Hydrolysis of α-Cyanobenzylideneanilines. Part I. Kinetic Studies in Acidic Media

By **Masaichiro Masui,* Hidenobu Ohmori, Chihiro Ueda,** and **Masashige Yamauchi,** Faculty of Pharmaceutical Sciences, Osaka University, Toyonaka, Osaka-fu, Japan

The hydrolysis of α-cyanobenzylideneanilines was studied kinetically in aqueous sulphuric acid (H_0 −2 to −6), 40% aqueous acetonitrile (pH 3—0), and 60% aqueous dioxan (H_0 1·5 to −2) at 25°. Benzoyl cyanide was demonstrated to be an intermediate. The rate of hydrolysis exhibited a maximum at H_0 *ca.* −1 to −2. The effect of substituents on the reaction rate and the Bunnett–Olsen ϕ values suggested that the hydration of the protonated substrate is rate determining on the less acidic side of the rate maximum and that the decomposition of the intermediate amino-alcohol is rate determining under more acidic conditions. It is suggested, from consideration of the shape of the acidity–rate profile, that aniline is expelled only from the dipolar form (or zwitterionic form) of the amino-alcohol intermediate, because the tendency for aniline to separate is weakened by the electron-withdrawing cyano-group.

α-CYANOBENZYLIDENEANILINES (I) are fairly readily hydrolysed in acidic or alkaline solution but not in neutral solution. The products depend on the nature

$$\underset{\text{(I)}}{XC_6H_4C(CN){=}NC_6H_4Y}$$

of the solution, benzanilides in alkaline solution,[1] benzoyl cyanides in strongly acid solution, such as relatively concentrated sulphuric acid,[2] and benzoic acids and anilines in slightly acidic solution. There have been no detailed kinetic studies on the hydrolysis of (I), although many studies have been reported on Schiff's bases and related compounds.[3] It seems interesting to investigate the role of the α-cyano-group, which must be responsible for the irreversible nature of the hydrolysis of (I) and the dependence of the products on the nature of medium. It has been suggested that for the attack of water on an azomethine compound, the molecule must have at least one positive charge.[3,4]

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[1] H. G. Aurich, *Chem. Ber.*, 1965, **98**, 3917; Y. Ogata and A. Kawasaki, *J.C.S. Perkin II*, 1972, 1792.

[2] W. Polaczkowa, J. Jaworski, and J. Wolinski, *Roczniki Chem.*, 1953, **27**, 468 (*Chem. Abs.*, 1955, **49**, 3181f).

[3] W. P. Jencks, *Progr. Phys. Org. Chem.*, 1964, **2**, 63, and references therein.

[4] M. Masui and H. Ohmori, *J. Chem. Soc.* (*B*), 1967, 762.

Thus it seemed of interest to determine whether a positive charge is also required for the hydrolysis of (I) with the strongly electron-withdrawing cyano-group in the α-position. This paper reports kinetic studies on the hydrolysis of (I) in acidic media.

RESULTS

Upon hydrolysis of α-cyano-*p*-methoxybenzylideneaniline (I; X = *p*-OMe, Y = H) in acidic aqueous acetonitrile (80% v/v) solution (pH 0—3), *p*-methoxybenzoyl cyanide was isolated as an intermediate, which could be hydrolysed further to give *p*-anisic acid. In the hydrolyses of other α-cyanobenzylideneanilines under the same conditions, the final products were benzoic acids, anilines, and hydrogen cyanide only. However, when ethanol was present in the hydrolysis media, the corresponding ethyl benzoates were isolated together with benzoic acids. The amounts of benzoic acids produced in the presence of ethanol were compared with the amounts produced on solvolysis of authentic benzoyl cyanides under the same conditions (Table 1). The values were in good agreement, indicating that benzoyl cyanides are intermediates in the hydrolysis of these α-cyanobenzylideneanilines.

TABLE 1

Amount of benzoic acid formed on hydrolysis of α-cyanobenzylideneanilines and benzoyl cyanides at 25° in acetonitrile (50 ml) and varying proportions of ethanol and water (50 ml) containing 0·2M-hydrochloric acid [a]

	Benzoic acid (%)	
$EtOH-H_2O$ (v/v)	PhC(CN)⁚NPh	PhCOCN
0·0	98·9	98·5
0·2	67·4	68·8
0·4	51·1	50·1
0·6	37·6	36·7
0·8	24·5	25·2
	p-Chlorobenzoic acid (%)	
	p-$ClC_6H_4C(CN)$⁚NPh	*p*-ClC_6H_4COCN
0·0	98·5	97·8
0·2	60·5	61·5
0·4	40·7	43·5
0·6	29·5	31·9
0·8	20·3	23·0

[a] Concentration of original substrates *ca.* 1 mM.

