NMR Centre funded by a grant from NSERC.

Registry No. 3a, 83313-92-2; **3b**, 83313-93-3; **5**, 83313-94-4; (*E*)-**6**, 83313-95-5; dicyclopropyl ketone acetylhydrazone, 83313-96-6; dicyclopropyl ketone propionylhydrazone, 83313-97-7; 1-acetoxyethylidene, 83313-98-8; *trans*-1,2-diacetoxy-1,2-dimethylcyclopropane, 67079-75-8; 1-acetoxy-2-methoxy-1,2-dimethylcyclopropane, 83313-99-9; acetylhydrazine, 1068-57-1; dicyclopropyl ketone, 1121-37-5; acetyl chloride, 75-36-5; biacetyl, 431-03-8; acetic anhydride, 108-24-7; propionyl chloride, 79-03-8; 2,3-pentanedione, 600-14-6; 2-acetoxypropene, 108-22-5; 2-methoxypropene, 116-11-0; $CH_3COOCCH_2CH_3$, 83350-10-1.

Fluoranthene: Synthesis and Mutagenicity of Four Diol Epoxides

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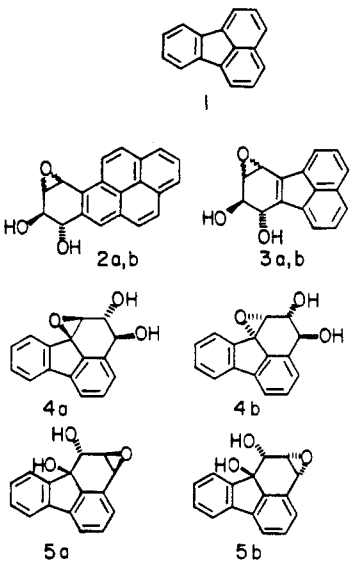
Received February 24, 1982

The syntheses of diol epoxides **4a,b** and **5a,b** of the mutagenic hydrocarbon fluoranthene (1) are described. Standard methodology is applied to the synthesis of targets **4a,b** but fails for the synthesis of **5a,b**. The latter two diol epoxides can be assembled by a route utilizing stereoselective, directed epoxidations. Simple molecular orbital calculations have been used to predict the reactivity of the diol epoxides in their opening to triol carbocations. Diol epoxides **4a,b** are predicted to be substantially more reactive than isomers **5a,b**. The more reactive pair, **4a,b**, may yield carbocations capable of alkylating cellular genetic material. This prediction is borne out in terms of the relative mutagenicity of the diol epoxides in a bacterial screen.

Fluoranthene (1, Chart I) occurs in various fossil fuels and combustion effluents at concentrations considerably greater than those of the most frequently studied polycyclic aromatic hydrocarbon, benzo[*a*]pyrene.[2] Further, we have found fluoranthene and benzo[*a*]pyrene to be approximately equipotent as mutagens for *Salmonella typhimurium*[3a] and as mutagens for human lymphoblasts.[3b] We have sought the syntheses of potential oxidative metabolites of fluoranthene to help identify the mode(s) of in vivo metabolism of the hydrocarbon and the structure(s) of the covalent adducts presumably formed from the activated hydrocarbon and DNA. Herein we outline our progress directed toward these ends. Specifically, we detail the syntheses and mutation assay of six possible metabolites of fluoranthene, the dihydrodiols **11** and **23** (see Schemes I and II), and the diol epoxides **4a,b** and **5a,b** (Chart I).

Chart I



syn-Isomers: epoxide oxygen syn to benzylic (allylic) OH, e.g., 4a and 5a

anti-Isomers: epoxide oxygen anti to benzylic (allylic) OH, e.g., 4b and 5b

Strategy

Extensive study of the metabolic activation of polycyclic aromatic hydrocarbons, such as benzo[*a*]pyrene,[4a] has identified the diol epoxides (see **2a,b**, Chart I) as agents responsible for the alkylation of cellular macromolecules. The genesis of the diol epoxides occurs through oxidation of the parent hydrocarbon to an arene oxide, followed by hydration of the oxide to the corresponding *trans*-dihydrodiol, and oxidation of the dihydrodiol to one or both

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(2) Prado, G. P.; Lee, M. L.; Hites, R. A.; Hoult, D. P.; Howard, J. B. In "16th International Symposium on Combustion"; The Combustion Institute: Cambridge, MA, 1973; pp 649–661.

(3) (a) Kaden, D. A.; Hites, R. A.; Thilly, W. G. *Cancer Res.* **1979**, *39*, 4152. (b) Thilly, W. G.; DeLuca, J. G.; Furth, E. E.; Hoppe, H., Iv; Kaden, D. A.; Krowelski, J. J.; Liber, H. L.; Skopek, T. R.; Slapikoff, S. A.; Tizard, R. J.; Penman, B. W. In "Chemical Mutagens"; de Serres, F. J., Hollaender, A., Eds.; Plenum Press: New York, 1980; Vol. 6, pp 331–363.

(4) (a) Harvey, R. G. *Acc. Chem. Res.* **1981**, *14*, 218. (b) Jerina, D. M., Yagi, H.; Lehr, R.; Thakker, D. R.; Schaefer-Rider, M.; Karle, J. M.; Levin, W.; Wood, A. N.; Chang, R. L.; Conney, A. H. In "Polycyclic Hydrocarbons and Cancer"; Gelboin, H. V., Ts'O, P. O. P., Eds.; Academic Press: New York, 1978; Vol 1, pp 173–188.

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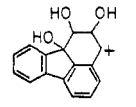
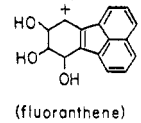
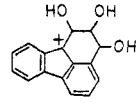
Table I. Triol Carbocation Delocalization Energies[a] and Carcinogenicities[b] for Fluoranthene

entry	triol carbocation[c]	$\Delta E\pi/\beta$[a]	$\Delta E_{deloc}/\beta$[a]	qualitative carcinogenicities
A	 (fluoranthene)	0.718	0.488	+++[d]
B	 (fluoranthene)	0.900	e	+++[d]
C	 (fluoranthene)	1.160	e	+++[d]

