

RATES OF SUPEROXIDE ANION RADICAL
REACTION WITH ALKYL BROMIDES

by

RICHARD JAY WARNER
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Approved by:

Wayne C. Plamen

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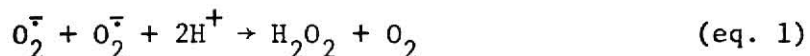
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INTRODUCTION

The superoxide ion, $O_2^{\cdot -}$, is the anion radical derived by addition of an electron to molecular oxygen. This species is capable of reacting with a variety of substrates owing to its anionic, radical, and redox nature. The relative dearth of knowledge concerning the chemical reactivity of $O_2^{\cdot -}$ as compared to other forms of oxygen is remarkable.

Being the first reduction product of aerobic cell respiratory processes, $O_2^{\cdot -}$ maintains widespread existence in nature. Fridovich and co-workers¹ found that superoxide dismutase, an enzyme which catalytically promotes decomposition of superoxide (eq. 1), is present in all aerobic



organisms. Since superoxide dismutase is so common among respiring organisms, $O_2^{\cdot -}$ is thought to be a deleterious species whose cytotoxicity has promoted the evolution of such defenses. In fact, superoxide has been suggested to be involved in various biological disorders such as radiation damage to tissue, cancer, aging processes and oxygen toxicity.

The superoxide anion radical is a reactive chemical species as indicated by the number of compounds for which reactions have been reported. Although capable of reacting through nucleophilic, radical, and redox modes, the nucleophilic and reducing electron transfer processes are predominate pathways. The following is a general, brief survey of literature concerning the reactions of $O_2^{\cdot -}$.

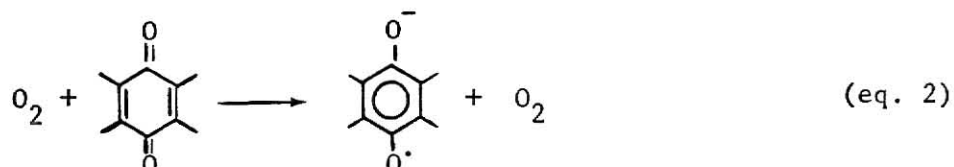
Chemical studies have employed either electrogenerated $O_2^{\cdot -}$ or suspensions of solid salts, e.g., KO_2 . Polar aprotic solvents are usually used in either case as $O_2^{\cdot -}$ is quite sensitive to proton sources. The electrogenerated tetraalkylammonium superoxides are both soluble and

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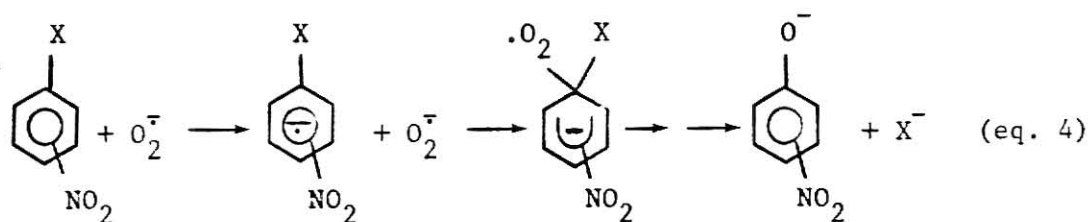
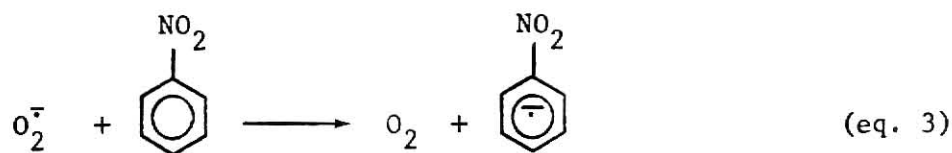
stable in a variety of dipolar aprotic solvents (DMSO, DMF, CH_3CN , pyridine, acetone, methylene chloride).²

The electron transfer reaction of $\text{O}_2^{\cdot-}$ has been demonstrated by such workers as Paupko and Rosenthal.³ Electron acceptors such as quinones readily react with $\text{O}_2^{\cdot-}$ to yield the corresponding anion radicals (eq. 2).



Rao and Hayon⁴ used this electron transfer reaction with a series of quinones, with known redox potentials, to determine the redox potential of $\text{O}_2^{\cdot-}$.

Nitro-substituted aromatics, which are likewise electron acceptors, are easily reduced to the corresponding radical anions³ (eq. 3). Nucleophilic radical aromatic substitution has been demonstrated by Frimer and Rosenthal⁵ for displacement of halogen ion by $\text{O}_2^{\cdot-}$ at the aromatic ring activated by electron withdrawing substituents such as nitro groups (eq. 4).

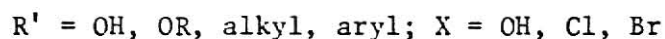
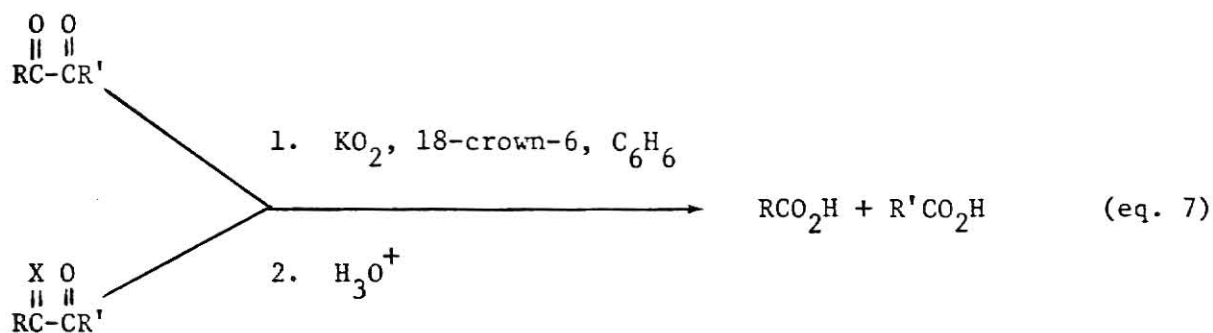
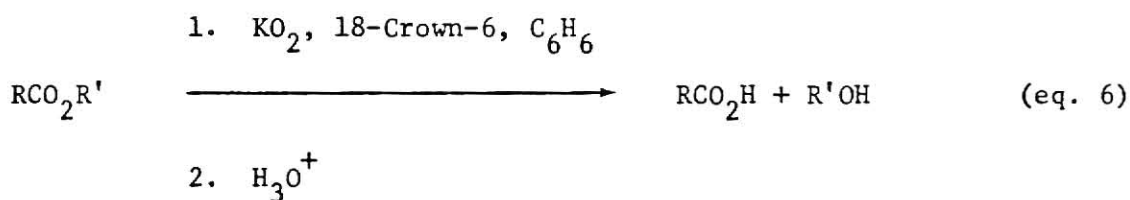


With amines, $O_2^{\cdot -}$ reacts as an oxidant to yield nitroxide free radicals (eq. 5).³



Superoxide oxidative cleavage reactions have been reported by several workers for various compounds, many of which are biologically important. A model compound of α -tocopherol was found to be oxidized by superoxide anion and, therefore, it is possible that this vitamin scavenges superoxide in vitro.⁶ The oxidative cleavage of various chalcones was determined by Rosenthal and Frimer⁷ and likely proceeds by a preliminary electron transfer from $O_2^{\cdot -}$ to the enone system of the substrate. A similar initiation step was suggested for the oxidation of 3,5-di-t-butyl catechol by KO_2 .⁸

San Filippo and co-workers^{9,10} have demonstrated oxidative cleavage reactions of α -keto, α -hydroxy, α -halo ketones, esters and carboxylic acids by KO_2 (equations 6 and 7).



Recently, Chern and San Filippo¹¹ have observed that various hydrazo compounds are readily oxidized by KO_2 and that certain related substances react in a variety of ways. These reactions are significant since hydrazo and related azo and azoxy compounds are concerned with a number of biologically important reactions (e.g. carcinogenesis).

The anionic character of superoxide enables nucleophilic reactions to occur and several displacement reactions have been reported. In the reaction of excess KO_2 with various alkyl halides and tosylates, the major product is the corresponding alcohol when the solvent used is DMSO.¹² However, the reaction of KO_2 with alkyl bromides and tosylates in benzene yields dialkyl peroxides.¹³ The difference in reaction products, as determined in these two solvents is explained¹⁴ by the fast reaction of the intermediate alkyl peroxy anion with DMSO to yield the corresponding alkoxide and dimethylsulfone rather than a displacement reaction with the halide substrate to yield the dialkyl peroxide. Diacyl peroxides are conveniently produced by reaction of KO_2 with acyl chlorides.¹⁵

The use of superoxide as a synthetically useful oxygen nucleophile has been discussed by Corey, et al.¹⁶ One of the more important uses of O_2^- concerns synthesis in the prostaglandin field; namely, the conversion of prostaglandin isomers by nucleophilic displacement.

OBJECTIVES

The underlying theme of this work was to broaden the base of chemical knowledge concerning the reactivity of superoxide ion. In particular, second-order rate constants for the reaction of O_2^- reacting as a nucleophile with alkyl halides will be determined. In contrast to previous kinetic studies of O_2^- , a new approach was implemented and optimized; namely,

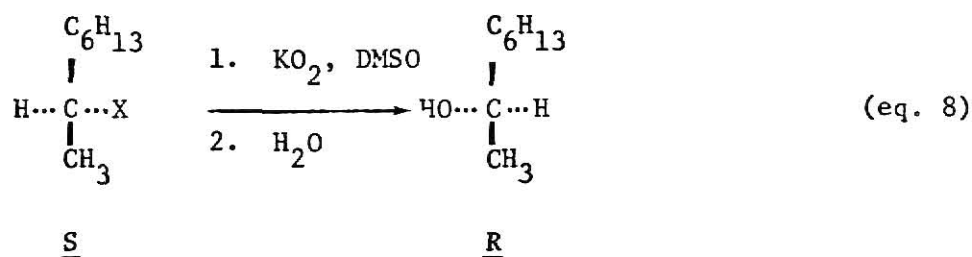
stopped-flow rapid kinetic techniques. The nucleophilicity, counter-ion effect, and activation parameters of $O_2^{\cdot -}$ were investigated by variation of substrate halides and the reaction conditions.

BACKGROUND

Nucleophilic Reactivity

That superoxide ion reacts with alkyl halides by an S_N2 mechanism has been demonstrated. Dietz¹⁷ observed a relative reactivity which fell in the series $n\text{-BuBr} > \text{sec-BuBr} > i\text{-BuBr} > t\text{-BuBr}$ for variation of alkyl group structure and in the series $n\text{-BuBr} > n\text{-BuOTs} > n\text{-BuCl}$ for variation of leaving group. The former order is consistent with a S_N2 reaction mechanism and the latter suggests that superoxide is a strong nucleophile.

Results obtained by San Filippo and co-workers¹² paralleled those of Dietz concerning substrate reactivity but indicate further that substitution was predominant with primary halides, whereas substantial elimination occurred with secondary and tertiary systems. Also reported was the essentially complete inversion of configuration at the chiral center in the carbon-oxygen bond formation which is typical of a S_N2 Walden inversion mechanism (eq. 8).



To date, reported rate constants for $O_2^{\cdot -}$ reactions have been limited to those of tetraalkylammonium superoxide as determined by electrochemical methods (Table I). In a chronopotentiometric study, Merritt and Sawyer¹⁸ determined the pseudo-first-order rate constants at 28°C for a series of

butyl chlorides in DMSO solvent. In two other studies, the fitting of potential step reduction data to i_k/i_d versus $\log kt$ working curves was used to determine rate constants. Dietz¹⁷ reported a pseudo-first-order rate constant for 1-bromobutane reacting with electrogenerated $O_2^{\cdot -}$ in DMF containing tetra-n-butylammonium perchlorate. Finally, Magno and Bontempelli¹⁹ have determined rate constants for the reaction of tetra-n-butylammonium superoxide in DMF with p-chlorophenyl benzoate and phenyl benzoate.

Table I.

Reported Rate Constants for Electrogenerated $O_2^{\cdot -}$ Reactions

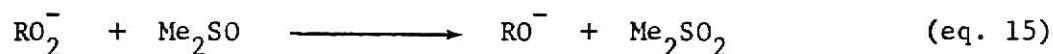
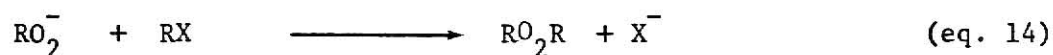
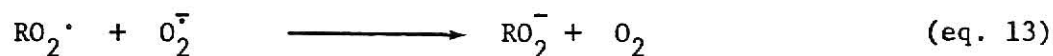
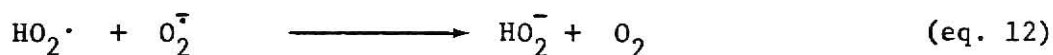
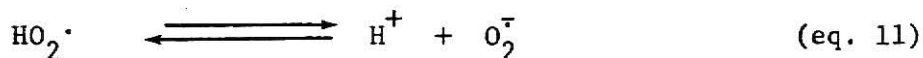
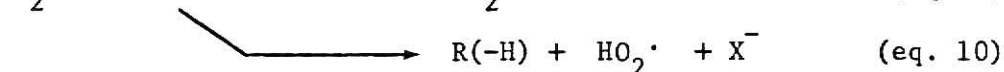
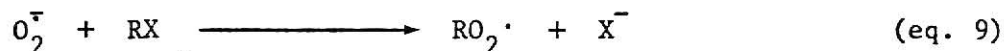
Reactant	Conc.	pseudo $k_1 (s^{-1})$	$k_2 (M^{-1}s^{-1})^a$	References
<u>n</u> -BuCl	0.1M	0.32	3.2	18
<u>sec</u> -BuCl	0.1M	0.06	0.6	18
<u>t</u> -BuCl	0.1M	0.04	0.4	18
<u>n</u> -BuBr	0.28M	140	500	17
<u>p</u> -ClC ₆ H ₄ CO ₂ Ph	0.1M	2.5	25	19
PhCO ₂ Ph	0.1M	0.3	3.0	19

^aDetermined by division of k_1 by reactant concentration.

There are several reactions that take place when $O_2^{\cdot -}$ is mixed with an alkyl halide. Reaction scheme I lists the overall mechanism originally proposed by Dietz, et al.¹⁷ which was subsequently expanded by Gibian and Ungermann.¹⁴ The course of the reaction is dependent upon both the alkyl halide structure and the reaction solvent. For a primary alkyl halide, the displacement of halide ion (eq. 9) is dominant over the elimination reaction (eq. 10) as determined by product analysis;

e.g., for the reaction of KO_2 with 1-bromooctane and 2-bromooctane in DMSO, olefins were isolated in yields of 1% and 34%, respectively.¹² It is apparent that secondary halides give significant olefin yields under these experimental conditions. The HO_2^\cdot formed in equation 10 may ionize to superoxide (eq. 11) or disproportionate (eq. 12). The bulk reaction of alkyl peroxy radical with O_2^\cdot (eq. 13) is the analogue to equation 12 and is equally exothermic. Finally, the peroxy anion can undergo either reaction 14 or 15 to form products. The displacement reaction of RO_2^- with an alkyl halide is quite facile but equation 15 is favored by at least a factor of four when DMSO is the solvent.¹⁴

Scheme I



Physical Properties

Some physical properties pertinent to this study are the solubility, spectral, and redox characteristics of superoxide. The solubility of KO_2 in DMSO is not particularly high as the estimated concentration of saturated KO_2 /DMSO solution is only about 0.02M.²⁰ However, the solubility is sufficiently high for kinetic determinations under pseudo-first-order-conditions where O_2^\cdot is the limiting reagent. The tetraalkylammonium

superoxides are inherently more soluble than their alkali metal counterparts but with the use of crown ethers the solubilization of KO_2 is greatly enhanced.

Superoxide ion exhibits spectral properties in the ultraviolet region. The λ_{max} for O_2^- is 250 nm in acetonitrile with a reported extinction coefficient of $2580 \pm 300 \text{ M}^{-1} \text{ cm}^{-1}$.²¹ Recently, McClune and Fee²² estimated an extinction coefficient of $500 \pm 50 \text{ M}^{-1} \text{ cm}^{-1}$ at a wavelength of 275 nm in DMSO. The ultraviolet spectrum of KO_2 dissolved in DMSO versus air is represented in Figure 1. Because the DMSO solvent cutoff is ca. 260 nm, the λ_{max} is not observable.

Peover and White² determined the halfwave potentials for the reduction of oxygen in various solvents at a dropping mercury electrode (e.g., in DMSO, $E_{1/2} = -0.77 \text{ V(SCE)}$).

