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Outer-sphere hexacyanoferrate(III) oxidation of organic substrates

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Contents

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Abstract

This review surveys the kinetics of the oxidation of organic substrates by hexacyanoferrate(III). Although a relatively poor oxidant, hexacyanoferrate(III) is a selective outer-sphere reactant applicable to the most easily oxidizable substrates, and frequently it is used as an interceptor of free radicals; this converts this species into an efficient one-electron oxidant particularly interesting in the comparative study of octahedral complexes. The major developments for each family of substrates are emphasized, comparing the mechanistic details for the various reaction types. © 1998 Elsevier Science S.A.

1. Introduction

Hexacyanoferrate(III) is one of the first compounds which was used as an oxidant, and many kinetic studies of its reactions have been carried out. Since the end of the last century, hexacyanoferrate(III) had been used to oxidize substrates such as aromatic hydrocarbons, quaternary heterocyclic salts and alkylthyoamides. After the comprehensive 1958 review by Thyagarajan reporting on hexacyanoferrate(III) oxidations [1], a great deal of work has been devoted to the elucidation of mechanistic aspects of a variety of organic substrates (oxygenated, sulphated, nitrogenated, unsaturated, etc.), most of them in basic media, describing experiments performed with modern techniques.

The key redox step in most, if not all, of these reactions involves an initial outer-sphere electron transfer (ox^-/red^+); for this step to occur, a substrate–oxidant ion-pair or outer-sphere (ox/red) precursor complex must be produced in a fast preequilibrium. Only the (ox/red) contact ion-pair is the critical precursor to the electrophile/nucleophile interaction, and the (ox/red) to (ox^-/red^+) electron transfer is the rate-determining step; the recent finding of a new near-infrared 800 nm intervalence hexacyanoferrate(II/III) transition [2] and the striking effect caused on this absorption band by replacing K^+ by larger cations such as $(CH_3)_4N^+$ in the outer-sphere shed abundant light into the crucial role played by the ion-pair configuration of the absorbing molecular entity.

2. A survey of the hexacyanoferrate(III/II) redox system

Hexacyanoferrate(III), $[Fe(CN)_6]^{3-}$, traditionally known as ferricyanide, is the anion (with neutral character regarding its acid–base behaviour, yellow colour in aqueous solution) of ferricyanic acid, $H_3[Fe(CN)_6]$; $H_3[Fe(CN)_6]$ is a very strong acid with $pK_1 = -6.25$, $pK_2 = -3.23$ and $pK_3 = -0.60$ [3], corresponding to the ionization equilibria

$$H_3[Fe(CN)_6] \overset{K_1}{\rightleftharpoons} H_2[Fe(CN)_6]^- + H^+ \quad (1)$$

$$H_2[Fe(CN)_6]^- \overset{K_2}{\rightleftharpoons} H[Fe(CN)_6]^{2-} + H^+ \quad (2)$$

$$H[Fe(CN)_6]^{2-} \overset{K_3}{\rightleftharpoons} [Fe(CN)_6]^{3-} + H^+ \quad (3)$$

This anion, $[Fe(CN)_6]^{3-}$, is a mild oxidant whose reduction potential remains essentially constant around 0.41 V within the pH range 4–13, referred to $[K^+]=0.1M$. Electrode potentials are normally only pH-dependent for anions whose protons are involved in the oxidation/reduction equation; thus, the reduction potential of the $[Fe(CN)_6]^{3-}/[Fe(CN)_6]^{4-}$ couple should not be pH-dependent, since H^+ is not included either in the oxidized or in the reduced form [4,5]. However, at higher acidity levels, the reduction potential increases from 0.56 to 0.93 V within $[H^+]=0.1$ to 8.0M [6] (Fig. 1), an effect ascribed to the formation of the mono-protonated $H[Fe(CN)_6]^{2-}$, bi-protonated $H_2[Fe(CN)_6]^-$ and tri-protonated $H_3[Fe(CN)_6]$ forms, and justifies the U-shaped rate constant profile with increasing proton concentration at acidities greater than 1M.

Hexacyanoferrate(III) is a stable octahedral complex with large energy gap between the ground state, $^2T_{2g}$, and the first excited state, ^2E_g, with $\Delta_o=34\,950\ cm^{-1}$; Fig. 2 shows the energy level diagram. The ground state corresponds to a paramagnetic complex of low spin [7–9]; the d^5 core in the octahedral symmetry of the $Fe(CN)_6^{3-}$ complex is split by spin–orbit coupling into a degenerate ^2E and a lower nondegenerate ^2A state with a small energy difference, $3/2\lambda_o$, the spin–orbit splitting parameter [10]. Introduction of one, two or three protons gives the $Fe(CN)_5(CNH)^{2-}$, $Fe(CN)_4(CNH)_2^-$ and $Fe(CN)_3(CNH)_3$ species, respectively, resulting in a lowering of the $^2T_{2g}$ energy level and a larger Δ_o energy gap. The UV spectral curves (Fig. 3) show five maxima at 416 nm ($\log\epsilon=3.01$), 318 nm ($\log\epsilon=3.05$, shoulder), 301 nm ($\log\epsilon=3.20$), 259 nm ($\log\epsilon=3.05$, shoulder) and 200 nm

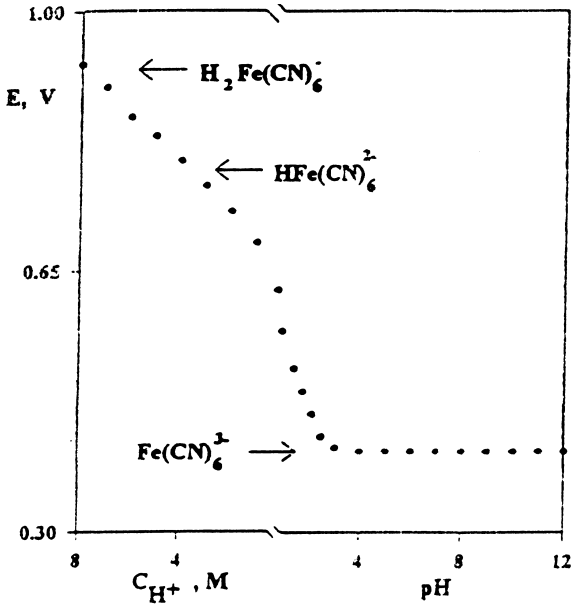


Fig. 1. Variation of the reduction potential E^o of the hexacyanoferrate(III/II) couple over a wide acidity range.

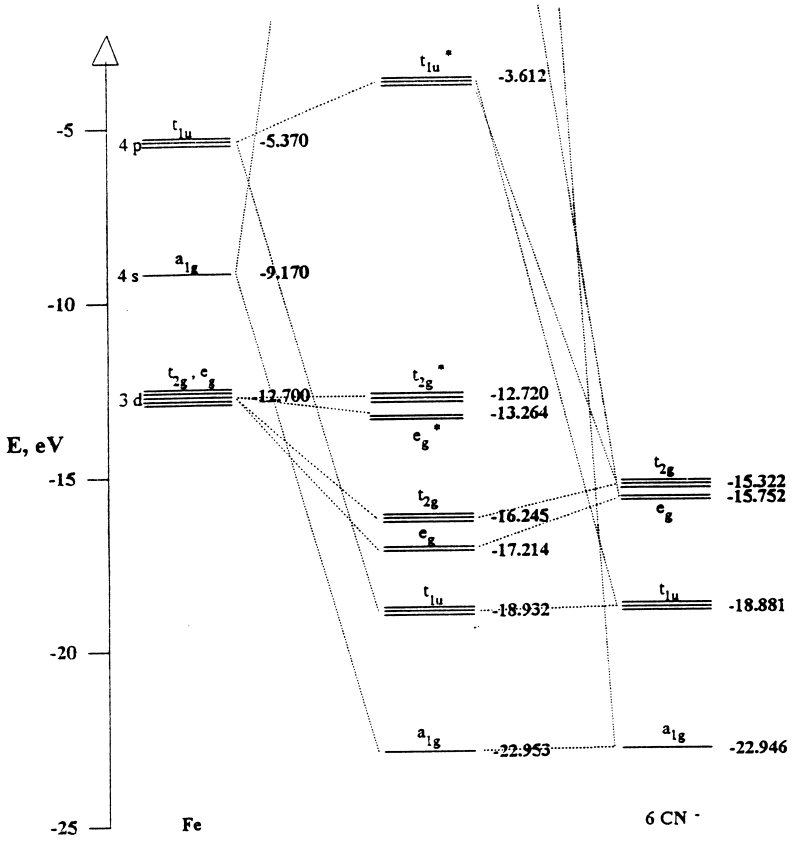


Fig. 2. MO energy diagram containing the most significant hexacyanoferrate(III) orbitals; the energies are based on an Extended Hückel Molecular Orbital calculation.

($\log \epsilon = 3.98$, shoulder). These intensities remain constant after addition of different cations, in spite of kinetic and conductometric evidence supporting ion-association effects [11,12]. $Fe(CN)_6^{3-}$ ions may form salts with different cations, especially with alkali-metal ions, $Fe(CN)_6^{3-}/Li^+$, Na^+, K^+ and Rb^+ according to

$$Y[Fe(CN)_6]^{2-} \overset{K_{YFe}}{\rightleftharpoons} Y^+ + [Fe(CN)_6]^{3-} \quad (4)$$

with $pK_{YFe} = (0.6–2.4)$ [6,13]. Kinetic evidence supporting a specific catalytic effect of these complexes in the oxidation of L-ascorbic acid [6] and substituted anilines [14] has been reported. The same effect was also detected in the reaction $Fe(CN)_6^{3-}/SO_3^{2-}$ where $[Fe(CN)_6–Y–SO_3]^{4-}$ was postulated in the transition state [15]; these ions bridge the two negatively charged species producing electrostatic screening and specific electronic effects, with the result of a decrease in the coulombic interaction and a relaxation of the need for a closer approach of the reactant anions,

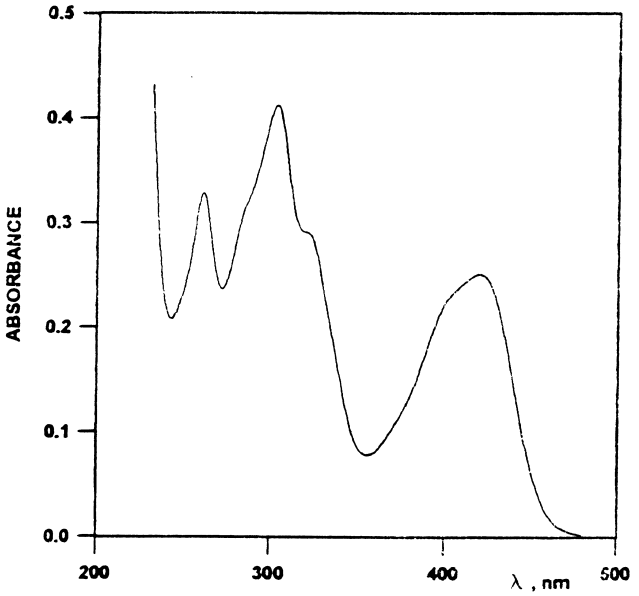


Fig. 3. UV-vis absorption of 2.5×10^{-4}M hexacyanoferrate(III).

thus playing a direct role in the electron transfer [16]. A band-shape analysis shows that extensive solvent and ion-pair reorganization occurs upon electron transfer [17].

Catalysis by ion-pairing is a general feature often found in many chemical reactions between two charged or an uncharged and a charged species [18–20]; this effect causes a decrease in the electrostatic repulsion between the reactants, the more so the larger the size of the cation. A weak near-infrared absorption band appears at 800 nm for equimolar mixtures $[Fe(CN)_6]^{3-}/[Fe(CN)_6]^{4-}$, which drops substantially upon stepwise replacement of K^+ ions by $(CH_3)_4N^+$ ions and even vanishes on full substitution [2]; replacement of K^+ by the larger $(CH_3)_4N^+$ cations increases the hexacyanoferrate(II/III) distance producing a decrease in the absorption band; this feature denotes that this intervalence transition involves ion-pairing. This argument has been used to rationalize the electron transfer between hexacyanoferrate(III/II), either in solution or at electrodes [21]. Moreover, hexacyanoferrate(III) ions are not prone to ligand substitution reactions and, if any, they are very slow. In basic media $Fe(CN)_6^{3-}$ is an inert complex regarding substitution of the cyano groups, and may be involved in one-electron transfer reactions retaining the inner coordination sphere. Given that HCN is a better π-acceptor ligand than CN^-, the protonation of $Fe(CN)_6^{3-}$ ions progressively increases the oxidizing power of this cyanometallate complex and facilitates the electronic flow from the organic substrate to the oxidant. This observation agrees well with the observed increase of the reduction potential with increasing acidity, for the lower the t_{2g} energy level (which means a higher reduction potential), the faster the electron transfer [22]. The oxidation of organic substrates proceeds through outer-sphere mechanisms, with the electron transfer

occurring from the reductant to the central atom via a cyanide ligand [23]. The cyano groups constitute bridging ligands, as they allow simultaneous C-bridging to the metal ion and N-bridging to the other electrophile.

In aqueous acidic solutions and in the presence of light the $Fe(CN)_6^{3-}$ ions hydrolyse slowly; this decomposition is noticeably inhibited in darkness. Depending on medium acidity, some hydroxo- or aquo-pentacyanoferrate(III) complexes can be formed [24], resulting in a change in solution pH if neutral, unbuffered media are used

$$[Fe(CN)_6]^{3-} + H_2O \overset{h\nu}{\rightleftharpoons} [Fe(CN)_5H_2O]^{2-} + CN^- \quad (5)$$

$$CN^- + H_2O \rightleftharpoons HCN + OH^- \quad (6)$$

If a $CN^{\cdot}$ radical rather than a CN^- ion is removed, then hexacyanoferrate(III) is reduced and the $CN^{\cdot}$ radicals combine to cyanogen. At room temperature and in 7M acid or greater concentration, we found that 80% of $Fe(CN)_6^{3-}$ decomposes to HCN and Fe^{3+}, and 20% is reduced to $Fe(CN)_6^{4-}$; we postulated both homolytic and heterolytic steps, with formation of $CN^{\cdot}$ radicals, $HCN^{\cdot -}$ radical anions and some Fe^{2+} complex species (Fig. 4) [3].

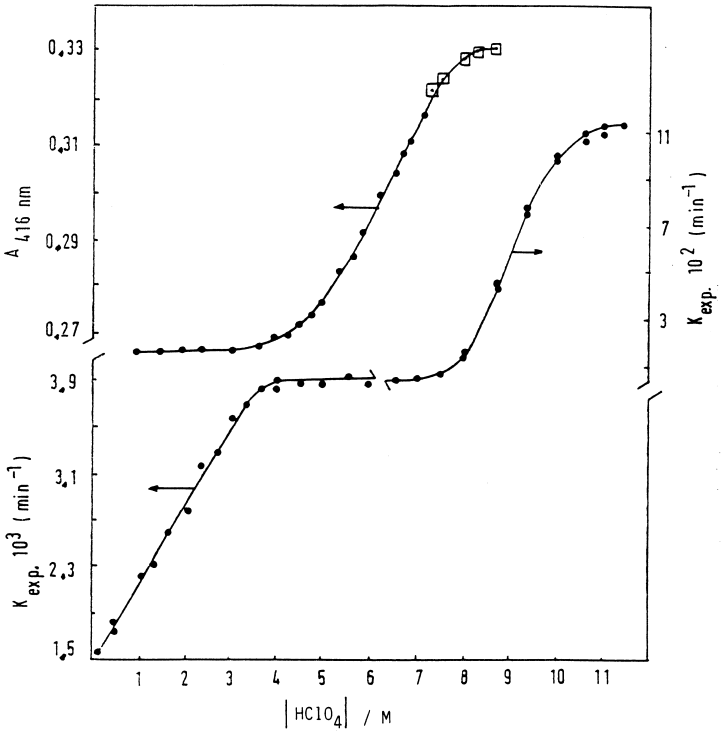


Fig. 4. Variation of absorbance ($A_{420\ nm}$) and k_{obs} rate constant for decomposition of hexacyanoferrate(III) with medium acidity [3].

Hexacyanoferrate(II), $Fe(CN)_6^{4-}$, also known as ferrocyanide, behaves as a tetravalent Brönsted-base and can react with four protons, forming ferrocyanic acid; it is the anion (pale-yellow in aqueous solutions) of ferrocyanic acid, $H_4Fe(CN)_6$, a strong acid in the dissociation of the two first protons, $pK'_1 = -2.54$ and $pK'_2 = -1.08$, and weaker in the dissociation of the third and fourth protons [25], $pK'_3 = 2.65$ and $pK'_4 = 4.19$. $Fe(CN)_6^{4-}$ protonates to a higher extent than $Fe(CN)_6^{3-}$ in the same medium acidity; this explains the observed increase in the electrode potentials with increasing acidity. The first two equilibria overlap with each other, as do the third and fourth ones

$$H_4[Fe(CN)_6] \overset{K'_1}{\rightleftharpoons} H_3[Fe(CN)_6]^- + H^+ \tag{7}$$

$$H_3[Fe(CN)_6]^- \overset{K'_2}{\rightleftharpoons} H_2[Fe(CN)_6]^{2-} + H^+ \tag{8}$$

$$H_2[Fe(CN)_6]^{2-} \overset{K'_3}{\rightleftharpoons} H[Fe(CN)_6]^{3-} + H^+ \tag{9}$$

$$H[Fe(CN)_6]^{3-} \overset{K'_4}{\rightleftharpoons} [Fe(CN)_6]^{4-} + H^+ \tag{10}$$

Hexacyanoferrate(II) is an octahedral, diamagnetic and stable complex of low spin and large energy gap [7], $\Delta_o = 33\,800\ cm^{-1}$, the ground state being $^1A_{1g}$. The UV-vis absorption spectral curves only display a noticeable maximum at 218 nm ($\log \epsilon = 4.35$), another absorption band of lower intensity at 425 nm ($\log \epsilon = 0.4$), and three shoulders at 322 nm ($\log \epsilon = 2.54$), 270 nm ($\log \epsilon = 3.25$) and 200 nm ($\log \epsilon = 4.05$) [26]. These intensities may be affected by addition of different cations due to ion-pair formation, especially with K^+

$$K[Fe(CN)_6]^{3-} \overset{K'_{YFe}}{\rightleftharpoons} [Fe(CN)_6]^{4-} + K^+ \tag{11}$$

with $pK'_{YFe} = 2.3$–2.4. In aqueous alkaline solutions hexacyanoferrate(II) is an even more inert ion than hexacyanoferrate(III) regarding the substitution of cyanide ligands. Although under normal laboratory conditions its aqueous acidic solutions decompose only negligibly, several authors have investigated thermal and photochemical decomposition over the 0–14 pH range [27]. Exposure of aqueous solutions to UV light, may result in an increase in pH due to hydrolysis of the cyanide released, according to

$$[Fe(CN)_6]^{4-} + H_2O \overset{h\nu}{\rightleftharpoons} [Fe(CN)_5H_2O]^{3-} + CN^- \tag{12}$$

$$CN^- + H_2O \rightleftharpoons HCN + OH^- \tag{13}$$

In sum, the hexacyanoferrate(II/III) redox couple constitutes a stable one-electron system categorized in a redox system group (ceric sulphate, ammonium–silver nitrate and Fehling's solution among others), the oxidant species being a one-electron acceptor complex ion

$$[Fe(CN)_6]^{3-} + e^- \rightleftharpoons [Fe(CN)_6]^{4-} \tag{14}$$

The rate constant $k = 5.45 \times 10^4 M^{-1} s^{-1}$ of this electron self-exchange reaction pathway involves reactants and products only in the lowest electronic state, and was determined by ^{13}C-line-broadening measurements and corrected for spin–orbit splitting effects [10]; temperature, high pressure and solvent isotope effects have shown that the H_2O molecules of the coordination sphere contribute noticeably to the reorganization Gibbs' energy of the optical transition [16].

$Fe(CN)_6^{3-}$ may be used to oxidize many organic substrates susceptible to extraction of one electron from the electron-rich site; this complex appeared in the organic chemistry literature along with a variety of available oxidants with specific and selective properties, such as selenium dioxide, lead tetraacetate, osmium tetroxide, *tert*-butyl chromate, chromium trioxide–pyridine complex, organic peroxiacids, periodic acid and peroxytrifluoroacetic acid; these compounds have extended the versatility of organic chemistry regarding the introduction of, or attack by functional groups either on simple or complex molecules. However, it should be pointed out that hexacyanoferrate(III) fails as an oxidant of many other organic species since it is most often an outer-sphere reagent applicable to the most easily oxidizable substrates only. This selectivity, however, makes the oxidant useful.

3. Oxidation of phenols

Phenols have been extensively used to protect living organisms and other organic materials from oxidative degradation; the oxidative coupling of phenols, ArOH, is an important reaction in the biosynthesis of many natural compounds, such as actinomycins and melanins [28]. The antioxidant action of phenols stems from their ability to trap peroxy radicals $ROO^{\cdot}$, forming aryloxy radicals $PhO^{\cdot}$ and hydroperoxide ROOH; phenoxy radicals are key intermediates in the oxidation of the small aromatic hydrocarbons which are constituents of lead-free gasoline. Phenol is the first complex real pollutant whose detailed supercritical water oxidation mechanism has been studied [29]. Chemical and biochemical phenol oxidations are complex reactions because they lack selectivity due to the different coupling reactions caused by phenoxy radicals; this has raised the challenge of exploring a practical method for selective oxidations. Recently, a biomimetic method for selective phenol oxidation by Lewis acid promoted migration using low valent ruthenium catalysts has been reported [30].

