1-(2-Hydroxy-3-methoxyphenyl)-2-vinyl-3-buten-1-ol. Method A, using 117 mg (0.8 mmol) of *o*-vanillin, 125 mg (0.85 mmol) of 1-bromo-2,4-pentadiene, and 52 mg (0.8 mmol) of zinc, gave crude alcohol, which was purified by preparative TLC, eluting with 15% ethyl acetate/ligroin to prove 63 mg of product (36% yield). TLC: silica gel, 10% ethyl acetate/ligroin, R_f = 0.17; 20% ethyl acetate/ligroin, R_f = 0.47. NMR: δ 3.32 (q, J = 7.5, 1 H), 3.92 (s, 3 H), 2 superimposed doublets 4.88 (J = 7.17) and 4.90 (J = 7.15), together (1 H, C*H*OH), 5.00–5.30 (m, 4 H), 5.71–5.85 (m, 1 H), 5.88–6.05 (m, 1 H), 6.8–6.9 (m, 3 H). The two superimposed doublets integrate roughly 1:1. When the decoupler was set at 3.322 ppm, the two superimposed doublets collapsed into two singlets at 4.88 and 4.90 ppm. They are broad and superimposed, too, and therefore integration is difficult. IR (Perkin-Elmer): 3600 (s), 3000 (m) with shoulder at 2950, 1500 (s), 1250 (s) cm^{-1}.

4-*tert*-Butyl-1-(2-propenyl)cyclohexanol. Method A with use of 0.168 g (1.1 mmol) of 4-*tert*-butylcyclohexanone, 0.1 mL (1.2 mmol) of allyl bromide, and 78 mg (1.2 mmol) of zinc gave 40% yield of the alcohol as a 60/40 axial/equatorial mixture by comparison with an authentic sample.[7]

1-Allyl-1,2-cyclohexanediol. Method A was used with 154.5 mg (1.36 mmol) of 2-hydroxycyclohexanone, 0.17 mL (2 mmol) of allyl bromide, and 130 mg (2 mmol) of zinc to produce the diol as a yellow oil (0.190 g, 89.7%). GC (3 ft): 5.12 min. TLC: silica gel, 50% ethyl acetate/ligroin: R_f = 0.6 (blue) and R_f = 0.48 (red, color indicated is obtained by visualizing the TLC plate with vanillin spray). NMR: δ 1.20–1.80 (m, 8 H), 2.06 (br s, 1 H), 2.13 (br s, 1 H), 2.26–2.47 (m, 2 H), 3.47 (d apparent, J = 7.83, 1 H), 5.15 (m, 2 H), 5.80–6.00 (m, 1 H). GC–MS (relative abundance): 115.0 (17.2), 97.0 (17.2), 79.0 (17.2), 69.9 (13.8), 69.1 (34.5), 58.1 (20.7), 57.1 (27.6), 55.1 (44.8), 43.1 (44.8), 41.1 (100.0). ^{13}C: δ 21.21, 23.37, 30.50, 34.46, 43.77, 73.43, 118.70, 133.94. IR (Nujol): 3500 (s), 3000 (s), 1650 (w), 1050 (br m), 970 (m), 910 (m) cm^{-1}. Accurate mass (EI^+): calcd for $C_9H_{16}O_2$ 156.1146, obsd 156.1150.

2-Methyl-1-decen-4-ol. Method B was used on 0.576 g (5.05 mmol) of heptaldehyde, 1 mL (10.1 mmol) of 3-chloro-2-methylpropene, 0.650 g (10 mmol) of zinc, and 0.5 g of C_{18} silica gel. The mixture was stirred for 16 h. The product was obtained in 56% yield (0.480 g). NMR data matches the reported values.[15]

(15) Hegedus, L. S.; Wagner, S. D.; Waterman, E. L.; Siirala-Hansen, K. *J. Org. Chem.* **1975**, *40*, 593.

1,8-Nonadien-4-ol. Method A was applied to 0.235 g (2.4 mmol) of 5-hexenal, 0.25 mL (2.9 mmol) of allyl bromide, and 0.199 g (3 mmol) of zinc in 2.5 mL of saturated aqueous solution of NH_4Cl and 0.5 mL of THF. After workup 0.254 g of crude product was obtained. A sample of 117.65 mg of crude product was purified by radial chromatography on a 1-mm plate, eluting with 10% ethyl acetate/ligroin to give 82.34 mg of 1,8-nonadien-4-ol as a yellow oil (70% yield). GC (3 ft): 2.34 min. TLC: silica gel, 10% ethyl acetate/ligroin, R_f = 0.30. NMR: δ 1.4–1.65 (m, 4 H), 1.65–1.75 (br s, 1 H), 2.05–2.40 (m, 4 H), 3.07 (br s, 1 H), 4.95–5.22 (m, 4 H), 5.75–5.95 (m, 2 H). GC–MS (relative abundance): 81.1 (91.3), 79.1 (13.9), 57.2 (35.7), 55.2 (70.9), 54.2 (15.9), 53.2 (18.7), 43.2 (65.2), 42.2 (21.5), 41.2 (100.0). ^{13}C: δ 25.09, 33.80, 36.37, 42.10, 70.67, 114.71, 118.23, 134.91, 138.77. IR (neat, Beckman IR-18): 3140 (s), 3060 (s), 3020 (w), 2800 (w), 1720 (s), 1650 (m), 1415 (s), 1250 (s), 990 (m), 910 (m) cm^{-1}.

1-Allylcyclohexanol. Method B was used on 0.490 g (5 mmol) of cyclohexanone, 0.86 mL (10 mmol) of allyl bromide, 0.650 g (10 mmol) of zinc, and 0.5 g of reverse-phase silica gel. The mixture was stirred for 2 h. 1-Allylcyclohexanol was obtained as a yellow oil (0.58 g, 82%). GC (3 ft): 2.16 min. TLC: silica gel, 10% ethyl acetate/ligroin, R_f = 0.52. NMR: δ 1.40–1.70 (m, 10 H), 2.25 (d, J = 7.45, 2 H), 5.08–5.24 (m, 2 H), 5.83–6.00 (m, 1 H). GC–MS (relative abundance): 99.1 (100.0), 81.0 (97.0), 79.0 (13.1), 57.1 (10.0), 55.1 (44.9), 43.0 (25.4), 41.0 (32.3).

7-Methyl-9-(trimethylsilyl)-4-hydroxy-1,7-nonadiene. Method B was used on 91.82 mg (0.5 mmol) of aldehyde, 0.09 mL (1 mmol) of allyl bromide, 65 mg (1 mmol) of zinc, and 50 mg of C_{18} silica gel. The mixture was stirred for 16 h. The crude product was purified by radial chromatography on a 1-mm plate, eluting with 7% ethyl acetate/ligroin. The product was obtained in 67.6% yield (76.4 mg). GC (3 ft): 5.28 min. TLC: silica gel, 10% ethyl acetate/ligroin, R_f = 0.42. NMR: δ 0.01 (s, 9 H, TMS), 1.59 (s, CH_3C=), 3.70 (br m, C*H*OH), 5.10–5.30 (m), and 5.60–6.00 (m), total area (4 H). GC–MS (relative abundance): 226.1 (M^+, 8.0), 95.1 (19.6), 75.1 (29.6), 73.1 (100.0), 68.1 (63.6), 67.1 (20.5), 45.0 (20.2), 43.0 (11.7), 41.0 (14.1).

