A Kinetic Study of the Anaerobic Reactions Between Adrenaline and Iron(III)

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Iron(III) reacts reversibly in aqueous acid with adrenaline [epinephrine, L-1-(3,4-dihydroxyphenyl)-2-(methylamino)ethanol, H_2LH^+] to give $FeLH^{2+}$ and $FeHLH^{3+}$. Both species decompose to yield iron(II) and the semiquinone, which in turn is oxidised further to the quinone. The latter cyclises to form leucoadrenochrome, which is finally oxidised by iron(III) to adrenochrome presumably *via* a semiquinone. The rate of appearance and disappearance of the complexes, quinone, and adrenochrome could be followed by stopped-flow photometric methods. Mechanisms are proposed for the various steps, rate constants evaluated, and the reversibility of the various redox steps discussed. These mechanisms are compared and contrasted with those of the analogous reactions between iron(III) and L-3-(3,4-dihydroxyphenyl)alanine.

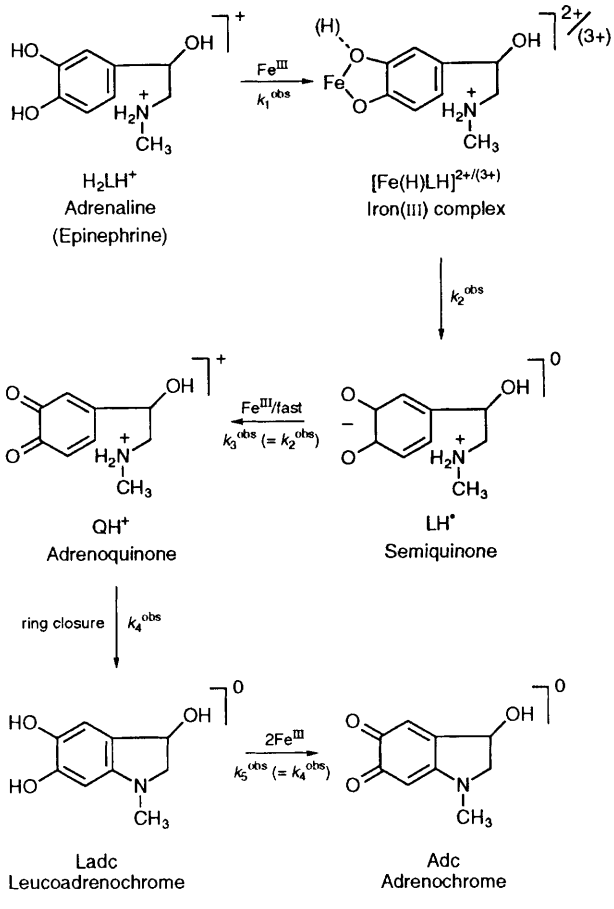
Brightly coloured complexes of catechols with iron(III) are well known and often used as qualitative analytical tests. In acid solution, however, the colours are not stable and slowly fade.[1,2] This can be ascribed to an internal electron transfer within the complexes that yields iron(II) and the respective semiquinone, which is unstable with respect to further oxidation to the quinone. The quinones of the catecholamines, however, are able to react further[3,4,5] *via* an internal Michael addition by which indole compounds are formed. These again contain a potentially complexing and oxidisable catechol function, which leads, in the case of adrenaline, to the formation of the bright red adrenochrome. How this is related to the present work is summarised in Scheme 1 in which the observed rate constants for each stage, k_n^{obs}, are depicted and any equalities noted.

In a previous paper[3] we investigated the analogous reactions of dopa [L-3-(3,4-dihydroxyphenyl)alanine] with iron(III) as oxidant. These investigations were made feasible by the fact that the complexes and the quinone absorbed at different wavelengths and the rate constants of complex formation and decomposition differed by a factor of 100. However, the overall product formation and detailed kinetics differ in some important aspects in the case of adrenaline.

Terminology.—In addition to the abbreviations noted in Scheme 1, the following terminology is employed throughout this paper.

$[Fe]_T$ = total concentration of unreacted iron(III)
$[L]_T$ = total ligand (adrenaline) concentration

Subscripts $_0$ and $_\infty$ are used to indicate initial and equilibrium values respectively. Solvating water molecules are not given in chemical equations.



Scheme 1

Experimental

Solutions of the required final pH were made up from deoxygenated stock solutions of adrenaline (free base supplied by Fluka, p.a.) and of iron(III) (as nitrate nonahydrate, Merck p.a.) that contained calculated amounts of HNO_3 and sufficient KNO_3 to maintain the final ionic strength at 0.10 mol dm^{-3}. Some experiments were also carried out with KCl as supporting electrolyte. The pH was measured immediately after each kinetic run and $[H^+]$ was calculated by the empirical relationship[7] $[H^+] = 10^{-[(pH-0.131)/0.982]}$. Since the iron concentration is well below 6×10^{-4} mol dm^{-3}, the changes of pH due to the released H^+ are negligible.

