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Recognition of Chiral Catechols Using Oxo−Titanium Phthalocyanine

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Abstract: Oxo−titanium phthalocyanine (TiOPc) derivatives of catechin and hematoxylin (natural ortho-diol type chiral compounds) have been prepared and characterized by spectral and chromatographic techniques. It is demonstrated that the TiOPc unit is an excellent template for chiral recognition through its isolated Q-transitions. The formation of a helical dimeric complex with hematoxylin induces strong CD-activity in the Q-band region. Ab initio geometry optimizations were combined with a Kuhn−Kirkwood coupled-oscillator mechanism to obtain the absolute configuration of hematoxylin. In addition, it is shown that the described chiroptical recognition method is sensitive to slight conformational changes.

Introduction

Catechol (1,2-dihydroxybenzene) units are often present in enzymes, antioxidants, and hormones, which play an important role in organisms. For example, the siderophore enterobactin possesses three catechol units and mediates Fe ion uptake into the cell in bacteria,[1] while catecholamines such as adrenalin and dopamine are mediators in the signal transmission in the nervous tissue.[2] It is therefore important to develop an efficient recognition method for these natural catechol compounds, because substrates which exhibit important biological activities are sometimes available in only limited amounts. In recent years, porphyrins and zinc porphyrins have been proposed as one of the most versatile circular dichroism (CD) reporter groups for structural studies of some chiral amines,[3] because these chromophores have intense absorption bands, known as the Soret (or B) bands, in the visible region (ca. 400 nm).[4] Due to the high conformational flexibility of the host−guest complexes, the chiroptical protocol in this case must be combined with a statistical analysis based on molecular mechanics calculations.[3c,e] Tetrabenzotetraazaporphyrins, conventionally called phthalocyanines (Pcs), have characteristic intense absorption bands called Q-bands at around 700 nm.[5] Because the Pc skeleton is rigid and the Q-bands consist mainly of two transitions (HOMO−LUMO and HOMO−LUMO+1 transitions), application of the Pc chromophore to chiral recognition has the potential to facilitate their CD analyses and leads to a neater recognition process. Some previous experimental studies have shown that oxo−titanium phthalocyanine (TiOPc) reacts readily with ortho-diol compounds under mild conditions (Scheme 1).[6] In this study, supramolecular chiral catechol recognition is achieved by applying CD spectroscopy to TiOPc linked with natural chiral compounds having one or two catechol units, catechin[7] and hematoxylin,[8] which are well-known natural chiral compounds extracted from plants. A combined quantum chemical[9]−coupled-oscillator model treatment[10] is set up to analyze the resulting TiPc−hematoxylin complex.

Experimental Section

Synthesis. TiPc−Catechin (1). A mixture of 20 mg of tetra-*tert*-butylated TiOPc (2.5×10^{-2} mmol) and 7.2 mg of catechin hydrate

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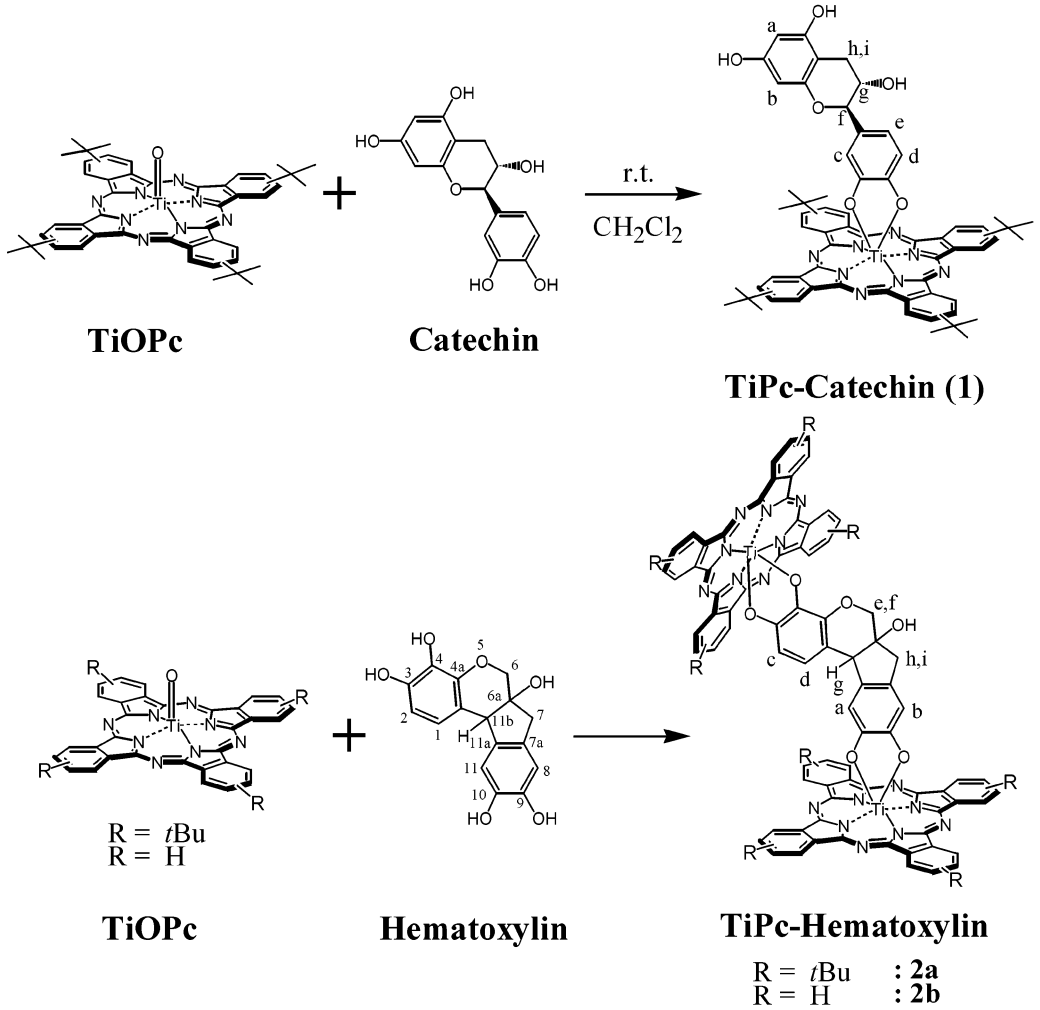
Scheme 1. Preparation of TiPc Complexes[a]



[a] Reaction conditions: **2a**, CH_2Cl_2, room temperature; **2b**, 1-chloronaphthalene, 180 °C.

