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ON THE MECHANISM OF AROMATIC HYDROXYLATION BY $O(^3P)$ ATOMS

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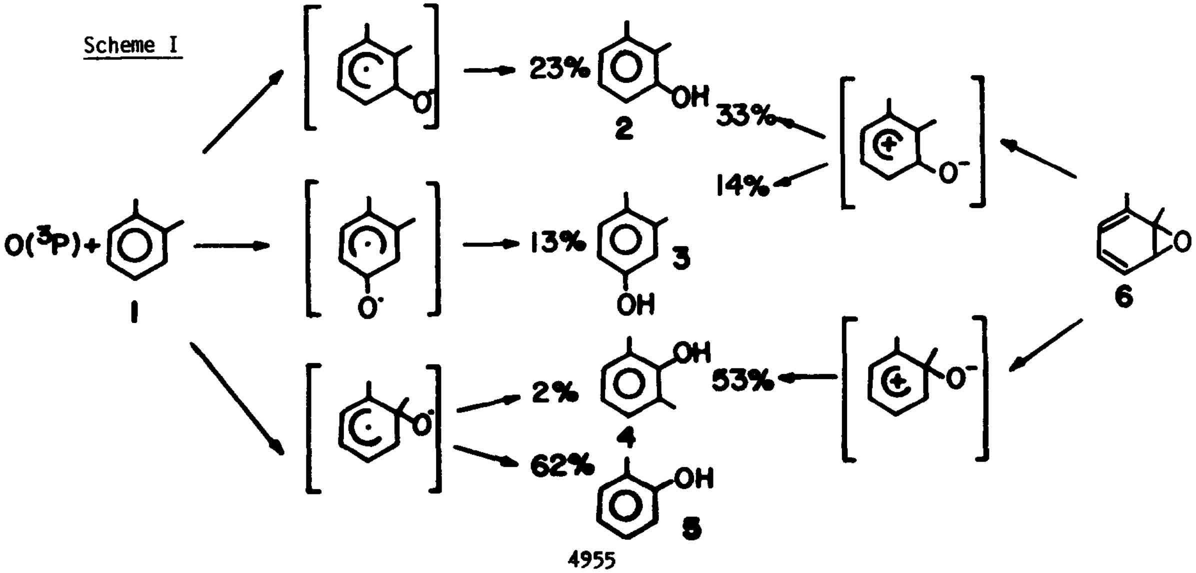
Summary: It is shown that $O(^3P)$ oxidation of aromatic compounds in the liquid phase leading to phenols may involve the intermediacy of triplet diradicals.

Unsaturated compounds in the liquid phase react with $O(^3P)$ atoms produced by microwave discharge of O_2 or N_2O and N_2, forming epoxides or undergoing 1,2-H migration,to give carbonyl compounds[1]. Reactions of $O(^3P)$ atoms with substituted benzene derivatives in the condensed phase lead to phenols and benzylic oxidation products[2]. An alternative procedure, previously reported for aromatic hydroxylation by $O(^3P)$ atoms in the condensed phase, is the gamma radiolysis of liquid CO_2 solutions[3]. Based on the results of this reaction, it has been recently stated that aromatic hydroxylation by $O(^3P)$ atoms proceeds via an ionic mechanism, involving a dipolar transient[3c]. Since this mechanism, and that of biological oxidations proceeding via arene oxide are similar[4], it has been proposed that $O(^3P)$ oxidation can be regarded as a model for these biological oxidations[3c].

We have found that oxidation of aromatic compounds in the liquid phase leads to a mixture of phenols[2] which differ in their compositions from the products obtained on rearrangement of arene oxides derived from the same aromatic compounds[5]. This is exemplified by $O(^3P)$ oxidation of ortho-xylene (**1**), leading to 2,3-, 3,4-, 2,6-xylenol (**2**), (**3**), (**4**) and ortho cresol (**5**) formed in 23, 13, 2 and 62 ratios[2] (Scheme I). Thus the attack of $O(^3P)$ atom results both in substitution of the aromatic ring and in replacement of methyl groups by OH, while the

Scheme I



product of methyl shift is formed only in traces. On the other hand, decomposition of the epoxide (**6**) derived from ortho-xylene[5c] (**1**) leading to a dipolar transient having a tertiary oxygen substituent, results in a high yield of the methyl shift product 2,6-xylenol (**4**), while ortho-cresol (**5**), the product of methyl cleavage, is not formed.

