Highly Efficient Chirality Inductors Based on (5*RS*,8*RS*)-*trans*-5,6,6a,7,8,12b-Hexahydrobenzo[*c*]phenanthrene-5,8-diol

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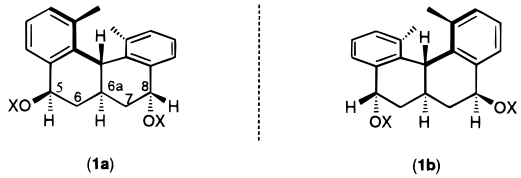
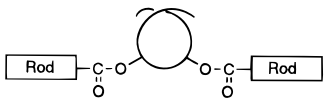
Received March 10, 1997

Introduction

In a previous paper,[1] we described the preparation and resolution of (5*RS*,8*RS*)-*trans*-5,6,6a,7,8,12b-hexahydrobenzo[*c*]phenanthrene-5,8-diol (**1**, X = H), a novel molecular template of the general shape depicted by structure (**2**). Esterification of the resolved diols (**1a**, X = H) and (**1b**, X = H) with a variety of acyl chlorides leads to a series of chiral molecules (**2**) with "rods" of variable length and nature.

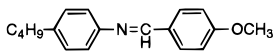


(**1a**) (**1b**)



(**2**)

It is possible to convert a nematic mesophase into a chiral nematic (cholesteric) mesophase by the addition of a chiral inducer[2] and to express the chirality-inducing power of the additive in terms of a molecular property, β_M.[2] This paper deals with the determination of the β_M values of five derivatives of the diol **1**, X = H, in the well-known[2] nematic phase, *N*-(4-methoxybenzylidene)-4′-butylaniline (MBBA) (**3**), to explore whether the chiral



(**3**)

template could transfer chirality intermolecularly. A search of the literature revealed few effective[2] (large β_M) chiral inducers except the very few compounds listed by Heppke.[3]

This work describes the preparation of five inducers of the general structure **2** synthesised from **1a**, X = H, and **1b**, X = H.

Results and Discussion

A series of (5*RS*,8*RS*)-*trans*-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl diesters (**1**, X = $COCH_3$, X = $CO(CH_2)_2CH_3$, X = $CO(CH_2)_{10}CH_3$, X = CO-*p*-$C_6H_4(CH_2)_6CH_3$, and X = CO-*p*-$(C_6H_4)_2(CH_2)_6CH_3$) were synthesized by esterification of (5*RS*,8*RS*)-*trans*-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diol (**1**, X = H) with acetic anhydride to give the diacetate (**1**, X = $COCH_3$),[1] and with the corresponding acyl chlorides to give the remaining esters.

Table 1. Helical Twisting Powers (β_M) of the Chiral Diesters 1[c]

entry	X		$[\alpha]^{20}_D$ [a] (c)	β_M[b]
1	$COCH_3$	(**a**)	−251.2 (0.3)	7.70 ± 0.01
		(**b**)	+230.7 (0.9)	7.87 ± 0.03
2	$CO(CH_2)_2CH_3$	(**a**)	−177.5 (0.2)	7.77 ± 0.07
		(**b**)	+207.9 (0.2)	7.83 ± 0.04
3	$CO(CH_2)_{10}CH_3$	(**a**)	−131.6 (0.5)	12.61 ± 0.14
		(**b**)	+156.1 (0.6)	12.10 ± 0.13
4	CO-*p*-$C_6H_4(CH_2)_6CH_3$	(**a**)	−110.0 (0.2)	59.3 ± 0.1
		(**b**)	+119.2 (0.1)	54.5 ± 0.1
5	CO-*p*-$(C_6H_4)_2(CH_2)_6CH_3$	(**a**)	−72.9 (0.5)	147.9 ± 0.1
		(**b**)	+87.1 (0.3)	142.6 ± 0.1

[a] Chloroform was used as solvent for the optical rotation measurements. The values are accurate to about 5% due to the small size of samples used. [b] Signs of β_M were not determined. [c] Measurements were taken at 22 °C.

The X-ray crystal structure of the diacetate (**1**, X = $COCH_3$)[1] indicated that the ester chains are in pseudoequatorial positions in relation to the helical framework and are approximately coplanar, thus giving an elongated shape. The ORTEP plot of the diacetate (**1**, X = $COCH_3$)[1] has a remarkable similarity to the conformation derived from ^{1}H NMR data,[1] indicating that the conformation of the diacetate (**1**, X = $COCH_3$) is the same in solution ($CDCl_3$) and in crystal form. All the remaining diesters produced from the diol (**1**, X = OH) were assumed to adopt a similar shape on the basis of the similarity of their ^{1}H NMR data, in particular the vicinal coupling constants of the protons on C5, C6, C6a, C7, and C8 (see the Experimental Section).

