Long-Range Exciton-Coupled Circular Dichroism: Application for Determination of the Absolute Configuration of Oligonaphthalenes
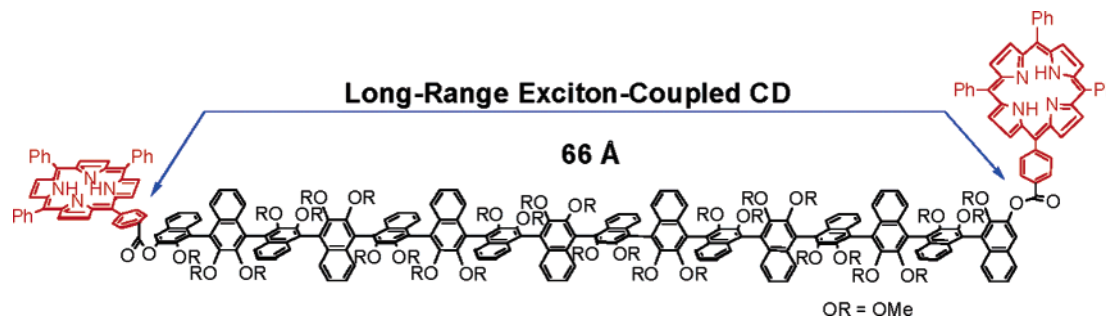
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ABSTRACT

Hexadecanaphthalenes (*S,S,S,S,S,S,S,S,S,S,S,S,S,S,S,S*)-4b and (*S,S,S,S,S,S,S,R,S,S,S,S,S,S,S*)-4b that possess two tetraphenylporphyrins (TPP) on the upper and lower naphthalene rings were synthesized. Long-range exciton-coupled CD in the Soret region of TPP (about 66 Å) was observed.

Since Nakanishi and Harada proposed the exciton-coupled circular dichroic (CD) method, which is based on the dipole−dipole interaction between two identical chromophores with strong $\pi-\pi^*$ transitions, this nonempirical method has been widely used to determine the absolute configurations of various chemical compounds.[1] 4-(Dimethylamino)benzoic acid was initially used as the chromophore,[2] but in 1995,

Nakanishi and Matile reported that tetraphenylporphyrin (TPP) carboxylic acid is about a 10 times more powerful and sensitive chromophore.[3] They demonstrated that long-range exciton-coupled CD (with an interchromophoric distance of about 50 Å) could be observed on a brevetoxin B derivative.[3b] In a theoretical sense, the total amplitudes of the CD are inversely proportional to the square of the interchromophore distance.[2b] Although numerous papers have theoretically and experimentally analyzed porphyrin−porphyrin exciton interactions,[4] the theoretical limit of a long-range exciton-coupled CD is unclear. The longest reported distance between the chromophores is still above "about 50 Å".

(1) (a) Harada, N.; Nakanishi, K. *Acc. Chem. Res*. **1972**, *5*, 257−263. (b) Harada, N.; Nakanishi, K. *Circular Dichroic spectroscopy − exciton coupling in organic stereochemistry*; University Science Book: Mill Valley, CA, 1983. (c) Berova, N.; Nakanishi, K. In *Circular Dichroism: Principles and Applications,* 2nd ed.; Berova, N., Nakanishi, K., Woody, R. W., Eds.; Wiley-VCH: New York, 2000; pp 337−382. (d) Koslowski, A.; Sreerama, N.; Woody, R. W. In *Circular Dichroism: Principles and Applications*; Berova, N., Nakanishi, K., Harada, N., Eds.; Wiley-VCH: New York, 2000; pp 55−95.

(2) (a) Chen, S.-M. L.; Harada, N.; Nakanishi, K. *J. Am. Chem. Soc*. **1974**, *96*, 7352−7354. (b) Harada, N.; Chen, S.-M. L.; Nakanishi, K. *J. Am. Chem. Soc*. **1975**, *97*, 5345−5352.

(3) (a) Matile, S.; Berova, N.; Nakanishi, K.; Novkova, S.; Philipova, I.; Blagoev, B. *J. Am. Chem. Soc*. **1995**, *117*, 7021−7022. (b) Matile, S.; Berova, N.; Nakanishi, K.; Fleischhauer, J.; Woody, R. W. *J. Am. Chem. Soc*. **1996**, *118*, 5198−5206.

