# Radical-induced Hydrogen Exchange in the Presence of Reducing Transition Metal Ions

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Fenton reagents (aqueous solutions of hydrogen peroxide and reducing metal ions) containing tracer tritium in the solvent are shown to effect a small amount of tritium exchange with a dissolved organic solute (dioxan or diethyl ether). The effectiveness of the metal ions (which are in stoicheiometric excess over hydrogen peroxide) follows the order $Cr^{II} > V^{II} > Ti^{III} > Fe^{II}$ and is thought to reflect their reducing power towards the organic radicals (which are formed by hydrogen abstraction by hydroxyl radicals from the substrates). The reduction of radicals by $Cr^{II}$ is known to proceed *via* the formation of isolable organochromium(III) complexes, and the trends in yields and rate constants suggest that the same sequence of steps may be involved with the other ions. The observation of exchange using the complex $Cr(bipy)_3{}^{2+}$ in place of an ordinary metal ion of a Fenton reagent points to the additional possibility of outer-sphere reduction of radicals to carbanions as unstable intermediates. The low yield of the hydrogen isotope exchange in all cases is attributed to the combined operation of (i) a substantial kinetic isotope effect and (ii) reactions of radicals competing with their reduction.

DURING the radiolysis of aqueous solutions of saturated aliphatic compounds, RH, organic radicals are formed *via* hydrogen abstraction, and subsequent reduction, either by the solvated electron or by low-valent metal ions, such as $Zn^+$, yields the corresponding carbanions.[1] Proton transfer from solvent water to the carbanion results in a net hydrogen-exchange reaction (Scheme 1).

$$H_2O \rightsquigarrow \cdot OH, \cdot H, e^-_{aq}$$

$$RH \xrightarrow{\cdot OH/\cdot H} R\cdot$$

$$R\cdot \xrightarrow{e^-_{aq}/M^+} R^- \xrightarrow{H^+/+T^+} RH/RT$$

SCHEME 1

The reduction of organic radicals in aqueous solutions by $Ti^{3+}$,[2,3] $Fe^{2+}$,[3] and $Cr^{2+}$ [4] has been reported in corresponding chemical systems using analogues of Fenton's reagent (Scheme 2) (generally referred to in the following as Fenton reagents). The formation of deuteriated products when related reactions are carried out in the presence of $D_2O$ has been interpreted as evidence for the reduction of radicals.[4,5] However, to date, no investigations into hydrogen-exchange reactions by the radical-reduction route starting with Fenton reagents have been made. We now report on such hydrogen exchange between saturated ethers and solvent water (in the presence of tritiated water at tracer level) with Fenton reagents based on reducing transition metal ions.

$$M^{n+} + H_2O_2 \longrightarrow M^{(n+1)+} + \cdot OH + OH^-$$

$$RH + \cdot OH \longrightarrow R\cdot + H_2O$$

$$R\cdot + M^{n+} + H^+_{aq} \longrightarrow RH + M^{(n+1)+}$$

SCHEME 2

## EXPERIMENTAL

Stock solutions of tritiated water (Radiochemical Centre) of nominal activity 2 mCi $ml^{-1}$ were prepared by serial dilution, and the activity determined as previously.[1]

