The Synthesis of Chiral Arene Oxide Metabolites of Benz[*a*]anthracene: Optically Active Benz[*a*]anthracene 10,11- and 5,6-Oxides

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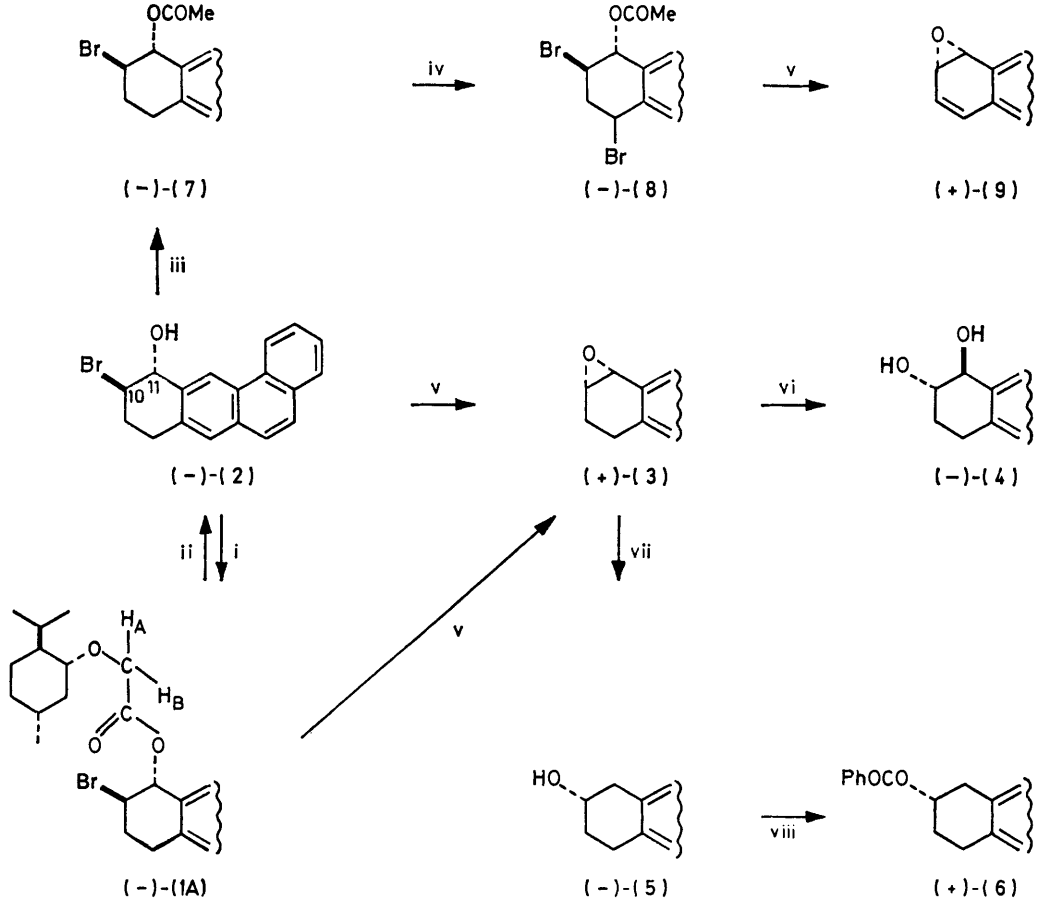
(+)-Benz[*a*]anthracene 10,11-oxide (9) has been obtained in optically pure form by a four-step synthesis from (−)-*trans*-(10R,11*R*)-10-bromo-11-(menthyloxyacetoxy)-8,9,10,11-tetrahydrobenz[*a*]anthracene (1A) which was separated from diastereoisomer (1B) by recrystallization. The absolute configuration of (+)-(9) was established as (10*S*,11*R*) by application of the exciton-chirality method to the circular dichroism curve of the benzoate (+)-(6) and by a correlation of stereochemistry between (+)-(6), (−)-(4), and (+)-(9). (+)-Benz[*a*]anthracene 5,6-oxide (15) has been synthesised in 30% optical yield using partially resolved (+)-*cis*-5,6-dihydroxy-5,6-dihydrobenz[*a*]anthracene (11) obtainable by chromatographic resolution of the (−)-*cis*-5,6-dimenthyloxyacetoxy-5,6-dihydrobenz[*a*]anthracene diastereoisomers (12A) and (12B). Both arene oxides, (+)-(9) and (+)-(15), showed configurational stability at ambient temperature in accord with perturbation molecular orbital calculations.

