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Perkin-Markovnikov Type Reaction Initiated with Electrogenerated Superoxide Ion

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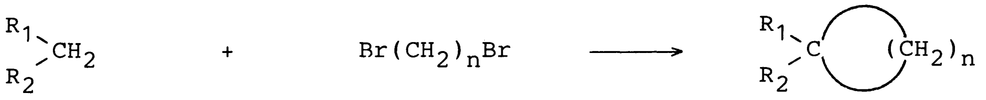
The cyclic condensation of α,ω-dihaloalkanes with activated methylene of malonic acid and acetoacetic acid esters is studied using an electrogenerated superoxide ion. Two possible mechanisms for this reaction are postulated.

In aprotic solvents, superoxide ion ($O_2^{\overline{\cdot}}$) acts as an electrogenerated base (EGB),1) and abstracts a proton of an activated methylene group to form a carbanion (EWG-$\bar{C}$H-EWG, EWG: electron-withdrawing group). Superoxide ion has another feature, as a nucleophile;2) it reacts with alkyl halides to form alkylperoxy radicals (R-OO•), which might be reduced further by superoxide ion to form alkylperoxy anions (R-OO$^-$).

We have investigated the difference in the reactivity of electrogenerated superoxide ion toward activated methylene and alkylene dihalide compounds. In this paper, we report a ring formation reaction by electrogenerated superoxide ion (Scheme 1).



1: $R_1=R_2=CO_2Et$
2: $R_1=R_2=CO_2Me$
3: $R_1=COCH_3$, $R_2=CO_2Et$

4: n=2
5: n=3
6: n=4
7: n=5

8: $R_1=R_2=CO_2Et$
9: $R_1=R_2=CO_2Me$
10: $R_1=COCH_3$, $R_2=CO_2Et$

Scheme 1.

This type of the reaction is known as Perkin-Markovnikov reaction.3,4) As described later, the reaction mechanism for the present electrochemical reaction is somewhat different from the ordinary chemical one.

Cyclic voltammetry was carried out using conventional electrochemical instruments in 0.1 mol dm^{-3} tetraethylammonium perchlorate (TEAP)/N,N-dimethylformamide (DMF) solution. DMF was dried by passing activated alumina column immediately before use.

The electrolyses were conducted at a constant potential (-1.5 V vs. Ag/Ag$^+$) in a H-type cell with a glassy carbon plate cathode and a platinum plate anode using a controlled potential analyzer. The electrolyte was 0.2 mol dm^{-3} TEAP/DMF solution. The products were identified and determined by comparison of TLC, GC, ^{1}H-NMR data with those of authentic samples prepared by the usual method.$^{5)}$

The cyclic voltammogram of dissolved oxygen in the absence of substrates shows a quasi-reversible shape with a peak separation of 180 mV (Fig. 1). The addition of diethyl malonate (**1**) to the electrolyte solution resulted in an increase in the cathodic peak current with an expense of the reoxidation peak. Similar cyclic voltammetric behavior was also observed in the presence of 1,4-dibromobutane (**6**) (Fig. 2). These phenomena indicate that electrogenerated superoxide ion reacts with both substrates and additional electron transfer reaction occurs at around the cathodic peak potentials. The rate constants for the reaction of $O_2^{\overline{\cdot}}$ with substrates have been estimated based on a simple ECE reaction and the values are listed in Table 1. The results indicate that $O_2^{\overline{\cdot}}$ is more reactive with α,ω-dibromoalkanes than with compounds containing an activated methylene group. The rate constant for ethyl acetoacetate (**3**) could not be obtained in the present study since the cyclic voltammogram of oxygen in the presence of **3** showed a prepeak which might be the indication of a rapid reaction between $O_2^{\overline{\cdot}}$ and **3**.

