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A General Rule for Circular Dichroism Induced by a Chiral Macrocycle

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Abstract: A general rule for induced circular dichroism (ICD) of a chromophore located inside or outside the cavity of a chiral macrocycle is derived from the Kirkwood–Tinoco equation. When a chromophore moves from the inside of the cavity to the outside, the sign of ICD tends to be reversed. Outside the cavity, the absolute value of ICD is larger on the narrower-rim side of a macrocycle than on the wider-rim side. Furthermore, ideally a parallel-polarized electronic transition along the axis of the cavity should give 2 times larger ICD with opposite sign as compared with ICD caused by a perpendicular-polarized one.

Introduction

There is a rule about induced circular dichroism (ICD) of a chromophore included in cyclodextrin (CDx)[1-3] which was derived from the Kirkwood–Tinoco equation.[4] This rule predicts that an electronic transition parallel to the axis of CDx gives positive ICD while that perpendicular to the axis gives negative ICD.[1-3] Recently we extended this rule to the outer field of the cavity of CDx.[5,6] According to our new rule, the sign of ICD should become reversed when a chromophore is situated outside the cavity. Recently Schuette et al.[7] and Hamai et al.[8] used this new rule to explain experimental results. This rule may be also useful for conformational analyses of CDx modified with various aromatic groups.[9-17] Here, however, one question has been raised. Is this new rule generally applicable to other chiral macrocycles? The purpose of the present study is to derive a general rule for ICD caused by chiral macrocycles.

Theory

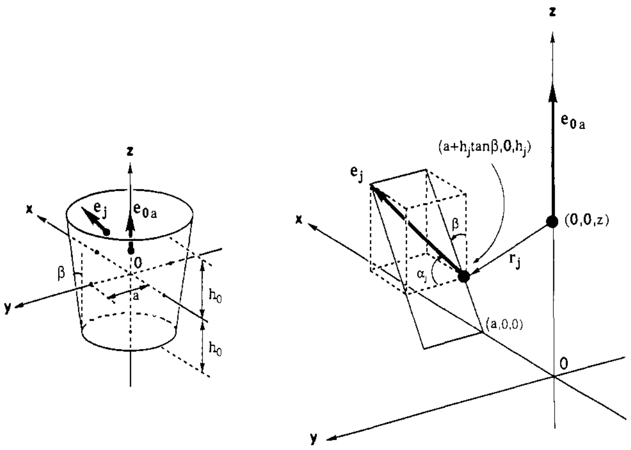

Figure 1. Definition of geometric parameters for a parallel-polarized transition moment and a bond of a host macrocycle.

The Kirkwood–Tinoco equation (1) suggests that circular dichroism is caused by dipole–dipole interaction between a transition moment of a guest molecule and those of bonds composing a chiral host molecule. Here R_{0a} is the rotational

$$R_{0a} = \pi\nu_a\mu_{0a}{}^2\sum_j \frac{\nu_{0j}{}^2(\alpha_{33}-\alpha_{11})_j(\mathrm{GF})_j}{c(\nu_{0j}{}^2-\nu_a{}^2)}$$

$$(\mathrm{GF})_j = \frac{1}{r_j{}^3}\left[\mathbf{e}_{0a}\cdot\mathbf{e}_j - \frac{3(\mathbf{e}_{0a}\cdot\mathbf{r}_j)(\mathbf{e}_j\cdot\mathbf{r}_j)}{\mathbf{r}_j{}^2}\right]\mathbf{e}_{0a}\times\mathbf{e}_j\cdot\mathbf{r}_j \qquad (1)$$

