

## Synthesis of Dibenz[*a,c*]anthracene 1,2-Oxide and 3,4-Oxide from Dibromo-trifluoroacetates: Concomitant Formation of Oxepines

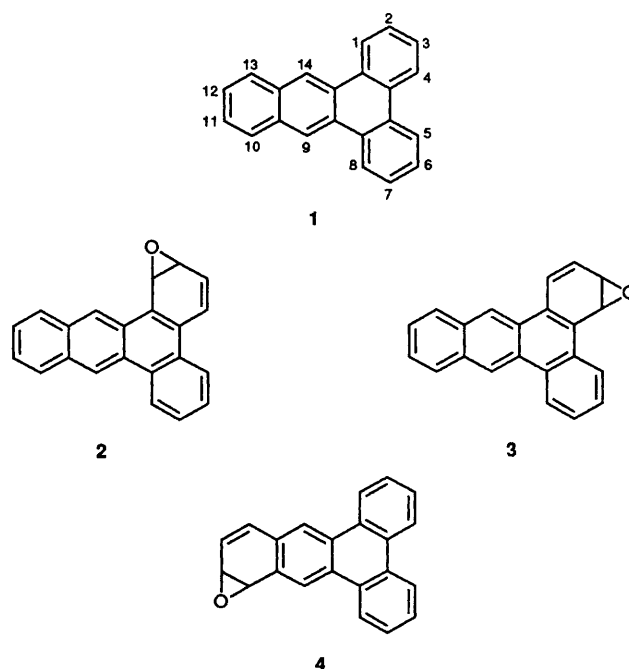
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The synthesis and spectral properties of 1 $\alpha$ -acetoxy-2 $\beta$ ,4 $\alpha$ -dibromo-, 4 $\alpha$ -acetoxy-1 $\alpha$ ,3 $\beta$ -dibromo-, 2 $\beta$ ,4 $\alpha$ -dibromo-1 $\alpha$ -trifluoroacetoxy- and 1 $\alpha$ ,3 $\beta$ -dibromo-4 $\alpha$ -trifluoroacetoxy-1,2,3,4-tetrahydrodibenz[*a,c*]anthracene are described. The reaction of the two dibromo acetates with anhydrous sodium methoxide produces labile dibenz[*a,c*]anthracene 1,2-oxide and dibenz[*a,c*]anthracene 3,4-oxide concomitantly with relatively major amounts of comparatively stable benz[1',2':3,4]anthra[1,2-*b*]oxepine or benz[1',2':3,4]anthra[2,1-*b*]oxepine, respectively. No improvement in the formation of the two arene oxides is noted when a similar reaction is carried out with the two dibromo trifluoroacetates in which the ester group is much more labile than that in the dibromo acetates. Under milder reaction conditions, the 2 $\beta$ ,4 $\alpha$ -dibromo-1 $\alpha$ -trifluoroacetate is hydrolysed to the 2 $\beta$ ,4 $\alpha$ -dibromo-1 $\alpha$ -alcohol which, on subsequent treatment with sodium methoxide, also produces benz[1',2':3,4]anthra[1,2-*b*]oxepine as one of the major products. These studies show for the first time that the use of dibromo esters with a labile ester group has no advantage in the synthesis of the two aforementioned arene oxides because dibromo alcohols produced in these reactions are the intermediates for the formation not only of arene oxides but also of oxepines as well.

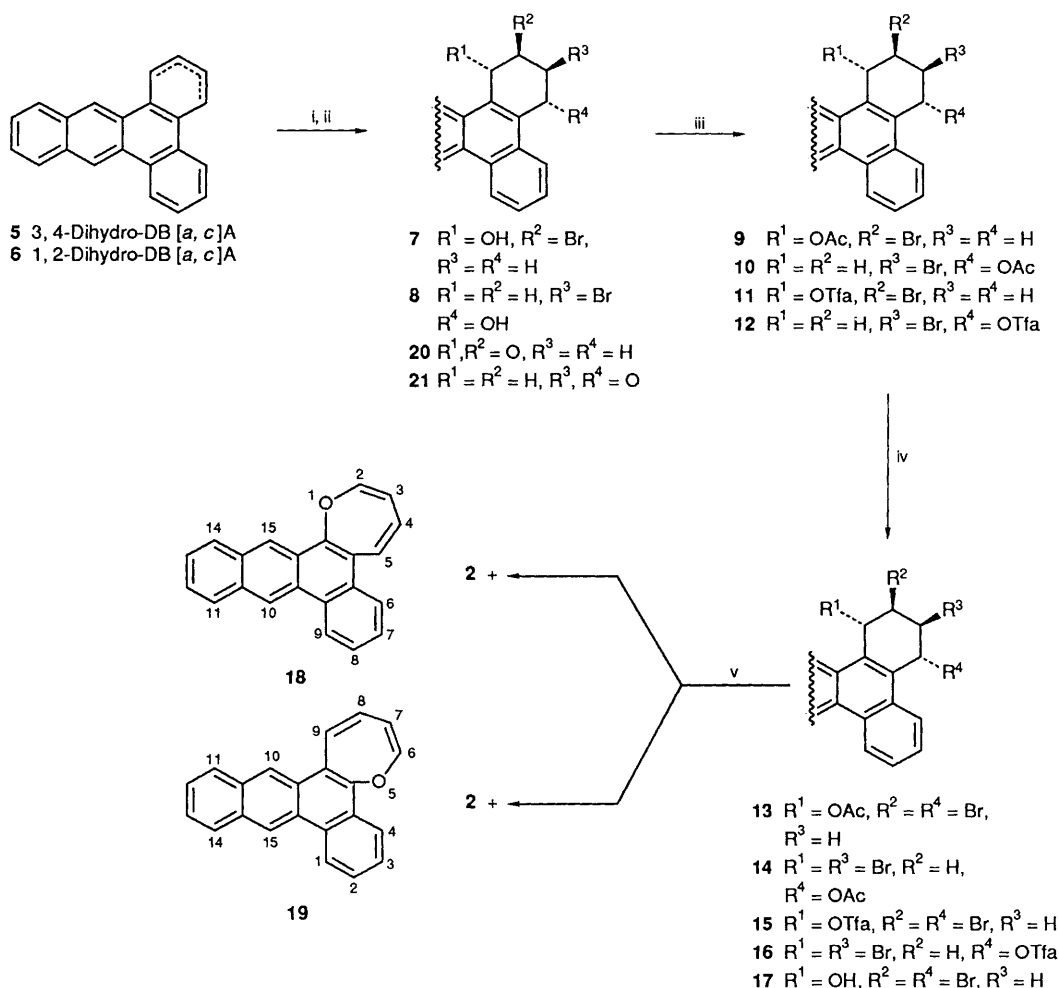
The environmental pollutant dibenz[*a,c*]anthracene **1** (DB[*a,c*]A), despite being a weak carcinogen,<sup>1</sup> is usually a more potent mutagen than are the environmental carcinogens benzo[*a*]pyrene<sup>2,3</sup> and dibenz[*a,h*]anthracene,<sup>4</sup> and exhibits tumour-initiating activity comparable to that of benz[*a*]anthracene<sup>5</sup> and chrysene.<sup>6</sup> DB[*a,c*]A **1** has previously been shown<sup>7</sup> to be metabolized by mammalian liver to its three theoretically possible dihydro diols, viz. *trans*-1,2-dihydroxy-1,2-dihydro-, *trans*-3,4-dihydroxy-3,4-dihydro- and *trans*-10,11-dihydroxy-10,11-dihydro-DB[*a,c*]A, presumably by the usual epoxide hydrolase-catalysed hydration of the initially formed arene oxide metabolites **2**, **3** and **4**, respectively. However, none of these dihydro diols appears to be the major metabolite responsible for the metabolic activation of the parent hydrocarbon.<sup>2,8</sup> Therefore, the chemical synthesis of DB[*a,c*]A 1,2-oxide **2** and DB[*a,c*]A 3,4-oxide **3** was undertaken in order to assess their potential role in the metabolic activation of DB[*a,c*]A.<sup>9</sup> The availability of these arene oxides, including the previously known DB[*a,c*]A 10,11-oxide **4**,<sup>10</sup> would permit one to study their biological activity (*e.g.*, mutagenicity, carcinogenicity) and behaviour as a substrate in solvolysis reactions and for the epoxide hydrolase enzyme.

