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Induced circular-dichroism spectra of complexes of cyclomalto-oligosaccharides and azo dyes containing naphthalene nuclei*

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ABSTRACT

In the circular-dichroism spectra of inclusion complexes of 7 types of cyclodextrin (CDs) with 6 kinds of azo dyes containing the naphthalene nucleus, the direction of inclusion and the stacking mode may be elucidated from patterns in the u.v. and the first $\pi \rightarrow \pi^*$ regions. The patterns in the former region indicate that the naphthalene fragment in almost all of complexes is incorporated equatorially into the cavity. Those azo dyes that have a tight fit in the CD cavity exhibit exciton interaction between two molecules of the chromophoric dye included in the complexes. The spectral pattern changes in sign according to the inclusion mode of the guest molecules and the angle between the chromophores. For example, the spectral pattern of the Orange II–cyclomaltoheptaose (β CD) complex indicates that the naphthalene nucleus is included axially, and that the angle between two molecules of the azo dye is $>90°$. On the other hand, the spectral pattern of the Croceine Orange–DM-β CD complex indicates equatorial inclusion and a stacking angle of $<90°$. The most important driving force for the host–guest interaction is van der Waals attraction; hydrogen bonding is not significant.

INTRODUCTION

Chiral cyclodextrins (CDs) induce circular dichroism (c.d.) spectra in achiral guest molecules[1]. The shapes and signs of these spectra should provide information concerning the host–guest structures. From the sign, it is possible to estimate the orientation of the chromophore in the cavity of the CD if the direction of the electric dipole moment in the chromophore is known[2–4]. The splitting pattern arises from exciton interaction of the associated chromophores and establishes that stacking of chromophores occurs[5–12].

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In the previous paper[13a], the c.d. spectra in the first $\pi\rightarrow\pi^*$ region of the CD–azobenzene derivative complexes were investigated. All single patterns show that the azobenzene derivatives are incorporated into the cavity from the long-axis side. The splitting patterns prove the occurrence of various stacking modes. Plots of the backbone lengths of the azo dyes *vs.* the molar circular-dichroism coefficients ($\Delta\varepsilon$) suggest that substituents play an important role in causing splitting and determining the sign and the amplitude of the Cotton effect.

In this paper, azo dyes containing naphthalene nuclei were used and c.d. spectra were investigated of all inclusion compounds with cyclomaltoheptaose (β CD), cyclomaltooctaose (γ CD), 2,6-di-*O*-methyl- and 2,3,6-tri-*O*-methyl-β-CDs (DM-β CD and TM-β CD), and fractions of glyceryl ethers of <2000 of water-soluble α-, β-, and γ-CDs–epichlorohydrin (Ep) polymer products. The aim was to determine what information the c.d. spectra can give on the structure of the CD complexes.

MATERIALS AND METHODS

Materials and instruments used were as described previously[13a], except as given here. Fast Red E was a standard sample distributed by the National Institute of Japanese Hygienic Science. Amaranth was purchased from Janssen Chimica (Belgium). The Azo dyes tested are listed in Table I.

For measurements of visible and c.d. spectra, 10^{-4} mol guest molecules and 10^{-3} mol host molecules were dissolved in 0.1M phosphate buffer at pH 6.0.

RESULTS AND DISCUSSION

The c.d. spectra. — It is known that Orange II (**2**) in neutral solution exists in a tautomeric equilibrium between its azo and hydrazone forms, and the latter form predominates[14]. The u.v.-visible spectrum of **2** is invariant in water within the pH range 2.0–6.0, indicating that no significant shifts in protonic equilibria occur under these conditions. Thus the data obtained from aqueous solutions buffered at pH 6 pertain to the Orange II monoanion[15]. The c.d. spectra in the **2**–β CD complex likewise do not change in shape at pH 2, 6, or 12, although the $\Delta\varepsilon$ values show slight deviation[13f]. The azo dye–CD complexes studied here induce single and split c.d. spectral patterns at the $\pi\rightarrow\pi^*$ band of the N = N group (Fig. 1 and Table II). Almost all single patterns have a positive peak. The split patterns show positive and negatieve split-type Cotton effects. In the former case, the $\Delta\varepsilon$ value of the longer-wavelength extremum is positive and that at shorter wavelength is negative; in the latter case, the signs become reversed.