POLYCYCLIC aromatic hydrocarbons (PAHs) are produced by combustion of fossil fuels and are thus widely distributed in the environment. The primary step in the ensuing metabolism of PAHs by mammalian and fungal systems is now generally accepted to involve the addition of an oxygen atom to form arene oxides.[1] The possibility of stereoselective mono-oxygenase-catalysed addition of an oxygen atom during arene oxide formation from PAHs prompted earlier reports from these laboratories on the synthesis of optically active arene oxides.[2,3,4,5] Thus, using a similar synthetic pathway, the chiral arene oxides of naphthalene (1,2-oxide [2]) and anthracene (1,2-oxide [2]) were both obtained as configurationally stable (+)-and (−)-enantiomers, whereas those of phenanthrene (1,2- and 3,4-oxides [3]) appeared to racemize spontaneously. This difference in con-



SCHEME 1 *Reagents*: i, (−)-Menthyloxyacetyl chloride–pyridine; ii, diborane–THF; iii, AcCl–pyridine; iv, *N*-bromosuccinimide; v, NaOMe–THF; vi, KOH–aqueous Bu^{t}OH; vii, $LiAlH_4$; viii, PhCOCl–pyridine

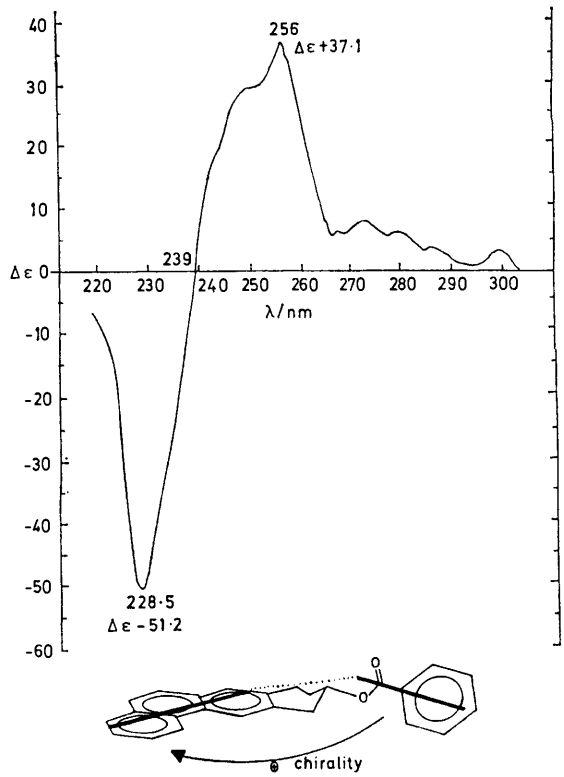
figurational stability between the chiral arene oxides of naphthalene (or anthracene) and phenanthrene was tentatively rationalized in terms of the ability of the arene oxide to isomerize rapidly with a very small (but undetected) proportion of the corresponding oxepin. A preliminary study,[3] using perturbation molecular orbital (PMO) methods to rationalize the racemization process, allowed predictions to be made concerning the configurational stability of arene oxide enantiomers derived from a range of PAHs.

The weak carcinogen benz[*a*]anthracene (BA) appeared to be the most interesting lower molecular weight PAH for intensive investigation since the total possible range of dihydrodiols (1,2-, 3,4-, 5,6-, 8,9-, 10,11-) was obtained optically active [7] from mammalian liver metabolism [6,7,8] which implied that all the corresponding arene oxide metabolites of BA (1,2-, 3,4-, 5,6-, 8,9-, and 10,11-) had been formed enzymatically (and were thus potentially present in optically active forms). Of these five possible arene oxides the PMO method predicted [3] that three should be configurationally stable (5,6-, 8,9-, and 10,11-) while two should racemize spontaneously (1,2- and 3,4-). At the commencement of this programme to examine the configurational stability of the arene oxides of BA only the 5,6- and 8,9-oxides had previously been chemically synthesised. The 8,9-oxide was the first arene oxide member of the BA series to be prepared in optically active form and showed no measurable degree of racemization at ambient temperature.[5] The present report describes the synthesis of optically active BA 10,11- and 5,6-oxides and examines their configurational stability.

The synthetic sequence now reported for BA 10,11-oxide (9) was directly parallel to that used previously for the preparation of optically active naphthalene 1,2-,[2] anthracene 1,2-,[2] and BA 8,9-oxides [5] and is outlined in Scheme 1. The bromohydrin (−)-(2) was prepared in *optically* pure form from the bromo-menthyloxyacetoxy-diastereoisomer (−)-(1A), $[\alpha]_D$ −74.0°. A combination of short-column chromatography or preparative high pressure liquid chromatography (h.p.l.c.) on silica gel (α 1.12) followed by fractional crystallization yielded a diastereoisomerically pure sample of the less soluble isomer (−)-(1A) from a mixture of (1A) and (1B).