On the other hand, we have been studying the bottom-up construction of optically active helical oligonaphthalenes and their properties.[5] Through the study, the development of a versatile method to determine the absolute configuration of the newly formed central axis chirality of oligonaphthalenes with any number of naphthalene rings and any kind of side chains still remains a big issue to be solved (Figure 1).
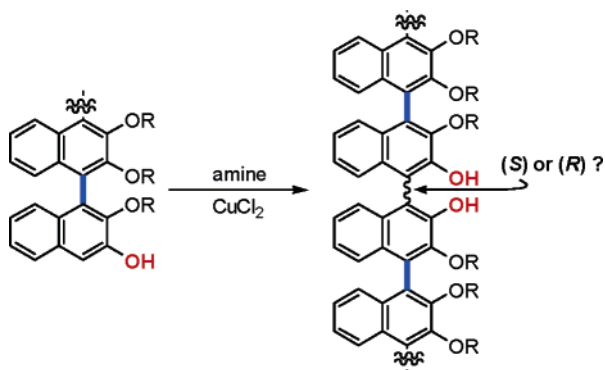

Figure 1. How does one determine the absolute configuration of the central axis bond? Blue bold bonds denote absolute-configuration-decided axis bonds.

In the present paper, we propose a convenient method, which is based on long-range exciton-coupled CD, to determine the absolute configuration of oligonaphthalenes with two TPPs on the top and bottom naphthalene rings. If the average dihedral angles of each axis are about 90°, then exciton-coupled CD between the two TPPs should reflect the torsion of the entire molecule and should decode the chirality of the target central axis bond (Figure 2). Figure 2A shows (S,S,S)-quaternaphthalene viewed from the top where each side chain is helically arranged every 90° in a clockwise direction. Consequently, the two TPPs are oriented in an anticlockwise direction, which leads to a negative exciton-coupled CD spectrum (Figure 2B). However, in
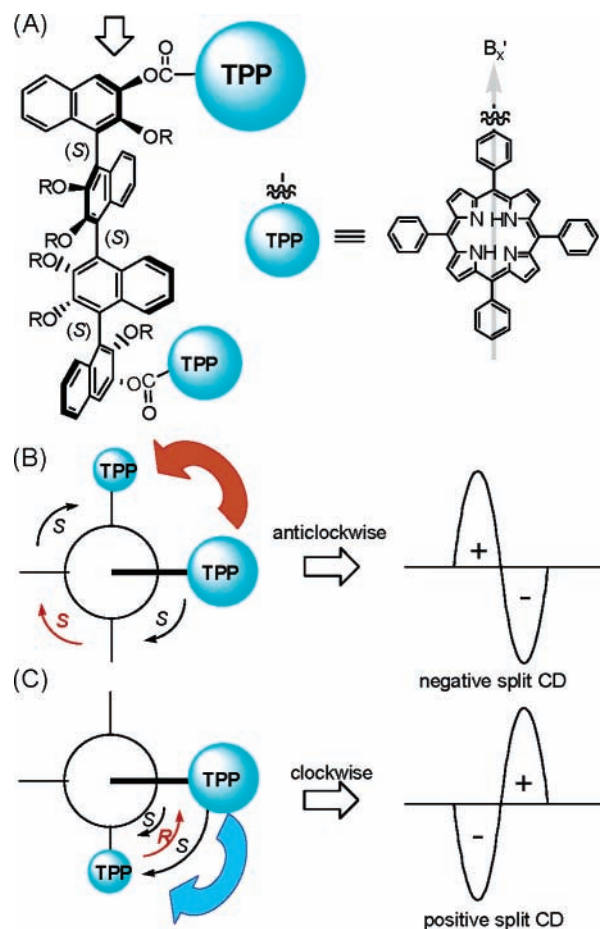
(4) (a) Crossley, M. J.; Mackay, L. G.; Try, A. C. *J. Chem. Soc., Chem. Commun.* **1995**, 1925−1927. (b) Ema, T.; Misawa, S.; Nemugaki, S.; Sakai, T.; Utaka, M. *Chem. Lett.* **1997**, *26*, 487−488. (c) Richman, B. H.; Matile, S.; Nakanishi, K.; Berova, N. *Tetrahedron* **1998**, *54*, 5041−5064. (d) Stomphorst, R. G.; Koehorst, R. B.; van der Zwan, G.; Benthem, B.; Schaafsma, T. J. *J. Porphyrins Phthalocyanines* **1999**, *3*, 346−354. (e) Huang, X.; Borhan, B.; Rickman, B. H.; Nakanishi, K.; Berova, N. *Chem.− Eur. J.* **2000**, *6*, 216−224. (f) Huang, X.; Nakanishi, K.; Berova, N. *Chirality* **2000**, *12*, 237−255. (g) Borovkov, V. V.; Lintuluoto, J. M.; Fujiki, M.; Inoue, Y. *J. Am. Chem. Soc.* **2000**, *122*, 4403−4407. (h) Redl, F. X.; Lutz, M.; Daub, J. *Chem.−Eur. J.* **2001**, *7*, 5350−5358. (i) Pescitelli, G.; Gabriel, S.; Wang, Y.; Fleischhauer, J.; Woody, R. W.; Berova, N. *J. Am. Chem. Soc.* **2003**, *125*, 7613−7628. (j) Proni, G.; Pescitelli, G.; Huang, X.; Nakanishi, K.; Berova, N. *J. Am. Chem. Soc.* **2003**, *125*, 12914−12927. (k) Borovkov, V. V.; Fujii, I.; Muranaka, A.; Hembury, G. A.; Tanaka, T.; Ceulemans, A.; Kobayashi, N.; Inoue, Y. *Angew. Chem., Int. Ed.* **2004**, *43*, 5481−5485. (l) MacMillan, J. B.; Linington, R. G.; Andersen, R. J.; Molinski, T. F. *Angew. Chem., Int. Ed.* **2004**, *43*, 5946−5951. (m) MacMillan, J. B.; Molinski, T. F. *J. Am. Chem. Soc.* **2004**, *126*, 9944− 9945. (n) Formaggio, F.; Peggion, C.; Crisma, M.; Kaptein, B.; Broxterman, Q. B.; Mazaleyrat, J.-P.; Wakselman, M.; Toniolo, C. *Chirality* **2004**, *16*, 388−397. (o) Balaz, M.; Holmes, A. E.; Benedetti, M.; Rodriguez, P. C.; Berova, N.; Nakanishi, K.; Proni, G. *J. Am. Chem. Soc.* **2005**, *127*, 4172− 4173.

