

# Redox Chemistry of Dioxygen Species

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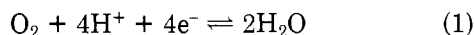
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*Vital elixir for life and technology from green plants beneath the sun.*

Dioxygen species are the various oxidation states and forms of diatomic oxygen, both as independent entities and as complexes in association with transition metal oxygen carriers. Included in this classification are the species  $O_2$ ,  $HO_2$ ,  $O_2^-$ ,  $H_2O_2$ ,  $HO_2^-$ , and  $O_2^{2-}$ . Because dioxygen is vital to many oxidation reactions and biological respiration processes, its oxidation-reduction chemistry has been the subject of numerous investigations. However, the mechanisms and energetics for the reduction of  $O_2$  and for the interconversion of the various dioxygen species have become known only during the last decade.

Although the highly exothermic free energy (316 kJ/mol at pH 7) for the four-electron reduction of  $O_2$  (eq 1, NHE = normal hydrogen electrode) makes the



$$E^{0'} = +0.82 \text{ V vs. NHE}$$

process attractive for energy transfer and storage,<sup>1</sup> mechanistic limitations preclude realization of this potential and energy for most redox reactions. Recent studies<sup>2,3</sup> indicate that the primary electron-transfer step for the reduction of  $O_2$  is a one-electron process which is followed by chemical disproportionation reactions to yield  $H_2O_2$  under acidic conditions (an overall two-electron process) and  $\cdot OH$  under basic conditions (an overall four-electron process). The effective potential for this reduction is  $-0.33 \text{ V vs. NHE}$  and is independent of pH. Hence, mechanistic restrictions on electron transfer to  $O_2$  cause the effective oxidizing energy of this species to be reduced by as much as 444 kJ/mol (relative to the thermodynamic value for eq 1).

The reverse reaction of eq 1 (generation of  $O_2$  from  $H_2O$ ) represents the net oxidation process for photosystem II in green plant photosynthesis.<sup>4,5</sup> Again the overall thermodynamics for the process is equivalent to that for eq 1, but the rate of the oxidation of  $H_2O$  to  $O_2$  is dependent upon the mechanistic pathway for the interconversion of various membrane-bound dioxygen species as well as for the formation of a diatomic oxygen species from two water molecules.<sup>6</sup> An understanding of the energetics and dynamics for the redox reactions of various dioxygen species is important

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to the development of a realistic model for photosystem II.

Besides its involvement in water formation and decomposition, dioxygen is the principal oxidant in most combustion processes. One major process is its reaction with hydrocarbons, which proceeds by a radical mechanism.<sup>7-11</sup> During the oxidation of normal paraffins,<sup>12</sup> a radical is formed by removal of a hydrogen atom from the paraffin. The radical in turn combines with another  $O_2$  molecule to give a radical peroxide chain as one mechanism of combustion (eq 2). Evi-



dence for the presence of alkyl peroxides is well established,<sup>13,14</sup> such peroxides undergo dehydration to aldehydes. An explosive decomposition also may occur through fission of the O-O bond to form  $\cdot OH$  and an alkoxy radical ( $RCH_2O \cdot$ ). Such radicals are known to be unstable.<sup>15</sup> These reactions all involve the reduction of  $O_2$  to either the  $-1$  or  $-2$  oxidation states as well as its incorporation in the oxidized products.

Beyond its biological origin via photosystem II of green plant photosynthesis, molecular oxygen is vital to a wide variety of biochemical reactions,<sup>16,17</sup> such as respiration, enzymatic redox processes, and enzymatic oxygenations. The studies of respiration have been concerned primarily with the structure and function of the active site in hemoglobin,<sup>18-21</sup> hemerythrin,<sup>22-27</sup> and

- (1) W. M. Latimer, "Oxidation Potentials", 2nd ed., Prentice-Hall, New York, 1952, pp 38-50.
- (2) D. T. Sawyer and E. T. Seo, *Inorg. Chem.*, **16**, 499 (1977).
- (3) J. L. Roberts, Jr., M. M. Morrison, and D. T. Sawyer, *J. Am. Chem. Soc.*, **100**, 329 (1978).
- (4) S. Ruben, M. Randall, M. Kamen, and J. L. Hyde, *J. Am. Chem. Soc.*, **63**, 877 (1941).
- (5) R. L. Health, *Int. Rev. Cytol.*, **34**, 49 (1973).
- (6) D. T. Sawyer, M. E. Bodini, L. A. Willis, T. L. Riechel, and K. D. Magers, *Adv. Chem. Ser.*, **No. 162**, 330 (1977).
- (7) A. D. Walsh, *Trans. Faraday Soc.*, **42**, 269 (1946).
- (8) A. D. Walsh, *Trans. Faraday Soc.*, **43**, 297 (1947).
- (9) A. D. Walsh, *Trans. Faraday Soc.*, **43**, 305 (1947).
- (10) R. A. Strehlow, "Fundamentals of Combustion", International Textbook Company, Scranton, PA, 1968.
- (11) V. N. Kondratiev and V. V. Azatyan, "HO<sub>2</sub> Radicals in Combustion Reactions", Fourteenth Symposium on Combustion, The Combustion Institute, Pittsburgh, PA, 1973, p 37.
- (12) B. Lewis and G. von Elbe, "Combustion, Flames, and Explosions of Gases", Academic Press, New York, 1961.
- (13) E. J. Harris and A. C. Egerton, *Proc. R. Soc. London, Ser. A*, **168**, 1 (1938).
- (14) E. J. Harris, *Proc. R. Soc. London, Ser. A*, **173**, 126 (1939).
- (15) F. O. Rice and E. L. Rodowskas, *J. Am. Chem. Soc.*, **57**, 350 (1935).
- (16) R. P. Hanzlik, "Inorganic Aspects of Biological and Organic Chemistry", Academic Press, New York, 1976.
- (17) E. I. Ochiai, "Bioinorganic Chemistry, An Introduction", Allyn and Bacon, Boston, 1977.
- (18) J. E. Falk, "Porphyrins and Metalloporphyrins", Elsevier, New York, 1964.
- (19) H. B. Gray, *Adv. Chem. Ser.*, **No. 100**, 365 (1971).
- (20) J. M. Rifkind in "Inorganic Biochemistry", Vol. 2, G. L. Eichhorn, Ed., Elsevier, New York, 1973, pp 832-901.
- (21) G. N. La Mar and J. Del Gaudio, *Adv. Chem. Ser.*, **No. 162**, 207 (1977).