In common with the n.m.r. spectral data obtained for the corresponding bromo-menthyloxyacetoxy-diastereoisomers in the naphthalene,[1,2] anthracene,[1,2] phenanthrene,[3] and benzo[*a*]pyrene [4] series, the more polar (lower R_F) isomer (1B), $[\alpha]_D$ −8.6°, was characterized by an AB quartet (centred at δ 3.88 and 4.03, J_{AB} 16.3 Hz) for the exocyclic methylene protons (H_A, H_B) while the less polar (higher R_F) isomer (1A), $[\alpha]_D$ −74.0°, gave a singlet (2 H, δ 3.96) for H_A and H_B. The configuration of (−)-(1A) was tentatively assigned as (10*R*,11*R*) based upon a comparison of the distinctive n.m.r. signals for protons H_A and H_B in (1A) and (1B) with the analogous bromo-menthyloxyacetoxy-compounds of known absolute stereochemistry in other members of the PAH series.

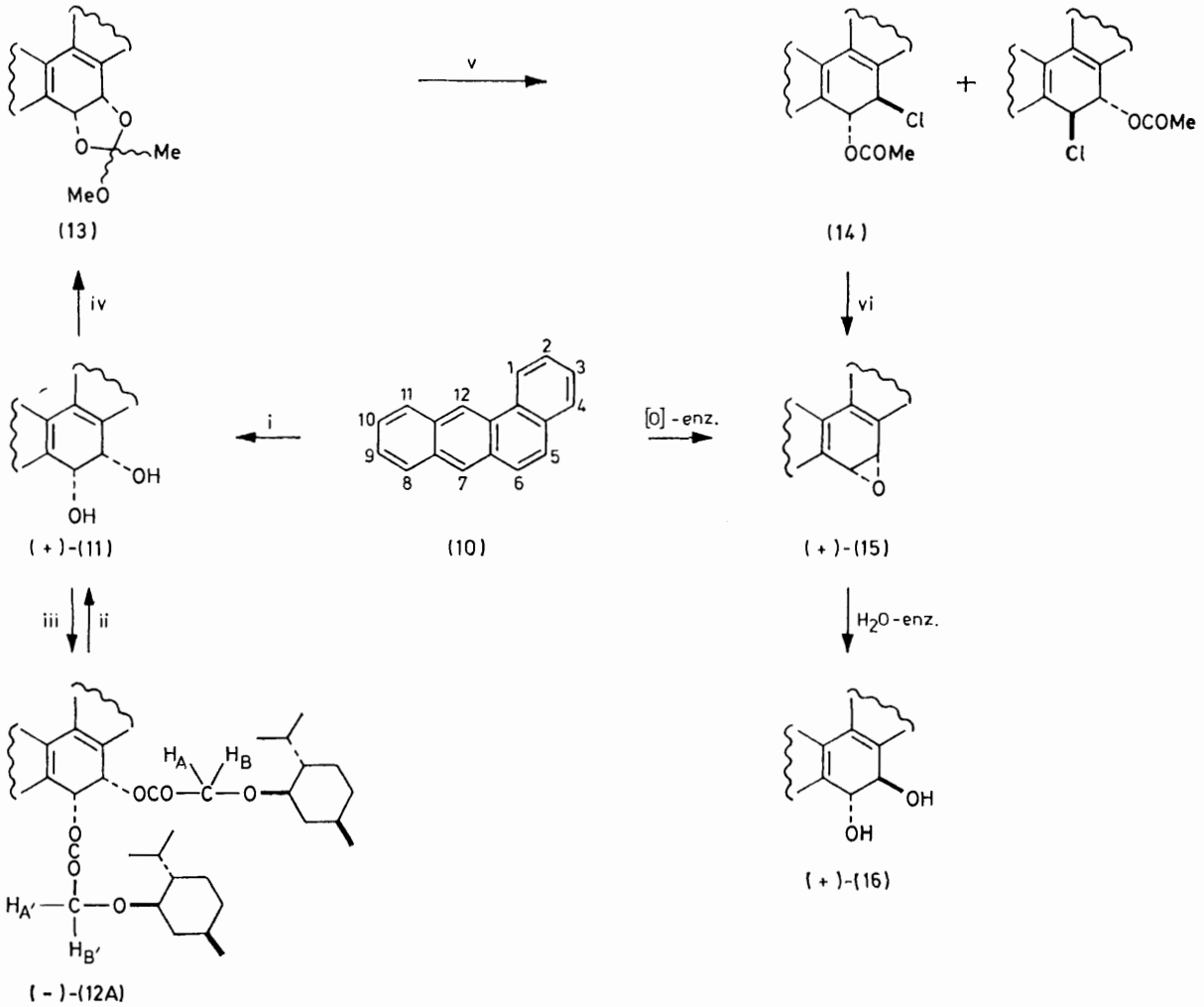
Confirmative evidence for the absolute stereochemistry of structures shown in Scheme 1 was obtained by conversion of (−)-(1A), *via* the epoxide (+)-(3) and the alcohol (−)-(5), to the benzoate derivative (+)-(6) which was amenable to stereochemical analysis by circular dichroism (c.d.). A bisignate c.d. couplet derived from $\pi \longrightarrow \pi^*$ transitions of the phenanthrene (256 nm, ε 135 000) and the benzoyloxy-ester (228 nm, ε 12 000) chromophores was observed for (+)-(6) (Figure). The strong positive and negative Cotton effects evident at 256 nm ($\Delta\varepsilon$ + 37.1) and 228.5 nm ($\Delta\varepsilon$ − 51.2) respectively, allied together form a typical exciton interaction pattern. These $\pi \longrightarrow \pi^*$ transitions are associated with polarization of both phenanthrene and benzoyloxy-systems along the long axes and the relative geometry of the coupled electric transition dipoles is as shown in the Figure. The positive Cotton effect at longer



