Synthesis and isomerization of arene oxide metabolites of phenanthrene, triphenylene, dibenz[*a*,*c*]anthracene and dibenz[*a*,*h*]anthracene

Suresh K. Balani, I. N. Brannigan, Derek R. Boyd,* Narain D. Sharma, Francis Hempenstall and Allison Smith

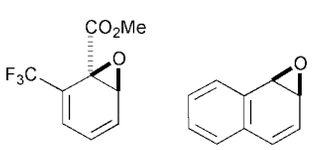
School of Chemistry, The Queen's University of Belfast, Belfast, UK BT9 5AG

Received (in Cambridge, UK) 4th December 2000, Accepted 21st February 2001
First published as an Advance Article on the web 22nd March 2001

Dibenz[*a*,*h*]anthracene 3,4-oxide $\mathbf{5A}_{RS}$, synthesised from the enantiopure dibromoMTPA precursor $\mathbf{9A}_{RRS*}$, was found to have totally racemized and to be accompanied by benz[5,6]anthra[1,2-*b*]oxepine **11A**. Phenanthrene 3,4-oxide $\mathbf{5B}_{RS}$, obtained from the enantiopure bacterial metabolite *cis*-3,4-dihydroxy-3,4-dihydrophenanthrene **12B** by a modified synthetic approach involving the chlorohydrin ester **16B**, was observed to racemize spontaneously at ambient temperature. Dibenz[*a*,*h*]anthracene 3,4-oxide $\mathbf{5A}_{RS}/\mathbf{5A}_{SR}$, phenanthrene 3,4-oxide $\mathbf{5B}_{RS}/\mathbf{5B}_{SR}$, triphenylene 1,2-oxide $\mathbf{5C}_{RS}/\mathbf{5C}_{SR}$, and dibenz[*a*,*c*]anthracene 1,2-oxide $\mathbf{5D}_{RS}/\mathbf{5D}_{SR}$, obtained from the corresponding racemic *cis*-tetrahydrodiol precursors **14A**–**14D** by the new method, were obtained without any evidence of the formation of benz[5,6]anthra[1,2-*b*]oxepine **11A**, naphth[1,2-*b*]oxepine **11B**, phenanthro[10,9-*b*]oxepine **11C**, or benz[3,4]-anthra[1,2-*b*]oxepine **11D** isomers respectively. The total racemization of arene oxide $\mathbf{5A}_{RS}$ and formation of oxepine **11A** from the bromoMTPA precursor $\mathbf{8A}_{RRS*}$ are in accord with earlier PMO predictions based on resonance energy considerations. Photoisomerization of arene oxides $\mathbf{5A}_{RS}/\mathbf{5A}_{SR}$, $\mathbf{5C}_{RS}/\mathbf{5C}_{SR}$, and $\mathbf{5D}_{RS}/\mathbf{5D}_{SR}$ was found to yield the corresponding oxepines **11A**, **11C**, and **11D**.

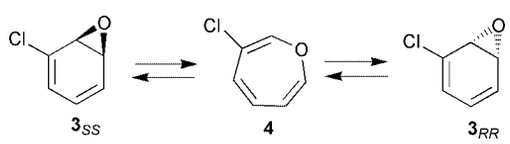
Introduction

Polycyclic aromatic hydrocarbons (PAHs) occur widely in the environment and can be cytotoxic, mutagenic and carcinogenic when activated *via* monooxygenase-catalysed arene and alkene epoxidations. The initially formed epoxide (arene oxide) intermediates are generally very difficult to detect due to their propensity to aromatize forming the corresponding phenols. The benzene oxide metabolite **1**, resulting from enzyme-catalysed epoxidation of 2-trifluoromethyl methylbenzoate in the fungus *Phellinus ribis*, was thus unusual, being isolable as a result of its remarkable stability.[1] By contrast, naphthalene 1,2-oxide **2**, the first reported example of a polycyclic arene oxide metabolite, was much less stable and could only be detected by using radiochemical tracer methods.[2]



1 2

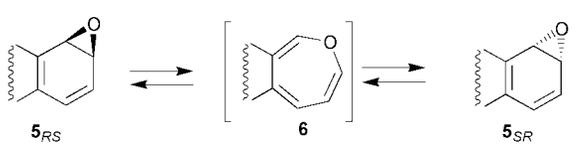
The formation of an arene oxide during metabolism could in principle involve facial stereoselectivity yielding either enantiomer.[3,4] Since the rates of further enzyme-catalysed reactions and biological activity are often dependent upon absolute configuration, it is important to determine if an arene oxide enantiomer is configurationally stable. In earlier reports we have shown that benzene oxide enantiomers *e.g.* chlorobenzene 2,3-oxide, **3**, spontaneously racemize *via* the corresponding oxepine valence tautomers *e.g.* oxepine, **4**[5] (Scheme 1). Conversely the configurational stability of naphthalene 1,2-oxide **2** was established by the synthesis of either enantiomer without evidence of spontaneous racemization.[6,7] Synthetic studies on polycyclic arene oxides **5** derived from single enantiomer precursors showed that configurational stability was variable



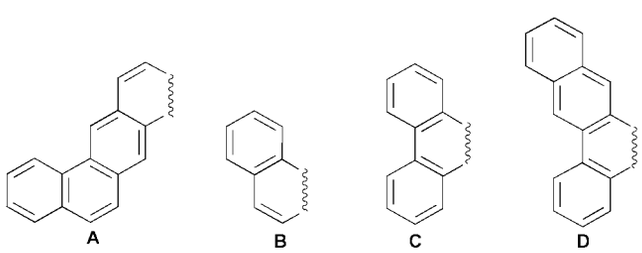
$\mathbf{3}_{SS}$ **4** $\mathbf{3}_{RR}$

Scheme 1

and that spontaneous racemization of some polycyclic arene oxides could occur through an electrocyclic rearrangement to yield undetected oxepine valence tautomers **6** (Scheme 2).[3,4,8]



$\mathbf{5}_{RS}$ **6** $\mathbf{5}_{SR}$



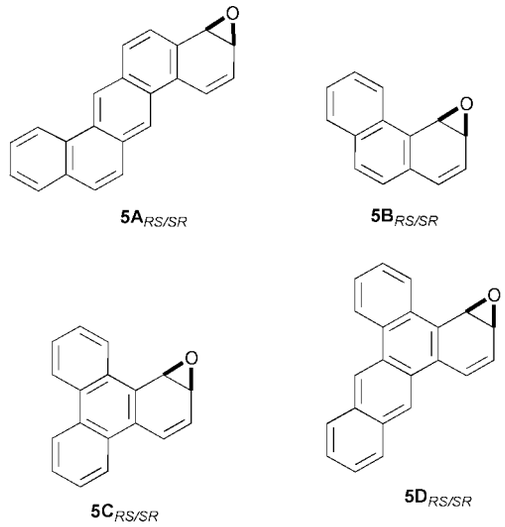
A **B** **C** **D**

Scheme 2

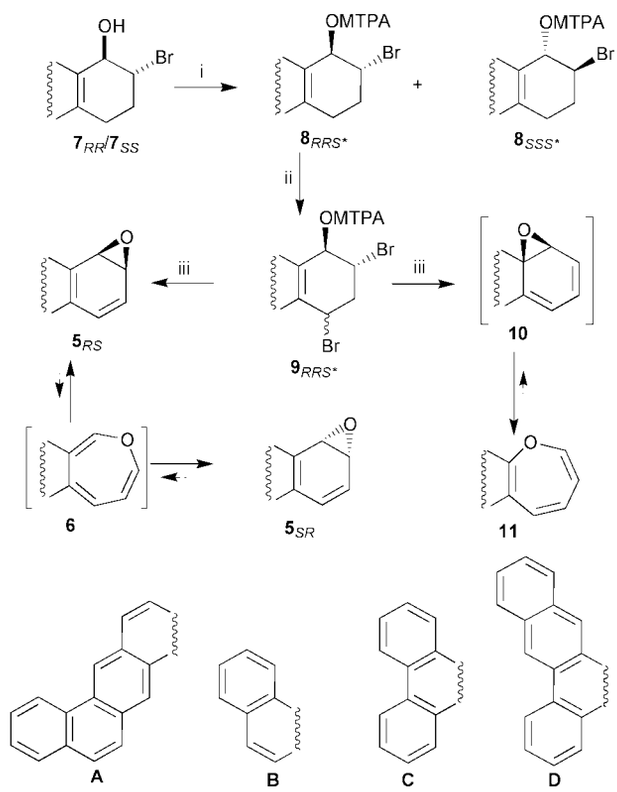
Perturbational molecular orbital (PMO) calculations of the arene oxide–oxepine equilibrium, and the associated loss of resonance energies, allowed the relative ease of racemization of particular arene oxide structures to be predicted.[8] Previous synthetic studies have provided experimental confirmation of the PMO-based prediction that monooxygenase-catalysed epoxidation of both tricyclic, *e.g.* phenanthrene (3,4-oxide **5B**),[8–10] and tetracyclic arenes, *e.g.* triphenylene (1,2-oxide **5C**),[11] could yield arene oxides which are prone to spontaneous

DOI: 10.1039/b009712h

racemisation. The same PMO method[8] also led to the prediction that several pentacyclic arene oxides, *e.g.* **5A**–**5D**, would spontaneously racemize.



