Hydrolysis of *N*-*p*-Nitrobenzylideneaniline: a Quantitative Study of Specific and General Catalysis

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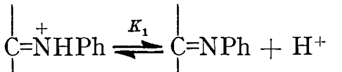
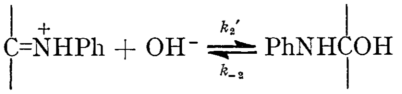
The pa_H^*–rate profile for the hydrolysis of *N*-*p*-nitrobenzylideneaniline was investigated in the pa_H^* range 2·72—10·94, in buffered aqueous methanol solutions (20·0% w/w H_2O) at 25° and ionic strength 0·045M. The dependence of rate coefficients on buffer concentration at constant pa_H^*, constant ratio of buffer components at each pa_H^*, and constant ionic strength was also studied in the pa_H^* range 3·02—8·25. The observed rate coefficients show the influence of catalysis, obeying the expression $k_{obs} = k_{ext} + k_{cat}[HA]$, in which the straight line parameters show a complex dependence on a_H^*. Starting from the generally accepted mechanism for these reactions, a steady-state rate equation for specific and general catalysis was developed. An analysis of this rate equation has given not only the entire set of parameters but also the rate-determining steps and the values of some individual rate coefficients. The risk of making erroneous conclusions in the absence of a quantitative study of general catalysis is underlined.

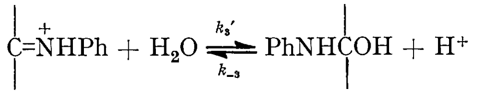
KINETIC studies of the pH, structure, and medium effects on the rate of hydrolysis of Schiff's bases has permitted the establishment of the general features of these rather complex reactions.[1-3] The general mechanism can be described by reactions (1)—(7).†



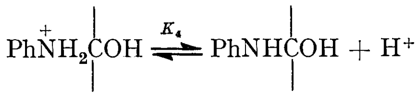
$$\overset{+}{\mathrm{C{=}NHPh}} \underset{}{\overset{K_1}{\rightleftharpoons}} \mathrm{C{=}NPh} + \mathrm{H^+} \tag{1}$$



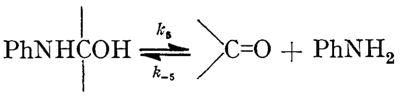
$$\overset{+}{\mathrm{C{=}NHPh}} + \mathrm{OH^-} \underset{k_{-2}}{\overset{k_2'}{\rightleftharpoons}} \mathrm{PhNHCOH} \tag{2}$$



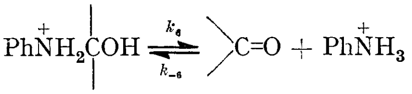
$$\overset{+}{\mathrm{C{=}NHPh}} + \mathrm{H_2O} \underset{k_{-3}}{\overset{k_3'}{\rightleftharpoons}} \mathrm{PhNHCOH} + \mathrm{H^+} \tag{3}$$



$$\mathrm{Ph\overset{+}{N}H_2COH} \overset{K_4}{\rightleftharpoons} \mathrm{PhNHCOH} + \mathrm{H^+} \tag{4}$$



$$\mathrm{PhNHCOH} \underset{k_{-5}}{\overset{k_5}{\rightleftharpoons}} \mathrm{{>}C{=}O} + \mathrm{PhNH_2} \tag{5}$$



$$\mathrm{Ph\overset{+}{N}H_2COH} \underset{k_{-6}}{\overset{k_6}{\rightleftharpoons}} \mathrm{{>}C{=}O} + \mathrm{Ph\overset{+}{N}H_3} \tag{6}$$

$$\mathrm{Ph\overset{+}{N}H_3} \overset{K_7}{\rightleftharpoons} \mathrm{PhNH_2} + \mathrm{H^+} \tag{7}$$

On the assumption that the formation of the carbinolamine intermediates and their decomposition are both slow steps, a steady-state rate equation was written for hydroysis in aqueous solutions;[4] subsequently, it was shown that the same equation holds in aqueous methanol as the influence of methanolysis can be neglected.[5] It was further established that for alkaline, pH-independent hydrolysis, the rate-determining step involves the attack of hydroxide ion on the conjugate acid of the substrate rather than that of water on the free base.[6]

In addition, previous studies have revealed that the addition of nucleophilic reagents to Schiff's bases is subject to general acid–base catalysis[7] but it has never been shown how the general catalysis accounts quantitatively for the observed rates.

In an attempt to obtain information pertinent to these questions, the kinetics of the hydrolysis of *N*-*p*-nitrobenzylideneaniline were studied at 25° in buffered aqueous methanol solutions (20·0% w/w H_2O). The dependence of the rate coefficient on buffer concentration at constant pa_H^* (a_H^* = activity of solvated hydrogen ions, with reference to the standard state in the mixed solvent),[8] constant ratio of buffer components, and constant ionic strength was checked as well as the dependence on pa_H^* at constant ionic strength.