The diesters were resolved directly using HPLC with a chiral column (Regis Pirkle type 1-A chiral column)[1] to give the enantiomers **1a** and **1b** in high enantiomeric purity (a single peak in HPLC using the same column), and their helical twisting powers (β_M) towards the nematic phase MBBA were examined by the droplet method.[4] The parameter β_M has been employed to define the twisting ability of the chiral solute in the nematic phase and is expressed as the inverse of the helical pitch value ($1/p$) of the macrohelical structure for a given molar solute concentration (c) by the relation: $1/p = \beta_M c$. The pitch values were obtained at a number of different concentrations, and the inverse of the pitch values were plotted against the molar solute concentration. β_M values were calculated as the slope of the line of best fit to the data points. The molar concentrations of the chiral solutes were generally between 0.5 and 5 mol %, at which point, the addition of more solute destroyed the macrohelical structures produced. There were no observable temperature effects over the nematic range of MBBA. The results are summarized in Table 1.

Assignment of absolute stereochemistry (that is, the attribution of the letter **a** or **b**) was based on the sign of $[\alpha]^{20}_D$ for entries 2−5 by analogy with entry 1, which is based on crystallographic data.[1] Significantly, all the enantimers with negative specific rotation were eluted first. However, if these assignments were wrong, it is unimportant for the present purposes, as this work is concerned only with the *absolute* values of β_M. It is

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(2) Solladié, G.; Zimmermann, R. G. *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 348, and references cited therein.
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S0022-3263(97)00431-3 CCC: $14.00

gratifying to note that the β_M values for each pair of **a** and **b** are very close, thus giving further confidence in the experimental accuracy of the determinations of the inducing powers.

It can be seen that while the extension of the "rods" in structure **2** from two to four atoms produces no significant increase in β_M (entries 1 and 2), and the significant lengthening involved in changing to the bis-laureate (entry 3, rods of 12 atoms length) produces only a modest increase. However, the "stiffening" of the rods without any increase in the numbers of atoms (entry 4) produces a dramatic increase of β_M from ca. 12 to 57. The incorporation of rods which are both longer (16 atoms) and stiffer (entry 5) produces a further ca. three-fold increase in β_M to give a chiral inducer of the same order of magnitude of β_M as the "chiral dopants with unusual twisting powers" reported by Heppke.[3]

We have thus synthesized a chiral molecular template which can serve as a basis for the preparation of a series of chiral inductors and appear to have determined a relationship between structure (length and stiffness of rods) and the twisting power β_M.

Experimental Section

(5*SR*,8*SR*)-*trans*-5,6,6a,7,8,12b-Hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl Dibutyrate (1, X = $CO(CH_2)_2CH_3$). Butyric acid (9.6 g, 0.12 mol) was added dropwise to thionyl chloride (10 mL) at reflux over a period of 30 min. When all of the acid had been added, the reaction mixture was heated at reflux under nitrogen for 30 min. The mixture was distilled and the fraction boiling between 70 and 100 °C was collected. Redistillation provided *butyryl chloride* (11 g, 86%), bp 100−101 °C (lit.[5] bp 101−102 °C). ν_{max} (chloroform) 1808 (s) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.00 (t, J = 6.0 Hz, 3H), 1.70−1.80 (m, 2H), 2.78 (t, J = 7.8 Hz, 2H).

