

Oxidation of Ascorbic Acid by Copper(II) and the Ferrocenium Ion in Acetonitrile–Water Mixtures

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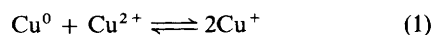
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Measurements are reported on the rates of oxidation of ascorbic acid (H_2A) by copper(II) and the ferrocenium cation $[Fe(C_5H_5)_2]^+$ in mixtures of water and acetonitrile. The stabilisation of Cu^+ by acetonitrile results in a rapid increase in E° for $Cu^{2+}-Cu^+$ and a simple, irreversible reaction between copper(II) and ascorbic acid to form copper(I) and dehydroascorbic acid upon addition of small amounts of acetonitrile to water. The acid dependence of the rate constant is consistent with the involvement of complexes of the monoanion, $[Cu^{II}(HA)]^+$, and the dianion $[Cu^{II}A]$, the former becoming relatively more important with increasing acetonitrile content of the solvent. The solvent dependence of the rate constant is discussed in relation to the solvation of copper(II) and copper(I) in the mixtures and it is suggested that the dominant influence is the solvation of copper(I) formed in the initial electron-transfer process. Redox potentials, E for $[Fe(C_5H_5)_2]^+-[Fe(C_5H_5)_2]$, and rates of oxidation of ascorbic acid by ferrocenium, a typical outer-sphere oxidant, have been measured under the same conditions and are compared with those of the copper(II)–copper(I) system.

The redox potential of the copper(II)–copper(I) system is very sensitive to solvent, especially in acetonitrile–water mixtures. An important feature of the nitrilic solvents is their ability to stabilise $Cu^+(d^{10})$ with respect to Cu^{2+} , as illustrated by equilibrium (1). In water Cu^+ is unstable and disproportionates

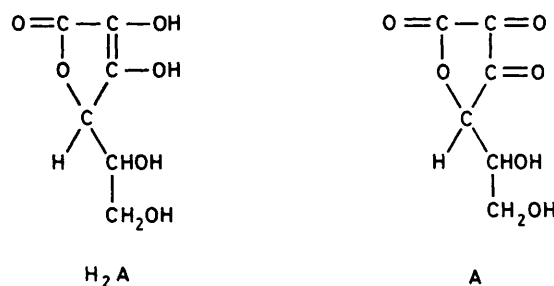


$[\Delta G^\circ(1) = 35 \text{ kJ mol}^{-1}$, $K = 10^{-6}]$,¹ reflecting the strong solvation of Cu^{2+} by water. The addition of only 6% acetonitrile to water, however, is sufficient to reverse the equilibrium, and in pure acetonitrile ΔG° for equilibrium (1) is *ca.* -85 kJ mol^{-1} ($K = 10^{16}$).² In mixtures of the two solvents, copper(II) salts are powerful oxidising agents and a number of useful applications have been reported.³

In recent years efforts have been directed towards the synthesis of ligands, especially macrocyclic ligands with S donor atoms, which are able to modify considerably copper(II)–copper(I) redox potentials, encompassing the range of potentials observed for copper proteins and enzymes (0.2–0.8 V).^{4–7} Reduction of co-ordinated Cu^{2+} frequently occurs in two successive, one-electron steps: the first step is a reversible reduction from a copper(II) complex to a copper(I) complex, and the second step, at a more negative potential, is the reduction of copper(I) to copper(0). The behaviour of Cu^{2+} when complexed with the various thioether ligands, and in acetonitrile–water mixtures, contrasts strongly with that in pure water, where the second reduction occurs at a more positive potential than the first ($E^\circ = 0.153$ for $Cu^{2+}-Cu^+$, 0.521 V for Cu^+-Cu).

Comparatively little information is available on the rates and mechanism of simple redox reactions involving $Cu^{2+}-Cu^+$ directly. Apart from their intrinsic interest, direct electron transfer from Cu^{2+} to various substrates is thought to be an integral part of the Cu^{2+} -catalysed oxidation by molecular oxygen of substrates such as ascorbic acid (vitamin C) and *p*-diphenols such as hydroquinone^{8–10} (the involvement of Cu^{3+} has also been implicated in the oxidation of ascorbic acid).^{11,12}

In the present paper we report a study of the influence of

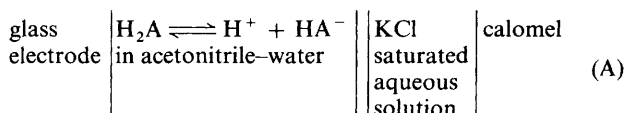


acetonitrile on the kinetics of the oxidation of ascorbic acid (H_2A) by Cu^{2+} . The reaction provides an opportunity to investigate the influence of the large increase in E° ($Cu^{2+}-Cu^+$) on the rate of the oxidation reaction. Furthermore the rapid increase in E° with increasing acetonitrile content of the solvent leads to a simple, irreversible reaction in contrast to the more complex behaviour observed in wholly aqueous media. For comparative purposes the outer-sphere oxidation by the ferrocenium ion and the redox potential of the ferrocenium–ferrocene couple have also been studied in the mixtures.

Experimental and Results

Materials.—Acetonitrile was purified by successive distillations at atmospheric pressure from P_2O_5 and CaH_2 .¹³ Ascorbic acid, methanesulphonic acid, and the inorganic chemicals were high-purity commercial samples used without further purification. Ferrocenium bromide solutions in the acetonitrile–water mixtures were prepared from a fresh stock solution generated by reaction of the required amount of saturated aqueous bromine (*ca.* 0.25 mol dm^{-3}) with 0.1 mol dm^{-3} ferrocene (B. D. H.) in acetonitrile. All solutions were prepared in oxygen-free distilled water obtained by bubbling N_2 through distilled water for several hours.

pK_a Determinations.—The pK_a values for the first dissociation of ascorbic acid were determined in acetonitrile–water mixtures containing up to 60% (v/v) acetonitrile ($x_{\text{CH}_3\text{CN}} = 0.341$). The determinations were carried out using standard techniques of pH measurements with glass electrodes in aqueous–organic solvent mixtures¹⁴ as in cell A. A Radiometer PM 64 – pH meter was used for all measurements. The true pH



is related to the observed pH, $(\text{pH})_{\text{obs.}}$ (based on calibration of the glass electrode–calomel system in aqueous buffers), by equation (2),¹⁴ where δ was obtained from measurements on a

$$\text{pH} = (\text{pH})_{\text{obs.}} + \delta \quad (2)$$

dilute solution of methanesulphonic acid (*ca.* 5×10^{-3} mol dm^{-3}) in the various mixtures (see footnote, Table 1). The pH values were determined for a number of $[\text{H}_2\text{A}]/[\text{HA}^-]$ ratios by titrating H_2A solutions (0.02 mol dm^{-3}) with NaOH (0.1 mol dm^{-3}) at a constant ionic strength of 0.1 mol dm^{-3} (NaClO_4) at 25°C . They were used in conjunction with equation (3) to

$$\text{p}K_a(\text{H}_2\text{A}) = \text{pH} + \log \frac{[\text{HA}]}{[\text{A}^-]_{\gamma_{\pm}}} \gamma_{\text{HA}} \quad (3)$$