EXPERIMENTAL

Materials.—Spectrograde methanol was rigorously dried by distillation over Na and then over Mg under dry nitrogen and redistilled. *N*-*p*-Nitrobenzylideneaniline was prepared by condensing equimolar amounts of aniline and *p*-nitrobenzaldehyde, as previously reported,[9] $\lambda_{max.}$ (MeOH) 290 (ε 14,000) and 335 nm (11,040).

Buffers.—In the pa_H^* range 2·5—7·7, buffer solutions were prepared by mixing the appropriate volumes *V* of solution A [*x*M-HCl–*y*M-KCl (2 : 1)] and B [*x*M-AcOK–*y*M-KCl (1 : 1)]. In the pa_H^* range 7·4—11 buffers were prepared from 0·01M-sodium tetraborate, 0·02M-NaCl, and aqueous 0·10M-NaOH. In each starting solution the methanol concentration was so calculated that the final solution contained 20·0% w/w water. In this solvent, it was considered that pa_H^* = meter reading + 0·06 at 25°.[10] The ionic strength of the final solutions was held constant at 0·045M.

Two series of acetate buffer solution were prepared. The

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† K_1, K_4, and K_7 are acid dissociation constants.

[1] For comprehensive reviews see (*a*) W. P. Jencks, *Progr. Phys. Org. Chem.*, 1964, **2**, 63; (*b*) 'Catalysis in Chemistry and Enzymology,' McGraw-Hill, New York, 1969, ch. 10.

[2] R. E. Barnett, *Accounts Chem. Res.*, 1973, **6**, 41.

[3] S. M. Silver and J. M. Sayer, *J. Amer. Chem. Soc.*, 1973, **95**, 5073.

[4] R. L. Reeves, *J. Amer. Chem. Soc.*, 1962, **84**, 3332.

[5] I. R. Bellobono and G. Favini, *Tetrahedron*, 1969, **25**, 57.

[6] J. Archila, H. Bull, C. Lagenaur, and E. H. Cordes, *J. Org. Chem.*, 1971, **36**, 1345.

[7] (*a*) K. Koehler, W. Sandstrom, and E. H. Cordes, *J. Amer. Chem. Soc.*, 1964, **86**, 2413; (*b*) G. M. Santerre, C. J. Hansrote, jun., and T. I. Crowell, *ibid.*, 1958, **80**, 1254.

[8] R. G. Bates, 'Determination of pH,' Wiley, New York, 1964, p. 223.

[9] D. Pitea, D. Grasso, and G. Favini, *Gazzetta*, 1970, **100**, 519.

[10] C. L. De Ligny, P. F. M. Luykx, M. Renbach, and A. A. Wienecke, *Rec. Trav. chim.*, 1960, **79**, 699, 727.

first by mixing solutions A and B (x 0·02—0·1, y 0·001—0·03) in a constant volume ratio; these buffers with constant ionic strength, with different concentrations but the same ratio of components at each pa_H*, were used for determining dependence of the rate coefficients on the buffer concentration at constant pa_H* values. The buffers for measurements of the dependence of rate coefficients on pa_H* at constant ionic strength were prepared by mixing solutions A and B ($x = y =$ 0·025) in various volume ratios.

Kinetics.—A solution of the *N*-*p*-nitrobenzylideneaniline in anhydrous methanol was prepared, care being taken to shield the solution from exposure to light, and the absence of any hydrolysis products was checked spectrophotometrically.[11] The solution (0·3 ml) was injected from a calibrated syringe into the thermostatted buffer (3·0 ml) contained in a 1 cm quartz cell.

Rate coefficients were evaluated at a fixed wavelength (285—295 nm) by measuring the absorbance of the solution with a Hitachi–Perkin-Elmer model 139 spectrophotometer at 25 ± 0·05°. For the runs with $t_{1/2}$ 0·25 min to a few hours, a home-made injection system was used to minimize the time lapse between mixing and the start of recording; the absorbance change was plotted continuously against time. For slow runs with $t_{1/2} > 10$ h, measurements were carried out on solutions kept in tightly stoppered cells and maintained in suitably thermostatted reactors; in each run, series of pairs of absorbance values were taken such that the time interval separating them was a constant.

At the conclusion of kinetic runs, the u.v. spectra were identical with those of equimolar samples of authentic *p*-nitrobenzaldehyde and aniline.

For all reactions, which were followed to 80—90% conversion pseudo-first-order kinetics were obeyed. Rate coefficients were calculated by Margerison's procedure [12a] or by Guggenheim's method.[13] For every run, the rate coefficient was obtained by a weighted,[12b] least-squares, linear regression method; only runs for which the index of determination (r^2) was $\geqslant$0·99 have been considered. The reported rate coefficients k_{obs} are the mean values for a group of duplicate experiments at different wavelengths and were tested for homogeneity.[12c]

In the overlap pa_H* range of the two buffers, the rate coefficients were practically independent of the choice of the buffer system. When the buffer capacity was low, pa_H* was checked during kinetic runs. The results were rejected when pa_H* variations exceeded 0·1 units.

