Tetrahedron Letters,Vol.30,No.46,pp 6357-6360,1989
Printed in Great Britain

0040-4039/89 $3.00 + .00
Pergamon Press plc

OXIDATION OF BENZYLIC METHYLENE COMPOUNDS TO KETONES WITH 2-NITROBENZENE PEROXYSULFONYL RADICAL FORMED FROM ITS CHLORIDE AND SUPEROXIDE

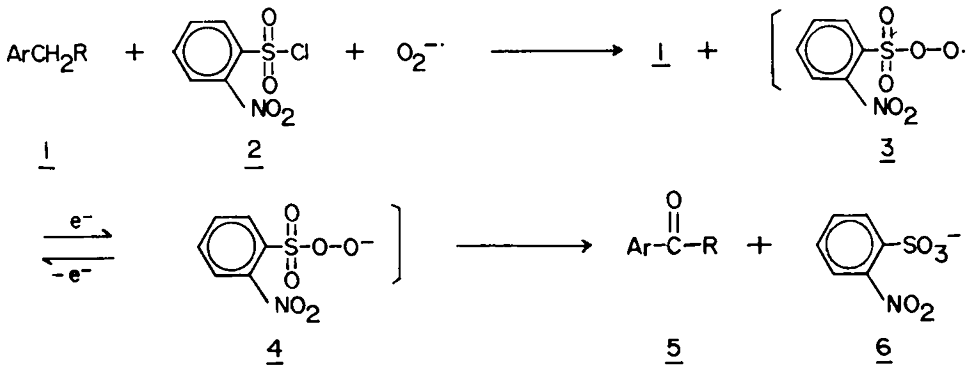
Yong Hae Kim*, Kyoung Soo Kim, and Hyeon Kyu Lee
Department of Chemistry
Korea Advanced Institute of Science and Technology
P.O. Box 150, Cheongyang-Ni
Seoul 130-650, Korea

Summary: 2-Nitrobenzene peroxysulfonyl radical intermediate generated from 2-nitrobenzenesulfonyl chloride and superoxide oxidized various substrates containing benzylic methylene group to ketones in excellent yields at -35 °C in acetonitrile under mild conditions.

Oxidation of active methylene group is important _in vivo_ metabolic process catalyzed by oxygenases[1] as well as in the organic synthesis. Active methylene group of lipids are known to be metabolized _in vivo_ to the hydroxy or carbonyl group with no evidence to show any intervention by activated species of oxygen such as superoxide.[2]

Though superoxide ($O_2^{-\cdot}$) alone is not so reactive in nonpolar solvents,[3] it can be expected to activate $O_2^{-\cdot}$ by the reaction with some substrates which turn out to be more reactive oxygen species.

In our previous works, it was reported that 2-nitrobenzene peroxysulfur intermediate generated _in situ_ by the treatment of 2-nitrobenzenesulfonyl chloride with $O_2^{-\cdot}$, showed sufficient oxidizing ability for the oxidation of olefins,[4] thiocarbonyl compounds,[5] sulfoxides,[6] and arenes.[7] However, there



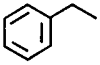
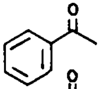
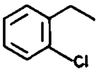
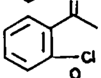
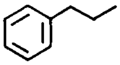
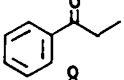
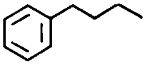
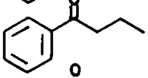
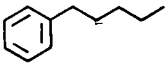
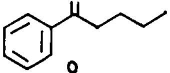
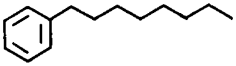
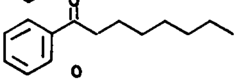
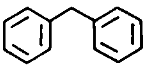
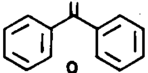
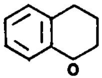
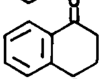
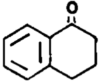
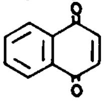
has been argument whether the intermediate exists as radical (3) or anion (4).

In this communication, we report that various substrates containing benzylic methylene group reacted readily with 2-nitrobenzene peroxysulfur intermediate at -35 °C under mild conditions to give the corresponding carbonyl compounds (5) in excellent yields. The oxidation can be best explained by a radical mechanism *via* formation of 3. The existence of 4 can not be ruled out, but formation of 3 was indirectly observed by spin trapping study.[8]

In a general procedure, a solution of 2-nitrobenzenesulfonyl chloride (666 mg, 3 mmol; CH_3CN, 8 ml) and propylbenzene (40 mg, 0.33 mmol) was added to a heterogeneous solution of potassium superoxide (639 mg, 9 mmol: CH_3CN,

Table 1. Oxidation of Substrates Containing Benzylic Methylene Group at ca. -35 °C.

