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Oxygenation by Superoxide Ion of 1,2-Dibromo-1,2-diphenylethane, 2,3-Dibromobutane, Ethylene Dibromide (EDB), and 1,2-Dibromo-3-chloropropane (DBCP)

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Abstract: In dimethylformamide (DMF) superoxide ion ($O_2^{-}\cdot$) reacts with PhCHBrCHBrPh, MeCHBrCHBrMe, and CH_2BrCH_2Br (EDB) via 2:1 stoichiometry to produce PhCH(O), MeCH(O), and $CH_2(O)$, respectively. A similar oxygenation occurs when $O_2^{-}\cdot$ and $CH_2BrCHBrCH_2Cl$ (DBCP) are combined in 5:1 stoichiometry to yield two $CH_2(O)$ and one $HOC(O)O^-$ per substrate. The relative rates of reaction are in the order CH_2BrCH_2Br > PhCHBrCHBrPh > MeCHBrCHBrMe. On the basis of the reaction rates and the products, the initial step for each substrate is believed to be a nucleophilic attack on a bromo carbon (R_2CHBr) with displacement of Br^- and formation of $R_2CHOO\cdot$. Subsequent steps involve reduction by a second $O_2^{-}\cdot$ and a dioxetane closing on an adjacent C–X group.

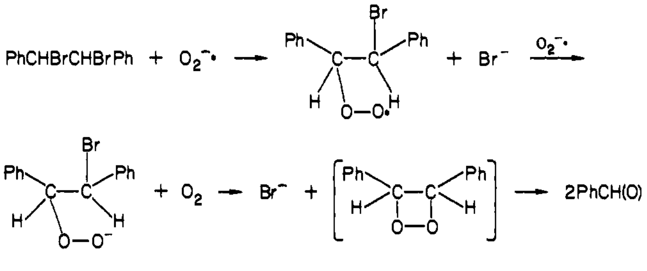
The chemistry of $O_2^{-}\cdot$ and its reactivity with a range of substrates (acids, electrophiles, oxidants, and activated secondary amines) have been discussed in several recent reviews.[1-4] Although the chemical reactivity of superoxide ion ($O_2^{-}\cdot$) with monohalogenated hydrocarbons has been known since 1970,[5,6] studies of multihalogenated molecules have been limited to CH_2Br_2,[7] chloromethanes and DDT,[8] trichloromethyl substrates,[9] and chloroalkenes.[10] The present report describes the reactivity of $O_2^{-}\cdot$ with α-dibromoalkanes (PhCHBrCHBrPh, MeCHBrCHBrMe, and CH_2BrCH_2Br) and an α-dibromo-β-chloroalkane ($CH_2BrCHBrCH_2Cl$) and characterizes the oxygenated products.

Experimental Section

Equipment. Conventional electrochemical instrumentation, cells, and electrodes were employed for the cyclic voltammetric and controlled-potential coulometric measurements,[11] and for the glassy carbon ring-disk kinetic measurements.[9] The volatile reaction products were separated and identified with a Hewlett Packard Model 5880 gas chromatograph that was equipped with a 12.5-m glass capillary column and by mass spectrometry. A Vacuum Atmosphere Corp. inert atmosphere glovebox was used for the storage and preparation of solutions of tetramethylammonium superoxide.

Chemicals and Reagents. Burdick and Jackson "distilled in glass" UV-grade dimethylformamide was used as received for all of the experiments. Tetraethylammonium perchlorate (TEAP) from G. Frederick Smith Chemical Co. was dried in vacuo and used as the supporting electrolyte (0.1 M TEAP) in the electrochemical experiments. The substrates PhCHBrCHBrPh (Aldrich), MeCHBrCHBrMe (Aldrich), CH_2BrCH_2Br (Aldrich), $CH_2BrCHBrCH_2Cl$ (Shell), *n*-BuBr (Aldrich), and CH_2ClCH_2Cl (Aldrich) were assayed by gas chromatography and found to be >99% pure and were used without further purification. Solutions of $O_2^{-}\cdot$ were prepared either by controlled-potential reduction of dissolved O_2 or by dissolution of weighted amounts of tetramethylammonium superoxide [$(Me_4N)O_2$].[12]

Scheme I



Methods. Addition of a quantity of substrate to known amounts of $O_2^{-}\cdot$ (such that about 80% of the $O_2^{-}\cdot$ was consumed) and subsequent measurement of the unreacted $O_2^{-}\cdot$ concentration by anodic voltammetry provided the stoichiometric ratios for the quantity of $O_2^{-}\cdot$ consumed per mole of substrate.