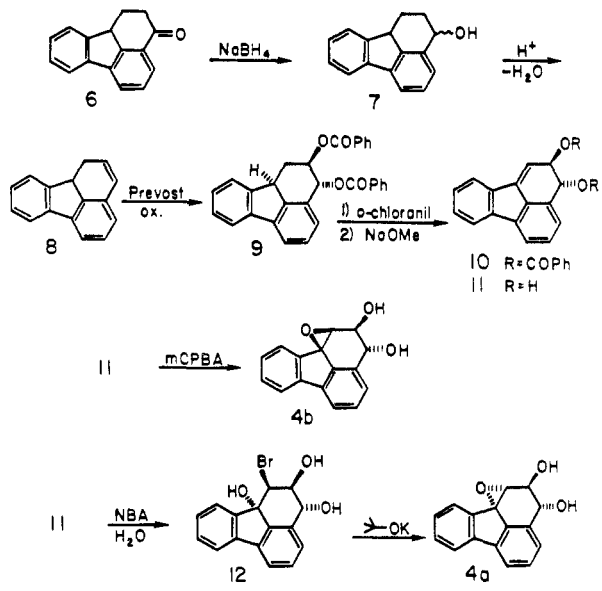
[a] $\Delta E\pi/\beta$ (HMO calculation) and $\Delta E_{deloc}/\beta$ (PMO calculation) are calculated values for the delocalization energy gained upon opening of a diol epoxide to the depicted triol carbocation. The HMO and PMO methods are π-system calculations only and methods do not take the hydroxyl substituents or the σ framework into account. [b] Qualitative carcinogenicities for the parent hydrocarbons from ref 5a. [c] The name of the parent aromatic hydrocarbon is given under each triol carbocation. [d] Qualitative carcinogenicity for fluoranthene, see ref 7. [e] PMO calculations cannot be made for nonalternant π systems.

of the stereoisomeric diol epoxides. The identification of *anti*-diol epoxide **2a** as a principal active metabolite of benzo[*a*]pyrene led Jerina et al.[4b] to comment on the exceptional stability of the triol carbocations formed from bay-region diol epoxides (e.g., **2a,b**). These workers and others[5a-d] have correlated theoretical parameters of the bay-region carbocations with the carcinogenic or mutagenic potency of the parent hydrocarbons. It is proposed that the reactivity of a diol epoxide toward genetic material correlates with the difference in delocalization energy between the diol epoxide and its derived triol carbocation. At least in theory, a readily formed carbocation, formed in situ from the corresponding diol epoxide, should show poor discrimination between strong (e.g., glutathione) and weak (e.g., DNA) cellular nucleophiles.[6] Such a correlation must be approximate, at best, when predicting the carcinogenicity of the parent polycyclic aromatic hydrocarbon (see Tables I and III in supplementary material), as other complex factors will ultimately govern the in vivo formation and detoxification of any given diol epoxide.[5e] The molecular orbital technique may fail also in predicting the reactivity of a diol epoxide in a biological assay (see e.g., ref 4a) owing among other factors to the requirement for absorption and intact delivery of the potential mutagen (carcinogen) to a crucial cellular target. Nonetheless, simple molecular orbital techniques may be of value in the *initial evaluation* of several potential metabolites of an aromatic hydrocarbon. Diol epoxides formed *within a cell* and capable of readily forming triol carbocations will likely

(5) (a) Loew, G. H.; Sudhindra, B. S.; Ferrell, J. E., Jr. *Chem. Biol. Interact.* **1979**, *26*, 75. (b) Smith, I. A.; Berger, D. G.; Seybold, P. G.; Serve, M. P. *Cancer Res.* **1978**, *38*, 2968. (c) Fu, P. P.; Harvey, R. G.; Belaıd, F. A. *Tetrahedron* **1978**, *34*, 857. (d) Osborne, M. R. *Cancer Res.* **1979**, *39*, 4760. (e) Sayer, J. M.; Yagi, H.; Croisy-Delcey, M.; Jerina, D. M. *J. Am. Chem. Soc.* **1981**, *103*, 4970.

(6) Hulbert, P. B. *Nature (London)* **1975**, *256*, 146.

Scheme I



react rapidly with cellular macromolecules. These diol epoxides and their dihydrodiol precursors are good candidates for synthesis and biological evaluation.

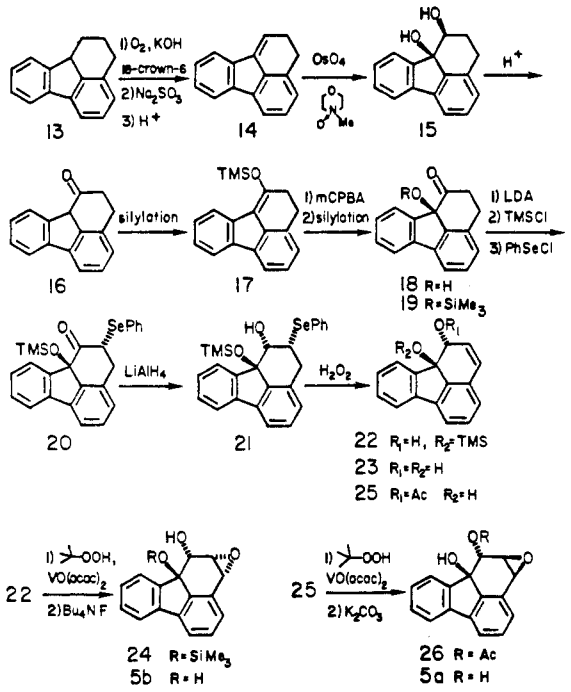
Given the number of polycyclic aromatic hydrocarbons that appear to be activated as the diol epoxides,[4a] we have sought the syntheses of the diol epoxides of fluoranthene. The symmetry of the hydrocarbon (1) limits the number of potential diol epoxide metabolites to a small group, viz., **3a,b**, **4a,b**, and **5a,b** (Chart I). Of these, only **5a,b** can be evaluated by the perturbational molecular orbital (PMO) method, which has been applied to benzo[*a*]pyrene and other polycyclic aromatic hydrocarbons.[4b] Diol epoxides **3a,b** and **4a,b** appear to be structurally related to the bay-region, benzo[*a*]pyrene diol epoxides (**2a,b**), but the PMO method is not applicable to their nonalternant π systems. We have examined all of the fluoranthene diol epoxides by using simple Huckel molecular orbital (HMO) theory; **5a,b** has been examined as well by the PMO method. Table I shows the results of these calculations. Values of $\Delta E\pi/\beta$ and $\Delta E_{deloc}/\beta$ for several other polycyclic aromatic hydrocarbons are given in Table III (see supplementary material).

In Table I the third column gives the value for $\Delta E\pi/\beta$, the difference in delocalization energies between diol epoxide and its corresponding triol carbocation, calculated by the simple Huckel molecular orbital (HMO) method. The fourth column gives the value of $\Delta E_{deloc}/\beta$, the difference in delocalization energy between the diol epoxides **5a,b** and their corresponding triol carbocation, calculated by the PMO method.[4b] The values for $\Delta E\pi/\beta$ are consistently larger than $\Delta E_{deloc}/\beta$ over a series of polycyclic aromatic hydrocarbons (Table III). Figure 1 (supplementary material) shows the close linear correlation between the two calculated values for several alternant π systems. The values of $\Delta E\pi/\beta$ for the nonalternant fluoranthene carbocations suggest that diol epoxides **3a,b** (entry B) and **4a,b** (entry C) will be at least as reactive as the bay-region diol epoxides from other polycyclic aromatic hydrocarbons (Figure 1). Diol epoxides **5a,b** are expected to be the least reactive of the fluoranthene metabolites. The routes to racemic diol epoxides **4a,b** and **5a,b** via their corresponding dihydrodiols are presented below.