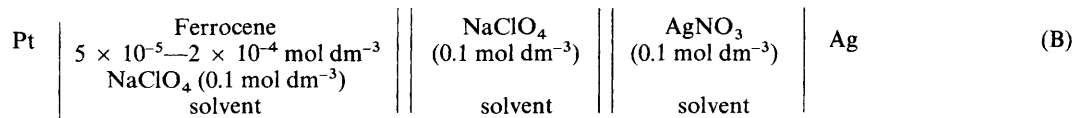
determine $\text{p}K_a(\text{H}_2\text{A})$. The activity coefficient of HA , γ_{HA} , was assumed to be unity, and γ_{\pm} values were calculated from the Davies equation (4)¹⁵ where I = ionic strength, A [=

$$\log \gamma_{\pm} = -\frac{Z^2 A I^{\frac{1}{2}}}{1 + I^{\frac{1}{2}}} + \frac{Z^2 A I}{3} \quad (4)$$

$(1.823 \times 10^6 / \epsilon T)^{\frac{1}{2}}$] is the Debye–Hückel parameter, and z = charge. Values of ϵ in the solvent mixtures were obtained from ref. 16.

Measured $\text{p}K_a$ values are given in Table 1. The value in water ($\text{p}K_a = 4.17$, $I = 0$) is in good agreement with earlier reported values ($\text{p}K_a = 4.04$, $I = 0.1$ mol dm^{-3} ,⁸ 4.15 , 0.05 mol dm^{-3} (20°C);¹⁷ 4.05 , 0.1 mol dm^{-3}). A value for the $\text{p}K_a$ of the second dissociation step of $\text{p}K_a(\text{HA}^-) = 11.81$ was also determined in water.

Redox Potential Measurements.—The E° values for ferrocenium–ferrocene in acetonitrile–water mixtures, relative to a reference half cell of Ag–AgNO_3 (0.1 mol dm^{-3}) in the same solvent were determined using cyclic voltammetry (PAR 170)



on solutions of ferrocene at platinum in cell B. Reversible waves were obtained in all cases over a range of sweep rates (peak separation 60 – 65 mV, sweep rates 10 – 300 mV s^{-1}). Measurements in highly aqueous solvent mixtures were more difficult because of the low solubility of ferrocene and the value in pure water was obtained from earlier literature measurements.^{18,19}

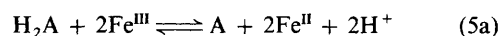
Cyclic voltammetry applied to cell B gives values of $E = E(0.1 \text{ mol dm}^{-3} \text{ Ag}^+/\text{Ag}) - E^\circ(\text{ferrocenium–ferrocene})$, assuming the diffusion coefficients of ferrocenium and ferrocene to be similar. The results are given in Table 2.

Reduction potentials of $\text{Cu}^{2+}/\text{Cu}^+$, Cu^+/Cu^0 , $\text{Cu}^{2+}/\text{Cu}^0$,

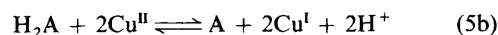
where $E^\circ(\text{Cu}^{2+}/\text{Cu}) = [E^\circ(\text{Cu}^+/\text{Cu}) + E^\circ(\text{Cu}^{2+}/\text{Cu}^+)]/2$, and Ag^+/Ag are available in acetonitrile–water mixtures relative to the reference electrodes 0.01 mol dm^{-3} Ag^+/Ag in CH_3CN ²⁰ or aqueous calomel.²¹ Using smoothed plots of E against solvent composition, redox potentials of these couples and ferrocenium–ferrocene at selected volume fractions/mole fractions of acetonitrile have been obtained by interpolation (Table 3). For the purpose of presentation, the values in Table 3 are placed on an absolute scale relative to the normal hydrogen electrode in water, based on the $\text{AsPh}_4^+/\text{BPh}_4^-$ assumption.^{22,23} The differences between any two sets (*e.g.* $\text{Cu}^{2+}/\text{Cu}^+$ vs. ferrocenium–ferrocene) are of course independent of any extrathermodynamic assumption. Figure 1 shows the change with solvent of the redox potential relative to water for the various couples, again based on the $\text{AsPh}_4^+/\text{BPh}_4^-$ assumption.

Kinetic Measurements.—The disappearance of the oxidising species (Cu^{2+} , ferrocenium) was followed using an all-glass, stopped-flow system contained a pair of platinum electrodes, with square-wave amperometric detection.²⁴ Square-wave signals were provided by a Farnell LFM4 sine-square generator, and the cell signal was measured using a sample-and-hold integrated circuit triggered by a delayed signal from the generator, as previously described.²⁵ The signal amplitude from the signal generator was $\pm(100$ – $200)$ mV at a frequency range of 50 – 400 Hz (normally 200 Hz). The electrodes were cleaned with concentrated HNO_3 prior to a series of measurements. The reactions were normally monitored over 4 – 6 half-lives and the rate constants were independent ($\pm 5\%$) of signal frequency, except in solvents containing $>40\%$ (v/v) acetonitrile when there was a non-linear response at higher frequencies (>200 Hz) of the cell signal to concentration.

Reaction stoichiometry. The stoichiometry of the oxidation of ascorbic acid by a wide range of iron(III) complexes has been shown to involve 2 mol of iron(III) per mol of ascorbic acid, as in equation (5a), where A represents the product dehydroascorbic



acid.^{8,26} We have assumed the same to be true for the ferrocenium oxidation. The reaction of Cu^{2+} was less certain because of the possibility of $\text{Cu}^{2+} \longrightarrow \text{Cu}^0$ occurring in preference to $2\text{Cu}^{2+} \longrightarrow 2\text{Cu}^+$. However, in acetonitrile–water mixtures analysis of the dehydroascorbic acid and its hydrolysis product, 2,3-dioxo-1-gluconic acid, by the method of Roe²⁷ established the stoichiometry as in equation (5b) over a



wide range of initial concentration ratios of $\text{Cu}^{2+}/\text{H}_2\text{A}$. The stoichiometry of the reaction in water is discussed below.

Ferrocenium oxidation. The rate of oxidation was measured in solvents containing 5 – 60% (v/v) CH_3CN , with initial $[\text{ferrocenium}] = 2 \times 10^{-4}$ (60% CH_3CN)– 5×10^{-5} mol dm^{-3} (5% CH_3CN), $0.02 \leq [\text{ascorbic acid}]/\text{mol dm}^{-3} \leq 0.10$, $2.8 \times 10^{-3} \leq [\text{CH}_3\text{SO}_3\text{H}]/\text{mol dm}^{-3} \leq 5.0 \times 10^{-2}$, and $I = 0.10$ mol dm^{-3} (NaClO_4). Under these conditions the observed rate law is given by equation (6), where k_e is the observed (pseudo)

$$-d[\text{ferrocenium}]/dt = k_e[\text{ferrocenium}] \quad (6)$$

first-order rate constant. The dependence of k_e upon [ascorbic acid] and $[H^+]$ was tested in 40% (v/v) acetonitrile as described below.