The alkaline oxidation of monohydric phenols, with *ortho* or *para* non-substituted positions, are quite complicated because the aryloxy radicals produced by the initial electron transfer may undergo a variety of reactions, thus yielding different products. The following observations apply:

(i) First-order in the oxidant and substrate concentrations.

(ii) First-order in base concentration, revealing that a phenolate anion, not the neutral molecule, is the reactive species. Polyphenols manifest a rather more complex behaviour.

(iii) An initial addition of hexacyanoferrate(II) to the reaction mixture inhibits

the oxidation, this denoting a reversible reaction in the kinetically significant step. Exceptions to this rule have also been reported [31].

(iv) The ionic strength effect points to a rate-controlling step between two negatively charged species. A specific catalytic effect of alkali-metal ions in the order $Na^+ < K^+ < Cs^+$ has been detected [32].

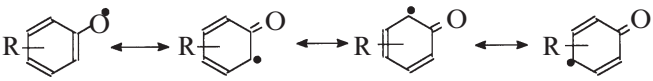
(v) Decreasing solvent relative permittivity results in an increase in reaction rate, consistent with reduction of ionic charge in the activated complex [33], and an easier formation of a radical intermediate in the rate-determining step.

In basic media it is reasonable to postulate a direct $Fe(CN)_6^{3-}$ oxidation of the phenolate anion in a one-electron rate-determining step with formation of phenoxy radical $PhO^{\cdot}$ [34].

(15)

(16)

Typical activation energies of 28, 32, 35, 24 and 10 kJ mol^{-1} for 1,3,5-trihydroxyphenol, α-naphtol, β-napthtol, resorcinol and orcinol, respectively, and activation entropies −174, −32 and −30 J K^{-1} mol^{-1} for 1,3,5-trihydroxyphenol, α-napthtol and β-napthtol, respectively, are consistent with an ion–ion interaction. The radical sites must be at the two *ortho* or the *para* positions, according to the following radical resonance structures [35].



(17)

The *meta* position should be less favourable, as a certain degree of ring strain is required. ESR measurements reveal the existence of an unpaired electron associated with the π-system of the aromatic ring with 17% of the unpaired spin density associated with both the O and the C atoms (the *p*- position 1.5 times that of the *o*- position) leading to a 17% O, 47% *o*-phenoxy and 36% *p*-phenoxy isomer distribution [28]. Conversion into stable nonradical products may occur by any one of the following routes:

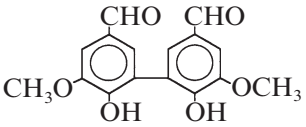
(1) Formation of oligomers via radical recombination.

(2) Oxidation of radicals yields reactive aryloxyl cations; the subsequent fast reaction with neutral phenol produces a variety of C–C and C–O dimers.

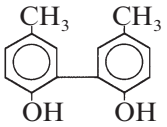
(3) Formation of stable halogen derivatives may follow if selective oxidants (like halogens) are present in the medium.

Phenoxy radicals are electron delocalized stable radicals resistant to oxygen addition, hence radical–radical processes become dominant; they are found in equilibrium with the dimer species [36] and become 100–300 times more reactive than peroxy radicals regarding the abstraction of phenolic hydrogen atoms [37]. The coupling

reactions in the second route, resulting from carbon–carbon, carbon–oxygen or oxygen–oxygen bonds involve cationic substitution and further oxidation of the substrate with formation of the mesomer aryloxy cation [38]. The C–C coupling may occur in *ortho–ortho*, *ortho–para* or *para–para* positions, and the carbon–oxygen in *ortho* or *para*; even though these couplings may give different products, the major products usually consist of species with little steric hindrance or susceptibility to resonance between the two rings. Examples of *ortho–ortho* C–C coupling are dehydrodivainillin (I) and dehydro-*p*-cresol (II), obtained by oxidation of vanillin and *p*-cresol [39]



(I)



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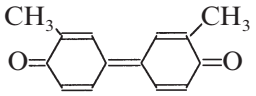
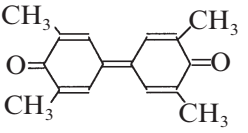
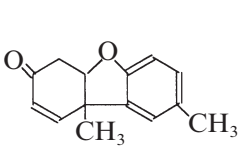


(III)



(IV)

while (III) and (IV) are examples of *para–para* coupling, by oxidation of *o*-cresol and 2,6-dimethylphenol, respectively [40]. The coupling mechanism depends on the reaction medium; phenoxy radical–phenoxy radical is the main route in aqueous solvent, whereas phenoxy radical–phenolate anion occurs in acetonitrile [41]. An example of *ortho–para* coupling is the ketone (V), obtained from cresol [36,38].



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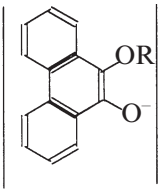
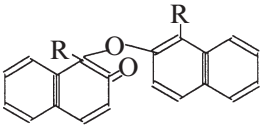


(VI)

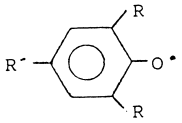


(VII)

Oxygen–oxygen coupling, quite unusual, occurs in the oxidation of the monoethyl- and monomethyl-ethers of phenanthrenehydroquinone, yielding species such as (VI). Carbon–oxygen coupling (VII), even more unusual, was reported in the oxidation of 1-methyl-2-naphthol or 1-bromo-2-naphthol [42]. In these examples the radical intermediates may exist in solution in equilibrium with the dimers, whereas in the solid phase only the dimer is stable.

Stable radicals can be isolated from phenol derivatives using carefully selected substituents: by introducing *o*- and *p*-substituents devoid of hydrogen atoms, the major oxidation product (99-100% yield) is the resonance-stabilized aryloxy radical; otherwise, a rapid conversion of phenoxy radicals into benzyl radicals and further

Table 1
Stable phenoxyl radicals obtained by basic hexacyanoferrate(III) oxidation of the corresponding phenols



R	R′	Colour	IR peaks (cm^{-1})
Tert-butyl	*Tert*-butyl	Blue	1507–1503
Tert-amyl	*Tert*-amyl	Blue	1507
Tert-butyl	Dimethylmethoxymethyl	Blue	–
Tert-butyl	Dimethylethoxymethyl	Blue	–
Tert-amyl	*Tert*-amyloxy	Red	–
Tert-amyl	Methoxy	Red	1590–1509
Tert-butyl	Ethoxy	Red	1590–1509
Tert-butyl	*Tert*-butoxy	Red	1590–1509

oxidation of the latter will occur; magnetic susceptibility measurements reveal the presence of an unpaired electron [43]; Table 1 lists the main features of some phenoxy radicals. Stable oxygenated biradicals may be produced by oxidation of substituted biphenols in benzene solution; in fact the appearance of a resin-type compound produced by oxidation of dimers and higher oligomers has been detected [44].

In sum, the phenoxy radicals produced in step (Eq. (16)) may follow several competing paths (dimers, higher oligomers, ring opening) depending on the particular phenol used. A range of reaction schemes may be postulated, hence the kinetic behaviour of most phenols may be described by any one of the following mechanisms (Schemes 1–5).

All five rate equations may be kinetically indistinguishable and identical with Eq. (22); the initial concentrations ratio $[Fe(CN)_6^{3-}]_o/[Fe(CN)_6^{4-}]_o$ exhibits a complicated inhibitory influence on k_{obs}. If $[phenol]_o < [Fe(CN)_6^{3-}]_o$, then the oxidant disappearance up to five half-lives may follow a second-order pattern. The reduction potentials for $Fe(CN)_6^{3-}/Fe(CN)_6^{4-}$ (0.41 V) and $ArO^-/Ar^{\cdot}$ (1.0 V) are consistent with the reversible formation of a phenoxy radical $ArO^{\cdot}$, stabilized by $Fe(CN)_6^{3-}$ in a second reversible step to produce the phenoxonium cation (ArO^+) in a rate-controlling step (Scheme 4).

The stoichiometric ratios are 1:1 or 2:1 oxidant:reductant and more rarely 3:1 [30]; detection of free radicals by ESR, IR and UV-vis has been reported [45,46]. Due to low solubility of the substrates, the kinetic experiments normally require

$$ArO^- + Fe(CN)_6^{3-} \xrightarrow{k_1} ArO^{\cdot} + Fe(CN)_6^{4-} \quad (18)$$

$$ArO^{\cdot} + ArO^{\cdot} \xrightarrow{\text{fast}} \text{Dimer} \quad (19)$$

or

$$ArO^{\cdot}(\text{mesomer}) + Fe(CN)_6^{3-} \xrightarrow{\text{fast}} ArO^{+}(\text{mesomer}) + Fe(CN)_6^{4-} \quad (20)$$

$$ArO^{+}(\text{mesomer}) + ArO^- \xrightarrow{\text{fast}} \text{Products} \quad (21)$$

consistent with the simplest rate equation:

$$-d[Fe(CN)_6^{3-}]/dt = (k_1 K_{AH}/K_W)\,[ArOH]\,[OH^-]\,[Fe(CN)_6^{3-}] \quad (22)$$

Scheme 1.

$$ArO^- + Fe(CN)_6^{3-} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ArO\cdot + Fe(CN)_6^{4-} \quad (18)$$

$$ArO\cdot \xrightarrow{k_2} \text{Products} \quad (23)$$

and rate law

$$r = \frac{K_{AH} k_1 k_2\,[ArOH]\,[OH^-]\,[Fe(CN)_6^{3-}]}{K_W k_{-1}\,[Fe(CN)_6^{4-}] + k_2 K_W} \quad (24)$$

Scheme 2.

$$ArO^- + Fe(CN)_6^{3-} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ArO\cdot + Fe(CN)_6^{4-} \quad (18)$$

$$2\ ArO\cdot \xrightarrow{k_2} \text{nonradical products} \quad (25)$$

leading to a more complex rate law:

$$r = k_1\,[Fe(CN)_6^{3-}]\,[ArO^-] - \frac{k^2_{-1}\,[Fe(CN)_6^{4-}]^2}{2k_2} \cdot \left\{ \left\{ 1 + \frac{4k_1 k_2\,[Fe(CN)_6^{3-}]\,[ArO^-]}{k^2_{-1}\,[Fe(CN)_6^{4-}]^2} \right\}^{1/2} - 1 \right\} \quad (26)$$

Scheme 3.

$$ArO^- + Fe(CN)_6^{3-} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ArO\cdot + Fe(CN)_6^{4-} \quad (18)$$

$$ArO\cdot + Fe(CN)_6^{3-} \rightleftharpoons [\text{ion pair}] \xrightarrow{k_2}$$

$$ArO^+ + Fe(CN)_6^{4-} \quad (27)$$

$$ArO^+ + ArO^- \xrightarrow{\text{fast}} \text{Dimers} \quad (28)$$

and rate law:

$$r = \frac{2k_1k_2\,[Fe(CN)_6^{3-}]^2[ArO^-]}{k_2\,[Fe(CN)_6^{3-}] + k_{-1}[Fe(CN)_6^{4-}]} \quad (29)$$

Scheme 4.

$$ArO^- + Fe(CN)_6^{3-} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ArO\cdot + Fe(CN)_6^{4-} \quad (18)$$

$$ArO\cdot \xrightarrow{k_2} R\cdot \quad (30)$$

$$R\cdot + Fe(CN)_6^{3-} \xrightarrow{\text{fast}} \text{Products} \quad (31)$$

and rate law:

$$r = \frac{k_1k_2\,[Fe(CN)_6^{3-}]\,[ArO^-]}{k_{-1}\,[Fe(CN)_6^{4-}] + k_2} \quad (32)$$

Scheme 5.

mixed solvents; an inert atmosphere is also convenient to avoid quenching of the radical cation by O_2 [47]. The oxidation of benzenediols follow [6]

$$H_2Q + Fe(CN)_6^{3-} \xrightarrow{\text{slow}} H_2Q^{\cdot +} + Fe(CN)_6^{4-} \quad (33)$$

$$H_2Q^{\cdot +} + Fe(CN)_6^{3-} \xrightarrow{\text{fast}} Q + 2H^+ + Fe(CN)_6^{4-} \quad (34)$$

where H_2Q stands for benzenediol and Q for benzoquinone.

The oxidation of carefully selected phenols yields naturally occurring compounds such as the indols serotonin, bufotenin, eserotola, fisostigmin and eserolin; adrenaline and its derivatives convert into indol in reasonably high yield [48]; these examples emphasize the role played by phenol oxidation in the biosynthesis of natural products.

4. Oxidation of alcohols

The kinetic features and the mechanism postulated are similar to those of phenols [49]: first-order in oxidant, substrate and base concentrations. The formation of an alkyloxy radical occurs in the rate-determining step by oxidation of the substrate anionic form, followed by further rapid oxidation to produce more unsaturated species.

The oxidation of aminoalcohols, diols and glycols does not occur via free radicals, but rather through an intermediate complex between the oxidant and the anionic substrate [50–52]. The reaction is first-order with respect to oxidant, substrate and base concentrations and exhibits alkali-metal ions specific catalytic effect. Contrary to phenols, an initial addition of $Fe(CN)_6^{4-}$ does not inhibit the reaction. Dissolved O_2 has no effect on the oxidation rate, but CO_2 inhibits the reaction due to partial neutralization of the medium. The effect of solvent relative permittivity on the rate constants, the activation energy ($40\ kJ\ mol^{-1}$) and the negative entropy ($-210\ J\ K^{-1}\ mol^{-1}$) for triethanolamine, is consistent with a rate-determining step involving ions carrying charges of same sign, consistent with the following mechanism.

$$R\text{–}OH + OH^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R\text{–}O^- + H_2O \tag{35}$$

$$R\text{–}RO^- + Fe(CN)_6^{3-} \xrightarrow{k_2} \text{Complex } (X^{4-}) \tag{36}$$

$$\text{Complex } (X^{4-}) + Fe(CN)_6^{3-} \xrightarrow{k_3} 2\ Fe(CN)_6^{4-} + \text{Prod} \tag{37}$$

Alkyloxy radicals are less stable than phenoxy radicals and alcohol oxidations normally require a catalyst. These oxidations follow Michaelis–Menten-type schemes: the substrate–catalyst complex diproportionates to give the products. The role of hexacyanoferrate(III) consists of regenerating a hydride catalyst by oxidizing its reduced form, hence most reactions are zero-order in oxidant, according to

$$r = \frac{k_1[\text{alcohol}][\text{catalyst}][OH^-]}{1 + k_2[\text{alcohol}] + k_3[OH^-]} \tag{38}$$

as in the Ru(VIII)-catalyzed oxidation of alcohols [53], the Ru(VI)-catalyzed oxidations of *n*-alkanols [54,55], unsaturated alcohols [56], the cycloalcohols [57], and the Ru(III)-catalyzed oxidation of alkanols [58–61], diols [62], glycols [63], benzyl alcohol [64] and ethylene glycols [65]; a similar pattern follows the Ru(VIII)-catalyzed oxidations of butanediols and cyclopentanol [66]; even though a rather more complex rate-law follows, it reduces to Eq. (38) at high alcohol and OH^- concentrations. The Os(VIII)-catalyzed oxidations of 1- and 2-propanol [67], butylglycol [68] and allyl alcohol [69] also adhere to Eq. (38), the catalytic species being $OsO_4(OH)_2^{2-}$, as do the Rh(III)-catalyzed oxidations of 2-propanol and 2-butanol [70]. These reactions produce the corresponding carboxylic acids or a mixture of organic acids for secondary alcohols; cyclic alcohols yield preferentially ketones. A somewhat different behaviour is exhibited by the alkaline Os(VIII)-catalyzed oxidation of 2-aminoethanol and 3-aminoethanol [71].

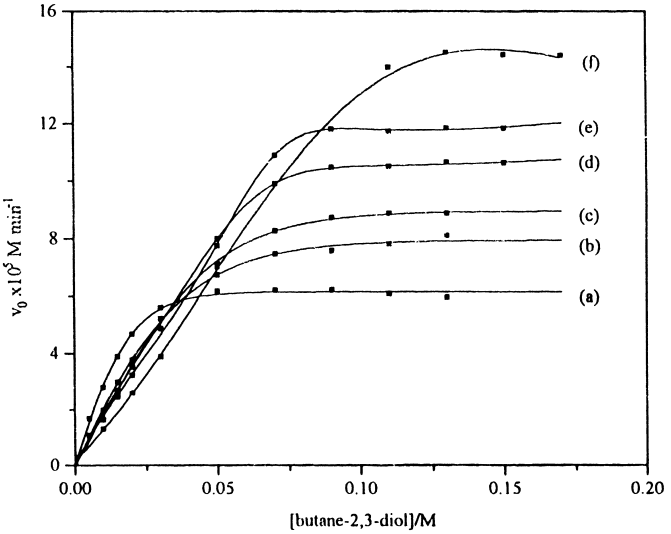
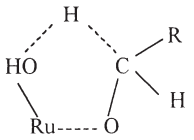


Fig. 5. Effect of substrate concentration on k_{obs} for the Ru(III)-catalyzed oxidation of butane-2,3-diol: $[RuCl_3] = 1 \times 10^{-6}$M; $[Fe(CN)_6^{3-}] = 0.003$M; [substrate] = 0.01M; [NaOH] (top to bottom): 0.45, 0.27, 0.21, 0.18, 0.15 and 0.03M [73].

It is only recently that the Ru(III)-catalyzed oxidation of propanol [72] and butane-2,3-diol [73] has been reported via free radicals, showing a Michaelis–Menten-type pattern on a substrate (Fig. 5); the intermediate substrate–catalyst complex is assumed to react with the oxidant in a rate-determining step involving abstraction of a hydrogen atom from the α-C to give a free radical which is further oxidized to products



$$+ Fe(CN)_6^{3-} \longrightarrow$$

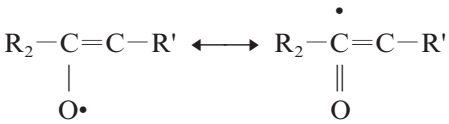
$$RCHO^- + Fe(CN)_6^{4-} + Ru(H_2O)_6^{3+} \quad (39)$$

The substrate–metal coordination in a cyclic complex prior to the H-transfer step [74] substantially lowers the activation energy, this explaining why hindered alcohols react slowly [75].

5. Oxidation of aldehydes, ketones and acyloins

The chemistry of simple enols is of great importance, and particularly the magnitude of the keto–enol conversion. These reactions are first-order both in alkali and substrate. The rate-controlling step depends on the particular substrate; dissolved oxygen gives rise to an induction period. If the oxidant is involved in the rate-determining step, then specific catalysis by K^+ ions occurs [76].

The dependence of base concentration denotes that the oxidizable species is the enol form, an assumption supported by the observation that benzaldehyde (which is not susceptible to keto–enol conversion) is not oxidized by $Fe(CN)_6^{3-}$, and furfuraldehyde is hardly oxidizable. The electron transfer from the anion of the enol form should generate the mesomer radical



(40)

Negative tests for vinyl polymerization point to an enol–$Fe(CN)_6^{3-}$ complex already suggested by Speakman and Waters [77] in the oxidation of aldehydes and ketones.

$$R\text{–}H + OH^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R^- + H_2O \tag{41}$$

$$R^- + Fe(CN)_6^{3-} \xrightarrow{k_2} \text{Complex } (X^{4-}) \tag{42}$$

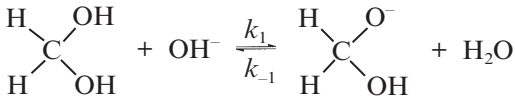
$$\text{Complex } (X^{4-}) + Fe(CN)_6^{3-} \longrightarrow \text{Prod} + 2\ Fe(CN)_6^{4-} \tag{43}$$

$$2\ (X^{4-}) \longrightarrow \text{Dimer} + 2\ Fe(CN)_6^{4-} \tag{44}$$

If Eq. (41) is rate-determining, then the reaction is first-order in OH^- and substrate, and zero-order in oxidant; if Eq. (42) is rate-determining, a first-order dependence in all three concentrations appears. With acetone, step (Eq. (42)) is reversible, Eq. (43) is rate-determining, and the reaction is second-order in oxidant. The general rate equation is

$$r = k[OH^-][\text{Substrate}][Fe(CN)_6^{3-}]'' \tag{45}$$

with $n = 0$, 1, 2. A free radical scheme has also been postulated [76,78]. Studies of substituent effects support the greater stability of the enol form for acetophenones ($\rho = 2.0$) and aliphatic ketones ($\rho = 3.0$) [79] and provide an extra kinetic proof of a mechanism to discriminate one-electron from two-electron transfers; the activation energies 48, 29 and 93 kJ mol^{-1} and activation entropies -112, -137 and -21 J K^{-1} mol^{-1}, for acetone, methyl-ethyl ketone and acetophenone, respectively, are consistent with a rate-controlling step involving species with charges of the same sign [80]. A striking exception is formaldehyde [81] (99% hydrated as $H_2C(OH)_2$), the reaction proceeds via free radicals



(46)

(RO^-)

$$RO^- + Fe(CN)_6^{3-} \xrightarrow{k_2} RO^{\cdot} + Fe(CN)_6^{4-} \quad (47)$$

$$RO^{\cdot} + Fe(CN)_6^{3-} \xrightarrow{\text{fast}} HCOOH + Fe(CN)_6^{4-} + H^+ \quad (48)$$

$$HCOOH + OH^- \rightarrow HCOO^- + H_2O \quad (49)$$

giving a rate-law

$$r = \frac{2k_1k_2[H_2C(OH)_2][OH^-][Fe(CN)_6^{3-}]}{k_{-1}[H_2O] + k_2[Fe(CN)_6^{3-}]} \quad (50)$$

The rate-determining step in the basic oxidation of α-hydroxy ketones (acyloins) [82,83] is the oxidation of the enolate to the mesomer radical Ph–CO–$HCO^{\cdot}$–Ph, forming benzil [84].

