Synthesis and Conformational Analysis of Nitropolycyclic Fluoranthenes

Bongsup P. Cho,*,†,§ Misoo Kim,† and Ronald G. Harvey‡

Department of Medicinal Chemistry, College of Pharmacy, University of Rhode Island, Kingston, Rhode Island, 02881, Division of Biochemical Toxicology, National Center for Toxicological Research, Jefferson, Arkansas 72079, and Ben May Institute, University of Chicago, Chicago, Illinois 60637

Received April 29, 1993•

Nitroarenes are ubiquitous environmental pollutants some of which exhibit mutagenic and tumorigenic activities. The first systematic investigation of the nitration reactions of the polycyclic fluoranthenes, a major class of nonalternant polyarenes, is described. The specific hydrocarbons studied were benz[*e*]acephenanthrylene (1), benz[*a*]aceanthrylene (2), indeno[1,2,3-*cd*]pyrene (3), indeno[1,2,3-*hi*]chrysene (4), dibenz[*a,e*]aceanthrylene (5), dibenz[*a,j*]aceanthrylene (6), and dibenz[*e,k*]acephenanthrylene (7). The nitration of all hydrocarbons, except 1, proceeded with remarkable regioselectivity to provide a single mononitro product. In the case of 1, 17% of a second mononitro isomer was isolated. The structures of the resulting mononitrofluoranthenes (8–15) were fully characterized by analysis of their high-resolution COSY, long-range COSY, and NOESY NMR spectra and by comparison with the spectra of the parent hydrocarbons. The observed nitration sites of the polycyclic fluoranthenes were in excellent agreement with theoretical predictions made by the DEWAR-PI method based on the relative energies of the Wheland intermediates for substitutions at various ring positions. The availability of the complete ^{1}H chemical shift assignments of the nitropolycyclic fluoranthenes (8–15), together with those of the parent hydrocarbons (1–7) and their UV-visible spectral data, enabled the molecular conformations of the nitro groups to be probed.

Introduction

Nitroarenes are ubiquitous environmental pollutants that are thought to arise from various human activities, including the incomplete combustion of fossil fuels.[1] Recent interest in nitroarenes stems from the fact that many of these compounds are metabolized to highly mutagenic and tumorigenic metabolites by mammalian and/or bacterial enzyme systems.[2,3] Importantly, some nitroarenes are reported to be more mutagenic and tumorigenic than their parent polycyclic aromatic hydrocarbons (PAHs).[2]

While much current attention has focused on the nitrated alternant PAHs, very little is known concerning the synthesis and chemical properties of the nitro derivatives of nonalternant PAHs.[4] The polycyclic fluoranthenes are a major class of nonalternant PAHs some of which, e.g., benz[*e*]acephenanthrylene and indeno[1,2,3-*cd*]pyrene, exhibit significant mutagenic and carcinogenic activities.[5,6] The widespread occurrence of polycyclic fluoranthenes in nature suggests that their nitro derivatives may be formed under environmental conditions. We have previously reported a general synthetic procedure[7] for the preparation of hydrocarbons of this class and the utilization of 2D-NMR methods for their complete ^{1}H and ^{13}C NMR assignments.[8]

We report herein the first systematic investigation on the nitration of polycylic fluoranthenes. The hydrocarbons studied include benz[*e*]acephenanthrylene (1), benz[*a*]aceanthrylene (2), indeno[1,2,3-*cd*]pyrene (3), indeno[1,2,3-*hi*]chrysene (4), dibenz[*a,e*]aceanthrylene (5), dibenz[*a,j*]aceanthrylene (6), and dibenz[*e,k*]acephenanthrylene (7) (Figure 1). The sites of nitro substitution of these hydrocarbons (1–7) are discussed in relation to the DEWAR-PI molecular orbital calculations devised specifically for this type of hydrocarbon.[9] In addition, complete ^{1}H NMR assignments of the nitropolycyclic fluoranthenes (8–15) isolated in this study and the parent hydrocarbons (1–7) were made by using a combination of nuclear Overhauser effects and COSY experiments. The extensive NMR data, along with UV-visible spectra of the compounds, allowed us to probe the orientations of the nitro groups with respect to the aromatic moiety. The conformations of the nitro substituents in nitroarenes have been shown to be important in determining their mutagenic activities.[2,10]

Results and Discussion

Nitration. The nitration of seven polycyclic fluoranthenes 1–7 (Figure 1) was carried out with 1.2 equiv of dinitrogen tetroxide (N_2O_4)[11] in methylene chloride or with 5 equiv of nitric acid (HNO_3) in acetic anhydride at room

* To whom correspondence should be addressed. Corresponding address: Department of Medicinal Chemistry, College of Pharmacy, University of Rhode Island, Kingston, RI 02881.
† University of Rhode Island.
‡ University of Chicago.
§ National Center of Toxicological Research.
• Abstract published in *Advance ACS Abstracts*, September 1, 1993.
(1) White, C. M., Ed. *Nitrated Polycyclic Aromatic Hydrocarbons*; Hüthig: Heidelberg, 1985.
(2) Fu, P. P. *Drug Metabol. Rev.* **1990**, *22* (2 & 3), 209–268.
(3) Howard, P. C.; Hecht, S. S.; Beland, F. A., Eds. *Nitroarenes: Occurrence, Metabolism, and Biological Impact*, Environmental Research, Vol. 40; Plenum Press: New York, 1990.
(4) Harvey, R. G. *Polycyclic Aromatic Hydrocarbons, Chemistry and Carcinogenecity*; Cambridge University Press: Cambridge, 1991.
(5) *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans: Polynuclear Aromatic Compounds*; IARC: Lyon, France, 1983; Vol. *32*, Part 1.
(6) Deutsch-Wenzel, R. P.; Brune, H.; Grimmer, G.; Dettbaun, G.; Misfeld, *J. Natl. Cancer Inst.* **1983**, *71*, 539–543.
(7) (a) Cho, B. P.; Harvey, R. G. *Tetrahedron Lett.* **1987**, *28*, 861–864, 2906. (b) Cho, B. P.; Harvey, R. G. *J. Org. Chem.* **1987**, *52*, 5668–5678.
(8) Cho, B. P.; Harvey, R. G. *J. Org. Chem.* **1987**, *52*, 5679–5684.
(9) Dewar, M. J. S.; Dennington, R. D., II. *J. Am. Chem. Soc.* **1989**, *111*, 3804–3808.
(10) Fu, P. P.; Chou, M. W.; Miller, D. W.; White, G. L.; Heflich, R. H.; Beland, F. A. *Mutat. Res.* **1988**, *209*, 115–122.
(11) Radner, F. *Acta Chim. Scand.* **1983**, *B37*, 65–67.

0022-3263/93/1958-5788$04.00/0

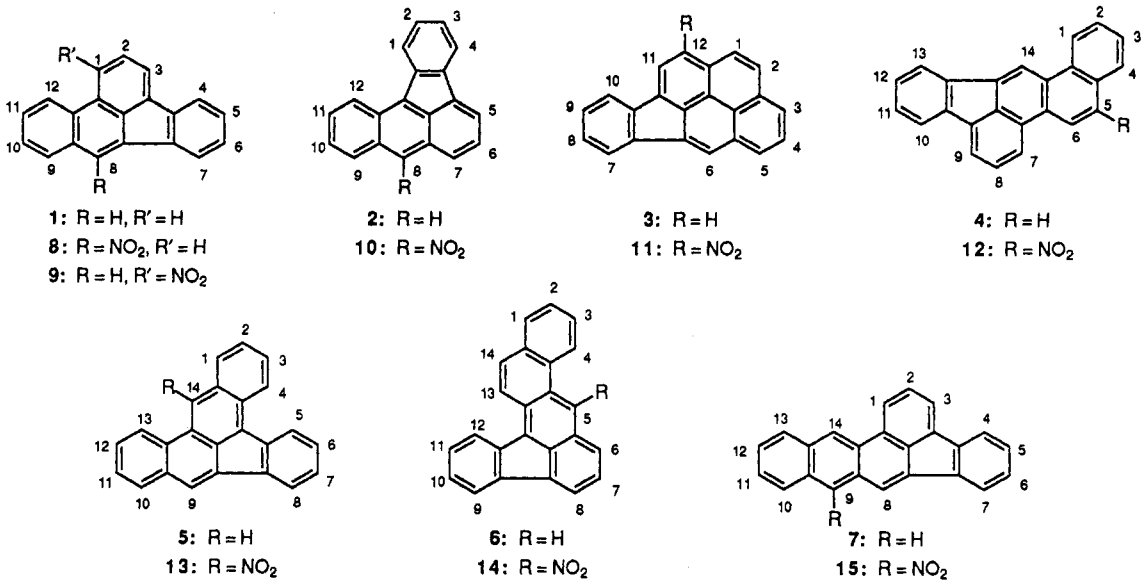


Figure 1. Structural formulas and numbering of polycyclic fluoranthenes: benz[*e*]acephenanthrylene (**1**), benz[*a*]aceanthrylene (**2**), indeno[1,2,3-*cd*]pyrene (**3**), indeno[1,2,3-*hi*]chrysene (**4**), dibenz[*a,e*]aceanthrylene (**5**), dibenz[*a,j*]aceanthrylene (**6**), dibenz[*e,k*]-acephenanthrylene (**7**); and their nitro derivatives, 8-nitrobenz[*e*]acephenanthrylene (**8**), 1-nitrobenz[*e*]acephenanthrylene (**9**), 8-nitrobenz[*a*]aceanthrylene (**10**), 12-nitroindeno[1,2,3-*cd*]pyrene (**11**), 5-nitroindeno[1,2,3-*hi*]chrysene (**12**), 14-nitrodibenz[*a,e*]aceanthrylene (**13**), 5-nitrodibenz[*a,j*]aceanthrylene (**14**), and 9-nitrodibenz[*e,k*]acephenanthrylene (**15**).

