DALTON

Anaerobic oxidation of dopamine by iron(III)

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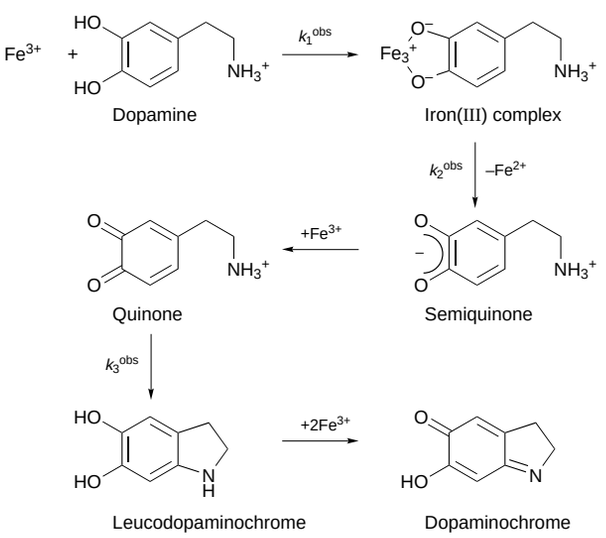
Iron(III) [in the form of $Fe(OH)^{2+}$] reacted reversibly in acid aqueous solution with dopamine, 2-(3,4-dihydroxyphenyl)ethylamine (H_2LH^+, in which the phenolic protons are written to the left of L) to give the complex ion $Fe(LH)^{2+}$. This species then decomposed to yield iron(II) and a semiquinone, which in turn is oxidised further to a quinone. The latter cyclised to form leucodopaminochrome (indoline-5,6-diol), which was finally oxidised by iron(III) to pink dopaminochrome (6-hydroxy-3*H*-indol-5-one), presumably *via* another semiquinone. The rate of appearance and disappearance of the complex and of the *ortho*-quinone were separately followed by stopped-flow photometric methods. Mechanisms are proposed for the various steps and these are supported by measurements at varying ionic strengths. Rate constants for the reversible formation of the iron–dopamine complex have been evaluated [$k_1 = (2.09 \pm 0.05) \times 10^3$ and $k_{-1} = 23 \pm 2$ dm^3 mol^{-1} s^{-1}]. The rate of decomposition of the protonated complex to yield iron(II) and the semiquinone was established as $k_2 = 0.23 \pm 0.02$ s^{-1} and $K_M^H = 33 \pm 0.9$ dm^3 mol^{-1} [for the protonation of $Fe(LH)^{2+}$]. The stability constant of the $Fe(LH)^{2+}$ complex has been calculated (log $K_1^M = 21.14$) and ε_{max} is 1260 dm^3 mol^{-1} cm^{-1} at 700 nm. The effect of chloride on the rate of complex formation at low pH has been explained by the fact that $FeCl^{2+}$ also reacts with dopamine ($k_{Cl} = 148 \pm 7$ dm^3 mol^{-1} s^{-1}) to form the complex but that this is predominantly reversible *via* the non-chloride route at low pH values. The stability constant for $FeCl^{2+}$ formation (a constant not readily accessible by standard methods) was extracted from the data (log $K_1^{Cl} = 1.53$). The rate of disappearance of the quinone enabled the ring-closure reaction (*i.e.* the formation of the indole) to be followed and the mechanism established. All measurements were carried out at 25 °C in solutions of ionic strength 0.10 mol dm^{-3} (KNO_3) except for ionic strength dependence studies.

Brightly coloured complexes of catechols with iron(III) are well known and often used as qualitative analytical tests. These colours are, however, not stable and slowly fade.[1,2] This can be ascribed to an internal electron transfer within the complexes which yields iron(II) and the respective semiquinone; the latter is unstable with respect to further oxidation (to the quinone). The quinones of the catecholamines are, however, able to react further[3–5] (*via* an internal Michael addition) to form indole compounds. These can usually be oxidised further to yield the pink aminochromes. How this is related to the present work is summarised in Scheme 1.