Diol Epoxide Syntheses

Diol Epoxides 4a,b. Diastereomers **4a,b** are prepared by the standard diol epoxide synthesis described by Jerina

Scheme II



et al.[8] (Scheme I). Details of our syntheses appear in the *Experimental Section.*

Diol Epoxides 5a,b. The syntheses of diastereomers **5a,b** by the standard route to diol epoxides[8] requires dihydrofluoranthene **14** (Scheme II) as starting material. Olefin **14** is prepared from tetrahydrofluoranthene[12] (**13**) by a modification[13] of the known hydroxylation/dehydration sequence.[14] Prevost oxidation[10] of **14**, however, fails to produce the corresponding *trans*-tetrahydrobenzoate (cf. **9**, Scheme I). An alternate route to **5a,b** therefore was sought.

Cis hydroxylation of **14** affords tetrahydrodiol **15** (87%). The *cis*-diol **15** is converted into α-hydroxy ketone **18** via dehydration (**15** → **16**, 97%), silylation (**16** → **17**, 96%), and oxidation (**17** → **18**, 61–79%).[15] Protection of the tertiary hydroxyl group of **18** (92%) and stereoselective phenylselenylation provides keto selenide **20** (50–61%). The desired trans relationship of the hydroxyl groups in the target diol epoxides is achieved by stereoselective (8:1, trans/cis) reduction of ketone **20** (80–90%, mixture of **21** and its *cis*-diol isomer).[16a,b] Selenoxide fragmentation from **21** affords the key intermediate, protected *trans*-dihydrodiol **22** (63%).

The hydroxyl-group directing effect used to advantage in Scheme I fails when applied to the peracid oxidation of *trans*-dihydrodiol **23** in which the hydroxyl groups are axially disposed.[11] Nonetheless, the stereoselective conversion of protected dihydrodiol **22** into the *syn*- (**5a**) and *anti*- (**5b**) diol epoxides is possible by use of a modified strategy. Epoxidation of **22** by *t*-BuOOH/VO(acac)$_2$[17] yields a single epoxide, **24** (82%). Upon desilylation (quantitative) **24** affords *anti*-diol epoxide **5b**. Deprotection and acetylation of **22** (92%) provides acetate alcohol **25**. Epoxidation of **25** by *t*-BuOOH/VO(acac)$_2$ yields a single epoxide, **26**. Upon deacetylation (82–90%) **26** affords *syn*-diol epoxide **5a**.

Table II. Mutagenicity of Polycyclic Aromatic Hydrocarbons and Metabolites to *Salmonella typhimurium*

compd	PMS[a]	significant[b] induced mutation	concn,[c] μM
fluoranthene (1)	O	–	50
	A	+	5
benzo[*a*]pyrene	O	–	100
	A	+	4
dihydrodiol 11	O	+	140
	A	+	30
diol epoxide 4a	O	+	2.5-3.1
	A	+	13-33
diol epoxide 4b	O	+	0.3-1.0
	A	+	10-18
dihydrodiol 23	O	–	300
	A	–	300
diol epoxide 5a	O	+	270
	A	–	300
diol epoxide 5b	O	–	300
	A	–	300

[a] O, no rat liver post-mitochondrial supernatant (PMS) added to assay; A, aroclor-induced PMS added to assay. [b] –, no significant induced mutation observed; +, significant induced mutation based on the 99% upper confidence limit of the historical negative controls. [c] Number listed is the lowest concentration range of significant induced mutation for positive responses, highest concentration tested for negative responses.

Biological Evaluation

The mutagenic potential of fluoranthene and its dihydrodiols and diol epoxides was assayed by determining bacterial (*Salmonella typhimurium* TM677) resistance to the purine analogue, 8-azaguanine (8-AG), in the presence of each compound as described by Skopek et al.[18] Normally, 8-AG enters the cell and is metabolized and incorporated into nucleic acids where the toxic effects of the analogue are manifested. However, mutants unable to transport or phosphoribosylate 8-azaguanine grow in the presence of 8-AG. The concentration of a given mutagen required to increase the frequency of cells capable of growth in the presence of 8-AG provides a measure of the mutagenicity of the compound.

The biological evaluation of fluoranthene and the fluoranthene dihydrodiols and diol epoxides is summarized in

(7) Preliminary results have indicated that fluoranthene is tumorigenic in an infant mouse lung adenoma bioassay; Busby, W. F. (M.I.T., Department of Nutrition and Food Science), personal communication.

(8) Yagi, H.; Thakker, D. R.; Hernandez, O.; Koreeda, M.; Jerina, D. M. *J. Am. Chem. Soc.* **1977**, *99*, 1604.

(9) Tucker, S. H. *J. Chem. Soc.* **1949**, 2182. Campbell, A.; Tucker, S. H. *Ibid.* **1949**, 2623.

(10) Newman, M. S.; Beal, P. *J. J. Am. Chem. Soc.* **1950**, *72*, 5163. Gunstone, F. D. *Adv. Org. Chem.* **1960**, *1*, 122.

(11) The Henbest effect observed during the epoxidation of allylic alcohols by peracids is more strongly manifested in pseudoequatorial alcohols. For a discussion of the lower stereoselectivity observed with pseudoaxial alcohols, see: Lee, H.; Harvey, R. G. *Tetrahedron Lett.* **1981**, *22*, 1657.

(12) Braun, J.; Manz, G. *Chem. Ber.* **1931**, *63*, 2608.

(13) KOH/18-crown-6 in benzene has also been used in the oxidation of fluorene to fluorenone, see: Gokel, G. W.; Durst, H. D. *Synthesis* **1976**, 168.

(14) Streitweiser, A.; Suzuki, S. *Tetrahedron* **1961**, *16*, 153.

(15) The Corey–Kim oxidation (see: (a) Corey, E. J.; Kim, C. U. *Tetrahedron Lett.* **1974**, 287; (b) Corey, E. J.; Kim, C. U. *J. Am. Chem. Soc.* **1972**, *94*, 7586) and the Swern oxidation (see: (c) Mancuso, A. J.; Huang, S.-L.; (d) Swern, D. *J. Org. Chem.* 1978, *43*, 2480; (e) Mancuso, A. J.; Brownfain, D. S.; Swern, D. *Ibid.* **1979**, *44*, 4148) give poor yields of α-hydroxy ketone **18**. The three-step sequence of Scheme II is preferable to either direct oxidation method.

(16) (a) The mixture of diol isomers is separated after the selenoxide fragmentation (at stage **22**); see Experimental Section. (b) For the reduction of acyclic keto selenides see: Leonard-Coppens, A. M.; Krief, A. *Tetrahedron Lett.* **1976**, 3227.

(17) Sharpless, K. B.; Verhoeven, T. R. *Aldrichimica Acta* **1979**, *12*, 63.

(18) (a) Skopek, T. R.; Liber, H. L.; Krolewski, J. J.; Thilly, W. G. *Proc. Natl. Acad. Sci. U.S.A.* **1978**, *75*, 410. (b) Skopek, T. R.; Liber, H. L.; Kaden, D. A.; Thilly, W. G. *Ibid.* **1978**, *75*, 4465.

