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The oxidizing nature of the hydroxyl Radical. A comparison with the ferryl ion (FeO_2^+)

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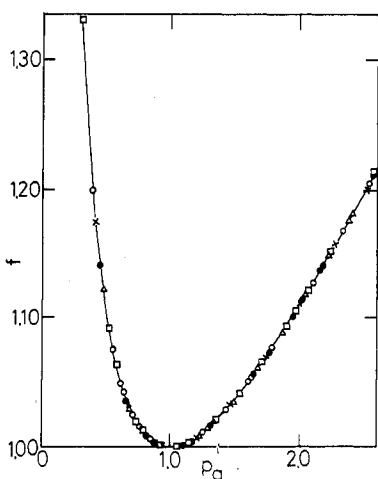


Figure 7. Variation of f with p_g for the prolate and oblate spheroids of various p , p_m , and m values.

the p is. The difference of f from 1.0 is less than 2% for $m < 1.30$, and less than 5% from $m < 1.50$ for isotropic particles. For the anisotropic particles of $p_m > 1$ the f is also larger, the larger the m is and the larger the p is, and the difference of f from 1.0 at $p_m = 1.6$ reaches to about 19% for $m = 1.50$ and runs into about 10% for $m = 1.20$. On the contrary, for the anisotropic particles of $p_m < 1$ the difference of f from 1.0 is smaller, the larger the m is and the larger the p is, because the form anisotropy of the prolate spheroid ($p > 1$) partially compensates the intrinsic anisotropy of $p_m < 1$. The difference of f from 1.0 at $p_m = 0.4$ reaches 14% for $m = 1.10$, reaches 10% for $m = 1.20$, and decreases to 2% for $m = 1.50$.

Figure 7 shows the relationship between the difference of f from 1.0 and the p_g value for the prolate and oblate spheroids of various axial ratios p , together with the limiting conditions for infinite

tesimally thin disk and rod, and of various m values. All data are fitted on one curve irrespective of the p and m values, whose curve is expressed by eq 23 as shown with the solid line in Figure 7. This means that the f value depends unequivocally on the p_g values.

Variation of Refractive Index Increment. The variation of the refractive index increment dn/dc (mL/g), with the axial ratio p of the prolate spheroids is calculated by eq 20 and 26 and the results are shown in Figures 4 and 5 by taking the quantity dn/dc on the ordinate at the right-hand side. The numerical values are obtained by assuming that the medium is water, whose refractive index is 1.340, and the density of the spheroid is 1.35, a value based on the fact that the density of normal protein materials is generally believed to be about 1.35.¹⁷ An appreciable dependence of dn/dc on p is observed even in the case of isotropic particles ($p_m = 1$). The value of the dn/dc at $p = 1$ increases with increasing the degree of the anisotropy. At any given m , the case of $m = 1.20$ being shown in Figure 4 and 5 as an example, the dn/dc increases steeply at first when a particle is deformed from a sphere to a prolate spheroid, and the increase is larger, the larger the p_m is, but the dn/dc increases scarcely when p has exceeded 10 for small p_m .

As shown in Figure 5, the dn/dc associated with a given p is single valued against p_m , if we know separately whether the optical anisotropy parameter p_m is larger or smaller than 1.0. As shown by eq 20, the dn/dc also depends on the density of the spheroids and the refractive index of the solvent. In general, the determination of the density of the compact spheroids is easy. Therefore, combined with the light scattering measurements and in conjunction with a knowledge of p which may be obtained by electron microscopy, the degree of anisotropy p_m is obtained with the known quantity dn/dc and the refractive index of the solvent n_0 .

