Synthesis, Spontaneous Racemization, and Photoisomerization of Benzo[e]pyrene 9,10-Oxide

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Benzo[e]pyrene 9,10-oxide (4) and the isomeric pyreno[4,5-b]oxepine (9) have been simultaneously synthesized from racemic and optically active bromo acetate precursors of known absolute configurations. Spontaneous thermal racemization of benzo[e]pyrene 9,10-oxide (4) [via the undetected oxepine intermediate (15)], and readily occurring photoisomerization of this arene oxide [via the putative arene oxide intermediate (16) to yield pyreno[4,5-b]oxepine (9)] occur as predicted from PMO calculations of resonance energy changes associated with these pericyclic reactions. Optically pure samples of the mammalian metabolites 9,10-epoxy-(12) and trans-9,10-dihydroxy-9,10,11,12-tetrahydrobenzo[e]pyrene (13) have been obtained.

Benzo[e]pyrene (1) is distributed widely in the environment since it is a common member of the polycyclic aromatic hydrocarbon (PAH) series produced by partial combustion of fossil fuels. Despite being isomeric with the potent carcinogen benzo[a]pyrene, and having two identical bay regions, benzo[e]pyrene (1) does not appear to be carcinogenic.[1-3]

The isolated major (3) and minor (5) trans-dihydro diol metabolites of benzo[e]pyrene (1) from mammalian liver

(1)

$\downarrow$ O$_2$ - enz.

(2) + (4)

$\downarrow$ H$_2$O - enz.　　　　$\downarrow$ H$_2$O - enz.

(3)　　　　　　　　(5)

Scheme 1.

systems[2] are assumed to have been formed by the usual enzyme-catalysed hydration of the initially formed arene oxide metabolites (2) and (4) respectively (Scheme 1). Racemic samples of the trans-dihydrodiols (3) and (5), and the achiral K-region epoxide (2), have previously been synthesized.[3,4] The chemical synthesis of benzo[e]pyrene 9,10-oxide (4) was undertaken since (a) availability of this arene oxide would allow its biological response (e.g. mutagenicity, carcinogenicity), and behaviour as a substrate for epoxide hydrolase enzyme, to be evaluated; (b) arene oxide (4) was predicted to have one of the lowest barriers to racemization for any arene oxide in the PAH series (from PMO calculations[5]); and (c) based upon earlier studies[6] of arene 1,2-oxides of triphenylene and benz[a]-anthracene, it was anticipated that arene oxide (4) would readily undergo a photochemical 'oxygen walk' to form a relatively stable oxepine (9).

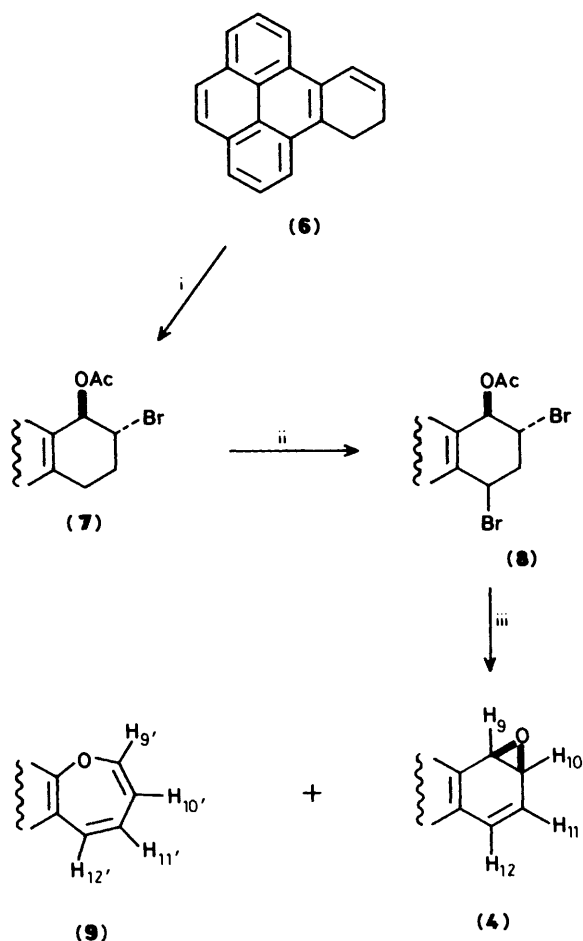The olefin (6) (obtained by the literature method[4,7]) was converted in good yield into bromo acetate (7) using N-bromoacetamide (NBA) and lithium acetate in glacial acetic acid solution (Scheme 2). Benzylic bromination of bromo acetate (7) yielded trans-9-acetoxy-10,12-dibromo-9,10,11,12-tetrahydrobenzo[e]pyrene (8) as an unstable compound whose structure was confirmed by n.m.r. analysis prior to treatment with sodium methoxide in tetrahydrofuran (THF) solvent. The resulting product was a mixture of arene oxide (4) and oxepine (9). Recrystallization from pentane (−70 °C) did not produce a pure sample of arene oxide (4). Further attempts to separate the mixture of arene oxide (4) and oxepine (9) by preparative t.l.c. (p.l.c.) (silica gel washed with triethylamine) resulted in the isolation of a pure sample of oxepine (9) only, due to aromatization of arene oxide (4). The proportion of arene oxide (4) relative to oxepine (9) varied during a range of experiments but appeared to be optimal [ca. 70% (4)] when the reaction was monitored in situ by n.m.r. spectroscopy (in [²H₈]THF). The structure of oxepine (9) was established on the basis of extensive decoupling experiments, an n.m.r. spectral comparison with 1-benzoxepine,[8] and aromatization to a phenol (18) upon addition of acid.

