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DIRECT EPOXIDATION OF POLYCYCLIC AROMATIC COMPOUNDS BY SUPEROXIDE IN THE PRESENCE OF PHOSGENE DIMER

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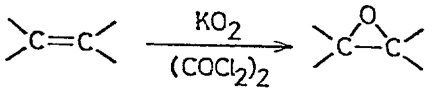
Abstract: Olefins and polycyclic aromatic compounds were oxidized to their epoxides by superoxide ($O_2^{\overline{\cdot}}$) in the presence of phosgene dimer. The reaction mechanisms are discussed.

During the past decade the possibility that superoxide $O_2^{\overline{\cdot}}$ might be an important intermediate in aerobic life has given new impetus to studies of this anion radical.¹⁾ The organic chemistry of superoxide has also been an area of intense interest in recent years.$^{2)}$ $O_2^{\overline{\cdot}}$, one of the simplest and most important anion radicals, reacts with various substrates owing to its anionic, radical and redox nature, although the nucleophilic and reducing electron transfer processes appear to be the predominate reaction pathways.

However some reports indicate that superoxide is relatively inactive and of limited use in organic synthesis.$^{3)}$ In this paper, we report that superoxide reacts with certain organic substrates to form oxidants that are more active than superoxide. That is, the more reactive species, acyl peroxy

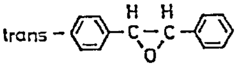
Scheme I



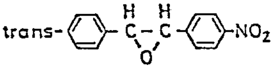
Reaction Conditions

Substrate: 1 mmol $(COCl_2)_2$: 5 mmol
KO_2: 40 mmol 18-crown-6: 1 mmol
benzene (4°C) or n-hexane (-10°C ~ -5°C): 30 ml

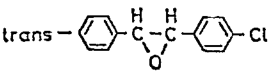
Table I



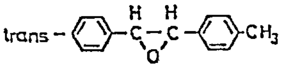
trans-Stilbene 89 %
cis-Stilbene 41 %
1



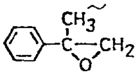
79 % 2



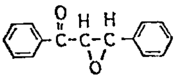
q.y. 3



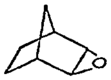
70 % 4



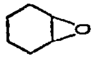
52% 5



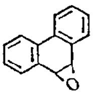
40 % 6



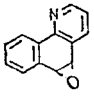
q.y. 7



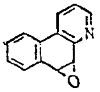
80 % 8



38 % 9



34 % 10



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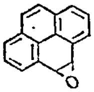
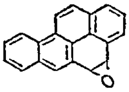
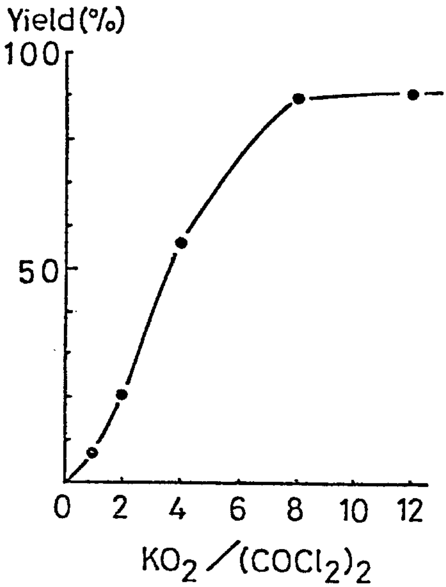


12 % 12



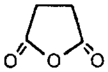
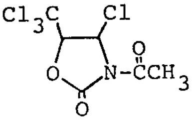
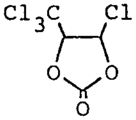
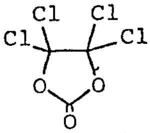
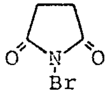
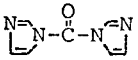
5 % 13

Fig. 1



The Relationship between the Yields of trans-Stilbene Oxide and $KO_2/(COCl_2)_2$ Ratio $(COCl_2)_2$:1 mmol, stilbene:0.2 mmol, 18-crown-6/KO_2=1/40, solvent:n-hexane(15 ml), reaction time: 2 hr, reaction temp.:-10°C~-5°C

Table II The Yield of Trans-Stilbene Oxide by Superoxide in the presence of Various Compounds other than $(COCl_2)_2$

$C_6H_5\overset{\overset{O}{\|}}{C}Cl$ 62% 14	$C_6H_5CH_2\overset{\overset{O}{\|}}{C}Cl$ 38% 15	$C_6H_5CH_2O\overset{\overset{O}{\|}}{C}Cl$ 59% 16
$(CF_3\overset{\overset{O}{\|}}{C})_2O$ 29% 17	$(CH_3\overset{\overset{O}{\|}}{C})_2O$ 52% 18	 8% 19
$Et_2N\overset{\overset{O}{\|}}{C}Cl$ 14% 20	$C_6H_5SO_2Cl$ 41% 21	$(EtO)_2\overset{\overset{O}{\|}}{P}Cl$ 39% 22
 14% 23	 56% 24	 13% 25
 18% 26	 0% 27	$CF_3\overset{\overset{O}{\|}}{C}CF_3$ 0% 28
$SOCl_2$ trace 29	SO_2Cl_2 trace 30	$Cl\overset{\overset{O}{\|}}{C}\overset{\overset{O}{\|}}{C}Cl$ trace 31

radical or anion, may be produced in the reaction of superoxide with acyl halide.