C.d. spectrum of (+)-(10*S*)-benzoyloxy-8,9,10,11-tetrahydrobenz[*a*]anthracene in cyclohexane and the configuration of the electric transition dipoles of the chromophores

wavelengths is consistent with a right-handed helical charge displacement and thus with an (*S*) configuration at C-10 in (−)-(5). Compound (−)-(5) showed weak c.d. absorption without bisignate exciton features, thus supporting the assignment of the strong bisignate c.d. in (+)-(6) with the origin described and implying the C-10 (*S*) configuration. This modified form of the exciton chirality method,[9,10] using benzoate and PAH chromophores, has been successfully applied in a similar manner to the corresponding benzoate derivatives of the anthracene [11] and phenanthrene [12] series.

Conversion of the dihydro-BA epoxide (+)-(3) to the diol (−)-(4) [under basic conditions known to effect



SCHEME 2 *Reagents:* i, OsO_4–pyridine; ii, (−)-menthyloxyacetyl chloride–pyridine; iii, KOH–MeOH; iv, trimethyl orthoacetate; v, Me_3SiCl–Et_3N; vi, NaOMe–THF

almost complete (*i.e. ca.* 90%) inversion of configuration at the benzylic centre (C-11) [4] allowed a convincing independent c.d. method of stereochemical analysis to be applied. Thus an examination of the c.d. curve of the dibenzoate of (−)-(4), which was obtained by a direct resolution method,[7] suggested (10*S*,11*S*) absolute stereochemistry in agreement with that presently assigned.

The chemical conversion of (−)-(1A) to the desired arene oxide (+)-(9) proceeded *via* the monobromo- (−)-(7) and dibromo-acetates (−)-(8). The arene oxide (+)-(9) decomposed on heating (*e.g.* during m.p. determination) or in the presence of a trace of acid as anticipated for a non-K region arene oxide. However, it appeared to be relatively stable under acid-free conditions either in the crystalline state or in $CDCl_3$ solution with no evidence of decomposition after 24 h at ambient temperature. The configurational stability of (+)-(9) over a similar period was established from the constant $[\alpha]_D$ values observed by polarimetry using $CDCl_3$ as solvent.

Benz[*a*]anthracene 10,11- and 5,6-oxides (9) and (15) appear to share a common role as initial products of mono-oxygenase-catalysed oxygen-atom transfer to BA during metabolism in mammalian liver systems. However, while the non-K region arene oxide (9) was neither previously synthesised chemically nor detected directly as a metabolite, the K-region arene oxide (15) was among the first members of the arene oxide series to be chemically synthesised [13] and identified as a direct metabolite.[14] The BA 5,6-oxide has also been synthesised from *trans*-[15] or *cis*-5,6-dihydroxy-5,6-dihydro-BA.[16] The latter route has been used in the present synthesis of (+)-(15) (Scheme 2).

A partial separation of the diastereoisomeric dimenthyloxyacetates (12A) and (12B) obtained from the *cis*-diol (11) was achieved by short-column chromatography or preparative h.p.l.c. (α 1.08) as for (1A) and (1B). Recrystallization of the enriched mixtures of (12A) and (12B) thus obtained yielded small quantities (*ca.* 0.02 g) of each of the pure (>97%) diastereoisomers (−)-(12A), $[\alpha]_D$ −7°, and (−)-(12B), $[\alpha]_D$ −88°. The n.m.r. spectra of (−)-(12A) and (−)-(12B) obtained at 220 MHz (C_6D_6) showed a non-equivalence pattern for the exocyclic

methylene protons H_A,H_B and $H_{A'}$,$H_{B'}$ of similar form to that observed for (−)(-1A) and (−)-(1B). Thus isomer (−)-(12A) showed a singlet (δ 4.08, 2 H) and an AB quartet centred at δ 3.87 (1 H, J_{AB} 16.3 Hz) and δ 4.10 (1 H, J_{AB} 16.3 Hz), while (−)-(12B) showed a similar pattern but with different chemical shifts, *i.e.* a singlet at δ 4.00 (2 H) and an AB quartet centred at δ 3.94 (1 H, $J_{A'B'}$ 16.3 Hz) and 4.10 (1 H, $J_{A'B'}$ 16.3 Hz). In common with the isomeric mixture of (−)-(1A) and (−)-(1B), it was thus possible to monitor the diastereoisomeric purity of mixtures of (−)-(12A) and (−)-(12B) both by h.p.l.c. and by n.m.r.