Kinetic data were obtained, for the visible spectra, with a Tracor Northern TN-1710 Multichannel Storage Unit, supplied by Applied Photophysics, Ltd. (London), and, for the spectra in the near UV-range, with an SF-3 instrument by Hi-Tech Scientific (Salisbury) coupled with a 514A transient recorder (Physical data inc., Portland). The appearance and disappearance of the green complex yielded the observed pseudo-first order rate constants k_1^{obs} and k_2^{obs}, respectively, as the

Table 1 Typical rate constants for complex formation (k_1^{obs}) of adrenaline with iron(III) and subsequent decomposition (k_2^{obs}), followed at 714 nm

pH	$10^2[H^+]$/mol dm^{-3}	$10^4[Fe]_T$/mol dm^{-3}	$10^2[L]_T$/mol dm^{-3}	k_1^{obs}/s^{-1}	$10^2k_2^{obs}$/s^{-1}
1.08	10.8	2.28	0.510	2.49	0.53
1.16	8.96	2.31	0.515	2.02	0.76
1.24	7.42	2.23	0.253	1.62	0.41
1.32	6.15	2.27	0.515	1.49	0.91
1.37	5.47	2.28	0.510	1.27	1.16
1.37	5.47	4.74	0.510	1.31	1.36
1.55	3.59	2.26	0.258	1.08	0.87
1.62	3.05	2.25	0.255	0.88	0.85
1.74	2.30	2.24	0.510	1.03	1.47
2.42	0.47	2.21	0.432	1.39	1.11

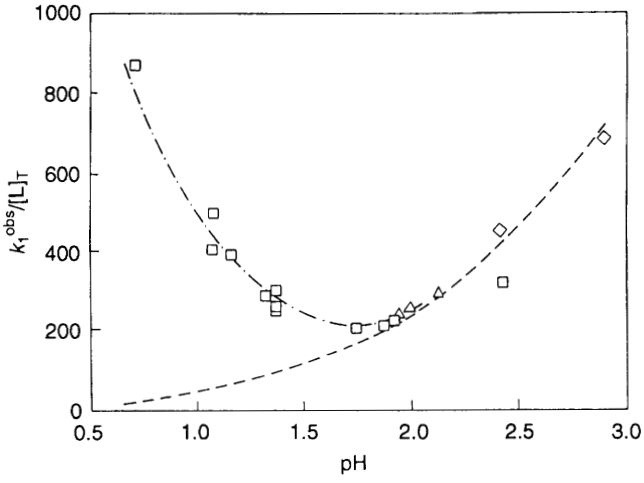


Fig. 1 Observed rate constants for the formation of the complex between iron(III) and adrenaline (k_1^{obs}) as a function of pH: (◇), $[L]_T$ = 1.7 × 10^{-3}; (Δ), $[L]_T$ = 3.3 × 10^{-3}; (□), $[L]_T$ = 5.0 × 10^{-3} mol dm^{-3}; ($[Fe]_T$ = 2.29 × 10^{-4} mol dm^{-3}). Theoretical curves are constructed from data given in the text. (- - -) Forward reaction alone; (- · · -) including back reaction.

appearance and the disappearance of the brown adrenoquinone gave k_3^{obs} and k_4^{obs}, respectively. The formation of the bright red adrenochrome yielded k_5^{obs}. The spectroscopic maxima used in this work are given in the Results and Discussion section under *Electronic Spectra*.

All kinetic runs were performed with adrenaline in great excess over iron(III) in order to work with pseudo (first)-order kinetics. The pH was measured with a Radiometer PHM-84 Research pH-meter.

Results and Discussion

Electronic Spectra.—From the primary absorption data it can be concluded that over the pH range 0.5–3.0 two complexes of iron(III) are formed with adrenaline, a protonated ($FeHLH^{3+}$) and an unprotonated species ($FeHL^{2+}$) with a protonation constant (1) of 75 mol dm^{-3} (log K_M^{H} = 1.75) whose

$$FeLH^{2+} + H^+ \overset{K_M^H}{\rightleftharpoons} FeHLH^{3+} \qquad (1)$$

spectra are virtually identical with those obtained using dopa as ligand.[3] The spectral characteristics of the iron(III) complexes with adrenaline and the quinone are as follows, with those for the corresponding dopa-compounds given in parentheses: For $FeLH^{2+}$, maxima at 453 (442) and at 714 (700) nm; ε_{714} = 1410 (ε_{700} = 1380) dm^3 mol^{-1} cm^{-1}. For $FeHLH^{3+}$, maxima at 421 (443) and at 673 (660) nm occur; $\varepsilon_{673} \approx 200$ (ε_{660} = 320) dm^3 mol^{-1} cm^{-1}. The quinone absorbs at 380 (385) nm, with a shoulder at 455 (458) nm; ε_{380} = 1670 (ε_{385} = 1650) dm^3 mol^{-1} cm^{-1}. Adrenochrome absorbs at 480 nm, ε_{480} = 3660 dm^3 mol^{-1} cm^{-1}.[6]

Complex Formation.—Typical first order rate constants, k_1^{obs}, for complex formation are given in Table 1 and presented graphically in Fig. 1. The kinetics of complex formation are independent of the relative concentrations of $FeLH^{2+}$ and for $FeHLH^{3+}$ thus suggesting the same route [*i.e.* $Fe(OH)^{2+}$ reacting with H_2LH^+] for the formation of both species, the subsequent loss or otherwise of a proton determining the final product [see eqn. (3), below].

Fig. 1 shows that the rate passes through a distinct minimum at pH *ca.* 1.8. Bearing in mind that $Fe(OH)^{2+}$ is far more reactive than Fe^{3+}, one can easily understand the acceleration with decreasing $[H^+]$ at higher pH [eqn. (2)]. To explain the

$$Fe(OH)^{2+} + H^+ \overset{K^{MOH}}{\rightleftharpoons} Fe^{3+} \qquad \log K^{MOH} = 2.28 \quad (2)$$

opposite effect at lower pH and the fact that the rate of complex formation becomes independent of the total adrenaline concentration, $[L]_T$, means that it is necessary to take reversibility into account. Therefore it is proposed that both complexes are formed according to reaction (3). Note that the

$$Fe(OH)^{2+} + H_2LH^+ \overset{k_1}{\rightleftharpoons} FeLH^{2+} + H^+ \quad (\text{or } FeHLH^{3+}) \qquad (3)$$

proton ambiguity involved here 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} mol^{-1} dm^3 s^{-1}). However, this restriction would not apply if the reactions were in parallel, but the data strongly suggest that any contribution from the reaction of Fe^{3+} with HLH must be extremely small (and indeed was shown to be negligible in the case of dopa[3]).

