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Evidence for covalent binding between copper ions and cyclodextrin cavity: a vibrational circular dichroism study

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Abstract

Vibrational absorption and circular dichroism (VCD) spectra were obtained for parent cyclodextrins, hydroxyl deuterated α-cyclodextrin, cyclodextrin–copper complexes, and for the cyclodextrin inclusion complexes with Methyl Orange, methyloxirane, 1-propanol, and substituted cyclohexanones, in the solution phase. Changes in the VCD spectra, reflecting perturbations of cyclodextrin cavity, were found in the case of an inclusion complex with Methyl Orange, but for the remaining inclusion complexes measurable changes in VCD were not found. Significant changes observed in the VCD spectra of cyclodextrin–copper complexes suggest that the covalent binding of copper ions to the hydroxyl groups of cyclodextrin is involved.

Keywords: Cyclodextrins; Inclusion complexes; Copper complexes; Vibrational spectra; Vibrational absorption; Circular dichroism; Infrared spectra

1. Introduction

Cyclodextrins are cyclic oligosaccharides with α-D-glucose units connected through α-(1→4) linkages. The most common forms of cyclodextrins are α-, β- and γ-cyclodextrins (cyclomaltohexa-, hepta-, and octaoses), which contain, respectively, six, seven, and eight glucose units. The structure of these molecules is toroidal containing an apolar cavity with primary hydroxyl groups lying on the outside and the secondary hydroxyl groups inside [1–3]. A wide variety of guest molecules can be incorporated into the cyclodextrin cavity, forming inclusion complexes. The formation of these complexes has been attributed to weak interactions (hydrophobic effect, van der Waals interactions and/or hydrogen bonding). Some of these inclusion complexes can be crystallized, and in such cases X-ray diffraction studies provide the most direct evidence for the structure of inclusion complexes in the crystalline state. In some cases the guest molecules have been found to be encapsulated inside the cyclodextrin cavity, while in others the guest molecules were found to be incorporated between the layers of arrays of host molecules, giving rise to intercalates or channel-type compounds. Inclusion complexes have also been reported in the solution phase. In particular, the binding of cyclodextrin to guest molecules in dimethyl sulfoxide solvent has been established [4]. Structures of the channel type are not known to be present in the solution phase,

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and so when an inclusion complex forms in the solution phase the guest molecule is present (either fully or partially) inside the cavity. A different type of complex is formed when cyclodextrins are complexed with metal ions [5]. In such metallo complexes, regular chemical bonds have been proposed to be formed between the guest and host, although spectroscopic evidence for this proposal was lacking. However, if such covalent bonding were present, then the perturbation by guest species would be expected to be much stronger, and should be verifiable with spectroscopic methods.

The ability of cyclodextrins to form inclusion complexes with a variety of guest molecules has attracted widespread interest with applications both in academic and industrial research [6–8]. Cyclodextrin complexes have been studied using different physical methods including X-ray crystallography [9,10], NMR [1–3], potentiometry [5,11], calorimetry [12], and spectroscopic methods including fluorescence [13], infrared [1–3], Raman [1–3] and mass spectrometry [14]. Chiroptical techniques such as optical rotation and electronic circular dichroism (ECD) have also been used to characterize the inclusion complexes [4,5,15–19], and to probe the chirality induced in achiral guest molecules by the chiral cyclodextrin cavity [15]. Optical activity in vibrational transitions, referred to as vibrational optical activity (VOA), is another chiroptical spectroscopic technique that has emerged more recently with greater potential for stereochemical applications [20]. The advantage of VOA is that all $3N-6$ vibrations, where N is the number of atoms in the molecule, can in principle exhibit VOA, and so there is a large spectral base for structural information and unlike ECD, the need for a chromophore to reveal that structural information is avoided. The disadvantage of VOA is that the signals are usually weak, so longer data collection and higher-sensitivity instrumentation are needed for VOA spectral studies. There are two different forms of VOA. One is vibrational circular dichroism (VCD), where differential absorption of left versus right circularly polarized infrared radiation is monitored in the vibrational spectral region [21]. The second is vibrational Raman optical activity (VROA), where differential Raman scattering for right versus left circularly polarized incident light is monitored [22]. VROA spectra of parent cyclodextrins and of cyclodextrin complexes have been reported [23], as well as resonance Raman and ROA spectra of cyclodextrin–azo dye complexes [24]. The vibrational spectra of solid-state samples of cyclodextrins [25] and of cyclodextrin–metal complexes [26] have also been reported.

