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Photooxygenation of Polycyclic Aromatic Hydrocarbons by Pyrimido[5,4-*g*]pteridine *N*-Oxide

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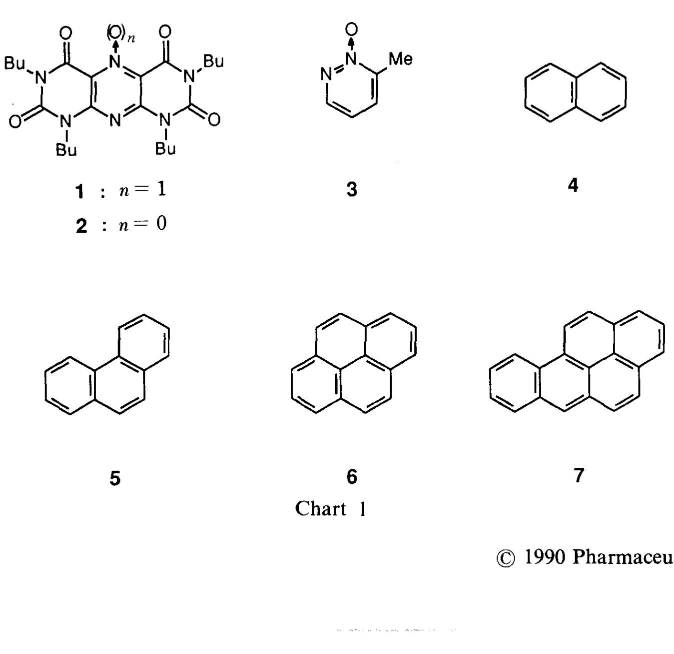
Photooxygenation of naphthalene (4), phenanthrene (5), pyrene (6), and benzo[*a*]pyrene (7) by pyrimido[5,4-*g*]pteridine *N*-oxide (1) was examined in comparison with that of benzene. These polycyclic aromatic hydrocarbons (PAHs) consumed 1 more smoothly than did benzene under irradiation with ultraviolet-visible light, as expected from the fact that their oxidation potentials for conversion to the corresponding phenols and/or further oxidized products are lower. The photooxygenation of the PAHs occurred predominantly at the most reactive position of the corresponding cation-radicals. These and other experimental results led us to conclude that the PAHs are oxygenated *via* photo-induced single-electron transfer (SET) from the PAHs to 1 followed by oxygen-atom transfer between the resulting radical-ion pairs. The occurrence of the SET in an excited charge-transfer complex formed between the PAHs and 1 is at variance with the case of benzene. The photooxygenation of 7 by 1 can be regarded as a simple reaction mimic for one of the metabolic activation processes involved in carcinogenesis by 7.

Keywords photooxygenation; polycyclic aromatic hydrocarbon; pyrimidopteridine *N*-oxide; single-electron transfer; charge-transfer complex; carcinogenesis; reaction mimic

Previous articles[1)] from our laboratory have documented that 1,3,6,8-tetrabutylpyrimido[5,4-*g*]pteridine-2,4,5,7-(1*H*,3*H*,6*H*,8*H*)-tetrone 10-oxide (**1**)[2)] functions as an efficient agent for oxygenation or dehydrogenation under photochemical conditions. A characteristic feature of the photooxygenation by **1** is the involvement of an initial single-electron-transfer (SET) process in contrast to the oxene mechanism which is generally accepted for photochemical oxygenation by heterocyclic *N*-oxides,[3–7)] *e.g.*, 3-methylpyridazine 2-oxide (**3**) and pyridine *N*-oxide. For example, it has been demonstrated that benzene undergoes photooxygenation by **1** *via* the SET from benzene to a singlet-excited **1** followed by coupling of the resulting radical-ions to give phenol.[8)]

The biological oxygenation catalyzed by hemoproteins such as cytochrome P-450 can be best explained in most cases in terms of the initial SET from substrates to the oxidizing species symbolized by $(\mathrm{Fe^{IV}=O})^{+\cdot}$.[9)] Thus, the photooxygenation by **1** can be considered as a reaction mimic for hemin-catalyzed oxygenation from the mechanistic point of view.

In this paper, we describe an extension of previous results[8)] to the photochemical oxygenation of a series of polycyclic aromatic hydrocarbons (PAHs), *i.e.*, naphthalene (**4**), phenanthrene (**5**), pyrene (**6**), and benzo[*a*]pyrene (**7**). The present results show that the photooxygenation of the PAHs by **1** is initiated by SET in an excited charge-transfer (CT) complex rather than that from the substrates to a singlet-excited **1** as documented in the case of benzene.



1 : *n* = 1
2 : *n* = 0

3

4

5

6

7

Chart 1

Results

Photooxygenation of Naphthalene (4) by the *N*-Oxide (1 or 3) A mixture of **4** (500 mM) and **1** [ultraviolet (UV), λ_{max}: 370 ($\varepsilon = 2.2 \times 10^4$) nm] (5 mM) in dry acetonitrile was irradiated externally with a 400W high-pressure mercury arc lamp through a $BiCl_3$ solution filter (>355 nm) at ambient temperature under argon. After irradiation for 10 min, 1- and 2-naphthols (**8**) (ratio, 7/1; by gas chromatography (GC)) were obtained in 71% yield based on the consumed **1**. Prolongation of the irradiation time resulted in a decrease of the conversion yield of **8** (*e.g.*, 30% yield after the complete consumption of **1**) as well as the formation of 1,4-naphthoquinone (**9**), indicating the occurrence of further photooxidation of the main product, 1-naphthol, by **1**.[10)]

The consumed *N*-oxide **1** was converted into pyrimido[5,4-*g*] pteridine (**2**) without the formation of a detectable amount of other photoproducts originated from **1**. This indicates the high efficiency of **1** as an oxidant.

