Temperature-Dependent Left- and Right-Twisted Conformational Changes in 1:1 Host-Guest Systems: Theoretical Modeling and Chiroptical Simulations

Nozomu Suzuki,[a,b]* Daisuke Taura,[c,d]* Yusuke Furuta,[d] Yudai Ono,[e] Senri Miyagi,[f] Ryota Kameda,[g] and Takeharu Haino[e,g]

[a] Dr. N. Suzuki
Department of Chemical Science and Engineering, Graduate School of Engineering
Kobe University
Rokko, Nada, Kobe 657-8501, Japan
E-mail: nsuzuki@port.kobe-u.ac.jp

[b] Dr. N. Suzuki
Department of Human Studies, Faculty of Arts and Humanities
Shikoku Gakuin University
3-2-1 Bunkyo-cho, Zentsuji, Kagawa 765-8505, Japan

[c] Dr. D. Taura
Department of Applied Chemistry, Faculty of Science and Technology
Meijo University
1-501 Shiogamaguchi, Tempaku-ku, Nagoya 468-8502, Japan
E-mail: dtaura@meijo-u.ac.jp

[d] Dr. D. Taura, Y. Furuta
Department of Applied Chemistry, Graduate School of Science and Technology
Meijo University
1-501 Shiogamaguchi, Tempaku-ku, Nagoya 468-8502, Japan

[e] Dr. Y. Ono, Prof. Dr. T. Haino
International Institute for Sustainability with Knotted Chiral Meta Matter (WPI-SKCM^2)
Hiroshima University
2-313 Kagamiyama, Higashi-Hiroshima, Hiroshima 739-8527, Japan

[f] S. Miyagi
Department of Chemistry, School of Science
Hiroshima University
1-3-1 Kagamiyama, Higashi-Hiroshima, Hiroshima 739-8526, Japan

[g] R. Kameda, Prof. Dr. T. Haino
Department of Chemistry, Graduate School of Advanced Science and Engineering
Hiroshima University
1-3-1 Kagamiyama, Higashi-Hiroshima, Hiroshima 739-8526, Japan

Supporting information for this article is given via a link at the end of the document.

Abstract: An efficient strategy for applying to chiral materials is to design and synthesize host molecules with left- and right-twisted conformations and to control their twisted conformations. For this, a quantitative analysis is required to describe the chiroptical inversion, chiral transfer, and chiral recognition in the host-guest systems, which is generally performed using circular dichroism (CD) and/or proton nuclear magnetic resonance (^{1}H-NMR) spectroscopies. However, the mass-balance model that considers the left- and right-twisted conformations has not yet been established. In this study, we derived novel equations based on the mass-balance model for the 1:1 host-guest systems. Then, we further applied them to analyze the 1:1 host-guest systems for the achiral calixarene-based capsule molecule, achiral dimeric zinc porphyrin tweezer molecule, and chiral pillar[5]arene with the chiral and/or achiral guest molecules by using the data obtained from the CD titration, variable temperature CD (VT-CD), and ^{1}H-NMR experiments. The thermodynamic parameters (ΔH and ΔS), equilibrium constants (K), and molar CD ($\Delta\varepsilon$) in the 1:1 host-guest systems could be successfully determined by the theoretical analyses using the derived equations.

Introduction

Since the pioneering discovery of the macrocyclic compound with the molecular recognition site, crown ether, by Pedersen in 1967,[1] the host-guest (supramolecular) chemistry has been developed over half a century using a variety of achiral and chiral host molecules, such as cyclodextrins, calixarenes, blue boxes, cucurbiturils, and pillararenes, as well as unique molecular tweezers and capsules. In particular, taking advantage of the host-guest systems, much interest has been focused on the versatility of chiral materials. The design and synthesis of host molecules with left- and right-twisted conformations play an essential role in chiral separation, chiral sensing, absorption and emission of circularly polarized light, and asymmetric catalysis because the twisted structures enable the control of chiroptical

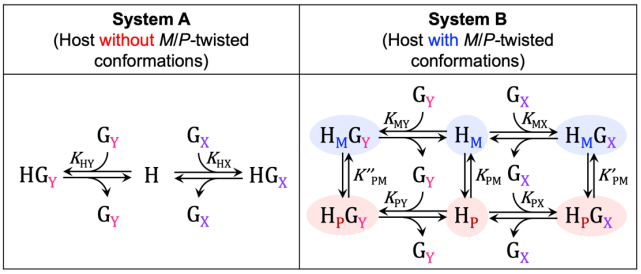
inversion, chiral transfer, and chiral recognition.[2] Thus, it is important to understand the host-guest system with left- and right-twisted conformations to maximize the potential of the host molecule.

There are two types of 1:1 host-guest systems (Systems A and B), as summarized in Scheme 1. System A is the conventional one, and its analytical method has been well-organized by Hirose,[3] Sessler, Anslyn, and co-workers,[4] and Thordarson.[5] They proposed the methods to analyze the 1:1, 1:2, and 2:1 host-guest systems but their models were limited within the variation in the stoichiometry of the host and guest molecules. Conversely, to the best of our knowledge, the mass-balance model for System B, which considers the left- and right- (*M*- and *P*-) twisted conformations of the host molecule, has not yet been established. It is noted that the chiral amplification of the helical supramolecular polymers has been successfully described based on the mass-balance model considering the *M*- and *P*-handed helical conformations,[2n,6] which supports the importance of distinguishing the *M*- and *P*-twisted conformations for understanding the chiral properties. The *M* and *P* notations are used as representative notations for the left- and right-handed conformers rather than those strictly defined by the IUPAC. Therefore, in this work, the left- and right-twisted conformations of the host molecule with planar chirality (*pS* and *pR*) are represented by the *M* and *P* notations, respectively. Moreover, there are two ways to describe the chirality of the host molecule in System B: chiral/achiral and non-racemic/racemic. We used the former description because the conformational changes between the left- and right-twisted structures of the host molecules in this work are mainly dynamic rather than static.

The following chiral phenomena are expected in Systems A and B (Scheme 1): (i) chiroptical inversion, (ii) chiral transfer, and (iii) chiral recognition. (i) If the *M*- or *P*-twisted conformation of the host molecule is inverted by complexation with a guest molecule, chiroptical inversion occurs. Chiroptical inversion can be observed in the systems for the achiral host/chiral guest, chiral host/achiral guest, and chiral host/chiral guest molecules. However, chiroptical inversion rarely occurs in systems for chiral host/achiral guest molecules. (ii) If the achiral host molecule interacts with the chiral guest molecule, the chirality of the chiral guest molecule can be transferred to the achiral host molecule (chiral transfer). (iii) If the chiral host molecule selectively interacts with either one enantiomer from the racemic mixture of the guest molecule, chiral recognition can be observed.

Quantitative analysis of the chiroptical inversion, chiral transfer, and chiral recognition through the host-guest interaction is generally performed by the titration and/or variable temperature (VT) experiments using circular dichroism (CD) and/or proton nuclear magnetic resonance (^{1}H-NMR) spectroscopies. As mentioned above, in contrast to System A, the systematic derivation of the equations based on the mass-balance model for System B has not yet been achieved. This could be because (i) many parameters are involved in System B, which appears to be complicated and (ii) conventional equations for System A can be used to analyze the system by ignoring the *M*- and *P*-twisted conformations even if the host molecule adopts them. However, if chiroptical inversion, chiral transfer, and chiral recognition are involved in the host-guest systems under the equilibrium between the left- and right-twisted conformations, the chiral property of the host molecule can be governed by its left- and right-twisted conformations. Thus, the quantitative analysis of System B is essential to evaluate and improve the chiral properties of the host molecules.

In this study, we propose useful equations based on the mass-balance model for System B to analyze the data obtained from the CD titration, VT-CD, and ^{1}H-NMR experiments. Among them, we mainly focused on the analysis of the VT-CD experiment rather than the CD titration and ^{1}H-NMR experiments because (i) it is difficult to analyze System B using the CD titration curve and (ii) the method to analyze System B using the ^{1}H-NMR data has been well-established, especially for diastereomeric host-guest systems. However, the ^{1}H-NMR experiment is not applicable when the conformational changes are faster than the timescale of the ^{1}H-NMR measurement. In contrast, the VT-CD experiment is free from such disadvantage. To the best of our knowledge, this is the first report describing an analytical method for System B using the VT-CD data.



Scheme 1. Host-guest systems. Guest molecules (G_X and G_Y) can be a pair of enantiomers or chiral and achiral molecules. System A: host molecule (H) without left- and right- (*M*- and *P*-) twisted conformations. System B: H with *M*- and *P*-twisted conformations (H_M and H_P).

Results and Discussion

Equations Based on the Mass-Balance Model for System B

On the basis of System B in Scheme 1, the following equation describes the equilibrium between the *M*- and *P*-twisted conformations of the host molecule ($H_P \rightleftarrows H_M$).

$$K_{PM} = \frac{[H_M]}{[H_P]} \quad (1)$$

The K_{PM} parameter denotes the equilibrium constant between the *M*- and *P*-twisted conformations of the free host molecule. If the host molecule is achiral (racemic, $[H_P] = [H_M]$), $K_{PM} = 1$ holds. However, if the host molecule is chiral (non-racemic, $[H_P] \neq [H_M]$) and the *M*- and *P*-twisted conformations are perturbed by the chiral moiety, $K_{PM} \neq 1$ holds.

