the bath was removed and stirring was continued for 20 min. Solvent was removed, and the product was purified by chromatography on silica gel (1:9 ether–pentane) to give, after recrystallization from ether–pentane, 0.212 g (83%) of 1-phenylethyl 2-nitrophenyl sulfide: mp 90.5–91.5 °C; ^{1}H NMR δ 1.70 (d, J = 7 Hz, 3 H), 4.47 (q, J = 7 Hz, 1 H), 7.1–7.4 (m, 8 H), 7.98 (d, J = 8 Hz, 1 H).

Anal. Calcd for $C_{14}H_{13}NO_2S$: C, 64.84; H, 5.05. Found: C, 64.81; H, 5.00.

The sulfide prepared above (67 mg, 0.259 mmol) in 15 mL of CH_2Cl_2 was cooled to 0 °C, and 52 mg (0.258 mmol) of *m*-chloroperbenzoic acid was added. After 10 min, the reaction mixture was filtered through Celite, and solvent was removed from the filtrate. Crystallization from CH_2Cl_2–pentane gave 54.7 mg (77%) of **45** as yellow needles: mp 98–99 °C; ^{1}H NMR ($CDCl_3$, major diastereomer, 3:1 ratio) δ 1.36 (d, J = 7 Hz, 3 H), 4.28 (q, J = 7 Hz, 3 H), 7.3–7.6 (m, 5 H), 7.67 (t m, J = 8 Hz, 1 H), 7.93 (t m, J = 8 Hz, 1 H), 8.24 (d m, J = 8 Hz, 1 H), 8.27 (d m, J = 8 Hz, 1 H).

The elimination rate was measured in $CDCl_3$ solution (0.2 M) containing 0.4 M Et_2NH at 38 °C in the NMR probe, k = (1.39 ± 0.09) × 10^{-5} s^{-1}.

1-Phenylethyl 2,4-dinitrophenyl sulfoxide (46) was prepared by a procedure similar to one above. Sulfide: mp 109–110 °C; IR 1590, 1535, 1518, 1355, 1340, 1055, 740, 705 cm^{-1}; ^{1}H NMR δ 1.68 (d, J = 7 Hz, 3 H), 4.60 (q, J = 7 Hz, 1 H), 7.2–7.6 (m, 6 H), 8.13 (dd, J = 9, 2 Hz, 1 H), 8.80 (d, J = 2 Hz, 1 H); MS 304.0511 (M^+), calcd for $C_{14}H_{12}N_2O_4S$, 304.0523. Sulfoxide (**46**): ^{1}H NMR ($CDCl_3$, partial) δ 4.25–4.3 (br q, J = 6 Hz), 8.65 (d, J = 8 Hz), 8.96 (s). Decomposed in $CDCl_3$ to styrene at 38 °C, k = 1.34 × 10^{-4} s^{-1}.

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Registry No. 1a, 83333-70-4; **1b**, 68099-13-8; **1c**, 60174-90-5; **2a**, 83333-71-5; **2b**, 68099-15-0; **2c**, 15619-32-6; **4**, 68099-18-3; **5a**, 17488-64-1; **5b**, 68099-38-7; **6**, 31952-17-7; **7**, 32363-86-3; **8**, 68099-17-2; **9**, 68099-19-4; (*E*)-**10**, 68099-20-7; (*E*)-**11** (isomer 1), 83333-72-6; *E*-**11** (isomer 2), 83334-14-9; (*E*)-**12**, 83333-73-7; (*Z*)-**12**, 83334-11-6; (*E*)-**13**, 83333-74-8; (*E*)-**14**, 83333-75-9; (*E*)-**15**, 83333-76-0; (*E*)-**16**, 83333-77-1; (*E*)-**17**, 83333-78-2; **18**, 83333-79-3; (*E*)-**19**, 5284-13-9; (*E*)-**20**, 83333-80-6; (*E*)-**21**, 83333-81-7; **22a**, 68099-24-1; **22b**, 68099-25-2; **22c**, 83333-82-8; **23a**, 15619-34-8; **24**, 83333-83-9; **25**, 21473-05-2; **26**, 57293-43-3; (*E*)-**27**, 68099-28-5; (*Z*)-**27**, 83334-03-6; (*E,E*)-**28**, 68099-29-6; (*E,Z*)-**28**, 68099-40-1; (*E*)-**29**, 77605-16-4; (*Z*)-**29**, 77605-17-5; (*E*)-**30**, 83333-84-0; (*Z*)-**30**, 83334-04-7; (*E*)-**31**, 55177-38-3; (*Z,E*)-**32**, 83333-85-1; (*E,E*)-**32**, 83334-12-7; (*Z,Z*)-**32**, 83334-13-8; (*E,E*)-**33**, 83333-86-2; (*Z,E*)-**33**, 83334-05-8; (*Z,E*)-**34**, 83333-87-3; **35**, 83333-88-4; (*E*)-**36**, 83333-89-5; (*Z*)-**36**, 83334-06-9; (*E*)-**37**, 83333-90-8; (*Z*)-**37**, 83334-07-0; (*E*)-**38**, 83333-91-9; **40** (isomer 1), 83333-92-0; **40** (isomer 2), 83333-93-1; **42a**, 83333-94-2; **42b**, 83333-95-3; **43a**, 83333-96-4; **43b**, 83333-97-5; **44**, 83333-98-6; **45**, 83333-99-7; **46**, 83334-00-3; PhLi, 591-51-5; 4-methyl-2-nitrobenzeneselenenyl chloride, 68099-14-9; 4-methyl-2-nitrophenylselenocyanate, 65275-29-8; 4-methyl-2-nitrophenyl methyl selenide, 83334-01-4; 2-iodotoluene, 615-37-2; 2-cyclohexenone, 930-68-7; prenyl phenyl selenide, 69690-81-9; 1-bromo-3-phenylpropane, 637-59-2; butyl phenyl selenide, 28622-61-9; 2-phenylpropionaldehyde, 93-53-8; propenyl bromide, 590-14-7; 1-decyne, 764-93-2; crotonaldehyde, 4170-30-3; 2-phenyl-3-penten-2-ol, 4743-67-3; 4-bromo-3-phenyl-2-pentanone, 83334-02-5; allyl phenyl selenide, 14370-82-2; acetophenone, 98-86-2; phenyl (4-phenyl-1-penten-4-ol-3-yl) selenide, 83334-08-1; phenyl (4-phenyl-2-penten-4-ol-1-yl) selenide, 83334-09-2; 4-phenyl-2-pentene-1,4-diol, 83334-10-5; 2,4-dinitrobenzenesulfenyl chloride, 528-76-7; 1-phenyl-4-*trans*-methylcyclohexanol, 30689-84-0; 1-phenyl-4-*cis*-methylcyclohexanol, 30689-83-9; 4-methylcyclohexenone, 5515-76-4; 2,5-dichloroiodobenzene, 29682-41-5; 4-methyl-2-cyclohexenone, 5515-76-4; 2-nitrophenylthiocyanate, 2769-30-4; 1-phenylethanol, 98-85-1; 1-phenylethyl 2-nitrophenyl sulfide, 19758-58-8.