The chemical synthesis of the arene oxides of polynuclear aromatic hydrocarbons (PAHs) is documented in the literature. Among various synthetic routes available,<sup>11–13</sup> the dibromo ester route<sup>11</sup> has been found quite successful in preparing various labile, non-K-region arene oxides of PAHs. Recently, Boyd *et al.*<sup>14</sup> observed that base treatment of a dibromo acetate normally produced a mixture of an arene oxide and a relatively stable by-product identified as an oxepine (see below). The ratio of arene oxide to oxepine formed varies greatly with the structure of the aromatic nucleus of a given dibromo acetate. Generally, those dibromo acetates in which the tetrahydrobenzo ring carrying the dibromo and acetoxy substituents is surrounded by two bay-regions produce significant amounts of oxepines as by-products. The presence of the variable amounts of oxepine in the reaction mixture has severely restricted the isolation and purification of benzo[*e*]pyrene 9,10-oxide<sup>15</sup> and DB[*a,c*]A 1,2-oxide **2**.<sup>16</sup> In a pioneering study, Yagi and Jerina<sup>11</sup> preferred to use a dibromo trifluoroacetate for the



synthesis of arene oxides since, in contrast to the dibromo acetate, it could be hydrolysed to a dibromo alcohol in the presence of the highly reactive bromine substituent present at the other benzylic position. The formation of arene oxides with high purity in this 'one-pot' reaction depends upon how efficiently dibromo esters are hydrolysed to dibromo alcohols. Therefore, in addition to dibromo acetates **13** and **14**, dibromo trifluoroacetates **15** and **16** were also synthesized in order that their utility in the preparation of DB[*a,c*]A 1,2-oxide and DB[*a,c*]A 3,4-oxide, respectively, could be studied. An analogous dibromo trifluoroacetate has recently been shown<sup>17</sup> to be converted efficiently into triphenylene 1,2-oxide without the formation of an oxepine as a by-product.

Both dihydro-DB[*a,c*]As **5** and **6** required for the synthesis



**Scheme 1** Reagents: i, NBA,  $H^+$ ; ii, NaOH; iii,  $Ac_2O$ , pyridine or TFAA; iv, NBS, AIBN; v, NaOMe

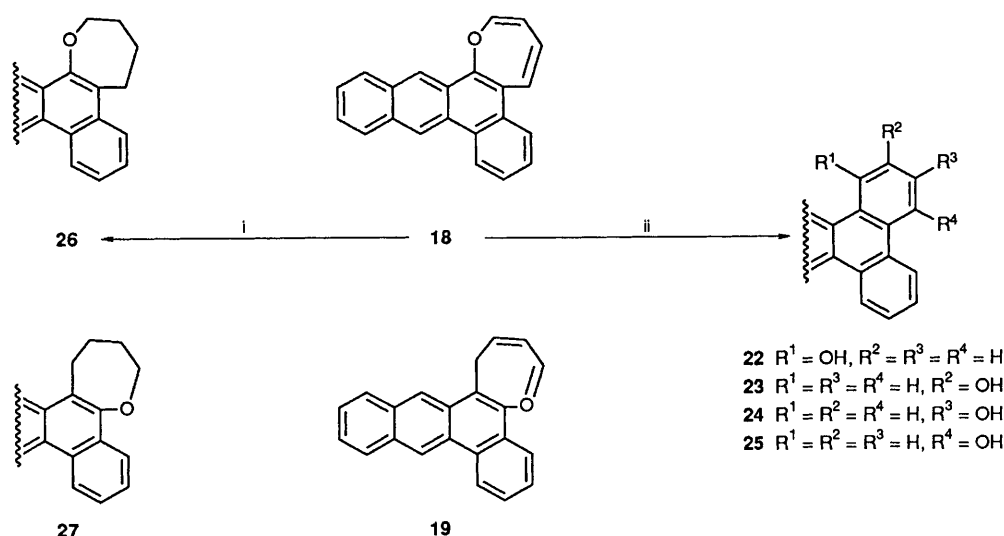
of dibromo esters were obtained as described earlier<sup>18</sup> and were then treated with *N*-bromoacetamide (NBA) in aq. tetrahydrofuran (THF) containing a trace of HCl to produce high yields of the corresponding bromohydrins **7** and **8**. Treatment of these bromohydrins with acetic anhydride–pyridine or with trifluoroacetic anhydride (TFAA) ( $Tf_2O$ ) produced the desired bromo acetates **9** and **10** or bromo trifluoroacetates **11** and **12** in almost quantitative yields. The  $^1H$  NMR spectrum of these bromo esters confirmed their structures and indicated that bromo ester groupings in these compounds prefer a *quasi*-axial conformation ( $J_{1,2}$  for **9** and **11** = 3.0 Hz;  $J_{3,4}$  for **10** and **12** = 2.0 Hz). Such a conformation was expected due to the presence of bromo ester substituents in the sterically hindered bay-region.<sup>11</sup> Treatment of bromohydrins or their acetates with NaOH (40%) at 0 °C produced the corresponding tetrahydro epoxides **20** and **21**.