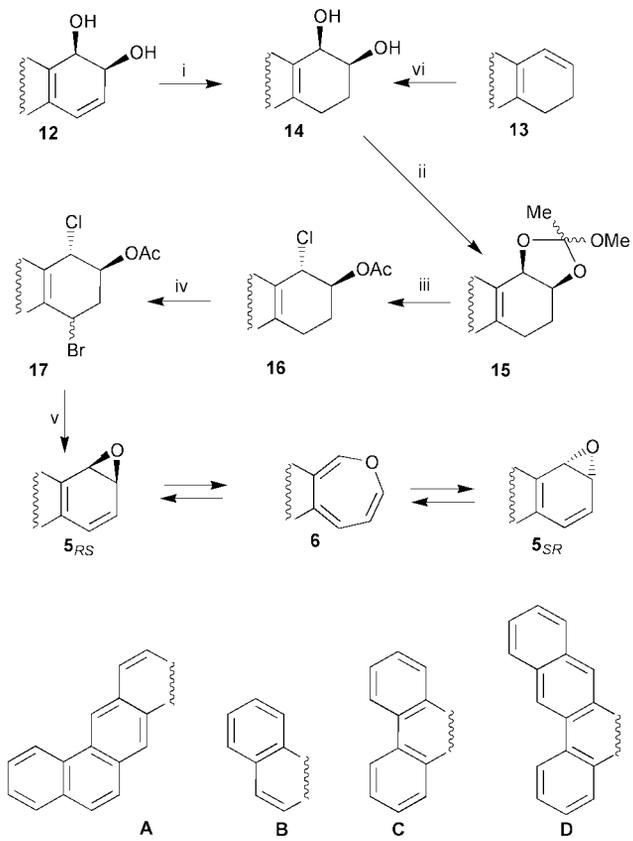
Prior to the preliminary report of this work,[12] the preferred method of synthesis of enantiopure polycyclic arene oxides has involved the formation and resolution of bromo-α-methoxy-α-(trifluoromethyl)phenylacetate (bromoMTPA) esters **8** and conversion of the resulting dibromoester intermediates **9** to arene oxides **5** *via* an intramolecular S_N2 mechanism as shown in Scheme 3.[10] However, when tetra- or penta-cyclic arenes



Scheme 3 i, (−)-MTPA Cl, pyridine; ii NBS–CCl_4; iii NaOMe–THF.

are synthesised from the dibromoester intermediate **9** the latter approach has often resulted in the concomitant formation of an isolable oxepine isomer **11**. The reaction is assumed to proceed *via* a competing S_N2' mechanism involving the unstable angular arene oxide intermediate **10** which remained undetected (Scheme 3).[8,13] It was also found that the formation and isolation of these relatively stable oxepine intermediates, **11**, could be predicted using the PMO method.[8,13]

In this report we present (i) the synthesis and spontaneous total racemization of a pentacyclic arene oxide (dibenz[*a*,*h*]-anthracene 1,2-oxide **5A**$_{RS}$) and the anticipated simultaneous formation of the corresponding oxepine isomer **11A** from an enantiopure bromoester precursor (**8**$_{RRS*}$) using the conventional synthetic route (Scheme 3). (ii) The synthesis and observed spontaneous racemisation of a tricyclic arene oxide (phenanthrene 3,4-oxide **5B**$_{RS}$/**5B**$_{SR}$), derived from an enantiopure *cis*-dihydrodiol bacterial metabolite (phenanthrene *cis*-3*S*,4*R*-dihydrodiol **12B**), using an alternative synthetic pathway (Scheme 4). (iii) The synthesis of pure samples of a tetracyclic

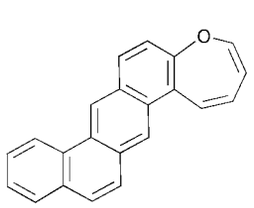


Scheme 4 i, Pd/C, H_2, MeOH; ii, $MeC(OMe)_3$; iii Me_3SiCl, CH_2Cl_2, Et_3N; iv NBS, AIBN, CCl_4; v NaOMe, THF; vi OsO_4, NMO, CH_2Cl_2 .

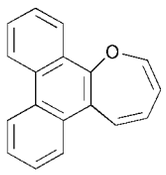
arene oxide (triphenylene 1,2-oxide **5C**$_{RS}$/**5C**$_{SR}$) and two pentacyclic arene oxides (dibenz[*a*,*h*]anthracene 3,4-oxide **5A**$_{RS}$/**5A**$_{SR}$, and dibenz[*a*,*c*]anthracene 1,2-oxide **5D**$_{RS}$/**5D**$_{SR}$) from racemic *cis*-tetrahydrodiol precursors (**13C**, **13A**, and **13D**) without formation of the corresponding stable oxepines (**11C**, **11A**, and **11D**) using a new method (Scheme 4) and (iv) the photoisomerization of arene oxides **5A**$_{RS}$/**5A**$_{SR}$, **5C**$_{RS}$/**5C**$_{SR}$ and **5D**$_{RS}$/**5D**$_{SR}$ to yield the corresponding oxepines **11A**, **11C**, and **11D**.

Results and discussion

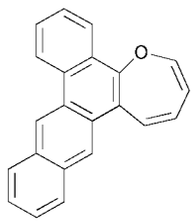
The established synthetic method, used earlier for the synthesis of enantiopure polycyclic arene oxides,[10] developed in these laboratories, was itself a modification of the method previously used by Yagi and Jerina[14] in the synthesis of racemic samples using resolved bromohydrin ester precursors (Scheme 3). To date this method[10] has been successfully applied to the synthesis of single enantiomers of three categories of arene oxides. The first group included the enantiopure arene oxides, **5**, of naphthalene (1,2-),[6] anthracene (1,2-),[6] benz[*a*]anthracene (8,9-, 10,11-),[15,16] and benzo[*a*]pyrene (7,8-)[17] which were found to be configurationally stable at ambient temperature. The second type included the arene oxides, **5**, of phenanthrene (1,2- and 3,4-),[9,10] chrysene (1,2- and 3,4-),[18,19] and benzo[*c*]phenanthrene



11A



11C



11D

(1,2-)[20] which were initially obtained in enantiopure form but were observed to racemize slowly at ambient temperature *via* undetected oxepine isomers, **6**. The final category included arene oxides, **5**, of triphenylene (1,2-),[21] benzo[*e*]pyrene (9,10-),[22] dibenz[*a*,*j*]anthracene (3,4-),[23] and benzo[*g*]chrysene (5,6-, 7,8-),[24] benz[*a*]anthracene (1,2-, 3,4),[21] which were all assumed to have been synthesised as single enantiomers, were found to have totally racemized (*via* unstable oxepine valence tautomers **6**) and were also accompanied by isolable oxepine isomers **11**. The loss of resonance energy associated with the isomerization of the third type of arene oxides **5** to the unstable oxepines **6** was calculated[8] to be much lower than for the first group and slightly lower than for the second category. The simultaneous formation of arene oxide derivatives, **5**, of dibenz[*a*,*c*]anthracene (1,2- and 3,4-) and the corresponding stable oxepine isomers, **11**, from racemic dibromoacetate precursors has also been reported.[25,26]

All of the earlier PMO predictions[8,13] have to date proved to be in accord with experimental observations on the relative ease of racemization of the arene oxides **5** and the concomitant formation of stable oxepine isomers **11** from these laboratories. Thus, it was surprising to find a report[27] that the 1,2- and 3,4-arene oxides of dibenz[*a*,*h*]anthracene, synthesised using the standard dibromoacetate route,[14] were unaccompanied by the corresponding stable oxepines, **11**. This apparent exception to our predictions[13] has been reinvestigated as part of our current programme to utilize arene *cis*-dihydrodiol metabolites in the synthesis of arene oxides.[5,7] A wide range of *cis*-dihydrodiol metabolites of the PAHs including naphthalene,[28,29] anthracene,[30,31] phenanthrene,[30,32] benz[*a*]anthracene,[33,34] chrysene,[35] and benzo[*a*]pyrene[33] and heteroPAHs[36] are available from bacterial biotransformations.

