Electrophilic Substitution of 3,4-Dihydrocyclopenta[*cd*]pyrene and the 3-Ketone

Masahiro MINABE,* Ryuuji NISHIMURA, Takao KIMURA, and Motohiro TSUBOTA
Department of Applied Chemistry, Faculty of Engineering, Utsunomiya University, Ishiicho, Utsunomiya 321
(Received November 12, 1992)

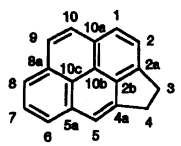
Brominaton of 3,4-dihydrocyclopenta[*cd*]pyrene (**1**) with bromine yielded predominantly the corresponding 8-bromide; on the other hand, a similar reaction of cyclopenta[*cd*]pyren-3(4*H*)-one (**2**) afforded the 4-bromide. The Friedel–Crafts acetylations of **1** and **2** with acetyl chloride in the presence of aluminum chloride occurred at sites 8, 6, and 1. The isomeric distribution in the acetylation of **1** was similar to that of **2**. The relative reactivity of **2** with 1-acetylpyrene in acetylation was 0.75. The partial rate factor of site 1 of **1** was less than that of the corresponding position of 1-acetylpyrene, in spite of the fact that sites 6 and 8 of **1** were more reactive than the corresponding positions of 1-acetylpyrene. Nitration of **2** using acetyl nitrate in acetic anhydride took place at positions similar to the case of the acetylation of **2**; however, the nitration of **1** gave the 5-nitro derivative in addition to the 8, 6, and 1-isomers.

Some polycyclic aromatic hydrocarbons (PAHs) having a pyrene moiety are widespread environmental pollutants that are contained in exhaust gas,[1] soot,[2] and other sources.[3] Some of them are mutagens[4,5] and/or carcinogens.[6] These facts focus considerably on current studies concerning the synthesis, electrophilic reactivity, and spectroscopic examination of PAHs having a pyrene moiety such as alkylpyrenes, nitropyrenes, ring-annulated compounds, and alkylene-bridged derivatives.

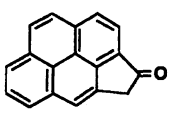
An electrophilic attack on pyrene is known to usually occur at site 1, based both on the experimental results[7] and on the consideration of a calculation.[8] The reaction of 1-substituted pyrenes usually takes place at the 3-, 6-, and 8-positions.[9,10]

3,4-Dihydrocyclopenta[*cd*]pyrene (**1**)[11] and cyclopenta[*cd*]pyren-3(4*H*)-one (**2**)[12] are detected as environmental contaminations; these are considered as 3,4-disubstituted pyrenes bearing ethylene and 1-oxoethylene bridges, respectively. However, the electrophilic substitutions of **1** and **2** have not been well-documented, in spite of an intriguing possibility that the presence of the distorted benzene rings on these PAHs may considerably alter the reactivities, compared to the parent hydrocarbon pyrene.[13] Hydrocarbon **1** gave the 6- and 8-derivatives by both electrophilic nitration[14] and the Vilsmeier reaction.[15] Some of the methyl-substituted derivatives of **1** have been synthesized from the derivatives of **2** (Scheme 1).[16]

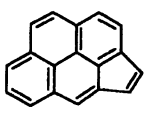
Cyclopenta[*cd*]pyrene (**3**), or 3,4-vinylenepyrene, is both a mutagen[4,5] and a carcinogen.[6] The reaction of **3** with an electrophile has not been reported, except for the reaction of **3** with nitric acid in acetic anhydride, which resulted in an extensive decomposition of **3**.[17]



1



2



3

Scheme 1.

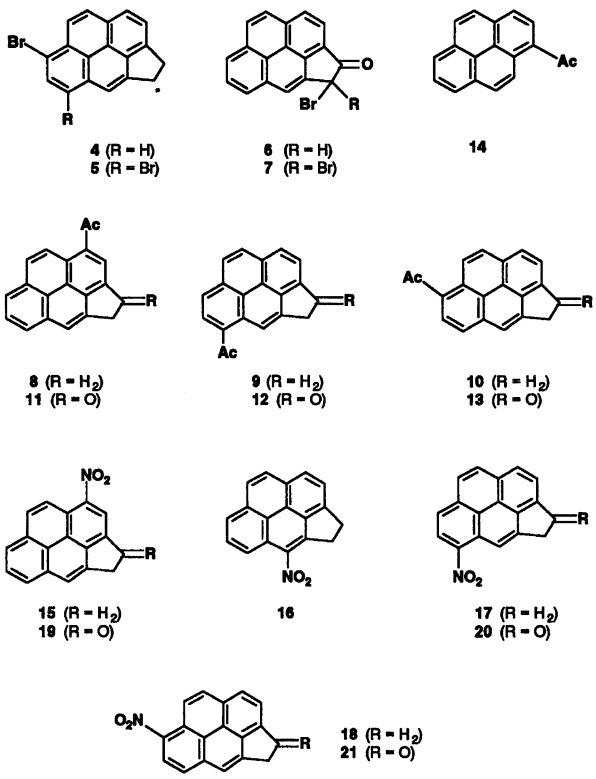
The reactions of **1** and **2** with electrophiles have been studied as part of a continuous program to investigate the syntheses and reactions of PAHs, in order to obtain further information regarding the reactivities of **1** and **2**. The results described herein may contribute to our understanding of the reactivities of disubstituted pyrenes as well as the environmental pollutant **3**.