The difficulties encountered in obtaining adequate samples of pure (−)-(12A) or (−)-(12B) resulted in the use of a sample of (−)-(12A) of lower (30%) diastereoisomeric purity for the reactions outlined in Scheme 2. Alkaline hydrolysis of (−)-(12) yielded the *cis*-diol (+)-(11), ($[\alpha]_D$ +40°, 31% enantiomeric excess [e.e]) The chemical transformation of (+)-(11) to (+)-BA 5,6-oxide (15) was carried out as reported.[16] Thus the crude isomeric mixtures of 2-methoxy-2-methyl-1,3-dioxolans (13) and *trans*-chlorohydrin acetates (14), which were formed as reaction intermediates, were identified by spectroscopic methods and were converted directly into (+)-BA 5,6-oxide (15) without further purification. Recrystallization of the final product gave a pure sample of (+)-(15) ($[\alpha]_D$ +36°, 30% e.e.), m.p. 134—135 °C with identical spectral characteristics to the racemic material. The configurational stability of (+)-(15) at ambient temperature was established by observation of a constant optical rotation over a period greater than 12 h.

An alternative method for the total resolution of (+)- and (−)-(11) has recently been developed [17] which, when applied to the synthetic route used in Scheme 2, also gave an optically active sample of (+)-BA 5,6-oxide (15) ($[\alpha]_D$ +120°) to which (5*S*,6*R*) absolute stereochemistry has been assigned.[17]

On the reasonable assumption that epoxide hydrolase-catalysed attack of water occurs at the C-10 position (based on analogy with the enzyme-catalysed hydration of a range of comparable non-K-region arene oxides), the (−)-(10*R*,11*R*) dihydrodiol metabolite isolated in 96% e.e. from metabolism of BA by liver microsomes [7] must have been formed by stereospecific mono-oxygenase enzyme-catalysed addition of an oxygen atom to BA to yield essentially optically pure (+)-(10*S*,11*R*)-arene oxide of BA (a similar conclusion is drawn in ref. 17). It should be noted however that the lower optical yield (62%) observed [7] for the (+)-(5*R*,6*R*)-*trans*-diol liver microsomal metabolite of BA (16) should not be considered to reflect the stereoselectivity of addition of an oxygen atom in the formation of (15) during the metabolism of BA, since regiospecificity in the enzyme-catalysed hydration of K-region arene oxides has yet to be established.

As previously determined [5] for the optically active 8,9-oxide of BA, the chiral 10,11- and 5,6-arene oxides are now also shown to possess configurational stability at ambient temperature as predicted by the PMO method.[3] The synthesis of the 1,2- and 3,4-oxides of BA from optically pure precursors (which, according to PMO calculations should racemize spontaneously) is currently under investigation and the final results will be reported elsewhere.

TABLE 1

Optical rotations, optical yields, and absolute configurations of compounds (1A)—(9), (11), (12a), and (15)

Compound	$[\alpha]_D$ (°)	Optical yield (%)	Absolute configuration
(1A)	−74 [a]	>98	(10*R*,11*R*)
(2)	−19	>98	(10*R*,11*R*)
(3)	+142	>98	(10*S*,11*R*)
(4)	−85 [b]	*ca.* 87	(10*S*,11*S*)
(5)	−25	>98	(10*S*)
(6)	+122	>98	(10*S*)
(7)	−127	>98	(10*R*,11*R*)
(8)	−152	>98	(10*R*,11*R*)
(9)	+383	>98	(10*S*,11*R*)
(11)	+40 [b]	*ca.* 31	(5*S*,6*R*) [d]
(12A)	−7 [c]	>98	(5*S*,6*R*) [d]
(15)	+36	*ca.* 30	(5*S*,6*R*) [d]

[a] (1B): $[\alpha]_D$ −8.6° (>98% diastereoisomeric purity). [b] In THF solution. [c] (12B): $[\alpha]_D$ −88° (>97% diastereoisomeric purity). [d] Ref. 17.

EXPERIMENTAL

M.p.s were determined using a Reichert Kofler hot-stage apparatus. N.m.r. spectra were recorded (Table 2) using Bruker WH90 and Varian HR-220 instruments, $CDCl_3$ as solvent and tetramethylsilane as reference. Chemical shifts and coupling constants which have previously been reported [16] for the racemic compounds (11), (13), (14), and (15), and which were found to be identical in the optically active forms, are not given. Specific optical rotations ($[\alpha]_D$) were recorded at 589 nm on Perkin-Elmer 141 and 241 polarimeters in $CHCl_3$ (or $CDCl_3$) solution unless stated otherwise. All new compounds (1)—(9) and (13) gave mass spectral data (AE1-MS9, 90 eV) consistent with the assigned structures.

