106296-67-7; **6c**, 106296-68-8; (*E*)-**8d**, 106296-84-8; (*Z*)-**8d**, 106318-60-9; **9i**, 106296-74-6; **9j** (isomer 1), 106296-75-7; **9j** (isomer 2), 106296-85-9; **9k** (isomer 1), 106296-76-8; **9k** (isomer 2), 106296-86-0; **9l** (isomer 1), 106296-77-9; **9l** (isomer 2), 106318-61-0; **9m**, 106296-78-0; **10a**, 106296-79-1; (*E*)-**11d**, 106296-69-9; (*Z*)-**11d**, 106296-70-2; (*E*)-**11e**, 106296-71-3; (*Z*)-**11e**, 106296-72-4; **11f**, 106296-73-5; **12j** (isomer 1), 106296-80-4; **12j** (isomer 2), 106296-81-5; **12k** (isomer 1), 106296-82-6; **12k** (isomer 2), 106296-83-7; **13o**, 17626-88-9; **13p**, 936-77-6; (*E*)-**15d**, 55059-13-7; (*Z*)-**15d**, 55059-14-8; **16**, 18032-18-3; $CH_3C(O)CH{=}CH_2$, 78-94-4; $PhCH_2Br$, 100-39-0; MeI, 74-88-4; $CH_3(CH_2)_5I$, 638-45-9; *p*-MeC_6H_4CHO, 104-87-0; $CH_3(CH_2)_2CHO$, 123-72-8; $CH_3(CH_2)_3CHO$, 110-62-3; Ph_2CO, 119-61-9; *t*-BuLi, 594-19-4; MeLi, 917-54-4; 2-cyclohexen-1-one, 930-68-7; cyclohexanone, 108-94-1.

Synthesis of the Major Metabolic Dihydrodiols of Benzo[*j*]fluoranthene

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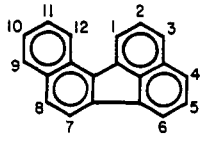
Syntheses are described for the major dihydrodiol metabolites of benzo[*j*]fluoranthene. *trans*-4,5-Dihydro-4,5-dihydroxybenzo[*j*]fluoranthene was prepared via 9-methoxy-11*H*-benzo[*a*]fluorene. Two of the intermediates in this synthetic sequence, 4-hydroxybenzo[*j*]fluoranthene and benzo[*j*]fluoranthene-4,5-dione, are also suspect metabolites of the parent hydrocarbon. An improved synthesis for *trans*-9,10-dihydro-9,10-dihydroxybenzo[*j*]fluoranthene is described. The key steps in this preparation are the Wittig reaction of acenaphthenequinone with (3-methoxyphenethyl)triphenylphosphonium bromide and the cyclization–dehydration of the intermediate, forming 10-methoxybenzo[*j*]fluoranthene exclusively. The synthesis of *trans*-2,3-dihydro-2,3-dihydroxybenzo[*j*]fluoranthene was accomplished through the intermediacy of 1,12c-dihydrobenzo[*j*]fluoranthen-3(2*H*)-one. This ketone was converted to its α-phenylseleno derivative which underwent selenoxide elimination in basic hydrogen peroxide, forming benzo[*j*]fluoranthene-2,3-dione directly. In each synthesis reduction of the appropriate quinone with potassium borohydride afforded the desired dihydrodiol.

Introduction

Benzo[*j*]fluoranthene (**1**) is a nonalternant polycyclic aromatic hydrocarbon[1] which is found throughout the environment in sources such as air, cigarette smoke condensate, soot, soil, drinking water, and smoked foods.[2-7] This compound is active as a tumor initiator and complete carcinogen on mouse skin and is carcinogenic in rat lung.[3,8-10] Studies in our laboratories have shown that **1** is metabolized to two dihydrodiols in rat liver homogenate. One of these has been identified, by comparison



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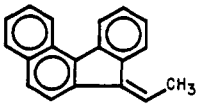

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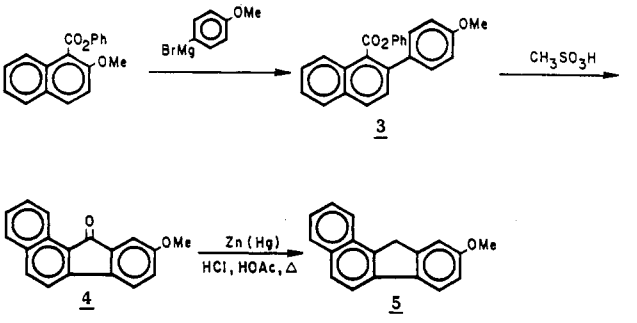
with a synthetic standard, as *trans*-9,10-dihydro-9,10-dihydroxybenzo[*j*]fluoranthene.[11,12] This dihydrodiol is mutagenic in *S. typhimurium* and is active as a tumor initiator on mouse skin.[8] The second dihydrodiol has been tentatively identified as *trans*-4,5-dihydro-4,5-dihydroxybenzo[*j*]fluoranthene by comparison of its UV spectrum with that of 7-ethylidine-7*H*-benzo[*c*]fluorene (**2**).[13] In this paper we describe for the first time the synthesis of the 4,5-dihydrodiol of **1**. Improved syntheses for the 9,10-dihydrodiol and the 2,3-dihydrodiol are also detailed.

Scheme I. Preparation of 9-Methoxy-11*H*-benzo[*a*]fluorene (5), the Key Intermediate in the Synthesis of the 4,5-Dihydrodiol of Benzo[*j*]fluoranthene



Results and Discussion

The key intermediate for the syntheses of the 4,5-dihydrodiol of benzo[*j*]fluoranthene is 9-methoxy-11*H*-benzo[*a*]fluorene. This compound was prepared by the general method of Fuson and Wassmundt[14] as illustrated

(1) Zahradnik, R. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 1039–1050.
(2) Hoffmann, D.; Wynder, E. L. In *Chemical Carcinogens*; ACS Monograph 173; Searle, C. E., Ed.; American Chemical Society: Washington, DC, 1976; pp 341–365.
(3) Wynder, E. L.; Hoffmann, D. *Cancer* **1959**, *12*, 1194–1199.
(4) Fischer, R. *Z. Anal. Chem.* **1970**, *249*, 110.
(5) Borneff, J.; Fischer, R. *Arch. Hyg. Bacteriol.* **1962**, *146*, 430.
(6) Olufsen, B. In *Polynuclear Aromatic Hydrocarbons: Chemistry and Biological Effects*; Bjorseth, A., Dennis, A. J., Eds.; Battelle: Columbus, OH 1980; pp 333–343.
(7) Masuda, Y.; Kuratsune, M. *Gann* **1971**, *62*, 27–30.
(8) LaVoie, E. J.; Amin, S.; Hecht, S. S.; Furuya, K.; Hoffmann, D. *Carcinogenesis*, **1982**, *3*, 49–52.
(9) Deutsch-Wenzel, R. P.; Brune, H.; Grimmer, G.; Dettbarn, G.; Misfeld, J. *J. Natl. Cancer Inst.* **1983**, *71*, 539–543.
(10) Grimmer, G.; Naujack, K. W.; Dettbarn, G.; Brune, H.; Deutsch-Wenzel, R. P.; Misfeld, J. In *Polynuclear Aromatic Hydrocarbons*; Cooke, M., Dennis, A. J., Eds.; Battelle: Columbus, OH, 1983; pp 571–582.
(11) LaVoie, E. J.; Hecht, S. S.; Amin, S.; Bedenko, V.; Hoffmann, D. *Cancer Res.* **1980**, *40*, 4528–4532.
(12) Hecht, S. S.; LaVoie, E. J.; Amin, S.; Bedenko, V.; Hoffmann, D. In *Poynuclear Aromatic Hydrocarbons*; *Chemistry and Biological Effects*; Bjorseth, A., Dennis, A. J., Eds.; Battelle: Columbus, OH, 1980; pp 417–433.
(13) Amin, S.; Hussain, N.; Huie, K.; Balanikas, G.; Rice, J. E.; LaVoie, E. J.; Hecht, S. S. In *Polynuclear Aromatic Hydrocarbons: Mechanisms, Methods, and Metabolism*; Cooke, M., Dennis, A. J., Eds.; Battelle: Columbus, OH, 1985; pp 99–111.