Supplementary Material Available: Spectroscopic data and/or experimental details for the preparation of the following compounds: 2,4-dinitrobenzeneselenocyanate, 2,4-dinitrobenzeneselenenyl bromide, **1c**, **4**, **6**, **8**, **9**, **14**, **18**, **19**, **20**, **21**, **40**, and **41** (5 pages). Ordering information is given on any current masthead page.

Induced Circular Dichroism of β-Cyclodextrin Complexes with Azanaphthalenes—Polarization Directions of the $\pi^* \leftarrow \pi$ Transitions in Azanaphthalenes

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Abstract: The induced circular dichroism (ICD) spectra of the β-cyclodextrin (β-CD_x) complexes with mono-, di-, and triazanaphthalenes were measured in the wavelength region 200–400 nm. The polarization analysis and spectral assignments of these azanaphthalenes were made from the comparison of the theoretical results calculated by using the CNDO/S-CI approximation with the observed ICD spectra. The polarization directions of the first $\pi^* \leftarrow \pi$ transitions in azanaphthalenes are closely related to the position of aza nitrogen atoms and can be determined by the coefficients of the configurations in the corresponding lowest $\pi^* \leftarrow \pi$ states. From the observation of the ICD band with mixed signs, the presence of the "forbidden" character is strongly suggested in the second absorption bands of isoquinoline, phthalazine, cinnoline, and quinazoline. In each case of azanaphthalenes, the observation of positive ICD bands in the third absorption band indicated the predominance of the long-axis-polarized electronic transitions.

Polarization analysis is one of the most useful techniques for spectral assignments of aromatic compounds, since it offers information on the transition-moment directions and vibronic structure. The measurements of polarized or linear dichroism[1] spectra require a partially oriented assembly of molecules achieved by the preparation of single and mixed crystals,[2,3] the dispersion of solute molecules in nematic liquid crystal[4] and stretched polymer sheet,[5-7] the application of electric or magnetic fields[8,9] and hy-

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drodynamic shear,[10] and the principle of photoselection.[11] Thulstrup et al. have analzyed the linear dichroism spectra in the stretched polymer sheet by the introduction of the observable orientation parameters and applied their method to a variety of organic aromatic molecules.[6,12] The direction of the electronic transition moments of organic aromatic compounds have been also studied on the basis of the signs of the extrinsic circular dichroism spectra measured in the cholesteric liquid crystal solutions.[13]

On the other hand, the induced circular dichroism (ICD) of β-cyclodextrin (β-CD_x) complexes with organic aromatic compounds has been shown to be useful for the determination of the relative direction of electronic transition dipole moment of the organic aromatic compounds.[14-18] ICD is the phenomenon in which the circular dichroism (CD) can be induced at the absorption frequency of the achiral molecule by the dissymmetric perturbation of the chiral species. In the case of the β-CD_x inclusion complex, CD is expected to be induced at the absorption bands of the achiral guest molecules that are included in the cavity of the β-CD_x host molecule, since β-CD_x is composed of chiral glucose units. The ICD method using inclusion phenomena of β-CD_x has some limitations; this method cannot be applied to the quantitative determination of the polarization angles in molecules of low symmetry and to separation of strongly overlapping transitions of opposite polarization. The ICD method is, however, said to be a new and simple technique for the study of the polarization direction of the electronic transition, which does not require any elaborate instrumentation.

Harata and Uedaira[14] have recently measured the ICD spectra of β-CD_x complexes with naphthalene derivatives and determined the structure of the β-CD_x complexes on the basis of the calculation of the rotational strengths by the Kirkwood–Tinoco equation.[19] Yamaguchi et al. have studied the ICD spectra of β-CD_x complexes with 2-hydroxytropone[15] and azulene[16] and have discussed the direction of the electronic transition moment of the guest molecules. In our previous papers,[17,18] we have studied the ICD spectra of β-CD_x inclusion complexes with a series of substituted benzenes in aqueous solution and have shown that the sign and intensity of ICD spectra depend on the transition-moment directions of substituted benzenes that are included in the cavity of β-CD_x.

On the other hand, the electronic structure of azanaphthalenes has received much attention.[20-28] Theoretical investigations have been performed to interpret the electronic spectra of azanaphthalenes within the semiempirical SCF-MO framework.[20-24] Furthermore, the photoelectron spectra of azanaphthalenes were measured, and the ordering of the π orbitals and the nitrogen "lone-pair" orbitals was discussed.[25,26] Similarly, from the viewpoint of the location and ordering of the $\pi^* \leftarrow$ n and low-lying $\pi^* \leftarrow \pi$ electronic transitions, the electronic spectra of azanaphthalenes have been observed in vapor phase[27] or in mixed crystals.[28] Despite these theoretical and experimental investigations, there are some unsettled problems with respect to the electronic-band assignments of azanaphthalenes.

Recently, the magnetic circular dichroism (MCD) spectra of azanaphthalenes were reported and the spectral assignments of these molecules were examined on the basis of the Faraday *B* terms.[24,29]

In this paper, we measured the ICD spectra of β-CD_x complexes with mono-, di-, and triazanaphthalenes in aqueous solution and discussed the polarization directions of these azanaphthalenes by the comparison with the results calculated by using CNDO/S-CI approximation.[30] We also attempt to derive the dependence of the ICD spectra on the polarization directions of the guest molecule from the theoretical model developed by Kirkwood–Tinoco.[19]

Table I. Averaged Wavenumber of the Electronic Transitions (ν_{bj}) and Polarizability (α) of the Bonds in a Glucose Residue

bonds	$(\alpha_{33} - \alpha_{11}) \times 10^{24}$, cm^3	$\nu_{bj} \times 10^{-3}$,[a] cm^{-1}
C–C	0.71[b]	70.85[e,f]
C–OC	0.43[c]	67.53[g,h]
O–H	0.45[d]	80.78[g,h]

[a] ν_{bj} is approximated by a wavenumber midway between the first absorption band and its ionization potential. [b] C. G. LeFevre and J. W. LeFevre, *J. Chem. Soc.*, 3549, (1956). [c] R. J. W. LeFevre et al., *ibid.*, 479, (1963). [d] C. G. LeFevre et al., *ibid.*, 123, (1960). [e] L. W. Pickett et al., *J. Am. Chem. Soc.*, 73, 4862 (1951). [f] R. F. Pottie et al., *ibid.*, 83, 3204 (1961). [g] A. J. Harrison et al., *J. Chem. Phys.*, 30, 355 (1959). [h] K. Watanabe, *ibid.*, 26, 542 (1957).

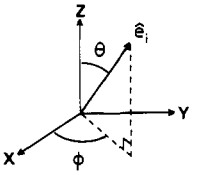

Figure 1. Coordinates of e_i.

Experimental Section

β-CD_x and azanaphthalenes were commercially available. β-CD_x was purified by recrystallization from aqueous solution. Phthalazine, quinazoline, and pyrido[2,3-*b*]pyrazine were recrystallized from ether, petroleum ether, and petroleum ether–ethanol (9:1 v/v), respectively. Quinoline, isoquinoline, and quinoxaline were distilled under reduced

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pressure. Cinnoline was purified by vacuum sublimation before use. 1,5-Naphthyridine was used without further purification (Tokyo Kasei Co., Ltd.). An inclusion complex was prepared by mixing β-CD_x and the corresponding azanaphthalene in an aqueous solution or in aqueous KOH.