(−)-Menthyloxyacetic acid was purchased from the Aldrich Chemical Company. The *cis*-diol (11) was prepared in racemic form by OsO_4 oxidation of BA.[16] The racemic bromohydrin (2) was obtained by the normal method [4,5] from 8,9-dihydrobenz[*a*]anthracene which was synthesised as reported.[18]

(−)-trans-10-*Bromo*-11-*menthyloxyacetoxy*-8,9,10,11-*tetrahydrobenz*[a]*anthracene* (1A *and* 1B).—A mixture of the diastereoisomers (1A) and (1B) was obtained in 95% yield from the racemic bromohydrin (2) and (−)-menthyloxyacetyl chloride in pyridine solution. Recrystallisation of this mixture ($CHCl_3$–n-C_6H_{14}) gave crystals, m.p. 137—139 °C (Found: C, 68.35; H, 7.0. $C_{30}H_{35}BrO_3$ requires C, 68.8; H, 6.7%) again consisting of almost equal proportions of (1A) and (1B). A partial separation of (1A) and (1B) was obtained using either a short-column chromatography method [19] (Kieselgel G type 60, Merck, 1 kg, column diameter 120 mm) with light petroleum–ether (9 : 1 v/v) as eluant or preparative h.p.l.c. [Waters Prep. 500, 4 silica-gel cartridges, cyclohexane–ether (19 : 1, v/v), α 1.18]. A sample of (−)-(1A) which appeared to have >98% diastereoisomeric purity was recrystallized from a $CHCl_3$–MeOH solution of the earlier chromatographic fractions [excess of (−)-(1A)]; m.p. 166—168 °C, $[\alpha]_D$ −74.0°. Similarly a sample of (−)-(1B) of high diastereoisomeric purity (>97%) could be

TABLE 2

N.m.r. spectral data for compounds (1)—(9), and (12) $CDCl_3$ at 90 MHz

Compound	δ Values (*J* values/Hz)
(1A) [a,b]	0.70 (d, 3 H, Me), 0.92 (d, 6 H, Me), 0.74—0.88 (m, 3 H), 1.23—1.52 (m, 4 H), 1.78—1.95 (m, 2 H), 2.25 (m, 1 H) (menthyl protons); 2.51—2.68 (m, 2 H, 9-H), 2.93—3.13 (m, 2 H, 8-H), 3.96 (s, 2 H, H_A and H_B), 4.39 (m, 1 H, 10-H), 6.71 (d, 1 H, 11-H, $J_{10,11}$ 4.1), 7.27—7.67 (m, 6 H, arom.), 8.47 (m, 1 H, 1-H), 8.77 (s, 1 H, 12-H)
(2)	1.60 (s, 1 H, OH), 2.38—2.74 (m, 2 H, 9-H), 3.09—3.25 (m, 2 H, 8-H), 4.49 (m, 1 H, 10-H), 5.15 (m, 1 H, 11-H), 7.54—7.91 (m, 6 H, arom.), 8.69 (m, 1 H, 1-H), 8.84 (s, 1 H, 12-H)
(3)	1.51—2.05 (m, 2 H, 9-H), 2.33—3.07 (m, 2 H, 8-H), 3.79 (m, 1 H, 10-H), 4.09 (d, 1 H, 11-H, $J_{10,11}$ 4.1), 7.45—7.87 (m, 6 H, arom.), 8.60 (m, 1 H, 1-H), 8.66 (m, 1 H, 12-H)
(4)	1.94—2.40 (m, 4 H, 9-H and OH), 3.03—3.18 (m, 2 H, 8-H), 3.88 (m, 1 H, 10-H), 4.76 (d, 1 H, 11-H, $J_{10,11}$ 8.0), 7.52—7.90 (m, 6 H, arom.), 8.65 (m, 1 H, 1-H), 8.82 (s, 1 H, 12-H)
(5)	1.79—2.10 (m, 3 H, 9-H and OH), 2.76—3.51 (m, 4 H, 8- and 11-H), 4.22 (m, 1 H, 10-H), 7.50—7.88 (m, 6 H, arom.), 8.34 (s, 1 H, 12-H), 8.60 (m, 1 H, 1-H)
(6)	2.11—2.40 (m, 2 H, 9-H), 3.05—3.55 (m, 4 H, 8- and 11-H), 5.60 (m, 1 H, 10-H), 7.31—8.05 (m, 11 H, arom.), 8.41 (s, 1 H, 12-H), 8.57 (m, 1 H, 1-H)
(7)	2.13 (s, 3 H, OAc), 2.20—2.80 (m, 2 H, 9-H), 2.89—3.55 (m, 2 H, 8-H), 4.59 (m, 1 H, 10-H), 6.46 (d, 1 H, 11-H, $J_{10,11}$ 4.15) 7.48—7.95 (m, 6 H, arom.), 8.57 (m, 1 H, 1-H), 8.60 (s, 1 H, 12-H)
(8)	2.30 (s, 3 H, OAc), 2.84—3.18 (m, 2 H, 9-H), 4.81 (m, 1 H, 10-H), 5.78 (m, 1 H, 8-H), 6.51 (d, 1 H, 11-H, $J_{10,11}$ 7.36), 7.51—8.00 (m, 6 H, arom.), 8.48 (m, 1 H, 1-H), 8.49 (s, 1 H, 12-H)
(9)	4.18 (m, 1 H, 10-H, $J_{10,11} = J_{10,9} = 3.9$, $J_{10,8}$ 1.5), 4.71 (d, 1 H, 11-H, $J_{11,10}$ 3.9), 6.49 (d of d, 1 H, 9-H, $J_{9,8}$ 9.3, $J_{9,10}$ 3.91), 6.95 (d of d, 1 H, 8-H, $J_{8,9}$ 9.3, $J_{8,10}$ 1.5), 7.50—8.00 (m, 6 H, arom.), 8.73 (m, 1 H, 1-H), 8.89 (s, 1 H, 12-H)
(12A) [c,d]	0.62—1.55 (m, 32 H), 1.86 (m, 1 H), 2.00 (m, 1 H), 2.55 (m, 2 H), 3.01 (m, 1 H), 3.22 (m, 1 H) (menthyl protons); 4.08 (s, 2 H, H_A and H_B), 3.87 (d, 1 H, $H_{A'}$, $J_{A'B'}$ 16.3), 4.10 (d, 1 H, $H_{B'}$, $J_{A'B'}$ 16.3), 6.55—6.63 (m, 2 H, 5- and 6-H), 7.08—7.43 (m, 5 H, arom.), 7.60—7.74 (m, 3 H, arom.), 7.83 (s, 1 H, 1-H), 8.07 (s, 1 H, 12-H)