VCD spectral studies of cyclodextrin complexes have, however, not yet been undertaken. The only report on VCD of cyclodextrins to date has been the study from this laboratory a few years ago, where the VCD spectra of α- and β-cyclodextrins in Me_2SO-d_6 solvent were reported in the 1600–1200 cm^{-1} region [27].

In this paper, we present the first VCD spectral studies on cyclodextrin complexes. The spectra of α- and β-cyclodextrins in Me_2SO-d_6 solvent are presented with higher signal quality than was achieved before. These are compared with the spectra of α-D-glucose to assess the influence of multiple glucose units. Crystalline inclusion complexes with 1-propanol, methyloxirane, and Methyl Orange are also studied in Me_2SO-d_6 solutions. In addition, the inclusion of substituted cyclohexanones in the α-cyclodextrin cavity in Me_2SO-d_6 solutions has been investigated. Based on these studies, the applicability of VCD spectroscopy for characterizing the inclusion complexes has been assessed. Next, VCD spectra of the complexes of α- and β-cyclodextrins with copper are compared with those of parent cyclodextrins and hydroxyl deuterated α-cyclodextrin, and implications of the structures of these complexes are discussed.

2. Experimental

Materials.—The chemicals were used as received from the following sources: α- and β-cyclodextrins from Janssen Chimica/Sigma; racemic 2-methylcyclohexanone, racemic 3-methylcyclohexanone, 4-methylcyclohexanone, racemic methyloxirane, and Methyl

Orange from Aldrich Chemicals; cyclohexanone from Matheson, Coleman and Bell; 1-propanol from Fisher-Scientific, and Me_2SO-d_6 from Cambridge Isotope Laboratories. The hydroxyl-deuterated α-cyclodextrin was prepared by dissolving α-cyclodextrin in an excess of D_2O, heating the solution (isolated from the atmosphere) in boiling water for ~1 h, followed by lyophilization. The inclusion complexes of 1-propanol and Methyl Orange with α- and β-cyclodextrins were crystallized from hot aqueous solutions using literature procedures [9,10]. A similar procedure was adapted for preparing the crystalline inclusion complex with racemic methyloxirane. These crystalline materials were dissolved in Me_2SO-d_6 as solvent for VCD studies. For studying the inclusion complexes formed in the solution phase (without crystallization), the optically inactive guest samples (cyclohexanone, racemic 2-methylcyclohexanone, racemic 3-methylcyclohexanone or 4-methylcyclohexanone) were mixed with α-cyclodextrin in a 1:1 mole proportion in Me_2SO-d_6 solvent. The copper complexes with α- and β-cyclodextrins were prepared using literature procedures [5]. To a 10 mL aq alkaline soln (0.5 M), cyclodextrin was added to yield 0.02 M in cyclodextrin, and then 15 mL of aq $CuSO_4$ soln (0.04 M) was added. The precipitated $Cu(OH)_2$ was filtered off and excess aq EtOH was added to the filtrate. The blue precipitate was filtered off, washed with aq EtOH, and air-dried at room temperature. The dried samples were dissolved in Me_2SO-d_6 for VCD studies.

Spectra.—The infrared and VCD spectra were recorded on a commercial Fourier-transform VCD spectrometer, Chiralir (Bomem-BioTools, Canada) with a ZnSe beamsplitter, BaF_2 polarizer, optical filter (transmitting below 2000 cm^{-1}) and a 2×2 mm HgCdTe detector. One difference from the standard Chiralir instrument is that the photoelastic modulator used was a PEM-80 model (Hinds Instruments) without AR coating on the ZnSe optical element. The VCD spectra were recorded using the supplied Chiralir software, with 1 h of data-collection time (two sets of 1247 ac scans and 138 dc scans) at 4 cm^{-1} resolution. The absorption spectra were obtained from 138 dc scans and the same number of background scans.

