Synthesis of Benzo[*g*]chrysene 5,6-Oxide and 7,8-Oxide and their Isomeric Oxepines

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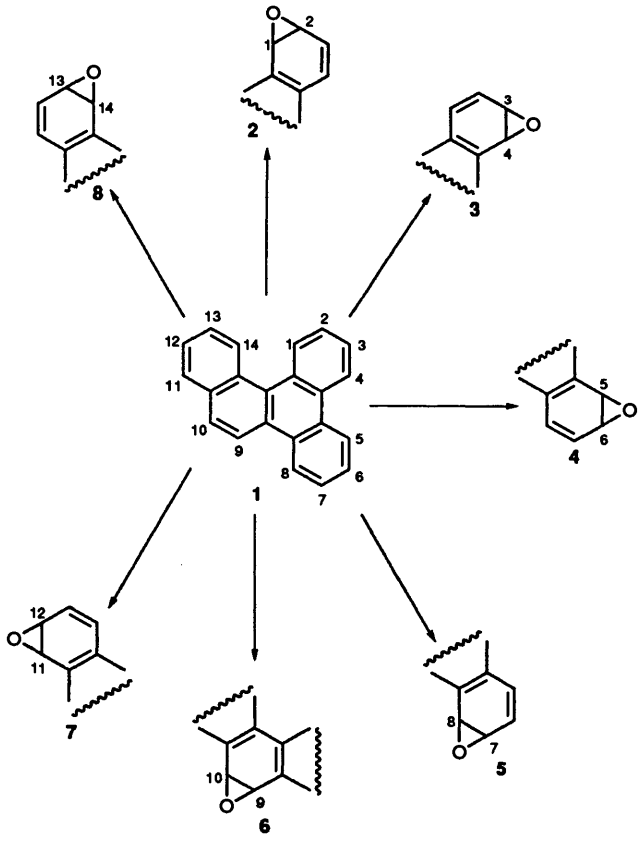
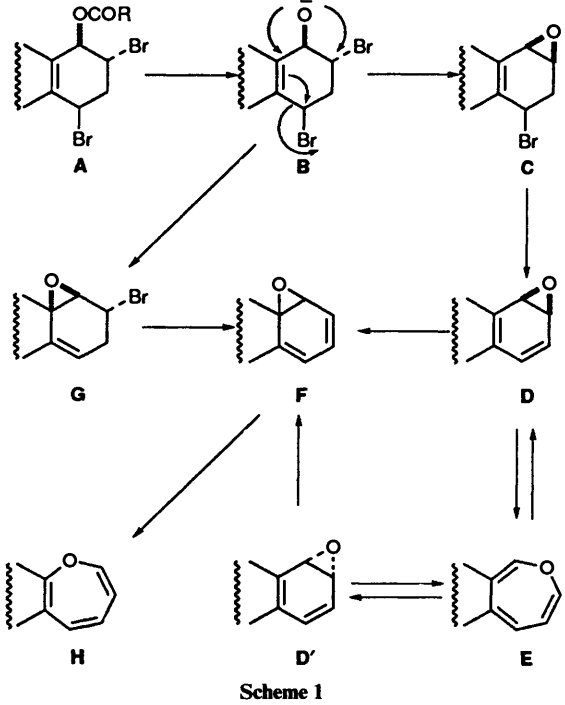
Benzo[*g*]chrysene 5,6-oxide and benzo[*g*]chrysene 7,8-oxide when synthesised from dibromo acetate precursors were accompanied by the stable oxepine isomers benzo[3,4]phenanthro[2,1-*b*]-oxepine and benzo[3,4]phenanthro[1,2-*b*]oxepine. The isolation of the latter oxepines, and their formation by photochemichal rearrangement of the isomeric arene oxides, are in accord with earlier predictions from PMO calculations.

Benzo[*g*]chrysene **1**, a carcinogenic member[1-3] of the polycyclic aromatic hydrocarbon (PAH) series, has been identified as a component of crude oil.[4] In common with other PAHs, the initial step in the mammalian metabolism of benzo[*g*]chrysene **1** involves enzyme-catalysed (cytochrome P450) epoxidation to yield arene oxides.[5] These arene oxides are not generally detected but their presence may be inferred from the isolation of *trans*-dihydro diols (from epoxide hydrolase-catalysed hydration) and glutathione conjugates (from glutathione *S*-transferase-catalysed attack of glutathione).[5] Benzo[*g*]chrysene **1**, is the simplest member of the PAH series to have a



combination of non-K-, K-, bay- and fjord regions. Thus, the non-K region, **7**, K-region, **6**, bay-region, **3** and **5**, and fjord-region, **2** and **8**, arene oxides could all, in principle, be produced by cytochrome P450-catalysed epoxidation. An earlier report from these laboratories[6] showed how the K-region arene oxide, **6**, was chemically synthesised. Furthermore, an early attempt to synthesise the fjord region arene oxide **2**, although unsuccessful,[6] provided a new synthetic route to diarene oxides of PAHs[7] including a diarene oxide of benzo[*g*]chrysene (benzo[*g*]chrysene 1,2:9,10-dioxide).

The application of PMO calculations to the isomerization of arene oxides to yield oxepines has allowed predictions to be made concerning the configurational stability of arene oxides within the PAH series.[8] Thus, for the benzo[*g*]chrysene series it was predicted[8] that (at ambient temperature) arene oxides **2–5** should rapidly racemize ($[\alpha]_D$ values would not be measurable due to racemization), arene oxide **6** should be configurationally stable (an $[\alpha]_D$ value could be obtained) and arene oxides **7** and **8** would be on the borderline of configurational stability ($[\alpha]_D$ values initially observable would slowly decrease at ambient temperature). Potential synthetic routes to arene oxides **2–5**, **7** and **8** from a dibromo ester precursor (**A** ⟶ **B** ⟶ **C** ⟶ **D**) and racemization *via* the unstable oxepine intermediate (**D** ⟶ **E** ⟶ **D'**) is shown in Scheme 1. The synthesis[9] of both enantiomers of the K-region



Scheme 1

arene oxide **6** (by simple modification of the original synthetic route[6]), without evidence of racemization, provides confirmation of the earlier prediction[8] that the oxepine tautomer (**E**) cannot readily be formed.