Table I. Nitration of Polycyclic Fluoranthenes

polycyclic fluoranthenes	method[a]	reaction time (h)	isolated yield (%)	product(s)
1	N_2O_4	3	75% of 8	8 (83%), 9 (17%)[b]
	HNO_3	12	64	
2	N_2O_4	0.6	94	10
	HNO_3	5	80	
3	N_2O_4	0.2	91% of 11	11 (94%), 5- & 3-nitro (6%)[b,c]
	HNO_3	1	71	
4	N_2O_4	1.5	91	12
	HNO_3	8	80	
5	N_2O_4	0.3	87	13
	HNO_3	10	71	
6	N_2O_4	0.3	82	14
	HNO_3	10	68	
7	N_2O_4	0.3	91	15
	HNO_3	8	75	

[a] N_2O_4 method: with 1.2 equiv of N_2O_4 in methylene chloride at room temperature. HNO_3 method: with 5.0 equiv of HNO_3 in acetic anhydride at room temperature. See Experimental Section for details. [b] Determined by HPLC monitored at 280 nm. [c] Tentative assignments (see text).

temperature. The results using these two nitrating reagents are summarized in Table I. Although nitrations with both reagents under controlled conditions proceeded with high regioselectivity, giving rise to virtually identical reaction profiles, nitration with N_2O_4 was more rapid, offered better workup procedures, and afforded cleaner products. In general, prolonged reaction times and use of excess reagents resulted in the formation of multiple mono- and dinitro products. The N_2O_4 reagent has been shown to be highly regioselective for the nitration of other types of PAHs.[11,12]

Benz[*e*]acephenanthrylene (1). Nitration of **1** with 1.2 equiv of N_2O_4 in methylene chloride was complete in 3 h at room temperature. HPLC analysis of the crude reaction mixture showed two peaks at 6.12 and 7.59 min, with an intensity ratio of 17:83 when monitored at 280 nm. Both products were identified as mononitro derivatives by mass analysis. The major product was isolated (75%) as golden needles after recrystallization from ethyl acetate and hexane. Nitration of **1** with 5 equiv of acetyl nitrate solution afforded an essentially identical reaction profile, but required a longer reaction time (12 h) and resulted in a lower yield (64%).

The 500-MHz ^{1}H NMR spectrum of the major product lacked the singlet signal of H8, consistent with its assignment as the 8-nitrobenz[*e*]acephenanthrylene (**8**) (Figure 1). The chemical shifts and coupling patterns exhibited in the ^{1}H NMR spectrum of **8** closely resemble those of the parent compound (**1**), whose complete ^{13}C and ^{1}H assignments were made previously.[8] Based on their spin-coupling networks, the eleven aromatic protons of **8** can be assembled into one AMX (H1,2,3), and two ABMX systems (H4,5,6,7 and H9,10,11,12). Complete ^{1}H assignments of these protons were made by a combination of COSY, long-range COSY (LRCOSY), and NOESY experiments, as described in detail in the next section. The results are listed in Table II in comparison with those of the parent hydrocarbon (**1**).

The polar minor isomer, which consisted of 17% of total by HPLC, was separated by means of HPLC. Its ^{1}H NMR spectral pattern was significantly different from those of the parent compound **1** and of the major mononitro isomer **8**. The retention of the characteristic high-field B-ring resonances (i.e., H5 and H6) at δ 7.47 and 7.46 and the D-ring resonances (i.e., H10 and H11) at δ 7.66 and 7.63, as well as the H8 singlet at δ 8.26, indicated that nitration had not occurred in the B-, or C-, or D-rings. An additional distinctive feature in the ^{1}H NMR spectrum of the minor isomer was the appearance of a AB-type spectral pattern centered around δ 7.91. This could only be possible with nitro substitution occurring at either the 1- or 3-position. A significant upfield shift (+0.41 ppm) of the angular bay-proton H12 is a strong indication that this proton is under the anisotropic effect of a nitro group located in the bay-

(12) Miller, D. W.; Herreno-Saenz, D.; Huang, K. H.; Heinze, T. M.; Fu, P. P. *J. Org. Chem.* **1992**, *57*, 3746–3748.

Table II. Comparison of ^{1}H Chemical Shift of Nitropolycyclic Fluoranthenes and Their Parent Compounds[a]

no.	8 (1)[b]	Δδ[c]	9 (1)[b]	Δδ	10 (2)	Δδ	11 (3)[b]	Δδ	12 (4)[b]	Δδ	13 (5)	Δδ	14 (6)	Δδ	15 (7)	Δδ
1	8.42 (8.42)[d]	0.00	– (8.42)		8.31 (8.38)	–0.07	9.03 (8.10)	–0.93	9.01 (8.90)	–0.11	7.94 (8.25)	+0.31	7.86 (7.87)	–0.01	8.47 (8.53)	+0.06
2	7.81 (7.73)	–0.08	7.87[e] (7.73)	–0.14	7.45 (7.47)	–0.02	8.34 (8.04)	–0.30	7.88 (7.74)	–0.14	7.72 (7.71)	–0.01	7.63 (7.62)	–0.01	7.78 (7.76)	–0.02
3	7.94 (7.90)	–0.04	7.96[e] (7.90)	–0.06	7.41 (7.39)	+0.02	8.39 (8.22)	–0.17	7.89 (7.64)	–0.25	7.78 (7.60)	–0.18	7.59 (7.68)	+0.09	7.92 (7.95)	+0.03
4	7.82 (7.90)	+0.08	7.92 (7.90)	–0.02	7.92 (8.01)	+0.09	8.16 (8.03)	–0.13	8.69 (7.99)	–0.70	8.84 (8.80)	–0.04	8.33 (8.85)	+0.52	7.85 (7.91)	+0.06
5	7.39 (7.40)	+0.01	7.47 (7.40)	–0.07	7.92 (8.01)	+0.09	8.52 (8.37)	–0.15	– (8.00)		8.37 (8.41)	+0.04	– (9.21)		7.44 (7.43)	–0.01
6	7.48 (7.39)	–0.09	7.46 (7.39)	–0.07	7.71 (7.65)	–0.06	8.66 (8.53)	–0.13	9.36 (8.66)	–0.70	7.50 (7.52)	+0.02	7.79 (8.05)	+0.26	7.43 (7.41)	–0.02
7	7.89 (7.97)	+0.08	7.98 (7.97)	–0.01	7.92 (8.02)	+0.10	8.13 (8.10)	–0.03	8.50 (8.52)	+0.02	7.43 (7.43)	0.00	7.72 (7.70)	–0.02	7.98 (8.01)	+0.03
8	– (8.17)		8.26 (8.17)	–0.09	– (8.47)		7.53 (7.40)	–0.13	7.87 (7.78)	–0.09	8.02 (8.08)	+0.06	7.95 (8.01)	+0.06	8.07 (8.27)	+0.20
9	7.94 (8.01)	+0.07	8.05 (8.01)	–0.04	8.16 (8.14)	–0.02	7.52 (7.45)	–0.07	8.05 (7.98)	–0.07	8.17 (8.24)	+0.07	7.92 (7.99)	+0.07	– (8.51)	
10	7.74 (7.60)	–0.14	7.66 (7.60)	–0.06	7.67 (7.51)	–0.16	8.07 (8.00)	–0.07	7.95 (7.93)	–0.02	8.01 (8.03)	+0.02	7.40 (7.40)	0.00	7.92 (8.06)	+0.14
11	7.78 (7.66)	–0.12	7.63 (7.66)	+0.03	7.70 (7.67)	–0.03	9.14 (8.33)	–0.81	7.50 (7.42)	–0.08	7.67 (7.66)	–0.01	7.42 (7.46)	0.00	7.69 (7.56)	–0.13
12	8.69 (8.62)	–0.07	8.21 (8.62)	+0.41	8.76 (8.76)	–0.00	– (8.20)		7.49 (7.43)	–0.06	7.66 (7.73)	+0.07	8.29 (8.37)	+0.08	7.67 (7.57)	–0.10
13									8.13 (8.08)	–0.05	8.34 (8.82)	+0.48	8.50 (8.58)	+0.08	8.14 (8.20)	+0.06
14									9.15 (9.19)	+0.04	– (9.00)		7.79 (7.80)	+0.01	9.16 (9.09)	–0.07

