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OXIDATION OF SUBSTRATES HAVING LABILE HYDROGENS BY SUPEROXIDE IN THE PRESENCE OF PHOSGENE DIMER

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Superoxide ($O_2^{\cdot-}$) oxidized substrates having labile hydrogens to ketones in the presence of phosgene dimer. Oxidations with similar treatment of alkynes were examined. The reaction mechanism was also discussed.

Superoxide ($O_2^{\cdot-}$), which is an anion radical and one of the activated oxygen species, is an important reactant in biological systems. It characteristically performs various functions (reduction, oxidation, nucleophilic reaction, disproportionation, etc.).1) Furthermore, $O_2^{\cdot-}$ may be an intermediate producing $\cdot OH$ or $^1O_2$ from O_2.2)

It is of great current interest whether $O_2^{\cdot-}$, itself, has super or innocuous reactivities.3) Our studies suggest that $O_2^{\cdot-}$ becomes a super active species in the presence of certain compounds which act as effectors. In the previous paper we reported that $O_2^{\cdot-}$ oxidizes polycyclic aromatic compounds to produce their oxides in the presence of phosgene dimer.4) $O_2^{\cdot-}$, by itself, is not as active as the species which can epoxidize polycyclic aromatic compounds. $O_2^{\cdot-}$ reacts with phosgene dimer to form a more active oxidant which facilitates epoxidations of polycyclic aromatic compounds.

In this paper, we report that $O_2^{\cdot-}$ oxidizes substrates having labile hydrogens to ketones in the presence of various effectors. In a typical experiment, phosgene dimer (2.5 mmol)5) was added to the mixture of tetralin (0.5 mmol), 18-crown-6 (0.25 mmol) and powdered potassium superoxide (10 mmol) in dry n-hexane (25 ml). The reaction mixture was stirred at -15° ~ -10° for 2 hr. As a result, tetralone was obtained after purification by silica gel column chromatography and identified with the authentic sample by IR, NMR and Mass spectra. Table I summarizes the yields of products obtained with similar treatment of other representative substrates. Tetralin was not oxidized at all by $O_2^{\cdot-}$ in the absence of phosgene dimer.6) However, tetralone was obtained first when the reaction mixture contained acyl halides, acid anhydride, benzene sulfonyl chloride or diethyl chloro phosphate (Table II). Tetralone was obtained in poor yields in the presence of thionyl chloride or oxalyl chloride, which were not effectors. Fluorene and xanthene were oxidized, respectively, to fluorenone (33%) and xanthone

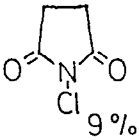
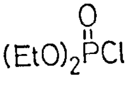
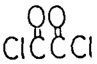
(23%) by $O_2^{\cdot-}$ only.[6a] However, in the presence of phosgene dimer these yields increased greatly (Table I Run 2,3). A more potent hydrogen abstracting agent than $O_2^{\cdot-}$ was formed in the reaction of $O_2^{\cdot-}$ with phosgene dimer. In the oxidation, the best yield was obtained in dry n-hexane at −15° ~ −10° (Table III). The low yields with the solvents CH_3CN or CH_3OH may be because these solvents reacted with $O_2^{\cdot-}$ in the presence of phosgene dimer.[7] The yields of tetralone were examined under various $KO_2/(COCl_2)_2$ ratios (Fig. 1). More than 4 mol of KO_2 is necessary for 1 mol of $(COCl_2)_2$. When the ratio was below 4, the yields decreased and 2-clorotetralone was formed as a by-product.

Table I Oxidation of Substrates Having Labile Hydrogens by $O_2^{\cdot-}$ in the Presence of $(COCl_2)_2$

Run	Substrate	Product	Yield (%)
1	tetralin	tetralone	34
2	fluorene	fluorenone	88
3	xanthene	xanthone	68
4	diphenylmethane	benzophenone	7
5	bis(4-nitrophenyl) methane	bis(4-nitrophenyl) methanone	9
6	9,10-dihydro-anthracene	anthraquinone	7
		anthracene	77
7	anthracene	anthraquinone	27
8	acridine	acridone	5
9	toluene	benzaldehyde	7
10	p-chlorotoluene	p-chlorobenzaldehyde	5
11	p-methoxytoluene	p-methoxybenzaldehyde	5

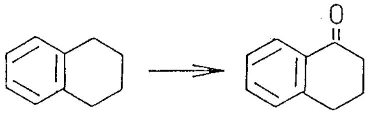
Reaction Time: 2 ~ 4 hr, Reaction Temp.: −15° ~ −10°
KO_2: 10 mmol, $(COCl_2)_2$: 2.5 mmol, 18-crown-6: 0.25 mmol
substrate: 0.5 mmol, solvent: n-hexane 25 ml,

Table II The Yields of Tetralone by $O_2^{\cdot-}$ in the Presence of Various Effectors besides $(COCl_2)_2$

