Dielectric Relaxation Study of Some Solutions Containing β-Cyclodextrin and Dimethylsulfoxide

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Dielectric spectra have been measured up to 72 GHz at 20 °C for solutions of β-cyclodextrin (CD) in the following solvents over the whole solubility range of CD: dimethylsulfoxide (DMSO), DMSO/1,4-dioxane mixture (2:1 molar ratio), DMSO/water mixtures (2:1 and 1:2). The spectra are analyzed into a sum of Debye type spectral components. These are likely to be caused by different physical processes. The discussion shows (*i*) that there is a preferential CD-DMSO interaction, by far exceeding the CD-water interaction, and (*ii*) that, concerning CD-DMSO, a loose interaction can be distinguished from the formation of an inclusion complex.

Key words: Association; Dielectric Spectroscopy; Liquids.

1. Introduction

Cyclodextrins are cyclic oligomers built up from α-(1–4)-linked D-glucose monomers. A cyclodextrin molecule has the form of a rigid torus with a cavity which allows for the inclusion of other molecules of appropriate size. For binding in those complexes, often relatively weak, non-specific interactions are sufficient, so that a broad variety of molecules is able to act as guest. This possibility makes cyclodextrins important for many applications [1].

In the instance of a liquid medium containing cyclodextrin as well as a compound capable of acting as guest, it is conceivable that the host-guest interactions lead to molecular assemblies of more fluxional character than in the solid state, the different stages of which could perhaps be pictured as more 'external' or more 'internal' complexation, depending on the interaction sites involved. Information on dynamical and structural circumstances in those liquid systems can be gathered by the method of dielectric spectroscopy, provided polar molecules are involved as suitable probes. To the best of our knowledge, however, studies of that kind have not yet been published.

Here we report the dynamic dielectric properties of solutions of β-cyclodextrin (CD) in dimethylsulfoxide (DMSO). The type of cyclodextrin chosen consists of seven glucose monomers; the inner diameter of the taper cavity is about 0.60 and 0.64 nm at the two gates, respectively [1]. The DMSO molecule is small enough to enter the cavity without steric difficulties. The solvent DMSO was chosen because CD is well soluble in it, so that a concentration series could be studied over the range $c_{CD} \lesssim 1$ mol/l. The dielectric behaviour of the highly polar substance DMSO is well known from previous work not only for its pure state but also for mixtures with various other components. To aid the assessment of the CD/DMSO dielectric spectra, we have additionally regarded a ternary CD solution system obtained by admixture of a practically non-polar diluent to DMSO, namely 1,4-dioxane (Dx), at a fixed DMSO/Dx molar ratio 2:1. The fact that the commercially available CD material contains always some water suggested the further study of CD solutions in mixed DMSO/water solvent. For that purpose two mixed solvents with relatively high water content were used, the DMSO/water molar ratios being 2:1 and 1:2. Hence, altogether four CD solution systems are dealt with.

2. Experimental

We have measured the dielectric relaxation spectra at up to 20 spot frequencies ranging between some MHz and 72 GHz, utilizing different lumped circuit, coaxial and waveguide setups. The conductivity was determined conventionally in the kHz region. Results will be regarded in terms of the (negative) imaginary part of the complex permittivity, $\varepsilon''(\omega)$, as already corrected for the conductivity contribution if significant.

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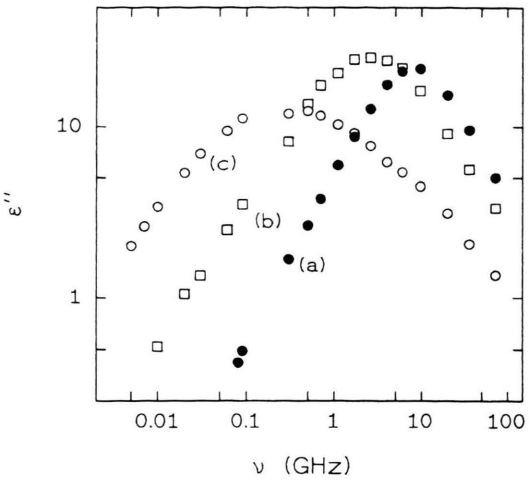

Fig. 1. Typical absorption spectra, dielectric loss ε'' against frequency ν. (a) Pure DMSO; (b) CD/DMSO/water (solvent DMSO/water 1:2, c_{CD} = 0.13 mol/l); (c) CD/DMSO (c_{CD} = 0.74 mol/l).

Chemicals were purchased from Fluka. According to the specifications of the supplier, CD is >99% β-cyclodextrin with about 10...13% water.

