Benzoquinone Imines. Part XII.[1] Reactions of 2-Aminoindamines [2-Amino-*N*-(4-aminophenyl)-*p*-benzoquinone Di-imines] in Aqueous Solution

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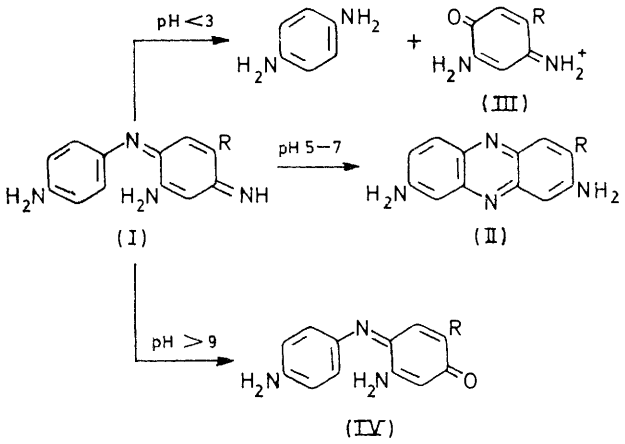
The fate of 2-aminoindamines [2-amino-*N*-(4-aminophenyl)-*p*-benzoquinone di-imines] in aqueous solution has been found to be highly pH dependent. At high pH (>9) the major reaction involves hydrolysis of the unsubstituted imino-group to produce 2-aminoindoanilines [2-amino-*N*-(4-aminophenyl)-*p*-benzoquinone monoimines]. At low pH (<4), the major reaction involves hydrolysis of the azomethine bridge to give a mixture of a *p*-phenylenediamine and a 2-amino-*p*-benzoquinone monoimine. In the intermediate pH range, the aminoindamines undergo intramolecular cyclisation to give 2,8-diaminophenazines. Mechanisms are proposed for these reactions on the basis of kinetic studies of the effect of pH on the rate.

2-AMINOINDAMINES [2-AMINO-*N*-(4-AMINOPHENYL-*p*-BENZOQUINONE DI-IMINES] (I) have been shown [2] to be the products of oxidative coupling of *p*-phenylenediamines with *m*-phenylenediamines. The 5-methyl derivative (I; R = Me) was first prepared by Bernthsen and Schweitzer,[3] who reported that it underwent cyclisation in 'dilute acid' solution to give 2,7-diamino-3-methylphenazine (II; R = Me). Similarly, Nietzki and Ernst[4] reported that oxidation of 2,4,4'-triaminodiphenylamine, on oxidation with 'Weldon manganese dioxide,' proceeded through a blue-violet intermediate, presumed to be (I; R = H) to give the red phenazine (II; R = H). The conversion of (I) into (II) has been given as an explanation of the fading to red of furs and hair dyed with *p*-phenylenediamine and an *m*-diamine.[5]

During the course of a study of the kinetics of the cyclisation reaction, we found the chemistry of the aminoindamines to be more complex than indicated by the earlier references. Attempts to obtain a sample of the phenazine (II; R = Me) by warming the indamine (I; R = Me) in 0·01M-hydrochloric acid were unsuccessful. Examination of the reaction mixture by t.l.c. showed it to contain *p*-phenylenediamine and a compound having a similar colour to the phenazine. This latter compound was isolated, as its hydrochloride, and shown by comparison with an authentic sample prepared by oxidation of 2,4-diamino-5-methylphenol, to be 2-amino-5-methyl-*p*-benzoquinone monoimine (III; R = Me). This structural assignment is supported by the n.m.r. spectrum which exhibits two sharp singlets (τ 3·46 and 3·84) ascribable to two isolated hydrogens on a quinonoid ring,[2] a singlet (τ 7·78) due to methyl hydrogens, and four broad absorptions in the region τ −1·0—2·0, which are removed on treatment with D_2O, ascrib-



SCHEME 1

[1] Part XI, J. F. Corbett and E. P. Gamson, *J.C.S. Perkin II*, 1972, 1531.
[2] J. F. Corbett, *J. Chem. Soc.* (*B*), 1969, 827.
[3] A. Bernthesen and H. Schweitzer, *Annalen*, 1886, **236**, 343.
[4] R. Nietzki and O. Ernst, *Ber.*, 1890, **23**, 1852.
[5] G. Siebert, 'Ullman's Encyklopadie der technischen Chemie,' Urban and Schwarzenberg, Berlin, 1962, vol. 13, p. 110; A. Ginzel, *Melliand Textilberichte*, 1948, **29**, 384; J. F. Corbett, 'The Chemistry of Synthetic Dyes,' ed. K. Venkataraman, Academic Press, New York, 1971, vol. V, p. 475.

able [2] to four amino and iminium hydrogens. A molecular weight of 137 was obtained from the mass spectrum.