General Approach

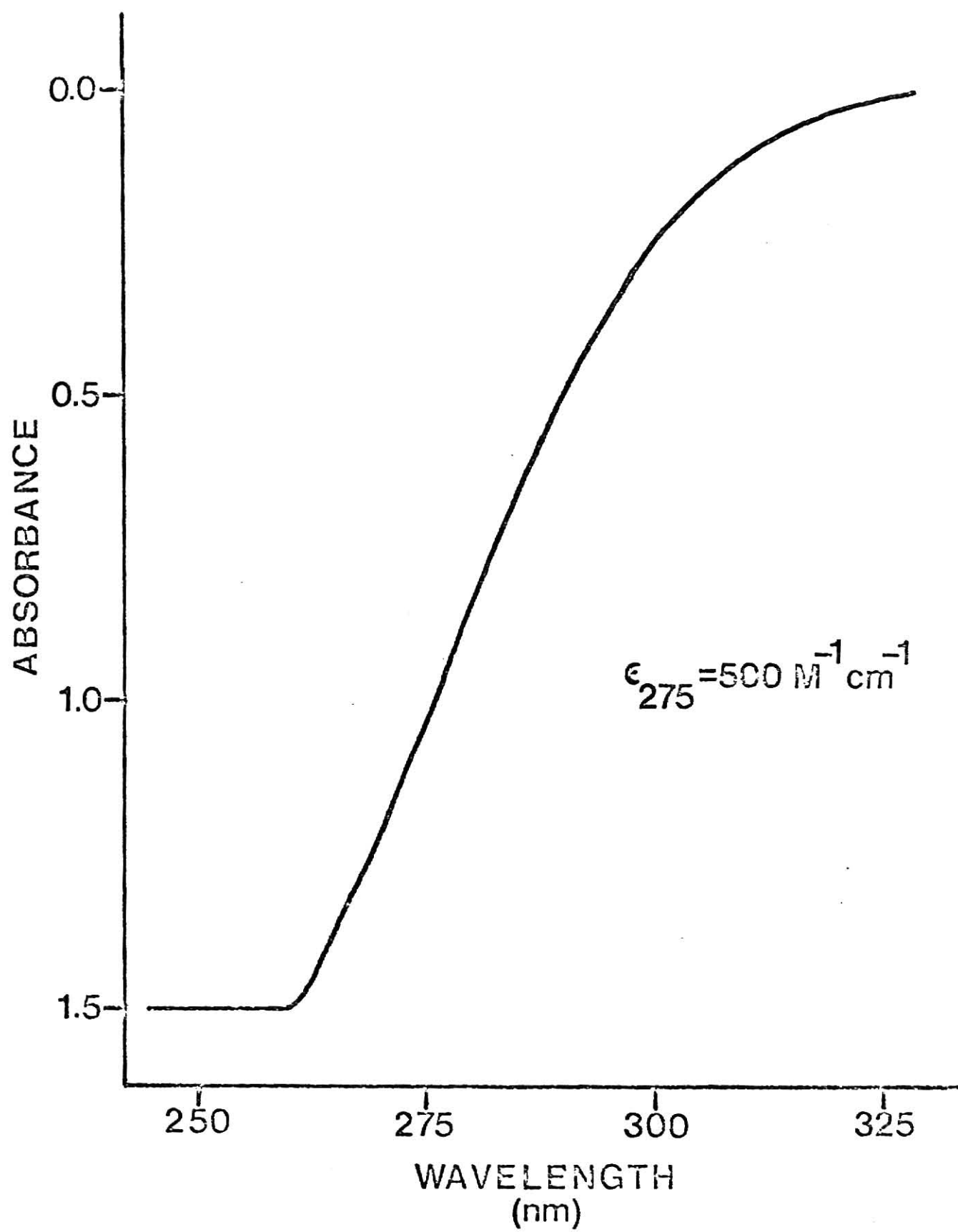
In order to determine the absolute rate constants for the $\text{S}_\text{N}2$ reaction of superoxide ion with a series of alkyl halides, stopped-flow rapid kinetic techniques were employed. Basically, the stopped-flow method allows the infusion of rapidly and efficiently mixed reactants into a cuvette where the concentration of a reactant can be monitored by spectrophotometric observation.

As indicated by Figure 1, the absorption of O_2^- in DMSO allows the monitoring of its decay by ultraviolet spectroscopy. Hence, stopped-flow determinations were conducted at a wavelength of 275 nm for reactions employing DMSO solvent. A criterion for observation of the reaction of O_2^- at 275 nm is that none of the other reactants, intermediates or reaction products absorb strongly in the same region and therefore interfere.

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Figure 1. Ultraviolet absorption spectrum of KO_2 in DMSO versus air.



for example, the kinetics of $O_2^{\cdot -}$ reactions with alkyl iodides can not be determined by this method since alkyl iodides absorb strongly in the observation region i.e., $\lambda_{\max}^{\text{EtI}} = 255$).²³

All stopped-flow experiments were conducted under pseudo-first-order-conditions with the alkyl halide in excess. Typically, a stock solution of $O_2^{\cdot -}$ was prepared in a dry box by saturating DMSO with finely powdered KO_2 . This saturated stock solution was then diluted approximately ten-fold which resulted in a $O_2^{\cdot -}$ concentration of about $2 \times 10^{-3} M$. This concentration corresponded to an absorbance of unity at 275 nm as calculated from the reported extinction coefficient of $500 M^{-1} cm^{-1}$. Adherence to this concentration was routinely determined by ultraviolet spectra taken prior to use in stopped-flow experiments.

Generally, alkyl halide solutions were prepared in concentrations ranging from 0.01M to 0.1M using distilled alkyl halides shown to be pure by glpc. It was observed that the purity of the alkyl halide was of the utmost importance since under pseudo-first-order-conditions any appreciable impurity could be of equal concentration with superoxide. Also, since DMSO possibly oxidizes alkyl halides slowly to the corresponding aldehydes, it was found that freshly prepared solutions of alkyl halides gave the most reproducible data.

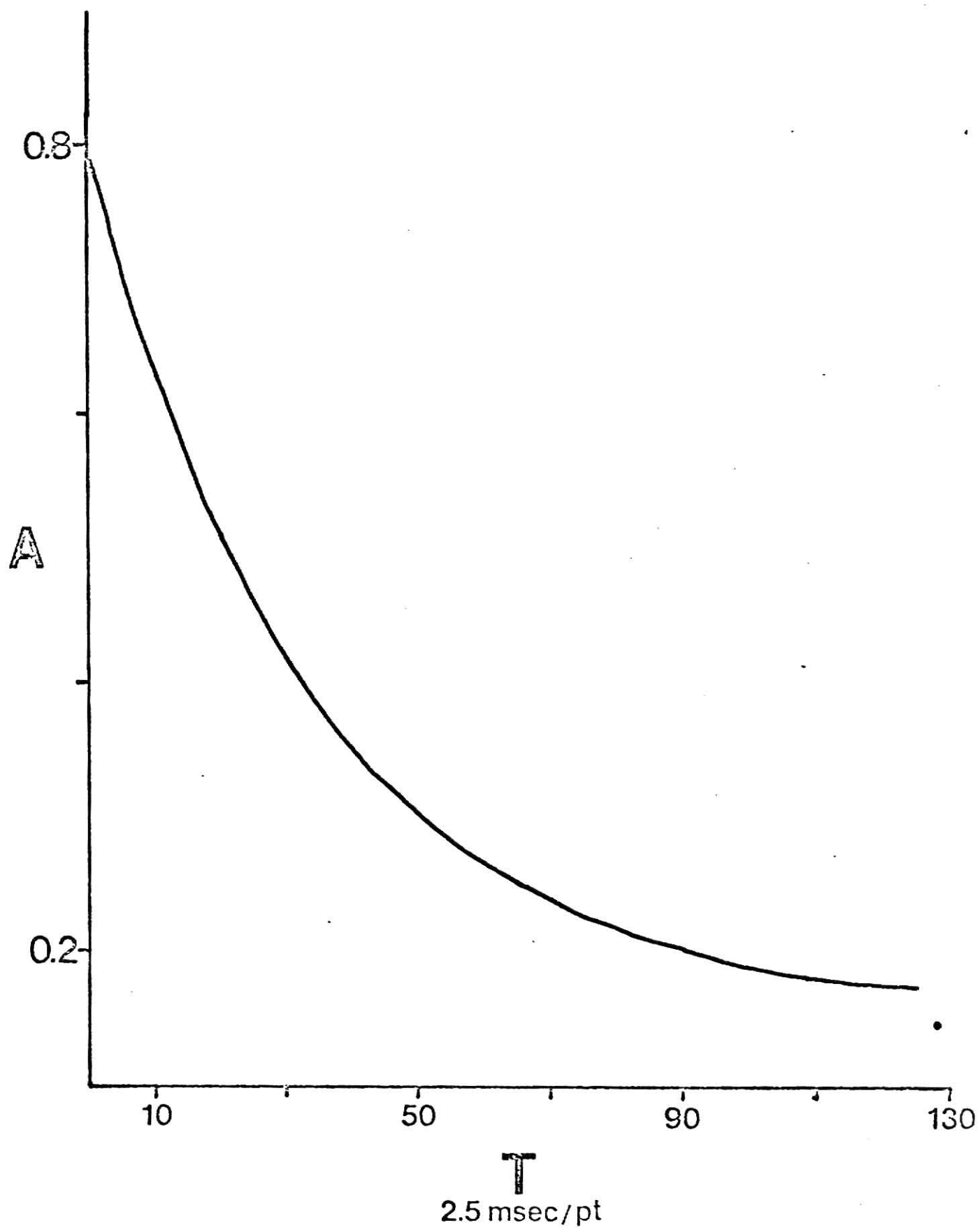
Due to the rapid dismutation of $O_2^{\cdot -}$ in the presence of protons, the exclusion of water was imperative. Therefore, all glassware used was oven-dried and manipulation of solid KO_2 was accomplished in a dry box. Dry DMSO (distilled from CaH_2 , stored over 4-A molecular sieves) was used for solution preparation and subsequent handling of solutions was done with all-glass syringes.

Most stopped-flow experiments were run at $25 \pm 0.1^\circ\text{C}$ as maintained by a Lauda/Brinkman K-2/R circulator. Data acquisition, storage, and calculations were handled by a PDP-8/E digital lab computer²⁴ (Digital Equipment Corporation). All the experimental variables and a co-averaged set of 128 data points were fed into the computer and subsequently saved on Dectape for later calculations. The data points represent absorbance at designated intervals of time and were simultaneously displayed on a oscilloscope. As an example of the typical decay observed, a plot of absorbance versus time for the reaction of 0.1M iso-propyl bromide with KO_2 in DMSO is depicted in Figure 2.

As a check for whether reactions followed good pseudo-first-order kinetics, the concentration of the excess reagent, RBr, was varied 5- to 10-fold. A corresponding 5- to 10-fold change in the observed pseudo-first-order rate constant indicated proper dependence upon RBr concentration. On the other hand, when variance of the RBr concentration did not result in the expected trend in observed rate constants the data were suspect. For a quick check, the half-life of the reaction was calculated using the stopped-flow computer program directly. An estimated pseudo-first-order rate constant was then obtained from the half-life ($k = \ln 2/t_{1/2}$) for comparison to another run using a different RBr concentration.

Calculation of pseudo-first-order rate constants, k_{obs} , was achieved by two methods: 1) by computer, using a revised program from Wiberg,²⁵ and 2) from plots of $\log A_t - A_\infty$ versus time. The computer program calculated k_{obs} by the least-squares method from data acquired by stopped-flow spectrophotometry. The rate equation for the pseudo-first-order rate constant, k_{obs} , is shown in equation 16, where t is the time between the initial absorbance, A_0 , used in the calculation and the absorbance at

Figure 2. Plot of absorbance versus time for the reaction of KO_2 with 0.1M iso-propyl bromide in DMSO. Data for this plot was determined by stopped-flow spectrophotometry at a time per point of 2.5 msec.

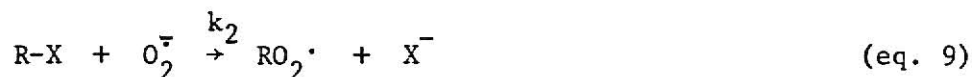


time t , A_t . Plots of the data were used mainly for visual representation

$$k_{\text{obs}} = \frac{\ln(A_0 - A_\infty) - (A_t - A_\infty)}{t} \quad (\text{eq. 16})$$

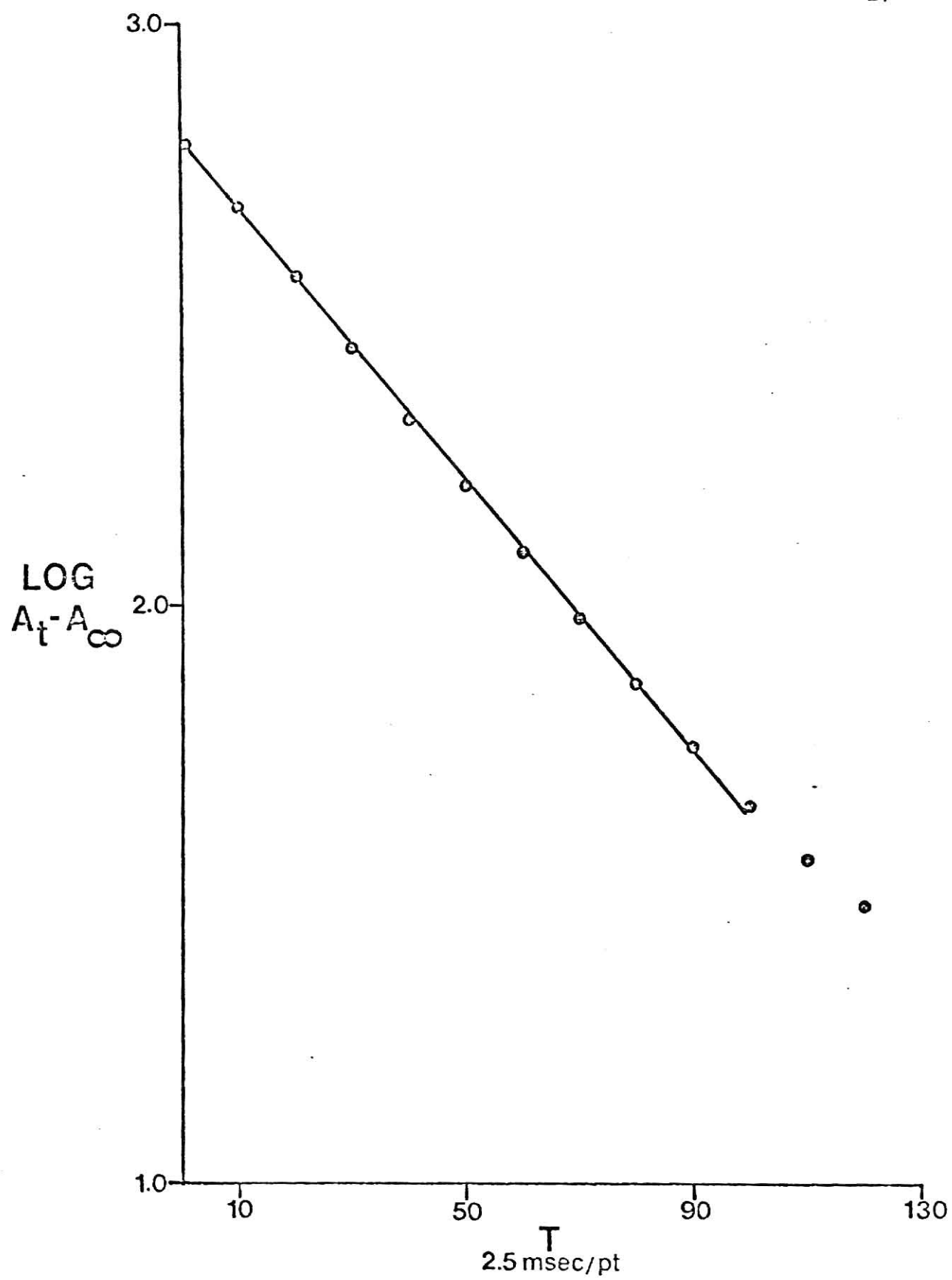
of the data in order to determine the linearity and therefore the reliability of each run. However, k_{obs} was routinely calculated from the slope of such plots for comparison to rate constants obtained from computer calculations. An example of a $\log A_t - A_\infty$ versus time plot is shown in Figure 3 for the reaction of KO_2/DMSO with 0.1M iso-propyl bromide.