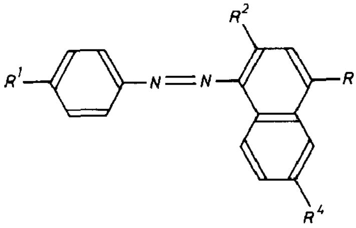
In the present examples, the α CD series cannot incorporate the guest molecules and the γ CD series plays an important role. In the γ CD series, the longest but slimmest example (Orange I, **1**) shows the smallest $\Delta\varepsilon$. Increase of molecular width by substitution has a large effect on the $\Delta\varepsilon$ value. Compound **2** shows a quite different pattern of complexation with the γ- and β-CDs.

The host: guest ratio in the complexes is[13e,15] 1:1, except for almost all of the γ CD

TABLE I

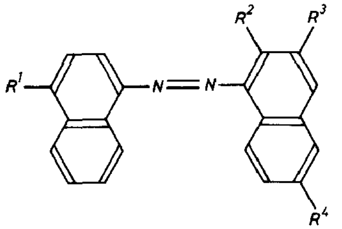
Guest molecules tested

Azo dyes



Compd.	*Name*	*R¹*	*R²*	*R³*	*R⁴*
1	Orange I	$NaSO_3$	H	OH	H
2	Orange II	$NaSO_3$	OH	H	H
3	Croceine Orange	H	OH	H	SO_3Na
4	Yellow V	$NaSO_3$	OH	H	SO_3Na

Azo dyes



Compd.	*Name*	*R¹*	*R²*	*R³*	*R⁴*
5	Fast Red E	$NaSO_3$	OH	H	SO_3Na
6	Amaranth	$NaSO_3$	OH	SO_3Na	SO_3Na

complexes, where the ratio was 1:2 and/or 2:2. In the **5**–γ CD-Ep complex, Job's plots of the c.d. and visible spectra show the formation of a 1:1 complex (Fig. 2).

The direction of inclusion. — The patterns in the u.v. region show negative, positive, and sometimes split peaks. The rotational strenghts of the β CD complexes with the substituted naphthalenes were calculated[4], applying the Tinoco[16] formulation of the coupled-oscillator model of Kirkwood[17]. When the angle between the symmetry axis of β CD and the electric dipole moment of the naphthalene group included in the β CD is parallel (axial inclusion), the ^1B_b and ^1L_a transitions show a large positive and a small negative sign, respectively, whereas when the foregoing angle is perpendicular (equatorial inclusion), these transitions change to a negative and a positive sign, respectively. Moreover, the theoretical calculation establish that the rotational strength of the ^1B_b transition is at its maximum when the electric dipole moment of the guest molecule is almost at the center of the cavity, whereas that of the ^1L_a transition does not show much penetration dependency.

In the present study, the transitions of azo dyes and their complexes were assigned according to ref. 18 (Table II). When the long axis of naphthalene nucleus in **2** is aligned

