Benzoquinone Imines. Part 14.[1] The Kinetics and Mechanism of the Coupling of *p*-Benzoquinone Monoimines with *m*-Aminophenols

By **Keith C. Brown,* John F. Corbett,** and **Robert Labinson,** Clairol Research Laboratory, 2 Blachley Road, Stamford, Connecticut 06902, U.S.A.

The coupling of *p*-benzoquinone monoimines with *m*-aminophenols involves rate-controlling electrophilic attack of the *p*-benzoquinone imine and/or its conjugate acid on the 4-carbon atom of the *m*-aminophenolate ion to give the corresponding aminodihydroxydiphenylamine. The latter undergoes rapid oxidation to afford the 2-aminoindophenol [2-amino-*N*-(4-hydroxyphenyl)-*p*-benzoquinone monoimine]. In concentrated solution, if the 2-aminoindophenol has no substituent in the 5-position, addition of *p*-aminophenols to give a trinuclear species occurs. The effect of methyl and chloro substituents on the reactivity of the imine and *m*-aminophenol, and on the spectrum of the 2-aminoindophenol are discussed.

EARLIER Parts have reported on the kinetics and mechanism of the reactions of *p*-benzoquinone monoimines with *m*-diamines [2] and with monohydric phenols.[3] We have now examined the reaction of monoimines with *m*-aminophenols.

Product Structure.—When dilute solutions (*ca.* 10^{-4}M) of *p*-aminophenol or its *C*-methyl derivatives are prepared at pH *ca.* 11 in the presence of oxygen, the *p*-aminophenol (I) is quantitatively oxidized to the *p*-benzoquinone monoimine (II) within 2 min. At higher concentrations, the solutions rapidly turn brown due to reaction of the monoimine with unoxidized *p*-aminophenol. The conversion of *p*-aminophenols into the colourless monoimines can be followed spectrophotometrically by observing the development of the characteristic absorption peak in the region 250—270 nm. If oxidation of the *p*-aminophenol is carried out at pH >11, in the presence of a 3-aminophenol having no substituent in the 4-position, a blue colour develops. In an attempt to isolate the coloured product, air was bubbled through an alkaline solution of *p*- and *m*-aminophenol (*ca.* 10^{-2}M). Although the characteristic blue colour developed initially, the solution rapidly turned brown. The isolated product had an elemental analysis and mass spectrum consistent with structure (VII). As further confirmation, acid hydrolysis of the precipitate gave 2,5-dihydroxy-*p*-benzoquinone, which clearly points to a trinuclear structure. However, in a similar experiment with 5-amino-2-methylphenol and *p*-aminophenol, the blue colour developed and no brown colour was observed. The product was isolated and shown to be 2-amino-5-methylindophenol (III). The elemental analysis corresponded to $C_{13}H_{12}N_2O_2$, while the n.m.r. spectrum showed the presence of four aromatic protons (τ 3.12), two different quinonoid protons (τ 3.27, 4.40) the latter *ortho* to an amino group,[4] three methyl protons (τ 8.20), and two amino protons (τ 3.27). Hydrolysis of the indophenol in dilute acid gave *p*-aminophenol, detected by t.l.c. of the hydrolysate, and 2-hydroxy-5-methyl-*p*-benzoquinone (IV), isolated by steam distillation and compared with an authentic sample.

Spectra and p*K*$_a$ *Values*.—Spectral data for a variety

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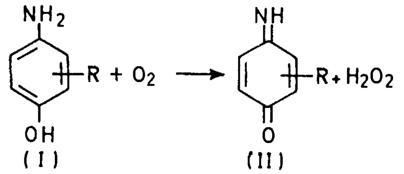
[1] Part 13, K. C. Brown and J. F. Corbett, *J.C.S. Perkin II*, 1977, 1125.

[2] J. F. Corbett, *J. Chem. Soc.* (*B*), 1969, 823.