Measurements of the rate of reaction of superoxide ion with the various substrates were made with a rotated ring-disk electrode. The pseudo-first-order rate constants (k_1) were determined with the method that has been described by Albery and Hitchman[13] and illustrated in a recent study of polyhalogenated hydrocarbons.[9]

The reaction products were characterized after stoichiometric amounts (at millimolar concentrations) of substrate and superoxide ion were combined. A negative voltage sweep provided a measure of the O_2 that was produced by the $O_2^{-}\cdot$–substrate reaction. Aliquots of the reaction mixture were analyzed for halide ion by potentiometric titration with $AgNO_3$ and for base by an aqueous pH titration with HCl. The product solution was diluted with H_2O and extracted with diethyl ether and the latter analyzed by gas chromatography.

Results

Substrates with vicinal dibromo groups readily react with superoxide ion in aprotic solvents such as dimethylformamide to yield bromide ion, dioxygen, and 2 equiv of aldehyde. Table I summarizes the reaction stoichiometries for the combination of $O_2^{-}\cdot$ with PhCHBrCHBrPh, MeCHBrCHBrMe, CH_2BrCH_2Br (EDB), $CH_2BrCHBrCH_2Cl$ (DBCP), *n*-BuBr, and CH_2ClCH_2Cl and the products from the dibromo substrates. These results confirm that $O_2^{-}\cdot$ promotes a net dioxygenation of each substrate to give two aldehydes.

The rates of reaction for $O_2^{-}\cdot$ with PhCHBrCHBrPh and the other dibromo substrates have been determined by the rotated ring–disk technique (O_2 is reduced at the disk to $O_2^{-}\cdot$, which reacts with substrate, and the unreacted $O_2^{-}\cdot$ is oxidized at the ring electrode),[9,13] and the normalized pseudo-first-order rate constants

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Table I. Stoichiometries and Kinetics for the Reaction of 0.1–5 mM $O_2^{-}\cdot$ with Multihalogenated Hydrocarbons in Dimethylformamide (0.1 M Tetraethylammonium Perchlorate) at 25 °C[a]

substrate [S], 1–10 mM	$O_2^{-}\cdot$ per S	X^- released per S	O_2 released per S	products per S	$k_1/[S]$,[b] $M^{-1}\ s^{-1}$
PhCHBrCHBrPh	2.0 ± 0.1	2.0 ± 0.1	1.0 ± 0.1	2PhCH(O)	1000 ± 100
MeCHBrCHBrMe	2.0 ± 0.1	2.0 ± 0.1	1.0 ± 0.1	2MeCH(O)	160 ± 20
CH_2BrCH_2Br (EDB)	2.0 ± 0.1	2.0 ± 0.1	1.0 ± 0.1	$2CH_2(O)$	2000 ± 200
$CH_2BrCHBrCH_2Cl$ (DBCP)	5.0 ± 0.2	3.0 ± 0.2	2.0 ± 0.1	$2CH_2(O)$, $1HOC(O)O^-$	4000 ± 400
n-BuBr	1.0 ± 0.1	1.0 ± 0.1			960 ± 100
CH_2ClCH_2Cl					24 ± 3

[a] Stoichiometries determined for $O_2^{-}\cdot$–substrate reactions by titration of excess $(Me_4N)O_2$ (with voltammetric detection), for released Br^- and Cl^- by titration with $AgNO_3$; for released O_2 by negative scan voltammetry, and for organic products by ether extraction and capillary-column gas chromatography. [b] Pseudo-first-order rate constants, k_1 (normalized to unit substrate concentration [S]), were determined from measurements with a glassy carbon–glassy carbon ring–disk electrode that was rotated at 900 rpm.

are tabulated in Table I. For comparison the rate constants for *n*-BuBr and CH_2ClCH_2Cl also are included.