Bromination of the unsubstituted benzylic position in bromo acetates **9** and **10** and bromo trifluoroacetates **11** and **12** with *N*-bromosuccinimide (NBS) in the presence of a radical initiator,  $\alpha, \alpha'$ -azoisobutyronitrile (AIBN), proceeded in high yield to produce the corresponding dibromo esters **13–16** (see Scheme 1). Although dibromo acetates **13** and **14** were fairly stable at –20 °C, dibromotrifluoroacetates **15** and **16** had a tendency to decompose at freezer temperature (–20 °C) with time. Inspection of the  $^1H$  NMR spectra of both the bromo esters and the resulting dibromo esters with extensive decoupling experiments suggested that, in contrast to bromo ester substituents in bromo esters **9–12**, the bromo ester substituents in dibromo esters **13–16** prefer a *quasi*-diequatorial

conformation as evident from the large coupling constant between the methine protons carrying these functional groups ( $J_{1,2}$  for **13** and **15** = 7.0 Hz and  $J_{3,4}$  for **14** and **16** = 6.0 Hz). Furthermore, the equality of  $J_{3,4}$  and  $J_{3',4'}$  in dibromo esters **13** and **15**, and that of  $J_{1,2}$  and  $J_{1,2'}$  in dibromo esters **14** and **16**, suggested that the benzylic bromine substituent in these compounds occupies a *quasi*-axial conformation.<sup>11</sup>

The existence of bromo ester groups of dibromo esters **13–16** in a *quasi*-diequatorial conformation is unusual, especially if these groups are part of the sterically hindered bay-region. Only recently have  $^1H$  NMR spectra of analogous dibromo ester derivatives of the structurally related PAHs benzo[*e*]pyrene and triphenylene been reported in the literature.<sup>15,17</sup> As observed for the dibromo esters **13–16** of DB[a,c]A, the bromo ester groups of the dibromo trifluoroacetate of triphenylene<sup>17</sup> also occupy a *quasi*-diequatorial conformation ( $J_{1,2}$  7.0 Hz). However, in contrast to the above observation, the analogous bromo ester groups of the dibromo acetate of benzo[*e*]pyrene<sup>15</sup> occupy, preferentially, a *quasi*-axial conformation as evident from the small coupling constant between the methine protons 9-H and 10-H ( $J_{9,10}$  1.6 Hz). The reason for the existence of the bromo ester groups of dibromo esters of DB[a,c]A and triphenylene in the *quasi*-diequatorial conformation, but not that of the dibromo ester of benzo[*e*]pyrene, is at present unknown.

Dibromo acetates **13** and **14** were treated with sodium methoxide at 0–4 °C (see Scheme 1) and the products were isolated by working up the reaction mixture at low temperature (0–5 °C).  $^1H$  NMR analysis of the products in each case

Scheme 2 Reagents: i,  $H_2/Pd-C$ ; ii,  $H^+$ 

indicated that none of the isolated products contained showed proton signals typical of those of the epoxide ring protons of arene oxides.<sup>11</sup> Careful column chromatography (basic alumina) of the crude mixture obtained as above from compounds **13** and **14** at  $-15^\circ C$  gave, in each case, a major compound identified as benz[1',2':3,4]anthra[1,2-*b*]oxepine **18** and benz[1',2':3,4]anthra[2,1-*b*]oxepine **19**, respectively (see Scheme 1). Further elution of the column gave a mixture of 1-hydroxy-DB[*a,c*]A **22** and 2-hydroxy-DB[*a,c*]A **23** from compound **13**, and 3-hydroxy-DB[*a,c*]A **24** and 4-hydroxy-DB[*a,c*]A **25** from compound **14**. The substitution of dibromotrifluoroacetates **15** and **16** for dibromo acetates **13** and **14**, respectively, in these reactions also produced the corresponding oxepines **18** and **19** and phenols **22**–**25**. Since arene oxides are known to be fairly stable in basic medium in the dark,<sup>14,15</sup> and may isomerize to phenols (*via* NIH shift) under isolation conditions, we attempted to analyse the product(s) formed after treatment of the dibromo esters **13**–**16** with NaOMe in [ $^2H_8$ ]THF solvent in an NMR tube at  $0^\circ C$  in the dark. The dibromo esters **13** and **15** were readily (within 1 h) transformed into a 60:40 mixture of the oxepine **18** and DB[*a,c*]A 1,2-oxide **2**. Similarly, dibromo esters **14** and **16** produced almost the same ratio of the oxepine **19** and DB[*a,c*]A 3,4-oxide **3**. A similar result has recently been reported from dibromo acetate **13** by Boyd and O'Kane.<sup>16</sup> No particular advantage was found in prior hydrolysis of the dibromo trifluoroacetate **15** by Amberlite-400 ( $OH^-$ ) at  $0^\circ C$  to give the dibromo alcohol **17** and subsequent treatment of compound **17** with NaOMe. This procedure also produced a high proportion of the oxepine **18**. The chemical structure of oxepines **18** and **19**, which showed a molecular ion  $M^+$  at  $m/z$  294, were established by comparison of their  $^1H$  NMR spectra with that of 1-benzoxepine<sup>19</sup> and analogous compounds<sup>15</sup> and by extensive decoupling experiments. As reported for the analogous 1-benzoxepine,<sup>19</sup> oxepines **18** and **19** also undergo catalytic hydrogenation (see Scheme 2) to produce the corresponding tetrahydro derivatives **26** and **27**, and acid-catalysed (trifluoroacetic acid) isomerization to produce 1-hydroxy-DB[*a,c*]A **22** and 4-hydroxy-DB[*a,c*]A **25**, respectively.