All measurements were made at 20 °C.

3. Results

While the dielectric spectrum of pure DMSO is practically of Debye type, the spectra of the solution systems are more or less broadened. Some typical examples are illustrated in Fig. 1, where the DMSO data can incidentally serve to illustrate the shape and width of a Debye type spectrum. All spectra are unstructured, and in some but not in all cases they can formally be described by one of the commonly used spectral functions based on a continuous relaxation time distribution (as combined in form of the Havriliak-Negami function). We desist from reporting those examples but restrict ourselves to a formal description scheme which is applicable to all systems studied, that is the superposition of Debye type spectral components C_i (viz. a discrete relaxation time distribution) according to

$$\varepsilon''(\omega) = \sum_i S_i \frac{\tau_i \omega}{1+\tau_i^2 \omega^2}, \qquad (1)$$

indexing the components in the order of increasing frequency. Up to four terms are required for satisfactory fitting. Thus the notation C_4 means always the highest frequency spectral component, regardless whether lower frequency components are present or not.

It should be added that for solutions with high CD concentration (e.g. example (c) in Fig. 1) and also for some systems containing water, the log-log slope on the high frequency side of the spectrum is indicative of an additional weak relaxation contribution in the range around or above the upper experimental frequency limit. This could be accounted for by adding a fifth Debye type component of minor relaxation strength (or equivalently, by changing C_4 to a Cole-Davidson function). However, the respective fitting parameters are rather uncertain and will, therefore, be left out of consideration.

The relaxation parameters, i.e. relaxation times τ_i and relaxation strengths S_i, $i = 1, \ldots, 4$, are represented in Fig. 2 for the four CD solution systems studied. Note that the molar CD concentrations c_{CD} have been calculated as if CD would be free of water (viz. putting $M_r = 1135$). Depending on the water content of the CD sample, the actual CD concentration may be about 15% lower. The concentration ranges are limited by the solubility of CD in the respective solvents.

Concerning the solvents used (cf. data for $c_{CD} = 0$ in Fig. 2), it should be noted at this point that one spectral component (C_4) is sufficient in case of DMSO and DMSO/Dx, while two components (C_3 and C_4) are required to describe the spectra of DMSO/water mixtures. Several physical properties of the binary DMSO/water system, among which the dielectric spectrum is a typical example, show a dependence on the mixture ratio which points towards hetero-interactions (presumably due to hydrogen bonding) with maximum intensity around the 1:2 molar mixture ratio. As the excess static permittivity [2], the relaxation strength S_3 passes through a maximum around the 1:2 ratio and vanishes for pure DMSO and for pure water, the spectra of which are describable by only the one term C_4 [3].

4. Discussion

It was stressed above that the representation of spectra by use of Eq. (1) is formal in character. However, there are indications that the spectral components C_i might actually result from physically distinguishable relaxation processes. Qualitatively, the spectra show at first glance that a noticeable absorption contribution around 10 GHz (the maximum absorption region of pure DMSO) continues to exist in all mixtures studied. This is confirmed by the fitting results (Fig. 2) which accordingly reveal a