The following equations (eqs 2–5) express the binding constants (K_{MX}, K_{MY}, K_{PX}, and K_{PY}) between the host molecule with the *M*- and *P*-twisted conformations and guest molecules (G_X and G_Y) through 1:1 host-guest interactions. It should be noted that G_X and G_Y can be a pair of enantiomers or chiral and achiral molecules.

$$K_{MX} = \frac{[H_M G_X]}{[H_M][G_X]} \quad (2)$$

$$K_{MY} = \frac{[H_M G_Y]}{[H_M][G_Y]} \quad (3)$$

$$K_{PX} = \frac{[H_P G_X]}{[H_P][G_X]} \quad (4)$$

$$K_{PY} = \frac{[H_P G_Y]}{[H_P][G_Y]} \quad (5)$$

Using eqs 1–5, the K'_{PM} and K''_{PM} parameters can be described as the following equations.

$$K'_{PM} = \frac{[H_M G_X]}{[H_P G_X]} = \frac{K_{MX} K_{PM}}{K_{PX}} \quad (6)$$

$$K''_{PM} = \frac{[H_M G_Y]}{[H_P G_Y]} = \frac{K_{MY} K_{PM}}{K_{PY}} \quad (7)$$

As only the total concentrations of the host ($[H]_T$) and guest ($[G_X]_T$ and $[G_Y]_T$) molecules are known, the concentrations of the free host ($[H_P]$ and $[H_M]$) and free guest ($[G_X]$ and $[G_Y]$) molecules should be estimated from $[H]_T$, $[G_X]_T$, and $[G_Y]_T$. By defining p, q, and r as the following equations (eqs 8–10), $[H_M]$ can be obtained by solving the cubic equation, $A[H_M]^3 + B[H_M]^2 + C[H_M] + D = 0$.

$$p = K_{MX} + \frac{K_{PX}}{K_{PM}} \quad (8)$$

$$q = K_{MY} + \frac{K_{PY}}{K_{PM}} \quad (9)$$

$$r = 1 + \frac{1}{K_{PM}} \quad (10)$$

$$A = pqr \quad (11)$$

$$B = pq([G_X]_T + [G_Y]_T - [H]_T) + r(p + q) \quad (12)$$

$$C = -(p + q)[H]_T + p[G_X]_T + q[G_Y]_T + r \quad (13)$$

$$D = -[H]_T \quad (14)$$

Although the analytical solution for the cubic equation is known as Cardano's formula, using commercially available software such as Origin or a spreadsheet based on the least square method could be more practical.[4] It may be worth mentioning that the cubic equation is also used for 1:2 and 2:1 host-guest equilibria.[4,5]

$[G_X]$ and $[G_Y]$ can be subsequently obtained using the following equations.

$$[G_X] = \frac{[G_X]_T}{1 + p[H_M]} \quad (15)$$

$$[G_Y] = \frac{[G_Y]_T}{1 + q[H_M]} \quad (16)$$

In the case of $[G_Y]_T = 0$, the equation for $[H_M]$ becomes a quadratic function, $B[H_M]^2 + C[H_M] + D = 0$, which coincides with the cubic equation with $q = 0$.

$$B = pr \quad (17)$$

$$C = p([G_X]_T - [H]_T) + r \quad (18)$$

$$D = -[H]_T \quad (19)$$

The value can be calculated analytically using the quadratic formula. Once $[H_M]$ is obtained, $[H_P]$ can be described as $[H_P] = [H_M]/K_{PM}$ using eq 1. By defining $[H] = [H_P] + [H_M] (= r[H_M])$, the quadratic function of System B can be described as $(B/r^2)[H]^2 + (C/r)[H] + D = 0$. Moreover, by replacing the coefficients of the equation with $B' = B/r^2$ and $C' = C/r$, the quadratic equation of System B becomes $B'[H]^2 + C'[H] + D = 0$. This equation is compared to the quadratic equation of System A (Table 1).[4]

Analysis of System B Using the CD Data

If the observed value of the molar CD ($\Delta\varepsilon$) originates from the host molecule and the contribution from the guest molecule(s) is negligible in the host-guest system, the $\Delta\varepsilon$ value is expressed by the following equation.

$$\Delta\varepsilon = \{\Delta\varepsilon_M + \Delta\varepsilon_P/K_{PM} + (\Delta\varepsilon_{MX}K_{MX} + \Delta\varepsilon_{PX}K_{PX}/K_{PM})[G_X] + (\Delta\varepsilon_{MY}K_{MY} + \Delta\varepsilon_{PY}K_{PY}/K_{PM})[G_Y]\} / (r + p[G_X] + q[G_Y]) \quad (20)$$

where $\Delta\varepsilon_M$, $\Delta\varepsilon_P$, $\Delta\varepsilon_{MX}$, $\Delta\varepsilon_{PX}$, $\Delta\varepsilon_{MY}$, and $\Delta\varepsilon_{PY}$ are the $\Delta\varepsilon$ values for H_M, H_P, H_MG_X, H_PG_X, H_MG_Y, and H_PG_Y, respectively. Eq 20 is described in general form, and the more specific conditions below (i–iv) can simplify the equation:

(i) If there is only a single guest molecule (G_X), $[G_Y] = 0$ holds.

(ii) If the host molecule is achiral, $K_{PM} = 1$ and $\Delta\varepsilon_M = -\Delta\varepsilon_P$ hold.

(iii) If the condition (ii) holds, and both guest molecules (G_X and G_Y) are enantiomers, $\Delta\varepsilon_{MX} = -\Delta\varepsilon_{PY}$, $\Delta\varepsilon_{MY} = -\Delta\varepsilon_{PX}$, $K_{MX} = K_{PY}$, and $K_{MY} = K_{PX}$ hold.

(iv) If the condition (ii) holds, and if one of the guest molecules (G_Y) is achiral, $K_{PY} = K_{MY}$ holds.

Further modification of the formula is necessary to analyze the results obtained from the VT-CD experiments. The following equation is derived if the conditions (ii) and (iii) are satisfied.

$$\Delta\varepsilon = \frac{(\Delta\varepsilon_{MX}K_{MX} + \Delta\varepsilon_{PX}K_{PX})([G_X] - [G_Y])}{2 + (K_{MX} + K_{PX})([G_X] + [G_Y])} \quad (21)$$

The following equation is obtained using the relations, $K_i = \exp(-\Delta G_i/RT)$ and $\Delta G_i = \Delta H_i - T\Delta S_i$, and applying the approximation, $\Delta\varepsilon_{MX} = -\Delta\varepsilon_{PX} = \Delta\varepsilon_{MY} = -\Delta\varepsilon_{PY}$.

$$\Delta\varepsilon = \{\Delta\varepsilon_{MX}(\exp(-\Delta G_1/RT) - 1)([G_X] - [G_Y])\} / \{2\exp(\Delta G_{PX}/RT) + (\exp(-\Delta G_1/RT) + 1)([G_X] + [G_Y])\} \quad (22)$$

where $\Delta G_1 = \Delta G_{MX} - \Delta G_{PX} = \Delta H_1 - T\Delta S_1 = \Delta H_{MX} - \Delta H_{PX} - T(\Delta S_{MX} - \Delta S_{PX})$. Furthermore, $2\exp(\Delta G_{PX}/RT)$ can be neglected when $2\exp(\Delta G_{PX}/RT) << \exp(-\Delta G_1/RT)([G_X] + [G_Y])$, indicating that almost all the host molecules form the complexes with the guest molecules. Then, eq 23 is obtained as follows by applying the above approximation.

$$\Delta\varepsilon = \frac{\Delta\varepsilon_{MX}\{\exp(-\Delta G_1/RT) - 1\}([G_X] - [G_Y])}{\{\exp(-\Delta G_1/RT) + 1\}([G_X] + [G_Y])} \quad (23)$$

In this work, eqs 22 and 23 are used when the analyses are carried out without and with the approximation, respectively.

For chiral host molecules, the K_{PM} parameter is necessary to be determined by analyzing the free chiral host molecule. The $\Delta\varepsilon$ value can be estimated using the VT-CD curve without guest molecules based on eq 20 substituting $[G_X]$ and $[G_Y]$ by 0.

$$\Delta\varepsilon = \frac{\Delta\varepsilon_M K_{PM} + \Delta\varepsilon_P}{K_{PM} + 1} = \frac{\Delta\varepsilon_M \exp(-\Delta G_{PM}/RT) + \Delta\varepsilon_P}{\exp(-\Delta G_{PM}/RT) + 1} \quad (24)$$

When there is only G_X (*i.e.*, $[G_Y] = 0$) and all chiral host molecules form the complexes with G_X, eq 20 is simplified as the following equation.

$$\Delta\varepsilon = \frac{\Delta\varepsilon_{MX}K_{MX} + \Delta\varepsilon_{PX}K_{PX}/K_{PM}}{K_{MX} + K_{PX}/K_{PM}} = \frac{\Delta\varepsilon_{MX}\exp\{(-\Delta G_2)/RT\} + \Delta\varepsilon_{PX}}{\exp\{(-\Delta G_2)/RT\} + 1} \quad (25)$$

where $\Delta G_2 = \Delta G_{PM} + \Delta G_{MX} - \Delta G_{PX}$.