Solutions of titanium(III) were prepared by the dissolution of titanium metal (sponge; B.D.H.) in excess of either sulphuric acid or hydrochloric acid under nitrogen. They were standardised by potentiometric titration against potassium permanganate. Vanadium(II) solutions were prepared by zinc wool reduction of the vanadyl salt (B.D.H.) and solutions of chromium(II) perchlorate by dissolving electrolytic chromium (B.D.H.; activated by dipping in 5M-HCl) in excess of perchloric acid under nitrogen. Tris-(2,2′-bipyridyl)chromium(II) perchlorate was prepared by Holah and Fackler's method.[6] All other inorganic reagents were AnalaR grade (Fisons). To remove peroxides, 1,4-dioxan was either kept over iron(II) sulphate (15 g $dm^{-3}$) for two days, decanted, and refluxed under nitrogen (8—12 h) with concentrated HCl (14 $cm^3$ $dm^{-3}$) and water (100 $cm^3$ $dm^{-3}$) or treated with tin(II) chloride and then distilled. Dioxan was salted-out from the mixture by addition of pellets of potassium hydroxide (whilst keeping the solution cool), and distilled under nitrogen (b.p. 100—101 °C). The pure dioxan was stored in a dark bottle at 5 °C, and was found to be peroxide-free [absence of reaction with iron(II) sulphate] even after 1—2 months. Diethyl ether (B.D.H.; AnalaR) was peroxide-free ($KI$–$H_2SO_4$ reagent).

*General Procedure.*—Into a solution (20—50 $cm^3$) of transition metal ion (0.01—0.3M) and ether (0.5—1.0M) in tritiated water ($\leqslant 2$ mCi $cm^{-3}$) under nitrogen, 1—2 $cm^3$ of an aqueous solution of hydrogen peroxide (to produce an initial stoicheiometric concentration of $10^{-3}$—$10^{-2}$M) was injected. After reaction, carrier ether (10—20 $cm^3$) was added. The ether layer was separated off and dried over sodium hydroxide. In the case of dioxan, sodium hydroxide or anhydrous potassium carbonate was added to salt out the substrate. The ether layer was then repeatedly washed with saturated potassium carbonate solution (20 × 2—3 $cm^3$ portions, to remove hydroxylic tritium), and dried (NaOH and $CaH_2$, or $K_2CO_3$). The tritiated ether was purified by preparative g.l.c. and the activity of the sample determined as previously.[1] To minimise evaporation of diethyl ether during work-up, all solutions were at 0 °C.

The degree of hydrogen exchange was calculated as:

$$\%\text{H exchange} = 100\left(\frac{\text{no. of moles of RT}}{\text{no. of moles of } H_2O_2}\right)\Bigg/\left(\frac{\text{no. of hydroxylic atoms of T in solvent}}{\text{no. of hydroxylic H atoms in solvent}}\right)$$

From the stoicheiometry in Scheme 2, in the absence of side reactions and provided hydrogen peroxide is present in stoicheiometric deficit (compared with metal ion), the number of moles of RH taking part in the hydrogen exchange reaction is equal to the number of moles of $H_2O_2$ added to the reaction mixture.

A solution of $(H_2O)_5CrCH(CH_3)OC_2H_5^{2+}$ was prepared by addition of $H_2O_2$ (1 mmol, corresponding to an initial concentration of 0.02M) to a solution of $Cr^{2+}$ (0.1M) and diethyl ether (0.5M) followed by ion-exchange chromatography on a column of Dowex 50w-X8 resin (15 × 1 cm). The column was washed with 0.1M-$HClO_4$, and the complex was then eluted with 0.1M-$HClO_4$–0.9M-$LiClO_4$. The concentration of the complex was determined spectrophotometrically (at 390 nm, $\varepsilon_{max.} = 440 \pm 40$ mol$^{-1}$ dm$^3$ cm$^{-1}$, compared with the literature value [7] $\varepsilon_{max.} = 490 \pm 50$ mol$^{-1}$ dm$^3$ cm$^{-1}$).

Experiments were performed under nitrogen to minimize scavenging of radicals by oxygen, and to prevent reaction of oxygen with reactants.

## RESULTS AND DISCUSSION

Under the conditions employed in these studies, *i.e.* $[RH] > [M^{n+}] > [H_2O_2]_0$, scavenging of hydroxyl radicals by organic substrate is essentially quantitative.[3,8] The degree of hydrogen exchange will therefore depend on the relative rates for the reaction of the radical with the reducing metal ion compared with rates for competing radical reactions, such as dimerization or oxidation. However, except for $Cr^{2+}$, which has been extensively studied, there are only few data relating to the reduction of radicals by transition metal ions.