When the aminoindamine (I; R = Me) was dissolved in 1% aqueous sodium carbonate, the solution showed a slight and rapid colour change and 2-amino-5-methylindoaniline [2-amino-*N*-(4-aminophenyl)-5-methyl-*p*-benzoquinone monoimine] (IV; R = Me) separated from the solution. The structure was proved by comparison with an authentic sample prepared by oxidation of a mixture of *p*-phenylenediamine and 2-methyl-5-aminophenol.[2]

The diaminophenazine (II; R = Me) was finally obtained by heating a solution of the aminoindamine in a buffer solution having pH 7·0. The structure was confirmed by mass spectrometry and elemental analysis.

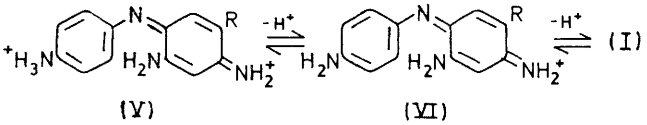
TABLE 1

Spectral data for 2-amino-5-methylindamine and its reaction products

	Diprotonated	pK_a	Monoprotonated	pK_a	Neutral
Indamine (I; R = Me)	455 (3·78)	3·6	549 (4·09)	10·6	464 (3·85)
Phenazine (II; R = Me)		<0	506 (4·39)	6·5	438 (4·20)
Quinone (III; R = Me)			508 (3·68)	8 *	~435 *
Indoaniline (IV; R = Me)					492 (3·96)

* The neutral form of the quinone imine (III; R = Me) is unstable.

Examination of the visible spectrum of the aminoindamine (I; R = Me) shows that in the pH range 0·5—12·5 it exists in three different forms. The pK_a values were found to be 3·6 and 10·6. It was previously shown [2] that the equilibria are represented by the structures shown in Scheme 2. The structure of the monocation



SCHEME 2

(VI) has been demonstrated previously.[2] Support for the structure of the dication (V) was obtained by comparing its spectrum, $\lambda_{max.}$ 455 nm (log ε 3·38), with that of 2-amino-*N*-phenyl-*p*-benzoquinone di-imine, $\lambda_{max.}$ 460 nm (log ε 3·6), indicating protonation of the amino-group of (VI) to give (V).

At first sight it would appear that the three different routes for reaction of the aminoindamine are related to the three different species existing in aqueous solution: the free base suffering terminal imino-group hydrolysis, the monocation undergoing intramolecular cyclisation, and the dication undergoing hydrolysis at the azomethine bridge. To test this hypothesis, a kinetic study of the three reactions was undertaken, employing spectrophotometric methods to follow the course and rate of the reaction. Spectral data for the compounds involved is given in Table 1.

When the visible spectrum of an aqueous solution of the aminoindamine at pH > 10 is repeatedly scanned, it can be seen that the absorption at 549 nm due to the monocation, or at 460 nm, due to the free base, gradually disappears while a new peak at 492 nm ascribable to 2-amino-3-methylindoaniline,[6] develops and an isosbestic point at 469 nm is observed. The change in optical density at constant wavelength follows the first-order rate law (1) where [Ind] is the concentration of indamine,

$$-\mathrm{d[Ind]}/\mathrm{d}t = k(\mathrm{O.D.}_t - \mathrm{O.D.}_\infty)/(\mathrm{O.D.}_0 - \mathrm{O.D.}_\infty) \quad (1)$$

O.D.$_0$ is the initial optical density, O.D.$_t$ is that at time t, and O.D.$_\infty$ is the final optical density. From experiments at different pH, it was found (Table 2) that the rate of hydrolysis increased with increasing pH up to pH *ca.* 11·5 and then becomes relatively independent of pH. This can be explained by the rate-controlling step involving reaction either between the free base (I) and water or between the conjugate acid (VI) and hydroxide ions. As has been pointed out by Tong and Glesmann,[7] salt effects cannot differentiate between mechanisms involving rapidly equilibrating sets of reactants. However, as shown in the Appendix, there is reason to prefer the latter mechanism.