PAHs constitute the first class of compounds to be confirmed as chemical carcinogens,[37] and dibenz[*a*,*h*]anthracene (DBA) was the first carcinogenic member to be identified.[38] The arene oxide metabolite $\mathbf{5A}_{RS}/\mathbf{5A}_{SR}$ has been proposed as one of three arene oxide intermediates formed during liver microsomal metabolism of DBA.[27] Enzyme-catalysed hydrolysis of this arene oxide has in turn been shown to yield the corresponding *trans*-dihydrodiol (*trans*-3,4-dihydroxy-3,4-dihydrodibenz[*a*,*h*]-anthracene), which has been identified as a precursor of the ultimate mutagenic and carcinogenic diol epoxide and tetraol epoxide metabolites of DBA.[39]

The first synthetic route to arene oxide $\mathbf{5A}_{RS}/\mathbf{5A}_{SR}$ was based on the use of bromohydrin $\mathbf{7A}_{RR}/\mathbf{7A}_{SS}$ as a precursor (Scheme 3). Compound **7A**, obtained from the corresponding bromoacetate,[27] was treated with (−)-α-methoxy-α-(trifluoromethyl)-phenylacetyl chloride (MTPA-Cl derived from *S*-MTPA and identified by *S**) to yield a mixture of bromoMTPA diastereoisomers, $\mathbf{8A}_{RRS^*}$ and $\mathbf{8A}_{SSS^*}$. This mixture was separated by PLC into the less polar ($\mathbf{8A}_{RRS^*}$) and more polar ($\mathbf{8A}_{SSS^*}$) fractions. The absolute configurations were assigned using the reported NMR method based upon the ^{1}H chemical shift values of the H-3 signal, the ^{19}F chemical shift values of CF_3, and the coupling constants $J_{3,4}$.[10] Thus the less polar bromoMTPA ester ($\mathbf{8A}_{RRS^*}$) having the smaller coupling constant ($J_{3,4}$), the smaller ^{1}H chemical shift ($\delta_{H\text{-}3}$) and the smaller negative ^{19}F chemical shift value for CF_3 (δ_F) was assigned the 3*R*,4*R* configuration. Benzylic bromination of the $\mathbf{8A}_{RRS^*}$ diastereoisomer using NBS yielded a relatively unstable mixture of dibromoMTPA esters, $\mathbf{9A}_{RRS^*}$. Treatment of this mixture with sodium methoxide in THF yielded dibenz[*a*,*h*]anthracene 3,4-oxide $\mathbf{5A}_{RS}/\mathbf{5A}_{SR}$ as the major component (*ca*: 65%) and the relatively stable oxepine **11A** as the minor component (35%). While the sample of arene oxide $\mathbf{5A}_{RS}/\mathbf{5A}_{SR}$ could not be chromatographically separated from oxepine **11A** without decomposition, the optical rotation value of zero from the crude mixture was consistent with the predicted initial formation of the $\mathbf{5A}_{RS}$ enantiomer followed by total spontaneous racemization (proceeding *via* the undetected unstable oxepine **6**). When the synthesis was repeated using a racemic sample of dibromoacetate, derived from bromohydrin **7**, a racemic mixture of arene oxide $\mathbf{5A}_{RS}/\mathbf{5A}_{SR}$ (*ca*. 40%) and stable oxepine **11A** (*ca*. 60%) was again formed. The arene oxide enantiomers $\mathbf{5A}_{RS}/\mathbf{5A}_{SR}$ decomposed to phenols during chromatography; a pure sample of the more stable oxepine **11A** was isolated. Further evidence of decomposition was found when the mixture of arene oxide $\mathbf{5A}_{RS}/\mathbf{5A}_{SR}$ and oxepine **11A** was dissolved in $CDCl_3$ solution containing a trace of benzoic acid. The arene oxide isomerized to the corresponding phenols leaving the residual oxepine **11A** unchanged.

No evidence for interconversion of the arene oxide $\mathbf{5A}_{RS}/\mathbf{5A}_{SR}$ to oxepine **11A** was obtained when a $CDCl_3$ solution of the mixture was heated at 50 °C or maintained at ambient temperature for an extended period (>24 h). However, UV irradiation (>300 nm) of the mixture of arene oxide $\mathbf{5A}_{RS}/\mathbf{5A}_{SR}$ and oxepine **11A** at ambient temperature for a short period (0.5 h), showed a concomitant increase in the proportion of oxepine (*ca*. 50%) and decrease in the amount of arene oxide. A similar type of photochemical circumambulatory rearrangement or "oxygen walk" process was observed for other arene oxide derivatives among tetra-and penta-cyclic members of the PAH series.[21–25] This observation clearly indicates that oxepine **11A** is formed during the synthesis of arene oxide $\mathbf{5A}_{RS}/\mathbf{5A}_{SR}$ from either dibromoacetate or dibromoMTPA (**9**) precursors. It was assumed that oxepine **11A** was formed *via* an S_N2' mechanism while the arene oxide **5A** resulted from the normal S_N2 pathway (Scheme 3). Thus, despite the earlier report on the synthesis of uncontaminated arene oxide **5A**,[27] the formation of oxepine **11A** in the present study has allowed our earlier prediction[13] about the concomitant formation of arene oxides and oxepines of this type, based on PMO calculations, to be confirmed. In view of the current results it appears that oxepine **11A** had escaped detection in the earlier study.[27]

Resulting from the importance of arene oxides and their derivatives in mechanism studies of chemically induced carcinogenesis caused by larger members of the PAH series,[38,39] and the difficulties experienced earlier in obtaining pure samples of arene oxides **5** of the tetracyclic series (triphenylene,[21] benz-[*a*]anthracene[21]), and pentacyclic (benzo[*e*]pyrene,[22] dibenz[*a*,*j*]-anthracene,[23] dibenz[*a*,*c*]anthracene,[25] and benzo[*g*]chrysene[24]) without the accompanying oxepines **11**, an alternative to the bromoester method shown in Scheme 3 was explored.

The synthetic sequence shown in Scheme 4 is based upon the availability of *cis*-tetrahydrodiol precursors **14**. The tricyclic tetrahydrodiol (3*S*,4*R*)-**14B** was derived by catalytic hydrogenation of the (3*S*,4*R*)-enantiopure *cis*-dihydrodiol metabolite **12B**, obtained from biotransformation of the corresponding PAH (phenanthrene) using mutant strains of the bacteria *Sphingomonas yanoikuyae* (B8/36)[32] and *Pseudomonas putida* (NCIB 9816/11).[40] Osmylation of the dihydroarenes **13A**, **13C**, and **13D**, synthesised by literature methods,[11,26,27] gave the

corresponding racemic *cis*-tetrahydrodiol precursors **14A**, **14C**, and **14D** in variable yields (15–80%) (Scheme 4).

Reaction of the tetrahydrodiols, **14A**–**14D**, with trimethylorthoacetate and a catalytic amount of benzoic acid provided the corresponding 1,3-dioxole derivatives **15A**–**15D**, as diastereoisomeric mixtures (63–82% yield) whose structures were confirmed by ^{1}H NMR and MS analysis. Separation of the diastereoisomeric pairs **15A**–**15D** was considered unnecessary as both gave the same chloroacetate products **16A**–**16D** in the next stage of the synthesis. The isomeric mixtures were considered to be of sufficient purity to be used without chromatography.

Reaction of the dioxolane diastereoisomers **15A**–**15D** with chlorotrimethylsilane in the presence of a trace of triethylamine yielded the corresponding *trans*-chloroacetates **16A**–**16D**. This reaction was earlier applied to the PAH bond of highest electron density (the 5,6- K-region band). The K-region arene *cis*-dihydrodiols were used for the synthesis of enantiopure *trans*-chloroacetate precursors of the K-region arene oxides of chrysene, 7,12-dimethylbenz[*a*]anthracene and benzo[*c*]-phenanthrene.[41] A qualitative comparison of the relative stabilities of the *trans*-halohydrin ester types exemplified by compounds **8** (containing a non-benzylic halogen, Scheme 3) and **16A**–**16D** (containing a benzylic halogen, Scheme 4) showed that the latter category was less stable. The *trans*-chloroacetates **16A**–**16D**, in common with other compounds bearing a halogen atom at a benzylic position *e.g.* compounds **9A**, **17A**–**17D**, were found to decompose during attempted purification during silica-gel chromatography. Fortunately these compounds were obtained in good yields (*ca*. 70%) and were of sufficient purity (^{1}H NMR analysis) for using directly in the next stage.

Treatment of the *trans*-chloroacetates **16A**–**16D** with *N*-bromosuccinimide in tetrachloromethane yielded the corresponding bromo *trans*-chloroacetates **17A**–**17D** as isomeric mixtures. Compounds **17A**–**17D** appeared to be relatively stable during their synthesis and isolation (^{1}H NMR spectral analysis). However, in order to avoid decomposition during chromatography they were converted directly to the corresponding arene oxides $\mathbf{5A}_{RS}/\mathbf{5A}_{SR}$–$\mathbf{5D}_{RS}/\mathbf{5D}_{SR}$ by treatment with sodium methoxide without chromatographic separation. The synthesis of the unstable arene oxides $\mathbf{5B}_{RS}/\mathbf{5B}_{SR}$, $\mathbf{5C}_{RS}/\mathbf{5C}_{SR}$, and $\mathbf{5D}_{RS}/\mathbf{5D}_{SR}$ from the corresponding *cis*-tetrahydrodiol precursors **14B**, **14C**, **14D** using the route shown in Scheme 4 eliminates the need for separation from the stable oxepines **11B**, **11C**,[20] **11D**[25,26] which are by-products from the method shown in Scheme 3. The unstable oxepine tautomers **6A**–**6C**, while not detected, were assumed to be present in solution and to be responsible for the spontaneous racemization of arene oxides **5A**, **5B**, and **5C** derived from enantiopure *trans*-bromoMTPA ester precursors **8A**, **8B**,[9,10] and **8C**.[21]

Since the tetrahydrodiol precursor **14B** ($[\alpha]_D$ −62, $CHCl_3$) was obtained by hydrogenation of the enantiopure *cis*-dihydrodiol bacterial metabolite of phenanthrene **12B** ($[\alpha]_D$ +35, MeOH), the product phenanthrene 3,4-oxide $\mathbf{5B}_{RS}$ must be a single enantiomer initially. However, based on the PMO calculations[8] and its earlier synthesis from an enantiopure *trans*-bromoMTPA precursor,[9,10] a degree of racemization was expected. The sample of phenanthrene 3,4-oxide obtained after recrystallization at −70 °C initially showed a significant optical rotation ($[\alpha]_D$ +165, $CDCl_3$) which decreased progressively to zero over 24 h at ambient temperature. Simultaneous ^{1}H NMR analysis of this sample of phenanthrene 3,4-oxide **5B** over the same period showed no decomposition and hence it was concluded that spontaneous racemization (yielding enantiomers $\mathbf{5B}_{RS}/\mathbf{5B}_{SR}$) was solely responsible for the decrease in $[\alpha]_D$ value.