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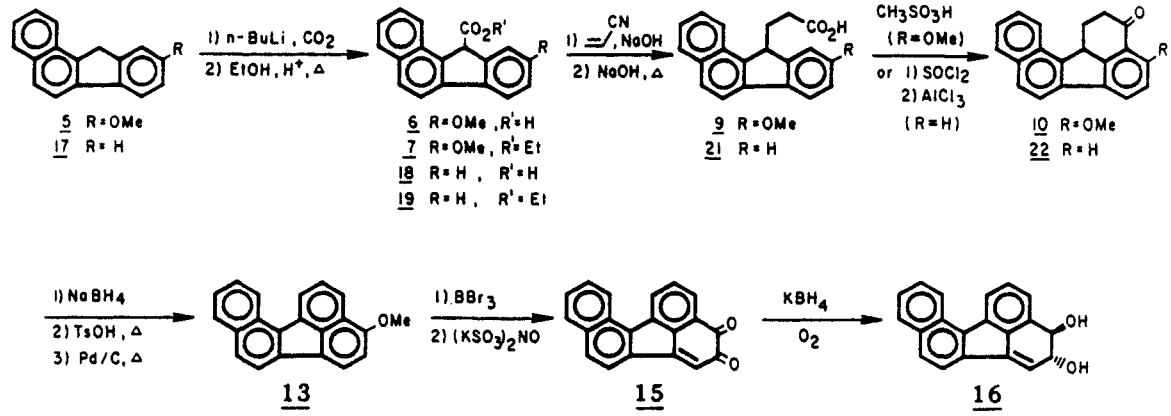
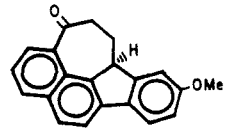
Scheme II. Synthesis of *trans*-4,5-Dihydro-4,5-dihydroxybenzo[*j*]fluoranthene (16) and 1,12c-Dihydrobenzo[*j*]fluoranthen-3(2*H*)-one (22)



in Scheme I. Displacement of the methoxy group of phenyl 2-methoxy-1-naphthoate with (4-methoxyphenyl)magnesium bromide gave **3** in good yield. Hydrolysis of the phenyl ester and Friedel–Crafts ring closure was effected with methanesulfonic acid. This reagent gave better yields than sulfuric acid which tended to give some water-soluble byproducts. Clemmensen reduction of **4** yielded 9-methoxy-11*H*-benzo[*a*]fluorene (**5**) in good yield. The benzo[*j*]fluoranthene skeleton was constructed from **5** by using the sequence outlined in Scheme II. Metalation at the 11-position using *n*-butyllithium, followed by treatment with carbon dioxide and esterification afforded the 11-carbethoxy derivative. This compound underwent Michael addition with acrylonitrile in the presence of sodium hydroxide. Upon heating at reflux in ethanol with 10 N sodium hydroxide, the ester and nitrile groups were hydrolyzed to carboxylic acids, and the tertiary carboxylic acid was decarboxylated to give **9**. Conversion of the acid to an acid chloride followed by Friedel–Crafts cyclization with aluminum chloride in carbon disulfide gave a mixture of ketones. The NMR spectrum of the minor component gives rise to a doublet (J = 9 Hz) at 7.03 ppm for the proton ortho to the methoxy group in the desired benzo[*j*]fluoranthene derivative **10**. In the NMR spectrum of the major component, however, an additional doublet (J = 1 Hz) is observed at 7.06 ppm. The presence of this proton ortho to the methoxy group indicates that the cyclization was directed away from the substituent-bearing ring, forming a seven-membered ring ketone (**11**). Ap-



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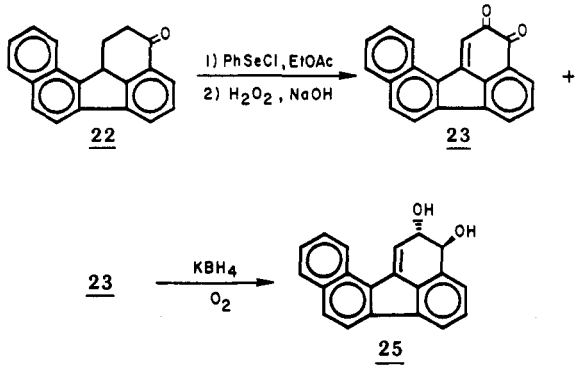
parently, coordination of the methoxy group with aluminum chloride decreases the electron density in that ring, directing the ring closure to the 1-position. The use of methanesulfonic acid for the closure of the propionic acid derivative **9** minimized this undesired side reaction, giving **10** as the major product. Reduction of **10** with sodium borohydride, followed by *p*-toluenesulfonic acid catalyzed dehydration, and aromatization in refluxing 1-methylnaphthalene over 10% palladium-on-charcoal yielded 4-methoxybenzo[*j*]fluoranthene (**13**) in almost quantitative yield. Treatment of **13** with boron tribromide in methylene chloride gave the corresponding phenol which was converted to the 4,5-quinone upon treatment with Fremy's salt in benzene in the presence of a phase-transfer catalyst.[15] Reduction of the quinone to the trans-dihydrodiol proved troublesome. The major products of this reduction (after acetylation) are the tetrahydrodiol diacetate and 6a-hydroxy-4,5,6,6a-tetrahydro-4,5-diacetoxybenzo[*j*]-fluoranthene. The latter product is most likely formed as a result of either base catalyzed or free-radical oxygenation at the doubly benzylic 6a-position. The use of a smaller ratio of potassium borohydride to quinone (2:1) or passing pure oxygen through the reaction mixture or conducting the reaction under 50 psi oxygen failed to minimize these overreduction products. Several other reducing agents including sodium borohydride, zinc borohydride, and tetrabutylammonium borohydride were used for this reaction but failed to improve the yield of dihydrodiol **16**. Warming the hydroxy diacetate with phosphorus oxychloride in pyridine resulted in the formation of the pure trans-4,5-dihydrodiol diacetate. The diacetate was converted to dihydrodiol **16** by treatment with methanolic ammonia.

The synthesis of the *trans*-2,3-dihydrodiol of benzo[*j*]-fluoranthene has been described previously.[13] That procedure suffered from low yields and extensive byproduct formation in the final steps. As a result of this, we have explored an alternative synthesis to circumvent many of these problems which relies on reduction of the 2,3-quinone of benzo[*j*]fluoranthene. The preparation of 1,12c-dihydrobenzo[*j*]fluoranthen-3(2*H*)-one is shown in Scheme II. In this case, cyclization of the acid chloride with aluminum chloride proceeded smoothly to give the desired ketone (**22**). Attempted dehydrogenation of this ketone over 10% palladium-on-charcoal gave very low yields of the desired 3-hydroxybenzo[*j*]fluoranthene. The major products of this reaction were 3-hydroxy-1,2,3,12c-tetrahydrobenzo[*j*]fluoranthene and 1,2,3,12c-tetrahydrobenzo[*j*]fluoranthene, resulting from reduction of the ketone and hydrogenolysis of the resulting benzylic alcohol. The use of sulfur or a mixture of sulfur and palladium-on-charcoal for the dehydrogenation did not increase the yield of this phenol. An alternate approach was explored based upon the formation of α,β-unsaturated ketones by thermal elimination of phenyl selenoxides which are adjacent to a ketone.[17,18] In the case of ketone **22**, the resulting enone should tautomerize to 3-hydroxybenzo-

(14) Fuson, R. C.; Wassmundt, F. W. *J. Am. Chem. Soc.* **1956**, *78*, 5409–5413.