The PMO calculations,[8] originally used to predict the ease of racemization of arene oxides (**D**) in the PAH series *via* an unstable oxepine intermediate (**E**), have also been used to predict[10] the concomitant formation of relatively stable oxepines (**H**) during the normal synthetic route to arene oxides (**D**) and (**D'**) and the facile photochemically induced sigmatropic rearrangement (oxygen walk mechanism) of arene oxides (**D** or **D'** ⟶ **F** ⟶ **H**). Thus, it was predicted (and *subsequently confirmed* experimentally) that the oxepines and arene oxides of benz[*a*]anthracene (1,2- and 3,4-),[11] triphenylene (1,2-),[11] benzo[*e*]pyrene (9,10-),[12] dibenz[*a*,*c*]-anthracene (1,2-, 3,4-),[13,14] dibenz[*a*,*h*]anthracene (3,4-)[10] and dibenz[*a*,*j*]anthracene (3,4-)[15] would be formed as indicated by Scheme 1. Of the 18 examples of arene oxides, **D**, predicted to be associated with stable oxepines, **H**,[8,10] thus far eight examples have been confirmed.

It is noteworthy that only one member of the PAH series, from the 18 considered[8] would be expected to yield more than two relatively stable oxepines, *i.e.* benzo[*g*]chrysene **1**. Thus, it has been predicted that the stable isomeric oxepines (**H**) should be found during the synthesis and photoisomerization of four arene oxides (**2**–**5**).

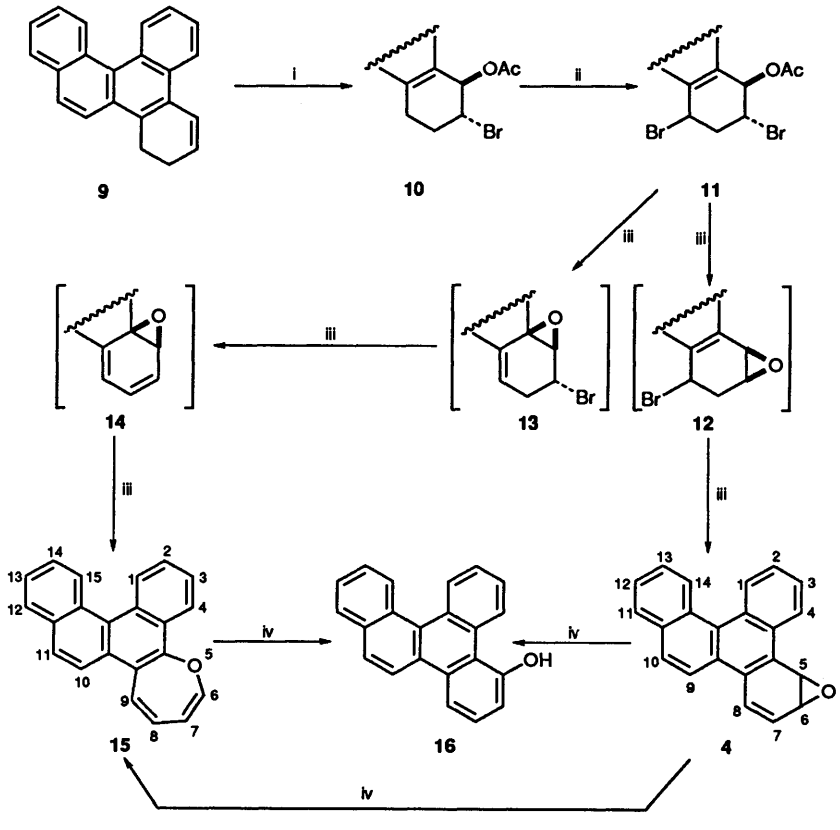
As part of a wider programme to make arene oxides and *trans*-dihydro diols of PAHs available for metabolism, mutagenicity–carcinogenicity studies, and to confirm earlier predictions[8,10] concerning the ease of racemization and stable oxepine formation in the PAH series, the synthesis of benzo[*g*]chrysene 5,6-oxide **4**, and 7,8-oxide **5**, is now reported.

The availability of the alkene 7,8-dihydrobenzo[*g*]chrysene **9**[3] provided a convenient precursor for the synthesis of arene oxide **4** by the normal dibromo acetate route (Scheme 2). Conversion of the alkene **9** in turn to bromo acetate **10** and dibromo acetate **11**, followed by treatment with sodium methoxide, yielded the expected mixture of 5,6-epoxy-5,6-dihydrobenzo[*g*]chrysene **4** (75%) and benzo[3,4]phenanthro[2,1-*b*]oxepine **15** (25%). Although neither bromo epoxide intermediates, **12** and **13** nor epoxide **14** were isolated or detected, their involvement was inferred from earlier studies where bromo epoxides of similar structure to compound **12** have been isolated after treatment of the analogous dibromo acetates with sodium methoxide. When similar types of 'reverse' bromoacetate precursors (*i.e.* with the positions of the bromine atom and acetate group interchanged) were converted into 'reverse' dibromo acetates and subsequently treated with NaOMe, no stable oxepine products were obtained.[16] The latter observation is consistent with the proposal[10] that these stable oxepines are produced by an S_N2' mechanism as shown in Scheme 1.

