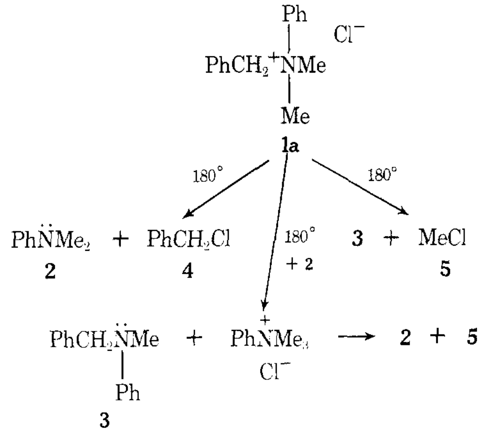
effect of the counterion change on the course of the thermolysis of the two halides **1a** (Cl) and **1b** (I) of the *N*-benzyl-*N*,*N*-dimethylanilinium ion.

When the chloride **1a** was heated at 175–180° without solvent, 90% of the salt reacted in 30 min to give the products arising from the two possible retro-Menschutkin reactions, namely *N*,*N*-dimethylaniline (**2**) and *N*-benzyl-*N*-methylaniline (**3**), as free bases together with the corresponding alkyl chlorides, benzyl chloride (**4**) and chloromethane (**5**). Amine **3** is in much larger amount than amine **2**, a fact which has a simple explanation in the operation of the Le Chatelier principle.

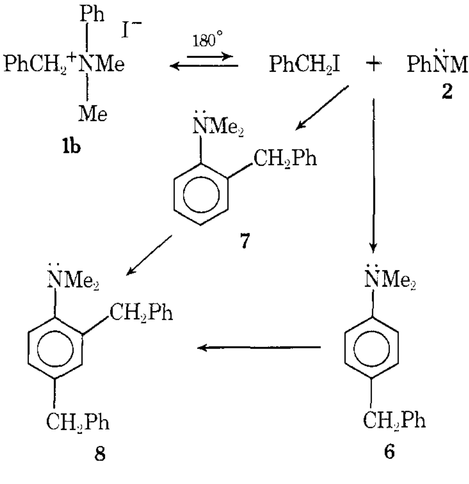
Scheme I



The reaction between **1a** and the *N*,*N*-dimethylaniline (**2**) being formed in the reaction may be an important source of **3**. In fact, independent experiments showed that *N*,*N*-dimethylaniline (**2**) reacts with the *N*-benzyl-*N*,*N*-dimethylanilinium cation to yield **3** at 180°.

The behavior of the iodide **1b** in the same experimental conditions was completely different, giving some amine **2** (~20%), no **3**, but three rearranged products: *p*-benzyl-*N*,*N*-dimethylaniline (**6**), *o*-benzyl-*N*,*N*-dimethylaniline (**7**), and *o*,*p*-dibenzyl-*N*,*N*-dimethylaniline (**8**). Products **6** and **7** were definitively different from all the Stevens and Sommelet isomers previously identified in the reaction of both **1a** and **1b** with strong bases.[3] The unequivocal identification of the reaction products from the thermolysis of **1b** was reached on the basis of gas chromatographic properties on widely different stationary phases (Carbowax 20M-KOH, silicones, etc.), mass spectrometry (electron impact at 70 and 15 eV), and spectroscopic characteristics (infrared and ^{1}H nuclear magnetic resonance on separated samples). Independent syntheses, which will be reported at a later time, confirmed the identifications.

Scheme II



The ortho/para ratio (~0.35) and the presence of the polyalkylated amine **8** does not suggest the operation of a radical mechanism recently advanced,[4] but rather indicates the possibility of a two-stage process: a predissociation (retro-Menschutkin, a reversible reaction, when no gaseous product is removed from the reacting mixture), followed by direct ring alkylation. Further study of these reactions is in progress.

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The Reaction of Superoxide with Alkyl Halides and Tosylates[1]

Summary: Alcohols are the major end product resulting from the reaction of alkyl halides and tosylates with an *excess* of potassium superoxide in an extraordinarily rapid process in which the carbon–oxygen bond-forming step proceeds with *inversion* of configuration.

