

Evidence for the Cyclodextrin Mediated Aggregation of Cyanine Dyes into Oligomers

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(Received: 19 March 1996; in final form: 11 June 1996)

Abstract. Based on the analysis of UV/Vis- and CD spectra of several cyanine dyes in β - and γ -cyclodextrin a case is made for the aggregation of the dyes into oligomers. The criteria for this new type of aggregates are: (i) the appearance of a concentration and temperature dependent shoulder on the high energy side of the dimer band in the UV/Vis-spectra; (ii) two oppositely signed high intensity CD absorptions, one centered at the shoulder, the other at about the energy of the monomer absorption. Calculations based on coupled-oscillator theory support the contention that chiral dye aggregates are formed in the presence of cyclodextrins, most probably trimers and tetramers. From UV/Vis- and CD-data a helically twisted sandwich structure is suggested for these aggregates. In contrast to the reported inclusion complexes these aggregates must form – at least partly – outside the chiral host.

Key words: Cyclodextrin, cyanine dyes, chiral aggregates, circular dichroism, exciton interaction.

1. Introduction

Cyclic oligosaccharides modify the natural propensity of cyanine dyes to form molecular aggregates: based on UV/Vis spectral studies of the interaction between α -, β -, and γ -cyclodextrins and a series of cyanine dyes, Sato and co-workers concluded that host–guest complexes are formed, provided certain steric requirements are met. Molecular modelling studies of the sandwich-like dye dimers stabilized inside the hydrophobic cyclodextrin cavity supported their conclusion [1]. With the chiral environment provided by the cyclodextrin hosts these aggregates should be amenable to chiroptical techniques, which has been shown to be the case in several instances [2]. Both the induced circular dichroism of sandwich-complexed dimers [3] as well as the inherent circular dichroism of twisted dimers have been observed [4]. Typical of the former is the almost constant g -factor, $\Delta\epsilon/\epsilon$, over the range of the dimer absorption band; the latter are detected by the high-intensity CD couplets corresponding to the two exciton states of the strongly coupled chromophores, symmetrically displaced from the monomer absorption.

The existence, in dye–cyclodextrin mixtures, of different monomeric and dimeric species, both complexed and uncomplexed, has been analyzed by Herkstroeter and coworkers [5]. We would like to add to this assortment evidence obtained from

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spectral and theoretical analysis, for higher aggregates, most probably trimers and tetramers, of cyanine dyes in the presence of β - and γ -cyclodextrins.

2. Experimental

Cyclodextrins were purchased and used without purification. 3,3'-Diethyl-9-methylthiacarbocyanine iodide (DMTC) and 3,3'-dipropylthiadibocyanine iodide (DPTD) were obtained from Aldrich; 3,3'-diethyloxatricarbocyanine iodide (DOTC) was a gift from Kodak. Absorption spectra were obtained with a Perkin-Elmer Lambda 5 spectrometer, CD spectra with a Jobin-Yvon CD6 and an AVIV 62 A DS. All spectrometers are equipped for controlled temperature measurements and for data acquisition and digital handling of spectral data.

Quantitative UV/Vis and CD measurements were performed on dye/cyclodextrin solutions, with ethylene glycol and water (1/1, v/v) as solvent. The spectra were taken at 0, -20, -40, -60 and -70 °C, with the exception of the DPTD/ β -cyclodextrin system which was measured only down to -60 °C. All spectra are corrected for the effects of volume contraction.

3. Results

3.1. UV/VIS AND CD DATA

3.1.1. DMTC (0.0008 mol/l)/ γ -Cyclodextrin (0.02 mol/l) (Figure 1, left)

The UV/Vis spectrum at 0 °C shows two prominent bands at 18450 cm⁻¹ (monomer) and 19782 cm⁻¹ (dimer). Decreasing the temperature increases the dimer band intensity at the cost of the monomer band (isosbestic point at 19210 cm⁻¹). At -40 °C an additional band ('band III') starts to develop at the high energy side of the dimer band. An exact determination of its energy is not possible due to extensive band overlap.

