INFLUENCE OF —M TYPE SUBSTITUENTS ON THE HYDROLYSIS RATE OF SALICYLIDENEANILINES

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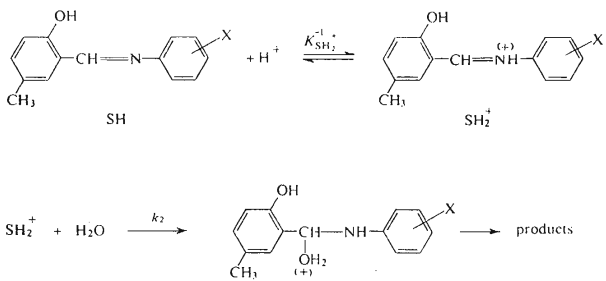
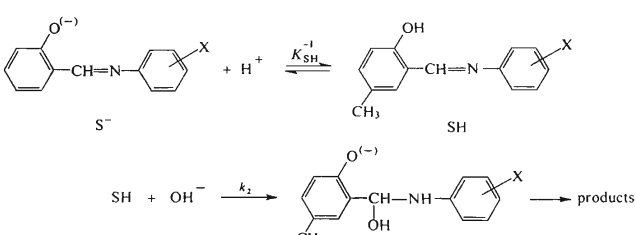
In the paper[1] we described the influence of pH and substituents on the hydrolysis rate of substituted salicylideneanilines in acid and basic media. The breaks found in the correlation with the Hammett σ constants were explained by a change in the rate limiting step of the reaction.

In the pH range 4—6 the hydrolysis rate was directly proportional to the proton concentration, and the attack of the protonated Schiff's base by a water molecule was the rate limiting step in the case of the substituents having a positive σ constant (Scheme 1).



Scheme 1

At pH > 12 the hydrolysis rate is independent of the proton concentration, and the reaction of the Schiff's base with hydroxyl ions is the rate limiting step (for the same substituents) (Scheme 2).



Scheme 2

In the previous work[1] we did not measure the derivatives with *p*-substituents having significant —M effects. After improving the experimental technics we have extended the study by several such *para* and *meta* derivatives, and, in order to be able to compare the results, we have once more measured the substances described in paper[1], too. The results are given in Tables I and II and Figs 1 and 2. From the Figs 1 and 2 it is obvious that the derivatives having —M type *p*-substituents deviate from the correlation in both acid and alkaline media. The correlation does not improve by using the σ_p^- or other constants, not any further change in the rate limiting step being possible either.

In the both cases the experimental rate constants used for correlation with the σ constants (in the case of electron-acceptors) are represented by the product of the reciprocal value of the equilibrium constant of the respective abovementioned equilibrium and the rate constant of the respective rate limiting step[1]; *i.e.* they are given by Eqs (*1*), (*2*) and (*3*), (*4*) in the acid and alkaline medium respectively.

$$v = k[\mathrm{SH}]\,, \tag{1}$$

$$k = k_2[\mathrm{H}^+]/K_{\mathrm{SH_2}^+}\,, \tag{2}$$

$$v = k[\mathrm{S}^{(-)}]\,, \tag{3}$$

$$k = k_2 K_w / K_{\mathrm{SH}}\,. \tag{4}$$

Eq. (*2*) can be transformed into Eq. (*5*) where ϱ' and σ' are the corresponding values of the relation of $K_{\mathrm{SH_2}^+}$.

$$\log(k/k^0) = \log(k_2/k_0^2) - \log(K_{\mathrm{SH_2}^+}/K^0_{\mathrm{SH_2}^+}) = \varrho_2\sigma_2 - \varrho'\sigma'\,. \tag{5}$$

Eq. (*4*) can be modified in the same way. Eq. (*5*) transforms into Eq. (*6*) in the case of the σ constants having the same values for both the equilibrium and the rate limiting step.