Scheme 1 Overall route of oxidation of dopamine

Experimental

Dopamine [4-(2-aminoethyl)benzene-1,2-diol] hydrochloride ($C_8H_{11}NO_2$·HCl) was supplied by Sigma Chemical Co. and used without further purification. The chloride was converted when necessary into the nitrate form by means of an ion-exchange column. Solutions of the required pH were made up from deoxygenated stock solutions of dopamine and of iron(III) (as nitrate nonahydrate, Merck) that contained calculated amounts of HNO_3 and KNO_3 to maintain the final ionic strength at 0.100 mol dm^{-3}. Some experiments were carried out with KCl or KBr as supporting electrolyte as well as various nitrate–halide mixtures. In order to investigate the dependence on ionic strength of these reactions, various salts of Li^+, Na^+, K^+ and Mg^{2+} were used. The pH was measured immediately after each kinetic run with a WTW pH 521 pH meter and the $[H^+]$ was calculated by use of the empirical relationship[6] $[H^+] = 10^{-[(pH - 0.131)/0.984]}$. Since the iron concentration was kept low, the change of pH due to H^+ released on complex formation was negligible.

The appearance and the disappearance of the (green) complex were followed at 700 nm with a Bio-sequential SX-17MV sequential stopped-flow ASVD spectrofluorimeter, and yielded observed pseudo-first-order rate constants, k_1^{obs} and k_2^{obs} respectively. Similarly, the appearance and the disappearance of the quinone were followed at 380 nm. [All kinetic runs were performed with dopamine in large excess over iron(III) in order to maintain pseudo-first-order kinetics.]

Results and Discussion

Complex formation

Above pH 1.8 the formation reaction of the complex between iron(III) and dopamine is accurately first order in both $[Fe]_T$ and $[L]_T$, but at lower pH the rate varies with, but is not first order in $[L]_T$. This behaviour has been found for the closely related catecholamines adrenaline and dopa [3-(3,4-dihydroxyphenyl)-L-alanine][3,7] and arises from reversibility of the reaction (as is explained below).

Typical first-order rate constants, k_1^{obs}, for complex form-

Table 1 Typical values of k_1^{obs}

$[L]_T$/mol dm^{-3}	pH	$10^3[H^+]$/mol dm^{-3}	$10^5[Fe]_T$/mol dm^{-3}	k_1^{obs}/s^{-1}	$k_1^{obs}/[H^+]$	$[L]_T/[H^+]^2$
0.01	0.79	186	50	4.53	24.4	0.289
	0.98	120	10	3.13	26.1	0.694
	1.00	115	25	2.40	20.9	0.756
	1.10	91.2	10	2.65	29.1	1.20
	1.21	70.8	25	2.05	29.0	1.99
	1.24	66.1	10	2.11	31.9	2.29
	1.27	61.7	50	1.78	28.8	2.63
	1.31	56.2	5	1.55	27.6	3.17
	1.46	39.8	25	1.66	41.7	6.31
	1.50	36.3	10	1.66	45.7	7.59
	1.68	24.0	50	1.78		
	1.75	20.4	10	2.01		
	2.00	11.5	10	2.48		
	2.13	8.51	50	3.55		
	2.37	4.90	100	5.75		
0.02	0.98	120	10	3.26	27.2	1.39
	1.23	67.6	10	2.51	37.1	4.38
	1.36	50.1	100	2.44	48.7	7.97
	1.48	38.0	10	2.55	67.1	13.9
0.04	1.23	67.6	10	3.45	51.0	8.75
	1.38	47.9	10	3.99	83.3	17.4
	1.40	45.7	50	3.76	82.3	19.2
	1.46	39.8	50	4.09	102	25.3
	1.49	37.2	10	4.30	116	28.9

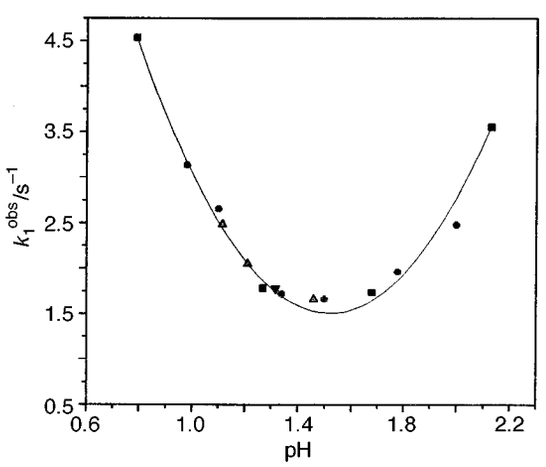


Fig. 1 Variation with pH of the observed rate constants, k_1^{obs}, for the formation of the iron(III)–dopamine complex ($[L]_T = 0.01$ mol dm^{-3}, various $[Fe]_T$ values). Data from Table 1

