

# Reactions of Di-, Tri-, and Hexamethylbenzenes with O(<sup>3</sup>P) Atoms in Liquid and on Adsorbed Phases

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**Abstract:** Oxidation of di- and trimethylbenzenes with O(<sup>3</sup>P) atoms produced by microwave discharge of CO<sub>2</sub> results in attack of the O(<sup>3</sup>P) atoms at C-H and ipso positions. At relatively higher temperatures, the ipso attack leads mainly to phenols derived from CH<sub>3</sub> cleavage, while at lower temperatures and on silica gel it leads to phenols derived from CH<sub>3</sub> migration and to cyclohexadienone derivatives. It is suggested that the former reaction occurs by decomposition of a diradical formed on O(<sup>3</sup>P) atom addition to the aromatic ring, but the latter occurs through the intermediacy of a dipolar transient. A similar oxidation of hexamethylbenzene adsorbed on silica gel results in hexamethylcyclohexadienone and its diepoxide derivatives, the latter formed through participation of <sup>1</sup>O<sub>2</sub> present in the discharged gases.

Oxygen atoms in their ground state react with methylbenzenes in the gas phase to give phenols derived both from C-H and ipso attack, the latter leading to the cleavage of methyl groups.<sup>1,2</sup> The relatively high yield of ortho substitution in these reactions is in accord with the electrophilic character of the oxygen atom as well as its low steric requirements.<sup>2</sup> It was suggested that gas-phase reactions of the O(<sup>3</sup>P) atom occur via a radical mechanism, the rate-determining step being the addition of O(<sup>3</sup>P) atom to the aromatic double bond, forming a triplet diradical which collapses to give a phenol derivative.<sup>2</sup>

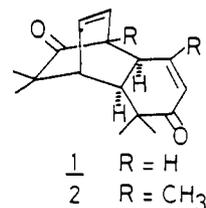
We have recently reported on reactions of O(<sup>3</sup>P) atoms, produced by microwave discharge of O<sub>2</sub> molecules, with aromatic compounds in the liquid phase.<sup>3</sup> We have shown that the distribution of phenolic products and relative rates of their formation as well as the low value of the primary kinetic isotope effect were comparable to those found for gas-phase reactions, pointing to similar reaction mechanisms in both phases.<sup>3</sup>

## Results

We report here on oxidations of dimethylbenzenes, trimethylbenzenes, and hexamethylbenzene, using microwave discharge of a mixture of He and CO<sub>2</sub> as a source of O(<sup>3</sup>P) atoms.<sup>5</sup> The oxidations of di- and trimethylbenzenes were performed in a flow system at 2 torr on neat liquids,<sup>6</sup> on substrates in solution at variable temperatures, and on substrates preadsorbed on silica gel (Merck 60, 70-200 mesh).<sup>7</sup> When the oxidations lasted for ca. 1-2 h, the conversions varied from 35% to 50%. Most of the converted material consisted of monooxygenated products: the rest included polyhydroxylated and polymeric products. In order to minimize over oxidations and to avoid loss of substrates in the low-pressure flow system, the reactions were conducted for 10 min only, whereby the conversions were lowered (ca. 5%) and most of the consumed material could be accounted for.

*o*-Xylene was reacted at variable temperatures in 10% hexane solution and adsorbed on silica gel (Table I). Total reaction mixture analysis by GC-MS revealed four phenolic and two neutral products: *o*-tolualdehyde (<3% realtive yield) and 2,2-dimethylcyclohexa-3,5-dienone. GC-MS analysis of reactions conducted with 1,2,3-trimethylbenzene, under similar conditions,

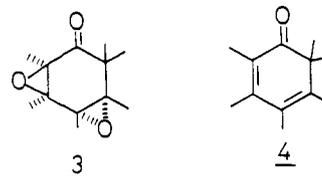
resulted in five methylated phenols, 2,2,6-trimethylcyclohexadienone, and traces (<3%) of another trimethylcyclohexadienone and a dimethylbenzaldehyde (Table I). Column chromatography of the neutral fractions of both reactions gave the corresponding dimers of 2,2-dimethylcyclohexadienone and of 2,2,6-trimethylcyclohexadienone, **1** and **2**. The structure and



stereochemistry of **2**, proposed previously<sup>8</sup> on the basis of its dipole moment, was confirmed by X-ray analysis<sup>9</sup> (Figure 1). It is conceivable that cyclohexadienone derivatives are primary reaction products, dimerizing spontaneously to **1** and **2**, which, in turn, decompose in GC to the respective monomers.<sup>10</sup> The main products of *p*-xylene, *m*-xylene, and mesitylene oxidations, performed under the above conditions, were methylated phenols (Table II).

Solvent effects (polarity and viscosity) were investigated by oxidation of *o*-xylene in different solvents at variable temperatures (Table I). The resulting product distributions did not differ significantly from those observed in 10% hexane solution.

Oxidations of hexamethylbenzene, a solid of low solubility, were performed only on silica gel or on Florisil (Floridin, 100-200 mesh).<sup>10</sup> The major product isolated after 2-h reaction on Florisil was keto diepoxide **3** (50%), the rest consisting mainly of the starting material. On silica gel, however, hexamethylbenzene



gave dienone **4** (25%), in addition to **3** (25%). The structure of

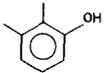
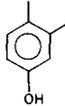
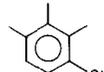
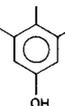
(1) Boocock, G.; Cvetanović, R. J. *Can. J. Chem.* **1961**, *39*, 2436.  
 (2) Grovenstein, E.; Mosher, A. J. *J. Am. Chem. Soc.* **1970**, *92*, 3310.  
 (3) Zadok, E.; Sialom, B.; Mazur, Y. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 1004.  
 (4) Zadok, E.; Mazur, Y. *Tetrahedron Lett.* **1980**, *21*, 4955.  
 (5) Capezuto, P.; Cramarossa, F.; d'Agostino, R.; Molinari, E. *J. Phys. Chem.* **1976**, *80*, 882. Wiegand, W. L. *Appl. Phys. Lett.* **1973**, *22*, 583.  
 (6) Zadok, E.; Amar, D.; Mazur, Y. *J. Am. Chem. Soc.* **1980**, *102*, 6369.  
 (7) Zadok, E.; Aronovitch, C.; Mazur, Y. *Nouv. J. Chim.* **1982**, *6*, 699.  
 Zadok, E.; Rubinraut, S.; Mazur, Y. *Isr. J. Chem.* **1983**, *Isr.* 457.

