Studies on Photochemical Reactions of Air Pollutants. XIII. Formation of Nitrophenols by the Reactions of Three Toluene Oxides with Nitrogen Dioxide in Air

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Received June 3, 1994; accepted July 27, 1994

Three toluene oxides reacted with nitrogen dioxide in air to give nitrocresols. 1-Methylbenzene oxide (1) and 3-methylbenzene oxide (2) gave the same nitrocresols, including 2-methyl-6-nitrophenol (1b) and 2-methyl-4-nitrophenol (1c), while 4-methylbenzene oxide (3) gave only 4-methyl-2-nitrophenol (3b). Irradiation with a xenon lamp through a Pyrex filter (cut-off below 290 nm) did not affect the product distribution. Only 1-methylbenzene oxide (1) generated fog when it was brought into contact with nitrogen dioxide in air.

Keywords toluene oxide; nitrogen dioxide; 2-methyl-6-nitrophenol; 2-methyl-4-nitrophenol; 4-methyl-2-nitrophenol; fog

Investigations on the photochemical reactions of aromatic hydrocarbons such as benzene and toluene with nitrogen dioxide in air have shown that they undergo hydroxylation and nitration to give nitrophenols as photo-products,[1,2] which have been observed in the ambient atmosphere in both the gas and particulate phases,[3] as well as in fog water, rain water, and snow,[2a,3b,4] and have been suggested as contributors to forest decline.[4b,5] We have suggested that the epoxidation of aromatic hydrocarbons by an oxygen atom, O (^{3}P),[5] formed by the photo-dissociation of nitrogen dioxide, might result in the formation of arene oxides as intermediates leading to nitrophenols.[6] Also, we have reported that benzene oxide isomerizes to phenol under the influence of nitrogen dioxide as a Lewis acid, followed by nitration with nitrogen dioxide as a nitrating agent to give *o*-nitrophenol and *p*-nitrophenol.[7] Therefore, in this study we examined the reactions of toluene oxides [1-methylbenzene oxide (**1**), 3-methylbenzene oxide (**2**) and 4-methylbenzene oxide (**3**)] with nitrogen dioxide in air to look at the possible involvement of these oxides in the formation of nitrophenols by the photochemical reaction of toluene with nitrogen dioxide in air. We also examined whether or not fog is produced when toluene oxides are brought into contact with nitrogen dioxide in air.

Experimental

Materials 1-Methylbenzene oxide (**1**) and 4-methylbenzene oxide (**3**) were prepared from 1,4-dihydrotoluene according to the methods of Vogel *et al.*[8] and Jerina *et al.*,[9] respectively. 3-Methylbenzene oxide (**2**) was obtained by dehydrobromination of the dibromo oxide prepared from the Diels–Alder adduct of 1,3-pentadiene and 1,2-dibromoethylene according to the method of the authors.[10] 2-Methyl-6-nitrophenol (**1b**) and 2-methyl-4-nitrophenol (**1c**) were synthesized through the nitration of *o*-cresol (**1a**) according to the method of Gibson.[11] Other nitrophenols and chemicals used in the experiments were supplied by Aldrich Chemical Co., Ltd., Tokyo Kasei Chemical Co., Ltd. and Wako Chemical Co., Ltd., and were purified before use, if necessary. Nitrophenols were treated with ethereal diazomethane[12] to convert them into nitroanisoles prior to their determination, since nitrophenols in which the nitro group is situated in the *p*-position to the hydroxyl group of a cresol are not volatile. Nitrogen monoxide was prepared from the reaction of sodium nitrite with iron(II) sulfate in aqueous sulfuric acid, and dried through a column packed with potassium hydroxide.

Dark Reactions and Photochemical Reactions of Toluene Oxides with Nitrogen Dioxide in Air Five μl of a toluene oxide [1-methylbenzene oxide (**1**), 3-methylbenzene oxide (**2**) or 4-methylbenzene oxide (**3**)] was taken in a 1 l Pyrex reaction vessel filled with air, and allowed to stand for 5 min to vaporize, then 1 ml of nitrogen monoxide was injected into the vessel.[13] The mixture was allowed to stand for 1 h in the dark or irradiated for 1 h at 25—30 °C with a xenon lamp (ozoneless type, Ushio Co., Ltd.).

