Synthesis of a Chiral Helical Molecular Template Based on *trans*-5,6,6a,7,8,12b-Hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-dione

Julie Cheung,[1a] Leslie D. Field,[1a] Trevor W. Hambley,[1b] and Sever Sternhell*,[1a]

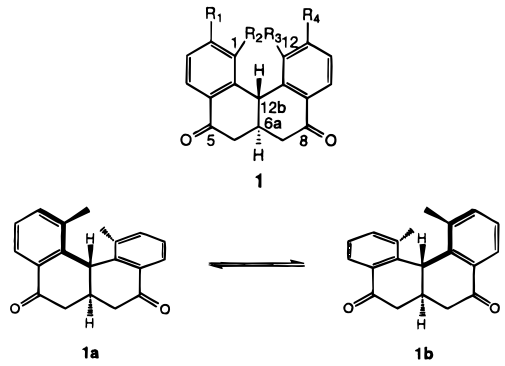
Department of Organic Chemistry and Department of Inorganic Chemistry, The University of Sydney, New South Wales 2006, Australia

Received July 2, 1996[⊗]

Reduction of *trans*-5,5,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-dione (**1**, $R_1 = R_4 = H$, $R_2 = R_3 = CH_3$) with lithium aluminum hydride yielded stereoselectively (5*RS*,8*RS*)-*trans*-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diols **2**, X = H. These diols proved to be configurationally stable chiral molecular templates capable of straightforward modification by attachment of molecular elements of different length and kind. The structures of the diacetate **2**, $X = COCH_3$, and (5*R*,8*R*)-(−)-*trans*-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo-[*c*]phenanthrene-5,8-diyl di-*p*-bromobenzoate (**2a**, X = *p*-BrC_6H_4CO), as well as the absolute configuration of the latter were obtained by X-ray crystallography.

Introduction

We have previously described[2] the synthesis of a series of helical ketones **1** and have shown that *trans*-5,6,-6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-dione (**1**, $R_1 = R_4 = H$, $R_2 = R_3 = CH_3$) was indefinitely stable at ambient temperature, i.e., that the inversion **1a** ⇄ **1b** is very slow.[3] We now wish to report the preparation of a chiral molecular template based on this compound.



Our basic design aim was to incorporate the chiral helical entity into a rodlike molecule in which we could control (a) the length of the rods and (b) the nature of the rods. This implies an attachment of molecular elements to the carbonyl groups of **1**. We have explored a number of possibilities of which the stereoselective reduction with lithium aluminum hydride was by far the most successful.

Preparation of Compounds

The dione **1**, $R_1 = R_4 = H$, $R_2 = R_3 = CH_3$, was reduced using lithium aluminum hydride to give the diol **2**, X = H. Depending on the directions of attack of the nucleophile on C5 and C8 (axial or equatorial), four possible diastereomers may be formed. For each sense of the helix, the hydroxy groups on C5 and C8 could be either both α, both *β*, or one α and the other *β*. The latter case would give rise to two diastereomers. The four diastereomers of one sense of the helix are each enantiomerically related to those of the other helical sense; thus, in total, there are four possible diastereomers of the diol **2**, X = H.

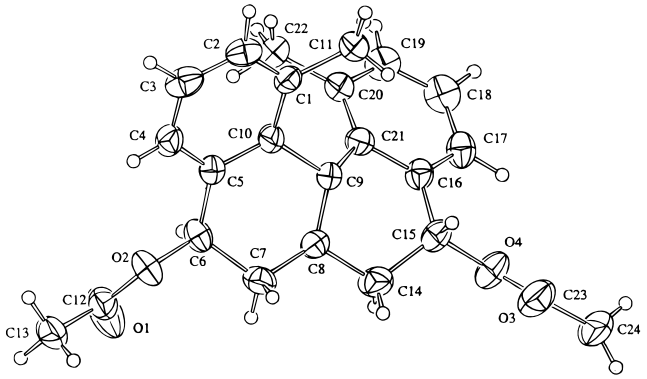


Figure 1. ORTEP plot of (5*R*,8*R*)-*trans*-(−)-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl diacetate (**2**, $X = COCH_3$) showing atomic labels (30% thermal ellipsoids).

However, according to the ^1H NMR spectrum (400 MHz) of the crude reaction product, the reaction proceeded to give exclusively *one* of the diastereomers. The stereoselectivity of lithium aluminum hydride reduction meant that only one of the four possible diastereomers was generated and the reaction proceeded in essentially quantitative yield. The diol **2** (X = H) forms the desired helical template, and esterification of this diol using acetic anhydride and various acyl chlorides would allow systematic variation of the molecular rods.

