Circular Dichroism of 9,10-Dihydrophenanthrene Derivatives Reveals both the Absolute Configuration and Conformation: A Novel Approach to Mislow's Helicity Rule

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Abstract: The absolute configuration and the conformation of 9,10-*trans*-disubstituted 9,10-dihydrophenanthrenes, known chiral metabolites of phenanthrene-9,10-oxide, have been determined by circular dichroism. The absolute configuration assignment is based on the sign of the long-wavelength Cotton effect (A-band), which is conformation invariant and originates from benzylic chirality. This provides a new interpretation of the Mislow biphenyl-helicity rule for the case of the 9,10-dihydrophenanthrene chromophore. The sign of the B-band Cotton effect reflects the conformation of the biphenyl chromophore in 9,10-dihydrophenanthrenes. It is shown that the origin of chiroptical properties of 9,10-dihydrophenanthrenes is closely related to those of 5,6-*trans*-disubstituted 1,3-cyclohexadienes.

Keywords: circular dichroism · configuration determination · conformation analysis · dihydrophenanthrenes

Introduction

Circular dichroism (CD) spectroscopy, along with X-ray diffraction analysis, is a widely used method for the determination of absolute configuration.[1] The advantages of the CD method are the small amounts of sample required and the simplicity of obtaining the spectra in solution. However, unlike X-ray diffraction results, CD spectra provide only a limited amount of structural information. Unless extensive theoretical calculations of the CD spectra of all possible conformers of configurational isomers are performed, and the results compared with the experimental CD curve,[2] the absolute configuration can only be obtained from simple analysis of the CD spectrum if the conformation is known. Conversely, the conformation can be determined if the absolute configuration of a molecule is known.[3] This notion is applicable, for example, to the well-known and widely used CD exciton chirality method,[4] or to the octant rule.[5]

The intrinsic limitation of the information available from the CD data could be eliminated if Cotton effects, arising by two different mechanisms from two different electronic transitions of the same chromophore, were observed and analyzed. Although such a situation is rare, we anticipated that a suitable chromophore to test is the bridged-biphenyl chromophore. This chromophore has received a great deal of attention, since it represents an important group of organic compounds whose stereochemistry has been thoroughly studied by the groups of Mislow[6] and Sandström.[7] The absolute configuration of suitably substituted 2,2′-bridged biphenyls (Figure 1), such as atropisomers when $n = 4$, or dominant conformers when $n = 2$ or 3, can be determined by CD spectroscopy.[8] In the case of 9,10-dihydrophenanthrene the barrier for enantiomer interconversion is low; the computed (MM2) planar transition state geometry is 5.25 kcal mol^{-1} above the molecular geometry of minimum energy.[9]

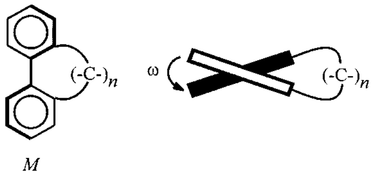

Figure 1. Bridged biphenyl chromophore: definition of the torsion angle ω (negative for M helicity).

Central to this problem is the nonplanarity of the biphenyl chromophore (D_2 symmetry). Its chiroptical properties are related to the sign and magnitude of the biphenyl twist angle ω.[10] Mislow and co-workers have proposed an experimental rule for the sign of the Cotton effect of the so-called conjugation band K (A-band according to Suzuki[11]): a positive Cotton effect is observed for bridged biphenyls of

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M helicity, which do not carry polar substituents in the benzene rings[6] and have $0^\circ > \omega > -90^\circ$. The position of the λ_{max} for this transition is highly dependent on the angle ω: the larger the angle ω (i.e., the longer the bridge), the more blue-shifted λ_{max}. Typically, for $n = 2$ ω is in the range 17–19° and λ_{max} is at approximately 265 nm, whereas for $n = 4$ ω increases to 60° and λ_{max} is shifted to 235–238 nm.[12] The electronic transition associated with the A-band is polarized parallel to the long axis, as determined by linear dichroism studies of Sagiv et al.[13a] and by polarized fluorescence studies of Edwards and Simpson.[13b] The location of the intense B-band appears less sensitive to the changes of the torsion angle ω.[14] This transition is found at around 210 nm and is polarized perpendicular to the long axis (Figure 2). It is particularly useful for stereochemical assignments as it generates an exciton-split Cotton effect through the in-phase and out-of-phase combinations of the ^1B_b transitions.