(8) Brown, T. L.; Curtin, D. Y.; Fraser, R. R. *J. Am. Chem. Soc.* **1958**, *80*, 4339. Cf.: Otieno, D. A.; Pattenden, G. Popplestone, C. R. *J. Chem. Soc., Perkin Trans. 1* **1976**, 196.

(9) The X-ray diffraction pattern of **2** resembles that of other cyclohexadienone dimers. Cf.: Alder, E.; Brasen, S.; Miyake, H. *Acta Chem. Scand.* **1971**, *25*, 2055. Karlsson, B.; Pilotti, A. M.; Wiehager, A. C. *Ibid.* **1973**, *27*, 2945, 2955. Alder, E.; Holmberg, K. *Ibid.* **1974**, *28B*, 465, 549.

(10) Berge, J. M.; Rey, M.; Dreiding, A. S. *Helv. Chim. Acta.* **1982**, *65*, 2230.

Table I. O(<sup>3</sup>P) Oxidation of *o*-Xylene and 1,2,3-Trimethylbenzene<sup>a</sup>

substrate	temp, <sup>b</sup> °C	conditions <sup>b</sup>	distribution of products (%) derived from					ipso subst., %	ratios of CH <sub>3</sub> cleavage vs. CH <sub>3</sub> shift
			C-H substitution		CH <sub>3</sub> cleavage		CH <sub>3</sub> shift		
									
	-10	hexane	33	25	38	3	1	42	9.5
		neat	30	26	41	3	c		
		<i>n</i> -decane	32	28	35	5	c		
		paraffin	29	30	38	3	c		
		<i>n</i> -butyl alcohol	27	28	38	7	c		
	-25	hexane	40	31	20	6	3	29	2.2
		neat	36	38	20	6	c		
		<i>n</i> -decane	38	38	17	6	c		
		<i>n</i> -butyl alcohol	37	36	20	7	c		
	-50	hexane	42	32	7	14	5	26	0.4
		<i>n</i> -butyl alcohol	41	39	6	14	c		
	-78	hexane	44	33	4	12	7	23	0.2
	-25	SiO <sub>2</sub>	40	34	1	15	10	26	<0.1
									
	-10	hexane	47	4	27	7	7	49	2.3
	-25	hexane	53	7	17	3	15	41	1.0
	-60	hexane	56	10	8	1	20	34	0.4
	-25	SiO <sub>2</sub>	58	6	8	1	23	35	0.3

<sup>a</sup> Relative yields determined by GC. <sup>b</sup> Reactions performed for 10 min in 10% solutions, neat liquids or 2% w/w on silica gel. <sup>c</sup> Not determined.

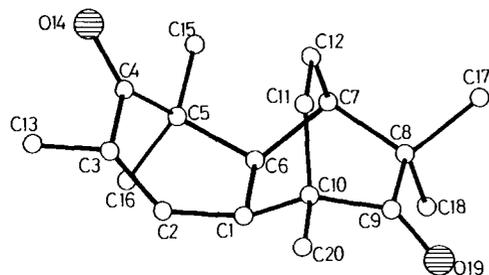


Figure 1. Molecular structure of dimer 2.

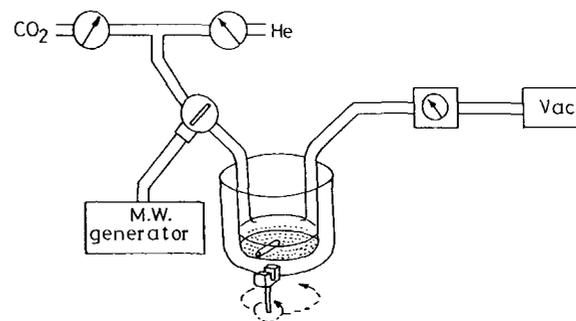
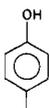
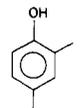


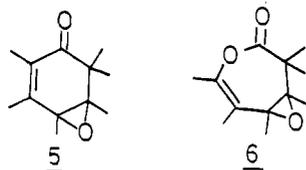
Figure 2. Schematic representation of experimental setup for reactions in adsorbed phases.

Table II. O(<sup>3</sup>P) Oxidation of *p*-Xylene, *m*-Xylene, and Mesitylene<sup>a</sup>

substrate	temp, <sup>b</sup> °C	conditions <sup>b</sup>	distribution of products (%) derived from		
			C-H subst.	CH <sub>3</sub> cleavage	CH <sub>3</sub> shift
	-25	hexane			
	-25	SiO <sub>2</sub>	86	10	4
			85	1	14
	-10	neat			
	-25	neat			
	-60	hexane	41	9	11
	-25	SiO <sub>2</sub>	44	8	6
			39	4	<0.5
			40	3	<0.5
	-10	neat			
	-25	neat	72	28	<0.1
	-25	SiO <sub>2</sub>	90	10	<0.1
			97	2	1

<sup>a</sup> Relative yields determined by GC. <sup>b</sup> Reactions performed for 10 min in 10% solution, neat liquids or 2% w/w on silica gel.