The room-temperature CD spectrum shows a small negative band at 19800 cm⁻¹ which remains unchanged down to -40 °C. Below -40 °C two new bands with opposite signs develop with a remarkably symmetric shape, consisting of a doublet with completely separated bands [6]. The band III position in the UV/Vis spectrum coincides with the position of the positive CD band. There is negligible CD absorption in the area of the dimer band.

3.1.2. DOTC (0.0005 mol/l)/ γ -Cyclodextrin (0.02 mol/l) (Figure 1, right)

Apart from the frequency shift due to the longer chromophore the UV/Vis spectra of DOTC and DMTC in γ -cyclodextrin are similar in their overall appearance and temperature dependency. However, the intensity ratio of the monomer and dimer band is shifted towards the latter. Also, the formation of band III, indicated by an asymmetry of the high-energy side of the dimer band (\sim 17000 cm⁻¹), starts at

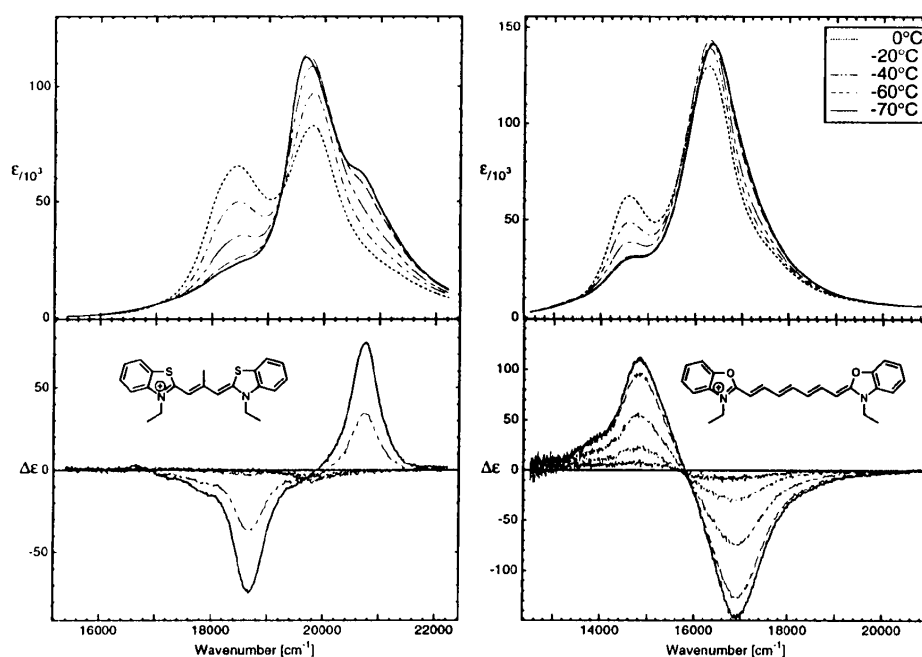


Figure 1. Temperature-dependent UV/Vis (top) and CD spectra (bottom) of DMTC (left) and DOTC (right) in the presence of γ -cyclodextrin. Concentrations: see text.

higher temperature, although it never reaches the intensity observed in the case of DMTC.

The CD spectra show a doublet with a strong temperature dependence, both bands increasing continuously with decreasing temperature. The energy separation of the bands is similar to that observed with DMTC, but due to their larger half width there is not a complete separation of the two oppositely signed bands. The amplitudes of the two bands, though similar, are not identical. As observed for DMTC, the low energy component is somewhat weaker ($\Delta\epsilon = 120$) than the high energy component ($\Delta\epsilon = -130$).

3.1.3. DPTD (0.00025 mol/l)/ β -Cyclodextrin (0.0082 mol/l) (Figure 2, left)

The UV/Vis spectra (Figure 2) show the monomer absorption decreasing and the dimer band increasing with decreasing temperature, the latter with a significant blue shift. Below -40 °C a shoulder at ~ 17900 cm^{-1} develops. In the CD spectrum a negative band develops at 15130 cm^{-1} and a positive one at 17905 cm^{-1} below -40 °C.