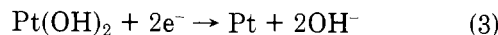
hemocyanin.<sup>28-32</sup> In spite of the considerable efforts to characterize these oxygen carriers, many of their fundamental chemical properties are poorly understood. For example, controversy rages over the oxidation state<sup>33-36</sup> and the mode of bonding of dioxygen to the iron in hemoglobin.<sup>35,37-39</sup> As a result, a wide variety of complexes<sup>40-44</sup> have been synthesized and studied as model compounds of the in vivo system.

Enzymatic oxidation processes also depend on the redox chemistry of dioxygen.<sup>45</sup> Examples of such systems include cytochrome oxidase,<sup>46</sup> nitrate reductase,<sup>47</sup> the peroxidases,<sup>48</sup> and the superoxide dismutases.<sup>49,50</sup>

The ensuing discussion summarizes the state of our understanding of the electron-transfer and atom-transfer reactions of dioxygen and the experiments (largely electrochemical) that have provided new insights into this chemistry.

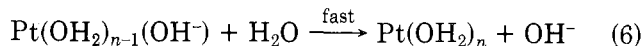
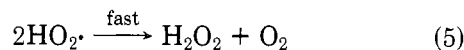
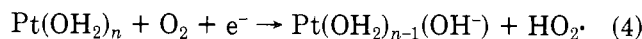
### Reduction Process for Molecular Oxygen

**Electron Transfer.** For many years dioxygen was believed to undergo a single, concerted, two-electron reduction to yield peroxide ion on the basis of aqueous<sup>51</sup> and nonaqueous polarographic data. Subsequent voltammetric results have established that the reduction process depends upon the electrode surface of solid electrodes in aqueous media. The pH-dependent O<sub>2</sub> reduction potential at a metal electrode surface is due to the reduction of the metal-hydroxide film,<sup>53,54</sup> for example,

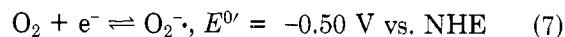


$$E^{0'} = -0.14 \text{ V vs. NHE}$$

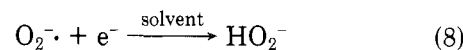
A pH-independent reduction of O<sub>2</sub> occurs at clean electrode surfaces in aqueous media. A set of reactions (eq 3-5) to account for this observation was proposed in 1961.<sup>53,54</sup>



At the time the idea of a one-electron mechanism was received with skepticism. However, in 1965-1966, the electrochemical reduction of dioxygen in aprotic solvents was reinvestigated by several groups.<sup>55-59</sup> These studies have established that O<sub>2</sub> is reduced by a quasi-reversible one-electron process to superoxide ion (eq 7), which in turn is reduced by a second one-electron



process (with the solvent Me<sub>2</sub>SO involved)<sup>60</sup> (eq 8). A



$$E_{\text{peak, cathodic (Me}_2\text{SO)}} = -1.75 \text{ V vs. NHE}$$

typical cyclic voltammogram for molecular oxygen in pyridine is illustrated in Figure 1.

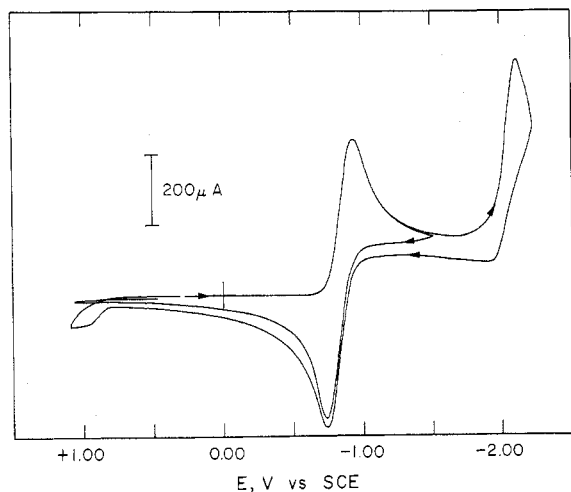
The stoichiometry of the electrochemical reduction of O<sub>2</sub> in aprotic media has been confirmed by controlled potential coulometry as well as by spectroscopic studies of the product species. In an acetonitrile solution with 0.1 M tetrapropylammonium perchlorate, superoxide ion has a single absorption band with a λ<sub>max</sub> at 255 nm (ε 1460 M<sup>-1</sup> cm<sup>-1</sup>).<sup>61,62</sup> The position of this maximum shifts with the supporting electrolyte that is used. Frozen glasses of this same solution at 77 K yield ESR spectra for O<sub>2</sub><sup>·-</sup> with g<sub>⊥</sub> = 2.008 and g<sub>∥</sub> = 2.083.<sup>57,60</sup>

Within experimental error, the reduction of molecular oxygen and the oxidation of O<sub>2</sub><sup>·-</sup> are independent of electrode material. The diffusion coefficients for these dioxygen species in Me<sub>2</sub>SO (0.1 M (C<sub>2</sub>H<sub>5</sub>)<sub>4</sub>NClO<sub>4</sub>) at 25 °C also have been determined.<sup>58</sup> D<sub>O<sub>2</sub></sub> = 3.23 × 10<sup>-5</sup> cm<sup>2</sup> s<sup>-1</sup>, D<sub>O<sub>2</sub><sup>·-</sup></sub> = 1.08 × 10<sup>-5</sup> cm<sup>2</sup> s<sup>-1</sup>. The fact that the diffusion coefficient for O<sub>2</sub><sup>·-</sup> is one-third that for O<sub>2</sub> indicates there is extensive ion pairing or solvation of the O<sub>2</sub><sup>·-</sup> species. Ion-pair formation occurs<sup>60</sup> when metal ions (Zn<sup>2+</sup>, Sr<sup>2+</sup>, Tl<sup>+</sup>, Cd<sup>2+</sup>, Y<sup>3+</sup>) are added to solutions of O<sub>2</sub><sup>·-</sup> in Me<sub>2</sub>SO. The resulting precipitates yield analyses which correspond to the metal superoxide.