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Synthesis of the K-Region Monofluoro- and Difluorobenzo[*c*]phenanthrenes

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Polycyclic aromatic hydrocarbons are metabolically activated by cytochromes P-450 and epoxide hydrolase to ultimate mutagens and carcinogens. Substitution by fluorine at specific positions has been used to elucidate metabolic activation and detoxication pathways of polycyclic aromatic hydrocarbons. Substitution by fluorine at the K-region C-6 position of the weak carcinogen benzo[*c*]phenanthrene (**1**) causes a >4-fold increase in its tumorigenicity. Out of the six possible monofluorobenzo[*c*]phenanthrenes, only 5-fluorobenzo[*c*]phenanthrene (**8a**) has not been evaluated as a carcinogen, presumably because a convenient synthetic method for the 5-fluoro derivative has not been available. Hence, a new method has been developed for the synthesis of **8a** from readily available starting materials. The method consists of selective bromination of benzo[*c*]phenanthrene (**1**) to 5-bromobenzo[*c*]phenanthrene (**3**), substitution of bromine by an amino group, and a modified Schiemann reaction of 5-aminobenzo[*c*]phenanthrene (**6a**) to yield 5-fluorobenzo[*c*]phenanthrene (**8a**). An improved method for the synthesis of 6-fluorobenzo[*c*]phenanthrene (**19**) has also been developed which consists of bromofluorination of β-naphthylstyrene, followed by selective dehydrobromination and photocyclization of the fluorostyrene to the 6-fluoro derivative **19**. The above methods, with minor modifications, also provided synthetic routes for the preparation of the difluoro derivatives 5,7-, 5,8-, and 6,7-difluorobenzo[*c*]phenanthrenes.

Polycyclic aromatic hydrocarbons are widespread environmental pollutants. They are metabolically activated by cytochromes P-450 and epoxide hydrolase to bay region diol epoxides which constitute an important class of ul-

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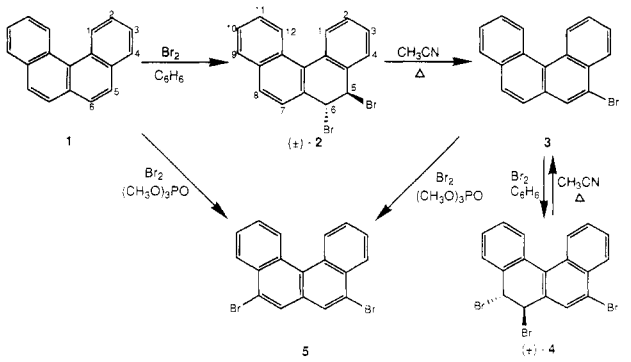
Scheme I



timate carcinogens formed from polycyclic aromatic hydrocarbons.[2] Because substitution by fluorine results in almost complete inhibition of oxidative metabolism at the substituted double bond of a polycyclic aromatic hydrocarbon,[3] fluoro derivatives have been used to elucidate metabolic activation and detoxication pathways of polycyclic aromatic hydrocarbons.[3,4] In case of benzo[*c*]phenanthrene (**1**), substitution by fluorine at the K-region[5] C-6 position causes a >4-fold increase in its carcinogenicity,[4c] at least in part, by blocking the oxidative metabolism at the K-region.[3d] The effect of fluorine substitution at the other carbon on a K-region, i.e. C-5, was not evaluated. In fact, Ittah and Jerina[6] had synthesized all the possible monofluoro derivatives of **1**, with the exception of 5-fluorobenzo[*c*]phenanthrene (**8a**), for the purpose of evaluating their tumorigenicity. Currently, a good synthetic procedure for the preparation of 5-fluorobenzo[*c*]phenanthrene (**8a**) is not available. Marx and Bergmann[7] had earlier reported that while they could readily synthesize 6-fluorobenzo[*c*]phenanthrene (**19**) by photocyclization of appropriately substituted β-naphthylstyrene, synthesis of **8a** required 10–13 steps and yielded the 5-fluoro derivative in less than 1% overall yield. We report here the synthesis of 5-fluorobenzo[*c*]phenanthrene (**8a**) from **1** in only four steps and with an overall yield of 25%. We also report a novel synthesis of 6-fluorobenzo[*c*]phenanthrene (**19**), which utilizes the intermediate β-naphthylstyrene, produced during the synthesis of benzo[*c*]phenanthrene (**1**) and its 5-fluoro derivative **8a**. Finally, we describe here the syntheses of three difluoro derivatives 5,7-, 5,8-, and 6,7-difluorobenzo[*c*]phenanthrenes.

Results and Discussion

Our approach to the synthesis of **8a** was based on the previous observation by Ittah et al.[8] that bromination of **1** yields 5-bromobenzo[*c*]phenanthrene (**3**) selectively (Scheme I). Position of bromine at C-5 in **3** was later confirmed by unequivocal assignment of all ^1H and ^{13}C resonances through the application of 2D NMR.[9] Bromination of **1** with bromine in benzene formed *trans*-5,6-dibromo-5,6-dihydrobenzo[*c*]phenanthrene (**2**) in quantitative yield.[8,10] A mixture of **1** and **3** in 1:2 ratio was obtained, respectively, when **2** was heated under reflux in acetonitrile. Two other minor products were also recovered which will be discussed later. It appears that two processes, i.e. elimination of hydrogen bromide vs dissociation of bromine are competing with each other. Sayer et al.[10] have reported that heating the dibromo derivative **2** in benzene under reflux for 10 min eliminated hydrogen bromide to form **3** in 90% yield. However, in our hands, over 50% of **2** was recovered after prolonged heating in benzene under reflux (>24 h). Furthermore, we did not observe significant change in the ratio of **1** to **3**, when they were formed from **2** under various reaction conditions, i.e. in different solvents and in the presence or absence of a base.

The 5-bromo derivative **3** was converted to 5-aminobenzo[*c*]phenanthrene (**6a**) when subjected to high-pressure ammonolysis by the procedure of Wisansky and Ansbacher[11] (Scheme II). The reaction of **3** with copper powder and cuprous chloride in 28% ammonium hydroxide in a sealed bomb at 170 °C yielded **6a** in 60% yield along with reduction product **1** (22%). Varying the amounts of copper or cuprous chloride or varying the temeprature had little effect on the percentages of the reduced product formed.