The question of spontaneous racemization of arene oxides from the larger PAHs, dibenz[*a*,*h*]anthracene 3,4-oxide $\mathbf{5A}_{RS}/\mathbf{5A}_{SR}$, triphenylene 1,2-oxide $\mathbf{5C}_{RS}/\mathbf{5C}_{SR}$, and dibenz[*a*,*c*]anthracene 1,2-oxide $\mathbf{5D}_{RS}/\mathbf{5D}_{SR}$ could not be addressed as these were synthesised from the corresponding racemic tetrahydrodiols **13A**, **13C**, and **13D**. An earlier observation using the enantiopure *trans*-bromoMTPA ester **8C**,[10] allied to results obtained in the present study using *trans*-bromoMTPA ester **8A**, has allowed the predicted[8,13] spontaneous racemization of the derived arene oxides $\mathbf{5A}_{RS}/\mathbf{5A}_{SR}$ and $\mathbf{5D}_{RS}/\mathbf{5D}_{SR}$ to be confirmed (in the presence of the corresponding oxepines isomers **11A** and **11C**).

Photoisomerization of the pure arene oxides $\mathbf{5A}_{RS}/\mathbf{5A}_{SR}$, $\mathbf{5C}_{RS}/\mathbf{5C}_{SR}$, $\mathbf{5D}_{RS}/\mathbf{5D}_{SR}$ yielded the corresponding isolable oxepines **11A**, **11C** and **11D** which were in turn found to yield phenolic products upon prolonged exposure to UV light. No evidence of oxepine **5B** was obtained from UV irradiation of phenanthrene 3,4-oxide $\mathbf{5B}_{RS}/\mathbf{5B}_{SR}$ under similar conditions.

Conclusion

Arene oxide enantiomers $\mathbf{5A}_{RS}/\mathbf{5A}_{SR}$ *and* oxepine **11A** have been simultaneously synthesised *via* the *trans*-bromoMTPA ester intermediate $\mathbf{8A}_{RRS^*}$ (Scheme 3) in contrast to an earlier report. An alternative synthetic route to arene oxides $\mathbf{5A}_{RS}/\mathbf{5A}_{SR}$–$\mathbf{5D}_{RS}/\mathbf{5D}_{SR}$ *via* the corresponding *cis*-tetrahydrodiols, **14A**–**14D**, and *trans*-chloroacetates, **16A**–**16D** involves exclusively an S_N2 pathway without formation of oxepine by-products **11A**–**11D** (Scheme 4). This is, in our view, the preferred method for the synthesis of pure arene oxide metabolites of PAHs. The roles of two distinct types of oxepines, **6** and **11**, have been established in the context of arene oxide chemistry of PAHs. Thus, spontaneous racemization *via* the unstable and unobserved oxepines, **6A** and **6B**, has been found to give arene oxides $\mathbf{5A}_{RS}/\mathbf{5A}_{SR}$ and $\mathbf{5B}_{RS}/\mathbf{5B}_{SR}$ while photoisomerization of arene oxides $\mathbf{5A}_{RS}/\mathbf{5A}_{SR}$, $\mathbf{5C}_{RS}/\mathbf{5C}_{SR}$, and $\mathbf{5D}_{RS}/\mathbf{5D}_{SR}$ was found to yield the stable and isolable oxepines **11A**, **11C** and **11D**.

Experimental

^{1}H NMR spectra were recorded at 250 MHz (Bruker WH250), 300 MHz (Bruker Avance DPX-500) and at 500 MHz (Bruker Avance DRX-500) in $CDCl_3$ solvent unless stated otherwise. Chemical shifts (δ) are reported in ppm relative to $SiMe_4$ and coupling constants (J) are given in Hz. Mass spectra were recorded at 70 eV on a VG Autospec Mass Spectrometer, using a heated inlet system. Accurate molecular weights were determined by the peak matching method with perfluorokerosene as standard. Elemental microanalyses were obtained on a Perkin-Elmer 2400 CHN microanalyser. Optical rotations were recorded at ambient temperature and are given in 10^{-1} deg cm^2 g^{-1}. PLC was carried out on glass plates (20 × 20 cm) coated with Merck Kieselgel $PF_{254+356}$.

The dihydroPAHs 1,2-dihydrodibenz[*a*,*h*]anthracene **13A**,[27] 3,4-dihydrotriphenylene **13C**,[11] and 3,4-dihydrobenzo[*a*,*c*]-anthracene **13D**[26] and (±)-*trans*-1-acetoxy-2-bromo-1,2,3,4-tetrahydrodibenz[*a*,*h*]anthracene[27] were obtained using the literature methods.

(±)-*trans*-3-Bromo-4-hydroxy-1,2,3,4-tetrahydrodibenz[*a*,*h*]-anthracene (7A)

To a stirring solution of (±)-*trans*-1-acetoxy-2-bromo-1,2,3,4-tetrahydrodibenz[*a*,*h*]anthracene (0.4 g, 0.72 mmol), in dry THF (4 cm^3) under N_2, was added dropwise diborane–THF solution (8 cm^3, 1.0 M solution) and the reaction mixture was stirred for a further 20 h. Water (25 cm^3) was added and the quenched reaction mixture extracted with chloroform (2 × 50 cm^3). PLC purification ($CHCl_3$–MeOH; 98 : 2) of the crude product, obtained after removal of chloroform, yielded bromohydrin **7A** (0.26 g, 70%), mp 175 °C (from CH_2Cl_2) (Found: M$^+$, 376.0465. $C_{22}H_{17}BrO$ requires M$^+$, 376.0463); ^{1}H NMR (250 MHz, THF-d_8–$CDCl_3$, 1 : 1) δ 2.50 (2 H, m, H-2), 3.30 (2 H, m, H-1), 4.49 (1 H, m, H-3), 4.88 (1 H, d, $J_{3,4}$ 4.7, H-4), 7.3–8.0 (7

H, m, Ar-H), 8.5 (1 H, s, Ar-H), 8.82 (1 H, d, *J* 4.7, Ar-H), 9.18 (1 H, s, Ar-H).

(−)-(3*R*,4*R*) and (+)-(3*S*,4*S*)-3-Bromo-1,2,3,4-tetrahydrodibenz[*a*,*h*]anthracen-4-yl 3,3,3-trifluoro-2-methoxy-2-phenylpropionate (8A$_{RRS*}$ and 8A$_{SSS*}$)

Bromohydrin **7A** (0.4 g, 1.03 mmol) dissolved in pyridine (1 cm^3) was converted into the corresponding bromoMTPA esters **8A**$_{RRS*}$ and **8A**$_{SSS*}$ by treatment with (−)-MTPA chloride (0.4 g, 1.5 mmol); the product was extracted using chloroform and purified by column chromatography (Found: C, 64.6: H, 4.2. $C_{32}H_{24}BrF_3O_3$ requires C, 64.8; H, 4.1%). Separation of the MTPA diastereoisomers by multiple elution PLC (EtOAc–hexane; 8 : 92) yielded the high R_f diastereoisomer **8A**$_{RRS*}$ (0.26 g, 41%), mp 173–174 °C (from $CHCl_3$–hexane); $[\alpha]_D$ −34 (c = 0.6 in $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.49 (2 H, m, H-2), 3.45 (2 H, m, H-1), 3.54 (3 H, s, OMe), 4.59 (1 H, m, H-3), 6.55 (1 H, d, *J* 4, H-4), 7.3–8.0 (12 H, m, Ar-H), 8.49 (1 H, s, Ar-H), 8.83 (1 H, d, *J* 8, Ar-H), 9.13 (1 H, s, Ar-H); δ_F (94.18 MHz, $CDCl_3$) −8.62 (3 F, s, CF_3). The low R_f diastereoisomer **8A**$_{SSS*}$ (0.24 g, 38%), mp 177–178 °C (from $CHCl_3$–hexane); $[\alpha]_D$ +1 (c = 0.5 in $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.6 (2 H, m, H-2), 3.45 (2 H, m, H-1), 3.56 (3 H, s, OMe), 4.67 (1 H, m, H-3), 6.55 (1 H, d, *J* 4, H-4), 7.4–7.9 (12 H, m, Ar-H), 8.49 (1 H, s, Ar-H), 8.82 (1 H, d, *J* 8, Ar-H), 9.10 (1 H, s, Ar-H); δ_F (94.18 MHz, $CDCl_3$) −8.64 (3 F, s, CF_3).