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The Oxidizing Nature of the Hydroxyl Radical. A Comparison with the Ferryl Ion (FeO^{2+})

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For the standard reduction potential of the hydroxyl radical/hydroxide couple, two values are found in the literature, 2.0 and 1.4 V. Thermochemical data yield 1.98 V for $E^\circ(\cdot\text{OH}_g/\text{OH}^-_{\text{aq}})$. Hydration of the hydroxyl radical by -5 kcal/mol changes this value to 1.77 V for $E^\circ(\cdot\text{OH}_{\text{aq}}/\text{OH}^-_{\text{aq}})$, which is still considerably higher than 1.4 V. It is concluded that the latter value is incorrect. The following thermodynamic quantities are derived from, or consistent with, the new E° value: $\Delta G^\circ_f(\cdot\text{OH}_{\text{aq}}) = +3.2$ kcal/mol; $E^\circ(\cdot\text{OH}_{\text{aq}}/\text{H}_2\text{O}) = 2.59$ V at pH 0; $\Delta G^\circ_f(\text{O}^-_{\text{aq}}) = 19.5$ kcal/mol, $E^\circ(\text{O}^-_{\text{aq}}/\text{OH}^-_{\text{aq}}) = 1.64$ V at pH 14; $\Delta G^\circ_f(\text{O}_3^-_{\text{aq}}) = 11.7$ kcal/mol; $E^\circ(\text{O}_3^-_{\text{aq}}/\text{O}_3^-_{\text{aq}}) = 1.19$ V, and $E^\circ(\text{H}_2\text{O}_{2\text{aq}}/\cdot\text{OH}_{\text{aq}}; \text{H}_2\text{O}) = 0.46$ V at pH 7. The reduction of hydrogen peroxide by ferrous complexes might yield the ferryl ion (FeO^{2+} -cholate). If the chelating agent is a porphyrin (compound II) the reduction potential of the couple ferryl/ferriporphyrin is estimated to be 0.9 V. For smaller chelating agents this potential is expected to be higher.

Introduction

Irradiation of aqueous solutions produces hydroxyl radicals as well as hydrated electrons and hydrogen atoms. From such experiments the hydroxyl radical is known to be a strongly oxidizing radical, reacting indiscriminately with proteins and other biomolecules at rates which are close to diffusion controlled.¹ In

biochemical systems and possibly in vivo it is thought to be formed through the one-electron reduction of hydrogen peroxide by metal ions and/or organic molecules.²⁻⁴ Others have expressed doubt at the formation of the hydroxyl radical in such systems since small molecules, known to react with the hydroxyl radical at certain

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rates, failed to protect. They invoke either the ferryl ion (FeO^{2+} -chelate) formed from the reaction of a ferrous chelate with hydrogen peroxide or the "crypto- $\cdot\text{OH}$ " radical, a rather undefined complex of an organic molecule with hydrogen peroxide.^{5,6} An attempt is made to distinguish these radicals on the basis of their oxidizing properties.

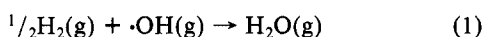
At low pH there is no doubt that the reduction of hydrogen peroxide by ferrous ions, the Fenton reaction, yields the hydroxyl radical.⁷ For the reason given above, we would like to entertain the possibility that at neutral pH an iron complex with a much lower reduction potential than that of the couple $\text{Fe}^{3+}_{\text{aq}}/\text{Fe}^{2+}_{\text{aq}}$ yields the ferryl ion. This species would be analogous to the compound II found in catalase and peroxidases.

A survey of the literature shows that there is considerable uncertainty about the value of the reduction potential of the hydroxyl/hydroxide couple, in spite of its importance in radiation chemistry. While various sources⁸⁻¹¹ quote values around 2.0 V, the "Handbook of Chemistry and Physics"¹² gives 1.4 V. The latter value probably finds its origin in two papers published in 1965.^{13,14} No thermodynamic data appear to exist for the ferryl ion, while for the related couple ferric/compound II in horse radish peroxidases A₂ and C and myoglobin values of about 0.9 V were found.^{15,16} No data are available for the crypto- $\cdot\text{OH}$ radical.

