Oxygenation by superoxide ion of halogenofluorocarbons (Freons and haloforms) in aprotic solvents.

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Oxygenation by Superoxide Ion of Halogenofluorocarbons (Freons and Haloforms) in Aprotic Solvents

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The reactivity of chloro- and bromofluoromethanes (Freons and others) with superoxide ion ($O_2^{\bullet-}$) has been evaluated by cyclic voltammetry in dimethylformamide (DMF). Substitution of fluorine atoms into chloromethanes results in a substantial decrease in their reactivity with $O_2^{\bullet-}$ (relative rates: $CCl_4 \gg CF_4$, $CCl_4 \gg FCCl_3$, $CCl_4 \gg F_2CCl_2$, $CCl_4 \gg F_3CCl$, $H_3CCl \gg F_3CCl$, and $H_2CCl_2 \gg F_2CCl_2$). The bromo derivatives react much faster with $O_2^{\bullet-}$ than the corresponding chloro compounds ($F_3CBr \gg F_3CCl$, $F_2CBr_2 \gg F_2CCl_2$, and $FCBr_3 \gg FCCl_3$). The rates of reaction for $HCCl_3$, $HCFCl_2$, and HCF_2Cl are approximately the same, and the reactions appear to have a common path via dehydrochlorination. Reaction stoichiometries, apparent second-order rate constants, and product profiles have been determined for these fluoromethanes and related chlorofluoroethanes.

Gases that can affect stratospheric ozone include the oxides of nitrogen (NO_2, NO, N_2O), chlorofluorocarbons, CH_3CCl_3, CCl_4, CH_4, and CO_2 (*1*). The halogenofluorocarbons (Freons and haloforms), which are widely used as refrigerants (F_2CCl_2, HCF_2Cl, etc.), fire extinguishants (F_2CClBr and BrF_2CCH_2Br), and aerosol propellants, constitute a major contributor to the destruction of the ozone layer. Because superoxide ion is ($O_2^{\bullet-}$) is one of the most abundant ions in the upper atmosphere, its reactivity with halocarbons will release halide ions that may initiate ozone destruction via halogen-mediated chain reactions.

Halogenofluorocarbons are used as anesthetics and, to the extent that they come into contact with $O_2^{\bullet-}$ that is generated within the microsomes of the liver, may lead to liver toxicity (*2*). Hence, an assessment of their reactivity in aprotic media with $O_2^{\bullet-}$ should provide insight to their relative hazard.

In aprotic media superoxide ion ($O_2^{\bullet-}$) reacts via nucleophilic displacement with many halogenated hydrocarbons [e.g., CCl_4, $HCCl_3$, C_6Cl_6, polychlorobiphenyls (PCB's), and hexafluorobenzene] (*3–6*). A recent report (*7*) discusses the reaction of perfluorodecalin ($C_{10}F_{18}$) with phenylthiolate ($C_6H_5S^-$). The present study has been undertaken to ascertain the effect of fluoro groups on the reactivity of chloro and bromomethanes with superoxide ion. A further question has been whether their reactivity with $O_2^{\bullet-}$ correlates with their impact on the ozone layer or with their toxicity.

Experimental Section

Equipment. Conventional three-compartment electrochemical cells (10-mL capacity) (*8*) were used for the voltammetric and coulometric measurements. The cyclic voltammetry was accomplished with a Bioanalytical Systems, Inc. (BAS) glassy-carbon electrode (0.08 cm²), a BAS Model CV-27 potentiostat, and a Houston Instruments Model 100 *x–y* recorder. Controlled-potential coulometry made use of a Pt-gauze electrode or a glassy-carbon plate (Tokai Carbon Co., LTD.) with a Princeton Applied Research Model 173/179 potentiostat/digital coulometer. The reference electrode was a Ag/AgCl electrode [filled with aqueous tetramethylammonium chloride solution and adjusted to 0.000 V vs SCE (*9*)]. A platinum wire in a glass tube closed with a medium-porosity glass frit was used as the auxiliary electrode.