Recently, Boyd *et al.*<sup>14</sup> have predicted the ease of formation of oxepines from dibromo alcohols by using Perturbational Molecular Orbital (PMO) calculations. According to these calculations, those dibromo alcohols or their precursor dibromo esters for which loss of resonance energy ( $\Delta E_R$ ) associated with the formation of oxepine is less than 4.9 kcal

$mol^{-1}$  should produce arene oxides simultaneously with a comparable amount of oxepines, and consequently are not appropriate intermediates for the synthesis of labile arene oxides with high purity. From over seventy arene oxide derivatives of PAHs considered,<sup>20</sup> the loss of resonance energy ( $\Delta E_R$ ) during the formation of DB[*a,c*]A 1,2-oxide **2** and DB[*a,c*]A 3,4-oxide **3** from the corresponding dibromo alcohols was predicted from PMO calculations to have the lowest value, *i.e.* 2.3 kcal  $mol^{-1}$ .

To date, the formation of oxepines **18** and **19** as products from liver microsomal metabolism of the highly mutagenic DB[*a,c*]A **1** has not been reported. However, the characterization of 1,2-dihydroxy-1,2-dihydro-DB[*a,c*]A and 3,4-dihydroxy-3,4-dihydro-DB[*a,c*]A as minor metabolites of DB[*a,c*]A indicates that the parent hydrocarbon is metabolized<sup>7</sup> by mixed-function oxidases to the arene oxides **2** and **3**. Since these and similar arene oxides can readily undergo 'oxygen walk' under ambient room-light conditions to produce oxepines,<sup>16</sup> it is likely that such oxepines, if produced, may contribute in part to the biological response exhibited by a parent hydrocarbon, especially *in vitro* bioassays performed under room-light condition. Our studies,<sup>21</sup> however, indicated that oxepines **18** and **19** were not predominantly involved in the mutagenic activity of DB[*a,c*]A.

## Experimental

$^1H$  NMR spectra were recorded on a JOEL-270FX spectrometer at the Department of Biochemistry, State University of New York at Buffalo. Coupling constants ( $J$ ) are recorded in hertz and chemical shifts in parts per million ( $\delta$ ) with tetramethylsilane as internal standard. Mass spectra were obtained on a KRATOS MS80RFA spectrometer in the Department of Biophysics, State University of New York at Buffalo. Elemental microanalyses were performed by the Galbraith Laboratories, Inc., Knoxville, TN. Dry-column-grade silica gel was purchased from ICN Pharmaceuticals. Preparative (PLC) and analytical silica gel plates were purchased from Analtech, Newark, DE. M.p.s were taken in a sealed capillary tube and are uncorrected. The designations  $\alpha$  and  $\beta$  are used to indicate relative stereochemistry. Light petroleum refers to that fraction boiling in the range  $30$ – $60^\circ C$ .

\* 1 cal = 4.184 J.

( $\pm$ )-1 $\alpha$ -Acetoxy-2 $\beta$ -bromo-1,2,3,4-tetrahydrodibenz[*a,c*]-anthracene **9**.—*Method A*. A solution of 3,4-dihydrodibenz[*a,c*]anthracene **5**<sup>18</sup> (560 mg, 2 mmol) in THF (8 cm<sup>3</sup>)–water (3 cm<sup>3</sup>) at 0 °C was treated with NBA (280 mg, 2.13 mmol) and a drop of 20% HCl. After being stirred for 20 min under Ar, the reaction mixture was quenched by the addition of 2–3 drops of aq. NaHCO<sub>3</sub> (pH 6.7). Most of the THF was distilled off under reduced pressure, and the residual crystalline solid was filtered, washed with water and dried under vacuum. The crude solid was recrystallized from diethyl ether–ethanol to produce bromohydrin **7** (655 mg, 87%) as a crystalline solid, m.p. 141–142 °C;  $\delta_{\text{H}}$ (270 MHz; CDCl<sub>3</sub>) 2.35–2.75 (3 H, m, 3-H<sub>2</sub> and OH), 3.20–3.40 (2 H, m, 4-H<sub>2</sub>), 4.80 (1 H, m, 2-H), 5.72 (1 H, m, 1-H), 7.52–8.15 (7 H, m, ArH), 8.73 (1 H, s, 14-H), 8.84 (1 H, d, *J*<sub>7,8</sub> 7.3, 8-H) and 9.15 (1 H, s, 9-H).

