KINETICS OF HYDROLYSIS OF N-BENZYLIDENE, HALOGENOANILINES IN AQUEOUS METHANOL SOLUTIONS

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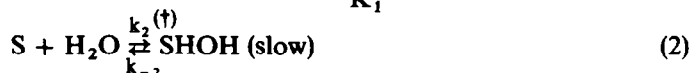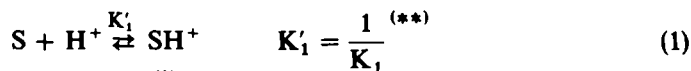Istituto di chimica fisica dell'Università, 20133 Milan, Italy

Abstract—The pa_H^*-rate profile for the hydrolysis of N-benzylideneaniline and fourteen N-benzylidene-anilines halogeno-substituted in the aniline ring were investigated in the range 0·5–11 pa_H^*, in buffered aqueous methanol solutions (20·0 wt% H_2O) at 25° and ionic strength 0·045M. They showed a first-order dependance of the rate of hydrolysis on a_H^* over a range of hydrogen ion activities. Two small pa_H^*-independent ranges were observed respectively at pa_H^* 10–11 and at $pa_H^* < 1$. Kinetics of methanolysis in 0·10N HCl solutions was studied, and the spectra of the conjugate acids of the anils were obtained by extrapolation at zero time in the kinetic runs, for the unsubstituted and for the *p*-monosubstituted anils. Their acid dissociation constants were also measured at 25° in aqueous methanol solution.

Rate of hydrolysis of N-benzylideneaniline was also investigated in aqueous solution (99·7 wt% H_2O) at 25°, in order to check the influence of ionic strength and buffer concentration. Rate constants were found to be independent from ionic strength at constant buffer concentration, both at pH 9·20, 6·20 and 4·50. This fact suggests a mechanism, which involves solvent and acid catalysis of the Schiff base, as well as hydrolytic cleavage of its conjugate acid. Following this mechanism, the single-step rate constants could be evaluated. The rate profiles are consistent with the proposed mechanism. The influence of steric and electronic factors is discussed.

KINETIC studies of the hydrolysis of N-benzylideneanilines in water-methanol solutions have established that these reactions are sensitive to specific and general acid catalysis,[1–14] as well as base catalysis. Evidence obtained[4,5] in unbuffered 50% aqueous methanol solutions suggests that in the hydrolysis reaction the addition of water to form the generally accepted amino-alcohol intermediate, in mobile equilibrium between benzylideneaniline and water, is rate determining. This intermediate is formed and cleaved in uncatalyzed and acid-catalyzed steps. Kastening *et al.*[2,3] have concluded from polarographic measurements in 30% methanol that the accumulation of intermediate amounts to 13% of the initial Schiff base concentration, while the absence of measurable concentrations of intermediate was stated by Willi[4] and confirmed in aqueous solutions by Reeves.[6]
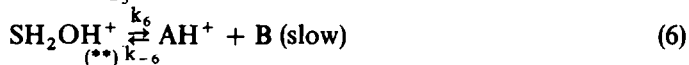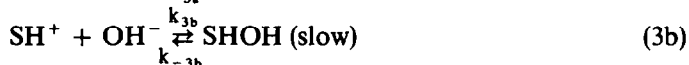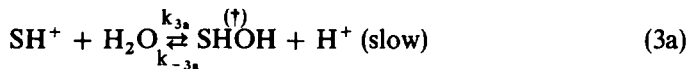
The following general mechanism by which the amino-alcohol intermediate, present in a low-steady-state concentration, forms and breaks down by uncatalyzed and acid-catalyzed paths was found to be in agreement with data:[6–9,14]

$$S + H^+ \underset{}{\overset{K_1'}{\rightleftarrows}} SH^+ \qquad K_1' = \frac{1}{K_1} \quad ^{(**)} \tag{1}$$

$$S + H_2O \underset{k_{-2}}{\overset{k_2 \, (\dagger)}{\rightleftarrows}} SHOH \text{ (slow)} \tag{2}$$

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** K_1, K_4, and K_7 are acid dissociation constants.
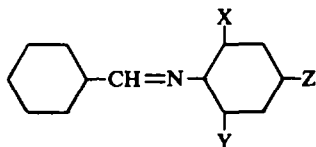† k_2 and k_{3a} are rate constants which include the water concentration.

$$SH^+ + H_2O \underset{k_{-3a}}{\overset{k_{3a}}{\rightleftarrows}} \overset{(\dagger)}{SHOH} + H^+ \text{ (slow)} \tag{3a}$$

$$SH^+ + OH^- \underset{k_{-3b}}{\overset{k_{3b}}{\rightleftarrows}} SHOH \text{ (slow)} \tag{3b}$$

$$SHOH + H^+ \underset{}{\overset{K_4'}{\rightleftarrows}} SH_2OH^+ \qquad K_4' = \frac{1}{K_4} {}^{(**)} \tag{4}$$

$$SHOH \underset{k_{-5}}{\overset{k_5}{\rightleftarrows}} A + B \text{ (slow)} \tag{5}$$

$$SH_2OH^+ \underset{(**) k_{-6}}{\overset{k_6}{\rightleftarrows}} AH^+ + B \text{ (slow)} \tag{6}$$

$$AH^+ \overset{K_7}{\rightleftarrows} A + \cdot H^+ \tag{7}$$

where $S = Ar{-}CH{=}N{-}Ar'$, $SH^+ = Ar{-}CH{=}\overset{+}{N}H{-}Ar'$, $SHOH =$ $Ar{-}CHOH{-}NH{-}Ar'$, $SH_2OH^+ = Ar{-}CHOH{-}\overset{+}{N}H_2{-}Ar'$, A and B are the products (aniline and benzaldehyde respectively). By the steady state approximation for the amino-alcohol intermediate the following equation can be derived for the hydrolysis rate constant k :

$$k = \frac{[H^+]}{[H^+] + K_1}$$
$$\times \frac{(k_{3b}'k_5 + k_2k_5K_1)/[H^+] + k_{3a}k_5 + k_2k_6K_4'K_1 + k_{3b}'k_6K_4' + k_{3a}k_6K_4'[H^+]}{k_{-3b} + k_{-2} + k_5 + (k_{-3a} + k_6K_4')[H^+]} \tag{8}$$

which is of the type:

$$k = \frac{A + B[H^+] + C[H^+]^2}{D + E[H^+] + F[H^+]^{2}} \tag{8a}$$

In order to unravel the proposed mechanism and examine the influence of electronic and steric factors on the rate of hydrolysis, fourteen N-benzylideneanilines, substituted by halogen atoms in the aniline ring, were studied in comparison with the unsubstituted Schiff base:

	Substituents					Substituents		
	X	Y	Z			X	Y	Z
I	H	H	H		X	F	H	F
II	H	H	F		XI	Cl	H	Cl
III	H	H	Cl		XII	Br	H	Br
IV	H	H	Br		XIII	I	H	I
V	H	H	I		XIV	Cl	Cl	H
VI	F	H	H		XV	Br	Br	H
VII	Cl	H	H					
VIII	Br	H	H					
IX	I	H	H					