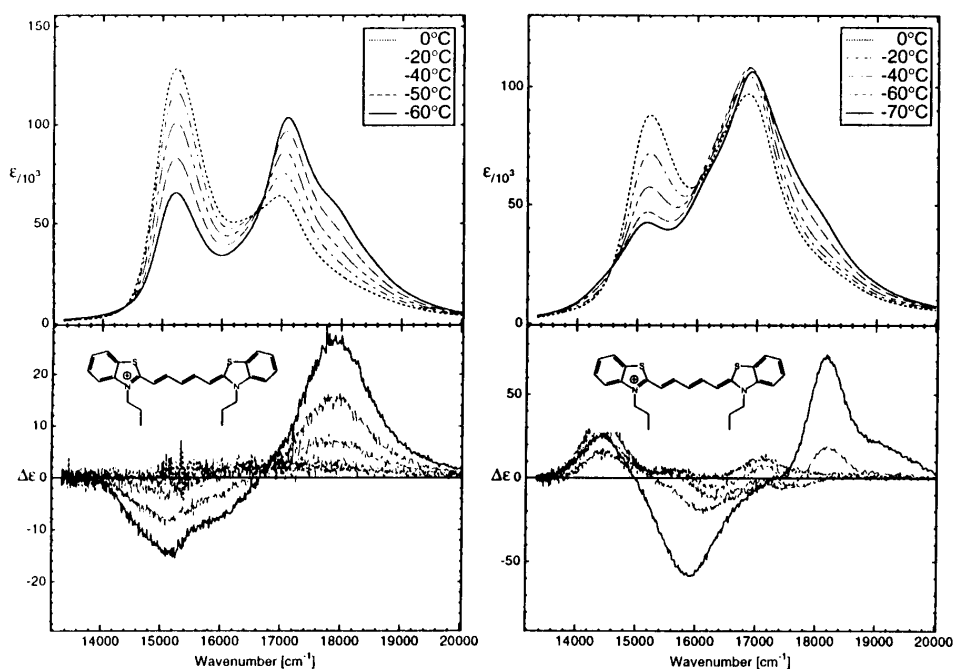


Figure 2. Temperature-dependent UV/Vis (top) and CD spectra (bottom) of DPTD in the presence of β -cyclodextrin (left) and γ -cyclodextrin (right). Concentrations: see text.

3.1.4. DPTD (0.0005 mol/l)/ γ -Cyclodextrin (0.02 mol/l) (Figure 2, right)

The UV/Vis spectra of DPTD in the presence of γ -cyclodextrin are more complicated than with β -cyclodextrin. At 0 °C only two bands with almost equal intensities are visible. Again at lower temperatures intensity is shifted towards the high energy absorption. The unsymmetric shape of this band suggests the presence of several different species.

This complicated behaviour is also reflected in the CD spectra. At 0 °C two positive bands at 14 450 and 17 090 cm^{-1} are observed. Lowering the temperature leads to an increase of the former and an decrease of the latter, with concomitant formation of a new negative band at 16 330 cm^{-1} . Below -60 °C the situation changes again. The spectrum is now dominated by three bands with alternating signs.

3.2. CALCULATIONS

In order to develop a theoretical description of the dye aggregates observed in the presence of cyclodextrins we assume a stacked geometry modified in the chiral environment to exhibit optical activity. This is most easily accomplished by

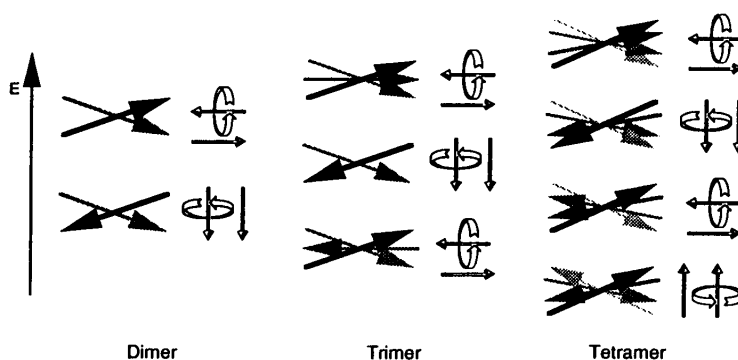


Figure 3. Coupled-dipole model for CD spectral properties of aggregated dye molecules (schematic). Thick arrows stand for coupled transition dipole moments of the dye molecules. Open arrows are the magnetic transition moment vectors (resulting from charge rotation) and electric transition moment (from charge translation). Parallel alignment of these vectors results in positive (+), antiparallel alignment in negative rotatory strength (−) for that particular coupled state.

twisting the aggregate helically, which results, as will be shown, in spectroscopic data basically in agreement with the observed chiroptical properties.