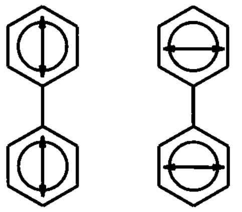
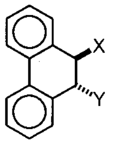


Figure 2. Polarization directions of the two biphenyl transitions important for stereochemical assignments. Left: Mislow K-band or Suzuki A-band. Right: Suzuki B-band.

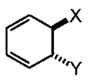
Results and Discussion

The 9,10-dihydrophenanthrene system ($n = 2$, Figure 1) is of exceptional importance as it is found in numerous chiral compounds of natural[15] and synthetic[16, 17] origin. Although this system is of lower symmetry (C_2), its transition polarizations and chiroptical properties were analyzed according to the biphenyl model. 9,10-Dihydrodiol (**1**) is the main metabolite of phenanthrene,[18] the simplest polycyclic aromatic hydrocarbon to contain both a K and a bay region (the structural features associated with carcinogenicity and mutagenicity).[19] Its absolute configuration was determined by chemical degradation to a (*R*,*R*)-tartaric acid derivative, but the CD/ORD spectra were assigned to the wrong conformer,[20] as later became evident from ^{1}H NMR data of Jerina et al.[18] These authors stated that "the sign of the CD band in the region of 230 nm is diagnostic of the helicity of the biphenyl chromophore and can be used for the assignment of absolute configuration if the conformation (…) of the C-9 and C-10 substituents is known".[19]

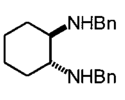
To demonstrate that there is direct relation between the CD spectra, the absolute configuration, and the conformation of 9,10-dihydrophenanthrene derivatives, we analyzed the conformation and CD spectra of derivatives **1**–**8** (Table 1). We also synthesized the optically active 9,10-dihydrophenanthrenes **9**–**11**, *trans*-9,10-disubstituted with carbon substituents, which were hitherto not reported.



	X	Y
1	OH	OH
2	OH	OG*
3	OH	NH_2
4	OH	SG*
5	OCH_2COOH	OCH_2COOH
6	OAc	OAc
7	OAc	N_3
8	OAc	Br
9	COOH	COOH
10	COOMe	COOMe
11	CH_2OH	CH_2OH
12	Me	Me



13 **X, Y** = OH
14 **X, Y** = OAc



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*OG = *O*-α-*D*-glucuronosyl
*SG = *S*-glutathionyl

Table 1. Comparative Cotton effects of *trans*-9,10-disubstituted phenanthrenes.

	A-band (260–275 nm)	B-band (210–235 nm)	Conformer (from NMR)[a]	Solvent	Ref.
1	−	+	dieq. *P*	MeOH	[b]
1	−	−	diax. *M*	H_2O	[21][c]
2	−	+	dieq. *P*	MeOH	[22]
2	−	−	diax. *M*	H_2O	[22]
3	−	+	dieq. *P*	MeOH	[19]
4	−	−	diax. *M*	[d]	[23]
5	−	−	diax. *M*	MeOH	[24]
6	−	−	diax. *M*	dioxane	[b]
7	−	−	diax. *M*	MeOH	[19]
8	−	−	diax. *M*	MeOH	[19]

[a] For dominant diequatorial conformer $J(9H,10H) > 8$ Hz, for dominant diaxial conformer $J(9H,10H) < 6$ Hz. [b] This work. [c] Data reported for (*S*,*S*)-enantiomer. [d] 0.025 M NH_4OAc in H_2O.

We note that the sign of the Cotton effect of the A-band is solvent/conformation independent without exception (see also the earlier observation of Armstrong[22]) It is also documented that a chromophoric substituent in the benzylic position of a 9,10-dihydrophenanthrene derivative induces Cotton effects owing to the bichromophoric exciton coupling.[17] Taking these two observations into account we propose here a reformulation of Mislow's rule: *benzylic chirality is the primary factor determining the sign of the 270 nm (A-band) Cotton effect in 9,10-dihydrophenanthrenes.* For the absolute configuration shown (Figure 3) the benzylic chirality is negative (left-handed) and the sign of the A-band Cotton effect is invariably negative (Table 1), regardless whether the conformation is diaxial or diequatorial.