* $k_{3b}' = k_{3b}[H^+][OH^-]$

Kinetics of hydrolysis was followed at 25° in aqueous methanol solutions (20·0 wt% H_2O), which were buffered in the pa_H^* range of 0·5–11 (a_H^* = activity of solvated hydrogen ions, with reference to the standard state in the mixed solvent).[15] The acid dissociation constant of the Schiff base conjugate acid was also measured for compounds I–V. For these latter kinetics of methanolysis in 0·10N HCl solutions was studied and the spectra of their conjugate acids were obtained by extrapolation at zero time in the kinetic runs. The influence of buffer concentration, as well as that of ionic strength, was furthermore investigated for the hydrolysis of N-benzylidene-
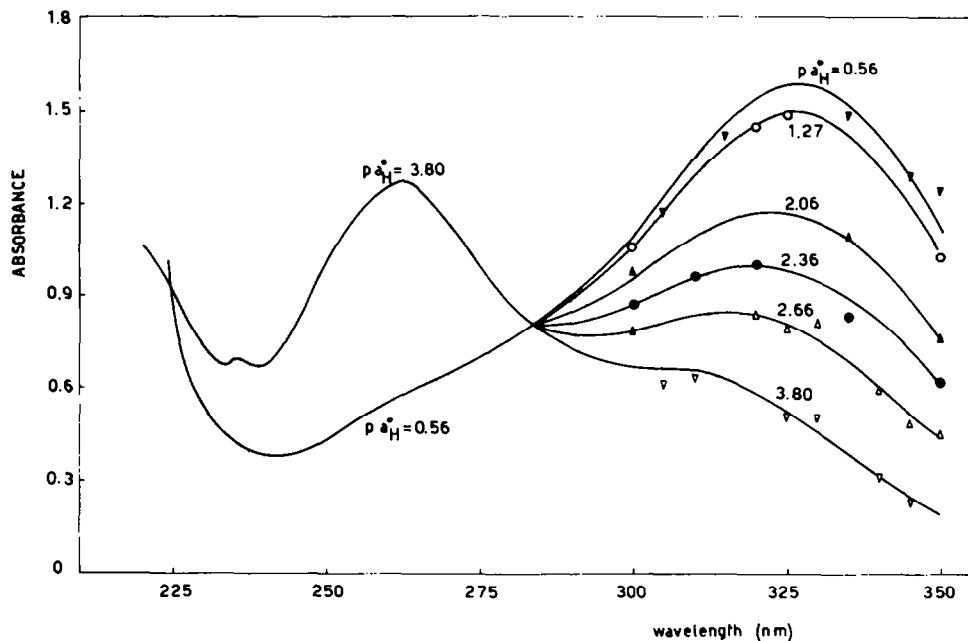

FIG. 1 Absorption curves, kinetically extrapolated at zero time, of a 7·4 × 10^{-4} M N-benzylideneaniline solution in aqueous methanol (20·0 wt% H_2O) at 25°C and various pa_H^* (ionic strength 0·045M); optical path 0·100 cm.

aniline and its p-halogeno derivatives in aqueous methanol and in water solution (0·3 wt% CH_3OH), in connection with the mechanism for the pH independent hydrolysis in basic solution, which has been indicated[8] to involve attack of OH^- on the conjugate acid (step 3b in the present paper) rather than reaction of solvent molecules with the anil molecule (step 2).

RESULTS

Acid dissociation constants. The acid equilibria involving the Schiff base and its conjugate acid were determined in the 20 wt% aqueous methanol solution at 25°, for anils I–V, from the change in the strong, long-wave absorption band of the conjugate acids with pa_H^*. Fig. 1 illustrates, as an example, the experimental absorbance curves for N-benzylideneaniline. Progressive decreasing of pa_H^* of solutions

TABLE 1. pK$_1$ AT 25° AND MOLAR ABSORBIVITIES IN AQUEOUS METHANOL (20 wt% H$_2$O) OF THE CONJUGATE ACIDS OF SOME SCHIFF BASES

Schiff base (S)	$\lambda_{max (SH^+)}$ (nm)	$\log \varepsilon_{max (SH^+)}$ (ε in M^{-1}cm^{-1})	pK$_1$ (25°) (K$_1$ in M)
N-Benzylideneaniline	328	4·335	2·266 ± 1·53 × 10^{-2}
N-Benzylidene, 4-fluoroaniline	328	4·290	2·072 ± 6·03 × 10^{-2}
N-Benzylidene, 4-chloroaniline	330	4·275	1·936 ± 7·20 × 10^{-3}
N-Benzylidene, 4-bromoaniline	335	4·305	1·807 ± 3·63 × 10^{-2}
N-Benzylidene, 4-iodoaniline	340	4·335	1·642 ± 6·80 × 10^{-3}

of N-benzylideneaniline from 3·80, at which the spectrum is substantially the same as that at higher pa$_H^*$ and in unbuffered methanol, results in diminution of the strong peak at 262 nm and increase in absorption in the region of 300–350 nm, with an isosbestic point at 283 nm. At pa$_H^* \leqslant 0.5$ the spectrum at zero reaction time remains again sensibly constant with an absorption peak at 328 nm. A similar behaviour was observed for the other Schiff bases. pK$_1$, as well as molar absorbivities of the conjugate acids at their maximum absorption, are reported in Table 1, with the probable error
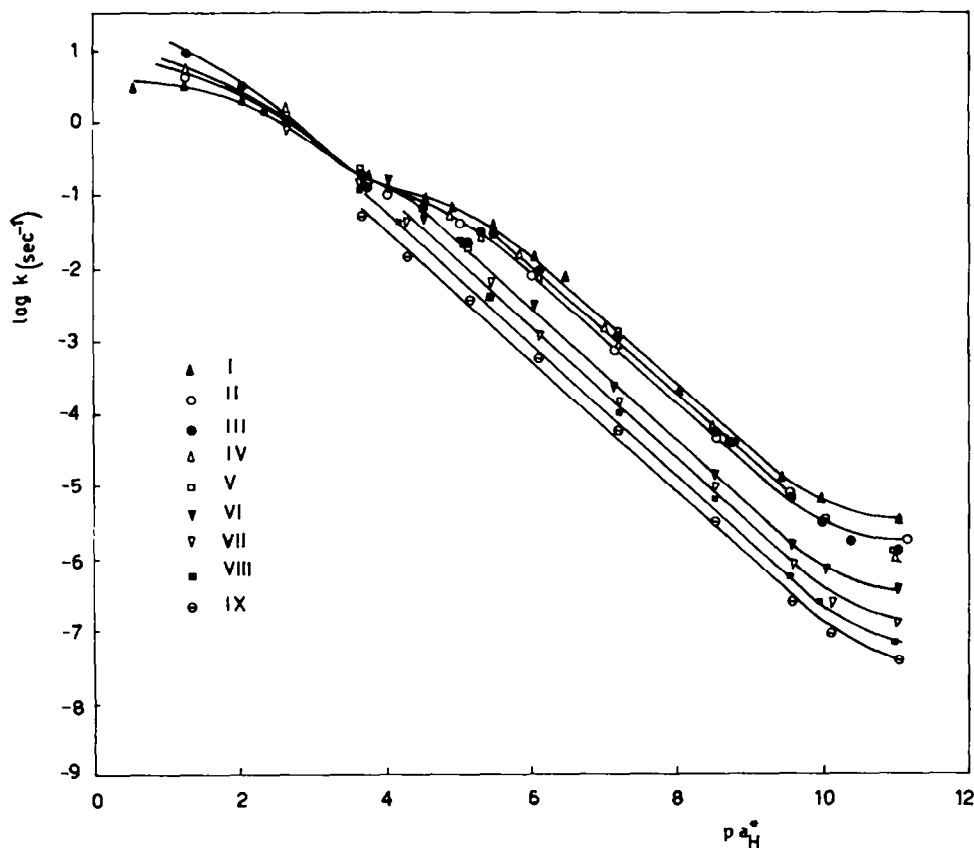