The circular dichroism and absorption spectra were measured at room temperature on a JASCO J-500 circular dichrograph with a J-DP 500 data processor and a Hitachi EPS-3T recording spectrophotometer, respectively.

In this paper, molar ellipticity was normalized by the concentration of the guest molecule.

Theory

Dependence of the Theoretical Rotational Strength on the Transition-Moment Directions of the Guest Molecule. The rotational strength is a fundamental quantity in circular dichroism. In the β-CD_x–aromatic compound systems, the theoretical rotational strength (R_{i0a}) of the transition from the ground state 0 to the excited state a in an aromatic compound is expressed as in eq 1, developed by Kirkwood and Tinoco: Here $\mathbf{e}_j$ is the unit

$$R_{i0a} = \pi\nu_{ai}\mu_{i0a}^2 \sum_j \frac{\nu_{bj}^2(\alpha_{33} - \alpha_{11})_j(GF)_{ij}}{\nu_{bj}^2 - \nu_{ai}^2} \quad (1)$$

$$(GF)_{ij} = \frac{1}{r_{ij}^3}\left[\mathbf{e}_i \times \mathbf{e}_j - \frac{3(\mathbf{e}_i \times \mathbf{r}_{ij})(\mathbf{e}_j \times \mathbf{r}_{ij})}{r_{ij}^2}\right]\mathbf{e}_i(\mathbf{e}_j \times \mathbf{r}_{ij}) \quad (2)$$

vector in the direction of the symmetry axis of the bond in β-CD_x; $\mathbf{e}_i$ is the unit vector in the direction of the electric dipole moment ($\vec{\mu}_{i0a}$) of the transition from the ground state (0) to the excited state (a) in the guest molecule, and ν_{ai} is its wavenumber; α_{33} and α_{11} are bond polarizabilities at zero frequency parallel and perpendicular, respectively, to the symmetry axis of the bond in β-CD_x; $\mathbf{r}_{ij}$ is the vector pointing from the center of the guest molecule to each bond in β-CD_x; and ν_{bj} is the averaged wavenumber of the electronic transitions of the bond in β-CD_x.

In this paper, ν_{bj} is approximated by a wavenumber midway between the first absorption band in the bond of β-CD_x and its ionization potential. The values of $(\alpha_{33} - \alpha_{11})$ and ν_{bj} for each bond are listed in Table I.

In the first place, the origin of the coordinates was chosen in the center of a ring of β-CD_x that was assumed to have a 7-fold symmetry axis. Next, $\mathbf{e}_i$, which is put at the origin of the β-CD_x-fixed Cartesian coordinates, is expressed by the spherical polar coordinates (Figure 1) resulting in eq 3. Here θ is the

$$\mathbf{e}_i = (\sin\theta\cos\phi)\mathbf{i} + (\sin\theta\sin\phi)\mathbf{j} + (\cos\theta)\mathbf{k} \quad (3)$$

inclination angle of $\mathbf{e}_i$ with respect to the z axis (the symmetry axis of β-CD_x), while ϕ is the angle in which the projection of $\mathbf{e}_i$ into the xy plane inclines to the x axis. In eq 3, **i**, **j**, and **k** are the orthogonal unit vectors along the x, y, and z axes, respectively, of the Cartesian coordinates. After substitution of eq 3 into eq 1, eq 1 can be expressed in terms of the angles θ and ϕ. Then, rotational strength (R_{i0a}) is given by expression 4:

$$R_{i0a} = (\sin^2\theta)[R_{xx}(\cos^2\phi) + R_{yy}(\sin^2\phi) + (R_{xy} + R_{yx}) \times (\cos\phi)(\sin\phi)] + (\sin\theta)(\cos\theta)[(R_{xz} + R_{zx})(\cos\phi) + (R_{yz} + R_{zy})(\sin\phi)] + (\cos^2\theta)R_{zz} \quad (4)$$

where

$$R_{zz} = \pi\nu_{ai}\mu_{i0a}^2 \sum_j \frac{\nu_{bj}^2(\alpha_{33} - \alpha_{11})_j(GF)_{zz}}{\nu_{bj}^2 - \nu_{ai}^2} \quad (5)$$

$$(GF)_{zz} = \frac{1}{r_{ij}^3}\left[\mathbf{e}_j - \frac{3\mathbf{r}_{ij}(\mathbf{e}_j \times \mathbf{r}_{ij})}{r_{ij}^2}\right]_z (\mathbf{e}_j \times \mathbf{r}_{ij})_z \quad (6)$$

Here R_{zz} is the zz component of R_{i0a} and contains the geometry factor $(GFe)_{zz}$ defined by eq 6. Each of other eight components of R_{i0a} can be expressed in a similar manner as above. All the components of R_{i0a} have two quantities in common, the bond polarizability difference $(\alpha_{33} - \alpha_{11})$ and averaged wavenumber ν_{bj} of the bonds in β-CD_x. Then, each of components of R_{i0a} at a transition wavenumber ν_{ai} is computed by the summation over all values of j, with the values of $(\alpha_{33} - \alpha_{11})$ and ν_{bj} listed in Table I. In this calculation the contributions of the C–C, C–O, and O–H bonds in β-CD_x are taken into account. The effect of all the C–H bonds is neglected, since these bonds may have isotropic polarizability. Among the evaluated components of R_{i0a}, the following relations have been found to be held, because the β-CD_x has a 7-fold axis.

$$R_{xx} = R_{yy} \quad R_{xy} = -R_{yx} \quad R_{xz} = -R_{zx} \quad R_{zy} = -R_{yz} \quad R_{zz} = -2R_{xx} \quad (7)$$

By using these relations, we can obtain the final form of R_{i0a} expressed as

$$R_{i0a} = \frac{1}{2}(3\cos^2\theta - 1)R_{zz} = \frac{1}{2}(3\cos^2\theta - 1)\mu_{i0a}^2 \times R_{zz} \quad (8)$$

In eq 8, the sign of R_{i0a} depends only on the angle θ, since both μ_{i0a}^2 and R_{zz} are positive values. Therefore, eq 8 suggests that the absolute direction of the transition dipole moment is determined by only the sign of observed ICD spectra, when the structure of inclusion complexes can be regarded as the axial inclusion in which the long axis of the guest molecule is parallel to the axis of the β-CD_x cavity (z axis).

On the contrary, the relationship in eq 7, $R_{xx} = R_{yy}$, implies that we can make no reference to the difference in the geometrical environment of the guest molecule with respect to the x and y axes. That is to say, in this theoretical model, the orientation of the guest molecule in the xz plane is equivalent to that in the yz plane. From the same reason, it is also suggested that the $\pi^* \leftarrow$ n (out of plane) transition may give rise to the negative ICD band as well as the short-axis-polarized $\pi^* \leftarrow \pi$ (in plane) transition when the guest molecule is included by the axial inclusion.