Table II. For fluoranthene and each potential metabolite the mutation assay was performed in the presence and in the absence of the post-mitochondrial supernatant (PMS) of aroclor-induced rat livers.[18] The PMS contains the metabolizing systems responsible for the oxidative conversion of polycyclic aromatic hydrocarbons into their mutagenic forms. A compound capable of alkylating nucleic acids without activation may induce mutations in the absence of PMS. By contrast, a compound requiring further oxidative elaboration, e.g., the conversion of a polycyclic aromatic hydrocarbon into one of its diol epoxides, will show a mutagenic effect only upon activation by the metabolizing system.

Fluoranthene is mutagenic only in the presence of PMS (Table II). Its mutagenic potency is comparable to that of benzo[*a*]pyrene tested under the same conditions. Mutagenic dihydrodiol **11** is more potent in the presence of PMS, suggesting a role for a diol epoxide (e.g., **4a,b**) in the mutagenic activation of the parent hydrocarbon. Both diol epoxides **4a** and **4b** are potent mutagens in the absence of the metabolizing systems (PMS). The lower activity in the presence of PMS may reflect destruction of the diol epoxides by the rat liver metabolizing systems. Dihydrodiol **23** does not display mutagenic activity up to 300 μM concentration in the presence or absence of PMS. Of the diol epoxides **5a,b**, the *syn*-diol epoxide (**5a**) displays weak mutagenic activity; the *anti*-diol epoxide (**5b**) is inactive even at high concentration.

Discussion

The mutagenic activity of diol epoxides **4a,b** and **5a,b** correlates well with the prediction of their reactivity by molecular orbital techniques (Table I). Triol carbocations should form more readily from diol epoxides **4a,b** ($\Delta E\pi/\beta$ = 1.160) than from the isomeric diol epoxides **5a,b** ($\Delta E\pi/\beta$ = 0.718). The former pair of diol epoxides also is the more mutagenic by a significant margin. Thus, the triol carbocation(s) shown in entry C of Table I becomes a good candidate(s) for the molecular species responsible for the covalent modification of cellular macromolecules by fluoranthene. In principle, the low activity of diol epoxides **5a,b** could be due to inefficient delivery of the compounds to the appropriate site of mutagenic action. Destruction of **5a,b** by solvolysis in the biological milieu is unlikely, however, given the predicted relative reactivities (**4a,b** > **5a,b**, Table I) and the potent mutagenicity of **4a,b** (Table II).

Conclusive testing of the involvement of diol epoxides **4a,b** during the activation of fluoranthene and in the alkylation of cellular genetic material must await further biological studies in our laboratories. Recently we have found[19] dihydrodiol **11**[20] as the major component of the fluoranthene metabolite profile formed by activation of the hydrocarbon in an in vitro system. This finding and the results of the present paper point suggestively to either diol epoxide **4a** or **4b** as the causative agent(s) of fluoranthene-induced mutation. The final details of the molecular basis of mutagenesis for fluoranthene must be learned through (a) the determination of structure for the fluoranthene–DNA adduct(s)[21] and (b) the demonstration that such adducts are, in fact, premutagenic lesions.

Experimental Section

General Procedures. ^{1}H NMR spectra were recorded on a Perkin-Elmer R-24B (60 MHz), Varian T-60 (60 MHz), JEOL HF-90 Q (90 MHz), Bruker WM-250 (250 MHz), or Bruker WM-270 (270 MHz) NMR spectrometer. ^{13}C NMR spectra were recorded on a Bruker WM-250 spectrometer at 62.8 MHz. Chemical shifts are reported downfield from tetramethylsilane (Me_4Si) on the δ scale. Infrared spectra were determined on a Perkin-Elmer 283 B spectrophotometer. Mass spectra were measured at 70 eV on a Varian MAT 44 mass spectrometer. High-resolution mass measurements were performed on a Mattauch-Herzog (Du Pont Instruments) CEC 110 B mass spectrometer. Elemental analyses were performed by Robertson Laboratories, Florham Park, NJ. Melting points were determined in open capillaries on a Thomas-Hoover Unimelt apparatus and are uncorrected.

All reactions were performed under an inert atmosphere unless otherwise specified. The following solvents were distilled before use: tetrahydrofuran (THF, from sodium/benzophenone ketyl), CH_2Cl_2 (from P_2O_5), MeOH (from Mg turnings), benzene (from CaH_2), pyridine (from CaH_2), dioxane (from CaH_2), and diisopropylamine (from CaH_2). Anhydrous *p*-toluenesulfonic acid was prepared from the hydrate by azeotropic distillation with benzene. Silver benzoate was dried over P_2O_5 in vacuo. Flash chromatography was performed according to Still et al.[22]

Diastereomeric Alcohols 7. Ketone 6[9] (0.368 g, 1.67 mmol) in dry MeOH (10 mL) at 0 °C was stirred overnight with $NaBH_4$ (0.196 g, 5.18 mmol). After evaporation of the solvent, the residue was purified by extraction (EtOAc/H_2O) and flash filtration (silica gel, 5:1 $CHCl_3$/EtOAc), affording the mixture of diastereomeric alcohols **7** (0.312 g, 84%). The mixture was routinely used in the subsequent dehydration, but the two alcohols were separated by flash chromatography (vide supra) for individual characterization. Data for faster-eluting isomer: mp 136–138 °C (recrystallized from EtOAc/hexanes); ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.43 (m, 1 H), 2.24 (m, 1 H), 2.37 (m, 1 H), 2.45 (m, 2 H), 3.61 (dd, 1 H), 5.05 (t, 1 H), 7.29 (m, 4 H), 7.48 (m, 1 H), 7.59 (m, 1 H), 7.71 (m, 1 H); ^{13}C NMR (62.8 MHz, $CDCl_3$) δ 147.7 (s), 145.5 (s), 141.5 (s), 139.4 (s), 137.0 (s), 128.3 (d), 127.2 (d), 126.9 (d), 124.8 (d), 124.2 (d), 120.7 (d), 119.1 (d), 65.8 (d), 45.3 (d), 33.9 (t), 20.9 (t); IR ($CHCl_3$) 3590, 1450, 1430 cm^{-1}; mass spectrum, *m/e* 222 (M^+). Anal. Calcd for $C_{16}H_{14}O$: C, 86.44; H, 6.35. Found: C, 86.30; H, 6.59. Data for slower-eluting isomer: mp 92–94 °C (recrystallized from EtOH/H_2O); ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.44 (m, 1 H), 2.12 (m, 2 H), 2.51 (m, 1 H), 2.62 (m, 1 H), 3.84 (dd, 1 H), 4.99 (t, 1 H), 7.29 (m, 4 H), 7.47 (m, 1 H), 7.59 (m, 1 H), 7.71 (m, 1 H); ^{13}C NMR (62.8 MHz, $CDCl_3$) δ 147.8 (s), 146.6 (s), 141.5 (s), 139.7 (s), 136.4 (s), 128.1 (d), 127.1 (d), 126.9 (d), 125.2 (d), 124.1 (d), 120.6 (d), 119.3 (d), 69.3 (d), 45.0 (d), 34.8 (t), 26.6 (t); IR ($CHCl_3$) 3590, 1448, 1430 cm^{-1}; mass spectrum, *m/e* 222 (M^+). Anal. Calcd for $C_{16}H_{14}O$: C, 86.44; H, 6.35. Found: C, 86.16; H, 6.58.