FIG. 2 pa$_H^*$-rate profile for the hydrolysis of N-benzylideneaniline (I) and its monohalogeno-substituted derivatives (II–IX), at 25° (ionic strength 0·045M) in aqueous methanol (20·0 wt% H$_2$O).

of the arithmetic mean of pK_1, calculated by Jeffreys' formula,[16] from 4 to 7 determinations at various wavelengths in the range 300–350 nm.

Kinetics. The decrease of concentration of the Schiff base *vs* time followed strictly first-order kinetics. Experimental values of the rate constants in the buffered aqueous methanol solutions were obtained from 5 to 8 determinations at various wavelengths in the region 230–350 nm, where decrease or increase of the initial absorbance was followed at different concentrations of the substrate. The arithmetic mean of results is reported graphically in Fig. 2 for N-benzylideneaniline and its monohalogeno derivatives, and in Fig. 3 for the parent compound and its dihalogeno substituted
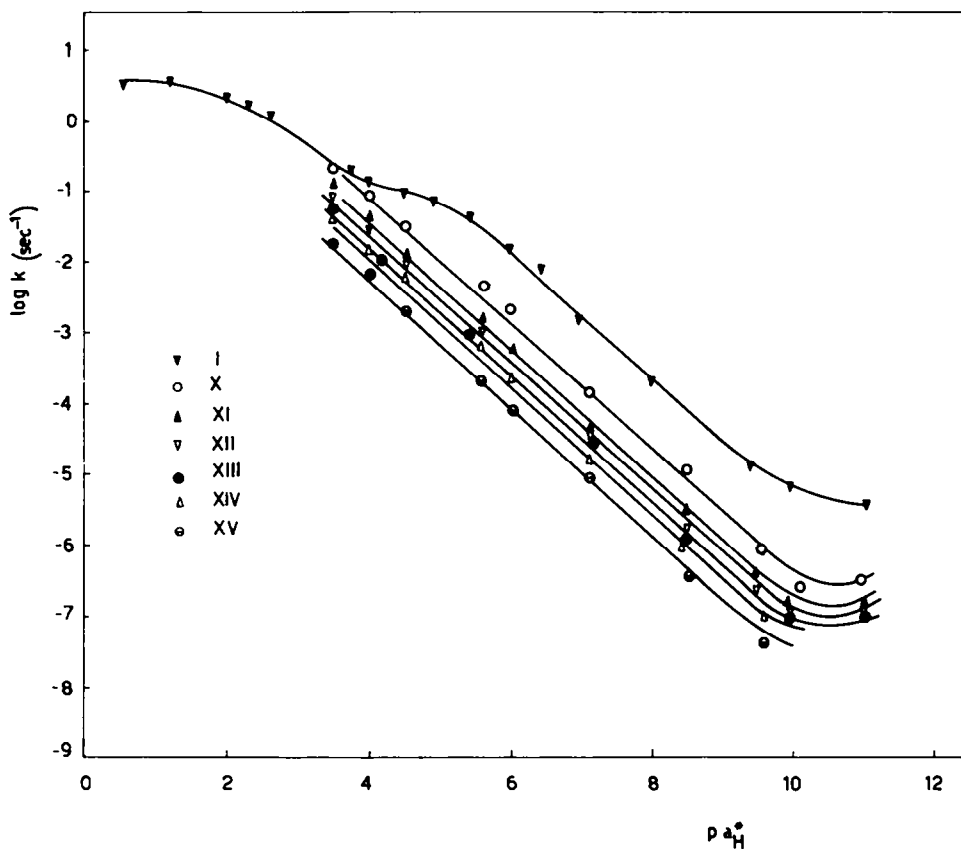

FIG. 3 pa$_H^*$-rate profile for the hydrolysis of N-benzylideneaniline (I) and its dihalogeno-substituted derivatives (X–XV), at 25°C (ionic strength 0·045M) in aqueous methanol (20·0 wt% H_2O).

derivatives. The measured rate constants for some of the examined anils are reported in Table 2, with the probable error of the arithmetic mean, calculated by Jeffreys' formula[16] from 6 to 10 determinations at various wavelengths in the range 245–350 nm. The whole set of values of rate constants is available upon request.

I. R. Bellobono and G. Favini

Table 2. The effect of acidity and ionic strength on the rate of hydrolysis of Schiff bases at 25°.

