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Reaction of Benzanthrone (7*H*-Benz[*d*,*e*]anthracen-7-one) with Nitrogen Dioxide Alone or in Admixture with Ozone. Implications for the Atmospheric Formation of Genotoxic 3-Nitrobenzanthrone

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The reaction of benzanthrone (7*H*-benz[*d*,*e*]anthracen-7-one, **1**) with nitrogen dioxide alone or in admixture with ozonized oxygen has been investigated in polar and nonpolar organic solvents at different temperatures. A remarkable change of product distribution was observed depending on the solvent employed; 3-nitrobenzanthrone (**4**) was the main product from the reaction in dichloromethane, while 2-nitrobenzanthrone was obtained as the major product in tetrachloromethane. Addition of protonic acid or inorganic solid support was found to promote the reaction, favoring the formation of the former nitro compound at the expense of the latter. All major products were identified. The variation of isomer distribution depending on the conditions employed has been discussed in terms of the competition between the homolytic and heterolytic mechanisms involved in the nitration of ketone **1**. On the basis of the results obtained, the atmospheric formation of the genotoxic nitro ketone **4** has been briefly discussed.

Many nitrated polycyclic aromatic hydrocarbons (nitro-PAHs) and derivatives are widespread as environmental contaminants; some of these are known to exhibit high mutagenic and/or carcinogenic activity.[1,2] They exist in emission gases and particles from Diesel engines, smoke and soot from burning wood, and ambient air particulate matters.[1,2] They are also formed by the reaction of parent PAHs with pollution gases such as nitrogen monoxide and dioxide (NO and NO_2) in the presence of ozone or hydroxylic radical species in atmospheric environment.[3,4]

Environmental nitration of PAHs by nitrogen oxides has been studied intensively during the past two decades. It takes place in gas phase as well as on the surface of airborne particulates.[5,6] Zielinska et al. reported that the environmental nitration of fluoranthene with dinitrogen pentaoxide (N_2O_5) gives mainly 2-nitrofluoranthene, which is not the major product from ordinary nitration using nitric acid. They explained this discrepancy in terms of an addition–elimination sequence involving a radical species as the reactive intermediate.[7,8] The nitration initiated by hydroxylic radical species has been suggested to contribute to the environmental formation of polycyclic nitroarenes.[4,8] A recent study has revealed that the isomer distribution of nitrofluoranthenes resulting from the reaction between NO_2 and solid-supported fluoranthene is considerably dependent on the inorganic oxides used as support material.[9]

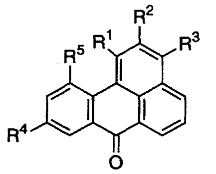
Benzanthrone (7*H*-benz[*d*,*e*]anthracen-7-one, **1**) represents an example of polycyclic aromatic ketones which are widely distributed as contaminants in atmospheric environment. It is especially abundant in exhaust gas and particles from motor engines and in smoke and soot from burning wood.[10—13] Very recently, we have reported that 3-nitrobenzanthrone (**4**) is a new class of powerful direct-acting mutagen of atmospheric origin. Since the ketone **1** readily reacts with NO_2 in inert organic solvent or on a solid support to form the nitration products,[14] it is quite reasonable to conceive that this genotoxic compound may be derived from the reaction of ketone **1** with nitrogen oxides in atmospheric environment.

In view of the highly toxic nature and environmental occurrence of compound **4**, more detailed knowledge about the products from the reaction of **1** and nitrogen dioxide seems to be of urgent importance. Direct gas phase reactions of arenes and NO_2 often parallel the corresponding reactions in nonpolar solvents, whereas the similar reactions on solid support are known to afford products whose compositions are close to those obtained from the corresponding reactions in polar organic solvents. Thus, the nitration of compound **1** by NO_2 in polar and nonpolar organic solvents is reasonably expected to provide a good probe to get an insight into the mechanism of the atmospheric formation of the toxic nitro ketone **4**. In the present study, therefore, we have carried out the reaction of compound **1** with NO_2 alone or in admixture with ozonized oxygen in inert organic solvents, such as dichloromethane and tetrachloromethane, and compared the composition of the resulting nitration product mixture with those obtained from conventional nitrations using nitric acid. For comparison, the reaction with dinitrogen pentaoxide (N_2O_5) has also been examined under similar conditions. On the basis of the results obtained, implications for the atmospheric formation of the genotoxic **4** has been discussed briefly.

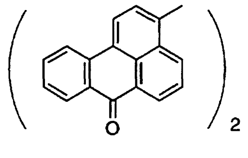
Results and Discussion

The nitration of benzanthrone (**1**) has not been studied so much previously. Although a few scattered papers have appeared in the past, the results reported therein are not always consistent. Lüttinghaus and Neresheimer treated a suspension of the ketone **1** in benzene with 87%-nitric acid to obtain 3-nitrobenzanthrone (**4**) as a golden yellow solid.[15] Lauer and Atarashi reacted **1** with gaseous NO_2 both in solution and in the solid state, obtaining the same product in good yield, where [3,3′-bi-7*H*-benz[*d*,*e*]anthracene]-7,7′-dione (**13**) was isolated as a minor product (Chart 1).[16] However, when the reaction was carried out using nitric acid in boiling acetic acid, the major product was 2-nitrobenzanthrone (**3**).[17] Later, concurrent formation of the 2- and 3-nitro derivatives was confirmed by Pandit et al.[18] and Sioda and Kato;[19] the latter authors performed the nitration in nitrobenzene and acetic acid, obtaining these two isomers in the ratios of 1 : 9 and 3 : 7, respectively. On further reaction with nitric acid–sulfuric acid at 50—60 °C, 3,9-dinitrobenzanthrone (**10**) was obtained in 23% yield.[20]