After standing or irradiation, the reaction mixture was dissolved in 30 ml of methanol, followed by concentration to 10 ml under reduced pressure. Aliquots (6 μl) of this solution were used for the analysis of cresols by the GLC method and the GLC-MS method. The residual solution was treated with ethereal diazomethane at room temperature overnight. The resulting solution was concentrated to 5 ml under reduced pressure and used for the analysis of nitroanisoles by the GLC method, the GLC-MS method and the HPLC method.

Photodecomposition of Nitrophenols in Air One ml of a solution of 2-methyl-6-nitrophenol (**1b**) or 2-methyl-4-nitrophenol (**1c**) in acetonitrile (each 44.6 μmol/ml = 1000 μl gas/ml) was taken in a 1 l Pyrex reaction vessel, and acetonitrile vapor was replaced with air. The nitrophenols (**1b** and **1c**) were deposited in the vessel. The mixture was irradiated at 25—30 °C for 5 h as mentioned above.

After irradiation, the reaction mixture was dissolved in 30 ml of methanol, followed by concentration to 10 ml under reduced pressure and by treatment with ethereal diazomethane at room temperature overnight. The resulting solution was treated as mentioned above and used for the analysis of nitroanisoles by the GLC method.

Analytical Equipment Gas liquid chromatography (GLC) was carried out with a Shimadzu 9A gas chromatograph equipped with a flame ionization detector. A coiled glass column (1.1 m × 3 mm i.d.) packed with 1.5% Silicone SE-30 on Chromosorb WAW-DMCS (60—80 mesh) was employed. Other conditions were the same as described in the previous paper.[2b]

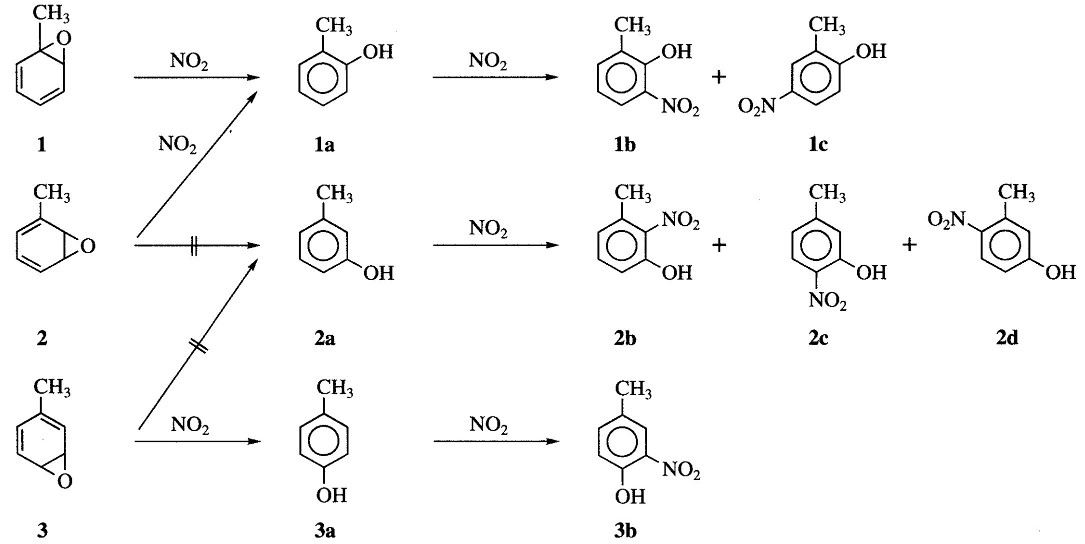
Gas liquid chromatography–mass spectrometry (GLC-MS) was done with a JEOL DX-300 spectrometer. A coiled glass column (2 m × 3 mm i.d.) packed with 1.5% Silicone SE-30 on Chromosorb WAW-DMCS (60—80 mesh) was used. Other conditions were the same as described in the previous paper.[2b]

High-performance liquid chromatography (HPLC) was carried out with a Waters LC Module I equipped with a UV (254 nm) detector and a Puresil (3.9 × 150 mm) column [the mobile phase was a mixture of methanol and water (4 : 3, v/v) at aflow rate of 1 ml/min].