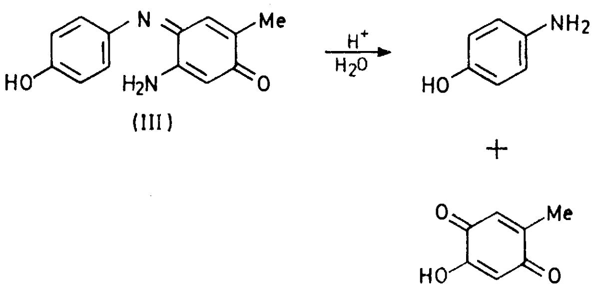
[3] J. F. Corbett, *J. Chem. Soc.* (*B*), 1970, 1502.

[4] J. F. Corbett, *J.C.S. Perkin II*, 1972, 539.

of 2-aminoindophenols were obtained by air oxidation of an alkaline solution (pH *ca.* 11) of the appropriate p-aminophenol (10^{-4}M) and excess of m-aminophenol (1.5×10^{-4}M).



(I) (II)



(III) (IV)

Spectral data for the 2-aminoindophenols are recorded in Table 1 along with the pK_a values. At pH >11.4 the dyes exist as the 2-aminoindophenolate ion. At pH <7 the neutral form is the stable species. The pK_a of 2-aminoindophenol is 8.9 and methyl and chloro substituents on the quinonoid ring have little effect (pK_a 8.8—9.0). Methylation of the benzenoid ring decreases the acidity, particularly when the methyl group is *meta* to the hydroxy group (pK_a 9.1—9.2). On the other hand an o-chloro group increases the acidity by a factor of 30. In general, methylation of the quinonoid ring produces a hypsochromic shift in the spectrum of both the anion and neutral species. Methylation of the benzenoid ring produces a somewhat larger bathochromic shift. Chlorination of the rings has the opposite effect.

TABLE 1

Spectra and dissociation constants of 2-aminoindophenols

Indophenol from				
p-Aminophenol	m-Aminophenol	$\lambda_{max.}$/nm (log ε) Neutral form	pK_a	$\lambda_{max.}$/nm (log ε) Anion
Parent	Parent	470 (3.92)	8.9	574 (4.24)
2-Me	Parent	482 (3.90)	9.1	605 (4.25)
3-Me	Parent	480 (3.84)	9.2	600 (4.10)
2-Cl	Parent	464 (3.94)	7.5	565 (4.21)
Parent	2-Me	470 (3.85)	9.0	563 (4.25)
Parent	6-Me	464 (3.92)	9.0	556 (4.22)
Parent	6-Cl	480 (3.90)	8.8	585 (4.27)
2-Me	2-Me	482 (3.86)	8.9	592 (4.28)
2-Me	6-Me	469 (3.92)	9.1	581 (4.25)
3-Me	2-Me	476 (3.78)	9.2	583 (4.11)
3-Me	6-Me	470 (3.79)	9.2	578 (4.12)

The shifts observed are similar, both in magnitude and direction, to those observed to result from substitution of indophenol itself.[3] Comparison of the spectrum of 2-aminoindophenol with that of indophenol[3] shows that the 2-amino group in the former has shifted the peak of the anion, hyposochromically, by 67 nm and that of the neutral form by 26 nm. These effects are in accord with the electron donor character of the amino group. It is also noteworthy that the amino group has no marked effect on the pK_a of indophenols.

Mechanism of the Dye-forming Reaction.—Preliminary kinetic experiments indicated that the rate of oxidation of p-aminophenol by molecular oxygen is of the same order of magnitude as that of the subsequent coupling to an m-aminophenol. Thus, in order to study the kinetics of the coupling reaction, it was necessary to work with preformed monoimine in the absence of oxygen. It has been shown previously[5] that, at pH >7, oxidation of p-aminophenol to the monoimine by ferricyanide is quantitative and almost instantaneous [equation (i)]. The stoicheiometry of the coupling

$$p\text{-Aminophenol} + 2[\mathrm{Fe(CN)_6}]^{3-} \rightleftharpoons \text{Monoimine} + 2\ [\mathrm{Fe(CN_6}]^{4-} \quad \text{(i)}$$

