A General Method for the Resolution of Cyclic *trans*-Bromohydrin Enantiomers. Absolute Configuration by Crystal Structure Analysis of a 2-Methoxy-2-phenyl-2-trifluoromethylacetate (MTPA) Diastereoisomer

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trans-Bromohydrins of 1,2,3,4-tetrahydronaphthalene (1a), 1,2,3,4-tetrahydroanthracene (1b), and 1,2,3,4-tetrahydrophenanthrene (1c) and (1d) were isolated in optically pure forms by reductive cleavage of the corresponding 2-methoxy-2-phenyl-2-trifluoromethylacetate (MTPA) diastereoisomers (2a—d) which had been separated by preparative h.p.l.c. Using reactions with established mechanisms and stereochemistry, the configurations at the chiral centres in the bromohydrins (1) were correlated with those in the tetrahydroepoxides (5), the arene oxides (7), and *cis*- (3) and *trans*- (4) tetrahydrodiols. An X-ray structure analysis of the 1,2,3,4-tetrahydroanthracene bromo-MTPA ester (+)-(2bₑ) indicated the *trans* equatorial quasi-equatorial conformation and confirmed the absolute stereochemistry of the MTPA group [derived from (−)-acid] as (*S*).

The enzymatic oxidation of polycyclic aromatic hydrocarbons (PAHs) to yield arene oxides is the initial metabolic step in mammalian liver systems. For the carcinogenic PAHs benzo[*a*]pyrene and benz[*a*]anthracene, this addition of an oxygen atom occurred exclusively on one stereoheterotopic face to yield a single arene oxide enantiomer.[1,2] Enzyme-catalysed hydration of these chiral arene oxide metabolites in animal livers subsequently led to the isolation of optically pure *trans*-dihydrodiols. An alternative metabolic pathway for PAHs occurred in bacteria to yield optically pure *cis*-dihydrodiols.[3,4] The determination of both optical purity and absolute stereochemistry of these and related mammalian and bacterial metabolites has been greatly facilitated by the development of several independent synthetic routes to the pure enantiomers.[1-7]

Previous reports on the attempted synthesis of the arene oxide enantiomers of naphthalene (7a),[5] anthracene (7b),[5] and phenanthrene (7c) and (7d)[6,7] have used the bromohydrins (1a—d) as precursors and (−)-menthyloxyacetic (MOA) acid as resolving agent. In these investigations,[5-7] the resolved bromo-MOA ester diastereoisomers were not cleaved and isolated as the pure bromohydrin enantiomers (1a—d), but were generally converted into other chiral derivatives including (4a—d), (5a—d), and (7a—d). The present study (and the preliminary report[8]) is primarily concerned with the use of the *trans*-bromo-MTPA esters (2a—d) in the resolution of the bromohydrins (1a—d). These compounds (2a—d) were also found to be of considerable value in the development of new or improved synthetic routes to optically pure forms of the arene oxides (7a—b), the *trans*-tetrahydrodiols (4a—d), and *cis*-tetrahydrodiols (3a—d). Since tetrahydrodiols of similar type to (3) and (4) have been converted by several methods into the corresponding dihydrodiol metabolites, the bromo-MTPA esters (2a—d) can provide a common synthetic and stereochemical link with the arene oxide, and dihydrodiol metabolites of naphthalene, anthracene, and phenanthrene in animals and micro-organisms.

The resolution of the bromohydrins (1a—d) into their enantiomers followed from the initial separation of the corresponding bromo-MTPA diastereoisomers (2a—d) which was readily achieved by preparative h.p.l.c. The use of the MTPA resolving agent for bromohydrins was found to have signifi-

Table 1. H.p.l.c. separation factors (α) and n.m.r. spectral data for compounds (2a—d)

Compd.	α-Values [a]	N.m.r. data		
		$\delta(^1H_B)$	$\delta(^{19}F)$	$J_{A,B}$ (Hz)
(2aₑ)		4.46	−8.65	4.2
	1.48 (1.15)			
(2aₗ)		4.53	−8.68	4.6
(2bₑ)		4.55	−8.51	4.2
	1.54 (1.21)			
(2bₗ)		4.60	−8.59	5.1
(2cₑ)		4.54	−8.62	3.7
	1.56 (1.18)			
(2cₗ)		4.62	−8.65	4.4
(2dₑ)		4.64	−8.53	2.75
	1.76 (1.31)			
(2dₗ)		4.78	−8.79	2.70

[a] $\alpha = (t_2 - t_0)/(t_1 - t_0)$, t = retention time; α-values for corresponding bromo-MOA esters in parentheses.

cant advantages over the MOA route which had previously been used in conjunction with the bromohydrins (1a—d).[3-7] Thus, prior to h.p.l.c. studies it was found that the individual diastereoisomers could be isolated by fractional crystallization of the bromo-MTPA product mixture from ether–pentane in both the anthracene (2b) and the phenanthrene (2d) series. Separation by preparative h.p.l.c. was more readily achieved since the separation factors (α) were consistently larger than those previously reported for the corresponding bromo-MOA esters (Table 1). The presence of the phenyl chromophore in the MTPA groups of compounds (2a—d) was of assistance during u.v. detection of h.p.l.c. fractions [particularly in example (2a)]. The availability of both (+) and (−) forms of the MTPA resolving agent has also proved to be of considerable value in the resolution of bromohydrins of precocene 1.[9]