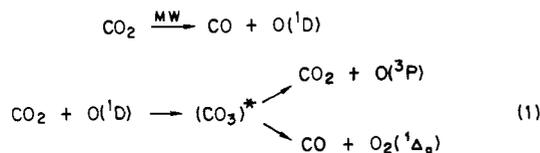
**3** was established by comparison with a product prepared by oxidation of keto epoxide **5**<sup>11</sup> with 1 equiv of *m*-chloroperbenzoic acid in the presence of NaHCO<sub>3</sub>.<sup>12</sup> **3** was also obtained, in low



yield, from **4**,<sup>13</sup> by using 2.5 mol equiv of this reagent, the major products being **5** and epoxy lactone **6**. <sup>1</sup>H NMR of **3**, which shows methyl signals at a relatively low field (1.25 ppm) but lacks a methyl signal at a higher field (expected for *cis*-diepoxide),<sup>14</sup> points to both epoxy groups being *trans* to each other.<sup>15</sup>

### Discussion

Microwave discharge of CO<sub>2</sub> produces O(<sup>3</sup>P) atoms accompanied by O<sub>2</sub> (<sup>1</sup>Δ<sub>g</sub>) (eq 1), similar to the discharge of O<sub>2</sub>.<sup>5</sup> However, the advantage of CO<sub>2</sub> discharge is the absence of ground-state O<sub>2</sub>, which otherwise might participate in the reac-



tions. The comparatively large amounts of substituted benzyl alcohols and benzaldehydes previously reported by us<sup>3</sup> are attributed to the presence of ground-state O<sub>2</sub>.

Product distribution and positional selectivity in the oxygenations of di- and trimethylbenzenes showed considerable temper-

ature dependence. At higher temperatures, the amounts of products formed by an ipso attack were larger than those formed at lower temperatures or on silica gel (Tables I and II). However, the largest differences were recorded in the ratios of products derived from CH<sub>3</sub> cleavage vs. CH<sub>3</sub> migration. At -10 °C, these ratios favored the demethylated phenols. At lower temperatures, the amounts of rearranged products became considerably larger than those of demethylated products. Product distributions from oxidations performed on silica gel were almost identical with those obtained in the liquid phase at -60 °C or at -78 °C.

Ipsos attacks, followed by either CH<sub>3</sub> cleavage or CH<sub>3</sub> migration, are well-established routes for hydroxylation by cationic reagents (i.e., trifluoroperacetic acid,<sup>16</sup> *tert*-butyl hydroperoxide,<sup>17</sup> and bis(trimethylsilyl) peroxide<sup>18</sup> in the presence of Lewis acids or by radical reagents (Fenton reagent),<sup>18,19</sup> respectively. An aryl radical and arenium cation were postulated to be intermediates in these reactions.<sup>18</sup>

Our results indicate that the reaction of O(<sup>3</sup>P) atoms with aromatic compounds also proceeds by either radical or ionic mechanisms. At relatively high temperatures, the oxygenations occur by a free radical mechanism involving the intermediacy of a triplet diradical, as previously suggested.<sup>1,2,4</sup> O(<sup>3</sup>P) atom attack on the unsubstituted position leads to a triplet diradical which may rearomatize either by 1,2-H migration (NIH shift) through the intermediacy of a cyclohexadienone derivative or by direct loss of a hydrogen atom (eq 2). However, it is reasonable to assume that the corresponding diradical formed by O(<sup>3</sup>P) attack on an ipso position (A, Scheme I) does not undergo 1,2-methyl migration but loses CH<sub>3</sub>, leading to a phenoxy radical.<sup>20</sup> At lower temperatures, however, the reaction pathway changes, proceeding

(16) Hart, H. *Acc. Chem. Res.* **1971**, *4*, 337.

(17) Hashimoto, S.; Koike, W. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 293.

(18) Apatu, J. O.; Chapman, D. C.; Heaney, H. *J. Chem. Soc., Chem. Commun.* **1981**, 1079.

(19) Davidson, A. J.; Norman, R. O. C. *J. Chem. Soc.* **1964**, 5404. Jeffcoate, C. R. E.; Lindsay-Smith, J. R.; Norman, R. O. C. *J. Chem. Soc. B.* **1969**, 1013.

(20) It was shown in a crossed molecular beam study that analogous reaction of O atoms with toluene leads to a long-lived complex, probably a triplet diradical which dissociates to methyl and phenoxy radicals: cf.: Baseman, R. J.; Buss, R. J.; Cassavecchia, P.; Lee, Y. T. *J. M. Chem. Soc.* **1984**, *106*, 4108.

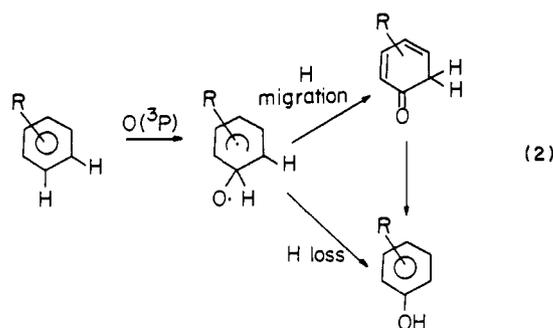
(11) Cf. Adam, W.; Cueto, O.; De Lucchi, O.; Peters, K.; Peters, E. M.; Von Schnering, H. G. *J. Am. Chem. Soc.* **1981**, *103*, 5822.

(12) Hart, H.; Collins, P. M.; Waring, A. J. *J. Am. Chem. Soc.* **1960**, *88*, 1005.

(13) Hart, H.; Huang, I.; Lavrik, P. *J. Org. Chem.* **1974**, *39*, 999.

(14) Hart, H.; Verma, M.; Wang, I. *J. Org. Chem.* **1973**, *38*, 3418.

(15) Small amounts of an isomeric product were observed in the GC-MS of reaction mixtures from both epoxidation of **4** and O(<sup>3</sup>P) oxidation of hexamethylbenzene.