The rates of hydrolysis in the region of appreciable protonation of *N*-*p*-nitrobenzylideneaniline were too fast to permit accurate extrapolations of optical density readings to zero time and so an accurate spectral titration curve of the protonation of the substrate could not be obtained.

RESULTS

The dissociation constant K_{HA} of acetic acid in the buffered, aqueous methanol solution was evaluated from a set of experimental values of pa_H* at different volume ratios (Table 1). Using the activity coefficients given by Shedlovsky and Kay [14] and $\gamma_{HA} = 1$, the parameters of the equation $\log[a_{(A^-)}{}^*/a_{HA}{}^*] = -\mathrm{p}K_{HA} + \mathrm{p}a_H{}^*$ were obtained by a least-squares treatment. The following values were obtained ($r^2 = 0{\cdot}999$; ± refer to 95% confidence limits): pK_{HA} = 6·23 ± 0·11 (slope 0·99 ± 0·02). The calculated value of K_{HA} [(5·88 ± 1·70) × 10⁻⁷] is in fairly good agreement with literature data.[5,14]

The dependence of rate coefficients on buffer concentration at constant pa_H*, constant ratio of buffer components at each pa_H*, and constant ionic strength 0·045M was studied in the 3·02—8·25 pa_H* range; the weighted mean values (k_{obs}) of the rate coefficients together with estimated standard errors and the corresponding number of degrees of freedom are given in Table 2.

TABLE 1

Experimental values of pa_H* at different volume ratios V_A/V_B [a]

V_A/V_B	0·248	0·245	0·236	0·234	0·211	0·187
pa_H* [b]	4·11	4·50	5·00	5·07	5·50	5·75

[a] For V_A/V_B see Experimental section. [b] Mean standard deviations are 0·002 for V_A/V_B and 0·02 for pa_H*. Each standard deviation is based on 5—7 determinations.

TABLE 2

Effect of acetic acid concentration on the rate of hydrolysis of *N*-*p*-nitrobenzylideneaniline at constant pa_H*, constant ionic strength (0·045M), and constant buffer component ratio at each pa_H* in aqueous methanol (20·0% w/w H_2O) at 25° [a]

pa_H *	10^2[HA]/M	$10^2k_{obs}/s^{-1}$ [b]	Degree of freedom
3·02	1·30	27·9 ± 0·9	5
	1·67	30·0 ± 1·0	5
	1·97	31·4 ± 1·0	6
	2·77	35·8 ± 1·2	5
3·96	1·23	16·8 ± 0·4	3
	1·45	17·6 ± 0·4	3
	1·81	18·8 ± 0·7	3
	2·54	22·2 ± 0·9	4
4·17	1·80	12·1 ± 0·2	3
	2·89	14·3 ± 0·2	4
	3·61	16·2 ± 0·1	3
	4·33	17·5 ± 0·2	3
4·56	1·43	5·70 ± 0·21	3
	1·79	6·08 ± 0·15	3
	2·15	6·48 ± 0·08	3
	2·51	6·81 ± 0·20	3
5·13	1·38	1·74 ± 0·04	3
	1·72	1·88 ± 0·01	4
	2·07	1·98 ± 0·02	3
	2·41	2·10 ± 0·06	3
5·81	1·15	0·442 ± 0·006	4
	1·43	0·466 ± 0·003	4
	1·72	0·490 ± 0·002	4
	2·00	0·512 ± 0·003	4
6·06	1·23	0·288 ± 0·001	4
	1·47	0·301 ± 0·001	4
	1·72	0·313 ± 0·001	4
	1·97	0·324 ± 0·001	4
	2·46	0·346 ± 0·002	4

[a] See text for runs at pa_H* >6·06. [b] Error refers to estimated standard error based on degrees of freedom.

Plots of k_{obs} against [HA] are linear; the coefficients of equation (8) are reported in Table 3. Although a small

$$k_{obs} = k_{ext} + k_{cat}[\mathrm{HA}] \qquad (8)$$

increase in the rate coefficients with the general acid concentration was also observed at pa_H* 7·15 (acetate buffer) and 8·25 (borate buffer) the statistic test at a 0·05 significance level shows that we cannot reject the hypothesis

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[11] D. Pitea, D. Grasso, and G. Favini, *Gazzetta*, 1970, **100**, 301.

[12] D. Margerison, 'The Practice of Kinetics,' eds. C. H. Bamford and C. F. H. Tipper, Elsevier, Amsterdam, 1969 (*a*) ch. 5; (*b*) method 2 on p. 375; (*c*) p. 382.

[13] E. A. Guggenheim, *Phil. Mag.*, 1926, **2**, 538.

[14] T. Shedlovsky and R. L. Kay, *J. Phys. Chem.*, 1956, **60**, 151.

that $k_{cat} = 0$; accordingly, the influence of buffer concentration can be neglected.

The dependence of rate coefficients on pa_H* at constant ionic strength 0·045M was studied in the pa_H* range 2·72—10·94 at intervals of *ca.* 0·25 units: representative values and average errors are reported in Table 4.