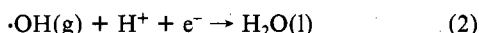
Some of these results have been presented earlier.¹⁷

Thermodynamics

The reaction



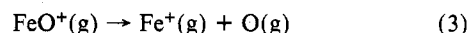
has a Gibbs energy change of -62.8 kcal/mol or -263 kJ/mol.¹⁸ Solvation of the water to the liquid state changes ΔG by -2.05 kcal,¹⁸ and yields a standard reduction potential of 2.81 V for the half-reaction



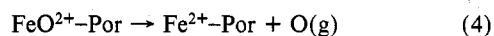
or 1.98 V for $E^\circ(\cdot\text{OH}_\text{g}/\text{OH}^-_\text{aq})$. For reactions of the hydroxyl radical in water, we need to correct E° for the Gibbs energy of hydration, which is unknown. Stein¹⁴ used a value of -6 kcal/mol, between that of HF, -5.6 kcal/mol,¹⁸ and that of H_2O_2 , -6.8 kcal/mol.¹⁸ Swartz¹⁹ employed a lower value of -3.7 kcal/mol as followed from comparison of Gibbs energies of hydration of ethanol, methanol, and water. George¹¹ assumed a low value of -1.2 kcal/mol, while Berdnikov and Bazhin¹⁰ calculated -2.0 kcal/mol. Pourbaix's value for $\Delta G_f(\cdot\text{OH}_\text{aq})$, 8.5 kcal/mol,²⁰ used by Henglein,²¹ would imply a small positive Gibbs energy of

hydration since $\Delta G_f(\cdot\text{OH}_\text{g}) = 8.2$ kcal/mol.¹⁸ Baxendale et al.²² intended to use the Gibbs hydration energy of water. However, the value of -2.1 kcal/mol corresponds to the transition $\text{g} \rightarrow 1$, not to $\text{g} \rightarrow 1\text{ m}$, which is -4.4 kcal. Since $\cdot\text{OH}$ is of comparable size and polarity as HF, a value of -5 kcal/mol seems reasonable. This value yields a Gibbs energy of formation of the hydroxyl radical in water of $+3.2$ kcal/mol, or $+13.4$ kJ/mol, and a value of 2.59 V for the couple $E^\circ(\cdot\text{OH}_\text{aq}/\text{H}_2\text{O}_\text{l})$ at pH 0, 2.18 V at pH 7 and 1.77 V for $E^\circ(\cdot\text{OH}_\text{aq}/\text{OH}^-_\text{aq})$. The pK of $\cdot\text{OH}$ is 11.9²³ which gives $E^\circ(\text{O}^-_\text{aq}/\text{OH}^-_\text{aq}) = 1.64$ V at pH 14. An estimated uncertainty in the Gibbs hydration energy of 1 kcal/mol leads to an error of 0.04 V in the reduction potentials. The value of pH 0 is not a standard reduction potential, since it refers to $[\text{OH}] = 1\text{ m}$.

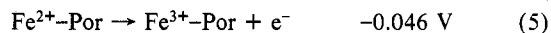
Turning to the ferryl ion, we first estimate the reduction potential of the couple compound II/ferric heme protein. Two assumptions can be made: first, that the effective charge of the Fe-O group is $+1\text{ e}$; second, that the solvation energies of FeO^{2+} - and Fe^{2+} -porphyrins can be neglected. These two energies are not expected to be very much different, and their contributions to the energetics of reaction 4 (see below) cancel. This assumption permits data from gas-phase studies to be used. As calculated from the following Gibbs energies of formation ($\text{FeO}(\text{g})$, 52 kcal/mol; $\text{Fe}(\text{g})$, 88 kcal/mol; and $\text{O}(\text{g})$, 55.4 kcal/mol) and ionization potentials (FeO , 8.7 eV and Fe , 7.7 eV),²⁴ reaction 3 has a ΔG° of $+69$ kcal or 289 kJ (equivalent to -3.00 V)



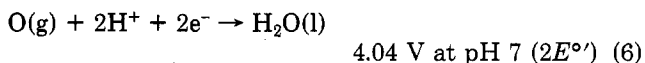
Thus



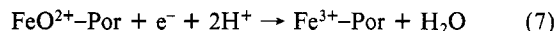
is assumed to have the same Gibbs energy change. Together with



and



we arrive at a value of 0.99 V at pH 7 for



The oxidation potential for reaction 5 is taken to be that of the myoglobin/metmyoglobin couple. The result, 0.99 V, agrees quite well with the experimental value of 0.9 V at pH 7 for the couple compound II/metmyoglobin.¹⁶

If we repeat the calculation for horse radish peroxidase A₂, which has a reduction potential E° (ferric/ferrous) at pH 7 of -190 mV,²⁵ we find a value of 1.23 V for reaction 7 while the experimental value is 0.88 V.¹⁵ The estimates obtained with our simple model appear to be of the right order of magnitude.

