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A Study of Superoxide Reactivity. Reaction of Potassium Superoxide with Alkyl Halides and Tosylates

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Abstract: The reaction of superoxide with a representative series of alkyl halides and tosylates in Me_2SO and benzene has been shown to proceed by a pathway involving an initial S_N2 displacement leading to alkylperoxy radicals which, in a subsequent one-electron reduction, are converted to peroxy anions. Processes involving the self-reaction of peroxy radicals play at most a very minor role in product determination. In most instances, the initially isolable principal product is the dialkyl peroxide which, in a subsequent, base-induced reaction(s), is converted into alkoxide. Product studies reveal that a number of factors can influence product ratios, including reactant ratios, the nature of the leaving groups, reaction time, reactant concentration, and workup conditions.

In recent years superoxide (O_2^-), the one-electron reduction product of molecular oxygen, has become the subject of considerable chemical and biological interest and investigation.[1] Much of the current interest about superoxide centers around its production and reactions in biological systems and in particular its role in certain biological oxidations.[2] There are a number of early (pre-1975) reports describing the chemical reactivity of superoxide;[3] however, much of the basic chemistry of superoxide remains ill defined. The work reported here details one avenue of an investigation we have pursued, designed to explore, elucidate, and define the chemical reactivity of superoxide.

Superoxide disproportionates rapidly in aqueous solvents,[4]

$$2O_2^- + 2H_2O \xrightarrow[\text{pH 5}]{k \simeq 2 \times 10^5} H_2O_2 + 2HO^- + O_2$$

complicating the study and interpretation of the reactions of superoxide in protic media. By contrast, superoxide has extended stability in certain aprotic solvents, specifically dimethyl sulfoxide, Me_2SO. For this reason, the studies reported here have been carried out in either dimethyl sulfoxide or benzene. Such studies provide the indirect opportunity to assess the feasibility of superoxide's participation in such reactions when conducted under largely aqueous conditions.

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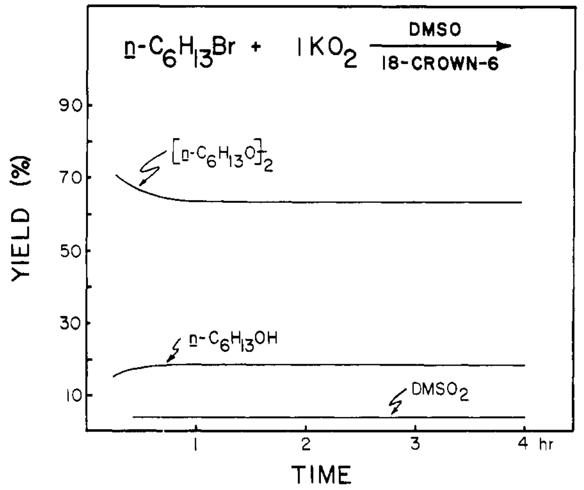


Figure 1. Reaction of KO_2 (3.00 mmol) with *n*-hexyl bromide (3.00 mmol) in Me_2SO (20 mL) containing 18-crown-6 ether (0.30 mmol) at 25 °C results in the formation of di-*n*-hexyl peroxide (63%), 1-hexanol (18%), and dimethyl sulfone (Me_2SO_2, 4%). Me_2SO_2 was analyzed by GLC prior to workup. Di-*n*-hexyl peroxide, *n*-hexyl hydroperoxide, and 1-hexanol were determined by LC following a workup procedure that consisted of treating individual reaction mixtures with a solution (20 mL) of acidified aqueous methanol. Control experiments established the stability of all these products under these conditions. Analysis (LC) for *n*-hexyl hydroperoxide showed none (<1%) of this material to be present. All yields are based on starting halides. For simplicity, actual data points are not shown here or in subsequent figures. All data points were determined at 30-min intervals and showed an esd of ±3% from the illustrated line.

The chemical nature of superoxide is unique in that it can function as either a reductant, nucleophile, base, or oxidant. Since all of these properties are subject to influence by the reaction solvent, unqualified extrapolation of a demonstrated behavior from one solvent system to another can be misleading. For example, the protonated form of superoxide, $HO_2\cdot$, has a pK_a in water of 4.5–4.9,[5] comparable to that of acetic acid. However, it is well known that anion basicity generally increases dramatically in an aprotic solvent such as Me_2SO. (The basicity of hydroxide ion, for example, is 14 orders of magnitude greater in dry Me_2SO than it is in water.[6]) Thus, it is reasonable to expect that superoxide is substantially more basic in Me_2SO than in water. Likewise, the oxidizing ability of superoxide can be anticipated to be substantially greater in protic systems where its one-electron reduction to peroxide is greatly aided by its protonation (or coordination to a metal center) to produce a *neutral* and, therefore, more readily reducible species, viz., the peroxy radical. In fact, the hydroperoxy radical and species derived from it (H_2O_2, HO_2^-, and $HO\cdot$) are in all likelihood the active oxidant(s) under these circumstances. These proposals are supported by two unrelated observations: (1) the early report of Maricle and Hodgson who found that, in the presence of an added proton source (e.g., phenol), the usually observed one-electron (electrochemical) reduction of oxygen to superoxide in Me_2SO is replaced by a two-electron reduction corresponding to the equation[7]

$$O_2 + H^+ \xrightarrow{2e^-} HO_2^-$$

and (2) by the more recent observations that the reaction of superoxide with various organic substrates in aprotic solvents (specifically, the oxidation of hydrazines, hydrazones, and selected α-substituted carbonyl compounds) does not proceed unless certain relatively acidic protons occur within the substrate molecule.[8,9] By contrast, the cleavage of simple carboxylate esters by superoxide in Me_2SO or benzene exhibits no such dependence, preferring to take place instead by a direct nucleophilic attack of O_2^- on the carbonyl carbon.[10]

Results

The early investigations of superoxide in aprotic media relied primarily on electrochemical means of generating O_2^-. At best, such techniques are relatively inconvenient and severely limit the quantity of reagent that can be prepared. By comparison, potassium and certain other alkali metal ions form stable, readily available salts with superoxide. The potential of such salts as convenient precursors to superoxide was realized when Valentine and Curtis observed that the otherwise very limited solubility of KO_2 in dimethyl sulfoxide (Me_2SO) could be increased to ca. 0.15 M by the addition of certain crown ethers.[11] The reactions we report here detail our study of superoxide's reactivity toward certain simple electrophilic substrates and were carried out using mixtures of potassium or sodium superoxide and 18-crown-6 ether (generally 10 mol % based on KO_2) in Me_2SO and benzene.

Reaction of *n*-Hexyl Bromide with KO_2 in Me_2SO. Equations 1 and 2 summarize the products produced by the reaction of a representative alkyl bromide, viz., *n*-hexyl bromide (**1**), with 3 equiv of KO_2 in Me_2SO and show that the product

$$\underset{\mathbf{1}}{n\text{-}C_6H_{13}Br} + 3KO_2 \xrightarrow[Me_2SO\ 0.5\ h]{18\text{-crown-6}} \xrightarrow{H_2O} \underset{<1\%}{[n\text{-}C_6H_{13}O\text{+}_2} + \underset{63\%}{n\text{-}C_6H_{13}OH} \quad (1)$$

$$\underset{\mathbf{1}}{n\text{-}C_6H_{13}Br} + 3KO_2 \xrightarrow[Me_2SO\ 0.5\ h]{18\text{-crown-6}} \xrightarrow[CH_3OH]{0.5\ M\ H_2SO_4} \underset{68\%}{[n\text{-}C_6H_{13}O\text{+}_2} + \underset{17\%}{n\text{-}C_6H_{13}OH} \quad (2)$$

distribution is substantially affected by the nature of the workup, suggesting that di-*n*-hexyl peroxide is possibly the initial principal product of the reaction of KO_2 with **1**, but that it is converted to 1-hexanol during aqueous workup. In fact, when authentic di-*n*-hexyl peroxide is subjected to conditions similar to those produced during the course of such a workup (treatment with 3 equiv of KOH in 5% aqueous Me_2SO for 15 min), 1-hexanol was produced in 60% yield and the yield of recovered peroxide was <1%.

Second, a comparison of eq 2, 3, and 4 reveals that the *initial* product distribution resulting from the reaction of *n*-hexyl bromide with KO_2 in Me_2SO is largely unaffected by reactant ratio.

$$n\text{-}C_6H_{13}Br + KO_2 \xrightarrow[Me_2SO\ 0.5\ h]{18\text{-crown-6}} \xrightarrow[CH_3OH]{0.5\ M\ H_2SO_4} \underset{66\%}{[n\text{-}C_6H_{13}O\text{+}_2} + \underset{16\%}{n\text{-}C_6H_{13}OH} \quad (3)$$

$$n\text{-}C_6H_{13}Br + 5KO_2 \xrightarrow[Me_2SO\ 0.5h]{18\text{-crown-6}} \xrightarrow[CH_3OH]{0.5\ M\ H_2SO_4} \underset{58\%}{[n\text{-}C_6H_{13}O\text{+}_2} + \underset{30\%}{n\text{-}C_6H_{13}OH} \quad (4)$$