Results

Bromination of **1** with bromine gave predominantly the 8-bromide (**4**) (Scheme 2) accompanied by a small amount of the 6,8-dibromo derivative (**5**), as is summarized in Table 1. The reaction of **2** with bromine afforded the 4-bromide (**6**) and 4,4-dibromide (**7**). The yield of **7** increased with increased reaction temperature and also increased in acetic acid. Bromides **6** and **7** were unstable; for example, ca. 59% of **7** was decomposed by allowing a solution of **7** in dichloromethane to stand for 1 d at room temperature.

The Friedel–Crafts acetylation of **1** with acetyl chloride in the presence of aluminum chloride afforded three isomers; namely, 1-acetyl- (**8**), 6-acetyl- (**9**), and 8-acetyl-3,4-dihydrocyclopenta[*cd*]pyrene (**10**). Isolation of pure **8** was not possible, since **8** could not be separated by HPLC from the major product **10**; the amount of **8** was then estimated by a comparison of the ^{1}H NMR signals of a mixture of **8** and **10**. Acetylation of **2** gave the 1-acetyl (**11**), 6-acetyl (**12**), and 8-acetyl isomers (**13**). The isomeric distribution of products from **2** (**11** : **12** : **13**=9 : 31 : 61) was similar to that observed from the same reaction of **1** (**8** : **9** : **10**=7 : 30 : 63). The relative reactivity between **2** and 1-acetylpyrene (**14**) was found to be 1.00 : 1.34 by a competitive method. The same ratio between **2** and **1** was found to be 1.00 : 4.23.

Nitration of **1** with acetyl nitrate yielded four compounds, namely 1-nitro- (**15**), 5-nitro- (**16**), 6-nitro- (**17**),[14] and 8-nitro-3,4-dihydrocyclopenta[*cd*]pyrene (**18**).[14] The isolation of pure **15** failed, and the amount of **15** was calculated from the ^{1}H NMR spectrum of



Scheme 2.

Table 1. Electrophilic Substitutions of **1** and **2**

Compd.	Reaction conditions[a]	Yield of each site [b]/%				
		1-	4-	5-	6-	8-
1	Br_2(1.1), Fe					88[+4]
	AcOH, 20 °C, 5 h					(100)
1	AcCl (2.8), $AlCl_3$(1.6)	6			27	56
	CH_2Cl_2, r.t., 5.5 h	(7)			(30)	(63)
1	$AcONO_2$ (1.9)	10		12	32	35
	Ac_2O, 0 °C, 3.5 h	(11)		(13)	(36)	(40)
1	HNO_3 (1.9)	3		4	43	50
	AcOH, 0 °C, 0.25 h	(3)		(4)	(43)	(50)
2	Br_2 (1.1)		57[+7]			
	CH_2Cl_2, 0 °C, 2 h		(100)			
2	Br_2 (1.1)		64[+21]			
	AcOH, 20 °C, 3 h		(100)			
2	AcCl (28), $AlCl_3$ (15)	8			28	53
	CH_2Cl_2, 40°C, 8 h	(9)			(31)	(61)
2	$AcONO_2$ (4.8)	16			35	41
	Ac_2O, r.t., 3 h	(17)			(38)	(45)
2	$AcONO_2$ (1.9)	17			29	34
	Ac_2O, 40 °C, 2 h	(21)			(36)	(43)

a) (): Molar ratio of reagent vs. substrate. b) []: Additional yield of dibromide. (): Isomer distribution of products.

the mixture. Although the reaction of **1** with nitric acid gave the same four products, the isomeric distribution of products (**15** : **16** : **17** : **18**=3 : 4 : 43 : 50) was somewhat different from that with acetyl nitrate (11 : 13 : 36 : 40). Nitration of **2** afforded the 1-nitro (**19**), 6-nitro (**20**), and 8-nitro derivatives (**21**), but not the 5-isomer. The ratio of the yield of **20** against that of **21** (**20** : **21**=38—36 : 45—43) was similar to that between **17** and **18** (36 : 40). The yield of **19** (17—21%) was roughly equal to the combined yield of **15** and **16** (total 24%). Competitive nitration showed that the relative reactivity between **2** and **14** was 1.00 : 1.87 and that between **2** and **1** was 1.00 : 25.8.

The assignment of signals in the ^1H and ^{13}C NMR spectra of the reaction products was facilitated by 2D NMR techniques, which included normal and long-range COSY and hetero-COSY procedures. The ^{13}C NMR spectra of **4** and **9**—**13** are summarized in Table 2.

Discussion

The structures of the reaction products were determined by comparing their spectral data with those of the parent compounds. In the IR spectra, the carbonyl absorption of **2** shifts reasonably to a higher wavenumber by substitution of a bromine atom at the C-4 position (ca. 11 cm^{-1} per one bromine atom).

In the ^1H NMR spectra (see Experimental section), the protons ortho to the bromine, acetyl, or nitro group resonate at lower fields ($\Delta\delta$=+0.21, +0.39 to +0.50, or +0.67 to +0.79, respectively) than do the corresponding protons of the parent compounds.[18] Similar low field shifts were observed on the protons peri to the bromo ($\Delta\delta$=+0.3), acetyl (+0.97 to +1.16), and nitro substituents (+0.79 to +1.02). The $^3J_{H-H}$ coupling constants ortho and peri to the acetyl or nitro group are larger (ΔJ=0.4—0.5 Hz) than that of the parent compounds. In the ^{13}C NMR spectra, the carbons which bear the bromine or acetyl group resonate at lower fields ($\Delta\delta$=+5.2, +6.7 to +7.4, respectively) than do the corresponding carbons of the parent materials. These findings are very similar to the case of the indeno[1,2,3-*cd*]pyrene derivatives[19,20] and are useful when considering the spectral analysis of substituted PAHs.