To a cooled, stirred solution of the above bromohydrin **7** (310 mg, 0.882 mmol) in pyridine (8 cm<sup>3</sup>) was added dropwise acetic anhydride (0.5 cm<sup>3</sup>). The reaction mixture was stirred at room temperature for 24 h, acidified with ice-cold 10% aq. HCl, and extracted with CH<sub>2</sub>Cl<sub>2</sub>. The extract was washed with water, dried (K<sub>2</sub>CO<sub>3</sub>) and evaporated under reduced pressure. The residual solid was recrystallized from diethyl ether to produce the title compound **9** (302 mg, 88%) as crystals, m.p. 177–178 °C (decomp.) (Found: C, 68.65; H, 4.6. C<sub>24</sub>H<sub>19</sub>BrO<sub>2</sub> requires C, 68.73; H, 4.53%);  $\delta_{\text{H}}$ (270 MHz; CDCl<sub>3</sub>) 2.10 (3 H, s, 1-OAC), 2.35–2.70 (2 H, m, 3-H<sub>2</sub>), 3.39 (2 H, m, 4-H<sub>2</sub>), 4.78 (1 H, dd, *J*<sub>2,3</sub> 3 and *J*<sub>2,3'</sub> 6, 2-H), 6.87 (1 H, br s, 1-H), 7.40–8.75 (7 H, m, ArH), 8.28 (1 H, s, 14-H), 8.87 (1 H, d, *J*<sub>7,8</sub> 7.6, 8-H) and 9.19 (1 H, s, 9-H).

*Method B*. A mixture of alkene **5** (560 mg, 2 mmol), acetic acid (15 cm<sup>3</sup>), CH<sub>2</sub>Cl<sub>2</sub> (5 cm<sup>3</sup>), NBA (331 mg, 2.2 mmol), and 1 drop of 20% HCl was stirred at 15–20 °C under Ar for 1 h. The reaction mixture was poured into ice-cold water (100 cm<sup>3</sup>), and then was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3  $\times$  50 cm<sup>3</sup>). The combined extracts were washed successively and carefully with 10% aq. NaHCO<sub>3</sub> (3  $\times$  50 cm<sup>3</sup>) and water (2  $\times$  50 cm<sup>3</sup>). After drying over anhydrous K<sub>2</sub>CO<sub>3</sub>, the solution was evaporated under reduced pressure to leave a solid, which was recrystallized from diethyl ether to give compound **9** (602 mg, 72%) as crystals, m.p. and mixed m.p. 177–178 °C (decomp.).

( $\pm$ )-2 $\beta$ -Bromo-1 $\alpha$ -trifluoroacetoxy-1,2,3,4-tetrahydrodibenz[*a,c*]anthracene **11**.—A solution of bromohydrin **7** (567 mg, 1.5 mmol) (see above) and TFAA (2 cm<sup>3</sup>) in anhydrous THF (5 cm<sup>3</sup>) was stirred at 0 °C for 50 min under argon. After evaporation of the solvent under reduced pressure, the residue was dissolved in anhydrous diethyl ether (100 cm<sup>3</sup>); the solution was stirred with anhydrous K<sub>2</sub>CO<sub>3</sub>, filtered, and evaporated to dryness to leave a solid, which was recrystallized from diethyl ether to give compound **11** (603 mg, 84%) as crystals, m.p. 134–135 °C (decomp.) (Found: M<sup>+</sup>, 472.0252. C<sub>24</sub>H<sub>16</sub>BrF<sub>3</sub>O<sub>2</sub> requires M, 472.0286);  $\delta_{\text{H}}$ (270 MHz; CDCl<sub>3</sub>) 2.35–2.68 (2 H, m, 4-H<sub>2</sub>), 3.43 (2 H, m, 3-H<sub>2</sub>), 4.81 (1 H, dd, *J*<sub>2,3</sub> 2 and *J*<sub>2,3'</sub> 6, 2-H), 7.04 (1 H, br s, 1-H), 7.45–8.35 (8 H, m, ArH), 8.88 (1 H, d, *J*<sub>7,8</sub> 7.5, 8-H) and 9.20 (1 H, s, 9-H).

( $\pm$ )-1 $\alpha$ -Acetoxy-2 $\beta$ ,4 $\alpha$ -dibromo-1,2,3,4-tetrahydrodibenz[*a,c*]anthracene **13**.—A stirred mixture of compound **9** (105 mg, 0.25 mmol), NBS (50 mg, 0.30 mmol), AIBN (5–10 mg) and anhydrous CCl<sub>4</sub> (10 cm<sup>3</sup>) was heated, at 60–65 °C with a sun lamp, under a current of Ar. The reaction was complete in 15 min. The mixture was cooled to room temperature, filtered to remove precipitated succinimide, and evaporated under reduced pressure. The residual solid was triturated with diethyl ether–light petroleum to give a relatively unstable light yellow crystalline solid accompanied by <5% of its isomer (90 mg, 72%), m.p. 127–128 °C (decomp.);  $\delta_{\text{H}}$ (270 MHz; CDCl<sub>3</sub>) 2.12

(3 H, s, 1-OAC), 2.82–3.22 (2 H, m, 3-H<sub>2</sub>), 4.98 (1 H, m, *J*<sub>2,3</sub> 4 and *J*<sub>2,3'</sub> 11, 2-H), 5.94 (1 H, t, *J*<sub>3,4</sub> and *J*<sub>3,4'</sub> 4, 4-H), 7.12 (1 H, d, *J*<sub>1,2</sub> 7, 1-H), 7.50–8.32 (7 H, m, ArH), 8.46 (1 H, s, 14-H), 8.86 (1 H, d, *J*<sub>7,8</sub> 9.7, 8-H) and 9.16 (1 H, s, 9-H); *m/z* 434, 436 and 438 (M<sup>+</sup>). This relatively unstable compound was used in the next step without further purification.

( $\pm$ )-2 $\beta$ ,4 $\alpha$ -Dibromo-1 $\alpha$ -trifluoroacetoxy-1,2,3,4-tetrahydrodibenz[*a,c*]anthracene **15**.—The conversion of compound **11** (472 mg, 1 mmol) into the title compound **15** was accomplished in 96% yield according to the procedure described above for compound **13**. The relatively unstable dibromo trifluoroacetate **15** was triturated with diethyl ether–light petroleum as an unstable, crystalline solid, m.p. 130–131 °C (decomp.);  $\delta_{\text{H}}$ (270 MHz; CDCl<sub>3</sub>) 2.85–3.24 (2 H, m, *J*<sub>2,3</sub> 4, *J*<sub>2,3'</sub> 11 and *J*<sub>3,3'</sub> 14.5, 3-H<sub>2</sub>), 5.16 (1 H, m, 2-H), 5.94 (1 H, t, *J*<sub>3,4</sub> and *J*<sub>3,4'</sub> 4, 4-H), 7.33 (1 H, d, *J*<sub>1,2</sub> 7, 1-H), 7.50–8.38 (8 H, m, ArH), 8.87 (1 H, d, *J*<sub>7,8</sub> 9.5, 8-H) and 9.18 (1 H, s, 9-H); *m/z* 356, 358 (M<sup>+</sup> – CF<sub>3</sub>CO<sub>2</sub>H – HBr). This product had a tendency to decompose during recrystallization and therefore was used crude in the next reaction.