[a] All samples were measured in $CDCl_3$ (~5 mg/mL) and chemical shifts are reported in ppm downfield from TMS. ^{1}H Chemical shifts of parent compounds are shown in parentheses. [b] Taken from ref 8. [c] Δδ = δ parent compound – δ nitro derivative, – indicates downfield shift and + indicated upfield shift of protons in the nitro derivatives. [d] Some relevant coupling constants of 1–15 are as follows: **1**, $J(1,2)$ = 8.13, $J(2,3)$ = 7.06, $J(9,10)$ = 7.71, $J(11,12)$ = 7.99; **8**, $J(1,2)$ = 8.21, $J(2,3)$ = 7.05, $J(9,10)$ = 7.89, $J(11,12)$ = 8.05; **9**, $J(11,12)$ = 8.01; **2**, $J(1,2)$ = 7.63, $J(9,10)$ = 8.54, $J(11,12)$ = 8.71; **10**, $J(1,2)$ = 7.44, $J(9,10)$ = 8.90, $J(11,12)$ = 8.71; **3**, $J(1,2)$ = 8.97, $J(3,4)$ = 7.53, $J(4,5)$ = 7.67; **11**, $J(1,2)$ = 9.44, $J(3,4)$ = 7.64, $J(4,5)$ = 7.66; **4**, $J(1,2)$ = 8.00, $J(3,4)$ = 8.00, $J(5,6)$ = 8.80, $J(7,8)$ = 8.40; **12**, $J(1,2)$ = 7.70, $J(3,4)$ = 8.05, $J(8,9)$ = 7.13; **5**, $J(1,2)$ = 8.60, $J(5,6)$ = 7.64, $J(7,8)$ = 7.40, $J(12,13)$ = 8.02; **13**, $J(1,2)$ = 8.54, $J(5,6)$ = 7.69, $J(7,8)$ = 7.35, $J(12,13)$ = 7.99; **6**, $J(1,2)$ = 8.21, $J(3,4)$ = 7.69, $J(6,7)$ = 8.29, $J(11,12)$ = 7.61, $J(13,14)$ = 9.24; **14**, $J(1,2)$ = 7.31, $J(3,4)$ = 8.34, $J(6,7)$ = 8.41, $J(11,12)$ = 7.44, $J(13,14)$ = 9.21; **7**, $J(1,2)$ = 8.02, $J(2,3)$ = 7.05; **15**, $J(1,2)$ = 8.03, $J(2,3)$ = 7.13. [e] Interchangeable.

region 1-position of the molecule.[13] The effect was expected to be smaller, if nitration had taken place on the 3-position. On the basis of these findings, the minor isomer was assigned as 1-nitrobenz[*e*]acephenanthrylene (**9**).

The observed sites of nitration of **1** are in complete agreement with the DEWAR-PI molecular orbital calculation devised by Dewar and Dennington (Figure 2).[9] The method predicts the most favorable electrophilic substitution at position 8 followed by position 1. Although the present results differ from an earlier bromination study,[14] which provided the 1-bromo isomer as the sole product, the 1-position is calculated to be less energetically favorable than the 8-position only by 3.8 kcal/mol, which is certainly within the limits of error of the DEWAR-PI predictions.

Benz[*a*]aceanthrylene (2). Nitration of **2** with N_2O_4 (0.6 h) in methylene chloride provided a single mononitro derivative as red crystals in 94% yield (Table I). The most revealing feature in the ^{1}H NMR spectrum of the product was the disappearance of the meso H8 singlet signal at δ 8.47, indicating that the nitro substitution occurred in the 8-position. Analysis of COSY and LR-COSY spectra of the product was entirely consistent with its assignment as 8-nitrobenz[*a*]aceanthrylene (**10**). The result is again in excellent agreement with the DEWAR-PI calculation,[9] which predicts preferential electrophilic substitution at the 8-position (Figure 2). It has been reported that bromination occurs preferentially at the 8-position as well.[14]

Indeno[1,2,3-*cd*]pyrene (3), in particular, has recently attracted considerable attention because of its environmental prevalence and reported mutagenicity and tumorigenicity.[5,6] The preferred sites of electrophilic substitution on **3** are predicted by DEWAR-PI to be the 3- and 5-positions followed by the 12-position which is only 1.4 kcal/mol higher in energy. Bolgar *et al.* have first reported the nitration of **3**, and the product was tentatively assigned as the 8- or 9-nitro derivatives.[15] A recent communication by Minabe and Shibuya,[16] however, has shown that the nitration of **3** with an acetyl nitrate solution actually occurred at position 12, which is the same site assigned for bromination and Friedel–Crafts acetylation.[14]

Nitration of **3** with N_2O_4 in methylene chloride at room temperature was complete in minutes. The relatively high reactivity of **3** toward nitration and other electrophilic substitution conditions (bromination and Friedel–Crafts acylation)[14] could be attributed to the electron-rich nature of the pyrene ring moiety. The HPLC analysis of the crude reaction mixture showed a retention time for the major mononitro product of 12.60 min. It was accompanied by two other minor mononitro products at 11.45 and 11.84 min. The relative peak intensity of the two minor isomers and the major isomer at 280 nm was 1:1:32.

The major product was isolated as bright yellow solid in 91% yield. It exhibited an essentially identical ^{1}H NMR spectral pattern as those reported by Bolgar *et al.*,[15] and by Minabe and Shibuya.[16] Analysis of the COSY and LRCOSY spectra confirmed its structure as 12-nitroindeno[1,2,3-*cd*]pyrene(**11**). A notable feature of the ^{1}H

(13) Miller, D. W.; Evans, F. E.; Fu, P. P. *Spectrosc. Int. J.* **1985**, *4*, 91–94.
(14) Minabe, M.; Cho, B. P.; Harvey, R. G. *J. Am. Chem. Soc.* **1989**, *111*, 3809–3812.
(15) Bolgar, M.; Hubball, J. A.; Cunningham, J. T.; Smith, S. R. *Polynuclear Aromatic Hydrocarbons: Mechanisms, Methods and Metabolisms*; Cooke, M., Dennis, A. J., Eds.; Battelle Press: Columbus, OH, 1985; pp 199–214.
(16) Minabe, M.; Shibuya, N. *Chem. Res. Tox.* **1989**, *2*, 357–358.

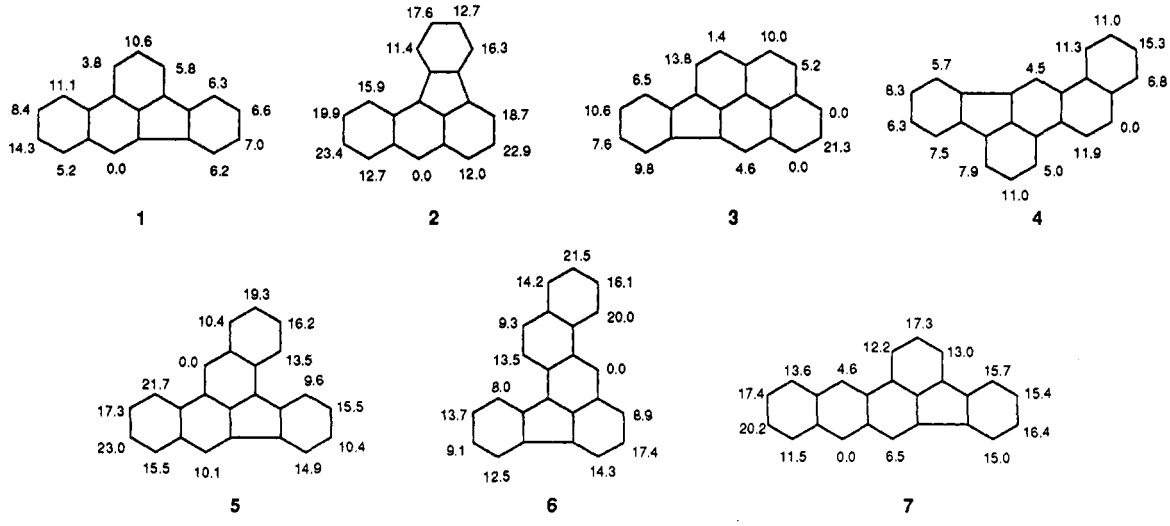


Figure 2. Calculated relative energies of the Wheland intermediates for electrophilic substitution at various ring positions of benz[*e*]acephenanthrylene (1), benz[*a*]aceanthrylene (2), indeno[1,2,3-*cd*]pyrene (3), indeno[1,2,3-*hi*]chrysene (4), dibenz[*a,e*]aceanthrylene (5), dibenz[*a,j*]aceanthrylene (6), and dibenz[*e,k*]acephenanthrylene (7). Energies are relative to the Wheland intermediates with the lowest energy calculated by the DEWAR-PI method.[9]