The transmission properties of optical filter and BaF_2 substrates used in the instrument restrict the range of measurements to 2000–900 cm^{-1}. The strong absorption of Me_2SO-d_6 precludes observing VCD features in the ~1100–900 cm^{-1} region. There are no fundamental vibrational absorption bands for cyclodextrins in the 2000–1500 cm^{-1} region, and so the presented spectra are limited to the 1500–1125 cm^{-1} region. The absorption and VCD spectra of Me_2SO-d_6 solvent obtained under identical conditions were subtracted from those of the samples dissolved in Me_2SO-d_6. For the sake of ease in direct comparison, the spectra are plotted on the same scale (x-axis: 1500–1125 cm^{-1}; y-axis: 0–0.75 for absorbance and -1.6×10^{-4} to $+1.8 \times 10^{-4}$ for VCD). The frequency positions of the bands labeled 1–5 in Figs. 1 and 2 are given in Table 1.

3. Results and discussion

It is first necessary to study the VCD of cyclodextrins themselves and of their inclusion complexes to establish the influence of complexation on the VCD spectral features.

Cyclodextrins.—The absorption and VCD spectra for α- and β-cyclodextrins in Me_2SO-d_6 solvent are presented in Fig. 1(a) and (b). The main VCD features in these spectra were: (1) a negative–positive pair (bands labeled 1 and 2) in the 1500–1400 cm^{-1} region; (2) another negative–positive pair (bands labeled 3 and 4) in the 1400–1300 cm^{-1} region; (3) a large negative VCD band (band labeled 5) at ~1149 cm^{-1} for α and at 1153 cm^{-1} for β-cyclodextrin. These three main features are the focus of our analysis, although we note in passing that a weak negative–positive VCD pair was also present in the 1300–1265 cm^{-1} region. For α-cyclodextrin in water solutions (not shown), the first pair could not be clearly seen (because of low absorbance), but the second pair and a negative VCD band at ~1149 cm^{-1} were present. Thus, no significant solvent-dependent changes were apparent on the VCD spectra as the solvent was changed from Me_2SO-d_6 to water.

Both cyclodextrins have essentially the same VCD features in Me_2SO-d_6 solutions, and no differences arising from the difference in the number of glucose units in the two cyclodextrins could be seen. The absorption coefficients (absorbance/(concentration × pathlength)) derived from the absorption-band peak intensities are approximately the same in two cyclodextrins. In addition, the dissymetry factors ($\Delta A/A$) calculated for the aforementioned VCD features are also approximately the same for both cyclodextrins (see Table 1). This result indicates that proceeding from six glucose units in α-cyclodextrin to seven glucose units in β-cyclodextrin, the absorption and VCD contributions per glucose unit remain the same.

In order to evaluate the role of coupling between different glucose units on the absorption and VCD intensities, the spectra of α-D-glucose in Me_2SO-d_6 solvent (see Fig. 1(c)) were also measured. The VCD spectrum of α-D-glucose has essentially the same features as those seen for α- and β-cyclodextrins, namely a negative–positive pair (bands labeled 1 and 2) in the 1500–1400 cm^{-1} region, another negative–positive pair (bands labeled 3 and 4) in the 1400–1300 cm^{-1} region, and a negative VCD band (band labeled 5) at 1147