Aminobenzo[*c*]phenanthrenes have not been used as precursors for the fluorobenzo[*c*]phenanthrenes because of the reported failure by Bergmann and Blum[12] in carrying out the Schiemann reaction on an amino derivative of **1**. However, we were able to convert **6a** to **8a** in good yield. We carried out diazotization of **6a** with *tert*-butyl nitrite in the presence of excess boron trifluoride etherate in dimethoxyethane (DME) to afford the diazonium tetrafluoroborate **7a** in quantitative yield (Scheme II). The diazotization of aromatic amines by alkyl nitrite and boron trifluoride etherate is believed to proceed via initial formation of nitrosyl fluoride.[13] Pyrolysis of the diazonium salt **7a** in refluxing chlorobenzene produced **8a** in 65% yield. *Carrying out pyrolysis of the diazonium tetrafluoroborate in a high-boiling solvent, such as chlorobenzene, affords a significant improvement in the yields of the fluoro derivatives over the conventional method in which the diazonium tetrafluoroborate salts are pyrolyzed as solids.*[14]

The major product obtained by bromination of **1** is the 5-bromo derivative **3**. However, when this reaction was

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(2) Thakker, D. R.; Yagi, H.; Levin, W.; Wood, A. W.; Conney, A. H.; Jerina, D. M. In *Bioactivation of Foreign Compounds*; Anders, M. W., Ed.; Academic Press: New York, 1985; pp 177–242.

(3) (a) Jerina, D. M.; Daly, J. W. In *Drug Metabolism from Microbe to Man*; Park, D. V., Smith, R. L., Eds.; Taylor and Francis: London, 1976; pp 13–32. (b) Buhler, D. R.; Unlu, F.; Thakker, D. R.; Slaga, T. J.; Newman, M. S.; Levin, W.; Conney, A. H.; Jerina, D. M. *Cancer Res.* **1982**, *42*, 4779. (c) Amin, S.; Camanzo, J.; Hecht, S. S. *Cancer Res.* **1984**, *44*, 3772. (d) Prasad, G. B.; Mirsadeghi, S.; Boehlert, C.; Byrd, R. A.; Thakker, D. R. *J. Biol. Chem.* **1988**, *263*, 3676.

(4) (a) Buening, M. K.; Levin, W.; Wood, A. W.; Chang, R. L.; Agranat, I.; Rabinovitz, M.; Buhler, D. R.; Mah, D. H.; Hernandez, O.; Simpson, R. B.; Jerina, D. M.; Conney, A. H.; Miller, E. C.; Miller, J. A. *J. Natl. Cancer Inst.* **1983**, *71*, 309. (b) Hecht, S. S.; Hirota, N.; Loy, M.; Hoffmann, D. *Cancer Res.* **1978**, *38*, 1694. (c) Jerina, D. M.; Sayer, J. M.; Croisy-Delcey, M.; Ittah, Y.; Thakker, D. R.; Wood, A. W.; Chang, R. L.; Levin, W.; Conney, A. H. *Adv. Exp. Med. Biol.* **1982**, *IIA*, 501.

(5) K-Region is defined by the double bond in polycyclic aromatic hydrocarbons flanked between two benzo rings. The 5,6-double bond in benzo[*c*]phenanthrene (**1**) is an example of a K-region.

(6) Ittah, Y.; Jerina, D. M. *J. Fluorine Chem.* **1980**, *16*, 137.

(7) Marx, G. S.; Bergmann, E. D. *J. Org. Chem.* **1972**, *37*, 1807.

(8) Ittah, Y.; Thakker, D. R.; Levin, W.; Croisy-Delcey, M.; Rayan, D. E.; Thomas, P. E.; Conney, A. H.; Jerina, D. M. *Chem.-Biol. Interact.* **1983**, *45*, 15.

(9) Bax, A.; Ferretti, J. A.; Nashed, N.; Jerina, D. M. *J. Org. Chem.* **1985**, *50*, 3092.

(10) Sayer, J. M.; van Bladeren, P. J.; Yeh, J. C.; Jerina, D. M. *J. Org. Chem.* **1986**, *51*, 452.

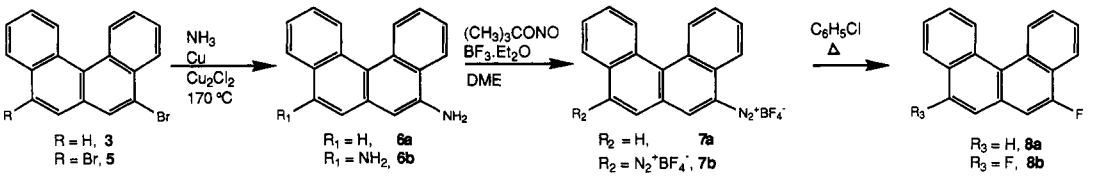
(11) Wisansky, W. A.; Ansbacher, S. *Org. Synth.* **1955**, *3*, 307.

(12) Bergmann, E. D.; Blum, J. *J. Org. Chem.* **1962**, *27*, 527.

(13) Doyle, M. P.; Bryker, W. *J. Org. Chem.* **1979**, *44*, 1572.

(14) By carrying out pyrolysis of the diazonium fluoroborates in refluxing chlorobenzene instead of pyrolyzing them as solids, we improved the yield of 5-fluorobenzo[*c*]phenanthrene (**8a**) from 21% to 65% and of 2-carbomethoxy-3-fluoronaphthalene from 25% to 75% (yields were calculated with respect to the amines).

Scheme II

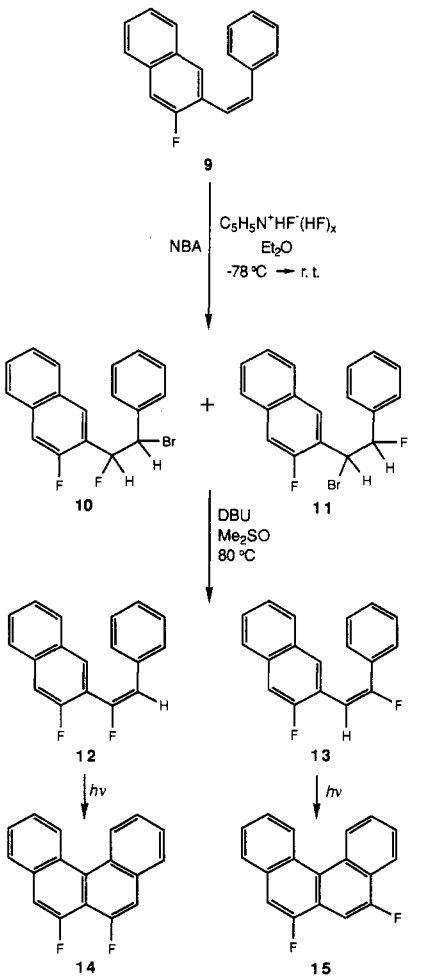


carried out on a preparative scale (14 mmol), small amounts of a tribromo derivative **4** (2%) and a dibromo derivative **5** (1%) (Scheme I) were also isolated in sufficient quantities to allow elucidation of their structures. ^{1}H NMR and mass spectra (cf. Experimental Section) of the tribromo and the dibromo derivatives were consistent with the structures **4** and **5** shown in Scheme I. The ^{1}H NMR spectrum of the dibromo derivative indicated that it is a symmetrical commpound. Positions of the two bromines were assigned at C-5 and C-8 based on approximately 0.4 ppm downfield movement of chemical shift for H-4 (H-9) in **5** relative to **1**. The tribrominated minor product **4** has a UV chromophore typical of a benzo[c]phenanthrene derivative in which one of the K-region double bond has been saturated,[15] indicating that bromine was added to a K-region double bond. The positions of the bromine substituents in **4** were assigned by our observation that **4** was exclusively formed upon reaction of **3** with bromine (Scheme I).