However, Figures 1 and 2 illustrate the influence which different reactant ratios have on product distribution when the reaction of KO_2 with **1** in Me_2SO is monitored over an extended reaction period. The product distribution produced by the reaction of **1** with 1 equiv of KO_2 remains unchanged after 45 min, while, in contrast, the reaction of **1** with 3 equiv of KO_2 produces an optimum yield of di-*n*-hexyl peroxide during the initial reaction period (~45 min), which then decreases accompanied by a corresponding increase in the yield of 1-hexanol. Taken together, these findings suggest that the initially formed di-*n*-hexyl peroxide is capable of further reaction with excess KO_2, producing, inter alia, 1-hexanol. As Figure 3 shows, authentic di-*n*-hexyl peroxide is rapidly converted to 1-hexanol by treatment with KO_2 in Me_2SO. In this regard, it is pertinent to note that authentic di-*n*-hexyl peroxide is consumed considerably more rapidly in the reaction profiled

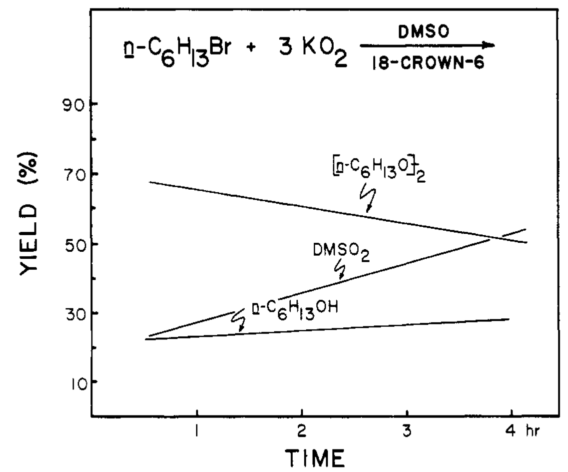


Figure 2. Analysis of the products from the reaction of KO_2 and *n*-hexyl bromide (3:1) in Me_2SO-18-crown-6 reveals the influence that reaction time has on product distribution (cf. Figure 1).

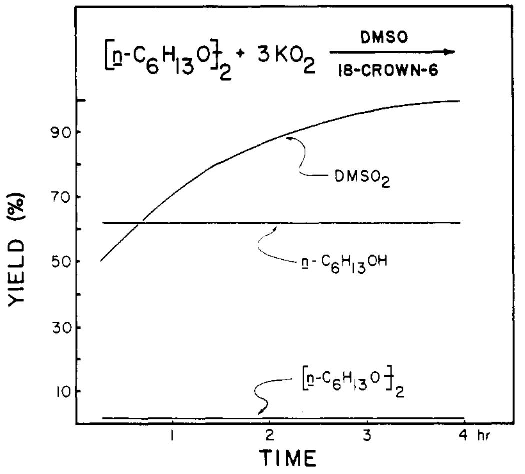


Figure 3. Plot showing the production of Me_2SO_2 and 1-hexanol and the recovery of $[n\text{-}C_6H_{13}O]_2$ resulting from the reaction of di-*n*-hexyl peroxide (3.33 mmol) with KO_2 (10.0 mmol) in Me_2SO (20 mL) containing 18-crown-6 ether (1.00 mmol). Workup and analytical procedures were equivalent to those described in Figure 1.

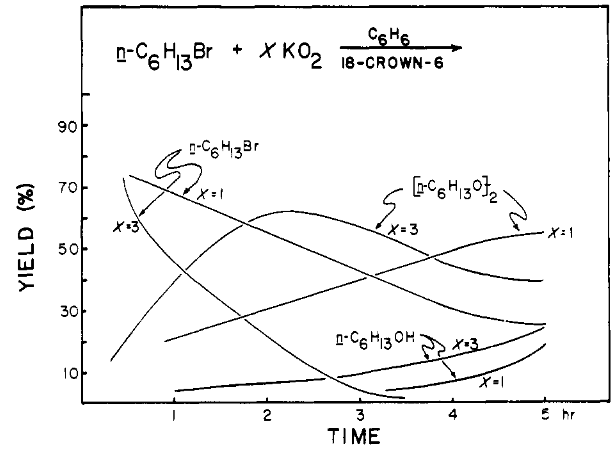


Figure 4. Influence of reaction time and reactant ratios on the product distribution produced by reaction of KO_2 with *n*-hexyl bromide (3.33 mmol) in benzene (20 mL)-18-crown-6 at 25 °C. Individual reaction mixtures were quenched with an acidified solution of methanol prior to analysis. Di-*n*-hexyl peroxide and 1-hexanol yields were determined by LC. Unreacted *n*-hexyl bromide was determined by GLC. The stability of these substances under these workup and analytical conditions was demonstrated by control experiments. All yields are based on alkyl bromide.

Table I. Effect of the Quantity of 18-Crown-6 Ether on the 1:3 Reaction of *n*-Hexyl Bromide with KO_2 in Me_2SO[a]

RBr, mM	KO_2, mM	18-crown-6, mM	reaction time, h	yield,[b] %	
				ROOR	ROH
3.33	10.0	1.00	0.5	68	21
			1	63	22
			2	60	23
			3	57	26
			4	50	29
3.33	10.0	3.33	0.5	44	37
			1	<1	60
			2	<1	61
			3	<1	59
			4	<1	60

[a] Reaction volume, 20 mL of Me_2SO. [b] Yields were determined by LC and are based on alkyl halide.

in Figure 3 than in Figure 2. This behavior is presumably a result of the increased solubility of KO_2 in the former reaction mixture, a conclusion that is consistent with the data in Table I which indicate that the di-*n*-hexyl peroxide produced in the 1:3 reaction of *n*-hexyl bromide with KO_2 is consumed much more rapidly when this reaction is carried out in the presence of an increased amount of 18-crown-6 ether.

Third, the generally high product balances observed in the reactions outlined above attest to the completeness of these product studies and sustain the accuracy of the analytical procedures used.

Finally, examination of these reaction mixtures for solvent-derived products revealed the presence of dimethyl sulfone. Peroxy anions are one of several likely intermediates formed during the reaction of KO_2 with **1** (vide infra) and it is, of course, well known that peroxy anions will oxidize most sulfoxides to the corresponding sulfone, the observed reaction being[12a]

$$ROO^- + R'_2SO \rightarrow RO^- + R'_2SO_2 \qquad (5)$$

(Control experiments established that dissolution of potassium superoxide in Me_2SO-18-crown-6 yields no significant (<2%) Me_2SO_2 after 5 h.) It follows from eq 5 that equal amounts of alcohol and sulfone are produced in this process. Indeed, Gibian has proposed that this process provides the principal pathway by which alcohol is produced in the reaction of KO_2 with alkyl halide.[12b]

Figure 2 shows the yield of Me_2SO_2 produced during the course of the reaction of 3 equiv of KO_2 with *n*-hexyl bromide in Me_2SO. A comparison of these data with those shown in Figure 1 reveals that depending on the ratio of KO_2 to *n*-hexyl bromide, the yield of 1-hexanol can greatly *exceed* the yield of Me_2SO_2. Thus, although a 1:1 ratio of these reactants produces an 18% yield of 1-hexanol, the corresponding yield of Me_2SO_2 is only 4%. In light of eq 6, it follows that greater than 75% of the alcohol produced in the 1:1 reaction cannot arise via eq 5.

It is further apparent from Figures 1 and 2 that the yield of sulfone increases as the ratio of KO_2 to *n*-hexyl bromide increases. In addition, the difference between the yield of 1-hexanol and Me_2SO_2 decreases as the ratio of KO_2 to *n*-hexyl bromide increases. Moreover, unlike the 1:1 reaction which was complete in $\lesssim$15 min, the yield of Me_2SO_2 in the 3:1 and 5:1 reactions increases with extended reaction times. These facts suggest that the slower secondary reaction of KO_2 with di-*n*-hexyl peroxide may also provide a pathway to Me_2SO_2. Figure 3 confirms this proposal.

Reaction of *n*-hexyl bromide with KO_2 in benzene is illustrated graphically in Figure 4. Aside from the limited side reaction involving the formation of Me_2SO_2 that accompanies reaction in Me_2SO, the principal difference between the two

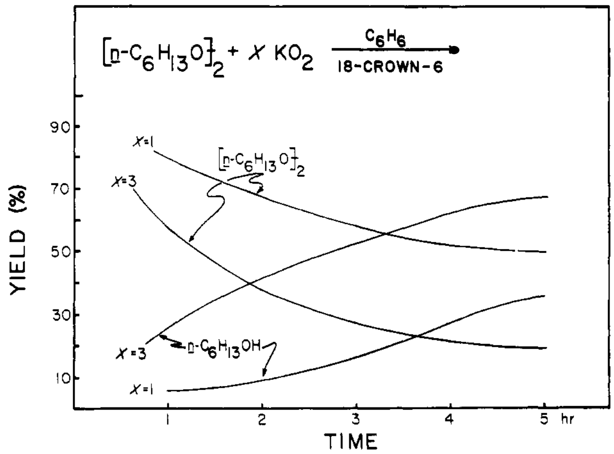


Figure 5. Data illustrating the influence of time and reactant ratios on product formation and reactant consumption during the reaction of KO_2 with di-*n*-hexyl peroxide in benzene-18-crown-6 at 25 °C. Reaction workup and analyses were carried out as described in Figure 4.