Anil	Wt % H_2O in the H_2O–CH_3OH solvent	Ionic strength (M)	pa_H^*	k (sec^{-1})
N-Benzylideneaniline	20·0	0·045	0·56	$3·10 \pm 0·08$
			1·27	$3·64 \pm 0·09$
			2·06	$2·13 \pm 0·13$
			2·36	$1·49 \pm 0·03$
			2·66	$1·15 \pm 0·05$
			3·80	$0·181 \pm 0·08$
			4·06	$0·130 \pm 0·05$
			4·56	$(8·09 \pm 0·09) \times 10^{-2}$
			4·97	$(6·63 \pm 0·08) \times 10^{-2}$
			5·50	$(3·78 \pm 0·09) \times 10^{-2}$
			6·06	$(1·49 \pm 0·03) \times 10^{-2}$
			6·47	$(7·41 \pm 0·08) \times 10^{-3}$
			7·02	$(1·50 \pm 0·02) \times 10^{-3}$
			7·99	$(2·13 \pm 0·04) \times 10^{-4}$
			8·06	$(2·04 \pm 0·03) \times 10^{-4}$
			9·45	$(1·25 \pm 0·02) \times 10^{-5}$
			10·00	$(6·67 \pm 0·04) \times 10^{-6}$
			11·06	$(3·33 \pm 0·02) \times 10^{-6}$
N-Benzylidene, 2-bromoaniline	20·0	0·045	3·68	$0·116 \pm 0·008$
			4·22	$(4·43 \pm 0·08) \times 10^{-2}$
			5·46	$(3·72 \pm 0·04) \times 10^{-3}$
			7·22	$(9·66 \pm 0·10) \times 10^{-5}$
			8·53	$(6·59 \pm 0·09) \times 10^{-6}$
			9·54	$(5·46 \pm 0·09) \times 10^{-7}$
			10·00	$(2·41 \pm 0·03) \times 10^{-7}$
			11·02	$(6·57 \pm 0·01) \times 10^{-8}$
N-Benzylidene, 2,6-dibromoaniline	20·0	0·045	3·56	$(1·75 \pm 0·03) \times 10^{-2}$
			4·05	$(6·52 \pm 0·08) \times 10^{-3}$
			4·56	$(2·10 \pm 0·04) \times 10^{-3}$
			5·64	$(1·95 \pm 0·05) \times 10^{-4}$
			6·06	$(7·94 \pm 0·06) \times 10^{-5}$
			7·16	$(8·61 \pm 0·17) \times 10^{-6}$
			8·56	$(3·18 \pm 0·04) \times 10^{-7}$
			9·63	$(6·38 \pm 0·15) \times 10^{-7}$
N-Benzylideneaniline	99·7	0·002	$9·20 \pm 0·05$	$(2·63 \pm 0·18) \times 10^{-4}$
		0·005	$9·20 \pm 0·05$	$(2·50 \pm 0·03) \times 10^{-4}$
		0·010	$9·20 \pm 0·05$	$(2·54 \pm 0·04) \times 10^{-4}$
		0·050	$9·20 \pm 0·05$	$(2·60 \pm 0·08) \times 10^{-4}$
		0·100	$9·20 \pm 0·05$	$(2·56 \pm 0·04) \times 10^{-4}$
N-Benzylideneaniline	99·7	0·001	$6·20 \pm 0·05$	$(3·56 \pm 0·05) \times 10^{-2}$
		0·010	$6·20 \pm 0·05$	$(3·35 \pm 0·15) \times 10^{-2}$
		0·050	$6·20 \pm 0·05$	$(3·62 \pm 0·16) \times 10^{-2}$
		0·100	$6·20 \pm 0·05$	$(3·58 \pm 0·10) \times 10^{-2}$

TABLE 2.—*Continued*

Anil	Wt% H$_2$O in the H$_2$O–CH$_3$OH solvent	Ionic strength (M)	pa$_H^*$	k (sec^{-1})
N-Benzylideneaniline	99·7	0·001	4·50 ± 0·05	3·55 ± 0·08
		0·050	4·50 ± 0·05	3·45 ± 0·11
		0·100	4·50 ± 0·05	3·68 ± 0·09

Rate constants for the catalyzed solvolysis reaction in anhydrous methanol containing 0·100N HCl are reported in Table 3. In this case the solvolysis products of the Schiff base were found to be the hydrochloride of the corresponding aniline and the dimethyl acetal of benzaldehyde, this latter being easily hydrolyzed, by addition of water, to the free aldehyde. The spectra at zero time agreed fairly well with those obtained at pa$_H^*$ 0·5 or lower from the kinetic runs in the buffered aqueous methanol system. Rate constants for the acid catalyzed methanolysis, on the contrary, differed
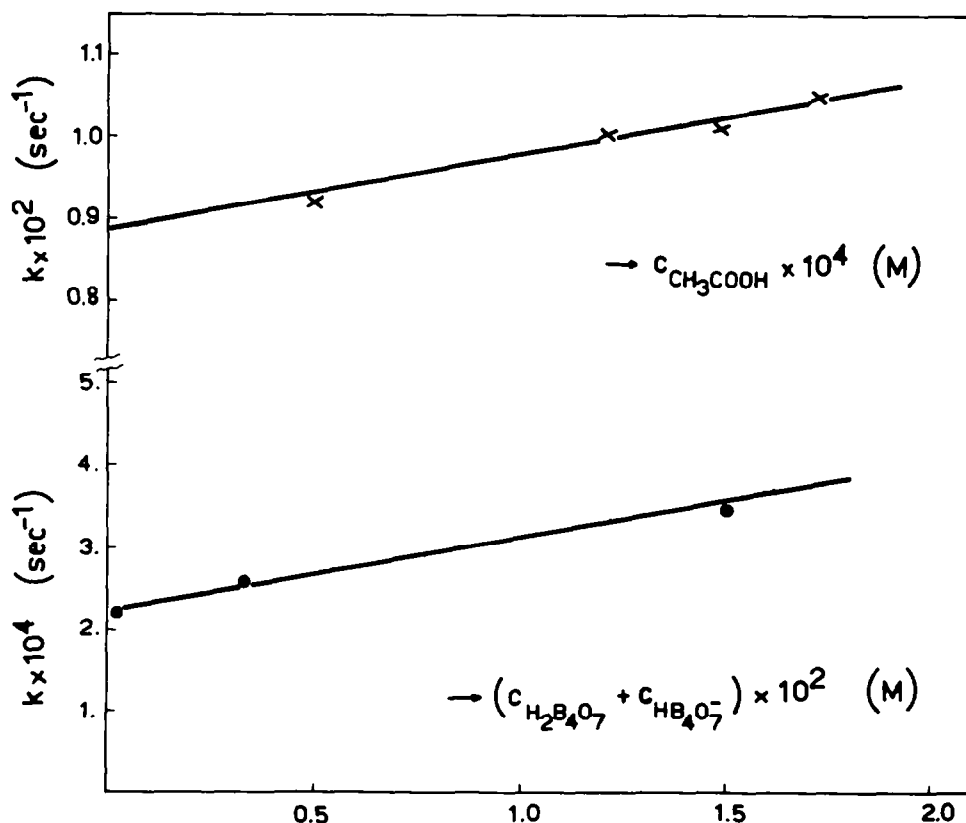

FIG. 4 Effect of acid concentration at constant ionic strength (0·045M) and pH on the rate of hydrolysis of N-benzylideneaniline in aqueous solution at 25°; × pH = 7·00 ± 0·05 (acetate buffer); ● pH = 9·20 ± 0·05 (borate buffer).

of two to three orders of magnitude from the corresponding values of the catalyzed hydrolysis in water–methanol solutions of comparable pa_H^*.

TABLE 3. SOLVOLYSIS RATE CONSTANTS IN 0.10 N HCl METHANOL SOLUTION AT 25°

Anil	$k^{(a)}$ (sec^{-1})
N-Benzylideneaniline	0·0110
N-Benzylidene, 4-fluoroaniline	0·0252
N-Benzylidene, 4-chloroaniline	0·0973
N-Benzylidene, 4-bromoaniline	0·1356
N-Benzylidene, 4-iodoaniline	0·1342

(a) mean of 18 determinations in the wavelength range 260–350 nm.

The effect of buffer concentration at constant ionic strength on the rate constant for hydrolysis of N-benzylideneaniline in 99·7 wt% H_2O solution is reported graphically in Fig. 4.

No dependance of rate constants on ionic strength at constant pH and activity of buffer (1×10^{-3}M), on the contrary, could be observed, within the limits of experimental error, both at pH 9·20 ± 0·05, 6·20 ± 0·05, and 4·50 ± 0·05, in the range 0·001–0·1M, as it can be seen from some data of Table 2. Similar results were also obtained in the aqueous methanol solution.