The characteristic differences in the degree of non-equivalence of protons Hₐ and H_B in the exocyclic methylene group in the n.m.r. spectra of the MOA ester diastereoisomers of bromohydrins (1a—d) have proved to be a useful indicator of absolute stereochemistry.[5-7] These differences however become less marked when the MOA group is located in the bay-

Table 2. Optical rotations and absolute stereochemistry of compounds (1)—(5) and (7)

| Compound | Specific rotation [a] (configuration [b]) | | | |
	a	b	c	d
(1)	−44 (1S,2S)	−61 (1S,2S)	+48 (1R,2R)	−71 (3R,4R)
(2E)	−93 (1R,2R)	+2 (1R,2R)	−93 (1R,2R)	−31 (3R,4R)
(2L)	+50 (1S,2S)	−35 (1S,2S)	+64 (1S,2S)	+48 (3S,4S)
(3)	−41 (1R,2S)	−65 [c] (1S,2R)	−91 [c] (1R,2S)	+35 [d,e] (3R,4S) +31 [d,f]
(4)	−106 (1S,2S)	+124 [c,g] (1R,2R) −117 [c,h] (1S,2S)	−35 [c] (1S,2S)	+30 [e] (3R,4R) +26 [f]
(5)	−131 (1S,2R)	−151 (1S,2R)	−140 (1S,2R)	−172 (3R,4S)
(7)	−128 (1S,2R)	−215 (1S,2R)	0	+271 or +141 ⟶ 0 (3S,4R)

[a] $[\alpha]_D$ (°) at ambient temperature with a concentration of ca. 10 mg ml⁻¹ in $CHCl_3$ unless stated otherwise. [b] Compounds (3), (4), (5), and (7) were not necessarily derived from the same configuration of diastereoisomer (2). [c] THF solvent. [d] Dioxane solvent. [e] From (+)-(2d_L). [f] From (−)-(5d). [g] From (−)-(5b). [h] From (+)-(2b_E).
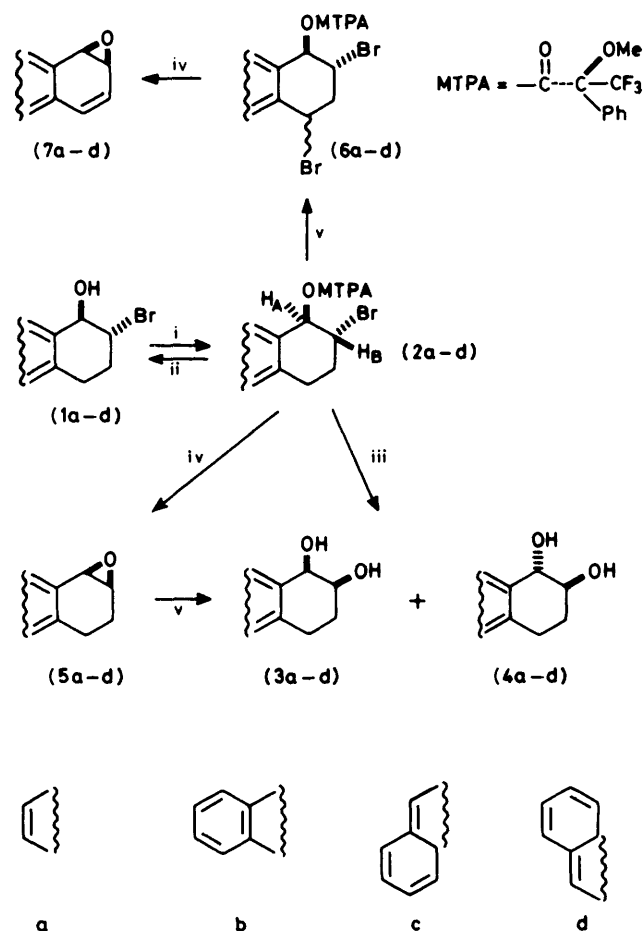
Scheme. Reagents: i, MTPA chloride–pyridine; ii, DIBAL–Et₂O; iii, AgOAc–CH₃CO₂H–H₂O or AgOAc–CH₃CO₂H–(CH₃CO)₂O; iv, NaOMe–Et₂O; v, THF–H₂O (pH 8)–CuSO₄

region of the bromohydrin, e.g. bromohydrin (1d) [7] and the corresponding chrysene bromohydrin.[10] In comparison with the bromo-MOA series, the bromo-MTPA esters [e.g. (2a–d)] gave much simpler n.m.r. spectra with a wider range of characteristic spectral features (Table 1). The chemical shift values for proton H_B [δ(¹H)] and the CF_3 group [δ(¹⁹F)] were consistently distinguishable for diastereoisomers eluted early (2a_E—d_E) or late (2a_L—d_L) from the h.p.l.c. column. The late non-

bay-region bromo-MTPA esters (2a_L—c_L) showed larger spin–spin coupling constants [J_{AB}(Hz)].