One concludes from the preceding studies of O<sub>2</sub> in both aprotic and aqueous media that the primary re-

- (22) M. Y. Okamura and I. M. Klotz in "Inorganic Biochemistry", Vol. 1, G. L. Eichhorn, Ed., Elsevier, New York, 1973, pp 320-343.  
 (23) I. M. Klotz, *Biol. Macromol.*, **5**, 55 (1971).  
 (24) C. C. Fan, Ph.D. Thesis, University of Arkansas, 1972.  
 (25) G. L. Klippenstein, D. A. Van Riper, and E. A. Oosterom, *J. Biol. Chem.*, **247**, 5959 (1977).  
 (26) J. W. Dawson, H. B. Gray, H. E. Hoenig, G. R. Rossman, J. M. Schredder, and R. H. Wang, *Biochemistry*, **11**, 461 (1972).  
 (27) W. A. Hendrickson and K. B. Ward, *Biochem. Biophys. Res. Commun.*, **66**, 1349 (1975).  
 (28) R. Lontie and R. Witters in ref 22, pp 344-360.  
 (29) K. E. Van Holde and E. F. J. Van Bruggen, *Biol. Macromol.*, **5**, 1 (1971).  
 (30) C. M. Kaneshiro, Ph.D. Thesis, University of Oregon, 1975.  
 (31) T. B. Freedman, J. L. Loehr, and T. M. Loehr, *J. Am. Chem. Soc.*, **98**, 2809 (1976).  
 (32) H. A. Kuiper, W. Gaastra, J. J. Beintema, E. F. J. Van Brugger, A. M. H. Schepman, and J. Drenth, *J. Mol. Biol.*, **99**, 619 (1975).  
 (33) J. J. Weiss, *Nature (London)*, **202**, 83 (1964).  
 (34) L. Pauling, *Nature (London)*, **203**, 182 (1964).  
 (35) J. J. Weiss, *Nature (London)*, **203**, 183 (1964).  
 (36) B. H. Huynh, D. A. Case, and M. Karplus, *J. Am. Chem. Soc.*, **99**, 6103 (1977).  
 (37) J. S. Griffith, *Proc. R. Soc. London, Ser. A*, **235**, 23 (1956).  
 (38) W. A. Goddard and D. B. Olafson, *Proc. Natl. Acad. Sci. U.S.A.*, **72**, 2335 (1975).  
 (39) C. A. Reed and S. K. Cheung, *Proc. Natl. Acad. Sci. U.S.A.*, **74**, 1780 (1977).  
 (40) T. G. Traylor and C. K. Chang, *J. Am. Chem. Soc.*, **95**, 5810 (1973).  
 (41) F. Basolo, B. M. Hoffman, and J. A. Ibers, *Acc. Chem. Res.*, **8**, 384 (1975).  
 (42) J. P. Collman, R. R. Gagne, T. R. Halbert, J. C. Marchon, and C. A. Reed, *J. Am. Chem. Soc.*, **95**, 7863 (1973).  
 (43) H. Goff and G. N. La Mar, *J. Am. Chem. Soc.*, **99**, 6599 (1977).  
 (44) J. P. Collman, *Acc. Chem. Res.*, **10**, 265 (1977).  
 (45) R. J. P. Williams, *Inorg. Chim. Acta Rev.*, **5**, 137 (1971).  
 (46) B. G. Malmstrom, *Adv. Chem. Ser.*, **No. 162**, 173 (1977).  
 (47) B. E. Smith in "Chemistry and Uses of Molybdenum", Proceedings of the Second International Conference, P.C.H. Mitchell and A. Seaman, Eds., Climax Molybdenum Co. Ltd., London, 1977, pp 237-241.  
 (48) B. C. Saunders in ref 20, pp 988-1021.  
 (49) I. Fridovich, *Annu. Rev. Biochem.*, **44**, 147 (1975).  
 (50) I. Fridovich, *Adv. Enzymol.*, **41**, 35 (1974).  
 (51) H. A. Laitinen and I. M. Kolthoff, *J. Phys. Chem.*, **45**, 1061 (1941).  
 (52) J. F. Coetzee and I. M. Kolthoff, *J. Am. Chem. Soc.*, **79**, 6110 (1957).  
 (53) D. T. Sawyer and L. V. Interrante, *J. Electroanal. Chem.*, **2**, 310 (1961).  
 (54) D. T. Sawyer and R. J. Day, *Electrochim. Acta*, **8**, 589 (1963).

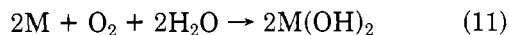
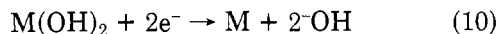
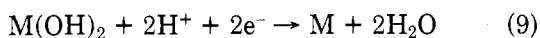
- (55) D. L. Maricle and W. G. Hodgson, *Anal. Chem.*, **37**, 1562 (1965).  
 (56) M. E. Peover and B. A. White, *J. Chem. Soc., Chem. Commun.*, 183 (1965).  
 (57) M. E. Peover and B. S. White, *Electrochim. Acta*, **11**, 1061 (1966).  
 (58) D. T. Sawyer and J. L. Roberts, Jr., *J. Electroanal. Chem.*, **12**, 90 (1966).  
 (59) W. Slough, *J. Chem. Soc., Chem. Commun.*, 184 (1965).  
 (60) E. L. Johnson, K. H. Pool, and R. E. Hamm, *Anal. Chem.*, **39**, 888 (1967).  
 (61) F. Ozawa, A. Hanaki, and H. Yamamoto, *FEBS Lett.*, **74**, 99 (1977).  
 (62) J. A. Fee and P. G. Hildenbrand, *FEBS Lett.*, **39**, 79 (1974).