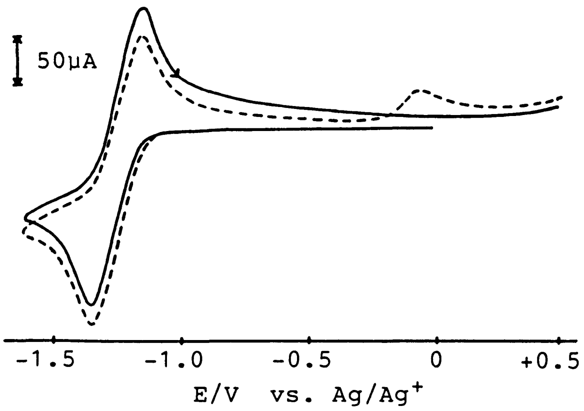


Fig.1. Cyclic voltammograms for O_2 in the absence (——) and in the presence (- - -) of 3 mmol dm^{-3} diethyl malonate (**1**). electrolyte: 0.1 mol dm^{-3} TEAP/DMF, electrode: glassy carbon disk (3mm diameter), sweep rate: 0.1 V s^{-1}.

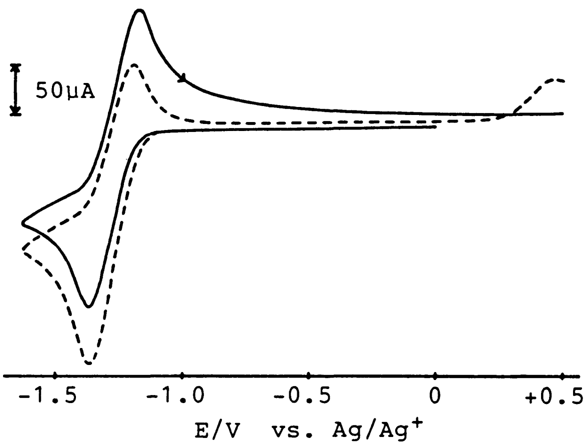


Fig.2. Cyclic voltammograms for O_2 in the absence (——) and in the presence (- - -) of 3 mmol dm^{-3} 1,4-dibromobutane (**6**). electrolyte: 0.1 mol dm^{-3} TEAP/DMF, electrode: glassy carbon disk (3 mm diameter), sweep rate: 0.1 V s^{-1}.

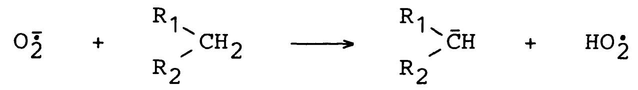
The macro-scale electrolyses were also carried out. The results are summarized in Table 2. The annulated products depend markedly on the methylene length of α,ω-dibromoalkanes. The yields of the products decrease in the order of $C_4 > C_5 > C_3 > C_2$, similarly to those observed in the ordinary chemical reaction.

Table 1. Reaction of electrogenerated $O_2^{\cdot-}$ with substrates

Substrate	Rate constant $k^{a)}$/mol^{-1} l s^{-1}
1	1×10^2
2	1×10^2
3	(1×10^2)
4	6×10^2
5	4×10^2
6	5×10^2
7	6×10^2

a) Determined by digital simulation based on the following mechanisms.

(1) $O_2 + e^- \longrightarrow O_2^{\cdot-}$



$O_2^{\cdot-} + R_1R_2CH_2 \longrightarrow R_1R_2\bar{C}H + HO_2^{\cdot}$

$HO_2^{\cdot} + e^- \longrightarrow HO_2^-$

(2) $O_2 + e^- \longrightarrow O_2^{\cdot-}$

$O_2^{\cdot-} + Br(CH_2)_nBr \longrightarrow Br(CH_2)_nOO\cdot + Br$

$Br(CH_2)_nOO\cdot + e^- \longrightarrow Br(CH_2)_nOO^-$

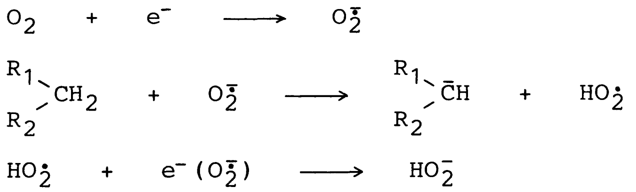
Table 2. Yields of **8**, **9**, **10** in the annulation reaction initiated by electrogenerated $O_2^{\cdot-}$

Substrate	Product	α,ω-Dibromoalkane $Br(CH_2)_nBr$ **4** (n=2)	**5** (n=3)	**6** (n=4)	**7** (n=5)
1	**8**	13%	35%	74%	64%
		(28%)	(43%)	(66%)	(50%)
2	**9**	11%	25%	67%	47%
3	**10**	22%	30%	30%	35%
		(<3%)	(37%)	(50%)	(34%)