ation are given in Table 1 and illustrated in Fig. 1. The plot of k_1^{obs} *vs.* pH (Fig. 1) shows that the rate passes through a distinct minimum at a pH of about 1.5. The acceleration with decreasing $[H^+]$ at higher pH is the result of $Fe(OH)^{2+}$ being far more reactive than Fe^{3+} [equation (1) shows the relationship between

$$Fe(OH)^{2+} + H^+ \rightleftharpoons Fe^{3+}; \quad \log K^{FeOH} = 2.82 \qquad (1)$$

these two species and the value[8,9] of $K^{FeOH} = 660$ dm^3 mol^{-1}] and to explain the opposite effect at lower pH it is necessary to take reversibility into account. The complex is formed according to reaction (2). Note that 'proton ambiguity' is involved

$$Fe(OH)^{2+} + H_2LH^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Fe(LH)^{2+} + H^+ \text{ or } [Fe(HLH)^{3+}] \qquad (2)$$

here and implies that the reaction of Fe^{3+} with HLH would equally well fit the data, but this would lead to an improbably high value for the rate constant (*ca.* 10^{11} dm^3 mol^{-1} s^{-1}). This restriction would not apply, of course, if the reactions were parallel, but the data strongly suggest that any contribution from the reaction of Fe^{3+} with HLH must be extremely small and this conclusion is reinforced by the dependence of the rate on ionic strength (see below).

At the pH under consideration, the observed rate law can, therefore, be written as in equation (3), where the subscript eq

$$d[\text{coloured complex}]/dt = k_1^{obs}([Fe]_{T,o} - [Fe]_{T,eq}) \qquad (3)$$

$$= k_1[Fe(OH)^{2+}][H_2LH^+] - k_{-1}[Fe(HL)^{2+}][H^+] \qquad (4)$$

implies the value of the quantity at equilibrium. Application of equilibrium (2) then leads to equation (4). The total uncomplexed iron(III), $[Fe]_T$, is given by equation (5), and the equilibrium condition (6) must also be valid.

$$[Fe]_T = [Fe^{3+}] + [Fe(OH)^{2+}] \qquad (5)$$

$$k_1/k_{-1} = [Fe(LH)^{2+}]_{eq}[H^+]/[Fe(OH)^{2+}]_{eq}[H_2LH^+] \qquad (6)$$

However, since (*i*) $[Fe(LH)^{2+}]_{eq} = ([Fe]_{T,o} - [Fe]_{T,eq})$, (*ii*) dopamine is used in great excess giving $[H_2LH^+] \approx [L]_T$ and (*iii*) only those data obtained below pH ≈ 1.6 are considered, then $K^{FeOH}[H^+] \gg 1$ and equation (6) becomes (7). Inserting this

$$[Fe]_{T,eq} = k_{-1}K^{FeOH}[H^+]^2[Fe]_{T,o}/(k_1[L]_T + k_{-1}K^{FeOH}[H^+]^2) \qquad (7)$$

result and the above assumptions into the rate law leads, after comparison with the observed rate law (3), to equation (8).

$$k_1^{obs} = (k_1/K^{FeOH})([L]_T/[H^+]) + k_{-1}[H^+] \qquad (8)$$

Thus a plot of $k_1^{obs}/[H^+]$ *vs.* $[L]_T/[H^+]^2$ should be linear with intercept corresponding to k_{-1} and a slope of k_1/K^{FeOH}. This is illustrated in Fig. 2 and, using $K^{FeOH} = 660$ dm^3 mol^{-1}, yields the results $k_1 = (2.09 \pm 0.05) \times 10^3$ dm^3 mol^{-1} s^{-1} and $k_{-1} = 23 \pm 2$ dm^3 mol^{-1} s^{-1}. The ratio k_1/k_{-1}, thus enables the stability constant for the formation of $Fe(LH)^{2+}$ to be calculated from the relationship $K_1^M = k_1\beta_2^H/k_{-1}K^{FeOH}$ (where β_2^H is the micro-

Table 2 Variation of k_1^{obs} with [Cl^-] (pH 1.27, $[L]_T = 0.01$ mol dm^{-3})

$[Cl^-]$/mol dm^{-3}	0.025	0.030	0.0325	0.045	0.0575	0.100
k_1^{obs}/s^{-1}	3.60	4.09	4.14	5.32	6.12	9.44