Second-order rate constants, k_2 , for the $\text{S}_{\text{N}}2$ reaction of $\text{O}_2^{\cdot -}$ with alkyl halides were extracted from the observed pseudo-first-order rate constants, k_{obs} , in the following manner. There are two major reactions involving superoxide with alkyl halide substrates that account for the observed decay of $\text{O}_2^{\cdot -}$ under the experimental conditions in the present study. The first is the $\text{S}_{\text{N}}2$ reaction (eq. 9) for which a rate constant is to be determined, and the second is the reaction of $\text{O}_2^{\cdot -}$ with the peroxy anion (eq. 13). Dietz¹⁷ has estimated by electron transfer theory that k_3 is diffusion-controlled. Since $k_2 \ll k_3$, then the observed rate will be simply that of a single second-order process but with the provision that two moles of $\text{O}_2^{\cdot -}$ are reacting for each mole of alkyl halide.



A second-order rate equation (eq. 17) can be derived for the initial $\text{S}_{\text{N}}2$ reaction (eq. 9) under pseudo-first-order conditions by use of the steady state approximation for the intermediate peroxy radical with the assumption of minimal contribution due to dimerization or radical decay.

Figure 3. Plot of $\log A_t - A_\infty$ versus time for the reaction of KO_2 with 0.1M iso-propyl bromide. Data for this plot was obtained by stopped-flow spectrophotometry and was shown as a plot of absorbance versus time in Figure 2. The time per point was 2.5 msec. The reaction solvent was DMSO.



$$k_2 = \frac{\ln[O_2^{\cdot-}]_o - \ln[O_2^{\cdot-}]_t}{2[RX]_t} \quad (\text{eq. 17})$$

Since the concentration of $O_2^{\cdot-}$ is proportional to its absorbance, A, then the rate equation for k_2 resembles that depicted in equation 16 with the exception of the inclusion of a stoichiometric factor of two and the alkyl halide concentration. The second-order rate constant, k_2 , for the initial S_N2 reaction can be expressed by equation 18 which is derived by the combination of equations 16 and 17. Therefore, second-order rate constants

$$k_2 = \frac{k_{\text{obs}}}{2[RX]} \quad (\text{eq. 18})$$

were obtained by dividing the observed pseudo-first-order rate constants by two times the concentration of the alkyl halide.

RESULTS AND DISCUSSION

Alkyl Bromide Series

The second-order rate constants for the reaction of KO_2 dissolved in DMSO with a series of alkyl bromides are compiled in Table II. The values given were determined by stopped-flow spectrophotometry under pseudo-first-order conditions. Pseudo-first-order rate constants were obtained for at least two alkyl bromide concentrations and the second-order rate constants were determined by using equation 18. The values listed are the averages of rate constants from runs showing good linearity in $\log A_t - A_\infty$ versus time plots and minimal variance in second-order rate constants for different alkyl halide concentrations.

The usual reactivity order characteristic of a S_N2 process is evident in the series $\text{MeBr} > \text{EtBr} > \text{n-BuBr} > \text{i-PrBr} \gg \text{1-bromoadamantane}$, which for the first four entries parallels the increasing inaccessibility of

Table II.

Rate Constants for the Reaction of KO_2 with
Alkyl Bromides in DMSO at 25.0°

Alkyl Bromide	$k_2 \text{ (M}^{-1}\text{s}^{-1}\text{)}$
CH_3Br	$(6.7 \pm 0.2) \times 10^2$
$\text{CH}_3\text{CH}_2\text{Br}^a$	$(3.5 \pm 0.2) \times 10^2$
$\text{CH}_3(\text{CH}_2)_3\text{Br}$	$(1.5 \pm 0.1) \times 10^2$
$(\text{CH}_3)_2\text{CHBr}$	$(6.5 \pm 0.1) \times 10^1$
$(\text{CH}_3)_3\text{CCH}_2\text{Br}$	b
$(\text{CH}_3)_3\text{CBr}$	b
1-bromoadamantane	$\ll 1.0^c$

^aDetermined at $\lambda = 280 \text{ nm}$.

^bDid not follow pseudo-first-order kinetics.

^cToo slow to measure by stopped-flow spectrophotometry.

the reaction center. However, the spread in reactivities is smaller than frequently observed.²⁶ This attenuation of rates is shown by comparing the average relative rates given by Streitwieser²⁶ to those of this study (Table III). This trend of little sensitivity to variation in the alkyl group is also noticeable in the rates reported by other workers for the reactions of O_2^- with alkyl halides. For the reaction of O_2^- with the alkyl chloride series n-butyl, sec-butyl, and tert-butyl, the relative rates are 1.0:0.19:0.13.¹⁸ An even smaller effect of substrate structure was reported by San Filippo and co-workers¹² for a 1°, 2°, and 3° series of alkyl bromides (1-bromooctane, 2-bromooctane, and 2-methyl-2-

bromopentane), where the relative reactivities were determined by competitive techniques to be 1.0:0.98:0.90.

Table III.

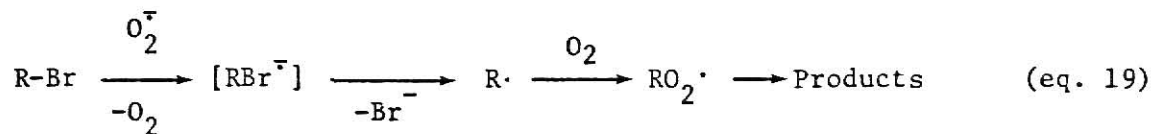
Relative Rates of Alkyl Systems Toward Nucleophilic Reactions

Alkyl Group	Average Relative Rate ^a	$O_2^{\cdot -}$ Relative Rate ^b
CH_3^-	30.0	1.9
$CH_3CH_2^-$	(1.0)	(1.0)
$CH_3(CH_2)_3^-$	0.4	0.44
$(CH_3)_2CH^-$	0.025	0.19

^aFrom Streitwieser.²⁶

^bThis study, Table 2.

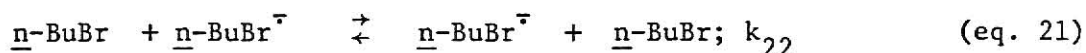
Gibian and Ungermann¹⁴ suggest that superoxide exhibits too flat of a distribution for a real S_N2 process, which may indicate a strong contribution of an electron-transfer character in the transition state or electron transfer followed by radical coupling (i.e., eq. 19). Attributing the attenuation of reactivity toward substrate structure change to electron transfer can be partially refuted by the low rate constant exhibited by 1-bromoadamantane. The unreactivity of this bridgehead bromide with $O_2^{\cdot -}$ demonstrated a lack of any appreciable electron transfer type substitution process (eq. 19). Although an electron transfer type mechanism has been proposed for nitroaromatic halides (eq. 4), the difference



in reduction potentials between $O_2^{\cdot -}$ and aliphatic bromides is apparently too great to allow such a transfer to occur. The halfwave potential of

$O_2^{\cdot -}$ is -0.77 V(SEC) in DMF² and is favorably close to that of a nitro-aromatic halide, i.e. p-bromonitrobenzene ($E_{1/2} = -1.15$ V).²⁷ On the other hand, the halfwave potential of an alkyl bromide is quite different, i.e. the $E_{1/2}$ for 1-bromobutane is -2.23 V(SEC) in DMF.²⁸

Electron transfer theory²⁹ allows the rate constant of the reaction shown in equation 19 to be estimated, e.g., where RBr is 1-bromobutane. The difference in potential between the redox couples $O_2/O_2^{\cdot -}$ and $n\text{-BuBr}/n\text{-BuBr}^{\cdot -}$ is about 1.46 V, thus, the equilibrium constant, K_{12} , of reaction (19) is approximately 10^{-25} as evaluated by the Nernst equation. Equation 22 relates the rate constant, k_{12} , of the electron transfer step to the equilibrium constant, K_{12} , and the rate constants of the two exchange reactions (20) and (21). The value of f is assumed to be unity and k_{11} and k_{22} can be assigned values of $10^{2.5} \text{ M}^{-1} \text{ s}^{-1}$ and $10^6 \text{ M}^{-1} \text{ s}^{-1}$, respectively.³⁰



$$k_{12} = (k_{11} k_{22} K_{12} f)^{1/2} \quad (\text{eq. 22})$$

Using equation 22, the rate constant, k_{12} , for the electron transfer step of (19) is estimated to be $\sim 10^{-9} \text{ M}^{-1} \text{ s}^{-1}$ for the example, 1-bromobutane. Reaction (19) is quite slow but possibly even slower since the value assigned to k_{22} is an upper limit.³⁰ From both the unreactivity of the bridgehead bromide and the extremely slow predicted rate, a strong contribution of electron-transfer does not adequately account for the trend in relative reactivities observed for $O_2^{\cdot -}$ reactions with substrate structural change.

Another more viable approach is perhaps that of selectivity versus reactivity. There are indications that for reactions with potent nucleophiles, a leveling effect on substrate structure is observed.³¹ The selectivity of a reagent toward a series of substrates usually decreases as the reactivity of the reagent increases. This relationship is usually interpreted as being the result of the transition state increasingly "resembling" reactants as the energies of the reactant and transition state becomes more nearly equal.³² The S_N2 reaction of KO_2 with 1-bromobutane has a very low enthalpy of activation (Table VII) and the reaction is exothermic by about 10.5 kcal/mole.^{33,34} From Hammond's postulate, this exothermicity implies an early transition state which reflects the lack of selectivity exhibited by superoxide.

The rate constants given in Table II indicate that O_2^- is a potent nucleophile. Since, at present, an absolute scale of nucleophilic reactivity in solution is not available, the assignment of a numerical nucleophilicity (e.g., Swain and Scott nucleophilic constant) to O_2^- would be of little comparative value. Brauman, et al.³⁵ goes as far as to suggest that it is impossible to establish any general scale or order of nucleophilicity without direct reference to the specific reaction. An example of the inherent difficulty in comparing the nucleophilicities of different anions is demonstrated by the change in reactivity order in going from protic to dipolar aprotic solvents. The nucleophilic order observed in protic solvents is $I^- > SCN^-$, $CN^- > N_3^-$, $Br^- > Cl^- > CH_3CO_2^-$ with methyl iodide, whereas in dipolar aprotic solvents the order becomes $CN^- > CH_3CO_2^- > Cl^-$, Br^- , $N_3^- > I^- > SCN^-$.³⁶ Another example of the difficulty in comparing nucleophilicities deals with symbiotic effects³⁷ on the rates

of nucleophilic displacement reactions. This effect suggests increased reaction rates for nucleophiles that resemble the leaving group of the substrate with respect to hardness or softness. Consequently, tosylates (hard) should react rapidly with hard nucleophiles and iodides (soft) should react rapidly with soft nucleophiles.

Since an absolute scale of nucleophilicity was not available, a qualitative comparison of the present kinetic values for $O_2^{\cdot -}$ with other nucleophiles reacting with the same substrates in dipolar aprotic solvent (Table IV) should reveal the reactivity exhibited by superoxide. Although there were relatively few data in DMSO solvent for direct comparison, it appeared that the dipolar aprotic solvents DMSO, DMF, and CH_3CN all exert similar effects on reaction rates.³⁸ The similarity of reactivity was demonstrated by comparing the second-order rate constants for the reaction of N_3^- with 1-bromobutane in the four dipolar aprotic solvents listed in Table IV.

The last six entries in Table IV were included due to the nonavailability of comparable data with the substrates of this study. Although I^- is a better leaving group than Br^- , the actual enhancement of reaction rates observed for CH_3I over CH_3Br is not readily estimated. Streitwieser²⁶ gave a ratio of 3:1 for the average relative displacement rate of the leaving groups I^- and Br^- for a number of reactions under various solvent conditions. Perhaps a more realistic value was determined by comparing rate constants listed in Table IV for CH_3I and CH_3Br reacting with Cl^- , N_3^- , and SCN^- . The data suggested that the CH_3I was at least 6 times more reactive than CH_3Br towards nucleophilic displacement under the same solvent conditions. This implied that the superoxide S_N2 reaction with CH_3Br (in DMSO) was conservatively one order of magnitude faster than that of the

Table IV.

Rate Constants for Reactions of Various Nucleophiles with Organic
Bromides in Dipolar Aprotic Solvents at 25° ³⁶

Reactants	Solvent	k_2 ($M^{-1} \text{ sec}^{-1}$)
$\text{CH}_3\text{Br} + \text{Cl}^-$	DMF	4.0×10^{-1}
$\text{CH}_3\text{Br} + \text{N}_3^-$	DMF	4.0×10^{-1}
$\text{CH}_3\text{Br} + \text{SCN}^-$	DMF	1.3×10^{-2}
$\text{CH}_3\text{Br} + \text{I}^-$	Me_2CO	4.0×10^{-1}
$\text{CH}_3(\text{CH}_2)_3\text{Br} + \text{N}_3^-$	Me_2CO	3.0×10^{-2}
$\text{CH}_3(\text{CH}_2)_3\text{Br} + \text{N}_3^-$	DMF	2.0×10^{-2}
$\text{CH}_3(\text{CH}_2)_3\text{Br} + \text{N}_3^-$	CH_3CN	4.0×10^{-2}
$\text{CH}_3(\text{CH}_2)_3\text{Br} + \text{N}_3^-$	DMSO	1.0×10^{-2} ⁴⁰
$\text{CH}_3(\text{CH}_2)_3\text{Br} + \text{C}_6\text{H}_5\text{S}^-$	DMF	5.0×10^{-1}
$(\text{CH}_3)_2\text{CHBr} + \text{N}_3^-$	DMF	4.0×10^{-3}
$(\text{CH}_3)_2\text{CHBr} + \text{C}_6\text{H}_5\text{S}^-$	DMF	2.0×10^{-1}
$\text{CH}_3\text{I} + \text{CN}^-$	DMF	3.2×10^2
$\text{CH}_3\text{I} + \text{AcO}^-$	DMF	2.0×10^1
$\text{CH}_3\text{I} + \text{CH}_3\text{O}^-$	DMSO	6.3×10^1
$\text{CH}_3\text{I} + \text{SCN}^-$	DMF	8.0×10^{-2}
$\text{CH}_3\text{I} + \text{N}_3^-$	DMF	3.2×10^0
$\text{CH}_3\text{I} + \text{Cl}^-$	DMF	2.5×10^0

heretofore acclaimed CN^- nucleophile. The only nucleophile exhibiting reaction rates that even rival those of O_2^- was thiophenoxide ($\text{C}_6\text{H}_5\text{S}^-$). Although more directly comparable data for nucleophiles reacting in DMSO would be desirable, it is still logical from the available data to conclude that O_2^- is a powerful nucleophile.

Why O_2^- is such a potent nucleophile is not readily explained. There are numerous factors (Bunnett lists 17)³⁹ involved in determining the relative nucleophilicity of anions toward organic substrates. The most widely mentioned factors are solvation, polarizability, basicity and the "alpha effect."⁴¹ A brief discussion of each of these factors with particular reference to O_2^- is given in the following text.

Before a nucleophile can attack carbon, the shell of solvent molecules surrounding the nucleophile must be removed.⁴² The importance of this desolvation process was demonstrated above in the reversal of nucleophilic order in going from protic to dipolar aprotic solvents, where the aprotic nature precludes solvation of the anion by hydrogen bonding. Thus, in dipolar aprotic solvents, anions apparently are poorly solvated and therefore are considerably more reactive than the heavily solvated species which occur in protic solvents. For solutions of KO_2 in DMSO, the superoxide anion radical should be solvated only by dipolar attractions which should enhance reactivity relative to hydrogen bonding solvents. The degree to which DMSO affects solvation of superoxide is discussed in the following section (Counter-ion effects).

Polarizability is one of the two parameters used by Edwards⁴³ to correlate nucleophilic reactivity. A common reason suggested for the dependence of polarizability is that as a reaction commences, the electron cloud is distorted toward the substitution site with greater ease for

polarizable nucleophiles.⁴⁴ This results in appreciable bonding between the entering anion and the substrate with little attendant increase in steric strain at the transition state. Since $O_2^{\bar{}}$ is made up of two electro-negative second row oxygen atoms, it is not expected to be particularly polarizable. Also, the effect of polarizability is the most pronounced in protic solvents and becomes less important in determining nucleophilicity in dipolar aprotic solvents.⁴⁵ Thus, due to both the low polarizability of $O_2^{\bar{}}$ and the fact that this effect is not as prominent in dipolar aprotic solvents, polarizability does not account for the observed nucleophilicity of superoxide.

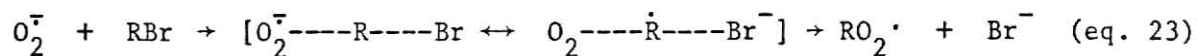
There is an obvious connection between nucleophilicity and basicity, since basicity is determined by the tendency to bond to a proton and nucleophilicity is determined by the tendency to bond to carbon. Edwards⁴³ uses the pK_a of the conjugate acid of the nucleophile as the second parameter in correlating S_N2 reaction rates. In the cases where attachment to a common atom is compared (i.e., all oxygen nucleophiles) the agreement between basicity and nucleophilicity is good. For example, both basicity and nucleophilicity decrease in the following series: $EtO^- > PhO^- > AcO^- > NO_3^-$.⁴³ This correlation breaks down upon changing the attacking atom or upon large variation in structure, i.e., the thiophenoxide anion is a much more effective nucleophile than the phenoxide anion, although it is the weaker base of the two.⁴⁴ With a pK_a of 4.88⁴⁶ for its conjugate acid, $O_2^{\bar{}}$ is not particularly basic. In comparison, the conjugate acid of the acetate anion (AcO^-) exhibits a comparable pK_a (i.e., 4.76)⁴⁵ but $O_2^{\bar{}}$ is a much more effective nucleophile.