Sir: The perspicacious observations of Fridovich and McCord[2] have led to the realization that superoxide is a common by-product produced by virtually all aerobic organisms. Moreover, recent studies suggest that superoxide may be involved in certain biological disorders and defense mechanisms.[3] Despite its apparent importance, much of the basic chemistry of superoxide remains ill-defined.[4] Of singular importance to the understanding of the reactivity of superoxide is a clarification of the ability of $O_2\cdot^-$ to act as either a one-electron reducing agent[6,7] or as a possible nucleophile. We have undertaken to answer this question by examining the reaction of superoxide with a particular class of electrophilic substrates, viz., alkyl halides and tosylates.

In a typical experiment, 1-bromooctane (0.644 g, 3.33 mmol) was added to a vigorously stirred mixture of powdered potassium superoxide[8] (0.710 g, 10.0 mmol) and 18-crown-6 ether[9] (0.264 g, 1.0 mmol) in dry DMSO (20 ml) at 25°.[10] The resulting mixture was allowed to stir for 75 min, then cautiously treated with 10 ml of water saturated with sodium chloride, and finally extracted with three 30-ml portions of petroleum ether. GLC analysis of the combined extracts indicated the presence of 1-octanol (63%), 1-octene (1%), and 1-octanal (12%). Results obtained on similar treatment of other representative substrates are given in Table I.

This sequence seems applicable to the production of alcohols from primary and secondary halides and tosylates; in our hands tertiary halides gave poor yields of alcohols

Table I
Reaction of Potassium Superoxide with Various Organic Halides and Tosylates[a]

Substrate	Products (%)[b]	Rel reactivity[c]
1-$C_8H_{17}I$	1-Octanol (46) 1-Octene (3) 1-Octanal (11)	4.5
2-$C_8H_{17}I$	2-Octanol (48) Octenes[d] (48) 2-Octanone (<1)	3.3
1-$C_8H_{17}Br$[e]	1-Octanol (63) 1-Octene (<1) 1-Octanal (12)	1.0
2-$C_8H_{17}Br$	2-Octanol (51) Octenes[d] (34) 2-Octanone (<1)	0.98
$CH_3(CH_2)_2C(CH_3)_2Br$	2-Methyl-2-pentanol (20) 2-Methylpentenes (30)	0.90
1-$C_8H_{17}Cl$	1-Octanol (34) 1-Octene (~1) 1-Octanal (5)	0.089
2-$C_8H_{17}Cl$	2-Octanol (36) Octenes[d] (12) 2-Octanone (<1)	0.020
1-$C_8H_{17}OTs$	1-Octanol (75) 1-Octene (<1) 1-Octanal (1)	1.0
2-$C_8H_{17}OTs$	2-Octanol (75) Octenes[d] (23) 2-Octanone (<1)	f
$C_6H_5CH_2Cl$	Benzyl alcohol (41) Benzaldehyde (6)	2.9

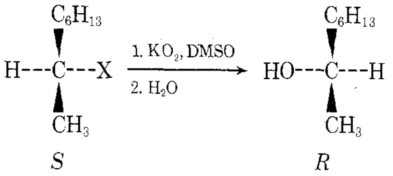
[a] Unless otherwise indicated, all reactions were carried out by adding 3.33 mmol of halide or tosylate to a vigorously stirred mixture of KO_2 (10.0 mmol) and 18-crown-6 ether (1.0 mmol) in dry DMSO (20 ml) at ambient temperature. Reaction time varied from 75 min for the alkyl bromides, iodides, tosylates, and benzyl chloride to 3 hr for the alkyl chlorides. Yields did not improve with increased reaction time. [b] Yields are based on alkyl halide or tosylate and were determined by GLC analysis using the internal standard procedure. [c] Reactivities were determined relative to 1-bromooctane (1.00) 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 substrates. [d] No attempts were made to distinguish possible octene isomers. [e] Repetition of this reaction using HMPA as solvent required an extended reaction time (17 hr) and yielded 1-octanol (55%), 1-octene (<1%), and 1-octanal (5%). Reaction in benzene also required longer reaction times (~20 hr) and produced lower yields of 1-octanol (29%), 1-octene (<1%), and 1-octanal (<1%). [f] Not determined.

while phenyl halides showed no significant reactivity. Optimum alcohol yields were obtained at superoxide to alkyl halide ratios of ≥3. Reaction was accompanied by an initially moderate to vigorous evolution of oxygen[11] which abated with time but otherwise continued throughout the course of the reaction. Finally, somewhat lower yields of alcohol were obtained when reactions were carried out in the absence of a macrocyclic polyether while the use of HMPA or benzene as solvent required longer reaction time, producing similar products but in diminished yields.