Figure 2. Application of the exciton chirality method to oligo-naphthalene skeletons.

(S,R,S)-quaternaphthalene, the two TPPs are positioned in a clockwise direction (Figure 2C).

To confirm this idea, compounds **1b**−**7b** were synthesized from chiral **1a**−**7a**[6] and TPP carboxylic acid **8** under WSC and DMAP conditions in 22−80% isolated yields (Scheme 1).

At the same time, two other approaches were also performed. First, the dihedral angles of three types of ternaphthalenes and one quaternaphthalene, whose structures were clarified by X-ray analysis, were scrutinized (Supporting Information, Figures S2 and S3). The dihedral angles defined C(2)−C(1)−C(1′)−C(2′), which ranged from 74.7° to 113°, and the average of the nine dihedral angles was

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(6) The diols **1a**−**7a** were synthesized from the corresponding dibenzyl derivatives.[5d,5e]

Scheme 1

1a: n = 0, R = Me
2a: n = 1, R = Me **5a**: n = 0, R = CH₂CON(Et)₂
3a: n = 3, R = Me **6a**: n = 1, R = CH₂CON(Et)₂
4a: n = 7, R = Me **7a**: n = 3, R = CH₂CON(Et)₂

1b: n = 0, R = Me
2b: n = 1, R = Me **5b**: n = 0, R = CH₂CON(Et)₂
3b: n = 3, R = Me **6b**: n = 1, R = CH₂CON(Et)₂
4b: n = 7, R = Me **7b**: n = 3, R = CH₂CON(Et)₂

90.02°. Second, the most stable conformations of the octinaphthalenes (Supporting Information, Figures S4−S7) were determined through molecular mechanics calculations (CONFLEX-MM2).[7] In any case, the dihedral angles of the corresponding binaphthyls were around 73.3−100.9° (average: 89.4°).