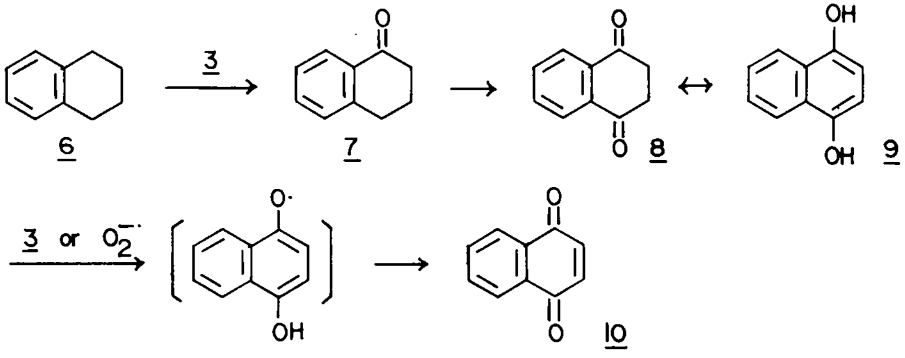
$$\underline{1} + \underline{2} + O_2^{-\bullet} \xrightarrow[-35\ ^{o}C,\ CH_3CN]{} \underline{5} + \underline{6}$$

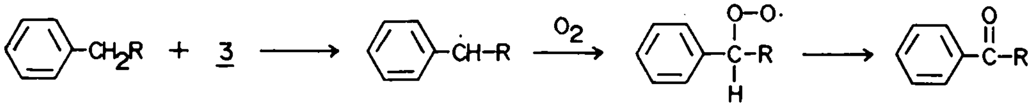
Run	Substrate	Ratio (2)/(1)	Reaction time (h)	Product	Yield (%)^{a}
1		9	4		92
2		9	8		82
3		9	6		98
4		9	8		91
5		9	8		84
6		9	8		90
7		4	6		92^{b}
8		4	6		$41^{b,c}$
9		8	6		85^{b}

a) Yields determined by GC. b) Isolated yields. c) Starting material was recovered in 45% yield.

5 ml) at ca. -35 °C. After being stirred for ca. 6 h at ca. -35 °C, the reaction mixture was filtered and then washed twice with acetonitrile (10 ml x 2) and methylene chloride (10 ml x 2). The yield of propiophenone was determined by GC analyses. Concentration and separation by preparative TLC (Merk, silica gel 60 GF$_{254}$, Et$_2$O : n-Hexane = 1 : 7, v/v) gave pure propiophenone (41 mg, 93 %). The products obtained were identified by comparing their IR and ^{1}H-NMR with those of authentic samples.

Results obtained are summarized in Table 1. Tetraline (6) which has two benzylic methylene groups is stepwise oxidized to 10 by 3. Tetraline is first oxidized to α-tetralone, 7 (Run 8) which was further oxidized to 1,4-naphtoquinone (10) through 1,4-dihydroxynaphthalene (8). The formation of an intermediate, 8 was confirmed by GC-Mass analysis (m/z 158 (base)) of an aliquot from the reaction mixture before the reaction is completed. Abstraction of a hydrogen atom from 1,4-dihydroxynaphthalene by 3 or $O_2^{-\cdot}$ remained produces semiquinone radical, which may quickly converted to 10. Oxidation of catechols to the quinones by the abstraction of hydrogen by $O_2^{-\cdot}$ has been reported.[9,10] When 7 was used as a starting material, it was actually oxidized to 10 (Run 9, 85 %) under the same conditions. Oxidation of ethylbenzene to acetophenone by electrogenerated superoxide[11] and oxidation of substrates containing more labile hydrogen to ketones using potassium superoxide at room temperature[12] are reported. However, substrates containing benzylic methylene group were not oxidized by potassium superoxide in the absence of 2 under the same conditions; starting materials were recovered quantitatively. A plausible reaction mechanism can be postulated as shown below.





One of the hydrogen atoms of benzylic methylene group is abstracted by 3, which is formed by a nucleophilic attack of superoxide anion to the sulfonyl sulfur of 2. The resulting benzylic radical may couple with molecular oxygen or $O_2^{-\cdot}$ to form peroxy radical and then converted to the corresponding carbonyl group.

The work described herein appears to be of synthetic use for the oxidation of various substrates containing benzylic methylene group to the corresponding carbonyl compounds and also sheds further light on the superoxide role in the biological system.

Acknowledgment: This work was supported by grants from Korea Science and Engineering Foundation.

References

1. J. Bland, **J. Chem. Educ.**, **55**, 151 (1978).
2. a) J.A. Matthew and T. Galliard, **Phytochemistry**, **17**, 1043 (1978). b) D.A. Wardale, E.A. Lambert, and T. Galliard, **Phytochemistry**, **17**, 205 (1978).
3. D.T. Sawyer and J.S. Valentine, **Acc. Chem. Res.**, **14**, 393 (1981).
4. Y.H. Kim and B.C. Jung, **J. Org. Chem.**, **48**, 1562 (1983).
5. Y.H. Kim, B.C. Jung, and H.S. Chang, **Tetrahedron Lett.**, **26**, 1079 (1985).
6. Y.H. Kim and H.K. Lee, **Chem. Lett.**, 1499 (1987).
7. H.K. Lee, K.S. Kim, J.C. Kim, and Y.H. Kim, **Chem. Lett.**, 561 (1988).
8. Y.H. Kim, S.C. Lim, M. Hoshino, Y. Ohtsuka, T. Ohishi, **Chem. Lett.**, 167 (1989).
9. Y. Moro-Oka and C.S. Foote, **J. Am. Chem. Soc.**, **98**, 1510 (1976).
10. D.T. Sawyer, M.J. Gibian, M.M. Morrison, and E.T. Seo, **J. Am. Chem. Soc.**, **100**, 627 (1978).
11. T. Matsue, M. Fujihira, and T. Osa, **J. Electrochem. Soc.**, **128**, 2565 (1981).
12. Y. Moro-Oka, P.J. Chung, H. Arakawa, and T. Ikawa, **Chem. Lett.**, 1293 (1976).

(Received in Japan 4 September 1989)