Results and Discussion

Arene oxides have been postulated as key intermediates in monoxygenase-catalyzed metabolism of aromatic substrates.[14] Jerina *et al.*[9c] have reported metabolism of toluene in rat liver microsomes, affording 2-hydroxytoluene as the major product, together with 4-hydroxytoluene as a minor product. They showed that the product

TABLE I. Schemes for the Dark or Photochemical Reactions of Toluene Oxides with Nitrogen Dioxide in Air



distribution was compatible with that obtained from the acid-catalyzed rearrangement of toluene oxides consisting of 1-methylbenzene oxide (**1**), 3-methylbenzene oxide (**2**) and 4-methylbenzene oxide (**3**).

It is well known that nitrogen dioxide dissociates photochemically into an oxygen atom, $O(^3P)$ and nitrogen monoxide.[5] Nitrogen dioxide under the influence of sunlight is therefore considered to be an oxidizer of aromatic substrates, like monoxygenase. We have noted that nitrogen dioxide can photochemically epoxidize not only olefinic compounds such as cyclohexene, *trans*-stilbene, *cis*-stilbene and aldrin, but also aromatic hydrocarbons such as benzene and phenanthrene.[6] Accordingly, toluene oxides might be intermediates in the formation of nitrophenols by the photochemical reaction of toluene with nitrogen dioxide in air. To investigate whether any nitrophenols are produced by the photochemical or dark reactions of toluene oxides with nitrogen dioxide in air, a series of nitrophenols [2-methyl-6-nitrophenol (**1b**), 2-methyl-4-nitrophenol (**1c**), 3-methyl-2-nitrophenol (**2b**), 5-methyl-2-nitrophenol (**2c**), 3-methyl-4-nitrophenol (**2d**) and 4-methyl-2-nitrophenol (**3b**)] shown in Table I were utilized as authentic substances, since it has been reported by the authors that cresols react with nitrogen dioxide in air to afford nitrophenols, the nitro group of which is always situated in the *o*-position or *p*-position to the hydroxyl group.[15] For the analysis of nitrophenols by the GLC method and the GLC-MS method, they were converted into volatile anisoles by treatment with ethereal diazomethane. The HPLC method was adopted so that 3-methyl-2-nitroanisole, 5-methyl-2-nitroanisole and 4-methyl-2-nitroanisole could be isolated individually.

Results in the dark and photochemical reactions of toluene oxides with nitrogen dioxide in air are summarized in Table II. It was found that 1-methylbenzene oxide (**1**) and 3-methylbenzene oxide (**2**) gave the same products, *o*-cresol (**1a**), 2-methyl-6-nitrophenol (**1b**) and 2-methyl-4-nitrophenol (**1c**), while 4-methylbenzene oxide (**3**) gave *p*-cresol (**3a**) and 4-methyl-2-nitrophenol (**3b**).

TABLE II. Products Obtained by the Dark or Photochemical Reactions of Toluene Oxides with Nitrogen Dioxide in Air[a]

Substrate	Products (yield)[b]	Fog
1[c] in dry air	**1a** (9.8%), **1b** (10%), **1c** (9.7%)	Not observed
1[c] in air[e]	**1a** (10%), **1b** (9.9%), **1c** (11%)	Observed
1[d] in dry air	**1a** (9.2%), **1b** (10%), **1c** (8.9%)	
1[d] in air[e]	**1a** (8.6%), **1b** (9.6%), **1c** (10%)	
2[c] in dry air	**1a** (11%), **1b** (7.3%), **1c** (7.9%)	Not observed
2[c] in air[e]	**1a** (10%), **1b** (7.8%), **1c** (8.4%)	Not observed
2[d] in dry air	**1a** (8.9%), **1b** (6.9%), **1c** (7.5%)	
2[d] in air[e]	**1a** (9.4%), **1b** (7.7%), **1c** (8.4%)	
3[c] in dry air	**3a** (9.7%), **3b** (14%)	Not observed
3[c] in air[e]	**3a** (10%), **3b** (15%)	Not observed
3[d] in dry air	**3a** (8.6%), **3b** (11%)	
3[d] in air[e]	**3a** (9.2%), **3b** (15%)	

a) Toluene oxide: 5 μl (liquid),[21] NO_2: 44.6 μmol. *b*) Yields were based on the quantity of NO_2 used. *c*) Standing for 1 h in the dark. *d*) Irradiated for 1 h. *e*) Relative humidity was in the range of about 50 to 60% during the experiments.