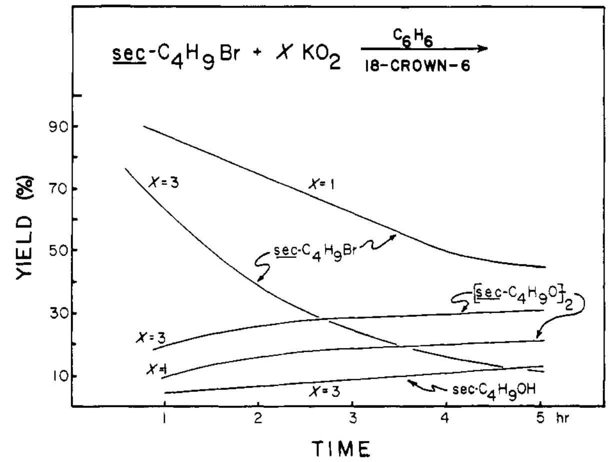


Figure 6. Reactant consumption and product formation during the course of the reaction of *sec*-butyl bromide (3.33 mmol) with KO_2 in benzene-18-crown-6 at 25 °C. Di-*sec*-butyl peroxide, *sec*-butyl alcohol, and 2-butanone were analyzed by LC following the workup procedure outlined in Figure 4. The yield of recovered *sec*-butyl bromide was determined by GLC.

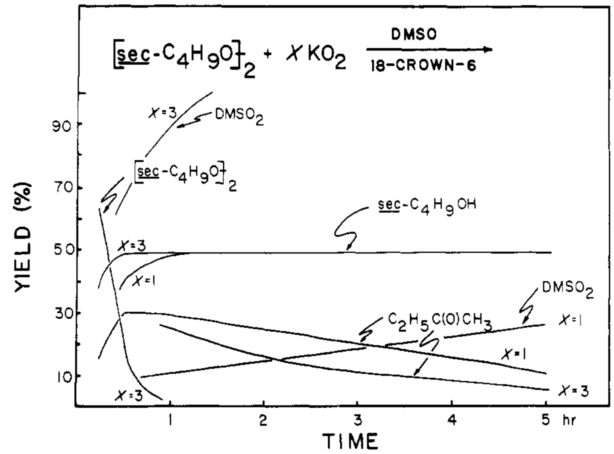


Figure 7. Data illustrating the influence of time and reactant ratio on the yield of products and consumption of peroxide during the reaction of di-*sec*-butyl peroxide with KO_2 in Me_2SO containing 18-crown-6 ether. Analyses were carried out as follows: di-*sec*-butyl peroxide, *sec*-butyl alcohol, and 2-butanone were determined by LC after a workup that consisted of treating individual reaction mixtures with an acidified solution of aqueous methanol. Me_2SO_2 was determined by GLC analysis prior to hydrolytic workup.

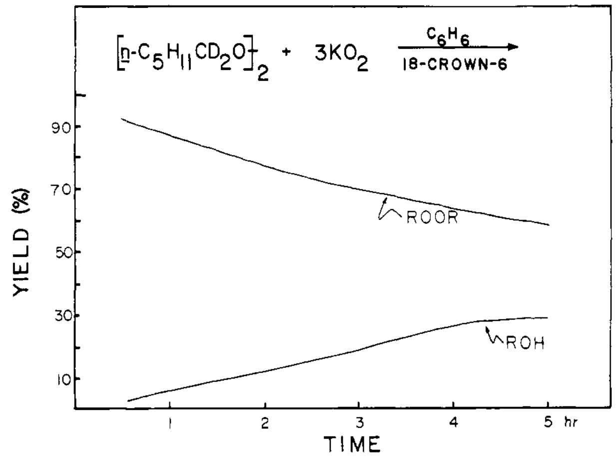


Figure 8. Reaction of di-*n*-hexyl-*1,1,1′,1′*-d_4 peroxide with KO_2 in benzene-18-crown-6 illustrating the influence which deuterium substitution at the α carbon has on reaction rate (cf. Figure 5).

processes seems to be one of rates, the reaction in Me_2SO being appreciably faster than in benzene. This fact is presumably a consequence of, inter alia, the enhanced solubility of KO_2 in Me_2SO-18-crown-6 relative to benzene-18-crown-6 mixtures.

Reaction of sec-Butyl Bromide with KO_2 in Me_2SO and Benzene. The reaction of *sec*-butyl bromide with potassium superoxide in Me_2SO- and benzene-18-crown-6 is summarized below and in Figure 6. These results reveal a reactivity which, allowing for the difference in structure of the alkyl groups, parallels that observed for the corresponding reaction with *n*-hexyl bromide: the principal isolated products are

$$sec\text{-}C_4H_9Br + KO_2 \xrightarrow[\text{18-crown-6, >3 h}]{Me_2SO} sec\text{-}C_4H_9OH\ (30\%)$$

$$+ C_4H_8\ (31\%)\ [sec\text{-}C_4H_9O\text{+}_2\ (20\%)$$

$$+ Me_2SO_2\ (18\%) + C_2H_5C(O)CH_3\ (4\%)$$

$$sec\text{-}C_4H_9Br + 3KO_2 \xrightarrow[\text{18-crown-6 >1 h}]{Me_2SO} sec\text{-}C_4H_9OH\ (31\%)$$

$$+ C_4H_8\ (31\%) + Me_2SO_2\ (63\%) + C_2H_5C(O)CH_3\ (4\%)$$

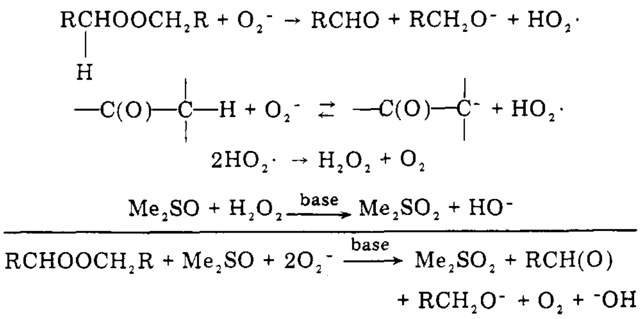
sec-butyl alcohol, di-*sec*-butyl peroxide, and butene(s). A further parallel is seen in the influence which reactant ratios have on product ratios: the yield of olefin is insensitive to the reactant ratios while that of *sec*-butyl alcohol increases and that of di-*sec*-butyl peroxide diminishes as the ratio of KO_2 to *sec*-butyl bromide increases.

Figure 8 illustrates the reaction of di-*sec*-butyl peroxide with KO_2 in Me_2SO. Again, the observed behavior is reminiscent of that exhibited by di-*n*-hexyl peroxide in its reaction with KO_2 (cf. Figures 3 and 5).

A similar reactivity is observed for the reaction of [*sec*-C_4H_9O+$_2$ with KO_2 in benzene-18-crown-6, although, as before, the reaction in benzene is significantly slower than the corresponding reaction in Me_2SO. It follows that the direct reaction of KO_2 with the initial product, di-*sec*-butyl peroxide, provides one plausible pathway for the production of *sec*-butyl alcohol produced during the course of the reaction of *sec*-butyl bromide with KO_2.

The most outstanding difference between the reaction of KO_2 with *n*-hexyl bromide and *sec*-butyl bromide appears to be the increased yields of olefin (and corresponding decreased yields of alcohol and peroxide) produced in the reactions of the latter. This difference is in qualitative accord with the proposition that the response of the product-determing step to the structure of the organic moiety is that expected for competing substitution and elimination reactions (vide infra). In contrast

Scheme I



$$\mathrm{RCH(H)OOCH_2R + O_2^- \rightarrow RCHO + RCH_2O^- + HO_2\cdot}$$

$$\mathrm{-C(O)-\overset{|}{\underset{|}{C}}-H + O_2^- \rightleftarrows -C(O)-\overset{|}{\underset{|}{C}}^- + HO_2\cdot}$$

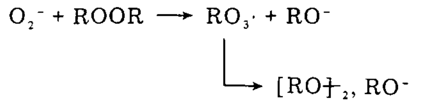
$$\mathrm{2HO_2\cdot \rightarrow H_2O_2 + O_2}$$

$$\mathrm{Me_2SO + H_2O_2 \xrightarrow{base} Me_2SO_2 + HO^-}$$

$$\mathrm{RCH(H)OOCH_2R + Me_2SO + 2O_2^- \xrightarrow{base} Me_2SO_2 + RCH(O) + RCH_2O^- + O_2 + {}^-OH}$$

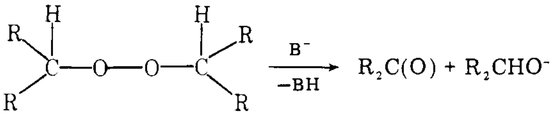
to *n*-hexyl bromide, the 1:1 reaction of *sec*-butyl bromide with KO_2 produces a moderate yield of Me_2SO_2 while the 1:3 reaction results in a substantial yield of this material. This difference, too, can be rationalized in terms of the effect which the structure of the organic moiety is expected to have on competing processes (vide infra).

Reaction of Dialkyl Peroxides with KO_2 in Me_2SO and Benzene.[16] It is apparent from the results presented here and elsewhere[20b] that dialkyl peroxides are intimately involved in the reaction of primary and secondary halides and tosylates (vide infra) with potassium superoxide in both Me_2SO and benzene. Given the nature of superoxide, its reaction with dialkyl peroxide might, a priori, take place by any of three pathways: (1) nucleophilic displacement on peroxide oxygen[13]



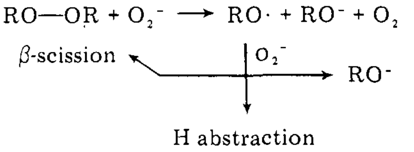
$$\mathrm{O_2^- + ROOR \longrightarrow RO_3\cdot + RO^-} \qquad \mathrm{RO_3\cdot \longrightarrow [RO\cdot]_2, RO^-} \tag{6}$$

(2) base-catalyzed decomposition of those peroxides bearing protons on the α carbon,[14]



(7)

and (3) electron transfer, similar to that observed in the facile reaction of organolithium and Grignard reagents with alkyl peroxides.[15]



$$\mathrm{RO{-}OR + O_2^- \longrightarrow RO\cdot + RO^- + O_2} \tag{8}$$

The reaction of *n*-hexyl and *sec*-butyl peroxide with KO_2 in Me_2SO and benzene is summarized in Figures 3, 5, 7, and 8 and shows that reaction in Me_2SO is much more rapid than in benzene. The reaction of *sec*-butyl peroxide with KO_2 in Me_2SO produces both *sec*-butyl alcohol and 2-butanone, suggesting that based-catalyzed cleavage is perhaps dominant. The former product is obtained in 50% yield but the yield of ketone passes through a maximum, presumably because of further base-catalyzed condensations. Indeed, 2-butanone is unstable in the presence of KO_2 in benzene-18-crown-6, and a 0.15 M solution is completely consumed in 8 h by 1 equiv of KO_2. The presence of carbonyl compounds also provides an explanation for the formation of Me_2SO_2 observed in the reaction of di-*n*-hexyl and di-*sec*-butyl peroxide (cf. Figures 3 and 7; Scheme I).