Reactions of Benzanthrone (1) with NO_2 in Dichloromethane and Tetrachloromethane. In the reaction of **1** with NO_2 in dichloromethane, we have confirmed the formation of five nitrobenzanthrones; these included 3-nitro- (**4**), 2-nitro- (**3**), 1,3-dinitro- (**7**), 9-nitro- (**5**), and 1-nitrobenzanthrones (**2**) in decreasing order of yield. These compounds were identified by direct comparison with the authentic specimens synthesized by independent routes. Theoretical calculations predicted the positional reactivity of **1** toward the nitryl cation to decrease in the order 3- > 1- > 9- ≈ 11-positions.[21] This order is in accordance with our experimental results, except for the cases of 2-nitro and 1,3-dinitro derivatives **3** and **7**. Therefore, these two compounds are highly likely to be formed via a mechanism different from that of ordinary ring nitration. In this nitration, **3** and **7** were produced as the main products only at the initial stage of the reaction, and their amounts did not increase in parallel with the progress of the reaction. At the final stage, the proportion of 3-nitro derivative **4** was predominant (Table 1, Run 1). The formation of dinitro compound **7** even at low conversion stage was quite unusual. If the dinitration of **1** occurs stepwise via the common electrophilic mechanism of aromatic substitution, the second nitro group should enter into the unsubstituted ring of the initial product **4**. As expected, attempted nitrations of both 1-nitro and 3-nitro derivatives **2** and **4** with nitric acid have failed to yield this anomalous product.



Compound	R^1	R^2	R^3	R^4	R^5
1	H	H	H	H	H
2	NO_2	H	H	H	H
3	H	NO_2	H	H	H
4	H	H	NO_2	H	H
5	H	H	H	NO_2	H
6	H	H	H	H	NO_2
7	NO_2	H	NO_2	H	H
8	NO_2	H	H	NO_2	H
9	H	NO_2	NO_2	H	H
10	H	H	NO_2	NO_2	H
11	H	H	NO_2	H	NO_2
12	H	H	NO_2	NO_2	NO_2



13

Chart 1.

When the reaction was run in the presence of 2,6-di-*t*-butylpyridine (DTBP) as an acid scavenger, the relative amount of the 2-nitro isomer **3** remarkably increased at the expense of the 3-nitro isomer **4** (Table 1, Run 2). In the NO_2–dichloromethane system, therefore, the nitric acid in situ generated during the course of the reaction no doubt plays an important role in the generation of nitryl cation, leading to the formation of the 3-nitro compound **4**. This finding suggests that the nitration of **1** with NO_2 in dichloromethane would probably start with a radical intermediate species **14** and would proceed via the addition–elimination sequence as shown in Scheme 2. With the progress of the reaction, the nitric acid gradually accumulated in the reaction system would come increasingly to act as the acid catalyst, switching over the mechanistic pathway from the radicalic to the ionic ones, as has recently been suggested for the *kyodai*-nitration of some substituted benzenes by NO_2.[22,23]

In dry tetrachloromethane in the dark, the reaction of benzanthrone (**1**) with NO_2 was quite slow. After standing overnight at room temperature, 2-hydroxy-2,3-dinitro-2,3-dihydro-7*H*-benz[*d*,*e*]anthracen-7-one (**20**) was isolated as the sole major product. Although much less in amount, 2-nitro and 3-nitro derivatives **3** and **4** were also obtained; the favored formation of the former isomer over the latter strongly suggests the reaction in tetrachloromethane to be radicalic in nature. Compound **20** was also obtained by the similar reaction of 2-nitro isomer **3**, but not so from 3-nitro isomer **4**. Hence, the reaction is considered to proceed according to the addition-elimination sequence involving the radical intermediates, as shown in Scheme 2. Unstable initial adduct **15** collapses under the elimination of a molecule of HNO_2 to produce the substitution products **3** and **4**, where the former compound is unoccupied at activated 3-position and further undergoes successive additions of two molecules of NO_2 to give an adduct **18**. Since the nitro substituent

Table 1. Nitration of Benzanthrone and the Resulting Product Distribution

					Isomer distribution (%)						
Run	Nitrating agent	Solvent	Temp (°C)	Conversion (%)	1-nitro	2-nitro	3-nitro	9-nitro	11-nitro	1,3-dinitro	3-nitro/1-nitro
1	NO_2–N_2O_4	CH_2Cl_2	25	82	2.8	13.3	53.2	2.1	0	7.1	19.0
2	NO_2–N_2O_4 a)	CH_2Cl_2	25	84	0.6	46.8	9.0	2.3	0	7.4	15.5
3	NO_2–N_2O_4	CH_2Cl_2	0	52	1.8	3.4	26.4	3.7	0	5.3	14.7
4	NO_2–O_3 b)	CH_2Cl_2	−70	98	7.7	0.6	58.8	Trace	Trace	0	7.6
5	NO_2–O_3	CH_2Cl_2	−70	46 c)	5.4	0	40.3	0	0	0	7.5
6	NO_2–O_3	CH_2Cl_2	0	100	6.6	2.1	80.0	1.6	0.4	0	12.1
7	NO_2–O_3	CH_2Cl_2	20	100	4.9	1.5	79.8	1.9	0.4	0	16.3
8	N_2O_5 d)	CH_2Cl_2	−70	90	12.5	0	67.3	1.5	0.7	0	5.3
9	N_2O_5 d)	CH_2Cl_2	0	91	7.3	0	75.6	1.4	Trace	0	10.4
10	N_2O_5 d)	CH_2Cl_2	20	99	6.8	0	83.0	1.3	Trace	Trace	12.2
11	NO_2–O_3	— f)	20	98	3.3	1.17	82.4	2.2	0	Trace	25.0
12	HNO_3	Nitrobenzene	20	100	5.8	0	83.5	3.0	1.2	0	14.4
13	NO_2–N_2O_4	CCl_4 g)	20	100	0	5.2	1.5	0.3	0	0	—
14	NO_2–O_3	CCl_4	20	100	0	67.3	0	1.6	0	6.3	—
15	NO_3–O_3 e)	CCl_4	20	90	3.8	7.8	57.1	3.2	0	0	15.0