The racemic bromohydrin (10) was obtained by treatment of 9,10-dihydrobenzo[e]pyrene (6) with NBA. It was resolved via the 2-methoxy-2-phenyl-2-trifluoromethylacetate (3,3,3-tri-fluoro-2-methoxy-2-phenylpropionate) (MTPA) derivatives (Scheme 3) using short-column chromatography (s.c.c.) and p.l.c. on silica gel. The high-R_F (11a) ([α]$_D$ −7.5°) and low-R_F (11b) ([α]$_D$ +34.5°) diastereoisomers were assigned absolute configurations on the basis of their n.m.r. characteristics.
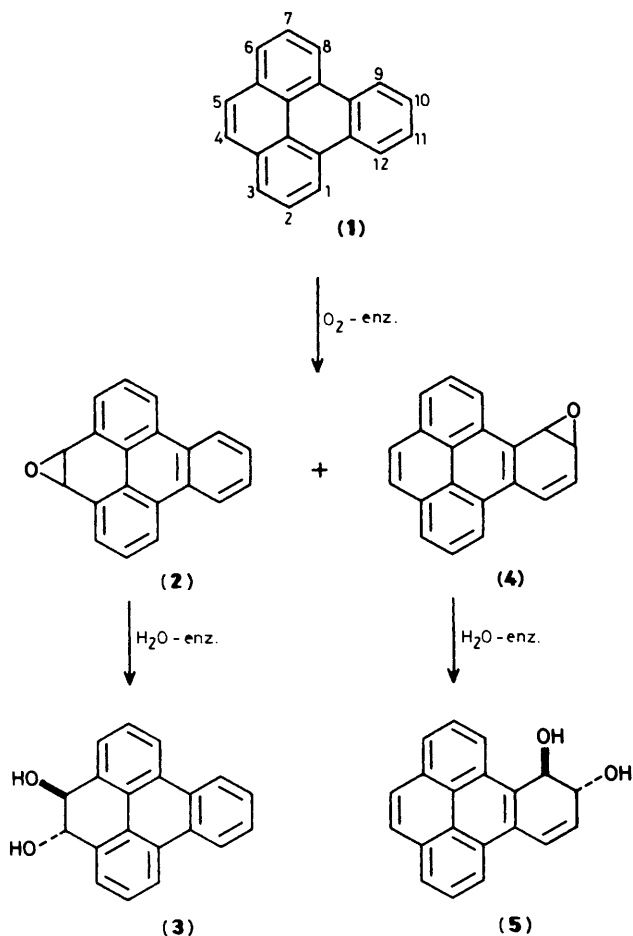
Extensive studies on analogous bromo MTPA diastereoisomers (some of whose absolute configurations have been unequivocally assigned by X-ray crystallography) have previously established[9,10] that the high-R_F isomer with a smaller positive δ_H value for the non-benzylic proton (H_B) and a smaller

(6)

i

OAc
-Br

(7)

ii

OAc
-Br

Br

(8)

iii

$H_{9'}$
O
$H_{10'}$
+
$H_{11'}$
$H_{12'}$

(9)

H_9 O
H_{10}
H_{11}
H_{12}

(4)

Scheme 2. *Reagents:* i, NBA, LiOAc, AcOH; ii, NBS; iii, NaOMe–THF

negative $\delta(^{19}F)$ value for the CF_3 group will have an (R,R) configuration and *vice-versa*. On this basis, the bromo MTPA diastereoisomers (11a) ($H_B \delta_H$ +4.76; $CF_3 \delta_F$ −8.43) and (11b) ($H_B \delta_H$ +4.91; $CF_3 \delta_F$ −8.68), will have (9R, 10R) and (9S,10S) absolute configurations respectively. Treatment of the bromo esters (11a) and (11b) with di-isobutylaluminium hydride (DIBAL) yielded the bromohydrin enantiomers (10) ($[\alpha]_D$ +14.1° and $[\alpha]_D$ −15.2° respectively).

Acetylation of the dextrorotatory enantiomer of bromohydrin (10), $[\alpha]_D$ +14.1°; 9R,10R, with acetic anhydride in pyridine yielded optically pure bromo acetate (7) ($[\alpha]_D$ −171°; 9R,10R absolute configuration as shown in Scheme 2). Dilution of the latter sample of bromo acetate (7) ($[\alpha]_D$ −171°) with the racemic form provided sufficient material of lower optical purity (*ca.* 20% e.e.) to permit the repeated synthesis of arene oxide (4). Thus, benzylic bromination of bromo acetate (7) ($[\alpha]_D$ −34°; 9R,10R) gave optically active dibromo acetate (8) ($[\alpha]_D$ −31°; 9R,10R) which was converted immediately into the arene oxide (4): oxepine (9) mixture by treatment with NaOMe. The highest ratio of arene oxide (4): oxepine (9) obtained from two independent experiments was 70:30 (by ^1H n.m.r. analysis). The

measurement of optical rotation values for the arene oxide (4) was made more difficult by the presence of the yellow-coloured oxepine (9). However, use of a wide-bore polarimeter tube, and different wavelengths of light (365—589 nm), ensured that an adequate transmission of light and thus reliable optical rotation measurements were possible. From duplicate experiments using optically active dibromo acetate precursor (8), the product arene oxide (4) was consistently found to have an $[\alpha]$ value of zero at all wavelengths. This result is as expected for the spontaneous racemization of the optically active arene oxide (4) *via* an undetected oxepine intermediate (15) (Scheme 4).