An Orion Research Model 701A digital potentiometer with a BAS Ag electrode was used to monitor the titration of halide ions (Cl^- and Br^-) with 0.01 M $AgNO_3$. Proton and ¹⁹F NMR spectra were recorded with a Varian Model XL 400 spectrometer.

Chemicals and Reagents. The halogenofluorocarbons [CF_4 (Freon 14), HCF_3 (Freon 23), F_3CCl (Freon 13), F_2CCl_2 (Freon 12), HCF_2Cl (Freon 22), $HCFCl_2$ (Freon 21), F_3CBr (Freon 13 B 1), and ClF_2CCF_2Cl (Freon 114)] were obtained from Aldrich Chemical Co., Inc., and were used as received. The other chloro and bromo hydrocarbons were reagent grade.

Dimethylformamide (DMF) and acetonitrile (MeCN), "distilled-in-glass" grade (0.012% H_2O and 0.004% H_2O, respectively; Burdick and Jackson), were used without further purification. Tetraethylammonium perchlorate (Et_4NClO_4) from GFS Chemicals was vacuum-dried over P_2O_5 and used as the supporting electrolyte (0.1 M). Aldrich DMF-d_7 (99%) was used for the proton NMR measurements, and Aldrich α,α,α-trifluorotoluene was used as the reference standard for the ¹⁹F NMR measurements.

Standard solutions of the substrate gases (0.1–1.0 M; 0.03 M in the case of F_3CCl) were prepared by introducing the gases into preweighed DMF solvent (~9 mL), which was subsequently adjusted to a total volume of 10 mL with DMF. Standard solutions (~1 M) of the chloro and bromo compounds were prepared by weighing into aliquots of DMF.

Tetramethylammonium superoxide [($Me_4N)O_2$] was prepared from KO_2 and ($Me_4N)OH \cdot H_2O$ by a solid-phase metathesis procedure (*10*). Superoxide ion (3–4 mM) also was generated (60–70% yield by coulombs) by the electrochemical reduction (at -1.1V vs SCE) of a DMF [0.1 M $Et_4N(ClO_4)$] solution through which dioxygen (at 1 atm) was continuously bubbled. The residual dioxygen was removed by purging with argon, and the concentration of $O_2^{\bullet-}$ was determined by anodic linear-sweep voltammetry. Approximately 20% of the $O_2^{\bullet-}$ decomposed within 30 min in the DMF solutions.

Methods. The apparent reaction rates for superoxide ion with the various substrates were determined from cyclic voltammetric peak-current measurements (*11*). The reaction stoichiometry of superoxide ion per substrate ($O_2^{\bullet-}/S$) was determined by adding a known amount of substrate to a known excess of $O_2^{\bullet-}$ in DMF. The unreacted $O_2^{\bullet-}$ was assayed by anodic voltammetry. The halide ion reaction products were assayed by $AgNO_3$ titration. For the potentiometric titration of chloride and bromide ions, 10 mL of distilled water and 0.5 mL of 98% H_2SO_4 were added to the 10-mL DMF solution. A KNO_3 agar bridge was used in order to eliminate the contamination by chloride ions from the reference electrode. Argon gas was introduced continuously into the solution during the titration.

Results

Reactivity of $O_2^{\bullet-}$ with Chlorofluoromethanes.

Figure 1 illustrates the cyclic voltammetry of O_2 (curve a)

Table I. Voltammetric Reduction Potentials ($E_{p,c}$) for Halogenofluorocarbons and Related Compounds, and Stoichiometries and Kinetics for Their Reactions with $O_2^{•-}$ in DMF at Room Temperature