When a solution of the aminoindamine (I; R = Me) is kept at constant pH, in the range 4·5—8, the protonated indamine absorption at 549 nm is slowly replaced by the phenazine absorption. Since the phenazine has pK_a 6·5, the new absorption may be at 506 nm for the cationic form, or 438 nm for the neutral form, or at both wavelengths, depending on the pH of the reaction mixture. The spectrophotometric course of the reaction shows an isosbestic point, and the rate of change follows first-order kinetics. The rate of reaction is independent of pH, over the range 4·5—8 (Table 3) indicating that the rate-controlling step involves intramolecular cyclisation of the major ionic species of the aminoindamine which, in this

TABLE 2

Rate data for the hydrolysis of 2-amino-5-methylindamine to 2-amino-5-methylindoaniline at 30·2° and ionic strength 1·0

pH (±0·02)	10^4k/s^{-1}	α *	$10k_3$ †/ l mol^{-1} s^{-1}
10·2	0·70 ‡	0·72	6·7
11·1	2·0	0·24	6·6
11·55	2·3	0·10	6·5
12·2	2·62	0·025	6·4

* α = Fraction of reactant present as monocation. † k_3 = $k/(\alpha[\mathrm{OH^-}])$. ‡ Corrected for phenazine formation (*ca.* 3%).

[6] J. F. Corbett, *J.C.S. Perkin II*, 1972, 539.
[7] L. K. J. Tong, and M. C. Glesmann, *J. Amer. Chem. Soc.*, 1956, **78**, 5827.

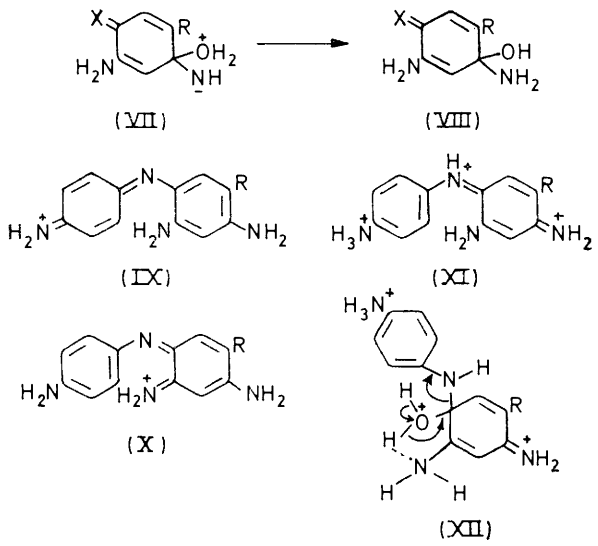
range, is the monocation (VI). The reaction can be considered to involve either the 1,4-addition of the 2-amino-group to the quinonoid ring of structure (IX) or electrophilic attack by the protonated imino-group on the benzenenoid ring of structure (X). The latter is analogous to the oxidative coupling of di-iminium ions with aniline.[1] On this basis, it can be seen that the formation of analogous structures from the neutral indamine (I) would involve separation of charge. In the case of the dication (V), the formation of (IX) or its analogue would require the loss or transfer of a proton while in the analogue of (X) the protonated amino-group would be expected to render the benzenoid ring resistant to electrophilic attack. Thus, the unique formation of the phenazine from the monocation (VI) can be understood.

TABLE 3

Rate data for the cyclisation of 2-amino-5-methylindamine at 67° and ionic strength 1·0

pH (±0·02)	$t_{1/2}$min	10^5k_{exp}/s^{-1}	k_2/s^{-1}
5·48	92·5	12·5	$1·5 \times 10^{-4}$
6·53	78·0	14·8	
7·52	70·7	15·7 *	
8·21	42·7	13·4 †	

* After correction for hydrolysis of the indamine ($6·3 \times 10^{-7}$ s^{-1}). † After correction for hydrolysis of the indamine ($1·3 \times 10^{-6}$ s^{-1}).



When a solution of the aminoindamine at pH < 2 is stored, the absorption at 455 nm, ascribed to the dication (V), rapidly disappears and is replaced by a new peak having a maximum at 508 nm, the isosbestic point being at 518 nm. The development of this peak is due to the formation of the conjugate acid of the amino-quinone imine (III). At fixed pH, the conversion of (V) to (II) follows the first-order rate law. Furthermore, the rate of reaction was found to be proportional to the hydrogen ion concentration (Table 4). Thus, the reaction involves acid catalysed hydrolysis of the dication (V), *i.e.* uncatalysed hydrolysis of the trication (XI), with the attack by a water molecule occurring at the carbon atom of the azomethine group. Such attack would obviously be facilitated by the presence of a positive charge on the adjacent nitrogen atom. Furthermore, delocalisation of this charge onto the rings is inhibited by the presence of positive charges on each of the terminal nitrogen atoms of the aminoindamine. The question as to why hydrolytic fission of the azomethine group should occur, rather than hydrolytic fission of the terminal imino-group of (V) or (XI), can be answered in terms of stabilisation of the transition state (XII) by hydrogen bonding to the *ortho*-amino-group. The presence of this amino-group may also facilitate collapse of the transition state into products, as indicated by the arrows. The requirement of base catalysis for the removal of a proton in the collapse of the transition state is shown by the finding that the hydrolysis is catalysed by phosphate ions. Thus, the reaction at a particular pH proceeds *ca.* 5 times faster in phosphate buffer than in unbuffered hydrochloric acid containing sodium chloride to give an equivalent ionic strength.