These differences can be explained by assuming that the O(^{3}P) oxidation is a free radical reaction, proceeding via a triplet diradical intermediate[6], and not by an ionic mechanism involving a dipolar transient. The negligible amounts of products derived from 1,2-alkyl shift in the aromatic oxidation[2] are in keeping with the oxidations of olefins, in which 1,2-alkyl shifts were observed only to a very small extent[1].

The compartively low negative value of ρ^+ (-1.4) found by us for the attack of O(^{3}P) at different positions of the substituted aromatic ring and that reported for the analogous reactions in the gas phase (ρ^+-1.3)[7] are consistent with the intermediacy of the triplet diradicals. It is of interest to note that a ρ^+-value of -7.3[8] was reported for the decomposition of arene oxides leading to phenols, which occurs by an ionic mechanism.

We have investigated the mechanism of the O(^{3}P) aromatic oxidation using specifically deuterated anisoles and toluenes, and oxygen atoms produced by microwave discharge of O_2[9].

Oxidation of anisole-4-d$_1$ (**7**)[10] and anisole-3,5-d$_2$ (**8**)[11] were performed at 0°C and -35°. The deuterium contents of the resulting ortho, meta and para hydroxy-anisoles, formed in 66:1:18 ratios, were analyzed by GC-MS (Table I)[12]. Comparison with the corresponding ratio of ortho and para hydroxy-anisoles formed from the non deuterated compound (65:19)[2] reveals

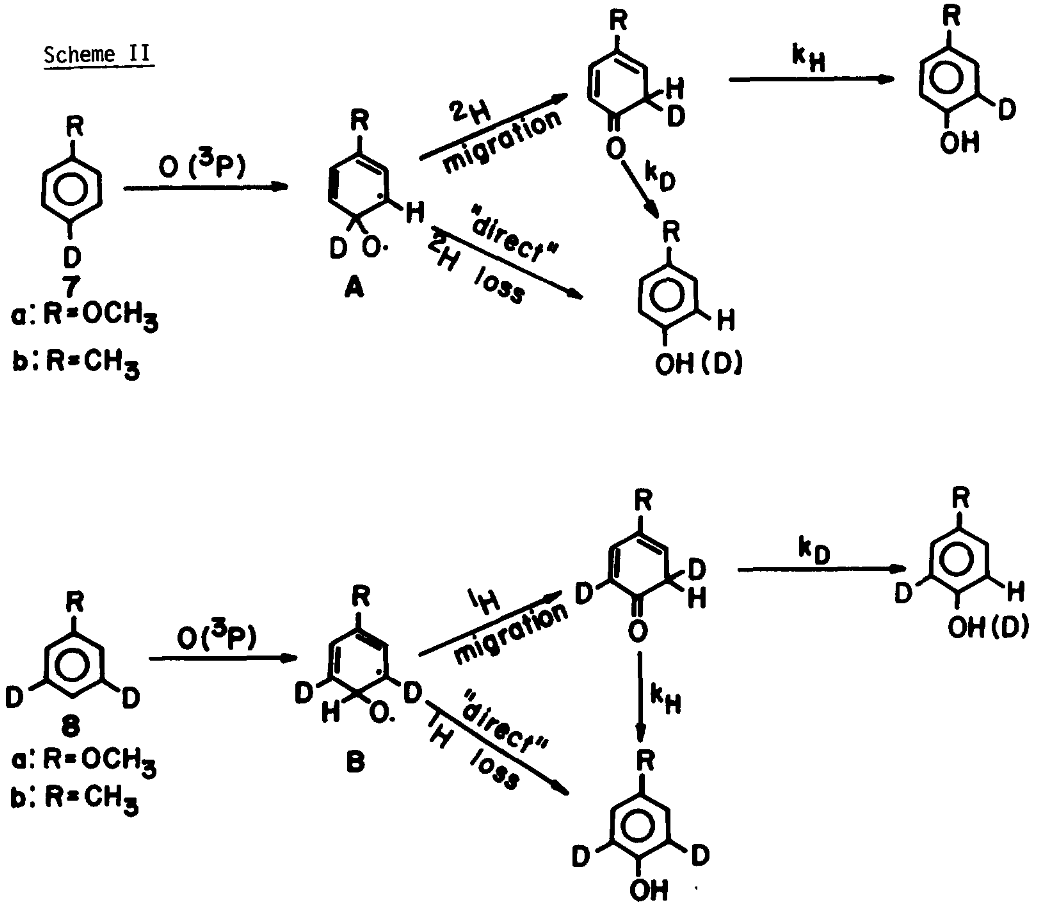
Table 1. Reactions with O(^{3}P) of Anisole-4-d$_1$ (**7a**), Anisole-3,5-d$_2$ (**8a**), Toluene-4-d$_1$ (**7b**) and Toluene-3,5-d$_2$ (**8b**).