(2.5×10^{-2} mmol) was reacted in dichloromethane (1 mL) at room temperature under nitrogen overnight. After evaporation of the solvent, the residue was applied to a size-exclusion column (Bio-beads S-X1, Bio-rad) using dichloromethane as eluent. The fast running dark-green portion was collected and recrystallized from dichloromethane/hexane to give 20 mg (1.9×10^{-2} mmol) of the desired compound as a green powder in 75% yield. MS (MALDI-TOF) (*m*/*z*): 1073 (M^+). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.61−9.33 (m, 8H, Pc), 8.37 (d, 4H, Pc), 5.68−5.50 (m, 2H, a,b), 5.44 (s, 1H, e), 4.56 (d, 1H, c), 4.50−4.34 (m, 1H, d), 3.64−3.61 (m, 1H, f), 3.13 (s, 1H, g), 2.53−2.46 (m, 1H, h or i), 2.16−2.00 (m, 1H, h or i). Anal. Calcd for $C_{63}H_{60}N_8O_6Ti\cdot 3H_2O$: C, 67.13; H, 5.90; N, 9.94. Found: C, 67.10; H, 6.11; N, 9.60. UV−vis (CH_2Cl_2) λ_{max} ($10^{-5}\epsilon$): 702(0.93), 634(0.19), 349(0.49), 293(0.49).

TiPc−Hematoxylin (2a). A mixture of 20 mg of tetra-*tert*-butylated TiOPc (2.5×10^{-2} mmol) and 3.8 mg of hematoxylin (1.3×10^{-2} mmol) was reacted in dichloromethane (1 mL) at room temperature under nitrogen overnight. After evaporation of the solvent, the residue was applied to a size-exclusion column (Bio-beads S-X1, Bio-rad) using dichloromethane as eluent. The fast running dark-green portion was collected and recrystallized from dichloromethane/hexane to give 19 mg (1.0×10^{-2} mmol) of the desired compound as a green powder in 80% yield. MS (MALDI-TOF) (*m*/*z*): 1870 (M + 2H). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 9.78−9.02 (m, 16H, Pc), 8.51−7.61 (m, 8H, Pc), 6.38−5.66 (m, 2H, a,d), 5.23−4.71 (m, 1H, b), 4.63−4.23 (m, 3H, c,e,f), 4.01−3.78 (m, 1H, g), 2.72−2.27 (m, 2H, h,i). Anal. Calcd for $C_{112}H_{106}N_{16}O_6Ti_2\cdot 2H_2O$: C, 70.65; H, 5.82; N, 11.77. Found: C, 70.62; H, 5.82; N, 11.20. UV−vis (CH_2Cl_2) λ_{max} ($10^{-5}\epsilon$): 705(2.72), 637(0.59), 347(1.09), 290(1.19).

TiPc−Hematoxylin (2b). To TiOPc without peripheral substituents, 60 mg (0.10 mmol) dissolved in 1-chloronaphthalene (2 mL) at 180 °C under nitrogen, was added 62 mg of hematoxylin (0.21 mmol), and the solution was stirred for 15 min and filtered. To the filtrate was added hexane to induce precipitation. The precipitate was collected and recrystallized from 1-chloronaphthalene/methanol to give 14.1 mg (19.1% yield) of a green powder of the desired compound. MS (MALDI-TOF) (*m*/*z*): 1419 (M + 1, calcd for $C_{80}H_{42}N_{16}O_6Ti_2$).

TiPc−Catechol. A mixture of 10 mg of tetra-*tert*-butylated TiOPc (1.3×10^{-2} mmol) and 4.2 mg of catechol (3.8×10^{-2} mmol) was reacted in dichloromethane (1 mL) at room temperature for 1 day. After evaporation of the solvent, the residue was recrystallized from acetonitrile to give the desired compound as a green powder in ca. 30−40% yield depending on the trials. Anal. Calcd for $C_{54}H_{52}N_8O_2Ti$: C, 72.64; H, 5.87; N, 12.55. Found: C, 72.69; H, 6.50; N, 11.54. UV−vis (CH_2Cl_2) λ_{max} ($10^{-5}\epsilon$): 700(1.16), 634(0.26), 351(0.48), 290(0.51).

Measurement. Electronic absorption spectra were recorded with a HITACHI 330LC spectrometer, and circular dichroism (CD) spectra were recorded with a JASCO J-725 spectrodichrometer. Magnetic circular dichroism (MCD) measurements were made with the above spectrodichrometer equipped with a JASCO electromagnet which produced magnetic fields of up to 1.09 T (1 T = 1 tesla) with parallel and antiparallel fields. The magnitudes were expressed in terms of molar ellipticity ($[\theta]$/deg dm^3 mol^{-1} cm^{-1}) for CD and molar ellipticity per

tesla ($[\theta]_M$/deg dm^3 mol^{-1} cm^{-1} T^{-1}) for MCD. FTIR spectra were recorded on a SHIMADZU FTIR-8100M spectrometer using KBr disks. 400 MHz ^{1}H NMR spectra were recorded with a JEOL GSX-400 spectrometer using $CDCl_3$ or CD_3OD (only catechin and hematoxylin). Size-exclusion chromatography was conducted using a Bio-beads S-X1 (Bio-rad) column. Mass spectra were recorded on a Perspective Biosystem MALDI-TOF Mass Voyager DE-SI2 spectrometer using a positive mode with dithranol (1,8-dihydroxy-9(10*H*)-anthracenone) as the matrix.

Calculation. The geometry optimizations of TiPc−catechol, catechin, and hematoxylin were initiated at the PM3 level using HyperChem,[11] and were refined further by the density-functional formalism with the B3LYP functional in conjunction with a def-SV(P) basis set, as implemented in TURBOMOLE 5.6.[12]

Different hematoxylin conformations were used as the starting point in the geometry optimizations, resulting in two stable conformers. These optimized geometries were used to construct TiOPc, TiPc−catechin, and TiPc−hematoxylin for which the optimization began at the aforementioned DFT level. The vibrational spectra of the TiPc−catechol complexes were calculated at the DFT level of theory, using C_{2v} symmetry restrictions, to discern between minima and transition states.

HyperChem was used to calculate the electronic absorption spectra of the DFT-optimized structures by the single excited configuration interaction method, taking only the singly excited configurations up to 8 eV into account, applying the ZINDO/S Hamiltonian.[13]

