



**FLUORINE-SUBSTITUTED DERIVATIVES OF THE CARCINOGENIC DIHYDRODIOL  
AND DIOL EPOXIDE METABOLITES OF 7-METHYL-, 12-METHYL- AND 7,12-  
DIMETHYLBENZ[*a*]ANTHRACENE**

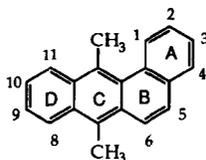
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**Abstract:** Stereospecific syntheses of the *trans*-3,4-dihydrodiol metabolites of 9- and 10-fluoro-7,12-dimethylbenz[*a*]anthracene, -7-methylbenz[*a*]anthracene, and -12-methylbenz[*a*]anthracene are described. These dihydrodiols are putative proximate carcinogenic metabolites that undergo activation by the P-450 microsomal enzymes to ultimate carcinogenic *anti*- and *syn*-diol epoxide metabolites that bind to nucleic acids *in vivo*. Syntheses of several of the *anti*- diol epoxide metabolites are also described.

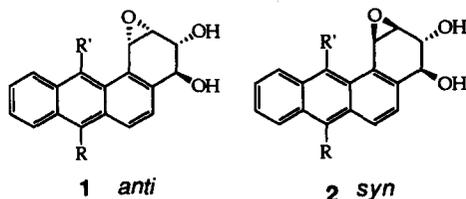
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The carcinogenic activities of polycyclic aromatic hydrocarbons (PAHs) are often strongly affected by substitution of fluorine in appropriate molecular sites.<sup>1-3</sup> In the light of current understanding of the need for metabolic activation of PAH procarcinogens to reactive forms that combine with DNA,<sup>1-4</sup> inhibition of activity by fluorine substitution is interpreted most simply as a due to interference with activation by the P-450 microsomal enzymes to reactive PAH diol epoxide metabolites.<sup>3</sup> Conversely, enhancement of activity by introduction of fluorine into other molecular regions may be considered primarily a consequence of restriction of oxidative metabolism leading to detoxification. One of the most thoroughly investigated examples of these effects is the highly potent PAH carcinogen 7,12-dimethylbenz[*a*]anthracene (DMBA).<sup>1-5</sup> While the 1-, 2-, and 4-fluoro-derivatives of DMBA in the angular benzo ring (A-ring) and the 5-fluoro derivative exhibit markedly reduced activity relative to the parent hydrocarbon, substitution of fluorine in the 8-, 9-, 10-, and 11-positions in the D-ring results in no significant loss of activity.<sup>6,7</sup> Indeed, 10-fluoro-DMBA exhibits substantially higher tumor-initiating activity in mouse skin and an enhanced level of mutagenic activity in a human hepatoma (HepG2) cell-



**DMBA**

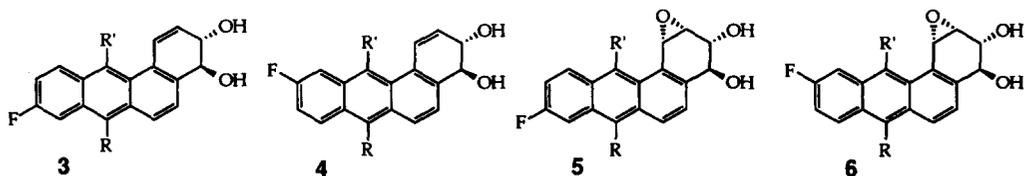
mediated assay than DMBA.<sup>7-9</sup> Similar effects are seen for the 7- and 12-monomethyl analogs, 7-MBA and 12-MBA.<sup>8,9</sup> These findings are consistent with involvement of the bay region *anti*- and *syn*-diol epoxide metabolites (**1** and **2**)<sup>10</sup> as the active forms of these methyl-substituted benz[*a*]anthracenes.<sup>1,2</sup> The intermediacy of **1** and **2** is further supported by development of methods for their synthesis<sup>11</sup> coupled with studies of their mutagenicity, tumorigenicity, and DNA binding.<sup>12</sup>



a: R = R' = CH<sub>3</sub>; b: R = CH<sub>3</sub>, R' = H; c: R = H, R' = CH<sub>3</sub>.

Analysis of the DNA of mouse skin treated with DMBA shows the presence of adducts shown to arise from the corresponding A-ring diol epoxide metabolites.<sup>13</sup> Treatment of mouse skin with 9- and 10-fluoro-DMBA affords covalently bound DNA adducts assumed to be formed from analogous adducts diol epoxide metabolites.<sup>14</sup> Metabolism of 10-fluoro-DMBA affords a higher level of DNA-bound adducts than DMBA, consistent with its greater tumorigenicity. However, the presence of fluorine at either the 9- or 10-positions also dramatically alters the relative extents of binding to deoxyadenosine and deoxyguanosine sites in DNA. This is potentially important in view of the recent evidence from metabolism and DNA binding studies which suggests that binding to deoxyadenosine sites may be of greater relevance for carcinogenicity than binding at other base sites.<sup>15,16</sup> This suggests the interesting possibility that the presence of a fluorine atom in the 9- or 10-positions of the DMBA diol epoxide isomers may remotely influence the reactivities of the epoxide function in the A-ring, thereby altering their selectivities of reaction with DNA sites.<sup>17</sup> In order to probe this hypothesis and to make these compounds available for biological studies, methods for the synthesis of the active metabolites of 9- and 10-fluoro-DMBA, 7-MBA, and 12-MBA are required.

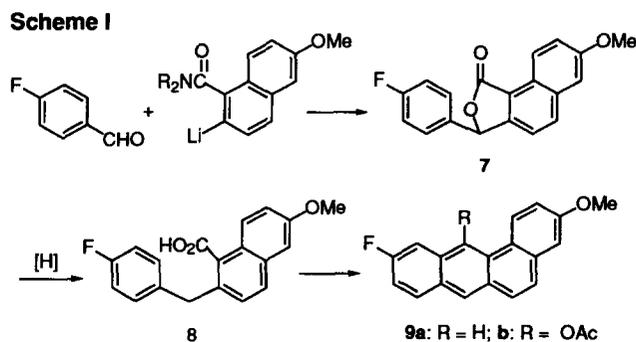
We now report efficient syntheses of the *trans*-3,4-dihydrodiols of 9- and 10-fluoro-DMBA, 7-MBA, and 12-MBA (**3,4**). These compounds are the first examples of fluorine-substituted active metabolites of carcinogenic PAHs to be reported. The dihydrodiols are putative proximate carcinogenic metabolites that are anticipated to be converted *in vivo* to the corresponding *anti*- and *syn*-diol epoxide metabolites by microsomal mixed function oxidase enzymes.<sup>1</sup> Syntheses of several of the *anti*-diol epoxide isomers (**5a,5c,6a**) are also described.



a: R = CH<sub>3</sub>, R' = H; b: R = H, R' = CH<sub>3</sub>; c: R = R' = CH<sub>3</sub>.

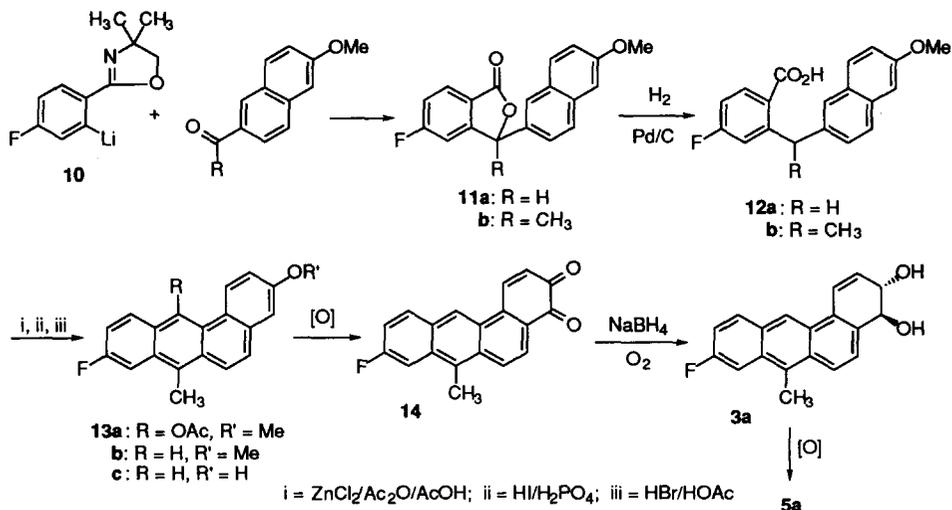
## RESULTS

The synthetic strategies employed previously for the preparation of the *trans*-3,4-dihydrodiols of 7-MBA, 12-MBA and DMBA<sup>11</sup> were less attractive as synthetic routes to the analogous 9- and 10-fluoro-substituted dihydrodiols because of the relative high cost of the starting compound, 3-fluorophthalic anhydride, and the likelihood of formation of mixtures of difficult to separate isomers in the initial step. Therefore, two alternative synthetic routes to the fluoro-substituted dihydrodiols (3,4) were examined. The first route entailed preparation of 10-fluoro-3-methoxybenz[*a*]anthracene (9a), a key intermediate in the synthesis of the 3,4-dihydrodiol (Scheme I). Reaction of 4-fluorobenzaldehyde with 2-lithio-6-methoxy-*N,N*-diethyl-1-naphthamide generated *in situ* by metalation of the amide with *sec*-BuLi and TMEDA in ether at -60 °C furnished the lactone 7.<sup>11d,18</sup> Reductive cleavage of 7 with zinc and alkali afforded the reduced acid (8) which was converted to 12-acetoxy-10-fluoro-3-methoxybenz[*a*]anthracene (9b) by treatment with ZnCl<sub>2</sub> and acetic anhydride in acetic acid. However, the yield of 9b was unacceptably low (10% in the initial step and 1.2% overall), and investigation of this route was abandoned.