reaction of p- to m-aminophenol was determined by varying the amounts of the three reactants in carbonate buffer solutions at pH 11.4 and 30 °C. The reaction was followed kinetically by recording the optical density of the solution at 574 nm as a function of time. From the data in Table 2 it is evident that m-aminophenol behaves as a four-equivalent coupler with the stoicheiometry [p-aminophenol] : [ferricyanide] : [m-aminophenol] of either 1 : 2 : 0.5 or 1 : 4 : 1. Furthermore, the reaction follows second-order kinetics, being first order in both monoimine and m-aminophenol. From this, we conclude that the rate-controlling step involves reaction of the monoimine with m-aminophenol to give 2,4,4'-aminodihydroxydiphenylamine [equation (ii)] which is rapidly oxidized to the 2-aminoindophenol either by one mole of monoimine [equation (iii)] when the stoicheiometry is 1 : 2 : 0.5, or by two moles of ferricyanide, when the stoicheiometry is 1 : 4 : 1. It should be noted that, in the latter case, the final optical density is always somewhat low. This was found to be due to oxidation of some m-aminophenol by the excess of ferricyanide as the reaction is proceeding. Indeed, if experiment 2 (Table 2) is performed by mixing m-aminophenol and ferricyanide and waiting 2 min before adding p-aminophenol, the maximum optical density achieved is reduced to 0.7. Thus, for kinetic experiments it was necessary to employ the 1 : 2 : 0.5 stoicheio-

TABLE 2

Stoicheiometry of the oxidative coupling reaction of p- and m-aminophenol at pH 11.4 and 30 °C

	10^4 Concentration (M)				
Experiment	p-Aminophenol	$[\mathrm{Fe(CN)_6}]^{3-}$	m-Aminophenol	$\mathrm{OD_{max.}}$/cell (cm)	$t_{\frac{1}{2}}$/s
1	2.0	4.0	1.0	1.70/1.0	11
2	1.0	4.0	1.0	1.62/1.0	24
3	0.5	1.0	0.25	1.68/4.0	46
4	0.5	1.0	0.5	1.70/4.0	
5	2.0	4.0	0.5	0.76/1.0	

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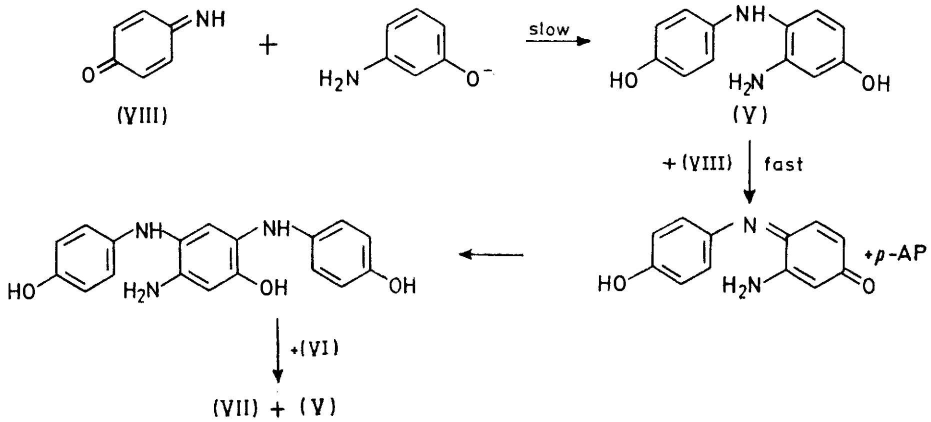
[5] J. F. Corbett, *J. Chem. Soc. (B)*, 1969, 207.

metry. When this stoicheiometry is employed the yield of indophenol is not quantitative due to a slow

$$\text{Monoimine} + m\text{-Aminophenol} \xrightarrow{\text{slow}} \text{Leucoindophenol (V)} \quad \text{(ii)}$$

$$\text{Leucoindophenol} + \text{Monoimine} \xrightarrow{\text{fast}} \text{Indophenol (VI)} + p\text{-Aminophenol} \quad \text{(iii)}$$

reaction between the indophenol and *p*-aminophenol which evidently involves addition at the 5-position of the indophenol (VI) to give a trinuclear leuco compound which is oxidized to the dye (VII) by a second molecule of indophenol (Scheme). Evidence for this was obtained by treating the monimine (10^{-4}M) with *m*-aminophenol (5×10^{-5}M) at pH 10.17 in the absence of oxygen. After 12 min the optical density (570 nm) reached 1.48. Thereafter it began to decrease at a rate of 0.01 min^{-1}. After 10 min, a further quantity of *p*-aminophenol was injected to increase its concentration to 2.5×10^{-4}M, *i.e.* a five-fold increase. The rate of decrease in optical density increased to 0.05 min^{-1}. After 2 h, the optical density at 570 nm had fallen to 0.46 and when air was admitted, it increased to 0.96, *i.e.* half the original drop.