a) 2,6-Di-*t*-butylpyridine (1 mmol) was added. b) Procedure for the *kyodai*-nitration was employed. c) A gasous mixture solidified in an inlet tube and hampered further reaction, resulting in a low conversion. d) N_2O_5 (3 mmol) was added. e) HNO_3 (50 µl) was added. f) SiO_2 was used as support material for benzanthrone. g) Compound **20** was obtained in 80% yield.

at 2-position in nitro ketone **3** does not influence much the orientation mode of the benzanthrone nucleus, compound **3** is still most reactive at 3-position.24) This would be easily understood by gazing on the framework of **1**, where the 3-position is doubly activated as the *para*-position of biphenyl moiety and also as the α-position of naphthalene nucleus. In the presence of excess NO_2, nitrite **18** is rapidly transformed to nitrate **19** via the NO–NO_2 exchange on the alcoholic oxygen atom.

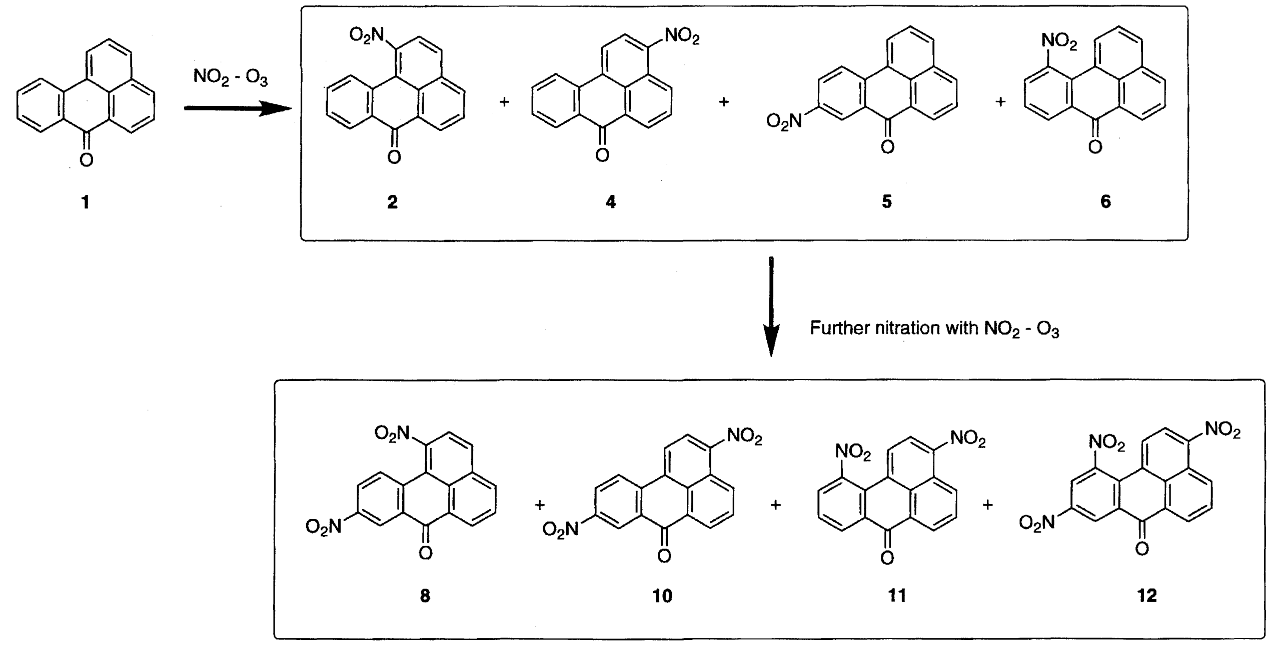
Nitration of Benzanthrone (1) with a Gaseous Mixture of NO_2 and Ozonized Oxygen. The nitration of arenes with NO_2 in the presence of ozone has been known as the *kyodai*-nitration, where the reaction proceeds via the dual mechanism involving either nitrogen trioxide (NO_3) or N_2O_5 as the initial electrophile.25,26) The *kyodai*-nitration of benzanthrone **1** has now been investigated in organic solvents of different polarity and also in the presence or absence of some solid support materials as the catalyst.

In Dichloromethane. When a premixed NO_2–O_3 gas was passed into a solution of **1** in dichloromethane at room temperature, five isomeric mononitro derivatives, 1-nitro-, 2-nitro-, 3-nitro-, 9-nitro-, and 11-nitrobenzanthrones (**2**—**6**), were formed and identified by direct comparison with the authentic samples. The distribution of these isomeric nitrobenzanthrones is shown in Table 1 (Runs 4—7). 3-Nitro isomer **4** was obtained as the major product in up to 80% yield, the relative amount of the accompanying isomers decreasing in the order 1-nitro > 2-nitro ≧ 9-nitro > 11-nitro derivatives. This result is consistent with the predicted positional reactivity, except for the case of the 2-nitro derivative **3**. The 2-nitro derivative **3** was the major product at the initial stage of the reaction, as was the case with the reaction of NO_2 alone.