Results and Discussion

Formation and Stoichiometry of TiPc Complexes. TiPc−catechin (**1**) and TiPc−hematoxylin (**2a**) complexes were formed in CH_2Cl_2 at room temperature by mixing *tert*-butylated TiOPc with commercially available catechin and hematoxylin, respectively (Scheme 1). Although TiOPc without peripheral substituents shows poor solubility in most organic solvents, the TiPc−hematoxylin complex (**2b**) was prepared at high temperature (180 °C) in 1-chloronaphthalene. When the reaction mixtures of *tert*-butylated complexes were introduced onto size-exclusion chromatography (SEC), a single main dark-green band was observed for each complex, while the color of the starting TiOPc was bright blue. The elution volume of TiPc−hematoxylin was substantially smaller than those of the starting TiOPc and TiPc−catechin complex, indicating that the molecular size of the hematoxylin complex is larger than that of the Pc monomer in solution.[14] A good correlation was found between the logarithm of the expected molecular weights and the elution volume, as plotted in Figure 1. In addition, the molecular ions of these compounds were detected by MALDI-TOF mass spectroscopy (m/z = 1073 for complex **1** and m/z = 1870 for complex **2a**). From these results, it is evident that the stoichiometry for the binding of the Pc chromophore with catechin and hematoxylin is 1:1 and 2:1, respectively. The stoichiometry was further confirmed by the integration of proton signals in ^{1}H NMR spectra. In addition, the NMR data support the structures shown in Scheme 1; that is, aromatic protons of benzene rings linked to Ti via two oxygen atoms appeared shifted to higher field by ca. 1.4−2.4 ppm, as compared to the corresponding signals of uncomplexed catechin or hematoxylin, due to the ring current of the Pc ring. We also measured the IR spectra of these complexes. TiOPc has a characteristic IR band at 972 cm^{-1} corresponding to Ti═O stretching.[15] This stretching band completely disappeared in the spectra of these new complexes. Thus, all of the data on SEC, MALDI-TOF mass, ^{1}H NMR, and IR support the formation of the desired compounds.

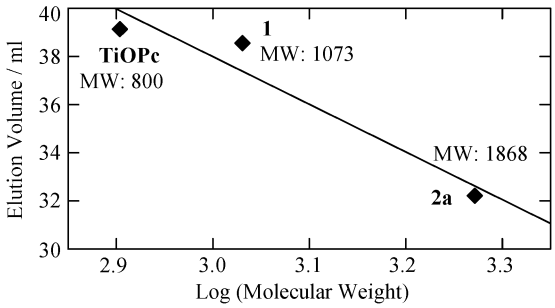


Figure 1. Size-exclusion chromatography of the TiPc complexes. A straight line was drawn by the least-squares method. Elution volume was determined by the maximum absorbance for the Q-band in the elution band.

We examined the reaction of *tert*-butylated TiOPc and an excess amount of resorcinol (1,3-dihydroxybenzene) under the same reaction conditions, to check the binding ability of nonadjacent OH groups in catechin. No spectral change was observed in this control experiment, so that we can conclude that a catechol unit with an ortho-substituted OH group is required for the binding to the central Ti atom in our systems.

Spectroscopic Properties of TiPc Complexes. As shown in Figure 2, the electronic absorption and magnetic circular dichroism (MCD) spectra of the starting TiOPc and TiPc with catechol as an axial ligand (TiPc−catechol) were measured to gain a better understanding of the change of the electronic structure upon ligation. MCD is sensitive to structural features that directly affect degeneracies in electronic energy levels.[4,5] In addition, MCD spectra give valuable indications of the exact energy and number of the excited states, because transitions of different polarizations generally have differently signed MCD signals.

In the absorption spectrum of TiPc−catechol, a broadening and small red-shift of the Q-bands (700 nm) were observed as compared to the Q-band of TiOPc (697 nm). A broad dispersion type MCD of this complex in the Q-band region is assigned to an "apparent" Faraday *A* term, which arises as a superposition of two closely lying Faraday *B* terms of opposite signs, that is, from transitions to near-degenerate states, whereas the sharp and intense dispersion type MCD in the Q-band of TiOPc is a Faraday *A* term arising from transitions involving degenerate final states.[16]

Figure 3 shows the spectra of the natural chiral catechols in methanol and TiPc−catechin (**1**) and TiPc−hematoxylin (**2a** and **2b**) complexes in CH_2Cl_2. The spectroscopic properties of

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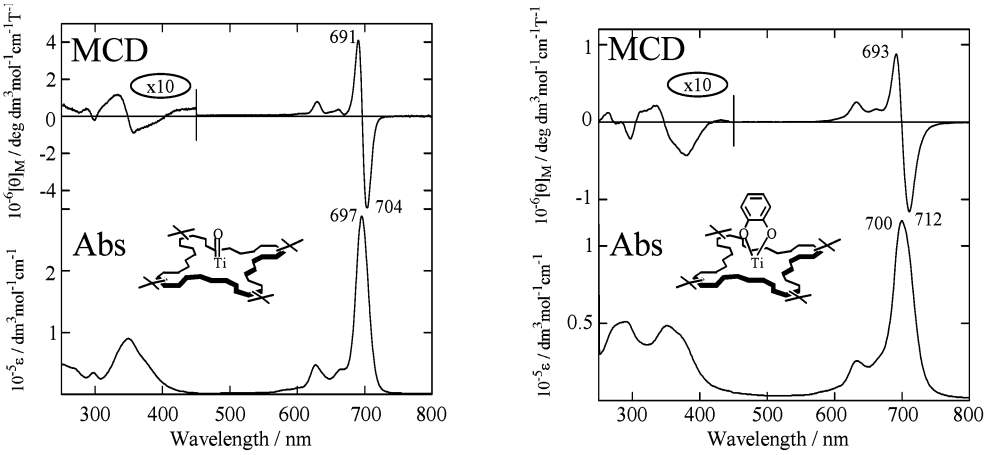

Figure 2. Electronic absorption (bottom) and MCD (top) spectra of TiOPc (left) and TiOPc with catechol (right) in CH_2Cl_2.