As with alcohols, OsO_4 has frequently been used in the oxidation of ketones, aldehydes and acyloins [85–88]; these reactions are zero-order in oxidant and obey the rate-law

$$r = k[\text{Substrate}][OH^-][OsO_4] \quad (51)$$

The mechanism involves the formation of an enolate–catalyst complex; as for alcohols, the role of the oxidant consists of regenerating the catalyst, and it is the species effectively consumed. Based on this effect, a potentiometric titration method for formaldehyde by Os(VIII)-catalyzed oxidation with $Fe(CN)_6^{3-}$ which excludes any interference of methanol, ethanol and other organic substrates has been utilized for a long time [89].

6. Oxidation of sugars and enediols

Basic oxidation of sugars, mono-, di- or oligosaccharides, aldo- or ketosugars, all follow the same pattern. The reaction is general base-catalyzed, and the rate is independent of the oxidant

$$r = k[\text{sugar}][\text{Base}] \quad (52)$$

Enolization is the initial and rate-determining step with formation of divalent enolate ions of 1,2-enediol, which is rapidly oxidized by the oxidant

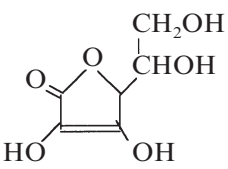
$$\begin{array}{l} CH_2OH \\ | \\ C{=}O \\ | \\ R \end{array} \text{ or } \begin{array}{l} HC{=}O \\ | \\ HCOH \\ | \\ R \end{array} + 2OH^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \begin{array}{l} HCO^- \\ | \\ CO^- \\ | \\ R \end{array} + 2H_2O \quad (53)$$

The reaction is inhibited by $Fe(CN)_6^{4-}$ and manifests a salt effect, in accordance with the prediction for an ion–dipole reaction [12]; dissolved O_2 causes an induction period. The rate constants increase with decreasing solvent relative permittivity using OHNa, but the opposite effect appears if NH_3 is used [90], because a decrease in

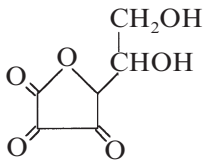
relative permittivity is accompanied by both a decrease in OH^- concentration and an increase in NH_3; the oxidation is retarded because the reaction rate is proportional to $k_{OH^-}[OH^-]+k_{NH_3}\cdot[NH_3]$, with $k_{OH^-}=500\cdot k_{NH_3}$. The negative activation entropies -61 and $-9\ J\ K^{-1}\ mol^{-1}$ for lactose and maltose, respectively, are consistent with an ion–dipole interaction.

Monosaccharides produce aldonic acids, and bisaccharides give bionic acids, which are easily hydrolyzed. Oxidation of the aldopentoses, aldohexoses and ketohexoses D-fructose, and the bisaccharides lactose, maltose, melobiose and celobiose follow the above mechanism [90–93]. Addition of sodium tetraborate produces a borate–sugar complex and the reaction is inhibited. The basic oxidation has long been used in the titration of sugars; the content of fructose–glucose mixtures can be determined using temperature and pH ranges where glucose is not oxidized [94].

The oxidation of enediols, an intermediate step in the oxidation of sugars, is a fast reaction, as is the oxidation of ascorbic acid or vitamin C (VIII) [95,96], an antioxidant and radical scavenger widely distributed in human tissues; its 2,3-enediol group is so effective as a reducing agent that it offers wide applications in analytical chemistry. Triose reductone (RH_2 or 2,3-dihydroxy-2-propenal), the simplest in structure of the compounds having an endiol group has these features, and knowledge of its kinetic behaviour is required for a better understanding of the physiological activity of the enediol group. The physiologically important ascorbic acid is a typical species with this structure; it is susceptible to oxidation in both acidic and basic media, and offers important applications in food industry [97]. Recently, there has been renewed interest in the protective role played by antioxidants in chronic diseases such as cancer, AIDS and celular damage caused by oxidants arising from normal metabolism [98]. Ascorbic acid (VIII) has been shown to mediate the N-deoxygenation and N-dealkylation of *N*,*N*-dimethylaniline N-oxide [99].



(VIII)



(IX)

This substrate is prone to attack by oxidant at the oxygen sites of the enediol group. The oxidation products depend on pH, but oxidation in acidic and basic solution produces dehydroascorbic acid (IX), a lactone whose ring can be easily hydrolyzed to give the free carboxylic group [100]; the reaction continues to L-xylose, lyxonic, oxalic and threonic acids.

Ascorbic acid is highly sensitive to heat, oxygen and alkaline conditions; the neutral or weakly acidic $Fe(CN)_6^{3-}$ oxidation can be monitored by conventional spectrophotometry, but it requires fast reaction techniques within pH 6.5–8.0, always using deoxygenated solvent to avoid self-decomposition (Fig. 6) [101]. Above pH 8 the oxidation is too fast, and can no longer be followed by stopped-flow techniques.

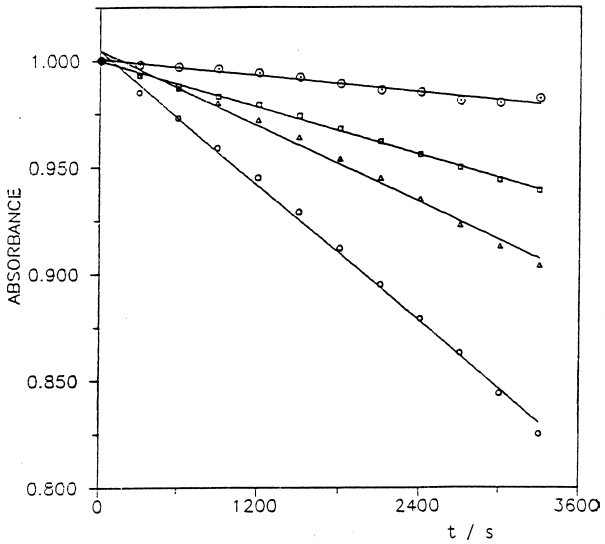


Fig. 6. Effect of ionic strength on the zero-order self-decomposition reaction of ascorbic acid by dissolved oxygen: pH = 6.8; $[H_2A] = 1 \times 10^{-4}$M; ionic strength (top to bottom): 0.25, 0.20, 0.15 and 0.10M.

The oxidation at pH < 7, follows the mechanism [102–107]

$$H_2A \overset{K_{H2A}}{\rightleftharpoons} HA^- + H^+ \quad (54)$$

$$HA^- \overset{K_{HA-}}{\rightleftharpoons} A^{2-} + H^+ \quad (55)$$

$$H_2A + Fe(CN)_6^{3-} \overset{k_a}{\longrightarrow} H_2A^{\bullet +} \; Fe(CN)_6^{4-} \quad (56)$$

$$HA^- + Fe(CN)_6^{3-} \overset{k_b}{\longrightarrow} HA^{\bullet} + Fe(CN)_6^{4-} \quad (57)$$

$$A^{2-} + Fe(CN)_6^{3-} \overset{k_c}{\longrightarrow} A^{\bullet -} + Fe(CN)_6^{4-} \quad (58)$$

$$H_2A^{\bullet +}/HA^{\bullet}/A^{\bullet -} + Fe(CN)_6^{3-} \overset{\text{fast}}{\longrightarrow} A + Fe(CN)_6^{4-} + 2/1/0\ H^+ \quad (59)$$

with rate law:

$$r = \frac{2k_a[H^+] + 2k_bK_{H2A}}{[H+] + K_{H2A}} [H_2A]_t [Fe(CN)_6^{3-}]_t \quad (60)$$

where subscript "t" denotes total concentration, and A dehydroascorbic acid. Comparison of the rate constants $k_a = 0.57M^{-1}s^{-1}$ and $k_b = 860M^{-1}s^{-1}$ reveals

the much greater reactivity of HA^- compared to H_2A (at this acidity level the A^{2-} concentration is negligibly small, $K_{HA^-}=11.9$, Fig. 7). The net reaction is often used in the quantitative determination of vitamin C in pharmaceuticals.

Two acidity regions with U-shaped rate constant profile allow one to discriminate two mechanisms at higher acidities [4,108–111]; within 0.01–0.20M acidity range, HA^- and H_2A are the only oxidizable substrates. The effect of varying concentrations of added salts YCl ($Y^+=Li^+$, Na^+, K^+, Rb^+) reveals the existence of a specific catalytic effect by binding of alkali-metal ions to oxidant, Eq. (4), so that the $YFe(CN)_6^{2-}$ complexes play an important oxidizing role (Fig. 8); the origin of the formally catalytic effect of the cations in this case may be the cation-dependence of the hexacyanoferrate(III/II) redox potential: $k(Rb)/k(Li)=1.45$ is consistent with $\Delta\Delta G^*$ 10 meV, whereas $E^f(Rb)/E^f(Li)=0.17$ mV (0.1M Cl) [4]. In addition to steps (Eqs. (4)), ((54)), ((56)) and ((57)) the mechanism postulated includes

$$H_2A^{\bullet+} \overset{k_{H_2A^{\bullet+}}}{\rightleftharpoons} AH^{\bullet} + H^+ \tag{61}$$

$$H_2A^{\bullet+}/HA^{\bullet} + Fe(CN)_6^{3-} \xrightarrow{\text{fast}} A + Fe(CN)_6^{4-} + 2/1\ H^+ \tag{62}$$

$$HA^- + YFe(CN)_6^{2-} \xrightarrow{k_1} HA^{\bullet} + YFe(CN)_6^{3-} \tag{63}$$

$$H_2A + YFe(CN)_6^{2-} \xrightarrow{k_2} H_2A^{\bullet+} + YFe(CN)_6^{3-} \tag{64}$$

$$H_2A^{\bullet+}/HA^{\bullet} + YFe(CN)_6^{2-} \xrightarrow{\text{fast}} A + YFe(CN)_6^{3-} + 2/1\ H^+ \tag{65}$$

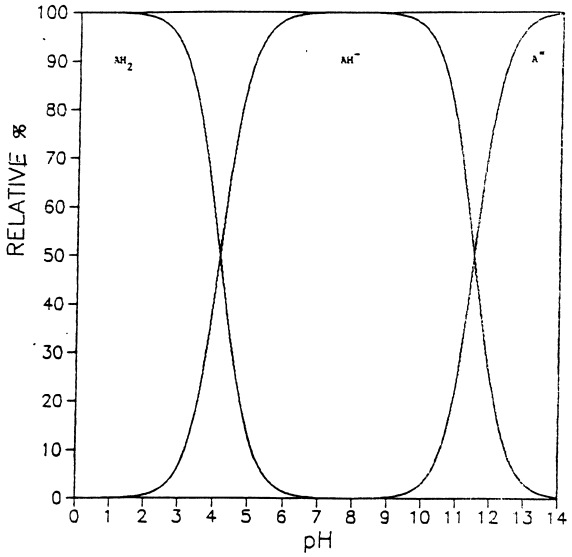


Fig. 7. Percentage distribution of the various ionized forms of ascorbic acid as a function of medium acidity.

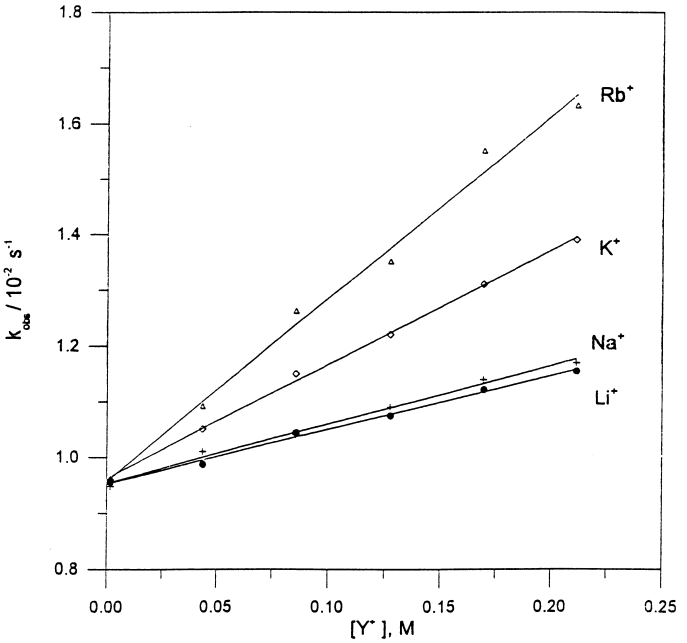


Fig. 8. Specific catalytic effect of alkali-metal ions on the hexacyanoferrate(III) oxidation of ascorbic acid: $[Fe(CN)_6^{3-}]=5\times10^{-4}$M, $[H_2A]=0.01$M, $[HClO_4]=0.15$M [6].

As occurs in most oxidations first-order in oxidant and reductant, the rate-determining steps (Eqs. (56) and (57)) involve an electron transfer with formation of ascorbate free radical, giving $Fe(CN)_6^{4-}$ and A in a subsequent diffusion-controlled step [112–114]. Nevertheless, recombination of two ascorbate radicals, forming H_2A and A in a fast diffusion-controlled step, should also be considered [115,116]. Eqs. (61)–(65) account for the specific catalysis by alkali-metal ions [4], steps (Eqs. (63)–(65)). The $AH^{\cdot}$ radicals do not disappear via radical recombination, but rather through reaction with $Fe(CN)_6^{3-}$ ions, since all steps are diffusion-controlled and the oxidant concentration is much higher than that of $AH^{\cdot}$ radicals [117]. This gives the following rate-law

$$r=2[Fe(CN)_6^{3-}]_t[AH_2]_t\left\{\frac{k_1K_{H2A}}{[H^+]}+k_2+\left(\frac{k_3K_{H2A}}{[H^+]}+k_4\right)K_{YFe}[Y^+]\right\} \qquad (66)$$

with $k_a=0.41M^{-1}s^{-1}$ and $k_b=139$, in good agreement with those of Eqs. (54)–(60). Comparison of the ratios $k_1/k_2=2.8\times10^4$ and $k_b/k_a=340$ reveals that the $YFe(CN)_6^{2-}$ ions are two orders of magnitude more reactive than $Fe(CN)_6^{3-}$; this effect reflects the important role played by binding of alkali-metal ions to bridge the cyanide ligands of the iron complex [19,118]. From a pressure-dependence study of the hexacyanoferrate(III)/L-ascorbic acid redox reaction the involvement of bicyclic ascorbate radicals and/or nonadiabatic pathways have been concluded [119].

Within the highest acidity range accessible by spectrophotometry (0.20–3.0M)

the amount of HA^- and A_2^- ions is negligibly small, and the species H_2A and H_3A^+ are the only oxidizable species present in solution. Moreover, the metal ions Y^+ can be replaced by H^+ in the sphere of the oxidant, since equilibrium (Eq. (3)) becomes predominant: the $[HFe(CN)_6^{2-}]/[Fe(CN)_6^{3-}]$ ratio is unity at acidity 0.5M. In addition to steps (Eqs. (3) and (56)) the scheme involves [3]

$$H_2A + HFe(CN)_6^{2-} \xrightarrow{k_{11}} H_2A\bullet^+ + HFe(CN)_6^{3-} \quad (67)$$

$$H_3A^+ \underset{}{\overset{K_{H3A}{}^+}{\rightleftharpoons}} H^+ + H_2A \quad (68)$$

$$H_3A^+ + Fe(CN)_6^{3-} \xrightarrow{k_{22}} H_2A\bullet^+ + Fe(CN)_6^{4-} + H^+ \quad (69)$$

$$H_3A^+ + HFe(CN)_6^{2-} \xrightarrow{k_{33}} H_2A\bullet^+ + HFe(CN)_6^{3-} + H^+ \quad (70)$$

$$H_2A\bullet^+ + Fe(CN)_6^{3-} \xrightarrow{\text{fast}} A + Fe(CN)_6^{4-} + 2H^+ \quad (71)$$

$$H_2A\bullet^+ + HFe(CN)_6^{2-} \xrightarrow{\text{fast}} A + HFe(CN)_6^{3-} + 2H^+ \quad (72)$$

with rate law:

$$r = 2[Fe(CN)_6^{3-}]_t [H_2A]_t \cdot$$

$$\cdot\left[\frac{k_{11}K_3K_{H3A+} + (k_{22}K_{H3A}{}^+ + k_{33}K_3)[H^+] + k_{44}[H^+]^2}{K_{H3A}+K_3 + (K_3 + K_{H3A+})[H^+] + [H^+]^2}\right] \quad (73)$$

with $k_{33} = 22M^{-1}s^{-1}$, and $k_a = 0.47M^{-1}s^{-1}$, in good agreement with k_1 in [61–65]; the step k_a is involved in different mechanisms, and was determined under different sets of experimental conditions with excellent agreement. The $HA^{\cdot}$ and $H_2A^{\cdot +}$ radicals both disappear in fast diffusion-controlled steps.

7. Oxidation of α-hydroxyacids, α-ketoacids and α,β-unsaturated acids

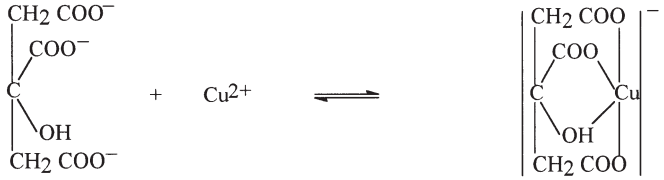
Investigations in basic media require intervention of catalysts because only few substrates are susceptible to direct oxidation; these reactions are first-order in oxidant, and first-order (or close to first, depending on the substrate) in substrate and $[OH^-]$; $Fe(CN)_6^{4-}$ causes no inhibition. Depending on pH, hydroxymalonic acid can exist in various ionized forms; its degradation is important in the oxidative purification of water [120]. The reaction products are low molecular weight carboxylic acids, HCHO and CO_2; oxidation of α-hydroxy acids often generates the corresponding α-ketoacid. The mechanism postulated involves the striking feature of a direct oxidant–substrate reaction with formation of a radical species via an oxidant–reductant complex; this pattern applies only for this type of substrate [121–123]. The catalyzed oxidations are zero-order in oxidant, except for Cu(II). The

route for the Os(VIII)-catalyzed oxidations is similar to that of alcohols, aldehydes and ketones; the mechanism involves an $OsO_4(OH)_{22}$–substrate complex, the alkaline rupture of which is rate-determining

$$r = \frac{k_1[\text{substrate}][\text{Os(VIII)}][\text{OH}^-]}{k_2 + k_3[\text{OH}^-]} \tag{74}$$

This scheme applies to pyruvic, glycolic, lactic, maleic, fumaric, glyoxylic, mandelic and 2-bromopropionic acids [124–129]; the oxidation of α-hydroxy acids involves the breaking of an αC–H bond with formation of an intermediate ketoacid. With Ru(III) the rate-law is similar for acrylic and α-hydroxy acids [130], but the formation of a Ru(III)–substrate complex is the rate-determining step. The fact that substrates devoid of hydrogen atoms at α-positions are not oxidized supports the assumption for a H-transfer from the α-carbon to Ru(III).

The Cu(II)-catalyzed oxidation of tartaric acid in basic medium [131] involves a Cu(II)–tartrate complex followed by slow oxidation, and obeys a fourth-order rate-law. The oxidation of citric acid [132] obeys a more complex rate-law and a similar reaction scheme.