Jerina *et al.*[11)] have reported that the photooxygenation of **4** by pyridine *N*-oxide in methylene chloride at 253.7 nm gives **8** (1-naphthol content, about 95%) in 1% yield and they detected the arene oxide, naphthalene 1,2-oxide, by nuclear magnetic resonance (NMR) spectroscopy. Careful monitoring of the present photoreaction by proton nuclear magnetic resonance (^{1}H-NMR) spectroscopy, however, did not show the presence of a detectable amount of the arene oxide.

Addition of ^{18}O-labeled water ($H_2{}^{18}O$) to the reaction medium of **4** with **1** resulted in no ^{18}O-incorporation into the product **8**, indicating that the oxygen of **8** originates from the *N*-oxide oxygen of **1** but not from a small amount of water contained in the medium.

Analogous irradiation (through a Pyrex filter) of a mixture of **4** (500 mM) and the *N*-oxide **3** [UV, λ_{max}: 323 ($\varepsilon = 1.4 \times 10^4$)nm] (5 mM) in dry acetonitrile for 20 min caused complete consumption of **3** and gave **8** (1- and 2-isomeric ratio, 4/1) in 25% yield. In this photoreaction, deoxygenated pyridazine was obtained in only 40% yield, suggesting the occurrence of the photochemical intramolecular rearrangement of **3** as previously demonstrated[12] and the lower efficiency of **3** as an oxidant.

The consumption rate of **1** in the photoreaction with **4** was distinctly dependent upon the concentration of **4** as shown in Fig. 1a. This observation reflects importance of interaction between **1** and **4** for the photooxygenation of **4**. In fact, ground-state CT interaction between **4** and **1** was observed, as evidenced by the UV-visible absorption spectrum. A strong wavelength dependence was observed in this photoreaction, and excitation of the CT-band (405 nm) gave the maximum yield of **8** (see Fig. 2). In sharp contrast, the consumption rate of **3** under photochemical conditions was independent of the presence of **4** as shown in Fig. 1b and no CT-band between **3** and **4** was observed in the difference UV-visible absorption spectrum of a mixture of **3** and **4** *vs*. **3**. These results indicate an apparent difference in reaction mode between **1** and **3**, as previously observed in the photooxygenations of benzene[8] and cyclohexene.[13]

Photooxygenation of Phenanthrene (5) by the *N*-Oxide (1 or 3) A mixture of **5** (100 mM) and **1** (5 mM) in dry acetonitrile was irradiated under conditions analogous to the foregoing case. After 40 min, **1** was completely consumed to give **2** in almost quantitative yield and 9-phenanthrol (**10**) was isolated in 21% yield together with bis(9-hydroxyphenanthrene-10-yl) (**11**)[14] (12%) and 9,10-phenanthrenedione (**12**)[15] (19%) as oxygenated products by column chromatographic separation of the reaction mixture. The structures of these products were confirmed by spectral comparison with the respective authentic samples.[14,15] The formation of **11** and **12** can be ascribed to the further photooxidation of the primary product **10** by **1** or by autoxidation, since **10** is unstable under photochemical conditions in the presence of **1**[10] or on exposure to air, being converted gradually into **11** and **12**.

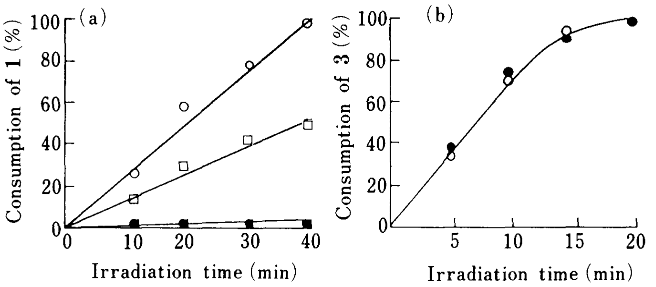


Fig. 1. Consumption of Pyrimido[5,4-*g*]pteridine *N*-Oxide (**1**) (Fig. 1a) and 3-Methylpyridazine 2-Oxide (**3**) (Fig. 1b) in the Absence or Presence of Naphthalene (**4**) as a Function of Irradiation Time

●, without **4**; □, with 10 eq of **4**; ○, with 100 eq of **4**.

Reaction conditions: the *N*-oxide **1** or **3** (5.0 mM) in dry acetonitrile was employed. Irradiation with a 400W high-pressure mercury arc lamp was carried out under argon at ambient temperature through a $BiCl_3$ solution filter for **1** and a Pyrex filter for **3**.