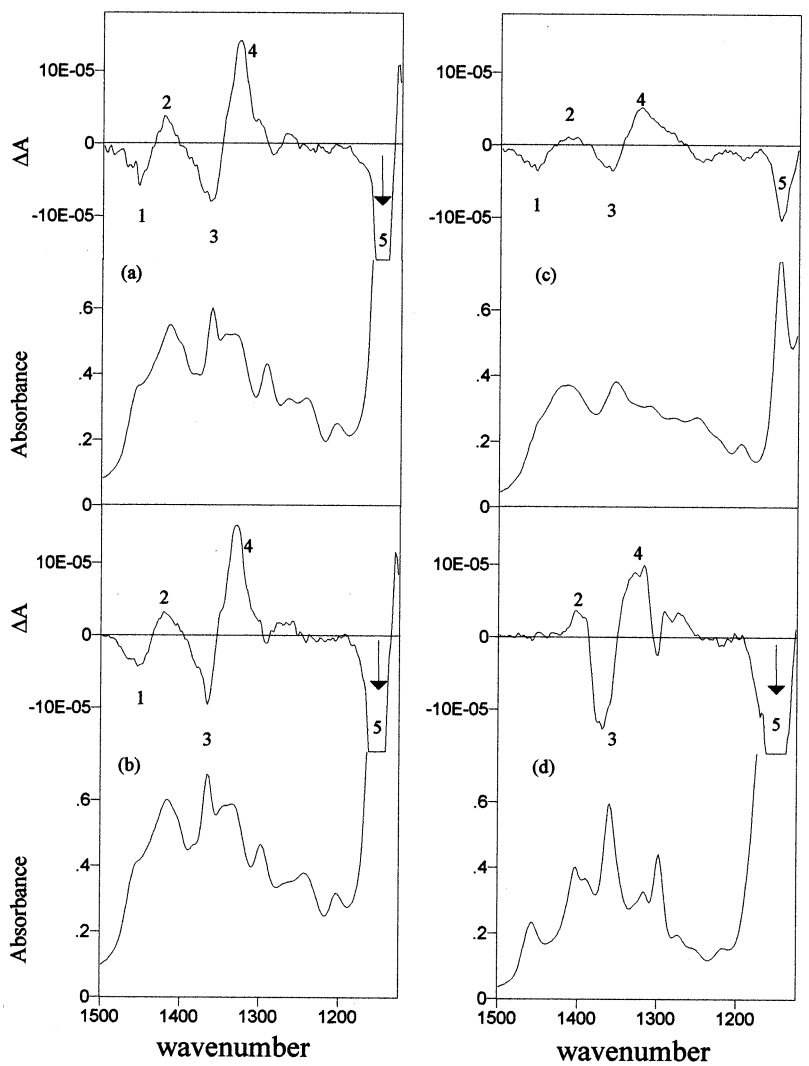


Fig. 1. Vibrational absorption (bottom) and VCD (top) spectra in the 1500–1125 cm^{-1} region in Me_2SO-d_6 solutions of: (a) α-cyclodextrin (conc 142 mg/mL; pathlength 107 μm; (b) β-cyclodextrin (conc 141 mg/mL; pathlength 107 μm); (c) α-D-glucose (conc 89.9 mg/mL, pathlength 77 μm); (d) α-cyclodextrin-$(OD)_{18}$ (conc 131 mg/ mL, pathlength 53 μm). The intensities of VCD bands at ~1150 cm^{-1} in (a), (b), and (d) are not reliable due to excessive absorbance and so they have been determined from lower pathlength measurements (see Table 1).

cm^{-1}. However, the absorption coefficients and dissymetry factors are significantly different for glucose. In cyclodextrins the absorption coefficients for the bands at ~ 1454, 1423, 1365 and 1327 cm^{-1} are enhanced by a factor of four, and the absorption coefficient for the 1149 cm^{-1} band is enhanced by a factor of 10 over those of corresponding bands in glucose. The dissymetry factor (see Table 1) for the ~ 1454 cm^{-1} band in cyclodextrins is not significantly different from that in glucose, but that for the remaining bands is enhanced in cyclodextrins by a factor of 1.5 to 2 over those for the corresponding bands in glucose. Thus, in general, the absorption coefficient and VCD intensities are enhanced in cyclodextrins over those in α-D-glucose, indicating that coupling among different glucose units substantially contributes to the observed vibrational absorption and VCD of cyclodextrins.

Assignments of vibrational bands in cyclodextrin have been suggested by Casu and Reggiani [25a]. They assigned the bands at ~ 1445 cm^{-1} to CH_2 bending, at ~ 1405, 1260, 1237, and 1199 cm^{-1} to OH bending, at 1363, 1330 and 1293 cm^{-1} to C–H bending, at ~ 1151 cm^{-1} to coupled CO (bridge) stretch-