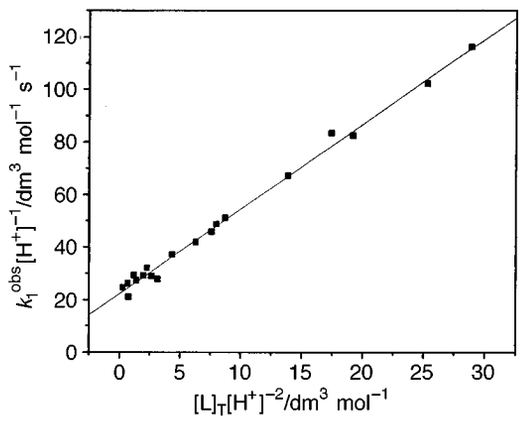


Fig. 2 Plot of $k_1^{obs}/[H^+]$ *vs.* $[L]_T/[H^+]^2$ for values obtained below pH 1.5 (data from Table 1)

constant for the protonation of the phenolic groups of the dopamine; the value log $\beta_2^H = 22.00$ was used). A value of log $K_1^M = 21.14$ was obtained, and accepting this value enabled the molar absorption, $\varepsilon_{max} = 1260$ dm^3 mol^{-1} cm^{-1} at 700 nm, to be calculated.

Effect of chloride ions on the rate of complex formation. At pH values below 1.5 the presence of chloride ions has a marked effect on the rate of complex formation. The results in Table 2 show clearly that the rate constant, k_1^{obs}, is directly proportional to [Cl^-]. Furthermore, when expression (8) is applied to data obtained in chloride media the rather surprising result is obtained that k_1 is unaffected, whereas the reverse reaction, represented by k_{-1}, is apparently proportional to [Cl^-]. This effect can be explained by assuming that the species $FeCl^{2+}$ is also able to react with H_2LH^+, equation (9), and since (9) is

$$FeCl^{2+} + H_2LH^+ \overset{k_{Cl}}{\rightleftharpoons} Fe(LH)^{2+} + Cl^- + 2H^+ \quad (9)$$

predominantly reversible *via* the non-chloride route at low pH values [equation (2)], resulting in the apparent effect of chloride ions of exclusively enhancing the reverse reaction.

The increase of k_1^{obs} with increased reverse reaction is a result of the mathematical behaviour of reverse first-order reactions for which $k_1^{obs} = k_1 + k_{-1}$.[10] Allowance must also be made for the fact that $[Fe]_T$ must now be written as in equation (10). By neglecting the value of $[Fe(OH)^{2+}]$ with respect to

$$[Fe]_T = [Fe^{3+}] + [FeCl^{2+}] + [Fe(OH)^{2+}] \quad (10)$$

$[FeCl^{2+}]$, equation (10) becomes (11) where K_1^{Cl} is the formation

$$[Fe]_T = [Fe^{3+}] + [FeCl^{2+}] = [Fe^{3+}](1 + K_1^{Cl}[Cl^-]) \quad (11)$$

constant for $FeCl^{2+}$. Thus, in the presence of chloride, equation (8) must be replaced by (12). Plots of k_{Cl}^{obs} *vs.* $[L]_T$ at constant

$$k_{Cl}^{obs} = k_1[L]_T/\{(1 + K_1^{Cl}[Cl^-])K^{FeOH}[H^+]\} + k_{-1}^{Cl}[H^+] + k_{Cl}K_1^{Cl}[Cl^-][L]_T/(1 + K_1^{Cl}[Cl^-]) \quad (12)$$

$[Cl^-]$ and $[H^+]$ should be linear and this is confirmed by Fig. 3 and Table 3, in which data for several $[H^+]$ values with $[Cl^-] = 0.05$ mol dm^{-3} are presented. These plots have intercepts = k_{-1}^{Cl} $[H^+]$ from which a mean value of $k_{-1}^{Cl} = 62$ dm^3 mol^{-1} s^{-1} was obtained and since $k_{-1}^{Cl} = k_{-1}(1 + K_1^{Cl}[Cl^-])$, K_1^{Cl}

Table 3 Values of k_{Cl}^{obs} for $[Cl^-] = 0.05$ mol dm^{-3}

pH	$10^3[H^+]$/mol dm^{-3}	$[L]_T$/mol dm^{-3}	k_{Cl}^{obs}/s^{-1}
1.07	97.7	0.005	6.28
		0.01	6.91
		0.02	8.33
		0.04	10.2
1.16	79.4	0.005	5.38
		0.01	5.91
		0.02	7.56
		0.04	—
1.30	57.5	0.005	4.18
		0.01	4.62
		0.02	5.65
		0.04	—
1.43	42.7	0.005	3.19
		0.01	3.72
		0.02	5.14
		0.04	7.22