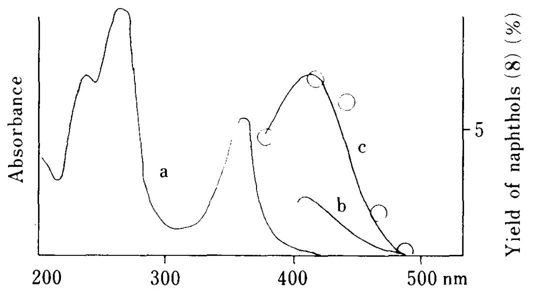


Fig. 2. Wavelength Dependence in the Photooxygenation of Naphthalene (**4**) by Pyrimido[5,4-*g*]pteridine *N*-Oxide (**1**)

a) UV-visible absorption spectrum of **1** (0.05 mM). b) Difference spectrum of a mixture of **1** (5.0 mM) and **4** (10.0 mM) *vs*. **1** (5.0 mM) in dry acetonitrile. c) The yield (%) of naphthols (**8**). Reaction conditions: a mixture of **1** (5.0 mM) and **4** (500 mM) in dry acetonitrile was irradiated with JASCO CRM-FA spectroirradiator (2 kW Xe lamp and 4 nm band width) under argon at ambient temperature for 10 min. Light in each wavelength region employed was irradiated at almost the same energy level.

Akhtar *et al.*[11] have reported that the photooxygenation of **5** by pyrazine *N*-oxide in methylene chloride at 253.7 nm gives 1- and 4-phenanthrols as the major products in addition to **10**. In analogy with their observations, UV-irradiation (through a Pyrex filter) of **5** with **3** in dry acetonitrile resulted in the formation of 4-phenanthrol (5%)[16] together with **10** (16%), **11** (3%), and **12** (8%). Careful inspection of the products in the photoreaction of **5** with **1**, however, showed no detectable formation of 4-phenanthrol.

Photooxygenation of Pyrene (6) and Benzo[*a*]pyrene (7) by the *N*-Oxide (1) Under analogous conditions to those described above, a mixture of **6** (10 mM) and **1** (5 mM) was irradiated until the complete disappearance of **1** (for 1 h) to give 1-hydroxypyrene (**13**) in 55% yield together with a trace amount of undetermined oxidized products. The 1-hydroxypyrene (**13**) was identified by comparing its spectral data with those of an authentic sample.[17]

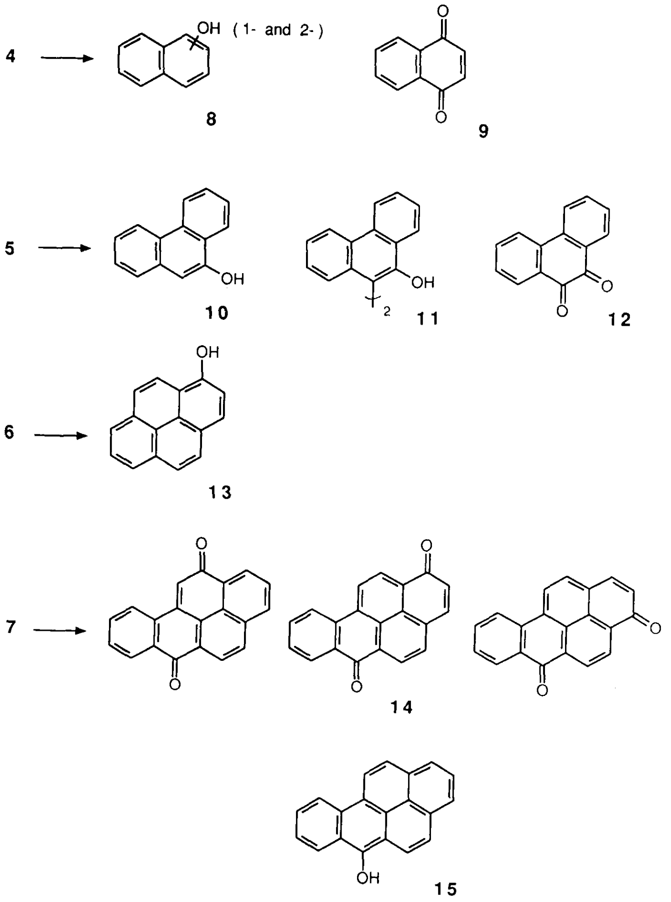


Chart 2

Irradiation of a solution of **7** (7.5 mM) and **1** (5 mM) in dry acetonitrile for 40 min followed by column chromatographic separation gave an inseparable mixture of 1,6-, 3,6-, and 6,12-benzo[*a*]pyrenediones (**14**) as oxygenated products in 25% yield. The mixture of the diones **14** showed a strong parent peak at *m*/*z* 282 in its mass spectrum (MS). Repeated preparative thin-layer chromatography (TLC) of **14** allowed isolation of the respective isomeric diones in a pure state, and their characteristic UV-absorption spectra are similar to those of the products obtained by electrochemical oxidation of **7**.[18] The formation of **14** apparently arises from the further photooxidation of 6-hydroxybenzo[*a*]pyrene (**15**) initially formed by **1** and to some extent by autoxidation. Facile oxidation of **15** leading to **14** has been well documented.[19]

A previous report[20] has shown that the photooxygenation of **7** by pyridine *N*-oxide results in the formation of 3-, 7-, and 9-hydroxybenzo[*a*]pyrenes. In the present photooxygenation, these oxidized products were not detected.

The formation of polymeric products of **6** and **7** in single-electron oxidation has been reported.[18,21] In the photooxygenation of **6** and **7** by **1**, some unidentified polymeric products were also produced.