substrate (S)	$E_{p,c}$[a] V vs SCE	$k/[S]$,[b] M^{-1} s^{-1}	$O_2^{•-}$ consumed per S	halide ions released per S
CF_4 (Freon 14)	<-3.0			
F_3CCl (Freon 13)	-2.7			
F_3CBr (Freon 13B1)	-1.6	$(2.6 \pm 1.0) \times 10$	2.0 ± 0.5	Br^-
F_2CCl_2 (Freon 12)	-2.2	$<1 \times 10^{-3\,c}$		
F_2CBr_2	-1.4	$(1.1 \pm 0.3) \times 10^3$	5.0 ± 0.5	$2Br^-$
$FCCl_3$	-1.7	4.2 ± 1.0	5.0 ± 0.5^d	$3Cl^-$
$FCBr_3$	-1.0	$(2.2 \pm 0.9) \times 10^3$	5.0 ± 0.5	$3Br^-$
CCl_4	-1.1	$(1.4 \pm 0.5) \times 10^{3\,e}$	5.0 ± 0.5^d	$4Cl^-$
CBr_4	-0.5	$>1 \times 10^5$	5.0 ± 0.5	$4Br^-$
HCF_3 (Freon 23)	<-3.0			
HCF_2Cl (Freon 22)	-2.5	$(2.0 \pm 0.5) \times 10^2$	4.0 ± 0.5^d	Cl^-
$HCFCl_2$ (Freon 21)	-2.2	$(2.4 \pm 0.5) \times 10^2$	4.0 ± 0.5	$2Cl^-$
$HCCl_3$	-2.0	$(1.0 \pm 0.3) \times 10^2$	4.0 ± 0.5	$3Cl^-$
$HCBr_3$	-1.3	$(1.1 \pm 0.4) \times 10^3$	4.0 ± 0.5	$3Br^-$
$F_3CCCl_3^d$	-1.3	$(4.0 \pm 1.0) \times 10^2$	4.0 ± 0.4	$3Cl^-$
$PhCCl_3$	-1.5	$(5.1 \pm 1.5) \times 10^e$	4.0 ± 0.4^d	$3Cl^{-\,d}$
H_3CCCl_3	-2.3			
ClF_2CCF_2Cl (Freon 114)	-2.2	$<1 \times 10^{-3\,c}$		
H_2CCl_2	-2.6	7.2 ± 2.0	2.0 ± 0.4^d	$2Cl^-$
H_2CBr_2	-2.0	$(2.3 \pm 0.5) \times 10^2$	2.0 ± 0.5	$2Br^-$
$H_3CCl_6^d$	<-3.0	$(8.0 \pm 2.0) \times 10^1$	1.0 ± 0.2	Cl^-
H_3CBr	-2.5	$(4.8 \pm 1.0) \times 10^2$	1.0 ± 0.2	Br^-
$H_3C(CH_2)_5Br$	-2.5	$(5.2 \pm 1.0) \times 10^2$	1.0 ± 0.2	Br^-

[a] At a GC electrode in DMF [0.1 M (Et_4N)ClO_4]. [b] Apparent pseudo-first-order rate constant k (normalized to unit substrate concentration [S]); [O_2] = 1 mM (0.2 atm). [c] Decrease of [$O_2^{•-}$] monitored by voltammetry. [d] From ref 3. [e] The ring-disk voltammetric technique for reaction rates gave values for $k/[S]$ of 3.8×10^3 M^{-1} s^{-1} and 50 M^{-1} s^{-1} for CCl_4 and $PhCCl_3$, respectively (ref 3).
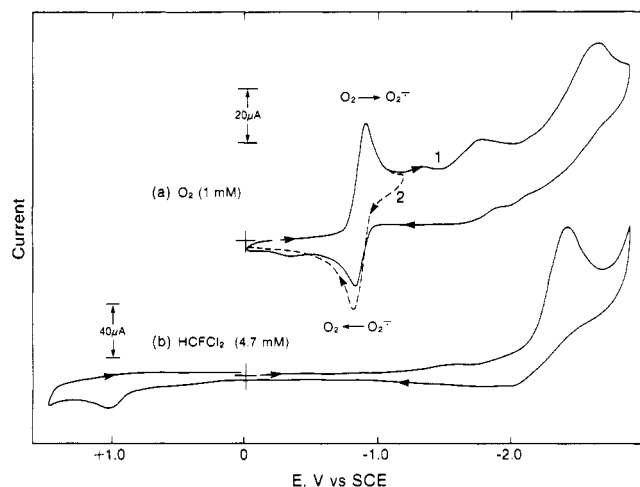

