

Synthesis of Triphenylene 1,2-Oxide (1,2-Epoxy-1,2-dihydrotriphenylene) and Absolute Configuration of the *trans*-1,2-Dihydro Diol Metabolite of Triphenylene. Crystal Structure of (-)-(1*R*,2*R*)-*trans*-2-Bromo-1-menthyl-oxyacetoxy-1,2,3,4-tetrahydrotriphenylene

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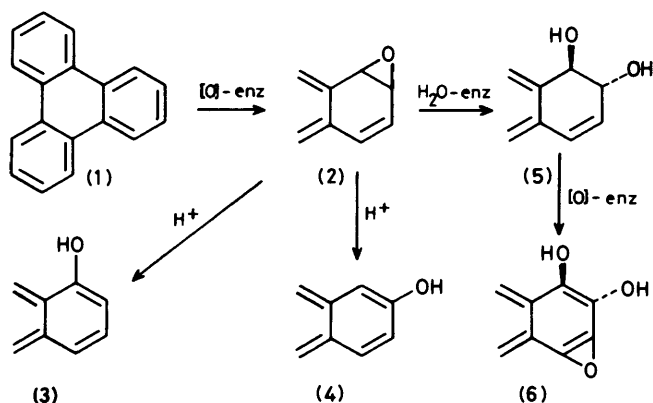
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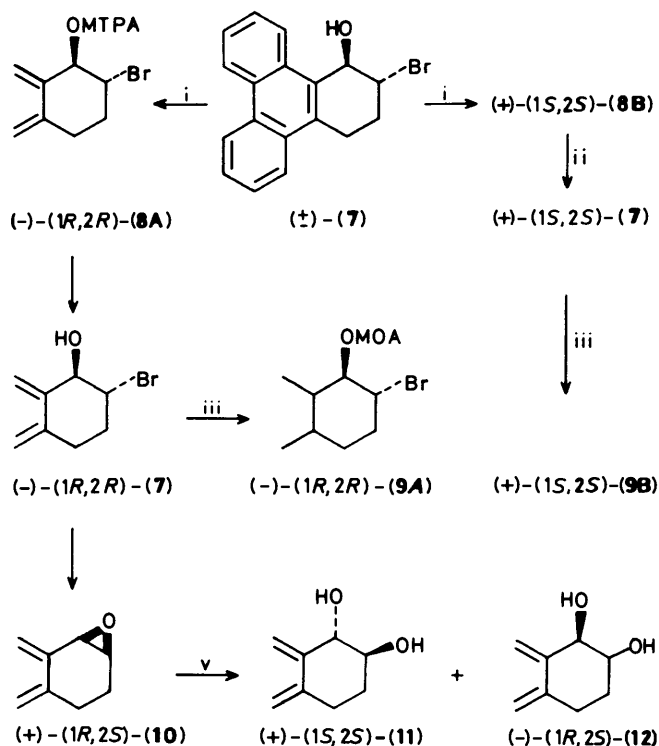
The synthesis of triphenylene 1,2-oxide (1,2-epoxy-1,2-dihydrotriphenylene) (**2**) from both racemic and optically pure precursors is reported. Racemic triphenylene 1,2-oxide (**2**) was obtained in each case, in accord with PMO calculations which predict rapid racemization. Liver microsomal metabolism of both triphenylene (**1**) and racemic triphenylene 1,2-oxide (**2**) yielded predominantly the (-)-enantiomer (**92** and 85%, respectively) of the *trans*-dihydro diol (**5**). The 1*R*,2*R* configuration for (-)-(**5**) has been established by preparative h.p.l.c. separation of the dimethylxyacetate diastereoisomers of the dihydro diol (**5**) and stereochemical correlation to (-)-(1*R*,2*R*)-*trans*-2-bromo-1-menthyl-oxyacetoxy-1,2,3,4-tetrahydrotriphenylene (**9A**) whose absolute configuration has been assigned by X-ray crystallographic analysis.

Triphenylene (**1**), the most stable member of the polycyclic aromatic hydrocarbon (PAH) series in terms of resonance energy per π -electron, occurs widely in the environment (e.g. air particulates, marine sediments) as a product of the combustion of fossil fuels.¹ Metabolites of triphenylene by mammalian liver enzymes are of particular interest since it is a non-carcinogenic PAH despite having three symmetrical bay regions. The phenols (**3**) and (**4**) and the *trans*-dihydro diol (**5**) are expected as liver enzyme metabolites of triphenylene. The dihydro diol (**5**) and the diastereoisomeric 1,2-diol 3,4-epoxides (**6**) have been synthesized,^{2,3} and the diastereoisomers of the 1,2-diol 3,4-epoxides derived from the *trans*-1,2-dihydro diol have been



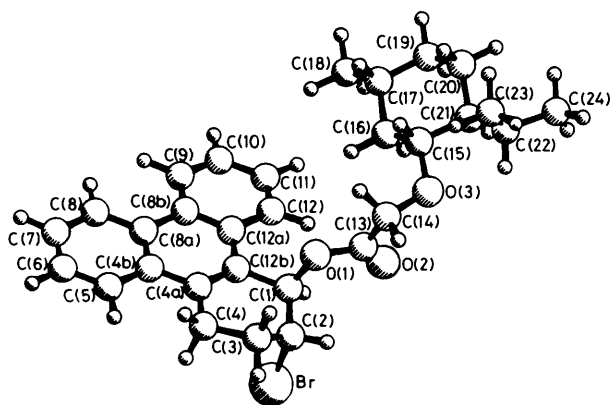
tested for mutagenic activity.⁴ The preparation of the initially formed arene oxide, triphenylene 1,2-oxide (**2**) (1,2-epoxy-1,2-dihydrotriphenylene), and the optically pure *trans*-1,2-dihydro diols (**5**) of known absolute configuration are described in the present report.

The bromohydrin (**7**) was obtained in good yield from 1,2-dihydrotriphenylene, and resolved *via* the (-)- α -methoxy-trifluoromethylphenyl (MTPA) esters (Scheme 1). Chromatographic separation (Chromatotron, Silica-gel) of the bromo-



Scheme 1. Reagents and reaction conditions: i, MTPA chloride-pyridine; ii, Dibal-H; iii, MOAc-pyridine; iv, OH⁻; v, H₂O-dioxane (pH 2.5)

MTPA ester diastereoisomers {(**8A**), [α]_D -41°; (**8B**), [α]_D +70°}, followed by treatment with Dibal-H yielded the pure bromohydrin enantiomers (**7**) ([α]_D ±24°). Unfortunately no suitable crystals for X-ray crystallographic analysis, and thus absolute configuration determination, could be obtained from either of the bromo-MTPA diastereoisomers (**8A**) or (**8B**). Analysis of the X-ray data obtained from a crystal of the



menthyloxyacetate (MOA) derivative **(9A)**, $[\alpha]_D -207^\circ$ however indicated that the 1,2,3,4-tetrahydro ring adopted a half-chair conformation with the bromine atom and the MOA group in a *trans*-pseudodiaxial relationship (Figure). The pseudodiaxial conformation of bromo ester **(9A)** in the crystalline state paralleled that of the bromo ester **(8A)** in solution ($J_{1,2}$ 2.2 Hz in C_6D_6) which resulted from steric strain in the congested bay region. Examples of both pseudodiaxial and pseudodiequatorial conformations of similar bromo-MOA diastereoisomers in the crystalline state have been observed.^{5,6} The absolute configuration of the menthyl group [derived from (-)-menthyloxyacetic acid] is well established⁷ and thus the configuration of the bromo-MOA ester (-)-**(9A)** was found to be 1*R*,2*R*. A direct stereochemical correlation between the bromohydrin (-)-**(7)** and the derived esters (-)-**(9A)** and (-)-**(8A)** indicates that all have the 1*R*,2*R* configuration as indicated in Scheme 1.