strength of the transition from a ground state (0) to an excited state (a), which is correlated with the molar ellipticity and therefore correlated with the area and sign of the CD band; $\mathbf{e}_{0a}$ is the unit vector in the direction of the electric transition moment (μ_{0a}) of a chromophore which has a frequency of ν_a; $\mathbf{e}_j$ is the unit vector along the symmetry axis of bond j of a host molecule; $\mathbf{r}_j$ is the vector directed from the center of a chromophore to bond j with the absolute value r_j; ν_{0j} is the frequency of the electronic transition of bond j; α_{33} and α_{11} are bond polarizability at zero frequency, respectively parallel and perpendicular to the symmetry axis of bond j; and c is the velocity of light. It should be pointed out here that the asymmetry of the whole system is contained in $(\mathrm{GF})_j$. Furthermore, since the polarizability term $(\alpha_{33}-\alpha_{11})_j$ is equal to $2\mu_{0j}{}^2/h\nu_{0j}$ (μ_{0j} is the electric transition moment of bond j), one can understand that R_{0a} is dependent on the dipole–dipole interactions between the electric transition dipole moment of the guest chromophore and those of the bonds in the host molecule.

1. Parallel-Polarized Transition. In the present study, a host molecule is assumed to be a truncated cone. When a transition

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(1) Harata, K.; Uedaira, H. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 375.
(2) Shimizu, H.; Kaito, A.; Hatano, M. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 2678.
(3) Shimizu, H.; Kaito, A.; Hatano, M. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 513.
(4) Tinoco, I., Jr. *Adv. Chem. Phys.* **1962**, *4*, 113.
(5) Kodaka, M.; Fukaya, T. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 1154.
(6) Kodaka, M. *J. Phys. Chem.* **1991**, *95*, 2110.
(7) Schuette, J. M.; Ndou, T. T.; Warner, I. M. *J. Phys. Chem.* **1992**, *96*, 5309.
(8) Hamai, S.; Ikeda, T.; Nakamura, A.; Ikeda, H.; Ueno, A.; Toda, F. *J. Am. Chem. Soc.* **1992**, *114*, 6012.
(9) Tabushi, I.; Kuroda, Y.; Shimokawa, K. *J. Am. Chem. Soc.* **1979**, *101*, 4759.
(10) Tabushi, I.; Yuan, L. C. *J. Am. Chem. Soc.* **1981**, *103*, 3574.
(11) Fujita, K.; Ueda, T.; Imoto, T.; Tabushi, I.; Toh, N.; Koga, T. *Bioorg. Chem.* **1982**, *11*, 108.
(12) Fujita, K.; Ueda, T.; Imoto, T.; Tabushi, I.; Toh, N.; Koga, T. *Bioorg. Chem.* **1982**, *11*, 72.
(13) Yoon, C.-J.; Ikeda, H.; Kojin, R.; Ikeda, T.; Toda, F. *J. Inclusion Phenom.* **1987**, *5*, 85.
(14) Ikeda, T.; Kojin, R.; Yoon, C.-J.; Ikeda, H.; Iijima, M.; Toda, F. *J. Inclusion Phenom.* **1987**, *5*, 93.
(15) Nakamura, A.; Saitoh, K.; Toda, F. *Chem. Lett.* **1989**, 2209.
(16) Ueno, A.; Minato, S.; Suzuki, I.; Fukushima, M.; Okubo, M.; Osa, T.; Hamada, F.; Murai, K. *Chem. Lett.* **1990**, 605.
(17) Parrot-Lopez, H.; Djedaini, F.; Perly, B.; Coleman, A. W.; Galons, H.; Miocque, M. *Tetrahedron Lett.* **1990**, *31*, 1999.

