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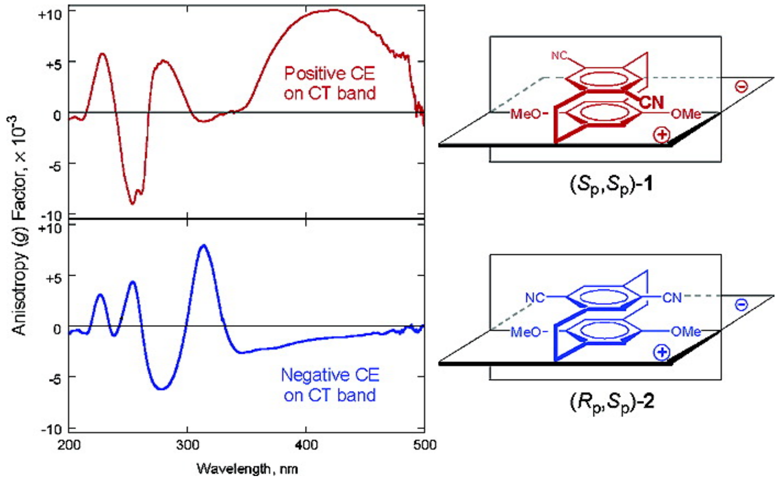

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Absolute Configuration of Chiral [2.2]Paracyclophanes with Intramolecular Charge-Transfer Interaction. Failure of the Exciton Chirality Method and Use of the Sector Rule Applied to the Cotton Effect of the CT Transition

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The exciton chirality method is a widely accepted and powerful tool for determining the absolute configuration of chiral organic and bioorganic molecules by using a small amount of optically pure sample.[1] The electronic transition moments of two chromophores positioned at an appropriate distance and angle in a chiral environment couple with each other, resulting in an energy level splitting which is most clearly displayed by a bisignate coupled circular dichroism (CD) spectrum. From the sign of the couplet, one can immediately assign the sense of chiral arrangement of the relevant chromophores or the absolute configuration.

The absolute configurations of [2.2]paracyclophanes have usually been determined by the sign of exciton coupling of the ^1L_a and ^1L_b transitions.[2] It is likely, however, that both boat-type deformation and electronic interactions of the two facing aromatic rings in cyclophanes will significantly affect the absorption and circular dichroism spectra.[3] Nevertheless, a variety of structurally well-defined cyclophanes have been employed as convenient rigid models in charge/electron-transfer studies, as well as catalysts in asymmetric syntheses but without paying significant attention to the above-mentioned structural and electronic features.[4]

In our ongoing project to elucidate the chiroptical properties of radical cations and/or charge-transfer (CT) complexes,[5] we now focus on chiral [2.2]paracyclophanes possessing CT interactions. A large number of such compounds have already been prepared by Staab and co-workers but have not been optically resolved.[6] In the present study, we found that the conventional exciton chirality method fails to correctly assign the absolute configuration of chiral paracyclophanes when intramolecular CT interactions are involved. Alternatively, we propose an empirical sector rule for assigning the absolute configuration of cyclophanes with CT character.

Staggered and eclipsed 4,7-dicyano-12,15-dimethoxy[2.2]paracyclophanes (**1** and **2**) were prepared as racemic mixtures[7] and were separated into enantiomers by preparative chiral HPLC (DAICEL OD column with hexane/2-propanol as an eluent). In both cases, the enantiomers were well separated to give enantiopure (+)-**1** and (+)-**2** as the first fractions, with (−)-**1** and (−)-**2** as the second fractions ($[\alpha]^{20}_D$ (c 0.2, $CHCl_3$) = +20.5°, +89.1°, −22.8°, and −90.3°, respectively). X-ray crystallographic studies were carried out with racemic **1** and **2** (CCDC 271472 and 271473, Figure 1 and Supporting Information).[8] The center-to-center distances between the two benzene rings of **1** (3.05 Å) and **2** (3.04 Å) are slightly shorter than that of the parent (nonsubstituted) [2.2]-paracyclophane (3.09 Å),[9] likely due to intramolecular CT interactions that reduce the deformation of the benzene rings to some extent. It is also noted that the projections of two aromatic rings in **1** and **2** are not completely overlapping each other but are slightly tilted in 3 and 7°, respectively. DFT-calculated structures are in excellent agreement with these X-ray structures (vide infra).