A striking similarity is observed between the long-wavelength Cotton effects of 9,10-dihydrophenanthrenes and 1,3-cyclohexadienes.[25, 26] In both systems the long-wavelength transitions are polarized perpendicularly to the molecular C_2 axis and have similar excitation energies (ca. 265 nm for 1,3-cyclohexadienes and ca. 270 nm for 9,10-dihydrophenanthrenes). The signs of the Cotton effects depend strongly on the configuration of the allylic substituents in the case of 1,3-cyclohexadienes or on the configuration of the benzylic substituents in the case of 9,10-dihydrophenanthrenes. The

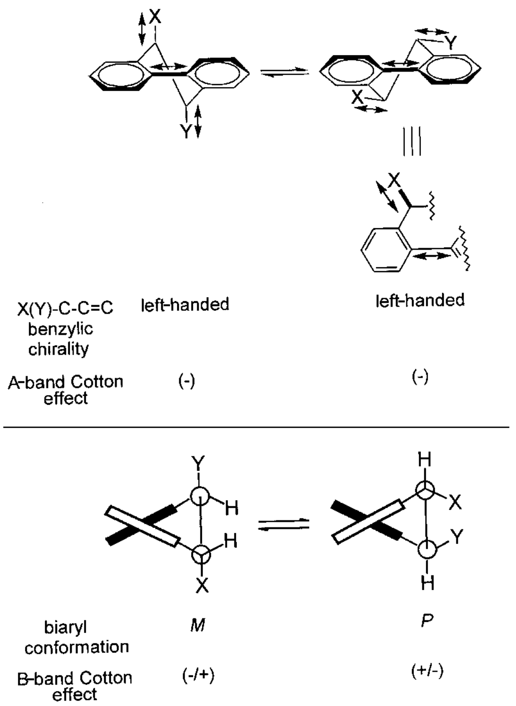

Figure 3. Configurational and conformational dependence of A- and B-band Cotton effects in derivatives of 9,10-dihydrophenantrene (one enantiomer shown).

Cotton effects in both cases are generated through the mechanism involving interaction of the π–π* transition dipole with the polarizabilities of the allylic (benzylic) C–X(Y) bonds. A comparison given in Table 2 serves as an example.

Table 2. Comparison of the long-wavelength Cotton effects (Δε).

	9,10-Dihydrophenanthrene	1,3-Cyclohexadiene[a]
X,Y = OH	**1**	**13**
	– 7.2 (270 nm)[b]	– 10.0 (256 nm)[b]
X,Y = OAc	**6**	**14**
	– 9.2 (262 nm)[c]	– 12.6 (254 nm)[b]

[a] Data from ref. [27], reported for *S,S* enantiomer. [b] In methanol. [c] In dioxane.

(*R*,*R*)-9,10-Dihydroxy-9,10-dihydrophenanthrene (**1**) in methanol displays a negative Cotton effect at 270 nm. From the coupling constant *J*(9H,10H) = 9.3 Hz measured by us in CD_3OD (satellite band), it is evident that the conformation is predominantly diequatorial. For the diacetoxy derivative **6** the Cotton effect at 262 nm is also negative despite the dominant diaxial conformation (*J*(9H,10H) = 5.1 Hz in CD_3OD and 5.2 Hz in $CDCl_3$ (satellite band)). Likewise, the diol **13** of *R*,*R* configuration displays a negative Cotton effect at 256 nm in a mostly diequatorial conformation, whereas the diacetoxy derivative **14** gives an even stronger negative Cotton effect in a presumably diaxial conformation.[27]

Further support for the A-band Cotton effect of 9,10-dihydrophenanthrenes originating from the benzylic-bond polarizability comes from the exceptionally large Cotton effects of derivatives **4** ($\Delta\varepsilon = -25$ at 273 nm)[23] and **8** ($\Delta\varepsilon = -43.5$ at 274 nm).[19] These derivatives are substituted with highly polarizable benzylic axial C–S and C–Br bonds, respectively.