[a] 250 MHz in C_6D_6. [b] (1B) gave a similar n.m.r. spectrum except for the exocyclic methylene proton signals at δ 3.88 (d, 1 H, H_A, J_{AB} 16.3) and 4.03 (d, 1 H, H_B, J_{AB} 16.3). [c] 220 MHz in C_6D_6. [d] (12B) gave a similar n.m.r. spectrum except for the exocyclic methylene proton signals at δ 3.94 (d, 1 H, $H_{A'}$, $J_{A'B'}$ 16.3) and 4.10 (d, 1 H, $H_{B'}$, $J_{A'B'}$ 16.3), and a singlet at δ 4.00 (s, 2 H, H_AH_B).

isolated from the later chromatography fractions [which were enriched in (−)-(1B)] by fractional crystallization from $CHCl_3$–n-C_6H_{14} solution; m.p. 136—140 °C, $[\alpha]_D$ −8.6°.

(−)-trans-10-*Bromo*-11-*hydroxy*-8,9,10,11-*tetrahydrobenz*[a]*anthracene* (2).—The synthesis of (−)-(2) from (−)-(1A) ($[\alpha]_D$ −74°) was carried out in 60% yield by the diboroane method.[2-5] Recrystallization from $CHCl_3$–n-C_6H_{14} gave the *bromohydrin* (−)-(2), m.p. 165—166 °C (racemic, m.p. 161—163 °C), $[\alpha]_D$ −19° (Found: C, 65.9; H, 4.85. $C_{18}H_{15}BrO$ requires C, 66.1; H, 4.6%).

(+)-8,9-*Dihydrobenz*[a]*anthracene* 10,11-*Oxide* (3).—Cyclization of the bromohydrin (−)-(2) was effected using NaOMe in Et_2O solution.[2-5] Recrystallization from $CHCl_3$–n-C_6H_{14} gave the *epoxide* (+)-(3); m.p. 134—135 °C (racemic, m.p. 131—132 °C), $[\alpha]_D$ +142° (Found: C, 87.65; H, 5.9. $C_{18}H_{14}O$ requires C, 87.8; H, 5.7%).

(−)-trans-10,11-*Dihydroxy*-8,9,10,11-*tetrahydrobenz*[a]*anthracene* (4).—Base-catalysed hydrolysis of (+)-(3) using KOH in aqueous t-butyl alcohol [2-5] gave the trans-*diol* (−)-(4) having 87% optical purity, m.p. 168—170 °C (from EtOAc), $[\alpha]_D$ −85° (THF) (Found: C, 81.5; H, 6.1. $C_{18}H_{16}O_2$ requires C, 81.8; H, 6.1%).

(−)-10-*Hydroxy*-8,9,10,11-*tetrahydrobenz*[a]*anthracene* (5).—$LiAlH_4$ reduction in ether solution of (+)-(3) gave the *alcohol* (−)-(5) (70%), m.p. 136—137 °C (from $CHCl_3$–n-C_6H_{14}) (racemic, m.p. 134—135 °C), $[\alpha]_D$ −25 ° (Found: C, 86.8; H, 6.4. $C_{18}H_{16}O$ requires C, 87.1; H, 6.5%).

