CHEMISTRY LETTERS, pp. 547-550, 1977. Published by the Chemical Society of Japan

REACTION OF POTASSIUM SUPEROXIDE WITH PHENOXY RADICALS. ON THE MECHANISM OF BASE-CATALYZED OXYGENATION OF PHENOLS

Akira NISHINAGA, Tadashi SHIMIZU, and Teruo MATSUURA

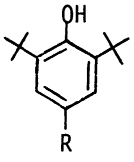
Department of Synthetic Chemistry, Faculty of Engineering,
Kyoto University, Sakyo-ku, Kyoto 606

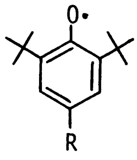
Superoxide ion (O_2^-) hes been found not to couple with 2,6-di-*tert*-butylphenoxy radicals but to reduce the radicals giving rise to the corresponding phenolates. Molecular oxygen attacks predominantly the para position of the phenoxy radicals and the regioselectivity is not affected by the nature of the reaction medium. A new mechanism involving an ionic process for the base-catalyzed oxygenation of 2,6-di-*tert*-butylphenols is proposed.

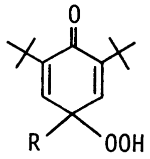
The oxidation of organic substrates with superoxide ion (O_2^-) is a current interest in connection with functional significance of O_2^- in biological oxygenations.[1-4] A mechanism involving combination of O_2^- with organic radicals has been postulated for the oxidation of phenols with O_2^-,[2,4] the oxygenation of carbanions,[5] and for the base-catalyzed oxygenation of phenols,[6] where hydroperoxides are the primary products. Little is, however, known about the reaction of O_2^- with organic radicals.[7]

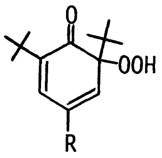
$$R\cdot \quad + \quad O_2^- \longrightarrow ROO^-$$

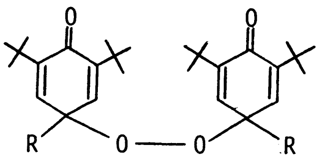
We have therefore investigated the reaction of O_2^- with 2,6-di-*tert*-butylphenoxy radicals (2) in view of the elucidation of mechanism by which the base-catalyzed oxygenation of 2,6-di-*tert*-butylphenols (1) leads to the quantitative formation of hydroperoxides 3 and 4[8-10] and found that O_2^- does not couple with these radicals but reduces the radicals affording the corresponding phenolates.


1


2


3


4


5

a: R = *t*-Bu, b; R = 4-MeOPh

A solution of phenoxy radicals 2 (0.5 mmol) in benzene (2.5 ml) was added to a suspension of

KO_2 (1 mmol) in an appropriate solvent (20 ml) containing dicyclohexyl-18-crown-6 (1 mmol) under nitrogen atmosphere. After a color of the radicals was disappeared, the reaction mixture was acidified with hydrochloric acid and extracted with ether. The extract was dried (Na_2SO_4) and evaporated to give a crystalline residue which was analyzed by tlc and NMR methods. The products were shown to be only phenols **1** and peroxides **5** (Table 1). As seen from Table 1, only the product ratio was changed by variation of the reaction conditions. In the case that the reaction proceeds fast, the yield of **1** is good. The reaction of **2b** with O_2 is very slow,[11] resulting in naturally the increase of yield of **1b**. The results indicate that the formation of **1** is resulted from the reduction of **2** by O_2^- through a one electron transfer process and the resulting O_2 reacts with **2** to give **5**,[12] and that hydroperoxide **3** or **4**[8-10] is not formed by the coupling of **2** with O_2^- in the base-catalyzed oxygenation.