Transformation of the bromo-MTPA diastereoisomer (-)-**(8A)** to the bromohydrin enantiomer **(7)** ($[\alpha]_D -24^\circ$) and base-catalysed cyclization provided a route to the tetrahydro epoxide (+)-**(10)** ($[\alpha]_D +145^\circ$, 1*R*,2*S*). Acid-catalysed hydrolysis of the latter epoxide gave both the *trans*-tetrahydro diol (+)-**(11)** ($[\alpha]_D +61^\circ$, 1*S*,2*S*) and the corresponding *cis*-isomer (-)-**(12)** ($[\alpha]_D -75^\circ$, 1*R*,2*S*) as shown in Scheme 1.

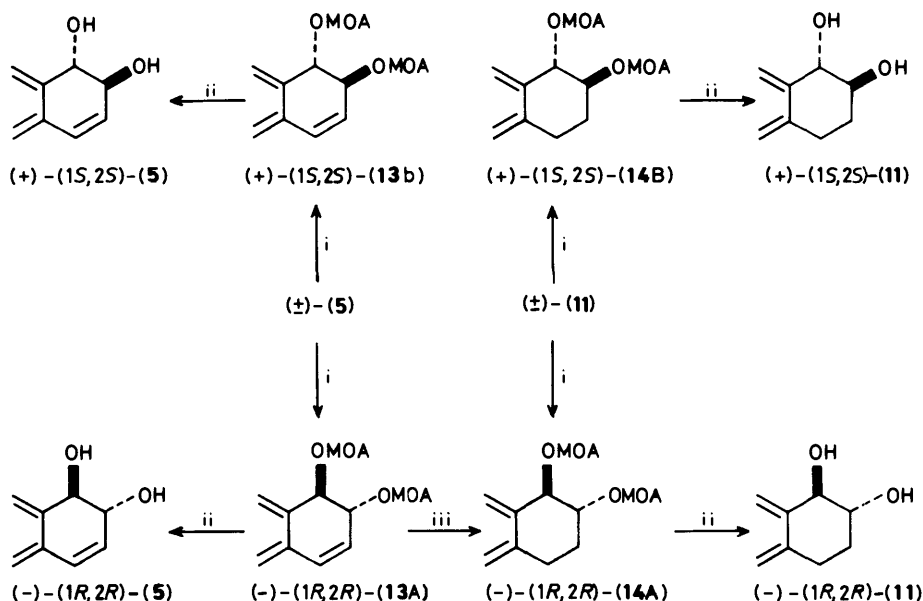
A racemic sample of the *trans*-1,2-dihydro diol **(5)** (available from earlier studies² was resolved *via* preparative h.p.l.c.

separation of the dimethyloxyacetate (diMOA) derivatives into the more polar isomer **(13B)** ($[\alpha]_D +331^\circ$) and the less polar isomer **(13A)** ($[\alpha]_D -506^\circ$) (Scheme 2). Treatment of the diMOA esters (+)-**(13B)** and (-)-**(13A)** respectively with sodium methoxide yielded the (+)- and (-)-enantiomers of the dihydro diol **(5)** ($[\alpha]_D \pm 452^\circ$). Catalytic hydrogenation of the 1,2-dihydrodiMOA diastereoisomer (-)-**(13A)** gave a sample of the 1,2,3,4-tetrahydrodiMOA ester **(14A)**, ($[\alpha]_D -164^\circ$). Individual diastereoisomers, **(14B)** ($[\alpha]_D +25^\circ$) and **(14A)** ($[\alpha]_D -164^\circ$) were obtained by preparative h.p.l.c. separation of the diastereoisomeric mixture **(14A)/(14B)** which was obtained from a racemic sample of the tetrahydro diol **(11)**. Base-catalysed hydrolysis of the diMOA esters **(14B)** and **(14A)** yielded the tetrahydro diol enantiomers (+)-**(11)** ($[\alpha]_D +61^\circ$) and (-)-**(11)** ($[\alpha]_D -61^\circ$) respectively. Since the absolute configuration of the *trans*-tetrahydro diol (+)-**(11)** has now been unequivocally assigned as 1*S*,2*S* in Scheme 1, it follows from Scheme 2 that the stereochemically related dihydro diol (+)-**(5)** will have the same 1*S*,2*S* configuration.

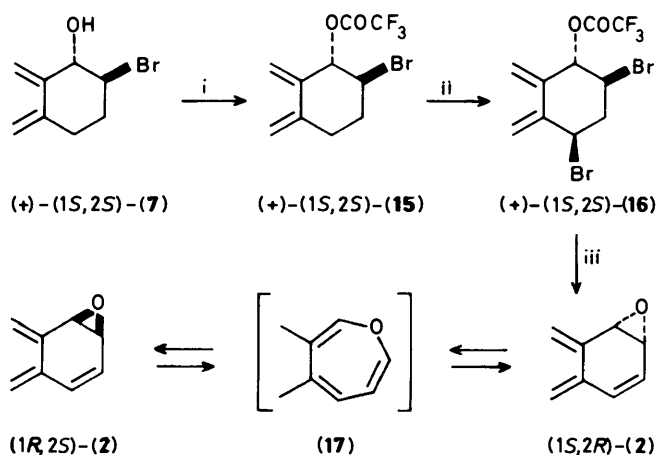
The n.m.r. splitting patterns of the exocyclic methylene signals (H_A, H_B) in bromo-MOA and diMOA esters in C_6D_6 solvent have previously been found to be distinguishable for each diastereoisomer and have been used to assign stereochemistry.^{5,6,8-16} The chemical shift (δ) and coupling constant values (J_{AB}) for the H_A and H_B protons in each of the bromo-MOA **(9A)/(9b)** and diMOA **(14A)/(14B)**, **(13A)/(13B)** diastereoisomers, and the absolute configurations of each, again show a consistent trend as indicated in Table 1. Thus the degree of nonequivalence ($\Delta\delta_{AB}$) between the diastereotopic geminal protons H_A (or H_A') and H_B (or H_B') is consistently larger for the 1*S*,2*S* configuration.