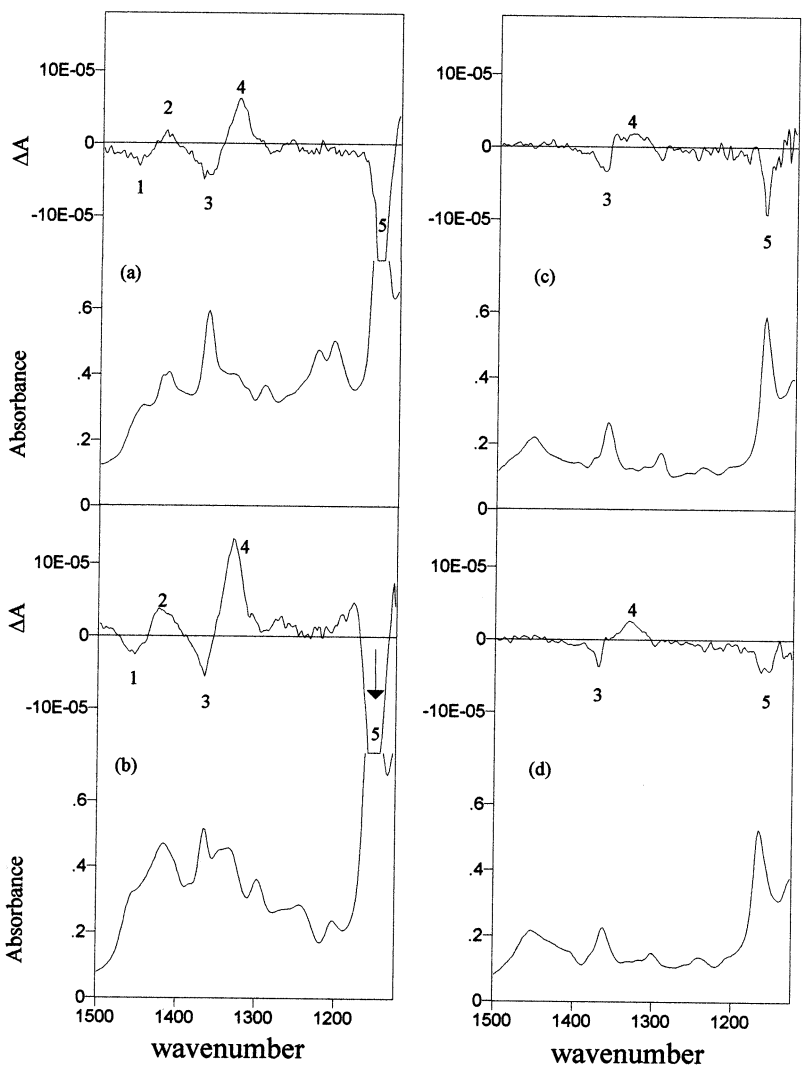


Fig. 2. Vibrational absorption (bottom) and VCD (top) spectra in the 1500–1125 cm^{-1} region in Me_2SO-d_6 solutions of: (a) Methyl Orange–α-cyclodextrin complex (conc 69 mg/mL, pathlength 118 μm); (b) Methyl Orange–β-cyclodextrin complex in Me_2SO-d_6 solution (conc 69.3 mg/mL, pathlength 193 μm); (c) copper–α-cyclodextrin complex (conc 36.1 mg/mL; pathlength 257 μm); (d) copper–β-cyclodextrin (saturated solution (54 mg/mL), pathlength 137 μm); the VCD intensities for the ~ 1150 cm^{-1} bands in (a), (b), and (c) have considerable uncertainty and so they have been determined from lower pathlength measurements (see Table 1).

ing and OH bending, and at ~ 1074 and 1028 cm^{-1} to CO/CC stretching. It is unlikely that the ~ 1151 cm^{-1} band is due to a C–O bridge (glycosidic) bond, since this band is present in the spectra of cyclodextrins as well as α-D-glucose and most monosaccharides [28]. Also, the assignment of O–H bending vibrations to this band is unlikely as this band is also present in hydroxyl deuterated monosaccharides [28] and α-cyclodextrin (see below). Instead, this band was assigned [28] to the exocyclic C–O stretching vibrations, which seems more likely (see below). Also, in the ROA spectrum of cyclodextrins, a couplet seen at ~ 1340 cm^{-1} has been assigned [23] to the CH_2OH group deformation and the main component of ROA seen in D-glucose at 1360 cm^{-1} was assigned [29] to the C–O–H bending vibrations.

To minimize the uncertainty in these assignments and to determine the origin of vibrational bands, the absorption and VCD spectra (Fig. 1(d)) of hydroxyl-deuterated α-cyclodextrin, α-cyclodextrin-$(OD)_{18}$, were measured. The negative–positive VCD pair seen for α-cyclodextrin in the 1500–1400 cm^{-1} region disappears upon deuteration of the hydroxyl groups. Instead a positive VCD band (band labeled 2) at ~ 1403 cm^{-1}, which is shifted from ~ 1423 cm^{-1} in α-cyclodextrin, appears in α-cyclodextrin-$(OD)_{18}$. Upon deuteration of the hydroxyl groups, the negative–positive pair seen for α-D-glucose in the 1500–1400 cm^{-1} region also disappears in D-glucose-$(OD)_5$ (not shown here). Then it is likely that the pair of VCD bands (labeled 1 and 2) seen in the 1500–1400 cm^{-1} region, both for α-D-glucose and cyclodextrins, originates from C–O–H bending vibrations. The negative–positive pair (bands labeled 3 and 4) in the 1400–1300 cm^{-1} region, however, is present in both α-cyclodextrin and α-cyclodextrin-$(OD)_{18}$. There are some differences in the shapes of VCD bands here, and the deuteration of hydroxyl groups leads to a significant enhancement of the dissymmetry factors for