Then, the UV and CD spectra of **1b**−**4b** (from a 2mer to a 16mer) were measured. Figure 3 and Table 1 show the data.

In the UV spectra (Figure 3b), the absorption near 310 nm is ascribed to the $\pi-\pi^*$ transition moments of the minor axis of the naphthalene ring, which increases as the number of naphthalene units increases.[5d,5g]

In contrast, the absorptions of the Soret band (420 nm) of **1b**−**4b** have nearly the same shapes and intensities. In the CD spectra (Figure 3a), clear split Cotton effects, which are

Table 1. UV−Vis and CD Data of **1b**−**4b**[a]

	$[\alpha]_D$ (CHCl₃)	UV λ_{max}	ϵ	CD λ	$\Delta\epsilon$	A_{CD}^b
(S)-**1b**	−1380	420.0	758 000	427	42.7	79.5
				419	−36.8	
(S,S,S)-**2b**	−2030	419.5	736 000	427	−36.2	75.4
				417	39.2	
(S,R,S)-**2b**	−1760	419.5	727 000	426	37.5	75.0
				416	−37.5	
homo-**3b**[c]	−2640	420.0	725 000	428	−10.1	22.7
				418	12.6	
hetero-**3b**[d]	−2530	420.0	755 000	428	10.7	21.8
				418	−11.1	
homo-**4b**[e]	−3000	420.0	756 000	434	−2.8	5.5
				418	2.7	
hetero-**4b**[f]	−2980	420.5	751 000	431	4.1	7.4
				417	−3.3	

[a] Conditions: CHCl₃, 1.0×10^{-5} M, 25 °C, light-path length = 1 mm. [b] Total amplitude of the CD. [c] (S,S,S,S,S,S,S)-**3b**. [d] (S,S,S,R,S,S,S)-**3b**. [e] (S,S,S,S,S,S,S,S,S,S,S,S,S,S,S,S)-**4b**. [f] (S,S,S,S,S,S,S,S,R,S,S,S,S,S,S,S)-**4b**.

attributed to the chiral exciton coupling between the two TPPs, are observed and the sign patterns are consistent with the assumption described in Figure 2. For example, (S,S,S)-**2b** and (S,R,S)-**2b** should have a negative and positive exciton-coupled CD, respectively (Figures 2B and 2C), which coincides with the experimental measurements. Clear split Cotton effects are detected even in diastereomers of 16mer **4b**. The estimated distance between the oxygen atoms on the top and bottom naphthalenes of **4b** is 66 Å. This long-range exciton-coupled CD is much longer than that of the

Figure 3. CD (a) and UV−vis (b) spectra of **1b**−**4b**. Conditions: CHCl₃, 1.0×10^{-5} M, 25 °C, light-path length = 1 mm.

(7) Calculations were performed with CONFLEX-MM2 implemented in *CAChe*, version 6.1.12 for Windows; Fujitsu Company Ltd.: Japan.