Results and Discussion

ICD Spectra and Polarization Directions. Figures 2–9 show the CD (upper) and UV (lower) spectra of the β-CD_x complexes with azanaphthalenes in aqueous solution. In each figure, ICD bands were observed at absorption frequencies of achiral azanaphthalenes. In these figures, the vertical lines indicate the theoretical spectra calculated by using the CNDO/S-CI method,[24] with the lengths of the lines representing relative values of oscillator strengths. The open circle designates the $\pi^* \leftarrow$ n transition at the frequency calculated. Numbers (1, 2, 3, ...) designate in turn the first $\pi^* \leftarrow \pi$, the second $\pi^* \leftarrow \pi$, the third $\pi^* \leftarrow \pi$ transitions of azanaphthalenes, and so on, respectively. The broken lines in structural formulas indicate the calculated directions of the respective transition dipole moments. Figure 2 shows the CD and UV spectra of the β-CD_x complex with quinoline, which contains a nitrogen atom at the α position. In this case, a positive ICD band with the vibrational structure observed in the lower wavenumber region was assigned to the first $\pi^* \leftarrow \pi$ transition, while one negative CD band was induced by the second $\pi^* \leftarrow \pi$ transition in the middle-wavenumber region. In the higher wavenumber region, a large positive ICD band originating from the third $\pi^* \leftarrow \pi$ transition was observed. As shown in this figure, the sign of the ICD bands are in agreement with the theoretical results in which the polarization directions of the first $\pi^* \leftarrow \pi$, the second $\pi^* \leftarrow \pi$, and the third $\pi^* \leftarrow \pi$ transitions of quinoline are nearly long, short, and long axes, respectively.

As shown in Figure 3, the β-CD_x complex with isoquinoline exhibited two negative ICD bands in the longer wavelength region, and these bands were attributed to the first and the second $\pi^* \leftarrow \pi$ transitions, which were both evaluated to be the roughly short-axis polarizations. One intensive positive CD band derived from the third and the fourth $\pi^* \leftarrow \pi$ transitions was observed in the shorter wavelength region and coincided with the calculated results in which both of the $\pi^* \leftarrow \pi$ transitions were approximately long-axis polarized. In the case of the β-CD_x–quinoxaline system, a weak negative CD band was induced by the $\pi^* \leftarrow$ n transition at 370 nm (Figure 4). Although the second absorption band of quinoxaline was supposed to be composed of the first $\pi^* \leftarrow \pi$ ($^1A_1$

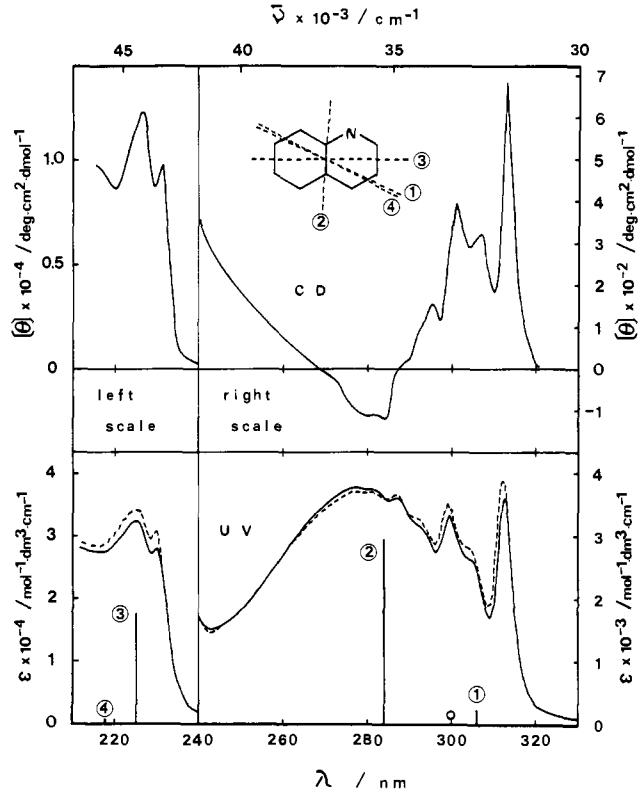

Figure 2. CD (upper) and UV (lower) spectra of the β-CD_x complex with quinoline in 1.0×10^{-5} M aqueous KOH (pH 7.45): (broken line) in the absence of β-CD_x, (solid line) β-CD_x (1.438×10^{-2} M) + quinoline (3.226×10^{-4} M).

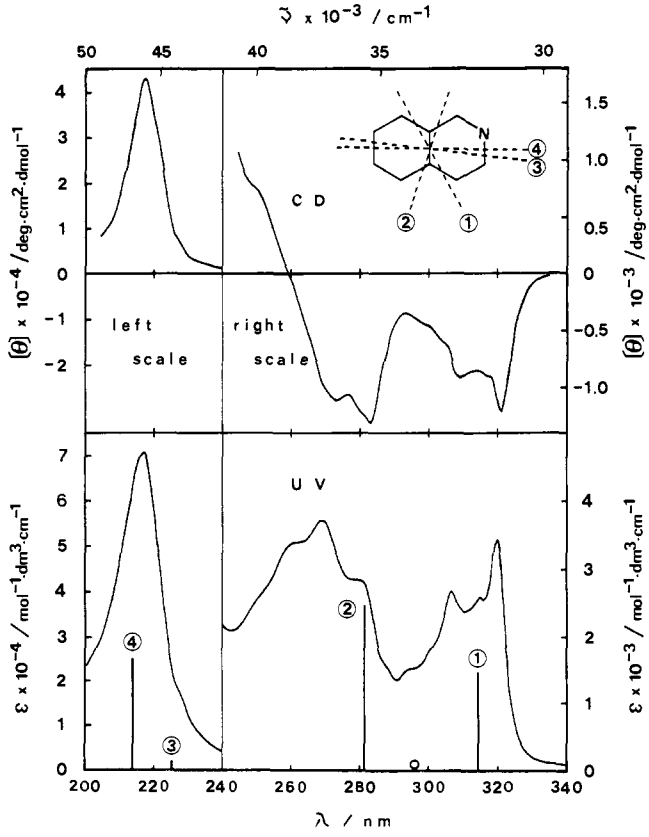

Figure 3. CD (upper) and UV (lower) spectra of the β-CD_x complex with isoquinoline in 1.0×10^{-4} M aqueous KOH (pH 9.06): β-CD_x (1.589×10^{-2} M) + isoquinoline (3.390×10^{-4} M).