C_6H_5COCl	$C_6H_5CH_2OCOCl$	$C_6H_5CH_2COCl$	$C_6H_5SO_2Cl$	
22 %	12 %	6 %	19 %	
$(CH_3CO)_2O$		 $(EtO)_2P(O)Cl$	$SOCl_2$	 $ClC(O)C(O)Cl$
9 %	9 %	4 %	trace	1 %

Reaction Time: 2 ~ 4 hr, Reaction Temp.: 4° ~ 6°, KO_2: 10 mmol
18-crown-6: 0.25 mmol, Tetralin: 0.5 mmol, Solvent: benzene 20 ml

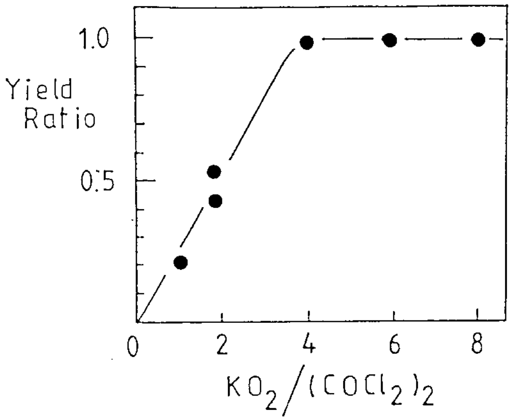
Table III
Effects of Solvent on the Oxidation of Tetralin by KO_2 in the Presence of $(COCl_2)_2$



		yield (%)	
Run	Solvent	0°	−15° ~ −10°
1	C_6H_6	19*	--
2	$n\text{-}C_6H_{14}$	11	34
3	CH_2Cl_2	10	17
4	CH_3CN	2	1
5	CH_3OH	3	2

Reaction Time: 2 ~ 4 hr, KO_2: 10 mmol, $(COCl_2)_2$: 2.5 mmol, 18-crown-6: 0.25 mmol, Tetralin: 0.5 mmol, *(4° ~ 6°)

Fig. 1 The Correlation Between the Ratios of $KO_2/(COCl_2)_2$ and the Yield Ratios of Tetralone

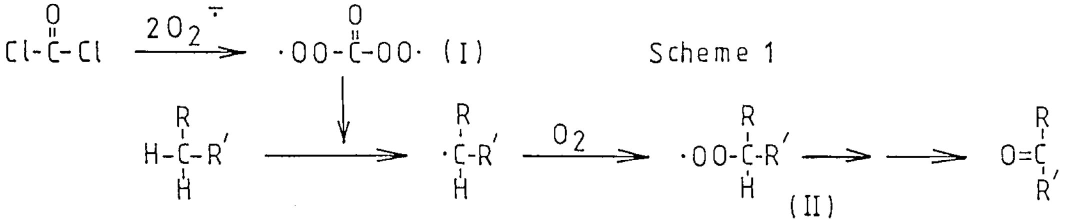


Reaction Time: 2 ~ 4 hr, Reaction Temp.: −15° ~ −10°, KO_2: 2.5 ~ 20 mmol, $(COCl_2)_2$: 2.5 mmol, 18-crown-6/KO_2=1/40, Tetralin: 0.5 mmol, Solvent: n-hexane 25 mml

Alkynes were oxidized to diketones on similar treatment. As a result $C_6H_5C(O)C(O)C_6H_5$ (11%) and $C_6H_5C(O)C(O)CH_3$ (7%) were produced from $C_6H_5C\equiv CC_6H_5$ and $C_6H_5C\equiv CCH_3$. respectively. $C_6H_5C\equiv CH$ was oxidized not to $C_6H_5C(O)CHO$ but to $C_6H_5C(O)CHCl_2$ (7%). Apparently $C_6H_5C(O)CHO$ was produced as a reaction intermediate, followed by chlorination to produce $C_6H_5C(O)CHCl_2$.

The assumed oxidation mechanism is shown in Scheme 1. The yield was maximal when the $KO_2/(COCl_2)_2$ ratio was ≧ 4. Substituents had little effect on oxidation yields (Table I Run 9,10,11). These suggest that the oxidation mechanism includes certain radical species. That is, 4 mol of $O_2^{\overline{\cdot}}$ reacted with 1 mol of $(COCl_2)_2$ to produce 2 mol of acyl peroxyradical(I) which abstracted labile hydrogen from the substrate. Then the produced substrate radical may have reacted with O_2 to become peroxyradical(II), and finally to form the ketone. In any event, the novel species acyl peroxyradical(I) appears to be a more potent oxidant than $O_2^{\overline{\cdot}}$ because it can oxidize substrates having labile hydrogen and alkynes.[8)] This species, which is different from organic peracids (e.g. mCPBA) or H_2O_2, seems to be significant not only in organic synthesis but also in the elucidation of reactivities of $O_2^{\overline{\cdot}}$ in the biological systems.

Further studies on biomimetic oxidation by $O_2^{\bar{\cdot}}$ and some effectors in the living systems are in progress.$^{9)}$



Scheme 1

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