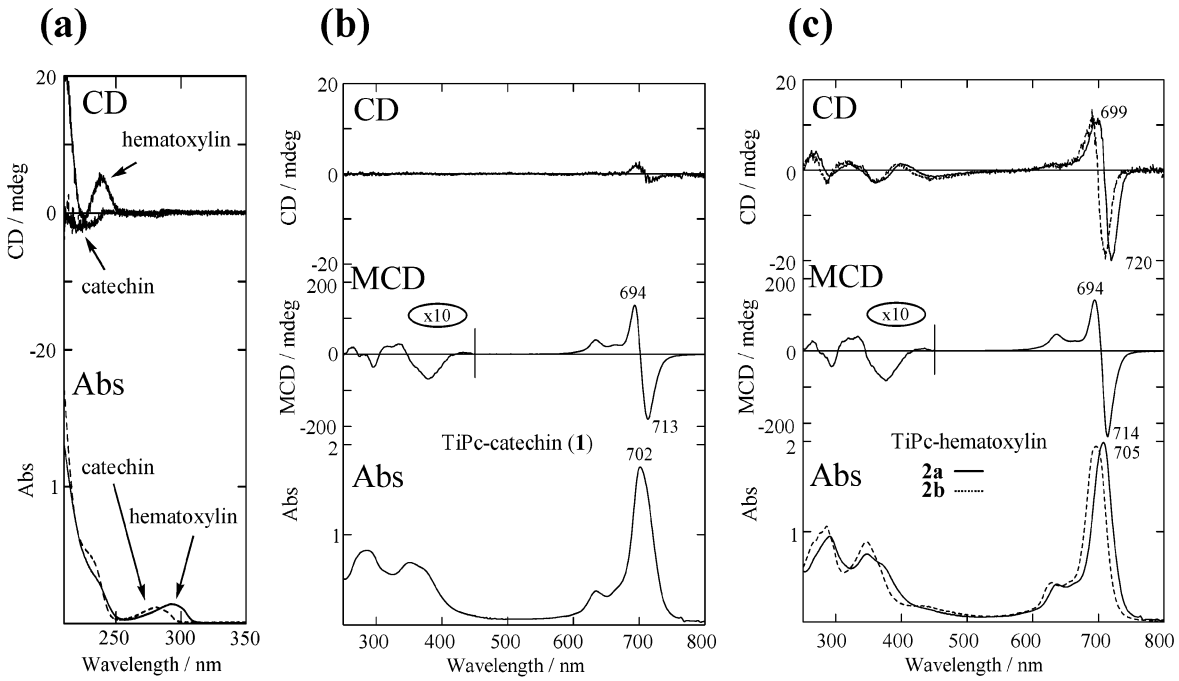

Figure 3. (a) Electronic absorption and CD spectra of catechin (1.0×10^{-4} M) and hematoxylin (1.5×10^{-4} M) in methanol. (b, c) Electronic absorption, MCD, and CD spectra of TiPc−catechin (**1**) (1.88×10^{-5} M) and TiPc−hematoxylin (**2a**, 7.29×10^{-6} M; **2b**, 9.1×10^{-6} M) in dichloromethane.

compound **1** are quite similar to those of the TiPc−catechol complex (Figure 3). The Q-band absorption peak of the TiPc dimer **2a** shifted to longer wavelength (705 nm), although the MCD patterns were essentially identical to those of TiPc−catechol.

The CD spectrum of TiPc−catechin (**1**) did not show any intense CD signal in the visible region. On the other hand, in the spectrum of the TiPc−hematoxylin complex (**2a**), an intense bisignate and several weak CD signals were detected in the Q- and Soret band regions, respectively. Because free hematoxylin shows CD signals only in the UV region (below 250 nm in methanol, see Figure 3a), the Q and Soret CD signals can be safely assigned to the CD exciton bands[17] arising from the interaction between the two Pc chromophores. The nonsubstituted TiPc−hematoxylin complex (**2b**) exhibits the same CD signal pattern as the *tert*-butylated complex (**2a**), suggesting that the perturbation of the *tert*-butyl group is small and therefore that the effect of the substituents can be neglected in the CD generation mechanism in our system. In addition, when the CD spectrum of compound **2a** was recorded in different solvents such as toluene, $CHCl_3$, and CH_2Cl_2:methanol = 1:1, the sign of the CD exciton couplets remained the same. As a result, we can assume that the skewed orientation of the two Pc chromophores in the TiPc−hematoxylin complex is crucial in analyzing the intense CD signal in the Q-band region. In this respect, the requirement of a dimeric chromophore system matches the chiroptical protocol based on dimeric porphyrin hosts.[3]

Structural Calculations. Absolute Structure of Hematoxylin. Hematoxylin is a long-known natural compound extracted from the plant *Hematoxylon campechianum* (Leguminosae)[18] and is easily oxidized to hematein, which has intense absorption

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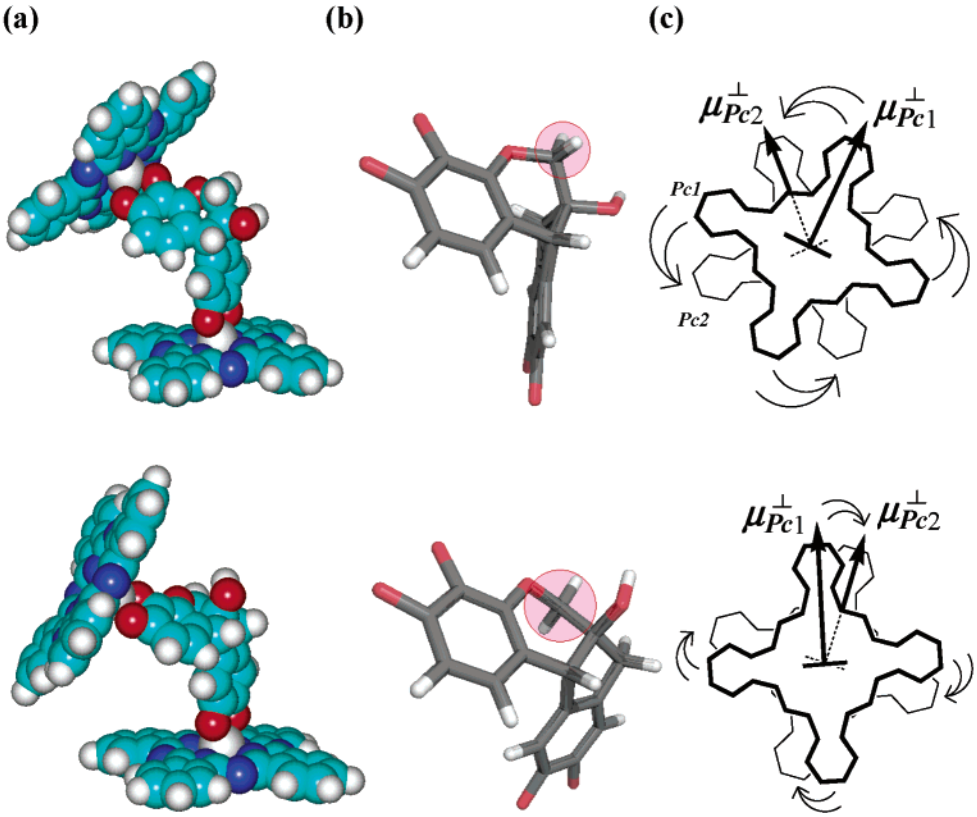

Figure 4. Two possible low-energy conformers of TiPc−(*6aS,11bR*)-hematoxylin obtained from DFT calculations (structure A, top; structure B, bottom). (a) Optimized geometries. (b) Hematoxylin sites in the two optimized structures. The circle indicates the flexible CH_2 group in the pyran ring. (c) Schematic representations of the supramolecular chirality.

bands in the visible region (at 445 nm in methanol).[19] Therefore, this compound has been widely used in histology and cytology, and has been used as a dye for human hair. The absolute configuration of hematoxylin, however, has been conjectured to date only by means of Horeau's partial resolution and the chemical correlation method.[20] In this study, we unambiguously determine the absolute configuration of hematoxylin by Kuhn−Kirkwood analysis of the CD spectrum observed for the TiPc−hematoxylin complex. There are four possibilities for the structural isomers of hematoxylin because this molecule possesses two asymmetric carbon atoms. From the ^{1}H NMR study,[21] the conformation of hematoxylin was assigned to the *cis*-form so that we consider only the two enantiomers. According to the chemical correlation study,[20] the natural hematoxylin was inferred to be the (*6aS,11bR*)-form.