At the pHs under consideration, the total uncomplexed iron(III) is given by eqn. (4), and the observed rate law can be

$$[Fe]_T = [Fe^{3+}] + [Fe(OH)^{2+}] \qquad (4)$$

written as eqn (5), whereas, in terms of reaction (3) the rate expression is eqn. (6).

$$d[\text{coloured complex}]/dt = k_1^{obs}([Fe]_{T,0} - [Fe]_{T,\infty}) \qquad (5)$$

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

The equilibrium condition (7) must also be valid, and since (i) $[FeLH^{2+}]_\infty = ([Fe]_{T,0} - [Fe]_{T,\infty})$, (ii) adrenaline is used in great excess giving $[H_2LH^+] = [L]_T$ and at these low pH values it may be assumed (iii) that $K^{MOH}[H^+] \gg 1$, the equilibrium condition (7) reduces to (8). Inserting this result and

the above assumptions into the rate law leads, after comparison with the observed rate law (5), to eqn. (9).

$$k_1/k_{-1} = [FeLH^{2+}]_\infty[H^+]/[Fe(OH)^{2+}]_\infty[H_2LH^+] \quad (7)$$

$$[Fe]_{T,\infty} = k_{-1}K^{MOH}[H^+]^2[Fe]_0/\{k_1[L]_T - k_{-1}K^{MOH}[H^+]^2\} \quad (8)$$

$$k_1^{obs}K^{MOH}[H^+] = k_1[L]_T + k_{-1}K^{MOH}[H^+]^2 \quad (9)$$

At low $[H^+]$, $k_1[L]_T \gg k_{-1}K^{MOH}[M^+]^2$, and the rate thus reduces to eqn. (10), from which k_1 can be easily extracted by

$$k_1^{obs}/[L]_T = k_1/K^{MOH}[H^+] \quad (10)$$

using the data above pH 1.8, yielding a value of 3130 ± 95 $dm^3\ mol^{-1}\ s^{-1}$, which is in remarkable agreement with the corresponding constant for dopa[3] (3100) and catechol[8] (3100 $dm^3\ mol^{-1}\ s^{-1}$). Using eqn. (9), k_{-1} can be obtained by plotting $(k_1^{obs}K^{MOH}[H^+] - k_1[L]_T)$ *vs.* $[H^+]^2$, yielding 17.3 ± 1.5 $dm^3\ mol^{-1}\ s^{-1}$. From k_1 and k_{-1} the formation constant K_1^M (= $[FeLH^{2+}]/[Fe^{3+}][LH^-]$) of $FeLH^{2+}$ can be evaluated, using $\log\beta_2^H = 21.94$ for adrenaline,[9] to give $\log k_1^M = 21.38$. This may be compared with a value obtained by potentiometric titration[10] of 20.5 (which, however, made no allowance for the electron transfer reaction) and a value of 20.64 for dopa.[3]

Electron Transfer in the Coordination Compounds.—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. In this respect, it is interesting to note that there is X-ray spectroscopic evidence that protonated catechols act as monodentate ligands towards iron(III),[11] whilst deprotonated ones are chelating.[12] This has been shown to be also valid in solution on the basis of electronic and NMR spectra.[13] That this could be relevant in our case is indicated by the fact that the shift between the absorption maxima of the protonated and the unprotonated catechol complexes[13] is the same as for the dopa complexes (namely *ca.* 40 nm).

At constant $[H^+]$ and $[L]_T$ the observed rate expression is given by eqn. (11) because the coloured complex here is acting as an indicator for total iron(III) by virtue of it being formed very much faster than it decomposes.

$$-\text{d[coloured complex]}/dt = k_2^{obs}[Fe]_T \quad (11)$$

Assuming that both complexes react according to reactions (12) leads to eqn. (13). The speciation of iron(III) is given by

$$FeLH^{2+} \xrightarrow{k_2} Fe^{II} + LH' \quad (12)$$

$$FeHLH^{3+} \xrightarrow{k_2^H} Fe^{II} + LH' + H^+$$

$$-\text{d[coloured complex]}/dt = k_2[FeLH^{2+}] + k_2^H[FeHLH^{3+}] \quad (13)$$

eqn. (14) and $[L]_T = [H_2LH^+]$, so that eqn. (13) can be

$$[Fe]_T = [Fe^{3+}] + [Fe(OH)^{2+}] + [FeLH^2] + [FeHLH^{3+}] = [Fe^{3+}]\{1 + 1/K^{MOH}[H^+] + K_1^M[L]_T/\beta_2^H[H^+]^2(1 + K_M^H[H^+])\} \quad (14)$$

expressed in terms of $[Fe]_T$ and $[L]_T$ and compared to eqn. (11) to give eqn. (15). The factor 2 on the left hand side (lhs) of eqn. (15) arises because the semiquinone is converted rapidly

$$2k_2^{obs}\beta_2^H[H^+]^2\{1 + 1/K^{MOH}[H^+] + K_1^M[L]_T/\beta_2^H[H^+]^2(1 + K_M^H[H^+])\}/K_1^M[L]_T = k_2 + k_2^HK_M^H[H^+] \quad (15)$$

(two free radicals) by another iron(III) to the quinone (see below).