The diacetate **2**, $X = COCH_3$, was synthesized by the acetylation of the diol **2**, X = H, with acetic anhydride in pyridine. The X-ray crystal structure of this compound was obtained, and the ORTEP plot is given in Figure 1.

The ORTEP plot and the structural data (see the Supporting Information) indicated that the ester chains are in pseudoequatorial positions in relation to the helical

⊗ Abstract published in *Advance ACS Abstracts,* December 1, 1996.

(1) (a) Department of Organic Chemistry. (b) Department of Inorganic Chemistry.

(2) Cheung, J.; Field, L. D.; Regaglia, F.; Sternhell, S. *Aust. J. Chem.* **1995**, *48*, 1707.

(3) Cheung, J.; Field, L. D.; Hambley, T. W.; Sternhell, S. *Aust. J. Chem.* **1995**, *48*, 1727.

S0022-3263(96)01254-6 CCC: $14.00

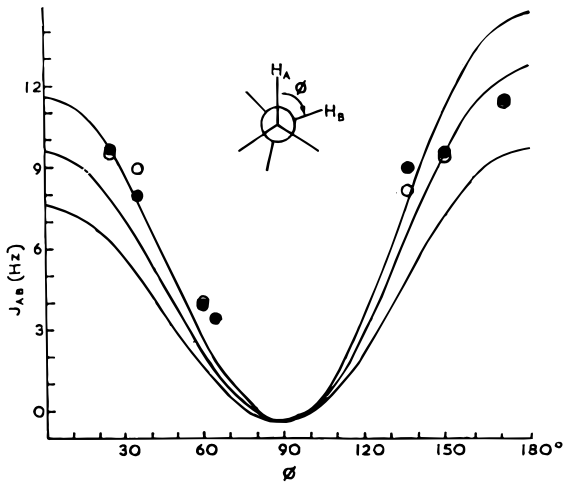


Figure 2. Values of the experimental vicinal coupling constants of the diol **2**, X = H (○), and the diacetate **2**, X = $COCH_3$ (●), and the dihedral angles (ϕ) obtained from the X-ray data of the diacetate **2**, X = $COCH_3$, fitted onto the Karplus plot.[4]

framework and are approximately coplanar, thus giving an elongated shape. Detailed analysis of the ^{1}H NMR spectra, in particular, the vicinal coupling constants of protons on C5, C6, C6a, C7, and C8, of the diol **2**, X = H, and the diacetate **2**, X = $COCH_3$, also indicate that H5 and H8 in both compounds are pseudoaxial. The conformations of these two compounds derived from the ^{1}H NMR data are remarkably similar to the conformation depicted in the ORTEP plot of the diacetate **2**, X = $COCH_3$, indicating the conformation of these helical molecules is the same in solution and in crystal form. This was established by plotting the dihedral angles between these vicinal C−H bonds, obtained from the X-ray structural data, against the observed vicinal coupling constants (Figure 2). It was found that the experimental data agreed well with the Karplus plot calculated for this type of molecules.[4]

The stereochemistry of the diol implies that the reduction of the dione **1**, $R_1 = R_4 = H$, $R_2 = R_3 = CH_3$, with lithium aluminum hydride is the result of axial attacks by the incoming nucleophiles generating pseudoequatorial alcohols and thus complying with the general rule of stereoselectivity of the reduction of cyclohexanones.[5−7]

Resolution of Derivatives of the Diol 2 and the Determination of Absolute Configurations of the Enantiomers. The diactete **2**, X = $COCH_3$, was resolved directly using HPLC with a chiral column (see Experimental Section) in high enantiomeric purity (determined by ^{1}H NMR with the addition of a chiral shift reagent).[8]

It was also found to be possible to resolve the diol **2**, X = H, by converting it into a mixture of diastereomeric diesters with the acyl chloride of (*S*)-α-methoxyphenylacetic acid **3**[9] according to Scheme 1. To show that racemisation had not occurred when the acid **3** was reacted with thionyl chloride, a portion of the product, (*S*)-α-methoxyphenylacetyl chloride **4**, was hydrolysed to the acid with water. The optical rotations of the hydrolysis product of the acyl chloride **4** and an authentic sample of the acid **3** were found to be identical. The diastereomeric diesters **5a** and **5b** could be easily separated on a silica column and, by hydrolysis, gave the resolved diols **2a**, X = H, and **2b**, X = H. The enantiomers of the diactete **2**, X = $COCH_3$, were prepared from the resolved diols **2a**, X = H, and **2b**, X = H (Scheme 1). The diacetates **2a**, X = $COCH_3$, and **b**, X = $COCH_3$, were found to be identical on the basis of their CD data to the pair of diacetates resolved by HPLC (Table 1).