The second, more satisfactory synthetic approach to the target compounds involves reaction of the *ortho*-lithium salt of 4,4-dimethyl-2-(4-fluorophenyl)oxazoline (10) generated *in situ* with an appropriate aryl aldehyde or ketone.<sup>19</sup> Application of this method to the synthesis of *trans*-3,4-dihydroxy-3,4-dihydro-9-fluoro-7-MBA (3a) (Scheme II) entails reaction of 10 with 2-(6-methoxynaphthyl)methylketone to give lactone 11b. Catalytic hydrogenation of 11b over a palladium-charcoal catalyst furnishes the carboxylic acid 12b essentially quantitatively. Hydrogenation was superior to the usual reduction with zinc in HOAc or zinc and KOH, both of which furnish lower yields. Cyclization of 12b takes place smoothly on treatment with ZnCl<sub>2</sub> and acetic anhydride in acetic acid to provide 12-acetoxy-9-fluoro-3-methoxy-7-methylbenz[*a*]anthracene (13a). Reduction of 13a with HI and hypophosphorus acid in HOAc<sup>20</sup> affords 9-fluoro-3-methoxy-7-methylbenz[*a*]anthracene (13b). Short reaction time (1.5 min) is essential to minimize reduction to the dihydro derivative. Demethylation of 13b with HBr in HOAc gives the phenol 13c which is oxidized with Fremy's salt [(SO<sub>3</sub>K)<sub>2</sub>NO] to the quinone, 9-fluoro-7-methylbenz[*a*]anthracene-3,4-dione (14). Reduction of 14 with NaBH<sub>4</sub> with O<sub>2</sub> bubbling through a heterogeneous solution in ethanol furnishes stereospecifically the *trans*-dihydrodiol *trans*-3,4-dihydroxy-3,4-dihydro-9-fluoro-7-MBA (3a). The use of O<sub>2</sub> for reoxidation of catechol byproducts back to quinones in reductions of this type is now well established.<sup>21</sup> The <sup>1</sup>H NMR spectrum of 3a is in good agreement with the structural assignment, with the pattern of chemical shifts and couplings for the protons in the A-ring matching closely those of *trans*-3,4-dihydroxy-3,4-dihydro-7-MBA lacking fluorine.<sup>11cd</sup>

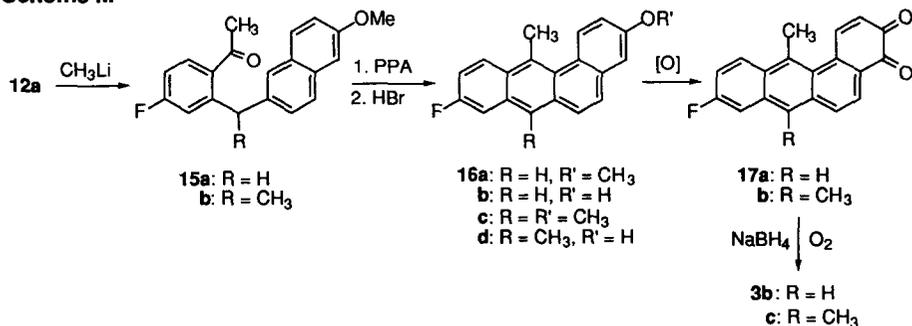
## Scheme II



Epoxidation of **3a** with *m*-chloroperbenzoic acid takes place stereospecifically to yield the target *anti*-diol epoxide metabolite, *trans*-3,4-dihydroxy-*anti*-3,4-epoxy-1,2,3,4-tetrahydro-9-fluoro-7-MBA (**5a**).<sup>22</sup> This assignment is supported by its <sup>1</sup>H NMR spectrum which matches closely that of the diol epoxide of 7-MBA lacking a fluorine substituent (**1b**) except for the resonances of the protons in the fluorine-substituted ring.<sup>11cd</sup>

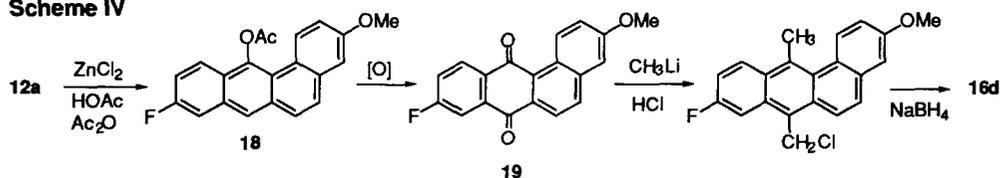
The synthesis of *trans*-3,4-dihydroxy-3,4-dihydro-9-fluoro-12-MBA (**3b**) is based on reaction of **10** with 6-methoxy-2-naphthaldehyde to furnish the lactone **11a**. Hydrogenation of **11a** over a palladium-charcoal catalyst provides the carboxylic acid **12a** which reacts with CH<sub>3</sub>Li to furnish the methylketone **15a** (Scheme III). Cyclodehydration of **15a** in polyphosphoric acid yields 9-fluoro-3-methoxy-12-methylbenz[*a*]anthracene (**16a**). Demethylation of **16a** with HBr in HOAc affords the phenol **16b** which is oxidized by Fremy's salt to the quinone, 9-fluoro-12-methylbenz[*a*]anthracene-3,4-dione (**17a**). Reduction of **17a** with NaBH<sub>4</sub>/O<sub>2</sub> furnishes *trans*-3,4-dihydroxy-3,4-dihydro-9-fluoro-12-MBA (**3b**), also stereospecifically. Conversion of this dihydrodiol to *trans*-3,4-dihydroxy-*anti*-3,4-epoxy-9-fluoro-1,2,3,4-tetrahydro-12-MBA (**5b**) was not attempted in view of the failure of previous attempts to synthesize the diol epoxide metabolite of the parent PAH lacking a fluorine substituent, presumably due to its instability due to steric crowding in the bay region.<sup>11de,23</sup>

## Scheme III



*trans*-3,4-Dihydroxy-3,4-dihydro-9-fluoro-7,12-dimethylbenz[*a*]anthracene (**3c**) is efficiently synthetically accessible from the carboxylic acid intermediate **12b** by a modification of the method used for the preparation of **3b** (Scheme III). Thus, reaction of **12b** with methyllithium furnishes the ketone **15b** which undergoes cyclodehydration in polyphosphoric acid to yield 9-fluoro-3-methoxy-7,12-dimethylbenz[*a*]anthracene (**16c**). Demethylation of **16c** with HBr in acetic acid furnishes 9-fluoro-3-hydroxy-7,12-dimethylbenz[*a*]anthracene (**16d**). An alternative route to **16c** based on **12a** was also examined (Scheme IV). Thus, treatment of **12a** with ZnCl<sub>2</sub> in acetic anhydride-acetic acid provides 12-acetoxy-9-fluoro-3-methoxybenz[*a*]anthracene (**18**) which is oxidized essentially quantitatively by sodium dichromate in AcOH to 9-fluoro-3-methoxybenz[*a*]anthracene-7,12-dione (**19**). This quinone is converted to **16c** by our modification of Newman's method for the synthesis of DMBA from benz[*a*]anthracene-7,12-dione, i.e. addition of methyllithium, followed by rearrangement to the 7-chloromethyl-12-methylbenz[*a*]anthracene derivative by treatment with anhydrous HCl in ether, and reductive dehalogenation with NaBH<sub>4</sub> in DMSO.<sup>11a,24</sup> Oxidation of **16d** with Fremy's salt provides the A-ring quinone, 9-fluoro-7,12-dimethylbenz[*a*]anthracene-3,4-dione (**17b**), and reduction of **17b** with NaBH<sub>4</sub>/O<sub>2</sub> gave the 9-fluoro-DMBA 3,4-dihydrodiol (**3c**). Epoxidation of **3c** with *m*-chloroperbenzoic acid takes place stereospecifically to yield the target *anti*-diol epoxide metabolite, *trans*-3,4-dihydroxy-*anti*-3,4-epoxy-9-fluoro-1,2,3,4-tetrahydro-7,12-dimethylbenz[*a*]anthracene (**5c**).<sup>22</sup>

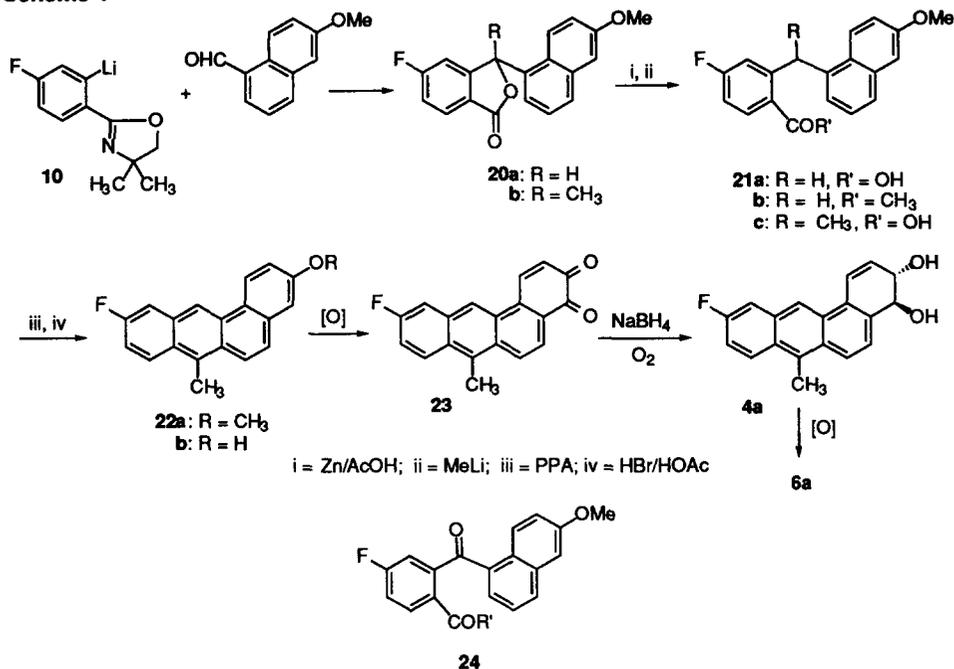
Scheme IV



The synthetic route to the *trans*-3,4-dihydrodiol of 10-fluoro-7-MBA (**4a**) and its *anti*-diol epoxide (**5a**) derivative is based on reaction of **10** with 6-methoxy-1-naphthaldehyde to provide lactone **20a** (Scheme V). Reduction of **20a** with Zn/HOAc provides 4-fluoro-2-[1-(3-methoxynaphthylmethyl)]benzoic acid (**21a**) quantitatively. Reaction of **21a** with MeLi in ether furnishes the corresponding methylketone (**21b**) which undergoes cyclodehydration in polyphosphoric acid to yield 10-fluoro-3-methoxy-7-methylbenz[*a*]anthracene (**22a**). Demethylation of **22a** with HBr in HOAc gives the free phenol, 10-fluoro-3-hydroxy-7-methylbenz[*a*]anthracene (**22b**), which is transformed to the quinone, 10-fluoro-7-methylbenz[*a*]anthracene-3,4-dione (**23**), by oxidation with Fremy's salt. Reduction of **23** with NaBH<sub>4</sub> and O<sub>2</sub> affords *trans*-3,4-dihydro-3,4-dihydro-10-fluoro-7-MBA (**4a**), and oxidation of the latter with *m*-chloroperbenzoic acid furnishes stereospecifically the corresponding *anti*-diol epoxide, **6a**.