The possibility of back reactions was examined by mixing benzoyl cyanide and aniline in 40% aqueous acetonitrile containing 0·1M-hydrochloric acid, in benzene, and in ether. The formation of α-cyanobenzylideneaniline was not detected in any of these solutions from u.v. or i.r. spectroscopic examination or by t.l.c., and using benzene and ether, benzanilide was isolated.

The effects of the acidity of the solution on the observed pseudo-first-order rate constants k_{obs} for the hydrolysis of α-cyano- and α-cyano-*p*-methoxy-benzylideneaniline are shown in Figure 1. In aqueous acetonitrile solution (40% v/v; pH 0—3) the rate constants showed first-order dependence on the acidity. The effect of the buffer concentration on the hydrolysis of α-cyanobenzylideneaniline was examined at pH 3·00 (phosphate), 2·50 (phosphate), and 1·00 (trichloroacetate). A slight increase (*ca.* 10%) in the rate was observed in trichloroacetate buffer, when the total buffer concentration was increased from 0·01 to 0·20M, but essentially no effect of buffer was detected at pH 3·00 or 2·50. The ionic strength, examined at pH 1·00 (HCl–KCl; μ 0·1—1·0), had no appreciable effect on the hydrolysis of the same substrate.

In 60% aqueous dioxan at H_0 1·5 to −2 the rate of hydrolysis of α-cyano-*p*-methoxybenzylideneaniline exhibited a maximum at an H_0 value of *ca.* −1. With the unsubstituted derivative the rate maximum could not be determined because H_0 values below −2 were not accessible in 60% dioxan, but results indicated the existence of a rate maximum.

In aqueous sulphuric acid (35—75% w/w) the rate of hydrolysis decreased with increase in acidity, and the slopes of the plots of log k_{obs} against H_0 were 1·25 and 1·00 for α-cyano- and α-cyano-*p*-methoxy-benzylideneaniline, respectively. Plots of log k_{obs} against $H_0 + \log[H^+]$,* the Bunnett–Olsen linear free energy relationships,[5] exhibited good straight lines (results not shown), and ϕ values of 1·18 and 1·08 were obtained for α-cyano- and α-cyano-*p*-methoxy-benzylideneaniline, respectively.

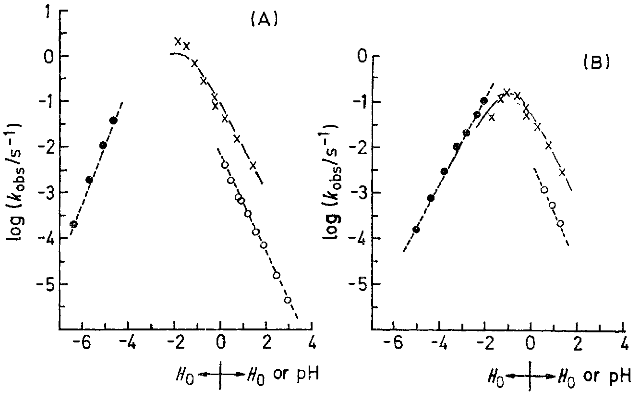

FIGURE 1 Plot of the observed pseudo-first-order rate constanst against acidity at 25° in the hydrolysis of (A) α-cyanobenzylideneaniline and (B) α-cyano-*p*-methoxybenzylidineaniline: ○, in 40% aqueous acetonitrile (against pH); ×, in 60% aqueous dioxan (against H_0); ●, in aqueous sulphuric acid (against H_0)

Figure 2 shows the effect of substituents on the rate of hydrolysis of (I) in 72% sulphuric acid. The rate constants for (I) with substituents on the benzylidene group were well correlated by the σ^+ constants with a ρ^+ value of 2·08, whereas the rate constants for (I) with substituents on the anline group were better correlated by σ constants with a ρ value of 2·70. At pH 1·00 in aqueous acetonitrile solution, the observed pseudo-first-order rate constants were scarcely affected by the nature of the substituents (Figure 3); † the rate varied less than four-fold on changing from α-cyano-*p*-nitrobenzylideneaniline (I; X = *p*-NO_2, Y = H) to α-cyanobenzylidene-*p*-toluidine (I; X = H, Y = *p*-Me).