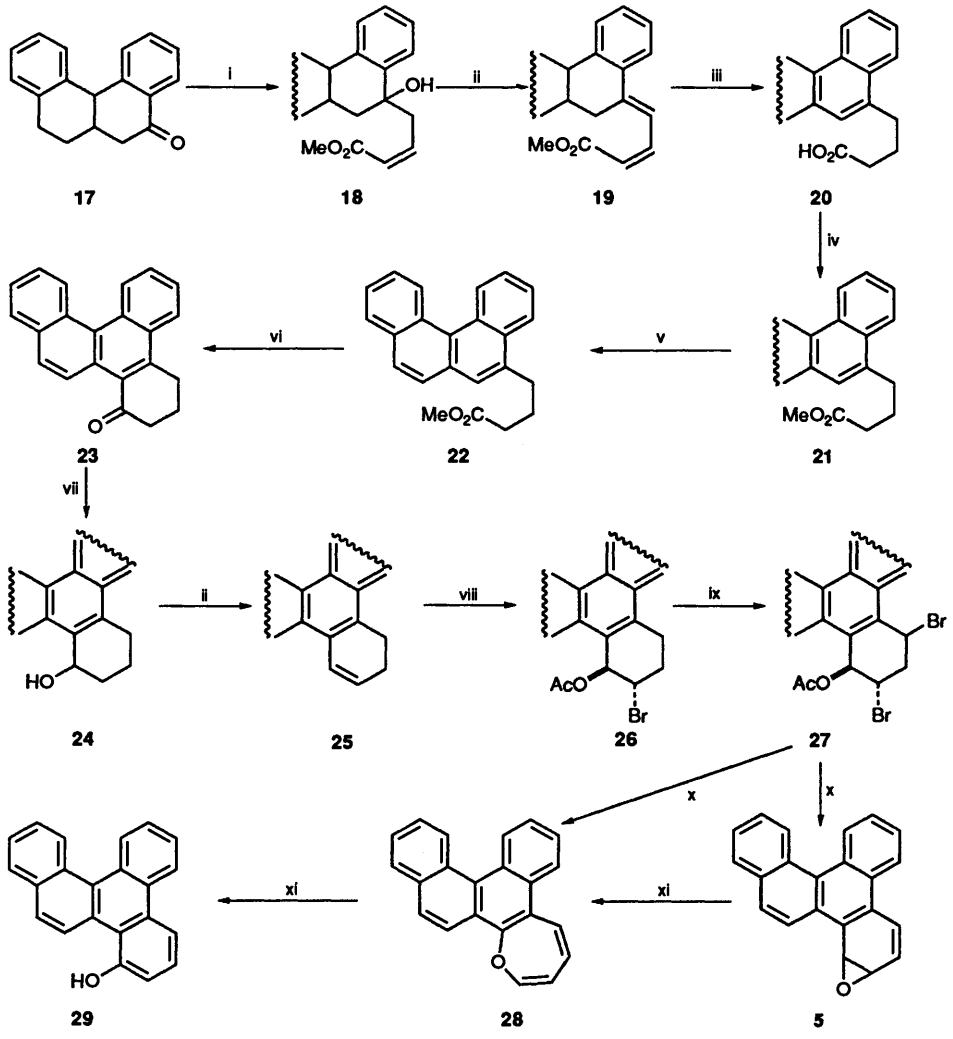
The mixture of arene oxide **4** and oxepine **15** was found to be very unstable and totally aromatized during attempted separation by fractional crystallization or preparative TLC on silica gel [hexane(75):diethyl ether(25)] to yield mainly benzo[*g*]chrysene-5-ol **16**. Decomposition of the arene oxide–oxepine mixture (**4**:**15**) to yield the phenol **16** was also found to occur on storage at low temperature. Irradiation of this mixture in $CDCl_3$ in an NMR tube (10 min at ambient temperature using UV light of wavelength > 300 nm) showed an increase in the proportion of oxepine **15** (from 25 ⟶ 52% relative to an internal reference peak), the formation of benzo[*g*]chrysene-5-ol **16**, (48%) and total disappearance of the arene oxide peak, **4**. Their instability precluded the isolation of pure samples of either arene oxide **4**, or oxepine **16**.

The synthesis of arene oxide **5** from the known precursor 6a,7,8,12b-tetrahydrobenzo[*c*]phenanthren-5(6*H*)-one **17**,[17] was carried out in 11 steps using established synthetic methods which have previously been successfully used in the synthesis of other arene oxides from the PAH series (Scheme 3).

The conversion of the tetracyclic ketone, **17**, through a series of intermediates (**18**, **19**, **20**, **21**, **22**) into the pentacyclic ketone **23** was found to proceed in a total yield of 15%. The remaining five synthetic steps from ketone **23** to benzo[*g*]chrysene 7,8-oxide, **5**, (Scheme 3), were completed using a sequence identical



Scheme 2 *Reagents and conditions:* I, *N*-bromoacetamide–AcOH; ii, *N*-bromosuccimide–AcOH; iii, NaOMe–THF; iv, *hν*



Scheme 3 *Reagents and conditions:* i, Methyl 4-bromocrotonate; ii, *p*-$MeC_6H_4SO_3H$–benzene; iii, KOH–ethylene glycol; iv, HCl–MeOH; v, Pd/C; vi, HF; vii, $NaBH_4$–MeOH; viii, NBA–AcOH; ix, NBS–CCl_4; x, NaOMe–THF; xi, *hν*

with that shown for arene oxide **4** (Scheme 2). Benzo[*g*]chrysene 7,8-oxide, **5**, obtained by the synthetic route shown (Scheme 3) was similarly found to be mixed with the isomeric oxepine, **28**. The ratio of arene oxide **5**: oxepine, **28** (75 : 25) observed in the crude product mixture (^{1}H-NMR analysis) appeared to be identical with that previously observed for arene oxide **4** and oxepine **15**. The arene oxide–oxepine mixture (**5**–**28**) appeared to be slightly more stable than the previously synthesised arene oxide–oxepine mixture (**4**–**15**) and thus relatively pure samples of both arene oxide, **5**, and oxepine, **28**, could be obtained by fractional crystallization from pentane at −70 °C. Arene oxide **5** crystallized out preferentially, while the mother liquors yielded a semi-solid product which appeared to be largely the more soluble oxepine **28**. Attempted further purification of the latter oxepine **28** by PLC on silica gel resulted in aromatization to yield a phenolic product which appeared to be largely chrysen-8-ol, **29**. This phenol was also obtained by allowing arene oxide **5** to remain at ambient temperature for several days. Photoisomerization of pure arene oxide **5** in an NMR tube ([$^2H_8$]THF, 10 mins, >300 nm) indicated a 67% conversion into oxepine **28** and aromatization of 33% to yield chrysen-8-ol, **29**.