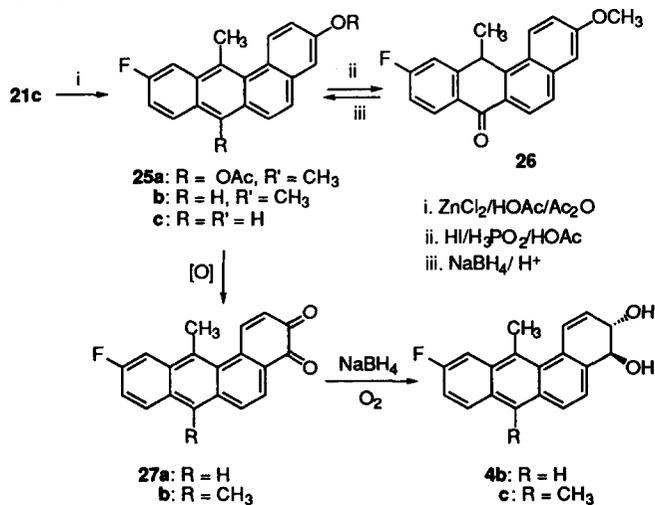
The *trans*-3,4-dihydrodiol of 10-fluoro-12-MBA (**4b**) is conveniently accessible via a synthetic sequence based on the methyl-substituted lactone **20b** (Scheme V). Oxidation of **20a** with KMnO<sub>4</sub> and 25% aqueous KOH in pyridine affords 4-fluoro-2-[1-(3-methoxynaphthoyl)]benzoic acid (**24**) which reacts with methyllithium to furnish the lactone **20b**. Reduction of **20a** takes place smoothly and essentially quantitatively to yield the carboxylic acid **21c** which cyclizes on treatment with ZnCl<sub>2</sub> and Ac<sub>2</sub>O in HOAc to provide 7-acetoxy-10-fluoro-3-methoxy-12-methylbenz[*a*]anthracene (**25a**) (Scheme VI). Treatment of **25a** with HI and hypophosphorus acid under the conditions employed for reduction of **13a** to **13b** yields not the expected 10-fluoro-3-methoxy-12-methylbenz[*a*]anthracene (**25b**) but provides instead the 7-keto compound **26** arising from deacetylation.

## Scheme V

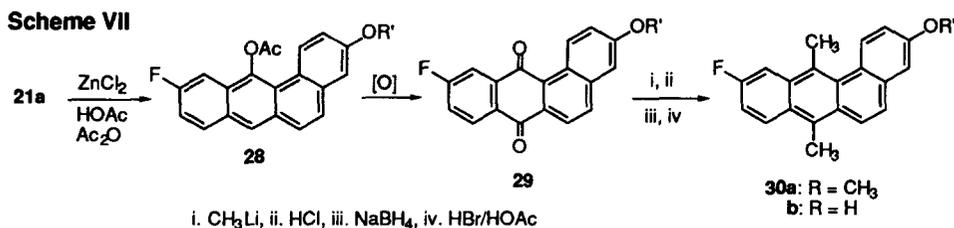


Compound **26** is readily transformed to **25b** by reduction with NaBH<sub>4</sub> in ethanol followed by acid-catalyzed dehydration. Demethylation of **25b** with HBr in HOAc provides 10-fluoro-3-hydroxy-12-methylbenz[*a*]-anthracene (**25c**). Oxidation of **25c** with Fremy's salt affords a mixture (~2:1) of 10-fluoro-12-methylbenz[*a*]-anthracene-3,4-dione (**27a**) and the related hydroquinone. Reduction of this with NaBH<sub>4</sub> and O<sub>2</sub> affords *trans*-3,4-dihydro-3,4-dihydro-10-fluoro-12-MBA (**4b**).

## Scheme VI



Finally, the *trans*-3,4-dihydrodiol of 10-fluoro-7,12-dimethylbenz[*a*]anthracene (**4c**) is prepared via a synthetic route based on the carboxylic acid **21a** (Scheme VII). Treatment of **21a** with ZnCl<sub>2</sub> and acetic anhydride in HOAc provides 7-acetoxy-10-fluoro-3-methoxybenz[*a*]anthracene (**28**) which is oxidized smoothly by sodium dichromate in AcOH to 10-fluoro-3-methoxybenz[*a*]anthracene-7,12-dione (**29**). This quinone is transformed to 10-fluoro-3-methoxy-7,12-dimethylbenz[*a*]anthracene (**30a**) by the reaction sequence employed for the synthesis of the 9-fluoro analog (**16d**) from the 9-fluoro-substituted quinone **19** (Scheme IV).<sup>11a,24</sup> Demethylation of **30a** with HBr in acetic acid provides the phenol **30b** which undergoes oxidation with Fremy's salt to the quinone 10-fluoro-7,12-dimethylbenz[*a*]anthracene-3,4-dione (**27b**) (Scheme VI). Reduction of **27b** with NaBH<sub>4</sub> and O<sub>2</sub> affords the 10-fluoro-DMBA 3,4-dihydrodiol (**4c**).



## DISCUSSION

The syntheses described provide efficient stereospecific routes to the *trans*-3,4-dihydrodiol derivatives of 9- and 10-fluoro-DMBA, -7-MBA, and -12-MBA and several of their *anti*-diol epoxide metabolites (**5a**, **5c**, **6a**). The synthetic accessibility of these compounds makes possible studies to probe the influence of fluorine substitution on metabolic activation, mutagenic and tumorigenic activity, and the relative reactivities of the diol epoxides as well as to determine their relative extents and sites of covalent binding to DNA *in vivo* in comparison with the unfluorinated parent compounds.

The methods devised earlier for the synthesis of the related unsubstituted dihydrodiols and diol epoxides of 7- and 12-MBA and DMBA<sup>11</sup> were less attractive for the preparation of the fluoro-substituted derivatives because of the relatively high cost of the starting compound and the likelihood of formation of mixtures of isomers in the initial stage. Two alternative synthetic approaches were investigated. The first method (Scheme I) involves reaction of a fluoro-substituted aldehyde, e.g. 4-fluorobenzaldehyde, with 2-lithio-6-methoxy-*N,N*-diethyl-1-naphthamide to furnish a lactone which is reductively cleaved to a carboxylic acid and cyclized in acidic media to provide a fluoro-substituted 3-methoxybenz[*a*]anthracene derivative, e.g. **9b**, a key synthetic precursor of the corresponding 3,4-dihydrodiol. However, the usefulness of the method was found to be limited by the relatively slow rates of the reactions and the low overall yields (~1%). This is partly a consequence of cyclization to a fluoro-substituted benzene ring. The second synthetic method (Scheme II) entails more favorable cyclization to a methoxy-substituted naphthalene ring. This approach is based on reaction of the *ortho*-lithium salt of 4,4-dimethyl-2-(4-fluorophenyl)oxazoline with an appropriate aryl aldehyde or ketone, e.g. 6-methoxy-2-naphthaldehyde, to furnish a lactone which is reduced to a carboxylic acid which in turn undergoes acid-catalyzed cyclization to a fluoro-benz[*a*]anthracene derivative. The reaction rates via this approach are considerably faster (hours vs days in the cyclization step) and the yields are substantially higher (~58% to the same stage).

Secondary processes involving metal exchange and loss of fluoride to form benzyne intermediates may occur in the steps involving the use of organolithium reagents, but they do not seriously interfere as long as excess RLi is avoided and reaction times are short. No significant loss of fluoride occurs in the reduction of the lactone intermediates or during deoxygenation with HI/P or H<sub>3</sub>PO<sub>2</sub>, providing that reaction times are kept short.

Syntheses of three of the six possible *anti*-diol epoxide derivatives of **3a-c** and **4a-c** are reported. At the time this work was carried out, it was anticipated that the remaining isomers might be too unstable to isolate as a consequence of the severe steric crowding of the methyl groups in the bay region 12-positions of benz[*a*]anthracene. Previous failure to isolate the corresponding *anti*- and *syn*-diol epoxides of unfluorinated 12-MBA and the very reactive nature of the *anti*-diol epoxide of DMBA was rationalized as a due to this steric effect.<sup>11</sup> However, the recent discovery<sup>11e</sup> that the apparent facility of decomposition of these isomers and the corresponding *syn*-diol epoxide isomers is due to impurities which may be removed by flash chromatography, suggests that the related *anti*- and *syn*-diol epoxides of the 9- and 10-fluorinated analogs are also sufficiently stable to isolate and characterize as well as to conduct a variety of biological experiments.

## EXPERIMENTAL SECTION

**Materials and Methods.** 4,4-Dimethyl-2-(4-fluorophenyl)oxazoline (**7**) was prepared by the literature procedure.<sup>19,25</sup> Fremy's salt [(SO<sub>3</sub>K)<sub>2</sub>NO] was prepared as described<sup>24</sup> and used fresh. *m*-Chloroperbenzoic acid (Aldrich) was purified by washing with pH 7.4 phosphate buffer and dried under reduced pressure. *N*-Bromosuccinimide was crystallized from water prior to use. *N,N,N',N'*-Tetramethylethylenediamine (TMEDA) was dried over LiAlH<sub>4</sub> and redistilled. THF was distilled from sodium benzophenone ketyl, and ether was dried over sodium. All melting points are uncorrected. The <sup>1</sup>H NMR spectra were obtained on the University of Chicago 300- or 500-MHz <sup>1</sup>H NMR spectrometers in CDCl<sub>3</sub> with tetramethylsilane as internal standard unless stated otherwise.

**Reaction of *N,N*-Diethyl-2-lithio-6-methoxy-1-naphthamide with 4-Fluorobenzaldehyde.** *N,N*-Diethyl-2-lithio-6-methoxy-1-naphthamide was synthesized *in situ* by metalation of the amide (6.12 g, 24 mmol) with *sec*-BuLi and TMEDA in ether at -60 °C by the published method.<sup>11d,18</sup> Reaction of the metalated amide with 4-fluorobenzaldehyde (3.0 g, 24 mmol) by the usual procedure<sup>11d,18</sup> gave the lactone **7** (770 mg, 10.4%), mp 124-126°C (benzene-hexane); NMR δ 3.94 (s, 3, CH<sub>3</sub>), 6.42 (s, 1, CH), 6.80-8.90 (m, 9, aryl). Anal. Calcd for C<sub>19</sub>H<sub>13</sub>O<sub>3</sub>F: C, 74.02; H, 4.25. Found: C, 74.11; H, 4.42.

**12-Acetoxy-10-fluoro-3-methoxybenz[*a*]anthracene (**9b**).** Reduction of **7** (550 mg, 1.8 mmol) with zinc and KOH by the usual procedure<sup>18</sup> (72 h) furnished the carboxylic acid **8**: NMR δ 3.92 (s, 3, CH<sub>3</sub>), 4.22 (s, 2, CH<sub>2</sub>), 6.70-8.25 (m, 10, aryl, OH). Reaction of **8** with ZnCl<sub>2</sub> in acetic anhydride and acetic acid by the usual procedure<sup>18</sup> gave **9b** (70 mg, 12% from **7**), mp 174-175°C (benzene-hexane); NMR δ 2.66 (s, 3, CH<sub>3</sub>), 3.95 (s, 3, CH<sub>3</sub>), 7.20-9.22 (m, 9, aryl). Anal. Calcd for C<sub>21</sub>H<sub>15</sub>O<sub>3</sub>F: C, 75.44; H, 4.52. Found: C, 75.55; H, 4.53.