DFT Optimized Structures of the TiPc Complex. Geometry optimization calculations of TiOPc and the TiPc−catechol complex have been carried out by the DFT method (B3-LYP functional). The optimized geometry of TiPc−catechol adopts an "eclipsed" conformation with respect to the pyrrole N atoms toward the O atoms in catechol. TiPc with catechol rotated by 45°, which is the "staggered" conformer, was also calculated. The energy difference between the two TiPc−catechol conformers is only ca. 1 kcal/mol, suggesting that the catechol ligand is freely rotating under the experimental conditions. This result agrees with ^{1}H NMR results of a Ti tetraphenylporphyrin−catechol complex, which indicated the free internal rotation of the catecholate ligand in d_8-toluene.[22] Figure 4a shows the optimized geometry of TiPc−hematoxylin ((*6aS,11bR*)-form) calculated by the DFT method. It should be noted that there are two possible optimized conformations ("structure A" and "structure B") for the TiPc−(*6aS,11bR*)-hematoxylin complex. The energy difference between the two conformers is less than 1 kcal/mol. The two conformers could be obtained by using various starting conformations. Figure 4b displays the hematoxylin units in the two optimized structures of the TiPc−hematoxylin complex. As is clearly seen, the main difference in the two optimized structures results from the relative orientation of the CH_2 group in the pyran ring: the six-membered ring is not planar but adopts a half-chair conformation. The conformational change occurs when flipping the pyran ring. In addition, the adjacent five-membered ring is also nonplanar. This conformation depends strongly on the conformation of the pyran ring, because the relative orientation of the CH_2 group in the pyran ring is always the "anti" conformation with respect to the adjacent OH group.

In the optimized conformations, one of the electric transition dipole moments of the Pc chromophore and an electric transition moment of the catechol unit, which is parallel to the Pc plane, adopt an "eclipsed" form in all cases, including the TiPc−catechin system. There is no distinct distortion of the Pc skeleton as compared to TiOPc, so that consequently the CD generation mechanism due to distortion of the Pc chromophore can be neglected.

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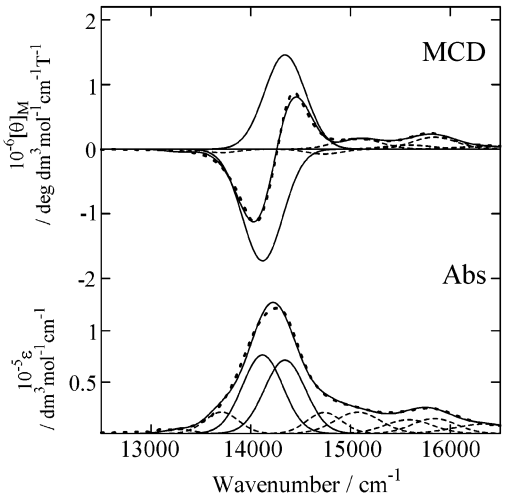


Figure 5. Gaussian band fit of the Q-bands in TiPc−catechol. The dotted line indicates the experimental spectra in CH_2Cl_2.

We use the labels Pc1 and Pc2 to distinguish between the two Pc chromophores in our dimer system; Pc1 and Pc2 denote the Pc chromophores connected with the catechol units adjacent to the five-membered ring and six-membered ring (pyran ring), respectively. As illustrated in Figure 4c, the geometry of the two Pc chromophores in "structure A" of TiPc−hematoxylin can be regarded as a "left-handed helix" system with a large dihedral angle when we choose the direction of one electric transition dipole moment of each Pc chromophore perpendicular to the plane of the catechol ($\mu_{Pc1}^{\perp}$ and $\mu_{Pc2}^{\perp}$). On the other hand, in the "structure B" conformer, the two Pc planes take on a nearly eclipsed conformation, adopting a "right-handed helix" system with a smaller dihedral angle. This result implies that the observed CD signals consist of a superposition of the left- and right-handed helices. As a result, to determine the absolute structure of hematoxylin, we must perform a quantitative exciton CD analysis for both structures.

Exciton Theory (Degenerate Coupled-Oscillator Systems). We consider the TiPc−hematoxylin system consisting of two identical TiPc−catechol molecules; each Pc chromophore has two nondegenerate transitions at energies $\epsilon_{Pc}^{\perp}$ and $\epsilon_{Pc}^{\parallel}$, of which transition dipole moments are denoted as $\mu_{Pc}^{\perp}$ and $\mu_{Pc}^{\parallel}$, respectively. For the quantitative analysis, a band deconvolution analysis[23] of the TiPc−catechol spectra has been performed to estimate accurate transition energies ($\epsilon_{Pc}^{\perp}$ and $\epsilon_{Pc}^{\parallel}$) and the magnitudes of the transition dipole moment ($\mu_{Pc}^{\perp}$ and $\mu_{Pc}^{\parallel}$) of the Pc monomer in CH_2Cl_2 solution. The Gaussian fits of the Q-bands for the TiPc−catechol complex are shown in Figure 5. Fitting parameters are listed in Table 1. The analysis was constrained by the requirement that a single set of Gaussian components be used for the fitting of both the absorption and the MCD spectra. The two dominant bands in absorption and MCD were assigned to the Q(0,0) bands and applied to the CD analysis. As would be expected, the $Q^{\parallel}$ and $Q^{\perp}$ bands have opposite signs within the MCD spectrum. The bands at higher energy can be assigned as Q(0,1) and Q(0,2), respectively, because there are two maxima within the vibrational envelope in both the absorption and the MCD spectra. At the lower energy side of Q(0,0), there appears to be a hot band arising from a 410 cm^{-1} vibration. The relatively high intensity of this band within the spectral deconvolution analysis is probably due to solvation-based band broadening effects. Band broadening due to a multiplicity of solvation environments tends to be more pronounced within the absorption spectrum due to the difference in the intensity mechanisms of absorption and MCD spectroscopy.[23c] The hot band can therefore be viewed as an artifact of the analysis, which would disappear if the spectra were recorded with vitrified solutions at cryogenic temperatures. Our analysis will therefore be restricted to the Q(0,0) bands.

Figure 6 displays the calculated absorption spectra from configuration interaction (CI) calculations at the ZINDO/S level. The calculation results are given in Table 2. TiOPc has a degenerate absorption band at 695 nm due to C_{4v} symmetry. In the case of the optimized structure of TiPc−catechol (Figure 6b), the degeneracy of the Q-band was lifted (690 and 701 nm).