The activation parameters for the hydrolysis of (I) with substituents on the benzylidene group were estimated at pH 0·60 in aqueous acetonitrile: rates were measured at 25, 30, and 49°. The values for both activation energy and entropy varied in a random fashion within a narrow range, reflecting the substituent effects in Figure 3 [E_a *ca.*

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* Both substrates were essentially fully protonated in solution at these concentrations of sulphuric acid (see Experimental section).

† The non-linear Hammett plot observed in Figure 3 is not due to differences in the dependence of the rates of hydrolysis of each substrate on acidity since all substituted α-cyanobenzylideneanilines showed strictly first-order dependence on acidity, at least between pH 0·5 and 1·5, and the rate constants in Figure 3 were obtained by interpolation of the pH–rate profiles to pH 1·00.

[5] J. F. Bunnett and F. Olsen, *Canad. J. Chem.*, 1966, **44**, 1917.

17 kcal mol^{-1}; $\Delta S^{\ddagger}$ *ca.* -14 cal mol^{-1} K^{-1} (rate constants used for estimating $\Delta S^{\ddagger}$ values were those obtained by dividing the observed pseudo-first-order rate constants by hydronium ion concentration)].

The pK_a' values of the cations of α-cyano-*p*-methoxy- and α-cyano-benzylideneaniline, estimated spectrophotometrically in 60% aqueous dioxan (see Experimental section), were $-1{\cdot}34$ and *ca.* $-2{\cdot}4$, respectively. These pK_a' values confirm that both substrates are essentially fully protonated in the aqueous sulphuric acid solution used in the present study.

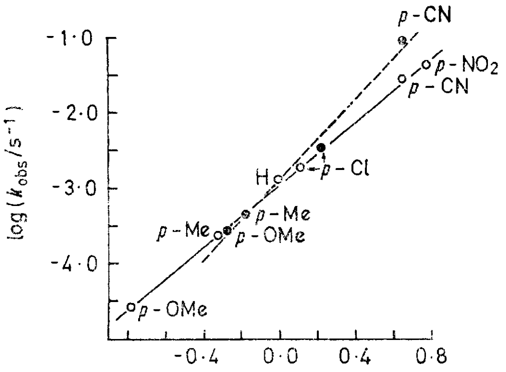


FIGURE 2 Logarithm of the observed pseudo-first-order rate constants for the hydrolysis of α-cyanobenzylideneanilines against σ^+ and σ constants in 72% sulphuric acid at 25°: ○, substituent on benzylidene ring (against σ^+; ρ^+ 2·08); ●, substituent on aniline ring (against σ; ρ 2·70)

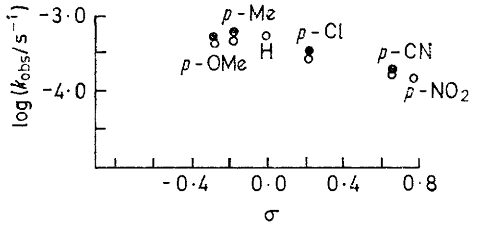
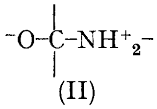


FIGURE 3 Logarithm of the observed pseudo-first-order rate constants for the hydrolysis of α-cyanobenzylideneanilines against σ constants at pH 1·00 in 40% aqueous acetonitrile at 25°: ○, substituent on benzylidene ring; ●, substituent on aniline ring

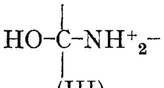
DISCUSSION

The mechanism of hydrolysis of (I) in acidic media cannot be elucidated from the present results alone. However, the mechanism can be deduced from the results in the light of the extensive studies reported on the hydrolysis of Schiff's bases and related compounds.[3] The acidity–rate profile shown in Figure 1 may be regarded as a bell-shaped pH–rate profile, in the sense described previously,[4] although a continuous acidity–rate profile could not be obtained over the whole acidity range studied, because of the low solubility of (I) in highly aqueous solution and the rapid hydrolysis in the region of the acidity–rate maximum.* A bell-shaped pH–rate profile was observed in the hydrolysis of azomethine compounds formed from strongly basic amines, such as Schiff's bases derived from aliphatic amines,[6,7] thiazolines,[8,9] and oxazolines.[10] On the other hand, in the hydrolysis of azomethine compounds formed from weakly basic amines, such as Schiff's bases derived from aromatic amines[11,12] and Girard hydrazones,[4,13] an inflection-type of pH–rate profile was observed. For both types of pH–rate profile, a change in the rate-determining step has been demonstrated; decomposition of the intermediate amino-alcohol occurs on the acidic side of the pH–rate maximum or the inflection point, and attack of water (or hydroxide ion) on the substrate takes place on the alkaline side. The hydrolysis of imidates formed from aliphatic amines gives a bell-type pH–rate profile similar to those of the other azomethine compounds described above.[14,15] However, the decrease in rate on increase in acidity has been ascribed to a salt effect rather than a change in the rate-determining step.[15,16] It has been stated that strongly basic amines can only be expelled from a dipolar intermediate (II), whereas weakly basic amines can be expelled from a cationic intermediate (III) also.[6] The reason for the two