Discussion and Conclusions

The stoichiometric data in Table I for vicinal dibromoalkanes are consistent with an overall net chemical reaction that yields two aldehyde molecules from the nucleophilic displacement by superoxide ion of the two bromo groups (e.g., for PhCHBrCHBrPh).

$$\mathrm{PhCHBrCHBrPh} + 2O_2^{-}\cdot \rightarrow 2\mathrm{PhCH(O)} + 2Br^- + O_2 \quad (1)$$

A reasonable mechanism for these dioxygenations is an initial nucleophilic attack of a bromo carbon followed by displacement of a bromide ion (Scheme I). A second $O_2^{-}\cdot$ reduces the peroxyl radical to a peroxide, which attacks the adjacent bromo carbon to displace the second bromide ion and give a dioxetane intermediate that dissociates to two benzaldehyde molecules. The data of Table I indicate that MeCHBrCHBrMe and CH_2BrCH_2Br (EDB) react in an analogous manner to yield MeCH(O) and $CH_2(O)$, respectively.

The initial reaction sequence for $CH_2BrCHBrCH_2Cl$ (DBCP) probably is the same as for EDB to give two aldehydes.

$$CH_2BrCHBrCH_2Cl + 2O_2^{-}\cdot \rightarrow CH_2(O) + CH_2ClCH(O) + 2Br^- + O_2 \quad (2)$$

The chloroacetaldehyde $[CH_2ClCH(O)]$ rapidly reacts with three additional $O_2^{-}\cdot$ ions to give bicarbonate ion and another formaldehyde (probably via another dioxethane intermediate to give a formate, which reacts with another $O_2^{-}\cdot$ and residual water).[9]

$$CH_2ClCH(O) + 3O_2^{-}\cdot \xrightarrow{H_2O} HOC(O)O^- + CH_2(O) + Cl^- + O_2 + 0.5H_2O_2 + OH^- \quad (3)$$

The overall process for DBCP is the sum of reactions 2 and 3;

$$CH_2BrCHBrCH_2Cl + 5O_2^{-}\cdot \xrightarrow{H_2O} 2CH_2(O) + HOC(O)O^- + 2Br^- + Cl^- + 2O_2 + 0.5H_2O_2 + OH^- \quad (4)$$

excess $O_2^{-}\cdot$ induces the polymerization of the formaldehyde.

If the normalized pseudo-first-order rate constants ($k_1/[S]$) of Table 1 for EDB, DBCP, and *n*-BuBr are divided by the stoichiometric factors ($O_2^{-}\cdot$ per S) of the second column, values for the apparent second-order rate constants (k_2) result. For the three substrates these are essentially equal (800 $M^{-1}\ s^{-1}$ for DBCP, 900 $M^{-1}\ s^{-1}$ for *n*-BuBr, and 1000 $M^{-1}\ s^{-1}$ for EDB), which is consistent with an initial nucleophilic attack for the methylenic bromo carbon as the rate-controlling step.

The formation of aldehydes from vicinal dihalo compounds via nucleophilic displacement by $O_2^{-}\cdot$ and a dioxetane intermediate (Scheme I) is similar to the oxygenation of *p,p′*-DDT by superoxide.[10]

$$(p\text{-}ClPh)_2CHCCl_3 + 4O_2^{-}\cdot \rightarrow (p\text{-}ClPh)_2C(O) + HOC(O)O^- + 3Cl^- + H_2O_2 + 1.5O_2 \quad (5)$$

As is the case with polyhalogenated ethenes,[10] the initial nucleophilic addition of $O_2^{-}\cdot$ to these substrates yields alkyl peroxyl radical intermediates ($CH_2BrCH_2OO\cdot$ in the case of EDB). The latter are effective initiators for the autoxidation of unsaturated fatty acids such as linoleic.[14] Hence, ingested vicinal dihalo compounds such as EDB and DBCH may react in vivo with superoxide to produce such peroxyl radical initiators for lipid peroxidation. This may represent the mechanism for the cytotoxicity of these pesticides.

In accord with previous reports,[8,15] the present results confirm that superoxide ion can be a useful and effective reagent for the degradation of halogenated pesticide wastes such as EDB and DBCP.

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Registry No. $O_2^{-}\cdot$, 11062-77-4; PhCHBrCHBrPh, 5789-30-0; MeCHBrCHBrMe, 5408-86-6; CH_2BrCH_2Br, 106-93-4; $CH_2BrCHBrCH_2Cl$, 96-12-8.

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