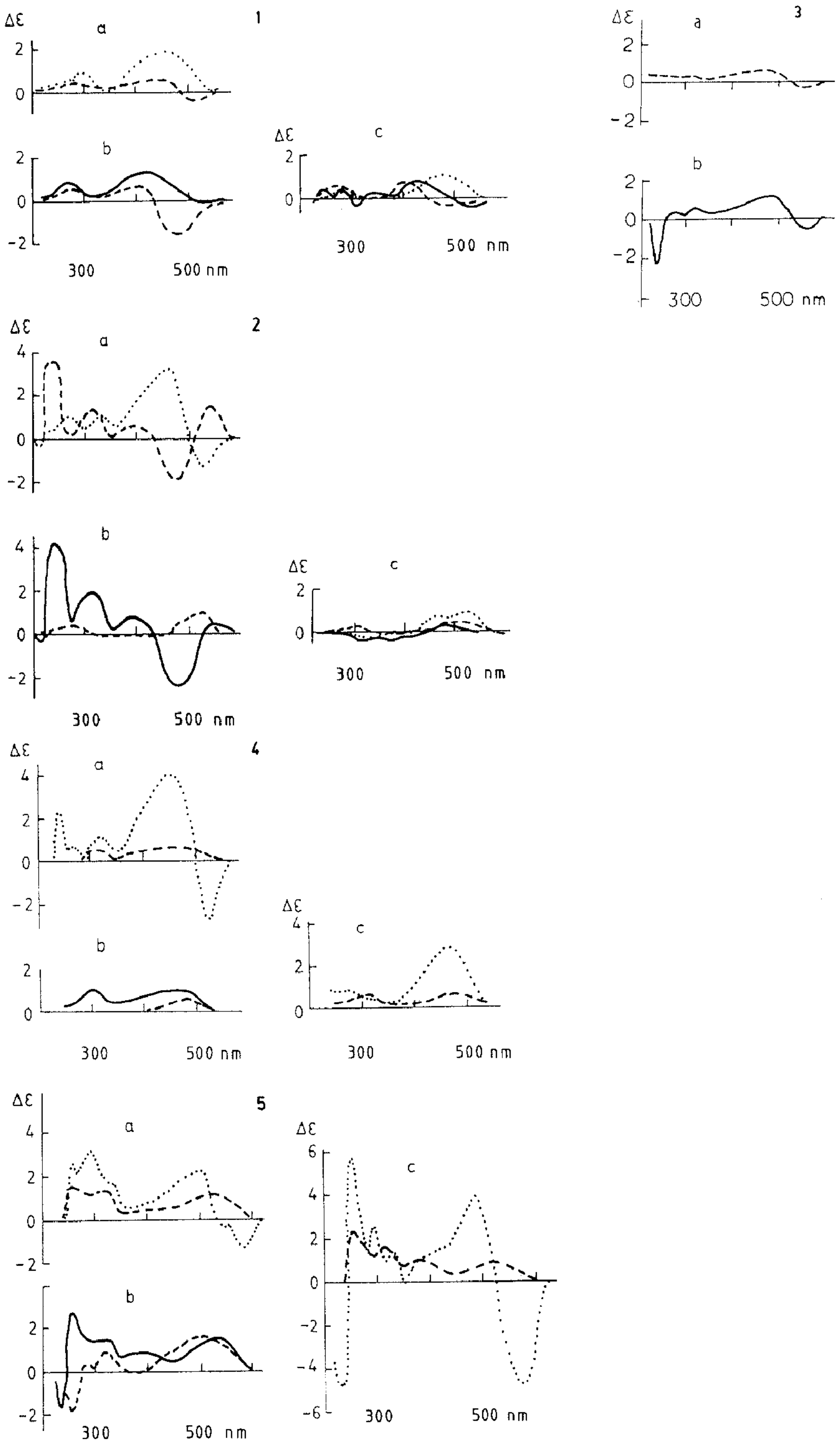


Fig. 1. C.d. spectra of azo dye complexes. Cyclodextrin *a*: cyclomaltoheptaose (β CD, -----); cyclomaltooctaose (γ CD, ···); *b*: 2,6-di-*O*-methyl-β CD (—); 2,3,6-Tri-*O*-methyl-β CD (-----); *c*: Products formed with the linking agents: α CD-epichlorohydrin (—); β CD-epichlorohydrin (-----); and γ CD-epichlorohydrin (···). The dyes **1-6** are listed in Table I.

TABLE II

Absorption maxima and induced c.d. values of complexes between azo dyes and cyclodextrin[a]

		Dye *nm$_{max}$*	*Complex* *α CD-Ep*	*TM-β CD*	*β CD-Ep*	*β CD*	*DM-β CD*	*γ CD-Ep*	*γ CD*
1	λ	473	470	472	466	470	476	468	464
	CD		427,525	400,480	405,485	452,514	415,512	490	450
	Δε		+0.9, −0.3	+0.6, −1.6	+0.9, −0.3	+0.5, −0.4	+1.2, −0.1	+1.2	+1.9
2 $^1B_b{}^b$	λ	229				229	229		231
	CD					240	240		–
	Δε					3.5	4.1		–
$^1L_a{}^b$	λ	260				260	256		260
	CD					s^c	s		270
	Δε					+	+		1.0
$^1L_b{}^b$	λ	310				310	310		311
	CD					312	318		318
	Δε					1.2	2.0		1.0
T^b	λ	486,513s	486	484	487	485,513s	485,513s	480	479,508s
	CD		480	500,527	520	480,540	485,542	520,528	465,530
	Δε		+0.3	+0.8, +1.0	+0.6	−2.0, +1.4	−2.5, +0.5	+1.5, +1.0	+3.2, −1.3

continued

TABLE II (continued)