NMR spectrum was the appearance of a downfield singlet at δ 9.14 and a doublet at δ 9.03 which were assigned to H11 and H1, respectively. The complete ^{1}H assignments of **11** were established by 1D NOE experiments and by the recognition of various long-range internuclear couplings in the LRCOSY spectrum (see next section). Furthermore, the magnitude of J(1,2) ortho coupling (9.44 Hz) of **11** represents a substantial increase (0.47 Hz) from that of the parent compound (**3**) and is comparable to that (9.5 Hz) observed for the electron-rich K-region J(9,10) coupling of 1-nitropyrene,[17] indicating a greater double bond character of the C1-C2 bond of **11**.[18]

Isolation of the two polar minor isomers, which consist of approximately 6% of the total, in pure state proved to be difficult. Analysis of the ^{1}H NMR spectrum of the partially purified material containing the two minor isomers (>70%) exhibited a noticeable downfield singlet at δ 9.19. A possible explanation for this peak is the presence of the 5-nitro isomer in the mixture. This would account for the downfield signal as the H6 peri proton is expected to be significantly deshielded. Indeed, the magnitude (−0.66 ppm) of a hypothetical downfield shift of H6 falls into the general range for a peri proton shift.[13] Furthermore, the 5- and 3-positions of **3** are predicted to be the most favorable sites for electrophilic substitution by the DEWAR-PI calculations (Figure 2).[9] According to photodiode-array analysis, the two minor isomers exhibit very similar UV characteristics to those of the 12-isomer, suggesting that they have similar nitro group orientations. On the basis of these data, the minor isomers were tentatively assigned as 5- and 3-nitroindeno[1,2,3-*cd*]-pyrene.

Indeno[1,2,3-*hi*]chrysene (4) is predicted by the DEWAR-PI MO calculations to react with electrophiles preferentially in the 5-position (Figure 2). In accordance with this prediction, bromination of **4** with bromine in methylene chloride at room temperature gave the 5-bromo derivative.[14]

Nitration of **4** with N_2O_4 stirring 1.5 h at room temperature furnished a single major mononitro derivative in 91% yield. Although nitration of **4** with acetyl nitrate solution required 8 h, this procedure afforded the same product in 80% yield. With the exception of appearance of a singlet at δ 9.36, the ^{1}H NMR spectrum of the product was nearly identical to that exhibited by the parent compound. This spectral feature ruled out the possibility of 14-nitro substitution. The downfield singlet was significantly deshielded as compared to the other bay-region protons, strongly suggesting that nitro substitution had occurred in the vicinity of this bay region. Analysis of the COSY and LRCOSY spectra (next section) assigned the product as 5-nitroindeno[1,2,3-*hi*]chrysene (**12**).

The formation of 5-nitroindeno[1,2,3-*hi*]chrysene is consistent with the theoretical predictions by the DEWAR-PI method.[9] The 5-position of **4** is equivalent to substitution at the 6- and 12-positions in chrysene. Although the relative energy (4.5 kcal/mol) calculated for the 14-position of **4** is within the limit of error, no such isomer was detected.

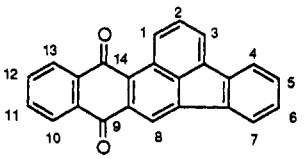
Dibenz[*a,e*]aceanthrylene (5). Nitration of **5** with N_2O_4 at room temperature proceeded rapidly (0.3 h), affording a single mononitro isomer in 87% yield (Table I). The disappearance of the downfield meso-bay H14 proton at δ 9.00 in the ^{1}H NMR spectrum indicated the occurrence of nitro substitution at the 14-position, which was predicted to be the most electrophilic site.[9] Again, the structure of **13** was fully characterized by ^{1}H NMR (next section).

Dibenz[*a,j*]aceanthrylene (6). Nitration of **6** with N_2O_4 was completed in 0.3 h to provide only one mononitro derivative. This pattern indicates that the electrophilic reactivity of **6** is comparable to **5**. The same product was obtained with acetyl nitrate solution in 10 h according to mainly ^{1}H NMR analysis. This nitrated analog was identified as 5-nitrodibenz[*a,j*]aceanthrylene (**14**). The ^{1}H NMR spectral pattern of the product is strikingly similar to that of the parent compound, with the exception of the absence of the downfield meso-bay proton signal at δ 9.21. The remaining 13 proton signals of **14** were well-separated and completely assigned by a combination of

(17) van den Braken-van Leersum, A. M.; Tintel, C.; van't Zelfde, M.; Cornellisse, J.; Lugtenburg, J. *Recl. Trav. Chim. Pays-Bas.* **1987**, *106*, 120–128.
(18) Karplus, M. *J. Am. Chem. Soc.* **1963**, *85*, 2870–2871.

COSY, LRCOSY, triple-quantum-filtered COSY (TQF-COSY), NOESY, and 1D NOE experiments, which are described in detail in the following section. The 5-nitro substitution of **6** is equivalent with the 12-position of benz[*a*]anthracene, and the finding is in complete agreement with the theoretical prediction (Figure 2).[9]

Dibenz[*e,k*]acephenanthrylene (7). Nitration of **7** with N_2O_4 in methylene chloride readily afforded a sole mononitro product **15** in 91% yield. Nitration of **7** with acetyl nitrate solution also gave **15**. In the latter case, HPLC photodiode-array analysis indicated formation of a small amount of an oxidation product, quinone **16**.[7b]



16

The distinct feature in the high resolution ^{1}H NMR spectrum of **15** was the disappearance of the H9 singlet at δ 8.51. This is one of the three singlets (H14, H9, and H8) present in the spectrum of **7**. Analysis of the COSY and LRCOSY spectral data fully supports the structure of **15** as 9-nitrodibenz[*e,k*]acephenanthrylene.

Nitration of **7** in the 9-position is totally consistent with the DEWAR-PI prediction (Figure 2).[9] This position is equivalent to the 7-position of benz[*a*]anthracene, which is the most reactive site of this arene. Nitro-substitution in the 14-position, which is predicted to be the second most reactive site (4.6 kcal/mol), was not observed.

Proton NMR Spectral Analysis. Complete ^{1}H NMR assignments were made for all eight nitropolycyclic fluoranthenes (**8–15**) isolated in this study and for four of the parent hydrocarbons (**2, 5, 6,** and **7**). Previously, similar analyses were made for the remaining parent compounds (**1, 3,** and **4**)[8] and their ^{1}H assignments are listed in Table II.

The majority of the ^{1}H resonances of these hydrocarbons were assigned primarily through the combined analysis of COSY and LRCOSY spectra by the reported procedures.[8] In addition to regular aromatic couplings (ortho, meta, and para couplings), recognition of various internuclear long-range through-bond (epi and peri) and through-space (bay) couplings were particularly useful to map out the proton coupling networks. Selected couplings for **6** are illustrated in Figure 3. In general, coupling constants of 0.6–0.8 Hz have been recorded for all the peri (^4J) and epi (^5J) protons and approximately 0.5 Hz for through-space bay couplings.[19] Although the magnitude of these couplings varies depending on the specific pathway between the PAH protons, they are clearly detectable employing appropriate delays (e.g., τ = 0.1–0.3 s) in LRCOSY experiments. In the cases where COSY experiments fail to give any detectable through-space couplings between the protons of the indeno ring and the alternant aromatic portion of the molecule (e.g., H3 and H4 of **8** or H8 and H9 of **14**), 1D NOE difference and NOESY experiments were conducted.