(5*SR*,8*SR*)-*trans*-5,6,6a,7,8,12b-Hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diol (**1**, X = H) (112 mg, 0.4 mmol) was dissolved in dry pyridine (10 mL) which was held at 40 °C. Butyryl chloride (100 mg, 0.9 mmol) was added dropwise to the solution and the mixture was heated at 40 °C under nitrogen for 1 h. The solution was poured into cold water, filtered, and the residue of *(5SR,8SR)-trans-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[c]phenanthrene-5,8-diyl dibutyrate* (**1**, X = $CO(CH_2)_2CH_3$) (130 mg, 75%) was collected. An analytical sample was recrystallised from methanol: mp 120−124 °C; ν_{max} (nujol) 1743 (m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 1.01 (t, J = 7.5, 3H), 1.05 (t, J = 7.5, 3H), 1.53 (s, 3H), 1.58 (ddd, J = 12.4, 11.4, 11.4, 1H), 1.72 (ddd, J = 12.8, 9.1, 8.1, 1H), 1.70−1.75 (m, 2H), 1.75−1.80 (m, 2H), 1.86−1.98 (m, 1H), 2.06 (s, 3H), 2.27 (ddd, J = 12.4, 4.1, 3.4, 1H), 2.35 (ddd, J = 12.8, 9.8, 9.8, 1H), 2.43 (t, J = 7.5, 2H), 2.51 (t, J = 7.5, 2H), 3.86 (d, J = 11.3, 1H), 5.99 (dd, J = 11.4, 3.4, 1H), 6.16 (dd, J = 9.8, 9.1, 1H), 6.91 (dd, J = 6.8, 1.1, 1H), 7.09 (dd, J = 6.8, 1.1, 1H), 7.13 (dd, J = 6.8, 6.8, 1H), 7.15 (dd, J = 6.8, 1.1, 1H), 7.21 (dd, J = 6.8, 6.8, 1H), 7.23 (dd, J = 6.8, 1.1, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.7, 18.5, 18.6, 20.6, 20.7, 33.9, 35.2, 35.7, 36.5, 36.6, 43.4, 68.9, 71.2, 120.8, 122.6, 125.5, 126.4, 129.1, 130.8, 132.6, 135.2, 137.0, 137.5, 138.6, 171.6, 172.0; MS m/z (relative intensity) 434 (M^+, 20), 243 (100). Anal. Calcd for $C_{28}H_{34}O_4$: C, 77.4; H, 7.8. Found: C, 77.6, H, 8.0.

(5*SR*,8*SR*)-*trans*-5,6,6a,7,8,12b-Hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl Dilaurate (1, X = $CO(CH_2)_{10}CH_3$). Lauric acid (20 g, 0.1 mol) was added gradually to thionyl chloride (50 mL) and the mixture was heated at reflux under nitrogen for 1 h. The excess thionyl chloride was removed under reduced pressure. *Lauryl chloride* was obtained as a clear oil (20.9 g, 86%) which was spectroscopically pure and was used in the next step without further purification: ν_{max} (Nujol) 1785s cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.89 (t, J = 6.0, 3H), 1.18−1.36 (m, 16H), 1.63−1.77 (m, 2H), 2.88 (t, J = 8.0, 2H).

Lauryl chloride (250 mg, 1.15 mmol) was added dropwise over a 30 min period at rt to a solution of (5*SR*,8*SR*)-*trans*-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diol (**1**, X = H) (100 mg, 0.36 mmol) in dry pyridine (5 mL). The reaction mixture was heated at 90 °C under nitrogen for 1 h. The solution was poured onto ice, stirred, and filtered. The residue was purified by flash chromatography over silica (eluant, CH_2Cl_2 (12%) in light petroleum) to give *(5SR,8SR)-trans-5,6,6a,7,8,12b-hexahydro-1,12-benzo[c]phenanthrene-5,8-diyl dilaurate* (**1**, X = $CO(CH_2)_{10}CH_3$) as the major fraction. Recrystallization from ethanol gave white needles (120 mg, 61%): mp 53−56 °C; ν_{max} (chloroform) 1728 (s) cm^{-1}; λ_{max} (chloroform) 265.8 nm (log ϵ, 2.84); ^1H NMR (600 MHz, $CDCl_3$) δ 0.88 (t, J = 7.5, 6H), 1.18−1.44 (m, 32H), 1.52 (s, 3H), 1.58 (ddd, J = 12.8, 11.4, 11.4, 1H), 1.79−1.91 (m, 5H), 1.86−1.98 (m, 1H), 2.05 (s, 3H), 2.27 (ddd, J = 12.5, 4.2, 3.6, 1H), 2.35 (ddd, J = 12.8, 9.7, 9.7, 1H), 2.44 (t, J = 7.5, 2H), 2.52 (t, J = 7.5, 2H), 3.86 (d, J = 11.4, 1H), 5.98 (dd, J = 11.4, 3.6, 1H), 6.15 (dd, J = 9.7, 9.1, 1H), 6.90 (dd, J = 8.0, 1.0, 1H), 7.10 (dd, J = 7.5, 0.8, 1H), 7.12 (dd, J = 8.0, 8.0, 1H), 7.14 (dd, J = 7.5, 0.8, 1H), 7.22 (dd, J = 7.5, 7.5, 1H), 7.23 (dd, J = 8.0, 1.0, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 12.1, 18.1, 18.7, 20.7, 23.1, 27.3, 27.5, 27.6, 29.9, 32.72, 31.9, 33.2, 33.7, 41.4, 66.9, 69.2, 118.8, 120.7, 123.5, 124.4, 127.1, 128.8, 130.6, 133.2, 135.0, 135.5, 137.5, 171.3, 171.8; MS (CI, NH_3) m/z 676.9 ($(M + NH_4)^+$, 100). Anal. Calcd for $C_{44}H_{66}O_4$: C, 80.2; H, 10.0. Found: C, 80.4; H, 10.2.