Scheme 1

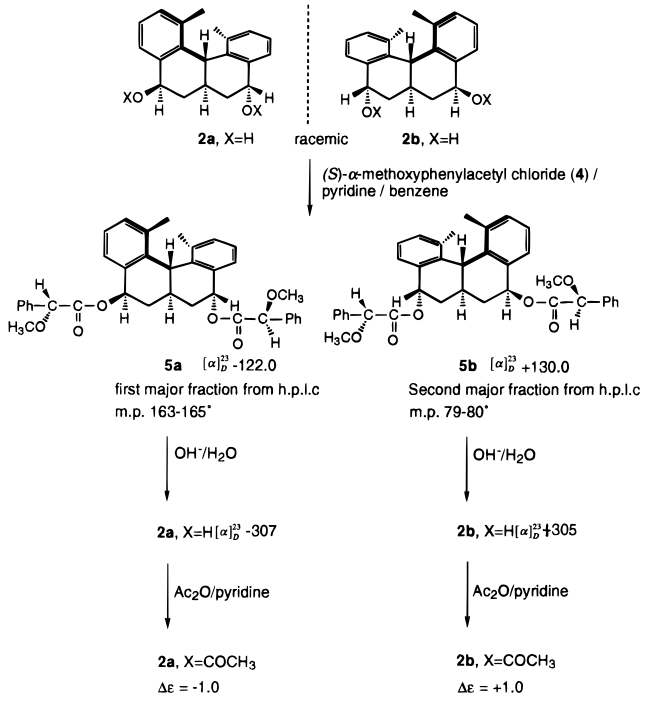


Table 1. Specific Rotations and Molar Differential Dichroic Absorptions for the Diols 2, X = H, and Their Derivatives

compd	$[\alpha]^{23}_D$	$\Delta\epsilon$ ($CHCl_3$)
2a, X = H[a]	−307 (*c* = 0.5, $CHCl_3$)[g]	
2b, X = H[b]	+305 (*c* = 0.2, $CHCl_3$)[g]	
2b, X = H[c]	+270 (*c* = 0.1, $CHCl_3$)[g]	
2a, X = $COCH_3$[d]	−251 (*c* = 0.3, $CHCl_3$)[g]	−1.1 (283 nm)
2b, X = $COCH_3$[d]	+231 (*c* = 0.9, $CHCl_3$)[g]	+1.1 (282 nm)
2a, X = $COCH_3$[e]		−1.0 (285 nm)
2b, X = $COCH_3$[f]		+1.0 (285 nm)

[a] Obtained from hydrolysis of the diester **5a**. [b] Obtained from hydrolysis of the diester **5b**. [c] Obtained from hydrolysis of the diester **2b**, X = *p*-BrC_6H_6CO. [d] Resolved by HPLC on a chiral column. [e] Obtained from acetylation of the resolved[a] diol **2a**, X = H. [f] Obtained from acetylation of the resolved[b] diol **2b**, X = H. [g] These values were determined on samples weighing between 0.9−5 mg and are therefore significant to approximately ±10%.

However, the relative configurations of the diastereomeric diesters **5a** and **5b** could not be determined by X-ray crystallography since neither of them produces good quality crystals. In order to determine the absolute configurations of the diols **2a**, X = H, and **2b**, X = H, and their derivatives, the diester **2**, X = *p*-COC_6H_4Br, was synthesized with the acyl chloride of 4-bromobenzoic acid. This diester **2**, X = *p*-COC_6H_4Br, was then resolved by HPLC with a chiral column. One of the enantiomers **2a**, X = *p*-COC_6H_4Br, was successfully recrystallized to produce a good quality crystal for X-ray crystallography, and the absolute configuration of this diester was determined. The ORTEP plot is shown in Figure 3. The other enantiomer of the diester **2b**, X = *p*-COC_6H_4Br, was

(4) Colucci, W. J.; Jungk, S. J.; Gandour, R. D. *Magn. Reson. Chem.* **1985**, *23*, 335.
(5) Anh, N. T.; Eisenstein, O. *Nouv. J. Chim.* **1976**, *1*(1), 61.
(6) Wigfield, D. C. *Tetrahedron* **1979**, *35*, 449.
(7) Chérest, M.; Felkin, H. *Tetrahedron Lett.* **1968**, *18*, 2205.
(8) (S_P)-*tert*-Butylphenylphosphinothioic acid was used as the chiral shift reagent. For preparation, see: Haynes, R.; Freeman, R.; Mitchell, C.; Vonwiller, S. C. *J. Org. Chem.* **1994**, *59*, 2919.
(9) McKenzie, A. *J. Chem. Soc.* **1899**, *75*, 761.