$\leftarrow {}^1A_1$) and the second $\pi^* \leftarrow \pi$ ($^1B_2 \leftarrow {}^1A_1$) transitions, only a positive ICD band was observed at 320 nm. This suggests that

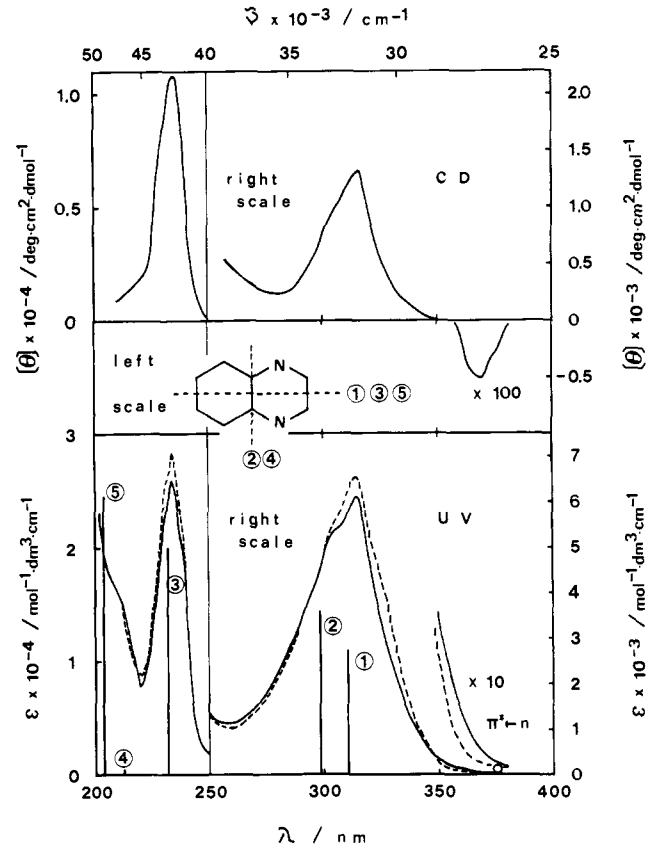

Figure 4. CD (upper) and UV (lower) spectra of the β-CD_x complex with quinoxaline in aqueous solution: (broken line) in the absence of β-CD_x, (solid line) β-CD_x (1.465×10^{-2} M) + quinoxaline (1.990×10^{-4} M).

the positive CD band originated from the $^1A_1 \leftarrow {}^1A_1$ transition predominates the adjacent one derived from the $^1B_2 \leftarrow {}^1A_1$ transition. A large positive ICD band observed at 230 nm was assigned to the third $\pi^* \leftarrow \pi$ ($^1A_1 \leftarrow {}^1A_1$) transition, i.e., long-axis polarization.

Figure 5 shows the CD and UV spectra of 1,5-naphthyridine with C_{2h} symmetry. From lower to higher wavenumber region, the signs of ICD bands observed were positive, negative, and positive, respectively. These results were in accord with the theoretical directions of the transition dipole moments, and each of these $\pi^* \leftarrow \pi$ transitions was attributed to the $^1B_u \leftarrow {}^1A_g$ transition.

As shown in Figure 6, the first $\pi^* \leftarrow \pi$ transition, which was assigned to the $^1A_1 \leftarrow {}^1A_1$ transition of phthalazine, gave rise to a positive ICD band. While the observation of two $\pi^* \leftarrow$ n transitions of phthalazine was reported[29,31] in the lower wavenumber region, the CD band originating from the $\pi^* \leftarrow$ n transition was hidden by the first $\pi^* \leftarrow \pi$ transition. On the contrary, the ICD band with two different signs was observed in the middle-wavenumber region (35 000–42 000 cm^{-1}) corresponding to the second absorption band of phthalazine. From the results calculated by using the CNDO/S-CI method, it is considered that there exists only an origin of the electronic transition, i.e., the second $\pi^* \leftarrow \pi$ ($^1B_2 \leftarrow {}^1A_1$) transition in this region. This result indicates the presence of "forbidden" character in the second absorption band, since the mixed polarization was observed in a single allowed electronic transition.[32] In other words, the "borrowed" long-axis-polarized moment was considered to be induced by the vibronic coupling with the adjacent intensive absorption band attributed to the third $\pi^* \leftarrow \pi$ ($^1A_1 \leftarrow {}^1A_1$) transition. In this case, the nontotally symmetric vibration mode, b_2,

(31) R. M. Hochstrasser and D. A. Wiersma, *J. Chem. Phys.*, 56, 528 (1972).
(32) A. C. Albrecht, *J. Chem. Phys.*, 33, 156 (1960).

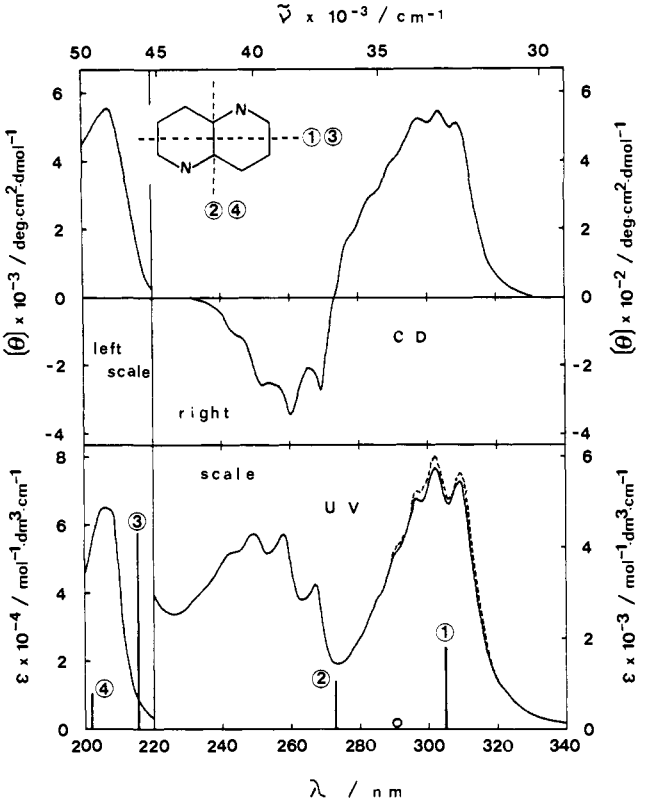

Figure 5. CD (upper) and UV (lower) spectra of the β-CD_x complex with 1,5-naphthyridine in aqueous solution: (broken line) in the absence of β-CD_x, (solid line) β-CD_x (1.434×10^{-2} M) + 1,5-naphthyridine (2.035×10^{-4} M).

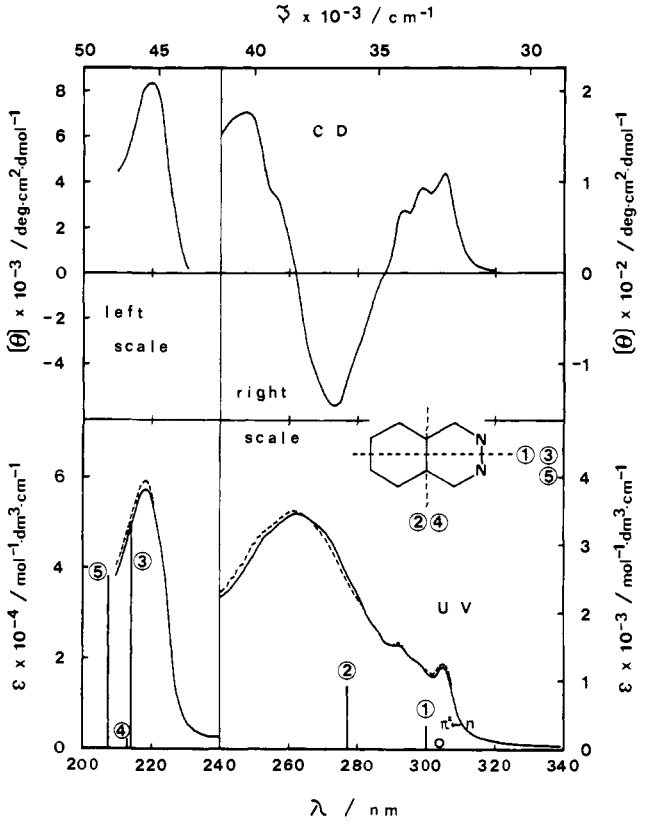

Figure 6. CD (upper) and UV (lower) spectra of the β-CD_x complex with phthalazine in aqueous solution: (broken line) in the absence of β-CD_x, (solid line) β-CD_x (1.428×10^{-2} M) + phthalazine (3.240×10^{-4} M).