**6-Methoxy-2-naphthaldehyde.** To a suspension of 6-methoxy-2-bromonaphthalene (23.7 g, 100 mmol) in anhydrous ether (500 mL) at -78 °C was added *n*-BuLi (125 mmol of a 1.6M solution in hexane). The

cold bath was removed and stirring was continued under argon for 1 h during which time the solid dissolved completely and the solution became light yellow. It was then cooled to  $-78\text{ }^{\circ}\text{C}$ , 20 mL of dimethylformamide was added, the cold bath was removed, and stirring was continued for 2 h. Conventional workup gave 6-methoxy-2-naphthaldehyde, mp  $82\text{--}83\text{ }^{\circ}\text{C}$  (92%); NMR  $\delta$  3.93 (s, 3,  $\text{CH}_3$ ), 7.14–7.22 (m, 3, aryl), 7.76 (d, 1, aryl,  $J = 8.5$ ), 7.80–7.89 (m, 2, aryl), 8.21 (s, 1, aryl), 10.05 (s, 1, CHO). Anal. Calcd for  $\text{C}_{12}\text{H}_{10}\text{O}_2$ : C, 77.40; H, 5.41. Found: C, 77.23; H, 5.42.

**2-(6-Methoxynaphthyl)methylketone.** Reaction of 6-methoxy-2-lithionaphthalene with acetaldehyde was carried out by the foregoing procedure and the resulting alcohol was oxidized with DDQ in THF. The reaction mixture was stirred at room temperature for 2 h, then water was added, the product was removed by filtration, washed with 10% NaOH and water, and dried. The ketone product was obtained as white solid, mp  $104\text{--}105\text{ }^{\circ}\text{C}$  (94%); NMR  $\delta$  2.68 (s, 3,  $\text{CH}_3$ ), 3.93 (s, 3,  $\text{CH}_3$ ), 7.13 (d, 1, aryl), 7.17 (d, 1, aryl), 7.19 (d, 1, aryl), 7.23 (s, 1, aryl), 7.74 (d, 1, aryl,  $J = 8.6$ ), 7.82 (d, 1, aryl,  $J = 8.9$ ), 7.99 (d, 1, aryl), 8.36 (s, 1, aryl). Anal. Calcd for  $\text{C}_{13}\text{H}_{12}\text{O}_2$ : C, 77.98; H, 6.04. Found: C, 77.86; H, 6.09.

**Reaction of *o*-Lithio-10 with 6-Methoxy-2-naphthaldehyde.** To a solution of **10** (15.82 g, 82 mmol) in anhydrous ether (150 mL) at  $-78\text{ }^{\circ}\text{C}$  was added dropwise 40 ml of a 2.5M solution of *n*-BuLi (98.4 mmol) in hexane over 20 min. The solution was stirred at this temperature for 1 h, then 6-methoxy-2-naphthaldehyde (15.25 g, 82 mmol) was added, the solution was allowed to warm to room temperature, and stirring was continued overnight. Conventional workup gave an oil. To this was added a solution of conc. HCl in 150 mL of water, and the mixture was heated at reflux for 4.5 h, then cooled, and the solid was collected, washed with water, then taken up in aqueous NaOH (10g in 100 mL) and heated at reflux for one h. The product was then precipitated by addition of HCl, extracted into ether, washed with water, dried, taken up in benzene, and chromatographed on a silica gel column eluted with benzene-hexane to yield the lactone **11a**, mp  $200\text{--}201\text{ }^{\circ}\text{C}$  (54%); NMR  $\delta$  3.91 (s, 3,  $\text{CH}_3$ ), 6.46 (s, 1, CH), 6.69 (dd, 1, aryl,  $J = 7.6$ ,  $J = 1.8$ ), 7.10–7.23 (m, 3, aryl), 7.33 (s, 1, aryl), 7.70 (s, 1, aryl), 7.72 (s, 2, aryl), 7.96 (m, 1, aryl). Anal. Calcd for  $\text{C}_{19}\text{H}_{13}\text{O}_3\text{F}$ : C, 74.02; H, 4.25. Found: C, 74.11; H, 4.25.

**Reaction of *o*-Lithio-10 with 2-(6-Methoxynaphthyl)methylketone.** This reaction was conducted by modification of the procedure used in the preceding synthesis. The lactone product (**11b**) had mp  $163\text{--}164\text{ }^{\circ}\text{C}$  (60%); NMR  $\delta$  2.12 (s, 3,  $\text{CH}_3$ ), 3.90 (s, 3,  $\text{CH}_3$ ), 7.08–7.21 (m, 3, aryl), 7.35 (dd, 1, aryl), 7.33 (s, 1, aryl), 7.70 (dd, 2, aryl,  $J = 8.8$ ), 7.80 (s, 1, aryl), 7.90 (m, 1, aryl). Anal. Calcd for  $\text{C}_{20}\text{H}_{15}\text{O}_3\text{F}$ : C, 74.52; H, 4.69. Found: C, 74.42; H, 4.74.

**Hydrogenation of Lactone 11 to Carboxylic Acid 12.** A solution of **11a** (2.2 g, 7.1 mmol) in EtOAc (60 mL) with a 10% palladium/charcoal catalyst (1.1 g) was shaken in a Parr hydrogenator at 40 psig for 4 h. The catalyst was removed by filtration, the resulting solution was evaporated to dryness, and the product recrystallized from benzene-hexane to yield **12a**, mp  $176\text{--}177\text{ }^{\circ}\text{C}$  (100%); NMR  $\delta$  3.89 (s, 3,  $\text{CH}_3$ ), 4.55 (s, 2,  $\text{CH}_2$ ), 6.86 (m, 1, aryl), 6.96 (m, 1, aryl), 7.08 (m, 2, aryl), 7.20 (s, 2, aryl), 7.48 (s, 1), 7.62 (m, 2, aryl), 7.90 (m, 1, aryl). Anal. Calcd for  $\text{C}_{19}\text{H}_{15}\text{O}_3\text{F}$ : C, 73.54; H, 4.87. Found: C, 73.62; H, 4.91.

Similar catalytic reduction of **11b** gave **12b**, mp 195-196 °C (85%); NMR  $\delta$  1.70 (d, 3, CH<sub>3</sub>,  $J = 7.1$ ), 3.88 (s, 3, CH<sub>3</sub>), 5.48 (q, 1, CH), 6.92 (m, 2, aryl), 7.09 (m, 2, aryl), 7.23 (m, 2, aryl), 7.61 (m, 1, aryl), 7.66 (d, 1, aryl,  $J = 8.9$ ), 8.03 (m, 1, aryl). Anal. Calcd for C<sub>20</sub>H<sub>17</sub>O<sub>3</sub>F: C, 74.06; H, 5.28. Found: C, 74.12; H, 5.30.

**12-Acetoxy-9-fluoro-3-methoxy-7-methylbenz[a]anthracene (13a)**. A solution of **12b** (700 mg, 2.2 mmol) and ZnCl<sub>2</sub> (70 mg) in Ac<sub>2</sub>O (25 mL) and AcOH (25 mL) was heated at reflux for 2 h. Addition of icewater precipitated out a white solid which was filtered off, dried, and dissolved in benzene. The solution was passed through a short Florisil column and recrystallized from benzene-hexane to yield **13a**, mp 195-196 °C (93%); NMR  $\delta$  2.60 (s, 3, CH<sub>3</sub>), 2.99 (s, 3, CH<sub>3</sub>), 3.89 (s, 3, CH<sub>3</sub>), 7.20-7.23 (m, 2, aryl), 7.35 (m, 1, aryl), 7.55 (d, 1, aryl,  $J = 9.4$ ), 7.85 (dd, 1, aryl,  $J = 11.4$ ), 8.02 (m, 2, aryl), 9.04 (d, 1, aryl). Anal. Calcd for C<sub>22</sub>H<sub>17</sub>O<sub>3</sub>F: C, 75.85; H, 4.92. Found: C, 75.80; H, 4.93.

**9-Fluoro-3-methoxy-7-methylbenz[a]anthracene (13b)**. Reduction of **13a** (700 mg, 2 mmol) with HI and hypophosphorus acid in acetic acid by the published method<sup>20</sup> and chromatography of the crude product through a short silica gel column eluted with benzene-hexane gave **13b**, mp 154-155 °C, recrystallized from benzene-hexane (77%); NMR  $\delta$  3.00 (s, 3, CH<sub>3</sub>), 3.96 (s, 3, CH<sub>3</sub>), 7.23 (s, 1, aryl), 7.25-7.32 (m, 1, aryl), 7.60 (d, 1, aryl,  $J = 9.4$ ), 7.82 (d, 1, aryl,  $J = 11.9$ ), 8.02-8.07 (m, 2, aryl), 8.67 (d, 1, aryl,  $J = 9.0$ ), 8.93 (s, 1, aryl). Anal. Calcd for C<sub>20</sub>H<sub>15</sub>OF: C, 82.74; H, 5.21. Found: C, 82.79; H, 5.25.

**9-Fluoro-7-methylbenz[a]anthracen-3-ol (13c)**. Hydrobromic acid, 48% (20 mL) was added dropwise over 10 min to a solution of **13b** (500 mg, 1.7 mmol) in refluxing HOAc, and the turbid reaction mixture was then heated at reflux for 3.5 h. Addition of ice water precipitated the solid product which was filtered and dried, then dissolved in benzene and passed through a short silica gel column eluted with benzene to provide **13c**, mp 222-223 °C, recrystallized from benzene-hexane (79%); NMR  $\delta$  3.03 (s, 3, CH<sub>3</sub>), 7.24-7.41 (m, 3, aryl), 7.64 (d, 1, aryl,  $J = 9.5$ ), 7.93 (m, 1, aryl), 8.12 (d, 1, aryl,  $J = 9.5$ ), 8.22 (m, 1, aryl), 8.77 (d, 1, aryl,  $J = 8.8$ ), 9.16 (s, 1, aryl). UVmax (EtOH) 288 (67 050), 244 (45 500), 211 (45 500) nm. Anal. Calcd for C<sub>19</sub>H<sub>13</sub>OF: C, 82.59; H, 4.74. Found: C, 82.42; H, 4.76.

**9-Fluoro-7-methylbenz[a]anthracene-3,4-dione (14)**. Oxidation of **13c** (200 mg, 0.72 mmol) with Fremy's salt by the procedure employed<sup>11d</sup> for the oxidation of 7-methylbenz[a]anthracen-3-ol furnished **14**, mp 220-221 °C, (95%); NMR  $\delta$  3.05 (s, 3, CH<sub>3</sub>), 6.62 (d, 1, vinyl,  $J = 10.6$ ), 7.37 (m, 1, aryl), 7.84 (dd, 1, aryl), 8.06 (m, 1, aryl), 8.12 (d, 1, aryl,  $J = 9.2$ ), 8.38 (d, 1, aryl,  $J = 9.4$ ), 8.48 (d, 1, vinyl,  $J = 10.6$ ), 9.16 (s, 1, aryl). Anal. Calcd for C<sub>19</sub>H<sub>11</sub>O<sub>2</sub>F: C, 78.61; H, 3.82. Found: C, 78.44; H, 3.89.