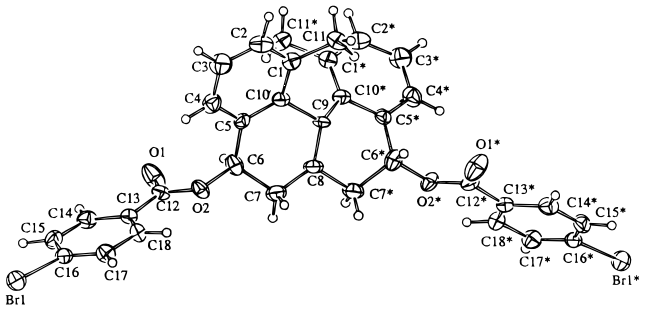
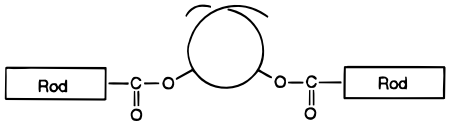


Figure 3. ORTEP plot of (5*R*,8*R*)-(−)-*trans*-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl di-*p*-bromobenzoate **2a**, X = *p*-BrC_6H_4CO, showing atomic labels (30% thermal ellipsoids).

hydrolyzed to an enantiomer of the diol **2**, X = H, which was correlated with the enantiomer of this diol obtained from the hydrolysis of the diastereomeric diester **5b** on the basis of their specific rotations (Table 1). Thus, the absolute configurations of the diols **2a**, X = H, and **2b**, X = H, and therefore the absolute configurations of the diacetates **2a**, X = $COCH_3$, and **2b**, X = $COCH_3$, synthesized from the diols were determined, and they are shown in Scheme 1.

Conclusions

Clearly, esterification of the diols **2a**, X = H, and **2b**, X = H, with a variety of acyl chlorides is straightforward and leads to a series of chiral templates with rods of variable type and length attached to it in a manner shown in structure **6**. It is apparent that these compounds, which are now under investigation in these laboratories, are similar in type to Cram's binaphthyl derivatives[10] because their chirality involves a large steric barrier to inversion of the helicene-like skeleton.



6

Experimental Section

General Methods. The term worked up in the usual way means that a solution of the product was washed with alkali and/or acid (as indicated) and with saturated saly solution. The solution was then filtered and dried over anhydrous magnesium sulfate and the solvent removed under reduced pressure. Analytical instruments and general procedures used in this work were previously described.[2,3] Both analytical and preparative chiral HPLC were carried out using a Regis Pirkle type 1-A chiral column, 10 mm i.d. × 25 cm (5 μm partical size), at a flow rate of 3.0 mL/min.

(5*RS*,8*RS*)-*trans*-5,6,6a,7,8,12b-Hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diols (2, X = H). A solution of *trans*-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-dione (**1**, $R_1 = R_4 = H$, $R_2 = R_3 = CH_3$) (100 mg, 0.3 mmol) in dry THF (10 mL) was added gradually to a suspension of powdered lithium aluminum hydride (0.5 g) in dry THF (50 mL). The mixture was heated at reflux under nitrogen for 2 h, ether (50 mL) was added, and the excess lithium aluminum hydride was decomposed with hydrochloric acid (3 M). The organic layer was worked up as usual, and the crude product was recrystallized from chloroform to yield (5*RS*,8*RS*)-*trans*-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diol (**2**, X = H) (98 mg, 98%) as colorless needles; mp 238−240 °C (lit.[12] mp 213−214 °C); UV (ethanol) 255.9 (log ϵ, 2.81) nm; ^{1}H NMR (600 MHz, CD_2Cl_2) δ 1.17 (ddd, J = 12.2, 11.4, 11.4 Hz, 1H), 1.32 (ddd, J = 12.7, 9.3, 8.3 Hz, 1H), 1.43−1.56 (m, 1H), 1.53 (s, 3H), 1.93 (ddd, J = 12.2, 4.1, 3.6 Hz), 1.96 (ddd, J = 12.7, 9.5, 9.5 Hz, 1H), 2.07 (s, 3H), 3.49 (d, J = 11.2 Hz, 1H), 4.43 (dd, J = 11.4, 3.6 Hz, 1H), 4.76 (dd, J = 9.5, 9.3 Hz, 1H), 6.89 (dd, J = 7.8, 1.3 Hz, 1H), 7.08 (dd, J = 7.8, 1.1 Hz, 1H), 7.15 (dd, J = 7.8, 7.8 Hz, 1H), 7.23 (dd, J = 7.8, 7.8 Hz, 1H), 7.45 (dd, J = 7.8, 1.3 Hz), 7.52 (dd, J = 7.8, 1.1, 1.1 Hz); MS m/e 294 (M^+, 30). Anal. Calcd for $C_{20}H_{22}O_2$: C, 81.6; H, 7.5. Found: C, 81.7; H, 7.5.