The nitration of **1** has been reported to give **17** and **18** in a ratio of 51 : 49.[14] The present experiment shows that the reaction of **1** gives four components. The product selectivity of nitration increases when nitric acid is used in acetic acid. On the other hand, bromination of **1** occurs predominantly at the C-8 position, giving **4**. The selectivity in acetylation of **1** is higher than that of nitration, and lower than that of bromination. This suggests that the product selectivity in electrophilic substitution of **1** is in accord with the reaction constant (ρ^+) of each reaction.

Bromination of **2** occurs predominantly at C-4, giving **6** and **7**. This is explained by saying that the reaction proceeds through a contribution of the corresponding enolate tautomer, as is the case regarding the bromination of **14**.[21] Therefore, one possibility concerning the reaction sequences in acetylation and nitration of **2** is that the formation of the corresponding enolate form (that is, enol acetate and enol nitrate, respectively), the

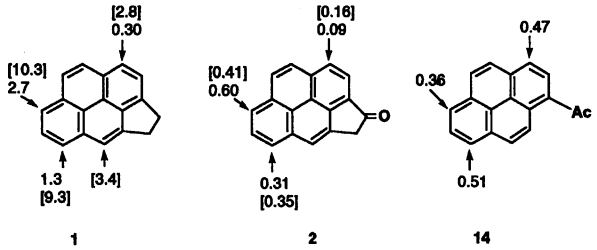
Table 2. ^{13}C NMR Spectra of **1**, **2**, Bromide **4**, and Acetyl Compds., **9**—**13**

Site	Chemical shift (δ/ppm)							
	1	**2**	**4**	**9**	**10**	**11**	**12**	**13**
1	124.8	125.6	125.3	126.4	126.0	132.1	126.9	126.5
2	121.4	120.6	122.0	122.0	122.0	122.2	121.1	120.9
2a	141.9	130.1	142.7	143.7	143.6	128.6	131.0	131.0
2b	136.5	144.4	136.4	135.7	136.3	145.7	143.3	144.1
3	31.7	202.2	31.7	31.7	31.7	201.4	201.9	201.4
4	30.4	42.2	30.7	30.9	30.4	41.9	42.4	41.8
4a	144.8	133.5	145.1	147.8	147.6	132.8	136.0	135.8
5	118.4	121.5	118.2	116.7	118.3	123.7	119.6	121.1
5a	133.4	131.8	132.8	132.0	136.7	131.4	130.0	134.6
6	123.8	127.2	124.4	130.6	122.7	128.4	134.6	126.1
7	126.0	126.9	129.7	127.7	128.0	127.3	127.7	128.2
8	122.7	125.6	117.5	121.7	129.1	126.6	124.7	131.9
8a	131.1	130.6	129.6	134.2	129.7	129.8	133.2	128.7
9	126.8	130.9	125.2	126.4	124.8	132.8	130.6	128.9
10	126.1	126.1	127.6	128.3	128.5	125.1	128.1	128.1
10a	128.1	134.3	127.9	128.1	127.6	132.6	134.1	133.5
10b	122.2	121.3	121.2	121.7	121.7	121.5	121.2	120.8
10c	123.6	122.7	124.8	123.9	123.8	122.1	123.2	123.0
Me	—	—	—	30.3	29.9	29.8	30.4	30.1
–CO–	—	—	—	202.1	201.4	200.8	202.1	201.3

substitution reaction of the enol form, and the decomposition of the products giving the corresponding keto forms during the reaction and/or separation procedure. However, no evidence has been detected regarding these intermediate products.

Although the reactivity of **2** is less than that of **1**, it is interesting that the regioselectivity observed for the acetylation and nitration of **2** is similar to that observed for **1**. Thus, the effect of the electron-withdrawing carbonyl group of **2** on the regioselectivity does not differ from that of the electron-releasing methylene group of **1**, except that the former retards the reaction rate. A similar tendency is recognized in the acetylation of **14**, 1-ethyl-, and 1-bromopyrene.[9,20] These observations may be ascribable to the fact that the electron density on the rings is decreased by the electron-attractive carbonyl group. However, the decrease in electrons on the rings is relatively small in the large PAHs which have abundant π-electrons. The electron-releasing methylene group acts in the opposite way. Consequently, the regioselectivity of **2** is similar to that of **1**, and substitution occurs at the most reactive C-1 of the pyrene moiety.[10]

The isomeric distribution of products in the Friedel–Crafts acetylation of **14** was 35 : 27 : 38 for 1,3-diacetyl-, 1,6-diacetyl-, and 1,8-diacetylpyrene, respectively.[22] The partial rate factor (f) of **1**, **2**, and **14** in acetylation (and nitration) is roughly estimated using the value "$f/6K$", where K is the relative reactivity of **2** with benzene, or $K = k_2/k_{PhH}$ (Scheme 3). This value indicates only the ratio of the reactivities between any two positions in one reaction, not the absolute reaction rate; therefore, the value obtained regarding the acetylation of **1** is not correlated to the value observed in the nitration of **1**. Since the reaction mechanism in the acetylation of **1** cannot be shown to be identical to that of **2**, the reaction rate obtained here is the apparent rate of the overall reaction under the stated conditions. Thus, the ratio of the partial rate factor between **1** and **2** is an apparent ratio.