Discussion

As previously reported,[8] benzene undergoes photochemical oxygenation by **1** to give phenol, and the mechanism of this reaction can be reasonably explained in terms of an initial SET from benzene to singlet-excited **1** followed by oxygen-atom transfer *via* coupling of the resulting radical-ions.

The present substrates **4**, **5**, **6**, and **7** possess lower oxidation potentials[22] (see Fig. 3) than that of benzene ($E^{\mathrm{ox}}_{1/2}=2.68$ V *vs.* SCE). Thus, the photooxygenation of these PAHs by **1** should occur through an initial SET process to give the corresponding radical cations.[23]

In the photooxygenations of **4** by **1** and **3**, there is some difference in the regioselectivity (1- and 2-isomeric ratio in **8**, 7/1 for **1**; 4/1 for **3**) and a distinct contrast in the substrate-concentration dependence of the *N*-oxide consumption (see Figs. 1a and b). In particular, the latter observation strongly supports the view that the photooxygenation by **1** proceeds by a different mechanism from that of **3** (the oxene mechanism).

Contrary to the case of **3**, a ground-state CT interaction between **1** and **4** (CT band: 405 nm, $\varepsilon=10$) was observed. The wavelength-dependence experiment (Fig. 2) showed the importance of CT-band excitation in the photooxygenation of **4** by **1**. Thus, the SET in the photoreaction of **4** with **1** can be considered to occur to a large extent in the excited CT complex.

The formation of CT-complexes between the other PAHs **5**—**7** and **1** in the ground state was also apparent from the UV-visible absorption spectra [CT band (ε): 405 (16) nm for **5**; 405 (50) nm for **6**; 415 (400) nm for **7**].

The photooxygenation of **5** by **1** exclusively gave **10** and its further oxidation products **11** and **12**, in contrast to the case with **3** as an oxidant. High regioselectivity was also observed in the photooxygenation of **6** and **7** by **1**.

The positions of oxygen-atom transfer from **1** into the PAHs are consistent with the most reactive sites proposed for the corresponding radical cations $4^{+\cdot}$,[24] $5^{+\cdot}$,[25] $6^{+\cdot}$,[24] and $7^{+\cdot}$[19,26] generated from the parent PAHs (see Chart 3).

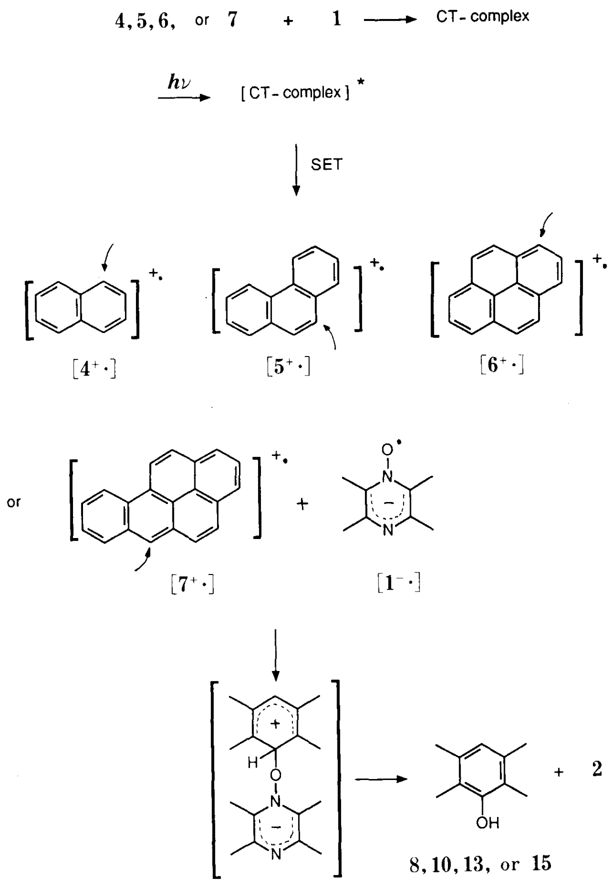


Chart 3

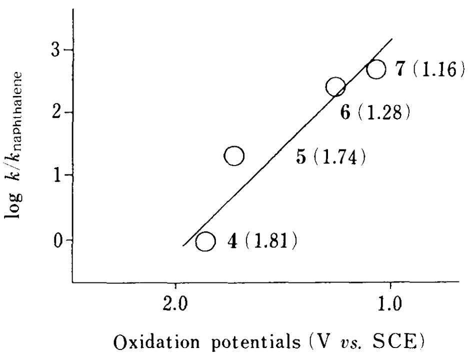


Fig. 3. Correlation between the Relative Consumption Rates (log $k/k_{\mathrm{naphthalene}}$) of Pyrimido[5,4-*g*]pteridine *N*-Oxide (**1**) in the Photoreactions of **1** with the PAHs **4**—**7** and Oxidation Potentials ($E^{\mathrm{ox}}_{1/2}$) of the PAHs

Reaction conditions: a mixture of **1** (5.0 mM) and **4**—**7** (5.0 mM) in dry acetonitrile was irradiated for 40 min. The oxidation potentials of the PAHs are shown in parenthesis (*cf.* ref. 22).