(5*RS*,8*RS*)-*trans*-5,6,6a,7,8,12b-Hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl Diacetate (2, X = $COCH_3$). Acetic anhydride (87 mg) was added dropwise to a solution of (5*RS*,8*RS*)-*trans*-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diol (**2**, X = H) (128 mg, 0.4 mmol) in dry pyridine (10 mL) at rt. The solution was heated at 40 °C for 1 h, poured into cold water, and stirred. The mixture was filtered, and the residue of (5*RS*,8*RS*)-*trans*-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl diacetate (**2**, X = $COCH_3$) (108 mg, 72%) was collected. Recrystallization from methanol gave an analytical sample that melted at 208−211 °C. Extraction of the filtrate failed to yield any additional product: UV (chloroform) 286.0 (log ϵ, 4.02), 238.5 (4.07) nm; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.53 (s, 3H), 1.59 (ddd, J = 12.6, 11.5, 11.5 Hz, 1H), 1.74 (ddd, J = 13.1, 9.0, 8.3 Hz, 1H), 1.86−1.98 (m, 1H), 2.10 (s, 3H), 2.20 (s, 3H), 2.28 (s, 3H), 2.29 (ddd, J = 12.6, 4.0, 3.6 Hz, 1H), 2.35 (ddd, J = 13.1, 9.7, 9.7 Hz, 1H), 3.85 (d, J = 11.2 Hz, 1H), 5.98 (dd, J = 11.5, 3.6 Hz, 1H), 6.14 (dd, J = 9.7, 9.0 Hz, 1H), 6.90 (dd, J = 7.5, 1.3 Hz, 1H), 7.10 (dd, J = 7.0, 1.3 Hz, 1H), 7.12 (dd, J = 7.5, 7.5 Hz, 1H), 7.15 (dd, J = 7.0, 1.3 Hz, 1H), 7.21 (dd, J = 7.0, 7.0 Hz, 1H), 7.22 (dd, J = 7.5, 1.3 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 20.1, 20.7, 21.3, 33.8, 35.2, 35.7, 43.3, 69.2, 71.5, 120.8, 122.7, 125.5, 126.5, 129.2, 130.8, 132.6, 135.2, 136.8, 137.3, 138.6, 138.6, 170.6, 171.0; MS m/z 378 (M^+, 19). Anal. Calcd for $C_{24}H_{26}O_4$: C, 76.2; H, 6.9. Found: C, 75.9; H, 6.9.

Resolution of (5*RS*,8*RS*)-*trans*-5,6,6a,7,8,12b-Hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl Diacetate (2, X = $COCH_3$). The resolution of the diacetates **2a**, X = $COCH_3$, and **2b**, X = $COCH_3$ (10 mg), was achieved by preparative HPLC with a chiral stationary phase (eluant: 2-propanol (2.0%) in light petroleum). (5*R*,8*R*)-(−)-*trans*-5,6,6a,7,8,12b-Hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl diacetate (**2a**, X = $COCH_3$) (4.5 mg, 45%) was obtained as the first fraction: $[\alpha]^{20}_D$ −251.2 (c = 0.3, $CHCl_3$); UV (chloroform) 282 (log ϵ, 2.78) nm; CD (chloroform) $[\theta]_{295}$ 0; $[\theta]_{270}$ −3630.

The second fraction consisted of (5*S*,8*S*)-(+)-*trans*-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl diacetate (**2b**, X = $COCH_3$) (4.0 mg, 40%): $[\alpha]^{20}_D$ +230.7 (c = 0.9, $CHCl_3$); UV (chloroform) 265 (log ϵ, 2.79) nm; CD (chloroform) $[\theta]_{295}$ 0; $[\theta]_{270}$ +3630. The ^{1}H NMR spectra of the racemic diacetate **2**, X = $COCH_3$, and the resolved diacetates **2a**, X = $COCH_3$, and **2b**, X = $COCH_3$, were identical.

(*S*)-α-Methoxyphenylacetyl Chloride (4). Thionyl chloride (1 mL) was added dropwise to a solution of (*S*)-α-methoxyphenylacetic acid (**3**) (200 mg, 1.87 mmol, $[\alpha]^{22}_D$ +143 (c = 1.7, C_2H_5OH) (lit.[13] $[\alpha]^{17}_D$ +150 (c = 1, C_2H_5OH))) in dry benzene (2 mL) at reflux and the reaction mixture stirred at rt under nitrogen for 3 h. The excess thionyl chloride and benzene were removed under reduced pressure to give (*S*)-α-methoxyphenylacetyl chloride (**4**) (186 mg, 80%), which was used in the next step without further purification: IR (chloroform) 1743 (C=O) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.53 (s, 3H), 5.01 (s, 1H), 7.30−7.60 (m, 5H).