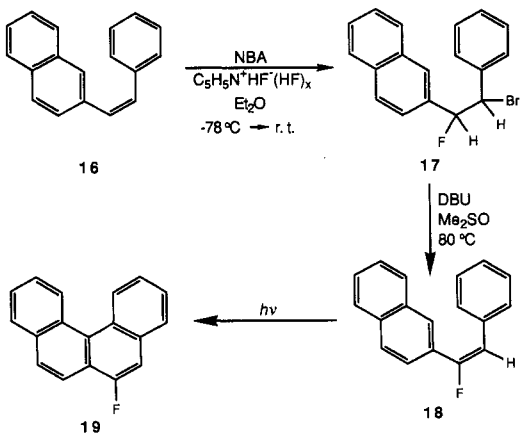
Since **3** could be converted to the corresponding fluoro derivative **8a** in good yield (Scheme II), the 5,8-dibromo derivative **5** was considered to be an excellent candidate as a precursor for 5,8-difluorobenzo[c]phenanthrene (**8b**). However, unlike **2**, the tribromo derivative lost bromine when it was heated in acetonitrile under reflux to yield **3** as the exclusive product (Scheme I). Subsequently, our attempts to dehydrobrominate **4** in the presence of either pyridine or sodium acetate also resulted in the loss of bromine and formation of **3** instead of **5**. Since hydrogen halide formed during halogenation of aromatic compounds in trimethyl phosphate combines rapidly with solvent to form methyl halide,[16] we anticipated that it might be possible to dehydrobrominate **4** in this solvent. Accordingly, **3** was treated with bromine in trimethyl phosphate at room temperature. It appears that the tribromo derivative **4**, formed in situ, was dehydrobrominated completely, since **5** was the only product isolated from the reaction mixture. Subsequently, we were able to convert **1** directly to **5** in excellent yield (95%) by treating it with 2 molar equiv of bromine in trimethyl phosphate (Scheme I). The conversion of **1** to **5** appears to proceed via the monobromo derivative **3**, because reaction of **1** with 1.1 molar equiv of bromine in this solvent results in the formation of approximately equal amounts of **3** and **5** as determined by HPLC. 5,8-Dibromobenzo[c]phenanthrene (**5**) was converted to the corresponding difluoro derivative **8b** via 5,8-diaminobenzo[c]phenanthrene, **6b**, and its 5,8-bis(diazonium tetrafluoroborate) salt **7b** by the procedures outlined for conversion of **3** to **8a** (Scheme II).

For synthesis of the other symmetrical K-region difluorobenzo[c]phenanthrene, i.e. 6,7-difluorobenzo[c]phenanthrene (**14**), the fluorostilbene **12** appeared to be a suitable precursor (Scheme III). Marx and Bergmann[7] had earlier reported that their attempts at direct photocyclization of a fluorostilbene with the fluorine atom on

Scheme III



Scheme IV



the olefinic double bond failed to give fluorophenanthrene under various reaction conditions. However, we have been successful in carrying out direct photocyclization reactions of fluorostilbenes to obtain benzo[c]phenanthrenes with one or two fluorine atom(s) at the K-region(s) (Schemes

(15) Croisy-Delcey, M.; Ittah, Y.; Jerina, D. M. *Tetrahedron Lett.* **1979**, *31*, 2849.
(16) Pearson, D. E.; Frazer, M. G.; Frazer, V. S.; Washburn, L. C. *Synthesis* **1976**, 621.

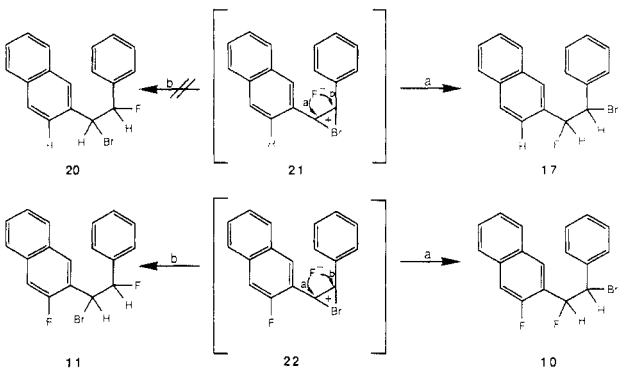
III and IV). Bromofluorination of β-(3-fluoronaphth-2-yl)styrene (**9**) with pyridinium poly(hydrogen fluoride)[17] and *N*-bromoacetamide (NBA) in ether gave two regioisomeric products **10** and **11** in equal amounts (Scheme III). These regioisomers were not separable by HPLC; however, their corresponding dehydrobrominated products, the fluoro olefins **12** and **13** (Scheme III), were separated. Several attempts to dehydrobrominate the bromofluoro adducts **10** and **11** with such bases as potassium hydroxide in dimethyl sulfoxide or triethylamine gave no reaction; whereas with the stronger base potassium *tert*-butoxide in dimethyl sulfoxide (Me_2SO), one product was detected which was assigned as naphthylphenylacetylene, the product of double dehydrohalogenation. Successful dehydrobromination of **10** and **11** was achieved when this mixture was heated (80 °C) with 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU) in dimethyl sulfoxide, which yielded products **12** and **13** in 76% overall yield (two steps), as shown in Scheme III. These fluoro olefins **12** and **13** were separated by reverse-phase HPLC. The ^1H NMR spectrum of each regioisomer exhibited the H–F coupling constant of 20 Hz, which is consistant with the reported cis H–F coupling constant (22 Hz) for (*Z*)-1-fluoro-1-(*p*-toluyl)-1-propene.[18] Because of the similarities in their ^1H NMR spectra, it is not possible to assign the position of the fluoro substituent in the fluoro olefins **12** and **13** isolated by reverse-phase HPLC. However, when the early HPLC fraction was irradiated in cyclohexane containing a trace amount of iodine with a 450-W Hanovia medium-pressure mercury arc lamp contained in a water-cooled quartz tube for 1.5 h, 6,7-difluorobenzo[*c*]phenanthrene (**14**) was obtained, indicating that this olefin must have the structure **12** (Scheme III). When the late eluting HPLC fraction was irradiated under the above photolysis conditions, the product obtained in modest yield was 5,7-difluorobenzo[*c*]phenanthrene (**15**), thus allowing assignment of the structure **13** to this late eluting fluoro olefin.