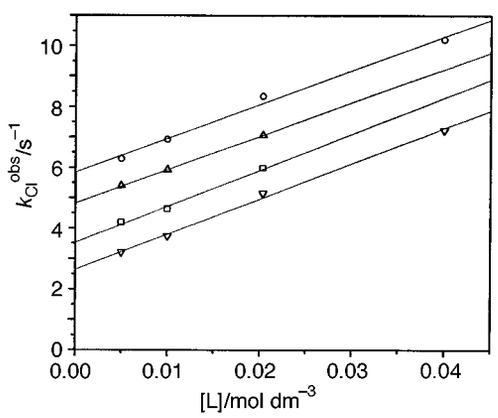


Fig. 3 Plots of k_{Cl}^{obs} *vs.* $[L]_T$ for $[Cl^-] = 0.05$ mol dm^{-3} and $10^3[H^+] =$ 97.7 (○), 79.4 (△), 57.5 (□) and 42.7 (▽) mol dm^{-3} (data from Table 3)

(the formation constant for $FeCl^{2+}$) is 34 dm^3 mol^{-1}, *i.e.* log $K_1^{Cl} = 1.53$. This constant is extremely difficult to obtain by other methods and the literature values vary over a vast range, but kinetically obtained values of stability constants are, in general, very reliable. The rate constant, k_{Cl}, for the reaction of $FeCl^{2+}$ with H_2LH^+ was obtained from the slopes of these lines {slope = $(k_1/K^{FeOH}[H^+] + k_{Cl}K_1^{Cl}[Cl^-])/(1 + K_1^{Cl}[Cl^-])$ for each $[H^+]$}: a mean value of 148 ± 7 dm^3 mol^{-1} s^{-1} was accepted.

The addition of bromide ions. Unlike chloride ions, bromide had no discernible effect on the rate.

Electron transfer in the coloured complex

The rate of decomposition of $Fe(LH)^{2+}$ passes through a minimum with pH ($pH_{min} \approx 1.8$), is independent of $[L]_T$ at lower pH, and independent of $[Cl^-]$. Now the rate of disappearance of the coloured complex monitors the rate of disappearance of $[Fe]_T$ and is therefore given by equation (13), and typical values of k_2^{obs} for pH < 1.75 are given in Table 4.

$$-d[\text{coloured complex}]/dt = -d[Fe]_T/dt = k_2^{obs}[Fe]_T \quad (13)$$

Since k_2^{obs} increases with decrease in pH it can be assumed that it is the protonated complex, $Fe(HLH)^{3+}$, that is the reactive species. In this respect it is interesting that there is X-ray spectroscopic evidence that protonated catechols act as monodentate ligands towards iron(III),[11] while deprotonated ones chelate.[12] The complex $Fe(LH)^{2+}$ can be protonated, yielding $Fe(HLH)^{3+}$, in which the dopamine presumably acts as a mono-

Table 4 Typical values of k_2^{obs} for pH < 1.75

pH	$10^3[H^+]$/mol dm^{-3}	$10^5[Fe]_T$/mol dm^{-3}	$[L]_T$/mol dm^{-3}	$10^2\ k_2^{obs}$/s^{-1}	(1/2 k_2^{obs})/s	$[H^+]^{-1}$/dm^3 mol^{-1}
1.20	72.4	25	0.02	8.04	6.22	13.8
1.38	47.9	10	0.01	6.94	7.20	20.9
1.39	46.7	10	0.04	6.43	7.78	21.8
1.43	42.7	5	0.02	6.76	7.40	23.4
1.53	33.9	10	0.02	6.03	8.29	29.5
1.62	27.5	10	0.01	5.63	8.88	36.5
1.71	22.4	5	0.04	4.91	10.2	44.2

dentate ligand, and electron transfer takes place within this protonated complex.

Furthermore, the decomposition of the coloured complexes can be treated assuming that they are formed in a rapid pre-equilibrium since the ratio $k_1^{obs}:k_2^{obs}$ was at least 50:1, *i.e.* the reaction can be written as in equation (14). Since the

$$Fe(OH)^{2+} + H_2LH^+ \rightleftharpoons Fe(LH)^{2+} + H^+ \xrightarrow{k_2} Fe^{II} + \text{semiquinone} \quad (14)$$

equilibrium constant is very large, it is $k_2[Fe(HLH)^{3+}]$ that is being followed and hence the rate equation becomes (15) in

$$-d[FeL]_T/dt = k_2[Fe(HLH)^{3+}] \quad (15)$$

which the total concentration of complex, $[FeL]_T$, is given by (16) in which the protonation constant $K_M^H = [Fe(HLH)^{3+}]/[Fe(LH)^{2+}][H^+]$. Introducing equation (16) into (15) yields (17).