A portion of this material (approximately 10 mg) was hydrolyzed by stirring in water (5 mL) for 30 min. The solution was extracted with ether; the ether layers were worked up in the usual manner to yield (*S*)-α-methoxyphenylacetic acid (**3**), $[\alpha]^{22}_D$ +145 (c = 2.1, C_2H_5OH) showing that

(10) Cram, D. J. *Angew. Chem., Int. Ed. Engl.* **1988**, *27(8)*, 1009.
(11) Newman, M. S.; Lednicer, D. *J. Am. Chem. Soc.* **1956**, *78*, 4765.
(12) Newman, M. S.; Wolf, M. *J. Am. Chem. Soc.* **1952**, *74*, 3225.
(13) McKenzie, A.; Walker, N. *J. Chem. Soc.* **1915**, *107*, 1700.

the formation of the acyl chloride **4** was not accompanied by racemization.

(5*R*,8*R*)-(−)-*trans*-5,6,6a,7,8,12b-Hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl Bis[(*S*)-α-methoxyphenylacetate] (5a) and (5*S*,8*S*)-(+)-*trans*-5,6,6a,7,8,-12b-Hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diols Bis[(*S*)-α-methoxyphenylacetate (5b). (5*RS*,8*RS*)-*trans*-5,6,6a,7,8,12b-Hexahydro-1,12-dimethylbenzo[*c*]-phenanthrene-5,8-diol (**2**, X = H) (120 mg, 0.37 mmol) was dissolved in a mixture of dry pyridine (0.38 mL) and dry benzene (12 mL) maintained at 40 °C. (*S*)-α-Methoxyphenylacetyl chloride **4** (185 mg, 1.0 mmol) was added dropwise to the solution and the mixture maintained at 40 °C for 1 h. The solution was poured into cold water and extracted with ether. The combined ether extracts were washed with saturated sodium bicarbonate solution and worked up in the usual way to give a white solid (164 mg, 75%) that was purified by flash chromatography over silica (eluant: ethyl acetate (10%) in light petroleum). The first major fraction, (5*R*,8*R*)-(−)-*trans*-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl bis[(*S*)-α-methoxyphenylacetate] (**5a**) (79 mg, 36%), was recrystallized from methanol to give white needles: mp 163−165 °C; $[\alpha]^{23}_D$ −122 (*c* = 0.3, $CHCl_3$); UV (chloroform) 240 (log ϵ, 2.04) nm; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40 (ddd, *J* = 12.0, 11.4, 11.4 Hz, 1H, H6α), 1.48 (s, 3H), 1.55 (ddd, *J* = 12.6, 9.0, 9.0 Hz, 1H), 1.71−1.82 (m, 1H), 1.95 (ddd, *J* = 12.0, 3.6, 3.4 Hz, 1H), 2.02 (s, 3H), 2.12 (ddd, *J* = 12.6, 9.8, 9.8 Hz, 1H), 3.49 (s, 3H), 3.54 (s, 3H), 3.75 (d, *J* = 10.4 Hz, 1H), 4.89 (s, 1H), 4.98 (s, 1H), 5.97 (dd, *J* = 11.4, 3.4 Hz, 1H), 6.11 (dd, *J* = 9.8, 9.0 Hz, 1H), 6.88 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.03 (d, *J* = 8.0, 0.8 Hz, 1H), 7.08 (d, *J* = 8.0, 0.8 Hz, 1H), 7.09 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.15 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.17, dd, *J* = 8.0, 8.0 Hz, 1H), 7.34−7.52 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 20.7, 33.2, 34.7, 35.2, 43.3, 57.4, 57.5, 69.8, 72.0, 82.7, 120.8, 122.7, 125.6, 126.5, 129.3, 130.9, 127.1, 128.6−128.8, 132.6, 135.1, 135.1, 136.0, 136.3, 136.8, 138.4, 138.6, 170.2, 170.6. Anal. Calcd for $C_{38}H_{38}O_6$: C, 77.3; H, 6.4. Found: C, 77.2; H, 6.6.