Finally, only the elimination mechanism can account for both the failure of di-*tert*-butyl peroxide to undergo any apparent reaction with KO_2 in Me_2SO even after 24 h and the substantial isotope effect observed in the reaction of KO_2 with di-*n*-hexyl-*1,1,1′,1′*-d_4 peroxide (Figure 8). However, the fact that alcohol is produced in greater than 50% yield in the reaction of excess KO_2 with certain alkyl halides and dialkyl peroxides (cf. Figures 2, 3, and 5) necessarily requires an additional pathway(s) leading to alcohol. Indeed, in a separate experiment when di-*n*-hexyl peroxide was allowed to react with powdered KOH in benzene-18-crown-6, analysis after 8 h revealed no unreacted di-*n*-hexyl peroxide and a 60% yield of 1-hexanol. Thus, even in the reaction of dialkyl peroxides with hydroxide ion, an alternative pathway(s) to base-induced decomposition (presumably involving nucleophilic displacement on oxygen) exists.

Effect of Halide. Reaction of KO_2 with *n*-Hexyl Iodide. The oxidation of halide ion by peroxides is well known.[13] Since peroxides are products in the reaction of alkyl halides with KO_2, we have investigated the possible ancillary role of halide in these reactions.

Potassium bromide shows no apparent reactivity toward di-*n*-hexyl peroxide in Me_2SO after several hours. Nor does added potassium bromide have any discernible influence on the yield of di-*n*-hexyl peroxide produced by the reaction of KO_2 with *n*-hexyl bromide. In contrast, iodide ion reacts readily with di-*n*-hexyl peroxide in Me_2SO, according to eq 10.[17]

$$\mathrm{ROOR + 2I^- \rightarrow 2RO^- + I_2} \tag{9}$$

$$\mathrm{I_2 + 2O_2^- \rightarrow 2I^- + 2O_2\ (ref\ 18b)} \tag{10}$$

This fact permits a reasonable explanation of the difference between the product distributions observed in the 1:3 reaction of *n*-hexyl bromide (Figure 2) and iodide (Figure 9) with KO_2 in Me_2SO. Comparison of these data reveals that the reaction of KO_2 with *n*-hexyl iodide produces a substantially greater yield of 1-hexanol than the corresponding reaction with *n*-hexyl bromide, presumably as a consequence of eq 9 and 10.

Influence of the Nature of the Crown Ether. Reaction of superoxide with alkyl halides and tosylates has been observed by a number of investigators.[18-20] Despite certain basic similarities, these studies are characterized by unusual inconsistencies in the reported product studies. Merritt and Johnson have suggested that these variations reflect the influence of the reaction conditions on the fate of the initially formed alkylperoxy radicals.[21] Such an explanation is unlikely (vide infra). We have shown that factors such as the nature of the workup conditions, the ratio of KO_2 to substrate, ratio of KO_2 to crown ether, nature of the halide, and reaction time can all influence product ratios; however, it remained to be determined what, if any, effect the nature of the macrocyclic ether has on the course of the reaction of KO_2 with alkyl halides. In an effort to determine if such an influence exists, we have examined the reaction of *n*-hexyl bromide with KO_2 in Me_2SO in the presence of different crown ethers. A comparison of these results is seen in Table II. They reveal that, in our hands, similar product distributions are observed with several 18-crown-6 ethers of differing grades suggesting that the nature of the crown ether does not substantially influence the course of this reaction.

Reaction of *n*-Hexyl Bromide with NaO_2 in Me_2SO. Based on a consideration of stability constants, K (determined in *water*), for the polyether-cation complex of dicyclohexyl-18-crown-6, with sodium and potassium ions,[22] and the estimated size of the cavity (2.6–3.2 Å) 18-crown-6[23] (ionic radii: Na^+ = 1.93 Å, K^+ = 2.66 Å; $K_{Na^+(H_2O)} = 1.7\ M^{-1}$, $K_{K^+(H_2O)} = 2.2\ M^{-1}$), NaO_2 might be expected to be less reactive than KO_2 because of its reduced solubility. Figure 10 shows that this is the case: even after 5 h, a substantial quantity of unreacted *n*-hexyl bromide remains in the 1:1 reaction of NaO_2 with **1**, whereas the equivalent reaction with KO_2 results in complete consumption of **1** in $\lesssim$15 min. It is interesting to note that in

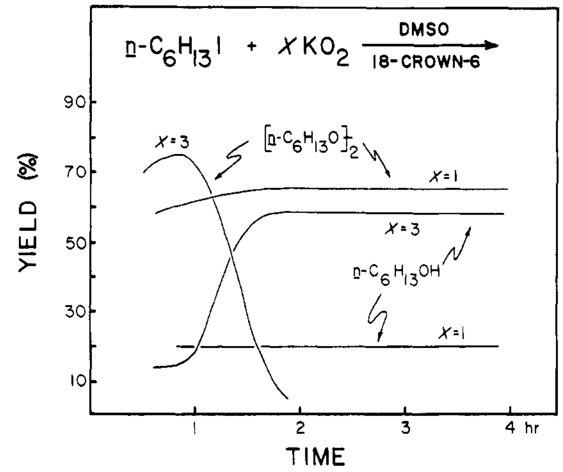


Figure 9. Reaction of KO_2 with *n*-hexyl iodide (1:1 and 3:1) in Me_2SO-18-crown-6 exhibits a different profile than the corresponding reaction with *n*-hexyl bromide (cf. Figures 1 and 2).

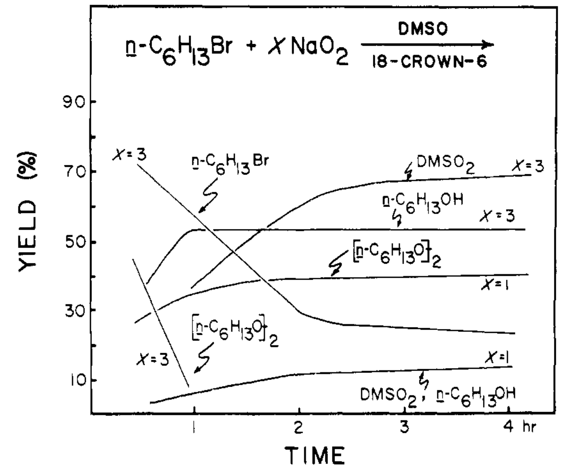


Figure 10. Plot showing the production of di-*n*-hexyl peroxide, 1-hexanol, and Me_2SO_2 as well as consumption of *n*-hexyl bromide during the course of the reaction of NaO_2 with **1** (1:1 and 3:1) in Me_2SO. Workup and analytical procedures were equivalent to those described in Figure 1.

Table II. Influence of Different 18-Crown-6 Ethers on the Reaction of KO_2 with *n*-Hexyl Bromide in Me_2SO[a]

RBr, mM	KO_2, mM	crown ether, mM	time h	products, % ROH	products, % ROOR
3.00	3.00	dicyclohexyl-18-crown-6[b] (0.30)	0.5	10	60
			1	13	63
			2	12	66
			3	12	68
			4	12	65
			5	15	65
3.00	3.00	dicyclohexyl-18-crown-6[c] (0.30)	0.5	6	54
			1	10	65
			2	12	68
			3	14	68
			4	12	70
			5	15	71
3.00	3.00	18-crown-6[c] (0.30)	0.5	11	74
			1	10	67
			2	14	70
			3	15	68
			4	15	72
			5	14	68

[a] Solution volume, 20 mL of Me_2SO. [b] Purchased from Fluka Chemical Co., "puriss" grade, and used without further purification. [c] Purchased from Aldrich Chemical Co., "technical" grade, and used without further purification.

contrast to the 3:1 reaction of KO_2 with **1** in which the yield of 1-hexanol increases gradually over a period of ca. 24 h to a maximum value of ~60%, the equivalent reaction employing NaO_2 is over $\lesssim 2$ h. A reasonable explanation of this result would seem to be that NaO_2 is more basic under these conditions than is KO_2; hence, the base-induced destruction of peroxide (Scheme I) occurs more rapidly.