$^{-}O{-}\overset{|}{\underset{|}{C}}{-}NH^{+}{}_{2}{-}$

(II)



$HO{-}\overset{|}{\underset{|}{C}}{-}NH^{+}{}_{2}{-}$

(III)

types of pH–rate profile seems to be explained well on the basis of this statement. The hydrolysis of 2-phenyliminotetrahydrofuran is exceptional.[17] In this case the reaction proceeds only through (II), and a bell-shaped pH–rate profile is observed, probably because the tendency for aniline to separate is weakened by the electron-withdrawing oxygen atom attached

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* The rate of hydrolysis was well within the range that can be measured by the stopped-flow method, but because of the requirement for an equivolume mixture it was impossible to prepare stable stock solutions of the substrates.

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

[7] K. Koehler, W. Sandstrom, and E. H. Cordes, *J. Amer. Chem. Soc.*, 1964, **86**, 2413; W. Bruyneel, J. J. Charette, and E. De Hoffmann, *ibid.*, 1966, **88**, 3808; J. Hine, J. C. Craig, jun., J. G. Underwood, jun., and F. A. Via, *ibid.*, 1970, **92**, 5194; C. V. McDonnell, jun., M. S. Michailis, and R. B. Martin, *J. Phys. Chem.*, 1970, **74**, 26.

[8] G. L. Schmir, *J. Amer. Chem. Soc.*, 1965, **87**, 2743.

[9] R. B. Martin, R. I. Hedrick, and A. Parcell, *J. Org. Chem.*, 1964, **29**, 3197; R. B. Martin, S. Lowey, E. L. Elson, and J. T. Edsall, *J. Amer. Chem. Soc.*, 1959, **81**, 5089; R. B. Martin and A. Parcell, *ibid.*, 1961, **83**, 4830.

[10] R. B. Martin and A. Parcell, *J. Amer. Chem. Soc.*, 1961, **83**, 4835; R. Greenhalph, R. M. Heggie, and M. A. Weinberger, *Canad. J. Chem.*, 1963, **41**, 1662.

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

[12] A. V. Willi, *Helv. Chim. Acta*, 1956, **39**, 1193.

[13] M. Masui and H. Ohmori, *J. Chem. Soc.*, 1964, 3951.

[14] M. Kandel and E. H. Cordes, *J. Org. Chem.*, 1967, **32**, 3061; R. K. Chaturvedi and G. L. Schmir, *J. Amer. Chem. Soc.*, 1968, **90**, 4413.

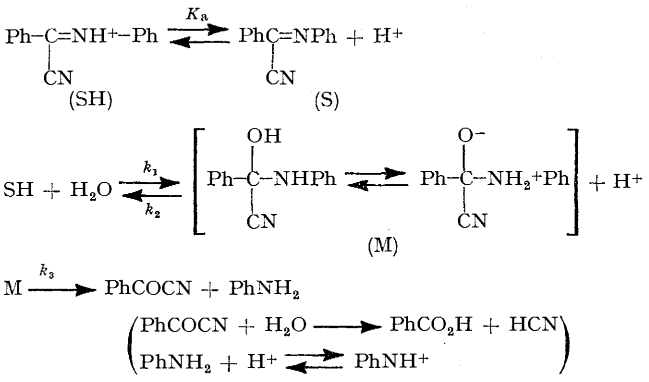
[15] G. M. Blackburn and W. P. Jencks, *J. Amer. Chem. Soc.*, 1968, **90**, 2638; the pH–rate profile reported for the hydrolysis of *N*-(methoxymethylene)morpholinium methosulphate is not actually bell-shaped. However, it can be classified as of the bell-type in the sense discussed previously (ref. 4).

[16] T. C. Pletcher, S. Koehler, and E. H. Cordes, *J. Amer. Chem. Soc.*, 1968, **90**, 7072.