In general, the assignments began with an assumption that the bay (e.g., H1 and H12 of **8**) or pseudo-bay (e.g., H4 and H5 of **13** or H12 and H13 of **14**) protons resonate

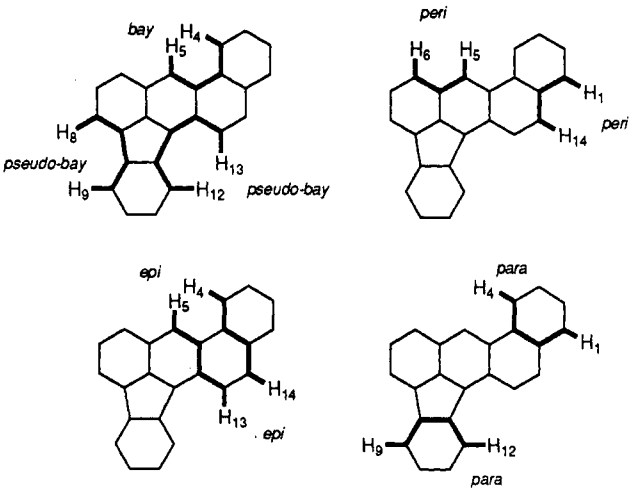


Figure 3. Various long-range couplings illustrated for **6**.

furthest downfield and the terminal indeno ring protons (the AB portion of ABMX, e.g. H5 and H6 of **8**) furthest upfield. In some cases, appearance (e.g. H11 of **11**, H6 of **12**) or disappearance (H8 of **8** and **10**, H14 of **13**, H5 of **14**, and H9 of **15**) of a singlet resonance was used as a convenient starting point. A typical example is the assignment of compound **14** and will be explained in detail below. This will be followed by brief assignment summaries of the remaining compounds (**2**, **5–13**, and **15**), whose pertinent 2D data are available as supplementary materials.

5-Nitrodibenz[*a,j*]aceanthrylene (14). As briefly mentioned in the previous section, the ^{1}H NMR spectral pattern of **14** was relatively unchanged from that of the parent hydrocarbon (**6**). The most notable feature was the absence of the downfield meso-bay proton H5 signal at δ 9.21 (Figure 4). With the exception of the two protons resonating near δ 7.79, the remaining 13 proton signals of **14** are well-resolved and grouped into four different spin systems, i.e., one isolated AX (H13,14), one AMX (H6,7,8), and two ABMX (H1,2,3,4 and H9,10,11,12) systems. It was assumed that the three most downfield doublets resonating in the δ 8.2–8.6 region arise either from the bay (H4) or the pseudo-bay (H12 and H13) protons and the most upfield protons centered around 7.44 ppm arise from the AB portion (H10,11) of the indeno ring.[8]

The most downfield doublet at δ 8.50 consistently showed a strong single cross peak in both high (Figure 4a) and low-resolution COSY (not shown) spectra, while the other two doublets at δ 8.33 and 8.29 exhibited multiple cross peaks. This implied that the former cross peak is a strong ortho coupling due to an isolated AX interaction between H13 and H14. This cross peak, arising from the only available two-spin system in the molecule, was too weak to be detected in both the LRCOSY and triple-quantum-filtered COSY spectra (TQF-COSY), as shown in Figure 4, parts b and c, respectively. Additional evidence for this conclusion was obtained from the observation of the relatively larger ortho J(13,14) coupling (9.21 Hz), which falls into a typical range (9.0–9.5 Hz) for the K-region double bond for benz[*a*]anthracene derivatives. This is a consequence of the higher double bond character of the C13–C14 bond of **14**. In COSY (Figure 4a), the resonance at δ 8.29 displayed a strong vicinal cross peak with one of the high-field protons resonating around δ 7.42, indicating its connection to the ABMX network arising from

(19) Evans, F. E.; Fu, P. P.; Cairns, T.; Yang, S. K. *Anal. Chem.* **1981**, *53*, 558–560.

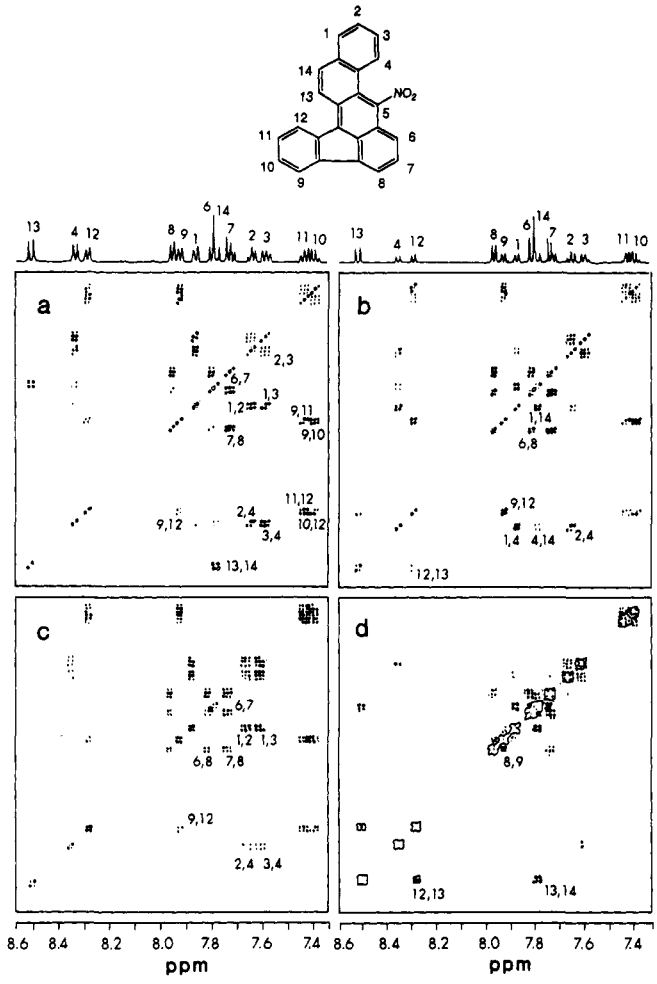


Figure 4. Contour plots of (a) COSY, (b) LRCOSY, (c) TQF-COSY, and (d) NOESY spectra of 14 are shown. Relevant through-bond and through-space couplings are indicated. Notice that a strong AX coupling between H13 and H14 is suppressed in the LRCOSY (b) and TQF-COSY (c) spectra.

H9,10,11,12 of the indeno ring. On the basis of these findings, the most downfield proton was assigned to H13 and the remaining two protons at δ 8.33 and 8.29 to H4 and H12, respectively.

Assignments of the remaining protons could then be carried out in a "walk-through" manner using a combination of COSY and LRCOSY spectra. Recognition of various internuclear long-range couplings in LRCOSY (τ = 0.2 s) facilitated the process of assigning protons.[8] For example, the K-region H14 exhibits a five-bond zig-zag epi coupling with H4, which is then connected with H3, H2, and H1 via ortho, meta, and para couplings, respectively (Figure 4a,b). An observation of a weak through-space interaction between the pseudo-bay protons, H12 and H13, was crucial in assigning the remaining protons (H9,10,11,12) of the indeno ring. An identical spatial interaction was also detected in the NOESY spectrum (Figure 4d). Also detected in the latter NOESY spectrum was an NOE between the pseudo-bay protons H8 and H9, which was crucial in assigning the protons (H6,7,8) of the isolated AMX system. These results were further verified by the NOE's observed on H8 and H13 upon saturation of H9 and H12 in 1D NOE difference experiments.

Complete ^{1}H NMR assignments of the parent compound **6** were made in a similar manner. The presence of the meso-bay proton H5 singlet in the ^{1}H NMR of **6** was a convenient starting point for the assignment process. For example, the H5 proton exhibited a peri coupling to H6 and a bay coupling to H4, as well as an epi coupling to H13, which in turn displayed a strong ortho coupling and a pseudo-bay coupling to H12. The connectivities (H12/H13 and H8/H9) between the protons of the indeno and the alternant aromatic portions of the molecule were also established by 1D NOE experiments. The results of the complete ^{1}H NMR assignments of **14** and the parent hydrocarbon **6** are listed and compared in Table II.

8-Nitrobenz[*e*]acephenanthrylene (8). The 500-MHz ^{1}H NMR spectrum of **8** was characterized by the disappearance of the H8 singlet signal of the parent compound **1**. The chemical shifts and coupling patterns exhibited in the ^{1}H NMR spectrum of **8** closely resemble those of **1**, whose complete ^{13}C and ^{1}H assignments have been determined.[8] The absence of the H8 singlet in the ^{1}H NMR spectrum of the product provides strong evidence for 8-nitro substitution. Recognition of a weak through-space interaction between the two downfield protons H12 and H1 in LRCOSY allowed the assignments of the protons belonging to the phenanthrene portion of the molecule to be completed. Unambiguous assignments of the indeno protons (H4,5,6,7) were made by recording an NOESY experiment, in which the H3 signal at δ 7.94 exhibited a weak through-space NOE to a multiplet at δ 7.82. This NOESY experiment confirmed the latter as H4, which in turn revealed a series of couplings, ortho, meta, para to H5, H6, and H7, respectively.