The synthesis of arene oxides **4** and **5** and concomitant formation of oxepines **15** and **28** is thus in accord with earlier predictions.[8,10] Similarly, the photoisomerization of arene oxides **4** and **5** to yield the corresponding oxepines (**15** and **28**), allied to earlier similar observations,[10,15] provide a total of 10 examples of relatively stable oxepines now isolated from the 18 predicted.[8,10] To our knowledge the synthesis of the remaining eight oxepines has not to date been attempted. Three of the seven possible arene oxide derivatives of benzo[*g*]-chrysene (**4**, **5** and **6**) have now been synthesised. The synthesis of the appropriate dihydrobenzo[*g*]chrysene precursors of arene oxides **2**, **3** and **7** have also been reported.[3,6,9] It has been predicted[9] that epoxidation at the 11,12-bond of benzo[*g*]chrysene to yield arene oxide **7**, followed by hydration to yield the corresponding *trans*-11,12-dihydro 11,12-diol and further epoxidation to yield the 13,14-epoxy-11,12,13,14-tetrahydrobenzo[*g*]chrysene-11,12-diols will account for the carcinogenicity of the benzo[*g*]chrysene.

Experimental

^{1}H NMR spectra were recorded at 300 MHz (General Electric QE 300 MHz) and *J* values are given in Hz. Tetramethylsilane was used as internal reference and $CDCl_3$ as solvent unless otherwise stated.

Mass spectra were recorded at 70 eV on an AEI-MS902 spectrometer updated by V.G. Instruments. Accurate molecular masses were determined by the peak-matching method using perfluorokerosene as standard reference and were accurate to within ±0.0000 06 amu. Analytical TLC was carried out on Merck Kieselgel $60F_{254}$ plates and spots were visualised using a Hanovia Chromatolite UV lamp. Flash chromatography was

carried out using Merck Kieselgel 60 (230–400 mesh) at a flow rate of *ca.* 2.5 cm^3 min^{-1}.

7.8-*Dihydrobenzo*[g]*chrysene* **9**.—5,6,7,8-Tetrahydrobenzo-[*g*]chrysen-5-ol (1.2 g, 4 mmol) in dry benzene (250 cm^3) was gently heated in the presence of a trace of toluene-*p*-sulfonic acid for 0.5 h according to the literature procedure.[3] The solution was cooled and diluted with water (300 cm^3) and the benzene layer was separated, washed, dried ($MgSO_4$), and concentrated. The residue was then purified by flash chromatography (hexane–diethyl ether, 90:10). Concentration of the chromatography fractions yielded 7,8-dihydrobenzo-[*g*]chrysene **9** (1.0 g, 90%) as a viscous oil, δ_H 2.45 (2 H, m, 7-H), 3.25 (2 H, t, $J_{8,7}$ 8.8, 8-H), 6.31 (1 H, dt, $J_{5,6}$ 9.8 and $J_{6,7}$ 4.6, 6-H), 7.29 (1 H, d, $J_{5,6}$ 9.8, 5-H), 7.51–7.58 (4 H, m, 2-H, 3-H, 12-H and 13-H), 7.83 (1 H, d, $J_{10,9}$ 9.0, 10-H), 7.92 (1 H, dd, *J* 7.7 and *J* 1.8, Ar-H), 8.04 (1 H, d, $J_{9,10}$ 9.0, 9-H), 8.22 (1 H, dd, *J* 6.7 and *J* 2.4, Ar-H) and 8.90–8.94 (2 H, m, 1-H and 14-H). The ^1H NMR spectrum was similar to that previously reported.[3]

trans-6-*Bromo*-5,6,7,8-*tetrahydrobenzo*[g]*chrysen*-5-*yl Acetate* **10**.—To a stirred solution of the benzo[*g*]chrysene **9** (0.6 g, 2.14 mmol) and lithium acetate (0.72 g, 7 mmol) in dry tetrahydrofuran (THF) (10 cm^3) and glacial acetic acid (50 cm^3) was added *N*-bromoacetamide (0.36 g, 2.6 mmol). Stirring was continued for 3 h. The reaction mixture was poured onto crushed ice and the precipitated product was filtered off and dissolved in diethyl ether. The latter solution was washed with water and aq. sodium hydrogen carbonate, dried ($MgSO_4$) and then concentrated to yield the crude bromo acetate **10**. Recrystallization of this from diethyl ether–pentane gave yellow crystals of the *title compound* **10** (0.627 g, 70%), m.p. 144 °C (Found: C, 68.9; H, 4.7. $C_{24}H_{19}BrO_2$ requires C, 68.9; H, 4.6%); δ_H 2.12 (3 H, s, OCH_3), 2.44–2.64 (2 H, m, 7-H), 3.46–3.52 (2 H, m, 8-H), 4.77 (1 H, dt, $J_{6,5}$ 2.1 and $J_{6,7}$ 6.0, 6-H), 6.84 (1 H, d, $J_{5,6}$ 2.0, 5-H), 7.61–7.69 (4 H, m, 2-H, 3-H, 12-H and 13-H), 7.92–7.95 (1 H, m, Ar-H), 7.97 (1 H, d, $J_{10,9}$ 9.1, 10-H), 8.00–8.04 (1 H, m, Ar-H), 8.13 (1 H, d, $J_{9,10}$ 9.1, 9-H) and 8.98–9.03 (2 H, m, 1-H and 14-H).

trans-6,8-*Dibromo*-5,6,7,8-*tetrahydrobenzo*[g]*chrysen*-5-*yl Acetate* **11**.—A mixture of the acetate **10** (0.2 g, 0.48 mmol), *N*-bromosuccinimide (0.093 g, 0.52 mmol) and α,α′-azoisobutyronitrile (0.005 g) in CCl_4 (25 cm^3) was heated at 50–60 °C using a heat lamp for 35 min under an atmosphere of N_2. The solution was filtered and concentrated to yield a pale yellow solid which was identified as the title compound **11** (0.168 g, 71%). Owing to instability this compound was identified on the basis of the ^1H NMR spectrum only and used in the next step without purification; δ_H 2.17 (3 H, s, OCH_3), 2.99–3.27 (2 H, m, 7-H), 4.98–5.04 (1 H, m, 6-H), 6.10 (1 H, dd, $J_{8,7} = J_{8,7'}$ 3.8, 8-H), 7.16 (1 H, d, $J_{5,6}$ 6.8, 5-H), 7.59–7.98 (4 H, m, Ar-H), 8.00–8.24 (4 H, m, Ar-H) and 8.93–8.96 (2 H, m, 1-H and 14-H).