Triphenylene 1,2-oxide **(2)** was initially synthesized from the racemic bromohydrin **(7)** using the halohydrin ester route¹⁶ and the trifluoroacetate intermediates **(15)** and **(16)**.

Using the (+)-1*S*,2*S* enantiomer of the bromohydrin **(7)** ($[\alpha]_D +24^\circ$) derived from the bromo-MTPA ester **(8B)**, ($[\alpha]_D +70^\circ$), the corresponding trifluoroacetate enantiomers (+)-**(15)** ($[\alpha]_D +147^\circ$) and (+)-**(16)** ($[\alpha]_D +184^\circ$) were synthesized (Scheme 3). Pure samples of triphenylene 1,2-oxide **(2)** from either racemic or optically pure dibromotrifluoroacetates **(16)** were obtained by low-temperature recrystallization from acetone were found to have no measurable optical



Scheme 2. Reagents and reaction conditions: i, MOAcI-pyridine; ii, NaOMe-MeOH-THF; iii, Pt-H₂-EtOAc



Scheme 3. Reagents and reaction conditions: i, $(CF_3CO)_2O-CHCl_3$; ii, NBS- CCl_4 ; iii, NaOMe-THF

rotation. This observation contrasted with previous optical rotation measurements on the configurationally stable arene oxide enantiomers of naphthalene (1,2¹⁷), anthracene (1,2¹⁷), benz[*a*]anthracene (8,9-⁶ and 10,11-¹⁸) and benzo[*a*]pyrene (7,8-⁵) which all gave large $[\alpha]_D$ values ($[\alpha]_D \pm 115 \rightarrow 383^\circ$). The enantiomerically pure sample of triphenylene 1,2-oxide (2) thus derived from the (+)-(1*S*,2*S*) enantiomer of the bromohydrin (7) appears to have racemized spontaneously. This conclusion is in accord with previous predictions concerning the configurational stability of chiral arene oxides.¹⁹ Thus, perturbational molecular orbital (PMO) calculations led to the proposal that racemization of triphenylene 1,2-oxide (2) would occur *via* a very minor contribution from the valence tautomeric oxepin structure (17) which would rapidly equilibrate with the arene oxide enantiomers (Scheme 3). Furthermore, it was predicted that the arene oxide (2) would racemize faster than any previously synthesized arene oxide including those of phenanthrene (1,2- and 3,4-), chrysene (1,2- and 3,4-), and benzo[*c*]phenanthrene (1,2-) which were predicted¹⁹ and found⁸ to racemize spontaneously.

The assignment of absolute configuration to each enantiomer of the *trans*-dihydro diol (5) shown in Scheme 2 may be used to explore the stereoselectivity of the mammalian liver metabolism of triphenylene. Thus, incubation of triphenylene (1) with liver microsomes from 3-methylcholanthrene-treated male rats of the Long-Evans strain (1 mg protein/ml, 10 min, 37 °C) resulted in the formation of 1- (3) and 2-hydroxytriphenylene (4) and the *trans*-dihydro diol (5) at a rate of 3 nmol of metabolites/mol of cytochrome P450/min. The rate of metabolism is similar to that observed with the much larger carcinogenic hydrocarbon, benzo[*a*]pyrene.²⁰ The *trans*-1,2-dihydro diol of triphenylene (5) is the major metabolite (*ca.* 75%) and consists predominantly (*ca.* 92%) of the 1*R*,2*R* enantiomer. Incubation of a sample of racemic triphenylene 1,2-oxide (2) with these same liver microsomes also results in the formation of *trans*-1,2-dihydro diol (5) (20–70% conversion dependent upon protein concentration) which in this case contains 85% of the 1*R*,2*R*-enantiomer. The preferred formation of the (*R,R*)-dihydro diol from triphenylene by the combined action of cytochrome P450 and epoxide hydrolase enzymes in liver microsomes is consistent with studies on several other hydrocarbons where the *trans*-dihydro diol metabolites were in all cases enriched in the (*R,R*)-enantiomer.^{8,21}

The 1*R*,2*R* configuration of the *trans*-1,2-dihydro diol metabolite (5) of triphenylene would have resulted from epoxide hydrolase catalysed attack at the C-2 position of the (1*R*,2*S*)-enantiomer of triphenylene 1,2-oxide (2). The benzylic-*S* allylic-*S* arene oxide enantiomer has previously been found

almost exclusively during metabolism of naphthalene (1,2-position²²), anthracene (1,2-position²²), benz[*a*]anthracene (8,9-position²³), and benzo[*a*]pyrene (7,8-position²⁴) by cytochrome P450c, the major isozyme in liver microsomes from 3-methylcholanthrene-treated rats. At present it is not possible to rationalize the difference in the proportion of the (*R,R*)-enantiomer (85–92%) found in the *trans*-dihydro diol metabolite (5) using triphenylene (1) or triphenylene 1,2-oxide (2) as substrates. Similarly, the degree to which spontaneous racemization of the arene oxide (2) occurs during liver microsomal metabolism is currently unknown.

Experimental

¹H N.m.r. spectra were obtained using Varian (100 and 220 MHz) and Bruker (250 and 300 MHz) n.m.r. spectrometers with tetramethylsilane as reference. ¹⁹F N.m.r. spectra were obtained in CDCl₃ solution using a Varian XL-100 instrument with α,α,α -trifluorotoluene as reference. Mass spectral data were recorded at 70 eV using an AEI-MS902 model (updated by V.G. instruments). Optical rotations were recorded at 589 nm using a Perkin-Elmer Model 241 instrument.

Chromatographic separations were achieved using Florisil (column) or silica-gel (radial t.l.c., Chromatotron Model 7924T and preparative h.p.l.c.) using the specified rotors, plates, columns, and eluants.

(–)-Menthylloxyacetic acid (MOA) and (–)-2-methoxy-2-phenyl-2-trifluoromethylacetic acid (MTPA) were purchased from the Aldrich Chemical Co.

1,2-Dihydrotriphenylene was obtained by the literature method.^{2,25} A sample of racemic *trans*-1,2-dihydroxy-1,2-dihydrotriphenylene was available from previous synthetic studies in the triphenylene system.²

(±)-*trans*-2-Bromo-1-hydroxy-1,2,3,4-tetrahydrotriphenylene (7).—A mixture of 3,4-dihydrotriphenylene (0.754 g, 3.28 mmol), *N*-bromoacetamide (0.5 g, 3.62 mmol), water (10 ml), THF (30 ml), and concentrated HCl (1 drop) was stirred at room temperature under argon for 18 h. The reaction mixture was neutralized by addition of sodium hydrogencarbonate and concentrated to yield a crystalline solid which was dissolved in chloroform (100 ml). The chloroform extract was washed with water, dried (K₂CO₃), concentrated, and recrystallized from diethyl ether to yield the bromohydrin (7) (0.87 g, 82%), m.p. 151–152 °C (Found: C, 66.0; H, 4.6. C₁₈H₁₅BrO requires C, 66.1; H, 4.6%); δ (250 MHz, CDCl₃) 2.37–2.57 (2 H, m, 3-H), 3.30 (2 H, m, 4-H), 4.71 (1 H, m, 2-H), 5.60 (1 H, d, *J*_{1,2} 2.8 Hz, 1-H), and 7.5–8.7 (8 H, m, ArH).