0002-7863/93/1515-3702$04.00/0

moment of a guest chromophore is parallel to the axis of a host molecule, coordinate system (x, y, z) and geometric parameters are defined as illustrated in Figure 1. Here the quantity a is defined as the radius of the circular section containing the x and y axes, and the quantity h_j is defined as the z coordinate of the bond j on the truncated cone. Generally, the asymmetry of the truncated cone is considered to arise from the disposition of the bonds and the angle α_j. The assumption that the bonds lie on the surface of the truncated cone must be reasonable, since the overall shape of most macrocycles may be regarded as a truncated cone. The following relations (2) and (3) are given. By substituting

$$\mathbf{e}_{0a} = \mathbf{k}$$

$$\mathbf{e}_j = (\sin\alpha_j \sin\beta)\mathbf{i} + (\cos\alpha_j)\mathbf{j} + (\sin\alpha_j \cos\beta)\mathbf{k}$$

$$\mathbf{r}_j = (a + h_j \tan\beta)\mathbf{i} + (h_j - z)\mathbf{k}$$

$$\mathbf{e}_{0a}\cdot\mathbf{e}_j = \sin\alpha_j \cos\beta \qquad (2)$$

$$\mathbf{e}_{0a}\cdot\mathbf{r}_j = h_j - z$$

$$\mathbf{e}_j\cdot\mathbf{r}_j = (a + h_j \tan\beta)\sin\alpha_j \sin\beta + (h_j - z)\sin\alpha_j \cos\beta$$

$$\mathbf{e}_{0a} \times \mathbf{e}_j\cdot\mathbf{r}_j = -(a + h_j \tan\beta)\cos\alpha_j$$

$$(\mathrm{GF})_j = (a + h_j \tan\beta)\{[2(z - h_j)^2 - (a + h_j \tan\beta)^2]\cos\beta - 3(a + h_j \tan\beta)(z - h_j)\sin\beta\} \sin 2\alpha_j/2[(z - h_j)^2 + (a + h_j \tan\beta)^2]^{5/2} \qquad (3)$$

eq 3 into eq 1, one obtains eq 4,

$$R_{0a}(\mathrm{para},z) = \sum_j A_j G_j(z) \qquad (4)$$

where $R_{0a}(\mathrm{para},z)$ is the rotational strength in the case of a parallel-polarized transition when a chromophore is situated at z and A_j and $G_j(z)$ are defined as follows: When h_0 is small as compared

$$A_j = \pi\nu_a\mu_{0a}{}^2\nu_{0j}{}^2(\alpha_{33} - \alpha_{11})_j \sin 2\alpha_j/2c(\nu_{0j}{}^2 - \nu_a{}^2) \qquad (5)$$

$$G_j(z) = (a + h_j \tan\beta)\{[2(z - h_j)^2 - (a + h_j \tan\beta)^2]\cos\beta - 3(a + h_j \tan\beta)(z - h_j)\sin\beta\}/[(z - h_j)^2 + (a + h_j \tan\beta)^2]^{5/2} \qquad (6)$$

with a (this seems to be true for CDx), eq 4 can be approximated by eq 7,

$$R_{0a}(\mathrm{para},z) \approx \Big(\sum_j A_j\Big)G_{\mathrm{av}}(z) \qquad (7)$$

where $G_{\mathrm{av}}(z)$ is the average of $G_j(z)$ in the region $-h_0 \leq h_j \leq h_0$. The smaller h_0 is, the better this approximation is. If the number of bonds in the macrocycle is large enough and each bond is assumed to be equally distributed on the surface of the truncated cone, $G_{\mathrm{av}}(z)$ may be given by integral form, eq 8 (cf. Appendix I). Then eq 7 is transformed to eq 9,

$$G_{\mathrm{av}}(z) \approx (1/2ah_0)\int_{-h_0}^{h_0}\{(a + p\tan\beta)^2\{[2(z-p)^2 - (a + p\tan\beta)^2]\cos\beta - 3(a + p\tan\beta)(z-p)\sin\beta\}/[(z-p)^2 + (a + p\tan\beta)^2]^{5/2}\}\mathrm{d}p \qquad (8)$$