The assignment of absolute stereochemistry to the bromo-MTPA ester diastereoisomers (2a—d) was achieved by a stereochemical correlation sequence (Scheme) with the corresponding enantiomers of the trans-tetrahydrodiols (4a), (4b), and (4d) and the tetrahydroepoxides (5a—d) of known configuration [3–7] (Table 2). The individual diastereoisomers of the bromo-MTPA esters (2a—d) were converted into the cis- (3a—d) and trans- (4a—d) tetrahydrodiols using the silver acetate method.[11–13] The dioxolane intermediates which have been proposed for this type of reaction [13] open exclusively with either retention of configuration [to yield the cis-diols (3a—d)] or with inversion of configuration [to yield the trans-diols (4a—d)] at the chiral benzylic centre. Confirmation of this stereochemical sequence and selectivity was obtained by hydration of the tetrahydroepoxide enantiomers of (5b) and (5d) to yield the corresponding cis- [(3b) and (3d)] and trans-[(4b) and (4d)] tetrahydrodiol enantiomers with retention of configuration at the non-benzylic chiral centre. The use of a copper sulphate catalyst [14] was found to improve both the yields and relative proportions of the cis-diols (3b) and (3d) formed during the epoxide hydration reaction.

The tetrahydroepoxides (−)-(5a—d) have previously been stereochemically assigned by several methods [3–7] including the geminal coupling constant values (J_{AB}) of the related bromo-MOA precursors. It is now also possible to relate the absolute stereochemistry of bromo-MTPA precursors (2a—d) to the tetrahydroepoxides (5a—d) and thus to devise a more general [8] empirical n.m.r. method for stereochemical assignment of bromo-MTPA esters based upon relative chemical shifts.

The early isomer (high R_F) with a smaller, positive δ (¹H) value for H_B, and a smaller, negative δ (¹⁹F) value for the CF_3 group, will have an (R,R) configuration.

The late isomer (low R_F), with a larger, positive δ (¹H) value for H_B, and a larger, negative δ (¹⁹F) value for the CF_3 group, will have an (S,S) configuration.

X-Ray crystallographic analysis has provided an unequivocal method for absolute stereochemistry determination for bromo-MOA esters in the benz[a]anthracene [15] and benzo[a]-pyrene [16] series. In view of the value of the bromo-MTPA resolution method it was considered important to examine the absolute stereochemistry of one bromo-MTPA ester diastereoisomer [(+)-(2b_E)] by X-ray structure analysis. All molecules adopted a conformation in which the cyclohexene half-chair ring, C(1)—C(10A), carried an equatorial bromine atom on C(2) and a quasi-equatorial MTPA group on C(1)
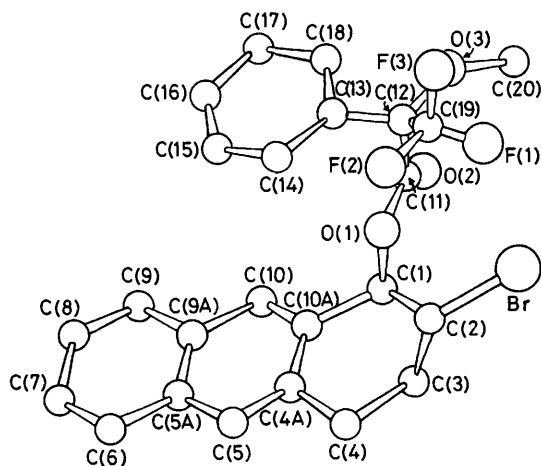
Figure. Molecular structure of the anthracene MTPA ester (+)-(2b$_E$) showing the crystallographic numbering scheme

(Figure). This is analogous to the conformation found in a similar type of bromo-MOA ester in the benzo[a]pyrene series [16] but differs from that found in a bromo-MOA ester in the benz[a]anthracene series [15] where the bromine atom and the MOA group were axial and quasi-axial respectively.

The crystal structure analysis showed the configuration at C(1) and C(2) of (+)-(2b$_E$) *relative* to that of the MTPA group. Since the absolute stereochemistry of (−)-(2b$_L$) has been unequivocally assigned as (1S,2S), by conversion into the (−)-(1S,2R) enantiomer of the tetrahydroepoxide (5b) [which had in turn been correlated with (+)-(R)-dimethyl β-methoxyadipate [17]], this analysis thus provides an unambiguous assignment of (S) configuration to (−)-MTPA. This absolute stereochemistry for (−)-MTPA had previously been deduced from empirical n.m.r.,[18] c.d.[19] and asymmetric synthesis[20] correlations.

A projection of the (+)-(2b$_E$) molecule [(1R,2R); (S)-MTPA] is shown in the Figure.

In contrast to the analogous bromo-MOA esters, the corresponding bromohydrins (1a—d) could not be obtained by selective diborane reduction of the bromo-MTPA esters (2a—d) under similar conditions (presumably owing to increased steric interactions). Fortunately, however, di-isobutylaluminium hydride (DIBAL), which had previously been shown to reduce ester groups in the presence of bromine atoms,[21] proved effective for this transformation. The optical rotations and configurations for the bromohydrin enantiomers (1a—d) obtained are summarized in Table 2.

The synthesis of the arene oxides (7a—d) from the corresponding bromo-MTPA esters (2a—d) required only two steps compared with the analogous bromo-MOA esters which (in order to circumvent bromination of the MOA group) required four steps.[5-7] Since the dibromo-MTPA esters (6a—d) were mixtures of isomers which frequently decomposed during attempted purification, they were not generally isolated and the overall recrystallized yields of (7a—d) from (2a—d) were found to be in the range (36—58%).