When the lhs of expression (15) is plotted against $[H^+]$, a straight line is obtained with a small but definite intercept of *ca.* $10^{-3}\ s^{-1}$. However, this is considered not to be significant because it is highly dependent on the few high (> 2.5) pH values and it is felt safe to assume that the reaction occurs solely *via* protonation of $FeLH^{2+}$. The slope leads to a value of $k_2^H = (5.11 \pm 0.20) \times 10^{-2}\ s^{-1}$ compared with a reported[3] value of $0.3\ s^{-1}$ for dopa. However, this difference may not be real because of uncertainties in the equilibrium constants used to evaluate the rate constants. The equality of the (log) values of the products $K_1^MK_M^Hk_2^H$ (21.78 for adrenaline, 21.73 for dopa) confirm that the kinetics are identical up to this point. Thus, the relatively large difference between k_2^H for dopa and adrenaline could be due to the use of an incorrect value of K_1^M (which could not be kinetically determined in the case of dopa); this is being re-evaluated potentiometically.

Formation of the Quinone.—Table 3 contains some typical first order rate constants (k_3^{obs}) for quinone formation and it is readily ascertained that, as stated above, k_3^{obs} equals k_2^{obs} *i.e.* the rate determining step in the formation of the quinone is the initial electron transfer in the complex, implying that no information as to the actual rate of formation of the quinone from the semiquinone (*i.e.* k_3) can be ascertained by this method of studying the reaction. The subsequent oxidation of the semiquinone is fast, as one could have expected for radical–radical reactions; this is the same result that has been established in the case of dopa.[3] As illustrated in Scheme 2, the quinone, Q, subsequently cyclises to form leucoadrenochrome, Ladc.

Cyclisation.—Fig. 2 is a plot of $\log k_4^{obs}$ *vs.* pH with the addition of high pH-data obtained electrochemically by Hawley *et al.*[14] and Ball and Chen[15] and this is seen to resemble strongly the corresponding curve for the cyclisation of dopaquinone.[3]

It is therefore quite safe to assume the same kinetic scheme for adrenaline as for dopa, which is given in Scheme 2. The derivation of the rate law from this Scheme is as follows. The basic rate expression is eqn. (16) in which $[Q]_T = [QH^+] + [HQH^{2+}]$ and from Scheme 2 the rate eqn. (17) follows. Under

$$-\text{d}[Q]_T/dt = k_4^{obs}[Q]_T \quad (16)$$

$$-\text{d}[Q]_T/dt = k_4[Q] + k_4^H[HQ^+] = (k_4 + k_4^HK_Q^H[H^+])[Q] \quad (17)$$

the present conditions [Q] can be assumed to be a steady state intermediate, *i.e.* $d[Q]/dt = 0$, and this condition leads to eqn. (18). Making use of eqn. (18) enables eqn. (17) to be expressed in

$$k_{-a}[QH] = k_a[Q][H^+] + k_4[Q] \quad (18)$$

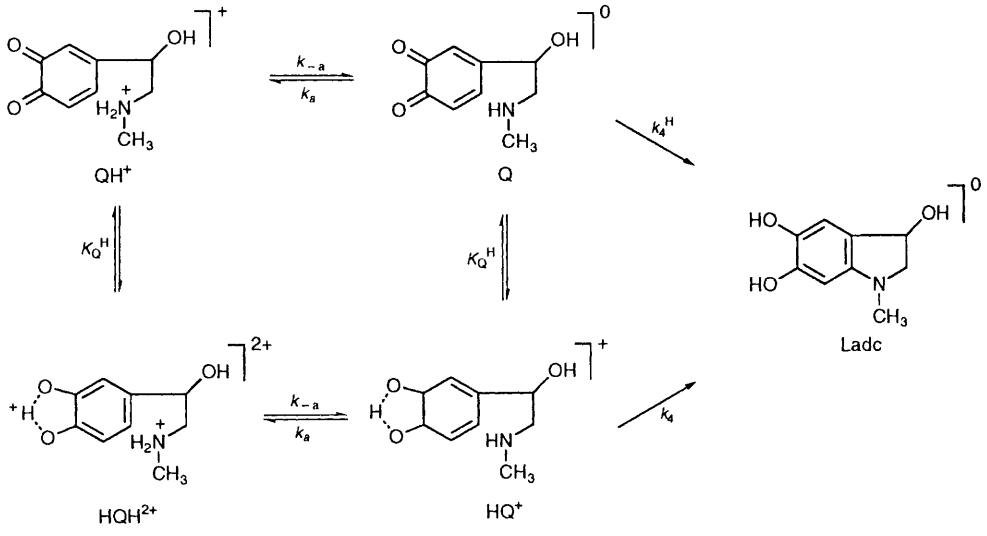
terms of $[Q]_T$ and thus, comparison with eqn. (16) leads to eqn. (19), in which $K_N^H = k_a/k_{-a}$ is the protonation micro-constant for the amino group. The value of K_N^H is known,[16] $\log K_N^H = 9.42$, the protonation constant for K_Q^H was obtained spectrophotometrically and has the value $\log K_Q^H = 1.55$ and k_{-a} has the

Table 2 Typical rate constants of the formation of adrenoquinone, followed at 380 nm, T = 25.0 ± 0.1 °C, I = 0.10 mol dm^{-3} (KNO_3)

pH	$10^2[H^+]$/mol dm^{-3}	$10^4[Fe]_T$/mol dm^{-3}	$10^3[L]_T$/mol dm^{-3}	$10^2\,k_3^{obs}$/s^{-1}
0.450	47.3	10.5	10.04	0.737
0.820	19.9	10.5	10.03	0.974
0.880	17.3	14.9	15.00	1.54
0.932	15.3	9.70	15.00	1.53
1.000	13.0	9.87	10.03	1.24
1.021	12.4	9.70	10.00	1.33
1.043	11.7	9.98	10.00	1.22
1.140	9.39	9.98	10.00	1.38
1.305	6.35	12.4	10.01	1.52
1.49	4.13	12.4	10.02	1.52
1.60	3.19	5.79	12.5	2.97
1.75	2.25	9.93	4.97	2.70
1.92	1.51	6.56	4.97	5.30

