sulfone and 5-(4-nitrophenyl)--2-furaldehyde.

-1-phenylsulfonyl-2-[5-(4-X-phenyl)-2-furyl]ethylenes and 1-(5-nitro-2-furyl)-1-phenylsulfonyl--2-(5-X-furyl) ethylenes were prepared by condensation reaction with 5-nitrofurfuryl phenyl sulfone with corresponding aldehydes[3,4] in the presence of ammonium acetate, piperidine and glacial acetic acid. 1-(5-Nitro-2-furyl)-1-methylsulfonyl-2-[5-(4-nitrophenyl)-2-furyl]ethylene was prepared analogously and had m.p. 235—237°C. For $C_{17}H_{12}N_2O_8S$ (392·3) calculated: 6·93% N, 7·91% S; found: 7·21% N, 7·61% S. UV spectrum: λ_{max} (nm) (log ε): 206 (4·22), 229 (4·20), 320 (4·35), 403 (4·29).

Kinetic Measurements

The measurement of the UV spectra, as well as the kinetic determinations were carried out on a recording spectrophotometer Specord UV VIS Zeiss in the 200—800 nm region. The samples were measured in 1 cm thermostated cells. The concentration of the substances for UV measurements was $2-5 . 10^{-5}$M in methanol and for the kinetic measurements it was $2·5-5 . 10^{-4}$M.

The determination of the rate constants was carried out in the following manner:

Method A: Composition of the reaction mixture: 0·01 mol of 5-nitrofurfuryl phenyl sulfone (resulting concentration in the mixture was $5 . 10^{-2}$M), 0·01 mol of the corresponding aldehyde (resulting concentration in the mixture $5 . 10^{-2}$M), 0·08 mol of piperidine, 0·16 mol of ammonium acetate, 200 ml of glacial acetic acid.

A solution of piperidine and ammonium acetate in 100 ml of acetic acid of the same temperature (118°C) was added at once into a stirred solution of sulfone and aldehyde in 100 ml acetic acid. The moment of mixing is considered as $t = 0$. Samples were withdrawn from the reaction mixture at regular intervals, which were immediately chilled in an ice-water bath, diluted with

methanol as necessary, and used for the measurement of UV spectra (the reference cell contained methanol). The concentration increase in the product formed was determined from the measured extinction at single time-intervals, the product displayed a band in the visible part of the UV spectrum. After substituting the values obtained into the kinetic equation of the second order a linear dependence of $X/C_0(C_0 - X)$ or $1/C_0 - X$ on time was obtained, and from this dependence we calculated and also graphically determined the values of the rate constant k_2. When the reaction was terminated (approx. 2—3 hours) the corresponding α,β-unsaturated sulfone was isolated from the reaction mixture.

Method B: The measurement was carried out at $41° \pm 0·2°C$ in methanolic solution of piperidine. The reaction course was followed directly in thermostated cells in a Specord UV VIS apparatus on the wave-length of the absorption maximum of the K-band of the condensation product formed.

The resulting concentrations of the sulfone and aldehyde in the reaction mixture were equal, within the $2-5 . 10^{-4}$M range. The working procedure and the calculation of the rate constants were carried out in the same manner as under method *A*.

The values of the measured rate constants k_2 and the half-times $t_{1/2}$ for both methods are given in Tables I and II.

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