Edwards and Pearson⁴⁷ recognized a class of nucleophiles which show exceptionally high reactivity toward a variety of substrates relative to

their basicity toward hydrogen. This class of nucleophiles is structurally characterized by an unshared pair of electrons on the atom adjacent or α -to the nucleophilic atom. The resulting rate enhancement is known as an "alpha-effect." For example, in the nucleophilic displacement of bromide ion from benzyl bromide, the hydroperoxide anion is about thirty-five times more reactive than the hydroxide ion, even though the latter is the stronger base by four orders of magnitude.⁴⁴ Due to the second oxygen atom adjacent to the nucleophilic site, O_2^- can be considered an "alpha effect" nucleophile. The inconsistent behavior of alpha nucleophiles makes the prediction of alpha effects rather risky and at the same time confirms the complicated nature of nucleophilic substitution. No single cause appears to account for all data but four categories have been used in explaining the enhanced reactivity displayed by α -effect nucleophiles.⁴⁸

First, the ground state destabilization due to considerable $p_\pi - p_\pi$ overlap has been suggested to describe the increased reactivity of α -nucleophiles. Adding electrons to the oxygen molecule causes a widening of the O-O distance (i.e., $O_2 = 1.21 \text{ \AA}$, $O_2^- = 1.28 \text{ \AA}$)⁴⁹ with a concomitant weakening of the bond which is indicative of higher repulsion energy. Secondly, since it is postulated that in the transition state of a displacement reaction a pair of electrons tends to leave the nucleophile, then α -effect can be partially explained in terms of the stabilization of the transition state due to orbital overlap of the alpha lone pair with the incipient positive charge developing at the nucleophilic center. The third category is concerned with solvation; however, recent data suggest that specific solvation should not be a major factor in determining the α -effect.⁵⁰ Finally, the thermodynamic product stability has been proposed as a factor but, as with solvation, this is not a dominant factor.

It is possible that an important factor in determining $O_2^{\cdot -}$ nucleophilicity is a significant electron-transfer contribution in the transition state (eq. 23). This transition state contribution should not be confused



with the electron-transfer followed-by radical coupling mechanism shown in equation 19. Since similar contributions can be drawn for all nucleophiles, the key factor in this particular instance is the inherent stability of molecular oxygen.

As indicated in Table II there were three alkyl bromides for which absolute rate constants were not obtained. The reaction of neopentyl bromide with $O_2^{\cdot -}$ gave stopped-flow spectrophotometric results that showed no dependence upon the substrate concentration. Also, tert-butyl bromide did not adhere to pseudo-first-order kinetics. In both instances, the reactions were slow in comparison to the other substrates of Table II. Finally, 1-bromoadamantane even in high concentration (i.e., 1.0M) gave only a very slow observed reaction rate and, therefore, was assigned a rate of $<1.0 \text{ M}^{-1} \text{ s}^{-1}$.

Counter-ion Effects

Chemical studies of $O_2^{\cdot -}$ in DMSO solvent here employed K^+ , R_4N^+ , or crown ether-complexed potassium ion ($\textcircled{K^+}$) as counter-ions. It has been implied that there is a difference in reactivity of $O_2^{\cdot -}$ due to its counter-ion. This conclusion was based on the observed lack of reactivity for suspensions of potassium and sodium superoxide with alkyl halides, whereas the tetraethylammonium salt exhibited measurable reactivity.¹⁸ The degree to which a counter-ion interacts with its corresponding anion has been shown to affect reaction rates dramatically. Tetraalkylammonium salts are usually

dissociated in organic solvents and their corresponding anions frequently exhibit increased reactivity over alkali metal salts.⁵¹ The extent to which ions are separated has a large effect on the reactivity of the anion. Separated ions are more reactive than their tight ion counterparts since less negative charge of the anionic species is being neutralized by the partner cation.⁵² Crown ethers are very efficient in converting contact ion pairs into separated ions and have been found to substantially increase nucleophilic reactivity.⁵⁰ Liotta and Grisdale coined the term "naked" fluoride to describe the physical effect of complexing KF with crown ether.⁵³ The effect of cation complexation is demonstrated by the kinetic data for nucleophilic displacement on *p*-nitrophenyl diphenylphosphine in toluene. An increase in rate of four orders of magnitude was observed on going from tight ion-paired $t\text{-BuOO}^-\text{K}^+$ to the same species in the crown ether complex form.⁵⁰

The extent to which counter-ion effects influence the reaction rates of $\text{O}_2^{\cdot-}$ in DMSO were studied by two experiments. First, the dependence upon the counter-ion was investigated by determining rate constants for $\text{O}_2^{\cdot-}$ reactions using either K^+ or K^+ in the presence of a large excess of Et_4N^+ cations. Secondly, 18-crown-6 ether was used in complexing K^+ to determine the role of ion pairing on reaction rates. Second-order rate constants were obtained by stopped-flow techniques under pseudo-first-order conditions as described previously. The results of the reaction of 1-bromobutane with $\text{O}_2^{\cdot-}$ under various cation conditions along with the rate constant for the reaction with KO_2 are listed in Table V.

The $\text{O}_2^{\cdot-}$ solutions used in determining rate constants listed were prepared by the following methods. Initially, use of electrogenerated $\text{Et}_4\text{N}^+\text{O}_2^{\cdot-}$ was attempted but decay of $\text{O}_2^{\cdot-}$ was not observed by monitoring the U.V.

absorption in stopped-flow experiments. However, solutions of $\text{Et}_4\text{N}^+\text{O}_2^-$ prepared by adding a DMSO solution approximately 0.002 M in KO_2 to 0.05 M tetraethylammonium perchlorate in DMSO resulted in an absorbance change upon reaction with 1-bromobutane. An assumption was made that for this solution, O_2^- pairs with the tetraalkylammonium cation since it is in 25-fold excess. The crown ether experiments were conducted using 18-crown-6-ether⁵⁴ in concentrations from 1.0×10^{-3} M to 5.0×10^{-2} M with little variance observed in second-order rate constants.

Table V.

Rate Constants for the Reaction of O_2^- with 1-bromobutane
in DMSO at 25.0° under Various Counter-ion Conditions

System	k_2 ($\text{M}^{-1}\text{s}^{-1}$)
$\text{K}^+\text{O}_2^- + \text{n-BuBr}$	$(1.5 \pm 0.1) \times 10^2$ ^a
$\text{Et}_4\text{N}^+\text{O}_2^- + \text{n-BuBr}$	$(1.5 \pm 0.1) \times 10^2$
$(\text{K}^+) \text{O}_2^- + \text{n-BuBr}$	$(1.7 \pm 0.1) \times 10^2$

^aFrom Table II.

The results furnish some information concerning the state of dissociation exhibited by KO_2 dissolved in DMSO. The rate constants for the two superoxide counter-ions shown in Table V are the same, thus, the potassium salt of O_2^- is evidently as reactive as tetraalkylammonium superoxide. This indicated that there was no significant ion-pairing in either case.

The effect of an ion-pairing equilibrium on the reaction rate of O_2^- can be partially determined by comparing the rate of KO_2 with that of the

crown ether complexed form. If KO_2 in DMSO was in a contact-ion pair, than a substantial increase in $\text{O}_2^{\cdot -}$ should have been observed upon complexation of potassium ion. Since no significant increase in rate was found by addition of crown ether, then KO_2 in DMSO apparently exhibited no appreciable ion-pairing.

Therefore, in DMSO solvent, $\text{O}_2^{\cdot -}$ finds itself essentially solvent-neglected, which is characteristic of polar aprotic solvents. This is accounted for by the ability of DMSO to bring about dissociation of ion pairs by "burying" the metallic cations in a solvent cluster.⁵² The lack of solvent interaction between DMSO and $\text{O}_2^{\cdot -}$ imparts higher chemical potential to this anionic species, and perhaps the term "naked"⁵³ is appropriate to describe its state of solvation.

Since $\text{O}_2^{\cdot -}$ reactions have been reported in other dipolar aprotic solvents, attempts were made at determining rate constants in acetonitrile. Stopped-flow experiments resulted in no absorbance change for $\text{KO}_2/\text{CH}_3\text{CN}$ solutions mixed with alkyl bromide solutions. No satisfactory explanation for these preliminary observations is available at present.⁵⁵

Dihalide Series

The effect of steric hindrance upon the rates of $\text{O}_2^{\cdot -}$ reacting with alkyl bromides was demonstrated in Table II. This section deals with the effects of polar substituents (i.e., halogen atoms) on the reaction rates for bromide displacement by superoxide.

Halogen atoms acting as substituents rather than leaving groups effect the $\text{S}_{\text{N}}2$ reactivity of the system in varying degrees depending partially upon their position relative to the reaction center. Placement of halogen atoms at a distance from the reacting center influences the reactivity of the system by their electron-withdrawing inductive effects.⁵⁶ On the other

hand, halogen substitution in the α -position, which causes substantial reduction in reactivity, is due to several reasons.⁵⁷ Halogen atoms, which are more electronegative than carbon, tend to destabilize the developing positive charge on carbon and, in turn, increase the energy of the transition state. Although this is a predominant effect of substitution in the β -position, it is even more pronounced in the α -position. Since reactivity is decreased by introduction of either an α -methyl (electron donating) or an α -halogen (electron withdrawing), it is likely that the decrease is at least partially due to steric hindrance. Finally, and closely related to steric hindrance, is the effect called neighboring orbital overlap, which is due to electron repulsion between the incoming nucleophile and the α -position halogen.

The effects of halogen atom substitution on the reactivity of alkyl bromides toward O_2^- were determined by obtaining second-order rate constants for a series of α -, β -, and γ -halogen substituted systems. Rate constants were determined by stopped-flow techniques and are listed in Table VI. Since displacement of chloride by O_2^- is much slower than that of bromide, the rate constants given are assumed to be for bromide displacement only.

The largest effect on reactivity was caused by α -halogen substitution as indicated by the relative rates shown in Table VI. These relative rates for the first two entries are characteristic of an $\text{S}_{\text{N}}2$ process. For example, the nucleophilic displacement reaction of KI in acetone with the same alkyl bromide series (Et- , $\text{ClCH}_2\text{-}$, $\text{BrCH}_2\text{-}$) gave the relative rates 1.0:0.13:0.041.⁵⁷

The effect of β -halogen substituents on the reactivity was in the anticipated direction but of less magnitude than usually observed, i.e., the rates of reaction of β -haloethyl bromides with thiophenoxide ion in methanol are a factor of five less than that of ethyl bromide.⁵⁶

In contrast to the decrease in reactivity exhibited by the other entries, the γ -halogen substituted example showed increased reactivity. This was a trend that had been previously observed for S_N2 reactions. Kiener and Richter⁵⁸ reported that a chlorine atom in the β -position to a given substituent group has a reactivity which is less than that observed when the chlorine atom is in the γ -position to the same group. Also, Hine and co-workers⁵⁹ reported data for reactions of thiophenoxide in methanol with dihalides where greater reactivity of the γ -chloro-substituted alkyl bromide over the β -chloro-substituted homolog was exhibited. A satisfactory explanation for these observations has not been advanced.

Table VI.

Rate Constants for the Reaction of KO_2 with Halogen Substituted Alkyl Bromides in DMSO at 25.0°

Dihalide	$k_2 (M^{-1}s^{-1})$	Relative Rate ^b
$BrCH_2Br$ ^a	$(1.28 \pm 0.02) \times 10^1$	0.037
$ClCH_2Br$	$(4.0 \pm 0.2) \times 10^1$	0.11
$BrCH_2CH_2Br$ ^a	$(2.42 \pm 0.02) \times 10^2$	0.69
$ClCH_2CH_2Br$	$(2.67 \pm 0.02) \times 10^2$	0.76
$ClCH_2CH_2CH_2Br$	$(4.71 \pm 0.04) \times 10^2$	1.35
CF_3CH_2Br	c	-
$BrCH_2CO_2C_2H_5$	c	-

^aCorrected for statistical factor of two.

^bRelative to ethyl bromide ($350 M^{-1}s^{-1}$).

^cA second-order rate constant was not obtained due to lack of reproducible data.

The rate constants derived from S_N2 reactions of dihalides can sometimes be used to calculate a ρ^* value via a Taft correlation. For example, Streitwieser⁶⁰ determined $\rho^* = -0.606$ for the S_N2 reaction of $RCH_2Br + PhS^-$ in methanol, which indicated a slight positive charge being formed in the transition state. An attempted Taft plot using data from Table VI is shown in Figure 4. Although the plot reveals no significant correlation, it does demonstrate at most a very slight influence due to inductive effects. This implies that little charge was formed in the transition state, which is characteristic of a concerted S_N2 process. There is possibly a "canceling out" of the expected effect of polar substituents due to an electron-transfer contribution in the transition state.

Two additional polar substituted alkyl bromides were included in Table VI, although no rate constants were listed. The reaction of these substrates with O_2^- was attempted for use in a Taft correlation. In the case of ethyl bromoacetate, there was a definite change in absorbance but dependence upon substrate concentration did not adhere to pseudo-first-order kinetics. Also, there is the possibility of competing reactions since this substrate can react with superoxide by oxidative cleavage. For CF_3CH_2Br , non-reproducible results were obtained with non-adherence to pseudo-first-order kinetics.

Enthalpy and Entropy of Activation

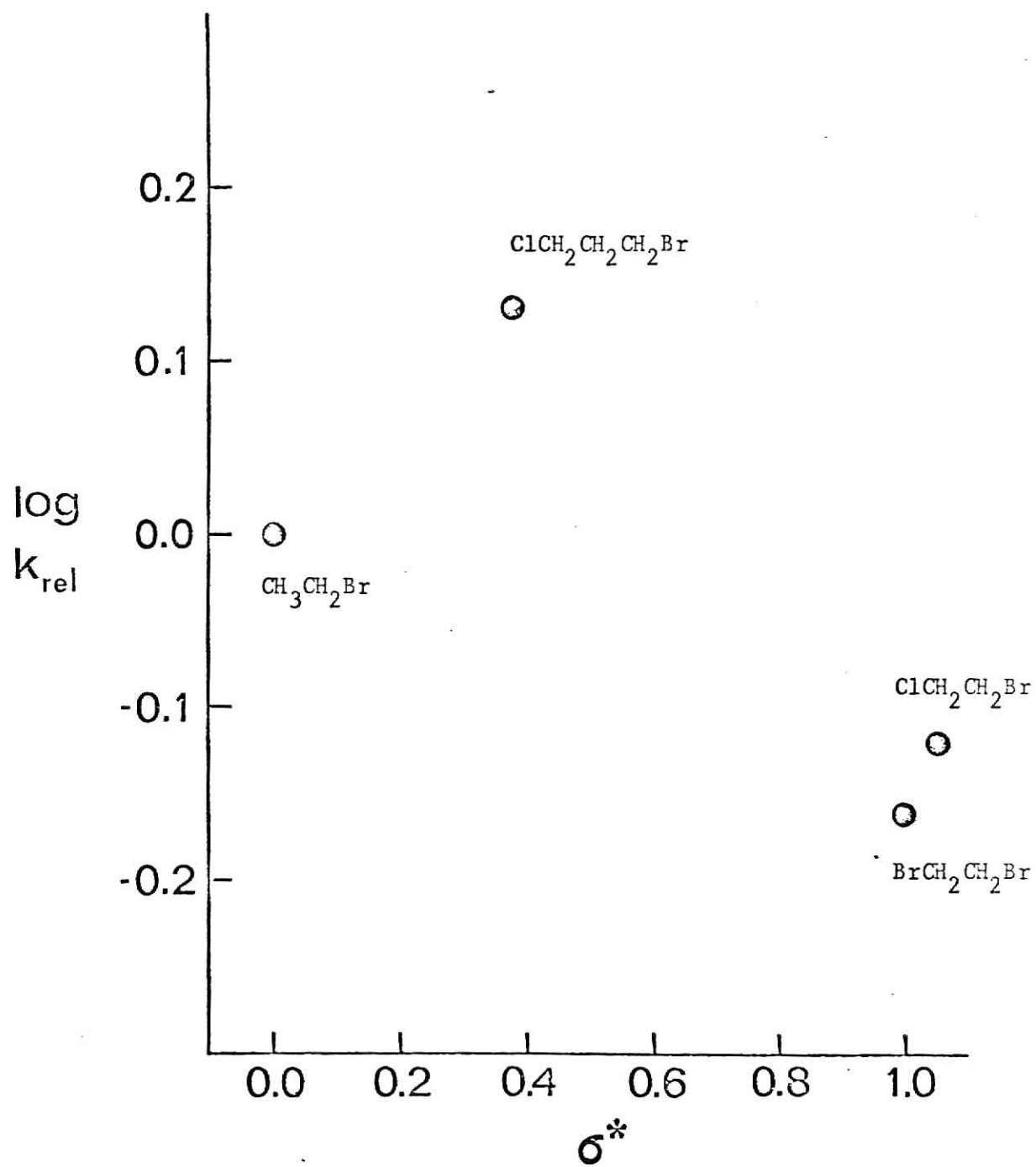
The variation of reaction rate with temperature is usually expressed as the Arrhenius equation (eq. 24) in the integrated form. The enthalpy

$$k = Ae^{-E_a/RT} \quad (\text{eq. 24})$$

of activation, ΔH^\ddagger , is related to the Arrhenius activation energy by equation 25. Actually, the uncertainty in the energy of activation is usually

$$\Delta H^\ddagger = E_a - nRT \quad (\text{eq. 25})$$

Figure 4. Plot of $\log k_{\text{rel}}$ for halogen substituted alkyl bromides versus Taft polar substituent constants, ρ^* . Values of ρ^* are from reference 25, page 415. The k_{rel} values are from Table VI.



about the same magnitude as the difference between the two parameters.⁶¹ Using the pre-exponential factor, A, from eq. 24, the entropy of activation, ΔS^\ddagger , can be calculated (eq. 26).