$$[FeL]_T = [Fe(HLH)^{3+}] + [Fe(LH)^{2+}] = [Fe(HLH)^{3+}](1 + K_M^H[H^+])/K_M^H[H^+] \quad (16)$$

$$-d[FeL]_T/dt = k_2K_M^H[H^+]/(1 + K_M^H[H^+])[FeL]_T \quad (17)$$

The semiquinone produced, however, reacts rapidly with another Fe^{3+} to yield the quinone and Fe^{2+} making $d[Fe]_T/dt = 2d[FeL]_T/dt$ and hence expressions (18) and (19) follow. Thus a

$$2k_2^{obs} = k_2K_M^H[H^+]/(1 + K_M^H[H^+]) \quad (18)$$

$$1/2k_2^{obs} = (1/k_2K_M^H[H^+]) + (1/k_2) \quad (19)$$

plot of $1/2k_2^{obs}$ *vs.* $1/[H^+]$ has slope $1/k_2K_M^H$ and intercept $1/k_2$. From this plot $k_2 = 0.23 \pm 0.02$ s^{-1} and $k_2K_M^H = 7.56 \pm 0.1$ dm^3 mol^{-1} s^{-1} which yields $K_M^H = 33 \pm 0.9$ dm^3 mol^{-1}. This value of $k_2K_M^H$ is identical to that obtained (using high pH data) for the dopa system[3] and shows that the redox potentials for the reduction of dopa and of dopamine to the respective semiquinones must be almost identical. These one-electron redox potentials have been shown[13] to have identical values of 18 mV, calculated by using the value of hydroquinone as a reference.

In a parallel study of the noradrenaline–iron(III) system[14] there is evidence for a small outer-sphere contribution to the redox reaction at low pH [*vis-à-vis* $Fe(OH)^{2+}$ reacting with H_2LH^+ to yield directly iron(II) and semiquinone]. However, it has not been possible to confirm any such effect in the dopamine–iron(III) system, although from the data obtained it certainly cannot be ruled out entirely.

Ionic strength effects

The kinetic salt effect on two reacting species A and B with charges z_a and z_b respectively can be expressed in terms of the Brønsted relationship (20) in which the constant A is 0.51 for aqueous solutions at 25 °C.

$$\log k = \log k_0 + 2Az_az_bI^{\frac{1}{2}} \quad (20)$$

Table 5 Variation of log (k/k_0) with ionic strength (pH 1.50, $[L]_T = 0.04$ mol dm^{-3})

Salt	I/mol dm^{-3}	$I^{\frac{1}{2}}$/ mol$^{\frac{1}{2}}$ dm$^{-\frac{3}{2}}$	log ($k_1^{obs}/k_{1,0}^{obs}$)	log ($k_2^{obs}/k_{2,0}^{obs}$)
LiCl	0.30	0.55	1.21	−0.09
	0.40	0.63	1.26	0.05
	0.50	0.71	1.43	0.06
	0.60	0.77	1.55	0.17
	0.80	0.89	1.76	0.17
	1.00	1.00	2.04	0.02
NaCl	0.30	0.55	1.09	0.11
	0.40	0.63	1.22	0.19
	0.50	0.71	1.41	0.23
	0.60	0.77	1.49	0.12
	0.80	0.89	1.85	0.12
	1.00	1.00	1.93	0.09
KNO_3	0.25	0.5	1.01	−0.15
	0.35	0.59	1.12	−0.09
	0.45	0.67	1.36	0.01
	0.55	0.74	1.37	0.03
	0.75	0.87	1.70	0.05
	0.95	0.97	1.75	0.15
$MgCl_2$	0.75	0.87	1.75	0.15
	1.05	1.02	2.19	0.11
	1.35	1.16	2.22	0.14
	1.65	1.28	2.55	0.25
	2.25	1.50	3.01	0.27
	2.85	1.69	3.34	0.31