(i) *Ascorbic acid dependence.* Table 4 lists values of k_e measured at various ascorbic acid concentrations in 0.02 mol dm^{-3} CH_3SO_3H . The results (Figure 2) show clearly that k_e is proportional to [ascorbic acid] giving an overall second-order rate constant as in equation (7), in which $k_2 = k_e/[H_2A]_T$ and

$$-d[\text{ferrocenium}]/dt = k_2[H_2A]_T[\text{ferrocenium}] \quad (7)$$

$[H_2A]_T$ represents the total concentration of ascorbic acid $\{[H_2A]_T = [H_2A] + [HA^-] + [A^{2-}]\}$.

(ii) *Acid dependence.* The rates of oxidation were determined at a fixed total ascorbic acid concentration with various concentrations of the strong acid, methanesulphonic acid. The results (Table 4, Figure 3) show an inverse dependence of k_2

Table 1. Values of pK_a for the dissociation of ascorbic acid ($H_2A \rightleftharpoons H^+ + HA^-$) in acetonitrile–water mixtures at 25 °C

% (v/v) CH_3CN^a	x_{CH_3CN}	pK_a^b
0	0	4.17
10	0.037	4.50
20	0.080	4.76
30	0.129	4.95
40	0.187	5.19
50	0.257	5.39
60	0.341	5.67

^a Values of δ [equation (2)] in the various mixtures are 0.16₃ (10), 0.19₁ (20), 0.20₄ (30), 0.23₆ (40), 0.336 (50), and 0.426 (69%). ^b ± 0.05 ; values refer to zero ionic strength.

Table 2. Results of cyclic voltammetry in cell B at 25 °C

% (v/v) CH_3CN	x_{CH_3CN}	$E(0.1 \text{ mol } dm^{-3} \text{ Ag}^+)^a - E^*(\text{ferrocenium-ferrocene})/mV$
0	0	340 ^b
5	0.018	315
10	0.037	283
15	0.058	255
20	0.080	228
30	0.129	180
40	0.187	149
60	0.341	87
80	0.580	34
100	1.00	-20

^a $AgNO_3$ except for pure acetonitrile, $AgClO_4$. ^b Literature value based on $E^* = 0.400 \text{ V}^{18}$ for ferrocenium–ferrocene.

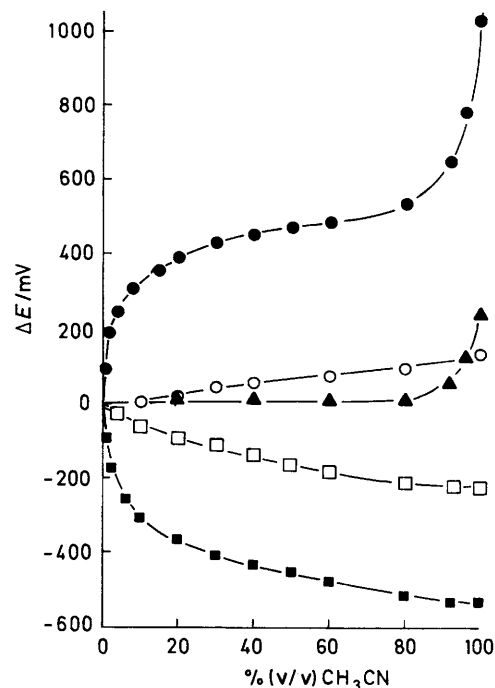


Figure 1. Variation in redox potentials of silver, copper, and ferrocene couples in acetonitrile–water mixtures at 25 °C: $Cu^{2+}-Cu^+$ (●); $Cu^{2+}-Cu^0$ (▲); $[Fe(C_5H_5)_2]^+-[Fe(C_5H_5)_2]$ (○); Ag^+-Ag^0 (□); and Cu^+-Cu^0 (■)

Table 3. Redox potentials^a of silver, copper, and ferrocene couples in acetonitrile–water mixtures at 25 °C

% (v/v) CH_3CN	x_{CH_3CN}	E^*/V				
		Ag^+-Ag	$Cu^{2+}-Cu^+$	Cu^+-Cu^0	$Cu^{2+}-Cu^0$	$[Fe(C_5H_5)_2]^+-[Fe(C_5H_5)_2]$
0	0	0.799 ^b	0.153 ^b	0.521 ^b	0.337 ^b	0.400 ^c
1	0.0035	0.793	0.248	0.431	0.340	0.399
2	0.0070	0.784	0.343	0.346	0.345	0.396
4	0.0142	0.774	0.400	0.311	0.356	0.394
6	0.0216	0.764	0.440	0.261	0.351	0.396
8	0.0292	0.753	0.458	0.239	0.349	0.399
10	0.0370	0.744	0.480	0.214	0.347	0.402
15	0.058	0.725	0.508	0.178	0.343	0.411
20	0.080	0.710	0.544	0.153	0.349	0.423
30	0.129	0.684	0.583	0.109	0.346	0.445
40	0.187	0.660	0.609	0.088	0.349	0.452
50	0.257	0.636	0.626	0.066	0.346	0.462
60	0.341	0.617	0.641	0.040	0.341	0.471
70	0.446	0.600	0.652	0.022	0.344	0.482
80	0.580	0.586	0.690	0.004	0.347	0.493
90	0.756	0.579	0.757	-0.003	0.337	0.515
95	0.868	0.576	0.873	-0.007	0.434	0.525
100	1.00	0.574	1.181	-0.011	0.585	0.535

^a Values relative to n.h.e. in water, based on $AsPh_4^+/BPh_4^-$ assumption; $\pm 0.005V$. ^b Ref. 1. ^c Ref. 18.

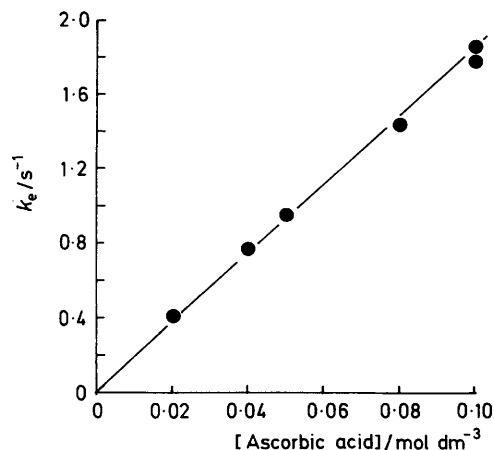


Figure 2. Ascorbic acid dependence of the rate of oxidation of ascorbic acid by ferrocenium in 40% (v/v) acetonitrile–water

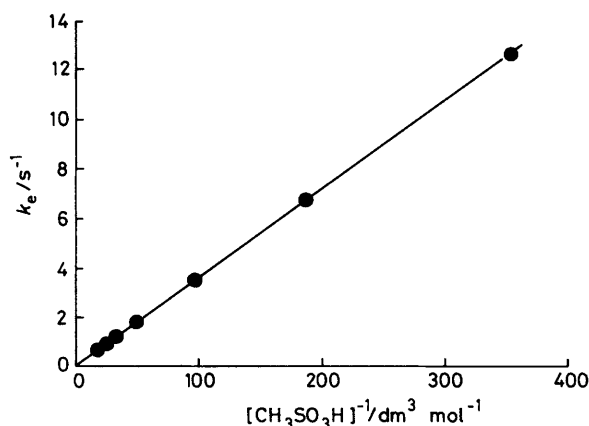


Figure 3. Acid dependence of the rate of oxidation of ascorbic acid by ferrocenium in 40% (v/v) acetonitrile–water

upon $[H^+]$ consistent with a rate-determining oxidation of the monoanion of ascorbic acid. This is illustrated in Table 5 by the constant value obtained when the second-order rate constant, k_2 , is divided by the fraction of H_2A existing as HA^- , $K_a/(K_a + [H^+])$.