Dihydrofluoranthene 8. The diastereomeric mixture of alcohols **7** (0.339 g, 1.52 mmol) and anhydrous *p*-toluenesulfonic acid (0.026 g, 0.152 mmol) were refluxed in dry benzene (20 mL). Water was removed azeotropically into a Dean–Stark trap. After 2 h the solution was concentrated and flash chromatographed (silica gel, benzene), affording pure **8** (0.310 g, quantitative) as a pale-yellow, crystalline solid: mp 71–72 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.03 (tt, 1 H), 2.89 (ddd, 1 H), 3.93 (dd, 1 H), 6.13 (ddd, 1 H), 6.66 (dd, 1 H), 6.99 (d, 1 H), 7.24–7.92 (m, 6 H); UV λ_{max} 260 nm; exact mass calcd for $C_{16}H_{12}$ (M^+) 204.093 90, found 204.092 86.

Tetrahydrobenzoate 9. Dry silver benzoate (AgOCOPh, 0.374 g, 1.64 mmol) and iodine (0.207 g, 0.817 mmol) in dry benzene (20 mL) were stirred until all the I_2 was consumed (color change from red to yellow).[10] To this suspension was added dihydrofluoranthene **8** (0.167 g, 0.818 mmol) and the mixture was stirred in the dark overnight. Filtration through Celite, evaporation of solvent, and flash chromatography (silica gel, 4:1, CH_2Cl_2/hexanes) afforded pure **9** (0.365 g, quantitative) as a white crystalline solid:

(19) Babson, J. R.; Wogan, G. N.; Wattley, R. V.; Russo-Rodriguez, S.; Rastetter, W. H.; Andon, B.; Thilly, W. G., paper in preparation.

(20) Presumably only one enantiomer of dihydrodiol **11** is formed metabolically; no assignment of absolute configuration has been made to the metabolic product.

(21) A covalent adduct of fluoranthene and DNA has been identified in our laboratories following incubation of tritiated fluoranthene and the PMS from arachlor-induced rat livers with DNA; ref 19.

(22) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

mp 152–153 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.76 (ddd, 1 H), 3.21 (ddd, 1 H), 4.17 (dd, 1 H), 6.09 (ddd, 1 H), 6.69 (d, 1 H), 7.28–8.08 (m, 17 H); ^{13}C NMR (62.8 MHz, $CDCl_3$) δ 166.6 (s), 166.1 (s), 146.3 (s), 141.5 (s), 139.6 (s), 133.3 (d), 131.6 (s), 130.0 (d), 129.9 (d), 129.8 (d), 128.5 (d), 127.6 (d), 127.3 (d), 126.5 (d), 124.3 (d), 120.9 (d), 120.3 (d), 76.2 (d), 74.4 (d), 42.5 (d), 32.6 (t); IR ($CHCl_3$) 1712, 1600, 1449, 1372 cm^{-1}; mass spectrum, *m/e* 446 (M^+). Anal. Calcd for $C_{30}H_{22}O_4$: C, 80.69; H, 4.97. Found: C, 80.47; H, 5.20.

Dihydrobenzoate 10. Tetrahydrobenzoate **9** (0.437 g, 0.980 mmol) and *o*-chloranil (0.301 g, 1.23 mmol) in dry dioxane (20 mL) were refluxed overnight. Evaporation of solvent and flash chromatography (silica gel, 5% EtOAc/hexanes) afforded **10** (0.209 g, 48%) as a pale-yellow, crystalline solid: mp 146–148 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.41 (t, 1 H), 6.76 (d, 1 H), 6.80 (d, 1 H), 7.26–7.52 (m, 10 H), 7.61 (dd, 1 H), 7.70 (t, 2 H), 8.01 (m, 4 H); ^{13}C NMR (62.8 MHz, $CDCl_3$) δ 165.8, 165.7, 141.9, 138.0, 137.1, 135.7, 135.0, 133.1, 129.8, 129.7, 129.5, 128.4, 128.3, 127.3, 125.8, 122.6, 120.9, 120.2, 117.2, 73.9, 71.5; IR ($CHCl_3$) 1712, 1448, 1264, 1101, 1090 cm^{-1}. Anal. Calcd for $C_{30}H_{20}O_4$: C, 81.07; H, 4.54. Found: C, 81.27; H, 4.71.

***trans*-Dihydrodiol 11.** Dihydrobenzoate **10** (0.082 g, 0.185 mmol) and sodium methoxide (0.41 mL of 1 N solution in dry MeOH) were stirred at −20 °C in dry THF (5 mL). After 1 h, EtOAc (10 mL) and 1 N HCl (aq, 0.5 mL) were added. Extractive purification (EtOAc/H_2O) and flash chromatography (silica gel, 1:1 EtOAc/hexanes) gave **11** (0.036 g, 83%) as a pale-yellow solid: mp 167–168 °C dec; ^{1}H NMR (250 MHz, acetone-d_6) δ 4.97 (dd, 1 H), 5.12 (d, 1 H), 6.61 (d, 1 H), 7.35 (m, 4 H), 7.59 (m, 1 H), 7.71 (m, 2 H); ^{13}C NMR (62.8 MHz, acetone-d_6) δ 143.0, 137.3, 137.0, 135.9, 135.8, 135.6, 129.8, 129.6, 128.0, 126.6, 125.2, 123.2, 121.7, 119.6, 76.9, 75.4; IR (KBr) 3240, 1430, 1050, 1025, 950, 772, 752, 723 cm^{-1}; exact mass calcd for $C_{16}H_{12}O_2$ (M^+) 236.083 73, found 236.082 70. Anal. Calcd for $C_{16}H_{12}O_2$: C, 81.34; H, 5.12. Found: C, 81.10; H, 5.16.

Bromo Triol 12. Dihydrodiol **11** (0.073 g, 0.310 mmol), *N*-bromoacetamide (0.051 g, 0.372 mmol), and HCl (1 drop, aq 12 N) were stirred in 3:1 THF/H_2O (15 mL) for 2 h in the dark. Extractive purification (EtOAc/NaCl (aq, half satd), $NaHCO_3$ (aq, satd), NaCl (aq, satd)) and preparative TLC (silica gel, 3:7 hexanes/EtOAc) yielded **12** (0.101 g, 98%) as a pale-yellow solid: mp 97 °C dec; ^{1}H NMR (250 MHz, acetone-d_6) δ 2.05 (br s, 3 H), 4.63 (d, 1 H), 4.94 (dd, 1 H), 5.00 (d, 1 H), 7.24–7.43 (m, 4 H), 7.51–7.60 (m, 2 H), 7.66–7.70 (m, 1 H); IR (KBr) 3260, 1432, 1382, 1320, 1300, 1230, 1055, 1020, 1010, 990, 935, 920, 755, 730 cm^{-1}. Anal. Calcd for $C_{16}H_{13}O_3Br$: C, 57.68; H, 3.93. Found: C, 57.46; H, 3.91.