PMO Calculations have previously suggested that the loss of resonance or stabilization energy (ΔE_R) associated with the arene oxide–oxepine isomerization (4) $\rightleftharpoons$ (15) and racemization of (4) will be very small in comparison with those arene oxide enantiomers which have been found to be configurationally stable ($\Delta E_R \geqslant$ 15 kcal mol^{-1}).[5,*] Although the barrier to racemization for arene oxide (4) has not been experimentally measured, the value of ΔE_R obtained from PMO calculations[5] (2.7 kcal mol^{-1}) was lower than that calculated for triphenylene oxide (4.3 kcal mol^{-1}) which was also found to have spontaneously racemized.[10]

The isolation of the *trans*-tetrahydrodiol product (13) as a mammalian liver metabolite of 9,10-dihydrobenzo[e]pyrene (6) results from initial formation of the tetrahydroepoxide metabolite (12) (Scheme 3, steps vi and vii).[3] In contrast with the parent hydrocarbon (1), the dihydro compound (6) and the epoxide metabolite (12) have both proved to be mutagenic.[3] In view of their establishment as metabolites and their mutagenic activities, the tetrahydroepoxide (12) and *trans*-tetrahydrodiol (13) were synthesized in optically pure forms. The configuration of epoxide (−)-(12) and *trans*-tetrahydrodiol (−)-(13) metabolites were related to the corresponding bromo MTPA diastereoisomer (11b) by stereochemical correlation (Scheme 3).

The laevorotatory enantiomer of epoxide (12) ($[\alpha]_D$ −110°; 9S,10R) was obtained after the bromohydrin enantiomer (10) ($[\alpha]_D$ −15.2°) had been stirred with the basic form of Amberlite IRA-900 ion-exchange resin in dry THF. Aqueous hydrolysis of the tetrahydroepoxide (12) ($[\alpha]_D$ −110°) under acidic conditions (water–dioxane, pH 2.5) yielded a mixture of optically pure *trans*-(13) and *cis*-(14) tetrahydrodiols. P.l.c. separation (silica gel; chloroform–methanol 97:3) yielded pure samples of the *trans*-diol (13) ($[\alpha]_D$ −22.7°; 9R,10R) and *cis*-diol (14) ($[\alpha]_D$ +24.6°; 9S,10R).

When the arene oxide (4)–oxepine (9) mixture (53:47) was briefly irradiated with u.v. light (0.5 h; $CDCl_3$; >300 nm), the arene oxide (4) was found to disappear. A degree of aromatization of (4) to an isomeric phenol (18) was observed, but the concentration of oxepine (9) was found to show a marked increase (*ca.* 45%) relative to a reference compound. This observation provides clear evidence of a readily occurring photochemical oxygen-walk process presumably proceeding *via* the undetected high-energy arene oxide (16). The relatively small loss in resonance energy calculated[5] for the arene oxide–oxepine electrocyclization (4) $\rightleftharpoons$ (15) leading to arene oxide racemization is similar to that associated with the arene oxide–arene oxide sigmatropic rearrangement (4) ⟶ (16) resulting in stable oxepine formation.