(–)-(1*R*,2*R*)- and (+)-(1*S*,2*S*)-*trans*-2-Bromo-1-(2-methoxy-2-phenyl-2-trifluoromethylacetoxy)-1,2,3,4-tetrahydrotriphenylene (8*A*) and (8*B*).—The racemic bromohydrin (7) (1.54 g, 4.7 mmol) was stirred with (–)-MTPA chloride (1.2 g, 5.0 mmol) and *p*-dimethylaminopyridine (0.097 g, 0.79 mmol) in pyridine (5-ml) at room temperature for 25 h. Water (50 ml) was added and the crude product was extracted into diethyl ether. The extract was washed with water, dried (MgSO₄), concentrated, and purified by column chromatography on Florisil using diethyl ether–light petroleum as eluant. The diastereoisomeric mixture (8*A*)–(8*B*) was obtained as a viscous oil (2.18 g, 85%) (Found: *M*, 542.070 46. C₂₈H₂₂BrF₃O₃ requires *M*, 542.070 48). Individual diastereoisomers (8*A*) and (8*B*) were separated using a Chromatotron (4 mm silica gel on a 240 mm diameter rotor plate, diethyl ether–light petroleum, 2:98).

(–)-(1*R*,2*R*)-(8*A*): High *R_F*, less polar isomer, m.p. 128–129 °C (diethyl ether–pentane), $[\alpha]_D -41^\circ$ (CHCl₃); δ (250 MHz, CDCl₃) 2.2 (2 H, m, 3-H), 3.28 (2 H, m, 4-H), 3.4 (3 H, s,

OMe), 4.67 (1 H, m, 2-H), 7.03 (1 H, d, $J_{1,2}$ 2.2 Hz, 1-H), and 7.2–8.7 (8 H, m, ArH); δ_F (94.2 MHz, CDCl_3) –8.49 (3F, s, CF_3).

(+)-(1*S*,2*S*)-(8*B*): Low R_F , more polar isomer, m.p. 177–179 °C (diethyl ether–pentane), $[\alpha]_D^{+70}$ (CHCl_3); δ (250 MHz, CDCl_3) 2.47 (2 H, m, 3-H), 3.40 (5 H, m, and s, 4-H and OMe), 4.82 (1 H, m, 2-H), 6.94 (1 H, d, $J_{1,2}$ 2.6 Hz, 1-H), and 7.2–8.7 (8 H, m, ArH); δ_F (94.2 MHz, CDCl_3) –8.72 (3 F, s, CF_3).

(–)-(1*R*,2*R*)- and (+)-(1*S*,2*S*)-trans-2-Bromo-1-hydroxy-1,2,3,4-tetrahydrotriphenylene (7).—The bromo-MTPA diastereoisomers (–)-(8*A*) or (+)-(8*B*) (0.867 g, 1.6 mmol) were dissolved in anhydrous THF (75 ml) and cooled to 0 °C under nitrogen. A solution of Dibal-H (1M solution in hexane; 5 ml) was added and the mixture was stirred at room temperature (12 h) before addition of methanol (10 ml) and light petroleum (b.p. 40–60 °C; 2 ml). After further stirring (2 h), dilute sulphuric acid was added dropwise and THF was removed under reduced pressure. The bromohydrin enantiomers were extracted and recrystallized as reported for the racemic sample (–)-(1*R*,2*R*)-(7): obtained from (–)-(8*A*) in 84% yield, m.p. 161–162 °C, $[\alpha]_D^{+24}$ (CHCl_3); (+)-(1*S*,2*S*)-(7): obtained from (+)-(8*B*) in 91% yield, m.p. 161–162 °C, $[\alpha]_D^{+24}$ (CHCl_3).

(–)-(1*R*,2*R*)- and (+)-(1*S*,2*S*)-trans-2-Bromo-1-menthyloxy-acetoxy-1,2,3,4-tetrahydrotriphenylene (9*A*) and (9*B*).—The laevorotatory ($[\alpha]_D^{+24}$) bromohydrin enantiomer (7) (0.055 g, 0.17 mmol), in pyridine (1 ml) was stirred with (–)-MOA chloride (0.043 g, 0.19 mmol) at room temperature for 12 h. The mixture was diluted with water (30 ml), extracted into diethyl ether, and the extract washed with dilute hydrochloric acid, dried, and concentrated to give the MOA ester (–)-(9*A*) (0.083 g, 94%), m.p. 163–164 °C (chloroform–hexane), $[\alpha]_D^{+207}$ (CHCl_3) (Found: M , 522.17662. $\text{C}_{30}\text{H}_{35}\text{BrO}_3$ requires M , 522.17693); δ (250 MHz, C_6D_6) 0.68–3.3 (23 H, m, 3-H, 4-H, and menthyl-H), 3.86 (1 H, d, J_{AB} 16.5 Hz, H_A), 3.95 (1 H, d, J_{AB} 16.5 Hz, H_B), 4.59 (1 H, m, 2-H), 7.29–7.62 (5 H, m, 1 H and ArH) and 7.82–8.44 (4 H, m, ArH).

Similar treatment of the other enantiomer (7) ($[\alpha]_D^{+24}$) gave the bromo-MOA ester (9*B*), m.p. 162–163 °C, $[\alpha]_D^{+81}$ (CHCl_3); δ (250 MHz, C_6D_6) 0.68–3.25 (23 H, m, 3-H, 4-H, and menthyl-H), 3.86 (1 H, d, J_{AB} 16.5 Hz, H_A), 3.97 (1 H, d, J_{AB} 16.5 Hz, H_B), 4.56 (1 H, m, 2-H), 7.29–7.62 (5 H, m, 1-H and ArH), and 7.82–8.84 (4 H, m, ArH).

(+)-(1*R*,2*S*)-1,2-Epoxy-1,2,3,4-tetrahydrotriphenylene (10).—A mixture of the bromohydrin (–)-(7) ($[\alpha]_D^{+24}$) (0.14 g, 0.43 mmol) and the basic form of Amberlite resin (IRA-900; 1.0 g) was stirred in dry THF (20 ml) at room temperature for 6 h. The mixture was filtered, the filtrate concentrated, and the residue triturated with diethyl ether to give the epoxide (10) (0.102 g, 97%), m.p. 149–150 °C, $[\alpha]_D^{+145}$ (CHCl_3) (Found: M , 246.104 34. $\text{C}_{18}\text{H}_{14}\text{O}$ requires M , 246.104 46); δ (250 MHz, CDCl_3) 1.90–2.04 (1 H, m, 3-H), 2.59–2.70 (1 H, m, 3-H), 2.81–2.97 (1 H, m, 4-H), 3.41–3.50 (1 H, m, 4-H), 3.92 (1 H, m, 2-H), 4.76 (1 H, d, $J_{1,2}$ 4.5 Hz, 1-H), 7.60–7.72 (4 H, m, ArH), 8.11–8.43 (2 H, m, ArH), and 8.71–8.77 (2 H, m, ArH).