**Figure 1.** Cyclic voltammogram for 5 mM molecular oxygen in pyridine (0.1 M tetrapropylammonium perchlorate) at a platinum electrode (area, 0.23 cm<sup>2</sup>). Scan rate, 0.1 V s<sup>-1</sup>. Saturated calomel electrode (SCE) vs. NHE, +0.244 V.

duction process is a one-electron transfer.<sup>2</sup> In aqueous media the reduction potential is -0.33 V vs. NHE and in aprotic media it is -0.55 V vs. NHE. The redox couple is essentially reversible and independent of the electrode material, and the primary process is first order in O<sub>2</sub> and independent of pH. In both aprotic and aqueous media the product species is affected by the presence of protons (or small cations), which cause the reduction potential to be shifted to more positive values and results in an overall two-electron process to yield H<sub>2</sub>O<sub>2</sub>.

**Oxygen Atom Transfer.** The reduction of dioxygen at a clean electrode surface is independent of both the electrode material and pH. In contrast, the reduction of dioxygen at oxidized electrodes is pH dependent, yields a negligible amount of H<sub>2</sub>O<sub>2</sub>, and occurs at the same potential as the metal oxide of the electrode material. A mechanism which is consistent with the results can be represented by eq 9-11. The metal oxide



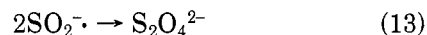
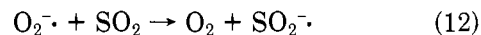
is electrochemically reduced to the metal and then re-formed by chemical reaction with the molecular oxygen in solution. The metal oxide behaves as a catalyst for the reduction of O<sub>2</sub> to H<sub>2</sub>O. The scheme accounts for the dependence of the reduction potentials and the rates of reaction on the electrode material and pH.<sup>53,54</sup>

Of considerable interest is the third step in the scheme in which the metal is spontaneously oxidized to yield the metal oxide. This is the general equation for the corrosion of metals. It apparently involves the splitting of the oxygen-oxygen bond and the transfer of oxygen atoms to the metal. While the mechanism of this reaction is unclear, extensive thermodynamic data are available for the oxidation of metals by molecular oxygen.<sup>63</sup>

(63) M. Pourbaix, "Atlas D'Équilibres Électrochimiques à 25 °C", Gauthier-Villars et Cie, Paris, 1963.

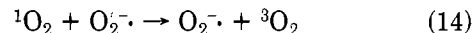
## Redox Processes for O<sub>2</sub><sup>-</sup>

**One-Electron Reductant.** Superoxide ion has been observed to be an effective reducing agent for organic substrates<sup>64,65</sup> and several transition-metal complexes.<sup>66-70</sup> The redox potential of superoxide ion indicates it has reducing capabilities in aprotic media which are roughly equivalent to those of dithionite ion ( $E^{0'} = -0.46$  V vs. NHE).<sup>71</sup> Confirmation of this assessment comes from a recent study which has established that O<sub>2</sub><sup>-</sup> reduces SO<sub>2</sub> to dithionite in dimethylformamide<sup>72</sup> (eq 12 and 13).



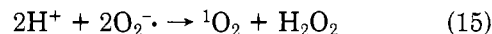
There is considerable interest in the reaction of O<sub>2</sub><sup>-</sup> with transition-metal ions. This results from the observation that a group of metalloenzymes which contain copper and zinc,<sup>73,74</sup> iron,<sup>75</sup> and manganese<sup>76</sup> catalyze the dismutation of superoxide to O<sub>2</sub> and H<sub>2</sub>O<sub>2</sub>.<sup>77</sup> Such enzymes are known as superoxide dismutases, and considerable effort has been expended in a search for complexes that mimic the enzymatic process. A copper(II)-phenanthroline complex, [Cu(phen)<sub>2</sub>](ClO<sub>4</sub>)<sub>2</sub>,<sup>66</sup> reacts with O<sub>2</sub><sup>-</sup> to form the copper(I) species, [Cu(phen)<sub>2</sub>]ClO<sub>4</sub>. A similar reaction occurs with manganese(III) tetraphenylporphyrin<sup>67</sup> to yield Mn<sup>II</sup>(TPP) and with tris(8-quinolinato)manganese(III)<sup>68</sup> to yield the corresponding manganese(II) derivative. Fe<sup>III</sup>EDTA<sup>70</sup> and cytochrome *c* also are reduced by O<sub>2</sub><sup>-</sup>. Superoxide ion reacts with quinones<sup>64</sup> and nitro-substituted aromatic hydrocarbons<sup>65</sup> to yield the corresponding radical anions.

There is also evidence that O<sub>2</sub><sup>-</sup> can "quench" singlet oxygen (eq 14). Although singlet oxygen also is thought



$$\Delta G = -91 \text{ kJ}$$

to result from the proton-induced dismutation of superoxide<sup>78</sup> (eq 15), this is still a matter of considerable



debate.<sup>79</sup> Recently, wavefunctions for the ground state of superoxide have been calculated.<sup>80</sup> The calculations indicate that the removal of the highest energy electron will produce a triplet state (favored by ~0.5 eV relative

(64) K. B. Patel and R. L. Willson, *J. Chem. Soc., Faraday Trans. 1*, **69**, 816 (1973).

(65) R. Poupko and I. Rosenthal, *J. Phys. Chem.*, **77**, 1722 (1973).

(66) J. S. Valentine and A. B. Curtis, *J. Am. Chem. Soc.*, **97**, 224 (1975).