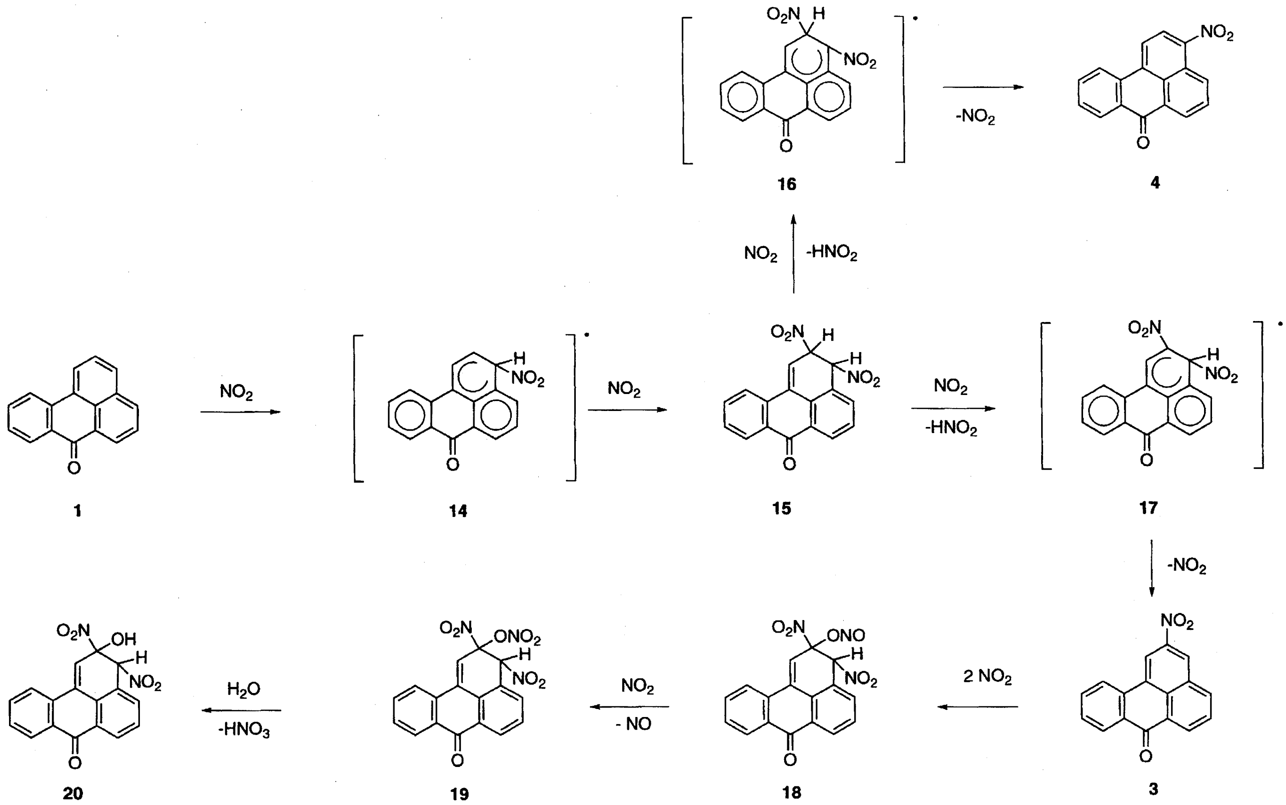
In the *kyodai*-nitration of **1**, the distribution of isomeric nitrobenzanthrones is similar to those observed in ordinary nitrations, based on the use of nitric acid or its equivalent (Table 1, Run 12). Thus, the reaction of ketone **1** with NO_2–O_3 may be regarded to bear an ionic nature like the classical nitration, where nitric acid is involved as the reagent and NO_2^+ ion as the attacking electrophile. However, the NO_2–O_3 system has been proved to be more effective as the nitrating agent than the nitric acid system.25,26) Hence, when subjected to the *kyodai*-nitration, the mononitration of benzanthrone (**1**) rapidly went to completion (within 20 min) and further nitration occurred quite smoothly even at temperatures as low as 0 °C, producing the polynitration products such as 3,9-dinitro- (**10**), 3,11-dinitro- (**11**), 1,9-dinitrobenzanthrones (**8**), and 3,9,11-trinitrobenzanthrone (**12**) shown in Scheme 1. Polynitration of **1** usually requires heating with nitric acid.

The product distribution in the *kyodai*-nitration of benzanthrone **1** was found to be dependent on the reaction temperatures employed. At room temperature (20 °C), the molar ratio of 3-nitro- to 1-nitrobenzanthrones (**4** : **2**) was 16.3. However, this ratio decreased as the reaction temperature was lowered; the ratio was 12.1 at 0 °C and 7.5 at −70 °C, lower reaction temperatures working favorably for the formation of 1-nitro isomer **2**.

The reaction of NO_2 and O_3 is well known to form N_2O_5, which reversibly dissociates to NO_2 and NO_3 radicals on the one hand and to NO_2^+ and NO_3^- ions on the other. Nonpolar conditions favor the former type dissociation, while polar conditions facilitate the latter. We have also examined the reaction of **1** with N_2O_5 in dichloromethane, where a similar product composition and temperature dependence of the isomer ratio **4** : **2** was observed; the product ratios **4** : **2** were 5.3 at −70 °C and 12.2 at 20 °C, respectively (Table 1, Runs 8—10). These values differ somewhat from those observed under the conditions of the *kyodai*-nitration, where the 3-nitro isomer **4** is more favored over the 1-nitro isomer **2**.



Scheme 1. Products from nitration of benzanthrone with NO_2–O_3 in dichloromethane.