Although the instability of the dibromo acetate precursor (8) and arene oxide product (4) have to date precluded a detailed mechanistic study, pathway 'a' (Scheme 4) has previously been accepted as the mechanism of formation of arene oxides from dibromo ester precursors in other members of the PAH series.[10] Based upon the currently observed photoisomerization of arene oxide (4) to oxepine (9), a similar isomerization pathway was
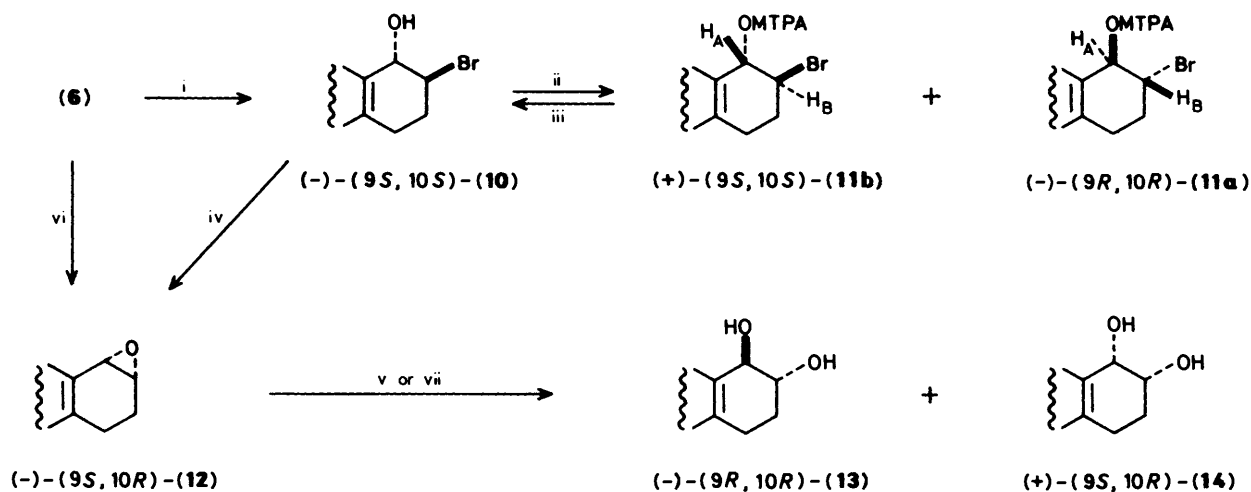
Scheme 3. *Reagents:* i, NBA–H$_2$O; ii, MTPA chloride–pyridine; iii, DIBAL; iv, OH$^-$ resin; v, water–dioxane (pH 2.5); vi, O$_2$–enz.; vii, water–enz.
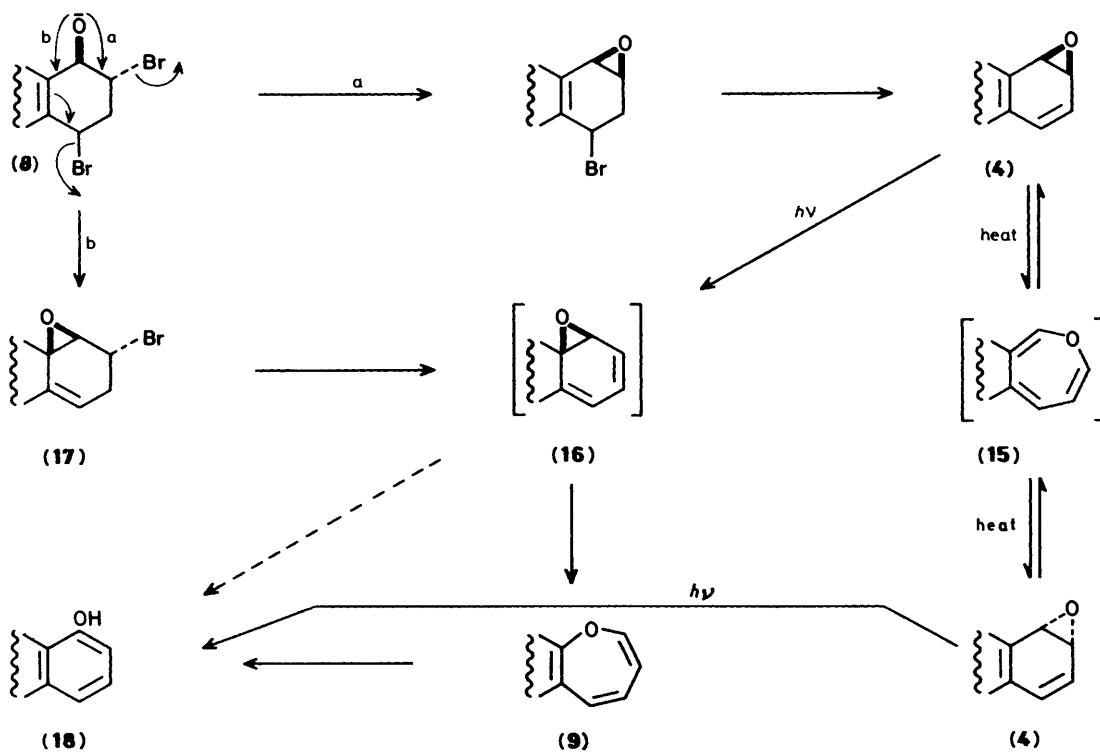
Scheme 4.

initially considered in order to account for the concomitant formation of both arene oxide (4) and oxepine (9) from dibromo acetate (8). The observation that a similar proportion of oxepine (9) was obtained at all stages of the reaction of dibromo acetate (8) with NaOMe (in [^{2}H$_8$]tetrahydrofuran), either in the presence or absence of room light, suggests that oxepine (9) was being formed directly rather than by photoisomerization. An S_N2' mechanism or a similar type of non-concerted pathway[11] involving the undetected arene oxide intermediate (16) (mechanism b, Scheme 4) could also provide an explanation for the isolated oxepine (9). The observation that comparable oxepines to compound (9) (in the benz[a]anthracene,[6] triphenylene,[6] dibenz[a,h]anthracene,[6] dibenz[a,j]anthracene,[6] and

dibenz[a,c]anthracene[12] series), are obtained from NaOMe treatment of the corresponding dibromo acetate precursors but only in association with arene oxides analogous to compound (4) (which are all predicted to have low barriers to racemization, ΔE_R 2.7—7.9 kcal mol^{-1}) is noteworthy. The loss in resonance energy (ΔE_R) associated with racemization of arene oxide (4) *via* oxepine (15) is very similar to that associated with the reaction of dibromo acetate (8) to form bromo epoxide (17) (Scheme 4, mechanism b). Thus, the S_N2' or related type of mechanism for the synthesis of stable oxepines [*e.g.* (9)] would be particularly favoured where arene oxides [*e.g.* (4)] with low barriers to racemization ($\Delta E_R \leqslant 8$ kcal mol^{-1}) are formed simultaneously.