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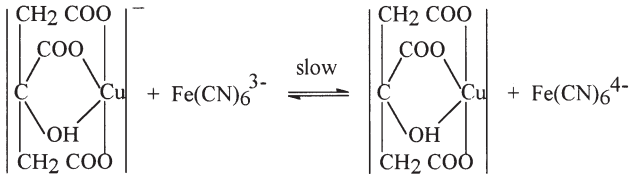

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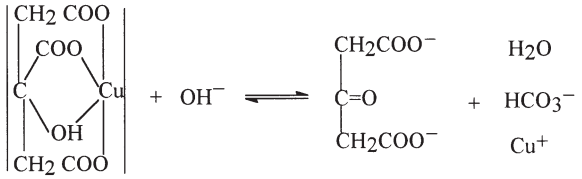


(77)

$$Cu^+ + Fe(CN)_6^{3-} \longrightarrow Cu^{2+} + Fe(CN)_6^{4-} \tag{78}$$

$$^-OOCCH_2COCH_2COO^- + Fe(CN)_6^{3-} \longrightarrow Fe(CN)_6^{4-} + \text{Prod} \tag{79}$$

and rate law:

$$r = \frac{k_1[\text{citrate}][\text{OH}^-]^2[\text{Cu(II)}][\text{Fe(CN)}_6^{3-}]}{1 + k_2[\text{OH}^-]^2} \tag{80}$$

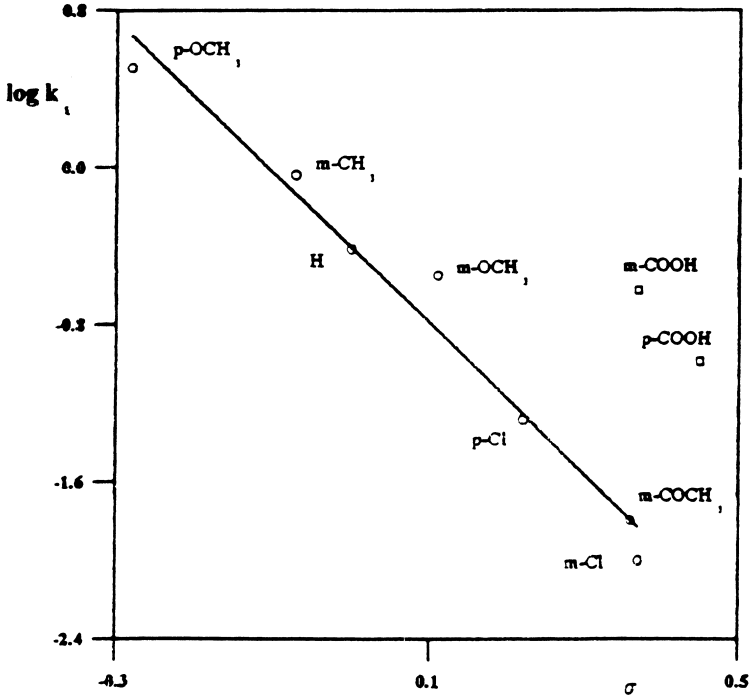


Fig. 9. Hammett plot for the oxidation of *m*- and *p*-substituted anilines by hexacyanoferrate(III) in alkaline medium [14].

8. Oxidation of amines

The oxidation of aromatic amines is a very interesting reaction, as these substrates have important chemical and physiological properties and play an important role in biotransformations such as carcinogenesis and drug metabolism [133,134]. Primary aromatic amines can be oxidized to azo, azoxy, nitroso or nitro compounds, depending on the oxidant [135]; the oxidation of anilines by basic $Fe(CN)_6^{3-}$ yields primarily azobenzenes, as shown by Nikishin et al. [136]. The stoichiometric ratios in the oxidation of aniline, $Ph–NH_2$ and substituted anilines [10,14,137,138], $R–C_6H_4–NH_2$, and the UV-vis band-shape parameters of the products [139] are consistent with formation of azocompounds, $R–C_6H_4–N=N–C_6H_4–R$; exceptions are 1,4-phenylenediamine and 4-aminophenol, which produce 1,4-benzoquinone diimine and 1,4-benzoquinone monoimine, respectively; further hydrolysis gives benzoquinone.

The oxidation of primary aliphatic amines yields the corresponding nitriles, but NH_3 and RCOOH are also feasible; amines with the NH_2 group at a secondary carbon, $RR'CHNH_2$, yield the dimer, $RR'CHNHN=CRR'$, (R, R′=Me, Me; Me, Et); the rate equation is first-order both in oxidant and reductant but it is independent of $[OH^-]$. The rate-determining step is the irreversible abstraction of an electron

from the nitrogen atom of the substrate with formation of an amine radical cation, confirmed by failure of $Fe(CN)_6^{4-}$ to inhibit the net reaction

$$RNH_2 + Fe(CN)_6^{3-} \overset{\text{slow}}{\rightarrow} R\overset{+\cdot}{N}H_2 + Fe(CN)_6^{4-} \quad (81)$$

The aminium radical cation may react with another radical forming either the dimer or an α-amino radical (if H atoms at α-C are available) which is dehydrogenated in a subsequent rate-determining step.

The oxidation of a set of *m*- and *p*-substituted anilines [14] provides evidence for a specific catalytic effect, by binding of alkali-metal ions to oxidant, increasing in the order $Li^+ < Na^+ < K^+ < Rb^+$, irrespective of the counterion used. Contrary to the oxidation of aliphatic amines [140], an initial addition of $Fe(CN)_6^{4-}$ inhibits the net reaction, denoting that the rate-determining step is the reversible abstraction of an electron from the nitrogen atom of the amino group with formation of a radical cation [141–143]. The following mechanism applies for the oxidation of aniline and substituted anilines in basic media.

$$YFe(CN)_6^{2-} + R\text{–}C_6H_4\text{–}NH_2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} YFe(CN)_6^{3-} + R\text{–}C_6H_4\text{–}\dot{N}H_2^+ \quad (82)$$

$$R\text{–}C_6H_4\text{–}\dot{N}H_2^+ + OH^- \xrightarrow{k_2} R\text{–}C_6H_4\text{–}\dot{N}H + H_2O \quad (83)$$

$$2\,R\text{–}C_6H_4\text{–}\dot{N}H \xrightarrow{\text{fast}} R\text{–}C_6H_4\text{–}NH\text{–}NH\text{–}C_6H_4\text{–}R \quad (84)$$

$$R\text{–}C_6H_4\text{–}NH\text{–}NH\text{–}C_6H_4\text{–}R + YFe(CN)_6^{2-} \xrightarrow{\text{fast}} R\text{–}C_6H_4\text{–}NH\text{–}\overset{\bullet+}{N}H\text{–}C_6H_4\text{–}R + YFe(CN)_6^{3-} \quad (85)$$

$$R\text{–}C_6H_4\text{–}NH\text{–}\overset{\bullet+}{N}H\text{–}C_6H_4\text{–}R + OH^- \xrightarrow{\text{fast}} R\text{–}C_6H_4\text{–}NH\text{–}\dot{N}\text{–}C_6H_4\text{–}R + H_2O \quad (86)$$

$$R\text{–}C_6H_4\text{–}NH\text{–}\dot{N}\text{–}C_6H_4\text{–}R + YFe(CN)_6^{2-} \xrightarrow{\text{fast}} R\text{–}C_6H_4\text{–}N{=}N\text{–}C_6H_4\text{–}R + YFe(CN)_6^{3-} + H^+ \quad (87)$$

The formation of radical cations at the nitrogen site also occurs in the oxidation of aromatic amines by Ce(IV) and Fe(III) [144]. The $YFe(CN)_6^{2-}$ complex, postulated in steps (Eqs. (82), (85) and (87)), is more reactive than $Fe(CN)_6^{3-}$ due to the lower electrostatic repulsion between the ion-pair and the electron-rich site of the aniline susceptible to attack [2,15,16]. The oxidation with other one-electron oxidants evolves through direct oxidant–reductant reversible rate-determining steps [145,146]. We found the following rate equation for substituted anilines [14]

$$r = 4k_1[Fe(CN)_6^{3-}]_t[R\text{–}C_6H_4\text{–}NH_2]\frac{k_2[OH^-]}{k_{-1}[Fe(CN)_6^{4-}] + k_2[OH^-]} \quad (88)$$

with $k_1 = 0.38 M^{-1} s^{-1}$ and $k_{-1}/k_2 = 18.6$ for aniline. The susceptibility factor $\rho = -3.8$, calculated from adherence to the Hammett equation, implies that electron-releasing groups facilitate the oxidation [147], suggesting that removal of one electron from the substrate is rate-determining (Fig. 9).

Particularly interesting is the oxidation of tertiary amines to give secondary amines and pyridones. The group to be dealkylated becomes determined by the acidity of the H atom at the α-carbon site, in the sequence: methyl > ethyl > *n*-butyl > *iso*-butyl. The rate-determining step for trialkylamines and alkyl-arylamines is similar to Eq. (81)

$$R_3N + Fe(CN)_6^{3-} \rightarrow R_3\overset{\cdot +}{N} + Fe(CN)_6^{4-} \quad (89)$$

The kinetic isotope effect caused by replacing a H atom by deuterium at the α-carbon results in the ratio $k_H/k_D = 1.04$, a value in accordance with an electron transfer rate-determining step rather than removal of an α-H. Conversely, deuteration influences noticeably the products distribution; the competitive deprotonation of the $R_3N^{\cdot +}$ radicals determines the reaction products. Substituents with an electron-donor effect on the nitrogen atom favour the transfer of an electron to the oxidant in the rate-determining step, so that the reactivity sequence tertiary > secondary > primary applies. The oxidation of tertiary amines is also susceptible to specific catalytic effect by alkali-metal ions, in the order $Li^+ < Na^+ < K^+ < Rb^+ < Cs^+$ caused by the bridging effect of the cation [148–151].

Two surprising observations not reported earlier display the oxidation of trialkylamines over a wide acidity range (pH 3.7–13.4) [152]: first, the oxidation may proceed outside the alkaline region, even though the reaction rate decreases with decreasing pH, and second, the initial addition of $Fe(CN)_6^{4-}$ inhibits the net reaction, this effect being greater the lower the pH. This necessitates a H-transfer from trialkylammonium ion to oxidant in a reversible rate-determining step (Eq. (90)) instead of (Eq. (89)), with formation of the radical species $R_3N^{\cdot +}$ already reported for aromatic amines

$$R_3\overset{+}{N}H + Fe(CN)_6^{3-} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R_3\overset{+\cdot}{N} + Fe(CN)_5(CNH)^{3-} \quad (90)$$

Only few catalyzed oxidations of amines have been investigated. The Os(VIII)-catalyzed oxidation of aliphatic amines are zero-order in oxidant, and first-order in the amine, catalyst and base concentrations [153]. The mechanism is similar to that described for other oxidations with the only exception of methylamine, which follows a rather more complicated kinetics: at low amine and base concentrations, the reaction is first-order in substrate, oxidant, catalyst and OH^- ions; at high amine and base concentrations the reaction order in oxidant and reductant is less than unity; NH_3 and HCHO appear among the reaction products of the net reaction

$$CH_3NH_2 + 2Fe(CN)_6^{3-} + 2OH^- \rightarrow HCHO + NH_3 + 2Fe(CN)_6^{4-} + H_2O \quad (91)$$

and the mechanism postulated involves the following steps

$$OsO_4(OH)(H_2O)^- + OH^- \rightleftharpoons OsO_4(OH)_2^{2-} + H_2O \quad (92)$$

$$OsO_4(OH)_2^{2-} + CH_3NH_2 \rightleftharpoons \text{Intermediate} \quad (93)$$

$$\text{Intermed} + Fe(CN)_6^{3-} \longrightarrow Os(VI) + Fe(CN)_6^{4-} + \text{Prod} \quad (94)$$

$$Os(VI) + 2Fe(CN)_6^{3-} \xrightarrow{\text{fast}} Os(VIII) + 2Fe(CN)_6^{4-} \quad (95)$$

The Cu(II)-catalyzed oxidation of butylamine is first-order in oxidant, substrate, Cu(II) and base concentrations; the rate equation is similar to Eq. (75) for citric acid, but it includes a reciprocal dependence with $[Fe(CN)_6^{4-}]$, consistent with a reversible rate-determining step. The mechanism involves a direct oxidant–reductant step like Eq. (81). Cu^{2+} ions may oxidize the $RNH^{\cdot}$ radicals (produced by the OH^- attack to $RNH_2^{+\cdot}$ radical cations) to hydroxylamine RNHOH in the presence of water; further oxidation gives the products.

The acidic oxidation of diphenylamine is the basis for the titration of the substrate; the diphenylamine ($pK_{In} = 9.9$)–$Fe(CN)_6^{3-}$ couple is often used as an indicator in acid–base titrations of the reaction product, diphenylbenzidine, changing from green (acidic form, $pH < 8.5$) to orange (basic form, $pH > 8.5$); both the direct and reverse titrations are reliable within 0.33% error for HCl, H_2SO_4, acetic, benzoic, oxalic, succinic and tartaric acids [154].

9. Oxidation of hydrazines

Hydrazine, N_2H_4, and parent compounds have attracted much interest among chemical engineers on account of their use as fuel reagents. The oxidation of hydrazine appears to be simple, but actually it is quite complex [155,156]. Hydrazines possess multiple ionization sites with small basicity differences [157]; at pH less than 3 hydrazine exists mainly as $N_2H_5^+$ ion, a non-oxidizable substrate in acidic medium [158]. The rate-law for the basic oxidation is similar to that of amines, with first-order in oxidant and reductant, and zero-order in base concentration; a decrease in solvent relative permittivity decreases significantly the reaction rate; the rate-determining step is similar to Eq. (81) for amines, but for hydrazines is reversible

$$N_2H_4 + Fe(CN)_6^{3-} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} N_2H_4^{\cdot +} + Fe(CN)_6^{4-} \quad (96)$$

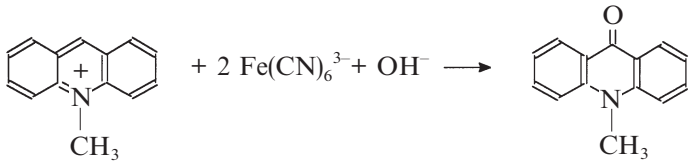
Pulse radiolysis experiments have shown that the reverse reaction is much less than diffusion controlled ($k_{-1} = 3 \times 10^6 M^{-1} s^{-1}$) and that k_1 is the rate limiting step [158,159]; alkali-metal ions cause a specific catalytic effect. Activation energies and entropies, ranging around 51 kJ mol^{-1} and -87 J K^{-1} mol^{-1}, respectively, are sim-

ilar to those for trialkylamines. These observations point to polyhydronitrogenated species as chemical intermediates [160], N_2 and NH_3 being among the final products. Arylhydrazines are extremely sensitive to oxidation in acidic media [161,162], in the range 0.025 to 2.5M $HClO_4$. The reaction rate is unaffected by addition of different salts including $Fe(CN)_6^{4-}$ and H_4EDTA, but it can be affected by medium acidity, depending on the substrate; this fact is explained assuming protonation of the hydrazine rather than protonation of the oxidant. The abstraction of an electron from the N site by oxidant is the rate-determining step, although prior formation of a complex species with oxidant often occurs [163]. The oxidation occurs through aryldiazene and diazonium ion as intermediates, to give azobenzenes and substituted anilines.

The basic oxidation of hydrazides $RCONHNH_2$ and arylhydrazides $XC_6H_4CONHNH_2$ has been only briefly investigated, despite this it gives an interesting method to produce aromatic and heterocyclic aldehydes from carboxylic acids previously converted to hydrazides. The reaction shows a fractional order in $[OH^-]$ and a positive specific salt effect [164].

10. Oxidation of heterocyclic cations

The base-catalyzed oxidation of heterocyclic salts, traditionally known as Decker's oxidation [165], is a very useful tool in organic synthesis to attain the functionalization of heteroaromatic rings [166,167]. This reaction can be extended to cations such as pyridinium, quinolinium, benzoquinolinium, phenanthrolinium and acridinium; the reaction products are the corresponding pyridone, quinolinone, benzoquinolinone, phenanthrolone and acridone; their reactivities should allow prediction of relative reactivities of a variety of substituted derivatives towards $Fe(CN)_6^{3-}$. When these salts are substituted at certain positions of the ring, some groups may be released with formation of pyridone or heterocyclic condensed derivatives [168].



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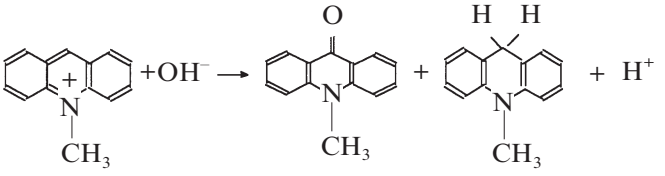
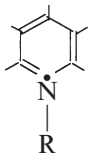
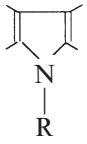


(98)

A drawback to Eq. (97) is the parallel disproportionation Eq. (98), as occurs with *N*-methylacridinium; these reactions have been known since the end of the last century, however, it is only recently that they have provoked kinetic interest; reactions (Eqs. (97) and (98)) can be studied independently from each other. If the pyridinium salt is substituted in position 3 (X) the oxidation is highly selective, and can afford penta-substituted pyrroles (XI) in high yields [169]. This conversion is the basis for a preparative method suitable for other substituents at position 1.



(X)



(XI)

The oxidation kinetics were investigated by Bunting et al. within the pH range 10–14, in mixed solvent [170–172]; the reaction is first-order each in oxidant and substrate. The initial rates, with the only exception of pyridinium, are extremely sensitive to inhibition by $Fe(CN)_6^{4-}$, this fact confirming a reversible rate-determining step. The influence of base concentration is consistent with an oxidant attack to the alkoxide ion of the pseudobase derived from the cation; unfortunately, ionic strength, solvent relative permittivity and temperature are effects not sufficiently investigated. For instance, an activation energy of $37\ kJ\ mol^{-1}$ and activation entropy of $-100\ J\ K^{-1}\ mol^{-1}$ for the *N*-(4-cyanobenzyl)-5-nitro-isoquinolinium cation, are similar to those for tertiary amines. The substituents effect is consistent with the abstraction of an electron by the oxidant from the endocyclic N atom. The radical generated undergoes a base-catalyzed deprotonation at the C_1 site, as supported by the isotope kinetic effect. Thus, the mechanism postulated is

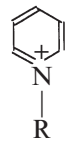
$$QOH \overset{K_{RO^-}}{\rightleftharpoons} QO^- + H^+ \tag{99}$$

$$QO^- + Fe(CN)_6^{3-} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} X + Fe(CN)_6^{4-} \tag{100}$$

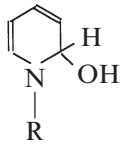
$$X + OH^- \xrightarrow{k_2} X' + H_2O \tag{101}$$

$$X' + Fe(CN)_6^{3-} \xrightarrow{\text{fast}} Q{=}O + Fe(CN)_6^{4-} \tag{102}$$

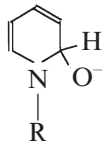
where Q^+ stands for the substrate, QOH for the pseudo-base; QO^- is the corresponding alkoxide, X represents the radical cation at the endocyclic nitrogen atom, X′ the radical at the C_1 site and Q=O the reaction product. In the case of pyridinium cation



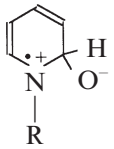
(Q^+)



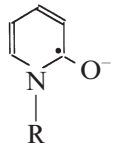
(QOH)



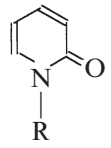
(QO^-)



(X)



(X')



(Q=O)

11. Oxidation of hydroxylamines

The preparative organic chemistry of hydroxylamines is well understood, and their industrial applications widely recognized; however, the structural chemistry is not completely developed [173]. Hydroxylamine is an intermediate species in the enzymatic oxidation of NH_3 to NO_2^- and NO_3^- or in the reverse reaction of these ions to NH_3, and can be either oxidized or reduced by transition metals and their complexes [174]. The oxidation rate of H_2NOH within the pH range 4.2–5.7 is proportional to oxidant and substrate, and to the reciprocal of proton concentration [175,176], suggesting that the rate-determining step involves hydroxylamine NH_2OH, rather than the H_3NOH^+ ion, a feature also supported by the positive solvent relative permittivity effect; the initial step follows the same radical pattern as trialkylamines Eq. (90) and hydrazynes Eq. (96)

$$H_2NOH + Fe(CN)_6^{3-} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} H_2NO^{\cdot} + Fe(CN)_6^{4-} + H^+ \quad (103)$$

The $H_2NO^{\cdot}$ and R–$NHO^{\cdot}$ radicals undergo further fast recombination to give the products

$$2H_2NO^{\cdot} \rightarrow N_2 + 2H_2O \quad (104)$$

however, if the [oxidant]/[reductant] ratio is large, the $NH_2O^{\cdot}$ radicals can also be oxidized to N_2O. The redox behaviour of NH_2OH with transition metal complexes is complicated, and a number of products can be formed; species such as N_2, NO, NO_2, N_2O, and others can be formed depending on the fate of the intermediate $NH_2O^{\cdot}$ radical. The oxidation of hydroxylamine has been proposed as a useful tool for the quantitative determination of the substrate, according to the net reaction

$$2H_2NOH + 2Fe(CN)_6^{3-} \rightarrow N_2 + 2H_3O^+ + 2Fe(CN)_6^{4-} \quad (105)$$

This reaction is so strongly catalysed by trace Cu^{2+} ions that there is no convincing report of the direct reaction [177]; the reaction rate increases linearly with $[Cu^{2+}]$, but it is unaffected by addition of ions such as Co^{2+}, Ni^{2+}, Mn^{2+}, Zn^{2+}, Fe^{2+}, Cr^{3+} and Fe^{3+}. The reaction mechanism consists of the following steps

$$Cu^{2+} + H_2NOH \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} Cu^{2+}(H_2NOH) \quad (106)$$

$$Cu^{2+}(H_2NOH) + Fe(CN)_6^{3-} \xrightarrow{k_2} Cu^{2+}(H_2NO\bullet) + Fe(CN)_6^{4-} + H^+ \quad (107)$$

$$Cu^{2+}(H_2NO\bullet) + NH_2OH \xrightarrow{k_3} Cu^+ + N_2 + H_3O^+ + H_2O \quad (108)$$

$$Cu^+ + Fe(CN)_6^{3-} \xrightarrow{k_4} Cu2^+ + Fe(CN)_6^{4-} \quad (109)$$

where k_2 is rate-determining. Addition of complexing agents such as EDTA or nitrilotriacetic acid (NTA) masks the Cu^{2+} effect but introduces the Fe^{3+}–EDTA or Fe^{3+}–NTA catalytic effect, and k_1 is rate-determining.