Analysis of System B Using the ^{1}H-NMR Data

If the interconversion between the diastereomeric left- and right- (*M*- and *P*-) twisted conformations is slower than the timescale of the ^{1}H-NMR measurement, each conformation can be quantified for System B without G_Y.[7] In the case of an achiral host molecule complexed with G_X, $[H_M] = [H_P]$ and $K_{PM} = 1$ hold for eq 6, and the diastereomeric excess (*de*) can be calculated as follows.

$$de = \frac{[H_M G_X] - [H_P G_X]}{[H_M G_X] + [H_P G_X]} = \frac{K_{MX} - K_{PX}}{K_{MX} + K_{PX}} \quad (26)$$

where $H_M G_X$ is assumed to be dominant ($K_{MX} > K_{PX}$). The equation coincides with the reported dataset of K_{MX}, K_{PX}, and *de*.[7a] Haino and co-workers successfully determined the K_{MX} and K_{PX} values of the achiral calixarene-based capsule molecule (**1**) as the host molecule and the chiral guest molecules (*i.e.*, **2a**–**2d**) (Figure 1a) by the competition experiment using the ^{1}H-NMR spectroscopy based on the known K_{MY} (= K_{PY}) value[8] of **1** and the achiral guest molecule (4,4'-diacetoxybiphenyl).[7a]

The Problem of Analyzing System B Using the CD Titration Curves

A question arises regarding an achiral (racemic) host molecule: "Why K_{MX} and K_{PX} cannot be determined for System B using the CD titration curve while K_{HX} can be determined for System A?" To answer this question, eqs 30 and 31 are compared in Table 1. One reason is that System A has only two unknown parameters, $\Delta\varepsilon_{HX}$ and K_{HX}, where $\Delta\varepsilon_{HX}$ can be determined if an excess amount of guest molecules is added, and all host molecules form complexes. In contrast, System B has four unknown parameters: $\Delta\varepsilon_{MX}$, $\Delta\varepsilon_{PX}$, K_{MX}, and K_{PX}. In some cases, $\Delta\varepsilon_{MX} = -\Delta\varepsilon_{PX}$ can be assumed if (i) the *M*- and *P*-forms are rigid and mirror images of each other, and (ii) the absorption peak of the guest molecule does not overlap with that of the host molecule in the same regions of the CD spectrum. This assumption ($\Delta\varepsilon_{MX} = -\Delta\varepsilon_{PX}$) reduces the number of unknown parameters from four to three. However, although $K_{MX} + K_{PX}$ can be estimated by varying the total concentration of the guest molecule ($[G_X]_T$), the three parameters cannot be determined from the CD titration curve. When the concentration of the guest molecule is high ($1 << (K_{MX} + K_{PX})[G_X]/2$), $(\Delta\varepsilon_{MX}K_{MX} + \Delta\varepsilon_{PX}K_{PX})/(K_{MX} + K_{PX})$ is obtained. The equation can be further simplified by assuming $\Delta\varepsilon_{MX} = -\Delta\varepsilon_{PX}$, resulting in $\Delta\varepsilon_{MX}(K_{MX} - K_{PX})/(K_{MX} + K_{PX})$. However, the two parameters, $K_{MX} + K_{PX}$ and $\Delta\varepsilon_{MX}(K_{MX} - K_{PX})/(K_{MX} + K_{PX})$, are not sufficient to determine the other three parameters: $\Delta\varepsilon_{MX}$, K_{MX}, and K_{PX}.

In the case of the interaction between the chiral host and achiral/chiral guest molecules, the parameters for the free chiral host molecule ($\Delta\varepsilon_M$, $\Delta\varepsilon_P$, and K_{PM}) are necessary to be determined in addition to those for the host-guest complex ($\Delta\varepsilon_{MX}$, $\Delta\varepsilon_{PX}$, K_{MX}, and K_{PX}). The equation for the CD titration curve of the system for chiral host and achiral/chiral guest molecules (eq 29) contains a larger number of parameters compared to that for achiral host and chiral guest molecules. Thus, it is impossible to determine these parameters solely by the CD titration curve.

Table 1: Comparison of the parameters for Systems A and B.[a]

	System	Parameters for $B'[H]^2 + C'[H] + D = 0$[b]			$\Delta\varepsilon$
		B'	C'	D	
Chiral host molecule with $[G_Y] = 0$	System A	K_{HX}	$K_{HX}([G_X]_T - [H]_T) + 1$	$-[H]_T$	$\frac{\Delta\varepsilon_H + \Delta\varepsilon_{HX}K_{HX}[G_X]}{1 + K_{HX}[G_X]} \cdots (28)$
	System B	$\frac{\left(K_{MX} + \frac{K_{PX}}{K_{PM}}\right)}{\left(1 + \frac{1}{K_{PM}}\right)}$	$\frac{\left(K_{MX} + \frac{K_{PX}}{K_{PM}}\right)}{\left(1 + \frac{1}{K_{PM}}\right)}([G_X]_T - [H]_T) + 1$	$-[H]_T$	$\frac{\Delta\varepsilon_M + \frac{\Delta\varepsilon_P}{K_{PM}} + \left(\Delta\varepsilon_{MX}K_{MX} + \Delta\varepsilon_{PX}\frac{K_{PX}}{K_{PM}}\right)[G_X]}{\left(1 + \frac{1}{K_{PM}}\right) + \left(K_{MX} + \frac{K_{PX}}{K_{PM}}\right)[G_X]} \cdots (29)$
Achiral host molecule with $[G_Y] = 0$	System A ($\Delta\varepsilon_H = 0$)	K_{HX}	$K_{HX}([G_X]_T - [H]_T) + 1$	$-[H]_T$	$\frac{\Delta\varepsilon_{HX}K_{HX}[G_X]}{1 + K_{HX}[G_X]} \cdots (30)$
	System B ($K_{PM} = 1$, $\Delta\varepsilon_M = -\Delta\varepsilon_P$)	$\frac{(K_{MX} + K_{PX})}{2}$	$\frac{(K_{MX} + K_{PX})}{2}([G_X]_T - [H]_T) + 1$	$-[H]_T$	$\frac{\frac{(\Delta\varepsilon_{MX}K_{MX} + \Delta\varepsilon_{PX}K_{PX})}{2}[G_X]}{1 + \frac{(K_{MX} + K_{PX})}{2}[G_X]} \cdots (31)$

[a] The parameters shown in blue coincide with Systems A and B, but those shown in red do not. [b] For both Systems A and B, the parameters, B', C', and D, for $B'[H]^2 + C'[H] + D = 0$ are given. For System B, $B' = B/r^2$, $C' = C/r$, and D, for $B'[H]^2 + C'[H] + D = 0$ are given, and $[H] = [H_M] + [H_P]$ hold.

Evaluation of Derived Equations: Analysis of System B Using the VT-CD Curves

To circumvent the problem of analyzing the CD titration curve, the analysis of the VT-CD data using eq 23 was considered. Eq 23 for the VT-CD experiment can determine the ΔG_1 (= $\Delta H_{MX} - \Delta H_{PX} - T(\Delta S_{MX} - \Delta S_{PX})$) value and $\Delta\varepsilon_{MX}$ for the achiral host molecule under approximations that $\Delta\varepsilon_{MX} = -\Delta\varepsilon_{PX} = \Delta\varepsilon_{MY} = -\Delta\varepsilon_{PY}$, and that almost all the host molecules form the complexes with the chiral guest molecules.

First, we chose the achiral calixarene-based capsule molecule (**1**) and the chiral guest molecules (**2a**–**2d**) as the model system of the 1:1 host-guest interaction (Figure 1a).[7a] This system is suitable to confirm the consistency between the novel VT-CD and well-established VT-^{1}H-NMR methods because of the following two reasons: (i) the host molecule is chiral ($de \neq 0$) when interacting with the appropriate chiral guest molecule, which is necessary for the VT-CD method; (ii) the host molecule is under a slow *M*- and *P*-twisted conformational equilibrium relative to the timescale of the ^{1}H-NMR measurement, which is necessary for the VT-^{1}H-NMR method.

The achiral **1** and chiral (*R*)-**2a** and (*R*)-**2b** used as the host and guest molecules were synthesized according to the previously reported methods.[7a,8] In the VT-CD measurements, we used the $CDCl_3$ solutions of **1** (H) in the presence of an excess amount of (*R*)-**2a** and (*R*)-**2b** (G_X) ($[G_X]_T/[H]_T = 10$) so that almost all **1** form the complexes with (*R*)-**2a** and (*R*)-**2b**. As shown in Figure S1, the *de* values for the systems of **1** with (*R*)-**2a** and (*R*)-**2b** ($de_{CD,exp}$) estimated from the $\Delta\varepsilon$ values at 325 nm in the experimental VT-CD spectra using eq S2, which is slightly modified from eq 23 to express the *de* value, were in good agreement with those ($de_{NMR,exp}$) estimated from the experimental VT-^{1}H-NMR spectra.[7a] Moreover, the calculated VT-CD curves ($de_{CD,calc}$) for the systems of **1** with (*R*)-**2a** and (*R*)-**2b** obtained

using eq S2 were also fitted well with the $de_{CD,exp}$ values (Figure S1).