Solvent-induced changes of the conformation of 9,10-dihydrophenanthrene derivatives bearing small hydroxy group(s) have been observed. Dominance of the diequatorial *P* conformer is observed in methanol (compounds **1**–**3** in Table 1) and in other solvents that allow for intramolecular hydrogen bonding to stabilize the arrangement of diequatorial hydroxy group(s).[22] Water brings about conformational changes to diaxial conformers (**1**, **2**), presumably by disrupting intramolecular hydrogen bonding. Our steric energy calculations at both semiempirical PM3 and B3LYP/6-31G(d,p)[28] levels predict that the diequatorial conformer of **1** is at least 3 kcal mol^{-1} more stable than the diaxial one, solvent effect not included.

In all these cases the diequatorial to diaxial conformational change results in a change of sign of the B-band exciton-type Cotton effect at 235–210 nm (Table 1) from positive (*P* helicity) to negative (*M* helicity). As noted previously by Jerina[19, 29] and Armstrong,[22] it is just the sign of the short-wavelength B-band Cotton effects of 9,10-dihydrophenanthrenes that correctly reports the helicity of the biaryl chromophore (Figure 3).

To provide additional support for the configurational/conformational model of optical activity of 9,10-dihydrophenanthrene, we synthesized the hitherto unknown optically active derivatives **9**–**11**, bearing the carboxy, methoxycarbonyl, and hydroxymethyl substituents in a *trans* configuration. The requisite racemic *trans*-diacid **9** was obtained from phenanthrene according to the literature procedure.[30] The racemate was efficiently resolved by crystallization of the 1:1 salt with (*R*,*R*)-*N*,*N*′-dibenzyl-*trans*-1,2-diaminocyclohexane (**15**). The (–) enantiomer of the diacid **9** had *S*,*S* absolute configuration, as determined by analysis of the X-ray diffraction of the salt **9** + **15** (Figure 4, top).

Strikingly, the bulky carboxy substituents occupy the axial positions in the near-perfect C_2-symmetric molecule of diacid **9**. The same C_2-diaxial structure has been also obtained from the analysis of the X-ray diffraction pattern of *rac*-**9**, which crystallizes as a racemic compound. The torsion angle ω of the biphenyl chromophore was –21.5° for the *S*,*S* enantiomer of *rac*-**9**.

The diester **10** and bishydroxymethyl derivative **11** were obtained from **9** by standard procedures (diazomethane, followed by $LiAlH_4$ reduction). X-ray diffraction analysis of **11** (Figure 4, bottom) confirmed the preference of the benzylic carbon substituents for the axial position in the 9,10-dihydrophenanthrene skeleton. The corresponding torsion angle of the biphenyl, $\omega = -21.3°$, is very close to that of **9**. Independent confirmation for the axial configuration of the benzylic-carbon substituents in solution has been obtained from the measurement of the *J*(9H,10H) coupling constant in the diester **10** (from the satellite band). Its low value of 3.0 Hz (in $CDCl_3$) is typical for a diequatorial hydrogen atom configuration. The diequatorial structure of diacid **9** is less stable than the diaxial one, according to both B3LYP/6-31G(d,p) ($\Delta E = 1.76$ kcal mol^{-1}) and PM3 semiempirical calculations ($\Delta E = 1.85$ kcal mol^{-1}). The torsion angle ω calculated by the DFT method for the diaxial conformer of **9** is –21.6°.