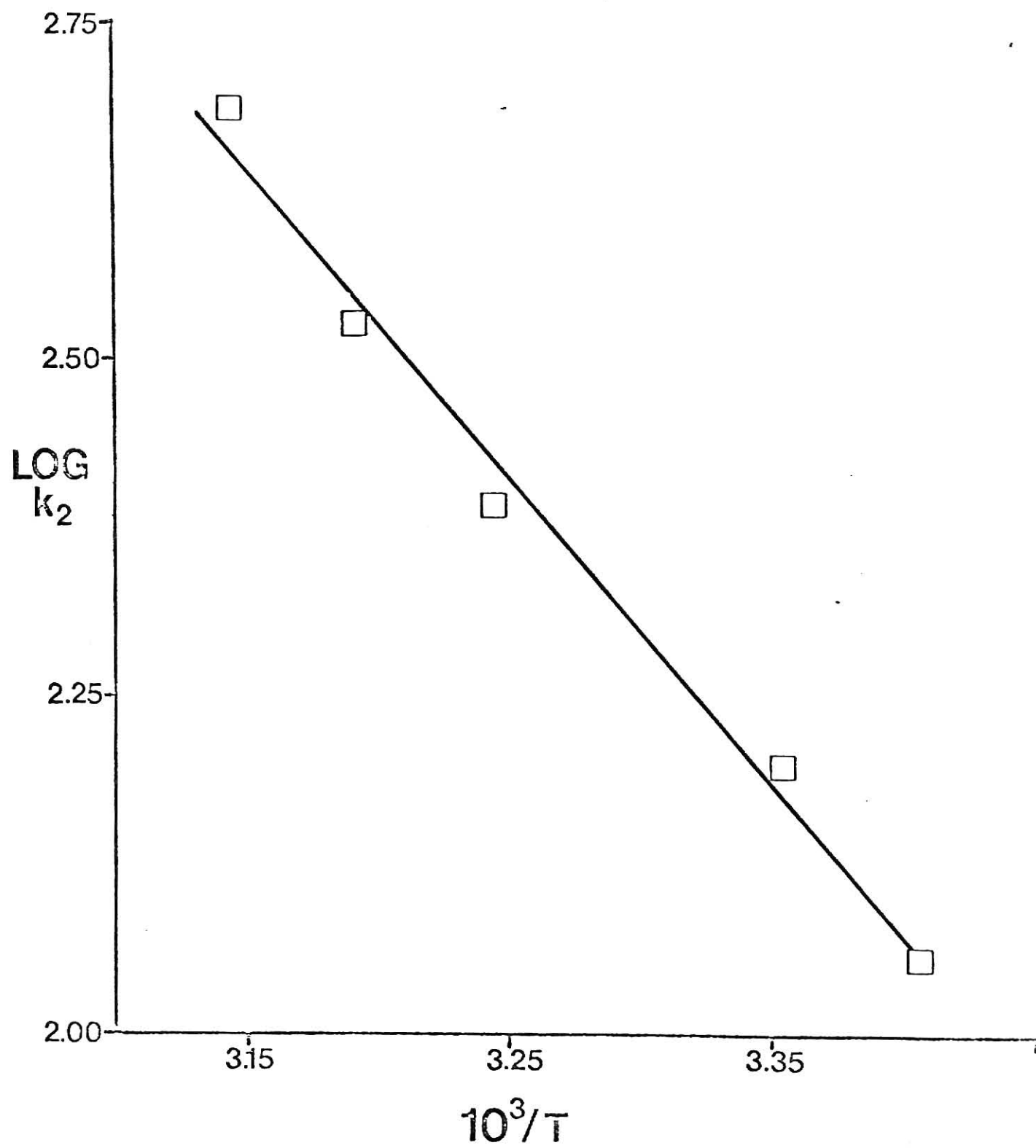
$$A = \left(\frac{kT}{h}\right) e^n e^{\Delta S^\ddagger/R} \quad (\text{eq. 26})$$

Of the two activation parameters, ΔS^\ddagger and ΔH^\ddagger , the former offers the most insight into the nature of the activated complex, as well as reaction mechanisms.⁶² For example, because entropy is measure of randomness or disorder, a negative ΔS^\ddagger implies that the transition state is more ordered than the reactants. This is the normal trend observed in most bimolecular reactions, since for reaction to take place two molecules in random motion must come together. For S_N2 Walden inversion reactions, where specific backside attack is required, a significantly negative ΔS^\ddagger value is usually observed. Typical ΔS^\ddagger values for bimolecular displacement reactions are in the range of -10 to -30 e.u.⁶²

Second-order rate constants for the reaction of KO_2 with 1-bromobutane in DMSO over a 25° temperature range were determined using stopped-flow techniques. Reaction temperatures were controlled by a Lauda/Brinkmann circulator. Temperature readings were taken at the cuvette/mixing jet assembly and the water bath which surrounds the valve block and drive syringes. The temperature values listed in Table VII and used in calculations were the average of these two readings.

Calculation of activation parameters from the data in Table VI was accomplished by two methods: 1) by a computer program which does a least square analysis⁶³ and 2) as a check, by hand employing equations 24-26. An Arrhenius plot of $\log k_2$ versus $1/T$ is given in Figure 5 where the

Figure 5. Arrhenius plot of $\log k_2$ versus $1/T$ for the reaction of KO_2 with 1-bromobutane in DMSO.



curve drawn is that obtained from a least square fit of the data. The computer calculated values of ΔH^\ddagger and ΔS^\ddagger for the reaction of KO_2 with

Table VII.

Rate Constants for the Reaction of KO_2 with 1-bromobutane
in DMSO at Various Temperatures

Temp, °C \pm 0.1°	k_2 ($\text{M}^{-1}\text{s}^{-1}$)
20.3	1.14×10^2
25.4	1.60×10^2
35.2	2.46×10^2
40.2	3.38×10^2
45.0	4.89×10^2

$n\text{-BuBr}$ are 9.8 ± 1 kcal/mole and -15.6 ± 1 e.u., respectively. Calculation of ΔH^\ddagger and ΔS^\ddagger from equations 24-26 yielded the same values, within the specified error limits.

For comparison purposes, the activation parameters for various nucleophiles reacting with alkyl bromides in dipolar aprotic solvents are presented in Table VIII, along with the values for superoxide. The low ΔH^\ddagger for superoxide is reflected in its nucleophilic reactivity. The entropy of activation for O_2^- is indicative of a bimolecular displacement reaction and also discloses some information about the degree of solvent interaction. If solvent molecules were being released in the transition state, a more positive entropy of activation would be expected. For example, the reaction of N_3^- with 1-bromobutane in DMSO exhibits a positive ΔS^\ddagger due to strong solvation of the nucleophile.⁵²

Table VIII
Energies and Entropies of Activation
of Some Displacement Reactions

<u>Nucleophile</u>	<u>Substrate</u>	<u>Solvent</u>	<u>E_a</u>	<u>ΔS[‡]</u>	<u>Reference</u>
O ₂ ⁻	<u>n</u> -BuBr	DMSO	11.0	-15.6	b
I ⁻	<u>n</u> -BuBr	acetone	20.5	-13.9	c
Cl ⁻	<u>n</u> -BuBr	acetone	17.5	-21.1	c
N ₃ ⁻	<u>n</u> -BuBr	DMSO	16.91	+ 1.62	52
C ₆ H ₅ S ⁻	<u>n</u> -BuBr	DMF	13.3	- 9.4 ^a	65
N ₃ ⁻	MeBr	DMF	16.7	-12.9 ^a	64
SCN ⁻	MeBr	DMF	16.0	-17.5 ^a	64

^aCalculated from log A using eq. 26.

^bFrom this study, E_a value was calculated from eq. 25.

^cFrom reference 26, Table X.

Control Experiments

In the course of this study, several types of experiments were conducted that can be grouped together as control experiments. These experiments were conducted to verify the stability of KO₂ in DMSO and the overall stoichiometry of the reaction of O₂⁻ with alkyl bromides. Also included in this section is a comparison of rate constants determined by a stopped-flow to those obtained in previous electrochemical studies.

Since rate constants in this study were determined by following O₂⁻ decay by U.V. absorption, it is critical that O₂⁻ is stable in DMSO over a reasonable time period. Fee and Hildenbrand observed that electrogenerated O₂⁻ behaves normally in DMSO and CH₃CN but abnormally in DMF with regard to oxygen evolution upon addition of water.²¹ Dietz, et al.,¹⁷ however, determined

that a 0.1M solution of superoxide in DMF had a half life of 76 minutes at 0°. The decay process of $O_2^{\cdot -}$ in dipolar aprotic solvents is not known.

To check the stability of $O_2^{\cdot -}$ in DMSO, a stopped-flow experiment was run as before, with the exception that the alkyl halide/DMSO solution was replaced by DMSO. The decay of this KO_2 /DMSO solution was followed by monitoring the absorption at 275 nm. Results of this experiment showed essentially no decay over a time period much longer than that employed in stopped-flow experiments using alkyl halide reactants. This observation rules out any appreciable background decay of $O_2^{\cdot -}$ so that in stopped-flow experiments reactions of $O_2^{\cdot -}$ can be attributed solely to the alkyl halide.

Another integral part of this study is the overall stoichiometry for the reaction of superoxide with an alkyl halide. From the work of Dietz,¹⁷ et al., there appears to be a 2:1 overall stoichiometry based on the initial S_N2 reaction being followed by a reduction step (see General Approach section, page 8). However, there are various conceivable reaction modes for the reactive peroxy radical formed in the initial reaction, other than reduction by $O_2^{\cdot -}$ to the peroxy anion. One such mode is simple radical-radical recombination via the Russell mechanism.⁶⁶ If the dimerization of peroxy radicals were competing favorably with the $O_2^{\cdot -}$ reduction step, then the concerted cyclic reaction mechanism would predict formation of aldehydes and ketones in addition to alcohols. In fact, San Filippo and Valentine¹² reported formation of aldehydes and ketones up to 12% under conditions comparable to those of this study. On the other hand, Johnson and Nidy¹³ reported no aldehyde or ketone formation. In order to substantiate the assumed stoichiometry, measurement of the amount of KO_2 reacting with an alkyl bromide was approached experimentally.

The basis of O_2^- determination usually relies on measurement of O_2 evolution upon reaction with a proton source (eq. 1). Evolved O_2 is then measured by a calibrated oxygen electrode or simply by volume. One inherent problem with simply quenching O_2^- with water is the erratic secondary decomposition of hydrogen peroxide. A procedure reported by Seyb and Kleinberg⁶⁷ alleviates this decomposition of H_2O_2 by using a glacial acetic acid-diethyl phthalate mixture. This method was adapted for stoichiometric determinations of KO_2 reacting with 1-bromobutane in DMSO. The measurement of evolved oxygen was accomplished by water displacement in an inverted buret.

Typically, a weighed amount of KO_2 was covered with DMSO and to this slurry was added 1 mmole of an alkyl bromide. The resulting O_2 evolution was recorded and then a 4:1 (by volume) acetic acid-n-butyl phthalate mixture was added. The amount of oxygen evolved in the second reaction corresponded to the amount of unreacted KO_2 and, by subtraction from the initial amount, a value for the KO_2 that reacted was obtained.

The results for the reaction of KO_2 with 1-bromobutane gave an overall stoichiometry of $1.8 \pm 0.2:1$ as determined by six experiments. This stoichiometry, although somewhat lower than predicted, was within experimental error and did tend to verify the 2:1 ratio used in kinetic calculations of this study.

As was indicated in the background section, the rate constants for several alkyl halides reacting with electrogenerated O_2^- have previously been reported (Table I). Although one comparison already exists, namely, 1-bromobutane, an additional example under more similar reaction conditions would be desirable. To accomplish this second comparison, a stopped-flow experiment was conducted for the reaction of KO_2 with 1-chlorobutane in DMSO.

A second-order rate constant was derived under pseudo-first-order conditions using 0.1M 1-chlorobutane in DMSO. This particular substrate reaction with $O_2^{\cdot -}$ has a rate constant determined by Merritt and Sawyer¹⁸ and it is compared to that obtained by stopped-flow in Table IX.

Table IX.

Comparison of Reported $O_2^{\cdot -}$ Rate Constants to Those of This Study

Reactant	Temp. °C	Cation	Solvent	k_2 ($M^{-1}s^{-1}$)	Method	Reference
<u>n</u> -BuBr	0	N^+Bu_4	DMF	5.0×10^2	i_k/i_d ^a	17
<u>n</u> -BuBr	25.0	K^+	DMSO	1.5×10^2	S.F. ^b	d
<u>n</u> -BuCl	28.0	N^+Et_4	DMSO	3.2	C.P. ^c	18
<u>n</u> -BuCl	25.0	K^+	DMSO	1.3 ± 0.2	S.F. ^b	d

^aDetermined by fitting of potential step reduction data to i_k/i_d vs. $\log kt$ working curves.

^bStopped-flow spectrophotometry

^cChronopotentiometry

^dThis study

The lack of agreement is evident from Table IX between the rate constant derived by Dietz for 1-bromobutane with that obtained from stopped-flow techniques. Even though the rate constants appear to be of the same order of magnitude, the electrochemical value was determined at 0°, which imparts even a greater difference. The rate constant extrapolated from the Arrhenius plot (Figure 5) is $30 M^{-1}s^{-1}$ at 0°. The variations can only partially be attributed to the different solvents and counter-ions employed and thus may be due to the methods of determination. A better comparison is between the two 1-chlorobutane values listed where DMSO was used mutually. Experimental evidence in DMSO indicates little or no variance in

reactivity of $O_2^{\cdot -}$ due to the cation. The temperature difference between the two determinations is small so that experimental methods again appear to be the major source of disagreement.

Electrochemical Studies of Superoxide

The reduction of oxygen to $O_2^{\cdot -}$ in aprotic solvents has been demonstrated by several workers.^{68,69} The intent of electrochemical generation of $O_2^{\cdot -}$ in this study was to obtain tetraalkylammonium superoxide for stopped-flow kinetic determinations. This section discusses the use of coulometry for the preparative scale reduction of oxygen and the analysis of subsequent solutions of $O_2^{\cdot -}$ by ultraviolet and electron spin resonance spectroscopy. Also included in this section are the results from cyclic voltammetry experiments of oxygen in DMSO.

Controlled-potential electrolysis was carried out in an all-glass cell using a stirred mercury cathode, a platinum foil anode separated from the cathode compartment by a sintered glass disc, and a silver wire reference electrode. Oxygen, dried by passage through a $CaCl_2$ drying tower, was continuously bubbled through the cathodic solution during electrolysis. Tetraethylammonium perchlorate (TEAP) was used as a supporting electrolyte. The potential of the working electrode was maintained by a controlled potential coulometer⁷⁰ typically preset at -1.0V.

To achieve similar concentrations as those prepared using KO_2 , between 20 and 40 coulombs were passed through 40 ml of DMSO solution (0.1M TEAP). The resulting solution was slightly yellow and the ultraviolet spectrum was identical to that obtained for KO_2 /DMSO solutions. Addition of an alkyl bromide to the $Et_4N^+O_2^{\cdot -}$ solution resulted in a decrease in absorption at 275 nm. The absorbance could also be quenched by addition of dilute HCl.