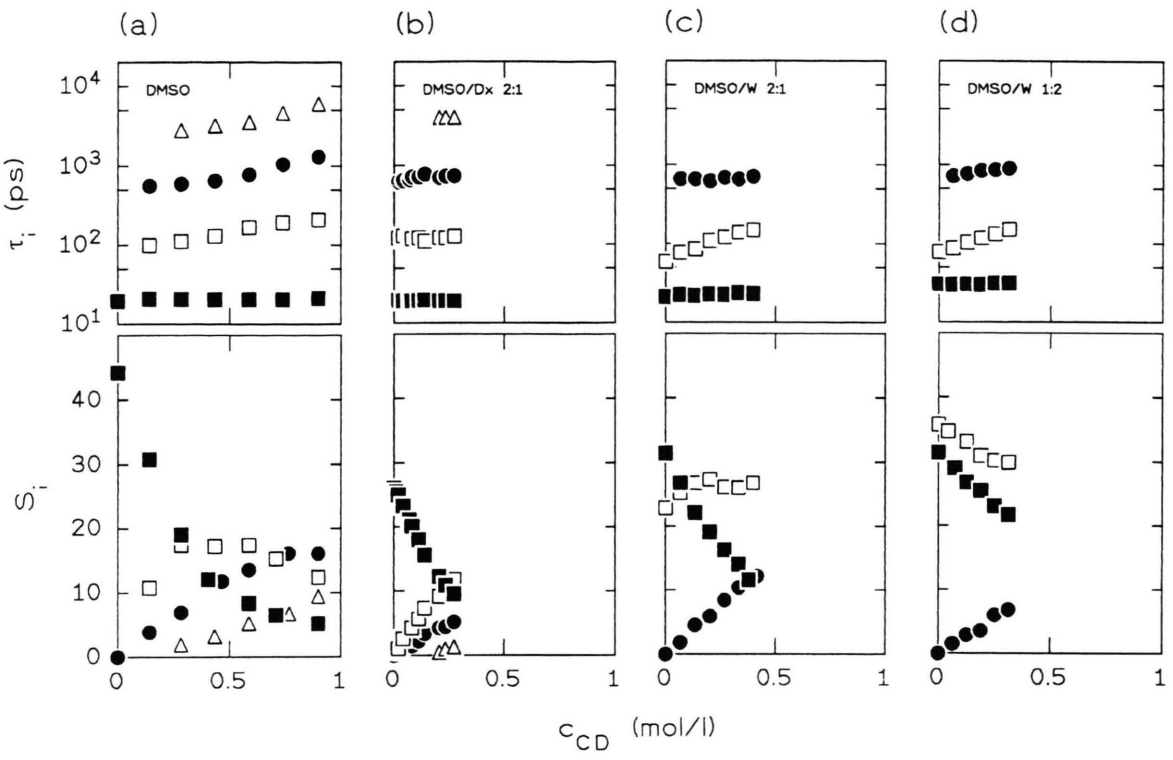

Fig. 2. Relaxation times τ_i and relaxation strengths S_i according to Eq. (1) against CD molar concentration c_{CD} in the following solvents: (a) DMSO; (b) DMSO/dioxane 2:1; (c) DMSO/water 2:1; (d) DMSO/water 1:2 (molar ratio). Symbols for spectral components: △ C_1, ● C_2, □ C_3, ■ C_4.

contribution C_4 with nearly unaltered relaxation time τ_4 for all solutions ($\tau_4 \approx 20$ ps ± 10%, except for the water-rich system, Fig. 2d, where $\tau_4 \approx 30$ ps ± 10%, staying, however, again nearly constant over the CD concentration range). Furthermore, the variation of relaxation strengths S_i for the system with the broadest CD concentration range (CD/DMSO, Fig. 2a) resembles the behaviour to be expected in the case that stepwise formation of certain species occurs on increasing CD content. Those findings lead us to tentatively discuss the spectral components C_i as due to certain relaxation processes.

Let spectral component C_4 accordingly be ascribed to DMSO relaxing as in its pure state (with some reservation concerning the water-rich system, Fig. 2d). The relaxation behaviour of pure DMSO is known to be somewhat peculiar in indicating the presence of intermolecular interactions which lead to a relaxation time longer than to be expected from the molecular size [4]. Nevertheless it has been found that, eventually besides other spectral components, this relaxation time remains nearly unchanged in binary systems of DMSO with various second components (e.g. polymer solutions such as polyvinylpyrrolidone/DMSO [5] and others), even if there are remarkable hetero-interactions (DMSO in mixtures with acetic acid [6] or water [3]). Moreover, the relaxation strength of DMSO in mixtures with nonpolar solvents has been found to be roughly proportional to the DMSO concentration, which means that the apparent dipole moment is only little altered on dilution [4, 7]. Those results support the present assignment of spectral component C_4. For the CD/DMSO and CD/DMSO/water systems, this implies microheterogeneity in the sense that solution regions exist which are unaffected by the presence of the cosolvent water or the solute CD.

A remarkable feature of all systems studied is the steep decrease of S_4 on increasing CD concentration (Fig. 2). The drop is much larger than to be expected from the slight dilution of DMSO by the solute CD. Adopting the above assumptions, it is possible to estimate the number z of DMSO molecules per CD molecule which are removed from contributing to the unaffected relaxation process C_4, thus necessarily being involved in another