Substrate	Temp. (°C)	Deuterium Retention (%)		Migration(%)[a] of ^{2}H or ^{1}H (NIH shift)	Direct loss[a] of ^{2}H or ^{1}H	Isotope effect[a] (k_H/k_D)
		ortho hydroxy-anisole	para hydroxy-anisole			
7a	0	100	35	52	48	2.1
8a		98	83			
7a	-35	100	50	69	31	2.6
8a		94	81			
		ortho cresol	para cresol			
7b	-78	100	69	95	5	3.0
8b		87	76			

[a] These data were derived from the values of deuterium retentions of the p-hydroxy-anisoles and p-cresols.

a small primary kinetic isotope effect of 1.1, similar to that found for the reaction in the gas phase[7]. Thus, the rate determining step in O(^{3}P) oxidations does not involve cleavage of C-H bonds, but the addition of O(^{3}P) to the aromatic double bond, consistent with the formation of a triplet diradical. The partial loss of the deuterium label in the para-hydroxy-anisole formed from dideuterated compound and the different deuterium retention values in the two para-hydroxylated anisoles formed from mono- and di-deuterated compounds respectively, point to two independent pathways for the collapse of the diradicals A and B (Scheme II), as already suggested for the reactions induced by γ-radiolysis of liquid CO_2 solutions[6]. One reaction pathway proceeds by 1,2-H migration leading to similar dienones from both deuterated

Scheme II



anisoles (NIH shift route - Scheme II). The alternative route, which involves loss of H at the position of hydroxylation, should lead to complete retention of ^{2}H in para-hydroxy-anisole-3,5-d$_2$ **(8a)** and to its total loss in para-hydroxy-anisole-4-d$_1$ **(7a)**. Using the data from Table I we have calculated the kinetic isotope effect associated with the enolization of the dienone intermediates. The magnitude of the isotope effect was found to increase with temperature decrease as has already been shown in analogous dienone-phenol rearrangements[13]. The ^{2}H retention values in para-hydroxy anisole (Table I) allow calculations of the partial contribution of the pathway involving H migration (NIH shift route) and H-loss.

It can be seen from these data that the relative contribution of the pathway involving H migration increases with lowered temperature. The same trend may be seen in both ortho, and meta-hydroxylated anisoles[14]. Utilization of toluene-4-d$_1$ **(7b)**[15] and toluene-3,5-d$_2$ **(8b)**[16] enabled us to increase the temperature range of O(^{3}P) oxidations to -78°. The relevant data (Table I) point to a high predominance (95%) of the dienone-phenol rearrangement at this temperature.

These results are also in accord with the intermediacy of a triplet diradical whose life time and decomposition mode are expected to be temperature dependent, possibly because of changes in the solvent viscosity.

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9. The technique used was described previously (see ref. 1).
10. Deuterium content: d$_1$-92%, d$_0$-8%.
11. Prepared in analogy to A.P. West and C.I. Wilson, J. Chem. Soc., 239 (1946); deuterium content: d$_3$-4%; d$_2$-92%, d$_1$-4%, d$_0$-negligible.
12. Using 6 m 1/8" 5% Carbowax on chromosorb W 80-100 mesh column at 180°C.
13. D.M. Jerina, D.R. Boyd and J.W. Daly, Tetrahedron Letters, 457 (1970).
14. Assuming the same kinetic isotope effect for the enolization of 2-methoxy- and 4-methoxy-cyclohexadienones, the calculated % of ^{1}H-shift in ortho-hydroxyanisole derived from anisole-3,5-d$_2$ was 6% at 0° and 22% at -35°. The ^{2}H-retention in meta-hydroxy anisole derived from anisole-3,5-d$_2$ was 40% at 0° and 46% at -35°.
15. Deuterium content: d$_1$-91%, d$_0$-9%.
16. Preparation: see ref. 11; Deuterium content: d$_2$-92%, d$_1$-8%, d$_0$-negligible; Separation of cresols was performed on 3m 1/8" 5% SE-30 and 15% Bentone-34 on Chromosorb W 80-100 mesh at 180°C.

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