As already mentioned, in contrast to eq 22, eq 23 is valid only if almost all the host molecules form the complexes with the chiral guest molecules. In addition, how the experimental error affects the result obtained using eq 23 is not known. Thus, we attempted to evaluate the validity of eq 23 generated by introducing artificial experimental error to eq 22 (see the detailed calculation in the XLSX file of the Supporting Information). All calculations were performed using Solver Add-in in Microsoft Excel based on the least square fitting. Eq 22 requires ΔH_{MX}, ΔH_{PX}, ΔS_{MX}, ΔS_{PX}, and $\Delta\varepsilon_{MX}$ as the parameters. The K_{MX} and K_{PX} parameters can be calculated from the values of enthalpy and entropy. These parameters were estimated using the data obtained from the previously reported VT-^{1}H-NMR experiments for this system with slow conformational changes relative to the timescale of the ^{1}H-NMR measurement.[7a] The values of ΔH_{MX}, ΔH_{PX}, ΔS_{MX}, and ΔS_{PX} were calculated by assuming ΔH_{MX}:ΔS_{MX} = ΔH_{PX}:ΔS_{PX} = $\Delta H_{MX} - \Delta H_{PX}$:$\Delta S_{MX} - \Delta S_{PX}$. Using the experimental parameters and eq 22, theoretical curves of $\Delta\varepsilon$ were obtained ($\Delta\varepsilon_{calc\text{-}1}$). The number of data points is limited for actual experimental data, and the experimental error is included. Therefore, data points of $\Delta\varepsilon$ were generated with a standard deviation of $\Delta\varepsilon_{MX}$ = 1 based on eq 22 ($\Delta\varepsilon_{calc\text{-}2}$). Using eq 23, ΔG_1 and $\Delta\varepsilon_{MX}$ were optimized by the least square method to give a good fit to $\Delta\varepsilon_{calc\text{-}2}$ ($\Delta\varepsilon_{calc\text{-}3}$). Figure 1b shows the $\Delta\varepsilon$ values calculated using the experimental parameters[7a] and eq 22 ($\Delta\varepsilon_{calc\text{-}1}$) (solid lines), the $\Delta\varepsilon_{calc\text{-}1}$ values with a standard deviation of $\Delta\varepsilon_{MX}$ = 1 ($\Delta\varepsilon_{calc\text{-}2}$) (circle, square, triangle, diamond, and cross marks),

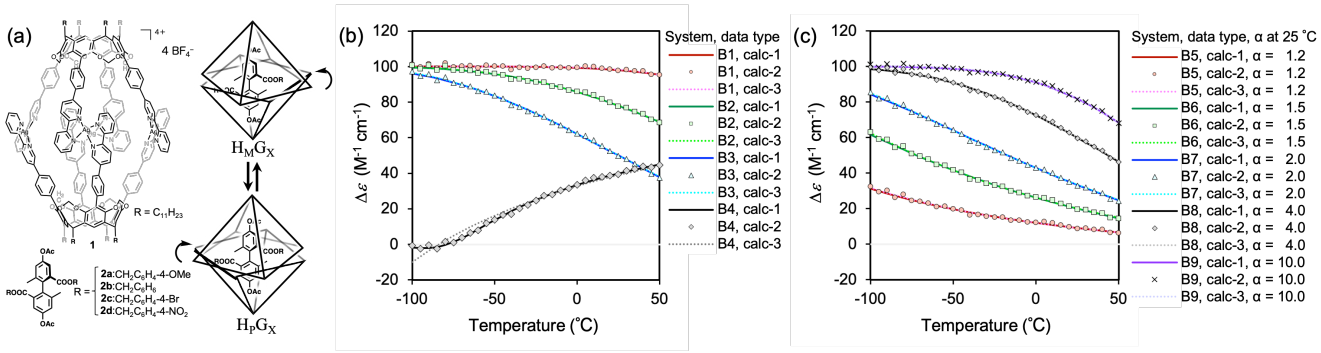


Figure 1. The theoretical VT-CD curves for Systems B1–B9 using the parameters obtained from the 1:1 host-guest system for the achiral calixarene-based capsule molecule (**1**) and the chiral guest molecules (**2a**–**2d**).[7a] The $\Delta\varepsilon_{calc\text{-}1}$ values were calculated using the experimental parameters (Table 2)[7a] and eq 22. The $\Delta\varepsilon_{calc\text{-}2}$ values were produced from the $\Delta\varepsilon_{calc\text{-}1}$ values by assuming the standard deviation of $\Delta\varepsilon_{calc\text{-}1}$ as 1.0 M^{-1} cm^{-1}, which is 1% of the $\Delta\varepsilon_{MX}$ value. Only one set of the $\Delta\varepsilon_{calc\text{-}2}$ values is shown in the Figure, although five sets of the $\Delta\varepsilon_{calc\text{-}2}$ values were produced. The $\Delta\varepsilon_{calc\text{-}3}$ values were obtained by fitting the parameters to $\Delta\varepsilon_{calc\text{-}2}$ using eq 23. (a) The chemical structures of **1** and **2a**–**2d** for Systems B1–B4, respectively. (b) The theoretical VT-CD curves for Systems B1–B4. The K_{MX} and K_{PX} parameters at 25 °C and the $\Delta H_{MX} - \Delta H_{PX}$ to $\Delta S_{MX} - \Delta S_{PX}$ ratios were taken from reference [7a] for the host-guest interactions of **1** with **2a**–**2d**. (c) The theoretical VT-CD curves for Systems B5–B9 with various α. The $\Delta H_{MX} - \Delta H_{PX}$ to $\Delta S_{MX} - \Delta S_{PX}$ ratio was also obtained from the reference for **1** with **2c**.[7a]

Table 2: Parameters and results obtained by fitting with the theoretical VT-CD curves of the systems for achiral host **1** and chiral guest **2a**–**2d** (Systems B1–B9).[7a]

System	Chiral guest molecule	K_{MX} [M^{-1}]	K_{PX} [M^{-1}]	α at 25 °C		$\Delta H_{MX} - \Delta H_{PX}$ [kJ mol^{-1}]		$\Delta S_{MX} - \Delta S_{PX}$ [kJ mol^{-1} K^{-1}]		$\Delta\varepsilon_{MX}$ [M^{-1} cm^{-1}]	
		calc-1	calc-1	calc-1	calc-3[a]	calc-1	calc-3[a]	calc-1	calc-3[a]	calc-1[b]	calc-3
B1	**2a**	158652[c]	1603[c]	99.0	102 ± 33	–26.2[d]	–27.5 ± 10.4	–0.0496[d]	–0.0541 ± 0.0323	100	100.1 ± 0.3
B2	**2b**	44761[c]	5532[c]	8.1	8.05 ± 0.19	–12.8[d]	–12.8 ± 0.5	–0.0257[d]	–0.0257 ± 0.0016	100	100.1 ± 0.5
B3	**2c**	8039[c]	2680[c]	3.0	2.99 ± 0.04	–9.6[d]	–9.7 ± 0.3	–0.0232[d]	–0.0233 ± 0.0009	100	100.1 ± 0.9
B4	**2d**	350[c]	150[c]	2.3	1.03 ± 0.01	3.9[d]	0.127 ± 0.009	0.0203[d]	0.0007 ± 0.0001	100	2700 ± 200
B5	**2c**	12000	10000	1.2	1.24 ± 0.15	–1.6[e]	–1.9 ± 1.3	–0.0038[e]	–0.0047 ± 0.0031	100	130 ± 100
B6	**2c**	15000	10000	1.5	1.51 ± 0.06	–3.6[e]	–3.6 ± 0.5	–0.0086[e]	–0.0088 ± 0.0014	100	100 ± 10
B7	**2c**	20000	10000	2	2.00 ± 0.04	–6.1[e]	–6.1 ± 0.3	–0.0146[e]	–0.0148 ± 0.0009	100	100 ± 3
B8	**2c**	40000	10000	4	3.99 ± 0.05	–12.2[e]	–12.2 ± 0.3	–0.0293[e]	–0.0293 ± 0.0010	100	100.1 ± 0.6
B9	**2c**	100000	10000	10	9.93 ± 0.26	–20.2[e]	–20.1 ± 0.7	–0.0486[e]	–0.0483 ± 0.0022	100	100.1 ± 0.3

[a] The averaged values and standard deviations for calc-3 were obtained by fitting the parameters to 5 independent data for calc-2 (N = 5). [b] The values for calc-1 were calculated using eq 22 by assuming $\Delta\varepsilon_{MX} = -\Delta\varepsilon_{PX} = \Delta\varepsilon_M = -\Delta\varepsilon_P$ = 100 M^{-1} cm^{-1}, $[H]_T$ = 1.0 × 10^{-4} M, $[G_X]_T$ = 1.0 M, and $[G_Y]_T$ = 0. [c] The values were taken from reference [7a]. Systems B1–B4 correspond to achiral calixarene-based capsule molecule (**1**) as the host molecule interacting with the chiral guest molecules (**2a**–**2d**), respectively. [d] The $\Delta H_{MX} - \Delta H_{PX}$ to $\Delta S_{MX} - \Delta S_{PX}$ ratios were taken from reference [7a] for the host-guest interactions of **1** with **2a**–**2d** (Systems B1–B4). [e] The $\Delta H_{MX} - \Delta H_{PX}$ to $\Delta S_{MX} - \Delta S_{PX}$ ratio was also obtained from the reference for **1** with **2c** (Systems B5–B9).[7a]

and the $\Delta\varepsilon$ values obtained by fitting the parameters to $\Delta\varepsilon_{calc\text{-}2}$ using eq 23 ($\Delta\varepsilon_{calc\text{-}3}$) (dotted lines) as a function of temperature. The parameters and resulting values are also summarized in Table 2. The selectivity (α) is defined as $\alpha = K_{MX}/K_{PX}$, where $K_{MX} > K_{PX}$ and $\alpha > 1$.

As shown in Figure 1b, the calculated values of all systems, except for System B4 (*i.e.*, Systems B1–B3), showed good agreement with $\Delta\varepsilon_{calc\text{-}1}$. However, the resulting thermodynamic parameters of System B1 had a large uncertainty, presumably due to the small change in $\Delta\varepsilon$ or large selectivity. To clarify this point, another approach to analyze the system with the left- and right-twisted conformations was carried out by combining the VT-CD and CD titration curves.