1-Nitrobenz[*e*]acephenanthrylene (9). The bay H12 proton of **9** exhibited a long-range epi coupling with the H8 singlet at δ 8.26 in addition to the ortho (H12/H11), meta (H12/H10), and para (H12/H9) couplings. The NOEs of H7 and H9 observed upon saturation of H8 at δ 8.26 provided unambiguous assignments of the indeno ring protons (H4,5,6,7). The relative assignment of the AB-type protons (H2 and H3), centered around δ 7.91, was difficult because they did not exhibit any long-range couplings to other protons. We attempted to solve this ambiguity by irradiating the H4 multiplet at δ 7.92 in the 1D NOE difference experiment or by recording an NOESY spectrum, but the data were not convincing due to their close chemical shifts.

8-Nitrobenz[*a*]aceanthrylene (10) and Benz[*a*]aceanthrylene (2). The absence of the characteristic H8 singlet and other features in the COSY and LRCOSY spectra of **10** were consistent with its assignment as 8-nitrobenz[*a*]aceanthrylene. The basic assumptions are that the indeno ring protons, H2 and H3, resonate furthest upfield and the pseudo-bay H12 and H1 protons furthest downfield. Thus, H1 at δ 8.31 was differentiated from the other pseudo-bay proton H12 at δ 8.76 on the basis of LRCOSY spectrum, which showed couplings with the most upfield signals at H2 (ortho), H3 (meta), as well as para coupling with H4 at δ 7.92, consistent with it being part of the indeno ring system. A through-space interaction between the two pseudo-bay protons (H1 and H12) was observed in LRCOSY. The NOE observed on H12 upon saturation of H1 in the 1D NOE difference experiment provided further evidence for their close spatial proximity. These findings allowed unambiguous assignment of the protons that belong to two ABMX systems (H9,10,11,12 and H1,2,3,4). In COSY, the ^{1}H signal, which appeared as a partially resolved triplet at δ 7.71 in the 500-MHz

NMR spectrum, coupled strongly with the multiplet at δ 7.92, which was integrated as three protons. This allowed assignment of the triplet at δ 7.71 to H6 and the two protons at δ 7.92 to H5 and H7, which are also degenerated with H4.

The ^{1}H assignments of the parent compound **2** were carried out in a similar manner. The most distinctive feature in the ^{1}H NMR spectrum of **2** was the presence of the meso H8 singlet at δ 8.47, which exhibited peri couplings to H7 and H9 and a five-bond zig-zag epi coupling to the pseudo-bay proton H12.

12-Nitroindeno[1,2,3-*cd*]pyrene (11). In accordance with the electron-rich nature of the pyrene ring, the LRCOSY spectrum of **11** displayed a number of useful long-range couplings. Some of these include the peri (H2/H3 and H5/H6) couplings and a five (H4/H6)- and six-bond zig-zag (H6/H11 and H6/H2) couplings. The NOEs on H5 and H7 upon saturation of H6 provided an unambiguous connectivity between the protons of the indeno (H7,8,9,10) and the pyrene portions of the molecule. The order of sequence of ^{1}H signal assignments of **11** was consistent with those reported by Minabe and Shibuya.[16] Complete ^{1}H and ^{13}C NMR assignments of the parent compound **3** were reported previously.[8]

5-Nitroindeno[1,2,3-*hi*]chrysene (12). A crucial coupling in the LRCOSY of **12** was a five-bond zig-zag epi coupling between the bay proton singlets H14 and H6, which were then further related to H1 and H7, respectively, by a through-space interaction. Irradiations of H14 and H9 yielded NOE's on H13 and H10, respectively, establishing the connectivity between the indeno and the chrysene portions of the molecule. Complete ^{1}H and ^{13}C NMR assignments of the parent hydrocarbons **4** were reported previously.[8]

14-Nitrodibenz[*a*,*e*]aceanthrylene (13) and Dibenz[*a*,*e*]aceanthrylene (5). The three ABMX spin systems (H1,2,3,4, H5,6,7,8, and H10,11,12,13) of **13** were related by the NOEs observed on H8 and H10 upon irradiation of H9 and by the NOE on H5 upon irradiation of H4. Using the singlet H9 at δ 8.17 as a convenient starting point, a complete ^{1}H assignment of **13** was accomplished. An epi coupling between H9 and H13 was observed in its LRCOSY spectrum. Complete ^{1}H NMR assignments of the parent hydrocarbon **5** were made in an analogous manner. In particular, the meso-bay H14 singlet at δ 9.00 of **5** displayed a peri coupling to H1 and a bay coupling to H13, which facilitated the assignment process.

9-Nitrodibenz[*e*,*k*]acephenanthrylene (15) and Dibenz[*e*,*k*]acephenanthrylene (7). Analysis of 2D spectral data of **15** was fully consistent with nitro substitution at the 9-position. In LRCOSY, the most downfield meso-bay H14 singlet at δ 9.16 exhibited epi couplings to H8 and H10, as well as a bay coupling to H1 and a peri coupling to H13. To confirm the close spatial proximity between the bay protons (H14 and H1), and between the pseudo-bay protons (H8 and H7), 1D NOE difference experiments were conducted. The latter NOE established the connectivity between the protons of the indeno and the benz[*a*]anthracene portions of the molecule. Complete assignments of the parent compound **7** were accomplished in a similar manner. The presence of meso-bay H9 singlet was characterized by its peri coupling to H8 and H10, an epi coupling to H13, and a para coupling to H14. The latter coupling represents a para coupling between the two meso protons (H9 and H14), which is unique for **7**.

Table III. Nitro Substitution Effect on Peri, Bay, and Ortho Proton Chemical Shifts of Polycyclic Fluoranthenes[a]

compound	peri proton Δδ[b]	bay proton Δδ	ortho proton Δδ
8	+0.07 (H9), +0.08 (H7)		
9		+0.41 (H12)	−0.14 (H2)
10	+0.10 (H7), −0.02 (H9)		
11	−0.93 (H1)		−0.81 (H11)
12	−0.70 (H4)		−0.70 (H6)
13	+0.31 (H1)	+0.48 (H13)	
14	+0.26 (H6)	+0.52 (H4)	
15	+0.20 (H8), +0.14 (H10)		

[a] Chemical shifts downfield from TMS. [b] Δδ = δ parent compound − δ nitro derivative, − indicates a downfield shift and + indicates an upfield shift relative to the parent polycyclic fluoranthenes.

Conformational Analysis. Orientation of the nitro substituent with respect to the aromatic ring of a nitroarene is a unique structural feature that can affect their spectroscopic and biological properties.[2,10,13,20] A nitro group in a sterically crowded position (such as in the bay region) is known to adopt a perpendicular or nearly perpendicular conformation to the plane of the aromatic ring system to relieve van der Waals interactions with adjacent protons. As a result, the anisotropy effect of the nitro group causes a significant shielding of nearby peri or bay protons. Nitroarenes containing only one adjacent peri proton or substituent adopt a coplanar or nearly coplanar orientation of the nitro group to the aromatic rings. This allows the maximum π-electron interaction between the nitro and the aromatic moiety. Accordingly, the protons (peri and ortho) in the vicinity of the nitro group of these compounds exhibit marked downfield shifts and significant changes in their UV-visible spectra.

Based on the degree of the anisotropic effect of the nitro substituent, the nitropolycyclic fluoranthenes **8**–**15** can be classified into three different categories. This classification was possible because of the availability of complete ^{1}H NMR assignments of the nitropolycyclic fluoranthenes and those of their parent hydrocarbons (Table II). The effect of nitro substitution on peri, bay, and ortho proton chemical shifts of the fluoranthenes **1**-**7** is summarized in Table III.

The first group represents those possessing only one peri proton, such as **11** and **12**. Significant downfield shifts (0.7–0.9 ppm) were observed for those protons peri (H1 of **11** and H4 of **12**) and ortho (H11 of **11** and H6 of **12**) to the nitro substituent, suggesting that the plane of the nitro substituent is nearly coplanar with the aromatic rings (Table III). Consistent with these observations, the UV-visible spectra of **11** and **12** were significantly different from those of the corresponding hydrocarbons. This indicates maximum π-electron conjugation between the nitro group and the aromatic ring due to the near coplanarity of the nitro substituent.