(iii) *Solvent dependence.* The rate constants, k_2 , for the oxidation reaction in various solvent mixtures are listed in Table 6. The rate constant in pure water was not measured because of problems associated with the precipitation of ferrocene, but has been estimated by extrapolation from 5% (v/v) acetonitrile. Also included are rate constants for the oxidation of the ascorbic acid monoanion (HA^-), where $k_{HA} = k_2(K_a + [H^+])/K_a$ (see Discussion).

Copper(II) oxidation. The rate of oxidation of ascorbic acid by Cu^{2+} was investigated over a range of solvent compositions [0–50 (v/v) acetonitrile] at various concentrations of ascorbic acid, methanesulphonic acid, and also in the presence of added Cl^- (0.1 mol dm^{-3}). The reactions were always carried out in the presence of a large excess of ascorbic acid (50-fold) with initial $[Cu^{2+}] = 2 \times 10^{-4}$ – 10^{-3} , normally ca. 5×10^{-4} mol dm^{-3} . Except in highly aqueous media [$< 4\%$ (v/v) CH_3CN , 1.4 mol %], as discussed below, the reactions displayed simple first-

Table 4. Oxidation of ascorbic acid by ferrocenium ion:^a ascorbic acid dependence

$[H_2A]_T$ ^b /mol dm^{-3}	k_e/s^{-1}
0.02	0.414
0.04	0.774
0.05	0.957
0.08	1.44
0.10	1.79
0.10	1.87

^a 40% (v/v) CH_3CN at 25 °C, $[CH_3SO_3H] = 0.02$, $I = 0.10$ mol dm^{-3} ($NaClO_4$). ^b Total ascorbic acid concentration.

Table 5. Oxidation of ascorbic acid by ferrocenium ion:^a acid dependence

$10^2[CH_3SO_3H]$ /mol dm^{-3}	k_e/s^{-1}	$10^{-4}k_2([H^+] + K_a)K_a^{-1}$ ^b / $dm^3 mol^{-1} s^{-1}$
0.284	12.7	5.59
0.543	6.71	5.64
1.034	3.48	5.57
2.034	1.79	5.64
3.034	1.18	5.55
4.034	0.880	5.50
5.034	0.707	5.51

^a 40% (v/v) CH_3CN at 25 °C, $[H_2A]_T = 0.10$, $I = 0.10$ mol dm^{-3} ($NaClO_4$). ^b $k_2 = k_e/[H_2A]_T$, K_a from Table 1.

Table 6. Oxidation of ascorbic acid by ferrocenium ion in acetonitrile–water mixtures at 25 °C

% (v/v) CH_3CN	x_{CH_3CN}	k_2 ^a /dm ³ mol ⁻¹ s ⁻¹	$10^{-3}k_{HA}$ ^b /dm ³ mol ⁻¹ s ⁻¹
0	0	5 ^c	1.7 ^c
5	0.018	6.55	2.80
10	0.037	7.65	4.84
20	0.080	10.5	12.1
30	0.129	14.5	25.9
40	0.187	18.7	57.9
50	0.257	20.1	98.7
60	0.341	22.3	209

^a $[CH_3SO_3H] = 0.02$, $[H_2A]_T = 0.1$, $I = 0.1$ mol dm^{-3} ($NaClO_4$).

^b Rate constant for oxidation of ascorbic monoanion, HA^- : $k_{HA} = k_2(K_a + [H^+])/K_a$. ^c By extrapolation.

Table 7. Oxidation of ascorbic acid by copper(II):^a ascorbic acid dependence

$[H_2A]_T$ ^b /mol dm^{-3}	k_e/s^{-1}	k_2 ^c /dm ³ mol ⁻¹ s ⁻¹
0.0207	0.578	28.4
0.0415	1.17	28.2
0.0834	2.33	27.2
0.104	3.01	28.9
0.167	4.74	28.4
0.209	6.05	29.0
0.417	11.6	27.8

^a 20% (v/v) CH_3CN at 25 °C, $[CH_3SO_3H] = 0.02$, $I = 0.10$ mol dm^{-3} ($NaClO_4$). ^b Total ascorbic acid concentration. ^c $k_2 = k_e/[HA]_T$.

order kinetics as in equation (8). A detailed study of the

$$-d[Cu^{2+}]/dt = k_e[Cu^{2+}] \quad (8)$$

dependence of k_e upon [ascorbic acid] and $[H^+]$ was made in 20% (v/v) acetonitrile.

(i) *Ascorbic acid dependence.* Table 7 lists values of k_e measured at various ascorbic acid concentrations in 0.02 mol

Table 8. Oxidation of ascorbic acid by copper(II):^a acid dependence

$10^2[\text{H}^+]/\text{mol dm}^{-3}$	k_e/s^{-1}	$10^{-4}k_2([\text{H}^+] + K_a)K_a^{-1}b/\text{dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$
0.66	28.4	18.8
1.14	10.1	11.5
2.12	3.35	7.11
3.11	1.69	5.26
4.10	1.07	4.39
5.10	0.72	3.64
10.05	0.24	2.41

^a 20% (v/v) CH_3CN at 25 °C, $[\text{H}_2\text{A}]_{\text{T}} = 0.575$, $I = 0.10 \text{ mol dm}^{-3}$ (NaClO_4). ^b $k_2 = k_e/[\text{H}_2\text{A}]_{\text{T}}$, K_a from Table 1.

Table 9. Oxidation of ascorbic acid by copper(II) in acetonitrile–water mixtures at 25 °C

% (v/v) CH_3CN	$x_{\text{CH}_3\text{CN}}$	$k_2/\text{dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$	
		<i>a</i>	<i>b</i>
0	0	5.4 ^c	—
1	0.0035	6.6 ^c	—
2	0.0070	8.9 ^c	(6) ^c
4	0.0142	12.4	14.6
5	0.018	16.0	16.7
6	0.022	18.8	20.0
8	0.029	26.8	25.0
10	0.037	33.0	32.0
15	0.058	—	51.3
20	0.080	87.4	80.9
30	0.129	139	130
40	0.187	203	176
50	0.257	—	203

^a $[\text{HCl}] = 0.02$, $[\text{H}_2\text{A}]_{\text{T}} = 0.1$, $I = 0.10 \text{ mol dm}^{-3}$ (NaCl).

