Is the CD Exciton Chirality Method Applicable to Chiral 1,1′-Biphenanthryl Compounds?

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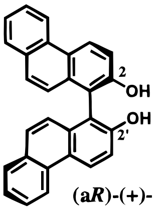
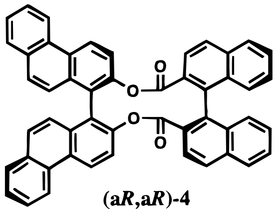
In the last two decades, many axially chiral 1,1′-binaphthyl derivatives have been successfully used as highly efficient chiral auxiliaries for chiral molecular recognition as well as asymmetric syntheses. In some cases, enhanced chiral recognition abilities have been brought by 4,4′- or 9,9′-biphenanthryl analogues by virtue of the more expanded aromatic plane.[1] To our knowledge, however, 1,1′-biphenanthryl compounds have never been utilized as chirality-recognizing auxiliaries, although members of this class of biaryl derivatives have often been isolated as natural products.[2] On the other hand, the CD exciton chirality method has been established as a nonempirical method for determining absolute stereochemistry of chiral organic compounds.[3] We report here the synthesis and absolute stereochemistry of chiral 1,1′-biphenanthryl compounds and also discuss their anomalous CD behavior which disagrees with the prediction by the CD exciton chirality method. It was disclosed that the apparent discrepancy was due to an extra hidden transition, and simple qualitative predictions by the CD exciton chirality method are not valid for the phenanthrene chromophores.

Prerequisite 2-phenanthrol was easily obtained by alkali fusion of barium phenanthrene-2-sulfonate which was prepared according to Fieser's procedure.[4] Oxidative coupling of 2-phenanthrol in the presence of 1-phenylethylamine−copper (II) complex afforded 1,1′-biphenanthryl-2,2′-diol (**1**) (72%).[5,6] Enantioresolution of (±)-**1** was achieved as follows: treatment of (±)-**1** with thiophosphoryl chloride and (*S*)-1-phenylethylamine in refluxing pyridine gave a diastereomeric mixture of *N*-[(*S*)-1-phenylethyl]-1,1′-biphenanthryl-2,2′-diyl thiophosphoramide (**2**) (70%).[7] The mixture was crystallized from ethanol/ethyl acetate (4:1), and crystals (a*S*,*S*)-(+)-**2a** obtained were washed with refluxing acetonitrile to remove the remaining more soluble diastereomer **2b**. Reduction of amide **2a** with $LiAlH_4$ in THF gave enantiopure (−)-**1** (72%), the enantiopurity of which was confirmed by HPLC on a Pirkle column [(*R*)-*N*-(3,5-dinitrobenzoyl)phenylglycine-modified column] with hexane/2-propanol (7:3).[6,8]



(a*R*)-(+)-1



(a*R*,a*R*)-4

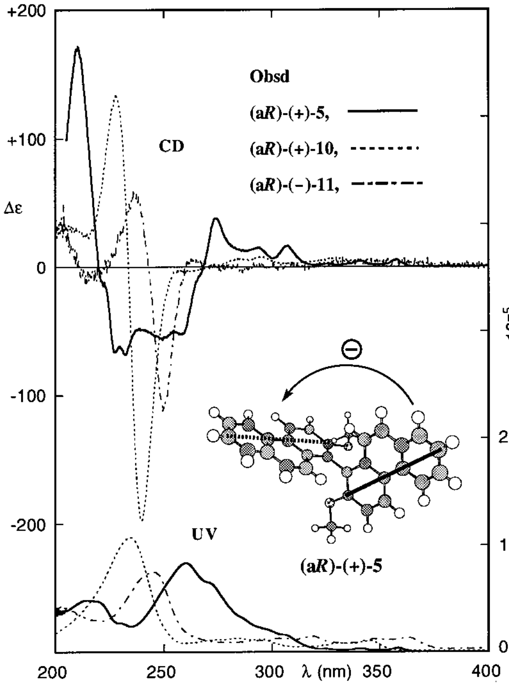


Figure 1. CD and UV spectra of (a*R*)-1,1′-biphenanthryl derivatives in EtOH or in 10% v/v 1,4-dioxane/EtOH. In (a*R*)-(+)-**5**, two long axes of phenanthrene chromophores constitute a counterclockwise screw sense.