Scheme 3. Ratio of partial rate factors in Friedel–Crafts acetylation. ([]: nitration using $AcONO_2$)

The factors at C-1 and C-6 of **2** are less than those of the correspondent positions (C-3 and C-8, respectively) of **14**; however, f_8 of **2** is larger than f_6 of **14**. Also, C-1 of **1** is less reactive than the corresponding position of **14**. These situations should be due to a distortion of the pyrene skeleton by 1-oxoethylene or an ethylene bridge. These are in some degree explained based on the chemical shift of the ^{13}C NMR spectra. The signals of the reactive positions (C-8, C-6, and C-1) of **1** resonate at 122.7, 123.8, and 124.8 ppm, respectively. Smaller reactivities at the C-2 position (121.4 ppm, gives no substitution product) and C-5 position (118.4 ppm, gives only nitrated product) of **1** may be due a steric factor during the formation of Wheland intermediates.

The electron density at each carbon is calculated using the CNDO/2 (complete neglect of differential overlap) procedure: the density of each carbon is large in the order $C_5 > C_6 > C_8 > C_1$ in **1**, and $C_1 > C_6 = C_8$ in **2**. These findings can hardly explain the experimental results mentioned above.

In conclusion, the reactions of **1** and **2** with electrophiles take place at the positions which correspond to more reactive position of the mother skeleton pyrene. However, the relative reactivities of each position depend on the substrate. The results are useful for assigning the nitro and methyl derivatives of **1** and **2**, which might exist as environmental pollutants.

Experimental

The melting points are uncorrected. The column, Zorbax SIL (Du Pont, 4.6 mm i.d., 15 cm) was used for analytical HPLC (flow rate, 1 ml min^{-1}). The IR spectra (KBr pellets) were recorded with a JASCO IR Report-100. The UV-vis spectra (EtOH) were obtained with a Shimadzu UV-180. The ^{1}H and ^{13}C NMR spectra (0.7 ml $CDCl_3$) were recorded with a Varian VXR-300. The sample used was ca. 2 mg for ^{1}H NMR and 10—30 mg for ^{13}C NMR spectra. The mass spectra were recorded with a Hitachi M-80 equipped with a direct inlet and operated at an ionization voltage of 70 eV.

Materials.[12] 1-(Bromoacetyl)pyrene was obtained either by bromination[21] of **14** (yield 57%) or by the reaction

of pyrene with bromoacetyl bromide in the presence of $AlCl_3$ in CH_2Cl_2 at 0 °C (yield 71%): Mp 127—128 °C (PhH–hexane) (lit,[12] mp 128—129 °C); IR 1660 cm^{-1}; UV λ_{max} 390 (log ε 4.07), 365 (4.25), 286 (4.31), 235 nm (4.61); ^{13}C NMR δ=34.1 (CH_2), 123.8 (C_3), 123.9 (C_{10c}), 124.5 (C_{10}), 124.9 (C_{10b}), 126.4 (C_8), 126.5 (C_7), 126.6 (C_6), 126.7 (C_2), 126.9 (C_4), 128.2 (C_1), 130.1 (C_5), 130.2 (C_9), 130.3 (C_{8a}), 130.5 (C_{10a}), 130.8 (C_{5a}), 134.5 (C_{3a}), 194.5 (CO).

Ketone **2** was synthesized by irradiation with a high-pressure mercury lamp via a Pyrex filter to a solution of the above-mentioned bromo ketone in CCl_4 for 3 h in 43% yield (78% yield by HPLC): Mp 203—205 °C (hexane) (lit, mp[12] 213—214 °C, mp[23] 201—203 °C); IR 1713 cm^{-1}. Hydrocarbon **1** was obtained by a Wolff–Kishner reducton of **2**[18] (97% yield): Mp 133—135 °C (hexane) (lit,[18] mp 134 °C).

Bromination of 1. Bromine (43 mg, 0.27 mmol) in AcOH (2 ml) was added to a mixture of **1** (57 mg, 0.25 mmol) and Fe (10 mg) in AcOH (10 ml) at 20 °C for 1 h. After stirring for an additional 4 h, the mixture was diluted with water. The resulting precipitate was dissolved in CH_2Cl_2, and the CH_2Cl_2 solution was washed with water and dried over Na_2SO_4; the solution was analyzed by HPLC (mobile phase, hexane): **4** (V_R 5.7 ml), **5** (4.6 ml), coronene (11.7 ml, added as an internal reference to the test solution).

The solvent of the solution was evaporated off, and the resulting residue was fractionally recrystallized from hexane to give 29 mg (38%) of **4**: Mp 136—137 °C; IR 3024, 2920, 1643, 1589, 1431, 1411, 1077, 913, 863, 834, 674 cm^{-1}; UV λ_{max} 384 (log ε 3.63), 363 (4.10), 355 (4.47), 338 (4.39), 281 (4.64), 276 (4.37), 246 nm (4.78); ^1H NMR δ=3.57—3.61 (2H, m, H_4), 3.67—3.71 (2H, m, H_3), 7.74 (1H, t, J=1.6 Hz, H_5), 7.91 (1H, d, J=7.7 Hz, H_2), 7.92 (1H, d, J=8.4 Hz, H_6), 8.14 (1H, d, J=9.2 Hz, H_{10}), 8.15 (1H, d, J=8.4 Hz, H_7), 8.16 (1H, d, J=7.7 Hz, H_1), 8.31 (1H, d, J=9.2 Hz, H_9); MS *m/z* 308, 306 (M^+), 227.