TABLE 3

Intercepts (k_{ext}) and slopes (k_{cat}) for the straight line plots of k_{obs} against [HA] [equation (8)]

pa_H*	r^2 [a]	$10^2\ k_{ext}/s^{-1}$ [b]	k_{cat}/l mol^{-1} s^{-1} [b]
3·02	0·998	20·8 ± 0·9	5·42 ± 0·12
3·96	0·995	11·7 ± 1·4	4·11 ± 0·50
4·17	0·997	8·11 ± 1·06	2·20 ± 0·85
4·56	0·997	4·19 ± 0·35	1·06 ± 0·35
5·13	0·983	1·31 ± 0·23	0·327 ± 0·168
5·81	0·999	0·350 ± 0·009	0·082 ± 0·007
6·06	0·999	0·229 ± 0·005	0·049 ± 0·004

[a] Index of determination. [b] Error refers to 95% confidence limits based on runs reported in Table 2.

TABLE 4

Effect of acidity on the rate of hydrolysis of *N-p*-nitrobenzylideneaniline at 25° and ionic strength 0·045M

pa_H* [a]	$-\log k_{obs}$ [b]	$-\log k_{ext}'$ [c]	pa_H* [d]	$-\log k_{obs}$ [b]
2·72	0·441	0·590	7·39	3·83
3·64	0·623	0·788	7·67	4·00
4·52	1·18	1·37	7·98	4·36
5·15	1·74	1·92	8·52	4·79
5·97	2·48	2·59	8·91	5·08
6·63	3·19	3·25	9·15	5·29
6·94	3·39	3·42	10·04	5·54
7·39	3·85	3·85	10·48	5·58
7·67	3·99	3·99	10·94	5·60

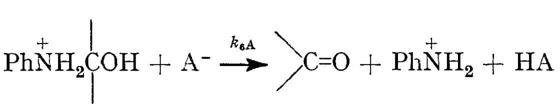
[a] Acetate buffer. [b] Weighted mean value of the observed rate coefficients based on 4—8 runs (s^{-1}); average errors based on 95% confidence limits are ±8% at pa_H* <4·2 and ±1% at pa_H* >4·2. [c] Observed rate coefficient corrected for general catalysis. [d] Borate buffer.

DISCUSSION

The observation that in acid solution (at constant pa_H* and constant ionic strength) the rate coefficients show significant variations with changes in the concentration of buffer solutions is characteristic of reactions showing general acid–base catalysis. General acid catalysis was previously observed under conditions in which the substrate exists as free base [7b,15] while general base catalysis was observed under conditions in which the substrate is fully protonated.[16]

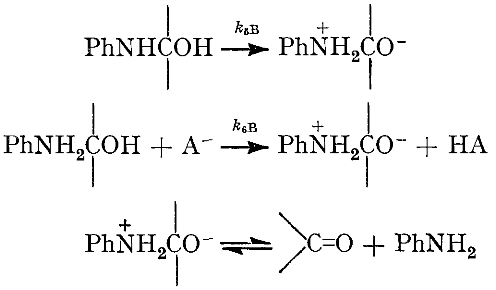
In our case, the lack of general catalysis at pa_H* >7 where the reactions governed by k_2' and k_3' are predominant, should indicate that the observed general catalysis is effective in reactions (5) and/or (6).

The usual mechanism for general catalysis is given in equation (9); the initially formed carbinolamine intermediate must undergo at least one proton transfer before it can break down to products. Such proton transfers have been assumed to be too fast to be rate determining.



$$\mathrm{PhNHCOH} \xrightarrow{k_{5A}} \mathrm{{>}C{=}O} + \mathrm{PhNH_2}$$
$$\mathrm{Ph\overset{+}{N}H_2COH} + \mathrm{A^-} \xrightarrow{k_{6A}} \mathrm{{>}C{=}O} + \mathrm{Ph\overset{+}{N}H_2} + \mathrm{HA} \qquad (9)$$

In the alternative mechanism (10) the rate-determining step is formation of the zwitterionic intermediate. It would also be expected that bifunctional catalysts could convert the neutral carbinolamine into the zwitterion directly.



$$\mathrm{PhNHCOH} \xrightarrow{k_{5B}} \mathrm{Ph\overset{+}{N}H_2CO^-}$$
$$\mathrm{PhNH_2COH} + \mathrm{A^-} \xrightarrow{k_{6B}} \mathrm{Ph\overset{+}{N}H_2CO^-} + \mathrm{HA} \qquad (10)$$
$$\mathrm{Ph\overset{+}{N}H_2CO^-} \rightleftharpoons \mathrm{{>}C{=}O} + \mathrm{PhNH_2}$$

Accordingly, there are two kinetically indistinguishable mechanisms. Both might be operative, possibly with a different weight depending on the pH range.