Table 1
Comparison of the dissymmetry factors for VCD bands

System	Band 1		Band 2		Band 3		Band 4		Band 5	
	Freq [c]	$\Delta A/A$ [d]	Freq [c]	$\Delta A/A$ [d]	Freq [c]	$\Delta A/A$ [d]	Freq [c]	$\Delta A/A$ [d]	Freq [c]	$\Delta A/A$ [d]
α-D-Glucose	1454	−1.4	1416	0.3	1360	−0.9	1323	1.7	1147	−1.3
α-Cyclodextrin	1454	−1.6	1423	0.8	1365	−1.5	1327	2.8	1149	−2.4
α-Cyclodextrin-$(OD)_{18}$			1403	0.9	1369	−3.2	1318	3.0	1149	−2.2
β-Cyclodextrin	1454	−1.1	1422	0.6	1365	−1.4	1329	2.6	1153	−2.4
α-Cyclodextrin–Cu [a]					1367	−1.7	1332	1.5	1165	−0.8
β-Cyclodextrin–Cu [a]					1371	−1.9	1332	1.9	1166	−0.8
α-Cyclodextrin–Methyl Orange [a]	1455	−1.1	1421	0.3	1364	−0.7	1328	1.6	1150	−1.7
β-Cyclodextrin–Methyl Orange [a]	1454	−0.8	1424	0.9	1365	−1.1	1329	2.8	1154	−2.9
α-Cyclodextrin–1-propanol [a]	1457	−1.0	1419	0.8	1365	−1.2	1327	3.0	1149	−2.7
β-Cyclodextrin–1-propanol [a]	1456	−0.7	1414	0.1	1366	−1.4	1331	2.6	1154	−2.4
α-Cyclodextrin–methyloxirane [a]	1455	−1.3	1420	1.0	1360	−1.3	1327	3.1	1149	−2.6
β-Cyclodextrin–methyloxirane [a]	1455	−1.7	1419	0.7	1361	−1.4	1329	3.0	1154	−2.5
α-Cyclodextrin–cyclohexanone [b]	1455	−1.4	1425	0.9	1365	−1.3	1327	2.9	1149	−2.6
α-Cyclodextrin–3-methylcyclohexanone [b]	1457	−1.7	1420	1.2	1363	−1.5	1325	3.0	1149	−2.7
α-Cyclodextrin–4-methylcyclohexanone [b]	1457	−1.1	1423	0.8	1365	−1.4	1328	2.9	1150	−2.6
α-Cyclodextrin-2-methylcyclohexanone [b]	1454	−1.0	1421	1.0	1365	−1.4	1326	2.7	1149	−2.7

[a] Crystalline complex (solid non-crystalline sample in the case of copper complexes) dissolved in Me_2SO-d_6 solvent.
[b] Guest and host samples mixed in 1:1 mole ratio in Me_2SO-d_6. The absorption and VCD of the guest samples in Me_2SO-d_6 obtained at the same concentrations were subtracted from those of the inclusion complex in obtaining these numbers.
[c] Frequencies in cm^{-1}
[d] The numbers listed under $\Delta A/A$ are to be multiplied by 10^{-4}.

this pair of VCD bands (see Table 1), suggesting some participation from the O–H bending vibrations in the parent undeuterated molecules. Since the pair of VCD bands seen in the 1400–1300 cm^{-1} region is present in both undeuterated and deuterated α-cyclodextrins, they originate most likely from the C–H bending vibrations. The large negative VCD band (band labeled 5) seen at 1149 cm^{-1} for α-cyclodextrin is also present in α-cyclodextrin-$(OD)_{18}$ with approximately the same dissymmetry factor. As mentioned earlier, this band is considered [28] to originate from the exocyclic C–O stretching motions.