(67) J. S. Valentine and A. E. Quinn, *Inorg. Chem.*, **15**, 1997 (1976).

(68) J. K. Howie, M. M. Morrison, and D. T. Sawyer, *ACS Symp. Ser.*, **38**, 97 (1977).

(69) K. Kovacs and B. Matkovic, *Enzyme*, **20**, 1 (1975).

(70) B. Halliwell, *FEBS Lett.*, **56**, 34 (1975).

(71) R. P. Martin and D. T. Sawyer, *Inorg. Chem.*, **11**, 2644 (1972).

(72) M. D. Stallings and D. T. Sawyer, *J. Chem. Soc., Chem. Commun.*, submitted for publication.

(73) J. M. McCord and I. Fridovich, *J. Biol. Chem.*, **244**, 6049 (1969).

(74) B. B. Keele, Jr., J. M. McCord, and I. Fridovich, *J. Biol. Chem.*, **246**, 2875 (1971).

(75) J. J. Villafranca, F. J. Yost, Jr., and I. Fridovich, *J. Biol. Chem.*, **249**, 3532 (1974).

(76) R. A. Weisiger and I. Fridovich, *J. Biol. Chem.*, **248**, 3582 (1973).

(77) I. Fridovich, *Acc. Chem. Res.*, **5**, 321 (1972).

(78) W. H. Koppenol and J. Butler, *FEBS Lett.*, **83**, 1 (1977).

(79) H. J. Guiraud and C. S. Foote, *J. Am. Chem. Soc.*, **98**, 1984 (1976).

(80) R. R. Birge, L. M. Hubbard, M. M. Morrison, and D. T. Sawyer, *J. Am. Chem. Soc.*, submitted for publication.

to the transfer of an electron to form singlet oxygen). Photon counting experiments<sup>80</sup> yield results that are in agreement with the calculations.

**Nucleophile.** That superoxide ion acts as a nucleophile toward organic compounds was first observed in 1970.<sup>81,82</sup> When molecular oxygen in Me<sub>2</sub>SO is reduced<sup>81</sup> by cyclic voltammetry, the ratio of anodic to cathodic peak currents is unity, which indicates that all of the O<sub>2</sub><sup>-</sup> that is formed during the cathodic sweep is stable and is reoxidized when the potential sweep is reversed. The addition of *sec*-butyl chloride causes the anodic peak height to be reduced, which indicates that some of the O<sub>2</sub><sup>-</sup> is consumed by the reaction with the alkyl chloride. A comparison<sup>81</sup> of the ratios of anodic-to-cathodic peak currents for the dioxygen redox couple in the presence of a variety of alkyl halides indicates a relative substrate reactivity of benzyl > primary > secondary > tertiary > aryl, and I > Br > Cl. The results indicate a direct S<sub>N</sub>2 displacement of the halide ion from the carbon by O<sub>2</sub><sup>-</sup>. Similar observations have been obtained for the reaction of various octyl halides and octyl tosylates with superoxide ion.<sup>83</sup>

Displacement of a halide ion by superoxide ion also has been observed on aromatic rings which are activated by electron-withdrawing substituents, such as nitro groups.<sup>84</sup> The order of reactivities (based on the rate of loss of O<sub>2</sub><sup>-</sup>) is F > Br ~ I > Cl for 1-halo-2,4-dinitrobenzene. There are two possible mechanisms for this reaction: (a) electron transfer from O<sub>2</sub><sup>-</sup> to the substituted benzene to yield an anion radical or (b) the direct addition of O<sub>2</sub><sup>-</sup> to the aromatic ring. Experiments with <sup>18</sup>O-enriched superoxide and mass spectral analysis of the products indicate that the oxygen atoms of superoxide are not assimilated into the products. Thus, mechanism a appears to dominate, unlike the reaction of O<sub>2</sub><sup>-</sup> with alkyl halides.

The reactivities of simple aldehydes, ketones, and esters with superoxide ion have been studied<sup>85</sup> in pyridine, toluene, and benzene. Typically, superoxide ion is generated in situ by controlled potential coulometry. A substrate then is added to the solution and the rate of reaction is determined by monitoring the concentration of O<sub>2</sub><sup>-</sup> as a function of time with linear sweep voltammetry. No loss of O<sub>2</sub><sup>-</sup> is observed when the substrates are benzophenone, cyclohexanone, acetone, or 2-butanone, or aromatic aldehydes, such as benzaldehyde. The addition of esters such as ethyl acetate or phenyl acetate to O<sub>2</sub><sup>-</sup> solutions results in reactions which are first order in O<sub>2</sub><sup>-</sup> and first order in ester. The esters are hydrolyzed to carboxylic acids and alcohols. The reaction mechanism that has been proposed is



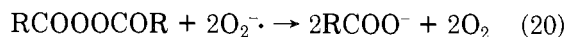
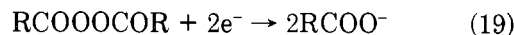
(81) M. V. Merritt and D. T. Sawyer, *J. Org. Chem.*, **35**, 2157 (1970).

(82) R. Dietz, A. E. J. Forno, B. E. Larcombe, and M. E. Peover, *J. Chem. Soc. B*, 816 (1970).

(83) J. San Filippo, Jr., C.-I. Chern, and J. S. Valentine, *J. Org. Chem.*, **40**, 1678 (1975).

(84) A. Frimer and I. Rosenthal, *Tetrahedron Lett.*, **32**, 2809 (1976).

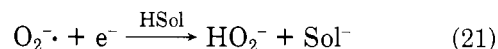
(85) M. J. Gibian, D. T. Sawyer, T. Ungermann, R. Tangpoonpholvivat, and M. M. Morrison, *J. Am. Chem. Soc.*, in press.