^b $[\text{CH}_3\text{SO}_3\text{H}] = 0.02$, $[\text{H}_2\text{A}]_{\text{T}} = 0.1$, $I = 0.10 \text{ mol dm}^{-3}$ (NaClO_4).

^c Rate constant for initial reactions, see Discussion section.

$\text{dm}^{-3} \text{CH}_3\text{SO}_3\text{H}$. Also included are values of $k_2 = k_e/[\text{H}_2\text{A}]_{\text{T}}$, corresponding to the second-order rate law in equation (9).

$$-d[\text{Cu}^{2+}]/dt = k_2[\text{HA}]_{\text{T}}[\text{Cu}^{2+}] \quad (9)$$

The constancy of k_2 , and in particular the lack of evidence for any levelling off of k_e at higher $[\text{H}_2\text{A}]_{\text{T}}$, suggests only an insignificant extent of complex formation between Cu^{2+} and ascorbic acid under these conditions (see Discussion).

(ii) *Acid dependence.* The rates of oxidation were determined at a fixed total ascorbic acid concentration with various concentrations of methanesulphonic acid. The results, listed in Table 8, show that the acid dependence cannot be accounted for by the reaction of the monoanion (or a contribution from oxidation of the neutral H_2A). Thus rate constants, $k_{\text{HA}} = k_2([\text{H}^+] + K_a)/K_a$, calculated on the basis of a rate-determining oxidation of HA^- , also decrease significantly with increasing $[\text{H}^+]$. This point is considered further below.

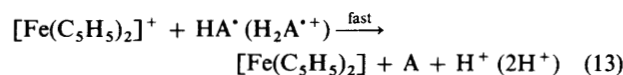
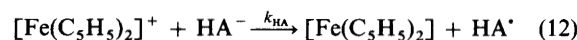
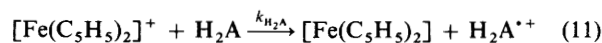
(iii) *Solvent dependence.* The rate constants, k_2 , for reaction in the various solvent mixtures were measured in the presence of $0.02 \text{ mol dm}^{-3} \text{CH}_3\text{SO}_3\text{H}$ ($I = 0.1 \text{ mol dm}^{-3}$, NaClO_4) or $0.02 \text{ mol dm}^{-3} \text{HCl}$ ($I = 0.1 \text{ mol dm}^{-3}$, NaCl). In solvent mixtures containing 4% (v/v) (1.4 mol %) CH_3CN or above, a single reaction, first order in $[\text{H}_2\text{A}]_{\text{T}}$ and $[\text{Cu}^{2+}]$, was observed. However, as the acetonitrile content was reduced from ca. 4% to zero, the amplitude of this reaction progressively decreased until in pure water it represented only about 20% of the total reaction. This was then followed by a slower (10–20 fold) reaction consuming the remainder of the Cu^{2+} . The amplitude of the slower reaction had decreased to ca. 10% of the total in

4% (v/v) acetonitrile, and was not detectable in the presence of higher concentrations of acetonitrile. Table 9 lists the k_2 values obtained in the various solvent mixtures, including those obtained by curve fitting to the initial part of the two-stage reaction in highly aqueous media. This behaviour is discussed further below.

Discussion

It is convenient to consider first the mechanism of the oxidation reactions involving the ferrocenium ion and Cu^{2+} and then the influence of solvent on the reactions.

For the oxidation of ascorbic acid by one-electron-acceptor metal complexes^{8,26,28} there is ample evidence that the observed kinetic behaviour can be accommodated within Scheme 1 (written for oxidation by ferrocenium). In Scheme 1,



Scheme 1.

H_2A^{*+} and HA^* represent radicals formed in a rate-determining, electron-transfer reaction between ferrocenium and H_2A or HA^- respectively.

In aqueous solution the redox potential for the two-electron reduction of ascorbic acid to dehydroascorbic acid is given by equation (14),²⁹ where K_{a2} is the acid dissociation constant for HA^- ($K_a K_{a2}$ is negligible compared with $K_a[\text{H}^+] + [\text{H}^+]^2$ in the dilute acid solutions used in the present study). With $[\text{H}^+] = 0.02 \text{ mol dm}^{-3}$ and ca. 2% conversion of H_2A into A the potential at the end of the oxidation calculated from equation (14) will be ca. 0.23 V. The E° values for H_2A^{*+} – H_2A and

$$E/V = 0.390 + 0.0295 \log (K_a K_{a2} + K_a[\text{H}^+] + [\text{H}^+]^2) + 0.0295 \log [\text{A}]/[\text{H}_2\text{A}] \quad (14)$$

$\text{HA}^* \text{--} \text{HA}^-$ have been estimated by the application of Marcus theory to kinetic data from a variety of reactions to be 1.25 and 0.82 V respectively.^{26,28} Thus the ferrocenium cation ($E^\circ = 0.400 \text{ V}$ for ferrocenium–ferrocene) is a sufficiently strong oxidant for the overall reaction to proceed to completion, but the radicals produced in the initial, one-electron processes will be present only as reactive intermediates.

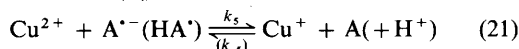
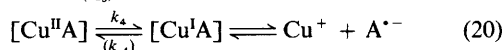
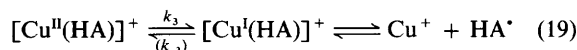
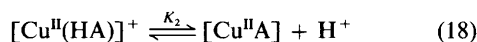
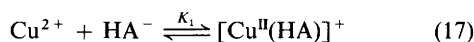
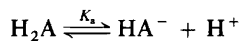
The results for the ferrocenium oxidation in solutions of various acid concentrations (Table 4, Figure 3) show reaction (12) to be the dominant reaction under the conditions studied as extrapolation to infinite acid concentration ($1/[\text{H}^+] = 0$) gives rise to a negligible intercept. Application of the steady-state approximation to $[\text{HA}^*]$ in Scheme 1 leads to the rate law in equations (15) and (16), in agreement with observed behaviour, with k_2 [equation (7)] = $k_{\text{HA}}K_a/(K_a + [\text{H}^+])$.

$$-d[\text{ferrocenium}]/dt = k_e[\text{ferrocenium}] \quad (15)$$

$$k_e = \frac{k_{\text{HA}}K_a}{K_a + [\text{H}^+]} \cdot [\text{ferrocenium}][\text{H}_2\text{A}]_{\text{T}} \quad (16)$$

The oxidation of ascorbic acid by copper(II) in aqueous solution (in the presence and absence of O_2) is normally also discussed within the framework of schemes broadly similar to Scheme 1, but with several differences in detail. Consideration of

the thermodynamics of the overall reaction [equation (5b)] shows (i) in dilute acid the reaction will be reversible, and (ii) there should be a contribution from a reaction involving the reduction of Cu^{2+} to Cu^0 (as has been reported).³⁰ For example, with $[\text{H}^+] = 0.02 \text{ mol dm}^{-3}$, equation (14) gives $E^\circ = 0.29 \text{ V}$ for $\text{A-H}_2\text{A}$ compared with $E^\circ = 0.521 \text{ V}$ for $\text{Cu}^{2+} - \text{Cu}^+$ ($E^\circ = 0.337 \text{ V}$ for $\text{Cu}^{2+} - \text{Cu}^0$); at pH 5, $E^\circ = 0.12 \text{ V}$ for $\text{A-H}_2\text{A}$. However, the results reported in Table 3 show that reaction (5b) becomes thermodynamically favourable upon addition of only 2% (v/v) acetonitrile to water, and we consider first the reaction in acetonitrile-water mixtures, according to Scheme 2.