Irradiation did not affect the product distribution or yields, suggesting that the reactions of toluene oxides with nitrogen dioxide in air might be faster than the dissociation of nitrogen dioxide by photolysis. The moisture in air also did not affect the product distribution or yields, but did influence the production of fog when toluene oxide was brought into contact with nitrogen dioxide. Leighton has reported that the conversion of nitrogen dioxide in air to nitrous acid and nitric acid is very slow in the homogeneous gas-phase reaction.[5a] Generally, air at 25 °C contains moisture ranging in concentration from about 11500 ppm (relative humidity 40%) to 20000 ppm (relative humidity 70%).[16] Indeed, nitrogen dioxide in a Pyrex reaction vessel filled with air remained unaltered during the observation of its color change on standing for 5 h.

Thus, it seems reasonable to consider that the reactions of toluene oxides with nitrogen dioxide should be faster than the conversion of nitrogen dioxide in air to nitrous acid and nitric acid.

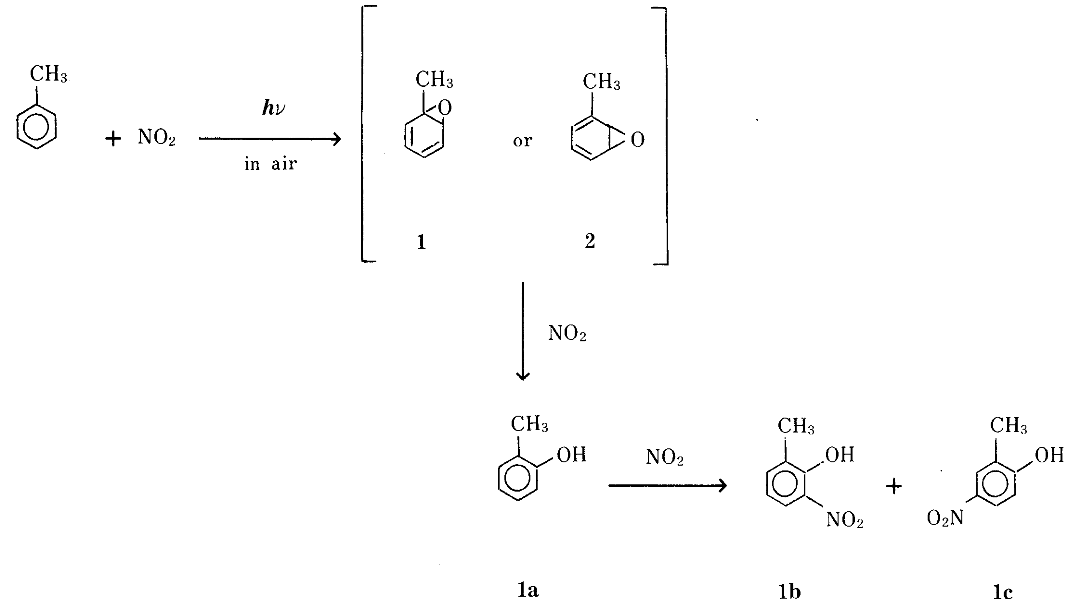


Chart 1

Of the toluene oxides, only 1-methylbenzene oxide (**1**), like benzene oxide described in the previous paper,[7)] produced fog. Therefore, 1-methylbenzene oxide (**1**) might participate in the occurrence of photochemical smog. Similar phenomena were observed when basic gases such as pyridine, *n*-propylamine and piperidine were brought into contact with nitrogen dioxide as a Lewis acid. Benzene oxide and 1-methylbenzene oxide (**1**) seem to behave like the basic gases. However, it is not clear why 3-methylbenzene oxide (**2**) and 4-methylbenzene oxide (**3**) did not produce fog.