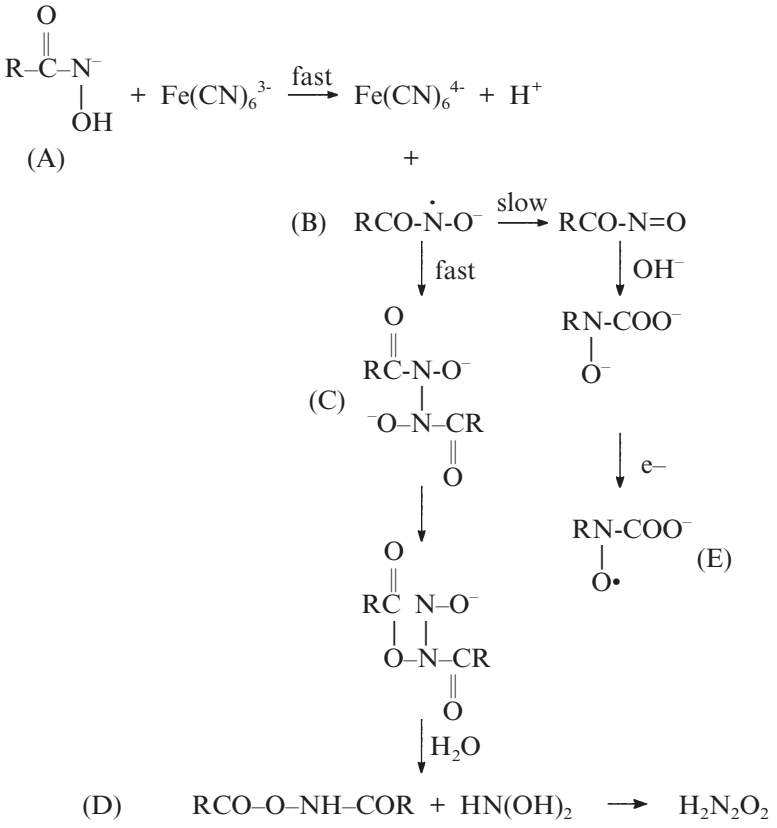
12. Oxidation of hydroxamic acids

The RCO–NH–OH (A) derivatives of hydroxylamine, are generally called hydroxamic acids. These reagents are important due to their properties (iron chelators, enzyme inhibitors, and their medical and biological applications); they are bases but also behave as weak acids due to the CO group [178]. The actual ionization sites have long been debated, but a strong controversy still remains; both O- and N-ionization have been proposed, depending upon the solvent [179]. Although these equilibria have been investigated in different solvents and using a variety of methods, so far the structure of the anionic species has not been unambiguously determined [180,181]. Hydroxamic acids are N-acids in DMSO and in the gas phase, but possibly O-acids in water and alcohols [182,183]. The observation that many oxidizing agents, $Fe(CN)_6^{3-}$ among others, can convert hydroxamic acids into active acylating agents, confers a great deal of interest to this reaction.

These acylations are important in connection with the carcinogenicity of urethane and many aromatic amines biologically oxidizable to hydroxylamines [184]. ESR measurements show that rapid basic oxidation of the substrate gives the $RCO–NO^{-\cdot}$ (B) radical anion. The reaction mechanism involves (D) as major product, produced by intramolecular rearrangement of (C), the dimer form of (B) [185].

The stoichiometry is determined by monitoring the oxidant at 415 nm: at pH 9.5 and above, 1 equivalent is consumed in only 4 min; 0.4 additional equivalents disappear in 60 min; moreover, addition of EDTA to exclude trace metals effect restricts the consumption of oxidant to only the first stage, yielding 95% NO–diacylhydroxylamine, RCO–NHOCOR (D). The dimer radicals produced by

oxidation of *o*-alkylhydroxamic acids can be isolated. The radical species $R–N(O^{\cdot})–COO^{-}$ (E) has been identified by continuous flow ESR measurements. A similar scheme explains the oxidation of *N*-arylhydroxamic acids [186].



13. Oxidation of amino acids

Oxidation of amino acids is a type of reaction not easily carried out with $Fe(CN)_6^{3-}$, and a catalyst is normally required; kinetic studies in the absence of a catalyst have been reported on the basic oxidations of *l*-histidine, phenylalanine, leucine, glycine and valine [187–189]; the keto acid species and NH_3 are found among the final products. The reactions are first-order in substrate, oxidant and base concentrations; although addition of $Fe(CN)_6^{4-}$ suggests a slow one-electron reversible step, complexes such as substrate–Fe(II), and substrate–$Fe(CN)_6^{4-}$ in basic media have been identified [190]. The basic oxidation of tyrosine proceeds via the α-imino acid, a mechanism supported by the oxidation reaction of tyrosine by the specific aminoacid oxidase. The oxidation of the α-aminoacids glutamic and aspartic acids to the respective α-ketoacids is independent of both base concentration

and $Fe(CN)_6^{4-}$ reaction product, and proceeds via the imino acid through a radical intermediate [191].

The kinetics of the Os(VIII)-catalyzed oxidation are more complex. The reaction is zero-order in oxidant and first-order in catalyst [192–196], and may change from one to zero for substrate and base concentrations. Oxidation of alanine, glycine, valine, phenylalanine, isoleucine and leucine is first-order both in alkali and substrate in the ranges [substrate] <0.025M, and $[OH^-]<0.13$M, but these reaction orders decrease at higher concentrations. Addition of $Fe(CN)_6^{4-}$ accelerates the reaction due to formation of the more reactive aminoacid–$Fe(CN)_6^{4-}$ complex, as occurs with lysine.

The reaction involves an intermediate complex species between catalyst and substrate (or its anionic form) which proceeds further to products; this implies a direct oxidation of the substrate by the catalyst. There are two important exceptions to this rule [194]: D-proline and L-methionine are first-order in oxidant and obey the rate-law

$$r=\frac{k_1[S][OH^-][Os(VIII)][Fe(CN)_6^{3-}]}{1+k_I[S](1+k_{II}[OH^-])} \tag{111}$$

involving the oxidation of the substrate–catalyst complex species in the rate-determining step

$$Os(VIII) + Substrate \overset{K_I}{\rightleftharpoons} C_1 \tag{112}$$

$$C_1 + OH^- \overset{K_{II}}{\rightleftharpoons} C_2^- + H_2O \tag{113}$$

$$C_2^- + Fe(CN)_6^{3-} \overset{k_1}{\longrightarrow} X_T + Fe(CN)_6^{4-} \tag{114}$$

$$X_T + Fe(CN)_6^{3-} \longrightarrow Prod + Os(VIII) + Fe(CN)_6^{4-} \tag{115}$$

The Ru(III) [196,197] and Ru(VI) [198,199]-catalyzed oxidations follow a different rate equation

$$r=\frac{k_1[S][OH^-][Ru(III)]}{k_2+k_3[S][OH^-]} \tag{116}$$

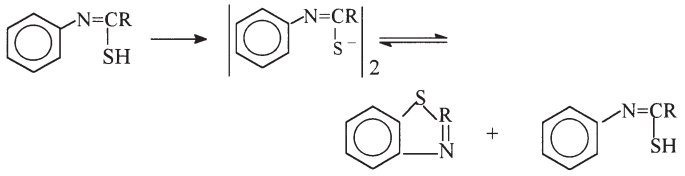
in agreement with a rate-determining step involving H abstraction from the α-carbon atom of the aminoacid by the catalyst, and are zero-order in oxidant.

14. Oxidation of thiols

The oxidation of thiols to disulphides is a reaction of considerable biological importance, since thiol groups are involved in cell biochemistry [200]. Biochemical

processes such as photosynthesis, plant-growth inhibition and cell metabolism bear relation to enzymes which depend for their function upon the thiol group at the active centre; due to their radical scavenging ability, thiols are widely used as antioxidants and in radiation protection [201]. Polythiols generated by in situ polymerization of benzenethiols play an important role as inhibitors for the corrosion of copper [202]. Many important reactions are facilitated by the ease of thiols to form sulfenyl (or thiyl) radicals through homolysis of the S–H bond. Most thiol reactions involve either the neutral form or the more reactive thiolate anion, RS^- [203,204].

The oxidation to disulphides, RSSR, can be easily achieved in a variety of ways and by many reagents, including transition metal ions and one-electron oxidants [205–208]. Recently, a new synthesis route to disulphides by disproportionation of thiols has been reported [209]. $Fe(CN)_6^{3-}$ has been utilized to synthesize benzothiazol derivatives starting from basic alkylthioanilides (Table 2), and other compounds useful as dyes or in pharmacological applications.



(117)

The oxidation is fast and quantitative, and proceeds to completion; for a long time this reaction has been a useful tool for chemical analysis of the thiol and mercapto groups in polyfunctional molecules [210,211], however, there are only very few kinetic studies on it [212]. This reaction may evolve either in basic or in acidic media and complexing agents such as EDTA slow down or even stop the reaction [213]. The statement of a unique mechanism is difficult due to complications arising from a variety of reactions involving thiyl radicals $RS^{\cdot}$. The following rate equation applies in basic medium

$$r = k[Fe(CN)_6^{3-}][RS^-][OH^-] \quad (118)$$

Table 2
Conversion of some thioacetanilides into benzothiazoles by basic hexacyanoferrate(III) oxidation

Benzothiazole	Yield (%)	Benzothiazole	Yield (%)
2-Methyl	71	2-Methyl-7-nitro	33
2,4-Dimethyl	73	2-Methyl-6-cyano	32
2,7-Dimethyl	52	2-Methyl-6-nitro-4-methoxy	24
2-Methyl-4-methoxy	70	2-Methyl-5-methoxy	7
2-Methyl-6-methoxy	6	2-Methyl-7-methoxy	38
2-Methyl-4-chloro	88	2-Methyl-4,5-tetramethylene	55
2-Methyl-5-chloro	87	2-Methyl-7-di-methylamine	52
2-Methyl-4-nitro	0	2,5,6-Trimethyl	10

The mechanism involves the abstraction of an electron by the oxidant from the anionic form of the substrate.

$$RSH + OH^- \overset{\text{fast}}{\rightleftharpoons} RS^- + H_2O \tag{119}$$

$$RS^- + Fe(CN)_6^{3-} \overset{\text{slow}}{\longrightarrow} RS\bullet + Fe(CN)_6^{4-} \tag{120}$$

$$2RS\bullet \overset{\text{fast}}{\longrightarrow} RSSR \tag{121}$$

Another source of difficulties stems from the catalytic effect of trace Cu^{2+} ions, frequently introduced as impurities in the chemicals used and even in distilled water samples [214–216]; this might explain the irreproducible kinetic behaviour often found with sulphur compounds. The acidic oxidation proceeds by a more complex scheme and in acidic non-aqueous solvents the dimer $(RSH)_2$ is the predominant form [217]. The mechanism postulated by Bridgart et al. [212] involves an electron abstraction from the substrate with formation of the $RS^{\cdot}$ radical, as supported by the ability of the thiol–$Fe(CN)_6^{3-}$ couple to promote olefin polymerization.

$$Cu^{II}(SR)^+ + RSH \overset{K_{Th}}{\longrightarrow} Cu^{II}(SR)_2 + H^+ \tag{122}$$

$$Cu^{II}(SR)_2 + Fe(CN)_6^{3-} \underset{k_{-1}}{\overset{k_1}{\longrightarrow}} Cu^{III}(SR)_2^+ + Fe(CN)_6^{4-} \tag{123}$$

$$(Cu^{III}(SR)_2)^+ \overset{k_2}{\longrightarrow} Cu^+ + RSSR \tag{124}$$

$$Cu^{II}(SR)_2 + RSH \overset{k_3}{\longrightarrow} Cu^{I}(SR) + RSSRH\bullet \tag{125}$$

$$RSSRH\bullet + Fe(CN)_6^{3-} \overset{k_4}{\longrightarrow} RSSR + Fe(CN)_6^{4-} + H^+ \tag{126}$$

$$RSSRH\bullet + Fe(CN)_6^{4-} \overset{k_5}{\longrightarrow} RS^- + RSH + Fe(CN)_6^{3-} \tag{127}$$

$$Cu^{I}(SR) + Fe(CN)_6^{3-} \overset{\text{fast}}{\longrightarrow} (Cu^{II}(SR))^+ + Fe(CN)_6^{4-} \tag{128}$$

$$Cu^+ + Fe(CN)_6^{3-} \overset{\text{fast}}{\longrightarrow} Cu^{2+} + Fe(CN)_6^{4-} \tag{129}$$

from which the following rate expression is derived

$$r = \frac{[Fe(CN)_6^{3-}][RSH][Cu]}{[H^+]} \cdot \left\{ \frac{2k_1k_2}{1 + k_1[Fe(CN)_6^{4-}]/k_2} + \frac{2k_2k_3[RSH]}{[Fe(CN)_6^{3-}] + k_5/k_4[Fe(CN)_6^{4-}]} \right\} \tag{130}$$

Step (Eq. (122)) involves the formation of a 1:2 Cu:thiol complex under excess of thiol [218,219]; disulphides may be formed by steps (Eqs. (124) and (126)), and the catalyst regenerated by Cu^+ reoxidation in steps (Eqs. (128) and (129)).

We checked the catalytic role of Cu^{2+} ions in the oxidation of the 2-mercaptopropionic or thiolactic acid, $CH_3CH(SH)COOH$, 3-mercaptopropionic acid, $HSCH_2CH_2COOH$, L-cysteine or L-2-amino-3-sulphopropionic acid, and thiomalic acid, $HOOCCH(SH)CH_2COOH$ [220]. The 1:1 stoichiometric ratio for the acidic oxidation was verified from the $Fe(CN)_6^{3-}$ absorbance remaining after completion of several kinetic runs. For 3-mercaptopropionic acid the products were checked by mixing at 25 °C two aqueous solutions of substrate (1.80 g in 50 ml) and oxidant (6.5 g in 50 ml); after two hours, the mixture yielded an abundant precipitate consisting of colourless needles and plates which were recrystallized. After filtering, washing and drying for 24 h, the solid gave 154–155 °C mp, in good agreement with that of the assumed disulphide, 3,3′-dithiodipropionic acid, 154 °C mp. A 0.0015M aqueous solution of the precipitate (0.0158 g in 50 ml, assuming the above disulphide) was neutralized with 29.9 ml of 0.005M NaOH, which means 0.00299M proton concentration (diprotic acid), a result consistent with 3,3′-dithiopropionic as final product.

The actual instantaneous reaction rates were determined at all absorbance/time data from disappearance of the $Fe(CN)_6^{3-}$ at 416 nm [221]. The non-linear plot rates vs absorbance give an overall kinetic order of 2.6, an indication of an intricate scheme (Fig. 10). An initial addition of disulphide to the reaction mixture does not inhibit the reaction rate, but addition of $Fe(CN)_6^{4-}$ in 10:1 excess over $Fe(CN)_6^{3-}$ retards the oxidation, and is zero-order in oxidant; under such conditions the thiols are actually oxidized by Cu^{2+} ions, $Fe(CN)_6^{3-}$ being co-oxidant, as occurs in the Os(VIII), Ru(VI) and Ru(VIII)-catalyzed oxidations [222]. Fig. 11 shows the catalytic effect of Cu^{2+} ions by comparing the oxidation of 3-mercaptopropionic acid in different kinetic runs, carried out (1) in the presence of trace ions (0.4 mM) and (2) in the absence of Cu^{2+} ions. An important feature is the crucial role played by the sequence of addition of reactants into the reaction vessel, for thiols and Cu^{2+} may give complex species (Table 3). If the reactants were added in the sequence

(a) (thiol + Cu^{2+}) + hexacyanoferrate(III) then the reaction proceeds much faster than in sequence (b)

(b) (hexacyanoferrate(III) + Cu^{2+}) + thiol

In option (a), the Cu^{2+} ions may form the 1:2 $Cu^{II}(SR)_2$ complex under excess of thiol; such a complex reacts with the oxidant releasing Cu^+ free ions; actually these sulphur-containing compounds have two or three coordination centres (N, O and S) [223]. In option (b) however the Cu^{2+} ions may be trapped by the oxidant, forming a yellow–green precipitate; this is verified by mixing 0.001 $Fe(CN)_6^{3-}$ ions with 0.001M Cu^{2+} ions, yielding a yellow suspension identified as $[Fe(CN)_6]_2Cu_3 \cdot 14H_2O$ [224]; given the concentrations ratio 4000:100:1 thiol:$Fe(CN)_6^{3-}$:Cu^{2+}, there is actually no appreciable amount of Cu^{2+} free ions in the mixture. In fact, the reduction of Cu(II) to Cu(I) with thiols proceeds through Cu(II)–thiol complexes, which depend upon the thiol structure and reaction condi-

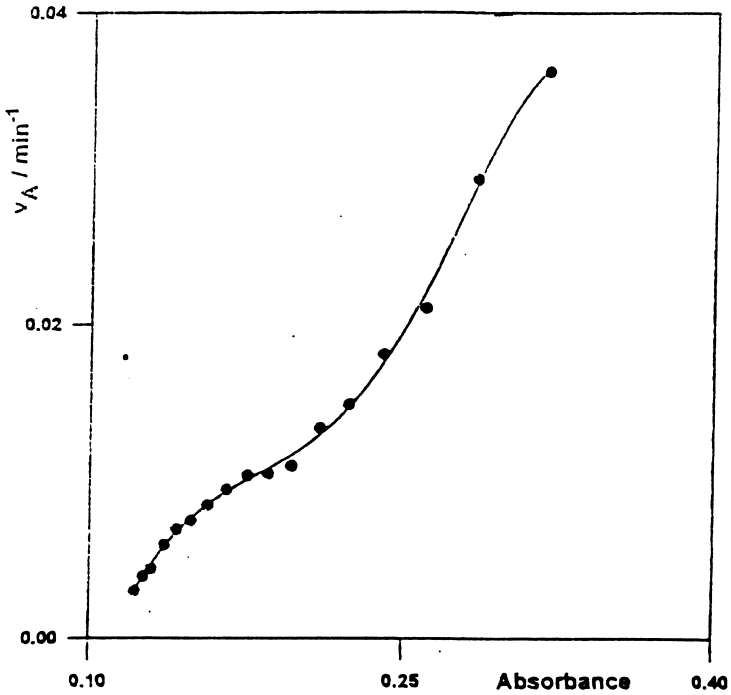


Fig. 10. Anomalous reaction rate vs absorbance plot in the oxidation of 3-mercaptopropionic acid: $[Fe(CN)_6^{3-}]=5\times10^{-4}$M, $[Cu^{2+}]=5\times10^{-6}$M, [thiol]$=9\times10^{-3}$M, $[H^+]=0.05$M, $T=25$ °C.

tions [225]. In sum, the formation of Cu(I) by internal electron transfer within a Cu(II)–thiyl precursor

$$(Cu^{II}RS)^+ \rightarrow RS^{\cdot} + Cu^+ \quad (131)$$

$$Cu^{II}(RS)_2 \rightarrow RS^{\cdot} + Cu^{I}(RS) \quad (132)$$

should also be taken into account [225,226]; under excess of thiol, step (Eq. (128)) may be more reliable than Eq. (129).