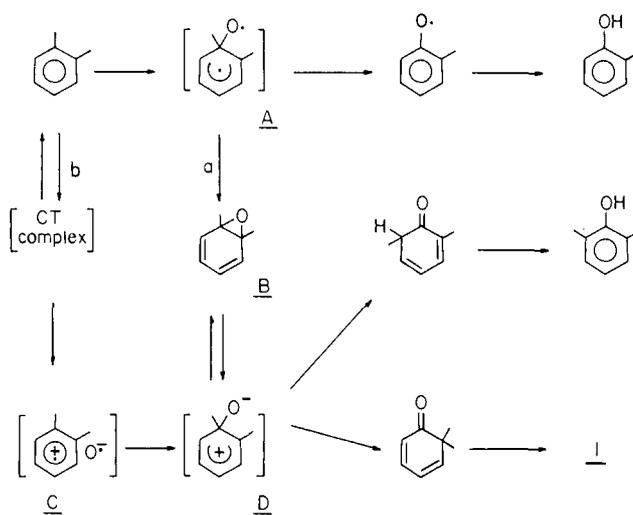
via a dipolar transient D, which undergoes NIH shift of the methyl group, resulting in a cyclohexadienone derivative. Enolizable cyclohexadienones give rise to phenols, while the nonenolizable ones are the final products of the reaction. Two pathways may be considered for the formation of this transient at low temperatures. Pathway a (Scheme I) suggests that the primary triplet diradical A formed by  $O(^3P)$  atom attack on the aromatic compound does not undergo methyl cleavage because of the relatively high energy of activation associated with this process. Instead, intersystem crossing takes place to give a singlet diradical, cyclizing to the arene oxide B, which rearranges to end products via dipolar transient D.

On the other hand, it is conceivable that the decrease in temperature may appreciably slow down the rate of  $O(^3P)$  addition to aromatic compounds.<sup>21</sup> Under these conditions, a contact charge-transfer complex between the  $O(^3P)$  atom and the aromatic compound may be formed. Electron transfer within the complex results in an ion pair C, the precursor of the dipolar transient D, which cyclizes reversibly to the arene oxide B. Charge-transfer interactions are known to exist between ground-state  $O_2$  and aromatic compounds.<sup>22</sup> These interactions are strengthened at lower temperatures or by adsorption on solid adsorbents, probably due to the closer proximity of  $O_2$  and aromatic compound.<sup>23</sup> Since  $O(^3P)$  atoms are more electrophilic than  $O_2$ ,<sup>1,2</sup> the formation of charge-transfer complexes at lower temperatures and on silica gel seems feasible. Moreover, the pronounced electrophilicity of  $O(^3P)$  atoms facilitates electron transfer to give the ion pair C. On the other hand, the fact that polarity and viscosity of solvents do not influence the product distribution (Table I) is in accord with pathway a, rather than with pathway b.

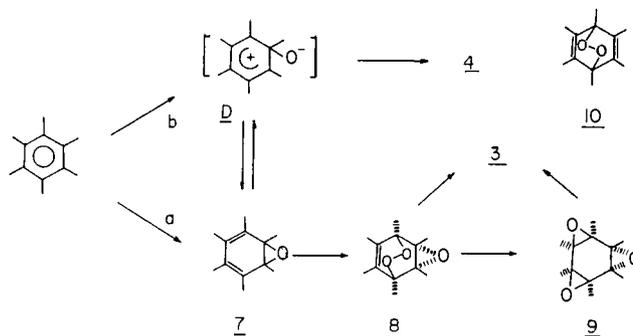
We have previously shown that the extent of the 1,2-H shift (NIH shift) in these oxidations is temperature-dependent.<sup>4</sup> Thus, it was found that by decreasing the reaction temperature from 0 to  $-35^\circ\text{C}$ , the relative amount of *p*-hydroxyanisole formed from deuterated anisoles by the NIH shift pathway increased from 52% to 69%. In the oxidations of deuterated toluenes to *p*-crescol at  $-78^\circ\text{C}$ , the contribution of this pathway reached 95%.<sup>4</sup> We have now performed similar experiments, using as substrates *tert*-butylbenzene-4-*d*<sub>1</sub> and *tert*-butylbenzene-3,5-*d*<sub>2</sub>. On the basis of deuterium retentions in the resulting *p*-hydroxy-*tert*-butylbenzenes (see Experimental Section), we have calculated the contributions of the NIH pathway to be 75%, 94%, and 97% at 0,  $-35$ , and  $-60^\circ\text{C}$ , respectively. The comparatively high values observed also at relatively higher temperatures indicate that 1,2-H migration (NIH shift) occurs not only in the dipolar transient but also in the diradical intermediate, although to a lesser extent.

Similar 1,2-H shifts, detected by deuterium migration retention, were previously observed, i.e., in some enzymatic oxidations,<sup>24</sup> in

Scheme I. Suggested Mechanism for  $O(^3P)$  Attack on Ipso Positions



Scheme II. Suggested Mechanism for the Oxidation of Hexamethylbenzene with  $O(^3P)$  and  $O(^1\Delta_g)$  Formed on  $\text{He}/\text{CO}_2$  Discharge at  $0^\circ\text{C}$



iodosylbenzene-porphyrin-mediated hydroxylations,<sup>25</sup> in aromatizations of arene oxides,<sup>26</sup> on photolysis of aromatic *N*-oxides<sup>27,28</sup> and on radiolysis of aromatic substrates in liquid  $\text{CO}_2$ .<sup>29,30</sup>

Generally, the occurrence of NIH shifts is accepted as a criterion, defining the polar nature of the intermediate in these reactions. Our results show, however, that these shifts do not define unequivocally the reaction mechanism. Polar or radical nature of the reaction pathway may be better distinguished by the results of hydroxylation at the ipso positions: formation of phenols derived from alkyl migration indicates polar intermediates, while formation of phenols derived from alkyl cleavage points to radical intermediates.<sup>18</sup>

Thus, the reported low relative yields of *o*-cresol (2–4%) formed from *o*-xylene by photooxygenation with aromatic *N*-oxides<sup>28</sup> are consistent with the polar mechanism as suggested by Jerina

(24) Jerina, D. M.; Daly, J. W.; Witkop, B. *J. Am. Chem. Soc.* **1968**, *90*, 6523. Jerina, D. M.; Daly, J. W.; Witkop, B. *Biochemistry* **1975**, *14*, 2024. Daly, J. W.; Jerina, D. M.; Witkop, B. *Arch. Biochem. Biophys.* **1968**, *128*, 517. Tomaszewski, J. E.; Jerina, D. M.; Daly, J. W. *Biochemistry* **1975**, *14*, 2024.