Reaction of *n*-Hexyl and *sec*-Hexyl Tosylate with KO_2 in Me_2SO and Benzene. Different leaving groups can influence the course of a substitution reaction in different ways and in so doing frequently provide additional insight into the mechanism of the reaction. With this purpose in mind, we undertook an investigation of the reaction of KO_2 with *n*-hexyl and *sec*-hexyl tosylate in Me_2SO and benzene. The results of this study are summarized below and in Figures 11-13. These data reveal a reactivity which in several ways parallels that observed for the corresponding bromides: the 1:1 reaction of KO_2 with *n*-hexyl tosylate in Me_2SO produces a reaction mixture consisting of two major components, di-*n*-hexyl peroxide and 1-hexanol, and two minor ($\lesssim 5\%$) components, Me_2SO_2 and hexene(s). Also, reactant ratios appear to influence product yields in a manner reminiscent of the effect caused by similar changes in the analogous reaction with *n*-hexyl bromide, viz., increasing the ratio of KO_2 to tosylate diminishes the yield of di-*n*-hexyl peroxide but increases the yield of alcohol and Me_2SO_2. Likewise, there are parallels between the reaction of KO_2 with *sec*-butyl bromide and *sec*-hexyl tosylate: both reactions produce equivalent products, the yields of which exhibit a parallel dependence on reactant ratios. The results summarized below show that in benzene-18-crown-6, reactions of KO_2 with *n*-hexyl and *sec*-hexyl tosylate, like the corresponding reactions with *n*-hexyl and *sec*-butyl bromide, display gross similarities (product yields, influence of reactant ratios on product distributions, etc.) to the same reaction performed in Me_2SO, the principal difference being one of reaction rate: reactions carried out in Me_2SO are significantly more rapid than the corresponding reactions in benzene. However, this difference in rate can be diminished by increasing the amount of 18-crown-6, thus,

$$n\text{-}C_6H_{13}OTs + 3KO_2 \xrightarrow[\text{18-crown-6 (100 mol \%) 0.5 h}]{C_6H_6} [n\text{-}C_6H_{13}O\text{+}_2\ (72\%) + n\text{-}C_6H_{13}OH\ (25\%)$$

$$n\text{-}C_6H_{13}OTs + 3KO_2 \xrightarrow[\text{18-crown-6 (100 mol \%) 3 h}]{C_6H_6} [n\text{-}C_6H_{13}O\text{+}_2\ (2\%) + n\text{-}C_6H_{13}OH\ (53\%)$$

A closer comparison of the reaction of KO_2 with alkyl halides and tosylates reveals two noteworthy differences. First, it is apparent that the reaction of KO_2 with *n*-hexyl and *sec*-hexyl tosylate in benzene to produce di-*n*-hexyl peroxide is substantially slower than the corresponding reaction with *n*-hexyl and *sec*-butyl bromides. Second, the reaction of KO_2 with *n*-hexyl and *sec*-hexyl tosylate in Me_2SO produces lower yields of the corresponding dialkyl peroxide but higher yields of the respective alcohol than is observed in the analogous reaction with *n*-hexyl and *sec*-butyl bromides. Although inverted from the reactivity order generally observed for displacements on alkyl bromides and tosylates in protic solvents, the first difference, i.e., an observed reactivity order of Br > OTs, is not unreasonable in this instance in view of the demonstrated and frequently dramatically different reactivities observed between displacement reactions in a protic solvent vs. the same reaction in an aprotic solvent. In DMF, for example, the leaving group tendencies for S_N2 reactions at saturated carbons are I > Br > OTs > Cl > $^+SMe_2$.[24]

Similar considerations provide a rational explanation of the

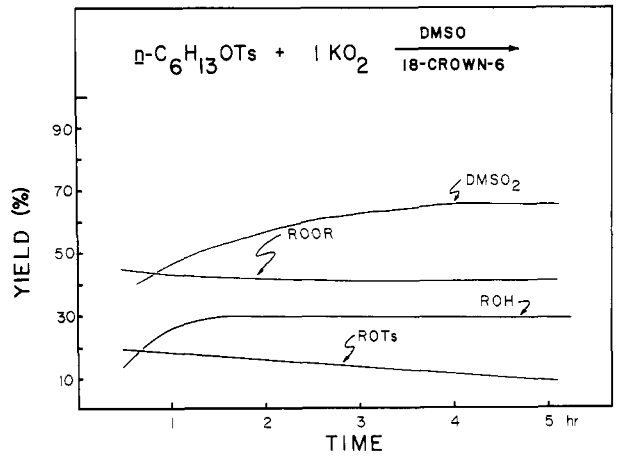


Figure 11. Analysis of the products and recovered tosylate resulting from the reaction of *n*-hexyl tosylate with 1 equiv of KO_2 in Me_2SO-18-crown-6. Me_2SO_2 was determined by GLC prior to workup. The analysis of di-*n*-hexyl peroxide, 1-hexanol, and recovered *n*-hexyl tosylate was performed by LC following individual reaction workup as described in Figure 1.

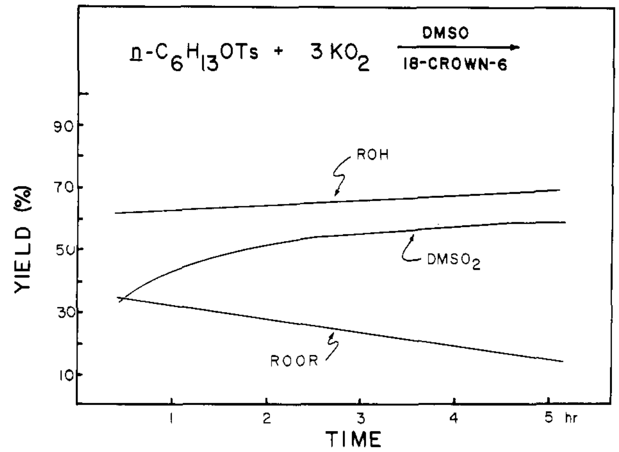


Figure 12. Plot showing the influence of time and reactant ratio (cf. Figure 13) on distribution of products produced by the reaction of *n*-hexyl tosylate (3.33 mmol) with KO_2 (10.0 mmol) in Me_2SO-18-crown-6 (20 mL, 1.00 mmol) at 25 °C. Analytical procedures are those described in Figure 13.

second difference. Thus, in view of the fact that the carbon-oxygen bond forming step is the same for both *n*-hexyl bromide and tosylate (vide infra), it follows that any difference in peroxide and alcohol yields observed in the reaction of KO_2 with these two substrates is a reflection of differences between the *subsequent* reaction sequences that lead from alkylperoxy radicals to these products. Of the three such pathways available (vide infra) only one (viz., that involving nucleophilic displacement by alkylperoxy anion on an alkyl halide or tosylate) can be expected to exhibit the significant leaving group influence and order observed in these reactions. Moreover, if, as required by this argument, tosylate is a poorer leaving group than bromide, it follows as a consequence of eq 5 (all other factors being equal), that the 1:1 reaction of *n*-hexyl tosylate with KO_2 in Me_2SO should result in a significant increase in the yield of Me_2SO_2 relative to that observed for the corresponding reaction with *n*-hexyl bromide. Indeed, a comparison of Figures 1 and 11 sustains this expectation.

Oxygen Evolution Studies. The reaction of alkyl halides and tosylates with KO_2 is characterized by the evolution of molecular oxygen. The rate of evolution, consonant with the rate of reaction, is rapid in Me_2SO and much slower in benzene. A summary of our brief study of this behavior is seen in Table III. It is apparent that all the alkyl halides and tosylates examined produce less than 50% yield of dioxygen. Indeed, 50% would appear to be the upper limiting value for the yield of molecular oxygen. Such a conclusion is certainly consistent with the stoichiometry of the reaction

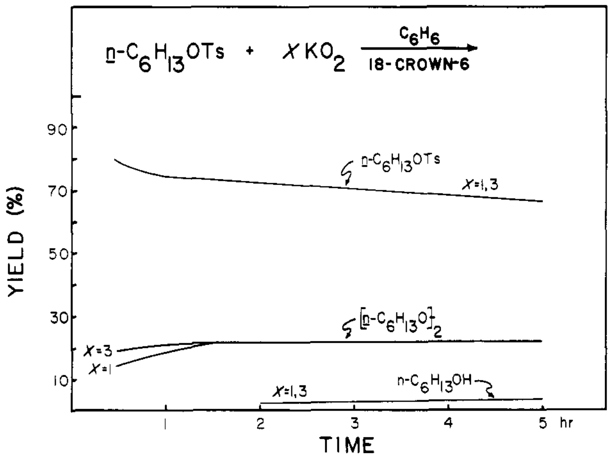


Figure 13. Analysis of the consumption of *n*-hexyl tosylate (3.33 mmol) and the production of di-*n*-hexyl peroxide and 1-hexanol during the reaction of *n*-hexyl tosylate with KO_2 (1:1 and 1:3) in benzene-18-crown-6 at 25 °C. Individual reactions were worked up by treatment with an acidified solution of aqueous methanol; analyses were performed by LC.

Table III. Oxygen Evolution from the Reaction of Alkyl Halides, Tosylates, and Related Substrates with Potassium Superoxide in Me_2SO-18-Crown-6[a]

substrate (3.33 mM)	O_2, %[b]	substrate (3.33 mM)	O_2, %[b]
n-$C_8H_{17}Br$	46	*n*-$C_6H_{13}OTs$	31
n-$C_6H_{13}Br$	42	*sec*-$C_8H_{17}OTs$	3.5
sec-C_4H_9Br	44	*sec*-$C_6H_{13}OTs$	3.5
n-$C_8H_{17}I$	43	[*n*-$C_6H_{13}O$-]$_2$	5.0
n-$C_8H_{17}OTs$	30		

[a] All reactions were carried out in Me_2SO (20 mL) containing 10 mol % 18-crown-6 (1.0 mM) and 10.0 mM of KO_2. [b] Oxygen evolution was metered with a gas buret; yields are based on substrate, i.e., $\% O_2 = \text{mM } O_2/\text{mM (substrate)} \times 10^2$.

$$2RX + 2O_2^- \rightarrow ROOR + O_2 + 2X^-$$

A dramatic reduction in oxygen evolution is observed in the reaction of KO_2 with secondary tosylates. The reason for this puzzling observation remains unclear.