is considered to contribute the vibronic coupling. The β-CD_x complex with cinnoline (α,β-diazanaphthalene), as demonstrated

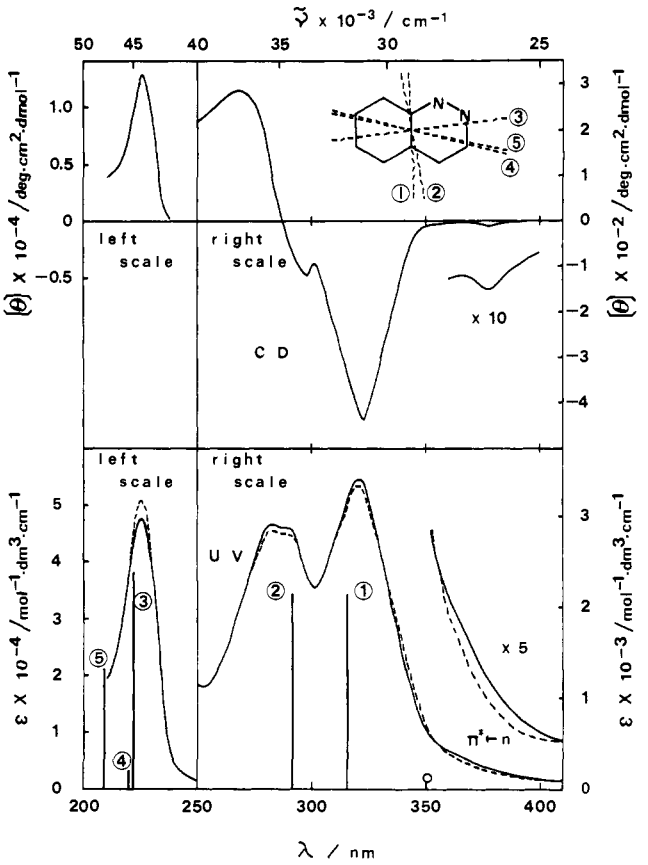

Figure 7. CD (upper) and UV (lower) spectra of the β-CD_x complex with cinnoline in aqueous solution: (broken line) in the absnece of β-CD_x, (solid line) β-CD_x (1.270×10^{-2} M) + cinnoline (3.750×10^{-4} M).

in Figure 7, exhibited a weak negative CD band that was derived from the $\pi^* \leftarrow$ n transition at 380 nm. The first $\pi^* \leftarrow \pi$ transition resulted in a negative CD band at 320 nm, and this is assigned to the short-axis-polarized $\pi^* \leftarrow \pi$ ($^1A' \leftarrow {}^1A'$) transition. Although the second $\pi^* \leftarrow \pi$ transition of cinnoline was evaluated to the nearly short-axis polarization, the ICD band with mixed signs was observed in the region corresponding to the second absorption band, similar to the case of phthalazine. It was supposed that the component of the long-axis-polarized moment in the second absorption band was caused by intensity borrowing through the vibronic interaction with the adjacent third $\pi^* \leftarrow \pi$ transition, which is approximated long-axis polarized. For the polarization directions of the first $\pi^* \leftarrow \pi$ and the second $\pi^* \leftarrow \pi$ transitions of cinnoline, Ridley and Zerner[23] using the INDO technique have reported results different from our calculations.[24] They evaluated the polarizations of both $\pi^* \leftarrow \pi$ transitions to the intermediate directions between long and short axes, whereas our calculation predicted short-axis polarization for these electronic transitions. Two negative ICD bands observed in this spectral region were in reasonable accord with our calculation. Figures 8 and 9 depict the spectra of quinazoline and pyrido[2,3-*b*]-pyrazine, respectively. The first $\pi^* \leftarrow \pi$ transition of quinazoline was assigned to the short-axis polarized $^1A' \leftarrow {}^1A'$ transition, while the sign of the CD band that was induced by the first $\pi^* \leftarrow \pi$ transition of pyrido[2,3-*b*]pyrazine was negative. In analogy with the case of phthalazine and cinnoline, the feature of the mixed polarization was observed in the second absorption band of quinazoline. This result also suggests the presence of the vibronic coupling in the second band. The totally symmetric vibration a′ for the molecule with C_s symmetry such as cinnoline and quinazoline seems to play an important role in the intensity borrowing by the vibronic interaction. The ICD band of pyrido[2,3-*b*]-pyrazine in the shorter wavelength region could not be practically measured because of the poor signal to noise ratio.

Origin of the Polarization Directions of the Lowest $\pi^* \leftarrow \pi$ States. It should be noted that the polarization directions of the

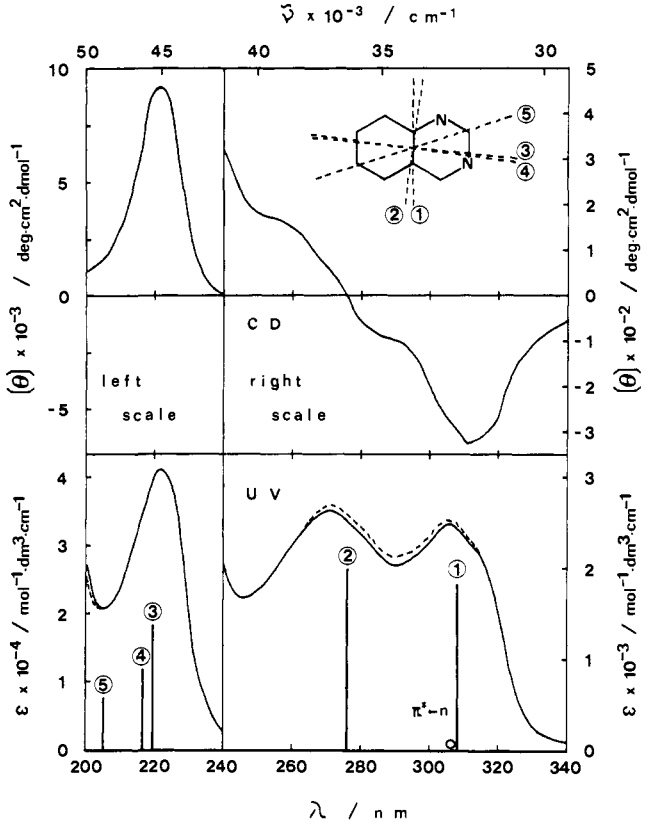

Figure 8. CD (upper) and UV (lower) spectra of the β-CD_x complex with quinazoline in aqueous solution: (broken line) in the absence of β-CD_x, (solid line) β-CD_x (1.406×10^{-2} M) + quinazoline (5.035×10^{-4} M).