**trans-3,4-Dihydroxy-3,4-dihydro-9-fluoro-7-methylbenz[a]anthracene (3a)**. Reduction of **14** (150 mg, 0.52 mmol) with NaBH<sub>4</sub> (1.5 g) in ethanol (100 mL) by the usual procedure<sup>11d</sup> with O<sub>2</sub> bubbling through the solution for 24 h furnished **3a** as a white solid, mp 226-228 °C, (53%); NMR (500 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  2.99 (s, 3, CH<sub>3</sub>), 4.37 (m, 1, H<sub>3</sub>), 4.75 (m, 1, H<sub>4</sub>), 5.25 (d, 1, OH), 5.59 (d, 1, OH), 6.20 (dd, 1, vinyl,  $J = 10.1$ ,  $J = 2.5$ ), 7.42 (m, 2, aryl), 7.80 (d, 1, aryl,  $J = 9.1$ ), 7.95 (dd, 1, vinyl,  $J = 12.3$ ,  $J = 2.0$ ), 8.20 (m, 1, aryl), 8.24 (d, 1, aryl,  $J = 9.0$ ), 8.86 (s, 1, aryl). UVmax (EtOH) 416 (10 600), 393 (11 000), 263 (159 500), 213 (31 900) nm. Anal. Calcd for C<sub>19</sub>H<sub>15</sub>O<sub>2</sub>F: C, 77.53; H, 5.14. Found: C, 77.44; H, 5.19.

***trans*-3,4-Dihydroxy-*anti*-1,2-epoxy-9-fluoro-7-methyl-1,2,3,4-tetrahydrobenz[a]anthracene (5a).** To a solution of **3a** (46 mg, 0.15 mmol) in dry THF (30 mL) in subdued light under argon was added *m*-chloroperbenzoic acid (258 mg, 1.5 mmol), and the resulting solution was stirred for 1 h.<sup>11,22</sup> The reaction was worked up as usual<sup>11</sup> except that the organic phase was washed 3X with 10% NaOH, and a small amount of Et<sub>3</sub>N was added to the ether layer before drying with MgSO<sub>4</sub>. Other precautions to minimize decomposition of the sensitive diol epoxide were also observed.<sup>11e,22</sup> It is likely that the yield could be improved by flash chromatography of the product through a short silica gel column deactivated with THF/hexane/Et<sub>3</sub>N, a procedure found to be effective for sensitive PAH diol epoxides.<sup>11e</sup> The diol epoxide **5a** was obtained as a white solid, mp 192-194 °C, (59%); NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 2.99 (s, 3, CH<sub>3</sub>), 3.79 (m, 1), 3.88 (m, 1), 4.47 (m, 1), 5.08 (m, 1), 5.59 (d, 1, OH), 5.75 (d, 1, OH). UVmax (EtOH) 377 (15 300), 260 (160 300), 200 (38 000) nm. Anal. Calcd for C<sub>19</sub>H<sub>15</sub>O<sub>3</sub>F: C, 73.54; H, 4.87. Found: C, 73.64; H, 4.99.

**Conversion of Carboxylic Acid 12a to the Methylketone 15a.** To a solution of **12a** (1.1 g, 3.5 mmol) in ether (100 mL) was added 6.3 mL of a 1.4M solution of MeLi in ether (8.9 mmol) and the solution was stirred at room temperature for 1.5 h. Conventional workup afforded 780 mg of a crude product which was chromatographed on a Florisil column eluted with hexane and ether-hexane to yield **15a**, mp 84-85 °C (73%); NMR δ 2.47 (s, 3, CH<sub>3</sub>), 3.89 (s, 3, CH<sub>3</sub>), 4.40 (s, 2, CH<sub>2</sub>), 6.88 (m, 1, aryl), 6.94 (m, 1, aryl), 7.08 (m, 2, aryl), 7.22 (m, 2, aryl), 7.46 (s, 1), 7.62 (m, 2, aryl), 7.69 (m, 1, aryl). Anal. Calcd for C<sub>20</sub>H<sub>17</sub>O<sub>2</sub>F: C, 77.90; H, 5.56. Found: C, 77.95; H, 5.60.

**9-Fluoro-3-methoxy-12-methylbenz[a]anthracene (16a).** A solution of **15a** (780 mg, 2.5 mmol) in polyphosphoric acid (50 mL) was heated at 100 °C for 45 min. The resulting reddish-purple solution was poured into icewater, and the crude product was filtered off, dried, then dissolved in benzene, and chromatographed on a column of silica gel. Elution with hexane gave crude **16a** which was recrystallized from benzene-hexane to yield pure **16a**, mp 144-146 °C (70%); NMR δ 3.32 (s, 3, CH<sub>3</sub>), 3.96 (s, 3, CH<sub>3</sub>), 7.17 (dd, 1, aryl, *J* = 9.1, *J* = 2.7), 7.23 (m, 1, aryl), 7.35 (m, 1, aryl), 7.47 (d, 1, aryl, *J* = 8.9), 7.56 (dd, 1, aryl), 8.28 (d, 1, aryl), 8.07 (s, 1, aryl), 8.28 (m, 1, aryl), 8.46 (d, 1, aryl, *J* = 9.0). Anal. Calcd for C<sub>20</sub>H<sub>15</sub>OF: C, 82.74; H, 5.21. Found: C, 82.58; H, 5.26.

**9-Fluoro-12-methylbenz[a]anthracen-3-ol (16b).** Demethylation of **16a** with HBr by the procedure for preparation of **13c** gave **16b**, mp 174-145 °C (84%); NMR δ 3.33 (s, 3, CH<sub>3</sub>), 7.18 (dd, 1, aryl, *J* = 9.0, *J* = 2.7), 7.29 (d, 1, aryl, *J* = 2.7), 7.44 (m, 1, aryl), 7.51 (d, 1, aryl, *J* = 8.9), 7.65 (d, 1, aryl, *J* = 8.9), 7.70 (dd, 1, aryl, *J* = 9.9, *J* = 2.7), 8.23 (s, 1, aryl), 8.42 (m, 1, aryl), 8.50 (d, 1, aryl, *J* = 9.0), 8.82 (s, 1, OH). UVmax (EtOH) 292 (77 900), 245 (31 500), 210 (37 000) nm. Anal. Calcd for C<sub>19</sub>H<sub>13</sub>OF: C, 82.59; H, 4.74. Found: C, 82.44; H, 4.80.

**9-Fluoro-12-methylbenz[a]anthracene-3,4-dione (17a).** Oxidation of **16b** (200 mg, 0.72 mmol) with Fremy's salt by the procedure employed<sup>11d</sup> for the oxidation of 7-methylbenz[a]anthracen-3-ol furnished **17a**, mp 206-207 °C, (71%); NMR δ 3.24 (s, 3, CH<sub>3</sub>), 6.40 (d, 1, vinyl, *J* = 10.7), 7.37 (m, 1, aryl), 7.53 (dd, 1, aryl), 7.94 (d, 1, aryl, *J* = 8.7), 7.99 (d, 1, aryl, *J* = 8.7), 8.17 (s, 1, aryl), 8.24 (m, 1, aryl), 8.26 (d, 1, vinyl, *J* = 10.6). Anal. Calcd for C<sub>19</sub>H<sub>11</sub>O<sub>2</sub>F: C, 78.61; H, 3.82. Found: C, 78.54; H, 3.93.

**trans-3,4-Dihydroxy-3,4-dihydro-9-fluoro-12-methylbenz[a]anthracene (3b).** Reduction of **17a** (120 mg, 0.52 mmol) with NaBH<sub>4</sub> (1.0 g) in ethanol (150 mL) by the usual procedure<sup>11d</sup> with O<sub>2</sub> bubbling through the solution for 24 h gave the dihydrodiol **3b** as a white solid, mp 203–205 °C, (50%); NMR (500 MHz, DMSO-*d*<sub>6</sub>) δ 3.11 (s, 3, CH<sub>3</sub>), 4.42 (m, 1, H<sub>3</sub>), 4.53 (m, 1, H<sub>4</sub>), 5.22 (d, 1, OH), 5.56 (d, 1, OH), 6.07 (dd, 1, vinyl, *J* = 10.1, *J* = 2.3), 7.03 (dd, 1, aryl, *J* = 10.1, *J* = 2.6), 7.43 (m, 1, aryl), 7.68 (d, 1, aryl, *J* = 8.6), 7.74 (dd, 1, vinyl, *J* = 10.2, *J* = 2.2), 7.87 (d, 1, aryl, *J* = 8.7), 8.30 (m, 2, aryl). UVmax (EtOH) 422 (10 500), 398 (11 300), 266 (105 000) 213 (29 000) nm. Anal. Calcd for C<sub>19</sub>H<sub>15</sub>O<sub>2</sub>F: C, 77.53; H, 5.14. Found: C, 77.62; H, 5.08.

**Conversion of Carboxylic Acid 12b to the Methylketone 15b.** Reaction of **12b** with MeLi was carried out by modification of the procedure used for the synthesis of **15a**. Purification of the crude product by chromatography on silical gel and recrystallization from benzene-hexane provided **15b**, mp 109–110 °C, (62%); NMR δ 1.65 (d, 3, CH<sub>3</sub>, *J* = 7.1), 2.39 (s, 3, CH<sub>3</sub>), 3.89 (s, 3, CH<sub>3</sub>), 5.10 (q, 1, CH), 6.90 (m, 1, aryl), 6.99 (dd, 1, aryl, *J* = 10.5, *J* = 2.4), 7.06 (s, 1, aryl), 7.10 (dd, 1, aryl, *J* = 9.0, *J* = 2.4), 7.18 (d, 1, aryl, *J* = 8.7), 7.54 (m, 2, aryl), 7.60 (d, 1, aryl, *J* = 8.5), 7.65 (d, 1, aryl, *J* = 8.9). Anal. Calcd for C<sub>21</sub>H<sub>19</sub>O<sub>2</sub>F: C, 78.24; H, 5.94. Found: C, 78.28; H, 5.99.

**9-Fluoro-3-methoxy-7,12-dimethylbenz[a]anthracene (16c).** (a) *From 15b.* Cyclodehydration of **15b** (200 mg, 0.62) in polyphosphoric acid was conducted by the procedure used for the synthesis of **16a**. The <sup>1</sup>H NMR spectrum of the crude product showed the presence of ~5% of the product of cyclization in the alternative ring position, 3-fluoro-5,12-dimethyl-8-methoxynaphthacene. Chromatography of this product on a silica gel column eluted with hexane followed by recrystallization from benzene-hexane gave **16c**, mp 172–173 °C, (96%); NMR δ 2.97 (s, 3, CH<sub>3</sub>), 3.29 (s, 3, CH<sub>3</sub>), 3.97 (s, 3, CH<sub>3</sub>), 7.15 (m, 1, aryl), 7.23 (s, 1, aryl), 7.37 (m, 1, aryl), 7.51 (d, 1, aryl, *J* = 9.3), 7.86 (dd, 1, aryl), 7.97 (d, 1, aryl, *J* = 9.4), 8.31 (m, 1, aryl), 8.35 (d, 1, aryl, *J* = 9.0). Anal. Calcd for C<sub>21</sub>H<sub>17</sub>OF: C, 82.87; H, 5.63. Found: C, 82.76; H, 5.67.

(b) *From 19.* The procedure described previously for the synthesis of 3-methoxy-7,12-dimethylbenz[a]anthracene was employed.<sup>11a</sup> Initial reaction of **19** (1.0 g, 3.3 mmol) reaction with MeLi (5.8 mL of 1.4M solution in ether, 8.2 mmol) in benzene-ether (1:1) (100 mL) gave the dimethyldiol adduct which rearranged on treatment with anhydrous HCl to 9-fluoro-7-chloromethyl-3-methoxy-12-methylbenz[a]anthracene which was reduced directly with NaBH<sub>4</sub> in DMSO to **16c**, mp 172–173 °C (42%) whose NMR spectrum agreed closely with that obtained by the alternative route.