The structure of **14** was assigned based on its ^1H and ^{19}F NMR spectra. The presence of only one signal for the bay-region protons H-1 (H-1′) and the benzo-ring protons H-4 (H-4′) (cf. Scheme I for numbering of the benzo[*c*]-phenanthrene ring system) in the ^1H NMR spectrum of **14** suggested that the two fluoro substituents are symmetrically placed on the benzo[*c*]phenanthrene skeleton. Although the chemical shifts of the two K-region protons were not identical, they were only 0.02 ppm apart, indicating a near equivalence of the two K-region protons. The same is true for the two fluoro substituents. As expected, the ^1H NMR spectrum of **15** did not show any symmetry, as H-6 and H-8 in this product are clearly detected as two doublets with H–F coupling constants of 11 and 10.5 Hz, respectively, and their chemical shifts being identical to those of H-6 and H-5 in **8a** and **19**, respectively. Furthermore, in the ^{19}F NMR spectrum of **15**, two distinct doublets ($J_{H,F}$ = 10.5 and 11.0 Hz) were observed that have very similar chemical shifts when compared to the ^{19}F NMR spectra of **8a** and **19**.

As shown in Scheme IV, we have employed the above methodology to synthesize 6-fluorobenzo[*c*]phenanthrene **19**. This synthesis of **19** represents a considerable improvement over those reported previously.[6,7] In this method, the β-naphthylstyrene **16**, an intermediate in the synthesis of **1**, is converted to **19** in just three steps. Bromofluorination of **16** with NBA and pyridinium poly-

(17) Olah, G. A.; Welch, J. T.; Vankar, Y. D.; Nojima, M.; Kercjes, I.; Olah, J. A. *J. Org. Chem.* **1979**, *4*, 3872.
(18) Eckes, L.; Hanack, M. *Synthesis* **1978**, 217.

Scheme V



(hydrogen fluoride) in ether gave an excellent yield (95%) of **17**. The position of the fluoro substituent in **17** was assigned based on its conversion exclusively to **19** via the intermediate olefin **18**. Interestingly, only one regioisomer **17** was detected upon bromofluorination of **16**; however, as discussed earlier, two products, **10** and **11**, were formed when similar reaction was carried out on the (fluoronaphthyl)styrene **9** (Scheme III). These results are consistent with the mechanism of bromofluorination of olefins with pyridinium poly(hydrogen fluoride) and NBA that involves bromonium ion intermediates **21** and **22** with the fluoride ion adding to the most stable carbocation (Scheme V). Thus in the case of compound **16**, the single product **17** formed is apparently due to a greater stabilization of the benzylic carbocation next to the naphthyl substituent than that next to the phenyl substituent, and therefore allowing the fluoride ion to add selectively at the benzylic carbon adjacent to the naphthyl moiety (Scheme V, path a). However, it appears that the fluoro group in the bromonium ion **22** derived from β-(3-fluoronaphth-2-yl)-styrene (**9**) destabilizes the carbocation adjacent to naphthyl substituent, perhaps due to strong inductive effect of fluorine, to the extent that the nucleophile (fluoride ion) does not discriminate between the two possible sites of attack, resulting in the formation of two regioisomeric products **10** and **11**. Dehydrobromination of bromofluoro adduct **17** with DBU in Me_2SO gave the β-fluoro-β-naphth-2-ylstyrene (**18**) (Scheme IV) in 74% yield. The position of the fluorine substituent in **18** was confirmed when this material was irradiated as described earlier to yield **19** (50% yield). This product is identical (MS and ^1H and ^{19}F NMR) with the 6-fluorobenzo[*c*]-phenanthrene prepared by the alternative method.[6]

Experimental Section

All reactions were carried out in oven-dried glassware under an inert atmosphere. The reactions with commerical pyridinium poly(hydrogen fluoride) [HF 70%, pyridine 30%] (Aldrich Chemical Co.) were carried out in polyolefin bottles. Melting points were measured with a Thomas-Hoover oil bath apparatus and are uncorrected. HPLC analyses were performed with a Perkin-Elmer series 4 liquid chromatograph equipped with a Hewlett-Packard 1040A diode array UV/vis detector. ^1H NMR spectra were obtained either with a General Electric GN-300 (300 MHz) spectrometer or with a JEOL GX-400 (400 MHz) spectrometer. ^{19}F NMR spectra were obtained with a Varian XL-300 (282 MHz) spectrometer. Chemical shifts were measured in ppm from internal standards in $CDCl_3$–tetramethylsilane (Me_4Si) for ^1H nuclei, and hexafluorobenzene (C_6F_6) for ^{19}F nuclei. Electron impact (EI) mass spectra were recorded on a VG Micromass 7070F mass spectrometer. UV spectra were recorded on a Hewlett-Packard 8451A diode array spectrophotometer.

Purity of each of the new compounds reported here was ensured by HPLC and TLC analyses, and every new compound was identified by accurate mass analysis and by ^1H NMR spectrom-

etry. For the fluorinated compounds, the isomeric purity was determined by ^{19}F NMR spectrometry. All of the fluorinated benzo[c]phenanthrenes were found to be isomerically pure except 5-fluorobenzo[c]phenanthrene (**8a**), which contained approximately 4% of the 6-fluoro isomer (**19**).

Bromination of Benzo[c]phenanthrene (Formation of 3, 4, and 5). To an ice-cooled solution of benzo[c]phenanthrene (1) (3.15 g, 13.8 mmol) in 200 mL of benzene was added bromine (0.82 mL, 15.8 mmol) dropwise over a period of 45 min. The resulting mixture was stirred at room temperature for 24 h. The solvent was removed under reduced pressure, CH_3CN was added (200 mL), and this mixture was refluxed for 2 h. The crude mixture was concentrated, and four products were separated by HPLC (Du Pont Zorbax ODS column (2.12 × 25 cm), CH_3CN (15 mL/min)). Benzo[c]phenanthrene (1) (734 mg, 23%, k' = 0.87) and 5-bromobenzo[c]phenanthrene (**3**) (2.02 g, 48%, k' = 2.12) were the major products recovered from the column which had spectral properties identical with those of the authentic compounds.[8] The third fraction recovered as an oil was 5,7,8-tribromo-7,8-dihydrobenzo[c]phenanthrene ((±)-**4**) (65 mg, 1%, k' = 0.68): ^1H NMR δ 5.62 (d, 1 H, H-7 or H-8, $J_{7,8}$ = 2.5 Hz), 5.65 (d, 1 H, H-7 or H-8, $J_{7,8}$ = 2.5 Hz), 7.46 (dd, 1 H, J = 8.0 and 7.0 Hz), 7.56 (m, 2 H), 7.68 (m, 2 H), 7.87 (s, 1 H, H-6), 8.03 (d, 1 H, J = 7.0 Hz), 8.36 (d, 1 H, H-1 or H-12, J = 8.0 Hz), 8.59 (d, 1 H, H-12 or H-1, J = 8.0 Hz); MS (EI) m/z calcd for $C_{18}H_{11}Br_2{}^{79}Br^{81}$ 465.8390, found 465.8347; UV λ_{max} at 256 and 325 nm (CH_3CN). A late eluting fraction (k' = 3.75) contained 5,8-dibromobenzo[c]phenanthrene (**5**) (90 mg, 2%), which was recrystallized from hexane as white crystalline solid: mp 137–139 °C; ^1H NMR δ 7.65 (m, 4 H, H-2, H-3, H-10, H-11), 7.9 (s, 2 H, H-6 and H-7), 8.38 (d, 2 H, H-4 and H-9, $J_{3,4} = J_{9,10}$ = 9.0 Hz), 8.92 (d, 2 H, H-1 and H-12, $J_{1,2} = J_{11,12}$ = 8.0 Hz); MS (EI) m/z calcd for $C_{18}H_{10}Br_2{}^{79}$ 383.9149, found 383.9140; UV λ_{max} at 292 nm (CH_3CN).