To date neither the absolute configurations nor the optical

purities of the initially formed arene oxide (4) [and derived *trans*-dihydrodiol (5)] or tetrahydroepoxide (12) [and derived *trans*-tetrahydrodiol (13)] products from liver microsomal metabolism of benzo[*e*]pyrene (1) or 9,10-dihydrobenzo[*e*]-pyrene (6) respectively have been determined. Based upon metabolism results with other members of the PAH series (including the similar PAH triphenylene [10]) it is anticipated that the initially formed arene oxide (4) and the derived *trans*-dihydrodiol (5) will also show an enantiomeric excess favouring the (9*R*,10*S*) and (9*R*,10*R*) configurations respectively.

Experimental

[1]H N.m.r. spectra were obtained using a Bruker WH250 MHz n.m.r. spectrometer with tetramethylsilane as reference. [19]F N.m.r. spectra were obtained in $CDCl_3$ solution using a Varian XL-100 n.m.r. spectrometer with α,α,α-trifluorotoluene as reference. Mass spectral data were recorded at 70 eV using an AEI-MS-902 model (updated by V.G. instruments). Optical rotations were recorded at 589 nm using a Perkin-Elmer Model 241 instrument.

(±)-trans-9-*Acetoxy*-10-*bromo*-9,10,11,12-*tetrahydrobenzo*-[*e*]pyrene (7).—A mixture of olefin (6) [4,7] (1.0 g, 3.9 mmol), NBA (0.57 g, 4.13 mmol), and lithium acetate (1.6 g, 15.7 mmol) was stirred in glacial acetic acid (100 ml) for 1.5 h at room temperature. After addition of cold water (200 ml), the mixture was extracted with diethyl ether. The extract was washed with water, dried ($MgSO_4$), and concentrated to yield the *bromo acetate* (7), which was recrystallized from chloroform–pentane (1.42 g, 92%), m.p. 165—166 °C (Found: C, 66.9; H, 4.5. $C_{22}H_{17}BrO_2$ requires C, 67.2; H, 4.3%); δ_H (250 MHz; $CDCl_3$) 2.12 (3 H, s, Ac), 2.54 (1 H, m, 11-H), 2.66 (1 H, m, 11-H), 3.59 (2 H, dd, $J_{11,12}$ 8.5, $J_{10,12}$ 3.9 Hz, 12-H_2), 4.83 (1 H, m, 10-H), 6.94 (1 H, d, $J_{9,10}$ 1.6 Hz, 9-H), 7.99—8.25 (7 H, m, ArH), and 8.44 (1 H, d, *J* 7.9 Hz, ArH).

(±)-trans-9-*Acetoxy*-10,12-*dibromo*-9,10,11,12-*tetrahydrobenzo*[*e*]pyrene (8).—A mixture of (±)-bromo acetate (7) (0.2 g, 0.51 mmol), *N*-bromosuccinimide (NBS) (0.97 g, 0.54 mmol), and α,α'-azoisobutryronitrile (0.005 g) was refluxed in carbon tetrachloride solution (30 ml) for 0.75 h. The insoluble succinimide product was filtered off from the cooled solution. Removal of the solvent at ambient temperature under reduced pressure yielded the crude dibromo acetate (8). The latter product was found to be rather unstable but yielded a solid after trituration with diethyl ether (0.2 g, 84%), m.p. 143—145 °C (decomp.); δ_H (250 MHz; $CDCl_3$) 2.18 (3 H, s, Ac), 3.07 (1 H, m, 11-H), 3.27 (1 H, m, 11-H), 5.03 (1 H, m, 10-H), 6.19 (1 H, $J_{11,12}$ 4.8 Hz, 12-H), 7.22 (1 H, d, $J_{9,10}$ 1.6 Hz, 9-H), 7.99—8.16 (4 H, m, ArH), 8.24—8.27 (3 H, m, ArH), and 8.62 (1 H, d, *J* 8.0 Hz, ArH).

(±)-*Benzo*[*e*]*pyrene* 9,10-*Oxide* (9,10-*Epoxy*-9,10-*dihydro*-benzo[*e*]pyrene) (4) and *Pyreno*[4,5-b]*oxepine* (9).—A solution of the (±)-dibromo acetate (8) (0.15 g, 0.32 mmol) in dry THF (20 ml) was stirred with freshly prepared sodium methoxide (0.13 g, 2.4 mmol) at 0 °C under nitrogen for 2 h. The mixture was maintained at 4 °C overnight, and then filtered. The solvent was removed at ambient temperature under reduced pressure and the residue was dissolved in diethyl ether containing triethylamine (2%). The ethereal solution was washed successively with water and aqueous sodium hydroxide, dried (K_2CO_3), and concentrated at room temperature to yield a crude product. Recrystallization of the product from pentane (−70 °C) yielded a crystalline sample, which was found to be very unstable and contained both arene oxide (4) and oxepine

(9) in varying proportions. The arene oxide (4) was generally the minor product.