It is generally recognized that arene oxides readily isomerize under the influence of Brönsted (proton) and Lewis acids to the corresponding phenols.[8a,9b)] In addition, Jerina *et al.*[9c,17)] have noted that the toluene oxide **3** rearranges exclusively to *p*-cresol (**3a**) in the presence of a Brönsted acid. The pathway leading to *p*-cresol (**3a**) has a slight energetic advantage arising from additional stabilization of a cationoid intermediate *via* hyperconjugation with the methyl group. This small, but apparently significant, added stabilization seems a dominant factor in controlling the opening of the arene oxides. The remaining two toluene oxides, **1** and **2**, rearrange exclusively to *o*-cresol (**1a**). Stabilization by hyperconjugation with the methyl group again causes selective opening.

As judged from the product distribution obtained by the reactions of toluene oxides with nitrogen dioxide in air, the ring opening is compatible with that in the above acid-catalyzed rearrangement. Since nitrogen dioxide is regarded as a Lewis acid according to the classification of electron donors and acceptors by Mulliken,[18)] nitrogen dioxide should be able to catalyze this isomerization. As described above, nitrogen dioxide can also act as a nitrating agent.[15,19)]

On the basis of these results and the above discussion, the reactions of toluene oxides with nitrogen dioxide in air can be explained by the processes shown in Table I. Toluene oxides, **1** and **2**, isomerize under the influence of nitrogen dioxide to *o*-cresol (**1a**), followed by nitration with nitrogen dioxide to afford 2-methyl-6-nitrophenol (**1b**) and 2-methyl-4-nitrophenol (**1c**), while toluene oxide **3** generates *p*-cresol (**3a**), followed by nitration to give only 4-methyl-2-nitrophenol (**3b**).

Table III. Photodecomposition of Nitrophenols (**1b** and **1c**) in Air[a)]

Substrate	Ratio of conversion[b)] (%)
1b	36.1 ± 1.3
1c	8.0 ± 1.6

Data reported represents the mean ± S.D. of three experiments. *a*) Nitrophenol, 44.6 μmol; irradiation time, 5 h. *b*) Ratio of conversions are [the molar amount of nitrophenol decomposed/the molar amount of nitrophenol used] × 100.

Accordingly, toluene oxides (**1** and **2**) are expected to lead to the formation of *o*-cresol (**1a**) and nitrophenols (**1b** and **1c**) observed in the smog chamber experiment using toluene and nitrogen dioxide in air.[2b)] Of the photoproducts obtained by the photochemical reaction of toluene with nitrogen dioxide in air, *o*-cresol (**1a**), 2-methyl-6-nitrophenol (**1b**) and 2-methyl-4-nitrophenol (**1c**) might be formed *via* toluene oxides, **1** and **2**, as intermediates, as shown in Chart 1. Here, the stability of 2-methyl-6-nitrophenol (**1b**) and 2-methyl-4-nitrophenol (**1c**) in air under the influence of 5 h irradiation was examined. As shown in Table III, 2-methyl-6-nitrophenol (**1b**) was more unstable than 2-methyl-4-nitrophenol (**1c**) under such conditions. This might be due to the difference of their absorption in the visible region, in other words, to the intramolecular hydrogen bonding derived from the hydroxyl group and nitro group. The fact that 2-methyl-4-nitrophenol (**1c**) was the main nitrophenol generated by the 5 h irradiation of toluene and nitrogen dioxide in air seems consistent with these results and the metabolism of toluene in rat liver, leading to *o*-cresol (**1a**) as the major product.[9c)]

On the other hand, Atkinson *et al.*[20)] have proposed that nitrophenols obtained by the photochemical reaction of toluene and nitrogen dioxide in air are formed through OH radical as an initiator. However, non-volatile nitrophenols (*i.e.*, *p*-nitrophenol type) were not determined in their experiments. The involvement of OH radical and oxygen atom O(^{3}P) as initiators for the formation of phenolic compounds leading to nitrophenols requires further study.

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