Table 3 Typical rate constants for the decomposition of the quinone followed at 380 nm, T = 25.0 ± 0.1 °C, I = 0.10 mol dm^{-3} (KNO_3)

pH	$10^2[H^+]$/mol dm^{-3}	$10^4[Fe]_T$/mol dm^{-3}	$10^2[L]_T$/mol dm^{-3}	$10^3\,k_4^{obs}$/s^{-1}	t_{max}/s	A_{max}
1.60	3.19	5.79	3.32	2.07	62	0.061
1.61	3.12	11.6	12.5	1.53	81	0.081
1.69	2.58	11.6	10.0	1.78	69	0.137
1.75	2.25	9.93	4.97	2.26	95	0.105
1.76	2.19	11.6	10.0	2.21	51	0.121
1.92	1.51	6.56	4.97	2.44	62	0.072
2.09	1.01	5.79	3.25	5.66	7.5	0.073



Scheme 2

value [15] 10.0 s^{-1}. Thus, the rate constants for the cyclisation reaction were readily obtained from eqn (19): k_4 = 1.86 × 10^4

$$k_4^{obs} = (k_4 + k_4^H K_Q^H[H^+])/\{(K_N^H[H^+] + k_4/k_{-a})(1 + K_Q^H[H^+])\} \quad (19)$$

and k_4^H = 1.56 × 10^5 s^{-1} and these can be compared with the corresponding values for dopa,[3] *i.e.* 1.41 × 10^2 and 4.80 × 10^4 s^{-1}, respectively.

Despite the close relationship of the above kinetic scheme to that of dopa the interpretation of the low-pH aspects of this scheme must be different. In the case of dopa, it was assumed [3] that the additional proton is located at the carboxy group of the amino acid, where it breaks an intramolecular hydrogen bond between the anionic carboxy group and a hydrogen of the amino group and therefore accelerates the cyclisation by liberating the amino group. We were led to this assumption by the close resemblance of the pK of the additional proton and the pK_a of the carboxylic acid group. But adrenaline does not have a carboxylic acid group and the only protonatable site in the quinone would appear to be one of the carbonyl groups; its protonation could possibly increase the rate of cyclisation due to its lowering the electron density at the 5-position of the ring and thus making it more reactive towards nucleophiles. A comparison of the values of the rate constants would suggest that it does not affect the arguments put forward for dopa; in the case of adrenaline the reaction is accelerated by protonation by a factor 10 whereas in the case of dopa this factor is 340. Although there is certainly some acceleration due to protonation of the quinone site of dopaquinone, the main influence must be due to its carboxylic acid group as previously proposed. Furthermore, the proton is almost certainly chelated by the two adjacent carbonyl groups since the influence of this protonation is small. Finally from the fact that adrenaline cyclises generally very much faster than dopa, it can be said that hydrogen bonds between the amino group and surrounding water molecules

Table 4 Typical rate constants for the formation of adrenochrome (k_5^{obs}), followed at 480 nm, T = 25.0 ± 0.1 °C, I = 0.10 mol dm^{-3} (KNO_3)

pH	$10^2[H^+]$/mol dm^{-3}	$10^4[Fe]_T$/mol dm^{-3}	$10^2[L]_T$/mol dm^{-3}	$10^4\ k_5^{obs}$/s^{-1}
1.08	10.8	2.28	0.510	6.94
1.16	8.96	2.31	0.515	5.62
1.24	7.42	2.23	0.253	3.25
1.32	6.15	2.27	0.515	9.45
1.37	5.47	2.28	0.510	14.5
1.55	3.59	2.26	0.258	14.6
1.62	3.05	2.25	0.255	18.9
1.74	2.30	2.24	0.510	29.6
2.42	0.47	2.21	0.432	58.5

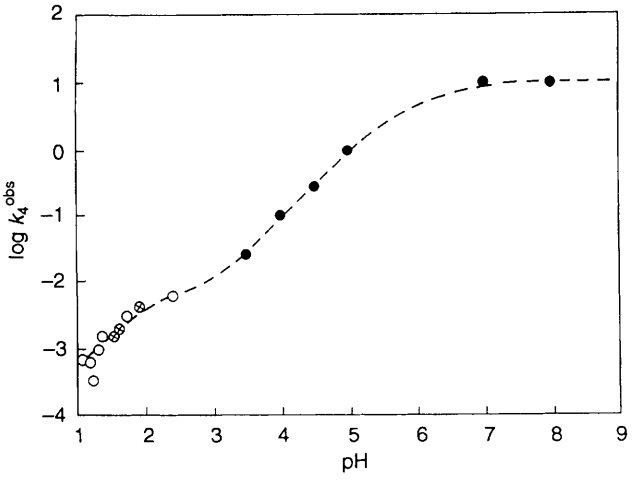


Fig. 2 Observed rates of cyclisation of adrenaline to form leucoadrenochrome: (⊗, ○), kinetically obtained values for k_4^{obs} and k_5^{obs}, respectively; (●), chronoamperometric results. The derivation of the curve is explained in the text.

(which are more or less absent in adrenaline due to its methyl group) are also retarding the cyclisation. However, further work using other catecholamines is in progress at our laboratories in an attempt to clarify the position.