(3*R*, 4*R*)-1,3-Dibromo-1,2,3,4-tetrahydrodibenz[*a*,*h*]anthracen-4-yl 3,3,3-trifluoro-2-methoxy-2-phenylpropionate (9A$_{RRS*}$)

A solution of bromoMTPA ester **8A**$_{RRS*}$ (0.16 g, 0.27 mmol) in CCl_4 (15 cm^3), containing *N*-bromosuccinimide (0.58 g, 0.3 mmol) and α,α′-azoisobutyronitrile (0.002 g), was refluxed (0.5 h). The reaction mixture was filtered and the filtrate concentrated to yield the dibromo product **9A**$_{RRS*}$ (0.16 g, 88% yield). ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.8–3.2 (2 H, m, H-2), 3.62 (3 H, s, OMe), 5.04 (1 H, m, H-3), 6.08 (1 H, t, *J* 3, H-1), 6.84 (1 H, d, *J* 9, H-4), 7.0–8.6 (12 H, m, Ar-H), 8.76 (1 H, s, Ar-H), 8.78 (1 H, d, *J* 7, Ar-H), 9.10 (1 H, s, Ar-H). Attempted PLC purification of compound **9A**$_{RRS*}$ resulted in its decomposition.

(±)-3,4-Dihydro-3,4-epoxydibenz[*a*,*h*]anthracene (dibenz[*a*,*h*]-anthracene 3,4-oxide) 5A$_{RS}$/5A$_{SR}$ and benz[5,6]anthra[1,2-*b*]-oxepine (11A)

Sodium methoxide (0.2 g, 4 mmol) was added to a solution of dibromoMTPA ester **9A**$_{RRS*}$ (0.15 g, 0.22 mmol) in THF (4 cm^3) and the reaction mixture stirred at 0 °C (16 h). Attempted PLC separation of the product mixture, arene oxide **5A**–oxepine **11A** (2 : 3), resulted in the isolation of oxepine **11A** and decomposition of arene oxide **5A** and hence the two compounds were characterized without separation (0.03 g, 45%) (Found: M$^+$, 294.10462. $C_{22}H_{14}O$ requires M$^+$, 294.10446).

(±)-3,4-Dihydro-3,4-epoxydibenz[*a*,*h*]anthracene (dibenz[*a*,*h*]-anthracene 3,4-oxide) (5A$_{RS}$/5A$_{SR}$). $[\alpha]_D$ 0 ($CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ 4.37 (1 H, m, H-3), 4.74 (1 H, d, *J* 4, H-4), 6.74 (1 H, dd, *J* 4, *J* 10, H-2), 7.61–9.15 (11 H, m, H-1 and Ar-H). ^{1}H NMR spectrum for compound **5A** was very similar to the literature report.[27]

Benz[5,6]anthra[1,2-*b*]oxepine (11A). Mp 180 °C (decomp.); ^{1}H NMR (250 MHz, $CDCl_3$) δ 5.75 (1 H, m, H-3), 6.41 (1 H, d, *J* 5.5, H-2), 6.53 (1 H, dd, *J* 4, *J* 11.4, H-4), 7.61–9.15 (11 H, m, H-5 and Ar-H).

Synthesis of *cis*-tetrahydrodiols (14A–14D) and the corresponding 2-methoxy-2-methyl-1,3-dioxole derivatives (15A–15D)

(−)-(3*S*,4*R*)-3,4-Dihydroxy-1,2,3,4-tetrahydrophenanthrene (14B). Typical procedure: a solution of (+)-(3*S*,4*R*)-3,4-dihydroxy-3,4-dihydrophenanthrene (**12B**), (0.2 g, 0.93 mmol; $[\alpha]_D$ +35, c = 0.4 in MeOH), isolated from the metabolism of phenanthrene using a mutant strain (B 8/36) of the bacterium *Sphingomonas yanoikuyae*,[28] in methanol (15 cm^3), was stirred (24 h) with 10% Pd/C catalyst (0.02 g) under hydrogen at atmospheric pressure. The filtrate, on concentration under reduced pressure yielded (−)-(3*S*,4*R*)-3,4-dihydroxy-1,2,3,4-tetrahydrophenanthrene (**14B**) as a white crystalline solid (0.19 g, 94%); mp 190–193 °C (from $CHCl_3$); $[\alpha]_D$ −62 (c = 0.5 in $CHCl_3$) (Found: C, 78.1; H, 6.4. $C_{14}H_{18}O_2$ requires C, 78.5; H, 6.6%); ^{1}H NMR (250 MHz, $CDCl_3$) δ 2.05 (2 H, m, H-2), 3.03 (2 H, m, H-1), 3.91–4.08 (1 H, m, H-3), 5.39 (1 H, d, $J_{4,3}$ 3.8, H-4), 7.23 (1 H, d, $J_{9,10}$ 8.5, H-9), 7.47 (1 H, dd, $J_{7,6}$ 7.0, $J_{7,8}$ 8.0, H-7), 7.57 (1 H, ddd, $J_{6,7}$ 7.0, $J_{6,8}$ 1.0, $J_{6,5}$ 8.5, H-6), 7.74 (1 H, d, $J_{9,10}$ 8.5, H-10), 7.81 (1 H, dd, $J_{8,7}$ 7.0, $J_{8,6}$ 1.0, H-8), 8.25 (1 H, d, $J_{5,6}$ 8.5, H-5).

(±)-*cis*-3,4-Dihydroxy-1,2,3,4-tetrahydrophenanthrene (14B). Typical procedure: 4-methylmorpholine *N*-oxide (NMO, 0.5 g) and osmium tetraoxide (0.01 g) were added to a stirred solution of alkene **13B** (1.0 g, 5.6 mmol) in CH_2Cl_2 (15 cm^3). On completion of the reaction (24 h) a saturated solution of Na_2SO_3 was added and stirring was continued (1 h). The solution was filtered and the filtrate washed with water. The racemic diol **14B** (0.93 g, 78%), obtained after removal of the solvent, was found to be spectrally identical with a sample of compound (−)-**14B**.

2-Methoxy-2-methyl-3a,4,5,11c-tetrahydrophenanthro[3,4-*d*]-[1,3]dioxole (15B). A solution of *cis*-tetrahydrodiol **14B** (0.2 g, 0.92 mmol), trimethylorthoacetate (0.5 cm^3) and benzoic acid (0.005 g) was refluxed (2 h); the cooled reaction mixture was filtered, dried (K_2CO_3) and concentrated to yield a mixture (70:30) of diastereoisomers **15B** (0.22 g, 79%) which could not be separated by PLC without partial decomposition. (Found: M$^+$, 270.1252. $C_{17}H_{18}O_3$ requires M$^+$, 270.1255); ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.40 (3 H, s, Me), 1.61 (3 H, s, Me′), 1.84–1.96 (2 H, m, H-4, H′-4), 2.0–2.3 (2 H, m, H-4, H′-4), 2.58–2.76 (2 H, m, H-5, H′-5), 2.84–2.99 (1 H, m, H′-5), 3.00–3.18 (1 H, m, H-5), 3.42 (3 H, s, OMe′), 4.66 (1 H, m, H-3a), 4.75 (1 H, d, H′-3a), 5.62 (1 H, d, $J_{11c,3a}$ 6.7, H-11c), 5.81 (1 H, d, $J_{11c,3a}$ 6.7, H′-11c), 7.14–8.17 (12 H, m, Ar-H, Ar-H′).

(±)-*cis*-1,2-Dihydroxy-1,2,3,4-tetrahydrotriphenylene (14C). Alkene **13C** (0.2 g, 0.87 mmol) on dihydroxylation (OsO_4) yielded tetrahydrodiol **14C** (0.160 g, 70%); mp 220 °C (from MeOH–$CHCl_3$) (lit.[11] mp 220 °C); ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.26 (1 H, br s, OH), 2.16 (1 H, m, H-3), 2.26 (1 H, m, H-3), 3.20 (1 H, m, H-4), 3.46 (1 H, m, H-4), 4.01 (1 H, m, H-2), 5.35 (1 H, d, $J_{1,2}$ 4.4, H-1), 7.64 (4 H, m, Ar-H), 8.10 (1 H, m, Ar-H), 8.38 (1 H, m, Ar-H), 8.71 (2 H, m, Ar-H).

12-Methoxy-12-methyl-9,10,10a,13a-tetrahydrotriphenyleno-[1,2-*d*][1,3]dioxole (15C). Yield 82% (Found: M$^+$, 320.1412. $C_{21}H_{20}O_3$ requires M$^+$, 320.1414); ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.45 (3 H, s, Me′), 1.71 (3 H, s, Me), 2.07 (1 H, m, H-10), 2.12 (1 H, m, H′-10), 2.40 (2 H, m, H-10, H′-10), 2.70 (3 H, s, OMe), 3.27 (4 H, m, H-9, H′-9), 3.52 (3 H, s, OMe′), 4.78 (1 H, m, H-10a), 4.84 (1 H, m, H′-10a), 5.79 (1 H, d, *J* 6.7, H-13a), 5.92 (1 H, d, *J* 6.2, H′-13a), 7.66 (8 H, m, Ar-H), 8.14 (2 H, m, Ar-H, Ar-H′), 8.32 (2 H, m, Ar-H, Ar-H′), 8.72 (4 H, m, Ar-H, Ar-H′).