Table 1. Results of the Gaussian Fit Analysis of TiPc−Catechol

band no.	assignment	energy (cm^{-1})	intensity (dm^3/mol cm)	bandwidth (cm^{-1})	oscillator strength	$\|\mu\|$ (D)
1		13 280	3838	335	0.0059	0.174
2		13 704	19 891	397	0.0363	1.035
3	$Q(0,0)^{\parallel}$	14 114	72 788	477	0.1597	4.417
4	$Q(0,0)^{\perp}$	14 339	68 080	483	0.1512	4.116
5		14 734	19 444	409	0.0366	0.970
6		15 068	19 748	536	0.0487	1.261
7		15 578	12 730	556	0.0325	0.815
8		15 836	13 902	518	0.0331	0.816
9		16 337	8713	716	0.0287	0.686

Table 2. CI Calculation Results of TiPc Compounds (ZINDO/S)

complex	energy (cm^{-1})	oscillator strength f	main configuration (wt %)
TiOPc	14 390	1.0667	HOMO−LUMO (80.6) (degenerate)
TiPc−catechol[a]	14 256	1.0323	HOMO−LUMO (94.1)
	14 490	1.0926	HOMO−LUMO+1 (94.0)
TiPc−catechol[b]	14 260	1.0582	HOMO−LUMO (94.3)
	14 620	1.0876	HOMO−LUMO+1 (94.2)

[a] Optimized structure. [b] 45° rotated structure.

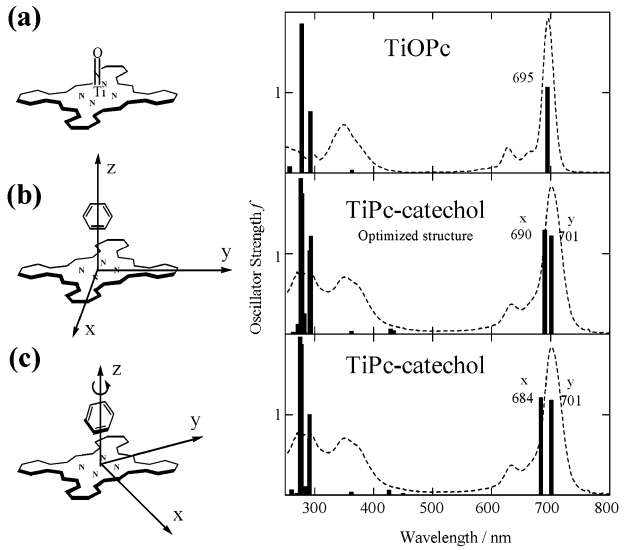
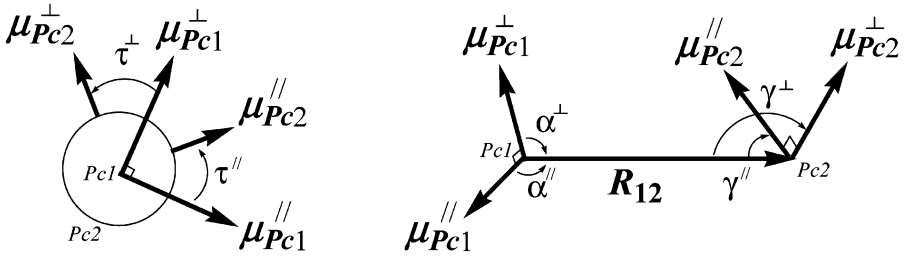


Figure 6. Conformations and calculated stick spectra of (a) TiOPc and (b and c) TiPc−catechol using the ZINDO/S Hamiltonian. The broken line indicates the observed absorption spectra in CH_2Cl_2.

(23) (a) Browett, W. R.; Stillman, M. J. *J. Comput. Chem.* **1987**, *11*, 73. (b) Mack, J.; Stillman, M. J. *J. Am. Chem. Soc.* **1994**, *116*, 1292. (c) Mack, J.; Stillman, M. J. *J. Phys. Chem.* **1995**, *99*, 7935.

Scheme 2. Geometrical Parameters for CD Analysis



The Q-band splitting obtained by the Gaussian fits (225 cm^{-1}) is in fair agreement with the ZINDO/S calculated splitting (234 cm^{-1}), although the total oscillator strengths from Table 1 (ca. 0.5) are less intense than the results of the CI calculations (ca. 2). This tendency to overestimate oscillator strength is a common feature of ZINDO/S calculations in the phthalocyanine system.[24]

The calculated absorption spectrum of the catechol unit-rotated (45°) system (Figure 6c) is essentially identical to that of the optimized structure. Thus, the lower and higher Q-band transitions are polarized parallel and perpendicular to the axial ligand plane, respectively, regardless of the rotation angle of this plane with respect to the rest of the Pc. Because the distance between the two Pc chromophores is at least 7−8 Å for both dimer structures, the free rotations of the constituent Pc chromophores in the *tert*-butylated Pc dimer system (**2a**), as well as the nonsubstituted system (**2b**), should be taken into consideration. Therefore, the precise conformation of the individual Pc chromophores is not important for analysis of the intense CD signal in the Q-band region: the important factors appear to be the absolute configuration and conformation of hematoxylin.

As we have already inferred from the spectra of the monomers, the CD intensity in the dimer is clearly caused by the Kuhn−Kirkwood coupled-oscillator mechanism of the Pc Soret and Q-bands. Stealing of CD intensity from the ligand transitions[25] seems to be ruled out by the high-energy separation of those transitions and is also confirmed by the near absence of rotatory strength in the Q-band of the TiPc−catechin complex (see Figure 3).

The exciton theory for degenerate coupled-oscillator systems predicts that the interaction energy between the two Pc chromophores should be inversely proportional to the cube of the interchromophoric distance (R_{12}) and proportional to the square of the transition moment (μ) of the interacting chromophore in the point-dipole approximation.[26] This approximation holds when the separation of the chromophores is much larger than the transition dipole lengths. In our system, the distance between the centers of gravity of the TiPc chromophores (R_{12}) is ca. 13 Å, and the transition dipole length calculated from the band fits is 0.8−0.9 Å, so that this approximation is justified. When we consider two degenerate coupled-oscillator systems within the point-dipole approximation, the exciton band energies $\epsilon^{\perp,\parallel}(\pm)$ and the rotatory strengths $R^{\perp,\parallel}(\pm)$ of the TiPc−hematoxylin complex can be written by the following equations using several angles defined in Scheme 2:

$$R^{\perp}(\pm) = \pm \frac{\epsilon_{Pc}{}^{\perp}(\mu_{Pc}{}^{\perp})^2 R_{12}}{4\hbar} \sin\alpha^{\perp} \sin\gamma^{\perp} \sin\tau^{\perp} \qquad (1)$$

$$\epsilon^{\perp}(\pm) = \epsilon_{Pc}{}^{\perp} \pm \frac{(\mu_{Pc}{}^{\perp})^2}{4\pi\epsilon_0 (R_{12})^3} (\sin\alpha^{\perp} \sin\gamma^{\perp} \cos\tau^{\perp} + 2\cos\alpha^{\perp} \cos\gamma^{\perp}) \qquad (2)$$

$$R^{\parallel}(\pm) = \pm \frac{\epsilon_{Pc}{}^{\parallel}(\mu_{Pc}{}^{\parallel})^2 R_{12}}{4\hbar} \sin\alpha^{\parallel} \sin\gamma^{\parallel} \sin\tau^{\parallel} \qquad (3)$$

$$\epsilon^{\parallel}(\pm) = \epsilon_{Pc}{}^{\parallel} \pm \frac{(\mu_{Pc}{}^{\parallel})^2}{4\pi\epsilon_0 (R_{12})^3} (\sin\alpha^{\parallel} \sin\gamma^{\parallel} \cos\tau^{\parallel} + 2\cos\alpha^{\parallel} \cos\gamma^{\parallel}) \qquad (4)$$

It should be noted that the angle τ is always taken in an anticlockwise direction when the system is viewed from Pc1 to Pc2. The notations plus and minus represent the in-phase and out-of-phase transition case, respectively. Table 3 lists the angle parameters calculated from the DFT-optimized structures.