The absolute configuration of **1** was determined by the axial chirality recognition method developed by us, which is based on the steric requirement for the formation of a 12-membered cyclic diester, e.g., compound **4**.[9] Treatment of (±)-**1** with 1.0 mol equiv of 1,1′-binaphthalene-2,2′-dicarbonyl dichloride (a*R*)-**3** in refluxing benzene/pyridine (60:1) in the presence of 4-(dimethylamino)-pyridine (DMAP, 2.0 mol equiv) allowed cyclization of only (a*R*)-**1** to yield diastereomerically pure cyclic diester **4**, which should have (a*R*,a*R*) configuration because of less steric hindrance (Supporting Information). Reductive cleavage of diester (a*R*,a*R*)-**4** with $LiAlH_4$ recovered (+)-**1**, the enantiomeric homogeneity of which was confirmed by chiral HPLC analyses. The a*R* absolute stereochemistry was thus assigned to (+)-**1**.

We were very surprised to observe the unexpected shape of the CD spectra of (+)-**1** and its dimethyl ether (+)-**5** (Figure 1 and Supporting Information);[10] we had expected that the CD spectra of (a*R*)-**1** and (a*R*)-**5** should show exciton split Cotton effects[3] of negative chirality in the $^{1}B_b$ transition region around 260 nm. Since the $^{1}B_b$ transition of phenanthrene is polarized along the long axis of the chromophore (perpendicular to the

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[1] Hayashi, T.; Iwamura, H.; Naito, M.; Matsumoto, Y.; Uozumi, Y. *J. Am. Chem. Soc.* **1994**, *116*, 775. Lee, G.-H.; Wang, Y.; Tanaka, K.; Toda, F. *Chem. Lett.* **1988**, 781 and references therein.

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[6] (±)-**1**, mp 297−299 °C (EtOAc); (a*S*)-(−)-**1**, mp 244−245 °C (EtOAc), $[\alpha]^{22}_{D}$ −34.0 (*c* 0.95, $CHCl_3$); (a*R*)-(+)-**1**, mp 243−244 °C (EtOAc), $[\alpha]^{19}_{D}$ +32.0 (*c* 1.60, $CHCl_3$).

[7] Fabbri, D.; Delogu, G.; Lucchi, O. D. *J. Org. Chem.* **1993**, *58*, 1748.

[8] Pirkle, W. H.; House, D. W.; Finn, J. M. *J. Chromatogr.* **1980**, *192*, 143.

[9] Koike, N.; Hattori, T.; Miyano, S. *Tetrahedron: Asymmetry* **1994**, *5*, 1899 and references therein.

[10] (a*R*)-(+)-**1**: UV (10% v/v 1,4-dioxane/EtOH) λ_{max} 258.6 nm (ϵ 101, 000); CD (10% v/v 1,4-dioxane/EtOH) λ_{ext} 273.8 nm ($\Delta\epsilon$ +48.7), 258.2 (−80.8). (a*R*)-(+)-**5**: UV (10% v/v 1,4-dioxane/EtOH) λ_{max} 260.6 nm (ϵ 83, 100); CD (10% v/v 1,4-dioxane/EtOH) λ_{ext} 274.2 nm ($\Delta\epsilon$ +38.5), 258.0 (−52.5).