The $\Delta\varepsilon_{MX}$ value with high accuracy was obtained from the VT-CD curve. Thus, subsequent CD titration curve analysis using eq 23 can be performed to determine K_{MX} and K_{PX} by assuming $\Delta\varepsilon_{MX} = -\Delta\varepsilon_{PX}$. Figure S2 and Table S1 show the CD titration curves using eq 31 and obtained parameters, respectively. Because the uncertainty of the selectivity was not improved for the CD titration curve, the large uncertainty is expected to be derived from the large selectivity rather than the small change in $\Delta\varepsilon$ in the VT-CD curves.

System B4 is an inappropriate example accompanied by the neglection of $2\exp(\Delta G_{PX}/RT)$ in the denominator of eq 22 at low temperatures. The theoretical curve obtained by calc-3 does not fit the plot of the $\Delta\varepsilon_{calc\text{-}2}$ values in the region from –100 to –50 °C (Figure 1b), and the $\Delta\varepsilon_{calc\text{-}3}$ values underestimate the magnitude of α, $\Delta H_{MX} - \Delta H_{PX}$, and $\Delta S_{MX} - \Delta S_{PX}$, and overestimate $\Delta\varepsilon_{MX}$ (Table 2). To compare the values of $2\exp(\Delta G_{PX}/RT)$ (= a) and $\exp(-\Delta G_1/RT)([G_X] + [G_Y])$ (= b) in the denominator of eq 22, the logarithms of a, b, and their ratio (a/b) were plotted as a function of temperature (Figure S3b). The plots indicate that a cannot be neglected in the region from –100 to 0 °C. When a cannot be neglected, it would be necessary to carry out VT-CD experiments with various concentrations of the achiral guest molecule (**2d**) and then analyze the data using eq 22 to determine the parameters.

In Systems B1–B3, the α values at 25 °C are relatively large (3.0–99.0 for calc-1 and 2.99–102 for calc-3) (Table 2). In addition, the $\Delta H_{MX} - \Delta H_{PX}$ to $\Delta S_{MX} - \Delta S_{PX}$ ratios are also different among the systems. Thus, the selectivity dependence of the VT-CD curve around $\alpha = 3.0$ was examined using the $\Delta H_{MX} - \Delta H_{PX}$ to $\Delta S_{MX} - \Delta S_{PX}$ ratio of System B3. In a similar way to Systems B1–B4, $\Delta\varepsilon_{calc\text{-}1}$, $\Delta\varepsilon_{calc\text{-}2}$, and $\Delta\varepsilon_{calc\text{-}3}$ were calculated by varying the α values in the range of 1.2–10 (Systems B5–B9). When the α value was relatively small (< 1.2), the obtained parameters deviated significantly from the $\Delta\varepsilon_{calc\text{-}1}$ values. However, the systems with an α value of larger than 1.5 would be acceptable and show a larger increase in $\Delta\varepsilon$ in the region of the lower temperature.

Analysis of a System for Achiral Host and Chiral Guest Molecules

When an achiral host molecule interacts with a chiral guest molecule, the chirality of the guest molecule can be transferred to the achiral host molecule.[7-9] The chiral transfer efficiency is generally evaluated by α or *de,* and these variables play a key role in understanding the chiral sensing capability of the host molecules.

The derived eq 23 was applied to the 1:1 host-guest system for the achiral dimeric zinc porphyrin tweezer molecule (**3**) and the chiral bidentate guest molecule (**4**) reported by Nakanishi, Berova, and co-workers (Figure 2a).[9d] The tweezer **3** adopts left- and right- (*M*- and *P*-) twisted conformations (H_M and H_P) (Figure 2a), exhibiting characteristic negative and positive bisignate Cotton effects, respectively. This is due to the exciton coupling between the electric dipole transition moments of the two zinc porphyrin units (Figure 2b). Curve fitting was performed for the plots of $\Delta\varepsilon$ at 423 and 434 nm ($\Delta\varepsilon_{423}$ and $\Delta\varepsilon_{434}$) in the VT-CD spectra (25, –40, and –80 °C) as the experimental data (Figure 2b) by assuming $\Delta\varepsilon_{MX} = -\Delta\varepsilon_{PX}$ (Figure 2c). As the results of the theoretical analysis using eq 23, the $\Delta H_{MX} - \Delta H_{PX}$ and $\Delta S_{MX} - \Delta S_{PX}$ values were estimated to be –24 kJ mol^{-1} and –0.071 kJ mol^{-1} K^{-1}, respectively. However, when either $\Delta H_{MX} - \Delta H_{PX} = 0$ kJ mol^{-1} or $\Delta S_{MX} - \Delta S_{PX} = 0$ kJ mol^{-1} K^{-1} was used for the calculations, the experimental values could not be fitted well with the theoretical curves. Interestingly, the fitting curves in Figure 2c indicate that an inversion of the Cotton effect signs would occur at *ca.* 65 °C, even though there were no VT-CD spectra above 25 °C.[9d] This is probably due to the lower boiling point of dichloromethane (40 °C). Therefore, if halogenated solvents with higher boiling points are used and the chiral bidentate **4** completely associates with the tweezer **3** above 65 °C, it may be possible to observe the inversion from H_M to H_P. If $\Delta S_{MX} - \Delta S_{PX} = 0$ kJ mol^{-1} K^{-1} or the complex dissociates with increasing the temperature, the $\Delta\varepsilon$ value in such system is expected to become zero at high temperature due to an equal amount of the *M*- and *P*-twisted conformations. However, since the entropy term is non-zero and when the concentration of the guest molecule is high enough to form complexes with all host molecules, the inversion of the Cotton effect signs can be predicted by the calculation. This is probably because, at low temperatures, the right-twisted conformation has higher steric hindrance but is flexible relative to the left-handed one, while the left-twisted conformation has lower steric hindrance[9d] but is rigid relative to the right-handed one (Figure 2a). Thus, the right-twisted conformation is entropically favorable at high temperatures.

The advantage of eq 23 is that it can be applied to a system in which achiral host molecule interacts with the enantiomerically impure guest molecules ($[G_X]$ and $[G_Y]$). The $\Delta\varepsilon_{MX}([G_X] - [G_Y])/([G_X] + [G_Y])$ term in eq 23 can be converted into $\Delta\varepsilon_{MX}(\%ee/100)$. The equation derived from eq 23 is still valid even if the maximum $\Delta\varepsilon$ values decrease with decreasing the %*ee* values of the guest molecules. We found one example of the system for the tweezer **3** and α-haloamides **4** (α-halocarboxylic acids derivatized with 1,4-phenylenediamine) reported by Borhan and co-workers.[9j] They used enantiomerically impure α-haloamides (%*ee* = 56–90) as guest molecules. Thus, we attempted to obtain the parameters for this system even though only two data points at 0 and –20 °C were provided in the reference and these complexes showed different bisignate CD spectral patterns. As anticipated, it was impossible to analyze the system using eq 23 due to insufficient data points. However, we believe that if three data points at sufficiently low temperatures are provided, the theoretical analysis of the VT-CD data can be applied not only to the system for the tweezer **3** and enantiomerically pure bidentate **4** but also to a variety of similar host-guest systems with enantiomerically impure chiral guest molecules.

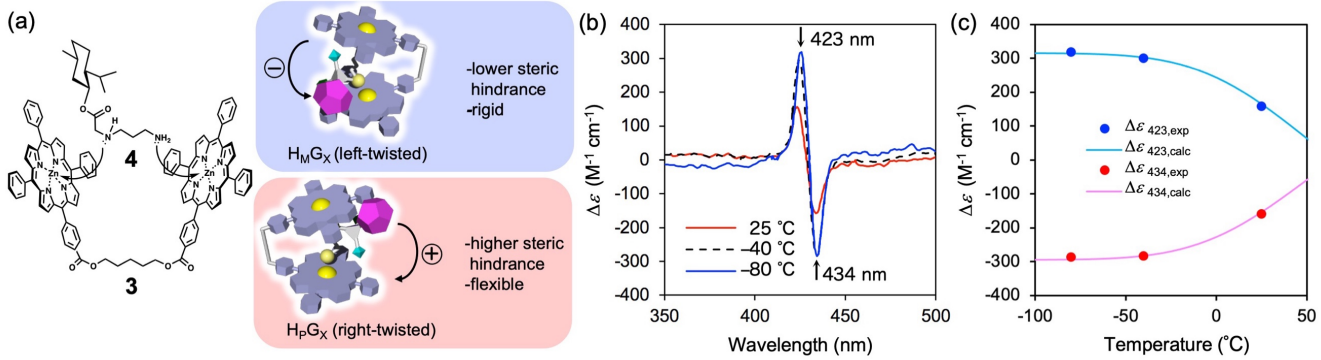
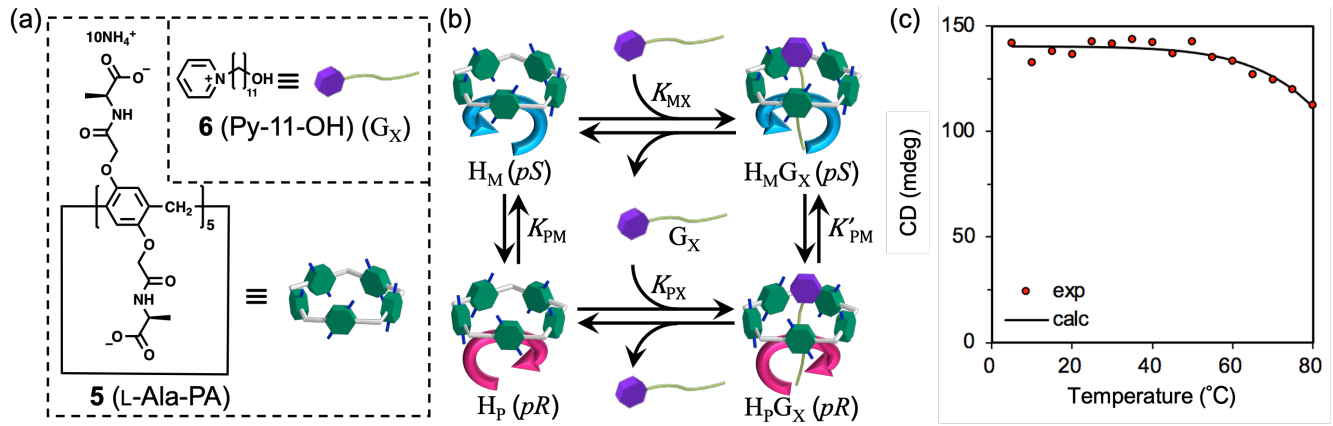