(25) Chang, C. K.; Ebina, F. *J. Chem. Soc., Chem. Commun.* **1981**, 778. (26) Jerina, D. M.; Kaubisch, N.; Daly, J. W. *Proc. Natl. Acad. Sci. U.S.A.* **1971**, *68*, 2545. Kasperek, G. J.; Bruice, T. C. *J. Am. Chem. Soc.* **1972**, *94*, 198. Kasperek, G. J.; Bruice, T. C. *J. Chem. Soc., Chem. Commun.* **1972**, 784. Chao, H. S.; Boyd, D. R.; Berchtold, G. A.; Jerina, D. M.; Yagi, H.; Dynak, J. *J. Org. Chem.* **1981**, *46*, 1948.

(27) Jerina, D. M.; Boyd, D. R.; Daly, J. W. *Tetrahedron Lett.* **1970**, 457. Akhtar, M. N.; Boyd, D. R.; Neill, J. D.; Jerina, D. M. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1693.

(28) Ogawa, Y.; Iwasaki, S.; Okuda, S. *Tetrahedron Lett.* **1981**, *22*, 2277, 3637.

(29) Hori, A.; Matsumoto, H.; Takamuku, S.; Sakurai, H. *J. Chem. Soc., Chem. Commun.* **1978**, 16; *Chem. Lett.* **1978**, 467.

(30) Takamuku, S.; Matsumoto, H.; Hori, A.; Sakurai, H. *J. Am. Chem. Soc.* **1980**, *102*, 1441.

(21) Activation energies for addition of the  $O(^3P)$  atom to benzene and toluene in the gas phase were reported to be in the range of ca. 3–4 kcal/mol (cf.: Atkinson, R.; Pitts, J. N., Jr. *Chem. Phys. Lett.* **1979**, *63*, 485 and references cited therein); the rates of these reactions were found to be temperature-dependent to a large extent, in contrast to the rates of  $O(^3P)$  addition to olefins.

(22) Evans, D. F. *J. Chem. Soc.* **1953**, 345. Pryor, W. A.; Patsiga, R. A. *Spectrosc. Lett.* **1969**, *2*, 61, 353. Tsubomura, H.; Mulliken, R. S. *J. Am. Chem. Soc.* **1960**, *82*, 5966.

(23) Ishida, H.; Takahashi, H.; Sato, H.; Tsubomura, H. *J. Am. Chem. Soc.* **1970**, *92*, 275.

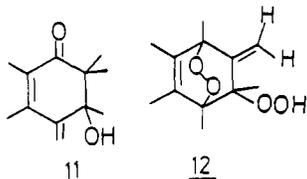
et al.<sup>27</sup> Moreover, the different product distribution pattern as compared to that reported by us makes it unlikely that this photolytic oxidation proceeds via direct interventions of "oxenes", [O(<sup>3</sup>P) atoms].<sup>28</sup> The radiolysis of methylbenzenes in liquid CO<sub>2</sub>, which was reported to involve O(<sup>3</sup>P) atoms and results in low relative yields of the demethylated phenols, or in their absence, is also in accord with intermediacy of a dipolar transient.<sup>30</sup>

The reactions of hexamethylbenzene on solid supports differ considerably from those of the other methylated benzenes. In order to explain the formation of keto diepoxide **2**, we must assume the participation not only of O(<sup>3</sup>P) atoms but also of <sup>1</sup>O<sub>2</sub> molecules.<sup>31,32</sup> The presence of <sup>1</sup>O<sub>2</sub> in the discharge gases, under our experimental conditions, is shown by isolating an endoperoxide (in 50–60%) from 9,10-dimethylanthracene adsorbed on silica gel or florisil, using Hg vapors to trap O(<sup>3</sup>P) atoms<sup>32,33</sup> (see Experimental Section).

The mechanism suggested for the formation of keto diepoxide **3** is formulated in Scheme II. The arene oxide **7** and its related dipolar transient **D** are formed by analogous pathways suggested above (Scheme I) for di- and trimethylbenzene reactions. Arene oxide **7** contains the electron-rich 1,3-cyclohexadiene system, which undergoes a facile cycloaddition with <sup>1</sup>O<sub>2</sub>, from the opposite face of the epoxide function, to give epoxyendoperoxide **8**.<sup>34</sup> Rearrangement of **8** either in one step<sup>35</sup> or through a triepoxide **9**<sup>36</sup> results in **3**. The fact that **3** is the only reaction product on Florisil but is accompanied by **4** on silica gel suggests that the slightly acidic silica gel catalyzes the opening of **7** leading to **4**.

Alternative mechanisms for the formation of **3** involving (a) intermediacy of **4** or (b) direct attack of <sup>1</sup>O<sub>2</sub> on hexamethylbenzene to give endoperoxide **10**, followed by O(<sup>3</sup>P) epoxidation, were shown to be less likely. Thus, reaction of **4** adsorbed on Florisil under the same experimental conditions led to a mixture of products (33% conversion after 3 h), including **3** (20% relative yield), hydroxyketone **11** (50%), epoxy lactone **6** (10%), and two C<sub>12</sub>H<sub>18</sub>O<sub>4</sub> compounds (20%) which were not identified.

The absence of the last four products in the reaction of hexamethylbenzene with O(<sup>3</sup>P) atoms speaks against the intermediacy of **4** in the formation of **3**. Reaction of hexamethylbenzene



adsorbed on Florisil with <sup>1</sup>O<sub>2</sub>, under the same experimental conditions, using Hg vapors as trap for O(<sup>3</sup>P) atoms, leads, after 5 h, only to traces of the hydroperoxide **12**,<sup>37</sup> indicating that direct addition of <sup>1</sup>O<sub>2</sub> to hexamethylbenzene in the presence of O(<sup>3</sup>P) atoms is also unlikely.