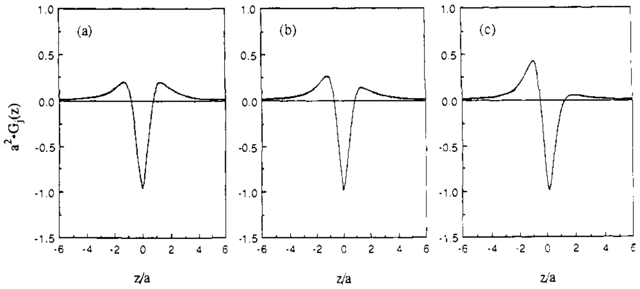


Figure 2. Dependence of $a^2G_j(z)$ on the position of a chromophore (z/a) for a parallel-polarized transition ($h_j = 0$). (a) $\beta = 0°$, (b) $\beta = 10°$, (c) $\beta = 30°$.

$$R_{0a}(\mathrm{para},z) \approx \Big[\sum_j (A_j/2ah_0)\Big]\int_{-h_0}^{h_0}\{(a + p\tan\beta)^2\{[2(z-p)^2 - (a + p\tan\beta)^2]\cos\beta - 3(a + p\tan\beta)(z-p)\sin\beta\}/[(z-p)^2 + (a + p\tan\beta)^2]^{5/2}\}\mathrm{d}p = DF(z) \qquad (9)$$

where

$$D = \Big[\sum_j (A_j/2ah_0)\Big] \qquad (10)$$

$$F(z) = \int_{-h_0}^{h_0}\{(a + p\tan\beta)^2\{[2(z-p)^2 - (a + p\tan\beta)^2]\cos\beta - 3(a + p\tan\beta)(z-p)\sin\beta\}/[(z-p)^2 + (a + p\tan\beta)^2]^{5/2}\}\mathrm{d}p \qquad (11)$$

The quantity D is the chiral part of $R_{0a}(\mathrm{para},z)$, the sign of which primarily depends on the directions of transition dipoles on the truncated cone, while $F(z)$ describes the relative position of a host molecule and a guest chromophore. Here we consider the interaction between one bond (j) of the host macrocycle and the transition moment of a guest chromophore. Typical dependency of $a^2G_j(z)$ on z/a when h_j is 0 is shown in Figure 2. Of special interest and importance is the finding that the integral value of $G_j(z)$ from $z = -\infty$ to $z = +\infty$ is always 0 (cf. Appendix II). This means that the integral value ($-\infty \leq z \leq +\infty$) of $R_{0a}(\mathrm{para})$, which is the linear combination of $G_j(z)$ (cf. eq 4), and that of $F(z)$ (cf. eq 9) are also always 0.

2. Perpendicular-Polarized Transition. When a transition moment of a guest chromophore is normal to the axis of a host molecule, coordinate system and geometry parameters are defined as shown in Figure 3, and relations 12 are given.

$$\mathbf{e}_{0a} = (\cos\theta)\mathbf{i} + (\sin\theta)\mathbf{j}$$

$$\mathbf{e}_j = (\sin\alpha_j \sin\beta)\mathbf{i} + (\cos\alpha_j)\mathbf{j} + (\sin\alpha_j \cos\beta)\mathbf{k}$$

$$\mathbf{r}_j = (a + h_j \tan\beta)\mathbf{i} + (h_j - z)\mathbf{k}$$

$$\mathbf{e}_{0a}\cdot\mathbf{e}_j = \sin\alpha_j \sin\beta \cos\theta + \cos\alpha_j \sin\theta \qquad (12)$$

$$\mathbf{e}_{0a}\cdot\mathbf{r}_j = (a + h_j \tan\beta)\cos\theta$$

$$\mathbf{e}_j\cdot\mathbf{r}_j = (a + h_j \tan\beta)\sin\alpha_j \sin\beta + (h_j - z)\sin\alpha_j \cos\beta$$

$$\mathbf{e}_{0a} \times \mathbf{e}_j\cdot\mathbf{r}_j = (a + h_j \tan\beta)\sin\alpha_j \cos\beta \sin\theta + (h_j - z)(\cos\theta \cos\alpha_j - \sin\theta \sin\alpha_j \sin\beta)$$