Scheme 2.

In Scheme 2 the rate-determining step involved electron transfer within the complex formed between Cu^{2+} and HA^- or A^{2-} [steps (19) and (20)]. No direct kinetic evidence for the formation of Cu^{2+} -ascorbic complexes has been obtained in the present study but such species are well established in aqueous solution at higher pH values, with K_1 ca. $40 \text{ dm}^3 \text{ mol}^{-1}$.^{8,31-33} A similar K_1 value applied to the results in Table 7 with $[\text{H}^+] = 0.02 \text{ mol dm}^{-3}$ suggests that less than 3% of the Cu^{2+} would be bound as a complex for the highest $[\text{H}_2\text{A}]$ used and hence would not show up in the kinetic data. Application of the steady-state approximation to the intermediate copper(i)-ascorbic and radical ascorbate species leads to the rate law given in equations (22) and (23), assuming $[\text{Cu}^{\text{II}}(\text{HA})]^+$, $[\text{Cu}^{\text{II}}\text{A}]$

$$-d[\text{Cu}^{2+}]_{\text{T}}/dt = k_e[\text{Cu}^{2+}]_{\text{T}} \quad (22)$$

$$k_e = \left(k_3 + \frac{k_4 K_2}{[\text{H}^+]} \right) \cdot \frac{K_1 K_a}{K_a + [\text{H}^+]} \cdot [\text{H}_2\text{A}]_{\text{T}} \quad (23)$$

$\ll [\text{Cu}^{2+}]_{\text{T}}$, where $[\text{Cu}^{2+}]_{\text{T}}$ is the stoichiometric concentration of copper(II) during the reaction.*

Equation (23) shows that, at constant $[\text{H}^+]$, k_e is proportional to $[\text{H}_2\text{A}]_{\text{T}}$, thus giving a constant value of $k_2 = k_e/[\text{H}_2\text{A}]_{\text{T}}$ (Table 7). Rearrangement of equation (23), and using $k_2 = k_e/[\text{H}_2\text{A}]_{\text{T}}$, gives equation (24) for the acid

$$\frac{k_a(K_a + [\text{H}^+])}{[\text{H}^+]} = k_3 K_1 + \frac{k_4 K_1 K_2}{[\text{H}^+]} \quad (24)$$

dependence of the oxidation rate. The results in Table 8, plotted according to equation (24), are shown in Figure 4. The fit over a 15-fold change in $[\text{H}^+]$ is reasonable and gives an intercept $k_3 K_1 (= k_{\text{HA}}) = 1.3 \times 10^4 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$ and slope $k_4 K_1 K_2 = 1.37 \times 10^3 \text{ s}^{-1}$ {relating to reaction *via* $[\text{Cu}^{\text{II}}\text{A}]$ }. There is some deviation from the line for the points at lower $[\text{H}^+]$ but this is the region of greatest experimental uncertainty. According to

* The kinetic equation allowing for significant formation of $[\text{Cu}^{\text{II}}(\text{HA})]^+$ includes an extra factor $1 + K_2 K_a [\text{H}_2\text{A}]_{\text{T}} / (K_a + [\text{H}^+])$ in the denominator.

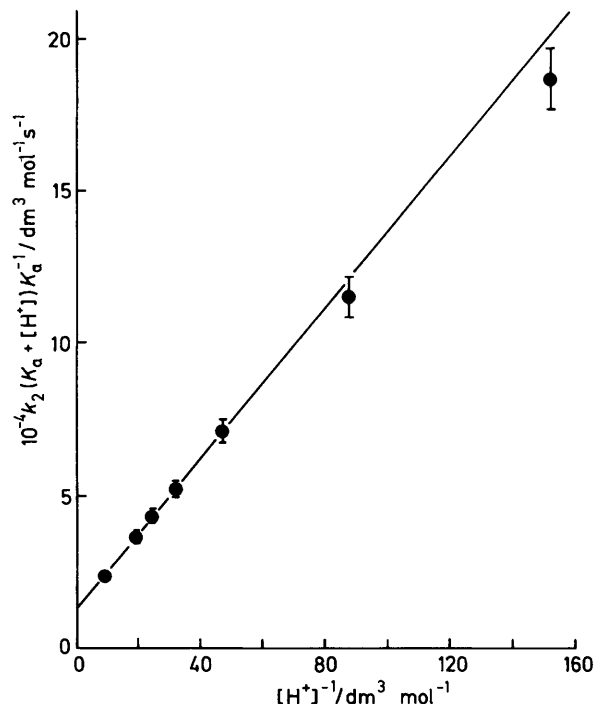


Figure 4. Acid dependence of the rate of oxidation of ascorbic acid by Cu^{II} in 20% (v/v) acetonitrile-water ($\pm 5\%$).

Scheme 2 and equation (24) then the higher-than-first-order inverse dependence of the oxidation rate on $[\text{H}^+]$ results from the participation of the dianionic ascorbate species. This has also been observed previously for oxidation reactions in water.

Similar behaviour to that shown in Table 8 and Figure 4 for 20% (v/v) acetonitrile was obtained in all solvent mixtures studied. However, it was noticeable that as the acetonitrile content of the solvent increased the relative contribution from the pathway involving A^{2-} [equation (20)] decreased. This is illustrated by the decrease in k_2 for a five-fold increase in $[\text{H}^+]$ from 0.02 to 0.10 mol dm^{-3} in various solvent mixtures: k_2 - $([\text{H}^+] = 0.02 \text{ mol dm}^{-3})/k_2([\text{H}^+] = 0.10 \text{ mol dm}^{-3}) = 16$ [10], 14 [20], 8.5 [30], 7.0 [40], and 5.8 [50% (v/v) CH_3CN]. This is not unreasonable as the formation of $[\text{Cu}^{\text{II}}\text{A}]$ involves liberation of two protons, the activities of which should increase significantly with increasing $x_{\text{CH}_3\text{CN}}$.