## Experimental Section

Infrared spectra were recorded on a Nicolet MX-1 spectrophotometer, <sup>1</sup>H NMR on a Varian FT-80A (80 MHz), and MS spectra on Finnigan GC-MS 4000 spectrometer. GC measurements were performed on a Varian Aerograph Series 1400 instrument, equipped with a flame ionization detector. GC analysis was carried out on 5% SE 30 + 15% Bentone 34 on Chromosorb W 80–100-mesh column (3 m). GC-MS

separations were performed on a SE-54 capillary column (0.25- $\mu$ m film thickness, 30 m, id 0.24 mm).

Microwave discharge reactions were performed on neat liquids,<sup>6</sup> in 10% solutions (2-mL total volume) or on substrates (0.25 g) preadsorbed from CH<sub>2</sub>Cl<sub>2</sub> on silica gel<sup>7</sup> (Merck 60, 70–100 mesh, 25 mL). Microwaves were generated by using a Kiva MPG-4 generator (2450 MHz, 100 W) transmitted to the discharge cavity using an air-cooled antenna. The vessel for the liquid-phase reactions consisted of a quartz U-tube of 15-mm diameter, containing the magnetically stirred solution.<sup>6</sup> The discharge cavity was placed ca. 5 cm above the level of the solution. The vessel for the adsorbed-phase reactions consisted of an 8 cm diameter closed Petri dish, 15-mm height, connected to a 15 mm diameter quartz inlet tube in which the discharged gases were passed (Figure 2). The solid support containing the substrate was magnetically stirred by using a specially designed rotating and revolving magnet (Figure 2). The outlets of reaction vessels were connected via a diaphragm manometer and a liquid nitrogen trap to the vacuum pump. The mixture of gases submitted to the discharge consisted of CO<sub>2</sub> and He (5:95) at a total flow rate of 0.6 L/min and a total pressure of 2 torr. All reactions were performed in a thermostatic bath.

**Oxidation of *o*-Xylene. (a) Liquid Phase.** Reactions were performed for 10 min at variable temperatures on the neat liquid and in 10% solutions (Table I). Total reaction mixtures were analyzed by GC and GC-MS at 160 °C. All the phenolic products were identified by comparison with authentic samples.

**(b) Adsorbed Phase.** Reactions were performed at –25 °C for 10 min. After elution with ether, the total reaction mixture was analyzed as in (a). Phenolic products were extracted from ether solution with 5% NaOH. The remaining neutral fraction was separated by flash chromatography on silica gel by using 10% ether in *n*-hexane as the eluent. Two products were isolated: *o*-tolualdehyde—identified by comparison with authentic sample—and dimer **1**: IR (neat)  $\nu$  2963, 2922, 2851, 1720, 1678, 1259, 1097 cm<sup>-1</sup>; UV (ether)  $\lambda_{\max}$  236 nm ( $\epsilon$  16 000). GC-MS, *m/e* 122 (C<sub>8</sub>H<sub>10</sub>O, M<sup>+</sup> monomer, 38%), 107 (7%), 93 (12%), 79 (100%), 77 (40%), 65 (6%).

**Oxidation of 1,2,3-Trimethylbenzene. (a) Liquid Phase.** Reactions were performed as with *o*-xylene. Total reaction mixtures were analyzed by GC and GC-MS at 180 °C (Table I). The phenolic products were compared to authentic samples.

**(b) Adsorbed Phase.** Reactions and workup were as above. The neutral phase obtained after NaOH extraction of the phenolic products was chromatographed to give dimer **2**:<sup>8,10</sup> mp 108–109 °C (ether–hexane); IR (CHCl<sub>3</sub>)  $\nu$  2968, 2925, 1716, 1672, 1455, 1360, 1032, 715 cm<sup>-1</sup>; UV (ether)  $\lambda_{\max}$  236 nm, ( $\epsilon$  16 500); <sup>1</sup>H NMR (CDCl<sub>3</sub>, TMS)  $\delta$  6.27 (2 H, m), 5.45 (1 H, dm, *J* = 6.8 Hz), 2.57 (3 H, m), 1.74 (3 H, brs), 1.26 (3 H, s), 1.11 (9 H, brs), 1.00 (3 H, s); GC-MS, *m/e* 136 (C<sub>9</sub>H<sub>12</sub>O, M<sup>+</sup> monomer, 48%); 121 (M<sup>+</sup> – CH<sub>3</sub>, 17%), 105 (21%), 93 (100%), 91 (52%), 77 (56%), 65 (19%).

**Oxidation of *p*-Xylene, *m*-Xylene, and Mesitylene.** Oxidations were performed in the liquid phase and on silica gel as above. Phenols were extracted and analyzed by GC and GC-MS (Table II) at 160–180 °C. 2,5-Xylenol and *p*-cresol were separated by GC-MS.

**Oxidations of Deuterated *tert*-Butylbenzenes. (a) *tert*-Butylbenzene-4-*d*<sub>1</sub>** was prepared from 4-bromo-*tert*-butylbenzene which was converted to a Grignard reagent and then quenched by D<sub>2</sub>O. The deuterium content (88% *d*<sub>1</sub>) was determined from the ratios of peaks at *m/e* 135 and 134 in the mass spectrum.

**(b) *tert*-Butylbenzene-3,5-*d*<sub>2</sub>** was prepared from 4-amino-*tert*-butylbenzene according to the procedure for the preparation of toluene-3,5-*d*<sub>2</sub>.<sup>38</sup> The deuterium content (97% *d*<sub>2</sub>, 3% *d*<sub>1</sub>) was determined from the ratios of peaks at *m/e* 136 and 135 in the mass spectrum.

**(c) Reactions with O(<sup>3</sup>P).** The deuterated compounds (0.8 g, 6 mmol) were reacted with O(<sup>3</sup>P) for 30 min (0 °C), 60 min (–30 °C), and 90 min (–60 °C). Total reaction mixtures were acetylated with acetyl chloride and trimethylamine. The resulting 4-hydroxy-*tert*-butylbenzene acetates were separated from the other isomers and analyzed by GC-MS at 140 °C by using a 3-m column containing 5% FFAP on Chromosorb G, 100–120 mesh, and their deuterium content was determined according to M<sup>+</sup> – 42 and M<sup>+</sup> – 57 peaks. Each analysis was conducted twice, and the results differed by less than 2%. 4-Hydroxy-*tert*-butylbenzene acetate derived from *tert*-butylbenzene-4-*d*<sub>1</sub> showed 61%, 80%, and 85% deuterium retention at 0, –30, and –60 °C, respectively, while the same compound derived from *tert*-butylbenzene-3,5-*d*<sub>2</sub> showed 86%, 86% and 88% deuterium retention at the same respective temperatures.