TABLE 4

Rate data for the hydrolysis of 2-amino-5-methylindamine to 2-amino-5-methylbenzoquinone monoimine and *p*-phenylenediamine, at 30·2° and ionic strength 1·0

pH (±0·05)	k_{exp}/s^{-1}	10^2k_1/l mol^{-1} s^{-1}
0·08	0·0152	1·6
0·25	0·0115	2·1
0·40	0·00582	1·45
0·46	0·00536	1·53
0·71	0·00417	2·20
0·78	0·00280	1·70
0·79	0·00367	2·30
0·89	0·00290	2·23
0·92	0·00169	1·41
1·03	0·00215	2·29
1·18	0·00166	2·51
1·38	0·000663	1·58
1·43	0·00101	2·72
1·91	0·000279	2·30
1·70	0·000557	2·73
1·98	0·000290	2·90

The rate constant for the disappearance of the aminoindamine from aqueous solutions, over the pH range 0—12, is given by equation (2), where α' and α are the

$$-\mathrm{d[In]}/\mathrm{d}t = k[\mathrm{In}]_t = (k_1\alpha'_1[\mathrm{H^+}] + k_2\alpha + k_3\alpha[\mathrm{OH^-}])[\mathrm{In}]_t \quad (2)$$

fractions of the indamine present as the di- and mono-protonated species respectively, at the pH to which k pertains, and k_1 is the specific second-order rate constant for hydrolysis at the azomethine link, k_2 is the specific first-order rate constant for the intramolecular cyclisation, and k_3 is the specific second-order rate constant for the hydrolysis at the terminal imino-group. Values of k_1—k_3 derived from our kinetic experiments are given in Table 5. Using these values and equation (2), theoretical plots of log k *versus* pH were plotted and compared with the experimental data (Figure 1). From these plots it is evident that, at a particular temperature, the amino-

indamine is most stable in the pH range 5—8, which is the range in which intramolecular cyclisation to the diaminophenazine is the preferred reaction.

TABLE 5

Rate constants for the reactions of 2-amino-5-methylindamine at various temperatures

Temp. (°C)	Hydrolysis at azomethine k_1/ l mol^{-1} s^{-1}	Phenazine formation k_2/s^{-1}	Hydrolysis at imino-group k_3/ l mol^{-1} s^{-1}
30·2	0·021	$2·7 \times 10^{-6}$	0·67
57·9	0·66	$6·4 \times 10^{-5}$	
60·0		$7·7 \times 10^{-5}$	5·7
67·0	1·9	$1·5 \times 10^{-4}$	
ΔE/kcal mol^{-1}	21·1	24·5	14·4

We have also examined the reactions of some other 2-aminoindamines in aqueous solution, over the pH range 0—8. Relevant data are given in Table 3. In every case, chromatographic and spectrophotometric examination of the reaction mixtures showed the formation of a diaminophenazine at pH > 5, and of the appropriate *p*-phenylenediamine and 2-amino-4-benzoquinone monoimine at the lower pH values.

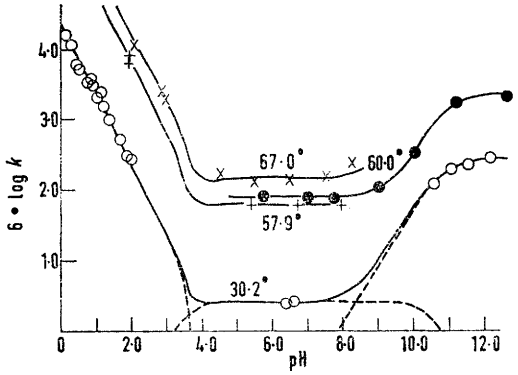


FIGURE 1 Experimental points and calculated plots for the rate of disappearance of 2-amino-5-methylindamine from aqueous solution as a function of pH. The broken lines represent the rates of the individual contributing reactions