(–)-(1*R*,2*S*)-cis- and (+)-(1*S*,2*S*)-trans-1,2-Dihydroxy-1,2,3,4-tetrahydrotriphenylene (12) and (11) by Acid-catalysed Hydrolysis of the Tetrahydro Epoxide (10).—A solution of the tetrahydro epoxide (10) ($[\alpha]_D^{+145}$), (0.102 g, 0.42 mmol) in dioxane (1 ml) was added to a mixture of dioxane (40 ml) and distilled water (100 ml) (previously adjusted to pH 2.5 by addition of HClO_4) containing 0.1M- NaClO_4 . The reaction mixture was stirred for 0.5 h after which it was neutralized (NaHCO_3) and concentrated under reduced pressure to yield a

white precipitate. This was extracted into ethyl acetate and the solution dried and concentrated. A preliminary purification was achieved using the Chromatotron (4 mm silica gel plate, dimethyl ether as eluant) and a final separation was obtained by preparative h.p.l.c. [DuPont Zorbax-Sil, 250 × 9.4 mm; eluted with ethanol (5%), ethyl acetate (15%), hexane (80%) at a flow rate of 8.8 ml min^{-1}]; (–)-(1*R*,2*S*)-cis-1,2-dihydroxy-1,2,3,4-tetrahydrotriphenylene (12) (0.018 g, 17%), $k' = 1.67$, m.p. 220 °C (sublimes), $[\alpha]_D^{-75}$ (THF) (Found: M , 264.115 13. $\text{C}_{18}\text{H}_{16}\text{O}_2$ requires M , 264.115 02); δ (250 MHz, CDCl_3 – CD_3OD) 2.13–2.27 (2 H, m, 3-H), 3.45–3.57 (2 H, m, 4-H), 4.05 (1 H, m, 2-H), 5.36 (1 H, d, $J_{1,2}$ 4.0 Hz, 1-H), 7.61–7.71 (4 H, m, ArH), 8.08–8.41 (2 H, m, ArH), and 8.68–8.74 (2 H, m, ArH).

(+)-(1*S*,2*S*)-trans-1,2-Dihydroxy-1,2,3,4-tetrahydrotriphenylene (11) (0.071 g, 65%), $k' = 2.5$, m.p. 199–200 °C, $[\alpha]_D^{+61}$ (THF) (Found: M , 264.115 13. $\text{C}_{18}\text{H}_{16}\text{O}_2$ requires M , 264.115 02); δ (250 MHz, CDCl_3 – D_2O) 2.14–2.42 (2 H, m, 3-H), 3.26–3.32 (2 H, m, 4-H), 4.34 (1 H, m, 2-H), 5.29 (1 H, d, $J_{1,2}$ 3.5 Hz, 1-H), 7.62–7.72 (4 H, m, ArH), 8.11–8.37 (2 H, m, ArH), and 8.68–8.73 (2 H, m, ArH).

1,2-Dimethyloxyacetoxy-1,2-dihydrotriphenylene. (–)-(13*A*) and (+)-(13*B*).—(–)-Menthylxyacetic acid chloride (0.1 g, 0.44 mmol) was added to a solution of the racemic trans-dihydro diol (\pm)-(5) (0.035 g, 0.13 mmol) in dry pyridine (2 ml) at 0 °C and the mixture was stirred overnight at room temperature. The product mixture was poured into benzene (50 ml) and the solution was washed (dilute HCl, water, and dilute aqueous NaHCO_3), dried (Na_2SO_4), and concentrated to yield a viscous oil which was separated into the diastereoisomers (13*A*) and (13*B*) by preparative h.p.l.c. [Perkin-Elmer Silica column, 1 in × 25 cm, eluted with diethyl ether (5%) and cyclohexane (95%)].

(–)-(1*R*,2*R*)-(13*A*). Less polar isomer ($k' = 3.60$) (0.013 g, 20%), m.p. 92–93 °C (MeOH), $[\alpha]_D^{+506}$ (CHCl_3), δ (100 MHz, C_6D_6) 0.5–3.2 (38 H, m, menthyl), 3.75 (2 H, s, COCH_2O), 3.87 (2 H, s, COCH_2O), 5.90 (1 H, dd, $J_{1,2}$ 1.5 Hz, $J_{2,3}$ 6.0 Hz, 2-H), 6.45–6.70 (1 H, m, 3-H), and 7.3–8.5 (10 H, m, ArH, 1- and 4-H).

(+)-(1*S*,2*S*)-(13*B*). More polar isomer ($k' = 5.45$) (0.0125 g, 19%), m.p. 114–115 °C (MeOH– Et_2O), $[\alpha]_D^{+331}$ (CHCl_3), δ (100 MHz, C_6D_6) 0.5–3.2 (38 H, m, menthyl), 3.68 (1 H, d, J_{AB} 16 Hz, H_A), 3.73 (1 H, d, J_{AB} 16 Hz, H_A), 3.82 (1 H, d, J_{AB} 16 Hz, H_B), 3.97 (1 H, d, J_{AB} 16 Hz, H_B), 5.90 (1 H, dd, $J_{1,2}$ 1.5 Hz, $J_{2,3}$ 6.0 Hz, 2-H), 6.45–6.70 (2 H, m, 3-H), and 7.30–8.5 (10 H, m, ArH and 4-H).

(–)-(1*R*,2*R*)- and (+)-(1*S*,2*S*)-trans-1,2-Dihydroxy-1,2-dihydrotriphenylene (5).—A mixture of the less polar isomer (13*A*) (0.043 g, 0.84 mmol) and dry sodium methoxide (0.04 g, 0.7 mmol) in methanol (3 ml), THF (5 ml), and water (1 ml) was stirred at room temperature for 2 h. The reaction was terminated by addition of aqueous ammonium chloride (10%, 30 ml). The solution was concentrated under reduced pressure and extracted into ethyl acetate. The extract was washed with water, dried (Na_2SO_4), and concentrated to yield the trans-dihydro diol (5) which was recrystallized from diethyl ether–hexane (0.2 g, 87%), m.p. 124–125 °C, $[\alpha]_D^{-451}$ (THF) (lit.,³ m.p. 153–154 °C).