Benzo[g]*chrysene* 5,6-*Oxide* (5,6-*Epoxy*-5,6-*dihydrobenzo*-[g]*chrysene*) **4** *and Benzo*[3,4]*phenanthro*[2,1-b]*oxepine* **15**.—A solution of the acetate **11** (0.168 g, 0.34 mmol) was stirred in dry THF (20 cm^3) under N_2 and sodium methoxide (0.05 g, 0.92 mmol) was added to the cooled solution (0 °C). After the mixture had been stirred at −20 °C for 12 h it was diluted with diethyl ether (60 cm^3), washed with water and aq. KOH, dried ($MgSO_4$) and then concentrated under reduced pressure at ambient temperature. The product proved to be a mixture of the title compounds **4** and **15**, and (0.047 g, 48%) in the ratio of 75:25. This mixture was very unstable and was found to aromatize during attempted purification/separation. Thus, identification of the arene oxide **4** and the oxepine **15** was confined to MS and ^1H NMR data on the isomeric mixture (Found: M, 294.10462, $C_{22}H_{14}O$ requires, *M*, 294.10446). Compound **4**: δ_H 4.41–4.44 (1 H, ddd, $J_{6,5}$ 4.0, $J_{6,7}$ 3.8 and $J_{6,8}$ 2.1, 6-H), 5.45 (1 H, d, $J_{5,6}$ 4.0, 5-H), 6.78 (1 H, dd, $J_{7,8}$ 9.9 and $J_{7,6}$ 3.7, 7-H), 7.51–7.92 (5 H, m, 8-H and Ar-H), 7.96 (1 H, d, $J_{10,9}$ 8.9, 10-H), 7.99–8.01 (2 H, m, Ar-H), 8.29 (1 H, d, $J_{9,10}$ 8.9, 9-H) and 9.00–9.05 (2 H, m, Ar-H).

Compound **15**: δ_H 5.83 (1 H, dd, $J_{8,9} = J_{8,7}$ 5.1, 8-H), 6.55 (1 H, dd, $J_{7,8}$ 5.1 and $J_{7,6}$ 8.0, 7-H), 6.60 (1 H, d, $J_{9,8}$ 5.2, 9-H), 7.51–7.72 (5 H, m, 6-H and Ar-H), 7.92 (1 H, m, Ar-H), 8.00 (1 H, dd, *J* 7.8 and 1.5, Ar-H), 8.05 (1 H, m, Ar-H), 8.50 (1 H, dd, *J* 7.7 and 1.6, Ar-H) and 9.00–9.02 (2 H, m, 1-H and 15-H).

During attempted purification of the mixture of the arene oxide **4** and the oxepine **15** by PLC using hexane–diethyl ether (80:20), aromatization occurred to yield benzo[*g*]chrysen-5-ol **16**, m.p. 103 °C (from diethyl ether–hexane) (Found: M, 294.10446, $C_{22}H_{14}O$ requires, *M*, 294.10446); δ_H(300 MHz, $CDCl_3$) 7.08 (1 H, d, $J_{6,7}$ 7.6, 6-H), 7.52 (1 H, dd, $J_{7,6}$ 7.8 and $J_{7,8}$ 8.1, 7-H) 7.55–7.98 (5 H, m, 2-H, 3-H, 11-H, 12-H and 13-H), 7.96 (1 H, d, $J_{10,9}$ 8.9, 10-H), 7.99 (1 H, d, *J* 7.1, Ar-H), 8.24 (1 H, d, $J_{8,7}$ 8.1, 8-H), 8.53 (1 H, d, $J_{9,10}$ 8.9, 9-H), 8.82 (1 H, d, *J* 7.8, Ar-H) and 8.90 (1 H, d, *J* 8.8, Ar-H).

Photoisomerisation of Benzo[g]*chrysene* 5,6-*Oxide* **4**.—A mixture of the preceding compounds **4** and **15** (0.005 g, 75:25) in $CDCl_3$ solvent (0.5 cm^3) was placed in a Pyrex glass NMR tube and pentamethylbenzene (0.001 g) was added to act as a reference peak. The ^1H NMR spectrum was recorded prior to irradiation. The NMR tube and contents were then placed in a water jacket and exposed to UV light of wavelength > 300 nm (Hanovia, Reading Photochemical Reactor, medium-pressure mercury-vapour arc tube, 500 W) for 10 min. A ^1H NMR spectrum on the irradiated sample showed that 52% of the original arene oxide, **4** had photoisomerized to oxepine **15**, while the remainder appeared to aromatize to benzo[*g*]chrysen-5-ol **16**.

Methyl (5-*Hydroxy*-5,6,6a,7,8,12b-*hexahydrobenzo*[c]*phenanthren*-5-*yl*)*crotonate* **18**.—A mixture of 6a,7,8,12b-tetrahydrobenzo[*c*]phenanthren-5-(6*H*)-one, **17** (8.0 g, 0.03 mol) (obtained by the literature method[17]), methyl 4-bromocrotonate (12 cm^3, 0.097 mol), amalgamated zinc (18 g), mercury(II) chloride (0.07 g) and iodine (0.07 g) was refluxed in a combination of dry benzene (100 cm^3) and diethyl ether (100 cm^3) under N_2 for 8 h. Methanol (15 cm^3) and acetic acid (2 cm^3) were added to the mixture and the excess of zinc was filtered off. A major portion of the solvent was removed under reduced pressure and then diethyl ether was added. The ethereal layer was washed with water, dried ($MgSO_4$) and then concentrated to yield a viscous oil. Flash chromatography of this on silica gel using hexane–diethyl ether (85:15) afforded the hydroxy ester **18** (10.2 g, 91%) as a viscous oil (Found: M, 348.17715, $C_{23}H_{24}O_3$ requires, *M*, 348.17253); δ_H 1.75–1.99 (1 H, m, 7-H), 2.49–2.59 (3 H, m, 7′-H and 6′-H), 2.72–2.84 (5 H, m, 6a-H, 4-H and 8-H), 3.64 (3 H, s, OCH_3), 3.78 (1 H, d, $J_{12b,6a}$ 9.5, 12b-H), 5.71 (1 H, d, $J_{2'',3'}$ 15.7, 2′-H) and 6.82–7.64 (9 H, m, 3′-H and Ar-H).