The arene oxides (−)-(7a) and (−)-(7b) derived from (−)-(2a$_E$) and (+)-(2b$_E$) respectively were found to be configurationally stable. These observations are in accord with those made using the corresponding bromo-MOA precursors[5] and with predictions based upon PMO calculations.[6,22] Similarly, the configurational instability (spontaneous racemization) of the arene oxides (7c) and (7d) derived from the corresponding bromo-MTPA precursors (2c) and (2d) was as expected.[6,22] Surprisingly, however, the initially observed [α]$_D$

values for (+)-(7d) in the present studies (within the range +141 ⟶ +271°) were much larger than the previously observed maximum value (+20°[7]). Spontaneous racemization at ambient temperature (without concomitant decomposition) did occur as before and a steady decrease in the initial [α]$_D$ value was observed at ambient temperature. The racemization process for (+)-(7d) was significantly slower than for the isomeric arene oxide (7c) where no optical rotation was observed after the normal work-up procedure from optically pure bromoacetate or bromo-MTPA precursors. This difference in rates of racemization between (7c) and (7d) was not predicted by the PMO calculations, but may result from increased steric interactions associated with the bay-region arene oxide (7d) and the corresponding oxepine valence tautomer (which would not be taken into account in the PMO calculations).

Experimental

The separation of the early (2$_E$) and late (2$_L$) diastereoisomers in each case from the bromo-MTPA mixtures (2a—d) was carried out using a Dupont Zorbax Sil semi-preparative (9.4 mm × 25 cm) column with cyclohexane–ether (ca. 97 : 3) as eluant. The separated diastereoisomers were detected using a u.v. detector (Cecil instruments CE272) operating at 254 nm. The diastereoisomeric purity and separation factor (α, Table 1) were determined using the same h.p.l.c. instrument (Spectra-Physics Model 3500B) and solvent system in conjunction with an analytical column (Dupont Zorbax Sil, 6.2 mm × 25 cm). Ether refers to diethyl ether.

The bromohydrins (1a—d) were synthesised by previously reported methods.[5,7] The MTPA esters (2a—d) were prepared from the corresponding bromohydrins by reaction of (−)-MTPA chloride [derived from (−)-MTPA acid, Aldrich] in pyridine at ambient temperature and purified by preparative h.p.l.c.

Separation of the Diastereoisomers of the MTPA Esters (2). —(−)-(1R,2R)- *and* (+)-(1S,2S)-trans-2-*Bromo*-1-(2-*methoxy-2-phenyl-2-trifluoromethylacetoxy*)-1,2,3,4-*tetrahydronaphthalene* (2a$_E$) *and* (2a$_L$). Recrystallization of the diastereoisomeric mixture from ether–pentane gave crystalline samples of (2a$_E$) and (2a$_L$) (84%) (Found: C, 54.0; H, 4.2. Calc. for C$_{20}$H$_{18}$BrF$_3$O$_3$: C, 54.2; H, 4.1%); (2a$_E$), early isomer, high R$_F$, m.p. 68—69 °C (pentane), [α]$_D$ −93° (CHCl$_3$); (2a$_L$), late isomer, low R$_F$, m.p. 68—69 °C (pentane), [α]$_D$ +50° (CHCl$_3$).

(+)-(1R,2R)- *and* (−)-(1S,2S)-trans-2-*Bromo*-1-(2-*methoxy-2-phenyl-2-trifluoromethylacetoxy*)-1,2,3,4-*tetrahydroanthracene* (2b$_E$) *and* (2b$_L$). These were obtained in 88% yield (Found: C, 58.4; H, 4.1. Calc. for C$_{24}$H$_{20}$BrF$_3$O$_3$: C, 58.4; H,

4.1%); (2b$_E$), early isomer, high R_F, m.p. 122 °C (ether–pentane), $[\alpha]_D$ + 2° (CHCl$_3$); (2b$_L$), late isomer, low R_F, m.p. 120 °C (ether–pentane), $[\alpha]_D$ − 35° (CHCl$_3$).

(−)-(1R,2R)- *and* (+)-(1S,2S)-trans-2-*Bromo*-1-(2-*methoxy*-2-*phenyl*-2-*trifluoromethylacetoxy*)-1,2,3,4-*tetrahydrophenthrene* (2c$_E$) *and* (2c$_L$). These were obtained in 81% yield (Found: C, 58.0; H, 3.9. Calc. for C$_{24}$H$_{20}$BrF$_3$O$_3$: C, 58.4; H, 4.1%); (2c$_E$), early isomer, high R_F, gum, $[\alpha]_D$ −93° (CHCl$_3$); (2c$_L$), late isomer, low R_F, m.p. 98—99 °C (ether–pentane), $[\alpha]_D$ +64° (CHCl$_3$).

(−)-(3R,4R)- *and* (+)-(3S,4S)-trans-3-*Bromo*-4-(2-*methoxy*-2-*phenyl*-2-*trifluoromethylacetoxy*)-1,2,3,4-*tetrahydrophenanthrene* (2d$_E$) *and* (2d$_L$). These were obtained in 79% yield (Found: C, 58.6; H, 4.2. C$_{24}$H$_{20}$BrF$_3$O$_3$ requires C, 58.4; H, 4.1%); (2d$_E$), early isomer, high R_F, m.p. 113—114 °C (ether–pentane), $[\alpha]_D$ −31° (CHCl$_3$); (2d$_L$), late isomer, low R_F, m.p. 128—129 °C (ether–pentane), $[\alpha]_D$ +48° (CHCl$_3$).