Inclusion complexes.—The absorption and VCD spectra of Methyl Orange–α-cyclodextrin and Methyl Orange–β-cyclodextrin inclusion complexes are shown in Fig. 2(a) and (b). The absorption spectrum of the Methyl Orange–α-cyclodextrin inclusion complex (Fig. 2(a)) is quite different from that of α-cyclodextrin (Fig. 1(a)), and the presence of Methyl Orange in the complex can be inferred from the new absorption bands in the spectrum of the complex at ~1601, 1558 and 1521 cm^{-1} (not shown). The band shapes of absorption bands in the 1500–1200 cm^{-1} region are also different in the two spectra. The VCD spectrum of the inclusion complex, however, appears qualitatively similar to that of α-cyclodextrin, with the two negative–positive pairs (bands labeled 1, 2, 3 and 4) in the 1500–1300 cm^{-1} region and a large negative VCD feature (band labeled 5) at ~1150 cm^{-1} being the dominant features. The dissymmetry factors of intense VCD bands (Bands 3–5 in Table 1), however, are smaller in the inclusion complex, by about a factor of ~1.5. It then appears that the perturbation by the guest molecule lowers the overall VCD of the α-cyclodextrin host. In the case of the Methyl Orange–β-cyclodextrin inclusion complex the VCD spectral pattern also appears qualitatively similar to that of the parent cyclodextrin. The perturbation of the host cavity appears in this case to be much smaller. This can be inferred from the facts that: (a) the absorption spectral pattern of the Methyl Orange–β-cyclodextrin complex (Fig. 2(b)) is much closer to that of β-cyclodextrin (Fig. 1(b)) and the Methyl Orange absorption bands seen in the absorption spectrum of the Methyl Orange–α-cyclodextrin complex are now much weaker; (b) the intensities (dissymmetry factors) of strong VCD bands (Bands 3–5 in Table 1) seen for the Methyl Orange–β-cyclodextrin complex are not much different from those of the parent β-cyclodextrin. These spectral observations suggest that Methyl Orange is held tightly in the cavity of α-cyclodextrin perturbing the host, but not as much in the cavity of β-cyclodextrin. These conclusions are supported by the physical observations that the Methyl Orange–α-cyclodextrin complex is brightly colored and dissolved slowly in Me_2SO-d_6, whereas the Methyl Orange–β-cyclodextrin complex is pale colored and dissolves more readily in Me_2SO-d_6.

For the remaining inclusion complexes studied, the VCD sign patterns are observed (see Table 1) to be similar to those seen for parent cyclodextrins and no major differences are apparent.

In order to investigate the influence, if any, on the magnitude of VCD intensities in these inclusion complexes, the dissymmetry factors for five major VCD bands are compared in Table 1. The parent cyclodextrins, hydroxyl deuterated α-cyclodextrin, and all inclusion complexes investigated are included in this Table. From a comparison of the numbers in this Table, it is apparent that the changes seen for the intense VCD bands in the 1400–1100 cm^{-1} region (except for copper complexes, see below) are rather small; some differences can be seen in the dissymmetry factors of the relatively weak VCD bands in the 1500–1400 cm^{-1} region. In the case of inclusion complexes with substituted cyclohexanones, we have also measured the VCD spectra in the carbonyl stretching region to investigate the induced chirality in guest molecules by the cyclodextrin cavity. We have not found any measurable VCD in this region, in contrast to the induced electronic circular dichroism seen in n–π* transitions of cylohexanones [15].

Copper complexes.—The effect of complexation with copper has a remarkable influence on the infrared absorption as well as VCD of both α- and β-cyclodextrin (Fig. 2(c) and (d)). The infrared absorption spectra of both complexes show sharpening of bands at ~1454,

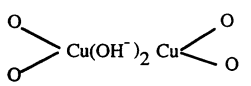
1361, and 1294 cm^{-1} and the broad background present in cyclodextrin absorption spectra is decreased upon complexation, indicating a decrease in the O–H bending absorptions. The strong absorption band seen at $\sim$1149 cm^{-1} in cyclodextrins is shifted upwards in frequency to 1165 cm^{-1} in the copper–α-cyclodextrin complex and to 1166 cm^{-1} in the copper–β-cyclodextrin complex. The relative absorption spectral features of the two complexes, however, are not quite the same. The absorption intensity of the 1361 cm^{-1} band is greater than that of the 1454 cm^{-1} band in the α-cyclodextrin complex, while they are about the same in the β-cyclodextrin complex.