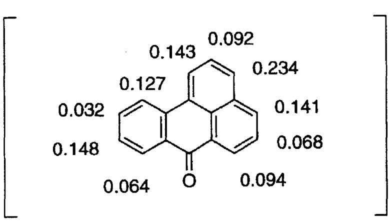
Scheme 2. Nitration of benzanthrone with NO_2 in tetrachloromethane.

In Tetrachloromethane. When tetrachloromethane was used as the reaction medium, the results were quite different from those obtained from the nitration in dichloromethane (Table 1, Runs 13—14). In this reaction system, 2-nitro- and 1,3-dinitro compounds **3** and **7** were always the major mono- and polynitration products obtained. 2,3-Dinitrobenzanthrone (**9**) was also detected in a trace amount. In this solvent system, the reaction was not subject to the effect of reaction temperatures. The use of other nonpolar aprotic solvents such as 1,1,2-trichloro-1,2,2-trifluoroethane and hexane gave similar results.

In spite of the well-established fact that the 2-position of **1** is not subject to preferential attack by electrophiles,[21)] the 2-nitro isomer **3** was obtained in most cases as the sole mononitration product in high yield. Besides, the adduct **20** was isolated in 10% yield. In a separate experiment where

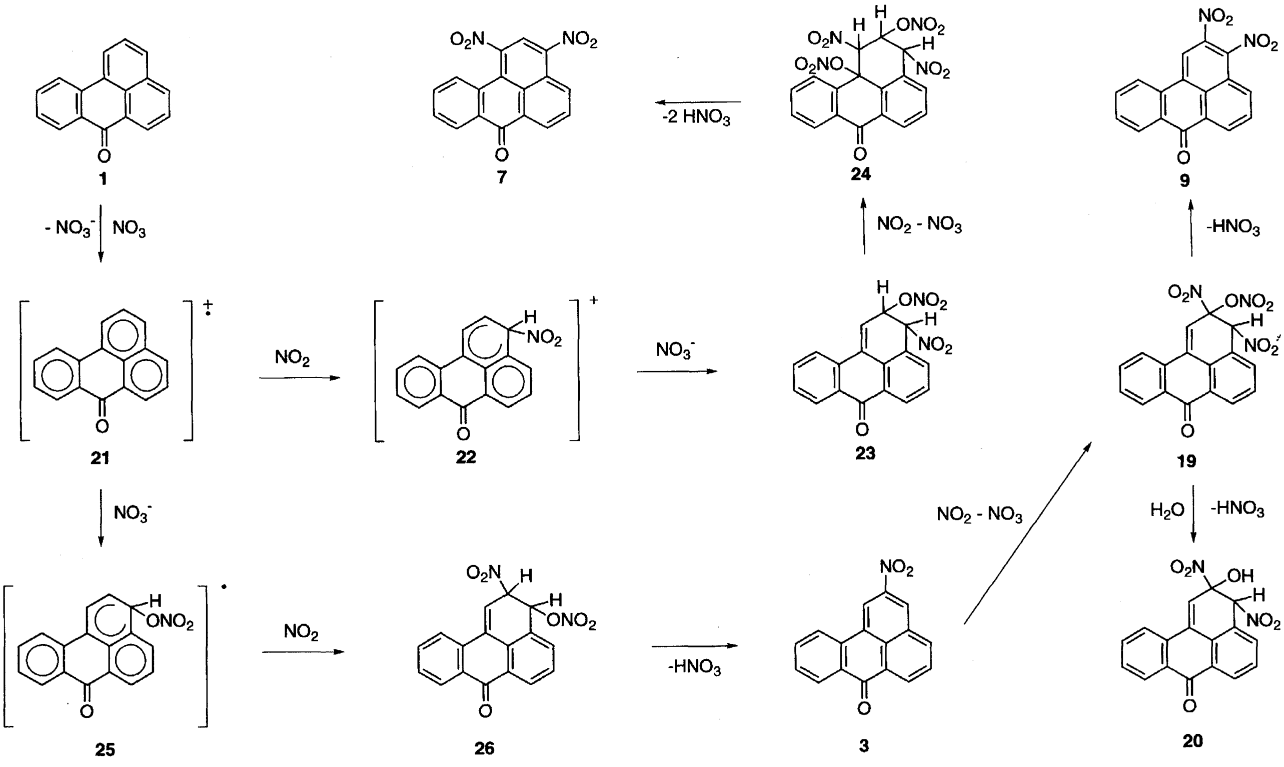
1 was reacted with NO_2 alone in tetrachloromethane, this compound was obtainable in 80% yield. Compound **20** was readily aromatized by the action of sulfuric acid to give 2,3-dinitro derivative **9**. Therefore, we may reasonably conclude that compounds **3**, **7**, and **9** were all derived from the corresponding nitro–nitrato adducts **19**, **23**, and **26** via the addition–elimination sequence. The isolation of addition product **20** as a side product endorses the operation of the addition–elimination mechanism, as depicted in Scheme 3. By the action of a protonic acid, the nitrato group at benzylic position of adduct **26** is eliminated as an HNO_3 molecule to give compound **3**. Successive additions of NO_2 and NO_3 molecules to compound **3**, followed by hydrolysis of the resulting adduct **19**, affords an alcohol **20**. A similar interpretation has previously been presented for the reaction of fluoranthene and N_2O_5 in tetrachloromethane.[7]

In Scheme 3, benzanthrone (**1**) (E° 2.0 V versus NHE) first reacts with the in situ generated NO_3 radical (E° 2.3—2.6 V versus NHE)[27] in an electron transfer way to give a cation radical (**21**), which combines with NO_2 to form an arenium ion intermediate (**22**). In the cation radical **21**, coupling with NO_2 would occur preferentially at 3-position, as predicted from the frontier electron distribution shown in Scheme 4. Under nonpolar conditions, the proton release from arenium ion **22** would be overshadowed by the preferential coupling with an intimate nitrate anion in the solvent cage, leading to the formation of addition product (**23**). Formation of these addition products was easily observed by ^1H NMR spectrum of the crude product mixture, which showed multiplet absorptions centered around $\delta = 4.5$, 5.0, 5.8, 6.2, and 6.5, attributable to aliphatic protons of the addition products.[28] The conjugated double bond present in the secondary allylic nitrate structure of addition product **23** would be more reactive than the corresponding bond in nitropropene structure of the counterpart (**26**). Therefore the former undergoes a further addition reaction across the 1, 11b-double bond to give an adduct (**24**), which, in the presence of acid catalyst, would rapidly aromatize by releasing two molecules of HNO_3 to afford 1,3-dinitro compound **7**.