Formation of Adrenochrome.—Since the catechol function of leucoadrenochrome is very similar to that in adrenaline one would expect that the oxidation of leucoadrenochrome to its quinone follows the same route as the oxidation of adrenaline to its quinone, *i.e.* complexation of iron, internal electron transfer, and subsequent fast oxidation of the produced semiquinone. However, as Table 4 reveals, the measured rate of formation of adrenochrome, k_5^{obs}, is identical to k_4^{obs} for the cyclisation. Thus the electron transfer reactions involving leucoadrenochrome and its semiquinone must be compared with this reaction. This is supported by the fact that oxygen does not have any influence on the rate of formation of adrenochrome and neither has chloride. The amount of adrenochrome formed, calculated by using the extinction coefficient[6] of 3660 dm^3 mol^{-1} cm^{-1}, is about 80% of the stoichiometric amount, which is explained by equilibrium between forward and reverse redox reactions being obtained. It is interesting to note that free adrenaline is required for the reverse reaction of iron(II) and adrenochrome to take place.[18] A previous study of the VO^{2+}-catalysed autoxidation of adrenaline led to a similar result.[17] The earlier suggestion by Hawley *et al.*[14] that adrenochrome is formed by oxidation of leucoadrenochrome by the adrenoquinone is not supported since we did not find any signs of autocatalysis in the disappearance of the quinone at these low pH values. It is perhaps surprising that the formation of dopachrome was not observed in the iron(III)–dopa system[3] but this might be due to loss of colour by protonation of the catechol function.

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Paper 3/02394J
Received 26*th April* 1993
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CONFERENCE DIARY †

1993

December

3rd Tohwa University International Symposium on Synthetic and Mechanistic Hydrocarbon Chemistry, Fukuoka, Japan **December 6–9**

Contact: Professor Dr. Y. Nagano, Tohwa Institute of Science, Tohwa University, Fukuoka 815, Japan
Fax +81 92 542 0813

27th Annual Meeting on Modern Aspects of Stereochemistry, Sheffield, UK **December 15**

Contact: Professor C. J. M. Stirling, Department of Chemistry, The University of Sheffield, Sheffield, UK S3 7HF
Tel +44 (0) 742 768555. Fax +44 (0) 742 738673

Free Radicals, Antioxidants, Lipids and Health, Belgrave Sq., London, UK **December 15**

Contact: SCI, Conference Dept., 14/15 Belgrave Sq., London, UK SW1X 8PS
Tel +44 (0) 71 235 3681. Fax +44 (0) 71 823 1698

Potential Energy Surfaces and Organic Reaction Paths, Oxford, UK **December 15–17**

RSC* (Mrs. Y. A. Fish)

1994

January

Natural Products and Medicinal Chemistry, Kingston, Jamaica **January 3–7**

Contact: Organising Secretary, Mona Symposium, Department of Chemistry, University of the West Indies, Mona, Kingston 7, Jamaica

Dynamics, Kinetics and Rate Equations in Heterogeneous Catalysis, Manchester, UK **January 6–7**

RSC* (Mr. S. S. Langer)

19th International Symposium on the Chemistry of Natural Products, Karachi, Pakistan **January 16–20**

Contact: Professor Atta-ur-Rahman, H.E.J. Research Institute of Chemistry, University of Karachi, Karachi-75270, Pakistan
Tel +92 21 470007. Fax +92 21 467887
E-mail atta%hejfirst@unet.uu.net

Trombay Symposium on Radiation and Photochemistry, Bombay, India **January 17–21**

Contact: Dr. S. N. Guha, Secretary, Symposium Organising Committee Chemistry Division, BARC, Bombay 400 085, India
Tel +91 22 556 3060 ext. 2280. Fax +91 22 556 0750

Renewable Resource Building Blocks for Polymer Science, SCI, London, UK **January 26**

RSC* (Mrs. Y. A. Fish)

March

Biotransformations in Action: A Practically Based Course on Opportunities and Techniques in Biocatalysis for Synthetic Organic Chemists, Blacksburg, VA, USA **March 3–7**

Contacts: Professor T. Hudlicky, Department of Chemistry, Virginia Polytechnic & State University, Blacksburg, VA 24061, USA *or* Professor S. M. Roberts, Department of Chemistry, University of Exeter, Stocker Road, Exeter, UK EX4 4QD

Reduction in Organic Synthesis, Scientific Societies Lecture Theatre, London, UK **March 15**

Contact: Dr. K. T. Veal, SmithKline Beecham, Coldharbour Road, Harlow, Essex, UK CM19 5AD
Tel +44 (0) 279 622269. Fax +44 (0) 279 622348

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* *Contact:* Dr. J. F. Gibson, Royal Society of Chemistry, Burlington House, Piccadilly, London, UK W1V 0BN. Fax +44 (0) 71 437 8883.
† Conference organisers are invited to provide details of meetings concerning organic, bio-organic or physical organic chemistry to: Dr. A. P. Kybett, Journals Department, Royal Society of Chemistry, Thomas Graham House, Science Park, Cambridge, UK CB4 4WF.

Physical Methods in Bioorganic Chemistry, Scientific Societies Lecture Theatre, London, UK **March 21**	RSC*
27th International Meeting: Electron Spin Resonance of Inorganic Radicals and Metal Ions in Inorganic and Biological Systems, Cardiff, UK **March 21–25**	*Contact:* Dr. C. C. Rowlands, School of Pure and Applied Chemistry, University of Wales College of Cardiff, PO Box 912, Cardiff, UK CF1 3TB Tel +44 (0) 222 874073. Fax +44 (0) 222 874030
Fatty Acid Biosynthesis, Belgrave Square, London, UK **March 22**	*Contact:* Dr. D. W. Holloman Tel +44 (0) 275 392 181. Fax +44 (0) 275 394 007