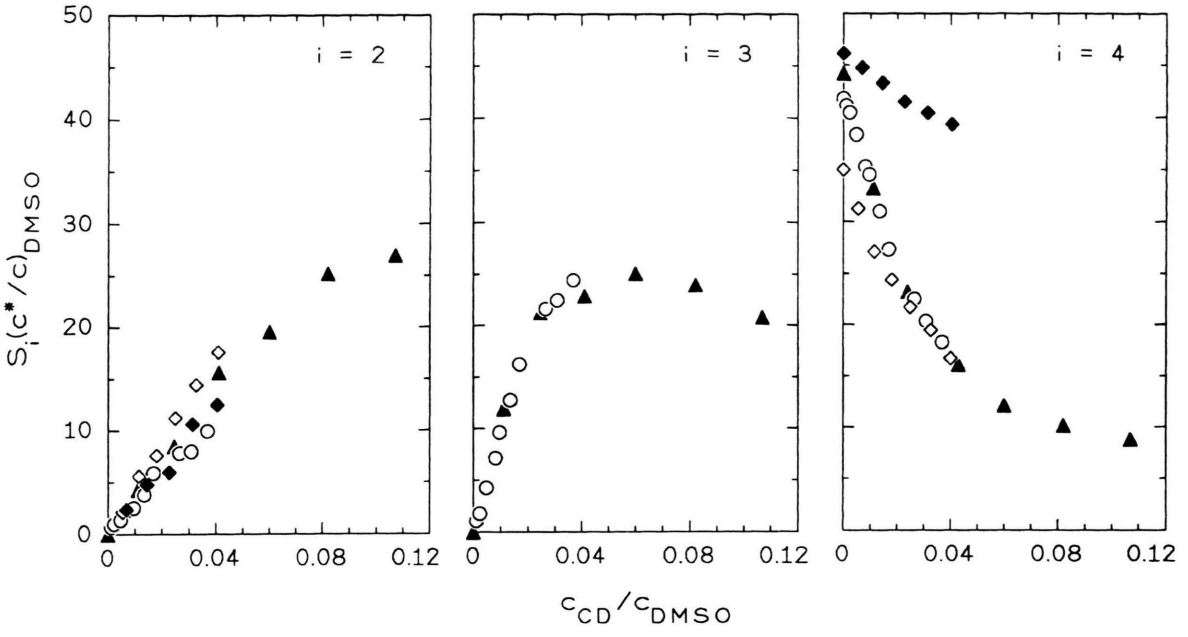

Fig. 3. Relaxation strengths S_i as normalized to the relative DMSO concentration c_{DMSO}/c^*_{DMSO} (the asterisk denoting pure DMSO) against the molar ratio c_{CD}/c_{DMSO} for spectral components C_2 (left), C_3 (middle) and C_4 (right). The symbols denote the four solvents used: ▲ DMSO (Fig. 2a); ○ DMSO/dioxane 2:1 (Fig. 2b); ◇ DMSO/water 2:1 (Fig. 2c); ◆ DMSO/water 1:2 (Fig. 2d).

process. For the CD/DMSO mixture series (Fig. 2a) we find roughly $z \approx 20$ for the lowest CD concentration (c_{CD} = 0.14 mol/l), decreasing monotonously to $z \approx 8$ for the highest concentration studied (c_{CD} = 0.90 mol/l). These are crude values, indicating, however, that a considerable number of DMSO molecules interact in some manner with the CD molecule.

In order to see whether CD-DMSO interactions play a similarly essential role in the ternary mixture systems (Figs. 2b to 2d) as in the CD/DMSO system (Fig. 2a), it is helpful to mutually compare the relaxation strengths as normalized to the actual DMSO concentration, referring to the CD/DMSO molar ratio as pertinent variable. Thus taking a certain spectral component C_i and regarding its normalized relaxation strengths found with the different mixture systems, the S_i data of Fig. 2 are converted into those of Fig. 3, which shows plots for $i = 2, \ldots, 4$. The case $i = 1$ is not suited for comparison since component C_1 is significant only for the one system CD/DMSO. For $i = 3$, on the other hand, data for the water containing systems are not taken into account since because of DMSO-water interactions these systems exhibit spectral component C_3 already in the absence of CD, so that the dependence of S_3 on the CD content will encompass unresolvable effects of overlapping relaxations due to both CD-DMSO and DMSO-water interactions.

Figure 3 shows some interesting features. For $i = 2$, the normalized relaxation strengths compare well for the four systems studied. The same holds for the $i = 3$ examples (viz. the two systems without water). For $i = 4$, rough agreement is seen for three of the systems, including the water containing system with DMSO/water ratio 2:1, but not the water-rich one with ratio 1:2. The accomodation between data for the different solution systems in the representation of Fig. 3 provides a strong argument in favour of the predominance of CD-DMSO interactions in comparison to those involving the diluent dioxane or the cosolvent water, with the reservation that this holds for the higher frequency relaxation contributions only if the water content is not too high, that is less than the 1:2 ratio which corresponds to the maximum of DMSO-water interactions. (Note that for this solvent composition also the τ_4 value deviates from that found for the other systems, as quoted earlier.)

In view of the findings with the water containing mixtures it is permissible to disregard effects possibly arising from the comparably small amount of water which is introduced with the CD samples.