Chromium(II) reacts rapidly with organic radicals [7] in an inner-sphere reaction to form penta-aquaorganochromium(III) ions, which decompose slowly in acidic aqueous solution [reactions (1)].[4,7] (Some relevant rate

$$(H_2O)_6Cr^{2+} + \cdot R \xrightarrow[-H_2O]{k_f} (H_2O)_5Cr^{III}R^{2+} \xrightarrow[+H_3O^+]{k_H} (H_2O)_6Cr^{3+} + RH \quad (1)$$

constants relating to the organic radicals studied by us are given in Table 1.) Under the experimental conditions used (see Table 2) in the reactions of 1,4-dioxan and diethyl ether with the Fenton reagent $Cr^{2+}$–$H_2O_2$, it might therefore be expected that the formation and subsequent reduction of the organic radicals would be a quantitative process. However, the 'yield' of the hydrogen exchange in these reactions is small (3—4%, Table 2). This suggests not only that there may be a large isotope effect in the protonolysis of the organochromium complex ions (an aspect examined in detail elsewhere) [9] but also opens the question whether there are other reactions which have not so far been considered.

TABLE 1

Rate constants in the formation and protonolysis of $(H_2O)_5CrR^{2+}$ ions

| R | $k_f$/l mol$^{-1}$ s$^{-1}$ | $k_H$/l mol$^{-1}$ s$^{-1}$ |
|---|---|---|
| $-CH(CH_3)OC_2H_5$ [a] | $3.4 \times 10^7$ [b] | $3.8 \times 10^{-5}$ [c]<br>$3.2 \times 10^{-5}$ [d] |
| $-\overline{CHOC_2H_4OCH_2}$ [e] | $1.0 \times 10^8$ [b] | $4.8 \times 10^{-1}$ [b] |

[a] The principal radical obtained in the reaction of diethyl ether and hydroxyl radical is $CH_3\dot{C}HOC_2H_5$ (W. T. Dixon, R. O. C. Norman, and A. L. Buley, *J. Chem. Soc.*, 1964, 3625). [b] H. Cohen and D. Meyerstein, *Inorg. Chem.*, 1974, **13**, 2434. [c] W. Schmidt, J. H. Swinehart, and H. Taube, *J. Am. Chem. Soc.*, 1971, **93**, 1117. [d] Ref. 9. [e] The radical derived from 1,4-dioxan.

Results in Table 3 show that three products other than dioxan are formed in the system $Cr^{2+}$–$H_2O_2$–dioxan (Table 3), and this confirms the latter possibility. However, the yield of these products is small (*ca.* 15%, Table 3), and is expected to have a correspondingly small effect on the observed degree of hydrogen exchange. The main reason for the low yield of the exchange reactions (4—5%, after allowing for the formation of other products) is a large isotope effect in the protonolysis of organochromium(III) ions. In the system $Cr^{2+}$–$H_2O_2$–diethyl ether, the degree of hydrogen exchange (3.4 ± 0.3%; Table 2), is significantly lower than that found in the protonolysis of $CrCH(CH_3)OC_2H_5^{2+}$ (Table 2). The result suggests that the formation and trapping of the radical derived from diethyl ether does not occur quite quantitatively under the experimental conditions (including concentrations) employed.

In a photochemical study [10] a ring-opening reaction of the dioxanyl radical has been shown to yield isomeric bidioxanyls, ethoxyacetaldehyde, and acetaldehyde. This report [10] suggests that these compounds may be the three by-products indicated by g.l.c. in the reactions of the $Cr^{2+}$–$H_2O_2$–dioxan system (Table 3) and that they are formed by an analogous mechanism.[10] At higher concentrations of reagents (and hence of radicals), the product of longest retention time (C) is formed in increased yield. It therefore probably results from a