Consumption rates of **1** in the photoreaction with the PAHs correlate well with the oxidation potentials of the respective PAHs as shown in Fig. 3. This also provides evidence supporting the involvement of an initial SET process in the photooxygenation of the PAHs by **1** as depicted in Chart 3. The reaction sequence for oxygen-atom transfer between the radical-ion pair is analogous to that of the photooxygenation of benzene by **1** as previously reported.[8]

1-Hydroxypyrene (**13**) has been identified as a major metabolite of **6**.[17] Thus, the formation of **13** in the present photooxygenation mimics the biological transformation of **6**.

Carcinogenesis by **7** can be understood in terms of metabolic activation involving two main pathways: single-electron oxidation of **7** to give a reactive cation-radical species $\mathbf{7}^{+\cdot}$[26,27] and the monooxygenation of **7** leading to the bay-region diol epoxide.[28] Both oxidations play a significant role in binding of **7** with cellular nucleophiles.[26–29] It has been demonstrated that peroxidases catalyze the single-electron oxidation of **7**,[27] whereas cytochrome P-450 catalyzes both the single-electron oxidation and the monooxygenation.[29] The occurrence of an initial SET from **7** to **1** to generate $\mathbf{7}^{+\cdot}$ thus mimics one of the enzymatic activation pathways of **7** involved in carcinogenesis.[30]

Conclusion

The radical cations of the PAHs, $\mathbf{4}^{+\cdot}$, $\mathbf{5}^{+\cdot}$, $\mathbf{6}^{+\cdot}$, and $\mathbf{7}^{+\cdot}$, are generated electrochemically[18] and chemically,[24–26] and their chemistry has been extensively studied. The generation of these PAH radical-cations by heterocyclic *N*-oxides under photochemical conditions, however, is unprecedented. The photooxygenation of the PAHs **4**—**7** by **1** is consistent with previous observations in the radical-cation chemistry of the PAHs and further demonstrates that **1** functions as an electron acceptor and an efficient oxygen-atom transfer agent under photochemical conditions. The experimental results show that the PAHs with low oxidation potentials undergo single-electron oxidation by **1** *via* the formation of the excited CT complex, in a manner different from the case of benzene. The photochemical oxygenation of the PAHs by **1** does not involve the oxene mechanism proposed for the heterocyclic *N*-oxides previously examined and mechanistically parallels the hemin-catalyzed biological oxygenation with respect to the involvement of the initial SET process. The present result is of interest in connection with metabolic activation of carcinogenic aromatic hydrocarbons such as **7**.

Experimental

Irradiation was carried out at ambient temperature under an argon atmosphere by using a 400W high-pressure mercury arc lamp (Riko Kagaku Sangyo) through a $BiCl_3$ solution filter (>355 nm, for **1**) or a Pyrex filter (for **3**). A grating monochromator (JASCO CRM-FA spectroirradiator with a 2 kW Xe lamp and 4 nm band-width) was used for the wavelength-dependence experiment. The spectroscopic measurements were performed with the following instruments: UV-absorption spectra with a Shimadzu 260 spectrophotometer; ^{1}H-NMR spectra with a JEOL JNX-270 (270 MHz) spectrometer using tetramethylsilane as an internal standard; MS with a JEOL JMS D-300 machine operating at 70 eV. Gas chromatographic analyses were performed with a Shimadzu GC-8APF instrument with 1.2 m column (polyethylene glycol, 5% on Uniport HP). TLC for the assay of **1** and **2** was performed on Silica gel 60 plates (Merck, art 5715) by using benzene–ethyl acetate (5 : 2) as an eluent and TLC-scanning was carried out with a Shimadzu CS-9000 dual-wavelength flying-spot scanner (detection, 370 nm for **1** and **2**). Column chromatographic and preparative TLC separation were accomplished by using silica gel (Wakogel C-300 or Merck Art 5717).

Photochemical Oxidation of Naphthalene (4), Phenanthrene (5), Pyrene (6), and Benzo[*a*]pyrene (7) by 1,3,6,8-Tetrabutylpyrimido[5,4-*g*]pteridine-2,4,5,7(1*H*,3*H*,6*H*,8*H*)-tetrone 10-Oxide (1) Photoreaction of **4** with **1**: A solution of **4** (12.8 g, 0.1 mol) and **1** (488 mg, 1.0 mmol) in dry acetonitrile (200 ml) was irradiated externally through a $BiCl_3$ solution filter. The reaction mixture was sampled every 10 min for 40 min. TLC and GC analyses of the samples showed a smooth consumption of **1** (by TLC densitometry, *Rf* 0.27) and the formation of pyrimido[5,4-*g*]pteridine (**2**) (*Rf* 0.35) and naphthols (**8**) (1-/2-isomers = 7/1, by GC). The consumed *N*-oxide **1** was converted almost quantitatively into **2**. The conversion yields of **8** based on the consumed **1** were as follows. Yields (irradiation time): 71% (10 min), 59% (20 min), 47% (30 min), and 30% (40 min).

The irradiation was stopped after 40 min and the mixture was evaporated to dryness under reduced pressure. The resulting residue was subjected to column chromatography (eluent, *n*-hexane and then benzene) to isolate **8** (40 mg, 28% yield based on the consumed **1**) and 1,4-naphthoquinone (**9**) (10 mg, 6%). The structures of the oxygenated products **8** and **9** were confirmed by comparison of their GC-retention times and GC-MS spectral data with those of authentic samples, which are commercially available.