15. Oxidation of thioamides

Sulphur chemistry has a close connection with nonlinear behaviour in chemistry. Thiourea and *N*-phenylthioureas constitute good model compounds for studying effects as varied as internal rotation, biological activity and inter and intramolecular hydrogen bonding. Thiourea is one of the simplest and most reactive sulphur compounds and may exhibit nonlinear behaviour upon oxidation [227]. The oxidation of thioamides has been investigated with different one-electron oxidants [228,229], but only a few references report the $Fe(CN)_6^{3-}$ oxidation. The oxidation

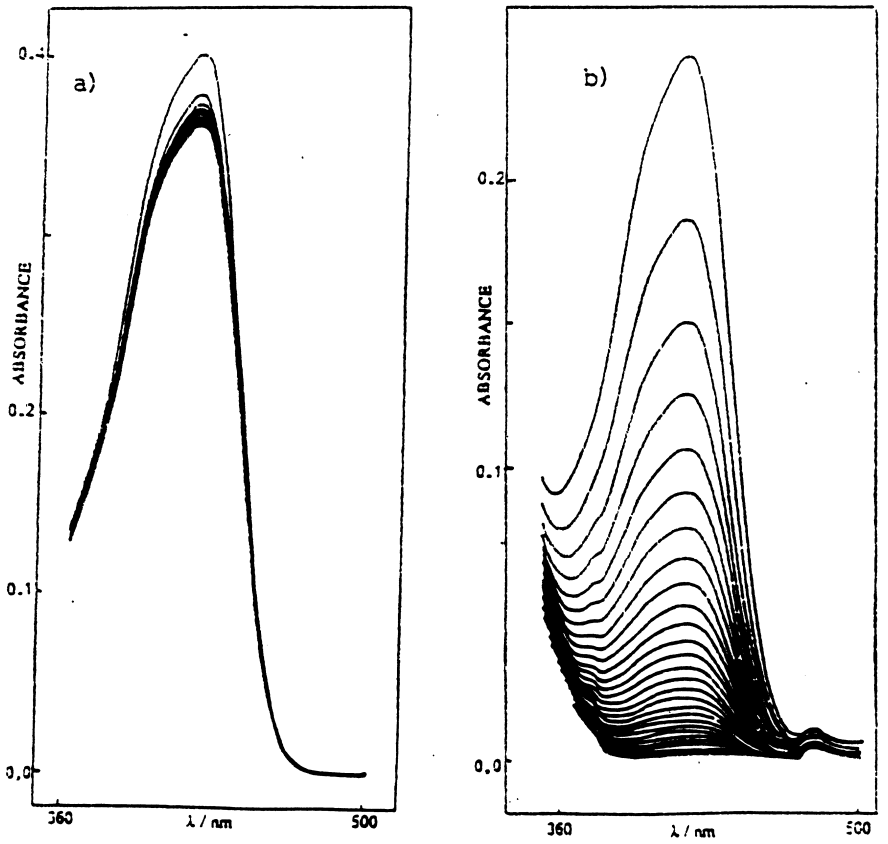


Fig. 11. Catalytic effect of Cu^{2+} ions in the oxidation of 3-mercaptopropionic acid: $[Fe(CN)_6^{3-}]=5\times10^{-4}$M, [thiol]=0.012M, $[H^+]=0.05$M, $T=25\,^{\circ}C$, time interval, 1 min: (a) in the absence of Cu^{2+} ions, (b) in the presence of 4×10^{-4}M Cu^{2+}.

Table 3
Evolution absorbance/time of two kinetics runs; $|Fe(CN)_6^{3-}|=5\times10^{-4}$M, |3-mercaptopropionic acid|= 0.02M, $|Cu^{2+}|=5\times10^{-6}$M; mixing of reactants: (a) (Cu^{2+} + thiol) + hexacyanoferrate(III); (b) (Cu^{2+} + hexacyanoferrate(III)) + thiol

t (min)	[a] $A_{416\ nm}$	[b] $A_{416\ nm}$
1	0.004	0.213
2	0.003	0.193
3	0.002	0.177
4	0.002	0.163
5	–	0.152
10	–	0.111
20	–	0.067
30	–	0.044
40	–	0.029

is carried out both in acidic [202,230] and in basic media [231]; the major reactive species is the thiol produced in the tautomer equilibrium thione–thiol, $H_2N–C(S)–NH_2 \rightleftharpoons HN=C(SH)–NH_2$. This effect is clearly seen in the basic oxidation of thioacetamide, a zero-order reaction in oxidant, and first-order both in alkali and substrate that involves the anionic enol form in the rate-determining step.

First-order in oxidant, however, is seen in the oxidation of thioureas [187,188] and dithizone [200], an effect interpreted by assuming that further oxidation of these thiols is the rate-determining step. The acidic oxidation of thioureas proceeds with $HFe(CN)_6^{2-}$ as the reactive oxidant. Addition of neutral salts causes no effect in acidic medium; in particular, the reaction is unaffected by addition of CN^- ions, consistent with an outer-sphere mechanism. The mechanism postulated by Lilani et al. [230] considers the thiol neutral molecule as the reactive species in the tautomer equilibrium, involving the thiourea free radical $TU^{\cdot}$ and its dimer $TU_2^{\cdot}$ as intermediates with rapid formation of formamidine disulphide.

$$HFe(CN)_6^{2-} + TU \rightleftharpoons [HFe(CN)_6TU]^{2-} \tag{133}$$

$$[HFe(CN)_6TU]^{2-} \xrightarrow{k_2} HFe(CN)_6^{3-} + \dot{T}U^+ \tag{134}$$

$$[HFe(CN)_6TU]^{2-} + TU \xrightarrow{k_3} HFe(CN)_6^{3-} + TU_2^{\dot{+}} \tag{135}$$

In basic medium an addition of neutral salts speeds up the reaction while an increase in solvent relative permittivity does retard the oxidation. The activation energies and entropies are similar assuming either oxidation (48 kJ mol^{-1} and -114 J K^{-1} mol^{-1}, respectively, for thiourea in basic medium) or enolate formation (69 kJ mol^{-1} and -89 J K^{-1} mol^{-1}, respectively, for thioacetamide) as rate-determining steps.

16. Oxidation of arylalkanes and aromatic hydrocarbons

One of the first applications of $Fe(CN)_6^{3-}$ was the oxidation of hydrocarbons to benzoic acids by boiling alkaline solutions in excess of oxidant; the yield is low, except with toluene derivatives (Table 4). Bhattacharjee and Mahanti investigated the oxidation kinetics of halotoluenes, xylenes and nitrotoluenes in acidic medium (0.25 to 1.5M) [232–234]; the stoichiometric ratio is 1:4 substrate:oxidant, and the oxidation products the corresponding aldehydes (80–95% yield) and a small per cent of polymeric material. The reaction is first-order in oxidant, acid and substrate.

The correlation constants $\log k$ vs σ^+ for the various substituents investigated give values for the susceptibility factor in the Hammett equation $\rho^+ = -1.8$ for halotoluenes, $\rho^+ = -1.3$ for nitrotoluenes and $\rho^+ = -0.90$ for xylenes. Reactions involving H-atom abstraction from toluene give ρ^+ values ranging from -0.75 to -1.5, while ρ^+ values ranging from -3.0 to -5.0 are inherent to reactions involving the formation of an electron-deficient C-atom adjacent to an aromatic ring [235–

Table 4
Oxidation of hydrocarbons to benzoic acid by basic hexacyanoferrate(III); yields given per gram of substrate

Hydrocarbon	Yield	Hydrocarbon	Yield
Toluene	0.009	3-Bromotoluene	0.011
2-Nitrotoluene	0.690	4-Bromotoluene	0.006
3-Nitrotoluene	0.052	*o*-Toluenesulphonamide	0.590
4-Nitrotoluene	0.730	*m*-Toluenesulphonamide	0.750
2-Bromotoluene	0.004	*p*-Toluenesulphonamide	0.800

237]; these data point to the abstraction of a H-atom to give benzil radical; furthermore, the strong isotope kinetic effect, $k_H/k_D = 6.0$, indicates that rupture of a C–H bond of the methyl group joined to the ring is the rate-determining step. This interpretation is also given to the chromic acid oxidation of diphenylmethane, with $k_H/k_D = 6.4$ [238].

The solvent polarity effect indicates the existence of an activated complex less polar than reactants, consistent with formation of radical intermediates rather than ionic species; these radicals have been detected by ESR measurements and confirmed by promoting as chain-initiators the acrylonitrile polymerization. The activation energies and entropies range from 58 kJ mol^{-1} and -29 J K^{-1} mol^{-1}, respectively, for xylenes, to 71 kJ mol^{-1} and -112 J K^{-1} mol^{-1}, respectively, for nitrotoluenes, and to 5 kJ mol^{-1} and -158 J K^{-1} mol^{-1}, respectively, for halotoluenes. The reaction mechanism postulated is

$$X\text{–}C_6H_4\text{–}CH_3 + HFe(CN)_6^{2-} \xrightarrow{\text{slow}} X\text{–}C_6H_4\text{–}\dot{C}H_2 + HFe(CN)_6^{3-} + H^+ \quad (136)$$

$$X\text{–}C_6H_4\text{–}\dot{C}H_2 + HFe(CN)_6^{2-} \xrightarrow{\text{fast}} X\text{–}C_6H_4\text{–}\overset{+}{C}H_2 + HFe(CN)_6^{3-} \quad (137)$$

$$X\text{–}C_6H_4\text{–}\overset{+}{C}H_2 + H_2O \xrightarrow{\text{fast}} X\text{–}C_6H_4\text{–}CH_2OH + H^+ \quad (138)$$

$$X\text{–}C_6H_4\text{–}CH_2OH + HFe(CN)_6^{2-} \xrightarrow{\text{fast}} X\text{–}C_6H_4\text{–}\dot{C}HOH + HFe(CN)_6^{3-} + H^+ \quad (139)$$

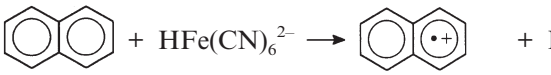
$$X\text{–}C_6H_4\text{–}\dot{C}HOH + HFe(CN)_6^{2-} \xrightarrow{\text{fast}} X\text{–}C_6H_4\text{–}\overset{+}{C}HOH + HFe(CN)_6^{3-} \quad (140)$$

$$X\text{–}C_6H_4\text{–}\overset{+}{C}HOH \longrightarrow X\text{–}C_6H_4\text{–}CHO + H^+ \quad (141)$$

with X = Cl, Br, I, NO_2 and CH_3. Steps (Eqs. (137) and (140)) seem reasonable given the radical trapping ability of $Fe(CN)_6^{3-}$. Recent measurements show that benzil radicals are rapidly oxidized in high yield to benzaldehyde under conditions similar to those used with toluene derivatives [239]; however, as electron-withdraw-

ing substituents considerably reduce the oxidation rate, the limited oxidizing ability of $Fe(CN)_6^{3-}$ could not be sufficient, depending upon the conditions, to complete the oxidation in competition with bimolecular termination reactions [240].

Oxidation of naphthalene normally produces naphthoquinone or phthalic acid, but the acidic $Fe(CN)_6^{3-}$ oxidation under N_2 atmosphere produces 35–45% of the unusual α-naphthol [10,236]; the reaction is first-order in [oxidant], $[H^+]$ and [substrate], and manifests a reverse isotope kinetic effect with $k_H/k_D = 0.6$. This effect, along with the susceptibility factor $\rho = -4$, determined from adherence to the Hammett equation, indicates that positive charge is developing at the reaction site in the activated complex, and suggests that the formation of a radical cation is rate-determining. Electron-donor substituents, e.g. $-CH_3$ and $-OCH_3$, increase the reaction rate, whereas electron-withdrawing substituents, e.g. NO_2, retard the reaction. The following scheme applies



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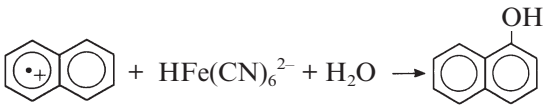

(143)

with 21 kJ mol^{-1} activation energy and -15 J K^{-1} mol^{-1} activation entropy. While the oxidation of phenanthrene by various oxidants normally gives phenanthroquinone or phenanthroic acids, the acidic $Fe(CN)_6^{3-}$ oxidation yields 30% of the unusual 9-hydroxyphenanthrene [10].

The alkaline oxidation of nitrotoluenes to nitrobenzyl alcohol in aqueous DMSO [237,238] is first-order in [oxidant], $[OH^-]$ and [substrate] and involves a second-order rate-determining step between two ions of same charge. The nucleophilic effect $Cl^- > Br^- > I^-$ is attributed to the solvent properties of DMSO [241]. Positive activation entropies 35 J K^{-1} mol^{-1} (2-nitrotoluene) and 21 J K^{-1} mol^{-1} (4-nitrotoluene), are quite unusual in $Fe(CN)_6^{3-}$ oxidations. The reaction mechanism is similar to that reported for other one-electron oxidants.

$$X\text{–}C_6H_4\text{–}CH_3 + OH^- \xrightarrow[\text{DMSO}]{\text{fast}} X\text{–}C_6H_4\text{–}CH_2^- + H_2O \quad (144)$$

$$X\text{–}C_6H_4\text{–}CH_2^- + Fe(CN)_6^{3-} \xrightarrow{\text{slow}} X\text{–}C_6H_4\text{–}\dot{C}H_2 + Fe(CN)_6^{4-} \quad (145)$$

$$X\text{–}C_6H_4\text{–}\dot{C}H_2 + H_2O \xrightarrow{\text{fast}} X\text{–}C_6H_4\text{–}CH_2OH + H\bullet \quad (146)$$

$$H\bullet + Fe(CN)_6^{3-} \xrightarrow{\text{fast}} H^+ + Fe(CN)_6^{4-} \quad (147)$$

The abstraction of an electron from the carbanion is the rate-determining step; the fast oxidation observed for 2,4-dinitrotoluene and 2,4,6-trinitrotoluene (which possess weaker methyl hydrogens) supports this assumption.

17. Oxidation of olefins

Direct $Fe(CN)_6^{3-}$ oxidation of olefins is very rare. The contribution by Mayell [242] describes the quantitative oxidation to glycols using OsO_4 as catalyst: a 0.1M KOH aqueous solution containing 0.1M $K_3Fe(CN)_6$ and 0.16 mM OsO_4 was bubbled with olefin gas at 30–40 $cm^3\,min^{-1}$ rate flow; the production of glycol is pH-dependent, and above pH 13 undesired products may be obtained. Table 4 lists yields from three olefins.

The oxidation of olefins to specific products using selective catalysts is an important reaction; the oxidation of ethylene to acetaldehyde and higher olefins to ketones using Cu^{2+}–Cu^{+} is feasible in the presence of $PdCl_2$; glycols may be suitably produced by addition of H_2O_2 to olefins in the presence of inorganic salts. By using black platinum certain olefins may be heterogeneously oxidized to CO_2. OsO_4 is an efficient catalyst to give *cis*-diols in non-aqueous media using H_2O_2 as co-oxidant, according to the net reaction

$$\mathrm{R{-}CH{=}CH{-}R' + 2Fe(CN)_6^{3-} + 2OH^- \rightarrow R{-}\overset{OH}{\underset{|}{CH}}{-}\overset{OH}{\underset{|}{CH}}{-}R' + 2Fe(CN)_6^{4-}} \quad (148)$$

The steps involved in the mechanism have been investigated separately. The Os(VIII)-catalyzed oxidation of propylene is consistent with the mechanism

$$\mathrm{CH_3{-}CH{=}CH_2 + OsO_4(OH)_2^{2-} \overset{k_1}{\rightarrow} |osmiate{-}ester|} \quad (149)$$

$$\mathrm{|osmiate{-}ester| + 2H_2O \overset{k_2}{\rightarrow} CH_3{-}\overset{OH}{\underset{|}{CH}}{-}\overset{OH}{\underset{|}{CH_2}} + OsO_2(OH)_4^{2-}} \quad (150)$$

Free radicals were not detected by ESR but an osmiate–ester intermediate complex [243] was observed in non-aqueous solvents, which undergoes further hydrolysis in accordance with step (Eq. (150)); the catalyst is regenerated rapidly and quantitatively in excess of oxidant, according to the net reaction

$$\mathrm{OsO_2(OH)_4^{2-} + 2Fe(CN)_6^{3-} + 2OH^- \rightarrow OsO_4(OH)_2^{2-} + 2Fe(CN)_6^{4-} + 2H_2O} \quad (151)$$

consistent with the following mechanism

$$\mathrm{OsO_2(OH)_4^{2-} + Fe(CN)_6^{3-} + OH^- \overset{k_3}{\rightarrow} |Intermediate|^{2-} + Fe(CN)_6^{4-} + H_2O} \quad (152)$$

$$\mathrm{|Intermediate|^{2-} + Fe(CN)_6^{3-} + OH^- \overset{k_4}{\rightarrow} OsO_4(OH)_2^{2-} + Fe(CN)_6^{4-} + H_2O} \quad (153)$$

The formation of such a short-lived intermediate is supported by the increase in absorbance at 518 nm, a wavelength where hexacyanoferrate(III)/(II) display no noticeable absorption, and the absorptivities of $OsO_2(OH)_4^{2-}$ and $OsO_4(OH)_2^{2-}$ are identical. Mayell also investigated the electrochemical regeneration of the oxidant consumed: H_2O_2 is used in the presence of OsO_4 to give glycols in mixed solvents such as *tert*-butyl alcohol or dry ether. This procedure allows to recover both the alkali and oxidant consumed. With a depolarized oxygen cathode the net cell reaction is

$$4Fe(CN)_6^{4-} + O_2 + 2H_2O \rightarrow 4Fe(CN)_6^{3-} + 4OH^- \quad (154)$$

Although this reaction should be spontaneous ($E^o = 0.041$ V), a small voltage is necessary due to the activation, concentration and polarization effects. If H_2 is released in the cathodic compartment, then the net cell reaction is

$$2Fe(CN)_6^{4-} + 2H_2O \rightarrow 2Fe(CN)_6^{3-} + H_2 + 2OH^- \quad (155)$$

the reduction potential being -1.188 V. The two processes differ by 1.229 V, equivalent to some 103.5% energy saving in favour of reaction (Eq. (154)); in practice this saving is only 43%. Table 5 lists the results corresponding to electrolysis of $Fe(CN)_6^{4-}$ determined at 100 mA current and ambient temperature; 95% graphite/5% polytetrafluoroethylene electrodes were used. Use of a H-type conventional electrolytic cell to produce glycol only requires consumption of olefin, oxygen, water and little energy.

$$\mathrm{R{-}CH{=}CH{-}R' + 1/2\ O_2 + H_2O \rightarrow R{-}\overset{\mathrm{HO}}{\overset{|}{\mathrm{C}}}{-}\overset{\mathrm{OH}}{\overset{|}{\mathrm{C}}}{-}R'} \quad (156)$$

Table 5
Second-order rate constants for the hexacyanoferrate(III) oxidation of free radicals

Radical	k ($M^{-1}\,s^{-1}$)	Radical	k ($M^{-1}\,s^{-1}$)
$\dot{C}H_3$	5.0×10^6	$\dot{C}H_2COOH$	2.0×10^6
$\dot{C}H_2CH_3$	5.0×10^7	$HOOC\dot{C}HOH$	1.0×10^8
$\dot{C}H(CH_3)_2$	1.2×10^9	$^-OOC\dot{C}HOH$	5.0×10^8
$\dot{C}(CH_3)_3$	3.6×10^9	$^-OOC\dot{C}HO$	7.5×10^8
$\dot{C}H_2Cl$	5.0×10^5	$\dot{C}OO^-$	1.1×10^9
$\dot{C}HCl_2$	5.0×10^5	$\dot{P}hOH$	1.8×10^7
$\dot{C}H_2CH_2OH$	5.0×10^7	$(CH_3O)_3\dot{C}$	1.7×10^9
$\dot{C}H_2OH$	4.0×10^9	$(CH_3O)_2CHO\dot{C}H_2$	1.7×10^9
$CH_3\dot{C}HOH$	5.3×10^9	$(C_2H_5O)_3\dot{C}$	1.6×10^9
$(CH_3)_2\dot{C}OH$	4.7×10^9	$(C_2H_5O)_2CHO\dot{C}HCH_3$	1.6×10^9
$\dot{C}H_2OCH_3$	4.3×10^9	$((CH_3)_2CHO)_3\dot{C}$	2.7×10^9
$CH_3\dot{C}HOCH_2CH_3$	4.0×10^9	$(CH_3O)_3CO\dot{C}H_2$	3.8×10^8
$(CH_3)_2\dot{C}OCH(CH_3)_2$	3.6×10^9	$(C_2H_5O)_3CO\dot{C}HCH_3$	1.8×10^9

18. Oxidation of metalloproteins

The interest in this type of reaction rests on the fact that the conclusions drawn may often be extrapolated on a physiological level; thus, the O_2/H_2O redox system may serve as the link between the biochemical routes of respiration and photosynthesis [244]. Heme proteins perform a variety of biological functions; cytochrome *c* is a simple low molecular weight heme electron transferase involving the Fe(II/III) redox couple and, as such, may undergo reversible changes in the mitochondrial electron transport system. The investigations carried out on electron-transfer reactions in metalloproteins indicate that the donor–acceptor electrostatic coupling depends on the structure of the bridging polypeptide medium [245,246]. These reactions need to be monitored by stopped-flow techniques. Metalloproteins are investigated in neutral media, under pH and ionic strength physiological conditions; the oxidation is normally first-order in [substrate], but the reaction order in [oxidant] decreases with increasing concentration, a feature also reported in electron-transfer reactions between metalloproteins and inorganic complexes [247,248], using the simplified mechanism

$$\mathrm{MP(Red)} + \mathrm{C(Oxid)} \overset{K}{\rightleftharpoons} |\mathrm{MP{-}C}| \tag{157}$$

$$|\mathrm{MP{-}C}| \overset{k_1}{\rightarrow} \mathrm{MP(Oxid)} + \mathrm{C(red)} \tag{158}$$

Step (Eq. (157)) involves an equilibrium association to form an intermediate complex, and Eq. (158) is the electron-transfer step, consistent with the rate expression

$$r = \frac{Kk_1[\mathrm{Fe(CN)_6^{3-}}][\mathrm{MP}]}{1 + K[\mathrm{Fe(CN)_6^{3-}}]} \tag{159}$$

With plastocyanin, PCu(I), and azurin, ACu(I) [249], the association constant *K* is small, the denominator tends to unity, and the rate equation is second-order. However, deviations from first-order in the oxidant are expected if *K* is large.