Figure 1. Cyclic voltammograms at a glassy carbon electrode (scan rate 0.1 V·s^{-1}) in DMF (0.1 M Et_4NClO_4) of (a) 1 mM O_2 and (b) 4.7 mM $HCFCl_2$.

and of $HCFCl_2$ (curve b) at a glassy-carbon electrode in dimethylformamide [0.1 M $Et_4N(ClO_4)$]. The first peak ($E_{p,c}$ -0.92 V vs SCE) is due to the one-electron reduction of dioxygen (O_2) to superoxide ion ($O_2^{•-}$). The reoxidation of $O_2^{•-}$ to O_2 occurs at -0.82 V. In contrast, the chlorofluorocarbons are reduced at much more negative potentials (Table I).

Figure 2 illustrates the effect of $FCCl_3$, $HCFCl_2$, and F_2CBr_2 on the cyclic voltammograms of O_2. The cathodic peak current ($i_{p,c}$) for O_2 increases and the anodic peak current ($i_{p,a}$) decreases in their presence. The enhancement of $i_{p,c}$ results from the rapid nucleophilic and electron-transfer reactions of $O_2^{•-}$, which regenerate O_2.

$$O_2^{•-} + RX \xrightarrow{k} ROO^• + X^- \qquad (1)$$
$$\downarrow O_2^{•-}$$
$$ROO^- + O_2$$
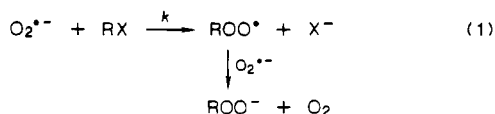
The apparent pseudo-first-order rate constants for the reaction of the voltammetrically generated $O_2^{•-}$ with the
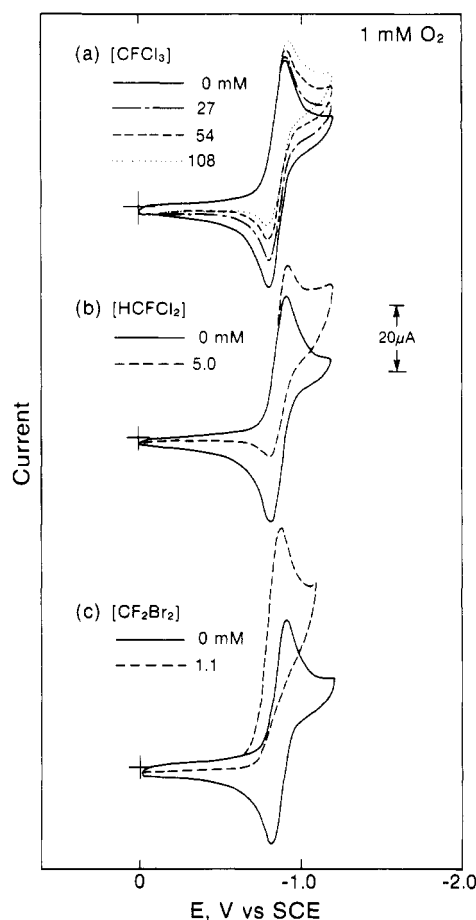

Figure 2. Effect of halogenofluorocarbons on the cyclic voltammogram of 1 mM O_2 at a GC electrode in DMF. (a) $CFCl_3$, (b) $HCFCl_2$, and (c) CF_2Br_2.