The second major fraction, (5*S*,8*S*)-(+)-*trans*-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl bis-[(*S*)-α-methoxyphenylacetate] (**5b**) (75 mg, 34%) was obtained as a white foam that was recrystallized from benzene/light petroleum to give white crystals: mp 79−80 °C; $[\alpha]^{23}_D$ +130 (*c* = 0.5, $CHCl_3$); UV (chloroform) 265.2 (log ϵ 1.48), 259.8 (1.48), 239.2 (1.74) nm; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.42 (s, 3H), 1.59 (ddd, *J* = 12.0, 11.2, 11.2 Hz, 1H), 1.74 (ddd, *J* = 12.8, 8.4, 8.4 Hz, 1H), 1.82−1.94 (m, 1H), 1.96 (s, 3H), 2.29 (ddd, *J* = 12.0, 3.6, 3.6 Hz, 1H), 2.35 (ddd, *J* = 12.8, 9.6, 9.6 Hz, 1H), 3.47 (s, 3H), 3.51 (s, 3H), 3.75 (d, *J* = 11.0 Hz, 1H), 4.85 (s, 1H), 4.97 (s, 1H), 5.97 (dd, *J* = 11.3, 4.1 Hz, 1H), 6.11 (dd, *J* = 8.6, 8.2 Hz, 1H), 6.34 (dd, *J* = 7.8, 1.0 Hz, 1H), 6.65 (dd, *J* = 7.8, 1.0 Hz, 1H), 6.79, dd, *J* = 7.8, 1.0 Hz, 1H), 6.87 (dd, *J* = 7.8, 7.8 Hz, 1H), 6.89 (dd, *J* = 7.8, 7.8 Hz, 1H), 6.99 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.39−7.58 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 20.6, 33.8, 35.1, 35.4, 43.2, 57.3, 57.3, 69.6, 72.0, 82.7, 82.8, 120.6, 122.6, 125.5, 126.3, 127.6, 128.8−129.2, 130.8, 132.5, 134.9, 136.2, 136.3, 136.5, 136.9, 138.3, 138.5, 170.1, 170.5. Anal. Calcd for $C_{38}H_{38}O_6$: C, 77.3; H, 6.4. Found: C, 77.5; H, 6.6.

(5*R*,8*R*)-(−)-*trans*-5,6,6a,7,8,12b-Hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl Diacetate (2a, X = $COCH_3$). Potassium hydroxide (3.0 mg) was added to a solution of (5*R*,8*R*)-(−)-*trans*-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl bis[(*S*)-α-methoxyphenylacetate] (**5a**) (10.0 mg) in 90% aqueous ethanol (4 mL). The reaction mixture was heated at reflux for 1 h, cooled, and diluted with brine. The mixture was extracted with ether, and the combined ether layers were worked up in the usual manner to give (5*R*,8*R*)-(−)-*trans*-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diol (**2a**, X = H) (3.7 mg, 88%) as a white solid: $[\alpha]^{23}_D$ −307 (*c* = 0.5, $CHCl_3$). This resolved diol **2a**, X = H, had an ^{1}H NMR spectrum identical to that of the racemic diol **2**, X = H.

Acetic anhydride (0.2 mL) was added to a solution of the diol **2a**, X = H (3.7 mg), in dry pyridine (1 mL). The mixture was stirred at 50 °C for 15 min. A second portion of acetic anhydride (0.2 mL) was added and the mixture stirred at that temperature for 1 h. The mixture was poured onto ice and extracted with ether. The ether layers were washed with dilute hydrochloric acid (3 M) and worked up in the usual manner to give (5*R*,8*R*)-(−)-*trans*-5,6,6a,7,8,12b-hexahydro-1,-12-dimethylbenzo[*c*]phenanthrene-5,8-diyl diacetate (**2a**, X = $COCH_3$) (2.9 mg, 60%): CD (chloroform) $[\theta]_{295}$ 0; $[\theta]_{270}$ −3630. The ^{1}H NMR spectrum of this diacetate **2a**, X=$COCH_3$, was identical to that of the racemic diacetate **2**, X = $COCH_3$.

(5*R*,8*R*)-(−)-*trans*-5,6,6a,7,8,12b-Hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl Diacetate (2b, X = $COCH_3$). (5*S*,8*S*)-(+)-*trans*-5,6,6a,7,8,12b-Hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl bis[(*S*)-α-methoxyphenylacetate] (**5b**) (10 mg was treated in the same manner as (5*R*,8*R*)-(−)-*trans*-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl bis[(*S*)-α-methoxyphenylacetate] (**5a**) to give (5*R*,8*R*)-(+)-*trans*-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diol (**2b**, X = H) (4.0 mg, 95%) as a white solid: $[\alpha]^{23}_D$ +305 (*c* = 0.2, $CHCl_3$). The ^{1}H NMR spectrum of this resolved diol was identical to that of the racemic diol **2**, X = H.

Esterification of the resolved diol **2b**, X = H, with acetic anhydride gave (5*R*,8*R*)-(+)-*trans*-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl diacetate (**2b**, X = $COCH_3$) (2.9, 75%) as a white solid: CD (chloroform) $[\theta]_{295}$ 0; $[\theta]_{270}$ +3630. The ^{1}H NMR spectrum of this resolved diacetate was identical to that of the racemic diacetate **2**, X = $COCH_3$.