(±)-*cis*-1,2-Dihydroxy-1,2,3,4-tetrahydrobenzo[*b*]triphenylene (14D). Alkene **13D** (0.05 g. 0.18 mmol) yielded tetrahydrodiol **14D** (0.03 g, 53%), mp 242 °C (from MeOH–$CHCl_3$) (Found: C, 83.6; H, 5.7. $C_{22}H_{18}O_2$ requires C, 84.0; H, 5.8%); ^{1}H NMR (300 MHz, $CDCl_3$–C_5D_5N) δ 1.29 (2 H, br s, OH), 2.10 (1 H, m, H-3), 2.54 (1 H, m, H-3), 3.00 (1 H, m, H-4), 3.28 (1 H, dd, $J_{4,4'}$ 1.7, $J_{4,3}$ 7.6, H-4), 4.21 (1 H, d, $J_{2,1}$12.4, H-2), 5.73 (1 H, s, H-1),

7.49–7.65 (4 H, m, Ar-H), 8.00–8.15 (3 H, m, Ar-H), 8.89 (1 H, d, $J_{8,9}$ 8.0, H-8), 9.18 (1 H, s, H-14), 9.29 (1 H, s, H-9).

2-Methoxy-2-methyl-3a,4,5,15c-tetrahydrobenzo[10,11]triphenyleno[1,2-*d*][1,3]dioxole (15D). Yield 73%; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.47 (3 H, s, Me), 1.77 (3 H, s, Me′), 2.11 (2 H, m, H-4), 2.35 (1 H, m, H-5), 2.62 (1 H, m, H′-4), 2.75 (3 H, s, OMe′), 3.14 (2 H, m, H-5, H′-4), 4.92 (2 H, m, H-3a), 5.90 (1 H, d, *J* 6.2, H′-15c), 6.03 (1 H, d, *J* 6.2, H-15c), 7.58 (4 H, m, Ar-H, Ar-H′), 7.71 (4 H, m, Ar-H, Ar-H′), 8.12 (6 H, m, Ar-H, Ar-H′), 8.79 (1 H, s, H′-14), 8.82 (1 H, s, H-14), 8.87 (1 H, s, H-8), 8.90 (1 H, s, H′-8), 9.20 (2 H, s, H-9, H′-9).

(±)-*cis*-3,4-Dihydroxy-1,2,3,4-tetrahydrodibenz[*a*,*h*]anthracene (14A). Phenylboronic acid (0.35 g) was added to the solution of alkene **13A** (0.15 g, 1.8 mmol) in CH_2Cl_2 during the osmylation procedure. The intermediate phenyl boronate (0.11 g, 15%) obtained was treated with propane-1,3-diol (2 cm^3) and the reaction mixture stirred (3 h) at room temperature to liberate the *cis*-tetrahydrodiol product **14A** (0.05 g, 10%); mp 250–252 °C (Found: M$^+$, 314.1312. $C_{22}H_{18}O_2$ requires M$^+$, 314.1307); ^{1}H NMR (300 MHz, THF-d_8) δ 2.08–2.32 (2 H, m, H-2), 3.07–3.23 (2 H, m, H-1), 3.96 (1 H, m, H-3), 4.02 (1 H, d, *J* 5.8, H-4), 7.62–7.81 (5 H, m, Ar-H), 7.94–8.02 (2 H, m, Ar-H), 8.68 (1 H, s, Ar-H), 9.04 (1 H, d, *J* 8.1, Ar-H), 9.38 (1 H, s, Ar-H).

2-Methoxy-2-methyl-3a,14,15,15a-tetrahydronaphtho-[2′,1′:6,7]phenanthro[1,2-*d*][1,3]dioxole (15A). Yield 70%; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.47 (3 H, s, Me), 1.68 (3 H, s, Me′), 2.11 (2 H, m, H-15), 2.24 (2 H, m, H-15), 2.75 (3 H, s, OMe′), 3.14 (2 H, m, H′-14), 3.30 (2 H, m, H-14, H′-14), 3.50 (3 H, s, OMe), 4.78 (1 H, m, H′-15a), 4.88 (1 H, m, H-15a), 5.40 (1 H, d, $J_{4,3}$ 6.1, H′-3a), 5.52 (1 H, d, $J_{4,3}$ 6.2, H-3a), 7.58 (4 H, m, Ar-H, Ar-H′), 7.70 (6 H, m, Ar-H, Ar-H′), 7.82 (4 H, m, Ar-H, Ar-H′), 8.08 (2 H, m, Ar-H, Ar-H′), 8.54 (2 H, m, Ar-H), 8.80 (2 H, m, Ar-H), 9.25 (2 H, m, Ar-H).

Typical procedure for the synthesis of *trans*-chloroacetates (16A–16D) and bromo-*trans*-chloroacetates (17A–17D)

(−)-(3*S*,4*S*)-3-Acetoxy-4-chloro-1,2,3,4-tetrahydrophenanthrene (16B). A mixture of chlorotrimethylsilane (0.2 cm^3, 1.5 mmol) and triethylamine (0.1 cm^3) in CH_2Cl_2 (5 cm^3) was stirred at 0 °C under nitrogen. A solution of 1,3-dioxolane **15B** (0.15 g, 0.5 mmol) in CH_2Cl_2 (5 cm^3) was then added and the reaction mixture stirred at 0 °C (2 h). The crude *trans*-chloroacetate **16B**, obtained as an oil, was used without purification as its attempted PLC purification resulted in partial decomposition (0.025 g, 81%); $[\alpha]_D$ −22 (*c* 0.5 in $CHCl_3$) (Found: M$^+$, 274.0782. $C_{16}H_{15}O_2Cl$ requires M$^+$, 274.0776); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.80 (3 H, s, $OCOCH_3$), 2.03 (1 H, m, H-2′), 2.43 (1 H, m, H-2), 2.79 (1 H, dd, $J_{1,1'}$ 11.6, $J_{1',2}$ 5.5, H-1′), 3.02 (1 H, m, H-1), 5.50 (1 H, m, H-3), 5.55 (1 H, m, H-4), 7.06 (1 H, d, $J_{9,10}$ 8.5, H-10), 7.32 (1 H, dd, $J_{6,7}$ 7.2, $J_{6,5}$ 8.2, H-6), 7.59 (1 H, d, $J_{9,10}$ 8.4, H-9), 7.66 (1 H, d, $J_{5,6}$ 8.4, H-5).

(−)-(3*S*,4*S*)-1-Bromo-3-acetoxy-4-chloro-1,2,3,4-tetrahydrophenanthrene (17B). *N*-Bromosuccinimide (0.74 g, 0.41 mmol) and azoisobutyronitrile (0.005 g) was added to a solution of the *trans*-chloroacetate **16B** (0.1 g, 0.36 mmol) in CCl_4 (20 cm^3). The reaction mixture was heated under reflux (0.75 h) cooled, filtered and concentrated under reduced pressure. (−)-(3*S*,4*S*)-1-Bromo-3-acetoxy-4-chloro-1,2,3,4-tetrahydrophenanthrene **17B** obtained was found to be a mixture of isomers which decomposed during attempted separation (0.96 g, 76%); $[\alpha]_D$ −12 (*c* 0.4 in $CHCl_3$) (Found: M$^+$, 274.0782. $C_{16}H_{14}BrClO_2$ requires M$^+$, 274.0776); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.04 (3 H, s, $OCOCH_3$), 2.90 (1 H, m, H-2), 3.08 (1 H, m, H-2′), 5.53 (2 H, m, H-3), 5.57 (1 H, d, $J_{4,3}$ 2.7, H-4), 5.67 (1 H, m, H-1), 7.14–8.10 (6 H, m, Ar-H).

(±)-*trans*-2-Acetoxy-1-chloro-1,2,3,4-tetrahydrotriphenylene (16C). 1,3-Dioxolane **15C** (0.100 g, 0.031 mmol) gave the crude chloroacetate **16C** (0.080 g, 79%) (Found: M$^+$, 324.0899. $C_{20}H_{17}O_2Cl$ requires M$^+$, 324.0917); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.95 (3 H, s, OCOMe), 2.39 (1 H, m, H-3), 2.70 (1 H, m, H-3′), 3.32 (1 H, m, H-4′), 5.64 (1 H, m, H-2), 5.66 (1 H, s, H-1), 7.67 (4 H, m, H-8, H-9, H-14, H-15), 8.15 (1 H, d, $J_{7,8}$, 9.1, H-7), 8.24 (1 H, d, $J_{15,16}$ 9.3, H-16), 8.73 (2 H, d, *J* 7.3, Ar-H).

(±)-4-Bromo-2-acetoxy-1-chloro-1,2,3,4-tetrahydrotriphenylene (17C). The *trans*-chloroacetate **16C** (0.07 g, 0.2 mmol) on bromination with *N*-bromosuccinimide gave the crude bromo-*trans*-chloroacetates **17C** (0.68 g, 80%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.10 (3 H, s, $OCOCH_3$), 2.39 (1 H, m, H-3), 2.71 (1 H, m, H-3′), 5.75 (1 H, d, $J_{1,2}$ 2.6, H-2), 5.83 (1 H, m, H-1), 6.11 (1 H, m, H-4), 7.61–8.82 (8 H, m, Ar-H).