Also, a trace amount of **5** was isolated: Mp 175—178 °C (decomp); ^1H NMR δ=3.56—3.64 (2H, m, H_4), 3.66—3.71 (2H, m, H_3), 7.94 (1H, d, J=7.7 Hz, H_2), 8.08 (1H, bs, H_5), 8.13 (1H, d, J=9.3 Hz, H_{10}), 8.18 (1H, d, J=7.7 Hz, H_1), 8.26 (1H, d, J=9.3 Hz, H_9), 8.43 (1H, s, H_7).

Bromination of 2. Bromine (43 mg, 0.27 mmol) in AcOH (10 ml) was added to a solution of **2** (60.5 mg, 0.25 mmol) in AcOH (40 ml) at 20 °C for 2 h, and the mixture was stirred for an additional 1 h. The organic matter was extracted with CH_2Cl_2, and the solution was analyzed by HPLC (hexane/THF, 9:1): **6** (V_R 13.4 ml), **7** (16.8 ml), **2** (18.7 ml), fluorene (2.52 ml, as a reference). The residual part of the solution was chromatographed on silica gel (PhH : hexane=1 : 1) to give 5.8 mg (6%) of **7**: Mp 254—255 °C (decomp) (PhH); IR 1735 cm^{-1}; UV λ_{max} 400 (log ε 3.94), 357 (4.23), 345 (4.11), 319 (3.84), 285 (4.32), 261 (4.45), 230 nm (4.58); ^1H NMR δ=8.20 (1H, t, J=7.8 Hz, H_7), 8.24 (1H, d, J=9.0 Hz, H_{10}), 8.40 (1H, d, J=9.0 Hz, H_9), 8.40 (1H, d, J=7.4 Hz, H_1), 8.41 (1H, d, J=7.8 Hz, H_8), 8.50 (1H, d, J=7.4 Hz, H_2), 8.53 (1H, d, J=7.8 Hz, H_6), 8.54 (1H, bs, H_5); MS *m/z* 402, 400, 398 (M^+), 321, 319 $(M-Br)^+$, 240.

The second eluate gave 34 mg (42%) of **6**: Mp 194—196 °C (decomp) (PhH); IR 1723 cm^{-1}; UV λ_{max} 395 (log ε 4.02), 371 (3.99), 358 (4.27), 343 (4.12), 287 (4.38), 247 nm (4.41); ^1H NMR δ=5.81 (1H, d, J=1.0 Hz, H_4), 8.15 (1H, t, J=7.5 Hz, H_7), 8.21 (1H, d, J=9.0 Hz, H_{10}), 8.27 (1H, bs, H_5), 8.34 (1H, d, J=8.1 Hz, H_1), 8.36 (1H, d, J=9.0 Hz, H_9), 8.36 (1H, d, J=7.5 Hz, H_8), 8.42 (1H, d, J=7.5 Hz, H_6), 8.42 (1H, d, J=8.1 Hz, H_2); ^{13}C NMR δ=44.8, 120.9, 121.6, 123.2, 123.8, 126.0, 126.0, 126.2, 126.5, 127.2, 128.0, 130.5, 131.3, 131.5, 134.5, 134.7, 142.6, 196.3; MS *m/z* 322, 320 (M^+), 241, 213.

Friedel–Crafts Acetylation of 1. Acetyl chloride (0.1 ml, 1.4 mmol) was added to a mixture of **1** (114 mg, 0.5 mmol) and $AlCl_3$ (110 mg, 0.82 mmol) in CH_2Cl_2 (10 ml) at r.t. for 2 min; the resulting mixture was stirred for 5.5 h. After quenching by the addition of crushed ice, a part of the organic layer was submitted to HPLC (hexane/THF, 98:2) : **8** (V_R 15.9 ml), **9** (12.6 ml), **10** (13.6 ml), fluorenone (6.8 ml, as a reference). The residual part was chromatographed on silica gel (PhH : hexane=1 : 1) to give 5.3 mg (4%) of **9**: Mp 168—169 °C (hexane); IR 1670 cm^{-1}; UV λ_{max} 400 (log ε 4.13), 364 (4.24), 349 (4.10), 290 (4.37), 244 nm (4.55); ^1H NMR δ=2.90 (3H, s, Me), 3.68 (2H, t, J=3.2 Hz, H_4), 3.69 (2H, t, J=3.2 Hz, H_3), 7.94 (1H, d, J=7.7 Hz, H_2), 8.02 (1H, d, J=9.1 Hz, H_9), 8.05 (1H, d, J=8.1 Hz, H_8), 8.15 (1H, d, J=9.1 Hz, H_{10}), 8.20 (1H, d, J=7.7 Hz, H_1), 8.38 (1H, d, J=8.1 Hz, H_7), 8.90 (1H, t, J=1.5 Hz, H_5); MS *m/z* 270 (M^+), 227. Found: C, 88.93; H, 5.24%. Calcd for $C_{20}H_{14}O$: C, 88.86; H, 5.22%.