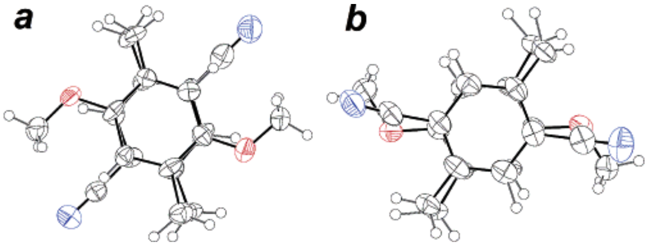

Figure 1. ORTEP drawings of (a) staggered **1** and (b) eclipsed **2**.

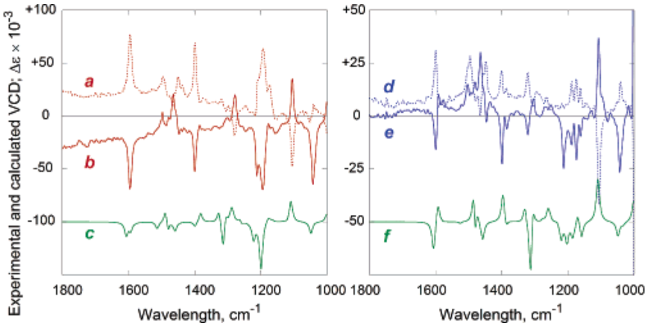

Figure 2. Experimental VCD spectra of (+)- and (−)-**1** (a and b) and (+)- and (−)-**2** (d and e) in dichloromethane-d_2. The levorotatory enantiomers (b and e) are assigned as (4S_p,12S_p)-**1** and (4R_p,12S_p)-**2** on the basis of the calculated VCD spectra (c and f).

Recent instrumental and theoretical advances in vibrational circular dichroism (VCD) spectroscopy have enabled the elucidation of the conformation of chiral organic and biological molecules in solution[10] and also determination of the absolute configuration of relatively rigid chiral molecules through the combined use of DFT calculations and a sophisticated FT-VCD instrument.[11] In contrast, calculations of the ECD spectra of such compounds that involve the CT interactions are still arguable.[3] Possessing a very rigid skeleton and less-flexible substituents, enantiomeric [2.2]paracyclophanes **1** and **2** are well-suited for this VCD/DFT analysis. Thus, the experimental VCD spectra were compared with the theoretical DFT-calculated ones at the B3LYP/6-31G(d) level for the most stable conformers. The global spectral profiles nicely coincide with each other, although some peaks are only reproduced by taking into account the minor conformers in the calculation. As shown in Figure 2, the (−)-enantiomers of **1** and **2** are assigned without difficulty as (4S_p,12S_p)-**1** and (4R_p,12S_p)-**2**.

The electronic circular dichroism (ECD) spectra of enantiopure **1** and **2** were also measured. As can be seen from Figure 3, both **1** and **2** show complicated coupling patterns with complete mirror images for the enantiomer pairs. The Cotton effects of the CT band

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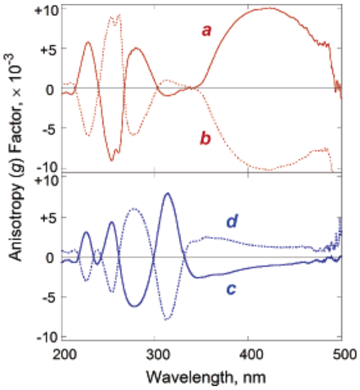

Figure 3. Electronic circular dichroisms of enantiopure **1** (a and b) and **2** (c and d) in acetonitrile. Only anisotropy (*g*) factors are shown for clarity (see Supporting Information for full UV−vis and ECD spectra). Solid lines are for the (−)-enantiomer.