For a qualitative model (Figure 3) consider what happens when two, three or four dye molecules are arranged in a helically twisted stack. Interaction of the transition dipoles leads to coupled states with different energies and electric and magnetic transition moments depending in size and orientation on the respective coupling modes. These orientations are constrained by the symmetry of the aggregate (C_2 ; horizontal orientation of the two-fold axes) alternating from state to state. As a consequence, the orientations of the two moments also alternate between parallel and antiparallel, as do the signs of the rotatory strength associated with these states.

These following general conclusions hold:

(i) While the energies of the coupled states are symmetrically displaced from the monomer absorption in all aggregates the rotatory strengths conform to this symmetry only in the case of the dimer, in which the negative value of the high-energy state is exactly balanced by the positive value of the low-energy state (zero-sum rule). For the trimer and tetramer, the rotatory strengths are associated mainly with the two highest-energy states where there is either strong charge translation or charge rotation. The increasing number of nodes in the lower-energy coupling modes leads to vanishing over-all electric and magnetic transition moments.

(ii) With an acute twist angle between consecutive monomers the sign of the highest-energy state (in-phase coupling of the transition dipoles) is opposite to the helicity of the aggregate, i.e. it is negative if the helicity is positive.

Calculations based on the coupled oscillator theory of extended dipoles [7] and modified for chiral aggregates [8] confirm these qualitative conclusions. Electronic transition moments for the dye monomers are approximated by extended dipoles

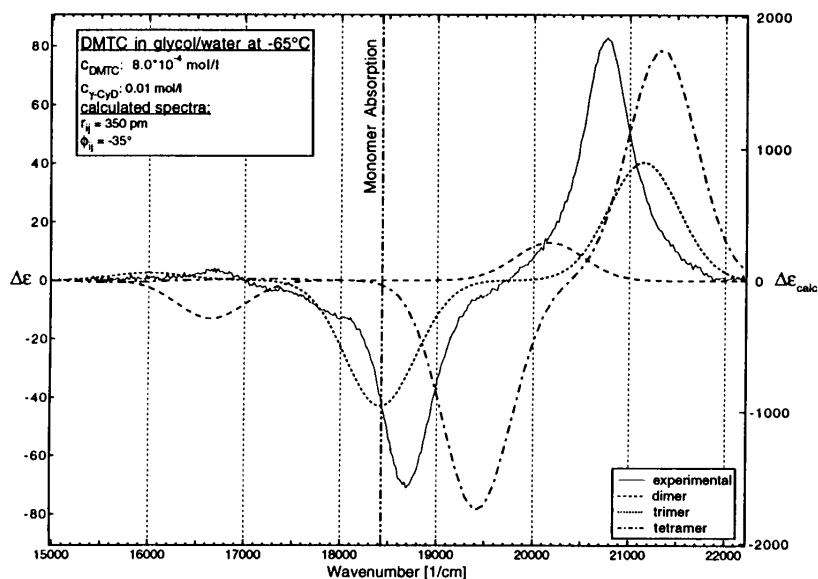


Figure 4. Comparison of experimental CD spectrum of DMTC/ γ -Cyclodextrin with calculated spectra for dimer, trimer, and tetramer aggregate.

in three dimensional space. Coulomb interactions between the monomers in the n -mer are calculated according to the assumed geometry. The interaction matrix is diagonalized resulting in eigenvalues and eigenvectors. From the former, the energies of the coupled states are calculated and from the latter the respective electric and magnetic transition moments, μ_{el_k} and μ_{m_k} . The rotatory strength R_k for each state is obtained according to

$$R_k = \mu_{m_k} \cdot \mu_{el_k} = |\mu_{m_k}| |\mu_{el_k}| \cos[\angle(\mu_{m_k}, \mu_{el_k})]$$

with the cosine argument referring to the angle subtended by the electric and the magnetic transition moment. Finally, CD curves are calculated as a superposition of Gaussian curves centered at energies ν_k and of half-widths $\Delta\nu$ [6]:

$$\Delta\varepsilon(\bar{\nu}) = \frac{\bar{\nu}_k}{(2.296 \cdot 10^{-39} \sqrt{\pi} \Delta\bar{\nu})} \cdot \sum_{k=1}^N R_k e^{-\left(\frac{\bar{\nu}-\bar{\nu}_k}{\Delta\bar{\nu}}\right)^2}.$$