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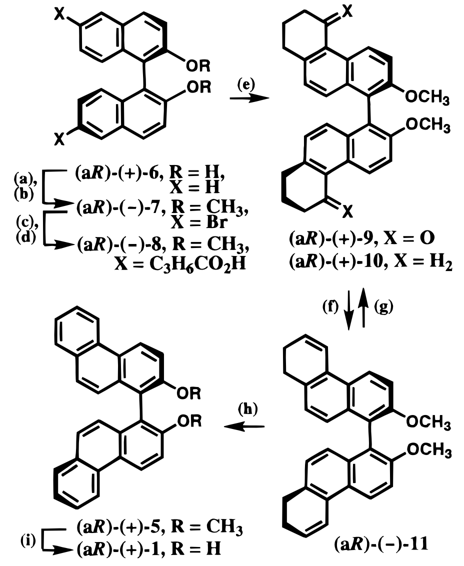
Scheme 1[a]



[a] (a) Br_2, CH_2Cl_2, 78 °C → room temp, 5 h, 80%. (b) NaH, CH_3I, DMF, 0 °C → room temp, 4 h. (c) 9-$MeO_2CC_3H_6$−BBN, $Pd(PPh_3)_4$, NaOH, THF, 65 °C, 24 h, 95%. (d) NaOH, aqueous EtOH, reflux, 1.5 h, 88%. (e) PCl_5, PhH, room temp, 2 h, and then $SnCl_4$, 5 °C, 1.5 h, 81%. (f) $LiAlH_4$, THF, room temp, 1 h, and then TsOH, acetone, reflux, 5.5 h, 92%. (g) H_2, Pd/C, EtOH, room temp, 21 h, 79%. (h) DDQ, PhMe, 80 °C, 20 h, 73%. (i) BBr_3, CH_2Cl_2, room temp, 2 h, 92%.

symmetry axis of C_{2v} phenanthrene),[11] two long axes of phenanthrene chromophores constitute a counterclockwise screw sense, i.e., negative exciton chirality, as illustrated in Figure 1. Both compounds (a*R*)-(+)-**1** and (a*R*)-(+)-**5**, however, exhibit positive and negative CD Cotton effects around 274 and 260 nm, respectively, although their $\Delta\epsilon$ values are relatively small.[10] This unexpected and strange CD behavior prompted us to reinvestigate the absolute stereochemistry of 1,1′-biphenanthryl derivatives.

The absolute stereochemistry of (+)-**1** and its derivatives was unambiguously determined by chemical correlation to 1,1′-binaphthyl-2,2′-diol (a*R*)-(+)-**6** (Scheme 1). Bromination of enantiopure (a*R*)-(+)-**6**, followed by methylation gave bis(bromo ether) (a*R*)-(−)-**7**, which was subjected to the Suzuki coupling reaction with 9-[(3-methoxycarbonyl)propyl]-9-borabicyclo[3.3.1]-nonane and then alkaline hydrolysis yielding dicarboxylic acid (a*R*)-(−)-**8**. The Friedel−Crafts cyclization of (a*R*)-(−)-**8** afforded diketone (a*R*)-(+)-**9**,[12] which was reduced with $LiAlH_4$ and then dehydrated with *p*-toluenesulfonic acid to give tetrahydrobiphenanthryl (a*R*)-(−)-**11**. Hydrogenation of (a*R*)-(−)-**11** gave octahydrobiphenanthryl (a*R*)-(+)-**10**. Hydrocarbon (a*R*)-(−)-**11** was dehydrogenated with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) affording dimethyl ether (a*R*)-(+)-**5**, which was converted to (a*R*)-(+)-**1** by demethylation with boron tribromide: total yield, 27% based on the starting binaphthol **6**. The a*R* absolute stereochemistry of (+)-**1** was thus established.