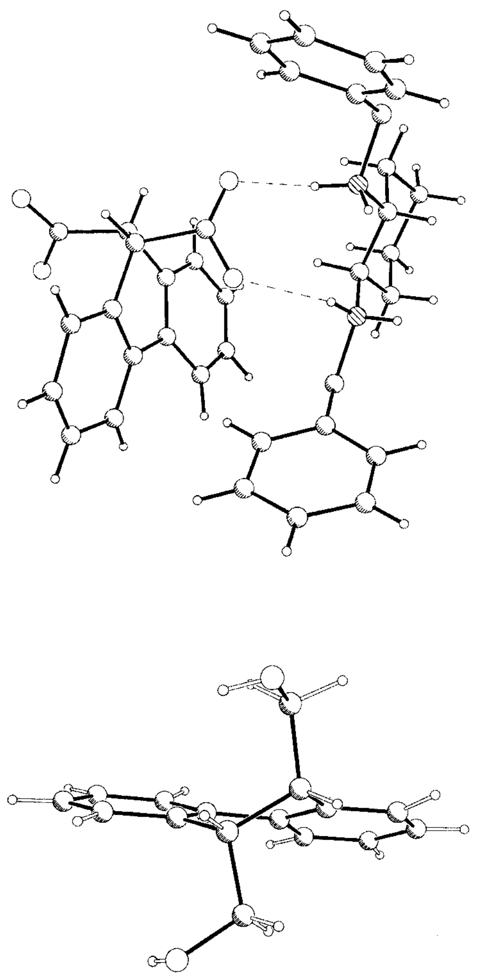

Figure 4. Structure of the salt **9**+**15** (top) and the diol **11** (bottom) as determined by X-ray diffraction analysis.

The CD spectra of **9**–**11** (Figure 5) show in all cases a negative A-band Cotton effect at approximately 268 nm and a negative exciton couplet at 232/210 nm due to the B-band transition. These Cotton effects correspond to the UV maxima at approximately 268 nm and 210–212 nm, respectively. The data are in full agreement with the general model of optical activity of 9,10-dihydrophenanthrenes substituted axially in the benzylic positions, as presented in Figure 3 and Table 1. In the light of these data the published[7c] CD data for *trans*-9,10-dimethyl-9,10-dihydrophenanthrene (**12**), which are of mirror image to those of **9**–**11**, strongly suggest that the absolute configuration of **12** is not 9*S*,10*S* as postulated, but rather 9*R*,10*R* (*ent*-**12**). This statement is in agreement with the results of force-field calculations of Sandström[7c] and our B3LYP/6-31G(d,p) energy optimization, both of which place the diequatorial conformer of **12** in a state of higher steric energy (by ca. 3 kcal mol^{-1}) than the diaxial one.

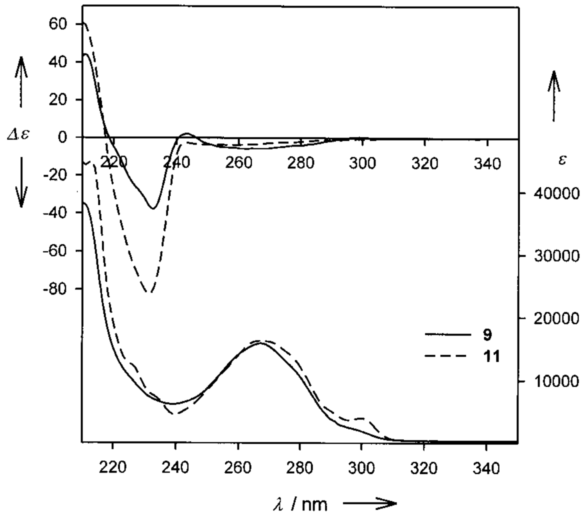

Figure 5. CD (top) and UV (bottom) spectra of 9,10-dihydrophenantrene derivatives **9** and **11** in methanol (CD and UV spectra of **10** are nearly identical to those of **9**).

Conclusion

We have been able to demonstrate that, in the case of 9,10-dihydrophenanthrenes, the primary origin of the long-wavelength Cotton effect (A-band) is not the nonplanarity of the biphenyl chromophore, as stated by Mislow's rule. Instead, we propose a new model that correlates the sign of the A-band Cotton effect with the configuration of benzylic carbon atoms (Figure 3). The sign of this Cotton effect is conformation (diequatorial/diaxial, *P*/*M*) invariant. On the other hand, the sign of the B-band Cotton effect, presumably of exciton-coupling origin, is a sensitive probe of biaryl helicity (*P* or *M*). Summarized, the CD spectrum of a *trans*-9,10-disubstituted 9,10-dihydrophenanthrene reports both the absolute configuration and the conformation of the molecule, thus abolishing the common belief that a limited amount of stereochemical information is available from CD measurements.

The present study also confirms the strong preference of 9,10-substituents for a diaxial position, the only exception to this being the small hydroxy substituent, capable of forming an intramolecular hydrogen bond with the neighboring substituent in the equatorial position.