(+)-10-*Benzoyloxy*-8,9,10,11-*tetrahydrobenz*[a]*anthracene* (6).—The *benzoate* (+)-(6) was obtained in 65% yield from the alcohol (−)-(5) using the standard benzoyl chloride–pyridine method; m.p. 138–140 °C (from n-C_5H_{12}), $[\alpha]_D$ +122° (Found: C, 85.2; H, 5.8. $C_{25}H_{20}O_2$ requires C, 85.2; H, 5.7%).

(−)-trans-11-*Acetoxy*-10-*bromo*-8,9,10,11-*tetrahydrobenz*[a]*anthracene* (7).—Reaction of (−)-(2) with acetyl chloride in pyridine gave the *bromo-ester* (75%), m.p. 144—146 °C (from EtOAc-n-C_6H_{14}) (racemic, m.p. 154—155 °C), $[\alpha]_D$ −127 ° (Found: *m/e*, 368.0415. $^{79}BrC_{20}H_{17}O_2$ requires *m/e*, 368.0412).

(−)-trans-11-*Acetoxy*-8,10-*dibromo*-8,9,10,11-*tetrahydrobenz*[a]*anthracene* (8).—The bromo-ester (−)-(7) was converted into the *dibromoacetate* (−)-(8) (60%) using *N*-bromosuccinimide in CCl_4 solution; m.p. 124—125 °C [from C_6H_6–light petroleum (b.p. 60—80 °C)] (racemic, m.p. 119—122 °C), $[\alpha]_D$ −152° (Found: *m/e* 445.9518. $C_{20}H_{16}{}^{79}Br_2O_2$ requires *m/e* 445.9519)

(+)-*Benz*[a]*anthracene* 10,11-*Oxide* (9).—The dibromoacetate (−)-(8) on treatment with sodium methoxide in THF gave the *arene oxide* (+)-(9) (56%), m.p. 136—140 °C (from THF–n-C_5H_{12}) (racemic, m.p. 136—140 °C), $[\alpha]_D$ +383°. No change in the $[\alpha]_D$ value was observed in $CDCl_3$ solution at ambient temperature over 24 h (Found: *m/e*, 244.0883. $C_{18}H_{12}O_2$ requires *m/e*, 244.0888).

(−)-cis-5,6-*Bis*(*menthyloxyacetoxy*)-5,6-*dihydrobenz*[a]*anthracene* (12A).— (−)-Menthoxyacetyl chloride when added to a pyridine solution of (±)-*cis*-5,6-dihydroxy-5,6-dihydrobenz[*a*]anthracene yielded a viscous high-boiling oil which on short-column chromatography on silica gel [eluting with light petroleum–ether (9 : 1 v/v)] gave the diastereoisomeric *dimenthyloxyacetates* (−)-(12A) and (−)-(12B) (80%) (Found: C, 77.15; H, 8.6. $C_{42}H_{54}O_6$ requires C, 77.0, H, 8.3%) which were partially separated by preparative h.p.l.c. [Waters Prep. 500, 4 cartridges, cyclohexane–ether (88 : 12 v/v), α 1.08]. The less polar diastereoisomer (12A) was obtained in >98% diastereoisomeric purity by fractional crystallization of the early h.p.l.c. fractions from pentane solvent; m.p. 111 °C, $[\alpha]_D$ −7°. The more polar diastereoisomer (12B) was isolated as a viscous, high-boiling oil after further chromatographic separation of the late h.p.l.c. fractions; $[\alpha]_D$ −88° (>97% diastereoisomeric purity).

Hydrolysis of the (−)-dimenthyloxyacetates (12A) and (12B) ($[\alpha]_D$ −30°) using methanolic KOH yielded (+)-(11) $[\alpha]_D$ +40° (THF) of *ca.* 31% optical purity.

(+)-*Benz*[a]*anthracene* 5,6-*Oxide* (15).—(+)-*cis*-5,6-Dihydroxy-5,6-dihydrobenz[*a*]anthracene (11) ($[\alpha]_D$ +40°) was converted *via* the 2-methoxy-2-methyl-1,3-dioxolan (13) and chloroacetate (14) intermediates in crude form into the 5,6-oxide (15) by the method of ref. 16. The optically active compounds (13), (14), and (15) showed identical n.m.r. spectral data to the racemic compounds.[16] Recrystallization of (+)-(15) from C_6H_6–n-C_6H_{14} yielded a

granular product (30%), m.p. 134—135 °C (racemic,[16] m.p. 130—132 °C), $[\alpha]_D$ +36° (*ca.* 30% optical purity). No change in $[\alpha]_D$ for (+)-(15) in $CDCl_3$ was observed during 24 h at ambient temperature.

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