Photoreaction of **5** with **1**: A solution of **5** (3.564 g, 20.0 mmol) and **1** (488 mg, 1.0 mmol) in dry acetonitrile (200 ml) was irradiated externally for 40 min under conditions analogous to those employed in the foregoing case. The assay of the reaction mixture by TLC densitometry showed the complete consumption of **1** and its almost quantitative conversion into **2**. After removal of the solvent, the residue was subjected to column chromatography (eluent, *n*-hexane–benzene (5 : 2) and then benzene) to isolate 9-phenanthrol (**10**) (41 mg, 21% yield based on the employed **1**), bis(9-hydroxyphenanthren-10-yl) (**11**) (46 mg, 12%),[14] and 9,10-phenanthrenedione (**12**) (40 mg, 19%).[15] The structures of these products were confirmed by examination of the MS and by comparison of the ^{1}H-NMR spectra with those of authentic samples prepared from **10** by treatment with ferric chloride or by autoxidation.[14,15]

Photoreaction of **6** with **1**: Under analogous conditions to those described above a solution of **6** (404 mg, 2.0 mmol) and **1** (488 mg, 1.0 mmol) in dry acetonitrile (200 ml) was irradiated externally until disappearance of **1** (monitored by TLC) was complete (1 h). After removal of the solvent, the resulting residue was subjected to column chromatography (eluent, benzene) to isolate 1-hydroxypyrene (**13**) (120 mg, 55% yield based on the employed **1**) and a trace amount of undetermined products. The structure of **13** was confirmed by comparison of the UV and ^{1}H-NMR spectra with those of the authentic compound previously reported.[17] In this reaction a faint colouring of the solution and the formation of a thin film on the surface of the filter were observed, indicating the occurrence of polymerization of **6** during the reaction.

Photoreaction of **7** with **1**: A solution of **7** (378 mg, 1.5 mmol) and **1** (488 mg, 1.0 mmol) in dry acetonitrile (200 ml) was irradiated for 40 min under the conditions used for the photooxygenation of **4**. The assay of the reaction mixture by TLC densitometry showed the complete consumption of **1** and the formation of **2**. After removal of the solvent, the residue was chromatographed by using benzene as an eluent to isolate benzo[*a*]pyrenediones (**14**) (71 mg, 25% yield based on the employed **1**) as an inseparable mixture of 1,6-, 3,6-, and 6,12-isomers. The ratio of these isomers could not be determined by GC and TLC analyses or from the ^{1}H-NMR spectrum because of the similar retention times and *Rf*-values, and the complexity of the spectrum. The MS of the product showed a strong peak at 282 (M^+ of **14**, relative intensity = 100), together with weak peaks at 254 (M^+-28, 38) and 226 (M^+-56, 26).[19] Repeated chromatographic separation (preparative TLC) of **14** by using ethyl ether–*n*-hexane (1 : 1) as an eluent allowed isolation of the respective isomers in a pure state. The structures of these three isomeric benzo[*a*]pyrenediones were all assigned by comparison of the UV and ^{1}H-NMR spectra with reported data.[18] In this reaction the formation of polymeric products of **7** was observed on the surface of the filter as a dark-colored thin film.

Photochemical Oxidation of 4 and 5 by 3-Methylpyridazine 2-Oxide (3) Photoreaction of **4** with **3**: A solution of **4** (320 mg, 2.5 mmol) in dry acetonitrile (5.0 ml) containing **3** (2.7 mg, 0.025 mmol) was irradiated externally through a Pyrex filter for 20 min under an argon atmosphere. GC analysis of the reaction mixture showed the complete consumption of **3** and the formation of **8** (25% yield based on the employed **3**, 1-/2-isomers = 4/1) and 3-methylpyridazine (40%) together with some unidentified products originated from **3**.

Photoreaction of **5** with **3**: Under analogous conditions to those described above a solution of **5** (3.564 g, 20.0 mmol) and **3** (110 mg, 1.0 mmol) in dry acetonitrile (200 ml) was irradiated for 20 min. The assay of the reaction mixture by GC showed the complete consumption of **3**. After removal of the solvent, the residue was subjected to column chromatography (eluent, *n*-hexane–benzene (5 : 2) and then benzene) to isolate 4-phenanthrol (10 mg, 5% yield based on the employed **3**) together with **10** (31 mg, 16%), **11** (12 mg, 3%), and **12** (17 mg, 8%). The structure of the product, 4-phenanthrol, was assigned on the basis of the MS and ^{1}H-NMR spectral data: m/z: 194 (M^+), 166, and 165, ^{1}H-NMR ($CDCl_3$) δ: 5.87 (1H, br s), 6.99 (1H, dd, $J=8$, 1 Hz), 7.42 (1H, t, $J=8$ Hz), 7.51 (1H, dd, $J=8$, 1 Hz), 7.55—7.68 (2H, m) 7.69 (1H, d, $J=8$ Hz), 7.73 (1H, d, $J=8$ Hz), 7.88 (1H, dd, $J=8$, 1 Hz), and 9.64 (1H, dd, $J=8$, 1 Hz) and by comparison of its UV and infrared (IR) spectra with reported data.[16)]

Wavelength-Dependence Experiment for the Photochemical Oxygenation of 4 by 1 A solution of **4** (500 mmol) and **1** (5.0 mmol) in dry acetonitrile was degassed carefully and irradiated at various wavelengths (329—460 nm, *ca.* 5.4×10^8 erg/cm^2) for 10 min. The yields of **8** were determined by GC analysis. The results were as follows. Yields of **8** (wavelength, nm): 2.4% (328), 3.2% (354), 4.4% (381), 6.9% (407), 6.3% (433), and 1.8% (460).