5-(3′-*Methoxycarbonyl-prop*-2′-*enylidene*)-5,6,6a,7,8,12b-*hexahydrobenzo*[c]*phenanthrene* **19**.—A solution of the hydroxy ester **18** (10 g, 0.029 mol) and toluene-*p*-sulfonic acid (0.005 g) in dry benzene (200 cm^3) was kept under reflux for 3 h. The solution was cooled, washed with water and aqueous Na_2CO_3 (10%), dried ($MgSO_4$) and then concentrated to yield the diene **19** (6.3 g, 67%) as the major component of a mixture. Fractional crystallization (diethyl ether–hexane) yielded the pure diene **19**, m.p. 113 °C (Found: C, 83.3; H, 6.9. $C_{23}H_{22}O_2$ requires C, 83.6; H, 6.7%); δ_H 1.57–1.60 (1 H, m, 6-H), 1.76–1.77 (1 H, m, 7-H), 2.06–2.09 (1 H, m, 6-H), 2.64–3.06 (4 H, m, 6-H and 8-H), 3.67 (1 H, d, $J_{12b,6a}$ 10.5, 12b-H), 3.78 (3 H, s, OCH_3), 6.00 (1 H, d,

$J_{2',3'}$ 15.2, 2'-H), 6.71, (1 H, d, $J_{1',2'}$ 11.0, 2'-H), 7.13–7.71 (8 H, m, Ar-H) and 7.74 (1 H, $J_{2',3'}$ 15 and $J_{3',1'}$ 11, 3'-H).

4'-(7,8-Dihydrobenzo[c]*phenanthren-5-yl)butanoic Acid* **20**.—A mixture of diene **19** (6 g, 0.018 mol), potassium hydroxide (8 g, 0.14 mol) and ethylene glycol (120 cm^3) was kept under reflux for 1 h at 120 °C. Excess of ethylene glycol was distilled off until the temperature of the residual solution reached 195 °C, when the mixture was kept under reflux for an additional 2 h. It was then poured onto ice and filtered before acidification (dil. HCl). The precipitate was washed with water, dried ($MgSO_4$) and then concentrated to yield the crude acid **20** which was purified by flash chromatography using dichloromethane–methanol (95:5) as eluent. Recrystallization from diethyl ether–hexane gave crystals of the acid **20** (4.07 g, 71%), m.p. 118 °C (Found: C, 83.3; H, 6.2. $C_{22}H_{20}O_2$ requires C, 83.5; H, 6.4%); δ_H 2.11–2.18 (2 H, m, 3'-H), 2.48 (2 H, t, $J_{2',3'}$ 7.3, 2'-H), 2.79–2.89 (4 H, m, 7-H and 8-H), 3.14 (2 H, t, $J_{4',3'}$ 7.6, 4'-H), 7.27–7.51 (6 H, m, Ar-H), 7.87 (1 H, d, *J* 7.7, Ar-H), 8.06–8.09 (1 H, m, Ar-H) and 8.55–8.58 (1 H, m, Ar-H).

Methyl 4'-(7,8-Dihydrobenzo[c]*phenanthren-5-yl)butanoate* **21**.—A stream of dry hydrogen chloride gas was bubbled into an ice-cold solution of acid **20** (3.5 g, 0.011 mol) in dry methanol (100 cm^3) for 2 h with stirring. The solution was then kept under reflux for 1 h. The methanol was removed by distillation and the crude product was extracted with dichloromethane. The extract was washed with water and aq. sodium hydrogen carbonate (10%), dried ($MgSO_4$) and then concentrated to yield the crude ester **21**. Purification of this by column chromatography on neutral alumina and elution using diethyl ether–hexane (10:90) gave the ester **21** as a viscous oil (3.54 g, 97%) (Found: M, 330.16182. $C_{23}H_{22}O_2$ requires, *M*, 330.16197); δ_H 2.03–2.08 (2 H, m, 3'-H), 2.38 (2 H, t, $J_{2',3'}$ 7.4, 2'-H), 2.72–2.80 (4 H, m, 7-H and 8-H), 3.05 (2 H, t, $J_{4',3'}$ 7.7, 4'-H), 3.61 (3 H, s, OCH_3), 7.20–7.39 (4 H, m, Ar-H), 7.40–7.42 (2 H, m, Ar-H), 7.80 (1 H, d, *J* 7.4, Ar-H), 8.00–8.03 (1 H, m, Ar-H) and 8.47–8.51 (1 H, m, Ar-H).

Methyl-4'-(Benzo[c]*phenanthren-5-yl)butanoate* **22**.—The ester **21** (3.2 g, 9.7 mmol) was dehydrogenated when stirred on an oil-bath at 240–260 °C for 2 h with 10% palladium on charcoal catalyst (0.8 g). The mixture was cooled, diluted with ethyl acetate (100 cm^3), filtered to remove the catalyst and concentrated under reduced pressure to yield the crude ester **22** (2.8 g, 88%). A small portion was purified by column chromatography on neutral alumina using diethyl ether–pentane (30:70), m.p. 70 °C (Found: C, 84.0; H, 6.15. $C_{23}H_{20}O_2$ requires C, 84.1; H, 6.1%); δ_H 2.17–2.24 (2 H, m, 3'-H), 2.48 (2 H, t, $J_{2',3'}$ 7.3, 2'-H), 3.24 (2 H, t, $J_{4',3'}$ 7.6, 4'-H), 3.68 (3 H, s, OCH_3), 7.61–7.70 (5 H, m, 2-H, 3-H, 6-H, 10-H and 11-H), 7.77 (1 H, d, $J_{8,7}$ 8.5, 8-H), 7.88 (1 H, d, $J_{7,8}$ 8.5, 7-H), 8.01 (1 H, dd, *J* 6.7, 1.0, Ar-H), 8.24 (1 H, dd, *J* 6.8 and 1.3, Ar-H) and 9.04–9.15 (2 H, m, 1-H and 12-H).