In an ideal case in which a transition moment of a guest chromophore has an equal probability in all directions ($0 \leq \theta < 2\pi$), $(\mathrm{GF})_j$ is given by eq 13 (cf. Appendix III). Since eq 13 is

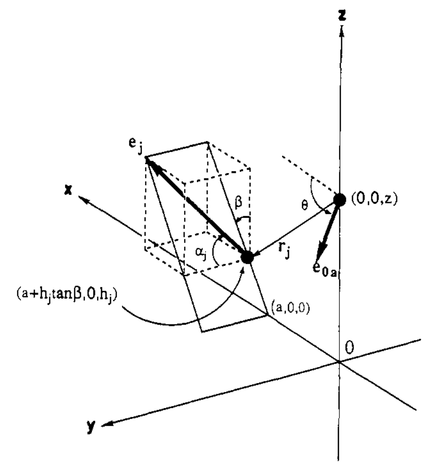


Figure 3. Definition of geometric parameters for a perpendicular-polarized transition moment and a bond of a host macrocycle.

$$(\mathrm{GF})_j = -(a + h_j \tan \beta)\{[2(z - h_j)^2 - (a + h_j \tan \beta)^2]\cos \beta - 3(a + h_j \tan \beta)(z - h_j)\sin \beta\}\sin 2\alpha_j / 4[(z - h_j)^2 + (a + h_j \tan \beta)^2]^{5/2} \quad (13)$$

different from eq 3 only in sign and coefficient (viz. $-^1/_2$ of eq 3), eq 14 holds for a perpendicular-polarized transition.

$$R_{0a}(\mathrm{perp},z) = (-^1/_2)R_{0a}(\mathrm{para},z) \approx (-^1/_2)DF(z) \quad (14)$$

Results and Discussion

Figures 4 shows the dependency of $F(z)$ on z for a parallel-polarized transition, which was numerically calculated by the Simpson method. It should be noted here again that the integral of $F(z)$ from $z = -\infty$ to $z = +\infty$ is always 0, as mentioned above. From Figure 4 and eq 14, we can qualitatively say the following. (1) In $F(z)$, there are one *negative* minimum inside the cavity ($-h_0 < z < h_0$) and two *positive* maxima outside ($z > h_0$ and $z < -h_0$). (2) The magnitude of the positive maximum value of $F(z)$ is larger when a chromophore is located in the *narrower-rim* outside ($z < -h_0$) of the host macrocycle than when it is in the *wider-rim* outside ($z > h_0$). This tendency becomes prominent as β increases. (3) In a perpendicular-polarized transition, ideally the ICD value should be $-^1/_2$ of that of a parallel-polarized one (cf. eq 14).

One of the macrocycles extensively studied so far is CDx, and therefore we compare the above-mentioned rule with the experimental data of CDx. According to the present conclusion, CDx can be classified as a macrocycle with a negative D value, since when D is negative the ICD curve obtained from eq 9 well reproduces the fundamental characteristics of the calculation curves of α- and β-CDx.[5,6] In the factor D, the summation of sin $2\alpha_j$ may primarily contribute to its sign, since the sign of the other factors in D is positive and their values do not change so widely as sin $2\alpha_j$, as can be seen from eqs 5 and 10. In fact, one can qualitatively see from the molecular structures of α- and β-CDx[5,6] that the sign of the summation of sin $2\alpha_j$ is negative, which means that the sign of D is also negative. One of experimental evidences supporting the present rule is that β-CDx capped with a trans azobenzene group (Scheme Ia) offers a positive ICD for the $\pi \rightarrow \pi^*$ transition at 355 nm which is polarized along the long axis of azobenzene group and therefore perpendicular to the axis of β-CDx.[18] On the other hand, methyl orange (the trans form) shows a positive ICD for the $\pi \rightarrow \pi^*$ transition when it is axially included inside β-CDx cavity (Scheme Ib).[19] Another experimental evidence obtained by us shows that 1,1′-di-*n*-heptyl-4,4′-bipyridinium (heptyl viologen, HV) gives a negative ICD corresponding to the $\pi \rightarrow \pi^*$ transition (long-axis polarized) in the presence of α- or β-CDx (Figure 5).[20] In 1,1′-dimethyl-4,4′-bipyridinium (methyl viologen, MV), however, no ICD was given under the same conditions.[20] Thus in this case the long alkyl chain of HV must be included in the cavity, as shown in Scheme II. Recently there has appeared much evidence which suggests the inclusion of long alkyl chains by CDx; typical examples are the behavior of viologen derivatives,[21-24] surfactants,[25,26] and rotaxanes.[27-29] Interestingly, when γ-CDx is used