Preparation of the Pure Enantiomers of the Bromohydrins (1a—d).—The bromohydrins (1a—d) were obtained as pure enantiomers by reduction of the corresponding bromo-MTPA diastereoisomers (2a—d) with an excess of DIBAL in ether solution at ambient temperature for 2 days.

(−)-(1S,2S)-trans-2-*Bromo*-1-*hydroxy*-1,2,3,4-*tetrahydronaphthalene* (1a). From the bromo-MTPA ester (+)-(2a) the yield of (−)-(1a) was ca. 80%, m.p. 106—107 °C (chloroform–pentane), $[\alpha]$ −44° (CHCl$_3$) (lit.,[23] racemic m.p. 102—103 °C).

(−)-(1S,2S)-trans-2-*Bromo*-1-*hydroxy*-1,2,3,4-*tetrahydroanthracene* (1b). The yield of (−)-(1b) obtained from the bromo-MTPA ester (−)-(2b$_L$) was 80%, m.p. 90—92 °C (ether–pentane), $[\alpha]_D$ −61° (CHCl$_3$) (lit.,[24] racemic m.p. 109—110 °C).

(+)-(1R,2R)-trans-2-*Bromo*-1-*hydroxy*-1,2,3,4-*tetrahydrophenanthrene* (1c). The yield of (+)-(1c) obtained from the bromo-MTPA ester (−)-(2c$_E$) was 80%, m.p. 82—84 °C (ether–pentane), $[\alpha]_D$ +48° (CHCl$_3$) (Found: C, 60.4; H, 4.7. Calc. for C$_{14}$H$_{13}$BrO: C, 60.7; H, 4.7%).

(−)-(3R,4R)-trans-3-*Bromo*-4-*hydroxy*-1,2,3,4-*tetrahydrophenanthrene* (1d). The yield of (−)-(1d) obtained from the bromo-MTPA ester (−)-(2d$_E$) was 86%, m.p. 148—149 °C (ether–pentane), $[\alpha]_D$ −71° (CHCl$_3$) {lit.,[7] m.p. 151—152 °C, $[\alpha]_D$ −68° (CHCl$_3$)}.

Preparation of the cis-*Diols*(3).—(−)-(1R,2S)-cis-1,2-*Dihydroxy*-1,2,3,4-*tetrahydronaphthalene* (3a). The yield of (−)-(3a) obtained from the bromo-MTPA ester (−)-(2a$_E$) using the silver acetate–acetic acid–water method[11] was 68%, m.p. 103—106 °C (chloroform–pentane), $[\alpha]_D$ −41°(CHCl$_3$) {lit.,[25] m.p. 129—130 °C, $[\alpha]_D$ −38° (CHCl$_3$)}.

(−)-(1S,2R)-cis-1,2-*Dihydroxy*-1,2,3,4-*tetrahydroanthracene* (3b). The yield of cis-diol (−)-(3b) obtained by the silver acetate–acetic acid–water method[11] was insufficient for accurate $[\alpha]_D$ measurements to be made. The (−)-(1S,2R)-cis-diol (3b) (36%) was obtained by hydrolysis of (−)-(1S,2R)-(5b) in aqueous THF solution containing copper sulphate,[14] m.p. 127—128 °C (ethyl acetate), $[\alpha]_D$ −65° (THF) (lit.,[24] racemic, m.p. 133—135 °C).

(−)-(1R,2S)-cis-1,2-*Dihydroxy*-1,2,3,4-*tetrahydrophenanthrene* (3c). The yield of (−)-(3c) obtained from bromo-MTPA ester (−)-(2c$_E$) by the silver acetate–acetic acid–water‚method[11] was 25%, m.p. 168 °C (ether–pentane), $[\alpha]_D$ −91° (THF) (Found: M, 214.09942. Calc. for C$_{14}$H$_{14}$O$_2$: M, 214.09937).

(+)-(3R,4S)-cis-3,4-*Dihydroxy*-1,2,3,4-*tetrahydrophenanthrene* (3d). The yield of (+)-(3d) obtained from the bromo-MTPA ester (+)-(2d$_L$) by the silver acetate–acetic acid–water method[11] was 28%, m.p. 191—193 °C (ethyl acetate), $[\alpha]_D$ +35° (dioxane) {lit.,[7] m.p. 168—169 °C, $[\alpha]_D$ −22° (dioxane)}.

The yield of (+)-(3d) obtained from the tetrahydroepoxide (−)-(5d) by the copper sulphate catalysed hydration method[14] was 31%, m.p. 192—193 °C (ethyl acetate), $[\alpha]_D$ +31° (dioxane).

Preparation of the trans-*Diols* (4).—(−)-(1S,2S)-trans-1,2-*Dihydroxy*-1,2,3,4-*tetrahydronaphthalene* (4a). The yield of (−)-(4a) obtained from the bromo-MTPA ester (−)-(2a$_E$) by the silver acetate–acetic anhydride method[13] was 49%, m.p. 109—111 °C (chloroform–pentane) $[\alpha]_D$ −106° (CHCl$_3$) {lit.,[26] m.p. 112—113 °C, $[\alpha]_D$ −111° (CHCl$_3$)}.