Discussion

The value of the reduction potential of the hydroxyl/hydroxide couple is higher than that presented by Stein¹⁴ and Landsberg and Heckner.¹³ These authors argue that $E^\circ(\cdot\text{OH}_\text{aq}/\text{OH}^-_\text{aq})$ should be close to that of $E^\circ(\text{Cl}_2/\text{Cl}^-)$. However, for the latter potential they take 1.36 V, which corresponds to $E^\circ(\text{Cl}_2/\text{Cl}^-)$,⁸ not $E^\circ(\text{Cl}_2/\text{Cl}^-)$. Furthermore, Stein's value of 1.25 V for $E^\circ(\cdot\text{OH}_\text{aq}/\text{OH}^-_\text{aq})$ has been criticized,¹⁰ since the difference with the standard reduction potential of 2.0 V cannot be accounted for by the solvation energy assumed for $\cdot\text{OH}$, -6 kcal. The value calculated here, 2.59 V for $E^\circ(\cdot\text{OH}_\text{aq}/\text{H}_2\text{O}_\text{l})$, is very close to the value of 2.55 V of the couple Cl_2/Cl^- .¹⁰ Another argument¹³ for a low value of 1.4 V for $E^\circ(\cdot\text{OH}_\text{aq}/\text{OH}^-_\text{aq})$ was based on the

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TABLE I: Gibbs Energies of Hydration of O^- , O_2^- , and O_3^- .^a

species	based on $\Delta G^\circ_f(\cdot OH)$	
	3.2 kcal/mol ^b	-6 kcal/mol ^c
O^-	-104.7	-114
O_2^-	-84.8 ^d	-84.8 ^d
O_3^-	-80.6	-90

^a Gibbs energies of hydration for O^- and O_3^- .²⁶ are calculated from thermodynamic data given in the text and from the electron affinity of O being 1.46 V.²⁸ The value for O_2^- is from ref 29. All values in kcal/mol. The hydration energies based on a Gibbs energy of formation of 3.2 kcal/mol for $\cdot OH$ decrease with increasing size of the ion O_x^- , as expected. ^b Corresponds to $E^\circ(\cdot OH_{aq}/OH^-_{aq}) = 1.77$ V. ^c Corresponds to $E^\circ(\cdot OH_{aq}/OH^-_{aq}) = 1.4$ V. ^d Independent of $\Delta G^\circ_f(\cdot OH)$.

observation that Ce^{4+} is able to oxidize $\cdot OH$. However, this reaction does not provide insight about $E^\circ(\cdot OH_{aq}/OH^-_{aq})$, but about $E^\circ(O_{aq}/\cdot OH_{aq})$. A third argument is based on the rate constant of the reaction of OH^- with MnO_4^- to form $\cdot OH$ and MnO_4^{2-} . Since $E^\circ(MnO_4^-/MnO_4^{2-})$ is known, and the backward reaction cannot be faster than diffusion controlled, an upper limit of 1.5 V was estimated.¹³ Considering that at pH 14 $\cdot OH$ is ionized and that the couple O^-/OH^- has a reduction potential of 1.64 V, we conclude that this estimate is in fair agreement with the value reported here. It is to be noted that under standard conditions, namely O^- in equilibrium with a P_{OH} of 1 atm at pH 14, the concentration of O^- is greater than 1 M. The value of 1.64 V refers to $[O^-] = [OH^-] = 1$ M and can therefore be compared with $E^\circ(MnO_4^-/MnO_4^{2-})$.

Adoption of $\Delta G^\circ_f(\cdot OH_{aq}) = 3.2$ kcal/mol leads to the following revised values for O^- and O_3^- :²⁶ $\Delta G^\circ_f(O^-_{aq}) = 19.5$ kcal/mol, $\Delta G^\circ_f(O_3^-_{aq}) = 11.7$ kcal/mol, $E^\circ(O_3^-/O_3^-_{aq}) = 1.19$ V, and $E^\circ(O_3^-_{aq}/O_2, H_2O_l) = 2.95$ V at pH 0. These new values do not affect the conclusions that ozone can be a strong one-electron oxidizing agent and a precursor of the hydroxyl radical.²⁶ The Gibbs energy change for the formation of the latter from the ozonide anion remains +1.1 kcal.