5-Aminobenzo[c]phenanthrene (6a). In a 90-mL stainless steel reaction vessel containing a magnetic stirring bar were added 5-bromobenzo[c]phenanthrene (**3**) (663 mg, 2.15 mmol), copper powder (135 mg, 2.15 mmol), cuprous chloride (420 mg, 4.2 mmol), and 60 mL of 28% ammonia. The bomb was sealed, and its contents were rapidly stirred and heated in an oil bath with the temperature maintained at 170 ± 5 °C for 15 h. After cooling, the reaction mixture was extracted with CH_2Cl_2 (5 × 50 mL). The combined organic phase was dried over $MgSO_4$ and concentrated. Analysis of the crude product by HPLC (Du Pont Zorbax ODS column (0.46 × 25 cm), CH_3CN (0.8 mL/min)) indicated the presence of two products, benzo[c]phenanthrene (1) (minor) and 5-aminobenzo[c]phenanthrene (**6a**) (major). These two were separated on a Du Pont Zorbax Silica column (2.12 × 25 cm) eluted with CH_2Cl_2 at a flow rate of 20 mL/min. 5-Aminobenzo[c]phenanthrene (**6a**) (300 mg, 60%, k' = 2.28) was obtained as an oil: ^1H NMR δ 4.3 (broad s, 2 H, NH_2), 7.10 (s, 1 H, H-6), 7.52 (dd, 1 H, H-3, J = 8.0 and 7.0 Hz), 7.66 (m, 4 H), 7.81 (d, 1 H, H-7 or H-8, $J_{7,8}$ = 8.0 Hz), 7.95 (d, 1 H, H-4, $J_{3,4}$ = 8.0 Hz), 8.03 (d, 1 H, H-9, $J_{9,10}$ = 8.0 Hz), 8.96 (d, 1 H, H-1, $J_{1,2}$ = 8.0 Hz), 9.13 (d, 1 H, H-12, $J_{11,12}$ = 8.0 Hz); MS (EI) m/z calcd for $C_{18}H_{13}N$ 243.1048, found 243.1054; UV λ_{max} at 290 nm (CH_3CN). The earlier eluting fraction collected was identified as benzo[c]-phenanthrene (1) (110 mg, 22%, k' = 0.49).

5-Fluorobenzo[c]phenanthrene (8a). To a solution of boron trifluoride etherate (60 μL, 0.48 mmol) in 1 mL of dimethoxyethane cooled to −7 °C (ice/salt bath) was added dropwise 5-aminobenzo[c]phenanthrene (**6a**) (95 mg, 0.39 mmol) dissolved in 4 mL of dimethoxyethane under nitrogen atmosphere. This mixture was stirred for 0.5 h at this temperature. To the reaction mixture was next introduced *tert*-butyl nitrite (48 μL, 0.4 mmol) in 2 mL of dimethoxyethane over a period of 5 min. The bath temperature was kept at 0 °C, and the reaction mixture was stirred for 1.5 h. The reaction mixture was concentrated under reduced pressure to a constant weight. The 5-diazonium tetrafluoroborate **7a** was taken up in 10 mL of chlorobenzene solvent and heated in an oil bath with the temperature set at 135 ± 5 °C for 45 min. The solvent was removed under reduced pressure, and the product was dissolved in CH_2Cl_2 (50 mL) and washed with 5% $NaHCO_3$ (4 × 20 mL). The organic phase was dried over Na_2SO_4 and concentrated. 5-Fluorobenzo[c]phenanthrene (**8a**) (62 mg, 65%) was obtained following chromatography of the crude product on silica gel (hexane). Recrystallization from hexane gave **8a** as a white crystalline solid: mp 93–94 °C (lit.[7] mp 57–59 °C); ^1H NMR δ 7.48 (d, 1 H, H-6, $J_{H,F}$ = 11.0 Hz), 7.62 (dd, 2 H, H-10 and H-11, J = 7.0 and 8.0 Hz), 7.70 (m, 2 H), 7.75 (d, 1 H, H-7 or H-8, $J_{7,8}$ = 8.0 Hz), 7.90 (d, 1 H, H-8 or H-7, $J_{7,8}$ = 8.0 Hz), 8.01 (dd, 1 H, H-9, J = 9.0 and 1.5 Hz), 8.32 (dd, 1 H, H-4, J = 8.0 and 1.5 Hz), 9.04 (d, 1 H, H-12, $J_{11,12}$ = 9.0 Hz), 9.13 (d, 1 H, H-1, $J_{1,2}$ = 8.0 Hz); ^{19}F NMR δ 36.75 (d, $J_{H,F}$ = 11.0 Hz); MS (EI) m/z calcd for $C_{18}H_{11}F$ 246.0845, found 246.0840; UV (CH_3CN) λ_{max} (ε, M^{-1} cm^{-1}) 272 (47 000), 282 nm (63 200). Anal. Calcd for $C_{18}H_{11}F$: C, 87.71; H, 4.52.

5,8-Dibromobenzo[c]phenanthrene (5). To a magnetically stirred solution of benzo[c]phenanthrene (1) (109 mg, 0.47 mmol) in 5 mL of trimethyl phosphate at room temperature was added bromine (55 μL, 1 mmol) in 1 mL of trimethyl phosphate. This reaction mixture, protected from light, was stirred for 20 h under nitrogen atmosphere. It was then poured into 20 mL of water, and the product was extracted into hexane (5 × 30 mL). The combined organic phase was washed with brine, dried over Na_2SO_4, and concentrated. Analysis of the crude product by HPLC (Du Pont Zorbax ODS column (0.46 × 25 cm), CH_3CN (2 mL/min)) indicated the complete conversion of starting material to 5,8-dibromobenzo[c]phenanthrene (**5**). Column chromatography of the product on 20 g of neutral Alumina eluted with hexane gave **5** (175 mg, 95%) which following crystallization from hexane had properties identical with those of the minor product isolated from bromination of benzo[c]phenanthrene (1).