The compounds **8**, **10**, and **15**, which belong to the second group, have an additional peri or pseudo-bay proton. The peri proton (H9) of **8** is slightly shielded (+0.07 ppm) as compared to that of the parent compound **1**. This contrasts with the magnitude and direction of chemical shift change (−0.42 ppm) observed for the same peri proton (H8) of 9-nitrophenanthrene,[13] indicating a significant difference in nitro group orientation. These results imply that the 8-nitro group of **8** is not exactly coplanar with the aromatic

(20) Fu, P. P.; Heflich, R. H.; Unruh, L. E.; Shaikh, A. U.; Wu, Y.; Lay, C.; Lai, J. *Mutat. Res.* **1988**, *209*, 115–122.

ring, presumably due to the steric hindrance between the 8-nitro group and H7 of the indeno ring. The close proximity of the two groups can be demonstrated indirectly by performing a 1D NOE experiment on the parent compound **1**, i.e., irradiation of H8 of **1** yielded a NOE to H7 which is consistent with the above steric argument. The chemical shift changes observed for the peri protons (+0.10 and −0.02 ppm, respectively for H7 and H9) of **10** upon 8-nitro substitution were not as significant as that (+0.15 ppm) observed for the similar peri protons (H1 or H8) of 9-nitroanthracene. The only structural difference between **10** and 9-nitroanthracene is the fusion of an indeno ring on the top side of the former. This may result in some distortion of the plane of the aromatic ring system due to steric interaction between H1 and H12 which may in turn affect the conformation of the nitro group. The chemical shift of the peri protons H8 and H10 of **15** are upfield (+0.20 and +0.14 ppm, respectively) as compared with those of **7**. The magnitude and direction of the chemical shift changes are quite comparable to that observed for the similar peri protons (H6 and H7) of 9-nitrobenz[*a*]anthracene.[13] The orientation of the nitro groups of this class (**8**, **10**, and **15**) is clearly out-of-plane, but not as perpendicular as those observed for the bay-nitro substituted compounds discussed below.

Compounds **9**, **13**, and **14**, containing a nitro group in the bay region, belong to the last category. As speculated, the bay protons located in the angular ring (H12, H13, and H4, respectively for **9**, **13** and **14**) were shielded significantly. The shielding effect was greater (+0.48–0.52 ppm) in the latter two, consistent with the fact that the nitro groups of **13** and **14** are more sterically crowded by the presence of an extra peri proton. These results suggest that the plane of the nitro group of these compounds is perpendicular or nearly perpendicular to the aromatic ring. This out-of-plane orientation of the nitro group would result in a minimal amount of π-electron delocalization between the nitro group and the aromatic ring. The UV-visible spectra (Figure 1, supplementary material) of **9**, **13**, and **14** were found to be virtually identical to those of the parent compounds, indicating that there are no π-electron interactions between the nitro group and the aromatic ring.

Finally, it should be noted that the upfield shift (+0.41 ppm) of the angular-bay proton H12 of 1-nitrobenz[*e*]acephenanthrylene (**9**) contrasts with the large downfield shift (−1.42 ppm) observed for the same proton of 1-bromobenz[*e*]acephenanthrylene.[14] This clearly demonstrates that the angular H12 of **9** is under the influence of the anisotropy of the sterically hindered nitro group in the 1-position, whereas that of 1-bromobenz[*e*]acephenanthrylene is solely under the influence of the long-range electrostatic effect.

Conclusions

The present investigation represents the first systematic study of the nitration of the polycyclic fluoranthenes. A total of eight mononitro derivatives (**8**–**15**) of polycyclic fluoranthenes were synthesized and characterized by analysis of their nuclear Overhauser effects, COSY, and LRCOSY spectra.

The observed sites of nitro substitution of the polycyclic fluoranthenes (**1**–**7**) are in excellent agreement with predictions based on DEWAR-PI molecular orbital calculations.[9] The preferred nitration site of polycyclic fluoranthenes could be predicted with high accuracy by the DEWAR-PI method.[9] For **1**, **4**, and **7**, the differences in the calculated energy between the lowest (8, 5 and 9-positions) and the second lowest sites (1, 14, and 14-positions, respectively, for **1**, **4**, and **7**) are well within the limits of error (<5 kcal/mol). The formation of a significant amount of **9** as the second isomer in the case of **1** may be a consequence of relatively less steric crowding in the 1-position of **1** as compared to the 14-positions of **4** and **7**. On the other hand, there does not seem to be any steric basis for the high regioselectivities observed for the nitration of **2**, **5**, and **6**, even though the relative energies of the second favored sites predicted for these hydrocarbons are far greater than 5 kcal/mol. This may be due to the fact that the bay-region nitro groups of **13**, **14**, and **15** can relieve steric crowding by rotation around the C–N bond.

The availability of the complete ^{1}H NMR assignments of these nitro compounds and the corresponding parent hydrocarbons made it possible to probe the orientation of the nitro groups with respect to the plane of aromatic ring systems. The orientation of nitro groups was previously shown to be an important structural factor for predicting the mutagenic activities of polycyclic nitroarenes.[2] On the basis of the present findings, the nitro-substituted polycyclic fluoranthenes **8**–**15** (Figure 1) can be classified into three categories: (1) those (**11** and **12**) in which the plane of the nitro group is coplanar, or nearly coplanar, with the aromatic rings, (2) those (**9**, **13**, and **14**) in which the nitro group is perpendicular to the aromatic ring system, and (3) those (**8**, **10**, and **15**) in which the nitro group is oriented between these two extremes.

Experimental Section

All seven polycyclic fluoranthenes (**1**–**7**) that were used as the starting materials were synthesized by methods described previously.[7] Dinitrogen tetroxide (N_2O_4, Aldrich Chemical Co., Milwaukee, WI.) solution was prepared by passing the gas into a preweighed stoppered Erlenmeyer flask containing about 100 mL of methylene chloride until a reddish saturated solution is obtained (0.3 mg/mL). Acetyl nitrate solution was prepared by diluting 1 mL of HNO_3 (70%, d = 1.413) 10-fold by acetic anhydride with ice-cooling. It is essential to prepare these solutions freshly before the reaction.

Melting points were measured using Büchi 535 melting point apparatus and uncorrected. Mass spectral data were obtained on a Finnigan-MAT 4023 mass spectrometer in the EI mode. Ultraviolet-visible spectra were taken on a Hitachi U-2000 spectrophotometer using methanol as solvent. HPLC analysis of nitration mixtures was carried out on a Waters liquid chromatography system equipped with a Hitachi L-3000 photodiode-array detector. Econosil (Alltex) ODS analytical column (4.6 mm i.d. × 25 cm) was used with 100% methanol and the flow rate was 1 mL/min. All TLC were run on Merck precoated silica gel 60 F 254 plastic plates using a ethyl acetate/hexane (1:4) solvent system.

NMR Experiments. Proton NMR spectra were obtained either on a Bruker AM500 NMR (500 MHz, National Center for Toxicological Research) or on a Bruker AM300 (300 MHz, The University of Rhode Island) spectrometer in $CDCl_3$ with trimethylsilane as internal standard. All ^{1}H chemical shifts and coupling constant data for **1**–**15** are listed in the Table II. All ^{13}C NMR measurements (75.5 MHz) were recorded on a Bruker AM300.

The COSY, long-range COSY (LRCOSY), triple-quantum-filtered COSY, and NOESY spectra were obtained using standard Bruker automation programs (COSY.AUR, COSYLR.AUR, COSYTQF.AUR, and NOESY.AUR, respectively). Appropriate τ delays (D_3 = 0.1–0.3 s) were used to detect various internuclear couplings (Figure 3) in the LRCOSY spectra. The NOESY

spectra were recorded with a mixing time of 1 s. All 2D experiments were acquired in magnitude mode. The F_2 dimension was zero-filled. The data were apodized with unshifted sine bell apodization function in each dimension and symmetrized along the diagonal. 1D NOE difference experiments were conducted using 1 s of mixing time. After an exponential line broadening of 2 Hz was applied, the FIDs were subtracted and Fourier transformed to obtain the NOE difference spectra.

Typical Nitration Procedure Using N_2O_4 Solution. To a solution of the appropriate polycyclic fluoranthene (10–50 mg) in 20 mL of dry methylene chloride was added 1.2 equiv of N_2O_4 in methylene chloride. After stirring for the appropriate time (Table I), the solvent was evaporated under a stream of nitrogen. The crude product was dissolved in methylene chloride, a small amount of silica was added to the solution, and the mixture was evaporated to dryness. It was then applied to silica column and eluted with ethyl acetate and hexane (1:9). In most cases, the nitro derivatives displayed characteristic yellowish bands in the silica column, which can be conveniently collected.

Typical Nitration Procedure Using Acetyl Nitrate Solution. To a solution of the polycyclic fluoranthene (10–50 mg) in acetic anhydride in an ice-bath was added 5 equiv of acetyl nitrate solution. After stirring at room temperature for the appropriate time (Table I), the mixture was poured onto crushed ice containing 2–5 mL of concd HCl and stirred vigorously for 3 h to hydrolyze excess acetic anhydride. The product was isolated either by filtration or by extraction with methylene chloride. The methylene chloride extracts were washed with saturated $NaHCO_3$ three times and water two times, dried over anhyd $MgSO_4$, and purified as described above.