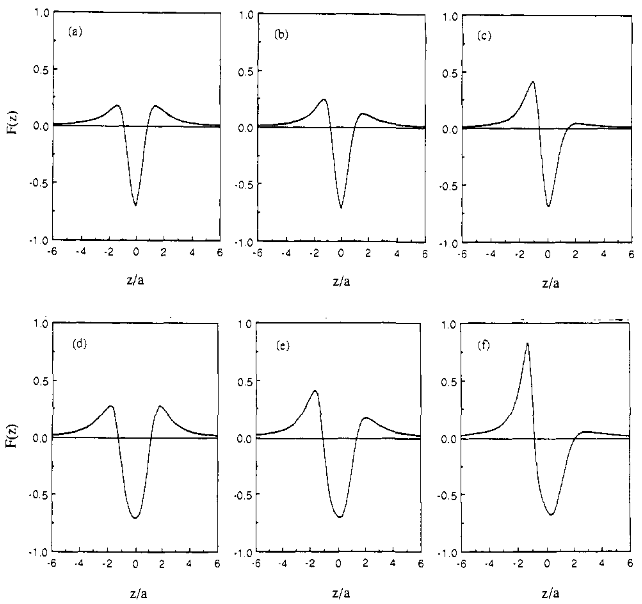
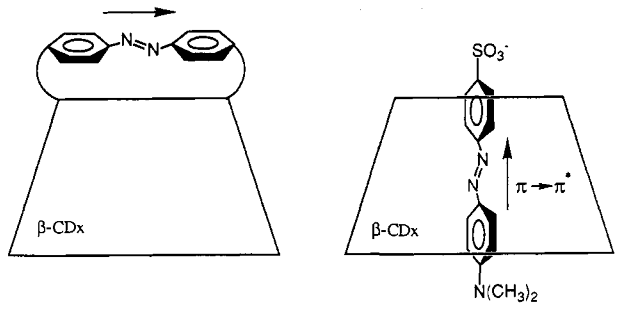


Figure 4. Dependence of $F(z)$ on the position of a chromophore (z/a) for a parallel-polarized transition. (a) $h_0/a = 0.5$, $\beta = 0°$; (b) $h_0/a = 0.5$, $\beta = 10°$; (c) $h_0/a = 0.5$, $\beta = 30°$; (d) $h_0/a = 1$, $\beta = 0°$; (e) $h_0/a = 1$, $\beta = 10°$; (f) $h_0/a = 1$, $\beta = 30°$.

Scheme I. Structures of (a) β-CDx Capped by Azobenzene Moiety (ref 18) and (b) Inclusion Complex between Methyl Orange and β-CDx (ref 19)



(a) ICD>0 (b) ICD>0

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[18] Ueno, A.; Yoshimura, H.; Saka, R.; Osa, T. *J. Am. Chem. Soc.* **1979**, *101*, 2779.

[19] Szejtli, J. *Cyclodextrins and Their Inclusion Complexes*; Akademiai Kiado: Budapest, 1982.

[20] Kodaka, M.; Fukaya, T. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2032.

[21] Yasuda, A.; Kondo, H.; Itabashi, M.; Seto, J. *J. Electroanal. Chem.* **1986**, *210*, 265.