Examination of the rate constants in Table 6, shows that the presence of an electron-donating group on the quinonoid ring decreases the rate of intramolecular cyclisation while the presence of an electron-withdrawing group increases the rate. This is consistent with the mechanism proposed earlier, since a similar effect of substituents on the rate of coupling of quinone imines has been observed previously. Thus, we can consider that electron-donating groups decrease the electrophilicity of the protonated imino group of structure (X), or that they reduce its contribution to the resonance hybrid. It can also be seen that the effect of substituents on the benzenoid ring of the aminoindamine on the rate of phenazine formation is the converse. Thus, the 3′-methoxy-derivative cyclises *ca.* 10 times faster than does the parent compound. This is to be expected since the presence of electron donor groups on this ring would render it more susceptible to intramolecular electrophilic attack through structure (X), or would increase the contribution of structure (IX).

The effect of substituents on either ring of the 2-aminoindamine on the rate of hydrolysis at the azomethine link is negligible. However, it must be remembered that the reaction involves the triprotonated species and, since the pK_a of these is not known, the apparent lack of effect of substituents may be due to the balancing of opposing effects.

EXPERIMENTAL

2-Amino-5-methylindamine (I; R = Me).—The indamine was prepared by the method of Bernthsen and Schweitzer.[3] The crude product was recrystallized from water to give the *indamine hydrochloride dihydrate* as fine black needles, m.p. 139—140° (Found: C, 52·6; H, 6·2; Cl, 11·6; N, 18·7. $C_{13}H_{15}ClN_4,2H_2O$ requires C, 52·6; H, 6·4; Cl, 11·6; N, 18·8%).

4′-Acetamido-5-methoxy-2,4-dinitrodiphenylamine.— A mixture of 5-chloro-2,4-dinitroanisole [8] (11·5 g), *N*-acetyl-*p*-phenylenediamine (7·5 g), and pyridine (5 g) was refluxed for 4 h in methanol (75 ml). On cooling the mixture to 0°, the crude product separated as yellow plates. The product was recrystallized twice from acetic acid to give the *diphenylamine* (6·5 g), m.p. 247·5—248·5° (Found: C, 51·95; H, 4·2; N, 16·05. $C_{15}H_{14}N_4O_6$ requires C, 52·0; H, 4·05; N, 16·2%).

4′-Amino-5-methoxy-2,4-dinitrodiphenylamine.— The above amide (1 g) was refluxed in 10% sulphuric acid in

TABLE 6

Kinetic and spectral data for the cyclisation (k_2) and azomethine hydrolysis (k_1) of 2-aminoindamines at 30·2°

2-Amino-indamine	Rate constants 10^2k_1/ l mol^{-1} s^{-1}	Rate constants 10^6k_2/s^{-1}	$\lambda_{max.}$/nm (log ε) Indamine: Dication	Indamine: Monocation	pK_a	$\lambda_{max.}$/nm Phenazine: Cation	Phenazine: Neutral	Quinone cation
Parent	2·19	6·1	453 (3·70)	552 (4·13)	3·4	502	431	~490
5-Methyl	2·11	2·7	462 (3·69)	549 (4·09)	3·6	506	438	508
5-Methoxy	1·50	0·08	434 (3·63)	511 (4·04)	4·1	490	430	490
5-Chloro	2·16	100	505	600	3·0	508	434	510
3′-Methyl	2·64	9·4	475 (3·66)	572 (4·06)	3·4	506	438	~490
3′-Methoxy	1·70	54	490 (3·73)	615 (4·18)	3·9	500	430	~490

[3] W. Borsche, H. Loibenstein, and R. Quast, *Ber.*, 1917, **50**, 1339.

ethanol (100 ml) for 2 h. The mixture was filtered while hot and was cooled to 0°. On cooling, crude product (0·7 g) separated. The product was washed with ammonia solution (50 ml; *d* 0·88) and was then recrystallized twice from ethanol to give the *diphenylamine* (0·5 g) as an orange solid, m.p. 202—203° (Found: C, 51·85; H, 4·2; N, 18·1. $C_{13}H_{12}N_4O_5$ requires C, 51·3; H, 3·95; N, 18·4%).