Attempted separation and purification of arene oxide (4) and oxepine (9) by p.l.c. [silica gel; diethyl ether–hexane 1:3, containing triethylamine (1%)] yielded a sample of the oxepine (9) as a relatively unstable pale yellow solid, which was recrystallized from acetone, m.p. 112—115 °C (decomp); δ_H (250 MHz; $CDCl_3$) 5.88 (1 H, dd, $J_{9',10'}$ = $J_{10',11'}$ = 5.1 Hz, 10'-H), 6.60 (1 H, d, $J_{9',10'}$ 5.1 Hz, 9'-H), 6.64 (1 H, $J_{11',12'}$ 11.2, $J_{10',11'}$ 5.1 Hz, 11'-H), 7.73 (1 H, d, $J_{11',12'}$ 11.2 Hz, 12'-H), 7.98—8.06 (4 H, m, ArH), 8.13—8.21 (2 H, m, ArH), 8.35 (1 H, d, *J* 7.8 Hz, ArH), and 8.65 (1 H, d, *J* 7.8 Hz, ArH); *m/z* 268 (16%), 259 (17), 241 (14), 147 (27), and 129 (100).

A much higher proportion (*ca.* 70%) of arene oxide (4) relative to the oxepine (9) (*ca.* 30%) was obtained when the dibromo acetate (8) was treated with $NaOCD_3$ in [$^2H_8$]tetrahydrofuran, and the progress of the reaction was monitored directly by n.m.r. analysis. Although a pure sample of arene oxide (4) could not be obtained due to instability, it was characterized by n.m.r. analysis from the mixture of arene oxide (4) and oxepine (9). Compound (4): δ_H(250 MHz; [$^2H_8$]THF) 4.21—4.25 (1 H, m, 10-H), 5.41 (1 H, d, $J_{9,10}$ 3.9 Hz, 9-H), 6.73 (1 H, dd, $J_{11,12}$9.9, $J_{10,11}$ 3.7 Hz, 11-H), 7.83 (1 H, dd, $J_{11,12}$ 9.8, $J_{10,12}$ 1.5 Hz, 12-H), 7.88—8.31 (6 H, m, ArH), 8.60 (1 H, d, *J* 8.1 Hz, ArH), and 8.75 (1 H, d, *J* 7.9 Hz, ArH).

Treatment of the mixture of arene oxide (4) and oxepine (9) in $CDCl_3$ solution with two drops of trifluoroacetic acid resulted in aromatization to yield mainly 9-hydroxybenzo[*e*]pyrene (18), which showed the characteristic blue colour of a phenol (with Gibbs reagent): m.p. 169—173 °C; δ_H (250 MHz; $CDCl_3$) 7.10 (1 H, d, *J* 7.8 Hz, ArH), 7.57 (1 H, t, *J* 8.0 Hz, ArH), 7.99—8.07 (5 H, m, ArH), 8.17 (1 H, d, *J* 7.6 Hz, ArH), 8.52 (1 H, d, *J* 8.4 Hz, ArH), 8.87 (1 H, d, *J* 8.0 Hz, ArH), and 9.91 (1 H, d, *J* 8.2 Hz, ArH); *m/z* 268 (100%), 269 (22), and 238 (36).

(±)-trans-10-*Bromo*-9-*hydroxy*-9,10,11,12-*tetrahydrobenzo*-[*e*]pyrene (10).—NBS (0.6 g, 4.3 mmol) was added to a stirred solution of 9,10-dihydrobenzo[*e*]pyrene (6) (1.0 g, 3.9 mmol) in a mixture of THF (100 ml) and water (50 ml) at 0 °C. The reaction mixture was stirred overnight at ambient temperature and the product mixture was diluted with water (100 ml) and extracted with ethyl acetate. The latter extract was washed successively with aqueous sodium sulphite and water and dried ($MgSO_4$). The product bromohydrin (10) was obtained as a crystalline solid after concentration, and recrystallization from chloroform (1.32 g, 95%), m.p. 164—166 °C (Found: M^+, 350.030 95. $C_{20}H_{15}BrO$ requires *M*, 350.030 97); δ_H (250 MHz; $CDCl_3$) 2.48—2.55 (1 H, m, 11-H), 2.73—2.79 (1 H, m, 11-H), 3.52 (2 H, m, 12-H_2), 4.85—4.89 (1 H, m, 10-H), 5.81 (1 H, d, $J_{9,10}$ 2.5 Hz, 9-H), 8.03—8.11 (4 H, m, ArH), 8.19—8.25 (2 H, m, ArH), 8.42 (1 H, d, *J* 8.0 Hz, ArH), and 8.57 (1 H, d, *J* 8.1 Hz, ArH).

(−)-(9R,10R)- *and* (+)-(9S,10S)-trans-10-*Bromo*-9-(3,3,3-*trifluoro*-2-*methoxy*-2-*phenylpropionyloxy*)-9,10,11,12-*tetrahydrobenzo*[*e*]pyrene (11a) *and* (11b).—A mixture of bromohydrin (10) (0.85 g, 2.4 mmol), (−)-3,3,3-trifluoro-2-methoxy-2-phenylpropionyl chloride (0.67 g, 2.9 mmol), and 4-dimethylaminopyridine (0.05 g) in dry pyridine (3 ml) was stirred at ambient temperature for 20 h. Water (100 ml) was added, and the ethereal extract of the product mixture was washed with water, dried, and concentrated under reduced pressure at ambient temperature.