5,8-Diaminobenzo[c]phenanthrene (6b). After ammonolysis of **5** by a procedure similar to that described earlier, three products were obtained when 5,8-dibromobenzo[c]phenanthrene (**5**) (150 mg, 0.38 mmol) was treated with copper powder (49 mg, 0.77 mmol), cuprous chloride (78 mg, 0.77 mmol), and 60 mL of 28% ammonia at 170 °C for 14 h. These products were separated by preparative HPLC (Du Pont Zorbax Silica column (2.12 × 25 cm), CH_2Cl_2–EtOAc (4:1), flow rate = 20 mL/min), and identified by ^1H NMR to be benzo[c]phenanthrene (1) (7 mg, 8%, k' = 0.55), 5-aminobenzo[c]pheanthrene (**6a**) (20 mg, 21%, k' = 0.97), and 5,8-diaminobenzo[c]pheanthrene (**6b**) (60 mg, 59%, k' = 2.52). Compound **6b** was obtained as an oil: ^1H NMR δ 4.0 (broad s, NH_2), 6.79 (s, 2 H, H-6 and H-7), 7.49 (dd, 2 H, H-3 and H-10, J = 8.0 and 7.0 Hz), 7.60 (dd, 2 H, H-2 and H-11, J = 8.0 and 7.0 Hz), 7.91 (d, 2 H, H-4 and H-9, $J_{4,3} = J_{9,10}$ = 8.0 Hz), 8.93 (d, 2 H, H-1 and H-12, $J_{1,2} = J_{12,11}$ = 8.0 Hz); MS (EI) mz calcd for $C_{18}H_{14}N_2$ 258.1156, found 258.1172; UV λ_{max} at 307 nm (CH_3CN).

5,8-Difluorobenzo[c]phenanthrene (8b). By a procedure similar to that described for the synthesis of **8a**, 5,8-diaminobenzo[c]pheanthrene (**6b**) (50 mg, 0.19 mmol) was converted to 5,8-difluorobenzo[c]phenanthrene (**8b**) when treated with boron trifluoride etherate (100 μL, 0.78 mmol) and *tert*-butyl nitrite (92 μL, 0.78 mmol) followed by pyrolysis of the 5,8-bis(diazonium tetrafluoroborate) **7b**. Following the usual workup, pure 5,8-difluorobenzo[c]phenanthrene (**8b**) (31 mg, 62%) was obtained after chromatography on silica gel (hexane): mp 144–148 °C dec; ^1H NMR δ 7.41 (d, 2 H, H-6 and H-7, $J_{H,F}$ = 10.5 Hz), 7.68 and 7.73 (2 dd, 4 H, H-2, H-3, H-10, H-11, $J_{2,1} = J_{2,3} = J_{10,9} = J_{10,11}$ = 7.0 Hz), 8.28 (d, 2 H, H-4 and H-9, $J_{4,3} = J_{9,10}$ = 8.0 Hz), 9.04 (d, 2 H, H-1 and H-12, $J_{1,2} = J_{12,11}$ = 8.0 Hz); ^{19}F NMR δ 37.85 (d, $J_{H,F}$ = 11.0 Hz); MS (EI) m/z calcd for $C_{18}H_{10}F_2$ 264.0751, found 264.0748; UV (CH_3CN) λ_{max} (ε, M^{-1} cm^{-1}), 272 (26 700), 282 nm (38 300).

***cis*- and *trans*-β-(3-Fluoronaphth-2-yl)styrene (9).** Compound **9** was prepared in an overall 53% yield from the commercially available 3-amino-2-naphthoic acid by a method similar to that published by Ittah and Jerina.[6] The conversion of 2-carbomethoxy-3-aminonaphthalene to its corresponding 2-carbomethoxy-3-fluoronaphthalene in 75% yield by the procedure described earlier in the synthesis of the compound **8a** represented a considerable improvement over that reported previously (lit.[7] 20% yield).

***cis*-β-(3-Fluoronaphth-2-yl)-β-fluorostyrene (12) and *cis*-β-(3-Fluoronaphth-2-yl)-α-fluorostyrene (13).** β-(3-Fluoronaphth-2-yl)styrene (**9**) (1.0 g, 4.0 mmol) in 40 mL of ether was added to a dry ice/acetone (−78 °C) cooled mixture of NBA (723 mg, 5.2 mmol) and 5 mL of pyridinium poly(hydrogen fluoride) (70%) in 90 mL of ether in a polyolefin bottle. The reaction mixture was stirred for 5 h at this temperature before

the bath was removed and allowed to warm up to room temperature (5 h). The reaction mixture was poured into ice water and extracted with ether. The ether phase was washed with aqueous bicarbonate and dried over anhydrous sodium sulfate. The solvent was removed, and the mixture of products **10** and **11** was dissolved in 60 mL of Me_2SO. To this stirred mixture was introduced DBU (657 μL, 4.4 mmol) and heated at 80 °C for 10 h. The reaction mixture was poured into water and extracted with hexane. The organic phase was dried and concentrated to obtain a mixture of **12** and **13** (820 mg, 76%). These products were separated by preparative HPLC (Du Pont Zorbax ODS Column (2.12 × 25 cm), CH_3CN–H_2O (5:1), 20 mL/min). The first fraction collected was pure olefin **12** (k' = 3.6): ^1H NMR δ 6.67 (d, 1 H, vinyl proton, $J_{H,F}$ = 20.0 Hz), 7.06 (m, 2 H), 7.14 (m, 3 H), 7.51 (m, 3 H), 7.78 (m, 2 H), 7.94 (m, 1 H); MS (EI) m/z calcd for $C_{18}H_{12}F_2$ 266.0907, found 266.0909; UV λ_{max} at 222 nm (CH_3CN). The second fraction collected was the olefin **13** (k' = 4.4): ^1H NMR δ 6.55 (d, 1 H, vinyl proton, $J_{H,F}$ = 20.0 Hz), 7.35 (m, 3 H), 7.45 (m, 4 H), 7.59 (m, 2 H), 7.73 (m, 2 H); MS (EI) m/z calcd for $C_{18}H_{12}F_2$ 266.0907, found 266.0900; UV λ_{max} at 222 nm (CH_3CN).

6,7-Difluorobenzo[*c*]phenanthrene (14). A solution of **12** (63 mg, 0.23 mmol) in 400 mL of cyclohexane containing a catalytic amount of iodine was irradiated in an immersion apparatus with a 450-W Hanovia medium-pressure mercury arc lamp contained in a water-cooled quartz probe. The solution was continuously purged with air during the irradiation, and the progress of the photocyclization reaction was monitored by HPLC. After 1.5 h, the solvent was evaporated and the crude product was chromatographed on basic Alumina (hexane) to obtain pure 6,7-difluorobenzo[*c*]pheanthrene (**14**) (22 mg, 37%): mp 131–132 °C; ^1H NMR δ 7.57 (dd, 2 H, H-5 and H-8, $J_{H,F}$ = 6.5 and 6.0 Hz), 7.64 (m, 4 H), 7.94 (dd, 2 H, H-4 and H-9, $J_{4,3} = J_{9,10}$ = 6.5 Hz and $J_{4,2} = J_{9,11}$ = 2.5 Hz), 8.99 (m, 2 H, H-1 and H-12); ^{19}F NMR δ 42.31 (dd, $J_{H,F}$ = 6.5 and 6.0 Hz); MS (EI) m/z calcd for $C_{18}H_{10}F_2$ 264.0750, found 264.0754; UV (CH_3CN) λ_{max} (ε, M^{-1} cm^{-1}), 278 (41 800), 284 nm (41 800).