DISCUSSION

The pa_H^*-rate profile, as it can be seen from Figs 2 and 3, shows a first-order dependance of the rate of hydrolysis on a_H^* over a certain range of hydrogen ion activities for all the Schiff bases studied (mean slope of the straight line log k/log a_H^* = 0·97 ± 0·03). Two small pa_H^*-independent ranges are observable respectively at pa_H^* 10–11 and at $pa_H^* < 1$. A break in the profile was observed for compounds I–V. As a consequence, the relative order

$$k_H > k_I \sim k_{Br} \sim k_{Cl} > k_F$$

which is valid at $pa_H^* > 4$, is inverted at $pa_H < 3$ and becomes:

$$k_H < k_F < k_{Cl} \gtrsim k_{Br} < k_I.$$

This break could not be detected for the other Schiff bases as far as the lower pa_H^* limit investigated.

The rate profile, particularly in the linear range and in the pa_H^*-independent ranges (at $pa_H^* < pK_1$ and for the solvent catalyzed reaction) is consistent with Eqs (1) to (7) and the general rate expression (8). Rigorously, Eq. (8) has been written for aqueous solutions: in aqueous alcoholic medium, also the parallel reactions with CH_3OH and CH_3O^- should be considered. In fact, as it is shown by comparison of hydrolysis and solvolysis rate constants respectively in the mixed solvent and in anhydrous methanol of comparable acidity, the acid catalyzed reactions in the non-aqueous

solvent are at least 100–1000 times slower than in the water containing solvent: the influence of methanolysis in the 20% aqueous solvent can therefore be neglected. The equilibrium[17]

$$OH^- + CH_3OH \rightleftarrows CH_3O^- + H_2O$$
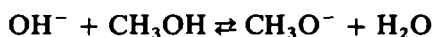
does not affect appreciably reaction rate, other than by limiting the actual OH^- concentration, and inhibiting the investigation of the base-catalyzed reaction in the aqueous methanol solution, which seems to become slightly effective at $pa_H^* > 11$ only for the disubstituted anils (Fig. 3).

As it was already stated by Reeves,[6, 8] it is obviously impossible to evaluate directly from kinetic experiments any of the individual rate constants in Eq. (8). However, some values can be assigned to ratios of the parameters (Eq. 8a). At high acidity in the pa_H^*-independent range:

$$k \cong \frac{k_{3a}k_6K_4'}{k_{-3a} + k_6K_4'} = \frac{C}{F} \tag{9}$$

as only the terms in $[H^+]^2$ prevail. In the pa_H^*-independent range of the alkaline side (solvent-catalyzed reaction):

$$k \cong \frac{k_2k_5K_1 + k_{3b}'k_5}{K_1(k_{-3b} + k_{-2} + k_5)} = \frac{A}{D}. \tag{10}$$

The experimental ratios of these parameters are reported in Table 4.

TABLE 4. VALUES OF PARAMETERS RATIOS (EQ. 8a) FOR THE RATE OF HYDROLYSIS OF N-BENZYL-IDENE, HALOGENOANILINES AT 25° IN AQUEOUS METHANOL (20·0 wt % H_2O) AT IONIC STRENGTH 0·045M

Anil	A/D (sec^{-2})	C/F (sec^{-1})
N-Benzylideneaniline	$3·36 \times 10^{-6}$ ($pa_H^* = 11·05$)	$3·10$ ($pa_H^* = 0·56$)
N-Benzylidene, 4-fluoroaniline	$1·87 \times 10^{-6}$ ($pa_H^* = 11·05$)	$4·14$ ($pa_H^* = 1·27$)
N-Benzylidene, 4-chloroaniline	$1·23 \times 10^{-6}$ ($pa_H^* = 11·05$)	$5·20$ ($pa_H^* = 1·50$)
N-Benzylidene, 4-bromoaniline	$1·12 \times 10^{-6}$ ($pa_H^* = 11·05$)	$5·83$ ($pa_H^* = 1·27$)
N-Benzylidene, 4-iodoaniline	$1·18 \times 10^{-6}$ ($pa_H^* = 11·05$)	$7·80$ ($pa_H^* = 1·27$)
N-Benzylidene, 2-fluoroaniline	$3·37 \times 10^{-7}$ ($pa_H^* = 11·05$)	—
N-Benzylidene, 2-chloroaniline	$1·28 \times 10^{-7}$ ($pa_H^* = 11·05$)	—
N-Benzylidene, 2-bromoaniline	$6·57 \times 10^{-8}$ ($pa_H^* = 11·05$)	—
N-Benzylidene, 2-iodoaniline	$3·94 \times 10^{-8}$ ($pa_H^* = 11·05$)	—
N-Benzylidene, 2,4-difluoroaniline	$2·95 \times 10^{-7}$ ($pa_H^* = 10·58$)	—
N-Benzylidene, 2,4-dichloroaniline	$1·35 \times 10^{-7}$ ($pa_H^* = 10·56$)	—
N-Benzylidene, 2,4-dibromoaniline	$9·33 \times 10^{-8}$ ($pa_H^* = 10·50$)	—
N-Benzylidene, 2,4-diiodoaniline	$7·58 \times 10^{-8}$ ($pa_H^* = 10·50$)	—
N-Benzylidene, 2,6-dichloroaniline	$5·25 \times 10^{-8}$ ($pa_H^* = 10·50$)	—
N-Benzylidene, 2,6-dibromoaniline	$2·63 \times 10^{-8}$ ($pa_H^* = 10·55$)	—

The independency of the rate of hydrolysis from ionic strength, at constant pa_H^* and buffer concentration, both in the acid and alkaline side of the profile, suggests that between the kinetically undistinguishable mechanisms (2) and (3b), the former

should be preferred in the rate determining step of the alkaline side, as the latter implies a net dependency on ionic strength following Brönsted's and Bjerrum's theory.[18]

Reaction (6) should also be relatively unimportant in the rate determining step for the same reason, as well as for the unobserved accumulation of amino-alcohol intermediate in appreciable concentration.

If these conclusions are valid, and if reverse reactions of Eqs (2), (3a), (5) and (6) are neglected in the hydrolysis conditions in which rates were measured, kinetic scheme reduces to reactions (1), (2), (3a) and (5). Eq. (8) simplifies to:

$$k = \frac{k_2 K_1 + k_{3a} a_H^*}{K_1 + a_H^*} \tag{11}$$

C/F and A/D ratios of Eq. (8a) become nearly equal to k_{3a} and k_2 respectively, and they should consequently represent values of individual rate constants.