The CD spectrum of octahydrobiphenanthryl (a*R*)-(+)-**10** shows typical and intense exciton split CD Cotton effects of negative chirality reflecting the counterclockwise screw sense between two long axes of naphthalene chromophores (Figure 1).[13] Tetrahydrobiphenanthryl (a*R*)-(−)-**11** also exhibits bisignate Cotton effects of negative exciton chirality. On the other hand, the CD spectra of 1,1′-biphenanthryl compounds (a*R*)-(+)-**1** and (a*R*)-(+)-**5** show positive first and negative second Cotton effects (Figure 1 and Supporting Information).[10] These CD data of 1,1′-biphenanthryl compounds disagree with the prediction by the CD exciton chirality method. To clarify the mechanism of such strange CD behavior of 1,1′-biphenanthryls and also to determine their absolute stereochemistry by the theoretical CD method, we carried out the theoretical calculation of CD and UV spectra of (a*R*)-1,1′-biphenanthryl **12** and (a*R*)-**5** by the π-electron SCF-CI-DV MO method.[3] The calculation of UV spectrum of phenanthrene revealed that there is another electric transition with short-axis polarization around 255 nm in addition to the main band of ^1B_b transition around 260 nm. It was also clarified that in the system of (a*R*)-**12**, these two transitions in each chromophore interact with one another (i.e., four sets of interactions) giving rise to positive first and negative second Cotton effects, which are opposite in sign to those expected from the qualitative application of the CD exciton chirality method. It should be emphasized that the CD exciton chirality method itself is correct, but the electronic transitions of phenanthrene are complex. For this reason, simple qualitative predictions based on the exciton method are not valid for 1,1′-biphenanthryl compounds.

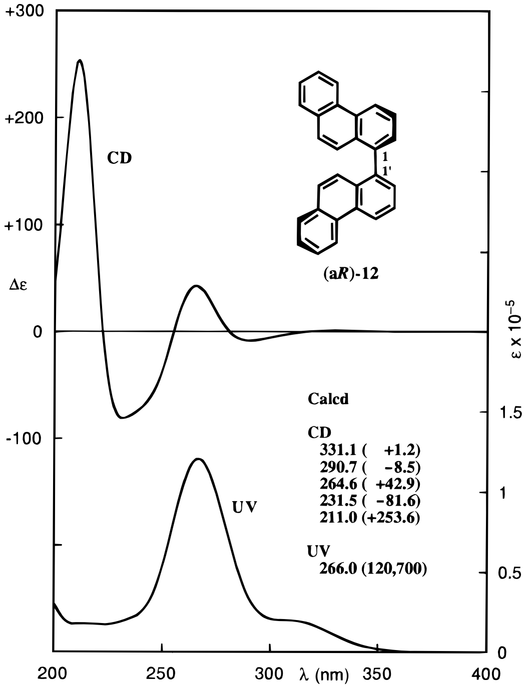


Figure 2. CD and UV spectral curves of (a*R*)-1,1′-biphenanthryl **12** calculated by the π-electron SCF-CI-DV MO method.

The CD and UV spectra of (a*R*)-**12** quantitatively calculated by the π-electron SCF-CI-DV MO method are shown in Figure 2; the calculated CD and UV curves are in a good agreement with the observed spectra, although there is a weak negative CD band around 290 nm (see also Supporting Information). The absolute stereochemistries of 1,1′-biphenanthryl-2,2′-diol (+)-**1** and its dimethyl ether (+)-**5** were thus theoretically determined to be a*R* in consistency with the chemical correlation results described above. Further studies for other biphenanthryl derivatives are now in progress.

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Supporting Information Available: Spectral and physical data of compounds **1**−**11**, CD and UV spectra of (a*R*)-(+)-**1**, and calculated CD and UV curves of (a*R*)-**5** (4 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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[12] Bachmann, W. E.; Cortes, G. D. *J. Am. Chem. Soc.* **1943**, *65*, 1329.

[13] (a*R*)-(+)-**10**: UV (EtOH) λ_{max} 233.8 nm (ϵ 116 000); CD (EtOH) λ_{ext} 239.8 nm ($\Delta\epsilon$ −197.1), 227.8 (+133.3). (a*R*)-(−)-**11**: UV (EtOH) λ_{max} 245.8 nm (ϵ 74 900); CD (EtOH) λ_{ext} 249.6 nm ($\Delta\epsilon$ −112.6), 236.4 (+60.5).