Corroboration for $E^\circ(\cdot OH_{aq}/H_2O_l) = 2.59$ V follows from the following considerations. (1) We note that the reduction potential of the ozone-ozonide couple is now in better agreement with $E^\circ(NO_2/NO_2^-)$ having the value 0.91 V, as discussed in ref 26. (2) One would expect Gibbs energies of hydration to increase when the size of the ion O_x^- becomes smaller.²⁷ This is the case for hydration energies based on the reduction potential of 1.77 V, but not when a value of 1.4 V is used (see Table I). (3) If the latter potential were correct and $E^\circ(O_3^-/O_3^-_{aq})$ were 1.6 V as calculated earlier,²⁶ O_3 should thermodynamically be able to oxidize the hydroxide ion, while the new values do not permit a reaction. Indeed, in a recent study on the decay of ozone in alkaline solutions, no evidence for the oxidation of OH^- by ozone could be found.³⁰ It is concluded that all available experimental evidence

agrees with a value of 1.77 V for $E^\circ(\cdot OH_{aq}/OH^-_{aq})$ while a value of 1.4 V seems less likely. The former value yields a Gibbs energy of hydration of -106 kcal/mol for OH^- , based on

$$\Delta G^\circ(\cdot OH_g + \frac{1}{2}H_{2g} \rightarrow OH^-_{aq} + H^+_{aq}) = EA + \Delta G^\circ_{aq} + \Delta G^\circ_f(H^+_{aq}) \quad (8)$$

in which the electron affinity of OH is 1.83 V²⁸ and the Gibbs energy of formation of H^+_{aq} is 102.5 kcal/mol.³¹

Likewise, the new value for $E^\circ(\cdot OH_{aq}/H_2O_l)$ has important consequences for the energetics of the one-electron reduction of hydrogen peroxide which produces the hydroxyl radical. Combination of the energetics of the two-electron reduction of hydrogen peroxide to water and the one-electron oxidation of water to the hydroxyl radical ($E^\circ_{oxidation} = -2.18$ V at pH 7) yields a reduction potential of 0.46 or 0.52 V at pH 7 for half-reaction 9, depending on whether one uses 1.32³² or 1.35 V⁹ for $E^\circ(H_2O_2/H_2O)$:



Previously a value of 0.8 V was reported for this reaction which was based on $E^\circ(\cdot OH_{aq}/OH^-_{aq}) = 1.4$ V.³³ A variety of metal ions, organic molecules, and radicals can be reductants of hydrogen peroxide. Complexes of the latter with those compounds which have one-electron reduction potentials close to 0.46 V such as hydroquinone, catechol, and *p*-aminophenol³⁴ might possibly be candidates for crypto- $\cdot OH$.

The estimates for the reduction potential of the couple compound II/ferric in myoglobin and horse radish peroxidase A₂ are much less accurate than that for the hydroxyl/water couple. The calculated reduction potentials are dependent on the net charges and ionization potentials of FeO and Fe. For instance had we calculated the energetics of reaction 3 for neutral FeO and Fe, we would have found that the potential of reaction 7 was close to 0 V. For iron complexes smaller than hemes the effective charge of the FeO group might well be more than +1 e. If one assumes a linear relationship between effective charge and reduction potential, the maximum value for $E^\circ(FeO^{2+}/Fe^{3+}\text{-chelate})$ is approximately 2 V. It would appear that the ferryl ion is less oxidizing than the hydroxyl radical.

Acknowledgment. W.H.K. thanks Dr. J. Butler, Dr. B. W. Griffin, and Professor A. Henglein for stimulating discussions. We thank Patricia Gagné for her help in the preparation of this paper.

Registry No. FeO^{2+} , 73133-33-2; $\cdot OH$, 3352-57-6; OH^- , 14280-30-9; O_3^- , 12596-80-4; O^- , 14337-01-0; H_2O_2 , 7722-84-1; O_3 , 10028-15-6; H_2O , 7732-18-5; peroxidase, 9003-99-0.

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