An esr signal was observed at -115°C for $\text{Et}_4\text{N}^+\text{O}_2^-$ in DMSO (Figure 6a). The spectrum was similar to that reported by Peover and White for $n\text{-Bu}_4\text{N}^+\text{O}_2^-$ in pyridine.² The signal in Figure 6a disappeared upon addition of dilute HCl (Figure 6b). Although the reaction of $\text{Et}_4\text{N}^+\text{O}_2^-$ with RBr was observed by ultraviolet spectroscopy, attempts at stopped-flow kinetic determinations yielded only small, unreproducible absorption changes.

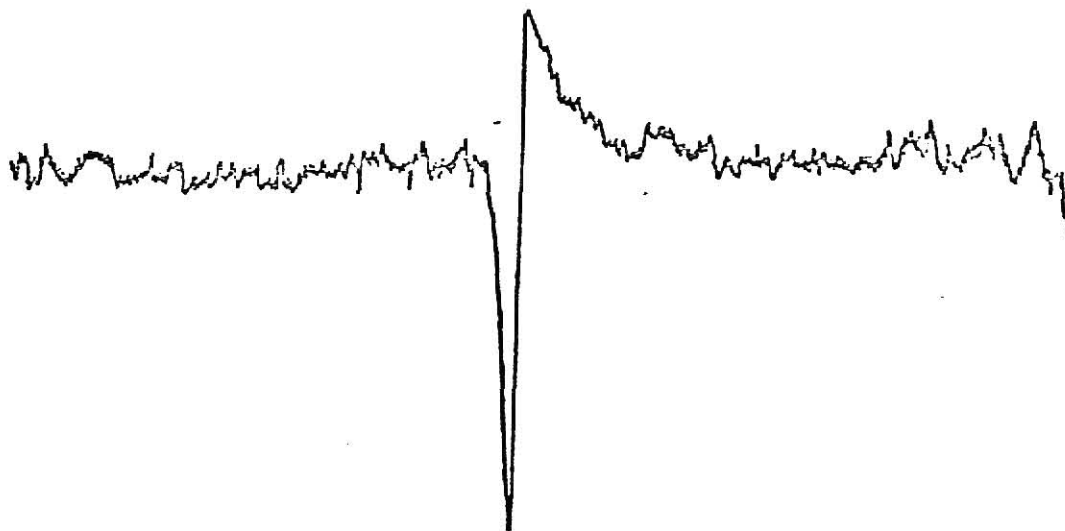
Because stopped-flow did not offer a method for obtaining kinetics of electrogenerated O_2^- , some preliminary work was done to determine the feasibility of using cyclic voltammetry. This method has previously been employed for determination of the stability of O_2^- solutions in various aprotic solvents and to indicate reactions of cathodically generated O_2^- with various substrates.^{17,18,69}

Cyclic voltammetry is a technique that involves the use of a triangular sweep, first in one direction and then symmetrically in the reverse direction. When the process is reversible, the electroactive material that is reduced in the cathodic (forward) sweep is re-oxidized in the anodic (reverse) scan.¹⁸ With cyclic voltammetry, the peak current is proportional to the concentration of the electroactive species. Therefore, if the chemical process is not reversible or a reaction takes place with the cathodically formed product, then the magnitude of the anodic (reverse) peak will be reduced relative to the cathodic peak.

The cyclic voltammogram obtained for a solution of DMSO (0.05M TEAP) saturated with oxygen is shown in Figure 7 where a reversible process is displayed, i.e., $i_p(\text{anodic})/i_p(\text{cathodic}) = 1.0$. This indicated that the superoxide formed in the cathodic sweep did not react but can be reoxidized when the potential sweep was reversed. On the other hand, Figure 8 shows the cyclic voltammogram for a DMSO solution (0.05M TEAP) containing

(A) $\text{Et}_4\text{N}^+\text{O}_2^-$

← 25 GAUSS →



(B) $\text{Et}_4\text{N}^+\text{O}_2^- + \text{dil. HCl}$

← 25 GAUSS →

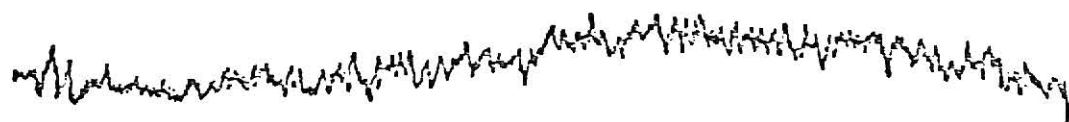


Figure 6. Electron spin resonance spectra of (A) electrogenerated $\text{Et}_4\text{N}^+\text{O}_2^-$ and (B) electrogenerated $\text{Et}_4\text{N}^+\text{O}_2^- + \text{dil. HCl}$. Both spectra were obtained at -115° .

1-bromobutane ($1.8 \times 10^{-3} \text{M}$). In the presence of 1-bromobutane, the anodic peak current was reduced in height, which indicated consumption of superoxide by the alkyl bromide. Also observable in Figure 8 is the appearance of two new anodic peaks at potentials indicative of the oxidation of bromide ions at mercury.¹⁷

A rate constant for $\text{Et}_4\text{N}^+\text{O}_2^-$ can be estimated from the cyclic voltammogram shown in Figure 8. This can be accomplished since the ratio of anodic to cathodic peak current is proportional to the amount of O_2^- reacting and the time for this reaction is known from the scan rate. The actual calculation relies on a working curve constructed for the ratio of peak currents i_a/i_c as a function of $k_f \tau$ and the knowledge of $E_{1/2}$.⁷² Evaluation by this method gave a first-order rate constant, k_f , of 0.2 s^{-1} which, by division of the 1-bromobutane concentration yields a second-order rate constant of $1.0 \pm 0.2 \times 10^2 \text{ M}^{-1} \text{ s}^{-1}$. This rate constant agrees favorably with that obtained by stopped-flow spectrophotometry for KO_2 reacting with the same substrate, i.e., $1.5 \pm 0.1 \times 10^2 \text{ M}^{-1} \text{ s}^{-1}$ (Table II). This agreement helps substantiate the small effect of counter-ion on the reactivity of superoxide noted earlier (i.e., Counter-ion Effect section).

Preliminary work with electrochemical techniques in this study resulted in the generation of $\text{Et}_4\text{N}^+\text{O}_2^-$ by coulometry. The electrogenerated O_2^- was observed by esr and the signal was found to be totally quenched by addition of dilute acid. Experiments in cyclic voltammetry yielded the expected results for both oxygen-saturated and oxygen-saturated containing 1-bromobutane solutions.

Figure 7. Cyclic voltammogram of oxygen-saturated DMSO, 0.05M in tetraethylammonium perchlorate as the supporting electrolyte. The scan rate was 0.3 V/s.

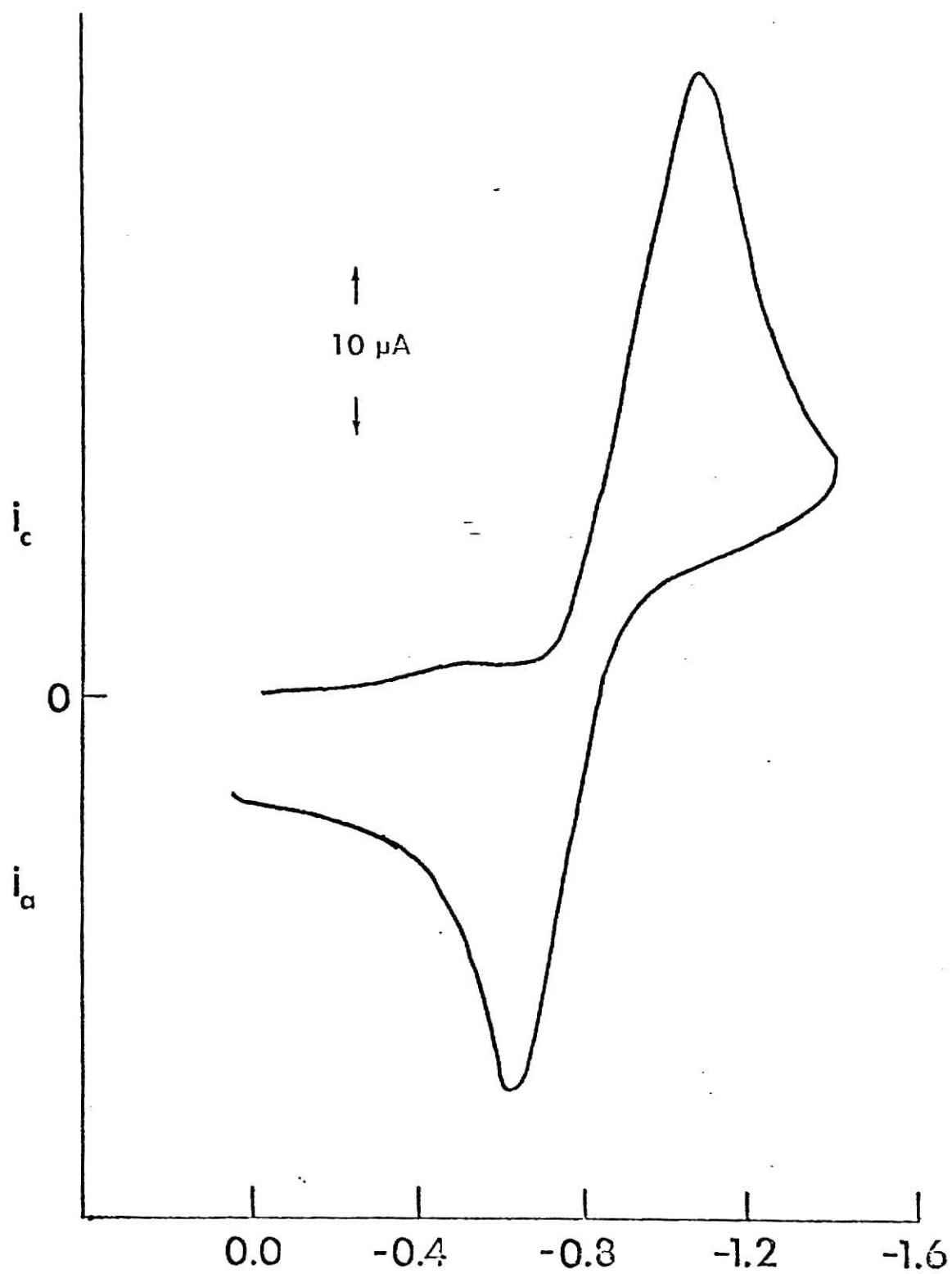
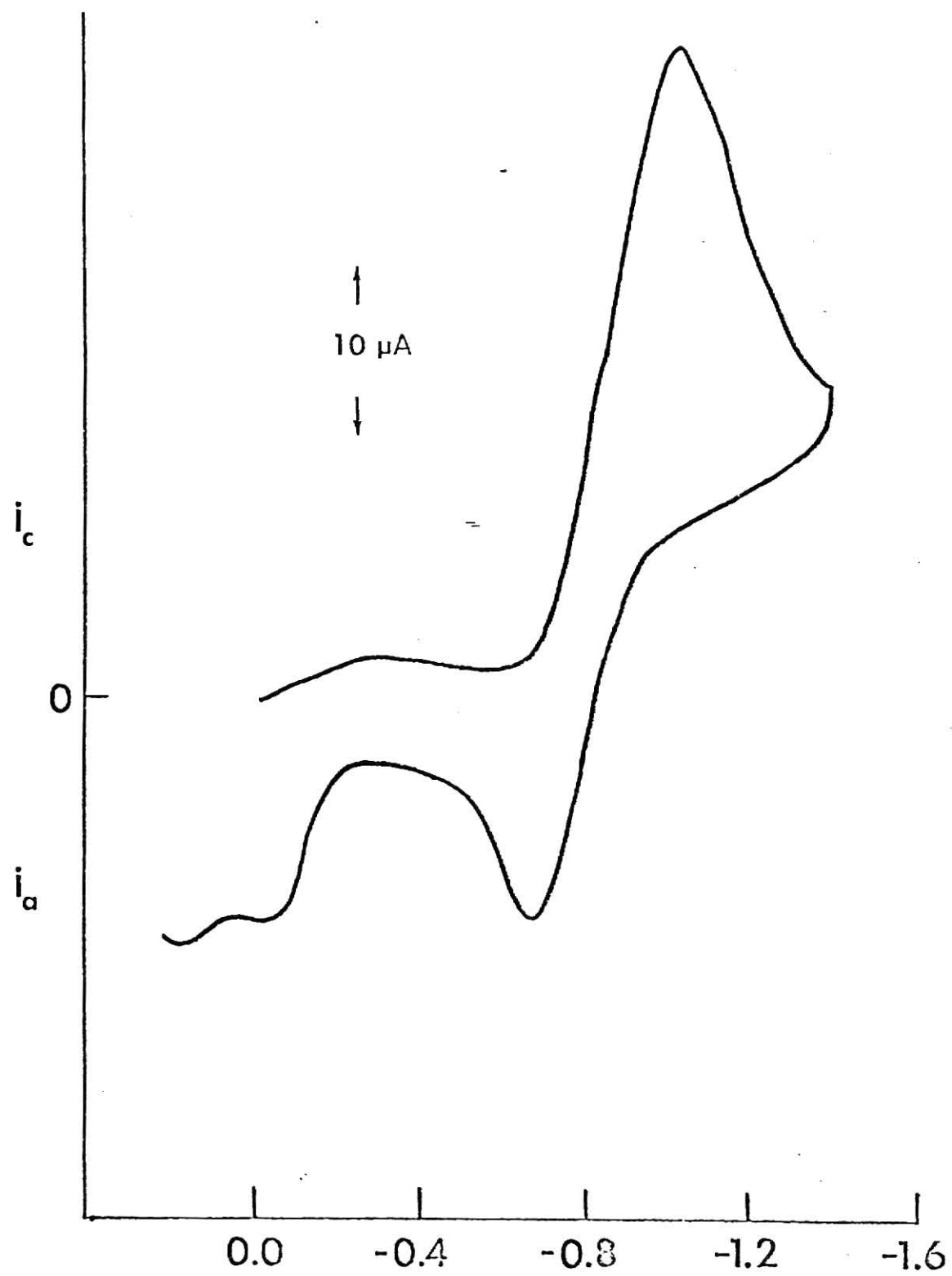


Figure 8. Cyclic voltammogram of oxygen-saturated DMSO, 0.05M in tetraethylammonium perchlorate as the supporting electrolyte in the presence of 1.8×10^{-3} M 1-bromobutane. The scan rate was 0.3 V/s.



CONCLUSIONS

The interfacing of stopped-flow spectrophotometry with a digital lab computer provides a powerful tool for the elucidation of rapid kinetics. The application of this technique to the determination of reaction rates for superoxide with alkyl halides using DMSO as a reaction solvent has been demonstrated in this study.

It was shown in the alkyl bromide series that $O_2^{\cdot -}$ is a potent nucleophile as compared to other previously acclaimed nucleophiles. Also, the flat distribution of relative rates exhibited by the primary and secondary alkyl bromides was partially explained by the reactivity versus selectivity argument. Although electron-transfer followed by radical coupling has been suggested to describe this distribution, the unreactivity of the bridgehead bromide (1-bromoadamantane), as well as the slow rate calculated by electron transfer theory, indicated a lack of viability for this explanation.

Of the factors influencing $O_2^{\cdot -}$ nucleophilicity, the best explanations are the possibility of an electron-transfer contribution in the transition state and the fact that $O_2^{\cdot -}$ is an "alpha effect" nucleophile. The extent to which $O_2^{\cdot -}$ is solvated is also a dominant effect since in DMSO solvent the anionic species is essentially free of solvation. Although crown ethers have been used to solubilize KO_2 and other anionic species have been found to show increased reactivity when their counter-ions were complexed, such was not the case for $O_2^{\cdot -}$. The major effect of crown ether on KO_2 in DMSO is only the increased solubilization of the salt. No counter-ion effect was found when the cation was varied from potassium to tetraethylammonium which demonstrated a lack of ion-pairing for DMSO solutions of superoxide.

The results of temperature studies for the reaction of KO_2 with 1-bromobutane showed the typical dependence upon temperature and gave a linear Arrhenius plot. Calculation of the activation parameters from the data gave reasonable values, depicting both the high reactivity of the species by the low enthalpy value and $\text{S}_{\text{N}}2$ type mechanism by the negative entropy value.

The introduction of polar substituents (i.e., halogen atoms) in β and γ positions from the reaction site resulted in only relatively small effects on the rate constants for displacement of bromide by superoxide. Halogen atoms placed α to the reaction center produced a dramatic decrease in reactivity which is typical of an $\text{S}_{\text{N}}2$ mechanism. Attempts at a Taft correlation did not yield an accurate ρ^* value but did indicate that limited charge formation was occurring in the transition state.