Scheme 4. Frontier electron density of benzanthrone cation radical.

Effect of Added Inorganic Solid Support on the Reaction of Benzanthrone (1) with NO_2 in Tetrachloromethane. When the *kyodai*-nitration of benzanthrone (**1**) was carried out in tetrachloromethane in the presence of a catalytic amount of HNO_3, the 3-nitro derivative **4** was the sole major product; it was formed at the expense of 2-nitro and 1,3-dinitro derivatives **3** and **7** (Table 1, Run 15). When a small amount of soot or a finely powdered metal oxide such as Fe_2O_3 or MnO_2 was added in place of HNO_3, a similar change of the product composition was again observed, indicating the switchover of the nitration mechanism from the radical to the ionic ones (Table 2). In the presence of added



Scheme 3. Nitration of benzanthrone with NO_2–O_3 in tetrachloromethane.

Table 2. Effect of Solid Additive on the Isomer Distribution in the Nitration of Benzanthrone with NO_2–O_3 in CCl_4

Additive	Conversion (%)	Product distribution (%)				
		1-nitro	2-nitro	3-nitro	9-nitro	11-nitro
None	100	0	67.3	0.0	1.6	0
Soot 100 mg	96	1.2	38.0	22.3	0.0	0
Soot 200 mg	100	2.5	13.6	52.6	0.0	0
Fe_2O_3 150 mg	100	0.0	7.8	56.8	0.0	0
MnO_2 200 mg	100	2.2	17.5	28.9	0.7	Trace
SiO_2 300 mg	45	0.0	8.6	35.7	0.0	0

inorganic solid support, the in situ formed N_2O_5 would be adsorbed and ionized on the solid surface. The resulting NO_2^+ ion would nitrate **1** to give 3-nitro derivative **4**.

In order to mimic the environmental formation of 3-nitrobenzanthrone (**4**), the ketone **1** supported on silica gel was allowed to stand under an atmosphere of NO_2 admixed with ozonized oxygen at room temperature. The product was extracted with dichloromethane and analyzed by HPLC to reveal that the only main product was nitro ketone **4**, as expected.

Environmental Relevance. The reaction of benzanthrone (**1**) with NO_2 alone or in admixture with ozone in organic solvents of different polarity has disclosed a remarkable dependence of the isomer distribution on the reaction temperature and solvent polarity, as shown in Table 1. The changeover of the product composition depending on the solvent employed may reasonably be attributed to the operation of two distinct mechanisms therein. The reaction under nonpolar conditions may proceed via the addition–elimination sequence involving the NO_2 and NO_3 radical species, as has previously been suggested for the nitrations of fluoranthene and naphthalene.[7,29,30] In atmospheric environment, this pathway would presumably be responsible for the gas phase nitration of volatile polycondensed arenes.

In ambient atmosphere, however, ketone **1** mostly occurs in adsorbed form on the surface of air-borne particulate matters.[10] Under these conditions, it is highly likely that the nitration of this ketone takes place via the competition between the homolytic process involving the NO_2 radical and the heterolytic process involving the NO_2^+ ion. Both processes would presumably proceed in parallel, since the homolytic addition–elimination pathway has been found to be easily switched to the heterolytic substitution pathway involving the arenium ion in the presence of a protonic acid or an inorganic solid support. In accordance with this, we have observed the concurrent formation of a varying ratio of 2- and 3-nitro isomers in the gas-solid phase reaction between NO_2 and ketone **1** on the solid support (Table 2).

Very recently, we have found 3-nitrobenzanthrone (**4**) in ambient air particles and Diesel exhaust particulates. The origin of environmental nitro ketone **4** can be sought in the gas–solid phase nitration of ketone **1** by NO_2 or NO_2–NO_3 during atmospheric transport, as well as in the direct interaction between ketone **1** and NO_2 inside motorcar engines. However, since we have so far failed to detect any 2-nitro isomer **3** in either ambient or Diesel particulates, we suspend our opinion about a possible role of the homolytic process in ambient as well as high-temperature nitrations of benzanthrone (**1**) with NO_2. We detected 9-nitro isomer **5** in Diesel exhaust particles, but not yet in airborne particles. This compound can be derived via both homolytic and heterolytic pathways. Quite difficult though it may be, further analytical study of the distribution of isomeric nitrobenzanthrones of atmospheric orign would provide a better key to understand the mechanistic aspect of environmental nitration of compound **1**.