The (+)-(1*S*,2*S*) enantiomer of (5) was obtained in a similar manner from the more polar isomer (13*B*) (0.04 g, 0.078 mmol) as colourless needles (0.02 g, 98%), m.p. 124–125 °C, $[\alpha]_D^{+452}$ (THF). N.m.r. data for individual enantiomers and for a racemic sample were identical with the reported values.²

(–)-(1*R*,2*R*)- and (+)-(1*S*,2*S*)-trans-1,2-Dimethyloxy-acetoxy-1,2,3,4-tetrahydrotriphenylene (14*A*) and (14*B*).—A

Table 1. Characteristic n.m.r. peaks of compounds **(9)**, **(13)**, and **(14)** and their absolute configuration

Compound	$\delta_{H_A}^b$	$\delta_{H_B}^b$	$\Delta\delta_{AB}$	$\delta_{H_A}^b$	$\delta_{H_B}^b$	$\Delta\delta_{A'B'}$	J_{AB}	Absolute configuration
(-)- (9A)	3.86 ^c (d)	3.95 ^c (d)	0.09				16.5	1 <i>R</i> ,2 <i>R</i>
(+)- (9B)	3.86 ^c	3.97 ^c (d)	0.11				16.5	1 <i>S</i> ,2 <i>S</i>
(-)- (14A)	3.97 ^d (s)	3.97 ^d (s)	0.0	3.71 ^d (d)	3.82 ^d (d)	0.11	16.0	1 <i>R</i> ,2 <i>R</i>
(+)- (14B)	3.90 ^d (d)	4.02 ^d (d)	0.12	3.67 ^d (d)	3.85 ^d (d)	0.18	16.0	1 <i>S</i> ,2 <i>S</i>
(-)- (13A)	3.75 ^e (s)	3.75 ^e (s)	0.00	3.87 ^e (s)	3.87 ^e (s)	0.0	16.0	1 <i>R</i> ,2 <i>R</i>
(+)- (13B)	3.77 ^e (d)	3.97 ^e (d)	0.20	3.65 ^e (d)	3.86 ^e (d)	0.21	16.0	1 <i>S</i> ,2 <i>S</i>

^a δ Values refer to the centre of each doublet, obtained in C₆D₆ solvent. ^b Peak multiplicity of the exocyclic methylene protons H_A and H_B. ^c At 250 MHz. ^d At 300 MHz. ^e At 100 MHz.

solution of the diMOA ester of the (-)-*trans*-(1*R*,2*R*)-dihydro diol (**13A**) (5 mg, 0.098 mmol) ($[\alpha]_D - 506^\circ$) in ethyl acetate (5 ml) was hydrogenated using a platinum catalyst (2 mg) with stirring for 0.25 h at room temperature under an atmosphere of hydrogen (1 atm). The catalyst was filtered off and the filtrate concentrated to give colourless needles of (-)-(1*R*,2*R*)-(**14A**) (4 mg, 80%), m.p. 115–116 °C (diethyl ether–hexane), $[\alpha]_D - 164^\circ$ (CHCl₃), δ (300 MHz, C₆D₆) 0.5–3.2 (38 H, m, menthyl), 2.1–2.3 (2 H, m, 3-H), 2.9–3.1 (2 H, m, 4-H), 3.97 (2 H, s, H_A and H_B), 3.71 (1 H, d, $J_{A'B}$ 16.0 Hz, H_A), 3.82 (1 H, d, $J_{A'B}$ 16.0 Hz, H_B), 5.75 (1 H, m, 2-H), 7.05 (1 H, d, $J_{1,2}$ 2.5 Hz, 1-H), and 7.1–8.5 (8 H, m, ArH).

A larger sample of (-)-(1*R*,2*R*)-(**14A**) and (+)-(1*S*,2*S*)-(**14B**) was obtained by treatment of the racemic tetrahydro diol (**11**) (0.20 g, 0.076 mmol) in dry pyridine (3 ml) with (-)-menthyl-oxyacetyl chloride (0.6 g, 2.6 mmol). The product mixture was isolated by a similar method to that used for (**13A**)/(**13B**) and separated by preparative h.p.l.c. [DuPont Zorbax SIL 9.4 × 250 mm, using diethyl ether (10%):cyclohexane (90%) at 6.6 ml min⁻¹ into pure diastereoisomers {Found [mixture of (**14A**)/(**14B**): *M*, 656.4082. C₄₂H₅₆O₆ requires *M*, 656.4077]}.

(-)-(1*R*,2*R*)-(**14A**): Less polar isomer, $k' = 2.3$ (0.21 g, 51%), m.p. 115–116 °C, $[\alpha]_D - 163.3^\circ$ (CHCl₃). The n.m.r. spectrum was identical with the sample of (-)-(**16A**) obtained by catalytic hydrogenation. (+)-(1*S*,2*S*)-(**14B**): More polar isomer, $k' = 3.35$ (0.19 g, 49%), viscous oil, $[\alpha]_D + 24.5^\circ$ (CHCl₃), δ (300 MHz, C₆D₆) 0.5–3.2 (38 H, m, menthyl), 2.1–2.4 (2 H, m, 3-H), 2.8–3.1 (2 H, m, 4-H), 3.67 (1 H, d, $J_{A'B}$ 16.1 Hz, H_A), 3.85 (1 H, d, $J_{A'B}$ 16.0 Hz, H_B), 3.90 (1 H, d, $J_{A'B}$ 16.0 Hz, H_A), 4.02 (1 H, d, $J_{A'B}$ 16.0 Hz, H_B), 5.75 (1 H, m, 2-H), 7.05 (1 H, d, $J_{1,2}$ 2.5 Hz, 1-H), and 7.1–8.5 (8 H, m, ArH).

Hydrolysis of the diMOA esters (**14A**) and (**14B**) using the method reported for the diesters (**13A**) and (**13B**) gave the tetrahydro diol enantiomers: (-)-(1*R*,2*R*)-(**11**) (0.073 g, 92%) from (-)-(**14A**), m.p. 199–200 °C, $[\alpha]_D - 61^\circ$ (THF); (+)-(1*S*,2*S*)-(**11**) (0.105 g, 92%) from (+)-(**14B**), m.p. 199–200 °C, $[\alpha]_D + 61^\circ$ (THF).

(±)- and (+)-(1*S*,2*S*)-2-Bromo-1-trifluoroacetoxy-1,2,3,4-tetrahydrotriphenylene (**15**).—A mixture of the racemic bromohydrin (**7**) (0.8 g, 2.45 mmol), trifluoroacetic anhydride (1.5 g, 7.14 mmol), and chloroform (50 ml) was stirred at room temperature for 2 h. Evaporation of solvent and excess of reagent under reduced pressure gave a solid which was recrystallized from diethyl ether to give the bromo ester (**15**) (0.78 g, 83%), m.p. 133 °C (decomp.); δ (300 MHz, CDCl₃) 2.45 (2 H, m, 3-H), 3.43 (2 H, m, 4-H), 4.54 (1 H, m, 2-H), 7.04 (1 H, d, $J_{1,2}$ 2.8 Hz, 1-H), 7.70 (5 H, m, ArH), and 8.20–8.78 (3 H, m, 5-, 8-, and 9-H).