The second eluate afforded 13.2 mg (10%) of **10**: Mp 143—145 °C (hexane); IR 1664 cm^{-1}; UV λ_{max} 391 (log ε 4.23), 377 (4.32), 291 (4.35), 245 nm (4.45); ^1H NMR δ=2.90 (3H, s, Me), 3.63 (2H, t, J=5.7 Hz, H_4), 3.72 (2H, t, J=5.7 Hz, H_3), 7.81 (1H, t, J=1.6 Hz, H_5), 7.95 (1H, d, J=7.8 Hz, H_2), 8.07 (1H, d, J=8.1 Hz, H_6), 8.21 (1H, d, J=7.8 Hz, H_1), 8.22 (1H, d, J=9.6 Hz, H_{10}), 8.40 (1H, d, J=8.1 Hz, H_7), 9.16 (1H, d, J=9.6 Hz, H_9); MS *m/z* 270 (M^+), 227. Found: C, 88.93; H, 5.26%. Calcd for $C_{20}H_{14}O$: C, 88.86; H, 5.22%.

The mother liquor after isolation of **10** contained **8** in addition to **10**; however, pure **8** could not be isolated. Characteristic ^1H NMR signals of **8**: δ=7.90 (bs, H_5), 8.00 (t, J=7.9 Hz, H_7), 8.32 (s, H_2), 9.01 (d, J=9.6 Hz, H_{10}).

Friedel–Crafts Acetylation of 2. Acetyl chloride (1.0 ml, 14 mmol) was added at once to a mixture of **2** (121 mg, 0.5 mmol) and $AlCl_3$ (1.0 g, 7.6 mmol) in CH_2Cl_2 (20 ml) and the resulting mixture was refluxed for 8 h. After treatment, a part of the organic layer was submitted to HPLC (hexane/THF, 9:1): **11** (V_R 6.7 ml), **12** (16.8 ml), **13** (22.1 ml), fluorene (2.52 ml, as a reference). The residual part was chromatographed on silica gel (PhH) to give 12 mg (8%) of **12**: Mp 238—239 °C (decomp) (PhH–hexane); IR 1715, 1685 cm^{-1}; UV λ_{max} 397 (log ε 4.24), 375 (4.26), 289 (4.25), 256 nm (4.39); ^1H NMR δ=2.94 (3H, s, Me), 4.04 (2H, d, J=1.1 Hz, H_4), 8.26 (1H, d, J=9.0 Hz, H_{10}), 8.29 (1H, d, J=8.2 Hz, H_8), 8.30 (1H, d, J=9.0 Hz, H_9), 8.34 (1H, d, J=8.0 Hz, H_1), 8.38 (1H, d, J=8.0 Hz, H_2), 8.47 (1H, d, J=8.2 Hz, H_7), 8.96 (1H, t, J=1.1 Hz, H_5); MS *m/z* 284 (M^+), 269, 241. Found: C, 84.10; H, 4.23%. Calcd for $C_{20}H_{12}O_2$: C, 84.49; H, 4.25%.

The second eluate gave 44 mg (31%) of **13**: Mp 212—214 °C (decomp) (PhH–hexane); IR 1708, 1674 cm^{-1}; UV λ_{max} 407 (log ε 4.39), 385 (4.24), 366 (4.45), 288 (4.44), 277 (4.30), 265 (4.25), 249 nm (4.46); ^1H NMR δ=2.95 (3H, s, Me), 4.02 (2H, d, J=1.1 Hz, H_4), 8.01 (1H, bs, H_5), 8.31 (1H, d, J=9.4 Hz, H_{10}), 8.32 (1H, d, J=8.1 Hz, H_6), 8.35 (1H, d, J=8.0 Hz, H_1), 8.39 (1H, d, J=8.0 Hz, H_2), 8.51 (1H, d, J=8.1 Hz, H_7), 9.31 (1H, d, J=9.4 Hz, H_9); MS

m/z 284 (M^+), 269, 241. Found: C, 84.30; H, 4.30%. Calcd for $C_{20}H_{12}O_2$: C, 84.49; H, 4.25%.

The other eluates after isolation of **12** and **13** were combined and treated with preparative HPLC to give 11 mg (8%) of **11**: Mp 224—225 °C (decomp) (PhH–hexane); IR 1712, 1678 cm^{-1}; UV λ_{max} 395 (log ε 4.25), 386 (4.28), 376 (4.29), 301 (4.19), 279 (4.34), 258 nm (4.11); ^1H NMR δ=2.96 (3H, s, Me), 4.03 (2H, bs, H_4), 8.12 (1H, bs, H_5), 8.16 (1H, t, J=7.7 Hz, H_7), 8.37 (1H, d, J=7.7 Hz, H_6), 8.39 (1H, d, J=7.7 Hz, H_8), 8.46 (1H, d, J=9.3 Hz, H_9), 8.80 (1H, s, H_2), 9.20 (1H, d, J=9.3 Hz, H_{10}); MS *m/z* 284 (M^+), 269, 241.

