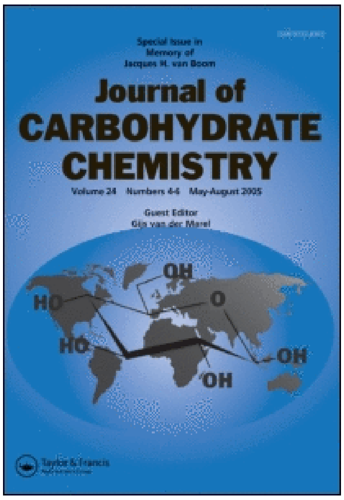

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Investigation of Temperature Effects on Cyclodextrin Compounds Through FT-IR Spectroscopy

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INVESTIGATION OF TEMPERATURE EFFECTS ON CYCLODEXTRIN COMPOUNDS THROUGH FT-IR SPECTROSCOPY

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ABSTRACT

The infrared spectra of inclusion compounds of terephthalaldehyde and two aromatic esters with α– or β– cyclodextrin are studied. A wide range of temperatures provides significant modifications of the spectra which are explained by rotational isomerism of the guest molecule.

INTRODUCTION

Cyclodextrins are cyclic compounds obtained by enzymatic transformation of starch. α-, β- and γ- Cyclodextrin correspond to the association of 6, 7 and 8 glucose units, respectively. Their geometry gives cyclodextrins the overall shape of a truncated cone whose wider side is formed by the 2- and 3- hydroxyl groups, and the narrower part by the 6-hydroxyl groups. The cavity of the cone is relatively hydrophobic, while the external faces are hydrophilic. References 1-6 give more detailed information about general properties of cyclodextrins.

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Cyclodextrins (CDs) are well known to be excellent hosts for accepting hydrophobic guest molecules, including aromatic esters.[3,4,7,8] We recently prepared a series of complex inclusion compounds and demonstrated their regioselective hydrolysis.[9-11] Electrospray ionization mass spectrometry, ESI-MS, has been used to characterize a series of supramolecular complexes of various CDs.[12-14] In this type of complex the guest molecules are enclosed within the hydrophobic cavity of CDs only by the combined action of van der Waals and hydrophobic interactions.[1,3] These complexes have been studied by different spectroscopic methods including IR and Raman spectroscopy.[1,15-17] Using IR and Raman spectroscopy, we recently demonstrated that the guest molecule in inclusion attains the physical properties of a liquid phase while it is still in a solid crystalline lattice.[18-19] It is well known that a molecule is bound to potential energy according to the environment. These potentials are different in the solid state and in the liquid state, which explains why the molecules are forced in some particular conformations according to their physical state, gas, liquid or solid. In the present work, we report the temperature dependence on the IR spectra of these compounds. Two phenomena were studied: the phase transition from the solid state to the liquid state, and for some of these compounds their rotational isomerism. In all cases, the similarity between the liquid state and the complexed state is evident.

The various CDs complexes described in this paper are only scarcely soluble in water since they are generally prepared by precipitation and/or recrystallisation in aqueous medium. All our attempts to study the weak interactions between the host and the guest molecules by NMR failed. No significant difference in chemical shifts could be detected, most probably due to rapid exchange on the NMR time scale.

RESULTS AND DISCUSSION

We have prepared and studied numerous inclusion compounds using α- or β-cyclodextrin. We report here the results obtained with three guest molecules in their natural state and in the inclusion state. The site of the cavity of the host molecules, α– or β-CD, was selected in order to obtain stable complexes in higher yield. While α-CD perfectly accepts terephthalaldehyde, all others guest molecules showed better fitting with β-CD. The aromatic aldehyde and the two esters exhibit rotational isomerism which can be observed through modification of the C=O stretching peak and sometimes of other frequencies (C=C stretching of the aromatic ring). Our experiments reveal that this isomerism is greatly influenced by temperature and by the physical state, solid or liquid, of the molecule. On the other hand our experiments show that the inclusion compound resembles more the liquid state than the solid state. The three compounds reported here are benzene para-dicarbonyl derivatives. One of these compounds is completely included in the host,[11] while the other two have only one ester group included in the host.