Reaction progress was monitored by silica TLC using a ethyl acetate/hexane (1:4) solvent system. In all cases, the nitrated products eluted slowly with visibly intense yellow and/or orange color on TLC. The reaction progress was also monitored by HPLC equipped with a photodiode-array detector, which provided additional structural information about the small amounts of minor products found in some reaction mixtures.

8-Nitrobenz[*e*]acephenanthrylene (8). Nitration of 1 (104 mg, 0.4 mmol) with 1.2 equiv of N_2O_4 by the general procedure (3 h) afforded 102 mg of the product as a mixture (83:17) of **8** and **9**. The major product **8** was isolated (89 mg, 75%) as yellow needles after recrystallization: mp (ethyl acetate/hexane) 207–208 °C; HPLC t_R 7.59 min; TLC R_f 0.50; ^{13}C NMR δ 141.5 (q), 141.2 (q), 137.7 (q), 134.0 (q), 131.3 (q), 131.2 (q), 130.3, 130.1, 128.4 (two overlapped methine carbons), 127.9 (q), 125.7 (q), 125.1 (q), 124.4, 123.7, 123.4, 121.9, 121.6, 120.7; UV λ_{max} (log ϵ) 336 nm (3.94), 299 (4.23), 289 (4.22), 253 (4.56), 220 (4.48); MS *m/e* 297 (M^+). Anal. Calcd for $C_{20}H_{11}NO_2$: C, 80.83; H, 3.73; N, 4.71. Found: C, 80.64; H, 3.85; N, 4.69. A small amount of the minor product **9** was separated from the filtrate by means of HPLC using a semiprep ODS column (Beckman Ultrasphere, 1 cm × 25 cm): HPLC t_R 6.12 min; ^{1}H NMR (see Table II); MS *m/e* 297 (M^+).

8-Nitrobenz[*a*]aceanthrylene (10). The N_2O_4 nitration of **2** (15 mg, 0.6 mmol) by the general procedure (40 min) afforded pure **10** (17 mg, 94%) as a red-brick solid: mp (ethyl acetate/hexane) 215–216 °C; HPLC t_R 7.38 min; TLC R_f 0.51 (orangish yellow); ^{13}C NMR δ 143.8 (q), 139.7 (q), 139.1 (q), 137.1 (q), 135.9 (q), 133.4 (q), 130.7, 129.6 (q), 128.7, 128.3, 128.2, 127.8, 125.8 (q), 124.8, 124.5, 123.8, 122.2, 122.2, 120.8, 120.2 (q); UV λ_{max} (log ϵ) 433 nm (3.95), 265 (4.59), 251 (4.56), 212 (4.59); MS *m/e* 297 (M^+). Anal. Calcd for $C_{20}H_{11}NO_2$: C, 80.83; H, 3.73; N, 4.71. Found: C, 80.71; H, 3.87; N, 4.56.

12-Nitroindeno[1,2,3-*cd*]pyrene (11). Nitration (83 mg, 0.3 mmol) of **3** with N_2O_4 solution by the general procedure gave a mixture of 12-nitro and two other mononitro isomers in 9:1 ratio. The major 12-nitro isomer **11** was obtained as bright yellow powder (88 mg, 91%) after recrystallization from ethyl acetate and hexane: mp (ethyl acetate/hexane) 246–249 °C (lit.[16] 238–240 °C); HPLC t_R 12.60 min (major isomer), 11.45, 11.84 min (minor mononitro isomers); TLC R_f 0.78; ^{13}C NMR δ 143.5 (q), 140.0 (q), 138.8 (q), 135.4 (q), 134.1 (q), 132.4 (q), 132.0 (q), 131.6, 131.2, 129.6 (q), 129.0, 129.0, 128.2, 127.8, 125.1 (q), 124.6, 123.0, 122.6, 122.3 (q), 122.2, 121.8 (q), 117.2; UV λ_{max} (log ϵ) 373 nm (4.25), 344 (4.23), 296 (4.37), 249 (4.69), 240 (4.64), 210 (4.58); MS *m/e* 321 (M^+).

5-Nitroindeno[1,2,3-*hi*]chrysene (12). Nitration (30 mg, 0.1 mmol) of **4** with N_2O_4 solution provided exclusively **12** (31 mg, 91%) as yellow solid after chromatography on silica gel, followed by recrystallization from ethyl acetate and hexane: mp (ethyl acetate/hexane) 243–245 °C; HPLC t_R 10.86 min; TLC R_f 0.73 (visibly yellow); ^{13}C NMR δ 145.9 (q), 140.8 (q), 139.2 (q), 138.5 (q), 137.6 (q), 133.5 (q), 132.5 (q), 132.1 (q), 129.7, 129.3, 128.6, 128.1, 128.1, 127.9 (q), 126.3 (q), 124.1, 123.9 (q), 123.8, 122.4, 122.2, 121.9, 120.8, 120.1 114.7; UV λ_{max} (log ϵ) 386 nm (4.01), 287 (4.34), 262 (4.33), 213 (4.29); MS *m/e* 347 (M^+). Anal. Calcd for $C_{24}H_{13}NO_2$: C, 82.98; H, 3.77; N, 4.03. Found: C, 83.27; H, 3.96; N, 4.30.

14-Nitrodibenz[*a,e*]aceanthrylene (13). Nitration (24 mg, 0.08 mmol) of **5** with N_2O_4 solution afforded exclusively **13** (24 mg, 87%) as golden yellow needles, mp (methylene chloride/hexane) 226–228 °C; HPLC t_R 11.38 min; TLC R_f 0.49; ^{13}C NMR δ 147.3 (q), 144.9 (q), 140.2 (q), 140.0 (q), 139.2 (q), 136.8 (q), 134.4 (q), 132.9 (q), 130.4, 130.3, 129.3, 128.8 (q), 128.6, 128.6, 128.2, 128.0, 127.4 (q), 125.8, 125.0, 122.2, 122.1, 121.8, 120.9, 120.8; UV λ_{max} (log ϵ) 428 nm (4.19), 298 (4.88), 253 (3.66), 224 (4.98); MS *m/e* 347 (M^+). Anal. Calcd for $C_{24}H_{13}NO_2$: C, 82.98; H, 3.77; N, 4.03. Found: C, 83.19; H, 4.00; N, 3.88.

5-Nitrodibenz[*a,j*]aceanthrylene (14). Nitration (30 mg) of **6** with N_2O_4 solution afforded exclusively **14** (29 mg, 82%) as golden yellow needles, mp (methylene chloride/hexane) 210–212 °C; HPLC t_R 10.69 min; TLC R_f 0.49; UV λ_{max} (log ϵ) 402 nm (3.02), 300 (4.53), 288 (4.82), 262 (4.63), 246 (3.67), 213 (4.61); MS *m/e* 347 (M^+). Anal. Calcd for $C_{24}H_{13}NO_2$: C, 82.98; H, 3.77; N, 4.03. Found: C, 82.76; H, 4.00; N, 4.30.

9-Nitrodibenz[*e,k*]acephenanthrylene (15). Nitration of **7** (24 mg, 0.8 mmol) with 1.2 equiv of N_2O_4 solution yielded (20 min) **15** (25 mg, 91%) as the sole product: mp (ethyl acetate/hexane) 255–257 °C; HPLC t_R 10.86 min; TLC R_f 0.42; ^{13}C NMR, all except one quaternary carbon was detected, δ 146.98 (q), 141.3 (q), 138.6 (q), 137.6 (q), 137.5 (q), 132.2 (q), 131.3 (q), 129.6, 129.5, 128.9, 128.5, 128.3(q), 127.9, 127.1, 126.8 (q), 124.8, 123.3 (q), 122.9, 121.5, 121.5, 121.4, 120.4, 113.5; UV λ_{max} (log ϵ) 410 nm (3.63), 388 (3.83), 367 (3.77), 353 (3.83), 318 (4.46), 280 (4.61), 260 (4.61), 249 (4.53); MS *m/e* 347 (M^+). Anal. Calcd for $C_{24}H_{13}NO_2$: C, 82.98; H, 3.77; N, 4.03. Found: C, 82.88; H, 4.00; N, 4.05. In some runs with acetyl nitrate solution, HPLC photodiode-array analysis indicated the formation of a small amount of the oxidative product quinone **16**, which exhibited an identical retention HPLC time (t_R 17.12 min) and UV-visible and ^{1}H NMR spectral chracteristics as those of authentic sample.[7b]

Acknowledgment. We thank Dr. Matthew S. Bryant for measuring mass spectra. The work was in part supported by The University of Rhode Island Proposal Development Award (1992–1993) to B.P.C. and by a grant from the National Institute of Health Sciences (ES 04266) to R.G.H.

Supplementary Material Available: UV-visible spectral data for 1–8 and 10–15 and 2D ^{1}H NMR data (COSY, LRCOSY, and NOESY) for 5–7, 8–13, and 15 (13 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.