Similar treatment of the bromohydrin (+)-(**7**) ($[\alpha]_D + 24^\circ$) afforded the (+)-trifluoroacetoxybromohydrin (**15**) in a comparable yield, m.p. 144–145 °C (ether), $[\alpha]_D + 147^\circ$.

Table 2. Atomic fractional co-ordinates (for non-hydrogen atoms)

Atom	x	y	z
Br	-0.155 8(1)	0.257 2(0)	0.225 4(1)
O(1)	0.114 4(4)	0.386 4(12)	0.422 1(4)
O(2)	0.084 5(6)	0.103 7(16)	0.499 0(5)
O(3)	0.233 0(4)	0.265 1(19)	0.654 1(4)
C(1)	0.043 4(6)	0.298 9(19)	0.336 5(5)
C(2)	-0.050 2(6)	0.421 2(17)	0.315 6(6)
C(3)	-0.042 2(8)	0.654 5(20)	0.283 3(7)
C(4)	-0.013 6(7)	0.653 7(20)	0.199 8(6)
C(4a)	0.061 7(6)	0.480 7(18)	0.203 7(6)
C(4b)	0.104 9(7)	0.483 3(19)	0.133 9(6)
C(5)	0.074 3(8)	0.644 0(26)	0.065 9(7)
C(6)	0.115 2(10)	0.653 6(30)	0.001 3(8)
C(7)	0.186 7(11)	0.509 3(35)	0.003 1(8)
C(8)	0.218 1(8)	0.341 0(23)	0.067 7(7)
C(8a)	0.176 2(7)	0.327 4(18)	0.135 5(6)
C(8b)	0.205 8(7)	0.162 1(20)	0.202 5(7)
C(9)	0.273 6(8)	-0.009 8(21)	0.203 5(8)
C(10)	0.297 1(8)	-0.175 4(20)	0.266 5(9)
C(11)	0.257 4(8)	-0.178 1(20)	0.333 0(8)
C(12)	0.192 6(7)	-0.015 3(18)	0.334 0(7)
C(12a)	0.162 3(7)	0.154 4(20)	0.269 3(6)
C(12b)	0.090 2(6)	0.318 6(16)	0.266 8(5)
C(13)	0.123 0(6)	0.272 7(24)	0.497 4(5)
C(14)	0.189 5(8)	0.407 7(21)	0.578 0(6)
C(15)	0.334 5(7)	0.215 0(18)	0.673 4(6)
C(16)	0.347 0(7)	0.055 1(21)	0.604 3(7)
C(17)	0.455 5(8)	0.000 4(20)	0.626 8(7)
C(18)	0.470 4(11)	-0.168 6(37)	0.559 0(9)
C(19)	0.499 6(8)	-0.096 0(26)	0.721 8(7)
C(20)	0.485 2(7)	0.055 1(20)	0.791 3(7)
C(21)	0.375 2(7)	0.108 1(19)	0.768 5(6)
C(22)	0.355 9(6)	0.254 8(27)	0.839 5(5)
C(23)	0.401 2(10)	0.473 2(23)	0.852 6(8)
C(24)	0.384 5(10)	0.128 3(28)	0.929 0(7)

(±)- and (+)-(1*S*,2*S*)-*trans*-2,4-Dibromo-1-trifluoroacetoxy-1,2,3,4-tetrahydrotriphenylene (**16**).—A mixture of the bromohydrin trifluoroacetate (0.43 g, 1.02 mmol), *N*-bromosuccinimide (0.216 g, 1.21 mmol), α,α' -azoisobutyronitrile (0.005 g) in carbon tetrachloride (100 ml) was maintained at 65 °C for 30 min with a heat lamp and under an atmosphere of argon. Activated charcoal (0.2 g) was added and the solution was filtered and concentrated to yield the dibromotrifluoroacetate (0.50 g, 98%). Fractional recrystallisation from diethyl ether-pentane gave the β -diastereoisomer (0.33 g, 65%), m.p. 120–123 °C; δ (100 MHz, CDCl₃) 2.6–3.4 (2 H, m, 3-H), 5.40 (1 H, ddd, $J_{2,3}$ 12 Hz, $J_{2,3'}$ 4.5 Hz, $J_{1,2}$ 7.0 Hz, 2-H), 5.96 (1 H, t, $J_{3,4} = J_{3',4'} = 3.5$ Hz, 4-H), 7.20 (1 H, d, $J_{1,2}$ 7 Hz, 1-H), and 7.6–8.7 (8 H, m, ArH).

Similar treatment of the (+)-trifluoroacetoxybromohydrin (**16**) ($[\alpha]_D + 147^\circ$) gave the (+)-dibromotrifluoroacetate, m.p. 102–103 °C, $[\alpha]_D + 184^\circ$ (CHCl₃).

Table 3. Bond lengths (Å) and angles (°)