**9-Fluoro-7,12-dimethylbenz[a]anthracen-3-ol (16d).** Demethylation of **16c** with HBr by the method used for preparation of **13c** gave **16d**, mp 200–202 °C (99%); NMR (500 MHz, acetone-*d*<sub>6</sub>) δ 2.99 (s, 3, CH<sub>3</sub>), 3.30 (s, 3, CH<sub>3</sub>), 7.15 (dd, 1, aryl, *J* = 8.9, *J* = 2.7), 7.27 (d, 1, aryl, *J* = 2.7), 7.45 (m, 1, aryl), 7.54 (d, 1, aryl, *J* = 9.4), 7.97 (dd, 1, aryl, *J* = 11.8, *J* = 2.6), 8.01 (d, 1, aryl, *J* = 9.4), 8.37 (d, 1, aryl, *J* = 8.9), 8.42 (m, 1, aryl), 8.82 (s, 1, OH). UVmax (EtOH) 298 (66 200), 247 (22 600), 211 (28 800) nm. Anal. Calcd for C<sub>20</sub>H<sub>15</sub>OF: C, 82.74; H, 5.21. Found: C, 82.63; H, 5.23.

**9-Fluoro-7,12-dimethylbenz[a]anthracene-3,4-dione (17b).** Oxidation of **16d** (150 mg, 0.52 mmol) with Fremy's salt by the procedure used for oxidation of **16b** furnished **17b**, mp 198–200 °C, (64%);

NMR  $\delta$  2.99 (s, 3, CH<sub>3</sub>), 3.19 (s, 3, CH<sub>3</sub>), 6.37 (d, 1, vinyl,  $J = 10.6$ ), 7.37 (m, 1, aryl), 7.81 (dd, 1, aryl,  $J = 11.3$ ,  $J = 2.5$ ), 8.00 (d, 1, aryl,  $J = 9.2$ ), 8.14 (d, 1, vinyl,  $J = 10.6$ ), 8.26 (m, 1, aryl), 8.28 (d, 1, aryl,  $J = 9.1$ ). Anal. Calcd for C<sub>20</sub>H<sub>13</sub>O<sub>2</sub>F: C, 78.94; H, 4.31. Found: C, 78.69; H, 4.42.

***trans*-3,4-Dihydroxy-3,4-dihydro-9-fluoro-7,12-dimethylbenz[*a*]anthracene (3c).** Reduction of **17b** (100 mg, 0.33 mmol) with NaBH<sub>4</sub> (100 mg) in ethanol (100 mL) by the usual procedure with O<sub>2</sub> bubbling through the solution for 24 h gave the dihydrodiol **3c** as a white solid, mp 200-202 °C, (50%); NMR (500 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  2.94 (s, 3, CH<sub>3</sub>), 3.06 (s, 3, CH<sub>3</sub>), 4.45 (m, 1, H<sub>3</sub>), 4.52 (m, 1, H<sub>4</sub>), 5.22 (d, 1, OH), 5.56 (d, 1, OH), 6.05 (dd, 1, vinyl,  $J = 10.2$ ,  $J = 2.2$ ), 6.92 (dd, 1, aryl,  $J = 10.2$ ,  $J = 2.0$ ), 7.44 (m, 1, aryl), 7.71 (d, 1, aryl,  $J = 9.1$ ), 7.96 (dd, 1, vinyl), 8.17 (d, 1, aryl,  $J = 9.1$ ), 8.31 (m, 1, aryl). UVmax (EtOH) 433 (10 700), 409 (11 000), 270 (107 250) 240 (29 900) nm. Anal. Calcd for C<sub>20</sub>H<sub>17</sub>O<sub>2</sub>F: C, 77.90; H, 5.52. Found: C, 77.58; H, 5.50.

**12-Acetoxy-9-fluoro-3-methoxybenz[*a*]anthracene (18).** A solution of **13** (1.70 g, 5.5 mmol) and ZnCl<sub>2</sub> (200 mg) in Ac<sub>2</sub>O (25 mL) and AcOH (25 mL) were heated at reflux for 2 h. Addition of icewater precipitated a white solid which was removed by filtration, air dried, then dissolved in a small volume of benzene and chromatographed on a short Florisil column eluted with hexane. Recrystallization from benzene-hexane gave **18** (1.52 g, 82%), mp 165-166 °C; NMR  $\delta$  2.64 (s, 3, CH<sub>3</sub>), 3.95 (s, 3, CH<sub>3</sub>), 7.21 (d, 1, aryl,  $J = 2.8$ ), 7.23 (s, 1, aryl), 7.34 (m, 1, aryl), 7.52 (d, 1, aryl,  $J = 9.0$ ), 8.17 (dd, 1, aryl,  $J = 9.5$ ,  $J = 2.4$ ), 7.67 (d, 1, aryl,  $J = 9.0$ ), 7.97 (m, 1, aryl), 8.15 (s, 1, aryl), 9.01 (d, 1, aryl,  $J = 9.0$ ). Anal. Calcd for C<sub>21</sub>H<sub>15</sub>O<sub>3</sub>F: C, 75.44; H, 4.52. Found: C, 75.38; H, 4.56.

**9-Fluoro-3-methoxybenz[*a*]anthracene-7,12-dione (19).** Oxidation of **18** to **19** was carried out by heating a solution of **18** (1.3 g, 3.89 mmol) with excess Na<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub>·H<sub>2</sub>O (2.4 g) in AcOH (20 mL) at reflux for 1 h. The product was precipitated by addition of icewater, filtered, dried, taken up in benzene, and chromatographed on a silica gel column to furnish **19** (1.1 g, 100%), mp 227-229 °C; NMR  $\delta$  3.94 (s, 3, CH<sub>3</sub>), 7.44 (dd, 1, aryl,  $J = 9.6$ ,  $J = 2.6$ ), 7.51 (d, 1, aryl,  $J = 2.5$ ), 7.72 (m, 1, aryl), 7.80 (dd, 1, aryl,  $J = 8.7$ ,  $J = 2.3$ ), 8.24 (m, 3, aryl), 9.45 (d, 1, aryl,  $J = 9.6$ ). Anal. Calcd for C<sub>19</sub>H<sub>11</sub>O<sub>3</sub>F: C, 74.51; H, 3.62. Found: C, 74.35; H, 3.66.

**6-Methoxy-1-naphthaldehyde.** To a stirred suspension of 6-methoxynaphthalene-1-carbonitrile<sup>27</sup> (3.6 g, 20 mmol) in 150 mL of heptane at -78 °C was added 40 mL of a 1M solution of *i*-Bu<sub>2</sub>AlH (40 mmol) in heptane.<sup>28</sup> Stirring was continued for 30 min, then the bath was removed and the solution was allowed to warm to room temperature for 3.5 h. Ethyl formate (4 mL) was added and stirring was continued for 1 h. The mixture was poured into a saturated solution of ammonium chloride, stirred for 20, then acidified and worked up conventionally to yield 6-methoxy-1-naphthaldehyde (3.6 g, 100%), mp 82-83 °C: NMR  $\delta$  3.93 (s, 3, CH<sub>3</sub>), 7.18 (d, 1, aryl,  $J = 2.5$ ), 7.31 (dd, 1, aryl,  $J = 2.5$ ), 7.56 (t, 1, aryl,  $J = 7.7$ ), 7.80 (d, 1, aryl,  $J = 7.1$ ), 7.95 (d, 1, aryl,  $J = 8.2$ ), 9.13 (d, 1, aryl,  $J = 9.3$ ), 10.30 (s, 1, CHO). Anal. Calcd for C<sub>12</sub>H<sub>10</sub>O<sub>2</sub>: C, 77.41; H, 5.41. Found: C, 77.51; H, 5.45.

**Reaction of *o*-Lithio-10 with 6-Methoxy-1-naphthaldehyde.** Reaction was carried out by the procedure employed for the analogous reaction with 6-methoxy-2-naphthaldehyde. The lactone product (**20a**)

(76%) had mp 82-83 °C: NMR  $\delta$  3.93 (s, 3, CH<sub>3</sub>), 7.04 (d, 1, aryl,  $J = 7.7$ ), 7.09 (d, 1, aryl,  $J = 7.9$ ), 7.10 (s, 1, CH), 7.19 (s, 1, aryl), 7.25 (m, 2, aryl), 7.33 (t, 1, aryl,  $J = 7.9$ ), 7.75 (d, 1, aryl,  $J = 8.2$ ), 7.95 (m, 1, aryl), 8.02 (d, 1, aryl,  $J = 9.2$ ). Anal. Calcd for C<sub>19</sub>H<sub>13</sub>O<sub>3</sub>F: C, 74.02; H, 4.25. Found: C, 74.01; H, 4.28.

**Reduction of Lactone 20a to Carboxylic Acid 21a.** Zinc metal (20 g) was activated by pre-washing with dilute HCl, water, and methanol, then added to a suspension of **20a** (2.0 g, 6.6 mmol) in acetic acid (100 mL). The mixture was heated at reflux for 24 h, then filtered to remove excess Zn, and poured into icewater. The solid product was filtered off, washed with water, and dried to furnish **21a** (1.97 g, 100%), mp 168-169 °C: NMR  $\delta$  3.89 (s, 3, CH<sub>3</sub>), 4.85 (s, 1, CH<sub>2</sub>), 6.55 (dd, 1, aryl,  $J = 10.1$ ,  $J = 2.4$ ), 6.93 (m, 1, aryl), 7.07 (m, 2, aryl), 7.14 (d, 1, aryl,  $J = 2.6$ ), 7.23 (s, 1, OH), 7.36 (t, 1, aryl,  $J = 7.5$ ), 7.65 (d, 1, aryl,  $J = 8.4$ ), 7.72 (d, 1, aryl,  $J = 9.2$ ), 8.14 (dd, 1, aryl,  $J = 8.8$ ). Anal. Calcd for C<sub>19</sub>H<sub>15</sub>O<sub>3</sub>F: C, 73.54; H, 4.87. Found: C, 73.60; H, 4.91.

**Conversion of 21a to the Methylketone 21b.** Reaction of **21a** with MeLi was carried out by the procedure employed for the synthesis of **15a**. The methylketone **21b** was obtained as an oil (98%); NMR  $\delta$  2.56 (s, 3, CH<sub>3</sub>), 3.88 (s, 3, CH<sub>3</sub>), 4.71 (s, 1, CH<sub>2</sub>), 6.58 (dd, 1, aryl,  $J = 10.2$ ,  $J = 2.2$ ), 6.90 (m, 1, aryl), 7.00 (d, 1, aryl,  $J = 7.1$ ), 7.06 (dd, 1, aryl,  $J = 9.2$ ,  $J = 2.5$ ), 7.14 (s, 1, aryl), 7.33 (t, 1, aryl,  $J = 7.5$ ), 7.63 (d, 1, aryl,  $J = 8.2$ ), 7.71 (d, 1, aryl,  $J = 9.2$ ), 7.74 (m, 1, aryl). **21b** was used directly in the next step.