Confirmation of the validity of this mechanism comes from the electrochemical stoichiometry and the observation of an easily reduced transient, a diacyl peroxide. The key step in the mechanism is the initial nucleophilic addition of O<sub>2</sub><sup>-</sup> to the carbonyl carbon, followed by the loss of alkoxide ion from the tetrahedral intermediate. For ketones and benzaldehyde, nucleophilic addition of superoxide to the carbonyl must occur as well, but the absence of a viable leaving group precludes a net reaction.<sup>85</sup>

**Nonoxidizing Agent.** Several groups have suggested that superoxide ion also is an effective oxidizing agent.<sup>86-88</sup> Although solutions of superoxide ion can result in a net oxidation of some substrates, O<sub>2</sub><sup>-</sup> does not act directly as an electron-transfer oxidant.<sup>89</sup>

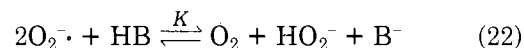
The electrochemical reduction of superoxide ion in pyridine or Me<sub>2</sub>SO occurs at -1.75 V vs. NHE<sup>58</sup> (eq 21).



Thus, from a thermodynamic standpoint, superoxide ion is an extremely weak oxidizing agent. In the presence of proton sources, however, superoxide disproportionates to form peroxide ion and oxygen.<sup>90</sup> Thus, the observed oxidation reactions may be due to the products of disproportionation.

The inertness of superoxide ion is confirmed by its nonreactivity with many substrates in aprotic solvents. Voltammetric studies have established that superoxide ion is thermodynamically unable to oxidize catechols or their anions in acetonitrile by electron transfer.<sup>89</sup> Indeed, the combination of O<sub>2</sub><sup>-</sup> with the anion of 3,5-di-*tert*-butylcatechol in pyridine results in no reaction. Furthermore, neither the monomethyl nor the dimethyl ether of catechol reacts with superoxide ion. Thus, from the chemical and voltammetric data, the initial reaction of superoxide with 3,5-di-*tert*-butylcatechol appears to involve a proton transfer from the catechol to the superoxide ion, followed by further chemistry of the resulting HO<sub>2</sub><sup>-</sup>. Presumably, the reported oxidations of hydrazines<sup>87,88</sup> and thiols<sup>91</sup> also involve an initial proton transfer to O<sub>2</sub><sup>-</sup>.

**Brønsted Base.** Another property of superoxide ions in solution is their effective basicity, in other words, their ability to effect proton removal from substrates.<sup>89</sup> The acid-catalyzed disproportionation of superoxide (eq 22) has a value for *K* of 2.5 × 10<sup>8</sup> when HB represents



water. Thus, weakly acidic organic compounds can be deprotonated efficiently in the presence of superoxide ion. In turn, deprotonation of H<sub>2</sub>O or other proton sources by O<sub>2</sub><sup>-</sup> results in the formation of a strong Brønsted base. Attack by this base, rather than by O<sub>2</sub><sup>-</sup>,

(86) Y. Moro-oka and C. S. Foote, *J. Am. Chem. Soc.*, **98**, 1510 (1976).

(87) H. P. Misra and I. Fridovich, *Biochemistry*, **15**, 681 (1976).

(88) C.-I. Chern and J. San Filippo, Jr., *J. Org. Chem.*, **42**, 178 (1977).

(89) D. T. Sawyer, M. J. Gibian, M. M. Morrison, and E. T. Seo, *J. Am. Chem. Soc.*, **100**, 627 (1978).

(90) D. Behar, G. Czapski, J. Rabini, L. M. Dorfman, and H. A. Schwarz, *J. Phys. Chem.*, **74**, 3209 (1970).

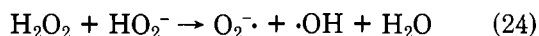
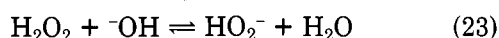
(91) K. Asada and S. Kanematsu, *Agr. Biol. Chem.*, **40**, 1891 (1976).

is the primary path for reaction with benzaldehyde.<sup>85,92,93</sup>

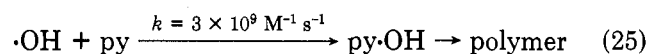
### Redox Processes for H<sub>2</sub>O<sub>2</sub> and HO<sub>2</sub><sup>-</sup>

**Base-Catalyzed Disproportionation to Superoxide Ion.** When tetraalkylammonium hydroxide is added to H<sub>2</sub>O<sub>2</sub> in pyridine, large quantities of superoxide ion are generated.<sup>94</sup> Spin trapping experiments and the subsequent ESR spectra of the products indicate that ·OH also is formed in the reaction. The addition of base to H<sub>2</sub>O<sub>2</sub> in acetonitrile yields O<sub>2</sub>, but there is no evidence of O<sub>2</sub><sup>-</sup>. The addition of base to H<sub>2</sub>O<sub>2</sub> in water results in the slow base-catalyzed disproportionation of hydrogen peroxide to water and oxygen.<sup>95</sup>

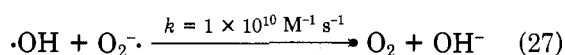
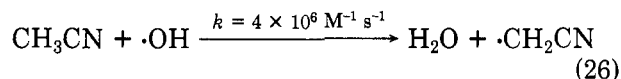
These results and other evidence indicate that superoxide ion is produced by the reaction of base with hydrogen peroxide (eq 23 and 24). Pulse radiolysis



data indicate that the reaction of ·OH with pyridine is rapid<sup>96</sup> (eq 25). Thus, pyridine traps hydroxyl radicals

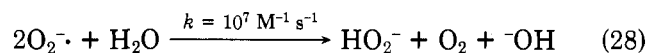


before they can react any further. The reaction of ·OH with acetonitrile is much slower than with pyridine<sup>96</sup> (eq 26). Thus, reaction 27 becomes competitive with



reaction 26. Reactions 23, 24, and 27 appear to represent a viable mechanism for the base-catalyzed decomposition of H<sub>2</sub>O<sub>2</sub> to oxygen and water.