2-*Amino*-5-*methoxyindamine* (I; R = OMe).—The above amine (6·5 g) was reduced in ethanol (100 ml) over Pd–C in a Paar hydrogenator. The solution of the product, 2,4,4′-triamino-5-methoxydiphenylamine, was initially colourless, but rapidly oxidized on exposure to air to deep blue-violet. The oxidation was completed by bubbling oxygen through the solution for 2 h. On cooling to −5°, 2-*amino*-5-*methoxyindamine* separated from the solution as black needles, m.p. 185—187° (Found: C, 63·5; H, 6·1; O, 8·9; N, 21·65. $C_{13}H_{14}N_4O,1/3H_2O$ requires C, 63·1; H, 5·9; O, 8·6; N, 22·7%). By a similar procedure were prepared 2-aminoindamine (I; R = H) and 2-amino-5-chloroindamine (I; R = Cl).

2-*Amino*-5-*methyl*-*p*-*benzoquinone Monoimine*.—5-Methyl-2,4-dinitrophenol [9] was reduced over Pt–C in methanol on a Paar hydrogenator. The resulting 2,4-diamino-5-methylphenol spontaneously oxidized in air to give a pale yellow solution. On acidifying, the solution turned deep red. Evaporation of the solvent left the *quinone imine* as a dark brown powder, $\nu_{max.}$ (KBr) 3360, 3230, 3050, 1683, 1650, 1570, 1520, 1463, 1417, 1390, 1290, 1145, 1093, 1040, 1020, 871, 812, 780, 755, 615, 600, and 505 cm^{-1}, *m/e* 139 (*M* + 1, 2·2%), 138 (*M*, 20), 137 (14), 136 (5·6), 121 (3·8), 108 (6·2), 93 (2·4), 92 (2), 81 (3·3), 80 (3·8), 68 (4), 67 (4), 38 (33), and 36 (100) (Found: C, 47·2, H, 5·5; N, 15·4. $C_7H_8N_2O,HCl,-1/3H_2O$ requires C, 47·0; H, 5·5; N, 15·7%). 2-Amino-5-methylbenzoquinone monoimine was also produced by the hydrolysis of 2-amino-5-methylindamine at pH 1.

3,7-*Diamino*-2-*methylphenazine* (II, R = Me).—This was prepared by the method of Bernthsen and Schweitzer.[3] The crude product was purified by repeated washing with hot benzene, *m/e* 225 (*M* + 1, 16·5%), 224 (*M*, 100), 222 (14·5), 208 (2·5), 207 (2·5), 206 (2·1), 197 (7·5), 196 (11·7), 183 (4·6), 179 (1·9), 112·5 (*m/2e*) (2·1), 112 (*m/2e*) (12), 111·5 (*m/2e*) (1·6), 98·5 (*m/2e*) (4·2), and 98 (2·9) (Found: N, 24·4. $C_{13}H_{12}N_4$ requires N, 25·0%).

TABLE 7

Typical rate data for the hydrolysis to 2-amino-5-methylindoaniline at 30·2° and ionic strength 1·0

pH 10·2

t/min	O.D.$_{500}$ (1 cm)	Reaction (%)	$10^5k/s^{-1}$
0	1·230	0	
65	1·115	25	7·34
160	1·05	50	7·22
330	0·995	75	7·00
∞	0·870	100	

pH 12·2

t/min	O.D.$_{500}$ (1 cm)	Reaction (%)	$10^4k/s^{-1}$
0	0·750	0	
20	0·785	25	2·48
44	0·820	50	2·62
92	0·855	75	2·5
∞	0·890	100	

Kinetic Experiments.—All reactions were run in a spectrophotometer. Pre-thermally equilibrated solutions of the indamine in water and of a suitable buffer solution were mixed and the reactions were followed, either by repetitive scanning of the visible spectrum or by recording the absorbance at constant wavelength as a function of time. The buffer concentration was chosen so as to give a total ionic strength of 1·0 in the reaction mixture. Typical experimental data are given in Tables 7—9.

TABLE 8

Typical rate data for the cyclisation of the aminoindamine (I; R = Me)

pH 5·44 at 57·9°

t/min	O.D.$_{600}$ (1 cm)	Reaction (%)	$10^5k/s^{-1}$
0	0·92	0	
40	0·82	13	5·8
100	0·70	28	5·5
160	0·58	41·5	5·4
280	0·41	62	5·8
400	0·30	77	6·2
∞	0·12	100	

pH 7·52 at 67°

t/min	O.D.$_{550}$ (1 cm)	Reaction (%)	$10^4k/s^{-1}$
0	1·07	0	
21	0·93	17	1·51
39	0·83	29	1·49
99	0·59	59	1·50
159	0·46	75	1·45
∞	0·25		

APPENDIX

Tong [10] has studied the effect of pH on the rate of hydrolysis of *p*-benzoquinone imines of type (XIII) over the pH range 7—12. For (XIII; R = alkyl) he found the rate increased by a factor of 10 for each unit increase in pH and concluded that the reaction involved hydroxide ion catalysed hydrolysis of the cationic imine. For *p*-benzoquinone diimine (XIV), he found that the rate of hydrolysis was independent of pH over the range 8·88—12·15 and concluded that, since this imine existed in the neutral form at pH > 8, the hydrolysis in this region is uncatalysed.