[22] Diaz, A.; Quintela, P. A.; Schuette, J. M.; Kaifer, A. E. *J. Phys. Chem.* **1988**, *92*, 3537.

[23] Yoneyama, H.; Saito, H.; Matsushima, S.; Nakamura, H.; Matsuo, T. *Tetrahedron Lett.* **1989**, *30*, 3143.

[24] Yonemura, H.; Kasahara, M.; Saito, H.; Nakamura, H.; Matsuno, T. *J. Phys. Chem.* **1992**, *96*, 5765.

[25] Junquera, E.; Aicart, E.; Tardajos, G. *J. Phys. Chem.* **1992**, *96*, 4533.

[26] Okubo, T.; Maeda, Y.; Kitano, H. *J. Phys. Chem.* **1989**, *93*, 3721.

[27] Isnin, R.; Kaifer, A. E. *J. Am. Chem. Soc.* **1991**, *113*, 8188.

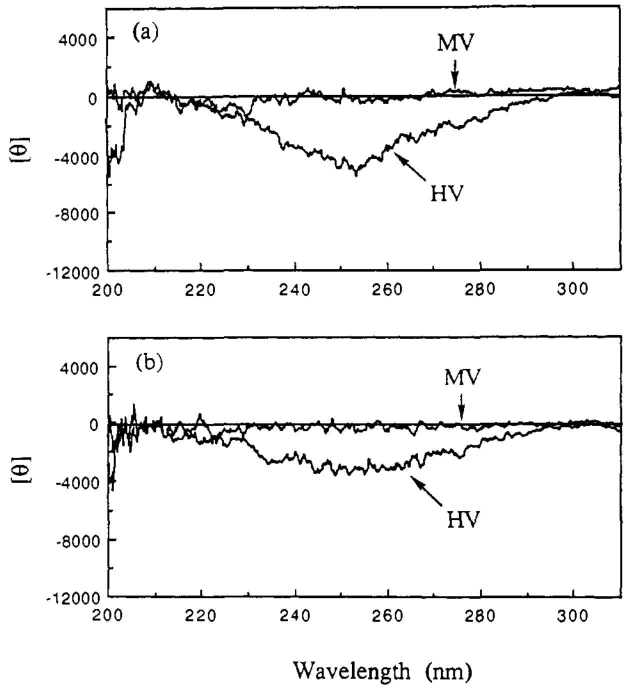
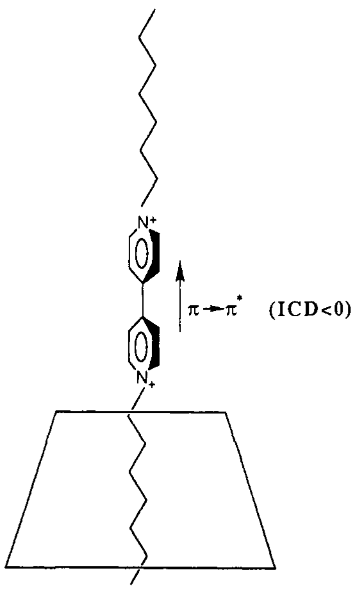


Figure 5. ICD spectra of (a) HV/α-CDx complex and (b) HV/β-CDx complex in H_2O (cf. ref 20). [HV] = 5×10^{-5} mol dm^{-3}, [α-CDx] = [β-CDx] = 5×10^{-3} mol dm^{-3}.

Scheme II. Estimated Structure of Inclusion Complex between HV and CDx (cf. ref 5)



as a host molecule either HV or MV showed little ICD, which is probably due to the cavity being too large to closely include a hydrophobic alkyl chain. We can also find further experimental results supporting our rule.[7,8]

In this study, a general rule for ICD by a chiral macrocycle has been proposed for the first time. Although the experimental examples are limited to CDx at present, this general rule may be applied to various types of new chiral macrocycles which will be synthesized or found naturally.