(15) Pataki, J.; Lee, H.; Harvey, R. G. *Carcinogenesis* **1983**, *4*, 399–402.
(16) Platt, K. L.; Oesch, F. *J. Org. Chem.* **1983**, *48*, 265–268.
(17) Sharpless, K. B.; Lauer, R. F. *J. Am. Chem. Soc.* **1973**, *95*, 2697–2699.
(18) Sharpless, K. B.; Lauer, R. F. *J. Org. Chem.* **1974**, *39*, 429–430.

Scheme III. Synthesis of *trans*-2,3-Dihydro-2,3-dihydroxybenzo[*j*]fluoranthene

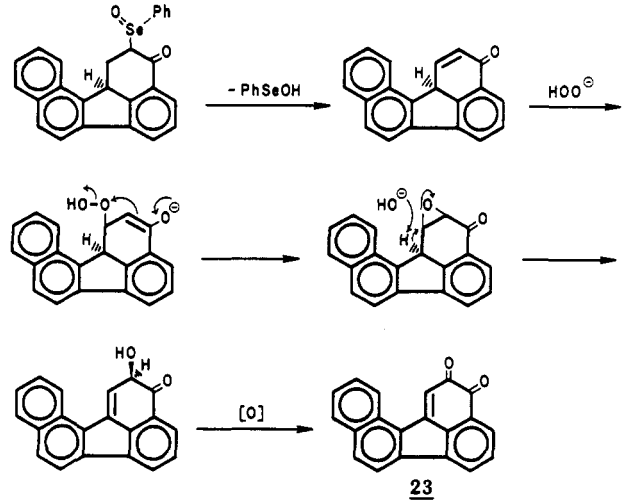


[*j*]fluoranthene. A solution of **22** was allowed to stir with phenylselenenyl chloride in ethyl acetate. This procedure as described by Sharpless[19] relies on reaction of the enol form of the ketone with phenylselenenyl chloride. Since HCl is eliminated in the course of the reaction, it is self-catalyzing and generally gives high yields of the α-phenylseleno ketone. In the present case, the necessity of generating an enolate under strongly basic conditions, which would result in reaction at both the 2- and the 12c-positions, is avoided. The α-phenylseleno ketone was isolated in high yield and fully characterized. A solution of this compound in THF–ethyl acetate (2:1) was treated with excess 30% hydrogen peroxide, and the mixture was stirred at room temperature for 18 h. However, no 3-hydroxybenzo[*j*]fluoranthene was obtained. Instead, benzo[*j*]fluoranthene-2,3-dione was isolated (Scheme III). Such a conversion of a ketone to an *o*-quinone is unprecedented for polycyclic aromatic hydrocarbons. It was later found that the addition of excess 1 N NaOH to the reaction mixture accelerates the formation of this quinone.

The formation of α-diketones from 2-(phenylseleno)-cyclooctanone has been studied by Reich et al.[20] who speculated that under acidic conditions these compounds are formed by Pummerer-like rearrangements. In the present case, tautomerization of the enone to the phenol might be retarded by unfavorable van der Waals interactions between H_1 and H_{12} in the fully aromatic structure. Reaction of this enone with alkaline hydrogen peroxide might result in formation of an α,β-epoxy ketone. This could then rearrange to the quinone by a mechanism such as is depicted in Scheme IV. The scope and limitations of this reaction are currently being explored in greater detail.

The synthesis of *trans*-9,10-dihydro-9,10-dihydroxybenzo[*j*]fluoranthene has been reported previously.[21] That preparation utilized 7-methylfluoranthene as a starting material, giving the dihydrodiol in 1% yield after 12 steps. Since this material is a proximate tumorigenic metabolite of benzo[*j*]fluoranthene, a more convenient synthesis was desirable. Wittig reaction of (*m*-methoxyphenethyl)triphenylphosphonium bromide with acenaphthenequinone afforded the desired enone **28** (Scheme V). Although treatment of **28** with a variety of acidic reagents including methanesulfonic acid, *p*-toluenesulfonic acid, and phosphorus oxychloride gave a methoxybenzo-[*j*]fluoranthene, Amberlyst-15 in refluxing benzene was the

Scheme IV. Possible Mechanism to Account for the Formation of 23 from the 2-Phenylseleno Derivative of Ketone 22



cleanest reagent. The identification of this compound as 10-methoxybenzo[*j*]fluoranthene was based upon its proton NMR spectrum. The two most upfield aromatic resonances occur as a doublet at 7.25 ppm for H_9 (J = 2.6 Hz) and a doublet of doublets at 7.30 ppm for H_{11}. The absorbance at 7.25 ppm with only a meta-coupling constant confirms the identity of this compound as the 10-methoxy derivative. No such absorbance would be detected for the isomeric 12-methoxy derivative. The absence of 12-methoxybenzo[*j*]fluoranthene from the product mixture is probably the result of unfavorable van der Waals interactions between the methoxy group and H_1 in the pseudo-bay region. 10-Methoxybenzo[*j*]fluoranthene was converted to the 9,10-quinone by treatment with boron tribromide followed by Fremy's salt oxidation. This same quinone has also been shown to be the exclusive product of Fremy's salt oxidation of 9-hydroxybenzo[*j*]fluoranthene.[22] The 9,10-quinone was reduced much more easily with potassium borohydride than either the 2,3- or the 4,5-quinone. Bubbling either air or pure oxygen through an ethanolic solution of the 9,10-quinone and excess potassium borohydride afforded the trans-9,10-dihydrodiol in good yield contaminated with only a small amount of the tetrahydrodiol.

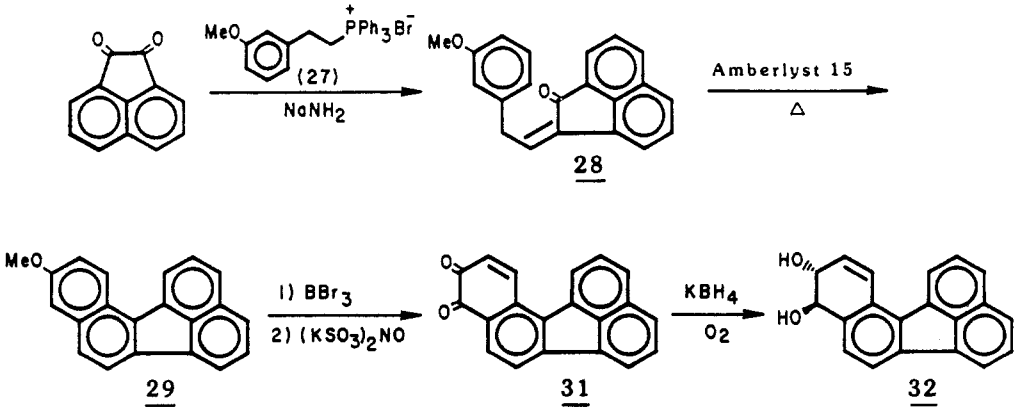
Experimental Section

Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 267 spectrophotometer as Nujol mulls unless otherwise specified. NMR spectra were recorded on a JEOL FX-90Q spectrometer. All NMR spectra were recorded in $CDCl_3$ solution unless otherwise noted with tetramethylsilane as an internal standard. UV spectra were obtained with a Cary Model 118 spectrophotometer. Mass spectra were determined with either a Hewlett-Packard Model 5982A instrument or a Hewlett-Packard Model 5988A instrument. High-resolution mass spectral data were obtained at the Rockefeller University Mass Spectrometric Biotechnology Resource Center, New York, NY. Combustion analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN.