In dilute aqueous acid solution it is clear from the thermodynamics discussed above that reaction (5b) must be reversible, and the simplest interpretation of the results involves establishment of an initial equilibrium *via* a mechanism analogous to Scheme 2, but allowing for the reverse reactions in equations (19)–(21) (k_{-3} , k_{-4} , and k_{-5} respectively). This equilibration presumably accounts for the initial, faster reaction, the rate of which is consistent with that extrapolated from acetonitrile-water mixtures in which stabilisation of Cu^+ by CH_3CN essentially removes the reversibility. The subsequent slower reaction may be accounted for in two ways, both of which lead to the same overall reaction. The first is the oxidation of ascorbic acid by Cu^{I} to give Cu^0 and A, analogous to the silver(I) oxidation of ascorbic acid.³⁴ The second is the disproportionation of Cu^{I} to give Cu^{II} and Cu^0 , equation (1), followed by oxidation of H_2A by the Cu^{II} so produced. Shtamm *et al.*³⁰ in a detailed study in dilute acid solution monitored $[\text{Cu}^{2+}]$, $[\text{Cu}^+]$, and $[\text{H}_2\text{A}]$, and reported a two-stage decrease in $[\text{H}_2\text{A}]$ and $[\text{Cu}^{2+}]$ as observed here. They also found that

the $[\text{Cu}^+]$ increased initially to a maximum and then decreased more slowly to zero as Cu^0 was deposited. At the point of maximum $[\text{Cu}^+]$ a constant ratio of concentrations represented by $K = [\text{Cu}^+]_{\text{max}}^2[\text{A}][\text{H}^+]^2/[\text{Cu}^{2+}][\text{H}_2\text{A}]$ was obtained, the value of which agrees well with the equilibrium constant for equation (5b) calculated from the difference in the redox potentials of $\text{Cu}^{2+}-\text{Cu}^+$ and $\text{A}-\text{H}_2\text{A}$. It may be noted that reaction *via* Scheme 2 combined with reoxidation of Cu^{I} to Cu^{II} by O_2 , a facile process even in acetonitrile-water mixtures, seems an obvious candidate for the mechanism of the Cu^{2+} -catalysed oxidation of ascorbic acid by O_2 .³⁵ The mechanism appears, however, to be somewhat more complicated.^{11,12}

At higher pH values in aqueous solution ($\text{pH} \geq 5$), reaction (5b) is thermodynamically favourable. Kinetic studies in acetate buffers have shown the initial rate to be second order with respect to $[\text{Cu}^{\text{II}}]$ and first order with respect to $[\text{HA}^-]$ and $[\text{A}^{2-}]$.³⁶ This again is consistent with Scheme 2 as competition between reaction (21) (k_5) and the reverse of reactions (19) and (20) (k_{-3} and k_{-4}) will lead to an order with respect to $[\text{Cu}^{\text{II}}]$ varying between 1 and 2, depending upon the relative magnitudes of the rate constants.

Finally, we consider the influence of varying acetonitrile concentration on the reaction rate for oxidation by Cu^{II} and ferrocenium. Although a large number of studies have been reported in which the overall free-energy change for electron-transfer reactions has been varied by altering substituents within a series of related complexes,^{26,37} little has been reported on the influence on reaction rate of redox potentials altered by solvation changes. In the present study we are able to compare the behaviour of the outer-sphere oxidation of ascorbic acid by the ferrocenium ion with that of the inner-sphere oxidation by copper(II).

Theoretical treatments of outer-sphere oxidation reactions generally divide the free energy of activation into two independent contributions: the work term (including changes in solvation) or energy required to bring the reactants into a suitable configuration for electron transfer, and the energy associated with the electron-transfer process.^{26,37,38} Neither of these terms is expected to be sensitive to solvent for ferrocenium oxidation because of shielding of the iron by the ligands. In agreement with this neither the redox potential (Table 2)* or the overall rate constant k_2 (Table 6) varies strongly with solvent. A somewhat larger increase in k_{HA} , the rate constant for oxidation of the ascorbic acid monoanion HA^- , is observed. This may be explained by reduced solvation of the anion (and hence a reduced work term in forming the active complex) as water is replaced by the aprotic acetonitrile in the mixtures. This latter factor will also contribute to the increase in $\text{p}K_{\text{a}}$ of ascorbic acid with increasing $x_{\text{CH}_3\text{CN}}$ and will be common to oxidation by both ferrocenium and Cu^{2+} .

The solvent effect on the copper(II) oxidation is somewhat more interesting. In this case the reaction proceeds *via* the complexes $[\text{Cu}^{\text{II}}(\text{HA})]^+$ and $[\text{Cu}^{\text{II}}\text{A}]$ formed in rapid pre-equilibrium between Cu^{2+} and H_2A .³¹ Addition of as little as 10–20% (v/v) acetonitrile (4–8 mol %) causes a very large increase in E° for $\text{Cu}^{2+}-\text{Cu}^+$ [ca. 0.4 V in 20% (v/v), Table 2] but the results in Table 2 and Figure 1 suggest that this is due almost entirely to solvation of Cu^+ by acetonitrile [cf. E° for Cu^+-Cu^0 and $\text{Cu}^{2+}-\text{Cu}^0$] with little effect on Cu^{2+} ; it is not until the removal of the last few percent of water that the free energy of Cu^{2+} increases substantially.^{20,21} Thus the question arises as to the extent to which these substantial solvation changes are confined to the work terms preceding and following the electron transfer or are able to influence the electron-transfer process itself. In the former case they would influence mainly the

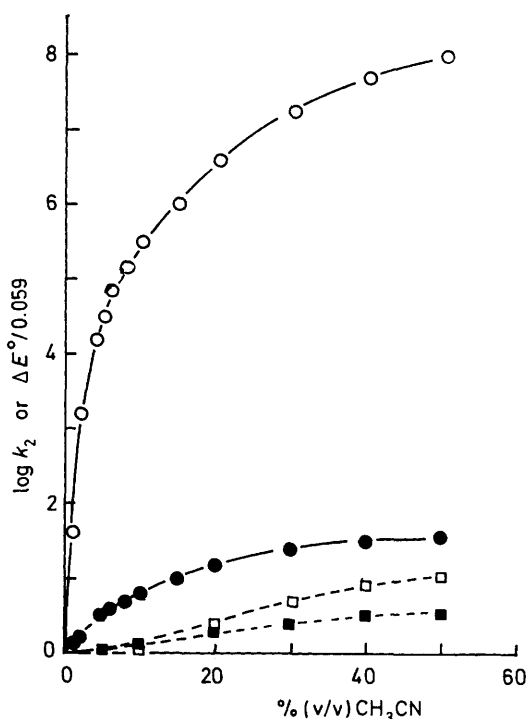
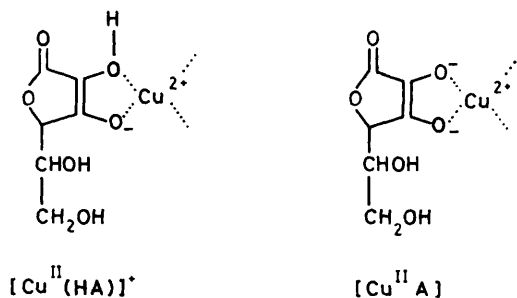


Figure 5. Comparison of E° values and rates of oxidation of ascorbic acid by Cu^{2+} and ferrocenium in acetonitrile-water mixtures: $\text{Cu}^{2+}-\text{Cu}^+$ ($\Delta E^\circ/0.059$) (O); $\text{Cu}^{2+}-\text{Cu}^+$ ($\log k_2$) (●); $[\text{Fe}(\text{C}_5\text{H}_5)_2]^+-[\text{Fe}(\text{C}_5\text{H}_5)_2]$ ($\Delta E^\circ/0.059$) (□); and $[\text{Fe}(\text{C}_5\text{H}_5)_2]^+-[\text{Fe}(\text{C}_5\text{H}_5)_2]$ ($\log k_2$) (■).

reverse reaction ($\text{Cu}^{\text{I}} \longrightarrow \text{Cu}^{\text{II}}$, $\text{A} \longrightarrow \text{H}_2\text{A}$) rather than the forward reaction ($\text{Cu}^{\text{II}} \longrightarrow \text{Cu}^{\text{I}}$, $\text{H}_2\text{A} \longrightarrow \text{A}$) as the reactants should be little affected by solvent (Tables 1 and 2) except at high $x_{\text{CH}_3\text{CN}}$. Thus the stabilisation of Cu^{I} by acetonitrile will only show up in correlations between the overall free-energy change and the activation free energy if CH_3CN is directly involved in the rate-determining step.