(±)-*trans*-2-Acetoxy-1-chloro-1,2,3,4-tetrahydrobenzo[*b*]triphenylene (16D). 1,3-Dioxolane **15D** (0.030 g, 0.081 mmol) gave the crude chloroacetate **16D** (0.023 g, 79%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.96 (3 H, s, OCOMe), 2.38 (1 H, m, H-3′), 2.68 (1 H, m, H-3), 3.34 (2 H, m, H-4), 5.69 (1 H, m, H-2), 5.81 (1 H, m, H-1), 7.42 (1 H, m, Ar-H), 7.56–7.64 (4 H, m, Ar-H), 8.07 (2 H, dd, $J_{12,13}$ 7, $J_{12,13}$ 7.5, H-13, H-10), 8.67 (1 H, s, H-14), 8.85 (1 H, d, $J_{8,7}$ 8.0, H-8), 9.17 (1 H, s, H-9).

(±)-1-Bromo-3-acetoxy-4-chloro-1,2,3,4-tetrahydrobenzo[*b*]-triphenylene (17D). The *trans*-chloroacetate **16D** (0.025 g, 0.067 mmol) was converted into the crude bromo-*trans*-chloroacetates **17D** (0.025 g, 83%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.10 (3 H, s, $OCOCH_3$), 3.22 (2 H, m, H-3), 5.76 (1 H, d, $J_{3,2}$ 2.6, H-2), 5.94 (1 H, m, H-1), 6.06 (1 H, d, $J_{4,3}$ 4.4, H-4), 7.60–7.71 (4 H, m, Ar-H), 8.09 (2 H, m, Ar-H), 8.33 (1 H, m, Ar-H), 8.74 (1 H, s, H-14), 8.85 (1 H, m, Ar-H), 9.16 (1 H, s, H-9).

(±)-*trans*-3-Acetoxy-4-chloro-1,2,3,4-tetrahydrodibenz[*a*,*h*]-anthracene (16A). 1,3-Dioxolane **15A** (0.030 g, 0.081 mmol) gave the crude chloroacetate **16A** (0.025 g, 81%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.98 (3 H, s, OCOMe), 2.35 (1 H, m, H-2), 2.64 (1 H, m, H-2), 3.46 (2 H, m, H-1), 5.35 (1 H, m, H-3), 5.50 (1 H, m, 4-H), 7.38–7.88 (5 H, m, Ar-H), 8.10 (2 H, m, Ar-H), 8.5 (1 H, s, Ar-H), 8.88 (1-H, d, *J* 8.0, Ar-H), 9.20 (1-H, s, Ar-H).

(±)-3-Acetoxy-1-bromo-4-chloro-1,2,3,4-tetrahydrodibenz-[*a*,*h*]anthracene (17A). The *trans*-chloroacetate **16A** (0.025 g, 0.067 mmol) formed the crude bromo-*trans*-chloroacetates **17A** (0.02 g, 72%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.10 (3 H, s, $OCOCH_3$), 3.18 (2 H, m, H-2), 5.45 (1H, d, $J_{3,2}$ 3.1, H-3), 5.62 (1 H, m, H-4), 6.09 (1 H, m, H-1), 7.42–7.78 (5 H, m, Ar-H), 8.18 (2 H, m, Ar-H), 8.63 (1 H, s, Ar-H), 8.80 (1 H, d, *J* 8.0, Ar-H), 9.18 (1 H, s, Ar-H).

Typical procedure for the synthesis of arene oxides ($5A_{RS}$/$5A_{SR}$–$5D_{RS}$/$5D_{SR}$)

(+)-(3*S*,4*R*)-3,4-Epoxy-3,4-dihydrophenanthrene ($5B_{RS}$/$5B_{SR}$). Sodium methoxide (0.055 g, 1.0 mmol) was added to a solution of the bromochloroacetate isomers **17B** (0.05 g, 0.14 mmol) in dry THF (40 cm^3) under nitrogen and the reaction mixture was then stirred (12 h) at 0 °C in the absence of light. The solvent was removed under reduced pressure at ice-bath temperature and the residue extracted with diethyl ether (30 cm^3). The ether layer was washed with KOH solution (1%) followed by cold water, dried (K_2CO_3) and concentrated to yield the crude oxide **5B**; it was recrystallized from diethyl ether–pentane at −70 °C (0.025 g, 60% yield); $[\alpha]_D$ +165 (*c* 0.7 in $CHCl_3$) (lit.[10] $[\alpha]_D$ +271, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.18 (1 H, m, H-3), 5.14

(1 H, d, $J_{4,3}$ 4.0, H-4), 6.44 (1 H, dd, $J_{2,3}$ 4.0, $J_{2,1}$ 9.5, H-2), 6.78 (1 H, dd, $J_{1,10}$ 1.7, $J_{2,1}$ 9.5, H-1), 7.47 (1 H, d, $J_{9,10}$ 8.4, H-10), 7.59 (1 H, dd, $J_{7,6}$ 7.1, $J_{7,8}$ 8.2, H-7), 7.65 (1 H, dd, $J_{6,7}$ 7.1, $J_{6,5}$ 7.9, H-6), 7.81 (1 H, d, $J_{9,10}$ 8.4, H-9), 8.44 (1 H, d, $J_{8,7}$ 8.2, H-8).

1,2-Epoxy-1,2-dihydrotriphenylene ($5C_{RS}$/$5C_{SR}$). A mixture of bromochloroacetate isomers **17C** (0.07 g, 0.17 mmol) was converted to 1,2-epoxy-1,2-dihydrotriphenylene $\mathbf{5C}_{RS}$/$\mathbf{5C}_{SR}$ (0.03 g, 70%); mp 165–167 °C (from $CHCl_3$) (lit.[21]mp 167–168 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.34 (1 H, m, H-2), 5.32 (1 H, d, $J_{1,2}$ 3.8, H-1), 6.73 (1 H, dd, $J_{2,3}$ 3.8, $J_{3,4}$ 9.8, H-3), 7.50–7.67 (5 H, m, H-4, H-6, H-7, H-10, H-11), 8.39 (1 H, m, H-12), 8.49 (1 H, m, H-5), 8.73 (2 H, m, H-8, H-9).

1,2-Epoxy-1,2-dihydrobenzo[*b*]triphenylene ($5D_{RS}$/$5D_{SR}$). The bromochloroacetate isomeric mixture **17D** (0.025 g, 0.06 mmol) was converted to a relatively unstable product which was identified as 1,2-epoxy-1,2-dihydrobenzo[*b*]triphenylene $\mathbf{5D}_{RS}$/$\mathbf{5D}_{SR}$ (0.010 g, 68%);^{1}H NMR (300 MHz, $CDCl_3$) δ 4.38 (1 H, m, H-2), 5.46 (1 H, d, $J_{1,2}$ 4.1, H-1), 6.78 (1 H, dd, $J_{2,3}$ 4.0, $J_{3,4}$ 10.0, H-3), 7.55–7.69 (5 H, m, H-4, Ar-H), 8.08 (3 H, m, Ar-H), 8.73–8.80 (1 H, m, Ar-H), 8.85 (1 H, s, H-14), 9.18 (1H, s, H-9).

3,4-Epoxy-3,4-dihydrodibenzo[*a*,*h*]anthracene ($5A_{RS}$/$5A_{SR}$). The bromochloroacetate isomers **17A** (0.025 g, 0.06 mmol) also gave a relatively unstable product 3,4-epoxy-3,4-dihydrodibenzo[*a*,*h*]anthracene $\mathbf{5A}_{RS}$/$\mathbf{5A}_{SR}$ (0.012 g, 70%); ^{1}H NMR (500 MHz, THF-d_8) δ 4.42 (1 H, m, H-3), 4.85 (1 H, d, $J_{3,4}$ 3.9, H-4), 6.94 (1 H, dd, $J_{2,3}$ 4.0, $J_{2,1}$ 10.0, H-2), 7.55–7.99 (5 H, m, H-1, Ar-H), 8.36 (3 H, m, Ar-H), 8.73 (2 H, m, Ar-H), 9.15 (1 H, m, Ar-H).

Typical photoisomerization reactions of arene oxides ($5A_{RS}$/$5A_{SR}$, $5C_{RS}$–$5C_{SR}$ and $5D_{RS}$/$5D_{SR}$) to yield oxepines (11A, 11C and 11D)

A mixture of benz[5,6]anthra[1,2-*b*]oxepine **11A** and arene oxide $\mathbf{5A}_{RS}$/$\mathbf{5A}_{SR}$ (0.1 g) was dissolved in $CDCl_3$ (1 cm^3) containing triethylamine (0.005 g) in a standard pyrex NMR tube; the solution was irradiated (0.5 h) under UV light generated from a medium pressure mercury lamp (>300 nm) at ambient temperature. The reaction mixture, on separation by PLC, gave oxepine **11A** and a minor phenolic product. Further irradiation resulted in isomerization of oxepine **11A** to phenolic isomers.