Table 1. The Reaction of **2** with O_2^-

2	Solvent	Reaction Temp. (°C)	Reaction[a] Time (min)	Product Ratio[b]	
				1	**5**[c]
2a	Benzene	20	3	44	56
2a	*t*-BuOH	20	0.4	69	31
2a	NMP[d]	20	0.5	54	46
2a	NMP	-20	15	56	44
2a	$NHEt_2$[d]	20	0.4	70	30
2b	Benzene	20	2	77	23
2b	*t*-BuOH	20	0.5	94	6
2b	NMP	20	2	96	4
2b	NMP	-20	10	95	5

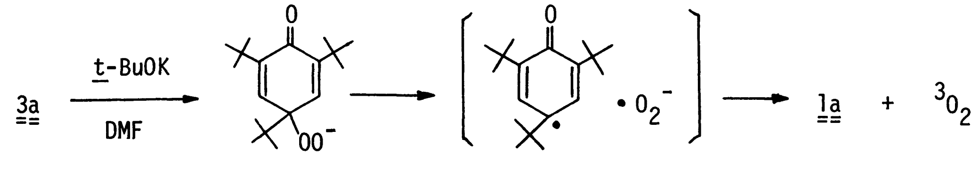
[a] Time required for the disappearance of color of the radicals. [b] Yields of the products were nearly quantitative and the product ratio was determined by NMR. [c] The peroxides contain a small amount of isomeric peroxides coupled at the ortho and para positions of **2**. [d] NMP = N-Methyl-2-pyrrolidone,in which the base-catalyzed oxygenation of **1a** gives **3a**. In $NHEt_2$ with $NaNH_2$, the oxygenation of **1a** gives exclusively the corresponding *p*-quinol.

It has been known that 1,3-diphenylisobenzofuran (**6**) reacts with an excited singlet-state molecular oxygen very easily to give 1,2-dibenzoylbenzene (**7**).[7] From the reaction of **2** with O_2^- in the presence of **6**, no compound **7** was obtained and **6** was recovered quantitatively. This indicates that the resulting O_2 from the reaction of **2** with O_2^- is of the ground-state.[13]

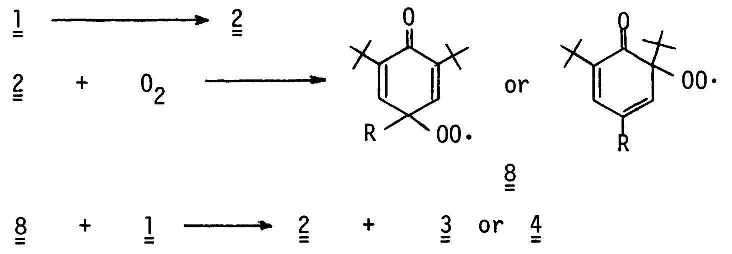
$$\mathbf{2} + O_2^- \longrightarrow \mathbf{1} + {}^3O_2$$

On the other hand, treatment of **3a** with *t*-BuOK in dimethylformamide results in the formation of

1a with the liberation of O_2.[10,14] The generated molecular oxygen has now been found to be of the ground-state (no compound **7** was formed from the base-catalyzed decomposition of **3a** in the presence of **6**). This is rationalized by considering the following mechanism involving a homolysis of the C-O bond of the peroxy moiety in **3a** followed by the electron transfer from the resulting O_2^- to **2a** in the cage, which is consistent with the results obtained in the reaction of **2a** with O_2^-. These results rule out the proposed mechanism involving the coupling of phenoxy radicals with O_2^-, which is just the reverse reaction of the base-catalyzed decomposition of **3a**, for the base-catalyzed oxygenation of **1**.

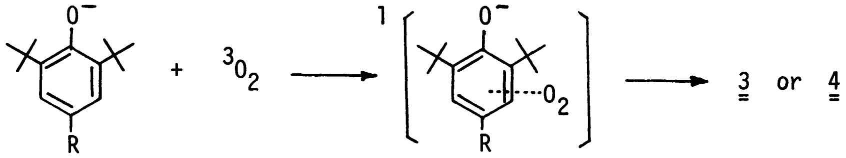


The base-catalyzed oxygenation of **1** occurs regioselectively depending on the reaction medium: p-hydroperoxide **3** is formed exclusively in polar aprotic solvents such as dimethylformamide and hexamethylphosphoric triamide, whereas the formation of o-hydroperoxide **4** is predominant in t-BuOH.[8-10] If the following free radical chain mechanism is applied for the base-catalyzed oxygenation, the reaction of **2** with O_2 must display the regioselectivity depending on the reaction medium.