The fraction of the product formed via the NIH shift, *f*, and the isotope effect for the aromatization of the dienone intermediate,<sup>4</sup>  $\alpha = k_H/k_D$ , were calculated by using the following equations:  $X = f\alpha/(1$

(31) Bader, L. W.; Ogryzlo, E. A. *Faraday Discuss. Chem. Soc.* **1964**, 37, 46.

(32) Gollnick, V.; Schade, G. *Tetrahedron Lett.* **1973**, 857.

(33) Gleason, W. S.; Broadbent, A. D.; Whittle, E.; Pitts, J. N., Jr. *J. Am. Chem. Soc.* **1970**, 92, 2068.

(34) Vogel, E.; Altenbach, H. J.; Sommerfeld, C. D. *Angew. Chem.* **1972**, 84, 986. Foster, C. H.; Berchtold, G. A. *J. Org. Chem.* **1975**, 40, 3743.

(35) Schulte-Elte, K. H.; Willhalm, B.; Ohloff, G. *Angew. Chem.* **1969**, 81, 1045. Turner, J. A.; Herz, W. *J. Org. Chem.* **1977**, 42, 1895. Maheshwari, K. K.; De Mayo, P.; Wiegand, D. *Canad. J. Chem.* **1970**, 48, 3265.

(36) Cf.: Foote, C. S.; Mazur, S.; Burus, P. A.; Lerdal, D. *J. Am. Chem. Soc.* **1973**, 95, 856. Easton, N. R.; Anet, F. A. L.; Burns, P. A.; Foote, C. S. *Ibid.* **1974**, 96, 3945. Boyd, J. D.; Foote, C. S.; Imagawa, D. K. *Ibid.* **1980**, 102, 3641.

(37) Van der Heuvel, C. J. M.; Hofland, A.; Steinberg, H.; de Boer, T. J. *Recl. Trav. Chim. Pays-Bas.* **1980**, 99, 275.

(38) Best, A. P.; Wilson, C. L. *J. Chem. Soc.* **1946**, 239. Brewster, R. Q.; Poje, J. A. *J. Am. Chem. Soc.* **1939**, 61, 2418.

$-\alpha)$  and  $Y = (1 - f) + f(\alpha/(1 - \alpha))$ , where  $X$  is the fraction of deuterated 4-hydroxy-*tert*-butylbenzene formed from *tert*-butylbenzene-4- $d_1$  and  $Y$ , the fraction of the same compound formed from *tert*-butylbenzene-3,5- $d_2$ . Substitution of  $X$  and  $Y$  with the measured deuterium retention values results in the following values:  $f = 75\%$ ,  $94\%$ , and  $97\%$  and  $\alpha = 4.3$ ,  $5.7$ , and  $7.1$  for reactions conducted at  $0$ ,  $-30$ , and  $-60$  °C, respectively.

**Oxidation of Hexamethylbenzene.** (a) On Florisil. Hexamethylbenzene (0.25 g, 1.5 mmol) adsorbed on Florisil (25 mL) was reacted by using He/CO<sub>2</sub> discharge at 0 °C for 2 h. The Florisil was washed with ether. Evaporation and flash chromatography on Merck Kieselgel 60 (230–400 mesh) under nitrogen, using 10% ether–hexane as the eluent, gave starting material (0.125 g, 0.75 mmol) and **3** (0.15 g, 0.71 mmol), as a colorless oil: <sup>1</sup>H NMR (CDCl<sub>3</sub>, TMS)  $\delta$  1.25 (s, 6 H), 1.35 (s, 3 H), 1.42 (s, 3 H), 1.55 (s, 6 H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, TMS)  $\delta$  14.00, 15.04, 15.58, 16.26, 20.87 and 23.26 (6 CH<sub>3</sub>), 47.27 (carbon bearing two methyls), 65.66, 65.93, 67.84, 70.70 (epoxides' carbons), 207.59 (CO); IR (neat)  $\nu$  2975, 2930, 1710, 1630, 1450, 1380, 1290, 1095, 1065, 850 cm<sup>-1</sup>; MS (CI),  $m/e$  211 (M<sup>+</sup> + 1, 100%); 183 (M<sup>+</sup> + 1 - CO, 25%), 151 (79%), 125 (74%). Anal. (C<sub>12</sub>H<sub>18</sub>O<sub>3</sub>) C, H. GC-MS revealed the presence of another C<sub>12</sub>H<sub>18</sub>O<sub>3</sub> compound (5%): MS (CI),  $m/e$  211, (M<sup>+</sup> + 1, 12%), 169 (10%), 151 (100%), 125 (60%).

(b) On Silica Gel. Reaction conditions and the isolation procedure are as in (a). Flash chromatography, as above, resulted in **3** (0.08 g, 0.38 mmol, 25%) and **4** (0.07 g, 0.39 mmol, 25%), identical with compound prepared according to the method described in the literature.<sup>11</sup>