Appendix I

We consider a case in which the number of bonds is large and each bond has an equal probability density (C) on the surface of the truncated cone. Here C is determined to be $1/4\pi a h_0$ from the next standardization condition, eq A-1. Thus the following

$$\int_{-h_0}^{h_0} 2\pi(a + p\tan\beta)C\,\mathrm{d}p = 1 \tag{A-1}$$

relation is given.

$$G_{\mathrm{av}}(z) \approx \int_{-h_0}^{h_0}(1/4\pi a h_0)\{(a + p\tan\beta)\{[2(z-p)^2 - (a + p\tan\beta)^2]\cos\beta - 3(a + p\tan\beta)(z-p)\sin\beta\}/[(z-p)^2 + (a + p\tan\beta)^2]^{5/2}\}2\pi(a + p\tan\beta)\mathrm{d}p = (1/2ah_0)\int_{-h_0}^{h_0}\{(a + p\tan\beta)^2\{[2(z-p)^2 - (a + p\tan\beta)^2]\cos\beta - 3(a + p\tan\beta)(z-p)\sin\beta\}/[(z-p)^2 + (a + p\tan\beta)^2]^{5/2}\}\mathrm{d}p$$

Appendix II

By replacing $z - h_j$ by q, the integral of $G_j(z)$ is given by

$$\int_{-\infty}^{\infty} G_j(z)\mathrm{d}z = (a + h_j\tan\beta)\int_{-\infty}^{\infty}\{\{[2q^2 - (a + h_j\tan\beta)^2]\cos\beta - 3(a + h_j\tan\beta)q\sin\beta\}/[q^2 + (a + h_j\tan\beta)^2]^{5/2}\}\mathrm{d}q = 2(a + h_j\tan\beta)\cos\beta\int_0^{\infty}\{[2q^2 - (a + h_j\tan\beta)^2]/[q^2 + (a + h_j\tan\beta)^2]^{5/2}\}\mathrm{d}q \tag{A-2}$$

Replacing q by $(a+h_j\tan\beta)/(t^{-2} - 1)^{1/2}$, one obtains

$$\int_{-\infty}^{\infty} G_j(z)\mathrm{d}z = 0$$

Appendix III

In a perpendicular transition, $(\mathrm{GF})_j$ is also derived in a similar manner. Here we assume that a transition moment of a guest molecule has an equal probability in all directions ($0 \le \theta < 2\pi$); viz., we average $\cos^2\theta$, $\sin^2\theta$, and $\cos\theta\sin\theta$ in this range by use of eq A-3. Finally, $(\mathrm{GF})_j$ has the following form.

$$\overline{\cos^2\theta} = \int_0^{2\pi}\cos^2\theta\,\mathrm{d}\theta\Big/\int_0^{2\pi}\mathrm{d}\theta = {}^1/_2$$

$$\overline{\sin^2\theta} = \int_0^{2\pi}\sin^2\theta\,\mathrm{d}\theta\Big/\int_0^{2\pi}\mathrm{d}\theta = {}^1/_2$$

$$\overline{\cos\theta\sin\theta} = \int_0^{2\pi}\cos\theta\sin\theta\,\mathrm{d}\theta\Big/\int_0^{2\pi}\mathrm{d}\theta = 0 \tag{A-3}$$

$$(\mathrm{GF})_j = -(a + h_j\tan\beta)\{[2(z-h_j)^2 - (a + h_j\tan\beta)^2]\cos\beta - 3(a + h_j\tan\beta)(z-h_j)\sin\beta\}\sin 2\alpha_j / 4[(z-h_j)^2 + (a + h_j\tan\beta)^2]^{5/2}$$

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[28] Harada, A.; Li, J.; Kamachi, M. *Nature* **1992**, *356*, 325.

[29] Wylie, R. S.; Macartney, D. H. *J. Am. Chem. Soc.* **1992**, *114*, 3136.