In the VCD spectra, the negative–positive pair (bands labeled 1 and 2) seen for cyclodextrins in the 1500–1400 cm^{-1} region disappears upon complexation. In fact the VCD spectrum of copper–α-cyclodextrin in the 1500–1200 cm^{-1} region looks very much like that of α-cyclodextrin-$(OD)_{18}$, except for the positive VCD band seen in the latter at 1403 cm^{-1}. This suggests that the exocyclic hydroxyl groups of cyclodextrin are involved in binding to copper ions. In addition, the strong negative VCD band (band labeled 5) seen for cyclodextrins (both deuterated and undeuterated) at $\sim$1149 cm^{-1} appears in the complexes as a weak negative VCD signal at $\sim$1165 cm^{-1}, suggesting that the exocyclic C–O stretching motions are effected by complexation with copper. There is a difference between the VCD spectra of α- and β-cyclodextrin complexes with copper, in that the positive VCD feature (band labeled 4) seen in the 1350–1315 cm^{-1} range for the α-cyclodextrin complex is broad, while the same for the β-cyclodextrin complex is somewhat sharper.

Based on the VCD spectra of deuterated and undeuterated α-cyclodextrins, VCD in the 1500–1400 cm^{-1} region is expected to have major contributions from the C–O–H bending vibrations. The disappearence of the negative–positive VCD pair and the disappearence of broad absorption background in this region upon complexation suggests that the exocyclic OH groups are involved in complexation. The shift of the strong absorption band $\sim$1149 cm^{-1} to higher frequencies and the decrease of associated VCD intensity upon complexation further confirms that the secondary hydroxyl groups are influenced by complexation. This is because this band is considered to originate from the exocyclic C–O stretching modes of the secondary hydroxyl groups.

In the cyclodextrin inclusion complexes (see above), where there are no covalent interactions between the host and guest, the changes seen in VCD spectra, if any, are small. So the significant VCD spectral changes seen for copper–cyclodextrin complexes can be safely interpreted to indicate the presence of covalent interactions between copper and cyclodextrins. The disappearence of VCD due to O–H bending vibrations and the reduction in the VCD of exocyclic C–O stretching vibration, upon complexation, provide evidence that exocyclic C–O groups are involved in this covalent interaction. Thus, the present studies provide spectroscopic evidence for covalent intercations between copper ions and the exocyclic C–O groups of cyclodextrins.

Based on potentiometric studies, Matsui et al. suggested [5] that copper forms a 2:1 complex with cyclodextrins and that the copper ion bonds to the oxygen atoms of two different secondary hydroxyl groups (at C-2 and C-3) on adjacent glucopyranose units. The two copper ions bound in this manner were proposed to make a diagonal link, as



between opposite glucose units of the cyclodextrin cavity. The observed absorption and VCD features of parent cyclodextrins and their copper complexes support the hypothesis [5] of covalent bonding between copper ions and exocyclic C–O groups of cyclodextrins.

The diagonal link made by copper ions cannot be identical in α- and β-cyclodextrins because of the difference in the number of glucose units present in forming their cavities. Since β-cyclodextrin is larger and more flexible than α-cyclodextrin, the degree of distortion of the cyclodextrin cavity was thought [5] to be smaller in β-cyclodextrin than in α-cyclodextrin. Evidence for differences in the binding of copper to α- and β-cyclodextrins can be seen both in the relative absorption intensities and VCD features of the two complexes summarized earlier.

4. Summary

In the inclusion complexes studied here, the perturbations of the cyclodextrin cavity from the interactions with guest molecules are not large enough to cause vibrational frequency shifts and changes in normal mode compositions so as to influence the VCD sign patterns. Obvious changes are not apparent either in absorption or VCD spectral patterns; the changes observed in the magnitudes of absorption and VCD intensities are small. Major changes in VCD spectral intensities, without obvious changes in VCD spectral patterns, are seen for the α-cyclodextrin–Methyl Orange inclusion complex. The formation of the complex in this case can be identified from an evaluation of absorption and VCD intensities. Since the corresponding changes seen for the β-cyclodextrin–Methyl Orange complex are small, and the β-cyclodextrin cavity is larger than that of α-cyclodextrin, it is possible that the changes in VCD spectral intensities become significant only when the guest molecule is tightly held (in a smaller cavity). Major changes in VCD spectral patterns seen for copper complexes support the notion of covalent binding of copper to cyclodextrin. The formation of complexes in this case can be identified from the visual inspection of the absorption and VCD spectra; the participation of exocyclic C–O groups in covalent bonding to copper ions could be inferred from the VCD spectral patterns.

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