Figure 2. The VT-CD analysis of the 1:1 host-guest system for the achiral dimeric zinc porphyrin tweezer molecule (**3**) and chiral bidentate guest molecule (**4**).[9d] (a) The chemical structures of **3** and **4**. In this system, the positive and negative bisignate Cotton effects are attributed to the left- and right- (*M*- and *P*-) twisted conformations (H_M and H_P) generated by zinc porphyrin–zinc porphyrin exciton coupling. (b) The VT-CD spectra of **3** in the presence of **4** in dichloromethane, reproduced from reference [9d]. (c) The experimental[9d] and calculated $\Delta\varepsilon$ values at 423 and 434 nm. The obtained parameters are as follows: $\Delta H_{MX} - \Delta H_{PX}$ = 24 kJ mol^{-1}, $\Delta S_{MX} - \Delta S_{PX}$ = 0.071 kJ mol^{-1} K^{-1}, $\Delta\varepsilon_{MX,423} = -\Delta\varepsilon_{PX,423}$ = 314 M^{-1} cm^{-1}, and $\Delta\varepsilon_{MX,434} = -\Delta\varepsilon_{PX,434}$ = –294 M^{-1} cm^{-1}. α = 3.2 (25 °C) was used for the calculations. The H_M was assumed to be the dominant form.



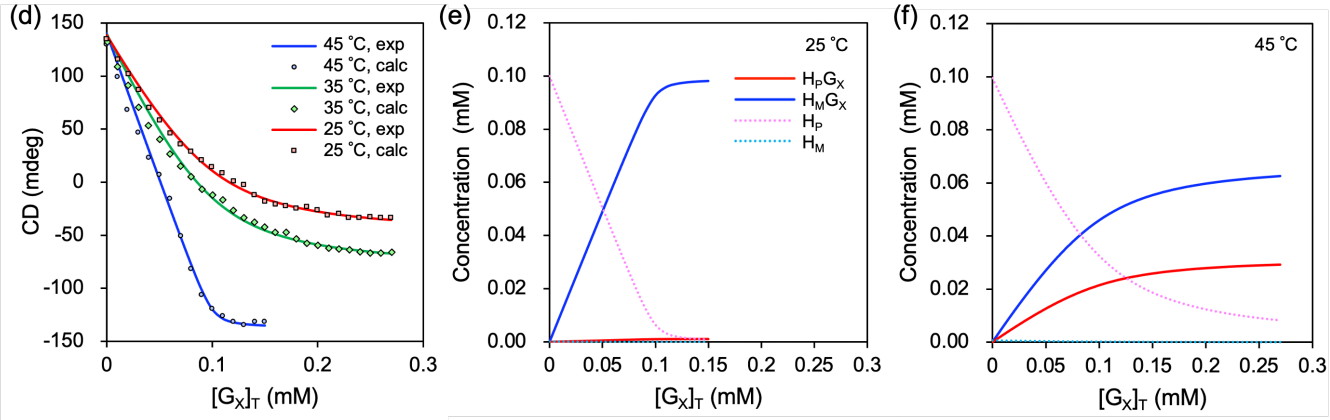


Figure 3. The VT-CD and CD titration analyses of the 1:1 host-guest system for the chiral pillar[5]arene derivative bearing the L-alanine residues (**5**) (L-Ala-PA) and the achiral guest molecule (**6**) (Py-11-OH).[10] (a) The chemical structures of **5** and **6**. (b) The equilibrium in the 1:1 host-guest system. The conformations of **5** with *pS* and *pR* are defined as H_M and H_P, respectively. (c) The plot of the CD intensities at 303 nm of free **5** (0.1 mM) in water at various temperatures was taken from reference [10]. The experimental plot was fitted to the calculated curve using eq 24. The obtained parameters were as follows: $\Delta\varepsilon_P = -\Delta\varepsilon_M$ = 42.5 M^{-1} cm^{-1}, ΔH_{PM} = 75 kJ mol^{-1}, and ΔS_{PM} = 0.194 kJ mol^{-1} K^{-1}. (d) The plots of CD intensities at 303 nm of **5** (0.1 mM) in the presence of **6** with various concentrations at 25, 35, and 45 °C. The data were also taken from reference [10]. The calculated curves were obtained using eq 29. (e,f) The molecular species in the 1:1 host-guest system for **5** (0.1 mM) in the presence of **6** with various concentrations at 25 (e) and 45 °C (f).

Table 3: Experimental conditions and obtained parameters of the system for chiral host **5** and achiral guest **6**.

System	Molecular species	Data type	T [°C]	$\Delta\varepsilon_P$ [M^{-1} cm^{-1}]	ΔH_{PM} [kJ mol^{-1}]	ΔS_{PM} [kJ mol^{-1} K^{-1}]	K_{MX} [M^{-1}]	K_{PX} [M^{-1}]	Data used
B10	H_M, H_P	VT-CD	5–80	42.5	75	0.194	–	–	Figure 3c
B11	H_M, H_P, H_{MX}, H_{PX}	CD titration	25	42.5[a]	75[a]	0.194[a]	2.8×10^9	2.2×10^4	Figure 3d
B12	H_M, H_P, H_{MX}, H_{PX}	CD titration	35	42.5[a]	75[a]	0.194[a]	2.6×10^7	1.5×10^4	Figure 3d
B13	H_M, H_P, H_{MX}, H_{PX}	CD titration	45	42.5[a]	75[a]	0.194[a]	7.7×10^6	2.0×10^4	Figure 3d

[a] The values ($\Delta\varepsilon_P$, ΔH_{PM}, and ΔS_{PM}) were obtained from System B10.

Analysis of a System for Chiral Host and Achiral Guest Molecules

Analysis of a chiral host molecule with a twisted structure is also important because of its chiral properties for chiral recognition and chiroptical inversion.[10,11]

The derived eqs 24 and 29 were applied to analyze the planar chirality inversion of the chiral pillar[5]arene derivative bearing the L-alanine residues (**5**) (L-Ala-PA) as the host molecule by inclusion complex formation with the achiral guest molecule (**6**) (Py-11-OH) reported by Choi, Jung, and co-workers (Figure 3a).[10] Pillar[5]arene was serendipitously discovered by Ogoshi, Nakamoto, and co-workers in 2008.[12] It shows the unique chiroptical properties originating from its planar chirality.[2h,2j,2m,2o,2q,2r,2y,2z] The five aromatic units in the chiral host **5** have planar chirality (*pR* or *pS*), indicating that the multiple conformations with *pR* and/or *pS* can exist in **5**. However, the chiral host **5** itself takes the right-twisted conformation (H_P or *pR* = *pR*, *pR*, *pR*, *pR*, *pR*) while **5** inclusion complexed with the achiral guest **6** adopts the left-twisted conformation (H_MG_X or *pS* = *pS*, *pS*, *pS*, *pS*, *pS*) in water. Thus, the equilibrium in this system can be described as shown in Figure 3b.

First, it is necessary to determine the K_{PM} parameter, which is a function of ΔH_{PM}, ΔS_{PM}, and T. Figure 3c shows the $\Delta\varepsilon$ values at 303 nm obtained from the VT-CD spectra of chiral host **5** in the absence of achiral guest **6** as a function of temperature.[10] The CD intensities were saturated from *ca.* 5 to 50 °C. Their averaged value, converted to $\Delta\varepsilon$, was calculated to be 42.5 M^{-1} cm^{-1} and can be used as $\Delta\varepsilon_P$. Moreover, a slight decrease in $\Delta\varepsilon$ is observed with increasing the temperature (42.5 M^{-1} cm^{-1} at 5 °C, and 34.1 M^{-1} cm^{-1} at 80 °C). Assuming $\Delta\varepsilon_P = \Delta\varepsilon_{PX} = -\Delta\varepsilon_M = -\Delta\varepsilon_{MX}$, the CD titration curve was analyzed using eq 24. The obtained parameters are summarized in Table 3 (System B10). The thermodynamic parameters were determined to be ΔH_{PM} = 75 kJ mol^{-1} and ΔS_{PM} = 0.194 kJ mol^{-1} K^{-1} from the calculation results obtained using $\Delta\varepsilon_P$ = 42.5 M^{-1} cm^{-1}. Second, plots of the $\Delta\varepsilon$ values obtained from the CD titration experiments at various temperatures (25, 35, and 45 °C) were analyzed using the parameters, shown in Table 3 (System B10) and eq 29 (Figure 3d). The K_{MX} and K_{PX} were determined at each temperature. It can be seen that the binding constant was specifically higher for H_M (*pS*), resulting in the inversion of the planar chirality of chiral host **5**. The concentrations of the molecular species (H_M, H_P, H_MG_X, and H_PG_X) at 25, 35, and 45 °C are shown in Figures 3e, S4, and 3f, respectively. At 25 °C, H_P and H_MG_X were the dominant species in the region of $[G_X]_T$. However, at 45 °C, the inclusion complex was no longer one chiral molecular species, and the two inclusion complexes (H_MG_X and H_PG_X) coexisted in this system. Thus, this analysis would be useful for quantifying molecular species at various temperatures.