It may be pertinent to mention briefly about the mode of formation of 3-nitrobenzanthrone (**4**) in combustion engines. Ketone **1** formed from incomplete combustion of fossil fuels is emitted from the combustion chamber to the exhaust pipe where, due to its low volatility, **1** deposits inside the pipings and is adsorbed on soot thereon. Inside the combustion chamber, nitrogen and oxygen react to form nitrogen monoxide (NO), which combines with molecular oxygen during the passage to the exhaust pipe, first forming an asymmetrical nitrogen trioxide (ONOO). This unstable nitrogen trioxide is further converted to NO_2 and a more stabilized symmetrical NO_3 according to the known reactions below:[31]

$$\begin{aligned} &\mathrm{ONOO\ (asym\text{-}NO_3) + NO \rightarrow ONO\text{–}ONO \rightarrow 2NO_2} \\ &\mathrm{ONOO\ (asym\text{-}NO_3) + NO_2 \rightarrow ONO\text{–}O\text{–}NO_2} \\ &\qquad\qquad \mathrm{\rightarrow NO_2 + O\text{–}N(O)\text{–}O\ (sym\text{-}NO_3)} \end{aligned}$$

The ketone **1** can be nitrated by either NO_2 alone or a combination of NO_3 and NO_2 inside the exhaust pipings, although we are not sure at present if the reaction proceeds in a manner similar to those described in the present paper. The possible contribution of molecular N_2O_5 as the nitrating agent may be ruled out, since this compound readily decomposes to lower nitrogen oxides and oxygen under such high temperature conditions as inside the running engines.

In the present study, we have shown a remarkable changeover of the isomer distribution of the nitration product of **1**, depending on the conditions employed. When supported on an inorganic solid material, ketone **1** can be readily nitrated with gaseous nitrogen dioxide to give a powerfully genotoxic nitroarene **4**. The formation of this hazardous substance is furthermore facilitated by the additional presence of ozone, where NO_3 plays a role as the initial electrophile.

Experimental

Melting points were determined on a Yanagimoto hot stage apparatus and are uncorrected. IR spectra were recorded on a Shimadzu FTIR DR 8000/8100 infrared spectrophotometer and only prominent peaks in 2000—700 $\mathrm{cm^{-1}}$ region were recorded. ^{1}H NMR spectra were obtained with a Varian Gemini-200 (200 MHz) spectrometer. *J* values are given in Hz. Electron impact mass spectra (EI-MS) were recorded on a Shimadzu QP-2000 at 70 eV and chemical ionization mass spectra (CI-MS) were determined on a Shimadzu QP-5000, using isobutane as a reacting gas. Ozone was generated from a Nippon Ozone Co., Ltd. type ON-1-2 apparatus, which produced ozone at a rate of 9 $\mathrm{mmol\,h^{-1}}$ under an oxygen flow of 10 $\mathrm{dm^3\,h^{-1}}$ and an applied voltage of 70 V. Semi-empirical calculations were carried out with the MOPAC (version 6.10) program using the PM3 Hamiltonian implemented on a Sony Tektronix CAChe system (version 3.5).

Chemicals: All solvents used were purified by distillation prior to use. Authentic nitrobenzanthrones used for calibration were synthesized by independent routes described elsewhere.[32] Benzanthrone was purchased from Tokyo Kasei Co., Ltd. and used after recrystallization from ethanol. Nitrogen dioxide (99% pure) was obtained from Sumitomo Seika Co., Ltd. and used after transfer distillation.

1,3-Dinitrobenzanthrone (7). To a stirred mixture of 1-iodo-2,4-dinitronaphthalene (5 mmol) and methyl 2-iodobenzoate (10 mmol) heated at 150 °C, copper bronze powder (500 mg) was added in four portions over 3 h. After cooling, the mixture was quenched with concentrated aqueous ammonia and then diluted with water. The organic phase was extracted with ethyl acetate (5×20 ml), dried over $\mathrm{Na_2SO_4}$, and evaporated. The thick oily residue was passed through a silica gel column using hexane–ethyl acetate (5 : 1) as the eluent and the fractions containing the Ullmann coupling products were collected. Evaporation of the solvent left an oil (200 mg), which was dissolved in a solution of lithium hydroxide (500 mg) in water–methanol (1 : 9; 50 ml) and heated under reflux for 1 h. After cooling, the solution was made acidic with hydrochloric acid and the organic phase was extracted with chloroform. The combined extracts were dried over $\mathrm{Na_2SO_4}$ and evaporated. The oily residue was chromatographed on a silica gel column using acetonitrile as the eluent to give 2-(2,4-dinitro-1-naphthyl)benzoic acid as a yellow powder.

The carboxylic acid (20 mg) thus obtained was dissolved into fuming $\mathrm{H_2SO_4}$ (1 ml) to form a yellow-colored solution, which after 30 min was poured onto crushed ice. The organic product was extracted with dichloromethane, dried over $\mathrm{Na_2SO_4}$, and evaporated. The residue was chromatographed on a silica gel using hexane–ethyl acetate (5 : 1) as the eluent to give 1,3-dinitrobenzanthrone (**7**). This compound was rather photo-sensitive and decomposed to **2**, **4** and other unidentified substances when left under diffused light. Mp = ca. 210 °C (decomp); ^{1}H NMR ($\mathrm{CDCl_3}$) $\delta = 7.7$—7.9 (m, 3H), 8.10 (dt, $J = 1.4$, 7.4 Hz, 1H), 8.50 (t, $J = 4.6$ Hz, 1H), 8.52 (s, 1H), 8.9—9.0 (m, 2H); IR (KBr) 1659, 1529, 1360, 1292 $\mathrm{cm^{-1}}$; Mass (CI) *m*/*z* 321 (M+1; 100), 291 (M+1−NO; 42). EI HRMS; Calcd for $\mathrm{C_{17}H_8N_2O_5}$: $[\mathrm{M}]^+$, 320.0433. Found: *m*/*z* 320.0429.