Using these equations, the oscillator strengths and rotatory strengths for the Q-bands in each TiPc−hematoxylin conformer are estimated (Table 4). In this calculation, the absolute configuration of hematoxylin was arbitrarily chosen to be the

Table 3. Geometrical Parameters for the TiPc−(*6aS,11bR*)-Hematoxylin Complex

structure		α	γ	τ	R_{12}/Å
A	$\mu_{Pc}{}^{\parallel}$	81.96	84.20	40.03	13.20
	$\mu_{Pc}{}^{\perp}$	61.00	65.20	38.23	13.20
B	$\mu_{Pc}{}^{\parallel}$	62.75	90.01	351.70	13.01
	$\mu_{Pc}{}^{\perp}$	66.97	61.17	339.00	13.01

Table 4. Results of Coupled-Oscillator Analysis for TiPc−(*6aS,11bR*)-Hematoxylin and Gaussian Fit Analysis of the Observed CD Spectrum for TiPc−Hematoxylin

		energy (cm^{-1})	wavelength (nm)	oscillator strength	rotatory strength ($D\mu_B$)
structure A	$\epsilon^{\parallel}(-)$	14 078	710.3	0.0337	−3.844
	$\epsilon^{\parallel}(+)$	14 149	706.7	0.2358	3.844
	$\epsilon^{\perp}(-)$	14 299	699.3	0.0653	−2.630
	$\epsilon^{\perp}(+)$	14 378	695.5	0.1600	2.630
structure B	$\epsilon^{\parallel}(-)$	14 075	710.5	0.0156	0.783
	$\epsilon^{\parallel}(+)$	14 153	706.5	0.2439	−0.783
	$\epsilon^{\perp}(-)$	14 295	699.5	0.0491	1.547
	$\epsilon^{\perp}(+)$	14 382	695.3	0.1762	−1.547
Gaussian fit		13 954	716.7	0.0927	−0.935
		14 245	702.0	0.7750	0.746

(24) Kobayashi, N.; Mack, J.; Ishii, K.; Stillman, M. J. *Inorg. Chem.* **2002**, *41*, 5350.
(25) (a) Schipper, P. E. *J. Am. Chem. Soc.* **1979**, *101*, 6826. (b) Kobayashi, N.; Higashi, R.; Titeca, B. C.; Lamote, F.; Ceulemans, A. *J. Am. Chem. Soc.* **1999**, *121*, 12018.
(26) Kasha, M.; Rawls, H. R.; El-Bayoumi, M. A. *Pure Appl. Chem.* **1965**, *11*, 371.

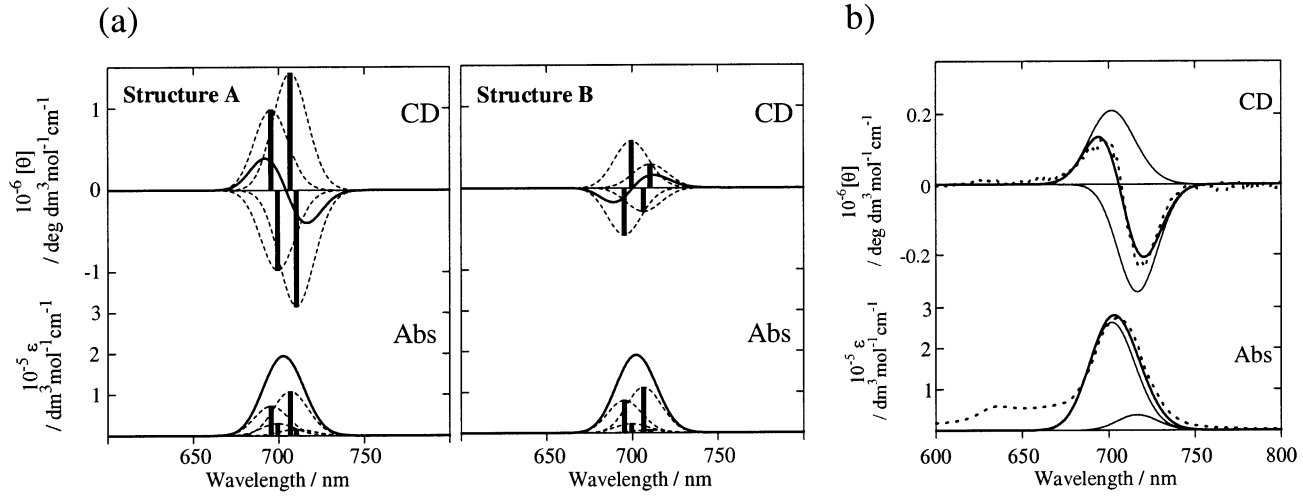


Figure 7. (a) Calculated electronic absorption and CD spectra of the two conformers in the TiPc−(*6aS,11bR*)-hematoxylin complex. Each band was described by a single Gaussian curve (broken line). The solid line indicates the superposition of all Gaussian curves. (b) Band deconvolution of the Q-band in TiPc−hematoxylin (**2a**) using two Gaussian components. The dotted line indicates the experimental spectra in CH_2Cl_2.

(*6aS,11bR*)-form. To reproduce a dispersion type CD signal, the calculated oscillator strength and rotatory strength are converted into the extinction coefficient (ϵ) and molar ellipticity ($[\theta]$) using the same bandwidths as for the band deconvolution of TiPc−catechol and then convoluted as shown in Figure 7a. Because of a very slight splitting of these exciton states, the resulting CD intensities are considerably weakened as compared to the intensity of each band. It is obvious that the signs of the CD signals for the two lowest-energy conformers are opposite. The CD intensity of the "structure A" conformer is approximately 3 times larger than that of the "structure B" conformer. For a comparison of these theoretical results with the observed CD signals, the Gaussian fit was performed for the observed spectrum (Figure 7b). Because the description of the experimental CD signal by a superposition of bands with such small splittings was impossible, the Q-band was deconvoluted in only two Gaussian curves. The resulting rotatory strengths are −0.935 and 0.746 Dμ_B.