**10-Fluoro-3-methoxy-7-methylbenz[a]anthracene (22a).** Cyclodehydration of **21b** (2.25 g, 7.3 mmol) in polyphosphoric acid by the method used for preparation of **16a** and **16c** gave **22a** (1.6 g, 76%), mp 143-144 °C (benzene-hexane): NMR  $\delta$  3.06 (s, 3, CH<sub>3</sub>), 3.96 (s, 3, CH<sub>3</sub>), 7.21-7.33 (m, 3, aryl), 7.56 (d, 1, aryl,  $J = 9.4$ ), 7.62 (dd, 1, aryl,  $J = 9.8$ ,  $J = 2.5$ ), 8.06 (d, 1, aryl,  $J = 9.4$ ), 8.25 (m, 1, aryl), 8.66 (d, 1, aryl,  $J = 8.9$ ), 8.84 (s, 1, aryl). Anal. Calcd for C<sub>20</sub>H<sub>15</sub>OF: C, 82.74; H, 5.21. Found: C, 82.68; H, 5.23.

**10-Fluoro-7-methylbenz[a]anthracen-3-ol (22b).** Demethylation of **22a** with HBr by the method used for preparation of **13c** gave **22b**, mp 211-212 °C (88%); NMR (500 MHz, acetone-*d*<sub>6</sub>)  $\delta$  3.08 (s, 3, CH<sub>3</sub>), 7.24-7.29 (m, 2, aryl), 7.39 (m, 2, aryl, OH), 7.60 (d, 1, aryl,  $J = 9.5$ ), 7.78 (dd, 1, aryl,  $J = 10.2$ ,  $J = 2.6$ ), 8.11 (d, 1, aryl,  $J = 9.5$ ), 8.40 (m, 1, aryl), 8.77 (d, 2, aryl,  $J = 8.8$ ), 9.08 (s, 1, aryl). UVmax (EtOH) 357 (6 700), 292 (62 750), 232 (32 200) 221 (31 800), 202 (32 900) nm. Anal. Calcd for C<sub>19</sub>H<sub>13</sub>OF: C, 82.59; H, 4.74. Found: C, 82.64; H, 4.77.

**10-Fluoro-7-methylbenz[a]anthracene-3,4-dione (23).** Oxidation of **22b** (600 mg, 2.2 mmol) with Fremy's salt by the procedure used for oxidation of **16b** furnished **23**, mp 197-198 °C, (95%), low solubility in organic solvents; NMR (500 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  3.13 (s, 3, CH<sub>3</sub>), 6.40 (d, 1, vinyl,  $J = 10.6$ ), 7.55 (t, 1, aryl), 7.84 (d, 1, aryl,  $J = 8.5$ ), 7.98 (d, 1, aryl,  $J = 12.0$ ), 8.13 (d, 1, aryl,  $J = 8.6$ ), 8.19 (m, 1, aryl), 8.23 (d, 1, vinyl,  $J = 10.6$ ), 8.53 (s, 1, aryl). Anal. Calcd for C<sub>19</sub>H<sub>11</sub>O<sub>2</sub>F: C, 78.61; H, 3.82. Found: C, 78.54; H, 3.93.

**trans-3,4-Dihydroxy-3,4-dihydro-10-fluoro-7-methylbenz[a]anthracene (4a).** Reduction of **23** (100 mg, 0.34 mmol) with NaBH<sub>4</sub> (100 mg) in ethanol (50 mL) by the usual procedure with O<sub>2</sub> bubbling through the solution for 24 h gave the dihydrodiol **4a** (80%) as a white solid, mp 222-224 °C; NMR (500 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  3.06 (s, 3, CH<sub>3</sub>), 4.37 (d, 1, H<sub>3</sub>,  $J = 10.1$ ), 4.74 (d, 1, H<sub>4</sub>,  $J = 11.0$ ), 5.22 (d, 1, OH), 5.56 (d,

1, OH), 6.19 (dd, 1, vinyl,  $J = 10.1$ ,  $J = 2.4$ ), 7.36 (m, 2, aryl and vinyl), 7.78 (m, 2, aryl), 8.26 (d, 1, aryl,  $J = 9.1$ ), 8.38 (m, 1, aryl), 8.75 (s, 1, aryl). UVmax (EtOH) 416 (11 500), 394 (12 600), 262 (143 000) 213 (35 200) nm. Anal. Calcd for C<sub>19</sub>H<sub>15</sub>O<sub>2</sub>F: C, 77.53; H, 5.14. Found: C, 77.59; H, 5.19.

***trans*-3,4-Dihydroxy-*anti*-1,2-epoxy-10-fluoro-7-methyl-1,2,3,4-tetrahydrobenz[*a*]-anthracene (6a).** Oxidation of **4a** (43 mg, 0.14 mmol) with *m*-CPBA by the procedure employed for the preparation of **5a** gave the *anti*-diol epoxide **6a** (31 mg, 71%), mp 188-189 °C; NMR (500 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  3.07 (s, 3, CH<sub>3</sub>), 3.82 (d, 1, H<sub>2</sub>,  $J = 4.4$ ), 3.89 (d, 1, H<sub>3</sub>,  $J = 8.3$ ), 4.48 (d, 1, H<sub>4</sub>,  $J = 8.5$ ), 5.06 (d, 1, H<sub>1</sub>,  $J = 4.5$ ), 7.45 (m, 1, aryl), 7.82 (d, 2, aryl,  $J = 9.4$ ), 8.35 (d, 1, aryl,  $J = 9.2$ ), 8.40 (m, 1, aryl), 8.99 (s, 1, aryl). UVmax (EtOH) 378 (8 700), 260 (125 800) nm. Anal. Calcd for C<sub>19</sub>H<sub>15</sub>O<sub>3</sub>F: C, 73.54; H, 4.87. Found: C, 73.66; H, 5.01.

**4-Fluoro-2-[1-(3-methoxynaphthoyl)]benzoic acid (24).** To a stirred mixture of the lactone **20a** (3.08 g, 10 mmol) in 40 mL of 25% KOH and 20 mL of pyridine was added 2.5 g of powdered KMnO<sub>4</sub>, and the mixture was heated at reflux for 5 h. The hot mixture was filtered, the residue was washed with water, and the filtrate was washed with ether to remove any unreacted lactone. The basic layer was acidified with HCl, and the precipitate was filtered, washed with water and dried to provide **24** (2.8 g, 86%), mp 204-205 °C (ether-hexane); NMR  $\delta$  3.93 (s, 3, CH<sub>3</sub>), 7.14-7.32 (m, 6, aryl and OH), 7.84 (d, 1, aryl,  $J = 8.1$ ), 7.98 (m, 1, aryl), 8.88 (d, 1, aryl,  $J = 9.4$ ). Anal. Calcd for C<sub>19</sub>H<sub>13</sub>O<sub>4</sub>F: C, 70.37; H, 4.04. Found: C, 70.44; H, 4.11.

**Reaction of 24 with Methylolithium.** To a stirred solution of **24** (2.25 g, 6.9 mmol) in 50 mL of THF was added 15 mL of a 1.4 M solution of MeLi (20.8 mmol) in ether. The solution was stirred at room temperature for 2 h and worked up conventionally to provide lactone **20b** (2.1 g, 95%), mp 149-150 °C (benzene-hexane); NMR  $\delta$  2.20 (s, 3, CH<sub>3</sub>), 3.91 (s, 3, CH<sub>3</sub>), 7.14-7.35 (m, 6, aryl and OH), 7.71 (d, 1, aryl,  $J = 7.8$ ), 7.95 (m, 1, aryl), 8.38 (d, 1, aryl,  $J = 9.4$ ). Anal. Calcd for C<sub>20</sub>H<sub>15</sub>O<sub>3</sub>F: C, 74.52; H, 4.69. Found: C, 74.55; H, 4.71.

**Reduction of Lactone 20b to Carboxylic Acid 21c.** Reduction of **20b** (1.5 g, 4.7 mmol) with zinc and acetic acid was carried out by the procedure employed for the reduction of **20a** to yield **21c** (1.5 g, 99%), mp 165.5-166.5 °C (benzene-hexane); NMR  $\delta$  1.70 (d, 3, CH<sub>3</sub>,  $J = 6.9$ ), 3.83 (s, 3, CH<sub>3</sub>), 6.04 (q, 1, CH), 6.72 (dd, 1, aryl,  $J = 10.0$ ,  $J = 2.2$ ), 6.88 (m, 1, aryl), 7.03 (dd, 1, aryl,  $J = 9.2$ ,  $J = 2.4$ ), 7.08 (s, 1, OH), 7.30 (d, 1, aryl,  $J = 7.1$ ), 7.42 (t, 1, aryl,  $J = 7.7$ ), 7.63 (d, 1, aryl,  $J = 8.2$ ), 7.79 (d, 1, aryl,  $J = 9.3$ ), 8.08 (m, 1, aryl). Anal. Calcd for C<sub>20</sub>H<sub>17</sub>O<sub>3</sub>F: C, 74.06; H, 5.28. Found: C, 74.07; H, 5.32.

**7-Acetoxy-10-Fluoro-3-methoxy-12-methylbenz[*a*]anthracene (25a).** Cyclization of **20b** (1.20 g, 3.7 mmol) with ZnCl<sub>2</sub> and Ac<sub>2</sub>O in acetic acid by the method used for preparation of **18** gave **25a** (1.2 g, 94%), mp 219.5-221.5 °C (benzene-hexane): NMR  $\delta$  2.61 (s, 3, CH<sub>3</sub>), 3.23 (s, 3, CH<sub>3</sub>), 3.96 (s, 3, CH<sub>3</sub>), 7.18 (dd, 1, aryl,  $J = 9.0$ ,  $J = 2.8$ ), 7.22 (d, 1, aryl,  $J = 2.8$ ), 7.35 (m, 1, aryl), 7.50 (d, 1, aryl,  $J = 9.2$ ), 7.62 (d, 1, aryl,  $J = 9.2$ ), 7.87 (dd, 1, aryl,  $J = 11.8$ ,  $J = 2.3$ ), 7.94 (t, 1, aryl), 8.43 (d, 1, aryl,  $J = 9.1$ ). Anal. Calcd for C<sub>22</sub>H<sub>17</sub>O<sub>3</sub>F: C, 75.85; H, 4.92. Found: C, 75.95; H, 4.95.

**10-Fluoro-3-methoxy-12-methylbenz[*a*]anthracene (25b).** Treatment of **25a** (1.20 g, 3.4 mmol) with HI/H<sub>2</sub>PO<sub>3</sub> by the procedure employed for reduction of **13a** to **13b** gave the ketone **26** arising from

deacetylation. The crude **26** was dissolved in benzene and chromatographed on a short column of Florisil. Evaporation of the fraction eluted with benzene gave **26** (1.0 g, 99%), mp 148-149 °C: NMR  $\delta$  1.54 (d, 3, CH<sub>3</sub>), 3.89 (s, 3, CH<sub>3</sub>), 4.70 (q, 1, CH), 6.90-8.45 (m, 8, aryl). Anal. Calcd for C<sub>20</sub>H<sub>15</sub>O<sub>2</sub>F: C, 78.42; H, 4.94. Found: C, 78.55; H, 4.96.