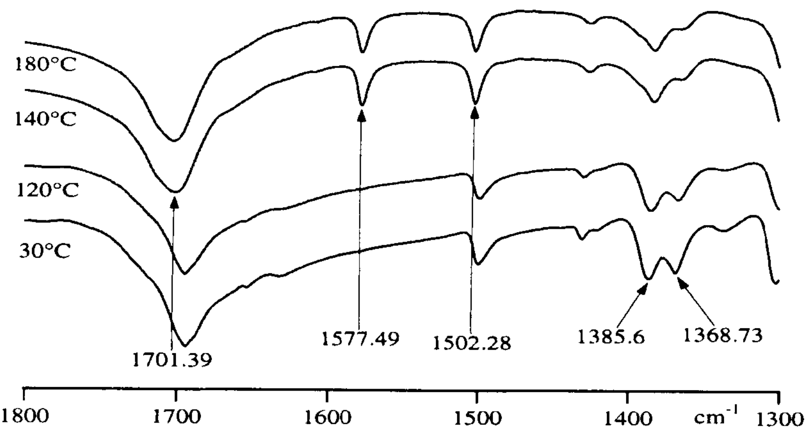
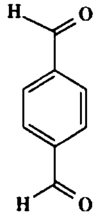


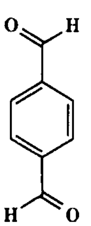
Figure 1. Temperature effect on the IR spectrum of pure terephthalaldehyde.

Inclusion Complex of Terephthalaldehyde in α-Cyclodextrin

Terephthalaldehyde has two main conformers resulting from the relative position of the carbonyl group. The *cis* conformation (1a) has a C_{2v} symmetry point group and a high dipole moment is expected. The *trans* conformation, (1b) has C_{2h} symmetry with a low dipole moment. The $s_{C=O}$, $s_{C=C}$ and $\delta_{O=C\text{-}H}$ have a symmetry A_g and B_u for C_{2h} point group and A_1 and B_2 in C_{2v} point group. In previous papers,[18,19] we stated that the C=O stretching peak appears as a doublet in the Raman spectrum while the IR spectrum shows a broad unresolved absorption with a peak at 1694 cm^{-1}. Another important feature appears if we consider C=C stretching of the aromatic ring.



cis
(1a)



trans
(1b)

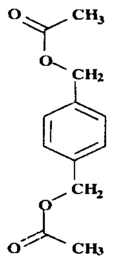
The peak at 1502 cm^{-1} is always present in the IR spectrum but is not observed in the Raman spectrum. This peak results from the E_u vibration of the C=C aromatic ring. The peaks at 1606 and 1577 cm^{-1} are observed in the Raman spectrum and are the result of the E_g component in D_{6h}. If this compound is dissolved in carbon tetrachloride or acetonitrile, the C=C stretching peak at 1577 cm^{-1} is clearly observed in the IR spectrum. We studied the effect of temperature on terephthalaldehyde in a KBr pellet in the range from -160 °C up to 180 °C. There is no important effect on the spectrum at low temperature. But as shown in Figure 1, the melting point temperature, around 116 °C, leads to important changes. The C=O peak at 1694 cm^{-1} suddenly shifts to 1701 cm^{-1}. More striking is the emergence of a strong peak at 1577 cm^{-1} corresponding to C=C stretching. Moreover, the $\delta_{O=C\text{-}H}$ which exhibits a doublet at 1385 and 1369 cm^{-1} shows a strong reduction in the strength of the second component.

Using symmetry considerations, especially the fact that A_g and B_g species are forbidden in the IR, we conclude that the most abundant conformation of the molecule is mainly C_{2h} in the solid state (*trans*)(1b) and essentially C_{2v} in the liquid state (*cis*)(1a).

Considering now the inclusion complex, Figure 2, we observe a similarity with the fused compound: the carbonyl peak shifted towards a higher wavenumber, 1701 cm^{-1} at 180 °C, and the C=C peak is well observed at 1577 cm^{-1}. Studying temperature effects, we observed a systematic shift of the carbonyl peak from 1695 cm^{-1} to 1701 cm^{-1} and a reduction of the OH bending peak due to cyclodextrin. This observation is not sufficient to ascertain whether this peak is modified by some residual water, or is due to hydrogen bonding between the guest molecule and an OH of cyclodextrin. The $\delta_{O=C-H}$ peaks are clearly observed but are somewhat blended by an OH bending peak of α-cyclodextrin. Figure 2 shows that the peak at 1366 cm^{-1} is due to C-H bending of α-cyclodextrin.

The conclusion of this study is that terephthalaldehyde, which is able to give rotational isomers around a C-C axis, attains a stable conformation close to that observed in the liquid state. The intermolecular potential inside the host molecule is close to that of the diluted state. This potential favours the *trans* conformation in the diluted and in the complexed state. In the crystalline state another potential favours the *cis* structure.

Di-*O*-acetyl-1,4-bis(hydroxymethyl)benzene in β-Cyclodextrin Inclusion Complex.