The rate law for mechanisms (9) and (10) is expressed by equation (11) where k_O, k_S, and k_{HA} refer to the solvent and specific and general catalysed reactions, respectively.

$$\text{Rate} = [\mathrm{PhNHCOH}]\{k_O + k_S + k_{HA}[\mathrm{HA}]\} \qquad (11)$$

The steady-state rate law for the overall reaction is (12)

$$k_{obs} = \frac{(k_2 + k_3a_H^*)\{k_O + k_Sa_H^* + k_{HA}[\mathrm{HA}]\}}{(K_1 + a_H^*)\{(k_O + k_{-2}) + (k_S + k_{-3})a_H^* + k_{HA}[\mathrm{HA}]\}} \qquad (12)$$

where $k_2 = k_2'a_H^*a_{OH}^*$ and $k_3 = k_3'$ [H$_2$O]. Two assumptions may be made: (*a*) $k_{-2} \ll k_O$, as shown for several similar reactions [16] and (*b*) $k_O + (k_S + k_{-3})a_H \gg k_{HA}[\mathrm{HA}]$, by comparison of equations (8) and (12). This results in equation (13).

$$k_{obs} = \frac{(k_2 + k_3a_H^*)(k_O + k_Sa_H^*) + k_{HA}(k_2 + k_3a_H^*)[\mathrm{HA}]}{(K_1 + a_H^*)[k_O + (k_S + k_{-3})a_H^*]} \qquad (13)$$
$$= k_{ext} + k_{cat}[\mathrm{HA}]$$

It is possible to discuss equation (13) by a 'semi-empirical' or by an 'analytical' approach.

In the 'semi-empirical' approach we use all the available information in order to simplify the calculation of parameters. An approximate pK_1 value for the *N-p*-nitrobenzylideneaniline might be inferred from the known pK_a of benzylidene-1,1-dimethylethylamine (pK_a 6·70 in water [16]), its *p*-nitro-derivative (pK_a 5·40 in water [16]) and benzylideneaniline [pK_a 1·50 in water and 2·27 in 4 : 1 (w/w) MeOH–H$_2$O [5]]. In benzylideneaniline, the 'aniline' ring is twisted out of the PhCHN plane; thus, the lone pair on nitrogen can partially interact with the delocalised orbitals of the ring. This effect adds to the electron-withdrawing power of the aromatic ring

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[15] E. H. Cordes and W. P. Jencks, *J. Amer. Chem. Soc.*, 1962, **84**, 832.

[16] E. H. Cordes and W. P. Jencks, *J. Amer. Chem. Soc.*, 1963, **85**, 2843.

and so a decrease in pK_a, relative to benzylidene-1,1-dimethylethylamine, is expected and observed. If the benzylideneaniline and its *p*-nitro-derivative have the same molecular conformation, the same effect observed for benzylidene-1,1-dimethylethylamines should be expected. Previously,[17] it was shown that the general behaviour of the $\Delta\nu$–σ correlation † and the ρ value for *p*-X-benzylideneanilines do not differ significantly from those for the *p*-X-benzylidenemethylamines. Therefore the ρ^+ value 1·6 reported for the dissociation constants of benzylidene-1,1-dimethylethylamines[16] was used and K_1 0·11 mol l^{-1} was estimated for *p*-nitrobenzylideneaniline in 1 : 4 H_2O–MeOH (w/w).‡ Since $K_1 \gg a_H^*$ over the entire pa_H^* range examined, the break in the pa_H^*–rate profile at pa_H^* *ca.* 3 requires that $k_O \gg k_S a_H^*$.

Moreover, in discussing the k_{cat} rate law, it must be observed that in the pa_H^* region of interest for general catalysis, the contribution to the observed rate from the attack of hydroxide ion on the protonated Schiff's base is negligible. Equation (13) yields (14).

$$k_{cat} = (k_3 k_{HA}/K_1 k_{-3}) a_H^* / [(k_O/k_{-3}) + a_H^*] \qquad (14)$$

Hyperbolic relationships of the form (14) may be written in a linear form in three different ways.[18,19] It is best to use all the transformations having different matrices when the function varies between wide limits.[19] The three possible transformations were applied to our k_{cat} data in Table 3; a good correlation between experimental and calculated data is obtained only when the matrix of equation (15) was used. The parameters

$$a_H^*/k_{cat} = K_1 k_O / k_3 k_{HA} + (K_1 k_{-3}/k_3 k_{HA}) a_H^* \qquad (15)$$

estimated by a weighted, least-squares treatment are reported in Table 5; experimental data are in good agreement with the curve calculated by equation (14) (Figure 1).

TABLE 5

Parameters for the k_{cat} [equation (15)] and k_{ext} [equation (16)] rate laws [a]

Equation (15) [b]	$K_1 k_O (k_3 k_{HA})^{-1}$/mol^2 l^{-2} s	(1·81 ± 0·21) × 10^{-5}
	$K_1 k_{-3} (k_3 k_{HA})^{-1}$/mol l^{-1} s	0·165 ± 0·006
	$k_O (k_{-3})^{-1}$/mol l^{-1} [c]	(1·09 ± 0·01) × 10^{-4}
Equation (16) [d]	$k_O k_2 (K_1 k_{-3})^{-1}$/mol l^{-1} s^{-1}	(2·49 ± 0·27) × 10^{-10}
	$k_O k_3 (K_1 k_{-3})^{-1}$/s^{-1}	0·260 ± 0·009
	$k_O (k_{-3})^{-1}$/mol l^{-1}	(0·985 ± 0·027) × 10^{-4}
	k_2/mol l^{-1} s^{-1} [c]	2·78 ± 10^{-7}
	k_3/s^{-1} [c]	2·90 ± 10^2

[a] Error refers to standard deviations. [b] $r^2 = 0.994$. [c] Value calculated from the estimated parameters. [d] The table of analysis of variance is not reported but is available on request.