***syn*-Diol Epoxide 4a.** Bromo triol **12** (0.054 g, 0.161 mmol) and freshly sublimed *t*-BuOK (0.018 g, 0.161 mmol) were suspended in dry Et_2O (5 mL) at 0 °C. After 30 min the mixture was filtered and the solvent removed in vacuo to afford **4a** (0.040 g, quantitative) as a pale-yellow solid: mp 75–78 °C dec; ^{1}H NMR (250 MHz, acetone-d_6) δ 4.63 (m, 3 H), 7.33–7.74 (m, 5 H), 7.80 (d, 1 H), 7.90 (d, 1 H); IR (KBr) 3280, 1440, 1065, 1016, 1010, 913, 751, 742 cm^{-1}; exact mass calcd for $C_{16}H_{12}O_3$ (M^+) 252.078 64, found 252.079 66.

***anti*-Diol Epoxide 4b.** Dihydrodiol **11** (0.045 g, 0.191 mmol) and 99% *m*-chloroperoxybenzoic acid[23] (0.106 g, 0.611 mmol) in $CHCl_3$ (10 mL, passed through basic alumina) were stirred at 0 °C for 1 h. The mixture was purified by extraction ($CHCl_3$/Na_2SO_3 (5% aq), $NaHCO_3$ (aq, half satd)) followed by liquid chromatography (Waters Radial-Pak, μBondapak CN Normal Phase, 3:7 EtOAc/hexanes), affording **4b** (0.032 g, 66%) as a white solid: mp 126–129 °C dec; ^{1}H NMR (250 MHz, acetone-d_6) δ 3.88 (dd, 1 H), 4.39 (d, 1 H), 4.86 (d, 1 H), 7.32–7.52 (m, 5 H), 7.72 (m, 1 H), 7.87 (d, 1 H); ^{13}C NMR (62.8 MHz, acetone-d_6) δ 143.6, 140.2, 138.3, 130.7, 130.6, 128.4, 124.2, 124.1, 122.1, 119.8, 76.5, 71.3, 61.2; IR (KBr) 3240, 1440, 1316, 1290, 1255, 1116, 1088, 1055, 1035, 890, 758, 730 cm^{-1}; mass spectrum, *m/e* 252 (M^+). Anal. Calcd for $C_{16}H_{12}O_3$: C, 76.18; H, 4.79. Found: C, 76.38; H, 4.95.

Dihydrofluoranthene 14. A mixture of tetrahydrofluoranthene **13**[12] (6.91 g, 33.5 mmol), KOH (3.11 g, 55.5 mmol), and 1,4,7,10,13,16-hexaoxacyclooctadecane (18-crown-6, 1.14 g, 4.49 mmol) in benzene (45 mL) was stirred vigorously in an open Erlenmeyer flask for 24 h. Na_2SO_3 (60 mL aq, satd) and H_2O (28 mL) were added to the orange suspension, and the mixture was stirred rapidly for 1 h. Extractive purification (benzene/H_2O) and evaporation of solvent from the organic phase afforded an oil, which was dissolved in CH_2Cl_2 (200 mL) and treated with a catalytic amount of $MeSO_3H$. The reaction was monitored by TLC (silica gel, 4:1 hexanes/EtOAc) and additional $MeSO_3H$ was added as needed to consume the starting material (a total volume of 5–8 drops of $MeSO_3H$ used). Upon observing disappearance of starting material, the mixture was washed with NaCl (aq, half satd), dried ($MgSO_4$), and concentrated in vacuo to provide the crude product. Flash chromatography (silica gel, 4:1 hexanes/EtOAc) afforded crystalline **14** (5.50 g, 80%): mp 61–63 °C; ^{1}H NMR (60 MHz, $CDCl_3$) δ 2.4–3.3 (m, 4 H), 6.4 (t, 1 H), 6.8–7.7 (m, 7 H); mass spectrum, *m/e* 204 (M^+).

***cis*-Diol 15.** To a solution of dihydrofluoranthene **14** (5.49 g, 26.91 mmol) and *N*-methylmorpholine *N*-oxide dihydrate[24] (6.90 g, 45.1 mmol) in THF/H_2O (26:5, 31 mL) was added OsO_4 (0.143 g, 0.56 mmol) in THF (1 mL). The mixture was stirred for 6 days at ambient temperature and then $NaHSO_3$ (5.0 g) in H_2O (40 mL) was added, and the phases were vigorously stirred for ca. 15 min. Extractive purification (Et_2O/H_2O), filtration of the organic layer through Florisil, and evaporation of solvent provided the crude product as a solid. Trituration with CH_2Cl_2/Et_2O afforded pure **15** as a white crystalline solid (5.54 g, 87%): mp 171–173 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.34 (s, 1 H), 2.36 (m, 2 H), 2.79 (m, 1 H), 3.03 (ddd, 1 H), 3.78 (dd, 1 H), 7.02–7.80 (m, 7 H); IR ($CDCl_3$) 3500–3100, 3030, 2950, 1605 cm^{-1}; mass spectrum, *m/e* 238 (M^+). Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.53; H, 6.03.

Ketone 16. *cis*-Diol **15** (5.51 g, 23.17 mmol) was suspended in CH_2Cl_2 (100 mL) and $MeSO_3H$ (3–5 drops) was added with stirring. When the mixture became homogeneous, the solvent was evaporated in vacuo, providing the crude, solid product. Recrystallization from CH_2Cl_2/hexanes and flash chromatography of the mother liquors (silica gel, 2:1 CH_2Cl_2/hexanes) afforded pure **16** as a white solid (4.94 g, 97%): mp 135–137 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.34 (ddd, 1 H), 2.89 (ddd, 1 H), 3.06 (ddd, 1 H), 3.46 (m, 1 H), 4.45 (s, 1 H), 7.20–7.92 (m, 7 H); IR ($CDCl_3$) 3160, 2950, 1725, 1610, 1450 cm^{-1}. Anal. Calcd for $C_{16}H_{12}O$: C, 87.24; H, 5.49. Found: C, 86.96; H, 5.61.