Our understanding of the details of this reaction is still incomplete. In this context, however, several specific points deserve brief comment. First, the organic groups bonded to the halogen and the nature of the leaving group exert an influence on the course of the reaction that is consistent with a mechanism for carbon-oxygen bond formation which involves a SN2 displacement at carbon.[12] Specifically, the observed substrate reactivity is benzyl > primary > secondary > tertiary > aryl and I > Br > Cl.

Second, substitution is predominant with primary halides; however, substantial elimination occurs with secondary systems whereas elimination is the predominant process observed from the reaction with the tertiary halide 2-bromo-2-methylpentane. These facts parallel similar observations involving the reactions of other nucleophiles with alkyl halides.[13]

Third, consistent with this conclusion is the fact that carbon–oxygen bond formation in at least two instances takes place with predominant *inversion* of configuration at the chiral center. Reaction of the tosylate of (+)-(*S*)-2-octanol ($\alpha^{20}{}_{589}$ +7.97°, optical purity 99.4%) with potassium superoxide produced (−)-(*R*)-2-octanol ($\alpha^{20}{}_{589}$ −7.71°) corresponding to an optical purity and overall stereoselectivity of 97%. Similar reaction with (−)-(*R*)-2-bromooctane[14] afforded (+)-(*S*)-2-octanol in 90% optical purity (95% net inversion).



Finally, we have carried out a comparison of the reactivity of potassium superoxide and potassium iodide toward a selected electrophilic substrate, viz., 1-bromooctane. The half-life for the reaction of 1-bromooctane (0.5 *M*) with potassium iodide (0.5 *M*) in dry DMSO containing 18-crown-6 ether (0.05 *M*) was ~20 hr.[15] By comparison, the reaction of potassium superoxide with 1-bromooctane under equivalent conditions has a half-life of *~45 sec.*

These results exclude as a principal reaction pathway leading to the production of the carbon–oxygen bond, a mechanism involving a one-electron transfer process since such a step would necessarily produce an alkyl radical which, in turn, would lead to products with loss of stereochemistry. The observed substitution reaction can in these instances be viewed as involving the direct displacement of halide at carbon by superoxide radical anion. The nature of the subsequent intermediates involved in this reaction sequence remain unclear although peroxo compounds are certainly reasonable possibilities. Further speculation on the details of the subsequent reactions that occur must be deferred until a clearer understanding of the nature of the intermediates in this reaction can be delineated.

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Superoxide Chemistry. A Convenient Synthesis of Dialkyl Peroxides

Summary: A convenient synthesis of dialkyl peroxides from the reaction of alkyl bromides or alkyl sulfonate esters with potassium superoxide, the latter solubilized in benzene by crown ethers, is described.

Sir: The chemistry of the superoxide radical anion, $O_2\cdot^-$, in organic systems has been studied very little. On a synthetic scale, superoxide is available to the chemist from two sources, either as the alkali metal salts, potassium superoxide (KO_2) and sodium superoxide (NaO_2), or from the electrochemical reduction of oxygen to $O_2\cdot^-$ (eq 1).[1] The use of

$$O_2 + e \rightleftharpoons O_2\cdot^- \qquad -0.75 \text{ V (SCE)} \quad (1)$$

$$RBr + O_2\cdot^- \longrightarrow \tfrac{1}{2}ROOR + Br^- + \tfrac{1}{2}O_2 \quad (2)$$

the alkali metal salts in organic reactions has not been fruitful owing to the lack of solubility of these salts in many organic systems.[2] The electrochemical method is experimentally more complex, but it has been used on a limited scale for several organic reactions.[1d,3] Two groups reported in 1970 that electrochemically generated superoxide will react with alkyl halides to form dialkyl peroxides according to eq 2.[4,5]

In view of the recently reported solubilization of KO_2 in dimethyl sulfoxide with the aid of dicyclohexyl-18-crown-6,[6] we wish to report our observations on the solubilization of KO_2 by crown ethers in various other aprotic solvents, including benzene, tetrahydrofuran, and dimethylformamide.[7] Using this method we have developed a convenient synthesis of dialkyl peroxides from various alkyl bromides and alkyl sulfonate esters (i.e., mesylates and tosylates). The following simple procedure can be used for this synthesis.