Stereochemistry of Carbon-Oxygen Bond Formation and the Relative Reactivity of Superoxide toward Alkyl Halides and Tosylates. The mild conditions and good yields associated with the reaction of superoxide with alkyl halides and tosylates afforded an opportunity to examine the stereochemistry of carbon-oxygen bond formation. Optically active (+)-(*S*)-2-octanol (α^{20}_{589} +7.97°, optical purity 99.4%) was converted to tosylate and thence to (−)-(*R*)-2-bromooctane (α^{20}_{589} −41.56°, optical purity 95.4%). Reaction of this tosylate with KO_2 in Me_2SO yields (−)-(*R*)-2-octanol (α^{20}_{589} −7.71°), corresponding to an optical purity and overall stereochemistry of 97% *inversion* of configuration. Similar reaction with (−)-(*R*)-2-bromooctane affords (+)-(*S*)-2-octanol in 90% optical purity (95% net *inversion* of configuration). A similar result (94% net

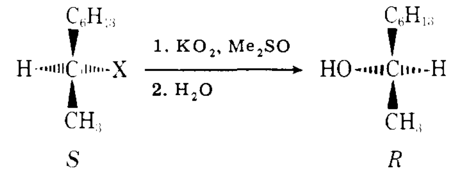


Table IV. Reaction of Potassium Superoxide with Various Organic Halides and Tosylates in Me_2SO[a]

substrate	rel reactivity[a]	substrate	rel reactivity[a]
$1\text{-}C_8H_{17}I$	4.5	$1\text{-}C_8H_{17}$	0.089
$2\text{-}C_8H_{17}I$	3.3	$2\text{-}C_8H_{17}Cl$	0.020
$1\text{-}C_8H_{17}Br$	1.00[a]	$1\text{-}C_8H_{17}OTs$	0.52 (0.55)[b]
$2\text{-}C_8H_{17}Br$	0.98	$2\text{-}C_8H_{17}OTs$	0.63 (0.27)[b]
$CH_3(CH_2)_2C(CH_3)_2Br$	0.90	$C_6H_5CH_2Cl$	2.9

[a] Reactivities were determined relative to 1-bromooctane (1.00) in Me_2SO by the standard competitive technique of allowing a mixture of a designated standard (1-bromooctane) and one additional substrate to react with a limited amount of potassium superoxide and determining the amount of unreacted starting substrate. [b] Determined in benzene.

inversion) has been observed by Johnson and Nidy for the reaction of KO_2 with (−)-(*R*)-2-bromooctane in benzene–18-crown-6.[19]

The data presented thus far suggest that the reaction of superoxide with *n*-hexyl bromide and tosylate in Me_2SO is rapid. In an effort to gain further insight into the reactivity of superoxide we carried out a series of experiments designed to determine the relative reactivity of KO_2 toward various organic halides and tosylates. A portion of the results of this study has been previously published[18] and is summarized in Table IV. Several points concerning these data deserve brief comment. First, it is apparent that the observed substrate reactivity is benzyl > primary > secondary > aryl and iodide > bromide > tosylate > chloride. Second, substitution is predominant with primary halides; however, substantial elimination occurs with secondary systems. Elimination is the predominant process observed from the reaction with the tertiary halide 2-bromo-2-methylpentane, but adamantyl bromide is quantitatively recovered after treatment with KO_2–18-crown-6 in Me_2SO and benzene for 24 h. These observations are in qualitative accord with the proposition that the response of the reaction of KO_2 with alkyl halides and tosylates in Me_2SO to changes in the nature of the leaving group and structure of the organic group bonded to it are those expected for an S_N2 reaction.[25]

It is noteworthy that the spread in reactivities is substantially smaller than that commonly observed for S_N2 reactions in protic solvents.[25] A similar leveling effect has been observed by others studying nucleophilic displacement in aprotic solvents.[24,26] Finally, although the differences in reactivity of KO_2 toward primary and secondary substrates is small, the nucleophilicity of superoxide is substantially greater than that of other nucleophiles under comparable conditions. For example, we previously reported data which indicated that the reaction of KO_2 with 1-bromooctane in Me_2SO–18-crown-6 occurs $\gtrsim 10^3$ times faster than KI reacts with the same substrate under equivalent conditions.[18] A similar conclusion has been presented by Danen and Warner, who recently determined the absolute rate constants for the reaction of KO_2 with several alkyl bromides.[27] Their relative rate (2.3) for the reaction of KO_2 with 1-bromobutane vs. 2-bromobutane in Me_2SO (determined in the absence of 18-crown-6) is in substantial agreement, considering the differences in reaction conditions, with the relative reactivity reported in Table IV for 1- vs. 2-bromooctane.

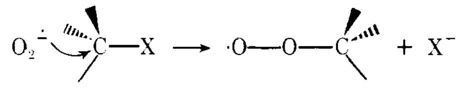
Discussion

The experimental data presented in this paper indicate that the reaction of potassium superoxide with alkyl halides and tosylates proceeds by a similar pathway, but at substantially different rates, in Me_2SO- and benzene–18-crown-6, by a mechanism which requires, in at least two instances, essentially complete inversion of configuration at the carbon originally bonded to halogen.

It has been calculated that direct electron transfer from superoxide to an alkyl bromide (eq 11) is thermodynamically disallowed.[21]

$$KO_2 + RBr \rightarrow O_2 + R\cdot + KBr \qquad (11)$$

A more accurate consideration of the thermodynamics for this reaction reveals its distinct plausibility.[28] We have argued, however, that the high stereoselectivity observed in this reaction is inconsistent with the intermediacy of free alkyl radicals.[18] Furthermore, the structure of the alkyl group bonded to the halogen, the nature of the leaving group, and the polarity of the solvent all exert an influence on the course of the carbon–oxygen bond forming step which is consistent with a mechanism that involves an S_N2 displacement at carbon. It follows that the initial reaction of superoxide with an alkyl halide produces an alkylperoxy radical, **2.** Three fundamentally



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different types of mechanistic schemes can be envisioned for the subsequent conversion of this intermediate to product. In one, self-reaction leads to a tetroxide, homolysis of which results in the production of geminate alkoxy radicals and oxygen, followed either by geminate coupling to yield the dialkyl peroxide or diffusion from the cage to produce free alkoxy radical.[29]

A second would involve the self-reaction of secondary and primary peroxy radicals by way of a tetroxide intermediate proceeding through a cyclic transition state in which one of the α-hydrogen atoms is transferred to give the observed products: ketone (aldehyde), alcohol, and oxygen.[30,31] Merritt and Johnson[21] have concluded that a concerted mechanism of this nature is largely responsible for the formation of alcohol and ketone (aldehyde) products produced in the reaction of alkyl halides with KO_2. It is clear, however, from the data presented here that such a reaction need not be invoked to explain the formation of alcohol and ketone (aldehyde). Indeed, our results demonstrate that these products probably arise from the direct reaction of superoxide with the initially formed alkyl peroxide (Scheme I).

A third pathway consists of the one-electron reduction of alkylperoxy radicals to peroxy anions, which in a subsequent step combine with alkyl bromide to produce dialkyl peroxide. It is possible to demonstrate that this process is the only one occurring to any significant extent during the reaction of KO_2 with alkyl halides. This conclusion rests on the reasonable assumption that the rate of reduction of alkylperoxy radicals by superoxide is approximately equal to or greater than the rate of reduction of $HO_2\cdot$ by O_2^-, i.e., $k_2 \gtrsim 8.5 \times 10^7\ M^{-1}\ s^{-1}$.[32] The three reactions of interest are given in the equations

$$O_2^- + RBr \xrightarrow{k_1} RO_2\cdot + Br^- \qquad (12)$$

$$RO_2\cdot + O_2^- \xrightarrow{k_2} RO_2^- + O_2 \qquad (13)$$

$$RO_2\cdot + RO_2\cdot \xrightarrow{k_3} RO_4R \qquad (14)$$

A consideration of the rate laws governing these reactions leads to the expression

$$\text{rate}_2 = \frac{k_2}{2k_3}\frac{[O_2^-]}{[RO_2\cdot]}\,\text{rate}_3$$

relating the relative rates of one-electron reduction (eq 13) and the bimolecular or self-reaction of two peroxy radicals (eq 14).

For all the reactions studied in this work the initial concentration of alkyl halide [RX] was ca. 0.2 M. Assuming a steady-state concentration of $[RO_2\cdot] \approx 1 \times 10^{-6}$ M[33] and the literature values for $k_1 = 1.5 \times 10^2$ M^{-1} s^{-1} [27] and $k_3 = 2 \times 10^8$ M^{-1} s^{-1},[30] it follows that $\text{rate}_2 \approx 10^3\ (\text{rate}_3)$. Thus, we conclude that the bimolecular coupling of peroxy radicals plays a negligible role in the reaction of KO_2 with alkyl halides. The elimination of this alternative mechanism leaves eq 13 as the only plausible description of the fate of the intermediate peroxy radicals. It should be recalled that this same conclusion was also reached from a consideration of the differences observed between the reactivity of alkyl bromides and tosylates with KO_2 as discussed above.