[17] G. L. Schmir and B. A. Cunningham, *J. Amer. Chem. Soc.*, 1965, **87**, 5692; 1966, **88**, 551.

to the azomethine carbon.[*] Although 2-phenyliminotetrahydrofuran is in fact an imidate, a change in the rate-determining step is demonstrated, in contrast to the imidates formed from aliphatic amines described above. It was suggested, however, that in the hydrolysis of the latter imidates, the amine is expelled only from the dipolar intermediate (II), and this is consistent with the foregoing statement. The relation between the pH–rate profile and reaction scheme in the hydrolysis of azomethine compounds is discussed elsewhere.[4]

In the hydrolysis of (I) in acidic media, a similar reaction process to that of 2-phenyliminotetrahydrofuran can be expected, because the strongly electron-withdrawing cyano-group will reduce the tendency for aniline to separate. Thus the Scheme seems compatible with the results obtained.



SCHEME

According to Bunnett–Olsen criteria, ϕ values $>0{\cdot}58$ indicate that water acts as a proton transfer agent in the transition state of a solvolytic reaction.[5] The ϕ values obtained in aqueous sulphuric acid solution (1·18 for α-cyano- and 1·08 for α-cyano-*p*-methoxybenzylideneaniline) strongly suggest that the rate-determining step is the decomposition of the amino-alcohol intermediate in these acidity regions. In the hydrolysis of *p*-chlorobenzylideneaniline, ϕ 1·34 was obtained, and the results were explained in a similar fashion.[11,†] The rate of hydrolysis of (I) in 72% sulphuric acid is strongly dependent on the nature of the polar substituent (ρ^+ 2·08 for substituents on the benzylidene ring and ρ 2·70 for these on the aniline ring). Similar substituent effects have been reported in the hydrolysis of benzylidene-1,1-dimethylethylamine at pH 1 (ρ^+ 2·17)[6] and of methyl 2-phenyl-Δ^2-thiazoline-4-carboxylate at pH 0·5 (ρ 2·08).[8] In both cases, the decomposition of the amino-alcohol intermediate was rate determining at the pH values studied, and the observed ρ^+ and ρ values were interpreted as the results of substituent effects on the pre-equilibrium addition of water to the substrates. It is uncertain why σ constants gave the best correlation in one case (thiazoline) while σ^+ values gave the best correlation in another (benzylidene-1,1-dimethylethylamine and the results in the present study). However, it seems reasonable that in the hydrolysis of (I), the effects of substituents on the aniline group are better correlated by σ constants, since the aniline ring is not conjugated with the carbon–nitrogen double bond.[20] The observed decrease in the rate in sulphuric acid solution (Figure 1) may, of course, be partly attributable to the decreased availability of water for pre-equilibrium hydration. The rate of hydrolysis, however, decreased more rapidly than the activity of water.

In aqueous acetonitrile solution the rate-determining step will be the attack of water on protonated substrate. The rate of hydrolysis is little affected by polar substituents, *i.e.*, the non-linear correlation in Figure 3 must be the result of the opposing effects of substituents on protonation and hydration of the substrates. A similar insensitivity of the hydrolysis rate to the nature of polar substituents was also reported in the hydrolysis of the azomethine compounds quoted above in the pH region where the attack of water and/or hydroxide ion on the protonated substrate is rate determining.[6,8] The values of the activation parameters obtained (see above) may be compared to those reported for a similar rate-determining step in the hydrolysis of azomethine compounds.[21,22]

In the hydrolysis of Schiff's bases, a general base catalysed attack of a water molecule on the protonated substrate was demonstrated.[3] Schmir and Cunningham proved that the magnitude of general base catalysis of this type exhibited a bell-shaped dependence on pH and that maximum catalysis was observed at pH $= (\mathrm{p}K_1 + \mathrm{p}K_2)/2$, where K_1 is the acid dissociation constant of the protonated substrate and K_2 is that of the buffer acid.[13] The pK_a' value of α-cyanobenzylideneaniline cation would be *ca.* −2 in aqueous acetonitrile (pK_a' *ca.* −2·4 in 60% aqueous dioxan), and hence maximum catalysis would be expected at H_0 *ca.* −0·7 for trichloroacetate and *ca.* 0 for phosphate. The pH values where buffer catalysis was examined (pH 1·00 for trichloroacetate, and 2·50 and 3·00 for phosphate) are 2—3 units from the expected maximum. The observed negligible buffer catalysis would thus be reasonable.