Choi, Jung, and co-workers also provided VT-CD spectra (5–80 °C) of chiral host **5** with achiral guest **6**.[10] Thus, eq 25 can be potentially used to analyze this system. However, eq 25 requires a high achiral guest molecule concentration to ensure that there is only a negligible amount of free chiral host molecules. On the basis of the composition of the molecular species at 45 °C, as shown in Figure 3f, the concentrations of the chiral host **5** and the achiral guest **6** in a 1:1 mixture were estimated to be [**5**] = $[H_M]$ = 0.1 mM and [**6**] = $[G_X]_T$ = 0.1 mM, respectively; more than 30% of the chiral host **5** did not form the inclusion complex with the achiral guest **6**. Therefore, eq 25 cannot be applied to analyze this system. Nevertheless, we believe that using eqs 24 and 25 would be a highly convenient and available way to analyze the system in which the chiral host molecule completely forms an inclusion complex in the presence of a sufficient amount of achiral guest molecule.

Conclusion

In this study, the novel equations based on the mass-balance model were derived for System B (the 1:1 host-guest system), in which the host molecules adopt left- and right-twisted conformations. It was found that System B cannot be analyzed solely by the theoretical curves for the CD titration experiments because the parameters of the equilibrium constants (K) and molar CD ($\Delta\varepsilon$) are coupled in the formula. Furthermore, theoretical analysis using the derived equations for the VT-CD experiments was applied to System B for the achiral calixarene-based capsule molecule, achiral dimeric zinc porphyrin tweezer molecule, and chiral pillar[5]arene as the host molecules with the chiral and/or achiral guest molecules, and resulted in successful determination of the thermodynamic parameters (ΔH and ΔS), K, and $\Delta\varepsilon$ in the 1:1 host-guest system.

The method to analyze System B using the VT-CD data had been uncommon, possibly because the theoretical framework was not established. However, it was revealed that the analytical method proposed for the VT-CD experiment was efficient for 1:1 host-guest systems under equilibrium between dynamic left- and right-twisted conformations of the host molecules. Therefore, we believe that the present findings open the door for theoretical analysis in a wide range of 1:1 host-guest systems using host molecules with left- and right-twisted conformations.

Until now, the applicability of the mass-balance model has been limited to 1:1 host-guest systems. Especially in the fields of supramolecular chemistry and polymer chemistry, chemists need theoretical analysis using models for 1:2 host-guest

systems and helical polymer systems, providing an in-depth understanding of supramolecules and polymers that undergo equilibria between left- and right-twisted and -handed conformations. This leads to the application to chiral separation, chiral sensing, absorption and emission of circularly polarized light, and asymmetric catalysis in the host-guest systems. Work along this line is now in progress.

Acknowledgements

The authors are thankful for Prof. Dr. Michiya Fujiki for stimulating us to work on this research. This work was supported in part by JSPS KAKENHI (Grant-in-Aid for Scientific Research B, No. 21H01740).

Conflict of Interest

The authors declare no conflict of interest.

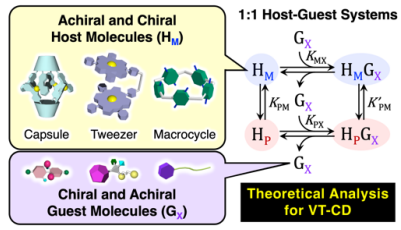
Data Availability Statement

The data that support the findings of this study are available from the corresponding author(s) upon reasonable request.

Keywords: Chirality • Host-Guest Systems • Molecular Recognition • Non-Covalent Interactions • Twisted Conformations