Finally, the nature of the principal side reaction observed during the reaction of superoxide with alkyl halides and tosylates deserves brief comment. Dehydrohalogenation is, of course, a well-known side reaction that occurs in varying degree in displacement reactions involving alkyl halides. In light of the earlier discussion concerning the substantially increased basicity of bases in Me_2SO, it is not unreasonable to suspect that superoxide is sufficiently basic in Me_2SO to affect dehydrohalogenation of an alkyl halide or tosylate. More intriguing is the possibility that this reaction possesses for the convenient,

$$RCH_2CH_2X + O_2^-\cdot \rightarrow RCH{=}CH_2 + HO_2\cdot + X^-$$

deliberate, and metered preparation of hydroperoxy radicals, $HO_2\cdot$.

In conclusion, it is worthwhile to make explicit two general points concerning the reaction of potassium superoxide with alkyl halides and tosylates. First, while it is clear from the work reported in this paper that reaction of most alkyl halides does not proceed through an electron-transfer process involving free alkyl radicals, it is not clear that the reaction of all classes of alkyl halides will follow a related mechanism. In particular, electron-transfer reactions are notoriously sensitive to changes in the structure of the alkyl moiety and halide center, the recognized order of facility of such reactions being benzyl, allyl, tertiary > secondary > primary, and I > Br > Cl.[32] Second, accepting the limitations on the generality of this reaction, the treatment of alkyl halides and tosylates with potassium superoxide provides a convenient method of generating free alkylperoxy radicals under mild conditions by a procedure that does not require autoxidation techniques. As such, the reaction merits further development as a probe for the study of this important class of free radicals.

Experimental Section

General. Melting points were obtained using a Thomas-Hoover capillary melting point apparatus and are uncorrected. All boiling points are uncorrected. ^1H NMR spectra were determined on Varian T-60 or Jeol MH-100 spectrometers. Chemical shifts are reported in parts per million relative to internal tetramethylsilane. Coupling constants are in hertz. Infrared spectra were recorded in sodium chloride cells on a Perkin-Elmer Model 727B grating spectrometer. Mass spectra were obtained on a Hitachi Perkin-Elmer Model RMU-7 mass spectrometer. Analytical GLC analyses were performed on Hewlett-Packard Model 5750 or Varian Model 1400 instruments equipped with flame ionization detectors and a Hewlett-Packard Model 3380A electronic integrator. Response factors were obtained with authentic samples. Analytical LC analyses were carried out on a Waters Model 6000A instrument equipped with UV and refractive index indicator. Response factors were determined with authentic samples. Unless otherwise indicated, all reagents were stored, weighed, and handled under a nitrogen atmosphere in a Vacuum Atmosphere glovebox. A static nitrogen atmosphere was employed in all reactions. Optical rotations were recorded as neat liquids in a 1-mm cell using a Perkin-Elmer Model 141 spectropolarimeter.

***n*-Hexyl iodide and bromide, *sec*-hexyl bromide, *sec*-butyl bromide, and 1-adamantyl bromide** as well as the halides listed in Table IV were purchased from commercial sources and used without further purification. **Dimethyl sulfone** and **di-*tert*-butyl peroxide** were also obtained from commercial distributors. Potassium superoxide was purchased from MSA (Evans City, Pa.). This material was ground to a fine powder in a mortar and pestle following preliminary dispersion in a Waring blender.

Dimethyl sulfoxide (Me_2SO) was dried by distillation at reduced pressure (96 °C, 25 Torr) from calcium hydride and stored over activated molecular sieves (4 Å). Benzene was distilled under nitrogen from benzophenone–sodium.

18-Crown-6 Ether. Unless otherwise noted, 18-crown-6 ether was prepared as described by Gokel, Cram, Liotta, and Harris,[34] purified by two successive applications of the purification procedure described therein, and stored over P_2O_5 under nitrogen, mp 39.5–41.0 °C (lit.[34] mp 36.5–38.0 °C).

Di-*n*-hexyl peroxide, prepared by the reaction of *n*-hexyl methanesulfonate and hydrogen peroxide,[35] had bp 59 °C (0.2 Torr) [lit.[35] bp 58 °C (0.5 Torr)]. *n*-Hexyl hydroperoxide was prepared in 42% yield as described by Williams and Mosher;[36] it had bp 42–43 °C (2.0 Torr) [lit.[36] bp 42–43 °C (2.0 Torr)].

Di-*sec*-butyl peroxide, prepared following the procedure of Welch, Homer, and Mosher,[35] had bp 52 °C (20 Torr) [lit.[35] bp 59 °C (50 Torr)].

***sec*-Butyl hydroperoxide** was prepared by the reaction of *sec*-butyl methanesulfonate and hydrogen peroxide as reported by Williams and Mosher,[37] bp 49 °C (1.0 Torr) [lit.[37] bp 41–42 °C (11.0 Torr)].

***n*-Hexyl, *sec*-hexyl, and *n*-octyl tosylates** were prepared from the corresponding alcohol by a recognized procedure.[38]

(−)-(*R*)-2-Octyl bromide, α^{20}_{529} −41.56°, 95.4% optically pure, was prepared from optically active (+)-(*S*)-2-octanol (Aldrich) according to the preferred literature procedure.[39]

Preparation of $CH_3(CH_2)_4CD_2OH$ and $[CH_3(CH_4)_2CD_2O\!+\!_2$. Hexanol-*1,1*-$d_2$ was prepared in 87% yield from ethyl caproate (62.58 g, 0.434 mol) by treatment with lithium aluminum deuteride by a procedure analogous to that described by Max and Deatherage[40] for the preparation of octanol-*1,1*-d_2. Hexanol-*1,1*-d_2 was converted into the corresponding peroxide by the procedure outlined above.

Procedures for Reactions. Similar procedures were used to carry out the reactions examined. Representative procedures for each reaction follow.

Reaction of Potassium Superoxide with *n*-Hexyl Bromide (1) in Me_2SO. In a typical experiment 0.711 g (10.0 mmol) of KO_2 was placed in a 100-mL flask equipped with a Teflon-coated magnetic stirrer bar. The vessel was capped with a rubber septum and 17 mL of Me_2SO added by syringe before adding 3.0 mL of a 0.33 M solution of 18-crown-6 in Me_2SO followed by 0.550 g (3.33 mmol) of *n*-hexyl bromide. The resulting mixture was stirred for 1 h, then treated with 20 mL of 95% methanol containing ~1 mL of 9 M H_2SO_4. Known amounts of *n*-decane and bromobenzene were added as internal standards along with methylene chloride (7.5 mL), added to provide a homogeneous mixture. This mixture was analyzed by LC for di-*n*-hexyl peroxide, 1-hexanol, 1-hexanal, and 1-hexene on a 10 × 0.25 in. column of μ-Bondapak-C_{18} (Waters Associates) using respectively 95/5, 70/30, 60/40, and 65/35 methanol-water as eluent.

To determine the yield of unreacted *n*-hexyl bromide, a separate reaction was carried out and worked up by addition of ca. 1 mL of 9 M H_2SO_4 followed by the addition of methylene chloride and a known amount of *n*-decane as internal standard. The resulting reaction mixture was transferred to a separatory funnel and a solution (20 mL) of saturated brine added before the contents of the flask was extracted with four 10-mL portions of petroleum ether (bp 30–60 °C). The combined ether extracts were dried ($MgSO_4$) and analyzed by GLC on a 10 ft × 0.125 in. column of 3% SE-30 on 80/100 Chromsorb Q.

To determine the yield of dimethyl sulfone, the above reaction was repeated adding, in addition to the reagents already described, a known amount of di-*n*-propyl sulfone as an internal standard. The resulting mixture was stirred vigorously at room temperature. Aliquots (0.20 mL) were removed by syringe at selected intervals and analyzed by GLC on a 3 ft × 0.25 in. column of 20% Carbowax 20M on Chromosorb W.

Oxygen evolution studies were performed in a flame-dried, 50-mL flask equipped with a Teflon-coated stirrer bar and a side arm connected by a length of flexible Tygon tubing to a mercury-filled gas buret. Reagents were added in the amounts described above and the flask was then stoppered with a rubber septum. With vigorous stirring,

Table V

LC Conditions for Reactions in Benzene

substrate	internal standard	column	solvent
di-*n*-hexyl peroxide	di-*n*-butyl ether	*μ*-Porasil	C_6H_6
di-*sec*-hexyl peroxide	di-*n*-butyl ether	*μ*-Porasil	C_6H_6
1-hexanol	2-butanol	Corasil II	C_6H_6
2-hexanol	*tert*-butyl alcohol	Corasil II	C_6H_6
hexanal	di-*n*-butyl ether	*μ*-Porasil	C_6H_6
2-hexanone	di-*n*-butyl ether	*μ*-Porasil	C_6H_6
n-hexyl tosylate	benzonitrile	*μ*-Porasil	$CHCl_3$
sec-hexyl tosylate	benzonitrile	*μ*-Porasil	$CHCl_3$
sec-butyl tosylate	di-*n*-butyl ether	*μ*-Porasil	C_6H_6
2-butanol	1-hexanol	Corasil II	C_6H_6
2-butanone	1-hexanol	*μ*-Porasil	$CHCl_3$

GLC Conditions for Reactions in Benzene

substrate	internal standard	column
sec-butyl bromide	*n*-octane	0.125 in. × 10 ft 10% Carbowax on 80/100 Chromosorb Q
n-hexyl bromide	*n*-decane	0.125 in. × 10 ft 3% SE-30
butenes	*n*-heptane	0.125 in. × 10 ft 10% Carbowax
hexenes	cyclopentane	0.125 in. × 10 ft 3% SE-30
1-bromoadamantane	*n*-tridecane	0.125 in. × 6 ft UCW 98

n-hexyl bromide (0.550 g, 3.33 mmol) was added by syringe. The resulting evolution of oxygen was monitored by the volume of mercury displaced. All readings were corrected for barometric pressure. This value was converted to millimoles of oxygen using the perfect gas equation.