( $\pm$ )-2 $\beta$ ,4 $\alpha$ -Dibromo-1,2,3,4-tetrahydrodibenz[*a,c*]anthracene-1 $\alpha$ -ol **17**.—( $\pm$ )-2 $\beta$ ,4 $\alpha$ -Dibromo-1 $\alpha$ -trifluoroacetoxy-1,2,3,4-tetrahydrodibenz[*a,c*]anthracene **15** (16 mg) was stirred with Amberlite-400 (OH<sup>−</sup>-form) (1.0 g) in dry THF (0.5 cm<sup>3</sup>), under argon, at 0 °C. After 4 min the mixture was filtered, the resin was washed with ice-cool, dry THF, and the solvent was evaporated to leave a residue. The structure of the major unstable product **17** (>75%) was assigned on the basis of the regular and decoupled <sup>1</sup>H NMR spectra of the mixture:  $\delta_{\text{H}}$ (270 MHz; CDCl<sub>3</sub>) 2.73–3.17 (2 H, m, *J*<sub>3,3'</sub> 14.7 and *J*<sub>3,4</sub> 3.7, 3-H<sub>2</sub>), 5.11–5.23 (1 H, m, 2-H), 5.90 (1 H, m, 4-H), 5.92 (1 H, d, *J*<sub>1,2</sub> 7.7, 1-H), 7.49–8.92 (8 H, m, ArH), 8.96 (1 H, s, 14-H) and 9.16 (1 H, s, 9-H).

( $\pm$ )-Dibenz[*a,c*]anthracene 1,2-Oxide **2** and Benz[1',2':3,4]-anthra[1,2-*b*]oxepine **18**.—A solution of dibromide **13**, **15** or **17** (30 mg) in freshly distilled THF (LiAlH<sub>4</sub>) (1 cm<sup>3</sup>) was stirred with freshly prepared NaOMe (90 mg) at 0 °C under argon for 4 h. The mixture was diluted with cold diethyl ether, and the ethereal solution was washed with water, dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated at 0–5 °C under reduced pressure to yield a crude product (25 mg), which was chromatographed at −15 °C over basic alumina with 20% diethyl ether–hexane as developing solvent. Relatively less polar benz[1',2':3,4]anthra[1,2-*b*]oxepine **18** was obtained as one of the major compounds. The polar fractions contained two major compounds which co-chromatographed with 1-hydroxy- **22**<sup>9</sup> and 2-hydroxy-dibenz[*a,c*]anthracene **23**<sup>9</sup> on silica gel TLC (15% EtOAc–hexane). The oxepine **18** had m.p. 179–180 °C (decomp.) (Found: M<sup>+</sup>, 294.1060. C<sub>22</sub>H<sub>14</sub>O requires M, 294.1045);  $\delta_{\text{H}}$ (270 MHz; [<sup>2</sup>H<sub>8</sub>]THF) 5.84 (1 H, t, *J*<sub>2,3</sub> = *J*<sub>3,4</sub> = 5.0, 3-H), 6.54 (1 H, dd, *J*<sub>3,4</sub> 5.0 and *J*<sub>4,5</sub> 11, 4-H), 6.58 (1 H, d, *J*<sub>2,3</sub> 5.0, 2-H), 7.43–8.98 (10 H, m, 5-H and ArH) and 9.24 (1 H, s, 10-H).

In another experiment, a solution of dibromide **13** or **15** in [2H<sub>8</sub>]THF was treated with NaOMe in an NMR tube, and the progress of the reaction was studied by NMR analysis. The reaction product consisted of a 60:40 mixture of the oxepine **18** and dibenz[*a,c*]anthracene 1,2-oxide **2**. Despite several efforts, arene oxide **2** could not be isolated in pure form due to its spontaneous isomerization to the phenols **22** and **23**; its formation was, however, confirmed by <sup>1</sup>H NMR analysis of the mixture of arene oxide **2** and the oxepine **18** produced in the NMR tube. Compound **2** showed  $\delta_{\text{H}}$ (270 MHz; [2H<sub>8</sub>]THF) 4.32 (1 H, m, 2-H), 5.54 (1 H, d, *J*<sub>1,2</sub> 4, 1-H), 6.84 (1 H, dd, *J*<sub>2,3</sub> 4 and *J*<sub>3,4</sub> 10, 3-H), 7.32–8.50 (8 H, m, ArH), 9.01 (1 H, d, *J*<sub>7,8</sub> 7.5, 8-H), 9.18 (1 H, s, 14-H) and 9.40 (1 H, s, 9-H).



( $\pm$ )-4 $\alpha$ -Acetoxy-3 $\beta$ -bromo-1,2,3,4-tetrahydrodibenz[a,c]anthracene **10**.—The title compound was prepared in 67% yield from compound **8** in a similar manner to the preparation of compound **9** (Method B), and was obtained as crystals, m.p. 144–145 °C (decomp.) (from THF–hexane) (Found: C, 68.5; H, 4.6. C<sub>24</sub>H<sub>19</sub>BrO<sub>2</sub> requires C, 68.73; H, 4.53%);  $\delta_{\text{H}}$ (270 MHz; CDCl<sub>3</sub>) 2.13 (3 H, s, 4-OAc), 2.35–2.75 (2 H, m, 1-H<sub>2</sub>), 3.52 (2 H, m, 2-H<sub>2</sub>), 4.77 (1 H, dd,  $J_{2,3}$  2.6 and  $J_{2,3'}$  6, 3-H), 6.70 (1 H, br s, 4-H), 7.50–8.30 (7 H, m, ArH), 8.64 (1 H, s, 14-H), 8.87 (1 H, d,  $J_{7,8}$  7.5, 8-H) and 9.19 (1 H, s, 9-H).