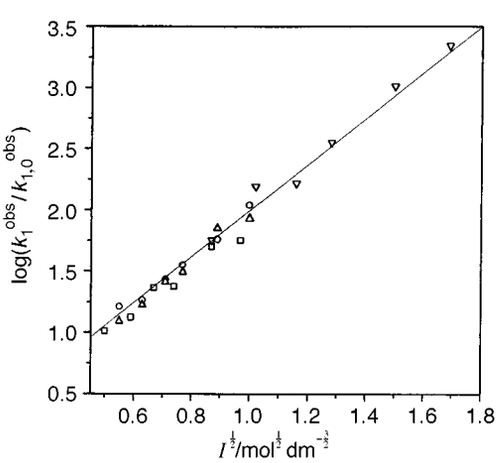


Fig. 4 Plot of log $(k_1^{obs}/k_{1,0}^{obs})$ *vs.* $I^{\frac{1}{2}}$ showing that $z_az_b = 2$ [see Table 5 and equation (19)]. Salts: ○, LiCl; △, NaCl; □, KNO_3; ▽, $MgCl_2$; theoretical line of slope 2.04

Both k_1^{obs} and k_2^{obs} were measured over a range of ionic strengths using a variety of salts and Table 5 gives some values of log $(k_1^{obs}/k_{1,0}^{obs})$ obtained. A plot of log $(k_1^{obs}/k_{1,0}^{obs})$ *vs.* $I^{\frac{1}{2}}$ is shown in Fig. 5 and is seen to correspond satisfactorily with the theoretical slope of 2.04 for $z_az_b = +2$ which is consistent with the formulation of the formation and reverse reactions (4) and (9). Table 5 also includes values of log $(k_2^{obs}/k_{2,0}^{obs})$ and it is seen

that these vary little with $I^{\frac{1}{2}}$ which confirms the postulate of $Fe(HLH)^{2+}$ reacting alone (or involving the participation of a solvent, *i.e.* water, molecule?).

Formation of the indole ring

The quinones of catecholamines such as dopamine spontaneously cyclise *via* an internal Michael addition to form the UV-transparent leucodopaminochrome (indoline-5,6-diol) (see Scheme 1). The kinetics of this cyclisation reaction for dopamine was followed by monitoring the quinone at 380 nm. Unfortunately this was only possible up to a pH of about 3, at which point the absorption of the iron(III) complexes begins to interfere. However, work in these laboratories[15] has shown that the quinone can be produced at higher pH by using periodate as the oxidant enabling measurements up to a pH of 7.

The rate of disappearance of the quinone follows the rate law (21) and typical results are summarised in Table 6 and

$$-d[Q]_T/dt = k_3^{obs}[Q]_T \quad (21)$$

illustrated in Fig. 6 [which also includes the results for the iron(III)–dopa system[3] for comparison purposes, see below]. The results strongly suggest that two quinone species are involved, one being protonated [equation (22)]. This must imply that protonation *of the quinone function* takes place at low pH. We further assume that deprotonation at the amino site is a requirement for cyclisation, and because the protonation constant of this functional group is very high [$\log K_N^H = \log(k_a/k_{-a}) = 9.95$] this (deprotonation) step is relatively slow and must be taken into account. These ideas are summarised in Scheme 2.

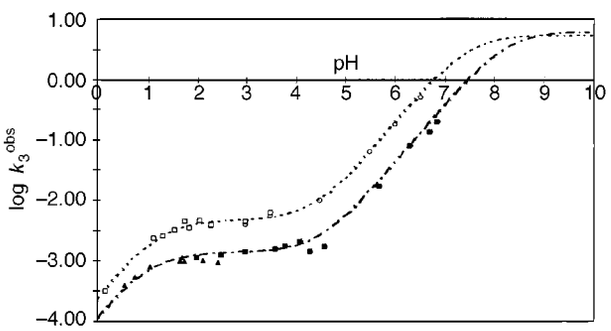


Fig. 5 Observed rates of cyclisation of dopaminoquinone (log k_3^{obs} *vs.* pH) with theoretical curve (derivation in text): ▲, values from Fe^{3+} oxidation; ■, oxidation with periodate (see Table 6). The theoretical curve for dopa (----) is included for comparison

Table 6 Typical values for the observed rate constants, k_3^{obs}, for indole formation (ring-closure reaction) following oxidation of the dopamine to the quinone

Using Fe^{3+} as oxidant		Using periodate as oxidant	
pH	$-\log k_3^{obs}$	pH	$-\log k_3^{obs}$
0.55	3.27	2.0	2.95
0.75	3.27	2.5	2.90
1.06	3.10	3.0	2.85
1.66	3.01	3.6	3.31
1.71	2.95	3.8	2.76
1.75	3.01	4.1	2.68
2.14	2.99	4.3	2.85
2.45	3.03	4.6	2.77
		5.7	1.77
		6.3	1.10
		6.7	0.88
		6.85	0.24