(+)-(1R,2R)- *and* (−)-(1S,2S)-trans-1,2-*Dihydroxy*-1,2,3,4-*tetrahydroanthracene* (4b). The yield of (−)-(4b) obtained from the bromo-MTPA ester (+)-(2b$_E$) by the silver acetate–acetic acid–water method was 40%, m.p. 160 °C (ethyl acetate), $[\alpha]_D$ −117° (THF) {lit.,[5] 160—162 °C, $[\alpha]_D$ −44° (acetone)}.

The yield of (+)-(4b) obtained from the tetrahydroepoxide (−)-(5b) by the copper sulphate catalysed hydration method was 62%, m.p. 160 °C (ethyl acetate), $[\alpha]_D$ +124 °(THF) and $[\alpha]_D$ +108° (acetone).

(−)-(1S,2S)-trans-1,2-*Dihydroxy*-1,2,3,4-*tetrahydrophenanthrene* (4c). The yield of (−)-(4c) obtained from the bromo-MTPA ester (−)-(2c$_E$) by the silver acetate–acetic acid–water method was 40%, m.p. 137—138 °C, $[\alpha]_D$ −35° (THF) (Found: C, 78.2; H, 6.4. Calc. for C$_{14}$H$_{14}$O$_2$: C, 78.5; H, 6.6%).

(+)-(3R,4R)-trans-3,4-*Dihydroxy*-1,2,3,4-*tetrahydrophenanthrene* (4d). The yield of (+)-(4d) obtained from the bromo-MTPA ester (+)-(2d$_L$) by the silver acetate–acetic acid water method was 42%, a viscous gum, $[\alpha]_D$ +30° (CHCl$_3$) {lit.,[7] m.p. 175—176 °C, $[\alpha]_D$ +25° (dioxane)}. The yield of (+)-(4d) obtained by copper sulphate catalysed hydrolysis of the tetrahydroepoxide (−)-(5d) was 45%, a viscous gum, $[\alpha]_D$ +26° (CHCl$_3$) and $[\alpha]_D$ −33° (dioxane).

Preparation of the Epoxides (5).—(−)-(1S,2R)-1,2-*Epoxy*-1,2,3,4-*tetrahydronaphthalene* (5a). Treatment of the (+)-bromo-MTPA ester (2a$_L$) with NaOMe in ether as previously reported for the corresponding bromo-MOA ester[5] gave (−)-(5a) (80%), m.p. 40—41 °C (pentane), $[\alpha]_D$ −131° (CHCl$_3$) {lit.,[5] m.p. 45—48 °C, $[\alpha]_D$ +135° (CHCl$_3$)}.

(−)-(1S,2R)-1,2-*Epoxy*-1,2,3,4-*tetrahydroanthracene* (5b). The yield of (−)-(5b) obtained from the (−)-bromo-MTPA ester (2b$_L$) was 88%, m.p. 147 °C (ether–pentane), $[\alpha]_D$ −151° (CHCl$_3$) {lit.,[5] m.p. 155—156 °C, $[\alpha]_D$ +140° (CHCl$_3$)}.

(−)-(1S,2R)-1,2-*Epoxy*-1,2,3,4-*tetrahydrophenanthrene* (5c). The yield of (−)-(5c) obtained from the (+)-bromo-MTPA ester (2c$_L$) was 75%, m.p. 125—128 °C (ether–pentane), $[\alpha]_D$ −140° (CHCl$_3$) (Found: C, 85.6; H, 6.0. Calc. for C$_{14}$H$_{12}$O: C, 85.7; H, 6.1%).

(−)-(3R,4S)-3,4-*Epoxy*-1,2,3,4-*tetrahydrophenanthrene* (5d). The yield of (−)-(5d) obtained from the (+)-bromo-MTPA ester (2d$_L$) was 79%, m.p. 50 °C (ether–pentane), $[\alpha]_D$ −172° (CHCl$_3$) (lit.,[7] m.p. 50—51 °C, $[\alpha]_D$ +156°).

Preparation of the Epoxides (7).—(−)-(1S,2R)-1,2-*Epoxy*-1,2-*dihydronaphthalene* (naphthalene 1,2-*oxide*) (7a). Reaction of the (+)-bromo-MTPA ester (2a$_L$) with N-bromosuccinimide in CCl$_4$, followed by treatment of the crude dibromo-ester (6a) with NaOMe [cf. the method of synthesis of (+)-(7a) from the corresponding bromoacetate derivative[5]] gave the arene oxide (−)-(7a) (58%). The arene oxide (7a), in common with the arene oxides (7b—d), decomposed rapidly on heating. Cooling the pentane solution to −60 °C gave crystals, $[\alpha]_D$ −128° (CHCl$_3$) {lit.,[5] $[\alpha]_D$ +149° (CHCl$_3$)}.

(−)-(1S,2R)-1,2-*Epoxy*-1,2-*dihydroanthracene* (anthracene 1,2-*oxide*) (7b). The yield of (−)-(7b) obtained from (−)-bromo-MTPA ester (2b$_L$) was 37%, as crystals from pentane (−60 °C), $[\alpha]$ −215° (CHCl$_3$) {lit.,[5] $[\alpha]_D$ +214° (CHCl$_3$)}.

(±)-1,2-*Epoxy*-1,2-*dihydrophenanthrene* (*phenanthrene* 1,2-*oxide*) (7c). The yield of (±)-(7c) obtained from (−)-bromo-MTPA ester (2c$_E$) was 36%, recrystallized from pentane (−60 °C), [α]$_D$ 0° (CHCl$_3$).