In aqueous dioxan, the rate-determining step in the region where the rate of hydrolysis increases with acidity will be the same as in aqueous acetonitrile, since the rate

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[*] When the basicity of the expelled aniline is greatly weakened by a strongly electron-withdrawing group in the aniline ring, a cationic amino-alcohol intermediate will again expel the aniline.[18,19]

[†] Ref. 11 appeared before the Bunnett–Olsen relationship was published. However, the slope of the plot of the logarithm of the observed rate constant against (H_0 + log[H$^+$]) is the ϕ value itself.

[18] T. Okuyama, T. C. Pletcher, D. J. Sahn, and G. L. Schmir, *J. Amer. Chem. Soc.*, 1973, **95**, 1253.

[19] T. Okuyama, D. J. Sahn, and G. L. Schmir, *J. Amer. Chem. Soc.*, 1973, **95**, 2345.

[20] K. Tabei and E. Saitou, *Bull. Chem. Soc. Japan*, 1964, **42**, 1440; M. A. El-Bayoumi, M. El-Aasser, and F. Abdel-Halim, *J. Amer. Chem. Soc.*, 1971, **93**, 586, 590; J. W. Pavlik and A. van Putten, *Tetrahedron*, 1971, **27**, 3007, 3301.

[21] C. J. O'Connor, E. J. Fendler, and J. H. Fendler, *J.C.S. Perkin II*, 1973, 1744.

[22] R. K. Chaturvedi and E. H. Cordes, *J. Amer. Chem. Soc.*, 1967, **89**, 1230 and references therein.

of hydrolysis of α-cyano-*p*-methoxybenzylideneaniline is almost the same as that of the unsubstituted compound (Figure 1). The rate maximum of the former compound can be regarded as due to the change in the rate-determining step. The absence of inflection in the acidity–rate profile, *i.e.* the bell-shaped acidity–rate profile, strongly suggests that in the hydrolysis of (I) aniline is expelled only through the dipolar form of the amino-alcohol intermediate (II) owing to the electron-withdrawing effect of the cyano-group, as in the case of 2-phenyliminotetrahydrofuran.[13] Assuming a steady-state approximation for the intermediate amino-alcohol, the observed pseudo-first-order rate constant for the disappearance of (I), k_{obs} is given by the equation (1)

$$k_{\mathrm{obs}} = \frac{k_1 k_3 h_0/K_{\mathrm{a}}}{(1 + h_0/K_{\mathrm{a}})(k_2 h_0 + k_3)} \qquad (1)$$

with the constants as defined in the Scheme and h_0 is the usual acidity function. Using the estimated pK_{a}' values, and adjusting the equation to fit the experimental plots, values of $k_1 = 18\cdot7\ \mathrm{s}^{-1}$ and $k_2/k_3 = 4\cdot18 \times 10^{-2}\ \mathrm{l\ mol}^{-1}$ are estimated for the hydrolysis of α-cyanobenzylideneaniline in aqueous dioxan, and values of $k_1 = 1\cdot51\ \mathrm{s}^{-1}$ and $k_2/k_3 = 1\cdot70 \times 10^{-1}\ \mathrm{l\ mol}^{-1}$ for that of α-cyano-*p*-methoxybenzylideneaniline. The solid lines in Figure 1 are the theoretical curves calculated from the equation and the values of the constants obtained above.

TABLE 2

M.p.s, analytical data, and absorption maxima of α-cyanobenzylideneanilines

Compound (I)			Found (%)			Required (%)				
X	Y	M.p. (°C)	C	H	N	C	H	N	λ_{max} (MeCN)/nm	λ_{max} (H_2SO_4)/nm
H	H [a]	71—72	81·75	5·4	12·6	81·5	4·9	13·35	362	403
p-NO_2	H [a]	149—150	67·3	3·6	16·5	66·9	3·6	16·7	378	418
p-CN	H	141—142	78·0	4·0	18·1	77·9	3·9	18·2	375	410
p-Cl	H	107—108	69·9	3·7	11·4	69·9	3·7	11·6	365	418
p-Me	H	97—99	82·1	5·4	12·6	81·8	5·5	12·7	361	415
p-OMe	H	118—119	76·2	5·1	11·7	76·25	5·1	11·9	355 [b]	447
H	*p*-CN	171—172	77·2	4·2	18·0	77·9	3·9	18·2	350	382
H	*p*-Cl	93·5—94·5	70·0	3·8	11·4	69·9	3·8	11·6	364	420
H	*p*-Me [a]	92·5—93·5	81·8	5·3	12·6	81·8	5·5	12·7	372	442
H	*p*-OMe [a]	80·5—81·5	76·2	5·35	11·6	76·25	5·1	11·9	389	455

[a] Known compound. [b] Shoulder.