(5*SR*,8*SR*)-*trans*-5,6,6a,7,8,12b-Hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl Bis(4-heptylbenzoate) (1, X = CO-*p*-$C_6H_4(CH_2)_6CH_3$). 4-Heptylbenzoic acid (3 g, 13.6 mmol) was added slowly to thionyl chloride (5 mL) at reflux. The mixture was heated at reflux for 2 h under nitrogen. The excess thionyl chloride was removed under reduced pressure and the residue of *4-heptylbenzoyl chloride* (3.2 g, 100%) was used in the next step without further purification: ν_{max} (chloroform) 1777s cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.88 (t, J = 6.8, 3H), 1.24−1.35 (m, 8H), 1.59−1.67 (m, 2H), 2.67 (t, J = 7.5 , 2H), 7.30 (d, J = 6.0, 2H), 8.04 (d, J = 6.0, 2H).

4-Heptylbenzoyl chloride (490 mg, 2.1 mmol) was added slowly to a solution of (5*SR*,8*SR*)-*trans*-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diol (**1**, X = H) (200 mg, 0.7 mmol) in dry pyridine (7 mL). The reaction mixture was heated at 90 °C under nitrogen for 5 h poured onto ice, stirred, and filtered. The residue was purified by flash chromatography over silica (eluant, CH_2Cl_2 (10%) in light petroleum) to give *4-heptylbenzoic acid* (110 mg) as the first major fraction. The second major fraction, *(5SR,8SR)-trans-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[c]phenanthrene-5,8-diyl bis(4-heptylbenzoate)* (**1**, X = CO-*p*-$C_6H_4(CH_2)_6CH_3$) (366 mg, 75%), was obtained as a white solid. An analytical sample was obtained by recrystallization from methanol: mp 118−120 °C; ν_{max} (chloroform) 1707 (m) cm^{-1}; λ_{max} (chloroform) 244.1 nm (log ϵ, 4.57); ^1H NMR (600 MHz, $CDCl_3$) δ 0.89 (t, J = 7.5, 6H), 1.25−1.36 (m, 16H), 1.63 (s, 3H), 1.61−1.69 (m, 4H), 1.75 (ddd, J = 12.4, 11.5, 11.5, 1H), 1.92 (ddd, J = 13.2, 8.9, 8.4, 1H), 2.02−2.14 (m, 1H), 2.18 (s, 3H), 2.43 (ddd, J = 12.4, 4.3, 3.5, 1H), 2.39 (ddd, J = 13.2, 9.8, 9.8, 1H), 2.67 (t, J = 7.5, 2H), 2.70 (t, J = 7.5, 2H), 3.99 (d, J = 11.1, 1H), 6.26 (dd, J = 11.5, 3.5, 1H), 6.42 (dd, J = 9.8, 8.9, 1H), 6.95 (dd, J = 8.0, 1.0, 1H), 7.13 (dd, J = 8.0, 1.0, 1H), 7.15 (dd, J = 8.0, 8.0, 1H), 7.22 (dd, J = 8.0, 1.0, 1H), 7.28 (dd, J = 8.0, 8.0, 1H), 7.37 (dd, J = 8.0, 1.0, 1H), 8.05 (dd, J = 8.0, 1.5, 4H), 8.13 (dd, J = 8.0, 1.5, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.1, 20.2, 20.8, 22.7, 29.1, 29.2, 31.2, 31.8, 36.1, 34.1, 35.3, 35.8, 43.6, 69.4, 72.0, 121.1, 123.0, 125.6, 126.6, 129.2, 130.8, 127.6, 127.7, 128.6, 129.9, 132.7, 135.4, 137.2, 137.7, 138.8, 148.8, 149.0, 166.1, 166.5. Anal. Calcd for $C_{48}H_{58}O_4$: 82.5; H, 8.3. Found: C, 82.7; H, 8.6.