Phenyl 2-(4-Anisyl)-1-naphthoate (3). (4-Methoxyphenyl)magnesium bromide was prepared by adding 4-bromoanisole (3.63 mL, 29 mmol) in ether (5 mL) to magnesium (0.7 g) in ether (25 mL). The mixture was heated at reflux for 6 h to complete the formation of the Grignard reagent. After the mixture cooled to room temperature, a solution of phenyl 2-

(19) Sharpless, K. B.; Lauer, R. F.; Teranishi, A. Y. *J. Am. Chem. Soc.* **1973**, *95*, 6137–6139.
(20) Reich, H. J.; Renga, J. M.; Reich, I. L. *J. Am. Chem. Soc.* **1975**, *97*, 5434–5447.
(21) Amin, S.; Bedenko, V.; LaVoie, E. J.; Hecht, S. S.; Hoffmann, D. *J. Org. Chem.* **1981**, *46*, 2573–2578.
(22) Rice, J. E., Unpublished results.

Scheme V. Preparation of *trans*-9,10-Dihydro-9,10-dihydroxybenzo[*j*]fluoranthene (32)



methoxy-1-naphthoate[14] (7.92 g, 28 mmol) in 1:1 ether–benzene (100 mL) was added dropwise. After the addition, the mixture was heated at reflux for 3 h and then stirred at room temperature overnight. The reaction mixture was poured into 500 mL of ice–NH_4Cl and the organic layer was separated. The aqueous solution was extracted twice with benzene, and the organic layers were combined. After washing with water and brine, the benzene solution was dried over sodium sulfate and evaporated to a red oil. Flash chromatography on silica eluting first with hexane and then 1–2% ethyl acetate/hexane yielded pure **3** (6.69 g, 68%), which was crystallized from aqueous acetone as white needles: mp 134–135.5 °C; IR (Nujol) 1740, 1610, 1592, 1490, 1290, 1245, 1210, 1185, 1122, 1027, 990, 905, 820, 730 cm^{-1}; NMR δ 8.2–7.83 (m, 3), 7.75–7.15 (m, 8), 7.07–6.80 (m, 4), 3.87 (s, 3); mass spectrum, *m/e* (relative intensity) 354 (1, M^+), 261 (100), 218 (16), 202 (10), 189 (26).

9-Methoxy-11*H*-benzo[*a*]fluoren-11-one (4). A solution of **3** (100 mg, 0.3 mmol) in methanesulfonic acid (3 mL) was stirred at room temperature for 90 min. The mixture was poured into 50 mL of cold water and extracted with ethyl acetate. The organic layer was washed with 5% $NaHCO_3$, water, and brine and dried over sodium sulfate. Evaporation of the solvent yielded **4** as a red oil (80 mg, 100%). Crystallization from methanol afforded red needles: mp 115–116 °C; NMR δ 8.90 (dd, 1, H_1), 7.95 (d, 1, H_5), 7.80–7.18 (m, 6, $H_{2,3,4,6,7,10}$), 6.88 (dd, 1, H_8), 3.88 (s, 3, OMe); mass spectrum, *m/e* (relative intensity) 260 (100, M^+), 245 (62), 217 (18), 189 (47). Anal. Calcd for $C_{18}H_{12}O_2$: C, 83.05; H, 4.66; Found: C, 82.89; H, 4.74.

9-Methoxy-11*H*-benzo[*a*]fluorene (5). Zinc amalgam was prepared by sonicating a mixture of zinc mossy (39.6 g), mercury(II) chloride (3.90 g), concentrated HCl (2.4 mL), and water (66 mL) for 5 min. The aqueous solution was decanted and glacial acetic acid added (48 mL) followed by concentrated HCl (48 mL) and **4** (3.1 g, 12 mmol) dissolved in toluene (200 mL). The mixture was heated at reflux for 23 h with mechanical stirring. An additional 48 mL of HCl was added, and reflux was continued for 4 h. The solution was cooled and decanted, washing the zinc with toluene. The toluene layer was separated and the acidic layer diluted with water and extracted with ether. The organic layers were combined and washed with water, 5% $NaHCO_3$, water, and brine. The solution was dried over sodium sulfate and evaporated in vacuo. Flash chromatography on silica eluting with 20% $CHCl_3$/hexane yielded pure **5** as a white crystalline solid; 1.73 g (59%). Recrystallization from methanol afforded **5** as white needles: mp 175.5–176 °C; NMR δ 7.96 (dd, 1, H_1), 7.83 (s, 2, $H_{5,6}$), 7.83–7.66 (m, 2, $H_{4,7}$), 7.53–7.38 (m, 2, $H_{2,3}$), 7.19 (d, 1, H_{10}), 6.96 (dd, 1, H_8), 4.13 (s, 2, Ar_2CH_2), 3.88 (s, 3, OMe); UV (MeOH) λ_{max} (ϵ) 317 nm (29100), 303 (30600), 293 sh (21700), 268 (81700), 259 (58200), 250 sh (32500), 217 (55800); mass spectrum, *m/e* (relative intensity) 246 (100, M^+), 230 (48). Anal. Calcd for $C_{18}H_{14}O$: C, 87.76; H, 5.74; Found: C, 87.92; H, 5.64.

Ethyl 9-Methoxy-11*H*-benzo[*a*]fluorene-11-carboxylate (7). A solution of **5** (500 mg, 2 mmol) in dry ether (150 mL) was stirred under N_2 at −30 °C as *n*-butyllithium (0.87 mL, 2.1 mmol, 2.42 M in hexane) was added in one portion. The yellow-orange solution was stirred at −30 °C for 1 h and then poured onto excess dry ice pieces. After warming to room temperature, the product was partitioned between water and ether. The aqueous layer was separated and acidified with 4 N HCl. Extraction into ether, followed by washing of the ether layer with brine and drying over sodium sulfate afforded the carboxylic acid **6** as a white solid upon removal of the solvent. The product was dissolved in ethanol (50 mL) and benzene (100 mL), and concentrated H_2SO_4 was added (0.5 mL). The solution was heated at reflux for 20 h, removing evolved water with a Dean–Stark trap. The solution was cooled and concentrated in vacuo. The residue was extracted into ether, which was then washed with 1 N NaOH, water, and brine and dried over sodium sulfate. The solution was evaporated to an oil, which was subjected to flash chromatography on silica gel, eluting with 50% CH_2Cl_2/hexane. **7** was obtained as a pale yellow oil; 0.44 g (69%). Crystallization from petroleum ether afforded **7** as white prisms: mp 105–106 °C; NMR δ 7.9–7.6 (m, 7), 7.24 (d, 1, H_{10}), 6.95 (dd, 1, H_8), 5.07 (s, 1, CH), 4.15 (m, 2, CH_2O), 3.85 (s, 3, OMe), 1.15 (t, 3, CH_3); mass spectrum, *m/e* (relative intensity) 318 (83, M^+), 245 (100).

3-(9-Methoxy-11*H*-benzo[*a*]fluoren-11-yl)propionic Acid (9). A solution of **7** (1.0 g, 3 mmol) in pyridine (4 mL) was cooled to 0 °C. Acrylonitrile (0.2 mL, 3 mmol) was added followed by 10 N NaOH (0.5 mL). The yellow solution was stirred for 15 min and was then allowed to warm to room temperature. Stirring was continued for 3 h, and the solution was poured into 65 mL of water containing 16 mL of concentrated HCl. The mixture was extracted with ether, and the ether was washed with 1 N HCl and brine and dried over sodium sulfate. Evaporation of ether left cyano ester **8** as an orange solid: 1.07 g (96%); NMR δ 7.98–7.35 (m, 7), 7.05–6.93 (m, 2, $H_{8,10}$), 4.02 (m, 2, CH_2O), 3.89 (s, 3, OMe), 3.04 (m, 2, CH_2CN), 1.37 (m, 2, CH_2CCN), 0.95 (t, 3, CH_3); mass spectrum, *m/e* (relative intensity) 371 (100, M^+), 298 (45), 258 (87), 243 (43).