Because the energy difference between $\epsilon_{Pc}{}^{\perp}$ and $\epsilon_{Pc}{}^{||}$ (225 cm^{-1}) is substantially larger than the exciton interaction energy (30−40 cm^{-1}), the CD contribution due to nondegenerate couplings (exciton interactions between $\mu_{Pc}{}^{\perp}$ and $\mu_{Pc}{}^{||}$) may be neglected. Nevertheless, we calculated the contribution of the nondegenerate coupling by solving the following matrix equation:

$$\begin{vmatrix} \epsilon_{Pc1}{}^{\perp} - \epsilon & 0 & V_{Pc1^{\perp}Pc2^{\perp}} & V_{Pc1^{\perp}Pc2^{||}} \\ 0 & \epsilon_{Pc1^{||}} - \epsilon & V_{Pc1^{||}Pc2^{\perp}} & V_{Pc1^{||}Pc2^{||}} \\ V_{Pc1^{\perp}Pc2^{\perp}} & V_{Pc1^{||}Pc2^{\perp}} & \epsilon_{Pc2^{\perp}} - \epsilon & 0 \\ V_{Pc1^{\perp}Pc2^{||}} & V_{Pc1^{||}Pc2^{||}} & 0 & \epsilon_{Pc2^{||}} - \epsilon \end{vmatrix} = 0 \quad (5)$$

$$V_{ij} = \frac{\mu_i \mu_j}{4\pi\epsilon_0 (R_{12})^3} (\sin\alpha \sin\gamma \cos\tau + 2\cos\alpha \cos\gamma) \quad (6)$$

where ϵ is the energy of the exciton state for the dimer, and V_{ij} is the excitonic interaction energy ($V_{Pc1^{\perp}Pc2^{\perp}}$ and $V_{Pc1^{||}Pc2^{||}}$ link degenerate levels, while $V_{Pc1^{\perp}Pc2^{||}}$ and $V_{Pc1^{||}Pc2^{\perp}}$ link nondegenerate levels). The calculated exciton state energies using these formulas were almost identical to the calculated energies using eqs 2 and 4 for both conformers: the energy difference was less than 3 cm^{-1} in all exciton states. This indicates that the contribution of the nondegenerate coupling is quite small.

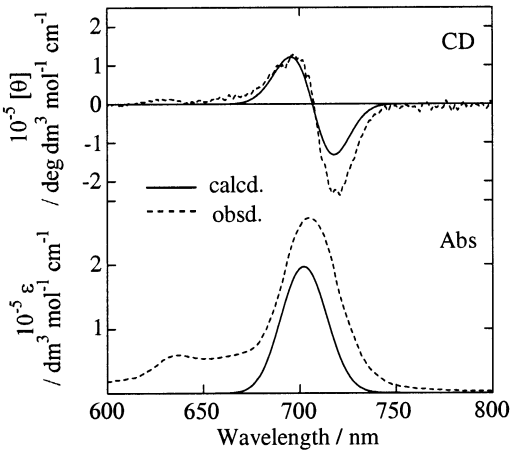


Figure 8. Comparison between the experimental spectra of TiPc−hematoxylin **2a** (broken line) and the calculated spectra (solid line) generated by superimposing the spectra of the two conformers for the (*6aS,11bR*)-form in a 50:50 mixture.

As a result, the total absorption and CD spectra were generated by superimposing the spectra of the two conformers for the (*6aS,11bR*)-form in a 50:50 mixture, as shown in Figure 8. The calculated CD spectrum closely reproduced the observed CD signals. Thus, because of the opposite CD signs for each conformer, the apparent rotatory strengths are reduced as compared to the theoretical values, which in turn might be correlated with the small values calculated from the band deconvolution analysis. Moreover, the apparent CD peaks were estimated at 718 and 696 nm, which are almost identical to the experimental values (720 and 699 nm).

Because the calculations using the (*6aS,11bR*)-form are in close agreement with the experimental data, while in contrast the (*6aR,11bS*)-form gives the mirror image of the CD spectrum, the absolute stereochemistry for hematoxylin can be assigned as (*6aS,11bR*). This assignment is also consistent with the model that was developed on the basis of the chemical correlation method.[20]

Conclusions

We have presented a method for chiroptical recognition of chiral catechol compounds (catechin and hematoxylin) using TiOPc under mild conditions. TiPc−catechin (**1**) and TiPc−hematoxylin (**2a**) complexes were characterized by means of size-exclusion chromatography (SEC), ^{1}H NMR, and IR spectroscopy. The stoichiometry for the binding of TiPc with the catechol ligand is 1:1 and 2:1. TiPc−hematoxylin (**2a**) exhibited an intense bisignate CD signal in the Q-band region, although TiPc−catechin (**1**) was CD-silent in the visible region. From these experimental results, we believe that the use of TiOPc has great potential for catechol recognition, because (1) the TiPc−catechol complexes are stable and can be isolated by SEC, (2) nonadjacent OH groups in catechol compounds have no binding ability to TiOPc, and (3) CD signals for the TiPc−catechol complexes depend strongly on the number of the catechol units.

The conformational study of DFT/B3LYP optimized structures suggested that the axial catechol unit is freely rotating in solution and that there are two lowest-energy structures for the TiPc−(*6aS,11bR*)-hematoxylin complex. The Kuhn−Kirkwood coupled-oscillator analysis demonstrated that the signs of CD signals for the two lowest-energy conformers are opposite, which is clear from the schematic representation of the coupled-chromophore helicities shown in Figure 4c. In structure A, the transition dipoles form a right-handed system,[17a] giving rise to a "normal" CD spectrum with a strong negative lower-energy branch and a positive upper-energy branch. For structure B, the helicity is opposite, but this feature is much less pronounced, because the CD intensity is weak. As a result, the convoluted CD spectrum assuming equal population of both conformations nicely reproduced the observed CD signals. Consequently, we have succeeded for the first time in assigning the absolute configuration of hematoxylin as the (*6aS,11bR*)-form on the basis of CD spectroscopy. This assignment lends support to the earlier estimation made using the chemical correlation method.[20]

In conclusion, we have shown that dimeric Pc complexes offer new possibilities for the recognition of absolute configurations and even open the prospect of obtaining direct conformational information. As compared to previously studied host−guest complex systems based on porphyrin dimers, the Pc units have distinct advantages for CD analyses. First, the CD resides in the well-separated Q-band of the chromophore, which is certainly well characterized spectroscopically and less contaminated by other transitions as compared to the Soret band in the porphyrin system. Second, free rotation of the Pc units around the metal ligation axis does not affect the CD because the underlying transitions are rotationally invariant and split by parallel and perpendicular transitions to the di-oxo bridging direction. Finally, conformational flexibility is limited to the conformational changes in the chiral unit itself, unlike the wide conformational freedom that is encountered in host−guest complexes. Interestingly, small conformational changes may give rise to widely differing helical geometries of the dimers, as is the case for structures A and B in the present compounds. In principle, this sensitivity could be exploited to obtain conformational information from the CD spectrum.

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