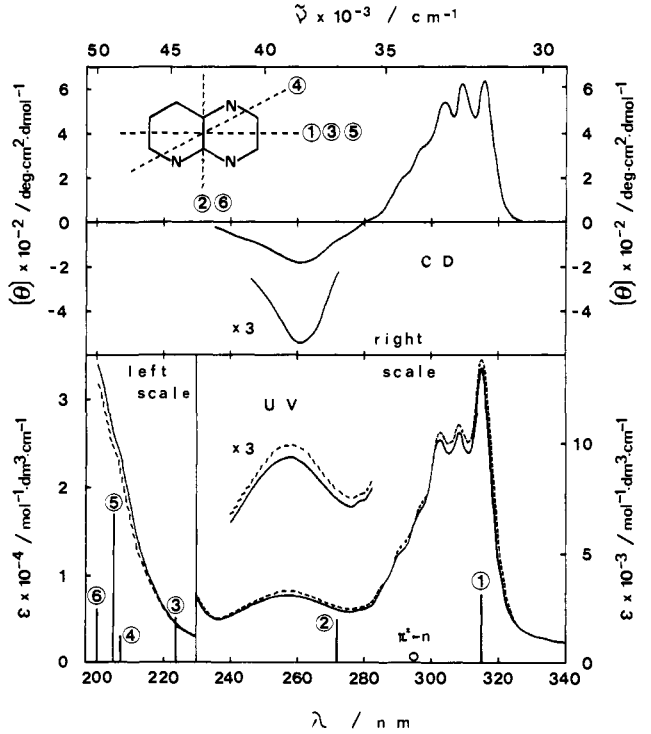

Figure 9. CD (upper) and UV (lower) spectra of the β-CD_x complex with pyrido[2,3-*b*]pyrazine in aqueous solution: (broken line) in the absence of β-CD_x, (solid line) β-CD_x (1.433×10^{-2} M) + pyrido[2,3-*b*]pyrazine (3.894×10^{-4} M).

first $\pi^* \leftarrow \pi$ transitions in azanaphthalenes are very sensitive to the position and number of aza nitrogen atoms. Koutecky has reported the theoretical analysis on the transition moments of the lowest two $\pi^* \leftarrow \pi$ transitions of heteroanalogues of alternant hydrocarbons and given the important rules,[21] two of which are summarized as follows.

Table II. State Functions of the First $\pi^* \leftarrow \pi$ States

compound	state functions
quinoline	$0.73\psi_{4\to6} - 0.65\psi_{5\to7}$
isoquinoline	$0.44\psi_{4\to6} - 0.61\psi_{5\to7} + 0.62\psi_{5\to6}$
quinoxaline	$0.83\psi_{4\to6} - 0.53\psi_{5\to7}$
1,5-naphthyridine	$0.77\psi_{4\to6} - 0.48\psi_{5\to7} + 0.37\psi_{5\to6}$
phthalazine	$0.56\psi_{4\to6} - 0.81\psi_{5\to7}$
cinnoline	$0.47\psi_{4\to6} - 0.49\psi_{5\to7} + 0.69\psi_{5\to6}$
quinazoline	$0.45\psi_{4\to6} - 0.47\psi_{5\to7} + 0.71\psi_{5\to6}$
pyrido[2,3-*b*]pyrazine	$0.82\psi_{4\to6} - 0.38\psi_{5\to7} + 0.36\psi_{5\to6}$

Rule 1: When one of the LCAO-MO coefficients of the atomic orbitals on the heteroatom in the two highest occupied molecular orbitals, ϕ_4 and ϕ_5, is small, the electronic configuration $|\alpha\rangle = (\Psi_{4\to6} - \Psi_{5\to7})/2^{1/2}$ does not mix with $|p\rangle = \Psi_{5\to6}$ so much and the transition moments of the first two transitions are approximately orthogonal. ($\Psi_{i\to j}$ stands for the one-electron-excitation configuration from the molecular orbital (MO) ϕ_i to the MO Ψ_j.)

Rule 2: On the contrary, when both of these LCAO-MO coefficients are large, a considerable mixing between $|\alpha\rangle$ and $|p\rangle$ takes place and the first two transitions have parallel transition moments. The experimental and calculated results in the present work coincide with these theoretical considerations.[21]

As shown in Table II, the lowest $\pi^* \leftarrow \pi$ state (ψ_1) of azanaphthalenes is approximately expressed as a linear combination of the configurations $\psi_{4\to6}$, $\psi_{5\to7}$, and $\psi_{5\to6}$, namely,

$$\psi_1 = C_1\psi_{4\to6} - C_2\psi_{5\to7} + C_3\psi_{5\to6} \tag{9}$$

where the coefficients C_1, C_2, and C_3 are taken to be positive. For quinoxaline and phthalazine, which belong to the C_{2v} point group, C_3 is zero.

Between molecular integrals of the electric moment operator, the following relations are obtained by using alternant pairing properties:[33]

$$\langle\phi_4|m_y|\phi_6\rangle \simeq \langle\phi_5|m_y|\phi_7\rangle \equiv m_y \tag{10}$$

$$\langle\phi_5|m_z|\phi_6\rangle \equiv m_z \tag{11}$$

where m_y and m_z are the y and z components of the one-electron operator of the electric moments.[34] From eq 9 to 11, the electric transition moment between ground state (ψ_0) and excited state (φ_1) is expressed as

$$\langle\psi_0|\mathbf{M}|\psi_1\rangle = 2^{1/2}(C_1 - C_2)m_y\mathbf{j} + 2^{1/2}C_3m_z\mathbf{k} \tag{12}$$

where $\mathbf{j}$ and $\mathbf{k}$ are the unit vectors along the y and z axes, respectively. Then, the polarization direction of the lowest $\pi^* \leftarrow \pi$ transition is determined by the relative magnitude of the coefficients C_1–C_3.

Quinoline, quinoxaline, 1,5-naphthyridine, and pyrido[2,3-*b*]-pyrazine, which are aza substituted at the α position, correspond to the case of rule 1. In this case, the lowest $\pi^* \leftarrow \pi$ state is mainly constituted of the configurations $\psi_{4\to6}$ and $\psi_{5\to7}$, and contamination of $\psi_{5\to6}$ to the lowest $\pi^* \leftarrow \pi$ state is very small. As C_3 is very small, the electric transition moment of the lowest $\pi^* \leftarrow \pi$ transition of α-azanaphthalenes dominantly arises from the difference between C_1 and C_2 (see eq 12) and is nearly parallel to the y axis (long axis).

On the other hand, in the case of β-azanaphthalene (isoquinoline) and α,β-diazanaphthalene (cinnoline, quinazoline), the electronic configurations $\psi_{4\to6}$ and $\psi_{5\to7}$ strongly mix with $\psi_{5\to6}$, according to rule 2. As C_3 has a large value, the polarization direction of the lowest $\pi^* \leftarrow \pi$ transition is approximately parallel to the z axis (short axis), similar to the second $\pi^* \leftarrow \pi$ transition.