various substrates are related to the ratio of $i_{p,a}/i_{p,c}$ for O_2 in the presence of excess substrate (RX) (3, 11). The measured rate constants for the various substrates are normalized to unit substrate concentration and summa-
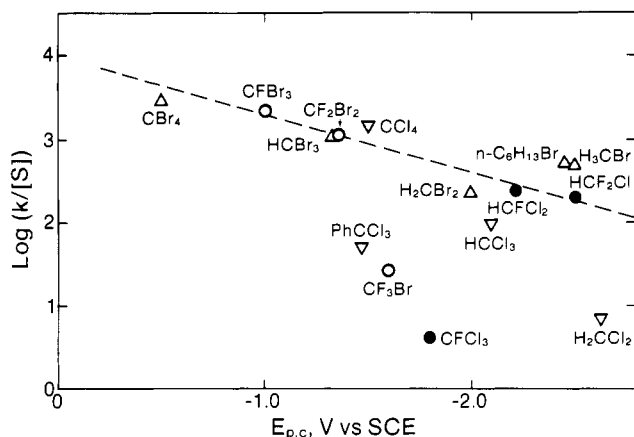
Figure 3. Reaction rates of halogenocarbons with $O_2^{\bullet-}$ in relation to their electrochemical reduction potentials ($E_{p,c}$) in DMF.

Figure 4. The apparent toxicities of the halogeno(fluoro)-methanes relative to their reaction rates with $O_2^{\bullet-}$. Toxicities classified by the Underwriters Laboratories; the higher the value, the lower is the toxicity (2).

rized in Table I. The values for CCl_4, F_3CCCl_3, $HCCl_3$, and several other substrates are from previous studies (3) but have been confirmed in the present investigation. The reaction and product stoichiometries for the substrates are also summarized in Table I, as is the reduction potential for each substrate in the absence of O_2. The ^{19}F NMR spectra for the product solutions from the reaction of $HCFCl_2$ and HCF_2Cl with excess $O_2^{\bullet-}$ establish that the former does not yield a product with a C–F bond, but the latter substrate yields products with C–F bonds.

Reactivity of $O_2^{\bullet-}$ with Bromofluoromethanes and Bromomethane. The bromofluoromethanes (F_3CBr, F_2CBr_2, $FCBr_3$), which are reduced at less negative potentials than their chloro analogues (Table I), react with $O_2^{\bullet-}$ at significantly faster rates. Thus, the respective values of $k/[S]$ for $FCBr_3$ and $FCCl_3$ are 2×10^3 M^{-1} s^{-1} and 4 M^{-1} s^{-1}.

Discussion and Conclusions

Although hexafluorobenzene reacts with $O_2^{\bullet-}$ to displace one fluorine (6), CF_4, F_3CCl, and HCF_3 are inert (Table I). This confirms that fluorine atoms are much less electron-withdrawing than chlorine atoms and consequently that fluoro-substituted methanes are less electrophilic toward the $O_2^{\bullet-}$ nucleophile. The reduction potentials for halogenofluorocarbons (Table I) provide a measure of their electrophilicity, and therefore of their reactivity with $O_2^{\bullet-}$. Thus, there is a rough correlation between the logarithms of the apparent second-order rate constants for the reaction of $O_2^{\bullet-}$ with halogenofluorocarbons and their reduction potentials (Figure 3). However, mechanistic constraints separate the substrates into several classes [primary alkyl halides (H_3CCl), S_N2 nucleophilic displacement; perhalocarbons (CCl_4), direct electron transfer; and substituted trichloromethanes ($FCCl_3$), direct electron transfer]. These classes each correlate well with substrate reduction potential.

A previous analysis (3b) has shown that the rate constants for substituted trichloromethanes decrease by approximately 10^5 M^{-1} s^{-1} per volt decrease (more negative) in their reduction potential. Hence, the observed rate constant for $FCCl_3$ (Table I, 4.2 M^{-1} s^{-1}) is consistent with its -1.8-V reduction potential. Within the group of $XCCl_3$ substrates, the relative electron-withdrawing propensity is in the order $X = Cl > F_3C > Ph > F > H \gg Me$.