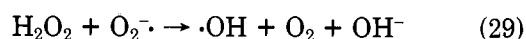
The same processes that dominate the base-induced decomposition of H<sub>2</sub>O<sub>2</sub> in acetonitrile probably occur in aqueous solution. A second pathway for superoxide decomposition also is likely in aqueous solutions at pH 7<sup>90</sup> (eq 28). Reaction 24 is presumed to be much faster



in pyridine and acetonitrile than in water, due to the general enhancement of the nucleophilic reactivity of HO<sub>2</sub><sup>-</sup> in aprotic solvents.

The reaction of H<sub>2</sub>O<sub>2</sub> and HO<sub>2</sub><sup>-</sup> may prove to be an important pathway leading to O<sub>2</sub><sup>-</sup> and ·OH in biological systems. Although the rate constant for the decomposition of H<sub>2</sub>O<sub>2</sub> in H<sub>2</sub>O at pH 7 is only 4 × 10<sup>-8</sup> M<sup>-1</sup> s<sup>-1</sup>,<sup>95</sup> the rate is rapid in aprotic media in the presence of base. Thus, for the hydrophobic regions of biomembranes, reaction 24 may become significant and an alternative to the so-called Haber-Weiss reaction<sup>97</sup> (eq

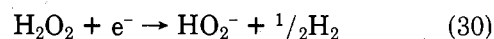
29) as a source of ·OH radical. Recent reports<sup>98</sup> indicate



that the rate constant for reaction 29 is less than 16 M<sup>-1</sup> s<sup>-1</sup>, and probably as low as 10<sup>-4</sup> M<sup>-1</sup> s<sup>-1</sup>, too low a value for this to be a significant source of ·OH radical.

**Electron-Transfer Reduction.** The electrochemical reduction of H<sub>2</sub>O<sub>2</sub> in pyridine yields superoxide ion.<sup>99</sup> That a reduction process generates a species with a higher oxidation state than H<sub>2</sub>O<sub>2</sub> is surprising and has prompted a series of experiments. The cyclic voltammogram for the reduction of H<sub>2</sub>O<sub>2</sub> in pyridine at a platinum working electrode exhibits a broad cathodic peak at -0.95 V vs. NHE and anodic peaks for the reverse scan at -0.50 V and -0.15 V vs. NHE. The latter is characteristic of electrolytically generated H<sub>2</sub>. Controlled-potential reduction of H<sub>2</sub>O<sub>2</sub> in pyridine at -1.0 V vs. NHE (with argon degassing) results in a solution that exhibits an anodic cyclic voltammogram that is characteristic of O<sub>2</sub><sup>-</sup>. ESR studies of the reduced solution confirm the presence of superoxide ion.

The products and the observed electron stoichiometries for the electrochemical reduction of H<sub>2</sub>O<sub>2</sub> are consistent with a mechanism in which the primary step is a one-electron transfer (eq 30) followed by a chemical

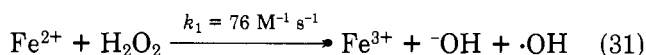


$$E^{0'} = -1.0 \text{ V vs. NHE}$$

reaction with another hydrogen peroxide molecule (reaction 24). The resultant ·OH is trapped by the pyridine solvent via reaction 25 to yield a stable solution of O<sub>2</sub><sup>-</sup>.

There is no evidence of superoxide ion, either by ESR or by cyclic voltammetry, from the electrochemical reduction of H<sub>2</sub>O<sub>2</sub> in acetonitrile. This can be explained by the slow rate of reaction of ·OH with CH<sub>3</sub>CN (reaction 6) which permits ·OH and O<sub>2</sub><sup>-</sup> to react via reaction 27 to give O<sub>2</sub>. The reduction of hydrogen peroxide in aqueous solution appears to be analogous to that in CH<sub>3</sub>CN, with the mechanism represented by reaction 30, followed by reactions 24 and 26. Thus, the reduction of H<sub>2</sub>O<sub>2</sub> yields H<sub>2</sub> and HO<sub>2</sub><sup>-</sup> initially, in a one-electron step. The final products are the result of the reaction of HO<sub>2</sub><sup>-</sup> with H<sub>2</sub>O<sub>2</sub> and are analogous to those for the base-induced decomposition of H<sub>2</sub>O<sub>2</sub>.

**Transition-Metal One-Electron Reduction (Fenton's Reagent).** In 1894, H. J. H. Fenton reported<sup>100</sup> that ferrous ion strongly promotes the oxidation of malic acid by hydrogen peroxide. Almost 40 years later Haber and Weiss<sup>97</sup> proposed that the hydroxyl radical is the oxidant in this reaction. There is considerable evidence<sup>101</sup> that the rate-determining step in the reaction is the generation of hydroxyl radical and that the overall process involves a second rapid oxidation of Fe<sup>2+</sup> (eq 31 and 32). This competing



(92) A. LeBerre and Y. Berguer, *Bull. Soc. Chim. Fr.*, 2368 (1966).

(93) E. Lee-Ruff, *Chem. Soc. Rev.*, 6, 195 (1977).

(94) J. L. Roberts, Jr., M. M. Morrison and D. T. Sawyer, *J. Am. Chem. Soc.*, 100, 329 (1978).

(95) F. R. Duke and F. W. Haas, *J. Phys. Chem.*, 65, 304 (1961).

(96) L. M. Dorfman and G. E. Adams, "Reactivity of the Hydroxyl Radical in Aqueous Solutions", NSRDS-NBS46, SD Catalog No. C 13.48:46, U.S. Government Printing Office, Washington, DC, June 1978.

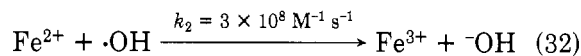
(97) T. Haber and J. J. Weiss, *Proc. R. Soc. London, Ser. A*, 147, 332 (1932).