The conclusions from the present study are strengthened by comparison with the results of the studies by Jerina et al. on the K-region *trans*-dihydrodiols from tetracyclic analogues of 9,10-dihydrophenanthrene.[29] Their results fit into the model of optical activity of 9,10-dihydrophenanthrene presented here. Further examples are to be published from this laboratory.

Experimental Section

Computational methods: Semiempirical PM3 and DFT computations were performed with Gaussian 98.[28]

X-ray diffraction studies (compounds 9 + 15, rac-9 and 11)

*Crystal data for **9**+**15***: It was difficult to obtain crystals of good X-ray quality. For a crystal grown from ethanol we were able to collect the data set that revealed the structure, but it could not be refined satisfactorily due to the poor diffracting power of the crystal and consequent low data-to-parameter ratio. However, the model provides unequivocal evidence that (*R*,*R*)-diamine **15** associates preferably with the (*S*,*S*)-enantiomer of **9**. $C_{36}H_{38}N_2O_4 \cdot 3H_2O$, $M_r = 616.73$. Crystal dimensions $0.4 \times 0.4 \times 0.3$ mm. X-ray measurements performed using $Cu_{K\alpha}$ radiation ($\lambda = 1.54178$ Å, $\mu = 0.68$ mm^{-1}), on a KM4 diffractometer, with a graphite crystal monochromator in the incident beam. Crystal system: tetragonal, space group $P4_12_12$, $a = 13.870(2)$, $b = 13.870(2)$, $c = 35.102(7)$ Å, $V = 6752.9(3)$ Å^3, $Z = 8$, $\rho_{calcd} = 1.213$ g cm^{-3}. Maximum θ was 62°, and *hkl* ranges were: 0/15, 0/15, 0/37, respectively. Of the 4884 reflections collected, 4421 were unique (Bijvoet pairs not merged) and 1015 were considered as observed with $I > 2\sigma(I)$. Final *R* value was 0.092 for 1015 observed reflections. The absolute structure of the crystal was assumed on the basis of the known absolute configuration of *N,N'*-dibenzyl-(*R,R*)-1,2-diaminocyclohexane.

*Crystal data for rac-**9***: The crystal of *rac*-**9**, of approximate dimensions 0.20 × 0.25 × 0.35 mm, was obtained from ethanol. The X-ray measurements were performed at 295 K with $Cu_{K\alpha}$ radiation. Crystal system: triclinic, space group $P\bar{1}$, $C_{16}H_{12}O_4$, $M_r = 268.26$, $a = 7.519(2)$, $b = 9.300(2)$, $c = 9.808(2)$ Å, $\alpha = 68.58(3)$, $\beta = 82.25(3)$, $\gamma = 81.70(3)^o$, $V = 629.3(3)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.416$ g cm^{-3}, $Cu_{K\alpha}$ radiation ($\lambda = 1.54178$ Å), $\mu = 0.85$ mm^{-1}, KM4 diffractometer,[31] with a graphite crystal monochromator in the incident beam. Maximum θ was 63.1°, and *hkl* ranges were: −8/8, −10/10, 0/11, respectively. Of the total 2065 reflections measured, 1984 were unique. Final *R* value was 0.038 for 1414 observed reflections [$I > 2\sigma(I)$] and 0.068 for all data.

*Crystal data for **11***: The crystal of **11**, of approximate dimensions 0.30 × 0.30 × 0.15 mm, was obtained from ethanol. The X-ray measurements were performed at 295 K using $Cu_{K\alpha}$ radiation. Crystal system: orthorhombic, space group $P2_12_12_1$, $C_{16}H_{16}O_2$, $M_r = 240.29$, $a = 7.1218(7)$, $b = 8.6384(7)$, $c = 21.108(2)$ Å, $V = 1298.6(4)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.229$ g cm^{-3}, $Cu_{K\alpha}$ radiation ($\lambda = 1.54178$ Å), $\mu = 0.63$ mm^{-1}, KM4 diffractometer,[31] with a graphite crystal monochromator in the incident beam. Maximum θ was 65.1°, and *hkl* ranges were: −8/8, 0/10, 0/24, respectively. Of the total 2992 reflections measured, 2202 were unique (Bijvoet pairs not merged). Final *R* value was 0.035 for 2018 observed reflections [$I > 2\sigma(I)$] and 0.041 for all data. Although the value of the Flack parameter[32] (0.006) indicates that the chosen enantiomorph is the correct one, the standard uncertainty (0.282) of this parameter indicates its weak inversion-distinguishing power. Since **11** was obtained from the (−)-enantiomer of **9**, its absolute configuration is known and does not need to be confirmed by X-ray diffraction.