( $\pm$ )-3 $\beta$ -Bromo-4 $\alpha$ -trifluoroacetoxy-1,2,3,4-tetrahydrodibenz[a,c]anthracene **12**.—The conversion of 1,2-dihydrodibenz[a,c]anthracene **6**<sup>18</sup> into bromohydrin **8** was achieved in 81% yield according to the procedure described for compound **7**. The bromohydrin **8** was obtained as a solid, m.p. 140–142 °C (decomp.);  $\delta_{\text{H}}$ (270 MHz; CDCl<sub>3</sub>) 2.41–2.72 (3 H, m, 2-H<sub>2</sub> and OH), 3.40–3.55 (2 H, m, 1-H<sub>2</sub>), 4.75–4.78 (1 H, m, 3-H), 5.56 (1 H, m, 4-H), 7.56–8.85 (8 H, m, ArH), 8.58 (1 H, s, 14-H) and 9.14 (1 H, s, 8-H).

The bromohydrin **8** (274 mg, 0.727 mmol) was acylated with TFAA in 88% yield following the procedure described for compound **11**. The bromotrifluoroacetate **12** was obtained as crystals (from EtOAc–hexane), m.p. 141–142 °C (decomp.) (Found: C, 60.7; H, 3.5. C<sub>24</sub>H<sub>16</sub>BrF<sub>3</sub>O<sub>2</sub> requires C, 60.90; H, 3.40%);  $\delta_{\text{H}}$ (270 MHz; CDCl<sub>3</sub>) 2.45–2.70 (2 H, m, 2-H<sub>2</sub>), 3.53–3.59 (2 H, m, 1-H<sub>2</sub>), 4.78–4.81 (1 H, m, 3-H), 6.87 (1 H, d,  $J_{3,4}$  2, 4-H), 7.57–8.90 (8 H, m, ArH), 8.66 (1 H, s, 14-H) and 9.20 (1 H, s, 8-H).

( $\pm$ )-4 $\alpha$ -Acetoxy-1 $\alpha$ ,3 $\beta$ -dibromo-1,2,3,4-tetrahydrodibenz[a,c]anthracene **14**.—Bromination of compound **10** (210 mg, 0.5 mmol) was accomplished in 70% yield according to the procedure described above for compound **13**. Trituration of the residue with ethyl acetate–hexane produced a slightly unstable diastereoisomeric mixture of the dibromoacetate **14** as a solid, m.p. 122–123 °C (decomp.);  $\delta_{\text{H}}$ (270 MHz; CDCl<sub>3</sub>) 2.17 (3 H, s, 4-OAc), 2.92–3.30 (2 H, m,  $J_{1,2} = J_{1,2'} = 4.6$  and  $J_{2,2'} = 14.5$ , 2-H<sub>2</sub>), 4.95 (1 H, m,  $J_{2,3}$  4 and  $J_{2,3'}$  11.0, 3-H), 6.09 (1 H, t,  $J_{1,2} = J_{1,2'} = 4.6$ , 1-H), 6.94 (1 H, d,  $J_{3,4}$  6, 4-H), 7.50–8.20 (7 H, m, ArH), 8.75 (1 H, s, 14-H), 8.83 (1 H, d,  $J_{7,8}$  7.5, 8-H) and 9.15 (1 H, s, 9-H).

( $\pm$ )-1 $\alpha$ ,3 $\beta$ -Dibromo-4 $\alpha$ -trifluoroacetoxy-1,2,3,4-tetrahydrodibenz[a,c]anthracene **16**.—The conversion of compound **12** (94.6 mg, 0.2 mmol) into the title compound **16** was accomplished in 94% yield according to the procedure described above for compound **13**. The unstable diastereoisomeric mixture of dibromo trifluoroacetate **16** was obtained as a light yellow crystalline solid, m.p. 124–125 °C (decomp.) (from diethyl ether–hexane);  $\delta_{\text{H}}$ (270 MHz; [2H<sub>8</sub>]THF) 3.11–3.17 (2 H, m, 2-H<sub>2</sub>), 5.16–5.25 (1 H, m, 3-H), 6.40 (1 H, t,  $J_{1,2} = J_{1,2'} = 4.3$ , 1-H), 7.28 (1 H, d,  $J_{3,4}$  6.6, 4-H), 7.57–8.98 (8 H, m, ArH), 8.89 (1 H, s, 14-H) and 9.34 (1 H, s, 8-H);  $m/z$  434, 436 and 438 (M<sup>+</sup>).

Dibenz[a,c]anthracene 3,4-Oxide **3** and Benz[1',2':3,4]-anthra[2,1-b]oxepine **19**.—Treatment of the dibromo ester **14** or **16** with freshly prepared anhydrous NaOMe in [2H<sub>8</sub>]THF in an NMR tube at 0–5 °C, followed by NMR analysis of the products as described above in the case of dibromides **13** and **15**, indicated that the reaction product consisted of a ca. 40:60 mixture of arene oxide **3** and the oxepine **19**.

Attempted separation and purification of arene oxide **3** and the oxepine **19** by low-temperature (–15 °C) column chromatography over basic alumina with 20% diethyl ether–hexane produced, first, the oxepine **19**, and then a mixture of two phenols characterized by co-chromatography on silica gel TLC (15% EtOAc–hexane) as 3-hydroxy- **24**<sup>9</sup> and 4-hydroxy-

dibenz[a,c]anthracene **25**.<sup>9</sup> The oxepine **19** had m.p. 113–114 °C (Found: M<sup>+</sup>, 294.1060. C<sub>22</sub>H<sub>14</sub>O requires M, 294.1045);  $\delta_{\text{H}}$ (270 MHz; CDCl<sub>3</sub>) 5.88 (1 H, t,  $J_{6,7} = J_{7,8} = 5.3$ , 7-H), 6.52 (1 H, d, 6-H), 6.64 (1 H, dd,  $J_{7,8}$  5.3 and  $J_{8,9}$  11, 8-H), 7.46–8.36 (8 H, m, 9-H and ArH), 8.52 (1 H, s, 10-H), 8.78 (1 H, d,  $J_{1,2}$  7, 1-H) and 9.14 (1 H, s, 15-H).