Although phthalazine contains aza nitrogen atoms at the β position, the polarization direction of the lowest $\pi^* \leftarrow \pi$ transition

(33) J. Michl, *J. Chem. Phys.*, **61**, 4270 (1974).

(34) The y and z axes are chosen as the long and short axes, respectively, of naphthalene, and the x axis is set perpendicular to the molecular plane.

is parallel to the long axis. This is because $\psi_{5\to6}$ and $(C_1\psi_{4\to6} - C_2\psi_{5\to7})$ belong to the different irreducible representations of the symmetry group C_{2v} and do not mix with each other.

As a result, aza substitution at the β position is considered to cause the short-axis polarization, except for phthalazine, for which the polarization direction is determined by symmetry rule. On the other hand, α-azanaphthalene holds to the same polarization direction as that of naphthalene, which is long-axis polarized.

Conclusion

The ICD spectra of the β-CD_x complexes with some azanaphthalenes were measured in the wavelength region 200–400 nm. For quinoxaline and cinnoline, weak negative CD bands were induced by the lowest allowed $\pi^* \leftarrow$ n transition.

The polarizaion directions of the first $\pi^* \leftarrow \pi$ transitions in azanaphthalenes are closely associated with the location of aza nitrogen atoms and can be evaluated by the coefficents of the configurations in the corresponding lowest $\pi^* \leftarrow \pi$ states.

From the observation of the ICD band with mixed signs, the presence of the forbidden character is strongly suggested in the second absorption bands of isoquinoline, phthalazine, cinnoline, and quinazoline. Though the third absorption band in each case of azanaphthalenes was regarded as the mixture of $\pi^* \leftarrow \pi$ states composed of many configurations, the observation of positive ICD bands in this region indicated the predominance of the long-axis-polarized electronic transitions.

Finally, it can be mentioned that the ICD method using the inclusion phenomena of β-CD_x is a useful tool for the analysis of the polarization in the aromatic molecules.

Registry No. β-Cyclodextrin·quinoline, 83528-62-5; β-cyclodextrin·isoquinoline, 83528-63-6; β-cyclodextrin·quinoxaline, 83528-64-7; β-cyclodextrin·1,5-naphthyridine, 83542-59-0; β-cyclodextrin·phthalazine, 83528-65-8; β-cyclodextrin·cinnoline, 83528-66-9; β-cyclodextrin·quinazoline, 83542-53-4; β-cyclodextrin·pyrido[2,3-*b*]pyrazine, 83528-67-0.

A New Total Synthesis of the Fungal Toxin Slaframine

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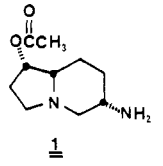
Contribution from the Department of Chemistry, The Pennsylvania State University, University Park, Pennsylvania 16802. *Received April 21, 1982*

Abstract: Slaframine (**1**) has been synthesized from diene aldehyde **2**. An intramolecular imino Diels–Alder reaction has been used to produce the indolizidine skeleton and to establish the requisite stereochemistry of this fungal metabolite.

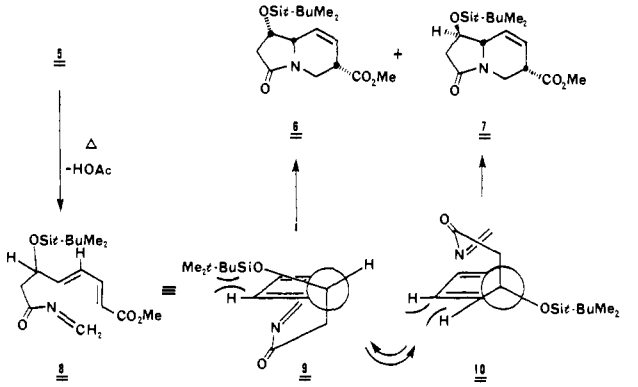
Slaframine (**1**), a neutrotoxic metabolite of *Rhizoctonia leguminicola*, is responsible for a disease characterized by excessive salivation in ruminants foraging on fungus-infected red clover hay.[1] The structure and absolute stereochemistry of this alkaloid were established by Rinehart et al.[2] in 1968. Aust has found that slaframine itself is not bioactive, but is oxidatively transformed in vivo to a compound that can then interact with muscarinic acetylcholine receptors, producing the observed symptoms.[3]



1

Work has also appeared recently on the biosynthesis of **1**.[4] To date, two total syntheses of slaframine have been reported.[5] Both relied heavily on classical Dieckmann chemistry to generate the indolizidine skeleton and upon catalytic hydrogenation to establish the three chiral centers of **1**. The first slaframine synthesis[5a] was nonstereoselective, but aided in confirmation of the proposed structure assignment. The second incorporated better stereocontrol,[5b] but it is not clear how selectively the stereochemistry contained in the six-membered ring of **1** was established. We now describe a completely new approach to slaframine that uses an intramolecular imino Diels–Alder cycloaddition[6] as the key step to efficiently construct the indolizidine ring system and to set the stereochemistry of **1**.

Scheme I



Our starting material for the synthesis was readily available[7] diene aldehyde **2** which was treated with the carbanion derived from bis(trimethylsilyl)acetamide (BSA)[8] in THF at −78 °C, followed by an acidic workup, affording β-hydroxy amide **3** (68%

(1) Rainey, D. P.; Smalley, E. B.; Crump, M. H.; Strong, F. M. *Nature (London)* **1965**, *205*, 203. Aust, S. D.; Broquist, H. P. *Ibid.* **1965**, *205*, 204.
(2) Gardiner, R. A.; Rinehart, K. L.; Snyder, J. J.; Broquist, H. P. *J. Am. Chem. Soc.* **1968**, *90*, 5639 and references cited therein.
(3) Guengerich, F. P.; Aust, S. D. *Mol. Pharmacol.* **1977**, *13*, 185 and references cited therein.
(4) Clevenstine, E. C.; Broquist, H. P.; Harris, T. M. *Biochemistry* **1979**, *18*, 3659. Clevenstine, E. C.; Walter, P.; Harris, T. M.; Broquist, H. P. *Ibid.* **1979**, *18*, 3663.
(5) (a) Cartwright, D.; Gardiner, R. A.; Rinehart, K. L. *J. Am. Chem. Soc.* **1970**, *92*, 7615. (b) Gensler, W. J.; Hu, M. W. *J. Org. Chem.* **1973**, *38*, 3848.
(6) Khatri, N. A.; Schmitthenner, H. F.; Shringarpure, J.; Weinreb, S. M. *J. Am. Chem. Soc.* **1981**, *103*, 6387 and references cited therein.
(7) Erhart-Subramanian, K. E. C.; Huisman, H. O.; de Koening, H. *Synth. Commun.* **1973**, *3*, 25.
(8) Morwick, T. *Tetrahedron Lett.* **1980**, *21*, 3227. We have found that the use of *sec*-butyllithium/TMEDA rather than *n*-butyllithium as originally reported significantly improved the yield of adduct **3**.

0002-7863/82/1504-7065$01.25/0