When the general and specific acid catalysis is considered, for reaction (2), as it is evident from Fig. 4, k_2 can be expressed as a function of hydrogen ion activity:

$$k_2 = k_{2_{(0)}} + k_{2_{(H^+)}} a_H^* + k_{2_{(HA)}} c_s \gamma_\pm \frac{a_H^*}{K_{HA} + a_H^* \gamma_\pm} \tag{12}$$

where c_s is the stoicheiometric concentration of a buffer constituted by a monoprotic acid HA and its salt, K_{HA} is the dissociation constant of this acid, and $k_{2_{(0)}}$, $k_{2_{(H^+)}}$, $k_{2_{(HA)}}$ represent the catalytic constants (solvent, specific, and general acid catalysis respectively). Eq. (11) becomes:

$$k = \frac{k_{2_{(0)}} K_1 + (k_{2_{(H^+)}} K_1 + k_{3a}) a_H^* + k_{2_{(HA)}} c_s \gamma_\pm K_1 \dfrac{a_H^*}{K_{HA} + \gamma_\pm a_H^*}}{K_1 + a_H^*} \tag{13}$$

The catalytic constant $k_{2_{(0)}}$ can be evaluated experimentally from the intercept of plots such as those of Fig. 4, in the pa_H^*-independent range of the alkaline side of rate profile; $k_{2_{(HA)}}$ from the slope of similar graphs, e.g. for the acetate buffer, in the linear range of rate profile. From one (or more) experimental values of k, the value of $(k_{3a} + k_{2_{(H^+)}} K_1)$ can finally be calculated. With the determined values of these constants, the validity of Eq. (13) can be checked either by determination of K_1 from observed rate constants k, and comparison with its independently determined value, or by comparison of the calculated values of k with experiment, when dissociation constants of conjugate acids of the anils are known. Both verifications were made. The first kind of calculation was carried out for the hydrolysis rate constants of N-benzylideneaniline in aqueous solution:

$k_{2_{(0)}} = 1\cdot67 \times 10^{-4} \text{sec}^{-1}$; $k_{2_{(HA)}} = 11 \text{ sec}^{-1} \text{M}^{-1}$; $(k_{3a} + k_{2_{(H^+)}} K_1) = 3\cdot00 \times 10^3$ sec^{-1}. A value of $pK_1 = 1\cdot50 \pm 0\cdot06$ was obtained. Unfortunately this value has not yet been measured; but from extrapolation of a Hammett plot of pK_1 for a series of substituted anils in aqueous solution[7] the value of $pK_1 = 1\cdot51$ was evaluated for the unsubstituted Schiff base, which is in excellent agreement with the present calculation.

By the rate constants for hydrolysis of N-benzylideneaniline and its p-halogeno

derivatives in aqueous methanol solution (20·0 wt% H_2O), the following parameters were obtained, at 25°:

	I	II	III	IV	V
$k_{2_{(0)}} \times 10^6$ (sec^{-1})	3·36	1·80	1·20	1·10	1·15
$k_{2(AA)}$ (sec^{-1} M^{-1})	1·13	0·65	0·83	0·88	0·95
$k_{3a} + k_{2(A^-)} K_1$ (sec^{-1})	3·39	4·44	6·73	8·18	12·5

In this calculation the values of K_1 from Table 1 were used. The value of K_{HA} (acetic acid) = 5·25 × 10^{-7}M was extrapolated from literature data[25] in 20% aqueous methanol: it is fairly consistent with the corresponding pK_{HA} in 20% aqueous ethanol solution[19] (6·87). The fitting of experimental points to the curve calculated by Eq. (13) could thus be tested. A satisfactory agreement was found over the whole pa_H^* range investigated, even if the experimental points at $pa_H^* > 8·5$ refer to a different buffer (borate buffer) from that adopted for calculation. In this range, however, where solvent catalysis is particularly operative, the contribution of $k_{2_{(0)}}$, rather than that of $k_{2(HA)}$ values only, is significant. The calculated curves practically coincide with the continuous lines of Fig. 2 for anils I–V. The slopes of the approximately linear range of k/a_H^* profiles, calculated by Eq. (13), are reported in Table 5: they agree with the observed values.

TABLE 5. RELATION BETWEEN THE ANGLE (θ) FORMED BY THE PLANES OF THE TWO PHENYL RINGS IN THE ANIL MOLECULE AND THE SLOPE OF THE RATE PROFILE k/a_H^* IN ITS LINEAR RANGE, AT 25° IN AQUEOUS METHANOL (20 wt% H_2O) AT IONIC STRENGTH 0·045M

| Anil	$\theta^{(20)}$ (°)	Slope of the rate profile (sec^{-1}M^{-1})	
		Experimental[a]	Calculated by Eq. (13)
N-Benzylideneaniline	30	1·41 × 10^4	1·53 × 10^4
N-Benzylidene, 4-chloroaniline	—	1·09 × 10$^{4\,b}$	1·10 × 10^4
N-Benzylidene, 4-bromoaniline	—	1·09 × 10^4	1·14 × 10^4
N-Benzylidene, 4-iodoaniline	—	1·09 × 10^4	1·18 × 10^4
N-Benzylidene, 4-fluoroaniline	—	8·29 × 10^3	8·16 × 10^3
N-Benzylidene, 2-fluoroaniline	37	2·14 × 10^3	—
N-Benzylidene, 2,4-difluoroaniline	—	1·35 × 10^3	—
N-Benzylidene, 2-chloroaniline	45	1·26 × 10^3	—
N-Benzylidene, 2,4-dichloroaniline	—	524	—
N-Benzylidene, 2-bromoaniline	51	868	—
N-Benzylidene, 2,4-dibromoaniline	—	371	—
N-Benzylidene, 2-iodoaniline	56	328	—
N-Benzylidene, 2,4-diiodoaniline	—	263	—
N-Benzylidene, 2,6-dichloroaniline	66	190	—
N-Benzylidene, 2,6-dibromoaniline	71	79·4	—

[a] Graphical values.

[b] Mean values, obtained from a unique straight line for N-benzylidene, 4-chloro-(bromo, iodo) anilines.

Hydrolysis reactions of Schiff bases in the experimental conditions adopted can then adequately be interpreted by a mechanism which involves conversion of the substrate into its conjugate acid, followed by hydrolytic cleavage of this latter, as well

as solvent and acid catalysis of the anil. The relative importance of Eqs (2) and (3a) is a function of pa_H^*, following Eq. (13).

The considerable carbonium-ion character of the conjugate acid or of the transition state, due to the resonance:

$$-CH=\overset{+}{N}H- \longleftrightarrow -\overset{+}{C}H-NH-$$
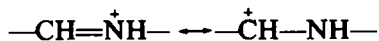
makes the substrate more subsceptible to solvent attack both by conversion to the conjugate acid and by hydrogen bonding of a general acid HA to the anil nitrogen. In the uncatalyzed hydrolysis (or solvolysis) solvent may play the dual role of acid and nucleophile. The transition state for the solvolysis and general acid catalysis can be represented respectively by:

$$\begin{array}{cc} -\overset{\cdots}{C}\overset{\cdots}{=}\overset{\cdots}{N}- & -\overset{\cdots}{C}\overset{\cdots}{=}\overset{\cdots}{N}- \\ H_2\overset{\delta+}{O} \; H_2\overset{\delta-}{O} & H_2\overset{\delta+}{O} \; H\overset{\delta-}{A} \end{array}$$

Two main factors can affect the stabilization of carbonium-ion:

(a) *Planarity of the anil molecule.* The carbonium-ion structure is stabilized by delocalization, which in turn decreases with increasing deviation from planarity. In fact, when the angle between the planes of the two phenyl rings increases, as a consequence of steric hindrance,[20] a lower hydrolysis rate is observed without exception in all the substituted anils in the pa_H^* range investigated. Quantitatively the influence brought about by this factor is showed by comparison of the angle θ of deformation from planarity, calculated from spectral data,[20] based on a theoretical value of $\theta = 30°$ for the unsubstituted anil, and the slope of the k/a_H^* profile in its linear range (Table 5).