The acidity effect on the rate constant is explained by the protonation of the protein. The oxidation of plastocyanin and azurin is unaffected by addition of the neutral salts, LiCl, NaCl or KCl; in the oxidation of stellacyanin (protein–Cu) [250] the observed rate constant varies linearly with $[K^+]$ regardless of the ionic strength used, an effect due to formation of the $KFe(CN)_6^{2-}$ ion-association complex. The activation entropies -158, -196 and $-217\ \mathrm{J\ K^{-1}\ mol^{-1}}$ and the activation enthalpies -3.7, -13.8 and $-17\ \mathrm{kJ\ mol^{-1}}$ for cytochrome *f*, plastocyanin and azurin, respectively, are interpreted in terms of the higher degree of solvation of the protein [251].

Elucidation of the reaction site of the metalloprotein is an important goal in this type of reaction; it is usually located in a region of the prosthetic group accessible to the solvent used. The electron transfer from the prosthetic group to the oxidant may occur either directly or through the polypeptide chain, as described for haemoglobin [252]. The oxidation of cytochrome-*C* is one of the kinetic studies

performed in more detail [253]. Cytochrome-*C* oxidase has four transition metal centres consisting of two heme groups and two copper sites [244]; the hexacyanoferrate–cytochrome-*C* association has been proved by NMR analysis, and some kinetic investigations have been carried out on it [254]. Solving for the simultaneous differential rate equations leads to a five-step mechanism that accounts for the experimental observations

$$\text{Cytochrome } (Fe^{2+}) + Fe(CN)_6^{3-} \rightleftharpoons C_1 \rightleftharpoons C_1' \rightleftharpoons C_2' \rightleftharpoons C_2 \rightleftharpoons \text{Cytochrome } (Fe^{3+}) + Fe(CN)_6^{4-} \quad (160)$$

C_1 and C_2 are collision complexes, and C_1' and C_2' are isergonic intermediates generated by solvent reorganization and rearrangement of bond lengths, so the redox potentials are related to first-order processes involving chemical and/or structural changes.

The chemical action of enzymes normally occurs via multistep kinetic processes, with the protein part involved in one or more first-order steps after the enzyme–substrate complex is formed, so the redox scheme of cytochrome-*C* is similar to Eq. (160), reported for different cytochromes [255–258]. In sum, it is reasonable to assume that the protein moiety controls the redox potential by forming intermediates that may undergo fast isergonic electron transformations.

19. Oxidation of free radicals

Most oxidations discussed above produce a radical as a first intermediate, i.e. species with a pronounced tendency to engage in one-electron transfer reactions to lose their radical nature; thus, it is interesting to study the oxidation of such species. The oxidation state of radicals can be changed easily, since radicals are species between two stable oxidation states [259]. $Fe(CN)_6^{3-}$ ions can be reduced quickly and quantitatively by e_{aq}^- and $H^\cdot$

$$Fe(CN)_6^{3-} + e_{aq}^- \rightarrow Fe(CN)_6^{4-} \quad (161)$$

$$Fe(CN)_6^{3-} + H^\cdot \rightarrow Fe(CN)_6^{4-} + H^+ \quad (162)$$

with second-order rate constants $k(e_{aq}^-) = 3 \times 10^9 M^{-1} s^{-1}$ in neutral media [260], and $k(H^\cdot) = 2 \times 10^8 M^{-1} s^{-1}$ in acidic media [261]. In N_2O-saturated solutions, solvated electrons react with N_2O yielding $OH^\cdot$ radicals which, in turn, oxidize the $Fe(CN)_6^{4-}$ ions to ferricyanide, $k = 1.2 \times 10^{10} M^{-1} s^{-1}$.

Other reactions have been described for obtaining free radicals [149,150]. If substrate concentrations are conveniently selected (500 to 1000 times that of the oxidant), $Fe(CN)_6^{3-}$ ions cannot react with either of the two radicals, and react solely with alkyl radicals

$$R^\cdot + Fe(CN)_6^{3-} \rightarrow R^+ + Fe(CN)_6^{4-} \quad (163)$$

This procedure allowed the oxidation kinetics of different alkyl radicals to be investigated [262]. These reactions are first-order both in substrate and oxidant

concentrations. Table 5 summarizes the second-order rate constants for the oxidation of some radical species [149–151], most of them corresponding to diffusion-controlled processes. A significant charge effect on the reaction rate is observed; radicals containing non-deprotonated COOH groups exhibit higher reactivity than those containing the ionized forms COO^-. These rate constants increase noticeably with decreasing ionization potential of the alkyl radicals; correlation with the σ Taft constants of the alkyl groups leads to a susceptibility reaction constant $\rho = -13.2$; this value points to an ionic activated complex, consistent with formation of carbocations. Species such as CH_3CN and CH_3CH_2CN were not found among the oxidation products of methyl and ethyl radicals, this fact excluding exchange of CN^- ligands. The oxidation of 4-chlorobenzyl radicals by $Fe(CN)_6^{3-}$ all have very similar rate constants, $k = (1–4) \times 10^7 M^{-1} s^{-1}$ [239].

20. Oxidation of chelating agents

The presence of trace metals introduced as impurities in commercial reagents is often the reason for obtaining irreproducible kinetic results; such behaviour has often been attributed to the catalytic action of trace metals. To avoid this undesired effect, impurities must be removed by action of chelating agents. Thus, knowledge of the interaction kinetics between the oxidant and the substrate is desirable. Although many chelating agents have been studied, either naturally occurring [263] or synthesized [264], the oxidation of EDTA by basic $Fe(CN)_6^{3-}$ is the only reaction kinetically investigated in detail [265]. The oxidation is first-order both in oxidant and chelating agent. Experiments in basic medium show that the anionic form $EDTA^{4-}$ is the reactive species and that the rate-determining step is not reversible; experiments at constant ionic strength and varying concentrations of alkali-metal ions show an increase in rate constant by a factor of 100 by replacing Na^+ by Li^+. The effect of structure on reactivity may be inferred from the influence of temperature on the rate constants of a series of chelating agents; Table 6 gives values of rate constants, activation enthalpies and activation entropies for the oxidation of 16 different substrates. The linear correlation between enthalpies and entropies denotes an isokinetic relationship ascribable to an attack on the amine N-atom present in almost all the substrates listed. The observed order in reactivity: tertiary amines > secondary > primary, is in agreement with that of Section 8. The oxidation of the complexes Ca^{2+}, Mg^{2+}, Cr^{3+} or Co^{3+} with $EDTA^{4-}$ is at least 100 times slower than oxidation of the $EDTA^{4-}$ ions, a result explained by the blocking effect of the reaction sites of the substrate by the metal ions. However, addition of CN^- ions does not inhibit the oxidation, in agreement with an outer-sphere rate-determining step.

21. Concluding remarks

$Fe(CN)_6^{3-}$ has proven to be an efficient oxidant of a wide variety of organic substrates, due to two major reasons:

Table 6
Rate constants (30 °C) and activation parameters for the oxidation of different chelating agents by basic hexacyanoferrate(III)

Substrate	10^3k ($M^{-1}\,s^{-1}$)	$\Delta H^{\ddagger}$ (kJ mol^{-1})	$\Delta S^{\ddagger}$ (J $K^{-1}\,mol^{-1}$)
Ethylenediaminetetraacetic acid	105	69.3	28.4
$MgEDTA^{2-}$	1.98	54.4	−38.5
$CaEDTA^{2-}$	0.044	70.7	−16.3
Ethylenediaminetetrapropionic acid	1.92	53.5	−41.8
Ethylenediaminepentaacetic acid	304	33.0	−79.5
Iminodiacetic acid	0.293	6.3	−209
Nitrilotriacetic acid	12.8	64.0	6.3
Ethylenebis(oxyethylenenitrilo)tetraacetic acid	61.8	63.2	2.1
β-Alanine	0.145	12.5	−197
α-Alanine	0.014	26.4	−171
Glycine	0.051	41.0	−121
Histidine	3.02	60.2	−22.2
Proline	0.042	79.1	30.1
Glutamic acid	0.24	93.7	74.1
Methionine	0.155	97.5	82.0
Imidazole	1.13	45.6	−79.5

(a) The reduction potential E^{o} of the $Fe(CN)_6^{3-}/Fe(CN)_6^{4-}$ pair remains essentially constant at 0.41 V over a wide pH range 4–13, which makes it a very convenient reagent for selective oxidations.

(b) Both the oxidized and reduced forms are stable, substitutionally inert complexes of low spin, and they exchange CN^- ligands in solution only very slowly, under high temperature and acidity. The CN^- ligands are resistant to substitution reactions, hence outer-sphere electron transfer is the preferred oxidation pathway. Therefore, oxidations are normally "clean", devoid of side reactions, which greatly facilitates the monitoring.

The reaction mechanisms normally involve the key redox step of an initial outer-sphere electron transfer with formation of free radicals. Depending on the fate of such radicals, different final products can be formed, especially if the radicals are susceptible to tautomer equilibrium.

The presence of cationic species in solution, particularly alkali-metal ions, plays an essential role in the kinetics reactions in acidic media since the high negative charge on $Fe(CN)_6^{3-}$ favours the ion-pair formation. However, the observed effect that larger Y^+ cations increase the reaction rate allows one to think of the transition state as a symmetrical Y^+ bridged dimer [17,266] of $Fe(CN)_6^{3-}$; thus use of the appropriate hexacyanoferrate salts rather than addition of the appropriate halides to solutions of the more generally available $K_3Fe(CN)_6$ should be advisable [2]. This fact, together with the electronically favourable nature of the CN^- ligands, considerably reduces the barrier to the electronic flow from the HOMO of the substrate to the LUMO of the metal complex.

The monitoring of most, if not all, oxidations can be performed by following the absorption band at 420 nm using either conventional spectrophotometry or stopped-flow techniques. The reactions are first-order in [substrate], since the substrate is always involved in the rate-determining step; however, the basic substrate form is normally more reactive than the neutral or the protonated species, since the electron transfer occurs from an electron-rich site of the substrate. The oxidations are also first-order in oxidant, except in reactions where enolization is the rate-determining step.

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References

[1] B.S. Thyagarajan, Chem. Rev. 58 (1958) 439.
[2] D.E. Khoshtariya, A.M. Kjaer, T.A. Marsagishvili, J. Ulstrup, J. Phys. Chem. 96 (1992) 4154.
[3] P.L. Domingo, B. García, J.M. Leal, Can. J. Chem. 68 (1990) 228.
[4] A. Messina, G. Gritzner, J. Electroanal. Chem. 101 (1979) 201.
[5] V. Gutman, G. Gritzner, K. Danksagmüller, Inorg. Chim. Acta 17 (1976) 81.
[6] J.M. Leal, P.L. Domingo, B. García, S. Ibeas, J. Chem. Soc. Faraday Trans. (1993) 3571.
[7] C. Meali, D.M. Proserpio, J. Chem. Educ. 67 (1990) 399.
[8] J.J. Alexander, H.B. Gray, J. Am. Chem. Soc. 90 (1968) 4260.
[9] H.B. Gray, N.A. Beach, J. Am. Chem. Soc. 85 (1963) 2922.
[10] D.E. Khoshtariya, R. Meusinger, R. Billing, J. Phys. Chem. 99 (1995) 3592.
[11] M.K. Mahanti, in: K.S. Gupta (Ed.), Topics in Chemistry Series 1; Chemical Kinetics and Reaction Mechanism, RBSA Publishers, Jaipur, 1991.
[12] W.A. Eaton, P. George, G.I.H. Hanania, J. Phys. Chem. 71 (1967) 2016.
[13] R.C. Wilkins, Kinetics and Mechanism of Reactions of Transition Metal Complexes, VCH, Weinheim, 1991, ch. 5.
[14] J.M. Leal, P.L. Domingo, B. García, S. Ibeas, New J. Chem. 18 (1994) 1233.
[15] D.V.S. Jain, F.S. Nandel, J. Chem. Soc. Dalton Trans. (1977) 949.
[16] D.E. Khoshtariya, R. Billing, M. Ackermann, R. van Eldik, J. Chem. Soc. Faraday Trans. 91 (1995) 1625.
[17] D.E. Khoshtariya, A.M. Kjaer, T.A. Marsagishvili, J. Ulstrup, J. Phys. Chem. 95 (1991) 8797.
[18] A. Loupy, B. Tchoubar, D. Astruc, Chem. Rev. 92 (1992) 1141.
[19] M.J. Pregel, E. Buncel, J. Am. Chem. Soc. 115 (1993) 10.
[20] T.M. Bockmann, J.K. Kochi, J. Am. Chem. Soc. 111 (1989) 4669.
[21] N.H. Hillal, S.A. Elshazly, A.M. Bekheet, W.A. Badawy, Ber. Bunsenges. Phys. Chem. 96 (1992) 643.
[22] D. Astruc, Electron Transfer and Radical Processes in Transition-Metal Chemistry, VCH, Weinheim, 1995, ch. 1.
[23] K.-M.F. Le Brocq, E. Leslie, I.R. Wilson, Aust. J. Chem. 39 (1986) 1411.
[24] P.G. Sim, E. Whalley, J. Phys. Chem. 91 (1987) 1877.
[25] P.L. Domingo, B. García, J.M. Leal, Can. J. Chem. 65 (1987) 583.
[26] R. Billing, D.E. Khoshtariya, Inorg. Chem. 33 (1994) 4038.

[27] V. Gaspar, M.T. Beck, Polyhedron 2 (1983) 387.
[28] W.I. Taylor, A.R. Battersby, Oxidative Coupling of Phenols, Marcel Dekker, New York, 1967, ch. 1.
[29] S. Gopalan, P.E. Savage, J. Phys. Chem. 98 (1994) 12646.
[30] S.I. Murahashi, T. Naota, N. Miyaguchi, S. Noda, J. Am. Chem. Soc. 118 (1996) 2509.
[31] M. Bhattacharjee, M.K. Mahanti, Int. J. Chem. Kinet. 15 (1983) 197.
[32] P.D. McDonald, G.H. Hamilton, J. Am. Chem. Soc. 95 (1973) 7752.
[33] F. Sanchez-Burgos, M.L. Moyá, M. Galán, Prog. Reaction Kinetics 19 (1993) 1.
[34] P.K. Panda, R.K. Panda, P.S. Radhakrishnamurti, Int. J. Chem. Kinet. 19 (1987) 155.
[35] T. Yu, A.M. Mebel, M.C. Lin, J. Phys. Org. Chem. 8 (1995) 47.
[36] E.T. Denisov, I.V. Khudyakov, Chem. Rev. 87 (1987) 1313.
[37] M. Foti, K.U. Ingold, J. Lusztyk, J. Am. Chem. Soc. 116 (1994) 9440.
[38] C.G. Haynes, A.H. Turner, W.A. Waters, J. Chem. Soc. (1956) 2823.
[39] G.W.K. Cavill, E.R. Cole, P.T. Gilham, D.J. McHugh, J. Chem. Soc. (1936) 1025.
[40] S.L. Cosgrobe, W.A. Waters, J. Chem. Soc. (1951) 388.
[41] P. Hapiot, P. Neta, J. Pinson, C. Rolando, S. Schneider, New J. Chem. 17 (1993) 211.
[42] R. Pummerer, I. Veit, Chem. Ber. 86 (1953) 412.
[43] C.D. Cook, N.G. Nash, H.R. Flanagan, J. Am. Chem. Soc. 77 (1955) 1783.
[44] P.L. Majumder, A. Kundu, J. Indian Chem. Soc. 61 (1984) 142.
[45] M. Bhattacharjee, M.K. Mahanti, Bull. Soc. Chim. Fr. 9 (1983) 225.
[46] G.N.R. Tripathi, D.M. Chipman, R.H. Schuler, D.A. Armstrong, J. Phys. Chem. 99 (1955) 5264.
[47] M. Bhattacharjee, M.K. Mahanti, Gazz. Chim. Ital. 113 (1983) 101.
[48] J. Harley-Mason, A.H. Jackson, J. Chem. Soc. (1954) 1165.
[49] H.S. Singh, V.P. Singh, D.P. Pandey, Monatsh. Chem. 110 (1979) 1455.
[50] S. Gupta, S.K. Upadhyay, Asian J. Chem. 4 (1992) 229.
[51] H.S. Singh, S.M. Singh, P. Singh, K.K. Singh, Proc. Indian Natn. Sci. Acad. 49A (1983) 173.
[52] M.P.K. Tandon, B. Krishna, Z. Phys. Chem. Leipzig 266 (1985) 1153.
[53] T.V. Latitha, B. Sethuram, Trans. Met. Chem. 17 (1992) 29.
[54] M.N. Pandey, H. Narayan, R.S. Shukla, K. Behari, Z. Phys. Chem. Leipzig 263 (1982) 1055.
[55] H.S. Singh, J.K. Singh, Indian J. Chem. 29 (1990) 1068.
[56] R.K. Dwivedi, M. Verma, P. Kumar, K. Behari, Tetrahedron 39 (1983) 815.
[57] K. Behari, H. Narayan, R.S. Shukla, K.C. Gupta, Int. J. Chem. Kinet. 16 (1984) 195.
[58] A. Mucientes, B. Cabañas, F.J. Poblete, An. Quím. 87 (1991) 127.
[59] A. Mucientes, B. Cabañas, F.J. Poblete, An. Quím. 87 (1991) 838.
[60] A. Mucientes, B. Cabañas, F.J. Poblete, An. Quím. 88 (1992) 104.
[61] A. Mucientes, B. Cabañas, F.J. Poblete, An. Quím. 88 (1992) 170.
[62] A. Mucientes, F. Santiago, An. Quím. 89 (1993) 313.
[63] T.V. Lalitha, M.P. Rao, B. Sethuram, Indian J. Chem. 31A (1992) 309.
[64] N. Nath, L.P. Singh, R.P. Singh, J. Indian Chem. Soc. 58 (1981) 1204.
[65] H.S. Singh, K.C. Tiwari, S.M. Singh, Indian J. Chem. 21A (1982) 520.
[66] M.K. Verma, P.K. Tandon, H.S. Singh, M.P. Singh, Z. Phys. Chem. Leipzig 267 (1986) 1219.
[67] H.S. Singh, S.P. Singh, S.M. Singh, R.K. Singh, A.K. Sisodia, J. Phys. Chem. 79 (1975) 1920.
[68] H.S. Singh, P. Singh, Ann. Soc. Sci. Bruxelles 97 (1983) 21.
[69] V.A. Morab, S.M. Tuwar, S.T. Nandibewoor, J.R. Raju, J. Indian Chem. Soc. 69 (1992) 862.
[70] H.S. Singh, K.K. Singh, S.M. Singh, P. Singh, P. Thakur, Indian J. Chem. 21A (1982) 816.
[71] S. Gupta, S.K. Upadhyay, Asian J. Chem. 4 (1992) 229.
[72] A. Mucientes, F.J. Poblete, M.A. Rodriguez, F. Santiago, J. Phys. Org. Chem. 10 (1997) 662.
[73] A. Mucientes, F. Santiago, F.J. Poblete, R. Varon, Int. J. Chem. Kinet. 29 (1997) 1.
[74] T.R. Cundary, R.S. Drago, Inorg. Chem. 29 (1990) 3904.
[75] S.L. Scott, A. Bakac, J.H. Espenson, J. Am. Chem. Soc. 114 (1992) 4205.
[76] B. Singh, B.B. Singh, S. Singh, J. Indian Chem. Soc. 57 (1980) 662.
[77] P.T. Speakman, W.A. Waters, J. Chem. Soc. (1955) 4045.
[78] K.B. Wiberg, W.G. Nigh, J. Am. Chem. Soc. 87 (1965) 3849.
[79] P.S. Radhakrishnamurti, S. Devi, Indian J. Chem. 10 (1972) 496.
[80] A.K. Kashyap, R.C. Mohapatra, N.C. Khandual, J. Indian Chem. Soc. 56 (1979) 748.