The cyano ester was dissolved in ethanol (100 mL) and 10 N NaOH added (25 mL). The mixture was heated at reflux for 17 h, cooled to room temperature, and concentrated under reduced pressure. The residue was acidified with 6 N HCl and extracted with ethyl acetate. The organic layer was separated, and the aqueous layer was extracted twice with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, and evaporated to an orange solid; 0.93 g (97%). Crystallization from aqueous acetic acid gave orange prisms of **9**: mp 168–170 °C; NMR δ 8.1–6.9 (m, 9), 4.47 (t, 1, Ar_2CH), 3.90 (s, 3, OMe), 2.65 (dd, 2, CH_2CO_2H), 1.73 (m, 2, CH_2CCO_2H); mass spectrum, *m/e* (relative intensity) 318 (100, M^+), 258 (39), 245 (66).

4-Methoxy-1,12c-dihydrobenzo[*j*]fluoranthen-3(2*H*)-one (10). A mixture of **9** (0.70 g, 2.2 mmol) and methanesulfonic acid (50 mL) was stirred at room temperature for 19 h. The red solution was poured into ice–water and extracted into ethyl acetate. The organic layer was washed with water and brine and dried over sodium sulfate. After removal of the solvent under reduced pressure, the residue was purified by flash chromatography on silica gel. Elution with CH_2Cl_2 yielded a yellow oil: 60 mg (9%); NMR δ 8.04–7.25 (m, 6), 7.06 (d, 1), 6.95 (dd, 1), 4.16 (dd, 1), 3.89 (s, 3), 3.16 (m, 2), 2.80 (m, 1), 2.00 (m, 1); mass spectrum, *m/e* (relative intensity) 300 (100, M^+), 285 (14), 258 (52). These data are consistent with this product being the

seven-membered ring ketone **11**.

Further elution with 10% EtOAc/CH_2Cl_2 yielded **10** as a yellow solid; 0.46 g (70%). Recrystallization from benzene–hexane afforded **10** as yellow needles: mp 200–201 °C; NMR δ 8.20–7.80 (m, 5), 7.50 (m, 2), 7.03 (d, 1, H_5), 4.28 (dd, 1, H_{12c}), 4.02 (s, 3, OMe), 3.03 (m, 3), 1.82 (m, 1, H_1); mass spectrum, *m/e* (relative intensity) 300 (100, M^+), 272 (25), 258 (35), 243 (20).

4-Methoxy-1,12c-dihydrobenzo[*j*]fluoranthene (12). A solution of **10** (460 mg, 1.5 mmol) in MeOH (100 mL) was stirred at room temperature for 40 min with sodium borohydride (230 mg, 6 mmol). The solution was acidified with 1 N HCl and MeOH was removed under reduced pressure. The residue was partitioned between water and benzene. The benzene layer was washed again with water and then *p*-toluenesulfonic acid (70 mg) was added. The solution was heated at reflux for 2 h while removing water azeotropically. After the solution cooled to room temperature, the solvent was removed and the crude product purified by flash chromatography on silica gel. Elution with 10% CH_2Cl_2/hexane yieled pure **12** as an off-white solid; 400 mg, 94%. Crystallization from MeOH afforded **12** as pale yellow needles: mp 161–162 °C; NMR δ 8.10 (dd, 1, H_{12}), 7.97–7.82 (m, 3), 7.65–7.40 (m, 3), 7.00 (m, 1, H_3), 6.90 (d, 1, H_5, $J_{5,6}$ = 8 Hz), 6.24 (m, 1, H_2), 4.26 (dd, 1, H_{12c}), 3.92 (s, 3, OMe), 3.29 (m, 1, H_1), 2.20 (m, 1, H_1); mass spectrum, *m/e* (relative intensity) 284 (100, M^+), 269 (14), 253 (82), 241 (35), 239 (64).

4-Methoxybenzo[*j*]fluoranthene (13). A mixture of **12** (0.40 g, 1.4 mmol), 10% Pd/C (100 mg), and 1-methylnaphthalene (30 mL) was heated at reflux for 7 h while N_2 was bubbled through the solution. After cooling to room temperature, the mixture was filtered through a pad of Celite, and the filter was rinsed with several portions of benzene. The benzene was removed on the rotary evaporator. 1-Methylnaphthalene was removed by Kugelrohr distillation (1 mmHg, 100 °C pot temperature). The residue remaining in the pot was purified by flash chromatography on silica gel. Elution with 2% EtOAc/hexane yielded **13** as yellow plates; 0.40 g (100%). Crystallization from MeOH gave yellow leaves: mp 192–193.5 °C; NMR δ 8.68 (m, 1), 8.47 (m, 1), 8.2–7.45 (m, 8), 6.88 (d, 1, H_5), 4.08 (s, 3, OMe); mass spectrum, *m/e* (relative intensity), 282 (100, M^+), 267 (61), 239 (58).

4-Hydroxybenzo[*j*]fluoranthene (14). A solution of **13** (98 mg, 0.35 mmol) in dry methylene chloride (25 mL) was cooled to −78 °C under N_2. Boron tribromide (1 mL, 1 M in CH_2Cl_2) was added to the solution via syringe. Stirring at −78 °C continued for 1 h, and the solution was then allowed to slowly warm to room temperature. An additional 1-mL aliquot of boron tribromide was added and stirring continued for 2 h. The solution was poured into 50 mL of water, the organic layer was separated, and the aqueous layer was extracted twice with small portions of ethyl acetate. The organic layers were combined, washed with water and brine, and dried over sodium sulfate. Evaporation of solvents left a yellow solid (90 mg, 96%), which was crystallized from benzene as yellow needles: mp 258–260 °C dec; UV (EtOH) λ_{max} (ε) 394 nm (5300), 374 (4000), 356 (2100), 330 (15 500), 317 (9700), 303 sh (3500), 277 sh (6200), 257 (14 900), 242 (22 700), 223 (16 700); mass spectrum, *m/e* (relative intensity) 268 (M^+, 100), 239 (38); high-resolution mass spectrum, exact mass calcd for $C_{20}H_{12}O$ 268.0888, obsd 268.0921.

Benzo[*j*]fluoranthene-4,5-dione (15). A solution of **14** (90 mg, 0.34 mmol) in benzene (20 mL) containing 5 drops of Adogen 464 was stirred at room temperature while a solution of potassium nitrosodisulfonate (265 mg, 1 mmol) in 1/6 M KH_2PO_4 (10 mL) and water (10 mL) was added in one portion with vigorous stirring. The reaction was monitored by TLC (5% MeOH in benzene) and was complete after 2 h at room temperature (product R_f 0.61 on silica gel). The benzene layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with water and brine and dried over sodium sulfate, yielding a red solid after evaporation of the solvents; 90 mg, 94%. Recrystallization from benzene afforded **15** as red needles: mp 227 °C dec; NMR δ 8.46 (m, 1, H_{12}), 8.25 (dd, 1, H_1), 8.04–7.49 (m, 7), 6.98 (s, 1, H_6); mass spectrum, *m/e* (relative intensity) 282 (M^+, 45), 254 (100), 225 (36), 224 (41).

***trans*-4,5-Dihydro-4,5-dihydroxybenzo[*j*]fluoranthene (16).** Quinone **15** (100 mg, 0.35 mmol) was added to a suspension of potassium borohydride (200 mg, 3.7 mmol) in 95% EtOH (70 mL) while air was bubbled through the solution. After 21 h, most of the solvent was removed in vacuo, and the residue was partitioned between EtOAc and water. The organic layer was washed with water and brine and dried over sodium sulfate. After evaporation of the solvents, the residue was treated overnight with 1 mL of dry pyridine and acetic anhydride (75 μL, 0.8 mmol) at 0 °C. Water was added, and the mixture was extracted with EtOAc. The organic layer was washed with water and brine and dried (Na_2SO_4). After removal of the solvents, the residue was purified by flash chromatography (silica gel, CH_2Cl_2 and then 10% EtOAc/CH_2Cl_2), yielding the dihydrodiol diacetate (8 mg, 6%), the tetrahydrodiol diacetate (49 mg, 37%), and 6a-hydroxy-4,5,6,6a-tetrahydro-*trans*-4,5-diacetoxybenzo[*j*]fluoranthene, (44 mg, 32%). The latter compound gave the following spectra: IR (neat) 3460, 3070, 3030, 2940, 2860, 1740, 1380, 1250, 1085, 1025, 980, 950, 830, 815, 755 cm^{-1}; NMR δ 8.58 (dd, 1, H_{12}), 8.15–7.1 (m, 9), 6.70 (d, 1, H_4) 6.15 (m, 1, H_5) 5.33 (m, 1, H_5), 3.20 (m, 1, H_6), 2.69 (m, 1, H_6), 2.18, 2.16, 2.06, 2.02 (s, OAc, 2 diastereomers), 2.0–1.6 (m, 1, H_6); mass spectrum, *m/e* (relative intensity) 388 (M^+, 74), 328 (2), 285 (100), 269 (90), 259 (54) , 231 (24), 202 (33).