Having a complete, quantitative catalytic profile, the observed rate coefficients were corrected for general catalysis; the corrected values (k_{ext}') are shown in Figures 2 and 3 and representative values are reported in Table 4. The k_{ext} rate law reduces to equation (16).

$$k_{ext} = \frac{(k_O k_2 + k_O k_3 a_H^*)/K_1 k_{-3}}{(k_O/k_{-3}) + a_H^*} \qquad (16)$$

The parameters of such an equation may be estimated by both a linear multiple regression analysis[20] [if equation (16) is linearized as $k_{ext} = k_2/K_1 + (k_{-3}/K_1) a_H^* - (k_{-3}/k_O) k_{ext} a_H^*$] and an optimization program.[21] The two sets of parameters, evaluated from experimental data, agree satisfactorily; the mean values are reported in Table 5. It may be observed that the two independent estimates of k_O/k_{-3} are in good agreement. The pa_H^*–rate profile for the hydrolysis of *N*-*p*-nitrobenzylideneaniline (Figure 2) is a theoretical curve calculated from equation (16).

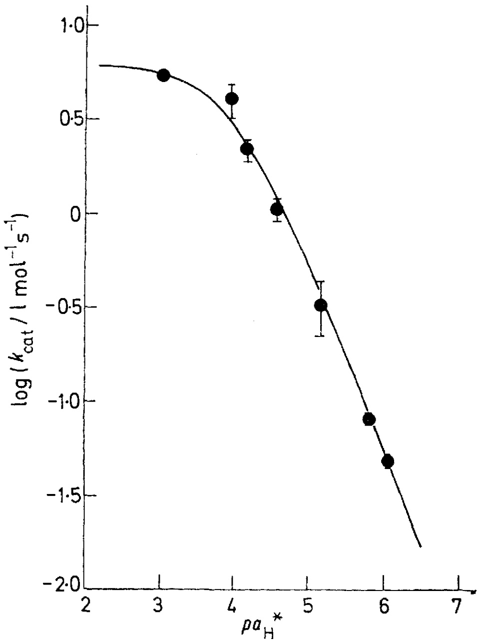
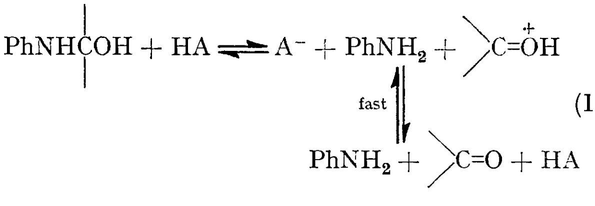


FIGURE 1 pa_H^*–log k_{cat} Profile for the hydrolysis of *N*-*p*-nitrobenzylideneaniline. The line is calculated from equation (14)

In the foregoing discussion, the possibility that the catalysts convert the neutral carbinolamine into products directly has not been envisaged. This mechanism corresponds to the general acid catalysis (17) and can be



$$\text{PhNHCOH} + \text{HA} \rightleftharpoons \text{A}^- + \text{PhNH}_2 + {>}\text{C=}\overset{+}{\text{O}}\text{H} \xrightleftharpoons{\text{fast}} \text{PhNH}_2 + {>}\text{C=O} + \text{HA} \qquad (17)$$

ruled out on the following grounds. In the reverse direction, mechanism (17) requires that the product of the catalytic coefficient for a general acid k_{HA}^*, its concentration [HA], and the concentration of aldehyde

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† $\Delta\nu = \nu_H - \nu_X$ is the difference in wavenumber between the absorption maxima of the H- and X-substituted compounds.

‡ This assumption implies that the ρ^+ value does not change much by reason of the effect of solvent.

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$[{>}C{=}O]$, equals the product of the concentrations of the protonated aldehyde $[{>}C{=}\overset{+}{O}H]$, conjugate base $[A^-]$, and the rate coefficients k^* for the formation step ($k^*[A^-][{>}C{=}\overset{+}{O}H] = k_{HA}^*[HA][{>}C{=}O]$ or $k^* = k_{HA}^*K_a/K_{HA}$, where $K_a = [{>}C{=}O][H^+]/[{>}C{=}\overset{+}{O}H]$). K_a, the equilibrium constant for the protonation of *p*-nitrobenzaldehyde is $2{\cdot}8 \times 10^8$ [22] and hence $k^* = 5 \times 10^{14}k_{HA}^*$.