(2)

The overall length of this guest compound (2) is greater than terephtalaldehyde (1a,1b) and more conformations are expected. The C=O stretching peak of (2) is observed as an unresolved broad peak at 1726 cm^{-1} in its IR spectrum, (Figure 3), and quite the same wavenumber in the Raman spectrum. [19] The complexed molecule displays a sharpened and shifted peak at 1741 cm^{-1} with an unresolved shoulder at a lower wavenumber, (Figure 4). The shift being positive, it is not possible to hold that hydrogen bonding may be responsible for this shift. Recording the spectra at various dilutions in CCl_4 provides some explanations. At high dilutions the peak appears very sharpened, and the measured wavenumber is 1740 cm^{-1}.

We therefore conclude that the C=O stretching band is broad and shifted not only because of the superposition of a great number of conformations, but also as the consequence of short-distance intermolecular forces due to the lattice, whose effect is reduced in CCl_4 solution. This phenomenon exists also for terephthalaldehyde.

The temperature effect on the IR spectrum of (2) is especially striking (Figure 3). At -140 °C, we clearly observe two peaks, one corresponding to a free C=O bond and one shifted by intermolecular bondings. This latter peak is broadened as the temperature is increased up to the melting point at 48 °C. The recorded spectrum at 50 °C shows the coexistence of the solid and liquid phase. In the liquid state, the peak at 1741 cm^{-1} remains and appears to be broadened by temperature. When di-*O*-acetyl-1,4-bis(hydroxymethyl)-

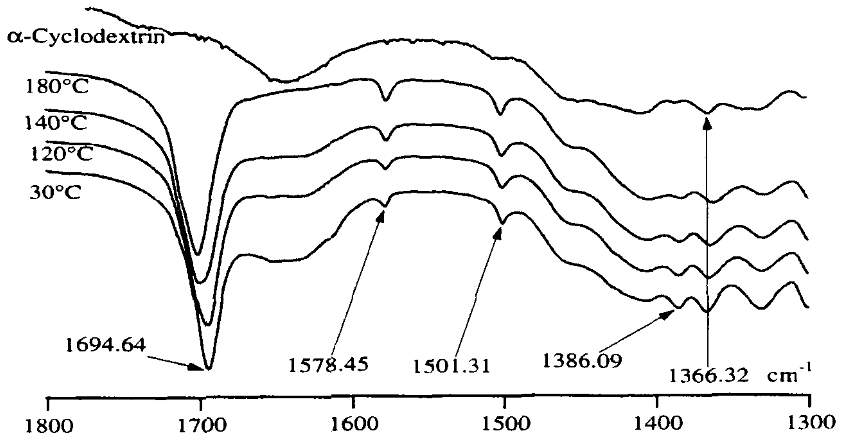


Figure 2. Absorption spectra of the terephthalaldehyde α-cyclodextrin inclusion complex.

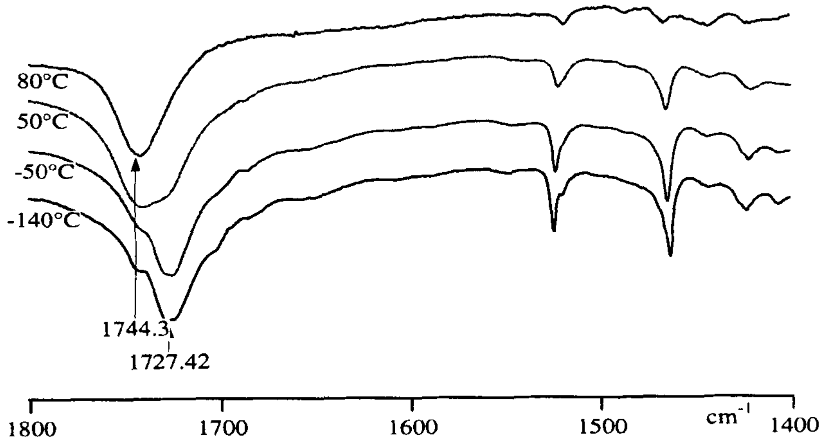


Figure 3. Infrared spectrum of di-*O*-acetyl-1,4-bis(hydroxymethyl)benzene for a set of temperature.

benzene is included in β-cyclodextrin, one acetate group absorbs as it was in solution, while the second acetate group is the object of intermolecular forces due to the environment. The infrared C=O peak appears as the superposition of a broad diffuse peak around 1725 cm^{-1} produced by the acetate group outside the the β-cyclodextrin cavity, and a sharp peak around 1740 cm^{-1} due to the acetate group inside the β-cyclodextrin cavity (Figure 4). The 1741 cm^{-1} peak appears at all temperatures, with a dissymmetry towards