Generation of $\text{O}_2^{\cdot -}$ was accomplished by coulometry in the presence of tetraethylammonium perchlorate. The esr signal exhibited by electrogenerated $\text{O}_2^{\cdot -}$ was found to be quenched by addition of dilute acid. A cyclic voltammogram of oxygen-saturated DMSO (0.05 TEAP) in the presence of 1-bromobutane yielded an estimated rate constant which agreed favorably with the rate constant determined for the same substrate by stopped-flow spectrophotometry.

EXPERIMENTAL

Stopped-flow Spectrophotometric Determinations

Rate constants were determined using a Durrum stopped-flow spectrophotometer system D-110, the flow subsystem of which is shown in Figure 9.⁷³ The two reactant solutions are loaded into separate reservoir syringes and then via rotary valves 1 and 2 into drive syringes. Upon initiation

of the stopped-flow experiment, a pneumatic plunger forces the reactants into a mixing jet. The design of the mixing jet creates turbulent flow which mixes the reactants before they enter the observation cuvette. The freshly mixed solution forces spent reactants from the previous experiment out of the cuvette into a "stop" syringe. When the "stop" syringe plunger makes contact with a mechanical stop, all flow is instantaneously stopped. At the same instant, a trigger switch is closed which initiates data acquisition. There is a dead time, which is the interval between mixing and observation, of 2-3 milliseconds for the 20 mm cuvette used in experiments of this study.

The optical subsystem consisted of a deuterium ultraviolet light source, 180-330 filter, prism monochromator, and an adjustable slit width normally opened to 0.3 mm. The monochromatic light passed through the observation chamber and to the photomultiplier tube. Output of the photomultiplier tube, after passing through a log buffer amplifier, was displayed on a Textronics oscilloscope. The data were fed to a PDP-8/E digital lab computer for storage and eventual calculations.

Constant temperature was maintained during experiments by a Lauda/Brinkman K-2/R circulator with distilled water used as the circulating liquid. The circulating liquid first flows through the cuvette/mixing jet assembly (A) and then into the water bath housing (B), which contains the valve block and drive syringes (Figure 9). Temperature readings were taken just before the circulating liquid entered the cuvette/mixing jet assembly (A) and in the water bath (B). By insulating the tubing which connects the circulator unit to the stopped-flow instrument and the tubing within the instrument itself, only a slight temperature drop was noted

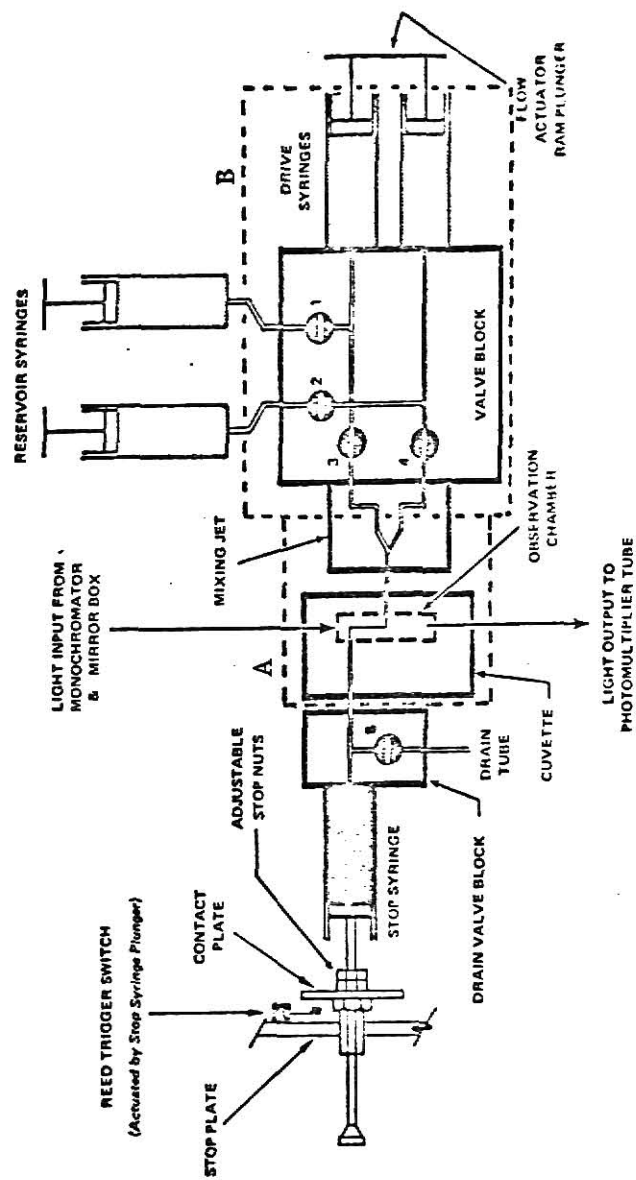


Figure 9. Flow Subsystem Diagram for a Durrum Stopped-flow Spectrophotometer⁷³

between measurement points A and B, i.e., at 10° above room temperature the variance was 0.15°.

The general procedure used in stopped-flow experiments was as follows: The instrument was first allowed to warm up for at least 15 minutes. Meanwhile, the circulator liquid flow and temperature were equilibrated and the flow system was washed out with DMSO solvent several times. Next, the computer program STFLOW was called and the photomultiplier tube was tuned to DMSO according to the instructions supplied with the Durrum instrument. Reactant solutions were then loaded into the drive syringe, a time per point constant was selected, and then experimental data were obtained.

Selection of a time per point value was arbitrary until several "test" runs were made allowing an optimum value to be selected. For example, if all the change in absorbance was in the first 20 data points, then the time per point constant selected is too small. The best results were obtained when the curve displayed on the oscilloscope at the time of the experiment resembles the data curve shown in Figure 2.

To keep data acquisition on scale (1-1000), the offset control was used. Also, the photomultiplier tube could be tuned to either the alkyl halide solution or the reaction mixture. The use of a gain higher than 1 was minimal but was used when the observed absorbance change was small.

Solution Preparation

Superoxide solutions were prepared inside a dry box by transferring a small amount of powdered KO_2 to a 25 ml erlenmeyer flask containing a stirring bar. The solid KO_2 was immediately covered with about 10 ml of dry DMSO. A rubber septum was used to seal the flask and the solution was then magnetically stirred. Also in the dry box, a 50 ml erlenmeyer flask was filled with 40 ml of dry DMSO and covered with a septum, several

25 ml volumetric flasks were filled almost to the mark, and a 20 ml syringe was filled and corked.

Outside the dry box, an approximate 10 to 1 dilution was made by syringing 4-5 ml of the stock (saturated) KO_2/DMSO solution into the 40 ml of DMSO. An ultraviolet spectrum was then taken of this dilute KO_2/DMSO solution using a Perkin-Elmer 202 ultraviolet-visible spectrophotometer. Spectra were taken using 10 mm cells and DMSO as the reference. Typically, absorption of 1 to 2 absorbance units were observed at 275 nm, which corresponds to a KO_2 concentration of $2-4 \times 10^{-3} \text{ M}$.⁷⁴ This diluted KO_2/DMSO solution was then used in stopped-flow experiments.

All the alkyl halide solutions (except methyl bromide) were prepared by syringing the appropriate volume of alkyl halide into a 25 ml volumetric flask partially filled with DMSO. The volumetric flask was then filled to the mark by addition of dry DMSO from the 20 ml syringe. These alkyl halide/DMSO solutions were generally prepared in the stopped-flow room and used immediately in experiments.

Methyl bromide/DMSO solutions were prepared, using a vacuum rack⁷⁵ where the amount of methyl bromide was measured by pressure using a calibrated volume of the rack. Measurement of the pressure was accomplished with a spiral gauge. The apparatus used to contain the solution was a 25 ml 3-neck round bottom flask which was connected to the vacuum rack via a teflon stopcock. One neck was covered with a rubber syringe septum and the other was stoppered. In the dry box, exactly 25 ml of dry DMSO was measured into this flask and the stopcock was closed. The sealed apparatus was then attached to the vacuum rack and the DMSO was frozen with liquid nitrogen. While the DMSO was freezing, it was degassed by periodic exposure to vacuum. Next, a predetermined pressure of methyl bromide was

achieved in the vacuum rack. The calibrated volume portion of the rack was then isolated and the remainder of the rack was pumped down. The flask containing the frozen DMSO was then opened to the portion of the rack containing the methyl bromide. When the pressure ceased dropping it was assumed that all the methyl bromide had condensed into the DMSO cold trap. Finally, the flask was brought to atmospheric pressure with short bursts of dry argon gas and the flask was allowed to warm to ambient temperature. The solution was then immediately syringed through the rubber septum into a 20 ml syringe and run in stopped-flow experiments.

Chemicals

Methyl bromide from Matheson was used without further purification.⁷⁶

Ethyl bromide (Fisher) was used without further purification as glc showed purity of > 99%

1-Bromobutane (Eastman) was either distilled through a vigreux or a spinning band column collecting the middle fraction. Purity was determined by glc (SE-30 column) to be > 99%,

Iso-propyl bromide (Eastman) was fractionally distilled under reduced pressure collecting the middle fraction, which was determined to be > 99% pure by glc.

Tert-butyl bromide (Eastman) was partially purified by fractional distillation. Analysis by glc showed purity of no greater than 98%.

1-Bromoadamantane (Aldrich) was used without further purification.

Dibromomethane (Aldrich) was determined to be > 99% pure and was used without further purification.

Bromochloromethane (Aldrich) was fractionally distilled collecting the middle cut and was determined by glc to be > 99% in purity.

1,2-Dibromoethane was obtained as a pure distilled sample.⁵⁴

1-Bromo-2-chloroethane (Eastman) was purified by spinning band distillation and the middle fraction was determined to be >99% pure by glc.

1-Bromo-3-chloropropane (Eastman) was fractionally distilled with the middle fraction showing >99% purity by glc.

Ethyl bromoacetate (Aldrich) was purified by spinning band distillation where the middle fraction was determined to be about 99% pure.

2,2,2-Trifluoroethyl bromide (PCR, Inc.) was determined to be 99% pure by glc and was used without further purification.

n-Butyl chloride (Fisher) was fractionally distilled collecting the middle fraction.

Tetraethylammonium perchlorate (Eastman) was recrystallized three times from water and dried for 5 days under vacuum at 47°C using a vacuum oven.

DMSO and acetonitrile were dried by heating to about 80°C over CaH_2 with stirring for at least 3 hours and then rapidly vacuum fractionally distilled. The middle fraction was collected and stored over 4-A molecular sieves (Aldrich).

Neopentyl alcohol (Aldrich) and bromine (Mallinckrodt) were used without further purification.

Synthesis of neopentyl bromide

Initially, synthesis of neopentyl bromide was attempted via bromination of the lithium salt. The lithium salt was prepared by addition of neopentyl chloride to powdered lithium. This procedure yielded no product.⁷⁷

Synthesis was achieved by reaction of neopentyl alcohol with triphenylphosphine dibromide as described by Wiley and co-workers.⁷⁸ Triphenylphosphine (0.1 mole) and neopentyl alcohol (0.1 mole) were dissolved in 75 ml dry DMF (dried over CaH_2 and vacuum distilled) with stirring. Bromine

(18 g) was added dropwise to the solution via an addition funnel, keeping the temperature below 55°. A dry nitrogen atmosphere was maintained with an overbubbler. A reflux condenser was attached and the solution was heated to about 70° with continuous stirring and then allowed to cool. The volatile material was removed under vacuum (<5 mm). Approximately 80 ml of distillate was collected and upon addition of 500 ml cold water a crude yield of 7.3 g (48%) of neopentyl bromide was obtained; nmr (neat) δ 2.92 (2H, singlet), δ 0.75 (9H, singlet). High purity neopentyl bromide was obtained by preparative glc using a SE-30 column with automatic collection.⁷⁹

Electrochemical Studies

The coulometer used in controlled-potential electrolysis experiments was a three-electrode potentiostat which compensated for the potential difference between the working and reference electrodes.⁷⁰ Also, a digital display of the number of coulombs passed had been incorporated into the instrument.

The cyclic voltammetric experiments were performed on a transistorized, three-electrode potentiostat.⁷¹

Cells and Electrodes

The solutions used in electrochemical experiments were added to cells and sealed inside a dry box. Originally, coulometry cells were constructed, using small wide-mouth jars with ground glass outer joints cemented to plastic lids for electrode placement. It was found that the solvents used, i.e. acetonitrile, dissolved the epoxy and the resultant solution exhibited strong absorption in the 270 nm region. All-glass cells were used in subsequent experiments. The coulometry cell consisted of a mercury pool cathode, platinum foil anode and a silver wire reference electrode.

Oxygen was bubbled in and vented via hyperdermic needles inserted through silicon septums. The needles also served as a means for anhydrous removal of electrogenerated O_2^- solutions.

The cyclic voltammetry cell employed a saturated calomel electrode (SCE), a mercury j-tube working electrode, and a platinum foil auxiliary electrode placed directly above and horizontal to the mercury sphere of the j-tube. The SCE compartment was separated from the other electrodes by a sintered glass disc and a bridge (TEAP/ CH_3CN) to minimize contamination of the cell solution.

Computer Programs

STFLOW

The most important PDP 8/E computer program used for determination of kinetics by stopped-flow spectrophotometry in this study was STFLOW.²⁴ This program acquires data strings of 128 points at specific increments of time and allows various routines to be performed. A list of the 22 routines that can be called from the keyboard can be obtained by typing in HE (Help). Of the functions available, the most commonly used commands are listed below along with a brief explanation of their functions.

CO = Co-add and average

HE = Help, print this list (complete)

HL = Half-life print-out

KE = Keep this file

OF = TTY off

ON = TTY on

SA = Save on mass storage

SC = Scale vertically to fill screen

TI = Time per point set-up

VO = Voltmeter mode

The normal order of the use of these commands are described in the following text. First, the stopped-flow photomultiplier tube and corresponding electronics were tuned up according to Durrum specifications⁷³ using the voltmeter mode (VO) which displays readings on the oscilloscope. Next, a time per point was selected and entered in response to the TI command. After the stopped-flow experiment was actuated, the data string consisted of only 127 points until the "Keep this file" command (KE) was given, at which time an infinity point was taken. Another data string could then be taken, kept or not, and this cycle was repeated until, usually, 4 to 6 data strings had been taken. The next step was to co-add and average (CO) the data strings into a scratch pad file. This initial average was then displayed together with the individual data strings and a decision was made as to whether or not each string would be included in the final average. After all the data strings had been presented, a new average was calculated using the data strings chosen in the previous step.

The final averaged data file could then be scaled up to fill the scope (SC) and a half-life for the reaction could be calculated (HL). Calculation of the half-life was accomplished using a cursor placed on the scope with the data file display.

The data file could be saved on mass storage by the SA command, which must be directly preceded by the CO command. Along with the data file, the save command allows the operator to enter experimental conditions. An example of this heading is shown in Figure 10 where, after giving the date, the next two lines are for free information (i.e. reactants, on what solution the photomultiplier tube was tuned, and the half-life calculated). In the next three lines the PM VOLT (photomultiplier voltage), NOISE FILTER, MODE (i.e., absorbance 1), OFFSET, GAIN, WAVELENGTH, and

Figure 10. Example of data file stored under "save" command of STFLOW program. The data listed is for absorbance of O_2 on a scale of 1-1000 taken at intervals of 0.5 msec.

ILLEGIBLE DOCUMENT

**THE FOLLOWING
DOCUMENT(S) IS OF
POOR LEGIBILITY IN
THE ORIGINAL**

**THIS IS THE BEST
COPY AVAILABLE**

DATE: 11-2-75

K02/D100 + CLO120H2DP/DH00

TUNED ON HALIDE TIN2=11FE-4

PH VOLT	NOISE FILTER	MODE
3.47	3.1	A1

OFFSET	WAVELENGTH(NM)	GAIN	RUNS	MSEC/POINT
2	275	1	5	0.5

CONC1(MM)	CONC2(MM)	CONC3(MM)
3.200	100.000	0.000

843	333	347	334	336	776	759	752
739	724	735	633	679	666	653	633
625	613	601	533	577	567	553	545
534	525	515	505	497	437	473	473
461	452	444	437	430	423	415	403
402	396	339	332	376	371	365	359
353	343	344	333	333	323	325	322
315	311	307	303	303	295	291	239
236	232	273	275	273	273	267	264
261	259	257	253	251	243	246	244
242	240	233	236	233	231	230	223
227	225	223	221	220	219	217	215
214	213	212	211	209	203	206	206
205	204	203	202	203	203	199	193
197	197	196	195	194	193	191	192
191	190	190	139	139	137	137	157

CONCENTRATION OF reactants are given in response to the save routine queries. The value under RUNS was determined by the number of data strings used in the final average and the MSEC/POINT value was from the time per point (TI) selected.