		Dye nm_{max}	*Complex* *α CD-Ep*	*TM-β CD*	*β CD-Ep*	*β CD*	*DM-β CD*	*γ CD-Ep*	*γ CD*
3 ^1B_b	λ	237				238	237		
	CD						236		
	$\Delta\varepsilon$						−2.2		
^1L_a	λ	263				265	266		
	CD						280		
	$\Delta\varepsilon$						+0.3		
T	λ	481,508s				478,507s	477,505s		
	CD					470,536	480,550		
	$\Delta\varepsilon$					+0.7, −0.3	+1.2, −0.5		
4 ^1B_b	λ	236							236
	CD								246
	$\Delta\varepsilon$								2.2
^1L_a	λ	258							265
	CD								270
	$\Delta\varepsilon$								0.7
^1L_b	λ	314							311
	CD								320
	$\Delta\varepsilon$								1.1
T	λ	481,500s		483	485	483	484	478	474,513s
	CD			480	480	480	480	470	470,525
	$\Delta\varepsilon$			+0.6	+0.6	+0.6	+1.0	+2.7	+3.9, −2.7

5 ^1B_b	λ	239		238	241	238	238s	238	238
	CD			252	255	255	235,255	234,258	260
	$\Delta\varepsilon$			− 1.9	2.2	1.4	− 1.7, + 2.9	− 4.7, + 5.6	2.7
^1L_a	λ	294		294	292	293	293	294	294
	CD			285	290	s	s	296	296
	$\Delta\varepsilon$			0.7	1.2	1.3	1.5	2.4	3.2
^1L_b	λ	323		325		323	323	327	321
	CD			325	320	320	318	325	320
	$\Delta\varepsilon$			0.9	1.7	1.4	1.5	1.3	1.9
T	λ	513		522	520	517	522	513	515
	CD			490	525	520	525	485,575	500,585
	$\Delta\varepsilon$			+ 1.7	+ 0.9	+ 1.2	+ 1.5	+ 4.5, − 5.8	+ 2.3, − 1.2
6 ^1B_b	λ	238s						238	238
	CD							233,258	258
	$\Delta\varepsilon$							− 7.2, + 5.5	3.3
^1L_a	λ	294						294	294
	CD							297	296
	$\Delta\varepsilon$							1.9	4.1
^1L_b	λ	321						327	321
	CD							323	
	$\Delta\varepsilon$							0.8	
T	λ	514						513	513
	CD							485,570	495,582
	$\Delta\varepsilon$							+ 5.7, − 7.1	+ 2.8, − 1.3

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[a] CD: cyclodextrin; Ep: epichlorohydrin; DM-β CD: 2,6-di-*O*-methyl-β CD; TM-β CD: 2,3,6-Tri-*O*-methyl-β CD. [b] ^1B_b, ^1L_a and ^1L_b: electronic transitions of local excitation of the naphthalene fragment in the dye molecules; T: intramolecular charge-transfer transition. [c] Shoulder.

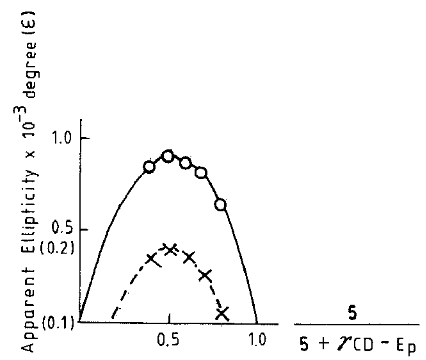

Fig. 2. Continuous-variation plots of Fast Red E and γ cyclodextrin epichlorohydrin complex: — ○ — ellipticity of the couplet; – – × – – absorption coefficient at 513 nm.

along the X axis, the band at 486 nm may be assigned to be a charge transfer directed along the longest conjugated chain in the molecular that forms an angle of 60° with the X axis. The ^1B_b and ^1L_a transitions of the naphthalene nucleus in **2** are 229 and 260 nm, respectively, and are aligned at angles of 11° (average) and 93° with the X axis. In the **2**–β CD and –DM-β CD complexes, the $\Delta\varepsilon$ value of the ^1B_b transition is ~ 4 and the ^1L_a transition is overlapped by the ^1B_b transition (axial inclusion). The larger $\Delta\varepsilon$ of the **2**–DM-β CD complex than that of the **2**–β CD complex may indicate that the axis of the naphthalene is situated deeper inside the DM-β CD. On the other hand, the $\Delta\varepsilon$ values of the u.v. region in the **3**–DM-β CD complex are -2.2 at the ^1B_b transition and 0.3 at the ^1L_a transition (equatorial inclusion). In the **2**–γ CD complex the ^1B_b transition does not appear, but other results establish equatorial inclusion. A space-filling molecular model indicates that two molecules of **2** are equatorially superimposed inside the γ CD[15]. In the **5**–γ CD-Ep complex, the ^1B_b transition appears as split-type and this complicates the information on the direction of inclusion.