(5*SR*,8*SR*)-*trans*-5,6,6a,7,8,12b-Hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diyl Bis(4′-heptylbiphenyl-4-carboxylate) (1, X = CO-*p*-$(C_6H_4)_2(CH_2)_6CH_3$). 4-Heptyl-4′-cyanobiphenyl (Aldrich) (200 mg, 0.7 mmol) was

(5) Brown, H. C.; Ash, A. B. *J. Am. Chem. Soc.* **1955**, *77*, 4019.

added to sulfuric acid (6 M) maintained at 150 °C. The mixture was heated for a further 3 h at 180 °C, cooled, and filtered. The residue was added to a solution of sodium hydroxide (2 M) and the precipitate of *4-heptyl-4′-biphenylcarboxylic acid* was collected (176 mg, 85%): ν_{max} (chloroform) 1678 (m) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.86 (t, J = 6.8, 3H), 1.22−1.32 (m, 8H), 1.64−1.71 (m, 2H), 2.64 (t, J = 7.5, 3H), 7.23 (d, J = 8.0, 2H), 7.55 (d, J = 8.0, 2H), 7.73 (d, J = 8.0, 2H), 8.23 (d, J = 8.0, 2H); MS m/z 296 (M^+, 70), 211 (100). Anal. Calcd for $C_{20}H_{24}O_2$: C, 81.1; H, 8.1. Found: C, 80.7; H, 8.3.

4-Heptyl-4′-biphenylcarboxylic acid (100 mg, 0.3 mmol) was added slowly to thionyl chloride (10 mL) at reflux. The mixture was heated at reflux for 3.5 h under nitrogen. The excess thionyl chloride was removed under reduced pressure and the residue of *4-heptyl-4′-biphenylcarbonyl chloride* (94 mg, 100%) was used in the next step without further purification: ν_{max} (chloroform) 1775 (s) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.88 (t, J = 6.8, 3H), 1.26−1.37 (m, 8H), 1.58−1.66 (m, 2H), 2.69 (t, J = 7.5, 2H), 7.27 (d, J = 6.0, 2H), 7.54 (d, J = 6.0, 2H), 7.73 (d, J = 6.0, 2H), 8.15 (dd, J = 6.0, 2H).

4-Heptyl-4′-biphenylcarbonyl chloride (94 mg, 0.3 mmol) was added slowly to a solution of (5*SR*,8*SR*)-*trans*-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[*c*]phenanthrene-5,8-diol (**1**), X = H (60 mg, 0.2 mmol) in dry pyridine (5 mL). The reaction mixture was heated at 90 °C under nitrogen for 2.5 h, poured onto ice, stirred, and filtered. The residue was purified by flash chromatography over silica (eluant, CH_2Cl_2 (10%) in light petroleum) to give *(5SR,8SR)-trans-5,6,6a,7,8,12b-hexahydro-1,12-dimethylbenzo[c]phenanthrene-5,8-diyl bis(4′-heptylbiphenyl-4-carboxylate)* (**1**, X = CO-*p*-$(C_6H_4)_2(CH_2)_6CH_3$) (60 mg, 35%). An analytical sample was obtained by recrystallization from toluene and methanol: mp 192−194 °C; ν_{max} (chloroform) 1708 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, J = 7.5, 6H), 1.24−1.36 (m, 16H), 1.61 (s, 3H), 1.62−1.69 (m, 4H), 1.75−1.84 (m, 1H), 1.93−2.01 (m, 1H), 2.06−2.14 (m, 1H), 2.14 (s, 3H), 2.46−2.58 (m, 2H), 2.65−2.69 (m, 4H), 4.02 (d, J = 11.1, 1H), 6.30 (dd, J = 12.0, 4.0, 1H), 6.46 (dd, J = 9.6, 8.4, 1H), 6.96 (d, J = 7.7, 1H), 7.15−7.20 (m, 2H), 7.24−7.32 (m, 6H), 7.40 (d, J = 7.6, 1H), 7.56 (d, J = 7.6, 2H), 7.58 (d, J = 7.6, 2H), 7.69 (d, J = 8.0, 2H), 7.74 (d, J = 8.0, 2H), 8.19 (d, J = 8.0, 2H), 8.28 (d, J = 8.0, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.7, 20.8, 21.4, 23.3, 29.8, 29.9, 32.1, 32.4, 34.7, 36.0, 36.3, 36.5, 44.2, 70.2, 72.6, 121.7, 123.6, 126.3, 127.3, 127.6, 127.8, 129.3, 129.7, 129.9, 130.9, 131.5, 133.4, 136.0, 137.8, 137.9, 139.4, 144.0, 166.4, 167.2. Anal. Calcd for $C_{60}H_{66}O_4$: 84.7; H, 7.8. Found: C, 84.5; H, 7.6.

Acknowledgment. The authors wish to express thanks to the Australian Research Council and to the Cooperative Research Centre for Molecular Engineering and Technology for financial support.

JO9704319