α-Hydroxy Ketone 18. To a solution of ketone **16** (4.94 g, 22.45 mmol) and hexamethyldisilazane (5.7 mL, 27.0 mmol) in CH_2Cl_2 (90 mL) at −20 °C was added freshly distilled trimethylsilyl iodide (3.5 mL, 24.6 mmol). The mixture was allowed to warm to ambient temperature and stirred overnight. The mixture was diluted with CH_2Cl_2 (to a volume of ca. 200 mL) and centrifuged, and the supernatant was washed with ice-cold $NaHCO_3$ (aq, satd). The organic phase was dried ($MgSO_4$) and concentrated in vacuo to give pure, H_2O-sensitive silyl enol ether **17** (6.27 g, 96%): ^{1}H NMR (90 MHz, $CDCl_3$) δ 0.3 (s, 9 H), 2.7 (m, 2 H), 3.1 (t, 2 H), 7.0–7.9 (m, 7 H); mass spectrum, *m/e* 292 (M^+).

A solution of **17** (4.79 g, 16.42 mmol) and 99% *m*-chloroperoxybenzoic acid[23] in CH_2Cl_2 (50 mL) was stirred at 0 °C for 35 min. Extractive purification (CH_2Cl_2/Na_2SO_3 (5% aq), $NaHCO_3$ (aq, satd)) and flash chromatography (silica gel, 10:1 CH_2Cl_2/EtOAc) provided crystalline **18** (2.30 g, 61%): mp 152–154 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.32 (s, 1 H), 2.45 (ddd, 1 H), 2.91 (ddd, 1 H), 3.10 (ddd, 1 H), 3.76 (ddd, 1 H), 7.14–7.80 (m, 7 H); IR ($CDCl_3$) 3560, 3500–3300, 3060, 2960, 2930, 1720 cm^{-1}; exact mass calcd for $C_{16}H_{12}O_2$ (M^+) 236.083 73, found 236.082 20.

α-Silyloxy Ketone 19. To a solution of α-hydroxy ketone **18** (1.06 g, 4.49 mmol) and hexamethyldisilazane (1.0 mL, 4.75 mmol) in pyridine (4.4 mL) was added trimethylsilyl chloride (0.70 mL, 5.50 mmol). The mixture was stirred at ambient temperature for 45 min. Extractive purification ($CH_2Cl_2/NaHCO_3$ (aq, satd)) and flash chromatography (silica gel, 1:1 CH_2Cl_2/hexanes) afforded crystalline **19** (1.26 g, 92%): mp 73–75 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ −0.33 (s, 9 H), 2.36 (ddd, 1 H), 2.87 (ddd, 1 H), 3.04 (ddd, 1 H), 3.63 (ddd, 1 H), 7.07–7.72 (m, 7 H); IR ($CDCl_3$) 3050, 2960, 1720 cm^{-1}; mass spectrum, *m/e* 308 (M^+). Anal. Calcd for

(23) Fieser, L. F.; Fieser, M. "Reagents for Organic Synthesis"; Wiley: New York, 1967; Vol. 1, p 135.

(24) Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, 1973.

$C_{19}H_{20}O_2Si$: C, 73.98; H, 6.54. Found: C, 73.83; H, 6.80.

Keto Selenide 20. To a cooled (−78 °C) solution of lithium diisopropylamide (10.4 mmol, prepared from 6.5 mL of 1.6 M *n*-BuLi and 1.5 mL of diisopropylamine) in THF (10.0 mL) was added over 10 min a solution of α-silyloxy ketone **19** (3.10 g, 9.90 mmol) in THF (6.0 mL). The resulting enolate was stirred for 30 min at −78 °C and quenched with trimethylsilyl chloride (2.50 mL, 19.82 mmol). The reaction was stirred an additional 30 min with continued cooling and then a solution of PhSeCl[25] (2.80 g, 14.66 mmol) in THF (4 mL) was added. The mixture was allowed to warm to ambient temperature and stirred for 5 h. Extractive purification (Et_2O/H_2O) and flash chromatography (silica gel, 2:1 CCl_4/CH_2Cl_2) gave pure **20** as an oily solid (2.20 g, 50%): ^1H NMR (250 MHz, $CDCl_3$) δ −0.32 (s, 9 H), 3.15 (dd, 1 H), 4.18 (dd, 1 H), 4.50 (dd, 1 H), 7.04–7.85 (m, 12 H); IR ($CDCl_3$) 3060, 2960, 2900, 1710, 1610 cm^{-1}; mass spectrum, *m/e* 464 (M^+, ^{80}Se), 462 (M^+, ^{78}Se).

Protected *trans*-Dihydrodiol 22. To a cooled (−15 °C) suspension of $LiAlH_4$ (0.244 g, 6.43 mmol) in Et_2O (30 mL) was added a solution of keto selenide **20** (1.95 g, 4.21 mmol) in Et_2O (18 mL, freshly distilled from $LiAlH_4$). The reaction was stirred for 10 min and quenched with a ground mixture of anhydrous Na_2SO_4 (6.98 g), H_2O (0.80 mL), and Celite (2.10 g). Dilution of the mixture with Et_2O (ca. 16 mL), filtration, and concentration of the filtrate afforded hydroxy selenide **21** as an oil (1.51 g, 80%): ^1H NMR (250 MHz, CD_2Cl_2) δ −0.458 (s, 9 H), 1.63 (s, 1 H), 2.75 (dd, 1 H), 3.48 (dd, 1 H), 4.47 (d, 1 H), 4.57 (dd, 1 H), 6.90–7.70 (m, 15 H).

A solution of hydroxy selenide **21** (1.51 g, 3.25 mmol) and 30% H_2O_2 (0.90 mL, 10.4 mmol) in THF (40 mL) at 0 °C was stirred for 1.5 h. The mixture was purified by extraction (Et_2O/H_2O, Na_2CO_3 (aq, satd)). Flash chromatography (silica gel, CH_2Cl_2) served to separate the minor *cis*-diol isomer (R_f 0.43) from the desired isomer **22** (R_f 0.29, crystalline solid, 0.612 g, 61%): mp 81–82 °C; ^1H NMR (250 MHz, $CDCl_3$) δ −0.45 (s, 9 H), 1.10 (s, 1 H), 4.48 (s, 1 H), 6.31 (dd, 1 H), 6.64 (d, 1 H), 6.99–7.60 (m, 7 H); IR ($CDCl_3$) 3580, 3420, 3040, 2960, 2900, 1640, 1600 cm^{-1}; exact mass calcd for $C_{19}H_{20}O_2Si$ (M^+) 308.123 30, found 308.1242.

Protected Diol Epoxide 24. To a solution of protected *trans*-dihydrodiol **22** (0.112 g, 0.360 mmol) and $VO(acac)_2$ (15.8 mg, 0.06 mmol) in dry benzene (1 mL) was added a solution of 6.5 M *t*-BuOOH (0.18 mL in CH_2Cl_2). After the mixture was stirred for 1 h at ambient temperature, Na_2SO_3 (5 mL, aq, half satd) was added. Extractive purification (benzene/H_2O) provided **24** (0.126 g, quantitative), which was routinely used in the subsequent step without purification (analytical TLC: trace base-line impurities). A small sample was purified by liquid chromatography (Waters Radial-Pak, μBondapak CN Normal Phase, hexanes) prior to characterization: ^1H NMR (270 MHz, $CDCl_3$) δ −0.50 (s, 9 H), 1.96 (d, 1 H), 4.01 (m, 2 H), 4.69 (dd, 1 H), 7.20–7.52 (m, 7 H); IR ($CDCl_3$) 3500, 3010, 2950, 1600 cm^{-1}; exact mass calcd for $C_{19}H_{20}O_3Si$ (M^+) 324.1182, found 324.1188.