5,7-Difluorobenzo[*c*]phenanthrene (15). Photolysis of **13** (117 mg, 0.44 mmol) in 400 mL of cyclohexane with a catalytic amount of iodine for 1.5 h with the same apparatus as described above gave the photocyclized product 5,7-difluorobenzo[*c*]pheanthrene (**15**) (35 mg, 26%) following chromatography on basic Alumina (hexane): mp 112–114 °C; ^1H NMR δ 7.57 (d, 1 H, H-8, $J_{H,F}$ = 10.5 Hz), 7.63 (m, 2 H), 7.76 (m, 2 H), 7.80 (d, 1 H, H-6, $J_{H,F}$ = 11.0 Hz), 7.96 (dd, 1 H, H-9, $J_{9,10}$ = 7.0 Hz and $J_{9,11}$ = 2.5 Hz), 8.35 (dd, 1 H, H-4, $J_{4,3}$ = 7.0 Hz and $J_{4,2}$ = 2.5 Hz), 9.02 (d, 1 H, H-1 or H-12, J = 7.5 Hz), 9.14 (d, 1 H, H-12 or H-1, J = 8.0 Hz); ^{19}F NMR δ 37.1 (d, $J_{H,F}$ = 10.5 Hz), 39.14 (d, $J_{H,F}$ = 11.0 Hz); MS (EI) m/z calcd for $C_{18}H_{10}F_2$ 264.0750, found 264.0738; UV (CH_3CN) λ_{max} (ε M^{-1} cm^{-1}), 276 (44 800), 282 nm (47 400).

α-Bromo-β-fluoro-β-naphth-2-ylstyrene (17). To a dry ice/acetone (−78 °C) cooled mixture of NBA (35 mg, 0.25 mmol), 2 mL of pyridinium poly(hydrogen fluoride) (70%), and 5 mL of ether in a polyolefin bottle was added the β-naphthylstyrene **16** (49 mg, 0.21 mmol) in 10 mL of ether. The reaction mixture was stirred for 5 h at this temperature and for an additional 5 h at room temperature, and then poured into water and extracted with ether. The organic phase was washed with aqueous bicarbonate, dried over Na_2SO_4, and concentrated to obtain **17** (67 mg, 95%). Recrystallization from $CHCl_3$/hexane gave pure **17**: mp 120–121 °C; ^1H NMR δ 5.23 (dd, 1 H, CHBr, $J_{H,F}$ = 15.0 Hz and $J_{\alpha H,\beta H}$ = 6.5 Hz), 6.00 (dd, 1 H, CHF, $J_{H,F}$ = 46.0 Hz and $J_{\beta H,\alpha H}$ = 6.5 Hz), 7.33 (m, 4 H), 7.41 (m, 2 H), 7.5 (m, 2 H), 7.82 (m, 4 H); MS (EI) m/z calcd for $C_{18}H_{14}BrF$ 328.0263, found 328.0231; UV λ_{max} at 224 nm (CH_3CN).

β-Fluoro-β-naphth-2-ylstyrene (18). A mixture **17** (198 mg, 0.6 mmol) and DBU (0.1 mL, 0.66 mmol) in 20 mL of Me_2SO was heated at 80 °C for 8 h. The reaction mixture was poured into water and extracted with hexane. The organic phase was dried over anhydrous Na_2SO_4 and concentrated. The crude product was purified by HPLC (Du Pont Zorbax Silica Column (2.12 × 25 cm), 10% CH_2Cl_2/hexane, 20 mL/min) and recovered as a mixture of cis and trans isomers of **18** (110 mg, 74%). A partial separation of the two isomers was achieved on a small scale: cis isomer **18**, ^1H NMR δ 6.54 (d, 1 H, vinyl proton, $J_{H,F}$ = 22.0 Hz), 7.45 (m, 5 H), 7.75 (m, 6 H), 7.98 (s, 1 H); trans isomer **18**, ^1H NMR δ 6.46 (d, 1 H, vinyl proton, $J_{H,F}$ = 40.0 Hz), 7.40 (m, 2 H), 7.51 (m, 2 H), 7.71 (m, 3 H), 7.86 (m, 4 H), 8.13 (s, 1 H); MS (EI) m/z calcd for $C_{18}H_{13}F$ 248.1001, found 248.0993; UV (both isomers) λ_{max} at 226 nm (CH_3CN).

6-Fluorobenzo[*c*]phenanthrene (19). A solution of **18** (30 mg, 0.12 mmol) in 300 mL of cyclohexane with a catalytic amount of iodine was irradiated as described earlier for 1.5 h. The solvent was evaporated, and the crude product was chromatographed on basic Alumina (hexane) to obtain pure **19** (15 mg, 50%): mp 71–72 °C (lit.[6] mp 72–73 °C); ^1H NMR δ 7.54 (d, 1 H, H-5, $J_{H,F}$ = 11.0 Hz), 7.7 (m, 4 H), 7.95 (m, 1 H, H-4 or H-9), 7.99 (d, 1 H, H-8, $J_{8,7}$ = 9.0 Hz), 8.03 (d, 1 H, H-9 or H-4, J = 7.3 Hz), 8.16 (d, 1 H, H-7, $J_{7,8}$ = 9.0 Hz), 9.12 (2 d, 2 H, H-1 and H-12, J = 10.0 and 9.0 Hz); UV λ_{max} at 274 nm (CH_3CN).

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Catalytic Cyclopropanation of Alkenes with Ethyl Nitrodiazoacetate. A Facile Synthesis of Ethyl 1-Nitrocyclopropanecarboxylates

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Ethyl 1-nitrocyclopropanecarboxylates are formed in the reaction between alkenes and ethyl nitrodiazoacetate using a catalytic amount of rhodium(II) acetate. Ethyl oxo[hydroxy(alkyl-2-propenyl)amino]acetates are obtained as side products. These result from an ene reaction between the alkene and an intermediate acyl nitroso compound. Relative reactivities and stereoselectivities for catalytic rhodium(II) acetate reactions of ethyl nitrodiazoacetate with 12 alkenes to yield cyclopropanes and ene products are reported. Electron-rich, sterically undemanding alkenes are the most reactive and give the best yields of cyclopropanes. Less reactive, crowded alkenes give poor yields of cyclopropanes and enhanced yields of ene products. A comparison with the relevant data for ethyl diazoacetate reveals that the reaction with ethyl nitrodiazoacetate is more sensitive to the electronic and steric nature of the reactant alkene. Doyle's model for catalytic cyclopropanation with rhodium(II) acetate is invoked to explain these data.

There has recently been considerable effort directed at the synthesis and study of strained ring nitro compounds as high-energy density materials.[1] Nitrocyclopropanes are the simplest members of this class of compounds. Al-

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