SCHEME Mechanism of the reaction of *p*-benzoquinone monoimine with *m*-aminophenol at pH > 9 in the absence of excess of oxidant

Because of these complications, which are more marked at higher concentrations, we were unable to isolate a sample of 2-aminoindophenol. However, we have been able to study its rate of formation in dilute solution. Table 3 shows the effect of pH on the rate of reaction of the monoimine (pK_a 3.7) [6] with *m*-aminophenol (pK_a 9.90).[4] Above pH 12 the rate is independent of pH. Below pH 11 the rate of coupling decreases with decreasing pH, reaching half the limiting rate at pH *ca.* 10. This indicates that the rate-controlling step in the pH range 9—13, involves reaction of the neutral monoimine with the *m*-aminophenolate ion (Scheme) and the observed rate constant is given by equation (iv) where k_a is the specific second-order rate constant and α_{P^-} and α_{M} are the fractions of *m*-aminophenolate and neutral monoimine present at the pH to which k pertains. From the data in Table 3 we get k_a 4.35×10^2 l mol^{-1} s^{-1}.

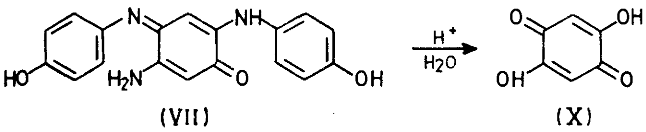
$$k = k_a\, \alpha_{\text{P}^-}\alpha_{\text{M}} \qquad \text{(iv)}$$

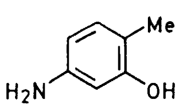
TABLE 3

Rate data for the reaction of *p*-benzoquinone monoimine with *m*-aminophenol at 30 °C

pH	$10^{-2}k$/l mol^{-1} s^{-1}	α_{P^-}	$10^{-2}k_a$/l mol^{-1} s^{-1}
12.4	4.55	1.0	4.55
12.2	4.53	0.99	4.58
11.6	4.36	0.98	4.45
11.4	4.12	0.97	4.25
11.3	4.16	0.96	4.33
10.9	3.70	0.90	4.11
10.2	2.78	0.67	4.15
9.1	0.52	0.13	(4.00)
			Mean 4.35 ± 0.19

5-Amino-2-methylphenol (IX) is even more susceptible to oxidation by ferricyanide than is *m*-aminophenol. Thus in a solution containing 10^{-4}M-compound (IX) and 4×10^{-4}M-ferricyanide, 75% of (IX) is destroyed within 15 s. For this reason all experiments with *C*-methylated *m*-aminophenols were performed using the 1 : 2 : 0.5 stoicheiometry.





(IX)

Table 4 gives data for the rate of reaction of *p*-benzoquinone monoimine with 3-amino-2-methylphenol. As before, the rate is independent of pH at pH >11.5 and decreases with decreasing pH below pH 11.5. In the pH range 9—10 a plot of log *k versus* pH has unit slope. In the pH range 7—8, the rate again becomes independent of pH. This is analogous to the rate–pH relationship for the reactions of monoimines with simple phenols [3] and indicates that, at pH 7—9, the contribution of a reaction between the conjugate acid of the monoimine and the *m*-aminophenolate ion becomes significant. Thus, over the pH range 7—13, the rate constant is

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[6] J. F. Corbett, *J. Chem. Soc.*, (*B*), 1969, 213.

given by equation (v) where k_a, α_M, and α_{P^-} are as above, k_b is the specific second-order rate constant for the

$$k = k_a \alpha_M \alpha_{P^-} + k_b \alpha_{M^+} \alpha_{P^-} \qquad \text{(v)}$$

reaction of the conjugate acid of the monoimine with the *m*-aminophenolate ion, the fractions of which are α_{M^+} and α_{P^-} at the pH to which k pertains. From the data in Table 4 we get k_a 4.8×10^3 and k_b 3.6×10^8 l mol^{-1} s^{-1}. The ratio of the reactivity of the conjugate acid to that of the neutral monoimine is given by k_b/k_a as 7.5×10^4, which is somewhat higher than the value of 3.2×10^3 obtained for the reaction with *m*-phenylenediamine[2] and somewhat lower than the value 2.4×10^5 obtained for the reaction with the 2,6-xylenolate ion.[3]