The observed rate constants (Table 9) show that there is a parallel between the rates and equilibria, illustrated by plots of $\log k_2$ and $E^\circ/0.059$ against % (v/v) acetonitrile (Figure 5). However, it does seem clear that the major influence of acetonitrile appears in the resolution of Cu^{I} following the electron transfer. Thus, for example, over the first 10% acetonitrile, $(\Delta G^\ddagger)/\Delta(\Delta G^\circ) \approx 0.1$, where ΔG^\ddagger is the overall free energy of activation and ΔG° is the overall free energy for reaction (5b). This is substantially lower than corresponding values for the outer-sphere oxidation of ascorbic acid by substituted iron(III)-phenanthroline complexes for which $\Delta(\Delta G^\ddagger)/\Delta(\Delta G^\circ) = 0.42$.²⁶

* Absolute values of the potential are of course dependent upon the use of an extrathermodynamic assumption.^{22,23}

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References

- 1 D. D. Wagman, W. H. Evans, V. B. Parker, I. Halow, S. M. Bailey, and R. H. Schumm, 'Selected Values of Chemical Thermodynamic Properties,' U.S. National Bureau of Standards Circular 500, technical note 270-4, January 1968.
- 2 A. J. Parker, *Proc. R. Aust. Chem. Inst.*, 1972, **39**, 163.
- 3 A. J. Parker, *Pure Appl. Chem.*, 1981, **53**, 1437.
- 4 J. P. Gisselbrecht and M. Gross, 'Electrochemical and Spectrochemical Studies of Biological Redox Components,' Advances in Chemistry Series No. 201, ed. K. M. Kadish, 1982, p. 110.
- 5 G. R. Dockal, T. E. Jones, W. F. Sokol, R. J. Engerer, D. R. Rorabacher, and L. A. Ochrymowycz, *J. Am. Chem. Soc.*, 1976, **98**, 4322.
- 6 L. S. W. Sokol, L. A. Ochrymowycz, and D. B. Rorabacher, *Inorg. Chem.*, 1981, **20**, 3189.
- 7 J. A. Fee, *Struct. Bonding (Berlin)*, 1975, **23**, 1.
- 8 M. M. T. Khan and A. E. Martell, *J. Am. Chem. Soc.*, 1967, **89**, 4176.
- 9 Y. Ogata, Y. Kosugi, and T. Morimoto, *Tetrahedron*, 1968, **24**, 4057.
- 10 E. V. Shtamm and Y. I. Shurlatov, *Zh. Fiz. Khim.*, 1974, **48**, 1454.
- 11 R. F. Jameson and N. J. Blackburn, *J. Chem. Soc., Dalton Trans.*, 1976, 543.
- 12 R. F. Jameson and N. J. Blackburn, *J. Chem. Soc., Dalton Trans.*, 1982, 9.
- 13 J. F. Coetzee, G. P. Cunningham, D. K. McGuire, and G. R. Podmanashan, *Anal. Chem.*, 1962, **34**, 1139.
- 14 R. G. Bates, 'Determination of pH: Theory and Practice,' 2nd edn., Wiley-Interscience, New York, 1973.
- 15 C. W. Davies, 'Ion Association,' Butterworths, London, 1962, equation 3.1.
- 16 C. Moreau and G. Douheret, *J. Chem. Thermodyn.*, 1976, **8**, 403.
- 17 R. Alexander, A. J. Parker, J. H. Sharp, and W. E. Waghorne, *J. Am. Chem. Soc.*, 1972, **94**, 1148.
- 18 H. M. Koepp, H. Wendt, and H. Strehlow, *Z. Elektrochem.*, 1960, **64**, 483.
- 19 C. Barraque, J. Vedel, and B. Tremillion, *Bull. Soc. Chim. Fr.*, 1968, 3421.
- 20 B. G. Cox, A. J. Parker, and W. E. Waghorne, *J. Phys. Chem.*, 1974, **78**, 1371.
- 21 A. J. Parker, D. A. Clarke, R. A. Couche, G. Miller, R. T. Tilley, and W. E. Waghorne, *Aust. J. Chem.*, 1977, **30**.
- 22 E. Grunwald, G. Baughan, and G. Kohnstam, *J. Am. Chem. Soc.*, 1960, **82**, 5801.
- 23 B. G. Cox, G. R. Hedwig, A. J. Parker, and D. W. Watts, *Aust. J. Chem.*, 1974, **27**, 477.
- 24 B. G. Cox and W. Jedral, *J. Chem. Soc., Faraday Trans. 1*, 1984, 781.
- 25 B. G. Cox and W. Jedral, *J. Electroanal. Chem.*, 1982, **136**, 93.
- 26 E. Pelizzetti, E. Mentasti, and E. Pramauro, *Inorg. Chem.*, 1978, **17**, 1181.
- 27 H. Roe, 'Methods of Biochemical Analysis,' Interscience, New York, 1954, vol. 1.
- 28 M. Kimura, M. Yamamoto, and S. Yamabe, *J. Chem. Soc., Dalton Trans.*, 1982, 423.
- 29 E. G. Ball, *J. Biol. Chem.*, 1937, **118**, 219.
- 30 E. V. Shtamm, A. P. Purmal, and Y. I. Skurlatov, *Zh. Fiz. Khim.*, 1974, **48**, 2229.
- 31 K. Hayakawa and Y. Hayashi, *J. Nutr. Sci. Vitaminol.*, 1977, **23**, 395.
- 32 Y. Yamamoto, K. Ishizu, and Y. Shimizu, *Chem. Lett.*, 1977, 735.
- 33 P. Martinez and J. Zuluaga, *An. Quim.*, 1984, **80**, 179.
- 34 S. P. Musharan, M. C. Agraval, R. M. Mehrotra, and R. Sanchi, *J. Chem. Soc., Dalton Trans.*, 1974, 1460.
- 35 H. Nord, *Acta Chem. Scand.*, 1955, **9**, 442.
- 36 R. D. Cannon, 'Electron Transfer Reactions,' Butterworths, London, 1980.
- 37 E. Pelizzetti, E. Mentasti, and E. Pramauro, *Inorg. Chem.*, 1976, **15**, 2898.
- 38 I. Bodek and G. Davies, *Coord. Chem. Rev.*, 1974, **14**, 269.

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