The hydroxy diacetate (50 mg, 0.13 mmol) was converted to the dihydrodiol diacetate by treatment of a pyridine solution (1 mL) at 0 °C under Ar with phosphorus oxychloride (14 μL, 0.15 mmol) for 30 min followed by heating at 50 °C for 4 h in an oil bath. After cooling to room temperature, the solution was diluted with water and extracted into EtOAc. The organic layer was washed with water and brine and dried over sodium sulfate. Purification by flash chromatography as described above afforded the pure dihydrodiol diacetate as a yellow solid; 20 mg, 42%. Recrystallization from ether–petroleum ether gave fine yellow needles: mp 154–156 °C; NMR δ 8.61 (m, 1, H_{12}), 8.16 (dd, 1, H_1, $J_{1,2}$ = 7.4 Hz, $J_{1,3}$ = 1.3 Hz), 7.96 (m, 1), 7.84 (s, 2, $H_{7,8}$), 7.7–7.4 (m, 4), 6.76 (d, 1, H_6, $J_{5,6}$ = 4.7 Hz), 6.36 (d, 1, H_4, $J_{4,5}$ = 3.7 Hz), 6.01 (dd, 1, H_5), 2.09 (s, 3), 2.08 (s, 3); mass spectrum, *m/e* (relative intensity) 370 (M^+, 4), 310 (19), 268 (100), 252 (33); high-resolution mass spectrum calcd for $C_{24}H_{18}O_4$, 370.1205; obsd 370.1164.

The diacetate (6.6 mg, 18 μmol) was dissolved in dry THF (10 mL) and treated with 10 mL of methanol which was saturated with ammonia. The solution was allowed to stand in the dark under argon at room temperature for 4 days. Solvents were removed in vacuo and the residue purified by flash chromatography on silica gel eluting with ethyl acetate. The pure dihydrodiol was obtained as a pale yellow solid (4.2 mg, 84%), which was recrystallized from EtOAc/hexane as fine yellow needles: mp > 170 °C dec; NMR (acetone-d_6) δ 8.73 (dd, 1, H_{12}, $J_{11,12}$ = 7.5 Hz, $J_{10,12}$ = 1.7 Hz), 8.22–7.84 (m, 4), 7.71–7.45 (m, 4), 6.91 (d, 1, H_6, $J_{5,6}$ = 2.9 Hz), 5.10 (d, 1, H_4, $J_{4,5}$ = 7.6 Hz), 4.94 (dd, 1, H_5); UV (MeOH) λ_{max} (ε) 344 nm (3600), 331 (4700), 320 (4300), 289 (6700), 278 (7200), 258 (15 200), 250 (15 100), 229 (9900); mass spectrum, *m/e* (relative intensity) 286 (M^+, 48), 268 (100), 240 (73), 239 (63).

11*H*-Benzo[*a*]fluorene (17). This compound was prepared by Clemmensen reduction of 11*H*-benzo[*a*]fluoren-11-one[14] (5.8 g, 25 mmol) as described above for **5**. Crystallization of the product from methanol afforded **17** as white needles: 4.11 g, 76%; mp 182–183 °C (lit.[23] mp 182 °C); NMR δ 8.08–7.75 (m, 5), 7.68–7.29 (m, 5), 4.20 (s, 3, OMe); mass spectrum, *m/e* (relative intensity) 216 (100, M^+), 215 (75).

Ethyl 11*H*-Benzo[*a*]fluorene-11-carboxylate (19). 11*H*-Benzo[*a*]fluorene (2.22 g, 10 mmol) was converted to the 11-carbethoxy derivative as described above for **7**. Pure **19** was obtained as a pale yellow oil; 2.15 g, 75%. Crystallization from petroleum ether afforded white needles: mp 66–67 °C; NMR δ 7.97–7.59 (m, 6), 7.55–7.30 (m, 4), 5.14 (s, 1, H_{11}), 4.15 (q, 2), 1.16 (t, 3); mass spectrum, *m/e* (relative intensity) 288 (M^+, 48), 215 (100).

3-(11*H*-Benzo[*a*]fluoren-11-yl)propionic Acid (21). This compound was prepared from **19** (1.05 g, 4 mmol) using the procedure outlined above for **9**. The intermediate cyano ester **20** was obtained as colorless prisms: mp 123–125 °C; IR 2240, 1720, 1240, 850, 825, 750, 730 cm^{-1}, mass spectrum, *m/e* (relative intensity) 341 (M^+, 100), 268 (80), 228 (80), 213 (40). The product propionic acid (**21**) was obtained as an orange solid (1.11 g). Crystallization from toluene afforded **21** as colorless prisms: mp 195–197 °C (lit.[24] mp 192–195.5 °C); NMR δ 8.45–7.30 (m, 10),

(23) Datta, B. B.; Bardhan, J. C. *J. Chem. Soc.* **1962**, 3974–3977.

4.48 (t, 1, H_{11}), 2.65 (m, 2), 1.69 (m, 2); mass spectrum, *m/e* (relative intensity) 288 (M^+, 37), 230 (100), 228 (50), 215 (67).

1,12c-Dihydrobenzo[*j*]fluoranthen-3(2*H*)-one (22). A mixture of **21** (1.0 g, 3.5 mmol), oxalyl chloride (10 mL), and benzene (100 mL) was heated at reflux for 2 h, cooled to room temperature, and evaporated. The residue was dissolved in carbon disulfide (30 mL) and cooled to 0 °C under argon. Aluminum chloride (700 mg, 5.3 mmol) was added in one portion, and the mixture was stirred for 16 h with the temperature gradually rising to room temperature. The mixture was poured into 1 N HCl and extracted with ethyl acetate. The organic layer was washed with water and brine and dried over sodium sulfate. After removing the solvents in vacuo the oily residue was purified by flash chromatography on silica gel. Elution with 25% CH_2Cl_2/hexane provided **22** as a straw-colored oil; 560 mg. Further elution with 10% EtOAc/CH_2Cl_2 yielded recovered starting material; 240 mg. The yield of **22** based on recovered starting material was 80%. Ketone **22** crystallized from MeOH as colorless needles: mp 92–93 °C (lit.[24] mp 97–98 °C); NMR δ 8.03 (m, 1, H_{12}), 7.94–7.79 (m, 4), 7.60–7.40 (m, 4), 4.26 (dd, 1, H_{12c}), 3.17 (m, 2), 2.98 (m, 1), 2.00 (m, 1); mass spectrum, *m/e* (relative intensity) 270 (100, M^+), 242 (11), 239 (27), 228 (76), 214 (30).