Although the reaction rates of chloroform ($HCCl_3$) and its fluoro derivatives ($HCFCl_2$ and HCF_2Cl) appear to be too fast and inconsistent with their reduction potentials, a previous discussion (3b) has noted that there are two
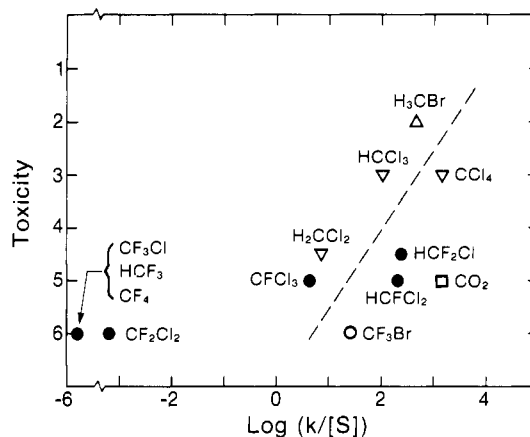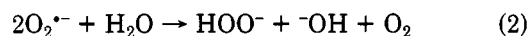
available reaction pathways: (a) direct electron transfer from $O_2^{\bullet-}$ to the chlorine of $HCCl_3$ ($k/[S]$ 0.4 M^{-1} s^{-1}) (3b) and (b) dehydrochlorination [Table I; $(k/[S])_{-HCl}$ 1×10^2 M^{-1} s^{-1}]. The latter is facilitated by the rapid decomposition of $O_2^{\bullet-}$ by the residual water present in the DMF solvent.

$$2O_2^{\bullet-} + H_2O \rightarrow HOO^- + {}^-OH + O_2 \qquad (2)$$

In turn, the resulting ${}^-OH$ deprotonates $HCCl_3$ (as well as $HCFCl_2$ and HCF_2Cl) to give a net dehydrochlorination.

$${}^-OH + HCCl_3 \rightarrow [:CCl_3^- + H_2O] \rightarrow :CCl_2 + H_2O + Cl^- \qquad (3)$$
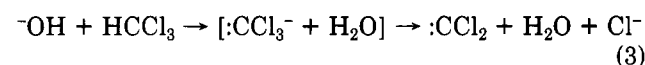
Combination of eq 2 and 3 gives the net reaction in the presence of residual water.

$$HCCl_3 + 2O_2^{\bullet-} \xrightarrow{H_2O} :CCl_2 + Cl^- + HOO^- + O_2 \qquad (4)$$
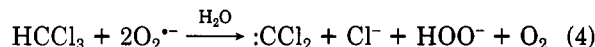
The observed rate constants ($k/[S]$) for $HCCl_3$, HCF_2Cl, and $HCFCl_2$ are essentially the same, which is consistent with dehydrochlorination (eq 4) as the dominant pathway and with the reasonable expectation that the three substrates are equivalent Brønsted acids. However, the facile reactivity of $HCBr_3$ ($k/[S]$ 1.1×10^3 M^{-1} s^{-1}) indicates that direct electron transfer by $O_2^{\bullet-}$ rather than dehydrohalogenation is the dominant reaction path.

With respect to the electron-transfer pathway $FCCl_3$ is 10 times *more reactive* than $HCCl_3$, but $FCBr_3$ is only twice as reactive as $HCBr_3$ (and F_2CBr_2 is 5 times as reactive as H_2CBr_2). In contrast, F_2CCl_2 is at least 10^4 times *less reactive* than H_2CCl_2 (probably because an S_N2 mechanism is viable for the latter). Thus, for direct electron-transfer substrates fluoro groups induce more reactivity than hydro groups, but substantially less than chloro groups.

Consideration of the results of Table I and Figure 3 leads to the conclusion that the fluoro derivatives of halogenomethanes are less reactive than their chloro and bromo analogues and somewhat more reactive than their hydro analogues. However, methyl chloride and bromide are much more reactive than their trifluoromethyl analogues.

The cytotoxicity of CCl_4 is believed to result from a CCl_4-stimulated peroxidation of unsaturated fatty acids via the $Cl_3COO^{\bullet}$ radical (13). The latter is the primary product of the $CCl_4/O_2^{\bullet-}$ reaction (3b). The much lower toxicity (2) of $FCCl_3$ may be due to its much slower reaction rate with $O_2^{\bullet-}$ (about 10^3 smaller than that for CCl_4). Figure 4 correlates the apparent toxicity of halogenofluoromethanes (2) with their ($RX + O_2^{\bullet-}$) reaction rates.

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In general, the larger the rate constant the greater is the toxicity.