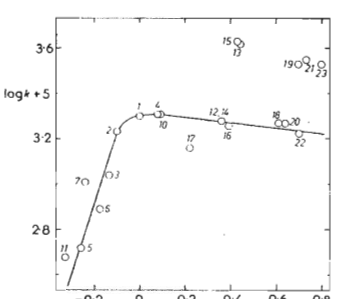


FIG. 1

Dependence of log *k* of Hydrolysis of Salicylideneanilines in Acid Medium (pH 5·5) on σ Constants

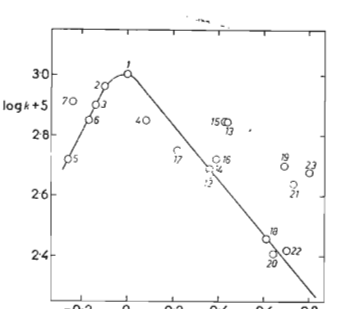


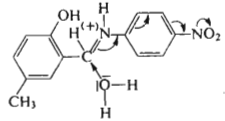
FIG. 2

Dependence of log *k* of Hydrolysis of Salicylideneanilines in Alkaline Medium (pH 12·5) on σ Constants

$$\log (k/k^0) = (\varrho_2 - \varrho') \sigma = \varrho_{exp}\sigma . \qquad (6)$$

This condition is fulfilled approximatively with all the derivatives having *meta* or *para* substituents without any significant —M effect.

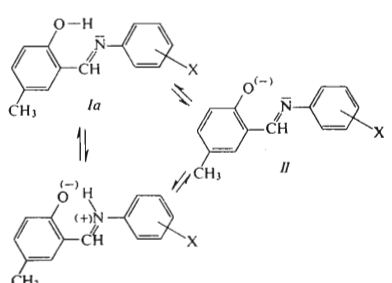
The —M effect does not make itself felt in the first reaction step of the hydrolysis in acid medium (Scheme 1), because no increase of the positive charge on the nitrogen atom is encountered with any of the possible resonance structures. On the contrary, these substituents facilitate the reaction with water in the rate limiting step, due to the conjugation with π electrons of $\rangle C{=}N{-}$ bond (Formula *A*). With respect to the application of the Hammett equation this means that the



A

exalted value σ should be used in Eq. (5) for the rate limiting step in the case of —M type *p*-substituents. Hence Eq. (6) cannot be used for these derivatives. The difference between the experimental values and those calculated from Eq. (6) is caused by the influence of —M effect on the rate limiting step and should be expressed quantitatively by the difference between σ_p and σ_p^- values which is roughly fulfilled as it can be seen in Fig. 1.

In alkaline medium the protonation of the anion of the Schiff's base takes place giving two tautomers (Scheme 3).



SCHEME 3

The equilibrium constant value of the reaction giving the tautomer *Ia* depends on the extent of the —M effect of *p*-substituent, whereas the equilibrium constant value of the reaction giving the tautomer *Ib* does not, the reasons being the same as with the protonation of the neutral Schiff's base. At the rate limiting step when the reaction of the Schiff's base with hydroxyl ion

takes place, the reaction is accelerated by —M effect again. As it can be seen in Figs 1 and 2, the influence of this effect is comparable in the both cases (acid and alkaline ranges). This means that even in this case we can presume that —M effect will make itself felt in the second, rate limiting step only. Therefrom we can conclude that the structure of the Schiff's base resembles that of the tautomer *Ib* in the moment of the reaction with hydroxyl ion. An analogous mechanism was proposed by McDonnell, Michailidis and Martin[2] for hydrolysis of the Schiff's base of the N-salicylidenealkylamine type.

A higher reaction velocity of *o*-hydroxy derivatives in alkaline medium (as compared to *o*-methoxy derivatives) was explained by Reeves[3] as being caused by an increased polarisation of >C=N— bond due to the protonation of the nitrogen. In contrast to the mechanism proposed by him (simultaneous formation of C—O and N—H bonds; Formula *B*) we suppose that the N—H bond formation precedes the C—O bond formation.