KINET1

KINET1 is a program derived from the first-order kinetics program obtained from Wiberg.²⁵ This program allows the calculation of first-order rate constants by the method of least squares. Also, the program contains a subroutine that can vary the infinity point to minimize the root mean square error and then recalculate a first-order rate constant.

After the program has been called, a file name is requested (i.e., DTAL:FILE.SF). The specified file is then read from mass storage and a printout of the data is produced, i.e., Figure 10. The program then offers the operator a choice as to whether or not a first-order rate constant calculation should be performed and, if so, what data points are to be used. A rate constant is then calculated from the designated data set and is printed on the CRT. The teletype then prints out the rate constant, errors, and a comparison of observed and calculated (least squares) values (Figure 11). Only an operator-specific fraction of points are printed, i.e., for Figure 11 only one-tenth of the points were printed. Next the same data set is used in another calculation where the infinity point is varied to achieve a better least squares fit. A first-order rate constant is then printed along with errors⁸⁰ and the observed/calculated comparison, which is again an operator controlled fraction of points. An example of the print-out of this second calculation is also shown in Figure 11.

Figure 11. Example of KINET1 calculation of first-order rate constants for the data listed in Figure 10 by (A) least squares method and (B) iterative variation of the infinity point followed by least square calculation of a rate constant.

(A)

RATE CONSTANT K1= 3.5201E+02

INTERCEPT 3.7373E+03

INFINITY VALUE 157.0337

RMS ERROR 2.6336

% ERROR IN SLOPE 0.24

POINT TIME(SEC) OBS CALC DIF

10	3.3345	724.3	714.4	9.57
20	3.3395	533.3	534.9	3.14
30	3.3145	437.3	435.4	1.59
40	3.3195	433.3	439.1	-1.07
50	3.3245	343.3	353.5	-2.43
60	3.3295	333.3	335.5	-2.51
70	3.3345	273.3	271.3	-3.99
80	3.3395	244.3	244.5	-0.19
90	3.3445	225.3	224.2	3.34
100	3.3495	211.3	233.5	2.45

(B)

ADJUSTED VALUES AFTER 3 ITERATIONS

RATE CONSTANT K1= 3.5494E+02

INTERCEPT 3.7136E+03

INFINITY VALUE 162.3194

RMS ERROR 1.3333

% ERROR IN SLOPE 23.72

POINT TIME(SEC) OBS CALC DIF

10	3.3345	724.3	723.2	3.77
20	3.3395	533.3	533.4	-0.43
30	3.3145	437.3	436.7	1.57
40	3.3195	433.3	433.2	-0.13
50	3.3245	343.3	349.1	-1.35
60	3.3295	333.3	334.1	-1.13
70	3.3345	273.3	273.3	0.31
80	3.3395	244.3	244.1	-0.33
90	3.3445	225.3	224.4	3.65
100	3.3495	211.3	239.4	1.62

BIBLIOGRAPHY

1. I. Fridovich, Acct. Chem. Res., 5, 321 (1972), and references therein.
2. M. E. Peover and B. S. White, Electrochim. Acta, 11, 1061 (1966).
3. R. Poupko and I. Rosenthal, J. Phys. Chem., 77, 1722 (1973).
4. P. S. Rao and E. Hayon, Biochem. Biophys. Res. Comm., 51, 468 (1973).
5. A. Frimer and I. Rosenthal, Tetrahedron Lett., 2809 (1976).
6. M. Nishikimi and L. J. Machlin, Arch. Biochem. Biophys., 179, 684 (1975).
7. I. Rosenthal and A. Frimer, Tetrahedron Lett., 2805 (1976).
8. Y. Moro-oka and C. S. Foote, J. Amer. Chem. Soc., 98, 1510 (1976).
9. J. San Filippo, Jr., L. J. Romano, C. Chern, and J. S. Valentine, J. Org. Chem., 41, 586 (1976).
10. J. San Filippo, Jr., C. Chern, and J. S. Valentine, J. Org. Chem., 41, 1077 (1976).
11. C. Chern and J. San Filippo, Jr., J. Org. Chem., 42, 178 (1977).
12. J. San Filippo, Jr., C. Chern, and S. S. Valentine, J. Org. Chem., 40, 1678 (1975).
13. R. A. Johnson and E. G. Nidy, J. Org. Chem., 40, 1680 (1975).
14. M. J. Gibian and T. Ungermann, J. Org. Chem., 41, 2500 (1976).
15. R. A. Johnson, Tetrahedron Lett., 331 (1976).
16. E. J. Corey, K. C. Nicolaou, M. Shibasaki, Y. Machida, and C. S. Shiner, Tetrahedron Lett., 3183 (1975).
17. R. Dietz, A. E. J. Forno, B. E. Larcombe, and M. E. Peover, J. Chem. Soc. (B), 816 (1970).
18. M. V. Merritt and D. T. Sawyer, J. Org. Chem., 35, 2157 (1970).
19. F. Magno and G. Bontempelli, J. Electroanal. Chem., 68, 337 (1976).
20. Ravindra Arudi, Kansas State University, Manhattan, Kansas personal communication, 1976.

21. J. A. Fee and P. G. Hildenbrand, FEBS Lett., 39, 79 (1974).
22. G. J. McClune and J. A. Fee, FEBS Lett., 67, 294 (1976).
23. J. G. Grasselli and W. M. Ritchey, "CRC Atlas of Spectral Data and Physical Constants for Organic Compounds," Vol. III, 2nd ed., CRC Press, Cleveland, Ohio, 1975, p. 253.
24. The author acknowledges Dr. M. van Swaay of this department for writing the computer program, STFLOW.
25. K. B. Wiberg, "Physical Organic Chemistry," Wiley, New York, NY, 1964, p. 560; The author acknowledges Dr. M. van Swaay and Dr. J. V. Paukstelis for revising KINET1.
26. A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill Book Co., New York, NY, 1962, p. 13.
27. C. K. Mann and K. K. Barnes, "Electrochemical Reactions in Nonaqueous Systems," Marcel Dekker, Inc., New York, NY, 1970, p. 354.
28. Reference 27, p. 230.
29. R. A. Marcus, J. Chem. Phys., 43, 679 (1965).
30. Dr. M. D. Hawley, Kansas State University, Manhattan, Kansas, personal communication, 1977.
31. C. L. Liotta, H. P. Harris, J. Amer. Chem. Soc., 96, 2250 (1974).
32. C. D. Ritchie, Acct. Chem. Res., 5, 348 (1972).
33. Calculated by $\sum \Delta H_f^\circ$ (products) - $\sum \Delta H_f^\circ$ (reactants) where the ΔH_f° values were obtained from the following references:
 - (a) G. V. Sonsonov, ed., "The Oxide Handbook," Ifi/Plenum, New York, NY, 1973, p. 38.
 - (b) S. W. Benson, F. R. Cruickshank, D. M. Bolden, C. R. Haugen, H. E. O'Neal, A. S. Rodgers, R. Shaw, and R. Walsh, Chem. Rev., 69, 279 (1969).

- (c) S. W. Benson and R. Shaw in "Organic Peroxides," Vol. I, D. Swern, editor, Wiley, New York, NY, 1970, p. 130.
- (d) "Handbook of Chemistry and Physics," 50th edition, the Chemical Rubber Co., Cleveland, Ohio, 1969-1970, p. D-68.
34. It should be noted that this heat of reaction value was calculated for the initial displacement reaction which results in the formation of a highly energetic peroxy radical.
35. J. I. Brauman, W. N. Olmstead, and C. A. Lieder, J. Amer. Chem. Soc., 96, 4030 (1974).
36. A. J. Parker, Chem. Rev., 69, 1 (1969).
37. R. G. Pearson and J. Songstad, J. Org. Chem., 32, 2899 (1967).
38. L. P. Hammett, "Physical Org. Chemistry," 2nd edition, McGraw-Hill Book Co., New York, NY 1970, p. 239.
39. J. F. Bunnett, Ann. Rev. Phys. Chem., 14, 271 (1963).
40. J. J. Delpuech, Tetrahedron Lett., 2111 (1965).
41. J. O. Edwards, J. Chem. Ed., 45, 386 (1968).
42. J. M. Harris and C. C. Wamser, "Fundamentals of Organic Reaction Mechanisms," Wiley, New York, NY, 1976, Chapter 4.
43. J. O. Edwards, J. Amer. Chem. Soc., 76, 1540 (1954).
44. S. R. Hartshorn, "Aliphatic Nucleophilic Substitution," Cambridge University Press, London, 1973, p. 45-7.
45. T. H. Lowry and K. S. Richardson, "Mechanism and Theory in Organic Chemistry," Harper and Row, New York, NY, 1976, p. 190.
46. D. Behar, G. Czapski, J. Rabani, L. M. Dorfman, and H. A. Schwarz, J. Phys. Chem., 74, 3209 (1970).
47. J. O. Edwards and R. G. Pearson, J. Amer. Chem. Soc., 84, 16 (1962).
48. N. J. Fina and J. O. Edwards, J. Int. Chem. Kinetics, 5, 1 (1973)

49. W. Bors, M. Saran, E. Lengfelder, R. Spottl, and C. Michel, Current Topics in Radiation Research Quarterly, 9, 247 (1974), and references therein.
50. R. Curci and F. D. Furia, International Journal of Chemical Kinetics, 7, 341 (1975).
51. D. J. Sam and H. F. Simmons, J. Amer. Chem. Soc., 96, 2252 (1974).
52. H. H. Szmant in "Dimethyl Sulfoxide," S. W. Jacob, E. E. Rosenbaum and D. C. Wood, editors, Marcel Dekker, Inc., New York, NY, 1971.
53. C. L. Liotta and E. E. Grisdale, Tetrahedron Lett., 4205 (1975).
54. The author acknowledges Ravindra Arudi, Kansas State University, Manhattan, Kansas, for providing this compound in a pure form.
55. One possible explanation is the absorbance of intermediates and products at the lower wavelengths employed with acetonitrile as solvent. Such intermediates are not detected in DMSO because of the rapidity of reaction 15 (p. 7).
56. Reference 26, p. 16.
57. Reference 26, pp. 25-6.
58. W. R. Kiener and G. H. Richter, J. Amer. Chem. Soc., 51, 3409 (1929).
59. J. Hine, S. J. Ehrensens, and W. H. Brader, Jr., J. Amer. Chem. Soc., 78, 2282 (1956).
60. A. Streitwieser, Jr., J. Amer. Chem. Soc., 78, 4935 (1956).
61. The RT term is small at ordinary temperatures, i.e., at 300°K the difference between E_a and ΔH^\ddagger is only about 0.6 kcal/mole.
62. Reference 42, pp. 109-10.
63. The author acknowledges Dr. R. N. McDonald of this department for providing this program. The calculations were performed on an IBM 360/50 computer.
64. B. O. Coniglio, D. E. Giles, W. R. McDonald, and A. J. Parker, J.

65. A. Alexander, E. C. F. Ko, A. J. Parker, and T. J. Broxton, J. Amer. Chem. Soc., 90, 5049 (1968).
66. G. A. Russell, J. Amer. Chem. Soc., 79, 3871 (1957).
67. E. Seyb, Jr., and J. Kleinberg, Anal. Chem., 23, 115 (1951).
68. E. L. Johnson, K. H. Pool, and R. E. Hamm, Anal. Chem., 38, 138 (1966).
69. D. L. Maricle and W. G. Hodgson, Anal. Chem., 37, 1562 (1965).
70. The author acknowledges Dr. M. van Swaay of this department for the design and building of the coulometer used in this study.
71. C. G. Santelices, M. S. Thesis, Kansas State University, Manhattan, Kansas, 1977; the author acknowledges the use of Dr. M. D. Hawley's instrument and the aid and cooperation of his group in obtaining cyclic voltammograms.
72. R. S. Nicholson and I. Shain, Anal. Chem., 36, 706 (1964).
73. From operational manual supplied with Durrum stopped-flow spectrophotometer system D-110.
74. Calculated from the reported extinction coefficient from reference 22.
75. The author acknowledges John Kolts of this department for gas phase manipulations and the use of Dr. D. W. Setser's apparatus.
76. The author acknowledges Dr. W. Setser of this department for providing methyl bromide.
77. (a) R. L. Bixler and C. Niemann, J. Org. Chem., 23, 743 (1958).
(b) P. T. Lansburg, V. A. Pattison, J. D. Sidler, and J. B. Bieber, J. Amer. Chem. Soc., 88, 78 (1966).
(c) G. E. Neal, Ph.D. Thesis, University of Illinois, Urgana, Illinois, 1965.
78. G. A. Wiley, R. L. Hershkowitz, B. M. Rein, and B. C. Chung, J. Amer. Chem. Soc., 85, 964 (1964).

79. The author acknowledges the use of Dr. J. V. Paukstelis' research glc and the assistance of Rod Bruckdorfer.
80. A program error exists in the % error in slope calculation and a float step is missing from the infinity variation subroutine. Neither of these have any effect on the rate constants reported in this study.

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VITA

Richard Jay Warner was born to Richard and Qwen Warner on July 27, 1952, in Salina, Kansas. He was reared in Solomon, Kansas, where he attended school for twelve years. He graduated from Solomon High School in 1970.

That same year he entered Kansas Wesleyan University where he majored in chemistry and biology. While at Kansas Wesleyan he was an American Chemical Society Student Affiliate member and was initiated into Beta Beta Beta. He was awarded a Bachelor of Arts degree in May, 1974.

After graduation he entered the Graduate School at Kansas State University to work toward the completion of a Master of Science degree in chemistry. While at Kansas State University he was initiated into Alpha Chi Sigma and was a member of the American Chemical Society.

RATES OF SUPEROXIDE ANION RADICAL
REACTION WITH ALKYL BROMIDES

by

RICHARD JAY WARNER

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KANSAS STATE UNIVERSITY

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ABSTRACT

The absolute rate constants for the nucleophilic displacement reaction of superoxide anion radical, $O_2^{\cdot -}$, with a series of aliphatic bromides and halogen-substituted alkyl bromides in DMSO were determined by stopped-flow spectrophotometry. The reactions were conducted under pseudo-first-order conditions with the disappearance of $O_2^{\cdot -}$ monitored at 275 nm.

In comparison to other, heretofore, acclaimed nucleophiles, $O_2^{\cdot -}$ was found to be a remarkably potent nucleophile. The second-order rate constants decreased in the series $MeBr > EtBr > n\text{-}BuBr > i\text{-}PrBr$ which is consistent with the previously proposed S_N2 reaction mechanism. The spread in relative reactivities for variation in substrate structure was smaller than frequently observed. The unreactivity of the bridgehead bromide (1-bromoadamantane) demonstrated the absence of any appreciable electron-transfer type substitution process.

Of the factors influencing $O_2^{\cdot -}$ nucleophilicity, the most viable explanations include the possibility of an electron-transfer contribution in the transition state and the fact that $O_2^{\cdot -}$ is an "alpha effect" nucleophile.

Although crown ethers have been used to solubilize KO_2 and other anionic species have been found to show dramatically increased reactivity when their counter-ions were complexed, such was not the case for superoxide. In the presence of excess 18-crown-6 ether no significant increase in reactivity was observed for KO_2 reacting with an alkyl bromide. Also, variation of the counter-ion from potassium to tetraethylammonium yielded no observable variation in $O_2^{\cdot -}$ reactivity. Both of these observations were related to the ability of DMSO to extensively solvate cations, whereas $O_2^{\cdot -}$ is essentially free of solvation. The data also indicated that solutions of KO_2 in DMSO exhibit no appreciable ion-pairing.

Temperature studies yielded rate constants that gave a linear Arrhenius plot. For the reaction of KO_2 with 1-bromobutane in DMSO, the values of ΔH^\ddagger and ΔS^\ddagger were 9.8 ± 1 kcal/mole and -15.6 ± 1 e.u., respectively. The calculated activation parameters depicted both the high reactivity displayed by $\text{O}_2^{\cdot-}$ and the $\text{S}_{\text{N}}2$ mechanism by which it reacts with alkyl halides.

The introduction of polar substituents (i.e., halogen atoms) in β and γ positions from the reaction center resulted in only minor effects on the rate constants for displacement of bromide by superoxide. Halogen atoms placed α to the reaction center produced a more substantial decrease in reactivity.

Electrogeneration of $\text{O}_2^{\cdot-}$ was accomplished by coulometry in the presence of tetraethylammonium perchlorate. The esr signal exhibited by $\text{Et}_4\text{N}^+\text{O}_2^{\cdot-}$ was found to be quenched by addition of dilute acid. A cyclic voltammogram of oxygen-saturated DMSO (0.05 TEAP) in the presence of 1-bromobutane yielded an estimated rate constant which agreed favorably with the rate constant determined for the same substrate by stopped-flow spectrophotometry.