TABLE 4

Rate data (k/l mol^{-1} s^{-1}) for the reaction of *p*-benzoquinone monoimine with 3-amino-2-methylphenol at 30 °C

Experiment	pH	$10^{-3}k_{obs}$	$10^{-3}\ k_a$ *		
1	12.0	5.00	5.10		
2	11.3	4.02	4.23		
3	11.0	3.27	4.06	k_a $4.80 \pm 0.5 \times 10^3$	
4	10.5	2.98	5.46		
5	10.1	1.82	5.08		
6	10.0	1.42	4.89		
			$10^{-3}\ k_a\ \alpha_{P^-}$ †	$10^{-3}\ k_b\ \alpha_{M^+}\ \alpha_{P^-}$	$10^{-8}\ k_b$ §
7	9.5	0.625	0.53	0.095	4.2
8	9.0	0.290	0.18	0.11	5.5
9	8.5	0.123	0.053	0.070	3.5
10	8.0	0.079	0.038	0.041	2.1
11	7.5	0.067	0.006	0.061	3.1
12	7.0	0.069	0.002	0.067	3.3
					Mean k_b $3.6 \pm 1.0 \times 10^8$

* Calc. from $k_a = k/\alpha_{P^-}$. † Calc. from k_a from experiments 1—6. ‡ Calc. from $k_b \alpha_{M^+} \alpha_{P^-} = k - k_a \alpha_{P^-}$. § Calc. from $k_b = (k - k_a \alpha_{P^-})/\alpha_{M^+} \alpha_{P^-}$.

Substituent Effects.—In order to determine the effect of substituents on the reactivity of *p*-benzoquinone monoimine and *m*-aminophenolate ion, the rate of reaction of various pairs was determined at pH 11.4 and the value of k_a calculated. From the data in Table 5 it is evident that *C*-methylation increases the reactivity of *m*-aminophenolate ion but decreases that of the monoimine. Conversely, *C*-chlorination increases the reactivity of the monoimine but decreases that of *m*-aminophenolate ion. This is in accord with the mechanism shown in the Scheme which involves rate-controlling electrophilic attack by the monoimine and/or its conjugate acid on the 4-carbon atom of *m*-aminophenolate ion.

TABKE 5

Rate data for the reaction of various *p*-benzoquinone monoimines with various *m*-aminophenols at 30° and pH 11.4

Reactant		$10^{-2}k_{obs.}$/ l mol^{-1} s^{-1}	$10^{-2}\ k_a$/ l mol^{-1} s^{-1}
4-Aminophenol	3-Aminophenol		
H	H		4.35
2-Me	H *		0.21
3-Me	H *		0.27
H	2-Me	44.5	48.0
H	6-Me	25.1	26.7
2-Me	2-Me	2.15	2.42
2-Me	6-Me	1.96	2.06
3-Me	2-Me	2.35	2.64
3-Me	6-Me	1.54	1.54
H	6-Cl	1.10	1.15
2-Cl	H	140	140

* Measured using excess of *m*-aminophenol.

Table 6 compares the effect of substituents on the reactivities of the monoimine and of the coupler for three classes of coupler. It can be seen that the effect of substituents on the reactivity of the monoimine is relatively independent of the nature of the coupler. While the qualitative effect of substituents on the reactivity of the different couplers is independent of the nature of the coupler, secondary effects are evident in the quantitative comparison. These secondary effects may well be of steric origin since methyl groups *ortho* to amino would be expected to decrease the activating effect of the amino group to a greater extent than methyl groups *ortho* to O$^-$ would decrease its effect. Nevertheless these differences are relatively small compared with the differences in reactivity of the three parent couplers, *viz.* phenolate : *m*-phenylenediamine : *m*-aminophenolate = 1 : 13 : 510.