The k_{HA}^* value may be estimated by the equation $k_{HA}^* = k_{HA}[PhNH_2]/K_{eq}$, where k_{HA} is the observed catalytic coefficient for the forward reaction, $[PhNH_2] = 1$M for simplicity's sake, and $K_{eq} = [PhNH_2][{>}C{=}O]/[PhNH\overset{|}{\underset{|}{C}}OH]$. K_{eq} may be estimated from the relation $K_{eq} = K_7/K_4K_f$, where $K_f = [Ph\overset{+}{N}H_2\overset{|}{\underset{|}{C}}OH]/[Ph\overset{+}{N}H_3][{>}C{=}O]$. Experimental or approximate values are available for all the equilibrium constants. For pK_7, the value 3·75 [in 4 : 1 (w/w) EtOH–H_2O] was used.[23] For K_4, a value higher than K_7 by one order of magnitude was estimated.[24] For K_f, only a rough estimate is possible; as values of the same order of magnitude were found in the literature for several secondary and tertiary amines ($0{\cdot}5 < K_f < 4{\cdot}3$ [24]), the approximate value 2 was used.

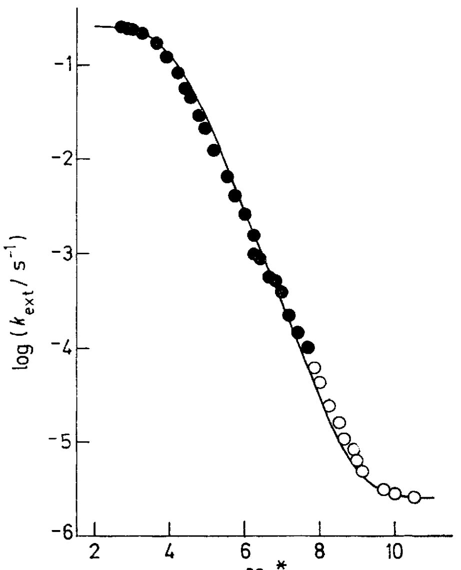

FIGURE 2 pa_H*-Rate profile for the hydrolysis of *N*-*p*-nitrobenzylideneaniline at 25° (ionic strength 0·045M) in aqueous methanol (20·0% w/w H_2O). The line is theoretical for equation (16): ●, extrapolated rate coefficients; ○, observed rate coefficients

The realization that $k_{HA} = K_1k_O/1{\cdot}81 \times 10^{-5}k_3 \cong 20k_O$ (Table 5), gives $k^* = 2 \times 10^{17}k_O$ l mol^{-1} s^{-1}. As the fastest diffusion-controlled processes have rate coefficients of 10^{11}—10^{12} l mol^{-1} s^{-1},[25] an unrealistic k_O value is required in order to obtain a k value lower than 10^{11}—10^{12}. Therefore, it seems possible to rule out mechanism (17). The same evidence was reported for acid-catalysed addition of semicarbazide to *p*-nitrobenzaldehyde,[26] the mutarotation of glucose,[27] and the hydration of aldehydes.[28]

In the 'analytical' approach, the k_{ext} rate law of equation (13) may be simplified by setting $k_a = k_2k_O/(k_{-3} + k_S)$, $k_b = (k_2k_S + k_3k_O)/(k_{-3} + k_S)$, $k_c = k_3k_S/(k_{-3} + k_S)$, $k_d = K_1(k_{-2} + k_O)/(k_{-3} + k_S)$, and $k_e = K_1 + (k_{-2} + k_O)/(k_{-3} + k_S)$. This gives the rate law (18). The calculation of the parameters in equation

$$k_{ext}' = \frac{k_a + k_b a_H^* + k_c a_H^{*2}}{k_d + k_e a_H^* + a_H^{*2}} \qquad (18)$$

(18) is based on the following principles. (1) At high acidity in the pa_H* independent range, equation (18) reduces to $k_{ext}' = k_3/(1 + k_{-3}/k_S)$, as only the terms in a_H^{*2} prevail. On the alkaline side of the pa_H* independent range the terms involving a_H^* are negligible and equation (18) simplifies to $k_{ext}' = k_2/K_1(1 + k_{-2}/k_O)$. Thus, the specification of rate-determining steps boils down to a quantitative evaluation of the k_{-3}/k_S and k_{-2}/k_O ratios. (2) To do this, two reasonable assumptions may be made. First, in slightly acidic conditions ($3 < pa_H^* < 6$) the parameters independent of a_H^* in equation (18) are negligible; this gives the rate law (19). Secondly,

$$k_{ext}' = (k_b + k_c a_H^*)/(k_e + a_H^*) \qquad (19)$$

in mildly basic solution ($8 < pa_H^* < 10$), the terms involving a_H^{*2} are negligible and equation (18) reduces to (20) where $k_h = k_a/k_e$, $k_i = k_b/k_e$, and $k_m = k_d/k_e$.

$$k_{ext}' = (k_h + k_i a_H^*)/(k_m + a_H^*) \qquad (20)$$

Equations (19) and (20) are of the form (16) and the parameters were estimated as previously reported. The parameters of equation (19), evaluated from the k_{ext} values at $pa_H^* < 6{\cdot}06$ (Table 3) and those of equation (20), evaluated from the k_{obs} values at $pa_H^* > 8$ (Table 4), are reported in Table 6. The variations of k_{ext}' with a_H^* calculated from equations (19) and (20) are shown as the dashed and dotted lines respectively in Figure 3.