A mixture of **26** (1.0 g, 3.4 mmol) and NaBH<sub>4</sub> (2.0 g) in 150 mL of ethanol was stirred at room temperature for 2 h, then the ethanol was evaporated, and the solid residue was washed with water, filtered, and dried. A solution of the crude alcohol product and *p*-toluenesulfonic acid (100 mg) in benzene was heated at reflux for 1 h, then cooled and passed through a short column of silica gel to provide **25b** (885 mg, 90%), mp 125-126 °C: NMR  $\delta$  3.27 (s, 3, CH<sub>3</sub>), 3.97 (s, 3, CH<sub>3</sub>), 7.18 (d, 1, aryl, *J* = 9.0), 7.24 (d, 1, aryl, *J* = 2.4), 7.30 (t, 1, aryl, *J* = 8.2), 7.46 (d, 1, aryl, *J* = 8.9), 7.62 (d, 1, aryl, *J* = 9.2), 7.87 (d, 1, aryl, *J* = 12.1), 7.98 (m, 1, aryl), 8.15 (s, 1, aryl), 8.50 (d, 1, aryl). Anal. Calcd for C<sub>20</sub>H<sub>15</sub>OF: C, 82.74; H, 5.21. Found: C, 82.55; H, 5.26.

**10-Fluoro-12-methylbenz[a]anthracene-3-ol (25c)**. Demethylation of **25b** (630 mg, 2.2 mmol) with HBr by the usual procedure gave **25c** (580 mg, 97%), mp 209-210 °C: NMR (500 MHz, acetone-*d*<sub>6</sub>)  $\delta$  3.28 (s, 3, CH<sub>3</sub>), 7.18 (dd, 1, aryl, *J* = 8.9, *J* = 2.6), 7.28 (d, 1, aryl, *J* = 2.7), 7.37 (m, 1, aryl), 7.47 (d, 1, aryl, *J* = 8.9), 7.65 (d, 1, aryl, *J* = 9.0), 7.94 (dd, 1, aryl, *J* = 12.4, *J* = 2.2), 8.10 (m, 1, aryl), 8.27 (s, 1, aryl), 8.52 (d, 1, aryl, *J* = 8.9), 8.72 (s, 1, OH). UVmax (EtOH) 290 (81 850), 238 (32 000) 209 (37 300) nm. Anal. Calcd for C<sub>19</sub>H<sub>13</sub>OF: C, 82.59; H, 4.74. Found: C, 82.66; H, 4.75.

**trans-3,4-Dihydroxy-3,4-dihydro-10-fluoro-12-methylbenz[a]anthracene (4b)**. Oxidation of **25c** (350 mg, 1.27 mmol) with Fremy's salt by the procedure used for oxidation of **16b** gave a ~2:1 mixture of 10-fluoro-12-methylbenz[a]anthracene-3,4-dione (**27a**) and the related hydroquinone (82%) (by NMR). A suspension of this mixture (200 mg) and NaBH<sub>4</sub> (2 g) in ethanol (150 mL) was stirred at room temperature with O<sub>2</sub> bubbling through the solution for 24 h and worked up in the usual manner to yield **4b** (82%), mp 226-228 °C: NMR (500 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  3.04 (s, 3, CH<sub>3</sub>), 4.43 (m, 1, H<sub>3</sub>), 4.55 (d, 1, H<sub>4</sub>, *J* = 11.3), 5.23 (d, 1, OH, *J* = 4.8), 5.57 (d, 1, OH, *J* = 6.0), 6.08 (dd, 1, vinyl, *J* = 10.2, *J* = 1.9), 7.03 (m, 1, vinyl), 7.41 (m, 1, aryl), 7.67 (d, 1, aryl, *J* = 8.6), 7.86 (m, 1, aryl), 7.93 (m, 1, aryl), 8.12 (m, 1, aryl), 8.40 (m, 1, aryl). UVmax (EtOH) 424 (12 500), 400 (14 200), 267 (144 400) 211 (40 900) nm. Anal. Calcd for C<sub>19</sub>H<sub>15</sub>O<sub>2</sub>F: C, 77.53; H, 5.14. Found: C, 77.27; H, 5.21.

**7-Acetoxy-10-Fluoro-3-methoxybenz[a]anthracene (28)**. Treatment of **21a** (1.35 g, 4.35 mmol) with ZnCl<sub>2</sub> and Ac<sub>2</sub>O in acetic acid by the method used for preparation of **18** gave **28** (1.40 g, 99%), mp 186-187 °C (benzene-hexane): NMR  $\delta$  2.62 (s, 3, CH<sub>3</sub>), 3.95 (s, 3, CH<sub>3</sub>), 7.20 (d, 1, aryl, *J* = 2.6), 7.20-7.35 (m, 2, aryl), 7.56 (d, 1, aryl, *J* = 9.3), 7.64 (dd, 1, aryl, *J* = 9.9, *J* = 2.3), 7.68 (d, 1, aryl, *J* = 9.3), 7.91 (m, 1, aryl), 8.61 (d, 1, aryl, *J* = 9.0), 8.82 (s, 1, aryl). Anal. Calcd for C<sub>21</sub>H<sub>15</sub>O<sub>3</sub>F: C, 75.44; H, 4.52. Found: C, 75.50; H, 4.51.

**10-Fluoro-3-methoxybenz[a]anthracene-7,12-dione (29)**. Oxidation of **28** (1.10 g, 3.3 mmol) with sodium dichromate by the method used to oxidize **18** to **19** gave **29** (1.00 g, 99%), as a yellow solid, mp 213-215 °C; NMR  $\delta$  3.96 (s, 3, CH<sub>3</sub>), 7.16 (d, 1, aryl, *J* = 2.5), 7.38 (m, 2, aryl), 7.90 (d, 1, aryl),

8.05 (d, 1, aryl,  $J = 8.5$ ), 8.26 (m, 1, aryl), 8.31 (d, 1, aryl,  $J = 8.5$ ), 9.56 (d, 1, aryl,  $J = 8.6$ ). Anal. Calcd for  $C_{19}H_{11}O_3F$ : C, 74.51; H, 3.62. Found: C, 74.38; H, 3.74.

**10-Fluoro-3-methoxy-7,12-dimethylbenz[*a*]anthracene (30a).** Conversion of **29** (950 mg, 3.1 mmol) to **30a** was carried out by the procedure used for the synthesis of **16c** from **19**.<sup>11a</sup> There was obtained **30a**, mp 141-142 °C (32%); NMR  $\delta$  3.03 (s, 3, CH<sub>3</sub>), 3.22 (s, 3, CH<sub>3</sub>), 3.97 (s, 3, CH<sub>3</sub>), 7.14 (d, 1, aryl,  $J = 9.0, J = 2.7$ ), 7.22 (m, 1, aryl), 7.33 (m, 1, aryl), 7.48 (d, 1, aryl,  $J = 9.3$ ), 7.87 (dd, 1, aryl,  $J = 11.9, J = 2.5$ ), 7.97 (d, 1, aryl,  $J = 9.4$ ), 8.29 (m, 1, aryl), 8.36 (d, 1, aryl,  $J = 9.0$ ). Anal. Calcd for  $C_{21}H_{17}OF$ : C, 82.87; H, 5.63. Found: C, 82.85; H, 5.65.

**10-Fluoro-7,12-dimethylbenz[*a*]anthracene-3-ol (30b).** Demethylation of **30a** with HBr in HOAc by the method used for preparation of **13c** gave **30b**, mp 191-192 °C (94%); NMR (500 MHz, acetone-*d*<sub>6</sub>)  $\delta$  3.05 (s, 3, CH<sub>3</sub>), 3.24 (s, 3, CH<sub>3</sub>), 7.15 (dd, 1, aryl,  $J = 8.9, J = 2.7$ ), 7.27 (d, 1, aryl,  $J = 2.6$ ), 7.42 (m, 1, aryl), 7.52 (d, 1, aryl,  $J = 9.4$ ), 7.94 (dd, 1, aryl,  $J = 12.1, J = 2.5$ ), 8.02 (d, 1, aryl,  $J = 9.4$ ), 8.40 (d, 1, aryl,  $J = 8.9$ ), 8.44 (m, 1, aryl). UVmax (EtOH) 297 (75 500), 210 (42 100) nm. Anal. Calcd for  $C_{20}H_{15}OF$ : C, 82.74; H, 5.21. Found: C, 82.68; H, 5.21.

**10-Fluoro-7,12-dimethylbenz[*a*]anthracene-3,4-dione (27b).** Oxidation of **30b** (290 mg, 1.0 mmol) with Fremy's salt by the procedure used for oxidation of **16b** furnished **27b**, mp 180-182 °C (66%), poorly soluble; NMR (500 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  3.04 (s, 3, CH<sub>3</sub>), 3.23 (s, 3, CH<sub>3</sub>), 6.37 (d, 1, vinyl,  $J = 10.4$ ), 7.57 (m, 1, aryl), 7.85 (d, 1, aryl,  $J = 9.0$ ), 7.97 (m, 1, aryl), 8.21 (m, 1, vinyl), 8.44 (m, 2, aryl). Anal. Calcd for  $C_{20}H_{13}O_2F$ : C, 78.94; H, 4.31. Found: C, 78.89; H, 4.50.

**trans-3,4-Dihydroxy-3,4-dihydro-10-fluoro-7,12-dimethylbenz[*a*]anthracene (4c).** Reduction of **27b** with NaBH<sub>4</sub>/O<sub>2</sub> by the usual procedure with O<sub>2</sub> bubbling through the solution for 48 h (monitored by TLC) gave the dihydrodiol **4c** as a white solid, mp 183-184 °C, (50%); NMR (500 MHz, DMSO-*d*<sub>6</sub>)  $\delta$  2.99 (s, 3, CH<sub>3</sub>), 3.00 (s, 3, CH<sub>3</sub>), 4.46 (m, 1, H<sub>3</sub>), 4.52 (m, 1, H<sub>4</sub>), 5.23 (d, 1, OH,  $J = 4.8$ ), 5.57 (d, 1, OH,  $J = 6.0$ ), 6.04 (dd, 1, vinyl,  $J = 10.0, J = 2.0$ ), 6.91 (dd, 1, vinyl,  $J = 10.2, J = 2.0$ ), 7.42 (m, 1, aryl), 7.69 (d, 1, aryl,  $J = 9.1$ ), 7.85 (dd, 1, aryl,  $J = 12.3, J = 2.3$ ), 8.22 (d, 1, aryl,  $J = 9.1$ ), 8.39 (m, 1, aryl). UVmax (EtOH) 435 (8 900), 410 (10 100), 271 (118 000) 211 (32 500) nm. Anal. Calcd for  $C_{20}H_{17}O_2F$ : C, 77.90; H, 5.56. Found: C, 77.72; H, 5.61.

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