Proceeding from the inference of preferential CD-DMSO effects and aiming at further structural and dynamical information about the very interactions, the lower frequency spectral components shall now briefly be discussed in some more detail. In that context it is reasonable to consider not only relaxation strengths but also relaxation times, which can give a hint at the nature of species formed. This is so if the relaxation process consists in the tumbling motion of quasi-rigid moieties since for that case there is a wealth of empirical material correlating relaxation time, viscosity and size of the moiety [8].

Concerning spectral component C_3, it seems unlikely from that correlation that the respective relaxation could be attributed to the tumbling motion of any rigid complex involving CD. Here a related example is worth mentioning, namely polyvinylpyrrolidone/DMSO solutions [5] (other polymer/small molecule systems behave similarly). They exhibit two relaxation times resembling τ_3 and τ_4 of the present systems. In that case the longer one (corresponding to τ_3) cannot be ascribed to quasi-rigid complexes but is very probably caused by DMSO in loose interaction with the polymer, appearing as some kind of solvation such that the motion of DMSO molecules is slowed down. In analogy, it may be adequate for the present systems to ascribe component C_3 to DMSO in loose, temporal interaction with CD, in any case being not firmly bound to CD, which thus acts like a small polymer molecule with, however, well-defined conformation. This picture is in accordance with the necessity that DMSO which has 'disappeared' from the bulk relaxation process C_4 must be found elsewhere. It was already noted that the relaxation time τ_3 caused by CD-DMSO interactions is in the same order as that caused by DMSO-water interactions, so that a resolution is not possible. With regard to the process underlying C_3, this may be considered a hint at similarly loose interactions of DMSO with the hydroxy groups of CD on the one hand, and with those of water on the other hand.

Turning to spectral component C_2, the relaxation time τ_2 (in contrast to τ_3) is not inconsistent with the tumbling motion of a moiety of roughly a size like the CD molecule. Let thus be assumed that CD molecules, either 'empty' or with inclusion, are responsible for component C_2. For all the present systems, this component is clearly related to CD ($S_2 = 0$ in the absence of CD). Thus an apparent moment μ_{app} per CD molecule can be calculated from S_2. Since fitting allows for some variability of parameters, among them S_2, only a rough estimate for the Onsager moment as found concurrently for the different systems may be given here, that is $\mu_{app} \approx 6 \ldots 10$ D. This is a remarkable result. It excludes the possibility that C_2 might be related to 'empty' CD molecules, since because of the high symmetry of conformationally optimized CD the moment is expected to be rather low (around 1 D) [9]. The dipole moment of DMSO is approximately 4.0 D. Thus C_2 may be related to CD including one or even two DMSO molecules, forming an inclusion complex which is long-lived on the timescale of the relaxation processes.

For component C_1, which exhibits the longest relaxation time but is significant only for relatively high CD concentrations (Fig. 2 a), one might conjecture the occurrence of higher association states.

Summing up, this paper has tried by means of dielectric spectroscopy to study interactions between CD and DMSO in the liquid state. First, it provides evidence of strong preference for CD-DMSO interactions as compared to those of CD-water, in accordance with theoretical considerations which conclude that water is only weakly bound [9]. Second, the dielectric spectra can be interpreted in the sense that concerning 'complexation' (including temporarily formed assemblies) there is a contribution from loose 'external' interaction of CD with a relatively large number of DMSO molecules as well as a contribution from 'internal' interaction leading to a long-lived inclusion complex of CD with one or two DMSO molecules.

[1] W. Saenger, Angew. Chem. **92,** 343 (1980).
[2] A. Luzar, J. Mol. Liq. **46,** 221 (1990).
[3] A. Galstian and M. Stockhausen, Z. Naturforsch. **53a,** 783 (1998).
[4] W. Dechert, R. Elsebrock, I. K. Hakim, and M. Stockhausen, Z. Naturforsch. **52a,** 807 (1997).
[5] M. Rohmann, E. Dachwitz, and M. Stockhausen, Colloid Polym. Sci. **268,** 326 (1990).
[6] V. Wessels, M. Stockhausen, and G. Schütz, Z. Phys. Chem. N. F. **168,** 193 (1990).
[7] W. Dechert, private communication.
[8] G. Turky, G. Wilke, U. Witt, A. Ghoneim, and M. Stockhausen, Proc. 3rd Conf. Dielectric and Related Phenomena, Zakopane 1994, p. 146.
[9] C. Margheritis and C. Sinistri, Z. Naturforsch. **51a,** 950 (1996).