The exciton-coupled c.d. spectra. — CD complexes often show c.d. splitting patterns (Fig. 1). These patterns may arise mainly from dipole–dipole interaction between the electric transition-moments of the intramolecular charge-transfer band of the two azo dye molecules[19-24]. According to this molecular exciton theory, the absorption maximum of the u.v.-visible spectrum and the crossover point of the c.d. couplet should coincide and the $\Delta\varepsilon$ values of both extrema in the splitting pattern should be the same. This theory was originally developed as a tool for determining the absolute configuration or conformation of natural products, and was later extended to the detection of stacking of the molecules[24]. The exciton splitting and molecular-orbital theories proved that the angle between the transition moments leads to changes in the c.d. and visible spectra. Calculations of the expected c.d. spectrum were performed by using a model for the interaction of two transition moments. When the angle between the transition moments is 120°, the calculated c.d. spectrum shows a positive split Cotton effect (positive chirality) and the visible spectrum moves to longer wavelength. On the other hand when the angle is 60°, the calculated c.d. spectrum shows a negative split Cotton effect (negative chirality), and the visible spectrum moves to shorter wavelength.

In the present **5**–γ CD-Ep complex, the absorption maximum and the crossover point of the c.d. couplet in the N=N region are practically coincident and both amplitudes of the splitting are almost the same. Negative exciton splitting indicates that the angle between the transition moments of two molecules of **5** included in the form of a 1:1 complex is <90°. A positive split Cotton effect appears in the **2**–β CD and **2**–DM-β CD complexes. The **2**–γ CD complex includes two molecules of **2** in one or two γ CDs[15]. If the long-axis side of the two molecules of **2** aligns parallel to the annular axis of the cavity, theoretically no interaction should be evident in the spectrum[16]. This c.d. spectrum shows negative chirality and the $\Delta\varepsilon$ values of both extrema are unequal. The γ CD may incorporate two molecules of **2** with crossing. The splitting arises when the guest molecules are incoporated with a tight fit to the host molecules[13a]. There is another possible cause for splitting of the c.d. spectrum. Deformation of the N=N group gives a similar pattern in the $\pi\rightarrow\pi^*$ region[8,25,26]; for instance, azo chromophores bound to poly (L-glutamic acid) generate dipole–dipole interactions and produce a positive couplet in the region of the $\pi\rightarrow\pi^*$ electronic transition. The *trans*-to-*cis* rearrangement shows a distorted split pattern[25]. Likewise in the present study, abnormal splitting, with unequal amplitudes of the splitting signals and deviation from the absorption maximum of the cross-over point of the c.d. couplet does not rule out the possibility of distortion in the azo dyes included, although their hydrazone forms stabilize the *trans* form of the azo group and a continuous change of amplitude in Job's plots can be observed[13e].

The driving force for inclusion. — Concerning the driving force for inclusion into the cavity, several types of intermolecular interaction have been proposed; *1*, hydrophobic interaction; *2*, van der Waals interaction; *3*, hydrogen bonding; *4*, the expulsion of high-energy water from the CD cavity upon substrate inclusion; and *5*, the relief of conformational strain in the CD–water adduct, together with the formation of a hydrogen-bonding network around the O-2, O-3 side of the CD macrocycle, upon substrate inclusion[27–30]. Concerning *1*, calculation of the correlation energy for complexation between α CD and benzenesulfonate indicates that this energy is lower in inclusions from the benzene nucleus side[31]. In the present series, inclusion from the sulfonate side is observed in the complexes of **4**, **5** and **6**; hydrophobic interaction is a lesser factor than is van der Waals interaction. Corcerning *2*, the $\Delta\varepsilon$ values in the N=N region in the γ CD complexes are in the order of **4**>**2**>**6**>**5**>**1** [6.8>4.5>4.1>3.5>1.9] (Fig. 1), and are related to widths of the part included in the guest molecules. The β CD derivatives cannot include **4**, because the trisubstituted naphthalene nucleus is too large. On the other hand, they can include **5** and **6**, suggesting that the included part is not the tri- and tetra-substituted naphthalene nucleus, but the disubstituted one. Concerning *3*, the molecules of **2**, **3** and **5** show larger amplitudes upon complexation with DM-β CD and TM-β CD than that with β CD; hydrogen bonding between host and guest molecules is not important. Factor *4* is dependent on the size of the CD cavity and is independent on the kind of guest molecules. Factor *5* is considered to be negligible for the β- and γ-CDs systems[29]. The foregoing facts suggest that van der Waals interaction is the most important driving force in this series.

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