**Epoxidation of Dienone 4.** (a) 2.5 mol equiv of *m*-Chloroperbenzoic Acid (mCPBA). To a solution of **4** (0.5 g, 2.80 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) at 0 °C, a solution of mCPBA (1.2 g, 7.00 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (20 mL) was added. The reaction mixture was stirred for 2 h at 0 °C and then overnight at room temperature. Workup and flash chromatography on Florisil (elution with 10% ether in hexane) afforded starting material (0.05 g, 0.28 mmol, 10%) and **5** (0.3 g, 1.5 mmol, 55%) having identical spectroscopic data with those published.<sup>12</sup> The second eluted product (0.145 g, 0.69 mmol, 25%) was identified as **6**: <sup>1</sup>H NMR (CDCl<sub>3</sub>, TMS)  $\delta$  1.03 (s, 3 H), 1.26 (s, 3 H), 1.33 (s, 3 H), 1.54 (s, 3 H), 1.80 (q,  $J = 0.9$  Hz, 3 H), 1.87 (q,  $J = 0.9$  Hz, 3 H); IR (CHCl<sub>3</sub>)  $\nu$  1735 cm<sup>-1</sup> (C=O, lactone); MS (CI),  $m/e$  211 (M<sup>+</sup> + 1, 43%), 179 (9%), 169 (M<sup>+</sup> + 1 - CO<sub>2</sub>, 45%), 166 (34%), 151 (53%), 141 (23%), 125 (28%), 123 (100%). Anal. (C<sub>12</sub>H<sub>18</sub>O<sub>3</sub>) C, H. The third eluted product (0.03 g, 0.14 mmol, 5%), **3**, was identified by comparison with the product described above.

(b) 1.1 mol equiv of mCPBA. **4** (0.5 g, 2.80 mmol) was treated with mCPBA (0.52 g, 3.00 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (20 mL) at 0 °C for 2 h and then at room temperature overnight, affording, after flash chromatography on Florisil (elution with 10% ether in hexane), **5** (0.39 g, 2 mmol, 72%) and **11** (0.065 g, 0.33 mmol, 12%), having identical spectroscopic data with those published.<sup>12</sup>

**Epoxidation of Keto Epoxide 5.** A solution of **5** (0.5 g, 2.80 mmol) and mCPBA (0.630 g, 3.65 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (30 mL) was stirred at room temperature for 3 days in the presence of solid NaHCO<sub>3</sub>.<sup>13</sup> Workup and flash chromatography on silica gel (elution with 10% ether in hexane) afforded **3** (0.44 g, 2.1 mmol, 75%), whose spectral data were identical with those obtained in the microwave discharge reaction described above. GC-MS revealed the presence of ca. 10% of another C<sub>12</sub>H<sub>18</sub>O<sub>3</sub> compound: MS (CI),  $m/e$  211, (M<sup>+</sup> + 1) 169, 151, 125.

**Oxidation of Dienone 4, Using He/CO<sub>2</sub> Discharge.** Dienone **4** (0.25 g, 1.4 mmol) prepared from hexamethylbenzene<sup>11</sup> adsorbed on Florisil (25 mL) was reacted by using He/CO<sub>2</sub> discharge at 0 °C for 3 h. After the usual workup, starting material (0.17 g, 0.94 mmol, 67%) was recovered, along with **3** (0.02 g, 0.1 mmol, 7%), epoxy lactone **6** (0.01 g, 0.05 mmol, 3%), hydroxyketone **11** (0.045 g, 0.23 mmol, 17%), and two unidentified C<sub>12</sub>H<sub>18</sub>O<sub>4</sub> compounds [MS (CI),  $m/e$  227 (M<sup>+</sup> + 1)] (0.02 g, 0.08 mmol, 6%).

**Oxidation of 9,10-Dimethylantracene with <sup>1</sup>O<sub>2</sub> Produced by Microwave Discharge.** The apparatus described above for microwave discharge

reactions was modified by adding a mercury saturator prior to the entrance of the He/CO<sub>2</sub> mixture to the discharge cavity.<sup>32,33</sup> The discharge zone was connected to the reaction vessel by an elongated horizontal quartz tube (15-mm diameter, 0.5-m length). O(<sup>3</sup>P) atoms formed in the discharge zone reacted with Hg vapors, producing mercuric oxide which deposited on the walls of the quartz tube. 9,10-Dimethylantracene (0.25 g, 1.2 mmol) adsorbed on silica gel (25 mL) was reacted with <sup>1</sup>O<sub>2</sub> by using He/O<sub>2</sub> discharge at -78 °C for 3.5 h. Chromatography (10% ether in hexane) of the reaction mixture eluted with CH<sub>2</sub>Cl<sub>2</sub> afforded 9,10-dimethylantracene endoperoxide (0.145 g, 0.61 mmol, 50%), identified by comparison with an authentic sample.<sup>39</sup> The reaction was repeated by using He/CO<sub>2</sub> discharge as the source of <sup>1</sup>O<sub>2</sub> at 0 °C, resulting also in the endoperoxide (60% yield).

**Oxidation of Hexamethylbenzene with <sup>1</sup>O<sub>2</sub> Produced by Microwave Discharge.** Reaction of hexamethylbenzene (0.25 g, 1.5 mmol) adsorbed on silica gel (25 mL) was performed as above for 5 h. NMR of the total reaction mixture was that of the starting material, with traces of new signals which were attributed to **12**<sup>37</sup> [<sup>1</sup>H NMR (CDCl<sub>3</sub>, TMS)  $\delta$  1.40 (s, 3 H), 1.43 (s, 3 H), 1.56 (s, 3 H), 1.78 (brs, 3 H); 1.83 (brs, 3 H); 5.10–5.20 (m, 2 H)]. The calculated yield (according to NMR) was less than 2%.

**X-ray Crystallography.** A transparent clear crystal of good quality of **2** was optically centered on a CAD-4 diffractometer. The intensities of all reflections were measured according to  $\omega$  technique using a scan range of 1.0° and constant scan speed of 3°/min. The structure was solved by the direct phase determination. The non-hydrogen atoms were refined anisotropically. Special X-ray operations, results, and tables containing structure factors, atomic, and bond parameters are presented as supplementary material.

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**Supplementary Material Available:** Tables containing data on X-ray operations, as well as results, atom coordinates, anisotropic temperature factors, hydrogen atom coordinates, bond lengths, and bond angles for **2** (6 pages). Ordering information is given on any current masthead page.

(39) Southern, P. E.; Waters, W. A. *J. Chem. Soc.* **1960**, 4340. Rigaudy, J.; Cunong, N. K.; Rothschild, J.-F. *Tetrahedron Lett.* **1973**, 4439.