[1] C. J. Pedersen, *J. Am. Chem. Soc.* **1967**, *89*, 2495-2496.
[2] a) V. V. Borovkov, Y. Inoue, in *Supramolecular Chirality*, 1st ed. (Eds.: M. Crego-Calama, D. N. Reinhoudt), Springer, Berlin, Heidelberg, **2006**, pp. 89-146; b) T. Brotin, J.-P. Dutasta, *Chem. Rev.* **2009**, *109*, 88-130; c) G. A. Hembury, V. V. Borovkov, Y. Inoue, *Chem. Rev.* **2008**, *108*, 1-73; d) H. Juwarker, J.-M. Suk, K.-S. Jeong, *Chem. Soc. Rev.* **2009**, *38*, 3316-3325; e) J. Crassous, *Chem. Soc. Rev.* **2009**, *38*, 830-845; f) N. Berova, G. Pescitelli, A. G. Petrovic, G. Proni, *Chem. Commun.* **2009**, 5958-5980; g) J. Leblond, A. Petitjean, *ChemPhysChem* **2011**, *12*, 1043-1051; h) T. Ogoshi, *J. Incl. Phenom. Macrocycl. Chem.* **2012**, *72*, 247-262; i) T. Ema, *J. Incl. Phenom. Macrocycl. Chem.* **2012**, *74*, 41-55; j) P. J. Cragg, K. Sharma, *Chem. Soc. Rev.* **2012**, *41*, 597-607; k) A. M. Castilla, W. J. Ramsay, J. R. Nitschke, *Acc. Chem. Res.* **2014**, *47*, 2063-2073; l) M. Matache, E. Bogdan, N. D. Hădade, *Chem.–Eur. J.* **2014**, *20*, 2106-2131; m) N. L. Strutt, H. Zhang, S. T. Schneebeli, J. F. Stoddart, *Acc. Chem. Res.* **2014**, *47*, 2631-2642; n) E. Yashima, N. Ousaka, D. Taura, K. Shimomura, T. Ikai, K. Maeda, *Chem. Rev.* **2016**, *116*, 13752-13990; o) T. Ogoshi, T. Yamagishi, Y. Nakamoto, *Chem. Rev.* **2016**, *116*, 7937-8002; p) S. Míguez-Lago, M. M. Cid, *Synthesis* **2017**, *49*, 4111-4123; q) T. Kakuta, T. Yamagishi, T. Ogoshi, *Acc. Chem. Res.* **2018**, *51*, 1656-1666; r) N. Song, T. Kakuta, T. Yamagishi, Y.-W. Yang, T. Ogoshi, *Chem* **2018**, *4*, 2029-2053; s) L. Zhao, X. Jing, X. Li, X. Guo, L. Zeng, C. He, C. Duan, *Coord. Chem. Rev.* **2019**, *378*, 151-187; t) X. Wang, F. Jia, L.-P. Yang, H. Zhou, W. Jiang, *Chem. Soc. Rev.* **2020**, *49*, 4176-4188; u) E. A. John, C. J. Massena, O. B. Berryman, *Chem. Rev.* **2020**, *120*, 2759-2782; v) M. Farinone, K. Urbańska, M. Pawlicki, *Molecules* **2020**, *25*, 4523; w) R. Joseph, *ChemistrySelect* **2021**, *6*, 3519-3533; x) G. Travagliante, M. Gaeta, R. Purrello, A. D'Urso, *Chemosensors* **2021**, *9*, 204; y) K. Kato, S. Fa, S. Ohtani, T. Shi, A. M. Brouwer, T. Ogoshi, *Chem. Soc. Rev.* **2022**, *51*, 3648-3687; z) S. Ohtani, K. Kato, S. Fa, T. Ogoshi, *Coord. Chem. Rev.* **2022**, *462*, 214503.
[3] K. Hirose, *J. Incl. Phenom. Macrocycl. Chem.* **2001**, *39*, 193-209.
[4] A. E. Hargrove, Z. Zhong, J. L. Sessler, E. V. Anslyn, *New J. Chem.* **2010**, *34*, 348-354.
[5] P. Thordarson, *Chem. Soc. Rev.* **2011**, *40*, 1305-1323.
[6] a) E. Yashima, K. Maeda, H. Iida, Y. Furusho, K. Nagai, *Chem. Rev.* **2009**, *109*, 6102-6211; b) T. F. A. De Greef, M. M. J. Smulders, M. Wolffs, A. P. H. J. Schenning, R. P. Sijbesma, E. W. Meijer, *Chem. Rev.* **2009**, *109*, 5687-5754; c) S. Cantekin, D. W. R. Balkenende, M. M. J. Smulders, A. R. A. Palmans, E. W. Meijer, *Nat. Chem.* **2011**, *3*, 42-46; d) A. J. Markvoort, H. M. M. ten Eikelder, P. A. J. Hilbers, T. F. A. de Greef, E. W. Meijer, *Nat. Commun.* **2011**, *2*, 509; e) S. Cantekin, H. M. M. ten Eikelder, A. J. Markvoort, M. A. J. Veld, P. A. Korevaar, M. M. Green, A. R. A. Palmans, E. W. Meijer, *Angew. Chem. Int. Ed.* **2012**, *51*, 6426-6431; f) H. M. M. ten Eikelder, A. J. Markvoort, T. F. A. de Greef, P. A. J. Hilbers, *J. Phys. Chem. B* **2012**, *116*, 5291-5301; g) Y. Nakano, A. J. Markvoort, S. Cantekin, I. A. W. Filot, H. M. M. ten Eikelder, E. W. Meijer, A. R. A. Palmans, *J. Am. Chem. Soc.* **2013**, *135*, 16497-16506; h) A. J. Markvoort, H. M. M. ten Eikelder, P. A. J. Hilbers, T. F. A. de Greef, *ACS Cent. Sci.* **2016**, *2*, 232-241; i) A. Das, G. Vantomme, A. J. Markvoort, H. M. M. ten Eikelder, M. Garcia-Iglesias, A. R. A. Palmans, E. W. Meijer, *J. Am. Chem. Soc.* **2017**, *139*, 7036-7044; j) B. Adelizzi, A. Aloi, A. J. Markvoort, H. M. M. Ten Eikelder, I. K. Voets, A. R. A. Palmans, E. W. Meijer, *J. Am. Chem. Soc.* **2018**, *140*, 7168-7175; k) L. N. J. de Windt, C. Kulkarni, H. M. M. ten Eikelder, A. J. Markvoort, E. W. Meijer, A. R. A. Palmans, *Macromolecules* **2019**, *52*, 7430-7438; l) H. M. M. ten Eikelder, B. Adelizzi, A. R. A. Palmans, A. J. Markvoort, *J. Phys. Chem. B* **2019**, *123*, 6627-6642; m) H. M. M. ten Eikelder, A. J. Markvoort, *Acc. Chem. Res.* **2019**; n) G. Vantomme, G. M. ter Huurne, C. Kulkarni, H. M. M. ten Eikelder, A. J. Markvoort, A. R. A. Palmans, E. W. Meijer, *J. Am. Chem. Soc.* **2019**, *141*, 18278-18285.
[7] a) Y. Tsunoda, K. Fukuta, T. Imamura, R. Sekiya, T. Furuyama, N. Kobayashi, T. Haino, *Angew. Chem. Int. Ed.* **2014**, *53*, 7243-7247; b) N. Ousaka, S. Yamamoto, H. Iida, T. Iwata, S. Ito, Y. Hijikata, S. Irle, E. Yashima, *Nat. Commun.* **2019**, *10*, 1457.
[8] T. Haino, M. Kobayashi, Y. Fukazawa, *Chem.–Eur. J.* **2006**, *12*, 3310-3319.
[9] a) S. Yagi, H. Kitayama, T. Takagishi, *J. Chem. Soc., Perkin Trans. 1* **2000**, 925-932; b) V. V. Borovkov, J. M. Lintuluoto, M. Fujiki, Y. Inoue, *J. Am. Chem. Soc.* **2000**, *122*, 4403-4407; c) Y. Mizuno, T. Aida, K. Yamaguchi, *J. Am. Chem. Soc.* **2000**, *122*, 5278-5285; d) T. Kurtán, N. Nesnas, F. E. Koehn, Y.-Q. Li, K. Nakanishi, N. Berova, *J. Am. Chem. Soc.* **2001**, *123*, 5974-5982; e) V. V. Borovkov, J. M. Lintuluoto, M. Sugiura, Y. Inoue, R. Kuroda, *J. Am. Chem. Soc.* **2002**, *124*, 11282-11283; f) V. V. Borovkov, J. M. Lintuluoto, H. Sugeta, M. Fujiki, R. Arakawa, Y. Inoue, *J. Am. Chem. Soc.* **2002**, *124*, 2993-3006; g) G. Proni, G. Pescitelli, X. Huang, K. Nakanishi, N. Berova, *J. Am. Chem. Soc.* **2003**, *125*, 12914-12927; h) X. Li, M. Tanasova, C. Vasileiou, B. Borhan, *J. Am. Chem. Soc.* **2008**, *130*, 1885-1893; i) M. Tanasova, C. Vasileiou, O. O. Olumolade, B. Borhan, *Chirality* **2009**, *21*, 374-382; j) M. Tanasova, Q. Yang, C. C. Olmsted, C. Vasileiou, X. Li, M. Anyika, B. Borhan, *Eur. J. Org. Chem.* **2009**, *2009*, 4242-4253; k) R. Katoono, H. Kawai, K. Fujiwara, T. Suzuki, *J. Am. Chem. Soc.* **2009**, *131*, 16896-16904; l) T. Haino, H. Shio, R. Takano, Y. Fukazawa, *Chem. Commun.* **2009**, 2481-2483; m) S. J. Wezenberg, G. Salassa, E. C. Escudero-Adán, J. Benet-Buchholz, A. W. Kleij, *Angew. Chem. Int. Ed.* **2011**, *50*, 713-716; n) I. C. Pintre, S. Pierrefixe, A. Hamilton, V. Valderrey, C. Bo, P. Ballester, *Inorg. Chem.* **2012**, *51*, 4620-4635; o) S. Brahma, S. A. Ikbal, S. Dey, S. P. Rath, *Chem. Commun.* **2012**, *48*, 4070-4072; p) J. M. Dragna, G. Pescitelli, L. Tran, V. M. Lynch, E. V. Anslyn, L. Di Bari, *J. Am. Chem. Soc.* **2012**, *134*, 4398-4407; q) S. Brahma, S. A. Ikbal, S. P. Rath, *Inorg. Chem.* **2014**, *53*, 49-62; r) J. Jiang, Z. Feng, B. Liu, C. Hu, Y. Wang, *Dalton Trans.* **2013**, *42*, 7651-7659; s) S. Barman, E. V. Anslyn, *Tetrahedron* **2014**, *70*, 1357-1362; t) A. Dhamija, S. A. Ikbal, S. P. Rath, *Inorg. Chem.* **2016**, *55*, 13014-13026; u) R. Katoono, S. Kawai, T. Suzuki, *Chem. Sci.* **2016**, *7*, 3240-3247; v) A. Dhamija, B. Saha, S. P. Rath, *Inorg. Chem.* **2017**, *56*, 15203-15215; w) Y. Yamasaki, H. Shio, T. Amimoto, R. Sekiya, T. Haino, *Chem.–Eur. J.* **2018**, *24*, 8558-8568; x) S. Olsson, C. Schäfer, M. Blom, A. Gogoll, *ChemPlusChem* **2018**, *83*, 1169-1178; y) C. Ni, D. Zha, H. Ye, Y. Hai, Y. Zhou, E. V. Anslyn, L. You, *Angew. Chem. Int. Ed.* **2018**, *57*, 1300-1305; z) M. Ito, T. Ikai, S. Yamamoto, D. Taura, N. Ousaka, E. Yashima, *Chem. Lett.* **2020**, *49*, 1030-1033; aa) H. Gholami, D. Chakraborty, J. Zhang, B. Borhan, *Acc. Chem. Res.* **2021**, *54*, 654-667; ab) H. Han, R. Fu, R. Wang, C. Tang, M.-M. He, J.-Y. Deng, D.-S. Guo, J. F. Stoddart, K. Cai, *J. Am. Chem. Soc.* **2022**, *144*, 20351-20362.
[10] J. Park, Y. Choi, S. S. Lee, J. H. Jung, *Org. Lett.* **2019**, *21*, 1232-1236.
[11] a) T. Ema, N. Ouchi, T. Doi, T. Korenaga, T. Sakai, *Org. Lett.* **2005**, *7*, 3985-3988; b) Y. Shoji, K. Tashiro, T. Aida, *J. Am. Chem. Soc.* **2006**, *128*, 10690-10691; c) H. Katagiri, Y. Tanaka, Y. Furusho, E. Yashima, *Angew. Chem. Int. Ed.* **2007**, *46*, 2435-2439; d) T. Ema, N. Ura, K. Eguchi, T. Sakai, *Bull. Chem. Soc. Jpn.* **2012**, *85*, 101-109; e) A. Schmitt, B. Chatelet, S. Collin, J.-P. Dutasta, A. Martinez, *Chirality* **2013**, *25*, 475-479; f) B. Saha, A. G. Petrovic, A. Dhamija, N. Berova, S. P. Rath, *Inorg. Chem.* **2019**, *58*, 11420-11438; g) B. Saha, S. A. Ikbal, S. P. Rath, *Inorg. Chem.* **2020**, *59*, 7795-7809; h) B. Teichmann, A. M. Krause, M. J. Lin, F. Würthner, *Angew. Chem. Int. Ed.* **2022**, *61*, e202117625; i) Y. Zhou, Y. Ren, L. Zhang, L. You, Y. Yuan, E. V. Anslyn, *Tetrahedron* **2015**, *71*, 3515-3521; j) W. Li, Y. Zhou, T. Gao, J. Li, S. Yin, W. Huang, Y. Li, Q. Ma, Z. Yao, P. Yan, H. Li, *ACS Appl. Mater. Interfaces* **2022**, *14*, 55979-55988.
[12] T. Ogoshi, S. Kanai, S. Fujinami, T. Yamagishi, Y. Nakamoto, *J. Am. Chem. Soc.* **2008**, *130*, 5022-5023.

Entry for the Table of Contents



Novel equations derived based on the mass-balance model were applied to analyze the 1:1 host-guest systems for the achiral and chiral host molecules with left- and right-twisted conformations (H_M and H_P) and the chiral and achiral guest molecules (G_X). Theoretical analysis for the variable temperature circular dichroism (VT-CD) experiments resulted in successful determination of the thermodynamic parameters, equilibrium constants, and molar CD.