TABLE 6

Effect of substituents on the relative activity of *p*-benzoquinone monoimines and various couplers

Substituents		Relative reactivities *		
		Coupler class		
Monoimine	Coupler	3-Amino-phenolate	Phenolate	*m*-Phenylene-diamine
H	H	1.0	1.0	1.0
2-Me	H	0.049	0.039	0.048
3-Me	H	0.056	0.059	0.054
2-Cl	H	31.1	40.0	
H	2-Me	11.0	29.0	4.8
H	6-Me	5.9	29.0	3.7
H	3-Me		10.0	
H	6-Cl	0.24	0.12	

* The specific second-order rate constants for the reaction of *p*-benzoquinone monoimine with 3-aminophenolate ion, phenolate ion, and *m*-phenylenediamine are, respectively, 430, 0.85, and 11.0 l mol^{-1} s^{-1}.

EXPERIMENTAL

Materials.—*p*-[3] and *m*-aminophenols[4] have been described previously.

2-*Amino-5-methylindophenol* (III). 2-Amino-5-methylindophenol, m.p. 198—199° (lit.,[7] 215°), was prepared by

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[7] G. Kalopissis, A. Bugaut, and F. Estradier, U.S.P. 3,884,625/1975.

the method of Kalopissis *et al.*[7] It was recrystallized from dimethylformamide–water (Found: C, 68.4; H, 5.4; N, 12.1. Calc. for $C_{13}H_{12}N_2O_2$: C, 68.4; H, 5.3; N, 12.3%).

2-*Amino*-5-(p-*hydroxyanilino*)*indophenol* (VII). A mixture of *p*- (1 g) and *m*-aminophenol (1 g) in pH 10 buffer (100 ml) was aerated for 24 h. The solution changed from blue to brown. The precipitate was crystallized from dimethylformamide–water to dark crystals of the *indophenol*, m.p. 255—257° (Found: C, 67.1; H, 4.9; N, 13.0. $C_{18}H_{15}N_3O_3$ requires C, 67.3; H, 4.7; N, 13.0%), *m/e* 321, 304, and 292. Dye (VII) was hydrolysed by boiling in dilute hydrochloric acid to 2,5-dihydroxy-*p*-benzoquinone (X) which was isolated by steam distillation and recognized by its characteristic u.v. spectrum.[8]

Spectra.—The visible spectrum of the indophenol (III) was determined in aqueous phosphate buffers at various pH values in the range 2—14. Between pH 2 and 7, the spectrum is independent of pH, indicating the weak basicity of the amino group.

Spectra of the other 2-aminoindophenols were obtained by injecting a solution (10 μl) of the *p*-aminophenol (3×10^{-2}M) into air-saturated carbonate buffer solution (3 ml) and, after 2 min, injecting a 50% excess of a solution (3×10^{-2}M) of the *m*-aminophenol. When maximum colour had developed, the spectrum of the 2-aminophenolate ion was recorded. The pH was adjusted by addition of strong acid by *ca.* 0.5 units and the spectrum was recorded at each pH down to 6.5. The pK_a values were calculated from these data.

Kinetics.—All kinetic measurements were made at 30 °C. Buffer solutions were prepared from 0.1M solutions of sodium dihydrogenphosphate, disodium hydrogenphosphate, and sodium phosphate, or, at pH >11, from 0.1M-sodium carbonate.

The reaction mixtures were prepared by previously described techniques.[9] Rate constants were calculated from the appropriate rate equation [3] using experimental data from 25—75% reaction. It is estimated that the rate constants are accurate to ±10%.

Dissociation Constants.—The dissociation constants of 4-methyl- and 6-methyl-3-aminophenol were reported previously.[4] Using the same technique, the following data were obtained: 3-amino-2-methylphenol pK_a 10.41, $\lambda_{max.}$ 280 (neutral) and 289 nm (anion); 5-amino-2-chlorophenol pK_a 9.05, $\lambda_{max.}$ 289 (neutral) and 297 nm (anion).

[8/028 *Received, 9th January*, 1978]

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[8] J. F. Corbett, *J. Soc. Dyers Colourists*, 1969, **85**, 71.

[9] J. F. Corbett, *J. Chem. Soc. (B)*, 1970, 1418.