***anti*-Diol Epoxide 5b.** To a cooled (0 °C) solution of protected diol epoxide **24** (0.127 g, 0.390 mmol) in THF (3 mL) was added 1 M n-$Bu_4N^+F^-$ in THF (0.39 mL, 0.39 mmol). After being stirred for 10 min, the mixture was purified by extraction (Et_2O/H_2O) to give **5b** as a pale-yellow solid (0.101 g, quantitative). For removal of residual colored impurities a small sample was rapidly flash chromatographed (silica gel, 80:20:1.5 CH_2Cl_2/EtOAc/NEt_3): mp 60 °C dec; ^1H NMR (270 MHz, $CDCl_3$) δ 2.14 (d, 1 H), 4.14 (m, 2 H), 4.85 (dd, 1 H), 7.32–7.62 (m, 7 H); IR ($CDCl_3$) 3560, 3510, 3060, 3020, 2960, 2930, 1600 cm^{-1}; exact mass calcd for $C_{16}H_{12}O_3$ (M^+) 252.078 64, found 252.0784.

***trans*-Dihydrodiol 23.** A mixture of protected *trans*-dihydrodiol **22** (0.178 g, 0.580 mmol) and anhydrous K_2CO_3 (0.218 g, 1.58 mmol) in MeOH (0.70 mL) was rapidly stirred at ambient temperature for 3 h. Extractive purification (CH_2Cl_2/H_2O) afforded **23** as an off-white solid (0.138 g, quantitative) routinely used in the subsequent reaction without further purification. A small sample was purified by flash chromatography (silica gel, 4:1 CH_2Cl_2EtOAc) prior to characterization: mp 128 °C; ^1H NMR (270 MHz, $CDCl_3$) δ 1.21 (d, 1 H), 2.20 (s, 1 H), 4.66 (dd, 1 H), 6.38 (dd, 1 H), 6.77 (d, 1 H), 7.06–7.66 (m, 7 H); IR ($CDCl_3$) 3575, 3400, 3040, 2920, 1600 cm^{-1}; exact mass calcd for $C_{16}H_{12}O_2$ (M^+) 236.083 76, found 236.0851.

Protected Diol Epoxide 26. To a solution of *trans*-dihydrodiol **23** (0.138 g, 0.59 mmol) in dry pyridine (0.60 mL) was added freshly distilled Ac_2O (0.06 mL, 0.63 mmol). The mixture was stirred at ambient temperature for 19 h and then purified by extraction (CH_2Cl_2/H_2O) and flash chromatography (silica gel, 6:1 CH_2Cl_2/EtOAc), affording pure acetoxy alcohol **25** (0.128 g, 78%) plus recovered starting material (19.8 mg). Data for **25**: R_f 0.63 (4:1 CH_2Cl_2/EtOAc); ^1H NMR (270 MHz, $CDCl_3$) δ 1.67 (s, 3 H), 2.03 (s, 1 H), 5.90 (d, 1 H), 6.25 (dd, 1 H), 6.84 (d, 1 H), 7.07–7.63 (m, 7 H).

To a solution of acetoxy alcohol **25** (0.118 g, 0.430 mmol) in dry benzene (1 mL) was added $VO(acac)_2$ (18.9 mg, 0.07 mmol) and 6.5 M *t*-BuOOH in CH_2Cl_2 (0.18 mL, 1.20 mmol). The reaction mixture was stirred at ambient temperature for 3 h and then additional 6.5 M *t*-BuOOH in CH_2Cl_2 (0.26 mL, 1.70 mmol) was added and stirring continued for 2 h. Extractive purification (benzene/Na_2SO_3 (aq, satd)) afforded **26** as a pale-yellow solid (0.127 g, quantitative): ^1H NMR (250 MHz, $CDCl_3$) δ 1.62 (s, 3 H), 3.74 (s, 1 H), 4.00 (dd, 1 H), 4.17 (d, 1 H), 6.25 (d, 1 H), 7.28–7.65 (m, 7 H); IR ($CDCl_3$) 3480, 3020, 2930, 2850, 1740 cm^{-1}; exact mass calcd for $C_{18}H_{14}O_4$ (M^+) 294.0892, found 294.0918.

***syn*-Diol Epoxide 5a.** To a cooled (−5 °C) solution of acetoxy alcohol **26** (0.075 g, 0.25 mmol) in MeOH (2.5 mL) was added anhydrous K_2CO_3 (3.9 mg, 0.28 mmol). The mixture was stirred for 10 min and then diluted with Et_2O and washed with H_2O. Evaporation of solvent from the organic phase and trituration with Et_2O afforded **5a** as a white solid (50 mg, 80%): mp 148–150 °C; ^1H NMR (270 MHz, $CDCl_3$) δ 3.77 (s, 1 H), 4.02 (dd, 1 H), 4.14 (d, 1 H), 4.96 (s, 1 H), 7.34–7.67 (m, 7 H); IR ($CDCl_3$) 3570, 3470, 3060, 3020, 2970 cm^{-1}; exact mass calcd for $C_{16}H_{12}O_3$ (M^+) 252.0786, found 252.0799.

Acknowledgment is made to the National Institutes of Health (Grant No CA-20574) and to the Department of Energy, Health Effects Research Division, Contract No. DE-AC02-77EV04267 A006, for generous support of this work. S.R.-R. thanks the Department of Health, Education and Welfare for a fellowship. We are grateful to Dr. C. Costello and Mr. A. Schkuta for exact mass measurements.

Registry No. 4a, 83349-66-0; **4b**, 83349-67-1; **5a**, 83291-40-1; **5b**, 83349-68-2; **6**, 38422-92-3; **7** (isomer 1), 83291-41-2; **7** (isomer 2), 83291-42-3; **8**, 35324-29-9; **9**, 83291-43-4; **10**, 83291-44-5; **11**, 82911-12-4; **12**, 83311-76-6; **13**, 20279-21-4; **14**, 30339-87-8; **15**, 83291-45-6; **16**, 83291-46-7; **17**, 83291-47-8; **18**, 83291-48-9; **19**, 83291-49-0; **20**, 83291-50-3; **21**, 83291-51-4; **22** (isomer 1), 83291-52-5; **22** (isomer 2), 83291-53-6; **23**, 83291-54-7; **24**, 83291-55-8; **25**, 83291-56-9; **26**, 83291-57-0.

Supplementary Material Available: Cation delocalization energies and carcinogenicities (Figure 1 and Table III (2 pages). Ordering information is given on any current masthead page.

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