(98) V. C. Maiboroda, E. P. Petryaev, V. M. Byakov, and L. F. Ivashkevich, *Khim. Vys. Energ.*, 8, 284 (1974) (*High Energy Chem.*, 8, 239 (1974)); G. J. McClure and J. A. Fee, *FEBS Lett.*, 67, 294 (1976); B. Halliwell, *ibid.*, 72, 8 (1976); A. Rigo, R. Stevanato, A. Finazzi-Agro, and G. Rotilio, *ibid.*, 80, 130 (1977).

(99) M. M. Morrison, J. L. Roberts, Jr., and D. T. Sawyer, *Inorg. Chem.*, submitted for publication.

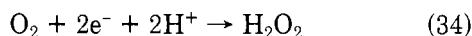
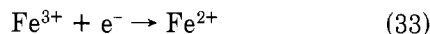
(100) H. J. H. Fenton, *J. Chem. Soc.*, 65, 899 (1894).

(101) T. Rigg, W. Taylor and J. J. Weiss, *J. Chem. Phys.*, 22, 431 (1954).



reaction always causes the yields of the organic oxidation by  $\cdot\text{OH}$  from Fenton's reagent to be lower than the 1:1 stoichiometry that is indicated by reaction 31.

Although there has been some resistance to the postulation of hydroxyl radicals as intermediates from Fenton's reagent, the evidence for their presence is considerable.<sup>102</sup> Perhaps the most convincing<sup>103,104</sup> is from a system that generates  $\cdot\text{OH}$  electrocatalytically. Reactions 33 and 34 occur simultaneously in aqueous



acid solution at 0.0 V vs. NHE. The  $\text{Fe}^{2+}$  and  $\text{H}_2\text{O}_2$  thus produced react via reaction 31 to give a controlled formation of  $\cdot\text{OH}$ . The products obtained in this manner are those expected from a Fenton's reaction, but the yields are significantly larger.

#### Oxygen Atom Transfer from $\text{HO}_2^-$ and $\text{H}_2\text{O}_2$ .

Unlike the reduction of oxygen to superoxide, which is a simple, reversible one-electron transfer process, the reduction of  $\text{O}_2^-$  is difficult and irreversible at  $-1.75$  V vs. NHE in pyridine or  $\text{Me}_2\text{SO}$ . An anodic wave for the reduction product of  $\text{O}_2^-$  is observed for the reverse scan of a cyclic voltammogram only at  $+1.0$  V vs. NHE. This peak initially was believed to be due to the oxidation of the peroxide anion.<sup>58</sup> However, subsequent studies<sup>105</sup> have shown that the anodic peak is due to the oxidation of hydroxide ion. A controlled-potential reduction (at  $-1.77$  V vs. NHE) of a solution of superoxide ion in dimethyl sulfoxide (0.1 M  $(\text{C}_2\text{H}_5)_4\text{NClO}_4$ ) followed by gas chromatography and infrared spectroscopy has established that the products of the reduction are hydroxide ion, ethylene, triethylamine, and dimethyl sulfone. An acid-base titration of the hydroxide ion confirms that 1 mol of  $^-\text{OH}$  is produced per mol of  $\text{O}_2^-$  that is reduced. The infrared spectrum of the reduced solution exhibits an absorption band at  $1134 \text{ cm}^{-1}$ , which is characteristic of dimethyl sulfone ( $\text{Me}_2\text{SO}$ ). The yield of dimethyl sulfone corresponds to 1 mol/mol of  $\text{O}_2^-$  reduced.

(102) C. Walling, *Acc. Chem. Res.*, **9**, 175 (1976).

(103) R. Tomat and E. Vecchi, *J. Appl. Electrochem.*, **1**, 185 (1971).

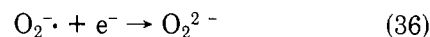
(104) R. Tomat and A. Rigo, *J. Appl. Electrochem.*, **6**, 257 (1976).

(105) A. D. Goolsby and D. T. Sawyer, *Anal. Chem.*, **40**, 83 (1968).

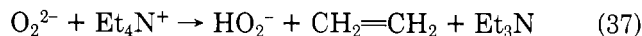
Strong IR bands also are observed at 1703 and 1200  $\text{cm}^{-1}$ , which are characteristic of triethylamine. A mechanism that is consistent with the data and the observed products is represented by eq 35-38. The last



$$E^{0'} = -0.50 \text{ V vs. NHE}$$



$$E^{0'} = -1.80 \text{ V}$$



two steps involve the deprotonation of the tetraethylammonium ion by the extremely basic peroxide ion and the conversion of  $\text{HO}_2^-$  to  $^-\text{OH}$  by transfer of an oxygen atom to  $\text{Me}_2\text{SO}$ .

#### Conclusions

In this discussion we have endeavored to demonstrate that the energetics for the redox chemistry of dioxygen is heavily dependent upon mechanistic pathway and reactive substrate. Under acidic conditions the stable product is  $\text{H}_2\text{O}_2$ , but for alkaline media the final product is  $^-\text{OH}$ . In either case, the redox potential for the reduction is limited to  $-0.33$  V vs. NHE. With appropriate substrates and/or catalysts the thermodynamic energy of eq 1 ( $+0.82$  V vs. NHE) can be approached, usually by processes that involve atom transfer. The redox chemistry of  $\text{O}_2^-$ ,  $\text{H}_2\text{O}_2$ , and  $\text{HO}_2^-$  is intimately connected to that for  $\text{O}_2$ . Atom transfer and disproportionation reactions are an important part of their chemistry. The base-catalyzed disproportionation of  $\text{H}_2\text{O}_2$  can produce a significant flux of  $\cdot\text{OH}$ . Further work is in progress to determine the controlling factors for this process and the mechanistic pathway.

*The material of the Account results primarily from the efforts of graduate students, colleagues, and postdoctoral associates as indicated by the citations. Their contributions are gratefully acknowledged, as is the support of the National Science Foundation under Grant No. CHE 76-24555 and the U.S. Public Health Service, National Institutes of Health, under Grant No. GM-22761.*