TABLE I

Values log k + 5 of Salicylideneaniline Hydrolysis in Acid Region

Salicylidene-aniline	X	λ nm	log k + 5 at a pH						Angular coefficient +K
			6·37	5·94	5·75	5·60	5·37	5·18	
1	H	305	2·44	2·88	3·02	3·23	3·46	—	−1·00
3	4′-CH_3	315	2·26	2·62	2·83	2·96	3·18	3·33	−0·97
4	3′-OCH_3	305	2·45	2·91	3·08	3·23	3·43	3·58	−0·89
5	4′-OCH_3	345	—	2·40	2·55	2·68	2·90	—	−0·87
18	3′-CN	280	2·47	2·86	3·05	3·17	3·38	3·56	−0·93
19	4′-CN	315	2·75	3·15	3·32	3·47	3·60	3·82	−0·90
20	3′-SO_2CH_3	280	2·39	2·82	3·01	3·15	3·38	3·55	−0·99
21	4′-SO_2CH_3	310	2·76	3·14	3·32	3·47	3·64	3·84	−0·93
		pH	6·32	5·93	5·73	5·58	5·34	4·98	
16	3′-Cl	305	2·49	2·83	3·06	3·19	3·41	—	−0·96
17	4′-Cl	325	2·45	—	2·95	3·07	3·28	3·60	−0·86
22	3′-NO_2	300	2·47	—	2·97	3·15	3·34	3·64	−0·90
23	4′-NO_2	315	2·79	3·12	3·28	3·45	3·64	3·94	−0·88
		pH	5·96	5·76	5·60	5·37	5·18		
2	3′-CH_3	300	2·81	3·00	3·14	3·34	3·52		−0·90
7	3′-CH_3-4′-CH_3	300	2·57	2·78	2·91	3·14	3·29		−0·93
10	3′-OH	300	2·88	3·08	3·22	3·43	3·60		−0·97
11	4′-OH	285	2·27	2·45	2·59	2·80	2·97		−0·90
6	4′-$C(CH_3)_3$	310	2·39	2·64	2·79	3·03	3·22		−0·99
12	3′-$COCH_3$	280	2·86	3·05	3·19	3·36	3·58		−0·92
13	4′-$COCH_3$	370	3·19	3·39	—	3·73	3·91		−0·92
14	3′-$COOCH_3$	285	2·85	3·03	3·17	3·40	3·55		−0·94
15	4′-$COOCH_3$	370	—	—	3·54	3·76	3·91		−0·90

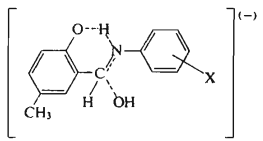


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TABLE II

Values log k + 5 of Salicylideneaniline Hydrolysis in Alkaline Region

Compound No	λ nm	log k + 5 at a pH				
		11·95[a]	12·33	12·66	13·02	13·27
1	305	2·98	3·00	3·01	3·01	3·01
3	315	2·84	2·89	2·90	2·90	2·89
4	305	2·81	2·84	2·85	2·85	2·87
5	345	2·68	2·71	2·72	2·72	2·74
9	345	2·68	2·72	2·72	2·74	2·76
18	295	2·43	2·46	2·47	2·46	2·46
19	315	2·66	2·70	2·70	2·71	2·70
20	295	—	—	2·41	2·40	2·43
21	310	2·63	2·64	2·64	2·65	2·64
	pH	11·41[a]	11·90[a]	12·36	12·86	13·16
16	305	—	2·69	2·72	2·73	2·72
17	315	2·68	2·77	2·75	—	2·74
22	300	2·36	2·42	2·41	2·48	2·41
23	315	2·66	2·69	2·67	2·68	2·69
	pH		11·85[a]	12·40	12·72	13·06
2	305		2·90	2·96	2·96	2·99
7	310		2·85	2·89	2·91	2·92
8	325		2·91	2·93	2·94	2·96
6	305		2·77	2·84	2·87	2·85
12	295		2·64	2·67	2·67	2·67
13	440		2·80	2·84	2·84	2·83
14	295		2·57	2·65	2·68	2·69
15	325		2·81	2·83	2·84	2·86

[a] The lower values of experimental rate constants found for hydrolysis in this medium are caused by the fact that a considerable portion of the salicylideneaniline (especially if it carries electropositive substituents) is still present in its undissociated form at this pH.

TABLE III

New-Prepared 5-Methylsalicylideneanilines

Compound No	M.p., °C colour[a]	Mol. formula (mol. weight)	Calculated/Found		
			% C	% H	% N
6	79 – 80	$C_{18}H_{21}NO$	80·86	7·92	5·24
	p.y.	(267·4)	80·92	7·97	5·15
10	152·5–154	$C_{14}H_{13}NO_2$	73·99	5·77	6·16
	o.	(227·3)	73·75	5·59	6·32
11	174·5–175	$C_{14}H_{13}NO_2$	73·99	5·77	6·16
	o.	(227·3)	74·31	6·01	6·42
7	102·5–103	$C_{16}H_{17}NO$	80·30	7·16	5·85
	d.y.	(239·3)	80·19	7·39	6·11
8	68·5– 69·5	$C_{16}H_{18}N_2O$	75·56	7·13	11·02
	d.y.	(254·32)	75·30	7·40	11·33
18	161·5–162	$C_{15}H_{12}N_2O$	76·25	5·12	11·86
	d.y.	(236·3)	76·15	4·96	11·72
20	113 –114	$C_{15}H_{15}NO_3S$	62·25	5·22	4·84
	d.y.	(289·4)	62·13	5·19	4·84
21	148·5–150	$C_{15}H_{15}NO_3S$	62·25	5·22	4·84
	d.y.	(289·4)	62·32	5·39	5·14