TABLE 2

The degree of hydrogen exchange in the reaction system $M^{n+}$ –$H_2O_2$–RH

| | | | | % Hydrogen exchange | |
|---|---|---|---|---|---|
| $M^{n+}$ | [RH] [e]/M | $[M^{n+}]$/M | $[H_2O_2]_0$ [f]/M | RH = Diethyl ether | RH = 1,4-Dioxan |
| $Fe^{2+}$ [a] | 0.7 | 0.20 | 0.10 | | 0.02 |
| $Ti^{III}$ [b] | 1.5 | 0.09 | 0.036 | 0.2 | 0.14 ± 0.01 |
| $Ti^{III}$ [a] | 1.0 | 0.3 | 0.06 | | 0.20 ± 0.02 |
| $V^{2+}$ [a] | 1.0 | 0.26 | 0.074 | | 0.60 ± 0.05 |
| $Cr(bpy)_3^{2+}$ [c] | 0.5 | 0.01 | 0.001 | 2 | 1 |
| $Cr^{2+}$ [c] | 0.5 | 0.05 | 0.01 | 3.4 ± 0.3<br>(5.0 ± 0.7) [d] | 3.7 ± 0.3 |

[a] As sulphate. [b] As chloride. [c] As perchlorate. [d] Obtained with purified $CrCH(CH_3)OC_2H_5^{2+}$. [e] RH is in excess over $M^{n+}$ to ensure efficient scavenging of ·OH by RH rather than by $M^{n+}$. When $[RH]/[M^{n+}]$ is reduced, the degree of hydrogen exchange is lower. [f] $M^{n+}$ is in stoicheiometric excess over $H_2O_2$ to prevent reactions of organic radicals with $H_2O_2$ rather than with $M^{n+}$.

TABLE 3

Organic products [f] in the reaction $Cr^{2+}$–$H_2O_2$–dioxan

| | A [e] | B | C |
|---|---|---|---|
| Relative [a] retention times | 0.7 | 1.2 | 4.4 |
| Yield (%),[b] Expt. 1 [c] | 2 | 3 | 10 |
| Yield (%),[b] Expt. 2 [d] | | 15 | |

Relative to propan-2-ol Carbowax High Polymer column at 150 °C (retention time 20 s). [b] Calculated from peak areas using propan-2-ol as internal standard. [c] [dioxan] 0.53M; [$Cr^{2+}$] 0.095M; $[H_2O_2]_0$ 0.0375M. [d] [dioxan] 0.54M; [$Cr^{2+}$] 0.057M; $[H_2O_2]_0$ 0.010M. [e] Same retention time as acetaldehyde from authentic sample. [f] No detectable impurities were present in solvent dioxan.

radical-radical reaction (formation of diastereoisomeric bidioxanyls).

The reactions of free radicals with reducing transition metal ions have been suggested to proceed *via* a carbon–metal bonded species, which may be six- or seven-co-ordinate. Thus the reduction of hydrogen atoms by $Fe^{2+}$ involves the formation of an iron(III) intermediate,[11] which must be seven-co-ordinate [12] since the rate of formation of the intermediate is considerably faster than the rate of substitution into the inner-co-ordination sphere of iron(II). It is expected that the analogous reduction of organic radicals by $Fe^{2+}$ will proceed by the same mechanism.[11,12] Metal–carbon bonded species have also been detected in the reactions of organic radicals with low-valent metal ions.[13,14] In aqueous solution these intermediates decompose *via* reaction (2) with aqueous hydrogen ion.

$$M^{n+} + \cdot R \longrightarrow M\text{-}R^{n+} \xrightarrow{H^+} M^{(n+1)+} + RH \quad (2)$$