Charge-Transfer Interaction between the PAHs and 1 The CT complex formation between the PAHs **4**—**7** and **1** was apparent in the difference UV-visible absorption spectra of mixtures of **1** (5.0 mmol) and the PAHs (10 mmol) *vs.* **1** (UV, λ_{max}: 370 nm) (5.0 mmol) for **4**—**6** or **7** (UV, λ_{max}: 402 nm) (10 mmol) for **7** in dry acetonitrile. The observed CT bands are presented under Discussion.

Photooxygenation of 4 by 1 in the Presence of $H_2{}^{18}O$ ^{18}O-Labeled water (^{18}O content = 99%) (500 mmol) was added to a solution of **4** (500 mmol) and **1** (5.0 mmol) in dry acetonitrile, and the mixture was irradiated for 40 min under the conditions described above. TLC and GC analyses of the reaction mixture showed the complete consumption of **1** and the formation of **8** in 30% yield. The absence of incorporation of labeled oxygen into the product **8** was confirmed by GC-MS analysis.

Concentration-Dependence Experiment for the Photooxygenation of 4 by the *N*-Oxide 1 or 3 A solution of **1** (5.0 mmol) in dry acetonitrile was irradiated in the absence or presence of **4** (50 or 500 mmol) through a $BiCl_3$ solution filter. Under analogous conditions (through a Pyrex filter) the photoreaction of **3** with or without **4** was carried out. The consumption yields of these *N*-oxides **1** and **3** were determined by TLC densitometry (for **1**) or GC analysis (for **3**) and are plotted as a function of irradiation time in Fig. 1 (see Figs. 1a and b).

Measurement of Relative Consumption Rates of 1 in the Photoreaction with the PAHs A mixture of an equimolar amount of **1** and the PAHs **4**—**7** (5.0 mM) in dry acetonitrile was irradiated externally under argon through a $BiCl_3$ solution filter. Consumption of **1** in this reaction was followed spectrophotometrically with a TLC scanner and its rate constants were calculated by plotting A_t/A_0 *vs.* time (A_0 = the initial peak area of **1**, A_t = the peak area of **1** after irradiation for t min). The relative consumption rates ($\log k/k_{\text{naphthalene}}$) of **1** based on the case of **4** are plotted in Fig. 3 as a function of the oxidation potentials ($E^{ox}_{1/2}$, V *vs.* SCE) of the PAHs employed.

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References and Notes

1) M. Sako, K. Shimada, K. Hirota, and Y. Maki, *Tetrahedron Lett.*, **26**, 6493 (1985); *idem*, *J. Am. Chem. Soc.*, **108**, 6039 (1986); *idem*, *Tetrahedron Lett.*, **27**, 3877 (1986); *idem*, *J. Chem. Soc., Chem. Commun.*, **1986**, 1704; K. Shimada, M. Sako, K. Hirota, and Y. Maki, *Tetrahedron Lett.*, **28**, 207 (1987); Y. Maki, K. Shimada, M. Sako, and K. Hirota, *Tetrahedron*, **44**, 3187 (1988); Y. Maki, K. Shimada, M. Sako, Y. Kitade, and K. Hirota, *Chem. Pharm. Bull.*, **36**, 1714 (1988).

2) Y. Maki, M. Sako, and E. C. Taylor, *Tetrahedron Lett.*, **1971**, 4271; E. C. Taylor, Y. Maki, and A. McKillop, *J. Org. Chem.*, **37**, 1601 (1972).

3) For a recent review on the photochemistry of the heterocyclic *N*-oxides, see A. Albini and M. Alpegiani, *Chem. Rev.*, **84**, 43 (1984).

4) H. Igeta, T. Tsuchiya, M. Yamada, and H. Arai, *Chem. Pharm. Bull.*, **16**, 767 (1968); T. Tsuchiya, H. Arai, and H. Igeta, *Tetrahedron Lett.*, **1969**, 2747.

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

6) H. Strub, C. Strehler, and J. Streith, *Chem. Ber.*, **120** 355 (1987).

7) For the radical mechanism, see W. H. Rastetter, T. R. Gadek, J. P. Tane, and J. W. Frost, *J. Am. Chem. Soc.*, **101**, 2228 (1979); H. J. Xu, S. O. Lin, S. Y. Shen, and L. Li, *J. Photochem. Photobiol.*, **48**, 53 (1989).

8) M. Sako, S. Ohara, K. Shimada, K. Hirota, and Y. Maki, *J. Chem. Soc., Perkin Trans. 1*, **1990**, 863.

9) For example, see F. P. Guengerich and T. L. Macdonald, *Acc. Chem. Res.*, **17**, 9 (1984); T. G. Traylor and F. Xu, *J. Am. Chem. Soc.*, **110**, 1953 (1988); J. T. Groves and M. K. Stern, *ibid.*, **110**, 8628 (1988); D. Dolphin, A. Matsumoto, and C. Shortman, *ibid.*, **111**, 411 (1989); P. Ostovic and T. C. Bruice, *ibid.*, **111**, 6511 (1989).