Nitration of 1.[14] An acetyl nitrate solution (1 ml, 0.95 mmol; prepared from 1 ml of fumed HNO_3 and 24 ml of Ac_2O under ice-cooling 30 min prior to use) was added to a solution of **1** (114 mg, 0.5 mmol) in Ac_2O (13 ml) at 0 °C for 2 min, and the resulting solution was stirred under ice-cooling for 3.5 h. The mixture was extracted with CH_2Cl_2 and the solution was analyzed by HPLC (hexane/THF, 199:1): **15** (V_R 12.4 ml), **16** (11.4 ml), **17** (12.4 ml), **18** (14.4 ml), fluorenone (17.5 ml, as a reference). The residual part was separated by means of preparative HPLC (hexane/THF, 49:1), and the first eluate afforded 7.8 mg (6%) of **16**: Mp 245—247 °C (decomp) (MeOH); IR 1500, 1322 cm^{-1}; UV λ_{max} 408, 366, 330, 316, 302, 265, 256, 240 nm; ^1H NMR δ=3.73 (2H, t, J=5.3 Hz, H_3), 3.99 (2H, t, J=5.3 Hz, H_4), 7.97 (1H, d, J=7.8 Hz, H_2), 8.06 (2H, s, $H_{9,10}$), 8.10 (1H, t, J=7.7 Hz, H_7), 8.19 (1H, d, J=7.7 Hz, H_8), 8.29 (1H, d, J=7.8 Hz, H_1), 8.89 (1H, d, J=7.7 Hz, H_6); MS *m/z* 273 (M^+), 227. Found: C, 79.07; H, 4.14; N, 5.09%. Calcd for $C_{18}H_{11}O_2N$: C, 79.11; H, 4.06; N, 5.13%.

The second eluate gave a mixture of **15** and **17**. The ^1H NMR spectrum of the mixture showed the formation ratio of **15** and **17**. Characteristic ^1H NMR of **15**: δ=7.93 (s, H_5), 8.05 (t, J=7.9 Hz, H_7), 8.59 (s, H_2), 8.85 (d, J=9.6 Hz, H_{10}). Evaporation of the solution and recrystallization of the residue from MeOH yielded 33.2 mg (24%) of **17**:[14] Mp 205—207 °C (decomp); IR 1500, 1321 cm^{-1}; MS *m/z* 273 (M^+), 227.

The third eluate of preparative HPLC gave 28.3 mg (21%) of **18**:[14] Mp 179—181 °C (decomp) (MeOH); IR 1492, 1308 cm^{-1}; MS *m/z* 273 (M^+), 227.

Nitration of 2. An acetyl nitrate solution (1 ml, 2.4 mmol) was added to a solution of **2** (121 mg, 0.5 mmol) in Ac_2O (13 ml) at r.t. for 2 min, and the resulting solution was stirred at r.t. for 3 h. After treatment as usual, HPLC (hexane/THF, 19:1) was carried out: **19** (V_R 26.2 ml), **20** (23.5 ml), **21** (29.3 ml), fluorene (2.43 ml, as a reference). The residual part of the solution was evaporated and the residue was chromatographed by preparative HPLC (hexane/THF, 17:3). The first fraction was evaporated and recrystallized from CH_2Cl_2 to give 25 mg (17%) of **20**: Mp 290—292 °C (decomp); IR 1716 cm^{-1}; UV λ_{max} 395 (log ε 3.95), 380 (3.90), 325 (3.70), 313 (3.74), 290 (3.81), 248 nm (4.14); ^1H NMR δ=4.10 (2H, d, J=1.2 Hz, H_4), 8.32 (1H, d, J=8.6 Hz, H_8), 8.34 (1H, d, J=8.9 Hz, H_{10}), 8.37 (1H, d, J=8.9 Hz, H_9), 8.46 (2H, s, $H_{1,2}$), 8.75 (1H, d, J=8.6 Hz, H_7), 8.84 (1H, t, J=1.2 Hz, H_5); MS *m/z* 287 (M^+), 257. Found: C, 75.39; H, 3.24; N, 4.64%. Calcd for $C_{18}H_9O_3N$: C, 75.26; H, 3.16; N, 4.88%.

The second fraction yielded 13 mg (8%) of **19**: Mp 266—267 °C (decomp) (CH_2Cl_2); IR 1720 cm^{-1}; UV λ_{max} 399 (log ε 4.24), 379 (4.21), 334 (3.89), 318 (3.92), 284 (4.16), 279 (4.15), 239 nm (4.35); ^1H NMR δ=4.07 (2H, d, J=1.2 Hz, H_4), 8.21 (1H, bs, H_5), 8.24 (1H, t, J=7.8 Hz, H_7), 8.45 (1H, d, J=7.8 Hz, H_8), 8.48 (1H, d, J=7.8 Hz, H_6), 8.56 (1H, d, J=9.5 Hz, H_9), 9.01 (1H, d, J=9.5 Hz, H_{10}), 9.07 (1H, s, H_2); MS *m/z* 287 (M^+), 257.

The third fraction gave 26 mg (18%) of **21**: Mp 295—297 °C (decomp) (CH_2Cl_2); IR 1718 cm^{-1}; UV λ_{max} 412 (log ε 4.23), 378 (4.15), 360 (s, 4.02), 289 (4.19), 234 nm (4.47); ^1H NMR δ=4.08 (2H, d, J=1.2 Hz, H_4), 8.10 (1H, bs, H_5), 8.36 (1H, d, J=8.6 Hz, H_6), 8.45 (1H, d, J=9.3 Hz, H_{10}), 8.46 (1H, d, J=8.3 Hz, H_1 or H_2), 8.47 (1H, d, J=8.3 Hz, H_2 or H_1), 8.83 (1H, d, J=8.6 Hz, H_7), 9.20 (1H, d, J=9.3 Hz, H_9); MS *m/z* 287 (M^+), 257. Found: C, 75.05; H, 3.26; N, 4.73%. Calcd for $C_{18}H_9O_3N$: C, 75.26; H, 3.16; N, 4.88%.