Potassium superoxide[8] (0.0050 mol) was weighed directly into a dry flask containing a magnetic stirring bar and was immediately covered with dry benzene (15 ml). The alkyl bromide or alkyl sulfonate ester (0.0050 mol) and dicyclohexyl-18-crown-6 (0.0050 mol) were then added to the flask. The pieces of KO_2 were carefully crushed with a heavy glass rod. The resulting mixture was protected from moisture with a $CaCl_2$ drying tube and was stirred vigorously. The reaction may be followed by VPC or TLC[10] and occasionally requires additional KO_2 to reach completion. The reaction was usually complete within 3 to 6 hr at room temperature. The reaction may be worked up by pouring it into saturated aqueous sodium chloride solution (50 ml) and extracting with methylene chloride or benzene.[12] The product can be isolated by chromatography on silica gel using, for example, benzene as the eluent.

Table I
The Reactions of Alkyl Bromides and Sulfonate Esters with KO_2 in the Presence of Crown Ethers[a]

	Products, %		
Substrate (R–X)	Peroxide (ROOR)	Alcohol (ROH)	Olefins[b]
n-C_5H_{11}–Br	53[c]		
n-C_6H_{13}–Br	54[c]		
n-C_7H_{15}–Br	56[c]		
n-$C_{16}H_{33}$–Br	44[d]	21	
n-$C_{18}H_{37}$–Br	77[e]	21	
n-$C_{18}H_{37}$–Br[f]	61	18	
c-C_6H_{11}–Br			67
c-C_5H_9–Br	42[e]		24
$C_6H_{13}CH(CH_3)$–Br	55[e]		37[g]
n-$C_{18}H_{37}$–OTos[h]	50	42	
n-$C_{18}H_{37}$–OMs[d]	46	40	
$C_6H_{13}CH(CH_3)$–OTos[i]	52	13	16[g]
$C_6H_{13}CH(CH_3)$–OMs[j]	44	19	14[g]

[a] Dicyclohexyl-18-crown-6 used except where noted otherwise. [b] VPC analyses for olefins were carried out using an F & M Scientific Model 5750 research chromatograph equipped with a flame ionization detector. A 3-ft stainless steel column packed with 26.6% Carbowax 20M on Gas-Chrom Z was used with a helium flow rate of 35–40 cc/min. The column was programmed for 4 min at 90° and then to increase 8° per minute to 225°. [c] Reference 16. [d] S. Wawzonek, P. D. Klimstra, and R. E. Kallio, *J. Org. Chem.*, **25**, 621 (1960). [e] Satisfactory analytical data has been obtained for this compound. [f] 18-Crown-6 was used in this experiment. [g] A mixture of 1-octene, *cis*-2-octene, and *trans*-2-octene was found. [h] V. C. Sekera and C. S. Marvel, *J. Am. Chem. Soc.*, **55**, 345 (1933). [i] A. Streitwieser, Jr., T. D. Walsh, and J. R. Wolfe, *ibid.*, **87**, 3682 (1965). [j] H. A. Weiner and R. A. Sneen, *ibid.*, **87**, 287 (1965).

Using this procedure, we have obtained the results summarized in Table I. Yields of peroxides and alcohols were determined from isolation of the products, whereas the yields of olefinic products were determined by VPC. In addition to these results we offer the following observations and comments on these reactions.

By analogy to recent reports of the solubilization of various inorganic salts in organic media by the crown ethers,[7] we assume that the equilibrium shown in eq 3 is responsible for the solubilization of KO_2. The dicyclohexyl-18-crown-6 used in these experiments was a mixture of stereoisomers. A stoichiometric quantity of crown ether was used in all the reactions reported in Table I. In a similar experiment, using only 0.1 equiv of crown ether relative to KO_2, 1-bromohexane was converted to di-n-hexyl peroxide in 50% yield. The reaction time was somewhat longer than when a full equivalent of crown ether was used. 18-Crown-6 and dibenzo-18-crown-6 also were effective in solubilizing KO_2 in benzene, although the latter was itself sparingly soluble in this solvent.

The formation of dialkyl peroxides by eq 2 was proposed by Dietz et al.[5] to occur stepwise according to eq 4–6. Sum-