The structures were phased by direct methods (SHELXS86 program[33]) and refined by full-matrix least-squares with the SHELXL97 program.[34] A Siemens computer graphics program was used to prepare drawings.[35] Anisotropic thermal parameters were refined for all non-hydrogen atoms. For *rac*-**9** the hydrogen atoms were located on difference Fourier maps, while those for **11** were placed at calculated positions (C–H = 0.96 Å), except for the hydroxyl hydrogen atoms, which were located on a difference Fourier map. Only the hydroxyl hydrogen atoms were allowed to refine freely. All remaining hydrogen atoms were refined in a "riding model" with their U_{iso} increased by 1.2 compared to U_{eq} of atoms to which they were bonded. CCDC-181879, CCDC-181878, and CCDC 185938 contain the supplementary crystallographic data for this paper (*rac*-**9**, **11**, and **9** + **15**, respectively). These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44)1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk).

(9*S*,10*S*)-9,10-Dihydrophenanthrene-9,10-dicarboxylic acid (9): Racemic diacid **9**[30] (1 mmol) and (1*R*,2*R*)-*N,N'*-dibenzyl-1,2-diaminocyclohexane (**15**)[36] (1 mmol) were dissolved in ethanol (4.5 mL), and the solution was left to crystallize. The crystalline 1:1 salt was filtered and recrystallized from ethanol twice. The salt (m.p. 87–95 °C, yield 80–85 %) was treated with 2 N NaOH and extracted with dichloromethane to recover **15**; the alkaline solution was then acidified with 4 N HCl. The diacid **9** was filtered and recrystallized from a methanol/water mixture. Yield 95 %; m.p. 227–230 °C; $[\alpha]_D^{20} = -141$ ($c = 2$ in methanol); ^{1}H NMR (300 MHz, CD_3OD, 23 °C, TMS): $\delta = 4.34$ (s, 2H), 7.26–7.38 (m, 6H), 7.80 (d, ^3J(H,H) = 7.2 Hz, 2H).

(9*S*,10*S*)-9,10-Dihydrophenanthrene-9,10-dicarboxylic acid dimethyl ester (10): Optically active diacid **9** (1 mmol) in tetrahydrofuran (5 mL) was methylated with excess diazomethane in diethyl ether. After removal of the solvents, diester **10** was crystallized from ethanol. Yield 96 %; m.p. 117–121 °C; $[\alpha]_D^{20} = -143$ ($c = 2$ in methanol); ^{1}H NMR (300 MHz, $CDCl_3$, 23 °C, TMS): $\delta = 3.55$ (s, 6H), 4.40 (s, 2H), 7.24–7.39 (m, 6H), 7.74 (d, ^3J(H,H) = 7.7 Hz, 2H).

Enantiomeric excess of **10** was determined by ^{1}H NMR spectra with a lanthanide-induced-shift reagent, tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorate]europium in $CDCl_3$. The methyl signals of the diester **10** were integrated to give *ee* 90 %.

(9*S*,10*S*)-9,10-Dihydro-9,10-bis(hydroxymethyl)phenanthrene (11): Diester **10** (1 mmol) in anhydrous diethyl ether (10 mL) was treated portionwise with $LiAlH_4$ (2 mmol), and the mixture stirred overnight at room temperature. Excess $LiAlH_4$ was destroyed by careful addition of water, followed by 5 % HCl. The mixture was extracted with diethyl ether, the extracts dried ($MgSO_4$), the solvent removed, and the product **11** crystallized from methanol. Yield 78 %; m.p. 160–165 °C; $[\alpha]_D^{20} = -172$ ($c = 2$ in methanol); ^{1}H NMR (300 MHz, CD_3OD, 23 °C, TMS): $\delta = 3.21$–3.32 (m, 4H), 3.42–3.47 (m, 2H), 7.22–7.34 (m, 6H), 7.81 (d, ^3J(H,H) = 7.4 Hz, 2H).

Acknowledgements

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