April

RSC Annual Congress (Horizons for Organic Chemistry in the 21st Century), Liverpool, UK **April 12–15**	RSC*
Transition Metals in Supramolecular Chemistry, Genoa, Italy **April 14–16**	*Contact:* Professor Luigi Fabrizzi, NATO ARW, Dipartimento di Chimica Generale, Viale Taramelli, 12, I-27100 Pavia, Italy Tel +39 382 392328. Fax +39 382 528544
Converging Methods for Determining Polypeptide Structures, Gregynog, UK **April 15–17**	RSC*
Florida Catalysis Conference, Palm Coast, FL, USA **April 18–22**	*Contact:* Professor R. S. Drago, Department of Chemistry, University of Florida, Gainesville, FL 32611, USA Fax +1 904 392 8758
5th Medicinal Chemistry Symposium, Hatfield, UK **April 21**	Dr. D. I. C. Scopes, Medicinal Chemistry Department, Glaxo Group Research Ltd., Park Road, Ware, Herts, UK SG12 0DP Tel +44 (0) 920 882656
Synthesis of Medicinally Important Carbohydrates and Analogues, Exeter, UK **April 21–22**	RSC*

May

29th ESF/Euchem Conference on Stereochemistry, Bürgenstock, Switzerland **May 1–7**	*Contact:* Professor A. Pfaltz, Institute of Inorganic Chemistry, University of Basel, St Johannsring 19, CH 4056, Basel, Switzerland
New Horizons in Anti-inflammatory Therapy, Scientific Societies Lecture Theatre, London, UK **May 11**	*Contact:* SCI Conference Secretariat, 14/15 Belgrave Square, London, UK SW1X 8PS Tel +44 (0) 71 235 3681. Fax +44 (0) 71 823 1698

June

12th European Experimental NMR Conference, Oulu, Finland **June 5–10**	*Contact:* Dr. Petri Ingman, Department of Chemistry, University of Oulu, FIN-90570, Oulu, Finland Tel +358 81 553 1622. Fax +358 81 553 1603
25th Reaction Mechanisms Conference, Notre Dame, IN, USA **June 10–15**	*Contact:* Dr. Daniel J. Pasto, 1994 Reaction Mechanisms Conference, Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, IN 46556, USA Fax +1 219 631 6652
XIX International Symposium on Macrocyclic Chemistry, Lawrence, KS, USA **June 13–17**	*Contact:* Professor Daryle H. Busch *or* Kristen Bowman-James, Department of Chemistry, University of Kansas, Lawrence, KS 66045, USA

* *Contact:* Dr. J. F. Gibson, Royal Society of Chemistry, Burlington House, Piccadilly, London, UK W1V 0BN. Fax +44 (0) 71 437 8883

July

Course and 2nd RSC International Symposium on Supported Reagents and Catalysis in Chemistry, Swansea, UK **July 5–8**	RSC*
16th International Conference on Organometallic Chemistry, Brighton, UK **July 10–15**	RSC*
35th IUPAC International Symposium on Macromolecules, Akron, OH, USA **July 11–15**	*Contact:* Cathy Manus-Gray, MacroAkron '94, The University of Akron, Akron, OH 44325-3909, USA Tel +1 216 972 5334. Fax +1 216 972 5463 E-mail Manusgray@uakron.edu
5th Belgian Organic Synthesis Symposium, Namur, Belgium **July 11–15**	*Contact:* Professor A. Krief, Facultés Universitaires Notre Dame de la Paix, Department of Chemistry, 61, rue de Bruxelles, B-5000 Namur, Belgium Tel +32 81 72 45 39. Fax +32 81 72 45 36
17th International Carbohydrate Symposium, Ottawa, Canada **July 17–22**	*Contact:* Dr. H. Jennings, Institute of Biological Sciences, National Research Council of Canada, 100 Sussex Drive, Ottawa, Ontario, Canada K1A OR6
Recognition Processes, Birmingham, UK **July 24–29**	RSC*
8th International Symposium on Molecular Recognition and Inclusion, Ottawa, Canada **July 31–August 5**	*Contact:* Mrs. Huguette Morin-Dumais, Steacie Institute for Molecular Sciences, National Research Council of Canada, 100 Sussex Drive, Ottawa, Ontario, Canada, K1A 0R6 Tel +1 613 990 0936. Fax +1 613 954 5242 E-mail ISMRI@NED1.SIMS.NRC.CA

August

Physical Organic Principles Applied to Supramolecular Chemistry. From Bioorganic Structures to New Materials, Geneva, Switzerland **August 25–28**	*Contact:* Professor P. Müller, Département de Chimie Organique, Université de Genève, 30, quai Ernest-Ansermet, CH-1211 Genève 4 Tel +41 (0) 22 702 6527. Fax +41 (0) 22 328 7396 E-mail MULLER@SC2A.UNIGE.CH
12th International Conference on Physical Organic Chemistry, Padova, Italy **August 28–September 2**	*Contact:* Professor G. Scorrano, Dipartimento Di Chimica Organica, Universita degli Studi di Padova, Via Marzolo 1, 35100 Padova, Italy. Fax +39 49 831222

September

European ESR Meeting on Recent Advances and Applications to Organic and Bioorganic Materials, Paris, France **September 5–9**	*Contact:* Dr. Bernard Catoire, GARPE, c/o ITF-Lyon, B.P. 60, F-69132 Ecully, France Tel +33 78 33 34 55. Fax +33 78 43 39 66
RSC Autumn Meeting [Organic Chemistry: Synthesis and Mechanisms (i) Mechanisms in Molecular Recognition and Bioorganic Chemistry (ii) Physical Organic Chemistry and Synthetic Methodology (iii) Organometallics in Organic Synthesis], Glasgow, UK **September 6–9**	RSC*
International Symposium on Cascade Reactions, Leeds, UK **September 12–14**	RSC*
6th Symposium on the Latest Trends in Organic Synthesis, Blacksburg, VA, USA **September 28–October 2**	*Contact:* Professor Tomas Hudlicky, Department of Chemistry, Virginia Polytechnic Institute and State University, Blacksburg, VA 24061-0212, USA Tel +1 703 231 4509. Fax +1 703 231 3941