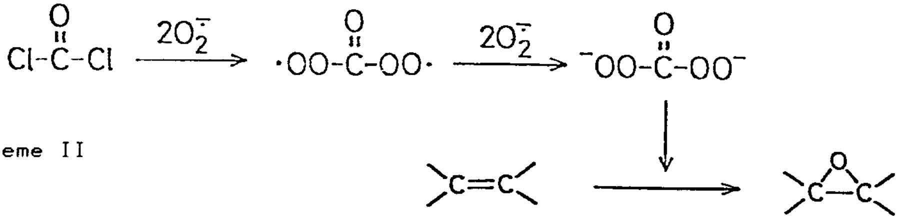
So far, our studies on biomimetic reactions involving superoxide have revealed the interchange reactions of disulfides,[4)] the desulfurizations of thiocarbonyl groups[5)] and the epoxidation of trans-stilbene by superoxide in the presence of acyl halide.[6)] The epoxidation is noteworthy because superoxide is presumed to be as one of the active intermediates in certain oxygenases.[7)] The previous paper reported that trans-stilbene oxide was produced from trans-stilbene by superoxide and benzoyl chloride. We examined the scope and limitations of this epoxidation and found that polycyclic aromatic compounds were epoxidized by superoxide in the presence of $(COCl_2)_2$ as acyl halide (Scheme I).

In a typical experiment, phosgene dimer (5 mmol) was added to the mixture of phenanthrene (1 mmol), 18-crown-6 (1 mmol) and powdered potassium superoxide (KO_2 40 mmol) in dry n-hexane (30 ml). The reaction mixture was stirred at -10°C ~ -5°C for 1 hr. The resulting phenanthrene oxide was purified by alumina column chromatography and recrystallized from $CHCl_3$/n-hexane. The oxide was found to be identical to the authentic sample by I.R., N.M.R., Mass spectra and E.A. etc.. Table I summarizes the results obtained under the described conditions; yields refer to pure, isolated products. Trans-stilbene and its derivatives were converted exclusively to oxides (**1**, **2**, **3**, **4**) in high yields. Nitro or chloro derivatives of trans-stilbene could hardly be oxidized by m-chloroperbenzoic acid. Cis-stilbene was oxidized to trans-stilbene oxide in the 41% yield. The yield of chalcone oxide (**6**) was low (40%) because of the decomposition by superoxide to benzoic acid and phenyl acetic acid. Also, olefins such as norbornene and cyclohexene were readily epoxidized. However the oxidation of cyclohexene was inhibited by 18-crown-6, though it is not clear why. Phenanthrene oxide was obtained in 38% yield with 48% recovery of the starting material. Of course no phenanthrene oxide was found when Na_2O_2 or 30% H_2O_2 was substituted for KO_2 in the reaction. The oxide of pyrene (**12**) or benzo(a)pyrene (**13**) was isolated in poor yield because of the difficult post-treatment of the unstable product.$^{8)}$

The yields of trans-stilbene oxide in various solvents were examined; n-C_6H_{14} (89%), C_6H_6 (62%), CH_2Cl_2 (32%), CH_3OH (25%), CH_3CN (16%), dioxane (2%). The last four were in low yields, probably because superoxide or an active intermediate arising from superoxide reacted with the solvents. The yields of trans-stilbene oxide were examined with various $KO_2/(COCl_2)_2$ ratios (Fig. 1). When the $KO_2/(COCl_2)_2$ ratio was below 4, the yield was extremely low because diacyl peroxide (RC(O)OO(O)CR) was formed by the reaction of acyl peroxyanion with phosgene. However the yield increased markedly at the ratio of $KO_2/(COCl_2)_2$=8. Therefore, 8 mmol of KO_2 is necessary for 1 mmol of $(COCl_2)_2$.

The epoxidation of trans-stilbene was investigated in the presence of acyl halides, diethylchlorophosphate,$^{9)}$ benzenesulfonyl chloride,$^{10)}$ acid anhydrides, NBS, etc. instead of phosgene dimer (Table II). Acyl halides (**14**, **15**, **16**, **20**) and acid anhydrides (**17**, **18**, **19**) were active reagents for superoxide. The epoxidation by superoxide proceeded with various halides (**21**,

Proposed Reaction Mechanism



Scheme II

22, 23, 24, 25 and 26). However, no active species were produced from compounds (27 and 28). In the presence of $SOCl_2$, SO_2Cl_2, or $(COCl)_2$, the product from trans-stilbene was dichlorodiphenylethane and no trans-stilbene oxide was obtained. The formation of dioxetane in the reaction of $(COCl)_2$ with KO_2 was confirmed by the emission of fluorescence from perylene.11)

Although the precise mechanism of these reactions is not clear, it is presumed that 1 mol of phosgene dimer $(COCl_2)_2$ reacts with 2 mol of superoxide to produce 1 mol of acyl peroxyradical ($\cdot OOC(O)OO\cdot$) and then acyl peroxyradical is reduced two electrons by 2 mol of superoxide to acyl peroxyanion ($^-OOC(O)OO^-$). Acyl peroxyanion seems to attack the substrates to produce the oxides (Scheme II). This reaction species is novel, since organic peracids (e.g. m-CPBA) are considered to have electrophilic reactivity (^+OH).

The biological significance of the above epoxidation will be clearly demonstrated in a following paper.

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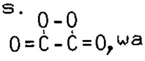
10). S.Oae, T.Takata and Y.H.Kim, Bull.Chem.Soc.Jpn., 54, 2172 (1980); J.S.Stanley, J.Org.Chem., 45, 1413 (1980), This paper reports the reaction of superoxide with peroxides.

11). The product, dioxetane  $\overset{O-O}{O=C-C=O}$, was obtained in the reaction of $(COCl)_2$ with KO_2. The emission of fluorescence was measured by Chem. Glow Photometer; Amico Co., Maryland, U.S.A.. Of course fluorescence of perylene by KO_2 in the absence of $(COCl)_2$ was not observed.

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