The pure diastereoisomers (11a) and (11b) were obtained either by multiple elution p.l.c. (silica gel; diethyl ether–hexane 5:95) or s.c.c. using an identical eluant.

(−)-(9R,10R)-(11a): *High* R_F *isomer* (0.47 g, 41%), m.p. 161—162 °C (from chloroform–pentane); $[\alpha]_D$ −7.5° ($CHCl_3$) (Found: C, 63.5; H, 4.1. $C_{30}H_{22}BrF_3O_3$ requires C, 63.5; H,

3.9%); δ_H(250 MHz; CDCl$_3$) 2.33—2.37 (2 H, m, 11-H$_2$), 3.41 (3 H, s, OMe), 3.50—3.54 (2 H, m, 12-H$_2$), 4.76 (1 H, m, 10-H), 7.18 (1 H, d, $J_{9,10}$ 1.4 Hz, 9-H), 7.21—7.31 (3 H, m, ArH), 7.43 (2 H, d, J 7.6 Hz, ArH), 7.97—8.37 (7 H, m, ArH), and 8.42 (1 H, d, J 8.0 Hz, ArH); δ_F (94.2 MHz; CDCl$_3$) −8.43 (3 F, s, CF$_3$).

(+)-(9S,10S)-(11b): Low-R_F isomer (0.42 g, 37%), m.p. 95—97 °C (from chloroform–pentane); [α]$_D$ +34.5° (CHCl$_3$) (Found: C, 63.3; H, 3.9. C$_{30}$H$_{22}$BrF$_3$O$_3$ requires C, 63.5; H, 3.9%); δ_H (250 MHz; CDCl$_3$) 2.53—2.64 (2 H, m, 11-H$_2$), 3.41 (3 H, s, OMe), 3.52—3.61 (2 H, m, 12-H$_2$), 4.91 (1 H, m, 10-H), 7.12 (1 H, d, $J_{9,10}$ 2.1 Hz, 9-H), 7.21—7.36 (3 H, m, ArH), 7.51—7.71 (2 H, m, ArH), 7.91—8.26 (7 H, m, ArH), and 8.39 (1 H, m, ArH); δ_F (94.18 MHz; CDCl$_3$) −8.68 (3 F, s, CF$_3$).

(+)-(9R,10R)- and (−)-(9S,10S)-trans-10-*Bromo-9-hydroxy-9,10,11,12-tetrahydrobenzo*[e]*pyrene* (10).—The bromo MTPA ester (11a) (0.35 g, 0.62 mmol) ([α]$_D$ −7.5°) was stirred in dry diethyl ether (50 ml) with DIBAL (7 ml; 1.0M solution in hexane) under nitrogen at 0 °C (0.5 h) and then at ambient temperature overnight. The product bromohydrin was obtained after successive addition of methanol (10 ml) and light petroleum (2 ml) with stirring (0.5 h), dil. sulphuric acid (0.5 ml), and water (100 ml), and extraction into diethyl ether. The extract was washed successively with aqueous sodium hydrogen carbonate and water, then dried (MgSO$_4$), and concentrated under reduced pressure to yield the bromohydrin (10) (0.18 g, 83%), m.p. 170—171 °C (from chloroform), [α]$_D$ +14.1° (CHCl$_3$).

The other bromo MTPA diastereoisomer (11b) ([α]$_D$ +34.5°) yielded the other bromohydrin (10), m.p. 165—166 °C (chloroform), [α]$_D$ −15.2° (CHCl$_3$). The (+) and (−) enantiomers of bromohydrin (10) were spectroscopically indistinguishable from the racemic sample.

(−)-(9R,10R)-trans-9-*Acetoxy*-10-*bromo*-9,10,11,12-*tetra-hydrobenzo*[e]*pyrene* (7).—(−)-Bromohydrin (10) ([α]$_D$ +14.1°) (0.1 g, 0.18 mmol) was converted into (−)-bromo acetate (7) (0.1 g, 87%) using the procedure outlined earlier. The crystalline product (−)-(7), m.p. 179—180 °C, [α]$_D$ −171° (CHCl$_3$), was spectroscopically identical to the racemic sample.

(−)-(9R,10R)-trans-9-*Acetoxy*-10,12-*dibromo*-9,10,11,12-*tetrahydrobenzo*[e]*pyrene* (8).—Using a similar procedure to that reported earlier for the racemic sample, the (−)-bromo acetate (7) (0.475 g, 1.21 mmol) ([α]$_D$ −35°; 20% e.e.) was converted into the dibromo acetate (8) (0.46 g, 84%), m.p. 144—145 °C; [α]$_D$ −30.5° (CHCl$_3$), which showed identical spectral characteristics to the racemic compound.

Racemization and Photoisomerization of Benzo[e]*pyrene* 9,10-*Oxide* (4).—The (−)-dibromo acetate (8) (0.02 g, 0.04 mmol) ([α]$_D$ −30.5°) in [^{2}H$_8$] THF (1.0 ml) was mixed with NaOCD$_3$ (0.016 g, 0.2 mmol) in a standard n.m.r. tube and the mixture was left overnight in the dark. N.m.r. analysis indicated that the reaction had gone to completion and that the product contained both arene oxide (4) (*ca.* 70%) and oxepine (9) (*ca.* 30%). The optical rotation measurement was carried out on the filtered [^{2}H$_8$]THF solution in a wide-bore short-path (10 mm) polarimeter cell which showed no trace of optical activity at any wavelength. An identical result was obtained when the experiment was repeated.