* *Contact:* Dr. J. F. Gibson, Royal Society of Chemistry, Burlington House, Piccadilly, London, UK W1V 0BN. Fax +44 (0) 71 437 8883

October

First Swiss Course on Medicinal Chemistry, Leysin, Switzerland **October 9–14**

Contact: Dr. Han van de Waterbeemd, F. Hoffmann-La Roche Ltd., CH-4002 Basel, Switzerland
Tel +41 61 688 8421. Fax +41 61 688 1745

November

Biotransformations in Action: A Practically Based Course on Opportunities and Techniques in Biocatalysis for Synthetic Organic Chemists, Blacksburg, VA, USA **November 3–7**

Contacts: Professor T. Hudlicky, Department of Chemistry, Virginia Polytechnic & State University Blacksburg, VA 24061, USA *or* Professor S. M. Roberts, Department of Chemistry, University of Exeter, Stocker Road, Exeter, UK EX4 4QD

6th International Kyoto Conference on New Aspects of Organic Chemistry, Kyoto, Japan **November 7–11**

Contact: Professor Yoshihiko Ito, Chairman IKCOC-6, Department of Synthetic Chemistry, Kyoto University, Yoshida, Kyoto 606-01, Japan. Fax +81 75 753 5668

December

10th International Conference on Organic Synthesis, Bangalore, India **December 11–16**

Contact: Professor G. S. R. Subba Rao, Department of Organic Chemistry, Indian Institute of Science, Bangalore 560 012, India
Tel +91 80 344411. Fax +91 80 341683
E-mail Ocgsrs@orgchem.iisc.ernet.in

28th Annual Meeting on Modern Aspects of Stereochemistry, Sheffield, UK **December 14**

Contact: Professor C. J. M. Stirling, Department of Chemistry, The University of Sheffield, Sheffield, UK S3 7HF
Tel +44 (0) 742 768555. Fax +44 (0) 742 768555

1995

March

Lipophilicity in Drug Research and Toxicology, Lausanne, Switzerland **March 21–24**

Contact: Professor Bernard Testa, School of Pharmacy, University of Lausanne, BEP, CH-1015 Lausanne, Switzerland
Tel +41 21 692 2851. Fax +41 21 692 2880

April

RSC Annual Congress, Edinburgh, UK **April 10–13**

RSC*

International Symposium on Protein Structure and Function, Exeter, UK **April 19–21**

Contact: Professor S. M. Roberts, Department of Chemistry, University of Exeter, Stocker Road, Exeter, UK EX4 4QD
Tel +44 (0) 392 263429/30. Fax +44 (0) 392 263431

July

12th RSC International Meeting: NMR Spectroscopy, Manchester, UK **July 2–7**

RSC*

XXth International Symposium on Macrocyclic Chemistry, Jerusalem, Israel **July 2–7**

Contact: Secretariat, XXth International Symposium on Macrocyclic Chemistry, PO Box 50006, Tel Aviv 61500, Israel
Tel +972 3 5140014. Fax +972 5175674

Biological Challenges for Organic Chemistry, St Andrews, UK **July 10–13**

RSC*

International Society of Magnetic Resonance Conference, Sydney, Australia **July 16–21**

Contact: Dr. Les Field, Chairman, ISMAR-95, Department of Organic Chemistry, University of Sydney, Sydney, NSW 2006, Australia. Tel +61 2 692 2060. Fax +61 2 692 3329
E-mail ISMAR-95@biochem.su.oz.au

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* *Contact:* Dr. J. F. Gibson, Royal Society of Chemistry, Burlington House, Piccadilly, London, UK W1V 0BN. Fax +44 (0) 71 437 8883

14th International Symposium—Synthesis in Organic Chemistry, Cambridge, UK **July 24–27** — RSC*

August

IUPAC General Assembly, Guildford, UK **August 7–15** — RSC*

September

8th Medicinal Chemistry Symposium, Cambridge, UK
September 10–13 — RSC* (Mr. S. S. Langer)

December

Pacifichem '95 (International Congress of Pacific Basin Chemical Societies), Honolulu, HI, USA
December 17–22

Contact: Mrs. C. Pruitt, Congress Manager Pacifichem '95, American Chemical Society, 1155–16th St., NW, Washington DC 20036, USA
Tel +1 202 872 4397. Fax +1 202 872 6128
E-mail cpp91@acs.org

DIARY OF MAJOR MEETINGS OF THE AMERICAN CHEMICAL SOCIETY

MEETING	YEAR	DATE	LOCATION
207th	Spring 1994	March 13–18	San Diego, CA
208th	Fall 1994	August 21–26	Washington, DC
209th	Spring 1995	April 2–7	Anaheim, CA
210th	Fall 1995	August 20–25	Chicago, IL
211th	Spring 1996	March 24–29	Seattle, WA
212th	Fall 1996	August 25–30	Boston, MA
213th	Spring 1997	April 6–11	San Antonio, TX
214th	Fall 1997	September 7–12	Las Vegas, NV
215th	Spring 1998	March 29–April 3	St. Louis, MO
216th	Fall 1998	August 23–28	Orlando, FL
217th	Spring 1999	March 21–26	Anaheim, CA
218th	Fall 1999	August 22–27	New Orleans, LA
219th	Spring 2000	March 26–31	Las Vegas, NV
220th	Fall 2000	August 20–25	Washington, DC
221st	Spring 2001	April 1–6	San Francisco, CA
222nd	Fall 2001	August 19–24	Chicago, IL

Contact: ACS Meetings, 1155–16th St., N.W. Washington DC 20036–4899, USA

* *Contact:* Dr. J. F. Gibson, Royal Society of Chemistry, Burlington House, Piccadilly, London, UK W1V 0BN. Fax +44 (0) 71 437 8883

Journal of Chemical Research, Issue 11, 1993

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