The resulting CD spectra for a dimer, trimer, and tetramer aggregate, calculated with assumed C_2 symmetry, an interplanar distance between neighboring dye monomers of 350 pm, a helical twist angle of -35° , and a constant band half-width of 950 cm^{-1} , are shown in Figure 4, together with the experimental low-temperature spectrum of DMTC/ γ -cyclodextrin.

The characteristic shapes of the calculated trimer and tetramer spectra – a high-intensity CD band, blue-shifted with respect to the (experimental and theoretical)

dimer band and an oppositely signed CD band in the area of, or slightly blue-shifted relative to, the monomer band – are in agreement with the experimental spectra. A superposition of these two types of spectra corresponding to an equilibrium mixture of the aggregate does not change these qualitative features. A third weak band at the low-energy side of the monomer absorption is indicative of tetramer (or higher) aggregation and corresponds possibly to the one observed in DPTD/ γ -cyclodextrin (at $14\,400\text{ cm}^{-1}$). Dimers, on the other hand, with their symmetrical splitting relative to the energy of the monomer absorption, can be ruled out.

By adjusting the interplanar distance or the dielectric constant for the calculation of the intermolecular interaction an even better agreement with experimental band positions could be obtained; we use standard values instead in order not to overburden this simple model. The difference between the measured and calculated $\Delta\varepsilon$ values (factor of ca. 100) is an indication of the low concentration of the aggregate relative to the total dye concentration in the solution, probably not more than a few percent. A quantitative analysis of the UV/Vis spectra is difficult due to the extensive overlap. In the case where the oligomer absorption band is most distinct (DMTC in γ -cyclodextrin; Figure 1 left) the ratio of the extinction coefficients at $20\,700$ and $19\,700\text{ cm}^{-1}$ is estimated to be 1 : 35. Assuming comparable molar extinction coefficients for the aggregate and the (achiral) dimer this gives an aggregate concentration in the same range as the theoretical estimate.

4. Discussion and Conclusion

Evidence is presented for a new type of chiral cyanine dye aggregate formed in the presence of β - and γ -cyclodextrin. The prominent features of these aggregates – their UV/Vis absorption, which is blue-shifted relative to the dimer band, and two exciton-like CD absorptions in the high-energy range of the split exciton states – suggest a stacked, sandwich-like, twisted geometry. For an assumed aggregate built of three or four dye monomers the calculated spectral data agree satisfactorily with the observed features; dimer aggregates, on the other hand, are ruled out.

Despite the overall similarities of the spectra subtle differences are observed. The low-temperature CD-spectra of DMTC and DOTC in the presence of γ -cyclodextrin (Figure 1) are most easily rationalized by the formation of trimers. Compared to DOTC the DMTC-aggregate forms only at lower temperature, certainly a consequence of the steric hindrance by the methyl group in the mesoposition of the conjugated chain. For DPTD in β - and in γ -cyclodextrin (Figure 2) significant differences are observed. The alternating signs of the CD-bands, their energies with respect to monomer and dimer absorption and the blue shift from β - to γ -cyclodextrin all point to a preponderance of trimers in the former and of tetramers (or higher) in the latter. We ascribe the band at $17\,000\text{ cm}^{-1}$ which forms at ambient temperatures to the absorption of an untwisted dimer (no exciton-splitting) of the type we have analyzed in detail in the case of DODC in β -cyclodextrin [3].

We have not observed any of these aggregations in the presence of α -cyclodextrin. This, and the effects just discussed with respect to DPTD, indicate that the size of the oligosaccharide cannot be neglected in the formation of these species. Complete inclusion of these oligomers is not possible for steric reasons. The contact between the saccharide and the aggregate, e.g. through partial inclusion, appears to be sufficient for the transfer of the chiral information.

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