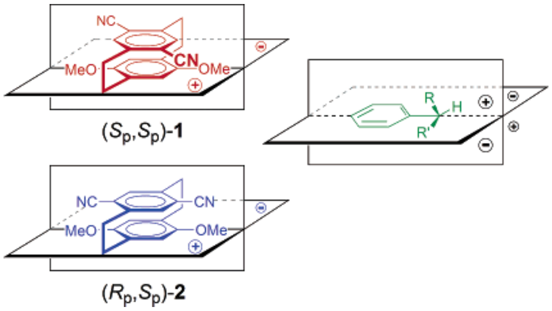

Figure 4. Sector rules applied to the CT cyclophanes **1** and **2**. Quadrant benzene sector is also shown for a comparison.

were noticeable. Conventionally, the couplet observed for the ^1L_b band is used for the assignment of the absolute configuration, while those at shorter wavelengths may not be suitable for the assignment due to complications arising from an overlap of several transitions. In the present case, (−)-enantiomers (traces a and c in Figure 3) exhibit negative couplets at the ^1L_b bands of **1** (280−350 nm) and **2** (300−380 nm).[12] The electronic transition dipole moments of the parent chromophores, that is, 2,5-dimethoxy-*p*-xylene and 2,5-dicyano-*p*-xylene, were calculated by the TDDFT method at the B3LYP/aug-cc-pVDZ level. By assuming that **1** and **2** have the same transition moments as the component chromophores, both (−)-enantiomers are assigned to the 4S_p configuration. This assignment is correct for **1** but clearly erroneous for **2** (Figure S6 for details).

For benzene derivatives, the quadrant projections (Figure 4, right), showing the sign of the ^1L_b Cotton effect, have been used for the empirical assignment of absolute configurations.[13] Similarly, we introduce here a sector rule for the CT cyclophane systems (Figure 4, left). The sector boundaries are defined by the two methoxy groups (polarization direction of the donor).[14] Thus, the sign of Cotton effect at the CT band of (S_p,S_p)-**1** is predicted to be positive since the cyano group resides in the first quadrant (although the methylene group of the ethano bridge is in the second quadrant, we assume CN > CH_2 employing the Cahn−Ingold−Prelog priority rule). For (R_p,S_p)-**2**, one of the methylene groups in the bridge sticks out into the second quadrant, thus giving a negative Cotton effect in the CT band region. This sector rule becomes valid because the contribution of the "dative" resonance structure is almost negligible, in agreement with the small electronic coupling elements[15] for **1** and **2**, H_{DA} being 300 and 530 cm^{-1}, respectively. Therefore, the CT transition can roughly be regarded as the HOMO(donor) → LUMO(acceptor) transition.

In this first study to elucidate the chiroptical properties of intramolecular CT complexes, we have shown that the exciton chirality method is not always valid in the absolute configuration assignment of CT−cyclophanes, and instead, we propose an alternative sector rule for predicting the absolute configuration using the sign of the CT band Cotton effect. Studies on the scope and limitations of this empirical rule and the theoretical interpretation of these apparently bizarre phenomena are currently in progress.[16]

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Supporting Information Available: Experimental details, X-ray crystal structure analyses (CIF files), UV−vis, CD, IR, and VCD spectra, and DFT calculations of **1** and **2** and attempted application of the exciton chirality method to ECD. This material is available free of charge via the Internet at http://pubs.acs.org.

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(16) This sector rule was successfully applied to the analysis of other CT cyclophanes, such as the staggered and eclipsed 4,7-bismethoxycarbonyl-12,15-dimethoxy[2.2]paracyclophanes, for which the exciton chirality method fails to give correct predictions for the absolute configurations; see Figure S7 in Supporting Information.

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