The <sup>1</sup>H NMR spectrum of the unstable arene oxide **3** was deduced by <sup>1</sup>H NMR analysis of the mixture of products **3** and **19**. Compound **3** had  $\delta_{\text{H}}$ (270 MHz; [2H<sub>8</sub>]THF) 4.24–4.26 (1 H, m, 3-H), 5.29 (1 H, d,  $J_{3,4}$  4.0, 4-H), 6.77 (1 H, dd,  $J_{1,2}$  7.26 and  $J_{2,3}$  3.6, 2-H), 7.40–7.90 (9 H, m, 1-H and ArH), 8.9 (1 H, s, 14-H) and 9.34 (1 H, s, 9-H).

Hydrogenation of the Oxepines **18** and **19**.—A small sample of the appropriate oxepine **18** or **19** in THF was catalytically hydrogenated in the presence of 10% Pd-C at atmospheric pressure for 30 min. The solution was filtered to remove the catalyst, and the filtrate was reduced to dryness under reduced pressure to produce the corresponding tetrahydro derivative **26** or **27** of the oxepine **18** or **19**. Compound **26** had  $\delta_{\text{H}}$ (270 MHz; CDCl<sub>3</sub>) 1.85–2.25 (4 H, m, 3- and 4-H<sub>2</sub>), 3.32 (2 H, m, 5-H<sub>2</sub>), 4.31 (2 H, t,  $J_{2,3}$  6.0, 2-H<sub>2</sub>), 7.45–8.88 (9 H, m, ArH) and 9.15 (1 H, s, 10-H);  $m/z$  298 (M<sup>+</sup>, 100%). Compound **27** (Found: M<sup>+</sup>, 298.1379. C<sub>22</sub>H<sub>18</sub>O requires M, 298.1358);  $\delta_{\text{H}}$ (270 MHz; CDCl<sub>3</sub>) 1.80–2.25 (4 H, m, 7- and 8-H<sub>2</sub>), 3.34 (2 H, m, 10-H<sub>2</sub>), 4.36 (2 H, t,  $J_{6,7}$  5.7, 6-H<sub>2</sub>), 7.50–8.82 (9 H, m, ArH) and 9.17 (1 H, s, 15-H).

Acid-catalysed Isomerization of the Oxepines **18** and **19**.—Treatment of the oxepines **18** and **19** with trifluoroacetic acid resulted in 1-hydroxydibenz[a,c]anthracene **22**<sup>9</sup> and 4-hydroxydibenz[a,c]anthracene **25**,<sup>9</sup> respectively, which had TLC and UV spectral data identical with those of the authentic phenols.

( $\pm$ )-1,2-Epoxy-1,2,3,4-tetrahydrodibenz[a,c]anthracene **20**.—A solution of bromohydrin **7** (1.8 g, 4.77 mmol) in THF (25 cm<sup>3</sup>)–water (20 cm<sup>3</sup>) was added dropwise to 40% aq. NaOH (0.6 cm<sup>3</sup>) during 10 min at 0 °C under argon. After being stirred for 1 h at 0 °C, the reaction mixture was diluted with ice-cold water (100 cm<sup>3</sup>), and extracted with ethyl acetate (3  $\times$  50 cm<sup>3</sup>). The combined extracts were washed with 10% aq. NaCl, dried (K<sub>2</sub>CO<sub>3</sub>), and distilled under reduced pressure to leave a solid. Recrystallization of the residue from diethyl ether gave the title compound as crystals (1.1 g, 78%), m.p. 131–132 °C (Found: C, 88.95; H, 5.4. C<sub>22</sub>H<sub>16</sub>O requires C, 89.16; H, 5.44%);  $\delta_{\text{H}}$ (270 MHz; CDCl<sub>3</sub>) 1.90–3.50 (4 H, m, 3- and 4-H<sub>2</sub>), 3.95 (1 H, br s, 2-H), 4.86 (1 H, d,  $J_{1,2}$  4.7, 1-H), 7.50–8.95 (9 H, m, ArH) and 9.20 (1 H, s, 9-H).

( $\pm$ )-3,4-Epoxy-1,2,3,4-tetrahydrodibenz[a,c]anthracene **21**.—To a solution of bromo acetate **10** (43 mg, 0.103 mmol) in 1:1 THF–MeOH (1 cm<sup>3</sup>) at 0 °C was added 2 drops of 40% aq. NaOH under argon. The reaction mixture was stirred at 0–5 °C for 30 min and was then diluted with ice-cold water (3 cm<sup>3</sup>). The mixture was worked up according to the procedure described above for compound **20**. The epoxide **21** was obtained as crystals, m.p. 174–175 °C (from diethyl ether) (Found: C, 88.1; H, 5.7. C<sub>22</sub>H<sub>16</sub>O $\cdot$  $\frac{1}{10}$  H<sub>2</sub>O requires C, 88.65; H, 5.44%. Found: M<sup>+</sup>, 296.1187. C<sub>22</sub>H<sub>16</sub>O requires M, 296.1201);  $\delta_{\text{H}}$ (270 MHz; CDCl<sub>3</sub>) 1.90–3.62 (4 H, m, 1- and 2-H<sub>2</sub>), 3.95 (1 H, br s, 3-H), 4.72 (1 H, d,  $J_{3,4}$  4.3, 4-H), 7.50–8.45 (7 H, m, ArH), 8.59 (1 H, s, 14-H), 8.88 (1 H, m, 8-H) and 9.20 (1 H, s, 9-H).

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