Concentration of **1**-**7**: 75 mM
Passed Charge: 2 x 96490 C mol^{-1}
Numbers in parentheses: Yields by chemical reaction

Besides the annulated products, diols (such as 1,4-butanediol from **6**) and cyclic ethers (such as tetrahydrofuran from **6**) were also detected as the minor products. Therefore, the mechanism of the present reaction is postulated as follows:

Mechanism 1: Superoxide as an electrogenerated base

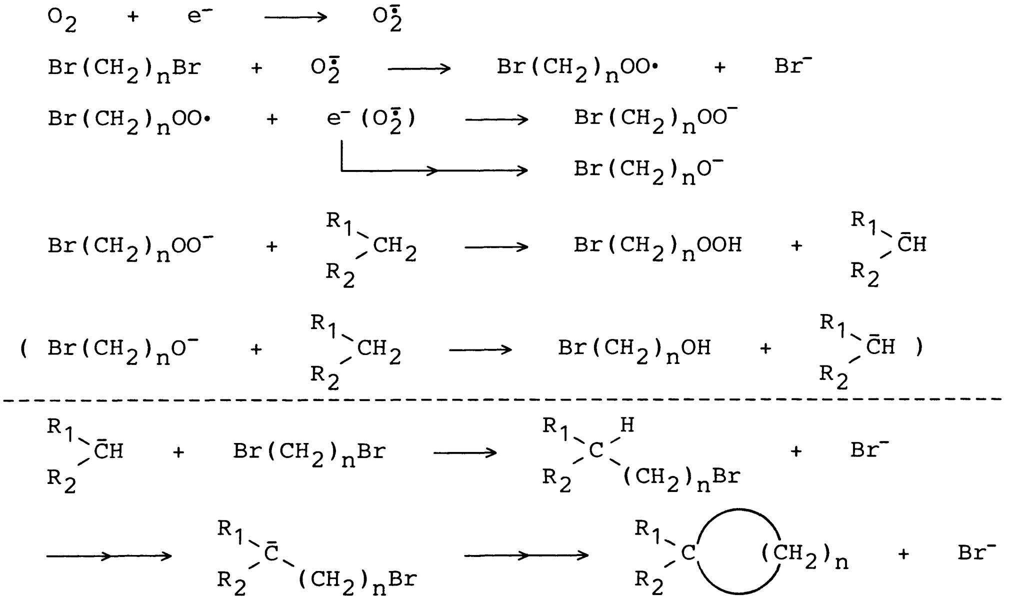


$$O_2 + e^- \longrightarrow O_2^{\bar{\cdot}}$$

$$R_1R_2CH_2 + O_2^{\bar{\cdot}} \longrightarrow R_1R_2\bar{C}H + HO_2^{\cdot}$$

$$HO_2^{\cdot} + e^-(O_2^{\bar{\cdot}}) \longrightarrow HO_2^-$$

Mechanism 2: Superoxide as a nucleophile



$$O_2 + e^- \longrightarrow O_2^{\bar{\cdot}}$$

$$Br(CH_2)_nBr + O_2^{\bar{\cdot}} \longrightarrow Br(CH_2)_nOO\cdot + Br^-$$

$$Br(CH_2)_nOO\cdot + e^-(O_2^{\bar{\cdot}}) \longrightarrow Br(CH_2)_nOO^-$$

$$\longrightarrow Br(CH_2)_nO^-$$

$$Br(CH_2)_nOO^- + R_1R_2CH_2 \longrightarrow Br(CH_2)_nOOH + R_1R_2\bar{C}H$$

$$(\ Br(CH_2)_nO^- + R_1R_2CH_2 \longrightarrow Br(CH_2)_nOH + R_1R_2\bar{C}H\ )$$

$$R_1R_2\bar{C}H + Br(CH_2)_nBr \longrightarrow R_1R_2C(H)(CH_2)_nBr + Br^-$$

$$\longrightarrow R_1R_2\bar{C}(CH_2)_nBr \longrightarrow R_1R_2C(CH_2)_n + Br^-$$

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