The experimental results can be interpreted on the basis of Scheme 2 and the associated equations (22) and (23). Under

$$-d[Q]_T/dt = k_{cyc}[Q] + k_{cyc}^H[HQ^+] \quad (22)$$

$$= (k_{cyc} + k_{cyc}^H K_Q^H[H^+])[Q] \quad (23)$$

reaction conditions [Q] will reach a steady state, equation (24)

$$d[Q]/dt = 0 = k_{-a}[QH^+] - k_a[Q][H^+] - k_{cyc}[Q] \quad (24)$$

or (25). However, the total quinone concentration, $[Q]_T$, is given

$$[Q] = [QH^+]/\{K_N^H[H^+] + (k_{cyc}/k_{-a})\} \quad (25)$$

by equation (26) and the combination of (23), (25) and (26)

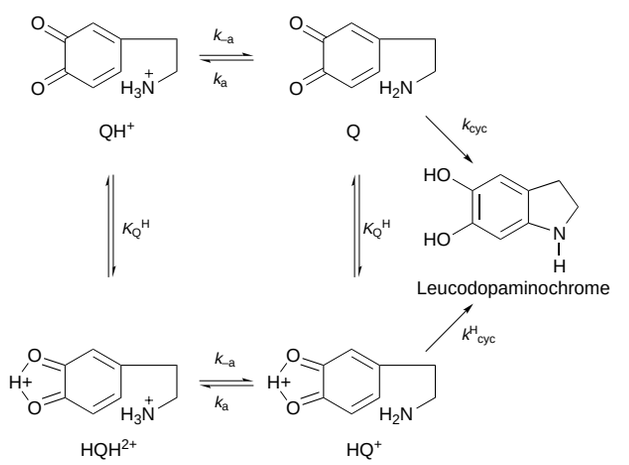
$$[Q]_T = [QH^+] + [HQH^{2+}] = [QH^+](1 + K_Q^H[H^+]) \quad (26)$$

and comparison with (21) leads to (27). The solution of

$$k_3^{obs} = (k_{cyc} + k_{cyc}^H K_Q^H[H^+])/\{(K_N^H[H^+] + k_{cyc}k_{-a}^{-1})(1 + K_Q^H[H^+])\} \quad (27)$$

equation (27) enables values of k_{cyc}, k_{cyc}^H, and K_Q^H to be obtained and these are given in Table 7.

Linert *et al.*[3] in their study of the iron(III)–dopa system had previously ascribed the protonation of the dopaquinone to protonation of the carboxyl group and therefore *assigned* the value



Scheme 2 Details of ring-closure reaction

Table 7 Comparison of results obtained for dopamine and dopa systems

(*a*) Oxidation of the catecholamines

	$\log K_N^H$	$\log \beta_2^H$	$\log K_1^M$	k_1/s^{-1}	k_{-1}/s^{-1}	k_2/s^{-1}	$k_2K_M^H/dm^3\ mol^{-1}\ s^{-1}$
Dopamine	9.95	22.00	21.14	2094	23	0.23	7.56
dopa	9.20	22.20	21.43	2100	22	0.3	7.52

(*b*) Formation of leucoaminochrome from quinone (ring-closure reaction)

	k_{-a}/s^{-1}	$\log K_Q^H$	k_{cyc}/s^{-1}	k_{cyc}^H/s^{-1}
Dopaminequinone	6.33	1.04	3.48×10^2	1.12×10^6
Dopaquinone	5.42	1.13	3.16×10^2	5.51×10^5

$10^{2.22}$ dm^3 mol^{-1} to K_Q^H (*i.e.* identifying K_Q^H with K_4^H for dopa). In the light of the present work this assignment is obviously erroneous and so Table 7 includes the results for the dopa system recalculated by the same method employed here: the agreement between the two (chemically very similar) systems is highly satisfactory. Reference to equation (27) shows that the displacement of the two log k_3^{obs} *vs.* pH curves for dopa and dopamine (Fig. 6) arises almost exclusively from the differences in the protonation constants for the respective amino groups. Furthermore, Linert *et al.*[3] had not allowed for the reverse reaction of complex formation in their calculation of k_1; this has now been done in Table 7 by using their published data at low pH.

Finally, the close correspondence between the dopa and dopamine systems is emphasised by Table 7 in which the present results for the formation of the coloured complexes and their subsequent redox decomposition are contrasted with those obtained for the interaction of iron(III) with dopa.

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