Reaction of Potassium Superoxide with *n*-Hexyl and *sec*-Hexyl Tosylate in Me_2SO. Procedures similar to those described for the reaction of KO_2 with *n*-hexyl bromide were employed in the reaction of KO_2 with *n*-hexyl and *sec*-hexyl tosylates in Me_2SO. Analysis for recovered tosylate was performed by LC on *μ*-Bondapak C_{18} using 70/30 methanol-water and bromobenzene as internal standard.

Reaction of Potassium Superoxide with Di-*n*-hexyl Peroxide in Me_2SO. In a procedure similar to that described above, Me_2SO (19 mL) and 0.90 mL of a 0.33 M solution of 18-crown-6 in Me_2SO was added to 0.213 g (3.00 mmol) of powdered KO_2 contained in a 100-mL flask equipped with a Teflon-coated stirrer bar and capped with a rubber septum. Di-*n*-hexyl peroxide (0.605 g, 3.00 mmol) was added by syringe and the resulting reaction mixture stirred for a selected period of time. Workup and analysis procedures were equivalent to those described above.

Reaction of Potassium Superoxide with n-Hexyl Iodide in Me_2SO. In a typical experiment, *n*-hexyl iodide (0.706 g, 3.33 mmol) and KO_2 (0.711 g, 10.0 mmol) were allowed to react as described above. Analytical conditions (LC and GLC) were equivalent to those already outlined.

Reaction of Potassium Superoxide with 2-Bromobutane in Me_2SO. In a typical experiment, 0.711 g (10.0 mmol) of powdered potassium superoxide was placed in a flame-dried, 100-mL round-bottom flask equipped with a Teflon-coated magnetic stirrer bar. The flask was capped with a rubber septum and flushed with nitrogen before adding Me_2SO (17 mL) by syringe. With stirring, a solution of 18-crown-6 in Me_2SO (3.0 mL, 0.33 M) followed by 0.456 g (3.33 mmol) of 2-bromobutane were added by syringe. The resulting mixture was stirred for 1 h, then treated with 20 mL of 95% methanol containing ~1 mL of 9 M H_2SO_4. A known amount of 1-butanol and bromobenzene were added as internal standards along with methylene chloride (7.5 mL), added to provide a homogeneous mixture. This mixture was analyzed by LC for di-*sec*-butyl peroxide, 2-butanol, and 2-butanone on a 10 × 0.25 in. *μ*-Bondapak-C_{18} column (Waters Associates) using respectively 75, 30, and 30% methanol-water solutions as eluent.

The yield of unreacted 2-bromobutane was obtained by repeating the above reaction followed by a workup consisting of the addition of 1 mL of 9 M H_2SO_4 followed by 7.5 mL of methylene chloride. A known amount of *n*-octane was added as internal standard, and the reaction mixture transferred to a separatory funnel. Saturated brine solution (20 mL) was added to the separatory funnel and the mixture extracted with four 10-mL portions of petroleum ether (bp 30–60 °C). The combined ether extracts were dried ($MgSO_4$) and analyzed by GLC on a 10 ft × 0.125 in. column of 3% SE-30 on 80/100 chromosorb Q.

The yield of butene(s) was determined as follows. Powdered potassium superoxide (0.711 g, 10.0 mmol) was placed in a flame-dried 100-mL flask equipped with a Teflon-coated magnetic stirrer bar. The flask was capped with a rubber septum and 17 mL of Me_2SO added by syringe followed by 3.0 mL of a 0.33 M solution of 18-crown-6 in Me_2SO. The flask was then placed under a positive pressure of nitrogen and the rubber septum replaced with a fresh septum which was then securely wired down. To the flask was then added by syringe 0.456 g (3.33 mmol) of 2-bromobutane and the reaction mixture stirred for 1 h as a sealed system. Methylene chloride (5.0 mL) was added by syringe followed by a known amount of *n*-heptane as internal standard. The reaction was immediately analyzed by GLC using a 10 ft × 0.125 in., 10% Carbowax on 80/100 GCQ.

The yields of Me_2SO_2 and oxygen evolution were obtained by procedures equivalent to those described for similar determinations carried out for the reaction of KO_2 with *n*-hexyl bromide in Me_2SO.

Reaction of Potassium Superoxide with Di-*sec*-butyl Peroxide in Me_2SO. The reaction of KO_2 with (*sec*-$C_4H_9O)_2$ in Me_2SO and subsequent analyses were carried out by procedures equivalent to those described for the reaction of 2-bromobutane with KO_2 in Me_2SO.

Reaction of Potassium Superoxide and 2-Butanone in Me_2SO. In a typical experiment, 0.711 g (10.0 mmol) of powdered potassium superoxide was placed in a flame-dried 100-mL round-bottom flask equipped with a Teflon-coated magnetic stirrer bar and capped with a rubber septum. To the flask were then added by syringe 17.0 mL of Me_2SO, 3.0 mL of a 0.33 M solution of 18-crown-6 in Me_2SO, and 0.239 g (3.33 mmol) of 2-butanone. The resulting mixture was stirred for 1 h, then treated with 20 mL of 95% methanol containing 1 mL of 9 M H_2SO_4. A known amount of 1-butanol was added as internal standard along with methylene chloride (7.5 mL), added to provide a homogeneous mixture. This mixture was analyzed by LC for recovered 2-butanone using a 10 × 0.25 in. *μ*-Bondapak-C_{18} column employing 30% methanol-water as eluent.

Reaction of Potassium Superoxide and 1-Bromoadamantane in Me_2SO. Into a flame-dried 50-mL round-bottom flask equipped with a Teflon-coated magnetic stirrer bar was placed 0.711 g (10.0 mmol) of powdered potassium superoxide. The flask was capped with a rubber septum and flushed with nitrogen. Then 17.0 mL of Me_2SO and 3.0 mL of a 0.33 M solution of 18-crown-6 in Me_2SO were added by syringe, followed by 0.7197 g (3.33 mmol) of 1-bromoadamantane. The resulting mixture was stirred for 24 h, then poured into a 125-mL Erlenmeyer flask containing 20 mL of water. The reaction flask was rinsed with 30 mL of benzene and the rinsings added to the Erlenmeyer flask along with a known amount of *n*-tridecane as an internal standard and 10 mL of a solution of saturated brine. The benzene layer was separated, dried over $MgSO_4$, and analyzed by GLC on a 6 ft × 0.125 in. UCW-98 on 80/100 Chromosorb W column.

Reaction of Potassium Superoxide with Dimethyl Sulfone in Me_2SO. Into a flame-dried, 50-mL flask equipped with a Teflon-coated magnetic stirrer bar was placed 0.213 g (3.00 mmol) of powdered potassium superoxide. The flask was capped with a rubber septum and 19.0 mL of Me_2SO added by syringe before 0.9 mL of a 0.33 M solution of 18-crown-6 in Me_2SO was added followed by 0.0941 g (1.00 mmol) of Me_2SO_2 and a known amount of di-*n*-propyl sulfone as internal standard. The resulting mixture was stirred and 0.20-mL aliquots removed at 1-h intervals and immediately analyzed without workup for recovered Me_2SO_2 by GLC on a 3 ft × 0.25 in. 20% Carbowax on Chromosorb W column.

Reactions in Benzene. The same general procedures employed for reactions carried out in Me_2SO were also used for reactions carried out in benzene. All reactions were run in 20 mL of benzene containing 10 mol % 18-crown-6 ether, based on superoxide. Reactions were worked up by adding ~1 mL of 9 M H_2SO_4 followed by the appropriate internal standards. Analysis for various products was carried out under the conditions in Table V.

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$$\begin{array}{lccccccccc} & KO_2 & + & CH_3Br & \rightarrow & O_2 & + & CH_3\cdot & + & KBr \\ \Delta G^\circ\ (\text{kcal/mol}) & -56 & & -5.9 & & 0 & & 21 & & -90 \end{array}$$

$$\Delta G^\circ_{\text{reaction}} \sim -7\ \text{kcal/mol}$$

This calculation neglects the free energy of solution of the species involved. Clearly, this is a valid assumption for the neutral species CH_3Br, O_2, and $CH_3\cdot$. An examination of the free energy of dissolution in water for a variety of potassium salts of monovalent anions similar in size to O_2^- reveals that they are substantially similar (ca. −85 ± 3 kcal/mol) and, in general, somewhat *less* than the corresponding value for potassium bromide. It seems reasonable to conclude that the difference between the free energy of solution for KO_2 and KBr is likely to be small in magnitude and such that it will reinforce the above conclusion.

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(33) Steady-state treatment of the processes outlined in eq 12–14 leads to the expression

$$[RO_2\cdot] = \frac{-k_2[O_2^-] + \sqrt{k_2^2[O_2^-]^2 + 8k_3k_1[O_2^-][RBr]}}{4k_3}$$

Assuming $[RBr] \approx 0.1$ M, $[O_2^-] \approx 0.01$ M, and $k_2 = 8.5 \times 10^7\ M^{-1}\,s^{-1}$, the steady-state value of $[RO_2\cdot] \approx 1 \times 10^{-6}\ M^{-1}$ leads to the relationship $\text{rate}_2 \approx 10^3\ \text{rate}_3$. Examination of this steady-state solution reveals that the relative difference between rate_2 and rate_3 is (1) only increased with higher values of k_2 and (2) relatively insensitive to the values of $[RBr]$ and $[O_2^-]$.

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