5,6-Dihydrobenzo[g]*chrysen-8(7H)-one* **23**.—The ester **22** (2.5 g, 7.6 mmol) was stirred with liquid hydrogen fluoride (50 cm^3) in a Polythene bottle (500 cm^3) equipped with inlet and outlet tubes. The reaction mixture was stirred overnight at ambient temperature under a slow stream of N_2 and the evolved HF was trapped (Na_2CO_3 solution). The traces of residual HF were removed and trapped by gentle warming. The reaction mixture was dissolved in dichloromethane, and the solution washed with aq. K_2CO_3 and water, dried ($MgSO_4$) and then concentrated under reduced pressure. Purification by flash chromatography using hexane–diethyl ether (90:10) as eluent and subsequent crystallization from this solvent mixture gave ketone **23** (1.46 g, 65%), m.p. 130 °C (Found: C, 89.0; H, 5.1. $C_{22}H_{16}O$ requires C, 89.3; H, 5.2%); δ_H 2.30–2.34 (2 H, m, 6-H), 2.88 (2 H, t, $J_{7,6}$ 7.0, 7-H), 3.49 (2 H, t, $J_{5,6}$ 6.0, 5-H), 7.59–7.75 (4 H, m, 2-H, 3-H, 12-H and 13-H), 7.95 (1 H, d, $J_{10,9}$ 9.2, 10-H), 7.98 (1 H, dd, *J* 7.3, 1.7, Ar-H), 8.28 (1 H, d, $J_{9,10}$ 9.2, 9-H), 8.86–8.93 (1 H, m, Ar-H), 8.95 (1 H, d, *J* 7.4, Ar-H) and 9.18 (1 H, d, *J* 9.1, Ar-H).

5,6,7,8-Tetrahydrobenzo[g]*chrysen-8-ol* **24**.—A mixture of the ketone **23** (1.3 g, 4.4 mmol) and sodium borohydride (1.9 g, 50 mmol) was stirred in methanol (70 cm^3) for 12 h and then evaporated under reduced pressure. Dichloromethane was added to the residue and the solution was washed with water, dried ($MgSO_4$) and then concentrated to yield a crude product. Crystallization of this from diethyl ether–hexane gave alcohol **24** (1.22 g, 94%), m.p. 146 °C (Found: C, 88.1; H, 6.2. $C_{22}H_{18}O$ requires C, 88.5; H, 6.1%); δ_H 1.91–2.34 (5 H, m, 6-H, 7-H and OH), 3.02–3.41 (2 H, m, 5-H), 5.54 (1 H, br s, 8-H), 7.55–7.65 (4 H, m, 2-H, 3-H, 12-H and 13-H), 7.93 (1 H, d, $J_{10,9}$ 9.0, 10-H), 7.97–8.00 (1 H, m, Ar-H), 8.18–8.20 (1 H, m, Ar-H), 8.34 (1 H, d, $J_{9,10}$ 9.0, 9-H) and 8.92–8.99 (2 H, m, 1-H and 14-H).

5,6-Dihydrobenzo[g]*chrysene* **25**.—The alcohol **24** (1.0 g, 3.36 mmol) was suspended in benzene (100 cm^3) containing toluene-*p*-sulfonic acid (0.005 g) and the mixture was refluxed for 1 h at 70 °C. It was then washed with aq. Na_2CO_3 and water, dried ($MgSO_4$) and concentrated to yield the crude alkene **25**. Column chromatography of the residue on neutral alumina using hexane–diethyl ether (90:10) as eluent yielded the pure alkene **25** as a viscous oil (0.742 g, 79%) (Found: M, 280.12588. $C_{22}H_{16}$ requires, *M*, 280.12519); δ_H 2.47–2.54 (2 H, m, 6-H), 3.31 (2 H, t, $J_{5,6}$ 8.6, 5-H), 6.37–6.40 (1 H, dt, $J_{7,8}$ 10.0 and $J_{7,6}$ 5.0, 7-H), 7.36 (1 H, d, $J_{8,7}$ 10.0, 8-H), 7.56–7.65 (4 H, m, 2-H, 3-H, 12-H and 13-H), 7.90 (1 H, d, $J_{10,9}$ 9.0, 10-H), 7.99 (1 H, dd, *J* 7.6 and 1.3, Ar-H), 8.17 (1 H, d, $J_{9,10}$ 9.0, 9-H), 8.25 (1 H, dd, *J* 7.7 and 1.7, Ar-H) and 8.97–9.01 (2 H, m, 1-H and 14-H).

trans-*7-Bromo-5,6,7,8-tetrahydrobenzo*[g]*chrysen-8-yl Acetate* **26**.—The *trans*-bromo acetate **26** was synthesised from the alkene **25** (0.6 g, 2.14 mmol), lithium acetate (0.607 g, 9.2 mmol) in a mixture of dry THF (15 cm^3) and glacial acetic acid (25 cm^3) containing *N*-bromoacetamide (NBA) (0.303 g, 2.2 mmol). The reaction procedure and work-up were identical with those reported for the bromo acetate **10**. The bromo acetate **26** was purified by flash chromatography using hexane–diethyl ether (70:30) and recrystallised from this combination of solvents (0.643 g, 72%), m.p. 150 °C (Found: C, 68.7; H, 4.8. $C_{24}H_{19}BrO_2$ requires C, 68.9; H, 4.6%); δ_H 2.08 (3 H, s, OCH_3), 2.46–2.56 (2 H, m, 6-H), 3.44–3.55 (2 H, m, 5-H), 4.77–4.79 (1 H, dt, $J_{7,8}$ 2.0 and $J_{7,6}$ 5.3, 7-H), 6.80 (1 H, d, $J_{8,7}$ 1.8, 8-H), 7.60–7.72 (4 H, m, 2-H, 3-H, 12-H and 13-H), 7.77 (1 H, $J_{10,9}$ 9.0, 10-H), 7.92 (1 H, d, $J_{9,10}$ 9.0, 9-H), 7.98–8.02 (1 H, m, Ar-H), 8.26–8.29 (1 H, m, Ar-H) and 8.94–9.03 (2 H, m, 1-H and 14-H).