TABLE 9

Typical rate data for hydrolysis of the aminoindamine (I; R = Me) at low pH

pH 2·23 at 67°

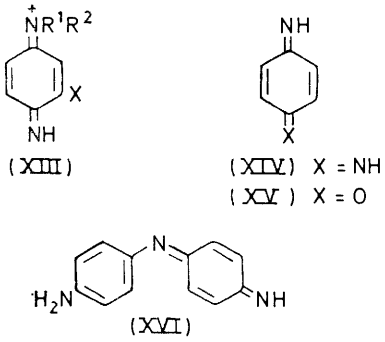
t/s	O.D.$_{440}$ (1 cm)	Reaction (%)	$10^2k/s^{-1}$
0	1·42	0	
25·5	1·20	25	1·16
61	0·98	50	1·13
80	0·90	59	1·12
122	0·76	75	1·13
∞	0·54	100	

pH 0·79 at 30·2°

t/s	O.D.$_{440}$ (1 cm)	Reaction (%)	$10^3k/s^{-1}$
0	1·23	0	
79	1·03	25	3·62
131	0·92	39	3·65
189	0·83	50	3·66
384	0·63	75	3·60
∞	0·43	100	

[9] W. Borsche, *Ber.*, 1917, **50**, 1350.
[10] L. K. J. Tong, *J. Phys. Chem.*, 1954, **58**, 1090.

Tong and Glesmann [11] determined the dependence of the rate of hydrolysis of (XIII; R = Et, X = Me) and of



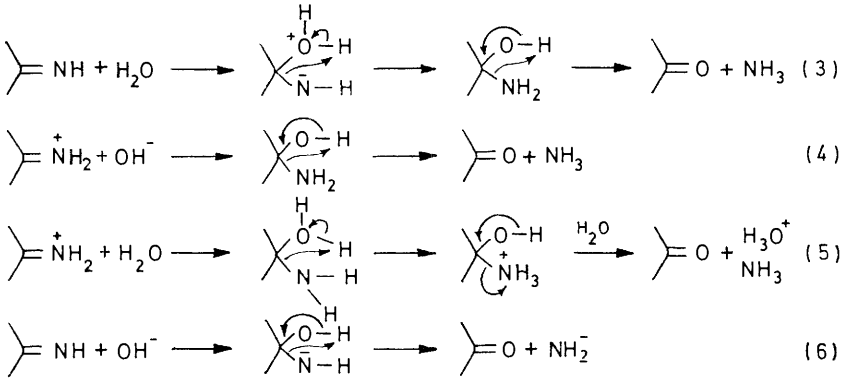
(XIV) on ionic strength I. Plots of log k/k_0 *versus* $I^{\frac{1}{2}}$ had a slope of −1 for (XIII; R = Et, X = Me) and of 0 for (XIV).

Over the pH range 2—10, the profile for *p*-benzoquinone monoimine (XV) is also a composite of curves A and B, although, at higher pH, there is evidence [10] for a contribution by C. In the case of indamine (XVI) [1] over the pH range 4·5—9, the profile is a composite of curves A and B, again indicating contributions from (5) with (3) and/or (4). For 2-amino-5-methylindamine (I; R = Me) the hydrolysis, at pH > 8·5, occurs by (3) or (4) with any contribution by other mechanisms at lower pH being masked by intramolecular cyclisation to a phenazine.

The rate constants for the above reactions are given in Table 10. It should be noted that the rate constant k_1', for (3) at pH $\gg$ pK_a' is related to that for (4), k_2', by equation (7). From Table 10, it is evident that the rate of hydrolysis,

$$\log k_1' = \log k_2' - (14 - \mathrm{p}K_a) \qquad (7)$$

when it is considered to occur by mechanism (3), is relatively independent of the structure of the di-imine while the rate for hydrolysis by mechanism (5), which is unambiguously



SCHEME 3

However, as they pointed out, the zero slope for (XIV) cannot be regarded as conclusive since any other pair of reactive species in rapid equilibrium with the free base and water [*e.g.* the conjugate acid of (XIV) and OH^-] would exhibit identical salt effects.