The pH-independent reaction reported in the hydrolysis of various azomethine compounds in the weakly acidic and/or neutral pH region[3] was not observed in the present study, because the reaction rate was too slow in this pH region. The negligible contribution of a pH-independent reaction such as this suggests that attack of a water molecule on the unprotonated substrate does not contribute to the overall reaction, at least in the acidity region studied. One rare example of the reaction of water with a neutral substrate was reported in the hydrolysis of methyl *N*-*p*-tolylsulphonylacetimidate, the pK_{a} value of which is $-6\cdot39$.[18]

The reaction processes so far discussed were limited to the formation of benzoyl cyanides. In the case of α-cyano-*p*-methoxybenzylideneaniline, hydrolysis of *p*-methoxybenzoyl cyanide may well be the rate-determining step in the overall reaction, because the latter compound was isolated as an intermediate. The hydrolysis of benzoyl cyanides also seems to be the rate-determining step in the overall hydrolysis of other α-cyanobenzylideneanilines, at least in sulphuric acid solution, since the formation of benzoyl cyanides in strong acid solution has been reported.[2] In the present study the reaction was followed by measuring the disappearance of (I) (see Experimental section), and no data were obtained on the hydrolysis of benzoyl cyanides. Kinetic studies on the hydrolysis of benzoyl cyanides have already been reported by Hibbert and Satchell.[23]

It is interesting to compare the hydrolysis of (I) with that of *N*-t-butylbenzaldoxime.[21] The acidity–profiles of hydrolysis of the latter compound were quite similar to those obtained in the present study, but more complete. The values of ϕ obtained in strong acid solution were also very similar to our values. However, throughout the acidity region studied the rate-determining step was concluded to be the attack of water on the protonated substrate, and no change in the rate-determining step was suggested. Our present results could be explained in a similar fashion, but we prefer the mechanism described above, because it is common to the hydrolysis of azomethine compounds and is compatible with the explanation of the reasons for the two types of pH–rate profile.[4]

EXPERIMENTAL

Materials.—α-Cyanobenzylideneanilines were prepared from the corresponding nitrones by the method of Krönke and Krönke.[24] Analytical results are summarized in Table 2. Benzoyl cyanides were prepared by a known method[25] and gave correct analyses. Acetonitrile was purified as described by Mann *et al.*[26] Dioxan was purified by a conventional method. Other chemicals were of reagent grade and were used without further purification. Deionized water was used throughout.

Apparatus.—Spectroscopic measurements were carried out in a Hitachi type 139 spectrophotometer. A Union stopped-flow reaction analyser type RA-1100 with digital

[23] F. Hibbert and D. P. N. Satchell, *J. Chem. Soc.* (*B*), 1967, 653.

[24] F. Krönke and G. Krönke, *Chem. Ber.*, 1958, **91**, 1474.

[25] T. S. Oakwood and C. A. Weisgerber, *Org. Synth.*, 1944, **24**, 14.

[26] J. F. O'Donnell, J. T. Ayres, and C. K. Mann, *Analyt. Chem.*, 1965, **37**, 1161.

memory equipment RA-108, was used to follow fast reactions. A Metrohm pH meter type E-300B, with a combined electrode was used for pH measurements.

Product Analysis.—Typical examples are described. (a) *Aniline and hydrogen cyanide.* Reaction mixtures for kinetic measurements in aqueous acetonitrile (see below) were analysed for aniline and hydrogen cyanide after 7—10 half-lives of hydrolysis. Aniline was determined colorimetrically by the Bratton–Marshall method modified by Schmir and Cunningham.[17] Quantitative formation of aniline was detected in each case. Hydrogen cyanide was detected by the method of Schapowalenko.[27]

(b) p-*Methoxybenzoyl cyanide.* α-Cyano-*p*-methoxybenzylideneaniline (200 mg) was subjected to hydrolysis in aqueous acetonitrile (80% v/v; 100 ml) containing 0·1M-hydrochloric acid at 25°. When the yellow colour of the substrate had disappeared (*ca.* 1 h), water (200 ml) was added. The solution was extracted with chloroform (3 × 30 ml). The chloroform layer was evaporated to dryness and the residue was subjected to column chromatography on silica gel with benzene as eluant. The crystals obtained from the first eluate were recrystallized from n-hexane to give needles which were identified as *p*-methoxybenzoyl cyanide by comparing the i.r. spectrum and m.p. with those of an authentic sample.