10) Details of the photochemical oxidation of phenols by the *N*-oxide **1** including its mechanism will be discussed in a forthcoming paper.

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

12) Igeta *et al.* have reported that **4** is photooxygenated by **3** in methylene chloride to give **8** (1-/2-isomers = 5/4) in 20—30% yield. See ref. 4.

13) Y. Maki, M. Sako, T. Murase, Y. Kitade, and K. Hirota, *Heterocycles*, **30**, 279 (1990).

14) F. Toda, K. Tanaka, and S. Iwata, *J. Org. Chem.*, **54**, 3007 (1989).

15) T.-L. Ho, T.-W. Hall, and C. M. Wong, *Synthesis*, **1973**, 206.

16) E. Mosettig and A. Burger, *J. Am. Chem. Soc.*, **57**, 2189 (1935); T. Horaguchi, *Bull. Chem. Soc. Jpn.*, **50**, 3329 (1977).

17) J. Jacob, G. Grimmer, G. Raab, and A. Schmoldt, *Xenobiotica*, **12**, 45 (1982); S. D. Keimig, K. W. Kirby, D. P. Morgan, J. E. Keiser, and T. D. Hubert, *ibid.*, **13**, 415 (1983).

18) L. Jeftic and R. N. Adams, *J. Am. Chem. Soc.*, **92**, 1332 (1970).

19) W. Caspary, B. Cohen, S. Lesko, and P. O. P. Ts'o, *Biochemistry*, **12**, 2649 (1973); R. J. Lorentzen, W. J. Caspary, S. A. Lesko, and P. O. P. Ts'o, *ibid.*, **14**, 3970 (1975); E. Lee-Ruff, H. Kazarians-Moghaddam, and M. Katz, *Can. J. Chem.*, **64**, 1297 (1986); G. Balanikas, N. Hussain, S. Amin, and S. S. Hecht, *J. Org. Chem.*, **53**, 1007 (1988).

20) B. Sergeev, M. Gubergrits, and V. Koblyakov, *Eesti NSV Tead. Akad. Toim., Keem.*, **28**, 278 (1979) [*Chem. Abstr.*, **92**, 93661*d* (1980)].

21) M. Wilk, W. Bez, and J. Rochlitz, *Tetrahedron*, **22**, 2599 (1966); A. C. Buchanan, III, A. S. Dworkin, and G. P. Smith, *J. Am. Chem. Soc.*, **102**, 5262 (1980).

22) T. Kubota, B. Uno, T. Kawakita, and M. Goto, *Bull. Chem. Soc. Jpn.*, **63**, 516 (1990).

23) In general, any organic molecule with an $E_{1/2}$ for oxidation of 2.2 V or less (*vs.* SCE) can be predicted to be susceptible to oxidation *via* a photo-induced SET process (*cf.* P. G. Gassman and K. J. Bottorff, *J. Am. Chem. Soc.*, **109**, 7547 (1987) and references cited therein).

24) A. C. Buchanan, III, R. Livingston, A. S. Dworkin, and G. P. Smith, *J. Phys. Chem.*, **84**, 423 (1980); M. Morita, K. Hirosawa, T. Sato, and K. Ouchi, *Bull. Chem. Soc. Jpn.*, **53**, 3013 (1980).

25) J. L. Courtneidge, A. G. Davies, and P. S. Gregory, *J. Chem. Soc., Perkin Trans. 2*, **1987**, 1527.

26) P. Cremonesi, E. L. Cavalieri, and E. G. Rogan, *J. Org. Chem.*, **54**, 3561 (1989) and references cited therein.

27) E. L. Cavalieri and E. G. Rogan, "Free Radicals in Biology," Vol. 6, ed. by W. A. Pryor, Academic Press, N.Y., 1984, p. 323; E. G. Rogan, E. L. Cavalieri, S. R. Tibbels, P. Cremonesi, C. D. Warner, D. L. Nagel, K. B. Tomer, R. L. Cerny, and M. L. Gross, *J. Am. Chem. Soc.*, **110**, 4023 (1988) and references cited therein.

28) E. C. Millor and T. A. Millor, *Cancer*, **43**, 2327 (1981); S. K. Balani, J. M. Sayer, and D. M. Jerina, *J. Am. Chem. Soc.*, **111**, 3290 (1989); D. R. Bushman, S. J. Grossman, D. M. Jerina, and R. E. Lehr, *J. Org. Chem.*, **54**, 3533 (1989) and references cited therein.

29) P. Sims and P. L. Grover, "Polycyclic Hydrocarbons and Cancer," Vol. 3, ed. by H. V. Gelboin and P. O. P. Ts'o, Academic Press, New York, 1981, p. 117; P. R. Ortiz de Montellano, "Cytochrome P-450, Structure, Mechanism, and Biochemistry," Plenum Press, New York, 1986.

30) G. Holder, H. Yagi, P. Dansette, D. M. Jerina, W. Levin, A. Y. H. Lu, and A. H. Conney, *Proc. Nat. Acad. Sci. U.S.A.*, **71**, 4356 (1974); L. J. Marnett and G. A. Reed, *Biochemistry*, **18**, 2923 (1979).