Just as the salt effect is not conclusive for the hydrolysis of benzoquinone di-imine, nor would it be for the hydrolysis of any other imine containing the group >C=NH, such as benzoquinone monoimine (XV), the indamine Phenylene Blue (XVI), or 2-amino-5-methylindamine (I; R = Me). It is thus evident that a definitive mechanism must be deduced by indirect means such as comparison of the rates of hydrolysis for a variety of imines *via* the various possible mechanisms.

The hydrolysis of imines can be considered to involve the mechanisms shown in Scheme 3.

Mechanisms (3) and (4) would show an identical pH–rate profile (Figure 2, curve A), while they could be distinguished from mechanisms (5) and (6) each of which would show a unique profile (Figure 2, curves B and C respectively).

Over the pH range 6—12 the rate–pH profile for *p*-benzoquinone di-imine (XIV) [12] can be considered a composite of curves A and B, suitably positioned relative to the log k axis, indicating contributions of (5) with (3) and/or (4). established, is very dependent on the nature of the di-imine. Furthermore, in the case of the indamines, the values for k_1' and k_3' suggest that water would attack the

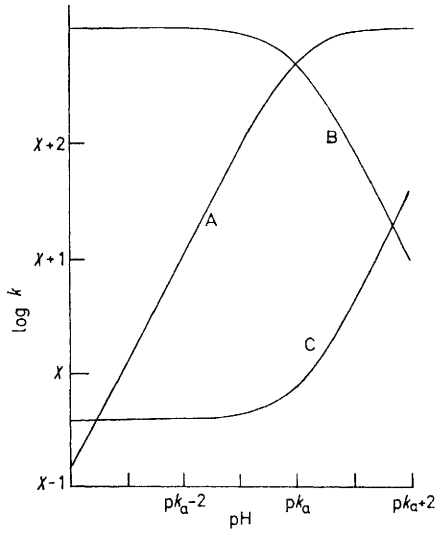


FIGURE 2 The theoretical rate–pH profiles for hydrolysis of imines occurring by mechanisms (3) and/or (4), curve A; (5), curve B; and (6), curve C

[11] L. K. J. Tong and M. C. Glesmann, *J. Amer. Chem. Soc.*, 1956, **78**, 5827.
[12] J. F. Corbett, *J. Chem. Soc.* (*B*), 1969, **213**.

neutral imine more readily than it would the conjugate acid. This would be surprising.

More likely, we would expect the hydrolysis rates to be highly dependent on the structure of the imine while the relative rates of the comprising mechanisms would be fairly independent of the nature of the imine. This is indeed borne out if we consider hydrolysis to involve reaction of the conjugate acid with water [mechanism (5)] and with hydroxide ions [mechanism (4)]. If this is so, it can be seen that the k_2'/k_3' ratios lie between 2×10^7 and 2×10^8, which seems reasonable.

TABLE 10

Specific rate constants for the hydrolysis of various imines at 30°

Imine		Di-imine (XIV)	Indamine (XVI)	2-Amino-5-methyl indamine (I; R = Me)	Monoimine (XV)
pK_a		5·75	7·55	10·6	3·7
Mechanism	Order	Rate constants *			
k_1' (3)	First	$4·5 \times 10^{-4}$	$3·6 \times 10^{-4}$	$2·6 \times 10^{-4}$	$1·1 \times 10^{-5}$
k_2' (4)	Second	$6·0 \times 10^{5}$	$1·0 \times 10^{3}$	0·67	$2·2 \times 10^{7}$
k_3' (5)	First	$5·0 \times 10^{-2}$	$5·0 \times 10^{-5}$	$(<10^{-5})$	$2·1 \times 10^{-1}$

* Expressed as s^{-1} or 1 mol^{-1} s^{-1}.

TABLE 11

Specific rate constants for the base catalysed hydrolysis of cationic *p*-benzoquinone di-imines at 25° *

Compound (XIII)			k'_2/l mol^{-1} s^{-1}
R^1	R^2	X	
H	H	H	$5·9 \times 10^{5}$ †
Me	Me	H	$2·5 \times 10^{4}$
Et	Et	H	$5·3 \times 10^{3}$
Et	Et	Me	$1·7 \times 10^{3}$

* Ref. 10. † Calc. from $k_1' = 3·3 \times 10^{-4}$ s^{-1} by equation (7).

The probability that the hydrolysis of imines at high pH occurs by mechanism (4) rather than (3) is further borne out by the comparison of k_2' with the analogous rate constants for some cationic imines (XIII) shown in Table 11. It can be seen that successive replacement of hydrogen by alkyl results in a decrease in the rate as would be anticipated for a series of compounds undergoing attack by a nucleophile.

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