Benz[5,6]anthra[1,2-*b*]oxepine **11A**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.80 (1 H, m, H-3), 6.40 (1 H, d, *J* 5.5, H-2), 6.53 (1 H, dd, *J* 5.0, *J* 11.4, H-4), 7.60–9.15 (11 H, m, H-5 and ArH).

Phenanthro[10,9-*b*]oxepine **11C**[21]: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.83 (1 H, dd, $J_{2,3} = J_{3,4}$ 5.1, H-3), 6.50 (1 H, d, $J_{2,3}$ 5.1, H-2), 6.57 (1 H, dd, $J_{3,4}$ 5.1, $J_{4,5}$ 11.3, H-4), 7.50–8.70 (9 H, m, H-5 and Ar-H).

Benz[3,4]anthra[1,2-*b*]oxepine **11D**[26]: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.84 (1 H, dd, $J_{2,3} = J_{3,4}$ 5.1, H-3), 6.53 (1 H, dd, $J_{3,4}$ 5.1, $J_{4,5}$ 11.2, H-4), 6.57 (1 H, d, $J_{2,3}$ 5.1, H-2), 7.50–7.73 (5 H, m, H-5 and Ar-H), 8.02–8.14 (3 H, m, Ar-H), 8.84–8.97 (1 H, m, Ar-H), 9.07 (1 H, s, Ar-H), 9.3 (1 H, s, H-9).

Acknowledgements

We thank DENI (I.N.B., A.S.), the Queen's University of Belfast (S. K. B., F. H.) and the BBSRC (N.D.S.) for funding.

References

1 D. R. Boyd, N. D. Sharma, J. S. Harrison, J. T. G. Hamilton, D. B. Harper and W. C. McRoberts, *J. Chem. Soc., Chem. Commun.*, 2000, 1481.
2 D. M. Jerina, J. W. Daly, B. Witkop, P. Zaltzman-Nirenberg and S. Udenfriend, *J. Am. Chem. Soc.*, 1968, **90**, 6525.
3 D. R. Boyd and D. M. Jerina, in *Small Ring Heterocycles*, *Chemistry of Heterocyclic Compounds*, part 3, ed. A. Hassner, vol. 42, Wiley, New York, 1985, 197.
4 D. R. Boyd and N. D. Sharma, *Chem. Soc. Rev.*, 1996, 289.
5 D. R. Boyd, N. D. Sharma, H. Dalton and D. A. Clarke, *Chem. Commun.*, 1996, 45.
6 M. N. Akhtar, D. R. Boyd and J. G. Hamilton, *J. Chem. Soc., Perkin Trans. 1*, 1979, 2437.
7 D. R. Boyd, N. D. Sharma, R. Agarwal, N. A. Kerley, R. A. S. McMordie, A. Smith, H. Dalton, A. J. Blacker and G. N. Sheldrake, *J. Chem. Soc., Chem. Commun.*, 1994, 1693.
8 D. R. Boyd and M. E. Stubbs, *J. Am. Chem. Soc.*, 1983, **105**, 2554.
9 D. R. Boyd, R. M. E. Greene, J. D. Neill, M. E. Stubbs, H. Yagi and D. M. Jerina, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1447.
10 S. K. Balani, D. R. Boyd, E. S. Cassidy, G. I. Devine, J. F. Malone, K. M. McCombe, N. D. Sharma and W. B. Jennings, *J. Chem. Soc., Perkin Trans. 1*, 1983, 2751.
11 D. R. Boyd, D. A. Kennedy, J. F. Malone, G. A. O'Kane, D. M. Jerina, D. R. Thakker and H. Yagi, *J. Chem. Soc., Perkin Trans. 1*, 1987, 369.
12 D. R. Boyd, N. D. Sharma, R. Agarwal, N. A. Kerley, R. A. S. McMordie, A. Smith, H. Dalton, A. J. Blacker and G. N. Sheldrake, *J. Chem. Soc., Chem. Commun.*, 1994, 1693.
13 D. R. Boyd, S. K. Agarwal, S. K. Balani, R. Dunlop, G. A. O'Kane, N. D. Sharma, W. B. Jennings, H. Yagi and D. M. Jerina, *J. Chem. Soc., Chem. Commun.*, 1987, 1633.
14 H. Yagi and D. M. Jerina, *J. Am. Chem. Soc.*, 1973, **95**, 243; H. Yagi and D. M. Jerina, *J. Am. Chem. Soc.*, 1975, **97**, 3185.
15 D. R. Boyd, K. A. Dawson, G. S. Gadaginamath, J. G. Hamilton, J. F. Malone and N. D. Sharma, *J. Chem. Soc., Perkin Trans. 1*, 1981, 94.
16 D. R. Boyd, G. S. Gadaginamath, N. D. Sharma, A. F. Drake, S. F. Mason and D. M. Jerina, *J. Chem. Soc., Perkin Trans. 1*, 1981, 2233.
17 D. R. Boyd, G. S. Gadaginamath, A. Kher, J. F. Malone, D. M. Jerina and H. Yagi, *J. Chem. Soc., Perkin Trans. 1*, 1980, 2113.
18 D. R. Boyd, M. G. Burnett and R. M. E. Greene, *J. Chem. Soc., Chem. Commun.*, 1981, 838.
19 D. R. Boyd and R. M. E. Greene, *J. Chem. Soc., Perkin Trans. 1*, 1982, 1535.
20 S. K. Balani, D. R. Boyd, R. M. E. Greene and D. M. Jerina, *J. Chem. Soc., Perkin Trans. 1*, 1984, 1781.
21 D. R. Boyd, N. D. Sharma, S. K. Agarwal, G. S. Gadaginamath, G. A. O'Kane, W. B. Jennings, H. Yagi and D. M. Jerina, *J. Chem. Soc., Perkin Trans. 1*, 1993, 423.
22 S. K. Agarwal, D. R. Boyd, R. Dunlop and W. B. Jennings, *J. Chem. Soc., Perkin Trans. 1*, 1988, 3013.
23 D. R. Boyd and G. A. O'Kane, *J. Chem. Soc., Perkin Trans. 1*, 1990, 2079.
24 R. Agarwal and D. R. Boyd, *J. Chem. Soc., Perkin Trans. 1*, 1993, 2869.
25 D. R. Boyd and G. A. O'Kane, *Tetrahedron Lett.*, 1987, **28**, 6395.
26 P. L. Kole and S. Kumar, *J. Chem. Soc., Perkin Trans. 1*, 1991, 2151.
27 K. L. Platt, H. Frank and F. Oesch, *J. Chem. Soc., Perkin Trans. 1*, 1989, 2299.
28 A. M. Jeffrey, H. J. C. Yeh, D. M. Jerina, T. R. Patel, J. F. Davey and D. T. Gibson, *Biochemistry*, 1975, **14**, 575.
29 D. R. Boyd, R. A. S. McMordie, H. P. Porter, H. Dalton, R. O. Jenkins and O. W. Howarth, *J. Chem. Soc., Chem. Commun.*, 1987, 1722.
30 D. M. Jerina, H. Selander, H. Yagi, M. C. Wells, J. F. Davey, V. Mahadevan and D. T. Gibson, *J. Am. Chem. Soc.*, 1976, **98**, 5988.
31 M. N. Akhtar, D. R. Boyd, N. J. Thompson, M. Koreeda, D. T. Gibson, V. Mahadevan and D. M. Jerina, *J. Chem. Soc., Perkin Trans. 1*, 1975, 2506.
32 M. Koreeda, M. N. Akhtar, D. R. Boyd, J. D. Neill, D. T. Gibson and D. M. Jerina, *J. Org. Chem.*, 1978, **43**, 1023.
33 D. T. Gibson, V. Mahadevan, D. M. Jerina, H. Yagi and H. J. C. Yeh, *Science*, 1975, **189**, 295.
34 D. M. Jerina, P. J. van Bladeren, H. Yagi, D. T. Gibson, V. Mahadevan, A. S. Neese, M. Koreeda, N. D. Sharma and D. R. Boyd, *J. Org. Chem.*, 1984, **49**, 3621.
35 D. R. Boyd, N. D. Sharma, R. Agarwal, S. M. Resnick, M. J. Schoken, D. T. Gibson, J. M. Sayer, H. Yagi and D. M. Jerina, *J. Chem. Soc., Perkin Trans. 1*, 1997, 1715.
36 D. R. Boyd and G. N. Sheldrake, *Nat. Prod. Rep.*, 1998, **15**, 309.
37 Y. Pommier, G. Kohlhagen, P. Pourquier, J. M. Sayer, H. Kroth and D. M. Jerina, *Proc. Natl. Acad. Sci. U.S.A.*, 2000, **97**, 2040.
38 E. L. Kennaway, *Biochem. J.*, 1930, **24**, 497.
39 K. L. Platt and M. Schollmeier, *Chem. Res. Toxicol.*, 1994, **7**, 89.
40 R. E. Parales, S. M. Resnick, C. L. Yu, D. R. Boyd, N. D. Sharma and D. T. Gibson, *J. Bacteriol.*, 2000, **182**, 5495.
41 S. K. Balani, P. J. van Bladeren, E. S. Cassidy, D. R. Boyd and D. M. Jerina, *J. Org. Chem.*, 1987, **52**, 137.