Benzo[*j*]fluoranthene-2,3-dione (23). A solution of **22** (0.16 g, 0.59 mmol) in ethyl acetate (50 mL) was stirred at room temperature with phenylselenenyl chloride (134 mg, 0.7 mmol) for 24 h. The pale yellow crystalline product was filtered, yielding 180 mg (72%) of 2-(phenylseleno)-1,12c-dihydrobenzo[*j*]-fluoranthen-3(2*H*)-one. An additional 30 mg was obtained upon flash chromatography of the concentrated mother liquor eluting with 50% CH_2Cl_2–hexane. The total yield of the α-phenylseleno ketone was (84%). An analytical sample was obtained by recrystallization from ether–petroleum ether as off-white needles: mp 196–198 °C; NMR δ 8.05 (m, 1, H_{12}), 7.91 (m, 2, $H_{7,8}$), 7.8–7.25 (m, 11), 4.77 (dd, 1, H_2), 4.25 (dd, 1, H_{12c}) 3.18 (m, 1, H_1), 1.85 (m, 1, H_1); mass spectrum, *m/e* (relative intensity) 428 (5, M + 3), 427 (8, M + 2), 426 (24, M + 1), 425 (3, M^+), 424 (11, M − 1), 423 (4, M − 2), 422 (4, M − 3), 269 (37), 239 (100). Anal. Calcd. for $C_{26}H_{18}SeO$: C, 73.24; H, 4.23; Found: C, 73.06; H, 4.35.

A solution of the α-phenylseleno ketone (0.4 g, 0.9 mmol) was dissolved in ethyl acetate (20 mL) and THF (40 mL). The solution was stirred vigorously as 1 N NaOH (10 mL) and 30% H_2O_2 (5 mL) were added. Stirring was continued for 18 h, EtOAc (50 mL) was added, and the organic layer was separated. After being washed with water and brine, the solution was dried over Na_2SO_4, filtered, and evaporated. Flash chromatography on silica gel, eluting with 50% CH_2Cl_2/hexane to 100% CH_2Cl_2 and then 10% EtOAc/CH_2Cl_2, yielded quinone **23** as a dark red solid; 100 mg (40%). Crystallization from benzene afforded **23** as red needles: mp >255 °C dec; NMR δ 8.39 (m, 1, H_{12}), 8.07 (m, 2), 7.84–7.30 (m, 6), 7.10 (s, 1, H_1); mass spectrum, *m/e* (relative intensity) 282 (M^+, 4), 254 (100), 226 (45).

***trans*-2,3-Dihdyro-2,3-dihydroxybenzo[*j*]fluoranthene (25).** Quinone **23** (44 mg, 0.16 mmol) was added in 15 mL of THF to a suspension of potassium borohydride (100 mg, 1.8 mmol) in 95% ethanol (50 mL). Air was bubbled through the mixture for 1.5 h. Solvents were removed under reduced pressure (below 40 °C), and the mixture was extracted with EtOAc. The organic layer was washed with water and brine and dried over Na_2SO_4. After removal of solvents in vacuo the residue was treated with 1 mL of dry pyridine and 1 mL of acetic anhydride at 0 °C overnight. The solution was poured into water and extracted with EtOAc. The EtOAc was washed with water and brine and dried over sodium sulfate. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography (silica gel, 50% to 75% CH_2Cl_2/hexane). The 2,3-dihydrodiol diacetate was obtained as a pale yellow solid (15 mg, 25%) which crystallized from ether–hexane as yellow needles: mp >198 °C dec; NMR δ 7.93–7.31 (m, 9), 6.98 (d, 1, H_1, $J_{1,2}$ = 6.4 Hz), 6.43 (d, 1, H_3, $J_{2,3}$ = 6.8 Hz), 6.04 (dd, 1, H_2), 1.92 (s, 3, OAc), 1.91 (s, 3, OAc); mass spectrum, *m/e* (relative intensity) 370 (M^+, 8), 310 (12), 268 (100), 239 (85); high-resolution mass spectrum, calcd for $C_{24}H_{18}O_4$ 370.1205, obsd 370.1176.

The dihydrodiol diacetate (15 mg, 0.041 mmol) was dissolved in dry THF (10 mL) and methanol saturated with ammonia (10 mL), and this solution was allowed to stand in the dark at room temperature for 41 h. The solvents were removed under reduced pressure (below 40 °C), and the residue was purified by flash chromatography on silica gel eluting with 50% hexane–EtOAc. Dihydrodiol **25** was obtained as a yellow solid (9.2 mg, 79%), which crystallized from $CHCl_3$/hexane as fine yellow needles: mp 206–215 °C dec; NMR (acetone-d_6) δ 8.1–7.8 (m, 5), 7.6–7.3 (m, 4), 7.13 (d, 1, H_1, $J_{1,2}$ = 3.1 Hz), 5.10 (d, 1, H_3, $J_{2,3}$ = 7.9 Hz), 4.81 (dd, 1, H_2); UV (MeOH) λ_{max} (ε) 353 nm (2500), 335 (3500), 320 (4000), 299 (11 500), 285 sh (14 600), 268 (25 300), 258 (26 000), 238 (21 500), 233 sh (19 400); mass spectrum, *m/e* ([relative intensity) 286 (M^+, 12), 268 (5), 255 (9), 240 (46), 239 (100), 226 (14).

3-Methoxyphenethyl Bromide (26). Phosphorous tribromide (8 mL, 85 mmol) was added dropwise at room temperature to a solution of 3-methoxyphenethyl alcohol (10 g, 66 mmol) in dry ether (35 mL). The solution was stirred overnight and then poured into ice–water. The mixture was extracted with chloroform, and the organic layer was then washed with 5% sodium bicarbonate and water and then dried over sodium sulfate. The residual oil remaining after removal of solvents was purified by flash chromatography on silica gel eluting with 1:1 hexane–chloroform, yielding **26** as a colorless oil: 11.5 g (81%); NMR δ 7.2 (m, 1, H_5), 6.75 (m, 3, $H_{2,4,6}$), 3.75 (s, 3, OMe), 3.55 (t, 2, CH_2Br, J = 7.2 Hz), 3.1 (t, 2, CH_2Ar); mass spectrum, *m/e* (relative intensity) 216 (92, M + 2) 214 (100, M^+), 199 (4), 77 (37).

(3-Methoxyphenethyl)triphenylphosphonium Bromide (27). A mixture of **26** (4.2 g, 20 mmol) and triphenylphosphine (5.65 g, 22 mmol) in dry DMF (60 mL) was heated at reflux for 60 h. After the mixture cooled to room temperature, ether was added, and the resulting precipitate was filtered and washed with ether until a white solid was obtained: 7.3 g (78%); mp 213–215 °C; NMR (Me_2SO-d_6) δ 7.84 (m, 15), 7.25 (dd, 1), 6.9 (m, 3), 4.2–3.8 (m, 2), 3.75 (s, 3), 3.1–2.6 (m, 2).

1-[2-(*m*-Anisyl)ethylidene]acenaphthenone (28). Sodium amide (0.9 g, 23 mmol) was added under N_2 to a solution of **27** (7.31 g, 15 mmol) in dry THF (175 mL). This mixture was heated at reflux for 1 h. Acenaphthenequinone (2.6 g, 14 mmol) was added rapidly and the solution heated at reflux for an additional 20 h. After cooling, the reaction mixture was poured into cold methanol. The precipitate was filtered, and the filtrate was evaporated. The residue was taken up in ethyl acetate washed with water, brine, and then dried over sodium sulfate. Flash chromatography on silica gel eluting with 0–30% ethyl acetate in hexane gave **28** as a yellow solid: 1.89 g (44%); IR 3042, 2937, 2830, 1700, 1662, 1590, 1040, 905, 770, 720, 692, 640 cm^{-1}; mass spectrum, *m/e* (relative intensity) 300 (100, M^+) 283 (31), 269 (42), 239 (29).