(c) *Benzoic acid and ethyl benzoate.* α-Cyanobenzylideneaniline (*ca.* 250 mg) or benzoyl cyanide (*ca.* 150 mg) was subjected to solvolysis at 25° in acetonitrile (150 ml) and varying proportions of ethanol and water (50 ml) containing 0·2M-hydrochloric acid. After complete solvolysis water (200 ml) was added. The solution was extracted with chloroform (3 × 30 ml), the chloroform layer was dried (Na_2SO_4), and evaporated to dryness under reduced pressure. The residue was dissolved in ethanol (20 ml), and the amount of benzoic acid was determined by titration with 0·1N-sodium hydroxide. In another run, the chloroform layer was washed with sodium hydroxide solution to remove benzoic acid. The resulting chloroform layer was evaporated to dryness under reduced pressure to give ethyl benzoate, which was identified by its i.r. spectrum.

Kinetic Measurements.—Kinetic measurements were made spectrophotometrically by following the disappearance of (I) at 25 ± 0·1° in aqueous sulphuric acid, aqueous acetonitrile (40% v/v), or aqueous dioxan (60% v/v). The absorption maxima of the substrates used are shown in Table 2. In aqueous acetonitrile and aqueous dioxan the absorption maxima obtained in acetonitrile were used. *p*-Methoxybenzoyl cyanide interferes with the absorption of α-cyano-*p*-methoxybenzylideneaniline, and when using this the reaction was followed at 390 nm, where absorption of *p*-methoxybenzoyl cyanide is negligible. In sulphuric acid all compounds (I) undergo a bathochromic shift, indicating that the substrates are converted into their conjugate acids.[28]

Aqueous dioxan solutions of various acidity were prepared by addition of perchloric acid. The H_0 values used for aqueous sulphuric acid and aqueous dioxan solutions are those given by Paul and Long.[29] Since no data on H_0 values in aqueous acetonitrile were available, the pH meter readings were employed as the measure of acidity. The buffer systems used were: pH 0—2, HCl–KCl; pH 1, trichloroacetate; pH 2·5—3, phosphate. The ionic strength of the systems, except those with pH $<0·3$, was adjusted to 0·5 by addition of potassium chloride by assuming the activity coefficient of hydronium ion to be unity. The pH values of the reaction solutions were measured at 25° both before and after the kinetic run, and the values agreed within 0·02 unit.

Except for slow reactions, hydrolysis was initiated by injecting a small amount (*ca.* 1—10 μl) of a concentrated stock solution of the substrate into 3 ml of the reaction medium, previously equilibrated at 25° in a cuvette. The initial concentrations of the substrates ranged from 10^{-3} to 10^{-4}M. Stock solutions of the substrates were prepared in acetonitrile, dioxan, or concentrated sulphuric acid. When the reaction was very slow, the reaction was carried out by a conventional method in a volumetric flask or in sealed ampoules. Kinetic runs carried out in a stopped-flow spectrophotometer were initiated by mixing a solution of the substrate in 80% dioxan with solutions of various concentrations of perchloric acid in aqueous dioxan. The water content of the latter solutions was adjusted so that the ratio water : dioxan in the resulting mixture was 2 : 3.[29] The values of rate constants were corrected for decrease in the water content with increase in the concentration of perchloric acid (<15%). Observed pseudo-first-order rate constants k_{obs} were estimated from the slope of the plot of log $(A_t - A_\infty)$ against time, where A_t and A_∞ represent the absorbances at time t and infinite time. A good first-order plot was obtained in every run.

Estimation of pK_a' *Values in Aqueous Dioxan* (60% v/v).—The hydrolysis of α-cyanobenzylideneaniline and α-cyano-*p*-methoxybenzylideneaniline were also followed at 403 and 447 nm (*cf.* Table 2), respectively, by the stopped-flow techniques described above at various concentrations of perchloric acid. The absorbances were extrapolated to zero time * and treated by the method of Reeves.[30] α-Cyanobenzylideneaniline is not fully protonated in aqueous dioxan even at the highest perchloric acid concentration available, and hence the value of the absorbance in concentrated sulphuric acid was used as that of the fully protonated substrate.

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* The rate constants obtained as described above were in good agreement with those obtained by following the absorption of unprotonated substrates (362 and 390 nm for the unsubstituted and *p*-methoxy-compound, respectively).

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