The results of Table I do not indicate a correlation between $O_2^{\cdot-}$ reactivity and the relative impact on the ozone layer for halogenofluorocarbons. Thus, unreactive Freon substrates (F_3CCl, HCF_3, F_2CCl_2, HCF_3, and ClF_2CCF_2Cl) are believed to be especially destructive of stratopheric ozone.

References

(1) Wakselman, C., and Kaziz, C. (1986) Recent advances in the chemistry of halogenofluorocarbons. *J. Fluorine Chem.* **3**, 347–359.

(2) Clayton, J. W., Jr. (1967) Fluorocarbon toxicity and biological action. *Fluorine Chem. Rev.* **1**, 197–252.

(3) (a) Roberts, J. L., Jr., and Sawyer, D. T. (1981) Facile degradation by superoxide ion of carbon tetrochloride, chloroform, methylene chloride, and p,p′-DDT in aprotic media. *J. Am. Chem. Soc.* **103**, 712–714. (b) Roberts, J. L., Jr., Calderwood, T. S., and Sawyer, D. T. (1983) Oxygenation by superoxide ion of CCl_4, $FCCl_3$, $HCCl_3$, p,p′-DDT, and related trichloromethyl substrates ($RCCl_3$) in aprotic solvents. *J. Am. Chem. Soc.* **105**, 7691–7696.

(4) Matsumoto, S., Sugimoto, H., and Sawyer, D. T. (1988) Formation of reactive intermediates [ROOOOR) from the addition of superoxide ion $O_2^{\cdot-}$ to CCl_4, CF_3CCl_3, $PhCCl_3$, $PhC(O)Cl$, n-BuBr, and n-BuCl in acetonitrile. *Chem. Res. Toxicol.* **1**, 19–21.

(5) (a) Sugimoto, H., Matsumoto, S., and Sawyer, D. T. (1987) Oxygenation of polychloro aromatic hydrocarbons by superoxide ion in aprotic media. *J. Am. Chem. Soc.* **109**, 8081–8082. (b) Sugimoto, H., Matsumoto, S., and Sawyer, D. T. (1988) Degradation and dehalogenation of polychlorobiphenyls and halogenated aromatic molecules by superoxide ion and by electrolytic reduction. *Environ. Sci. Technol.* **22**, 1182–1186.

(6) Sugimoto, H., Matsumoto, S., Sawyer, D. T., Kanofsky, J. R., Chowdhury, A. K., and Wilkins, C. L. (1988) Oxygenation of hexafluorobenzene by superoxide ion. *J. Am. Chem. Soc.* **110**, 5193–5195.

(7) MacNicol, D. D., and Robertson, C. D. (1988) New and unexpected reactivity of saturated fluorocarbons. *Nature* **332**, 59–61.

(8) Tang, P. K. S., Cofré, P., and Sawyer, D. T. (1987) Electrochemical oxidation of hydroxide ion in acetonitrile and its facilitation by transition-metal complexes. *Inorg. Chem.* **26**, 3604–3609.

(9) Sawyer, D. T., and Roberts, J. L., Jr. (1974) *Experimental Electrochemistry for Chemists*, pp 44–46, 144–145, and 336–339, Wiley, New York.

(10) Yamaguchi, K., Calderwood, T. S., and Sawyer, D. T. (1986) Corrections and additional insights to the synthesis and characterization of tetramethylammonium superoxide [(MeN)O$_2$]. *inorg. Chem.* **25**, 1289–1290.

(11) Nicholson, R. S., and Shain, I. (1964) Theory of stationary electrode polarography. *Anal. Chem.* **36**, 706–723.

(12) Sawyer, D. T., Chiericato, G., Jr., Angelis, C. T., Nanni, E. J., Jr., and Tsuchiya, T. (1982) Effects of media and electrode materials on the electrochemical reduction of dioxygen. *Anal. Chem.* **54**, 1720–1724.

(13) Slater, T. F. (1979) Mechanisms of protection against the damage produced in biological systems by oxygen-driven radicals. *Ciba Found. Symp.* **65**, 143–163.