The degree of hydrogen exchange with Fenton reagents containing various metal ions is in the order $Cr^{2+} > Cr(bipy)_3^{2+} > V^{2+} > Ti^{3+} > Fe^{2+}$ (Table 2) which is also the order of reducing power of the ions. This order is attributed to the reduced efficiency of the reduction of the organic radicals by the various metal ions in competition with radical reactions such as dimerization or oxidation. This is corroborated by reported rate constants in the reactions of organic radicals with metal ions. In the case of chromium(II) these reactions lead to the formation or organochromium(II) species ($k_f$ in the range $3 \times 10^7$—$4 \times 10^8$ dm$^3$ mol$^{-1}$ s$^{-1}$). With $Ti^{III}$ and for $Fe^{II}$ values of *ca.* $10^7$ and *ca.* $5 \times 10^5$ dm$^3$ mol$^{-1}$ s$^{-1}$, respectively, are reported [3] for the reactions observed as disappearance of α-acylmethyl radicals from aqueous solution. The same order ($Cr^{2+} > Ti^{3+} > Fe^{2+}$) has been observed in the reaction of the methyl radical with metal ions.[5]

The reduction of organic radicals by vanadium(II) has been postulated,[15] but to date no kinetic information has been reported. However, in the reaction of vanadium(II) with the methyl radical methane is produced in high yield (≥99%), with only traces of ethane (≤2%),[16] suggesting that radical reduction is rapid in order to compete with dimerisation.

The results obtained for the reduction of radicals by $V^{2+}$, $T_i^{3+}$, and $Fe^{2+}$ in the systems are thus seen to be consistent with the $Cr^{2+}$ system. This suggests that the reduction of organic radicals by $V^{2+}$, $Ti^{3+}$, and $Fe^{2+}$ occurs *via* the formation of unstable organometallic intermediates which decompose by reaction with a proton donor, as in the analogous reduction of radicals by $Cr^{2+}$.[13] On the other hand, $Cr(bipy)_3^{2+}$ is an outer-sphere reducing agent,[17] which might be expected to react with radicals *via* the outer-sphere mechanism to form the corresponding carbanions [reaction (3)]. However, the result

$$Cr(bipy)_3^{2+} + \cdot R \longrightarrow Cr(bipy)_3^{3+} + {}^{-}R \quad (3)$$

obtained with $Cr(bipy)_3^{2+}$ is somewhat uncertain owing to the low solubility of $Cr(bipy)_3^{2+}$ in aqueous solution,[18] and hence no mechanistic conclusion can be drawn from the values reported in Table 2.

Ethylenediaminetetra-acetic acid has been used in Fenton reagents with $Ti^{III}$ in order to stabilize $Ti^{III}$ at high pH (>2.5) and to permit the study of these reactions of organic radicals in weakly acidic solutions.[3] In the present study we have used complex formation between $Ti^{III}$ and methyl-lactic acid or with 5-sulphosalicylic acid to allow weakly acidic media to be used in the system $Ti^{III}$–$H_2O_2$–RH. However, as the concentration of ligand is increased, the degree of hydrogen exchange decreases, and this is attributed either to scavenging of hydroxyl radicals by the organic ligands, or by the effect of complex formation on the reduction potential of the metal ion.

The effect of the nature of the anion in all these systems is expected to be small. Thus, although chloride ions react with hydroxyl radicals to form chlorine atoms, these behave similarly to •OH, and scavenging of Cl• by substrate to form the organic radical is efficient.[19] Formation of metal–sulphate complexes in the presence of $SO_4^{2-}$ may slightly affect the rate constants in the reaction of organic radicals with metal ions, and may modify the decomposition of organometallic intermediates formed in these reactions.[20]

The formation of tritiated organic products in the reactions of reducing transition metal ions with hydrogen peroxide and organic substrate thus confirms the conclusions reached in the earlier radiolytic studies,[1] *viz.* that hydrogen exchange occurs *via* formation of organic radicals and their subsequent reduction. The calculated degree of hydrogen exchange in these systems is very small. This is attributed to the presence of a large primary isotope effect [9] which is suggested to arise in the protonolysis of an organometallic intermediate formed in the reaction of a transition metal ion with an organic radical, and to the competition between radical reduction and other reactions of the organic radicals.

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