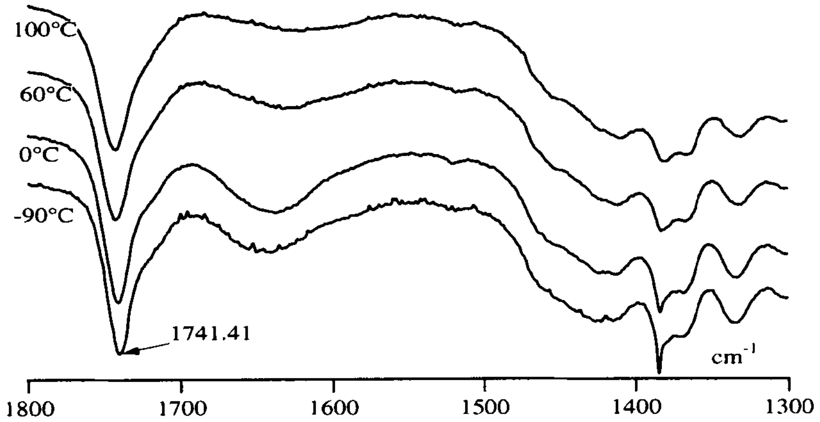
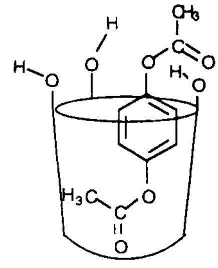


Figure 4. Infrared spectrum of di-*O*-acetyl -1,4-bis(hydroxymethyl)benzene complexed in β-cyclodextrin for a set of temperatures.

lower wavenumbers. At higher temperatures the profile is broadened and the dissymmetry becomes more important indicating the beginning of expulsion of the guest molecule.

Hydroquinone Diacetate in β-Cyclodextrin Inclusion Complex.



(3)

The size of the guest molecule provides an opportunity to consider that the aromatic ring and one acetate group are included in the β-cyclodextrin, while the other acetate group is outside the host (3). Preliminary molecular modeling studies [11] confirm this structure and propose a difference of conformation between the acetate within the cavity and the acetate group which protrudes. For the isolated molecule, one may expect rotation of the acetate group around the C-O bond giving rise to multiple conformations. In the pure solid state the peaks at 1754 and 1761 cm^{-1}, both in IR and Raman spectra may be a consequence of this feature, but we cannot ignore the possibility of intermolecular bondings with the carbonyl group. When hydroquinone diacetate is observed in solution in CCl_4 or $CHCl_3$, the peak at 1761 cm^{-1} remains while the peak at 1754 cm^{-1} appears like an elbow.

A similar doublet is observed with hydroquinone monoacetate and we expect that this doubling is the result of two main conformers acting on one acetate group. We have mentioned[19] that the magnitude of the peak at 1761 cm^{-1} is higher in the IR spectrum and lower in the Raman spectrum. As a consequence, the strengths ratio S_A/S_B between the two components shows only different probabilities in the transition moment and is not directly related to the abundance of the conformers. We can only assume that one conformer,

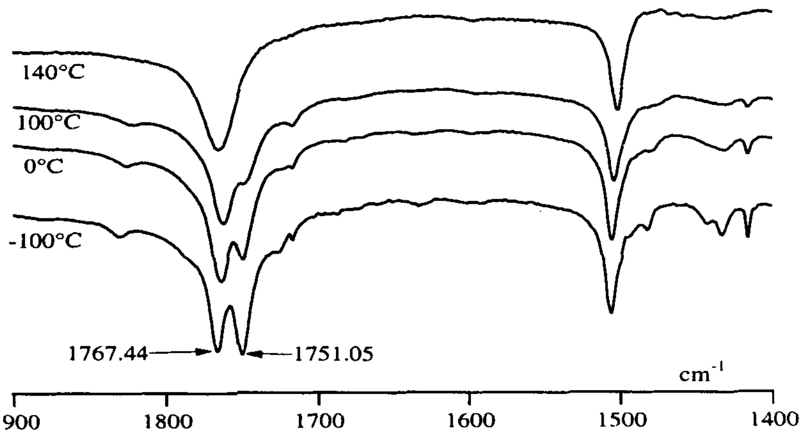


Figure 5. Infrared spectra of hydroquinone diacetate for a set of temperatures.