10-Methoxybenzo[*j*]fluoranthene (29). A mixture of **28** (131 mg, 0.4 mmol) and Amberlyst 15 (1.4 g) in dry benzene (170 mL) was heated at reflux for 22 h. The reaction mixture was filtered and the resin washed with several portions of benzene. After removal of benzene in vacuo the residue was purified by flash chromatography on silica gel eluting with hexane and then 10% CH_2Cl_2/hexane, yielding **29** as a yellow solid: 28 mg (25%). Recrystallization from methanol afforded **29** as yellow plates: mp 126–127 °C; UV (MeOH) λ_{max} (ε) 385 nm (7800), 366 (900), 320 (41 900), 307 (29 400), 254 (28 600), 238 (42 000); NMR δ 8.61 (d, 2, H_{12}, $J_{11,12}$ = 9.5 Hz), 8.40 (d, 1, H_1, $J_{1,2}$ = 7.5 Hz), 8.06–7.52 (m, 7, H_{2-8}), 7.30 (dd, 1, H_{11}, $J_{9,11}$ = 2.6 Hz), 7.25 (d, 1, H_9), 3.97 (s, 3, OMe), mass spectrum, *m/e* (relative intensity) 282 (100, M^+), 267 (11), 239 (57). Anal. Calcd for $C_{21}H_{14}O$: C, 89.33; H, 5.01. Found: C, 89.33; H, 5.10.

10-Hydroxybenzo[*j*]fluoranthene (30). This compound was prepared from **29** by the procedure described above for **14**. 10-Hydroxybenzo[*j*]fluoranthene was obtained as a yellow crystalline solid, which was recrystallized from benzene as yellow needles: 37 mg (77%); mp >220 °C dec; UV (EtOH) λ_{max} (ε) 388 nm (8000), 369 (6000), 352 (3300), 324 (43 500), 311 (30 100), 282 (14 400), 272 (14 700), 257 (27 100), 242 (35 500), 219 (50 200); mass spectrum, *m/e* (relative intensity) 268 (90, M^+), 239 (56); high-resolution mass spectrum; exact mass calcd for $C_{20}H_{12}O$ 268.0888, obsd, 268.0887.

Benzo[*j*]fluoranthene-9,10-dione (31). The conversion of **30** to **31** was performed with the procedure detailed above for **15**. The pure quinone **31** was obtained after flash chromatography

(24) Orchin, M.; Reggel, L. *J. Am. Chem. Soc.* **1951**, *73*, 436–442.

on silica gel eluting with CH_2Cl_2 and then 10% EtOAc/CH_2Cl_2 as an orange solid; 30 mg (77%). Recrystallization from benzene afforded **31** as fine red needles; mp >265 °C dec; NMR δ 8.45 (d, 1, H_{12}, $J_{11,12}$ = 10 Hz), 8.3-7.65 (m, 8), 6.60 (d, 1, H_{11}); mass spectrum, (chemical ionization, methane), *m/e* (relative intensity) 283 (M + 1, 100), 255 (6).

***trans*-9,10-Dihydro-9,10-dihydroxybenzo[*j*]fluoranthene (32).** A suspension of quinone **31** (30 mg, 0.11 mmol) in 95% EtOH (20 mL) was stirred in the dark at 0 °C with potassium borohydride (60 mg, 1.1 mmol). Oxygen was bubbled through the solution for 2 h. After that time, the colorless solution was poured into water and extracted several times with EtOAc. The extracts were combined, washed with 0.1 N HCl, water, and brine and dried over K_2CO_3. After removal of the solvent, the residue was purified by flash chromatography on silica gel eluting first with $CHCl_3$ and then 5% MeOH/$CHCl_3$. The dihydrodiol **32** was obtained as a white solid; 18 mg (58%). The spectral characteristics and chromatographic behavior of this compound were identical with those previously described.[21]

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Dichotomous Regiochemistry of Aldehyde and Ketone in the Reaction with Dithio-Substituted Crotyllithium

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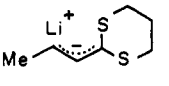
The crotyllithium compound **1** generated from (*E*)-2-(1-propen-1-yl)-1,3-dithiane reacted with an aldehyde to give γ-products in favor of the anti isomer. This regio- and diastereoselective reaction is applicable to syntheses of trans β,γ-disubstituted γ-lactones, including natural products of (±)-eldanolide and (±)-trans quercus lactone. The γ(1,2)-adducts obtained from the reaction of **1** and enals underwent alkoxy-Cope rearrangements on treatment with KH. The consequence is virtually complete α(1,4)-addition of crotyllithium **1** to α,β-unsaturated aldehydes. Crotyllithium **1** reacted with ketones at either the α- or the γ-site, depending on the nature of respective ketone. The regiochemistry is well interpreted by the hard and soft acids and bases principle, when the steric effect is a minor controlling factor. The effects of HMPA and reaction temperature on the regioselectivity were also evaluated.

The regioselective reactions of unsymmetric allylic anions have been extensively studied.[1] The controlling factors of regioselectivity include the effect of substituents,[2] the nature of attacking electrophiles,[3,4] the nature of solvents,[5] and the nature of counter cations.[6] However, no consistent rule is so far established to interpret the observed regioselectivity. The dithianylidene anion, an unsymmetric allylic anion with dithio substituents, can function as an equivalent of α,β-unsaturated acyl anion when reaction takes place at the α-site, while the anion can function as an equivalent of β-anion of carboxylic acid when reaction occurs at the γ-site. Thus, a proper manipulation of the ambident property of dithianylidene anions would provide a versatile method in organic synthesis. Furthermore, enlightened by the recent research on the diastereoselective reaction of crotyl anions,[7] we have found that dithio-substituted crotyllithium **1** indeed adds to aldehydes in a regio- and diastereoselective manner.[8] We herein report the unusual dichotomous regiochemistry of aldehyde and ketone in the reaction with crotyllithium **1**.

Table I. Reaction of Crotyllithium 1 and Aldehydes

entry	electrophile	addition products α:γ	addition products (anti/syn)	total yields, %
1	MeCHO	<5:95	(80/20)	86
2	$MeCH_2CHO$	<5:95	(~100/0)	91
3	$Me(CH_2)_2CHO$	<5:95	(~100/0)	89
4	Me_2CHCHO	<5:95	(~100/0)	93
5	$Me(CH_2)_3CHO$	<5:95	(~100/0)	93
6	$Me_2C{=}CHCH_2CHO$	<1:100	(~100/0)	90
7	$CH_2{=}CHCHO$	<1:100	(75/25)	87
8	$MeCH{=}CHCHO$	<1:100	(84/16)	88
9	$PhCH{=}CHCHO$	<1:100	(85/15)	86
10	2-furaldehyde	<1:100	(~100/0)	84
11	PhCHO	<1:100	(75/25)	92



1

Results and Discussion

Treatment of crotonaldehyde with an equivalent amount of 1,3-propanedithiol in the presence of magnesium perchlorate yielded the vinylogous dithiane **2** in the *E* form.[8] Dithiane **2** was readily deprotonated by *n*-BuLi in THF solution to give the desired crotyllithium **1**.[9] Previous

(1) Evans, D. A.; Andrews, G. C. *Acc. Chem. Res.* **1974**, *7*, 147.
(2) Ikeda, Y.; Furuta, K.; Meguriya, N.; Ikeda, N.; Yamamoto, H. *J. Am. Chem. Soc.* **1982**, *104*, 7663.
(3) Murphy, W. S.; Wattanasin, S. *J. Chem. Soc., Perkin Trans 1* **1980**, 2678.
(4) Atlani, P. M.; Biellmann, J. F.; Dube, S.; Vicens, J. J. *Tetrahedron Lett.* **1974**, 2665.
(5) Ziegler, F. E.; Fang, J. M.; Tam, C. C. *J. Am. Chem. Soc.* **1982**, *104*, 7174.
(6) Ziegler, F. E.; Tam, C. C. *J. Org. Chem.* **1979**, *44*, 3428.
(7) Hoffmann, R. V. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 555.
(8) Fang, J.-M.; Liao, L.-F.; Hong, B.-C. *J. Org. Chem.* **1986**, *51*, 2828.
(9) Ziegler, F. E.; Mencel, J. J. *Tetrahedron Lett.* **1983**, *24*, 1859.

0022-3263/87/1952-0855$01.50/0