[81] V.N. Singh, M.C. Gangwar, B.B.L. Saxena, M.P. Singh, Can. J. Chem. 47 (1969) 1051.
[82] A.A. Jarrar, R.A. El-Zaru, Nat. Sci. 6 (1979) 7.
[83] A.A. Jarrar, R.A. El-Zaru, A.S. Shahin, Arabian J. Sci. Eng. 13 (1988) 65.
[84] L. Ferrari, F. Gutierrez, An. Quím. 78 (1982) 15.
[85] G.K. Kletawat, G.D. Menghami, J. Indian Chem. Soc. 64 (1987) 766.
[86] P.S. Radhakrishnamurti, B. Sahu, Indian J. Chem. 17A (1979) 93.
[87] P.V. Somahia, K.B. Reddy, B. Sethuram, T.N. Rao, Indian J. Chem. 26A (1987) 402.
[88] P. Misra, S.C. Mohapatra, N.C. Khandual, J. Indian Chem. Soc. 63 (1986) 291.
[89] F. Solymosi, Chemist–Analyst 51 (1962) 71.
[90] K.C. Gupta, M.P. Singh, Bull. Chem. Soc. Jpn. 42 (1969) 599.
[91] R.K. Srivastava, N. Nath, Tetrahedron 23 (1967) 1189.
[92] K.C. Gupta, A. Sharma, V.D. Misra, Tetrahedron 37 (1981) 2887.
[93] D.G. Lambert, M.M. Jones, J. Inorg. Nucl. Chem. 29 (1967) 579.
[94] S. Shahine, R. Mahmoud, Mikrochim. Acta 1 (1980) 119.
[95] C.M. Paleos, E. Papaconstantinou, J. Colloid Interface Sci. 113 (1986) 297.
[96] B.M. Tolbert, J.B. Ward, Ascorbic acid: chemistry, metabolism, and uses, in: Advances in Chemistry Series, vol. 200, ACS, Washington, DC, 1982, pp. 101–123.
[97] M.B. Davies, J. Austin, D.A. Partridge, Vitamin C: Its Chemistry and Biochemistry, Royal Society of Chemistry, Cambridge, 1991, ch. 5.
[98] B.N. Ames, M.K. Shigenaga, T.M. Hagen, Proc. Natl. Acad. Sci. USA 90 (1993) 7915.
[99] K. Wimalasena, S.W. May, J. Am. Chem. Soc. 117 (1995) 9.
[100] W. Friedrich, Vitamins, Walter de Gruyter, Berlin, 1988, ch. 1.
[101] J.F. Martínez, Thesis, Valladolid Univ., 1992.
[102] P. Martínez, J. Zuluaga, An. Quím. 80 (1984) 179.
[103] P. Martínez, J. Zuluaga, C. Sieiro, Z. Phys. Chem. 265 (1984) 1225.
[104] P. Martínez, J. Zuluaga, C. Sieiro, An. Quím. 84 (1988) 310.
[105] B. Bänsch, P. Martínez, J. Zuluaga, D. Uribe, R. van Eldik, Z. Phys. Chem. 170 (1991) 59.
[106] L.J.A. Martins, J. Barbosa, J. Chem. Educ. 65 (1988) 176.
[107] S. Acharya, G. Neogi, R.K. Panda, Z. Phys. Chem. 267 (1986) 1189.
[108] N. Sharma, A. Agrawal, S.K. Misra, Transit. Metal Chem. 17 (1992) 181.
[109] L. Ferrari, A. Alonso, An. Quím. 79 (1983) 531.
[110] P. Martínez, J. Zuluaga, D. Uribe, R. van Eldik, Inorg. Chim. Acta 136 (1987) 11.
[111] P. Martínez, J. Zuluaga, A.P. Rodríguez, Z. Phys. Chem. 271 (1990) 597.
[112] S. Steenken, P. Neta, J. Am. Chem. Soc. 104 (1982) 1244.
[113] S. Steenken, J. Buschek, R.A. McClelland, J. Am. Chem. Soc. 108 (1986) 2808.
[114] S. Steenken, Free radicals. Chemistry, Pathology and Medicine, Richelieu Press, London, 1988, ch. 3.
[115] I. Yamazaki, L.H. Piette, Biochim. Biophys. Acta 50 (1961) 62.
[116] B.H.J. Bielski, D.A. Comstock, R.A. Bowen, J. Am. Chem. Soc. 93 (1971) 5624.
[117] N.H. Williams, J.K. Yandell, Aust. J. Chem. 35 (1982) 1133.
[118] T.J. Meyer, H. Taube, Comprehensive Coordination Chemistry, vol. I, Pergamon Press, Oxford, 1987.
[119] N. Kagayama, M. Sekiguchi, Y. Inada, H.D. Tagaki, S. Funahashi, Inorg. Chem. 33 (1994) 1881.
[120] M.N. Schuchmann, H.P. Schuchmann, C. Sonntag, J. Phys. Chem. 99 (1995) 9122.
[121] M.P. Singh, S.H. Singh, B.S. Arya, A.K. Singh, V. Tripathi, A.K. Singh, Indian J. Chem. 15A (1977) 716.
[122] K.K. Gupta, T. Sarkar, S. Gupta, H.R. Chatterjee, Indian J. Chem. 14A (1976) 583.
[123] V.S. Singh, Indian J. Chem. 20A (1981) 586.
[124] K.K. Gupta, S. Gupta, H.R. Chatterjee, Indian J. Chem. 14A (1976) 586.
[125] J.C. Soni, B.L. Chandwani, G.D. Menghani, J. Indian Chem. Soc. 51 (1974) 693.
[126] M.P. Singh, H.S. Singh, B.S. Arya, A.K. Singh, A.K. Sisodia, Indian J. Chem. 13 (1975) 112.
[127] R.K. Shukla, N. Anandam, Acta Cienc. Indica Chem. 11 (1985) 242.
[128] S.S. Shivastava, P.C. Mathur, Pol. J. Chem. 60 (1986) 531.
[129] B. Singh, B.B. Singh, R.P. Singh, J. Inorg. Nucl. Chem. 43 (1981) 1283.
[130] B. Singh, S. Saxena, S.P. Singh, J. Indian Chem. Soc. 60 (1983) 795.

[131] R.N. Singh, P.K. Tikoo, Indian J. Chem. 19A (1981) 1210.
[132] S. Kumar, P.C. Mathur, J. Inorg. Nucl. Chem. 40 (1978) 581.
[133] F.A. Beland, F.F. Kadluber, Carcinog. 6 (1985) 1989.
[134] D.W. Potter, J.A. Hinsone, Drug Metab. Rev. 20 (1989) 341.
[135] M. Hudlický, Oxidations in Organic Chemistry, ACS Monograph 186, Washington, DC, 1990, ch. 3.
[136] G.I. Nikishin, E.I. Troyanskii, V.A. Ioffe, Izv. Acad. Nauk SSSR (1982) 2758.
[137] T.W.G. Solomon, Organic Chemistry, Wiley, New York, 1992, ch. 19.
[138] P.S. Radhakrishnamurti, R.K. Panda, Indian J. Chem. 9 (1971) 1247.
[139] C.N.R. Rao, Ultra-violet and Visible Spectroscopy, Butterworth, London, 1970, ch. 3.
[140] M.M. Al-subu, J. Indian Chem. Soc. 67 (1990) 966.
[141] A.J. Miralles, R.E. Armstrong, A. Haim, J. Am. Chem. Soc. 99 (1977) 1416.
[142] U.R. Lindsay, L.A. Mead, J. Chem. Soc. Perkin Trans. (1983) 206.
[143] J. Huang, H.B. Dunford, Can. J. Chem. 68 (1990) 2159.
[144] T.J. Kemp, P. Moore, J.R. Quick, J. Chem. Res.-S. (1981) 33.
[145] V.K. Gupta, Z. Phys. Chem. Leipzig 267 (1986) 204.
[146] U. Nickel, B. Mao Zhou, G. Gulden, Ber. Bunsenges. Phys. Chem. 89 (1985) 999.
[147] C. Hänsch, A. Leo, R.W. Taft, Chem. Rev. 91 (1991) 165.
[148] G. Dasgupta, M.K. Mahanti, Afinidad 45 (1988) 35.
[149] G. Dasgupta, M.K. Mahanti, Croat. Chem. Acta 59 (1986) 407.
[150] G. Dasgupta, M.K. Mahanti, Croat. Chem. Acta 59 (1986) 895.
[151] A.K. Awasti, S.K. Upadhyay, J. Indian Chem. Soc. 64 (1987) 125.
[152] E.P. Burrows, D.H. Rosenblatt, J. Org. Chem. 48 (1983) 992.
[153] S.K. Upadhyay, M.C. Agrawal, Indian J. Chem. 19 (1980) 478.
[154] K.S. Sidhu, W.R. Bansal, S. Kaur, Indian J. Chem. 26 (1987) 740.
[155] Y. Zhong, P.K. Lim, J. Am. Chem. Soc. 111 (1989) 8398.
[156] Y. Zhong, P.K. Lim, J. Am. Chem. Soc. 111 (1989) 8404.
[157] A. Garrone, R. Fruttero, C. Tironi, A. Gasco, J. Chem. Soc. Perkin Trans. II (1989) 1941.
[158] J.C. Leipoldt, L.D. Bok, A.J. van Wyk, C.R. Dennis, React. Kinet. Katal. Lett. 6 (1977) 467.
[159] D.M. Stanbury, Inorg. Chem. 23 (1984) 2879.
[160] A. Kumar, R.K. Prasad, J. Indian Chem. Soc. 51 (1974) 366.
[161] M.M. Al-Subu, R. Abu El-Halawa, M.M. Abed, Int. J. Chem. Kinet. 22 (1990) 1027.
[162] A.K. Gupta, B. Gupta, Y.K. Gupta, J. Chem. Soc. Dalton Trans. (1984) 2599.
[163] M.S. Frank, P.V.K. Rao, Indian J. Chem. 19A (1980) 476.
[164] M.M. Al-Subu, R. Abu El-Halawa, H.M. Abed, Indian J. Chem. 30A (1991) 717.
[165] H. Decker, A. Kaufmann, J. Prakt. Chem. 84 (1911) 425.
[166] M.F. Powell, J.C. Wu, T.C. Bruice, J. Am. Chem. Soc. 106 (1984) 3850.
[167] P. Nesvabda, J. Kuthan, Collect. Czech. Chem. Commun. 48 (1983) 511.
[168] P. Nesvabda, P. Strop, J. Kuthan, Collect. Czech. Chem. Commun. 48 (1983) 3307.
[169] S. Böhm, H. Slavik, J. Kuthan, Collect. Czech. Chem. Commun. 54 (1989) 200.
[170] J.W. Bunting, G.M. Kaufmann, Can. J. Chem. 62 (1984) 729.
[171] J.W. Bunting, D. Stefanidis, J. Org. Chem. 51 (1986) 2060.
[172] J.W. Bunting, D. Stefanidis, J. Org. Chem. 51 (1986) 2068.
[173] N.W. Mitzel, B.A. Smart, S. Parsons, H.E. Robertson, D.W.H. Rankin, J. Chem. Soc. Parkin Trans. II (1996) 2727.
[174] M.N. Hughes, The Inorganic Chemistry of Biological Processes, Wiley, New York, 1981, pp. 204–211.
[175] V.K. Jindal, M.C. Agrawal, S.P. Mushran, J. Chem. Soc. (A) (1970) 2060.
[176] V.K. Jindal, M.C. Agrawal, S.P. Mushran, Z. Naturforsch. 25B (1970) 100.
[177] G.J. Bridgart, W.A. Waters, I.R. Wilson, J. Chem. Soc. Dalton Trans. (1973) 1582.
[178] K. Tanaka, K. Matsuo, K. Nakanishi, Y. Kataoka, K. Takase, S. Otsuki, Chem. Pharm. Bull. 36 (1988) 2323.
[179] K.K. Ghosh, S.K. Rajput, K.K. Krishnani, J. Phys. Org. Chem. 5 (1992) 39.
[180] O. Exner, M. Hradil, J. Mollin, J. Collect. Czech. Chem. Commun. 58 (1993) 1109.
[181] A. Bagno, C. Comuzzi, G. Scorrano, J. Am. Chem. Soc. 116 (1994) 916.

[182] F.G. Bordwell, H.E. Fried, D.L. Hughes, T.Y. Lynch, A.V. Satish, Y.E. Whang, J. Org. Chem. 55 (1990) 3330.
[183] M. Decouzon, O. Exner, J.F. Gal, P.C. Maria, J. Org. Chem. 55 (1990) 3980.
[184] E. Boyland, R. Nery, J. Chem. Soc. (C) (1966) 354.
[185] T.R. Oliver, W.A. Waters, J. Chem. Soc. (B) (1971) 677.
[186] A.R. Forrester, M.M. Ogilvy, R.H. Thomson, J. Chem. Soc. (C) (1970) 1081.
[187] S.K. Upadhyay, M.C. Agrawal, J. Indian Chem. Soc. 58 (1981) 871.
[188] D. Laloo, M.K. Mahanti, Oxid. Commun. 109 (1987) 205.
[189] D. Laloo, M.K. Mahanti, Afinidad 44 (1987) 123.
[190] D. Laloo, M.K. Mahanti, Afinidad 48 (1991) 45.
[191] D. Laloo, M.K. Mahanti, J. Phys. Org. Chem. 3 (1990) 799.
[192] R.N. Mehrotra, R.C. Kapoor, S.K. Vajpai, J. Chem. Soc. Dalton Trans. (1984) 999.
[193] R.C. Acharya, N.K. Saran, S.R. Rao, M.N. Das, Int. J. Chem. Kinet. 14 (1982) 143.
[194] S.K. Upadhyay, Int. J. Chem. Kinet. 15 (1983) 669.
[195] S.K. Upadhyay, M.C. Agrawal, Monatsh. Chem. 110 (1979) 413.
[196] B. Singh, J.P. Singh, Natl. Acad. Sci. Lett. (India) 5 (1982) 323.
[197] B. Singh, A.K. Singh, J. Indian Chem. Soc. 60 (1983) 704.
[198] R.S. Shuka, R.K. Dwivedi, K.C. Gupta, K. Behari, Natl. Acad. Sci. Lett. (India) 5 (1982) 297.
[199] R.S. Shuka, R.K. Dwivedi, K.C. Gupta, K. Behari, Natl. Acad. Sci. Lett. (India) 5 (1982) 323.
[200] R.C. Smith, V.D. Reed, T.R. Webb, J. Inorg. Biochem. 52 (1993) 173.
[201] G. Capozzi, G. Modena, The chemistry of the thiol group, in: S. Patai (Ed.), The Chemistry of Functional Groups, Wiley, New York, 1974.
[202] S. Sankarapapavinasam, M.F. Ahmed, J. Appl. Electrochem. 22 (1992) 390.
[203] G. Stochel, P. Martinez, R. van Eldik, J. Inorg. Biochem. 54 (1994) 131.
[204] A.Y. Kassim, Inorg. Chim. Acta 27 (1978) 243.
[205] B. Pispisa, G. Paradossi, A. Palleschi, A. Desideri, J. Phys. Chem. 92 (1988) 3422.
[206] S.P. Mezyk, J. Phys. Chem. 99 (1995) 13970.
[207] C. Srinivasan, P. Subramanian, J. Chem. Soc. Perkin Trans. II (1990) 1061.
[208] M.E. Niyazymbetov, L.D. Konyshkin, Z.I. Niyazymbetov, V.P. Litvinov, V.A. Petrosyan, Synth. Commun. 23 (1995) 1659.
[209] J.S. Choi, N.M. Yoon, J. Org. Chem. 60 (1995) 3266.
[210] K.G. Kalla, K.K. Mishra, Phosphorus Sulphur 35 (1988) 183.
[211] G. Dasgupta, M.K. Mahanti, Pol. J. Chem. 60 (1986) 583.
[212] G.J. Bridgart, M.W. Fuller, I.R. Wilson, J. Chem. Soc. Dalton Trans. (1973) 1274.
[213] S.C. Askew, D.J. Barnett, J. McAninly, D.L.H. Williams, J. Chem. Soc. Perkin Trans. II (1995) 741.
[214] G. Scrivens, B.C. Gilbert, T.C.P. Lee, J. Chem. Soc. Perkin Trans. II (1995) 955.
[215] P.K. Lim, Y. Zhong, J. Am. Chem. Soc. 111 (1989) 8398.
[216] Y. Zhong, P.K. Lim, J. Am. Chem. Soc. 111 (1989) 8404.
[217] R.C. Kapoor, P.C. Potter, O.P. Kachhwaha, B.P. Sinha, Indian J. Chem. 20 (1981) 89.
[218] T. Kamidate, T. Kinkou, H. Watanabe, J. Biol. Chem. 11 (1996) 123.
[219] A.E. Martell, R.M. Smith, Critical Stability Constants, vol. 6, Plenum Press, New York, 1989, p. 20, 181.
[220] P.L. Domingo, J.M. Leal, unpublished results.
[221] J.M. Leal, P.L. Domingo, J. Chem. Soc. Perkin Trans. II (1990) 407.
[222] S.C. Hiremath, S.A. Chimatadar, J.R. Raju, Transit. Metal Chem. 19 (1994) 636.
[223] W.G. Nigh, Oxidation by cupric ions, in: W.S. Trahanovsky (Ed.), Oxidations in Organic Chemistry, vol. 5B, Academic Press, New York, 1973, p. 84, 85.
[224] R.C. Smith, V.D. Reed, V.E. Hill, Phosphorus Sulphur 90 (1994) 147.
[225] S.P. Ghosh, S.K. Saha, R.N. Bose, J.W. Reed, M.C. Ghosh, E.S. Gould, Inorg. Chem. 32 (1993) 2261.
[226] S.K. Ghosh, S.K. Saha, M.C. Ghosh, R.N. Bose, J.W. Reed, E.S. Gould, Inorg. Chem. 31 (1992) 3358.
[227] R.H. Simoyi, I.R. Epstein, K. Kustin, J. Phys. Chem. 98 (1994) 551.
[228] A. McAuley, R. Shanker, J. Chem. Soc. Dalton Trans. (1973) 2321.

[229] H.N. Po, E. Harutynn, K. Yongjoo, T.E. Byrd, Inorg. Chem. 18 (1979) 197.
[230] M.D. Lilani, G.K. Sharma, R. Shanker, Indian J. Chem. 25A (1986) 370.
[231] M.C. Agrawal, S.P. Mushran, J. Phys. Chem. 72 (1968) 1497.
[232] A.K. Bhattacharjee, M.K. Mahanti, Int. J. Chem. Kinet. 14 (1982) 1113.
[233] A.K. Bhattacharjee, M.K. Mahanti, B. Soc. Chim. Fr. 1 (1983) 270.
[234] A.K. Bhattacharjee, M.K. Mahanti, B. Kor. Chem. Soc. 4 (1983) 120.
[235] A.K. Bhattacharjee, M.K. Mahanti, Gazz. Chim. Ital. 113 (1983) 1.
[236] A.K. Bhattacharjee, M.K. Mahanti, Indian J. Chem. 22B (1983) 74.
[237] P.S. Radhakrishnamurti, S.N. Mahapatro, Indian J. Chem. 13 (1975) 1029.
[238] P.S. Radhakrishnamurti, S.N. Mahapatro, Indian J. Chem. 14A (1976) 613.
[239] G. Merga, H.P. Schuchmann, B.S.M. Rao, C. von Sonntag, J. Chem. Soc. Perkin Trans. II (1996) 551.
[240] G.V. Buxton, J.R. Langan, J.R. Lindsay, J. Phys. Chem. 90 (1986) 6309.
[241] K.A. Connors, Chemical Kinetics. The Study of Reactions in Solution, VCH, Weinheim, 1990, ch. 8.
[242] J.S. Mayell, Proc. Res. and Dev. 7 (1968) 129.
[243] S. Ege, Organic Chemistry, D.C. Head and Co., Lexington, 1994, ch. 8.
[244] S.C. Lee, R.H. Holm, J. Am. Chem. Soc. 115 (1993) 11789.
[245] J.R. Winkler, H.B. Gray, Chem. Rev. 92 (1992) 369.
[246] D.R. Casimiro, J.H. Richards, J.R. Winkler, H.B. Gray, J. Phys. Chem. 97 (1993) 13073.
[247] A.G. Lappin, M.G. Segal, D.C. Weatherburn, R.A. Henderson, A.G. Sykes, J. Am. Chem. Soc. 101 (1979) 2302.
[248] F.A. Armstrong, R.A. Henderson, A.G. Sykes, J. Am. Chem. Soc. 102 (1980) 65454.
[249] S.K. Chapman, I. Sanemasa, A.D. Watson, A.G. Sykes, J. Chem. Soc. Dalton Trans. (1983) 1949.
[250] R.J. Kurland, M.E. Winkler, J. Biochem. Biophys. Methods 4 (1981) 215.
[251] D. Beoku-Betts, A.G. Sykes, Inorg. Chem. 24 (1985) 1142.
[252] J. Butler, S.K. Chapman, D.M. Davies, A.G. Sykes, S.H. Speck, N. Osheroff, E. Margoliash, J. Biol. Chem. 258 (1983) 6400.
[253] F.E. Wood, C.B. Post, M.A. Cusanovich, Arch. Biochem. Biophys. 184 (1977) 586.
[254] E. Cheung, A.M. English, Can. J. Chem. 73 (1995) 1181.
[255] G. Cheddar, T.E. Meyer, M.A. Cusanovich, C.D. Stout, G. Tollin, Biochemistry 28 (1989) 6318.
[256] P.L. Drake, R.T. Hartshorn, J. McGinnis, A.G. Sykes, Inorg. Chem. 28 (1989) 1361.
[257] L.M. Peerey, N.M. Kostic, Biochemistry 28 (1989) 1861.
[258] P.R. Rich, P. Heathcote, D.A. Moss, Biochim. Biophys. Acta 892 (1987) 138.
[259] S. Steenken, Chem. Rev. 89 (1989) 503.
[260] S. Gordon, E.J. Hart, M.S. Matheson, J. Rabani, J.K. Thomas, J. Am. Chem. Soc. 85 (1963) 1375.
[261] G. Czapski, J. Rabani, G. Stein, Trans. Faraday Soc. 58 (1962) 2160.
[262] R.B. Draper, M.A. Fox, E. Pellizzetti, N. Serpone, J. Phys. Chem. 93 (1989) 1938.
[263] T. Ozawa, K. Jitsukawa, H. Masuda, H. Einaga, Ber. Bunsenges. Phys. Chem. 98 (1994) 66.
[264] T. Ozawa, K. Jitsukawa, H. Einaga, Ber. Bunsenges. Phys. Chem. 98 (1994) 59.
[265] D.G. Lambert, M.M. Jones, J. Am. Chem. Soc. 88 (1966) 4615.
[266] M.D. Newton, Chem. Rev. 91 (1991) 767.