brevetoxin B derivative (about 50 Å).[3b] Because the ratio of the distances between the top and bottom TPPs of oligo-naphthalenes **2b** (4mer)/**3b** (8mer)/**4b** (16mer) is about 0.5: 1:2 and the total amplitudes of the CDs are inversely proportional to the square of the interchromophore distance, the estimated ratio of the CD amplitudes is 4:1:0.25, respectively. This ratio is consistent with the observed values 75:22:6 (=3.4:1:0.27). Conversely, the data clearly show the long-range exciton coupling of **4b** (66 Å). However, this relationship is not applicable to 2mer **1b**. Currently, we speculate that the torsion angle between the transition moments of the TPPs in **1b** is narrower than those of **2b**–**4b**.[8]
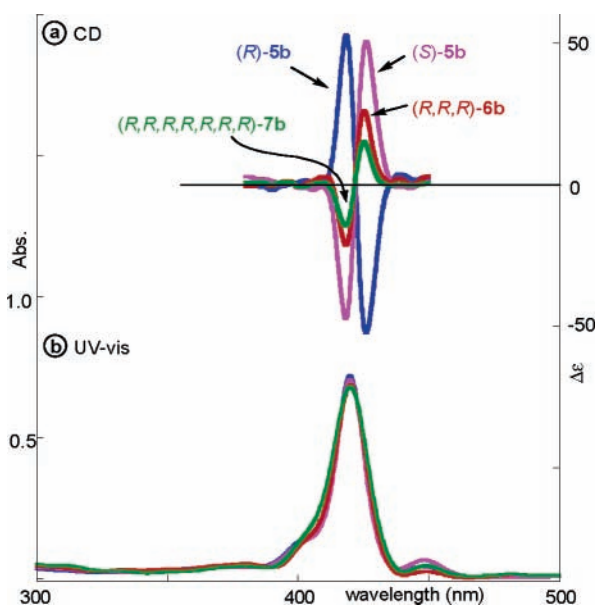
Figure 4. CD (a) and UV−vis (b) spectra of **5b**–**7b**. Conditions: CHCl₃, 1.0×10^{-5} M, 25 °C, light-path length = 1 mm.

It is noteworthy that oligonaphthalenes with TPPs **1b**–**4b** have large specific rotations (about 9−35 times larger than the parent compounds **1a**–**4a**).[9] Despite the decreased TPP concentration per unit volume, the specific rotations increase as the corresponding molecular weight increases.

(8) The lowest-energy structure (calculated with CONFLEX-MM2) of (*S*)-**1b** is shown in Figure S8 (Supporting Information).

(9) (a) Katzenelson, O.; Edelstein, J.; Avnir, D. *Tetrahedron: Asymmetry* **2000**, *11*, 2695−2704. (b) Polavarapu, P. L. *Chirality* **2002**, *14*, 768−781.

Thus, the data indicate that the number of both TPP and naphthalene units influences the specific rotations of oligo-naphthalenes **1b**–**4b**.

These long-range exciton-coupled CDs are clearly detected for oligonaphthalenes with amide side chains **5b**–**7b** (Figure 4 and Table 2) and butyl side chains (Supporting Information, Figure S1). In all cases, the sign patterns of exciton-coupled CD are congruent with our hypothesis.

Table 2. UV−Vis and CD Data of **5b**–**7b**[a]

	$[\alpha]_D$ (CHCl₃)	UV λ_{max}	ϵ	CD λ	$\Delta\epsilon$	A_{CD}[b]
(*R*)-**5b**	−3460	420.0	720 000	426	−51.9	104.8
				418	52.9	
(*S*)-**5b**	+3380	420.0	706 000	426	50.6	97.7
				418	−47.1	
(*R,R,R*)-**6b**	−3480	420.0	688 000	425	26.0	47.7
				418	−21.7	
homo-**7b**[c]	−3570	420.0	680 000	425	15.1	29.6
				418	−14.5	

[a] Conditions: CHCl₃, 1.0×10^{-5} M, 25 °C, light-path length = 1 mm. [b] Total amplitude of the CD. [c] (*R,R,R,R,R,R,R*)-**7b**.

In conclusion, the association between exciton-coupled CD (signs, shapes, and amplitudes) and torsion of the entire molecule was systematically investigated using a series of chiral oligonaphthalenes that possessed two TPPs on the upper and lower naphthalene rings. Hexadecanaphthalene derivative **4b** exhibited a clear exciton coupling over an interchromophore distance of ca. 66 Å. This method should conveniently determine the absolute configuration of oligo-naphthalenes with naphthalene rings (up to 16mer) and various side chains on the naphthalenes synthesized through the bottom-up route.

Supporting Information Available: The CD and UV spectra of oligonaphthalene with butyl side chains, full experimental details and characterization data of all new compounds, X-ray structures of ter- and quaternaphthalenes, and calculated structures of oligonaphthalenes. This material is available free of charge via the Internet at http://pubs.acs.org.

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