(+)-(3S,4R)-3,4-*Epoxy*-3,4-*dihydrophenanthrene* (*phenan-threne* 3,4-*oxide*) (7d). The yield of (+)-(7d) obtained from (−)-bromo-MTPA ester (2d$_E$) was 32%. The initially isolated sample of (+)-(7d) was rapidly crystallised at −60 °C from pentane to give a maximum [α]$_D$ value of +271° (CHCl$_3$). The optical rotation was found to decrease spontaneously at ambient temperature while simultaneous n.m.r. analysis indicated that no significant decomposition had occurred relative to a reference peak. Consistently high [α]$_D$ values [> +150° (CHCl$_3$)] for (+)-(7d) were observed when the precursor (−)-(2d$_E$) was used.

Table 3. Fractional atomic co-ordinates for the anthracene MTPA ester (+)-(2b$_E$) with e.s.d.s in parentheses

Atom	x	y	z
Br	−0.078 9(1)	0.250 0(0)	0.440 3(1)
F(1)	−0.290 1(8)	0.405 7(14)	0.556 0(6)
F(2)	−0.175 8(7)	0.521 2(10)	0.717 3(7)
F(3)	−0.376 9(7)	0.460 1(12)	0.673 6(7)
O(1)	−0.024 8(5)	0.266 9(10)	0.708 6(5)
O(2)	−0.113 4(8)	0.020 3(12)	0.686 1(7)
O(3)	−0.340 3(6)	0.144 2(14)	0.684 6(6)
C(1)	0.084 9(8)	0.212 8(11)	0.685 4(8)
C(2)	0.081 0(10)	0.301 2(19)	0.580 5(9)
C(3)	0.206 9(10)	0.262 7(22)	0.565 5(8)
C(4)	0.325 2(11)	0.345 4(30)	0.669 4(12)
C(4A)	0.326 9(9)	0.310 6(18)	0.787 7(9)
C(5)	0.434 0(9)	0.357 5(20)	0.884 8(12)
C(5A)	0.441 8(8)	0.327 6(18)	0.998 1(10)
C(6)	0.556 4(11)	0.377 9(20)	1.103 4(13)
C(7)	0.559 2(12)	0.349 5(23)	1.210 6(14)
C(8)	0.450 5(13)	0.266 4(23)	1.220 5(10)
C(9)	0.338 3(11)	0.222 6(23)	1.120 3(10)
C(9A)	0.332 9(9)	0.254 6(18)	1.007 2(8)
C(10)	0.223 0(8)	0.213 3(15)	0.905 2(8)
C(10A)	0.215 0(8)	0.247 4(16)	0.795 8(7)
C(11)	−0.116 1(8)	0.158 5(16)	0.703 3(7)
C(12)	−0.227 0(7)	0.240 3(16)	0.727 5(6)
C(13)	−0.177 4(7)	0.253 4(17)	0.861 0(6)
C(14)	−0.064 9(8)	0.340 9(20)	0.930 3(8)
C(15)	−0.021 3(10)	0.344 0(17)	1.052 6(8)
C(16)	−0.086 8(11)	0.260 8(23)	1.104 8(8)
C(17)	−0.199 3(13)	0.177 9(21)	1.033 8(10)
C(18)	−0.245 7(9)	0.173 5(18)	0.913 5(8)
C(19)	−0.263 6(9)	0.407 7(18)	0.670 4(9)
C(20)	−0.403 5(12)	0.091 8(24)	0.563 4(9)

Crystal Data for the Anthracene MTPA Ester (+)-(2b$_E$).—C$_{24}$H$_{20}$BrF$_3$O$_3$, M = 493.3, monoclinic, space group $P2_1$, a = 11.217(5), b = 8.270(4), c = 12.716(5) Å, β = 115.8(2)°, U = 1 061.7 Å^3, Z = 2, D_c = 1.54 g cm^{-3}, $F(000)$ = 500, μ(Mo-$K_α$) = 19.1 cm^{-1}.

The crystals were well-formed, colourless, hexagonal prisms. Initial lattice characterisation was by means of oscillation and Weissenberg photographs. Diffraction intensities were recorded on a Stoe STADI-2 two-circle diffractometer using the ω scan technique with graphite-monochromated Mo-$K_α$ radiation. Data were measured to a maximum 2θ of 55°.

The 2 017 reflections with $I > \sigma(I)$ were corrected for Lorentz and polarization effects and were used in the subsequent analysis and refinement. The structure was determined by direct methods using SHELX but as many of the atoms lay close to a false mirror plane (because of the polar space group) the correct atomic co-ordinates were derived from a series of difference Fourier syntheses after refinement of the Br parameters. Least squares refinement, initially with isotropic and finally with anisotropic temperature factors for all non-hydrogen atoms, produced convergence at R = 8.2%, R_w = 9.3%. The enantiomer was fixed by choosing the set of co-ordinates consistent with the known (1R,2R) configuration of the anthracene moiety. This established the absolute configuration of (−)-MTPA as (S). A projection of the molecule is shown in the Figure.