(a) Bond lengths			
Br—C(2)	1.949(9)	C(10)—C(11)	1.394(17)
C(1)—C(2)	1.480(12)	C(11)—C(12)	1.369(15)
C(1)—C(12b)	1.518(11)	C(12)—C(12a)	1.407(15)
C(1)—O(1)	1.477(9)	C(12a)—C(12b)	1.437(14)
C(2)—C(3)	1.520(16)	O(1)—C(13)	1.355(12)
C(3)—C(4)	1.545(13)	O(2)—C(13)	1.169(15)
C(4)—C(4a)	1.502(15)	C(13)—C(14)	1.532(15)
C(4a)—C(4b)	1.477(12)	O(3)—C(14)	1.435(13)
C(4a)—C(12b)	1.357(13)	O(3)—C(15)	1.432(11)
C(4b)—C(5)	1.404(16)	C(15)—C(16)	1.532(15)
C(4b)—C(8a)	1.398(14)	C(15)—C(21)	1.558(13)
C(5)—C(6)	1.378(16)	C(16)—C(17)	1.528(15)
C(6)—C(7)	1.353(21)	C(17)—C(18)	1.564(20)
C(7)—C(8)	1.401(20)	C(17)—C(19)	1.534(15)
C(8)—C(8a)	1.438(13)	C(19)—C(20)	1.514(16)
C(8a)—C(8b)	1.410(14)	C(20)—C(21)	1.546(14)
C(8b)—C(9)	1.431(16)	C(21)—C(22)	1.548(16)
C(8b)—C(12a)	1.437(13)	C(22)—C(23)	1.454(20)
C(9)—C(10)	1.370(16)	C(22)—C(24)	1.542(15)
(b) Angles			
C(2)—C(1)—C(12b)	115.3(7)	C(8b)—C(12a)—C(12)	118.0(9)
C(2)—C(1)—O(1)	107.7(6)	C(8b)—C(12a)—C(12b)	118.8(9)
O(1)—C(1)—C(12b)	107.6(6)	C(12)—C(12a)—C(12b)	123.2(8)
C(1)—C(2)—Br	109.1(7)	C(1)—C(12b)—C(4a)	120.6(9)
C(1)—C(2)—C(3)	110.8(8)	C(1)—C(12b)—C(12a)	117.0(8)
C(3)—C(2)—Br	110.9(6)	C(4a)—C(12b)—C(12a)	122.3(8)
C(2)—C(3)—C(4)	112.0(9)	C(1)—O(1)—C(13)	116.7(8)
C(3)—C(4)—C(4a)	113.4(8)	O(1)—C(13)—O(2)	125.1(9)
C(4)—C(4a)—C(4b)	118.4(8)	O(1)—C(13)—C(14)	107.7(10)
C(4)—C(4a)—C(12b)	123.2(8)	O(2)—C(13)—C(14)	127.2(9)
C(4b)—C(4a)—C(12b)	118.4(9)	O(3)—C(14)—C(13)	110.0(11)
C(4a)—C(4b)—C(5)	119.7(10)	C(14)—O(3)—C(15)	113.9(7)
C(4a)—C(4b)—C(8a)	120.4(9)	O(3)—C(15)—C(16)	111.7(8)
C(5)—C(4b)—C(8a)	119.9(9)	O(3)—C(15)—C(21)	106.7(7)
C(4b)—C(5)—C(6)	120.8(13)	C(16)—C(15)—C(21)	110.2(9)
C(5)—C(6)—C(7)	120.4(13)	C(15)—C(16)—C(17)	111.0(8)
C(6)—C(6)—C(8)	121.4(10)	C(16)—C(17)—C(18)	112.2(10)
C(7)—C(8)—C(8a)	119.1(11)	C(16)—C(17)—C(19)	109.4(8)
C(8)—C(8a)—C(4b)	118.3(9)	C(18)—C(17)—C(19)	109.2(12)
C(4b)—C(8a)—C(8b)	120.3(8)	C(17)—C(19)—C(20)	112.5(11)
C(8)—C(8a)—C(8b)	121.4(10)	C(19)—C(20)—C(21)	111.6(9)
C(8a)—C(8b)—C(9)	122.4(9)	C(15)—C(21)—C(20)	107.6(8)
C(8a)—C(8b)—C(12a)	119.7(9)	C(15)—C(21)—C(22)	112.1(9)
C(9)—C(8b)—C(12a)	117.8(10)	C(20)—C(21)—C(22)	113.8(8)
C(8b)—C(9)—C(10)	121.3(11)	C(21)—C(22)—C(23)	115.2(9)
C(9)—C(10)—C(11)	120.8(11)	C(21)—C(22)—C(24)	110.0(12)
C(10)—C(11)—C(12)	119.2(11)	C(23)—C(22)—C(24)	111.2(10)
C(11)—C(12)—C(12a)	122.9(10)		

(±)-Triphenylene 1,2-Oxide [(+)-1,2-Epoxy-1,2-dihydrotriphenylene] (**2**).—A solution of the racemic trifluoroacetoxy dibromide (**16**) (0.170 g, 0.34 mmol) was stirred in dry THF (5 ml) and dry sodium methoxide (0.25 g) was added at 0 °C in the dark. The mixture was stirred at ca. 2 °C for 18 h, diluted with cold diethyl ether (100 ml), and then washed with cold water (2 × 10 ml). The dried (K₂CO₃) extract was concentrated to a mixture of products from which the title compound (**2**) was isolated by low-temperature recrystallization from acetone (0.034 g, 41% yield) as colourless needles, m.p. 167–168 °C (Found: *M*, 244.0884. C₁₈H₁₂O requires *M*, 244.0884); δ [300 MHz, (CD₃)₂CO] 4.37 (1 H, sextet, *J*_{1,2} 4.0 Hz, *J*_{2,3} 3.8 Hz, *J*_{2,4} 1.6 Hz, 2-H), 5.44 (1 H, d, *J*_{1,2} 4.0 Hz, 1-H), 6.85 (1 H, q, *J*_{3,4} 10.0 Hz, *J*_{2,3} 3.8 Hz, 3-H), 7.82 (1 H, q, *J*_{3,4} 10.0 Hz, *J*_{1,4} 1.6 Hz, 4-H), and 7.70–8.92 (8 H, m, ArH).

Treatment of the (+)-dibromo ester (**16**) ([α]_D +184°) using identical conditions again yielded a mixture of products from

which the title compound (**2**) was obtained pure by fractional recrystallization, m.p. 167–168 °C, [α]_D 0.0° (CHCl₃).

Crystal Data for (-)-(1R,2R)-(9A).—C₃₀H₃₅BrO₃. *M* = 523.5, monoclinic, *a* = 14.636(5), *b* = 6.030(3), *c* = 16.053(5) Å, β = 111.8(2)°, *U* = 1315.1 Å³, λ(Mo-K_α) = 0.710 69 Å, space group *P*2₁, *Z* = 2, *D*_c = 1.32 g cm⁻³, *F*(000) = 548. Colourless, elongated rectangular prisms; crystal dimensions 0.15 × 0.20 × 0.80 mm, μ(Mo-K_α) = 15.3 cm⁻¹.

Initial lattice characterization was by means of oscillation and Weissenberg photographs (Cu-K_α radiation) and accurate cell dimensions were obtained by refinement of diffractometer angles. 1971 Independent diffraction intensities were recorded on a Stoe STADI-2 two-circle diffractometer using the ω-scan technique with graphite-monochromated Mo-K_α radiation (2° < θ < 30°). The bromine atom position was determined by the program MULTAN²⁶ and all other atoms were located in a difference Fourier synthesis after refinement of the Br parameters using SHELX.²⁷ In the final stages of least-squares refinement the 1787 reflections with *I* > σ(*I*) were used, all non-hydrogen atoms were allowed anisotropic temperature factors, and hydrogens were included in positions calculated from the geometry of the molecule (C–H = 1.08 Å). Common isotropic temperature factors were applied to tertiary CH, methylene, methyl and phenyl-type hydrogen atoms and these refined to final values of *U* = 0.06(1), 0.07(1), 0.13(2), and 0.09(1) Å² respectively. The enantiomer was fixed by choosing the set of co-ordinates consistent with the known absolute stereochemistry of the menthyl group and this established unequivocally as 1*R*,2*R* the absolute stereochemistry of the triphenylene moiety (see Figure). The final weighting scheme was *w* = 1.124/[σ²(*F*) + 0.002 35*F*²]. Final *R* and *R*_w values were 0.055, and 0.058. Atomic co-ordinates are given in Table 2 and bond lengths and angles in Table 3. A complete listing of co-ordinates, anisotropic temperature factors, bond lengths, angles, and hydrogen atom co-ordinates are available on request from the Cambridge Crystallographic Data Centre.*

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