When the same experiment was carried out using identical quantities of a racemic sample of dibromo acetate (8), but with one sample exposed to room light throughout and a second sample in the dark, no significant changes in the proportion of arene oxide:oxepine were observed.

A Pyrex n.m.r. tube containing a solution of arene oxide (4) (53%) and oxepine (9) (47%) (0.01 g, in 0.5 ml [^{2}H$_8$]THF) and an internal reference compound (pentamethylbenzene) was exposed to u.v. light (>300 nm; 0.5 h) at ambient temperature (water-cooled jacket). N.m.r. analysis showed that *ca.* 45% of the original arene oxide (4) had photoisomerized to oxepine (9) with the remainder isomerizing to 9-hydroxybenzo[e]pyrene (18). Further irradiation (0.5 h) showed a slight decrease (<20%) in the proportion of oxepine (9) with associated aromatization.

(−)-(9S,10R)-9,10-*Epoxy*-9,10,11,12-*tetrahydrobenzo*[e]-*pyrene* (12).—A solution of bromohydrin (10) (0.07 g, 0.2 mmol) ([α]$_D$ −15.2°) in dry THF (25 ml) was stirred with the basic form of Amberlite resin (IRA-900; 1.5 g) under nitrogen at ambient temperature for 2 h. The resin was filtered off and the THF was removed at ambient temperature under reduced pressure to yield *epoxide* (12) (0.05 g, 92%), m.p. 175—177 °C (from diethyl ether at −70 °C); [α]$_D$ −110° (CHCl$_3$) (Found: M^+, 270.104 46. C$_{20}$H$_{14}$O requires M, 270.104 46); δ_H (250 MHz; CDCl$_3$) 1.99—2.13 (1 H, m, 11-H), 2.70—2.80 (1 H, m, 11-H), 2.92—3.08 (1 H, m, 12-H), 3.60—3.70 (1 H, m, 12-H), 4.00—4.03 (1 H, m, 10-H), 4.97 (1 H, d, $J_{9,10}$ 4.5 Hz, 9-H), 8.02—8.17 (4 H, m, ArH), 8.20 (2 H, d, J 7.6 Hz, ArH), 8.42 (1 H, d, J 8.4 Hz, ArH), and 8.68 (1 H, d, J 7.8 Hz, ArH).

(−)-(9R,10R)-trans-9,10-*Dihydroxy*-9,10,11,12-*tetrahydro-benzo*[e]*pyrene* (13) and (+)-(9S,10R)-cis-9,10-*Dihydroxy*-9,10,11,12-*tetrahydrobenzo*[e]*pyrene* (14).—A solution of tetra-hydroepoxide (12) (0.05 g, 0.19 mmol) ([α]$_D$ −110°) in dioxane (5 ml) was added to a buffer solution of dioxane (50 ml) and water (70 ml) (adjusted to pH 2.5 by addition of NaClO$_4$ and HClO$_4$) and stirred at ambient temperature for 0.5 h. The dioxane was removed under reduced pressure, and the residual solution was neutralized (NaHCO$_3$), and extracted with ethyl acetate. The extract was washed with water, dried (MgSO$_4$), and concentrated to yield a mixture of *trans* (13) and *cis* (14) tetrahydrodiols (0.044 g, 80%), which were separated by p.l.c. on silica gel with chloroform–methanol (97:3) as eluant.

(−)-(9R,10R)-(13): Low-R_F isomer (0.015 g, 34%), m.p. 172—174 ° (from THF–pentane); [α]$_D$ −22.7° (THF) (Found: M^+, 288.114 96. C$_{20}$H$_{16}$O$_2$ requires M, 288.115 02); δ_H (250 MHz; CD$_3$COCD$_3$) 2.14—2.51 (2 H, m, 11-H$_2$), 3.28—3.45 (2 H, m, 12-H$_2$), 4.37—4.41 (1 H, m, 10-H), 5.40 (1 H, d, $J_{9,10}$ 2.8 Hz, 9-H), 8.02—8.10 (4 H, m, ArH), 8.18—8.24 (2 H, m, ArH), 8.42 (1 H, d, J 7.8 Hz, ArH), and 8.70 (1 H, d, J 7.8 Hz, ArH).

(+)-(9S,10R)-(14): High-R_F isomer (0.007 g, 16%), m.p. 212—215 °C (from THF–pentane); [α]$_D$ +24.6° (THF) (Found: M^+, 288.114 96. C$_{20}$H$_{16}$O$_2$ requires M, 288.115 02); δ_H (250 MHz; CD$_3$COCD$_3$–CD$_3$OD) 2.14—2.59 (2 H, m, 11-H$_2$), 3.28—3.45 (2 H, m, 12-H$_2$), 4.48—4.50 (1 H, m, 10-H), 5.52 (1 H, d, $J_{9,10}$ 3.4 Hz, 9-H), 8.00—8.18 (4 H, m, ArH), 8.21—8.24 (3 H, m, ArH), 8.45 (1 H, m, ArH), and 8.72 (1 H, m, ArH).

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