(b) *Electron-donating or electron-withdrawing power of substituents.* When the substrate is chiefly the conjugate acid of the anil ($pa_H^* \ll pK_1$) the presence of electron-withdrawing substituents delocalizes the developing negative charge from the nucleophile in the transition state and consequently increases the rate of hydrolysis. The Hammett plot for log ($k_{halogen}/k_H$), where k are the rate constants, the subscripts referring to the values of p-halogenosubstituted (II–V) and unsubstituted N-benzylideneaniline (I) respectively, are reported in Fig. 5, both as a function of σ_p or of σ_p^+.[21] The Hammett σ_p(I) value of 0·276, obtained from pK of substituted benzoic acid, was adopted, instead of the value σ_p(I) = 0·18 ± 0·10, which was proposed by Brown.[22] A ρ value (substitution in the aniline ring) of 0·95 ± 0·05 results at $pa_H^* < 3$ for the hydrolysis reaction, indicating that in the acid side of the rate profile reaction is facilitated by low electron density at the azomethine bond. The linear correlation is satisfactory only when log k values are plotted against σ_p constants. A much poorer correlation coefficient is obtained from the plots as a function of σ_p^+.

The rate constants, on the contrary, are nearly independent of the substituent for Schiff bases I–V at $pa_H^* > 4$ ($\rho \cong -0·2$). A substantially similar plot would be obtained with the values of $k_{2(HA)}$ (Eq. (13)).

The Hammett plot for the acid dissociation constants K_1 of anils I–V yields again a satisfactory correlation against σ_p with a ρ value of 1·62 ± 0·02.

The stabilization of carbonium-ion by halogens in the *para* position of the aniline ring follows consequently the relative order of the Hammett σ_p values (F < Cl $\gtrsim$ Br < I). Similar conclusions were reached in the reaction between N-benzylideneanilines substituted in the aniline ring and p-nitrophenol,[23] and in the

cis-trans isomerization of the anils.[24] In the hydrolysis reaction of Schiff bases at $pa_H^* \gtrsim pK_1$, the preequilibrium between the anil and its conjugate acid is rapidly established and the latter is slowly converted into the amino-alcohol and hydrolysis products. Prevailing reactions are those of Eq. (3a), followed by (5). At $pa_H^* \gg pK_1$, acid or solvent catalysis involves primarily the conversion of the Schiff base into its conjugate acid. The very small negative value of the Hammett plot for reaction rate constants at $pa_H^* \gg pK_1$ could indicate a compensation of the two opposing effects brought about by the halogen substituent during the electrophilic and nucleophilic attack of azomethine bond by the acid and solvent or by the solvent alone in the transition state. In this range of the rate profile, both steric and electronic factors decrease the rate of hydrolysis. This may be observed, besides the small negative ρ value of the Hammett plot of Fig. 5 at $pa_H^* > 4$, by comparison of the slope of rate
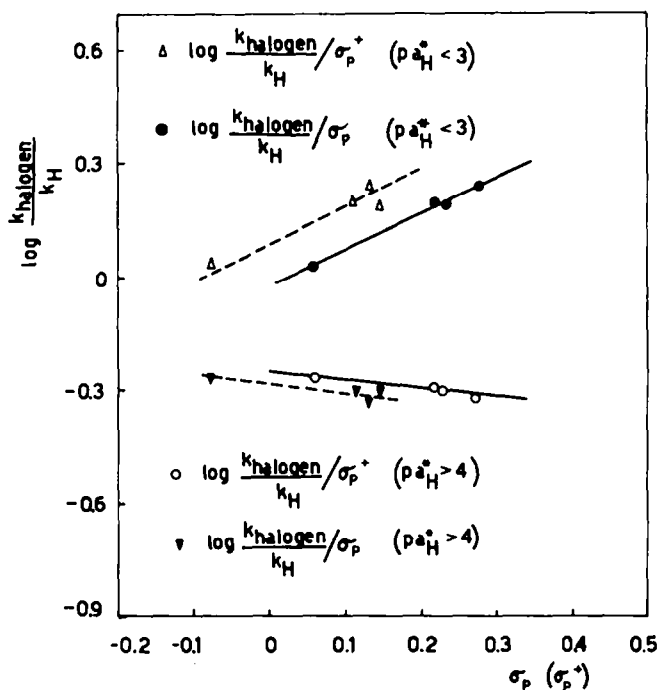

FIG. 5 Plot of log ($k_{halogen}/k_H$) for the hydrolysis of N-benzylideneaniline and its p-halogeno-derivatives (II–V) against σ_p (or σ_p^+) constants. Temperature 25°C; aqueous methanol solution (20·0 wt% H_2O); ionic strength 0·045M.

profiles in Table 5, for the 2-mono and 2,4-disubstituted anils. For these compounds, from UV spectra,[20] the same angle of deformation from planarity was calculated. The decrease of the rate parameters of Table 5 for the 2,4-disubstituted Schiff bases relatively to the monosubstituted compounds should consequently reflect the in-influence of the electronic factors in these molecules. Of the two factors, which principally influence the rate of hydrolysis of the series of structurally related anils I–XV, the steric effect seems hitherto to play the most important role.

When the substrate which undergoes hydrolysis, on the contrary, is principally constituted by the conjugate acid of the anil (pa$_H^*$ $\gtrsim$ pK$_1$), the electronic effect increases the rate of hydrolysis (Fig. 5 at pa$_H^*$ < 3). No observations can be made at present on the influence of steric factors in this latter range of the pa$_H^*$ rate profile, which has not been as yet investigated for the sterically hindered Schiff bases.

EXPERIMENTAL

Materials. Anils I–XV were prepared starting from equimolar amounts of the appropriate amine and benzaldehyde.[20] The solvents from which they were recrystallized, with the m.ps or b.ps, analyses, and UV absorption data have already been given.[20] All reagents were purified and prepared as previously described. Spectrograde methanol was rigorously anhydrified by distillation over Na and then over Mg in a dry N$_2$ stream, and again rectified.