5,7-Dibromo-5,6,7,8-tetrahydrobenzo[g]*chrysen-8-yl Acetate* **27**.—The bromo acetate **26** (0.160 g, 0.38 mmol) and *N*-bromosuccinimide (NBS) (0.072 g, 0.4 mmol) were treated in the same manner as that reported for compound **11**. A similar work-up procedure yielded the dibromo acetate **27** (0.138 g, 73%) as an unstable product which was used without further purification in the next step; δ_H 2.13 (3 H, s, OCH_3), 3.07–3.26 (2 H, m, 6-H), 4.79–4.84 (1 H, m, 7-H), 6.15 (1 H, dd, $J_{5,6}$ 6.1, 5.8, 5-H), 6.99 (1 H, d, $J_{8,7}$ 4.7, 8-H), 7.66–8.01 (7 H, m, Ar-H), 8.43 (1 H, d, *J* 8.1, Ar-H) and 8.91–8.98 (2 H, m, 1-H and 14-H).

Benzo[g]*chrysene 7,8-Oxide* (*7,8-Epoxy-7,8-dihydrobenzo*-[g]*chrysene*) **5** and *Benzo*[3,4]*phenanthro*[1,2-b]*oxepine* **28**.—The crude dibromo acetate **27** (0.138 g, 0.27 mmol) and sodium methoxide (0.2 g, 3.7 mmol) in dry THF (20 cm^3) were stirred at 0 °C in an ice-bath under a nitrogen atmosphere. The mixture

was maintained at −20 °C over 12 h and then stirred for a further 0.5 h at 0 °C in the absence of light. Diethyl ether was added to the solution which was then washed with cold water and aq. KOH, dried ($MgSO_4$) and evaporated at *ca.* 10 °C to give a crude mixture of the arene oxide **5** and oxepine **28** (0.042 g, 52%). ^1H NMR spectroscopy indicated that compounds **5** and **28** were present in the ratio 75:25. The arene oxide **5** and oxepine **28** were separated by careful fractional crystallization from diethyl ether–pentane.

Compound **5**: m.p. 83–85 °C (decomp.) (Found: M, 294.10755. $C_{22}H_{14}O$ requires, *M*, 294.10446); δ_H 4.44–4.45 (1 H, m, 7-H), 5.43 (1 H, d, $J_{8,7}$ 4.1, 8-H), 6.79 (1 H, dd, $J_{6,5}$ 9.7 and $J_{6,7}$ 3.8, 6-H), 7.64–7.76 (4 H, m, 2-H, 3-H, 12-H and 13-H), 7.78 (1 H, dd, $J_{5,6}$ 9.7 and $J_{5,7}$ 1.5, 5-H), 8.02 (1 H, d, $J_{10,9}$ 8.8, 10-H), 8.04–8.06 (1 H, m, Ar-H), 8.43–8.45 (1 H, m, Ar-H), 8.47 (1 H, d, $J_{9,10}$ 8.9, 9-H), 8.96–9.03 (2 H, m, 1-H and 14-H).

Compound **28**: semi-solid (Found: M, 294.10316. $C_{22}H_{14}O$ requires, *M*, 294.10446); δ_H 5.84 (1 H, dd, $J_{7,8} = J_{7,6}$ 5.1, 7-H), 6.55 (1 H, dd, $J_{6,7}$ 5.1 and $J_{6,5}$ 8.2, 5-H), 6.60 (1 H, d, $J_{8,7}$ 5.2, 8-H), 7.51–7.74 (5 H, m, 2-H, 3-H, 5-H, 13-H and 14-H), 7.94 (1 H, d, $J_{10,11}$ 9.0, 11-H), 8.02 (1 H, dd, *J* 7.5 and 1.7, Ar-H), 8.22 (1 H, dd, *J* 7.5 and 1.7, Ar-H), 8.36 (1 H, d, $J_{10,11}$ 9.0, 10-H) and 9.00–9.05 (2 H, m, 1-H and 15-H).

Photoisomerization of Benzo[g]*chrysene* 7,8-*Oxide* **5**.—A sample of the arene oxide **5** (0.005 g, 0.017 mmol), dissolved in [$^2H_8$]THF (0.5 cm^3) containing pentamethylbenzene (0.002 g), was irradiated for 10 min under similar conditions to those specified for the arene oxide **4**. The ^1H NMR spectrum indicated that 67% of the arene oxide **5** had photoisomerized to the oxepine **28** while the remainder was found to have aromatized to a phenolic product. During attempted purification of the oxepine **28** by TLC on silica gel using hexane–diethyl ether (75:25) as eluent total aromatization occurred to yield the same phenolic product as that formed by photoisomerization. Recrystallization of the phenol from diethyl ether–hexane gave a product which was identified as benzo[*g*]chrysen-8-ol **29**, m.p. 97 °C (Found: M, 294.10446. $C_{22}H_{14}O$ requires, *M*, 294.10446); δ_H 7.04 (1 H, d, $J_{7,6}$ 7.6, 7-H), 7.52 (1 H, dd, $J_{6,7}$ 7.9 and $J_{6,5}$ 8.1, 6-H), 7.56–7.67 (4 H, m, 2-H, 3-H, 12-H and 13-H), 7.94 (1 H, d, $J_{10,9}$ 9.1, 10-H), 8.00 (1 H, dd, *J* 6.1 and 3.3, Ar-H), 8.33 (1 H, d, $J_{5,6}$ 8.3, 5-H), 8.67 (1 H, dd, *J* 7.6 and 1.7, Ar-H), 8.80 (1 H, dd, *J* 7.3 and 1.8, Ar-H), 8.87 (1 H, dd, *J* 6.2 and 3.4, Ar-H) and 9.51 (1 H, d, $J_{9,10}$ 9.1).

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