(5*RS*,8*RS*)-*trans*-5,6,6a,7,8,12b-Hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl Di-*p*-bromobenzoate (2, X = *p*-BrC_6H_4CO). *p*-Bromobenzoyl chloride, prepared from *p*-bromobenzoic acid (400 mg, 2.0 mmol), was added to a solution of (5*RS*,8*RS*)-*trans*-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diol (**2**, X = H) (200 mg, 0.7 mmol) in dry pyridine (4 mL) held at 40 °C. The reaction mixture was heated at that temperature for 1 h, at which time it was poured into cold water. The mixture was filtered, and the solid collected was purified by column chromatography over silica (eluant: dichlorometane (10%) in light petroleum) to give (5*RS*,8*RS*)-*trans*-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl di-*p*-bromobenzoate (**2**, X = *p*-BrC_6H_4CO) (180 mg, 42%). It was recrystallized from chloroform/methanol to give pale yellow crystals: mp 230 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.59 (s, 3H), 1.75 (ddd, *J* = 12.3, 11.1, 11.1 Hz, 1H), 1.93 (ddd, *J* = 12.7, 8.7, 8.7 Hz, 1H), 2.03−2.10 (m, 1H), 2.12 (s, 3H), 2.44 (ddd, *J* = 12.3, 3.6, 3.6 Hz, 1H), 2.49 (ddd, *J* = 12.7, 9.6, 9.6 Hz, 1H), 3.98 (d, *J* = 11.0 Hz, 1H), 6.26 (dd, *J* = 11.1, 4.1 Hz, 1H), 6.42 (dd, *J* = 8.8, 8.7 Hz, 1H), 6.95 (d, *J* = 7.6, 1.0 Hz, 1H), 7.14−7.16 (m, 4H), 7.31 (d, *J* = 7.6 Hz, 1H), 7.62 and 7.99 (AA′BB′, *J* = 8.6 Hz, 4H), 7.67 and 8.08 (AA′BB′, *J* = 8.6 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.7, 20.7, 33.7, 35.0, 35.3, 43.3, 70.0, 72.7, 120.5, 122.7, 125.4, 126.4, 128.4, 129.1, 129.4, 130.7, 131.7, 132.0, 132.5, 135.4, 135.7, 137.4, 138.6, 139.1, 166.3, 166.7.

Resolution of (5*RS*,8*RS*)-*trans*-5,6,6a,7,8,12b-Hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diols Di-*p*-bromobenzoate (2, X = *p*-BrC_6H_4CO). The resolution of the diesters **2a**, X = *p*-BrC_6H_4CO, and **2b**, X = *p*-BrC_6H_4CO (40 mg), was achieved by preparative HPLC with a chiral stationary phase (eluant: 2-propanol (0.4%) in light petroleum). (5*R*,8*R*)-(−)-*trans*-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl di-*p*-bromobenzoate (**2a**, X = *p*-BrC_6H_4CO) (15 mg) was obtained as the first fraction, $[\alpha]^{23}_D$ −198 (*c* = 0.3, $CHCl_3$). A sample was recrystallized from chloroform/methanol, mp 211 °C, and the X-ray crystal structure was obtained.

The second fraction consisted of (5*S*,8*S*)-(+)-*trans*-5,6,-6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl di-*p*-bromobenzoate (**2b**, X = *p*-BrC_6H_4CO) (10 mg), $[\alpha]^{23}_D$ +200 (*c* = 0.2, $CHCl_3$). The ^{1}H NMR of the racemic diester **2**, X = *p*-BrC_6H_4CO, and the resolved diesters **2a**, X = *p*-BrC_6H_4-CO, and **2b**, X = *p*-BrC_6H_4CO, were identical.

Hydrolysis of (5*S*,8*S*)-(+)-*trans*-5,6,6a,7,8,12b-Hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl Di-*p*-bromobenzoate (2b, X = *p*-BrC_6H_4CO). (5*S*,8*S*)-(+)-*trans*-5,6,6a,7,8,12b-Hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-

5,8-diyl di-*p*-bromobenzoate (**2b**, X = *p*-BrC_6H_4CO) (6.3 mg, 0.01 mmol) was added to a 90% aqueous ethanol solution of sodium hydroxide (3 mg in 4 mL). The reaction mixture was treated in a similar manner as for the base hydrolysis of diester **5a** to give (5*S*,8*S*)-(+)-*trans*-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diol (**2b**, X = H) (1 mg, 36%), $[\alpha]^{23}_D$ +270 (*c* = 0.1, $CHCl_3$). This resolved diol has an ^1H NMR spectrum identical to that of the racemic diol **2**, X = H.

Structure Determination. The authors have deposited atomic coordinates for the structures depicted in Figures 1 and 3 with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, upon request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

Acknowledgment. We thank the Australian Research Council for financial support (to S.S., L.D.F., and T.W.H.) and the Australian Government for an Australian Postgraduate Research Award (to J.C.).

JO961254Z