TABLE 6

Parameters for the rate laws (19) and (20) [a,b]

Equation (19)	k_b/mol l^{-1} s^{-1}	$(8{\cdot}37 \pm 0{\cdot}64) \times 10^{-8}$
	k_c/s^{-1}	$0{\cdot}236 \pm 0{\cdot}052$
	k_e/mol l^{-1}	$(1{\cdot}30 \pm 0{\cdot}03) \times 10^{-4}$
Equation (20)	k_h/mol l^{-1} s^{-1}	$(3{\cdot}61 \pm 0{\cdot}23) \times 10^{-13}$
	k_i/s^{-1}	$(5{\cdot}99 \pm 0{\cdot}16) \times 10^{-4}$
	k_m/ mol l^{-1}	$(1{\cdot}45 \pm 0{\cdot}04) \times 10^{-7}$

[a] See text for details and definitions of symbols. [b] Error refers to standard deviation.

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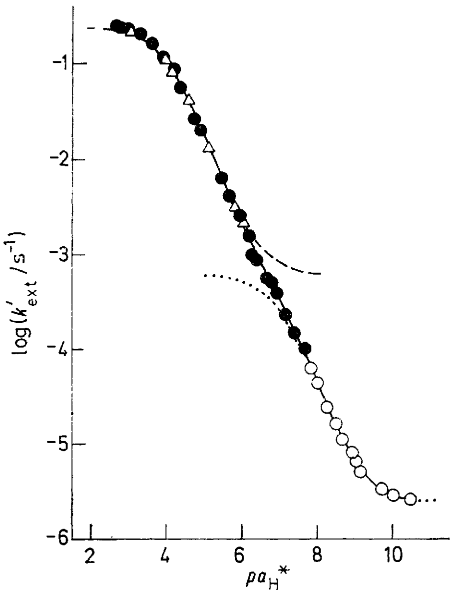

FIGURE 3 pa_H*–Rate profile for the hydrolysis of *N*-*p*-nitrobenzylideneaniline. The lines are theoretical for: equation (19), dashed; equation (20), dotted; equation (21), full; ○ and ●, see Figure 2; △ value of k_{ext} used for calculation of parameters in equation 19

(3) From the parameters k_e and k_m, the two following roots are obtained for K_1: $K_1 = 1{\cdot}29 \times 10^{-4}$ and *ca.* 10^{-7} mol l^{-1}. The former value corresponds to a *ca.* 40-fold increase in basicity of benzylideneaniline due to the *p*-nitro-substituent. This is surprising but, when the pK_a value of *p*-chlorobenzylideneaniline is taken into account (pK_a 2·80 [15]), it can be explained by smaller twisting of the ' aniline ' ring in the two *para*-derivatives than in the unsubstituted compound. (4) Starting from $K_1 = 1{\cdot}29 \times 10^{-4}$, subsequent calculations (which are not reported in detail) on the parameters in Table 6 give the following values: $10^{-9}k_3/k_2$ 1·79 ± 0·05 l mol^{-1}, $10^7k_{-2}/k_O$ 2·27 ± 0·33, k_{-3}/k_S 1·45 ± 0·18, $10^{10}k_2$ 3·22 ± 0·23 l mol s^{-1}, and k_3 0·58 ± 0·05 s^{-1}. The alternative calculation with K_1 *ca.* 10^{-7} gives a negative k_{-3}/k_S ratio. (5) Using the preceding values, equation (18) reduces to (21). The pa_H*–rate profile shown as a full line in

$$k_{ext}' = \frac{(k_2k_O + k_3k_Oa_H^* + k_3k_Sa_H^{*2})/(k_{-3} + k_S)}{[K_1k_O/(k_{-3} + k_S)] + K_1a_H^* + a_H^{*2}} \quad (21)$$

$$= \frac{4{\cdot}68 \times 10^{-17} + 8{\cdot}34 \times 10^{-8}a_H^* + 0{\cdot}236a_H^{*2}}{1{\cdot}89 \times 10^{-11} + 1{\cdot}29 \times 10^{-4}a_H^* + a_H^{*2}}$$

Figure 3 is a theoretical curve calculated from equation (21). It must be observed that the fitting of experimental data to the curve calculated by equation (21) is more satisfactory than that calculated by (16); however, the experimental pa_H*–log k_{cat} profile cannot be explained.

Many alternative kinetic schemes were tested, but we cannot envisage any other mechanism by which the experimental data may be explained. In the absence of an independent determination of the K_1 value, quantitative study of the general catalysis is essential to establish the mechanism.

We thank the C.N.R. (Italy) for support.

[4/258 *Received, 11th February,* 1974]