Competitive Acetylation. Acetyl chloride (0.08 ml, 1.1 mmol) was added at once to a stirred mixture of **2** (20.0 mg, 0.08 mmol), **14** (20.0 mg, 0.08 mmol), $AlCl_3$ (0.13 g, 1 mmol), and $PhNO_2$ (12.0 mg, 0.10 mmol, as a reference) in CH_2Cl_2 (7 ml) at r.t. A small portion of the mixture was taken out at one min intervals and analyzed by HPLC (hexane/THF, 9:1; V_R of $PhNO_2$, 3.82 ml). Each of the conversions was plotted and the ratio of the reaction rates of **2** and **14** at time=0 was calculated from each slope. The average ratio of the three trials was 1.34/1.00 for **14/2**.

A mixture of **1** (19.4 mg, 0.085 mmol), **2** (41.0 mg, 0.169 mmol), $AlCl_3$ (0.4 g, 3 mmol), and $PhNO_2$ (24.0 mg, 0.20 mmol) in CH_2Cl_2 (7 ml) was acetylated at 40 °C with AcCl (0.15 ml, 2.1 mmol); the relative reactivity was 4.23/1.00 for **1/2** as an average.

Competitive Nitration. A mixture of **2** (20.0 mg, 0.08 mmol), **14** (20.0 mg, 0.08 mol), and $PhNO_2$ (12.0 mg, 0.10 mmol) in Ac_2O (20 ml) was mixed with $AcONO_2$ (0.34 mmol) at r.t. The average ratio of the reaction rate was 1.87/1.00 for **14/2**.

The average ratio of **1/2** was 25.8/1.00 by the reaction of **1** (9.7 mg, 0.043 mmol), **2** (41.0 mg, 0.169 mmol), $PhNO_2$ (48.0 mg, 0.40 mmol), and $AcONO_2$ (0.19 mmol) in CH_2Cl_2 (20 ml).

The work described here was supported in part by a Grant-in-Aid for Scientific Research No. 02640381 from the Ministry of Education, Science and Culture. The authors thank Professor T. Toda of Utsunomiya University for helpful discussions and Mr. H. Nambu and Mr. K. Ishiwa for their assistance.

References

1) P. H. Ruehle, D. L. Fischer, and J. C. Wiley, Jr., *J. Chem. Soc., Chem. Commun.*, **1979**, 302.

2) E. Eisenstadt and A. Gold, *Proc. Natl. Acad. Sci. U.S.A.*, **75**, 1667 (1978).

3) A. Greenberg, *Atoms. Environ.*, **23**, 2797 (1989).

4) A. W. Wood, W. Levin, R. L. Chang, M. Huang, D. E. Ryan, P. E. Thomas, R. E. Lehr, S. Kumar, M. Koreeda, H. Akagi, Y. Ittah, P. Dansette, H. Yagi, D. M. Jerina, and A. H. Conney, *Cancer Res.*, **40**, 642 (1980).

5) D. A. Kaden, R. A. Hites, and W. G. Thilly, *Cancer Res.*, **39**, 4152 (1979).

6) W. F. Busby, Jr., E. K. Stevens, E. R. Kellenbach,

J. Cornelisse, and J. Lugtenburg, *Carcinogenesis*, **9**, 741 (1988).

7) H. Vollmann, H. Becker, M. Corell, H. Streeck, and G. Langbein, *Liebigs Ann. Chem.*, **531**, 1 (1937); *Chem. Abstr.*, **32**, 145 (1938).

8) M. J. S. Dewar and R. D. Dennington, II, *J. Am. Chem. Soc.*, **111**, 3804 (1989).

9) M. Minabe, H. Mochizuki, M. Yoshida, and T. Toda, *Bull. Chem. Soc. Jpn.*, **62**, 68 (1989).

10) K. K. Laali and P. E. Hansen, *J. Org. Chem.*, **56**, 6795 (1991).

11) L. Wallcave, *Environ. Sci. Technol.*, **3**, 948 (1969).

12) N. M. Spijker, A. M. van den Braken-van Leersum, J. Lugtenburg, and J. Cornelisse, *J. Org. Chem.*, **55**, 756 (1990).

13) R. A. Hites and W. J. Simonsick, Jr., "Calculated Molecular Properties of Polycyclic Aromatic Hydrocarbons," Elsevier, New York, NY (1987), p. 58.

14) A. M. van den Braken-van Leersum, N. M. Spijker, J. Lugtenburg, and J. Cornelisse, *Recl. Trav. Chim. Pays-Bas*, **106**, 628 (1987).

15) R. Sangaiah and A. Gold, *J. Org. Chem.*, **56**, 6717 (1991).

16) E. R. Kellenbach, J. Lugtenburg, and J. Cornelisse, *Recl. Trav. Chim. Pays-Bas*, **108**, 437 (1989).

17) A. M. van den Braken-van Leersum, J. Cornelisse, and J. Lugtenburg, *Tetrahedron Lett.*, **26**, 4823 (1985).

18) C. Tintel, J. Cornelisse, and J. Lugtenburg, *Recl. Trav. Chim. Pays-Bas*, **102**, 14 (1983).

19) M. Minabe, B. P. Cho, and R. G. Harvey, *J. Am. Chem. Soc.*, **111**, 3809 (1989).

20) M. Minabe, M. Ishida, T. Kimura, M. Tsubota, and M. Yoshida, *J. Org. Chem.*, **57**, 1012 (1992).

21) Sankyo Co., Ltd., Jpn Kokai Tokkyo Koho, JP 81113728 (1981); *Chem. Abstr.*, **96**, 52044 (1982).

22) M. Minabe, unpublished results.

23) Y. Ittah and D. M. Jerina, *Tetrahedron Lett.*, **1978**, 4495.