The final weighting scheme was w = 0.937/[σ^2(F) + 0.011 74 F^2]. A final difference synthesis revealed no peaks

Table 4. Bond lengths (Å) for the anthracene MTPA ester (+)-(2b$_E$) with e.s.d.s in parentheses

Br−C(2)	1.946(9)	C(1)−O(1)	1.456(12)
C(1)−C(2)	1.505(17)	O(1)−C(11)	1.340(13)
C(2)−C(3)	1.539(18)	C(11)−O(2)	1.166(16)
C(3)−C(4)	1.564(18)	C(11)−C(12)	1.560(14)
C(4)−C(4A)	1.524(21)	C(12)−C(13)	1.544(11)
C(4A)−C(10A)	1.404(16)	C(13)−C(14)	1.387(14)
C(4A)−C(5)	1.351(14)	C(14)−C(15)	1.413(14)
C(5)−C(5A)	1.427(21)	C(15)−C(16)	1.370(20)
C(5A)−C(9A)	1.412(17)	C(16)−C(17)	1.373(18)
C(5A)−C(6)	1.455(15)	C(17)−C(18)	1.385(15)
C(6)−C(7)	1.369(26)	C(18)−C(13)	1.385(17)
C(7)−C(8)	1.452(24)	C(12)−C(19)	1.534(19)
C(8)−C(9)	1.393(15)	C(12)−O(3)	1.393(12)
C(9)−C(9A)	1.437(18)	O(3)−C(20)	1.454(14)
C(9A)−C(10)	1.388(11)	C(19)−F(1)	1.352(14)
C(10)−C(10A)	1.383(15)	C(19)−F(2)	1.302(14)
C(10A)−C(1)	1.548(10)	C(19)−F(3)	1.359(14)

Table 5. Bond angles (°) for the anthracene MTPA ester (2b$_E$) with e.s.d.s in parentheses

O(1)−C(1)−C(2)	109.2(0.8)	C(7)−C(8)−C(9)	120.1(1.4)	C(13)−C(12)−O(3)	107.5(0.8)
O(1)−C(1)−C(10A)	107.8(0.8)	C(8)−C(9)−C(9A)	119.6(1.3)	C(19)−C(12)−O(3)	108.6(0.7)
C(2)−C(1)−C(10A)	111.5(0.8)	C(9)−C(9A)−C(5A)	120.0(0.9)	C(12)−C(13)−C(14)	121.9(0.9)
Br−C(2)−C(1)	111.5(0.8)	C(9)−C(9A)−C(10)	121.6(1.1)	C(12)−C(13)−C(18)	119.1(0.8)
Br−C(2)−C(3)	111.8(0.8)	C(5A)−C(9A)−C(10)	118.4(1.0)	C(14)−C(13)−C(18)	119.0(0.8)
C(1)−C(2)−C(3)	109.6(0.9)	C(9A)−C(10)−C(10A)	122.2(1.0)	C(13)−C(14)−C(15)	119.5(1.1)
C(2)−C(3)−C(4)	107.0(1.1)	C(10)−C(10A)−C(4A)	118.8(0.7)	C(14)−C(15)−C(16)	121.5(1.0)
C(3)−C(4)−C(4A)	113.1(1.3)	C(10)−C(10A)−C(1)	119.8(0.9)	C(15)−C(16)−C(17)	117.7(1.0)
C(4)−C(4A)−C(10A)	121.0(0.8)	C(4A)−C(10A)−C(1)	121.5(0.9)	C(16)−C(17)−C(18)	122.4(1.4)
C(4)−C(4A)−C(5)	118.1(1.2)	C(1)−O(1)−C(11)	118.7(0.9)	C(17)−C(18)−C(13)	119.9(1.0)
C(10A)−C(4A)−C(5)	120.5(1.2)	O(1)−C(11)−O(2)	125.7(1.0)	C(12)−C(19)−F(1)	112.7(1.1)
C(4A)−C(5)−C(5A)	120.8(1.2)	O(1)−C(11)−C(12)	111.0(1.0)	C(12)−C(19)−F(2)	116.1(0.7)
C(5)−C(5A)−C(9A)	118.8(0.8)	O(2)−C(11)−C(12)	123.3(1.0)	C(12)−C(19)−F(3)	109.6(1.0)
C(5)−C(5A)−C(6)	121.4(1.2)	C(11)−C(12)−C(13)	108.1(0.6)	F(1)−C(19)−F(2)	105.7(1.1)
C(9A)−C(5A)−C(6)	119.7(1.2)	C(11)−C(12)−C(19)	111.7(0.9)	F(1)−C(19)−F(3)	105.4(0.8)
C(5A)−C(6)−C(7)	119.7(1.3)	C(11)−C(12)−O(3)	110.2(1.0)	F(2)−C(19)−F(3)	106.7(1.1)
C(6)−C(7)−C(8)	120.8(1.1)	C(13)−C(12)−C(19)	110.5(1.0)	C(12)−O(3)−C(20)	121.7(1.0)

higher than possible hydrogen atoms, which were not included in the refinement.

Final atomic co-ordinates are given in Table 3 and bond lengths and bond angles in Tables 4 and 5. A complete listing of co-ordinates, anisotropic temperature factors, bond lengths, angles, and observed and calculated structure factors have been deposited as a Supplementary Publication * (SUP No. 23680, 17 pages).

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* For details of the Supplementary Publications Scheme see Instructions for Authors (1983), *J. Chem. Soc., Perkin Trans. 1*, 1983, Issue 1.

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