We, however, find that molecular oxygen attacks predominantly the para position of **2** affording **5** regardless of the nature of the medium (Table 1).[12] Accordingly, the regioselectivity observed in the oxygenation of **1** cannot be interpreted either by the free radical chain mechanism.

Our results therefore strongly suggest an ionic mechanism for the base-catalyzed oxygenation of **1** although the ionic mechanism has been excluded so far by reason of the violation of the spin conservation rule.[15] A diamagnetic transition state is imaginable.



The ionic mechanism may be rationalyzed by assuming that the phenolate anion of 1, which is a strong electron donor, attacks a π^* orbital of O_2, causing the perturbation of this level. The donating electron pair of the phenolate will occupy one of the perturbed orbitals of the π^* level, in consequence, the π^* electrons of O_2 will be forced to pair in the resulting lowered orbital. The mechanism can be considered to be analogous to that operated in the reaction of diamagnetic (singlet-state) d^8 and d^{10} metal complexes with O_2 giving rise to diamagnetic (singlet-state) oxygen complexes, MO_2.[16]

Recently, Turro and his coworkers have reported that the theraml reaction of a certain kind of cyclic acetylene derivative with O_2 involves an ionic process,[17] which may be analogous to that in our case.

The authors are indebted to the Ministry of Education for a financial support.

References and Notes

1) O. Hayaishi, "Molecular Mechanism of Oxygen Activation," Academic Press, New York and London, 1974, pp 678.
2) Y. Morooka and C. S. Foote, J. Am. Chem. Soc., 98, 1570 (1975).
3) M. Tetsuka, Y. Ohkatsu, and T. Osa, Bull. Chem. Soc. Jpn., 48, 1471 (1975).
4) Y. Morooka, P. J. Chung, H. Arakawa, and T. Ikawa, Chem. Lett., 1293 (1976).
5) G. A. Russell, A. G. Bemis, E. J. Geels, E. G. Janzen, and J. Moye, Adv. Chem. Ser., 75, 174 (1968).
6) R. K. Haynes and H. Musso, Chem. Ber., 107, 3723 (1974).
7) An electrochemical study has revealed the reaction of radical cations with O_2^- to give $^1O_2$: E. A. Mayeda and A. J. Bard, J. Am. Chem. Soc., 95, 6223 (1973).
8) A. Nishinaga, T. Itahara, T. shimizu, and T. Matsuura, Tetrahedron Lett., 2467 (1976).
9) A. Nishinaga and A. Rieker, J. Am. Chem. Soc., 98, 4667 (1976).
10) A. Nishinaga, T. Itahara, and T. Matsuura, Chem. Lett., 667 (1974); Tetrahedron Lett., 4481 (1974).
11) E. Müller, A. Schick, and K. Scheffler, Chem. Ber., 92, 474 (1959).
12) The formation of peroxides of type 5 from the reaction of 2 with O_2 is well known: reference 11, E. Müller and K. Ley, Chem. Ber., 87, 922 (1954); C. D. Cook and R. C. Woodwarth, J. Am. Chem. Soc., 75, 6242 (1953). The reaction of 2 with O_2 in t-BuOH/t-BuOK also gave 5 predominantly.
13) We find that stable 2,5-dialkyl-1,4-dimethoxybenzene radical cations oxidize KO_2 to give $^1O_2$ in 82-84% yield (determined by means of $^1O_2$ quencher 6). The results will be published elsewhere. It is quite interesting that different radical species oxidizes O_2^- in different way.
14) The liberation of O_2 from a hydroperoxide derived from di-tert-butylresorcinol monomethyl ether has also been reported: R. Zunker and H. Musso, Liegigs Ann., 717, 73 (1968).
15) W. von E. Doering and R. M. Haines, J. Am. Chem. Soc., 76, 482 (1954).
16) J. S. Valentine, Chem. Rev., 73, 235 (1973).
17) N. J. Turro, V. Ramamurty, and K-C, Liu, J. Am. Chem. Soc., 98, 6759 (1976).

(Received April 12, 1977)