Buffers. In the range 0·5–8·5 pa$_H^*$, buffer solns were prepared from a 0·025M KOAc, 0·025M KCl, and a 0·05M KCl, 0·10M HCl soln. In the range 8·5–11 pa$_H^*$, buffers were prepared from 0·01M sodium tetraborate, 0·02M NaCl, and 0·10M NaOH aq. The MeOH concentration of buffers was so calculated, that by dilution of 1·00 volume with 0·100 volumes of anhyd MeOH, the resulting soln contained 20·0 wt% of water. In this solvent[25] the difference between the measured pH and pa$_H^*$ was considered to be −0·06 pH units at 25°. The ionic strength of these solns was held constant in most runs at 0·045M. In aqueous solns the same buffers were employed. Buffer concentration and/or ionic strength was varied at constant pa$_H^*$, in some instances, both in the aqueous MeOH and aqueous solns. pH Measurements were performed with a glass-electrode (vs saturated calomel electrode) by means of a S.I.S. (Milan) precision pH-meter. The standard reference buffers were the National Bureau of Standards borax (pH 9·18 at 25°) and phtalate (pH 4·01 at 25°).[26]

Kinetic measurements. The Schiff base and its hydrolysis products were determined spectrophotometrically by means of a recording Beckman DK-2A spectrophotometer, equipped with the time-drive accessory. A soln of the anil in anhyd MeOH was prepared and the absence of any hydrolysis products was checked spectrophotometrically, 0·300 ml of this soln was injected from a calibrated syringe into 3·00 ml of the thermostated buffer contained in a 1-cm quartz cell. The water concentration of the final soln was thus 20·0 wt% and the ionic strength 0·045M. The time lapse between mixing and the beginning of the record was 10–15 sec (as measured with a stopwatch).

For the slow runs, with half-times greater than 10 hr, periodic absorbance measurements were carried out on solns kept in the tightly stoppered quartz cells and maintained in suitable thermostated reactors.

For the runs with half-times from 0·25 min to a few hours, the absorbance change at a fixed wavelength was plotted continuously vs. time on the recording spectrophotometer.

The very fast runs (half-times ≤ 0·1 min), using the stopped-flow method, were followed by a non-recording spectrophotometer (Optica, Milan, model CF4) connected to a Textronix oscillograph, type 532. The bright trace on the screen of this latter was recorded photographically on a calibrated transmittance scale. Complete mixing of the buffer (0·150 ml) with the anil soln (0·0150 ml) occurred directly into a 0·100-cm spectrophotometric cell, within a maximum time interval of 100 msec, owing to the geometry of apparatus.

Kinetic measurements in aqueous solns were effected similarly: 10 μl of the alcoholic soln of the anil were injected into 3·00 ml of the aqueous buffer. The water concentration of the final soln was thus 99·7 wt%.

All kinetic runs were carried out at 25 ± 0·05°.

First-order kinetics was always observed up to 80–90% conversion throughout any run. Calculations, which were effected by means of a I.B.M. 1620/20K computer, allowed to obtain rate constants and absorbances at zero time from the measured values of absorbances during the run and after the reaction was completed (absorbances at infinite time).

In the pa$_H^*$ range of superposition of buffers (about 7–8·8), the measured rate constants of the N-benzylideneanilines at constant pa$_H^*$ and ionic strength (0·045M) were practically independent, within the limit of experimental error, from the choice of the two buffer systems employed. When the buffer capacity was low, pa$_H^*$ was controlled during kinetic runs. The results of these latter were rejected when pa$_H^*$ variations exceeded 0·1 pa$_H^*$ units.

Acid dissociation constants. For the equilibrium between the Schiff base (S) and its conjugate acid (SH$^+$)

in the 20% aqueous MeOH solution (ionic strength 0·045M) at 25^c, the dissociation constants:

$$K_1 = \frac{a_S \cdot a_{H^+}}{a_{SH^+}} \quad (a = \text{activities})$$

were determined from the change in the absorption curves (extrapolated by the calculation to zero reaction time) with pa_H^* in the region $(pK_1 - 2) \leqslant pa_H^* \leqslant (pK_1 + 2)$. Activity coefficients $\gamma_\pm$ were evaluated by Debye–Hückel expression $-\log \gamma_\pm = A\sqrt{I}/(1 + \sqrt{I})$, where $A = 1\cdot275$ $(\text{gmole/l})^{-\frac{1}{2}}$, for 20% aqueous methanol at 25°C.

By plotting $\log \left[(D_{SH^+} - D)/\gamma_\pm (D - D_S) \right]$ vs. pa_H^*, where D are the absorbances at zero reaction time of SH^+, S, and their equilibrium mixtures respectively, the pK_1 values were obtained by a least square treatment. All solutions were thermostatically equilibrated at 25°C prior to and during the measurements. The constancy of temp was maintained within $\pm 0\cdot05°$.

REFERENCES

[1] O. Bloch-Chaudé, C.R. Acad. Sci. Paris 239, 804 (1954).
[2] L. Holleck and B. Kastening, Z. Elektrochem. 60, 127 (1956).
[3] B. Kastening, L. Holleck, and G. A. Melkonian, Ibid. 60, 130 (1956).
[4] A. V. Willi and R. E. Robertson, Canad. J. Chem. 31, 361 (1953).
[5] A. V. Willi, Helv. Chim. Acta 39, 1193 (1956).
[6] R. L. Reeves, J. Am. Chem. Soc. 84, 3332 (1962).
[7] R. L. Reeves and W. F. Smith, Ibid. 85, 724 (1963).
[8] R. L. Reeves, J. Org. Chem. 30, 3129 (1965).
[9] E. H. Cordes and W. P. Jencks, J. Am. Chem. Soc. 84, 826, 832 (1962); Biochemistry 1, 773 (1962).
[10] K. Koehler, W. A. Sandstrom, and E. H. Cordes, J. Am. Chem. Soc. 86, 2413 (1964).
[11] M. T. A. Behme and E. H. Cordes, Ibid. 87, 260 (1965).
[12] L. Do Amaral, W. A. Sandstrom, and E. H. Cordes, Ibid. 88, 2225 (1966).
[13] R. K. Chaturvedi and E. H. Cordes, Ibid. 89, 1230 (1967).
[14] cf. W. P. Jencks, Progr. Phys. Org. Chem. 2, 63 (1964).
[15] R. G. Bates, Determination of pH p. 223. Wiley, New York (1964).
[16] H. Jeffreys, Proc. Roy. Soc. 138A, 48 (1922)
[17] See E. F. Caldin and C. Long, J. Chem. Soc. 3737 (1954).
[18] E. S. Amis, Solvent effects on reaction rates and mechanism, p. 21. Academic Press, New York (1966).
[19] E. Grunwald and B. J. Berkowitz, J. Am. Chem. Soc. 73, 4939 (1951); B. Gutbezahl and E. Grunwald, Ibid. 75, 559 (1953); see Ref. 15, page 195.
[20] G. Favini and I. R. Bellobono, Gazz. Chim. Ital. 96, 1423 (1966).
[21] H. H. Jaffe, Chem. Rev. 53, 191 (1953); H. Brown and Y. Okamoto, J. Am. Chem. Soc. 80, 4979 (1958); see Refs cited therein.
[22] H. C. Brown, J. Org. Chem. 23, 425 (1958).
[23] J. Weinstein and E. McIninch, J. Am. Chem. Soc. 82, 6064 (1960); cf. D. Anderson and G. Wettemark, Ibid. 87, 1584 (1965).
[24] G. Wettemark, J. Weinstein, J. Sousa, and L. Dogliotti, J. Phys. Chem. 69, 1584 (1965).
[25] C. L. De Ligny, P. F. M. Luykx, M. Renbach, and A. A. Wienecke, Rec. Trav. Chim. 79, 699 (1960); Ibid. 79, 727 (1960).
[26] see Ref. 15, page 123.