2-Hydroxy-2,3-dinitro-2,3-dihydro-7*H*-benz[*d*,*e*]anthracen-7-one (20). To a solution of benzanthrone (230 mg, 1,0 mmol) in tetrachloromethane (50 ml), liquid nitrogen dioxide (1 ml, 15 mmol) was added in one portion. The resulting mixture was stirred overnight at room temperature. As the reaction proceeded, a solid product separated out from the solution. The product was collected by filtration and recrystallized from acetone to give compound **20** as a yellow solid. The structure of the product was assigned by ^{1}H-2D-COSY and NOE experiments; irradiation of a singlet peak at $\delta = 6.96$ enhanced the proton at 11-position (ca. 5%) and irradiation of a peak at $\delta = 8.70$ enhanced the proton at 4-position (3%). Treatment of **20** with triethylamine in dichloromethane resulted in the formation of a quinoid compound, probably 3-nitro-2,3-dihydrobenz[*d*,*e*]anthracen-2,7-dione. Mp = 197 °C; ^{1}H NMR (DMSO-d_6) $\delta = 7.06$ (s, 1H, H-1), 7.34 (s, 1H, OH), 7.69 (t, $J = 7.9$ Hz, 1H, H-9), 7.79 (t, $J = 7.8$ Hz, 1H, H-5), 7.89 (dt, $J = 1.4$, 7.9 Hz, 1H, H-10), 8.22 (dd, $J = 1.4$, 7.8 Hz, 2H, H-4,8), 8.30 (dd, $J = 1.3$, 7.8 Hz, 1H, H-6), 8.37 (d, $J = 7.9$ Hz, 1H, H-11), 8.70 (s, 1H); IR 3427, 1662, 1556, 1525, 1329; Mass (CI) *m*/*z* 339 (M+1; 10) 321 (7), 276 (100). Found: C, 59.96; H, 2.96; N, 8.21%. Calcd for $\mathrm{C_{17}H_{10}N_2O_6}$: C, 60.36; H, 2.98; N, 8.28%.

2,3-Dinitrobenzanthrone (9). Compound **20** was dissolved in cold concentrated $\mathrm{H_2SO_4}$ and left to stand overnight. The reaction mixture was poured into ice water and a solid which separated was taken up with dichloromethane. The solvent was removed and the residue was chromatographed on silica gel using hexane/ethyl acetate (5 : 1) as the eluent. The structure of the product was assigned by ^{1}H-2D-COSY and NOE experiments. Mp = 237—238 °C; ^{1}H NMR ($\mathrm{CDCl_3}$) $\delta = 7.74$ (dt, $J = 8.0$, 1.1 Hz, 1H, H-9) 7.90 (t, $J = 7.6$, 1.8 Hz, 1H, H-10), 8.07 (dd, $J = 7.1$, 8.3 Hz, 1H, H-5), 8.22 (dd, $J = 8.3$, 1.2 Hz, 1H, H-6), 8.39 (dd, $J = 7.6$, 1.1 Hz, 1H, H-11), 8.53 (dd, $J = 8.0$, 1.8 Hz, 1H, H-8), 8.95 (dd, $J = 7.1$, 1.2 Hz, 1H, H-4), 9.06 (s 1H, H-1); IR (KBr) 1660, 1541, 1336, 1280 $\mathrm{cm^{-1}}$; Mass (CI) 321 (M+1; 66), 291 (M+1−NO; 22), 276 (M+1−$\mathrm{NO_2}$; 100). EI HRMS; Calcd for $\mathrm{C_{17}H_8N_2O_5}$: $[\mathrm{M}]^+$, 320.0433. Found: *m*/*z* 320.0432.

Nitration of Benzanthrone 1. With $\mathrm{NO_2}$ Alone; Typical Procedure. To a stirred solution of benzanthrone [(230 mg; 1.0 mmol) in dichloromethane (50 ml) or (115 mg, 0.5 mmol) in tetrachloromethane (50 ml)] kept at an appropriate temperature, nitrogen dioxide (1 ml, 15 mmol) was added in one portion. The resulting mixture was stirred overnight. The solvent was evaporated and the product was analyzed by HPLC.

With a Mixture of $\mathrm{NO_2}$ and Ozone; Typical Procedure. Into a stirred solution of benzanthrone [(230 mg; 1.0 mmol) in dichloromethane (50 ml) or (115 mg, 0.5 mmol) in tetrachloromethane (50 ml)] kept at an appropriate temperature, a stream of nitrogen dioxide (20 $\mathrm{mmol\,h^{-1}}$) admixed with ozonized oxygen (9 $\mathrm{mmol\,h^{-1}}$) at inlet tubing was passed slowly. After 20 min, the reaction mixture was evaporated and the product was analyzed by HPLC.

With $\mathrm{N_2O_5}$; Typical Procedure. $\mathrm{N_2O_5}$ was prepared by distilling fuming $\mathrm{HNO_3}$ in the presence of excess of $\mathrm{P_2O_5}$ under a constant stream of ozonized oxygen. Benzanthrone (230 mg, 1.0 mmol) was dissolved in dichloromethane (35 ml). A solution of $\mathrm{N_2O_5}$ in the same solvent (15 ml, 3 mM = 3 $\mathrm{mmol\,dm^{-3}}$) was added in one portion at an appropriate temperature. After 20 min, the reaction mixture was evaporated under reduced pressure and the product was analyzed by HPLC.

With $\mathrm{NO_2}$ in the Presence of $\mathrm{O_3}$ (*kyodai*-nitration); Typical Procedure. A solution of benzanthrone (230 mg, 1.0 mmol) in dichloromethane (50 ml) was mixed with liquid $\mathrm{NO_2}$ (1 ml, 15 mmol) and some ozonized oxygen was passed slowly into this solution. After 20 min, the reaction mixture was worked up in the manner described above and the product was analyzed by HPLC.

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