[a] p.y. Pale yellow; d.y. deep yellow; o orange.

EXPERIMENTAL

The melting points were determined with the use of a Kofler apparatus. The samples for elemental analyses were dried over phosphorus pentoxide in the vacuum of oil pump 24 hours.

Substituted salicylideneanilines were prepared from 5-methylsalicylaldehyde and *meta* or *para* substituted anilines in methanolic solutions. The yields were within 50–80% th. The melting points of the derivatives not described so far are given in Table III, physical properties of the other derivatives prepared are given elsewhere[4,5].

Kinetic measurements were carried out in aqueous-alcoholic buffers in the same way as in the previous work[1]. In addition to it a mixture of solutions 0·2M-KCl and 0·2M-NaOH was used for strongly alkaline region. Constant ionic strength 0·100 was maintained by addition of potassium chloride. Again, the measurements were carried out with the use of Unicam SP 800 spectrophotometer at 22°C, but the cells used were thicker (3 and 4 cm). It was thus possible to measure also those *para* substituted salicylideneanilines which were slightly soluble in the reaction medium, and to repeat the previous measurements[1] with a higher accuracy. The measurements were carried out as follows: 7·5 ml (or 10 ml) buffer solution was placed in the 3 cm (or 4 cm) cell and after adjusting the temperature, 0·3 ml (or 0·4 ml) Schiff's base stock solution was added from a syringe. Ethanol concentration in the reaction mixture was 22% by vol., concentration of the Schiff's base was $2-5 \cdot 10^{-5}$ mol/l. Absolute ethanol had to be used for preparation of the stock solutions of Schiff's bases; 96% ethanol could only be used for preparation of the solutions

immediately before measurements, because the dissolved anils underwent more than 50% hydrolysis on several days standing in this medium.

pH *of the solutions* was measured by means of a PHM 4c apparatus (Radiometer, Copenhagen) and a glass electrode type B of the same firm (correction for the salt error only over pH 11·5).

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NUCLEIC ACID COMPONENTS AND THEIR ANALOGUES. CXLIV.*
SYNTHESIS OF 5¹,5²-AZINODI(2-β-D-RIBOFURANOSYL-*as*-TRIAZIN-3(4*H*)-ONE)

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The reaction of 5-chloro-2-(2,3,5-tri-O-acetyl-β-D-ribofuranosyl)-*as*-triazin-3(2*H*)-one[1] (*V*) and hydrazine in benzene–methanol affords a yellow substance the elemental analysis and molecular weight of which is in accordance with the formula $C_{28}H_{34}N_8O_{16}$. Deacetylation with methanolic ammonia leads to the parent nucleoside $C_{16}H_{22}N_8O_{10}$ the ultraviolet spectrum of which in acidic and neutral media exhibits a significant maximum at 350—351 nm; in alkali, the spectrum shows a bathochromic shift of the maximum to 388 nm. From the theoretically possible tautomeric structures of this nucleoside, both lactam forms are the most probable, namely, the azino form *I* and the hydrazo form *II*. The infrared spectrum of the chloroform-soluble acetyl derivative shows a single band of the stretching vibration of the free NH group at 3360 cm^{-1}. The wavenumber of this band corresponds well to the $N_{(4)}$—H triazine group situated between two exocyclic double bonds. Thus under analogous conditions, the ν(NH) band is situated at 3374 cm^{-1} with 1-methyl-6-azauracil[2] and at 3 363 cm^{-1} with 1-methyl-4-thio-6-azauracil[2]. It is noteworthy that the ν(NH) band of hydrazobenzene (solution in chloroform) as model of the form *II* is also situated in this region (3380 cm^{-1} and shoulder at 3 330 cm^{-1}).

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