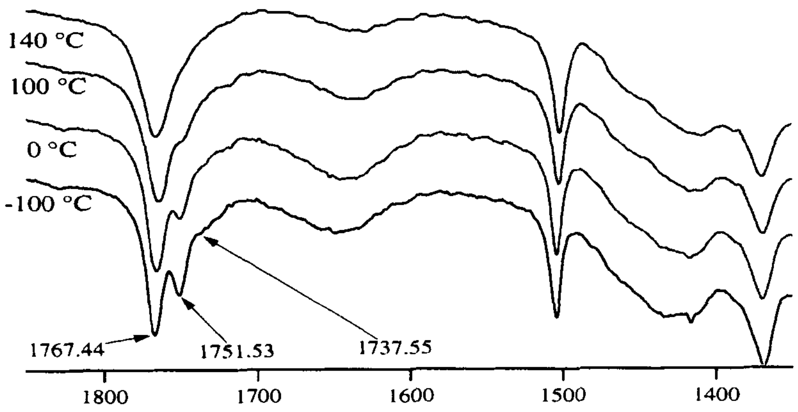


Figure 6. Infrared spectra of inclusion complex of hydroquinone diacetate in β-cyclodextrin.

which we call A, has a higher polarity, and gives a peak at 1761 cm^{-1} while the other one, which we call B, has a lower polarity and gives a peak at 1754 cm^{-1}. The action of temperature confirms this tentative assignment.

A study of the strengths of the components of A and B versus temperature was performed from 100 K up to 450 K with the pure and the complexed compounds. The decomposition of the profile of the doublet was achieved using the multi-peak procedure, IGOR Pro, (Wavemetrics). A statistical curve fitting of overlapping peaks locates the maximum or the minimum of a peak by analyzing first and second derivatives. This fit is a

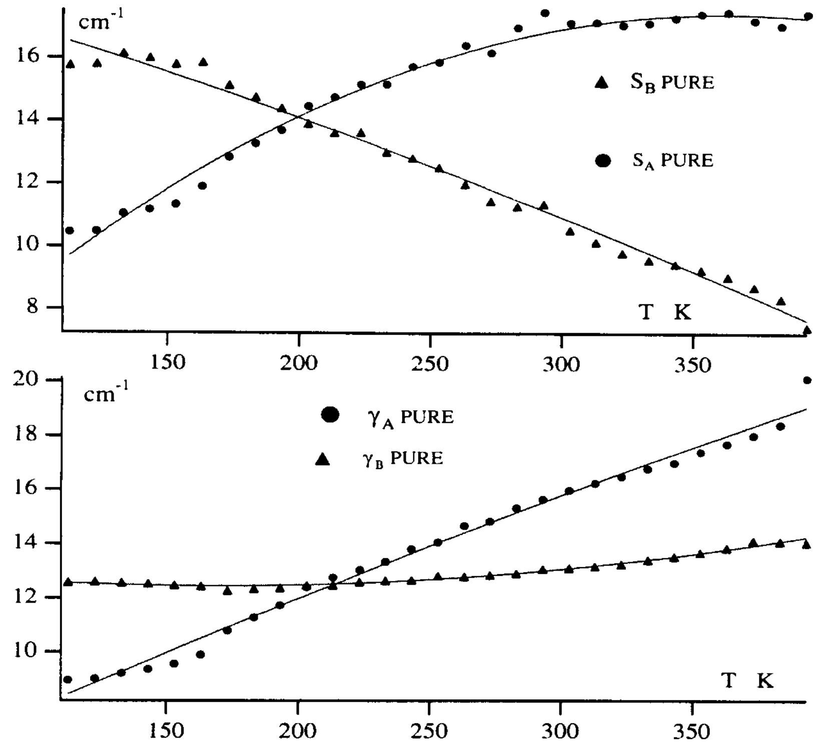


Figure 7. Strength and half-width of the two components of the carbonyl stretching peak versus temperature in pure hydroquinone diacetate.

decomposition and not a deconvolution. We observe two peaks and this procedure allows the determination of the area of the absorbance profile, S_A and S_B, and the half-width, γ_A and γ_B, for each component respectively.

The first observation (Figure 7) is the high abundance of conformer B at low temperature, with a regular decrease up to the melting temperature, 123 °C. This conformer disappears in the liquid state. This implies that the rotational motion around the C-O bond has a potential with two minima, one with a low energy E_B corresponding to conformation B, and one with a high energy E_A corresponding to the conformation A in the solid state. In the liquid state, the potential has only one minimum corresponding to conformer A. Figure 7 shows the result of the measurement for the solid state. We can check a Boltzmann law to these measurements according to :

$$\frac{N_A}{N_B} \propto \frac{2S_A}{2S_B} \propto e^{\frac{hc}{kT}(E_A-E_B)}$$

A fit of this ratio was performed between 170 K and 350 K (Figure 9). It allows determination of the energy difference: $\Delta E^{*}hc/k = 284.52$.

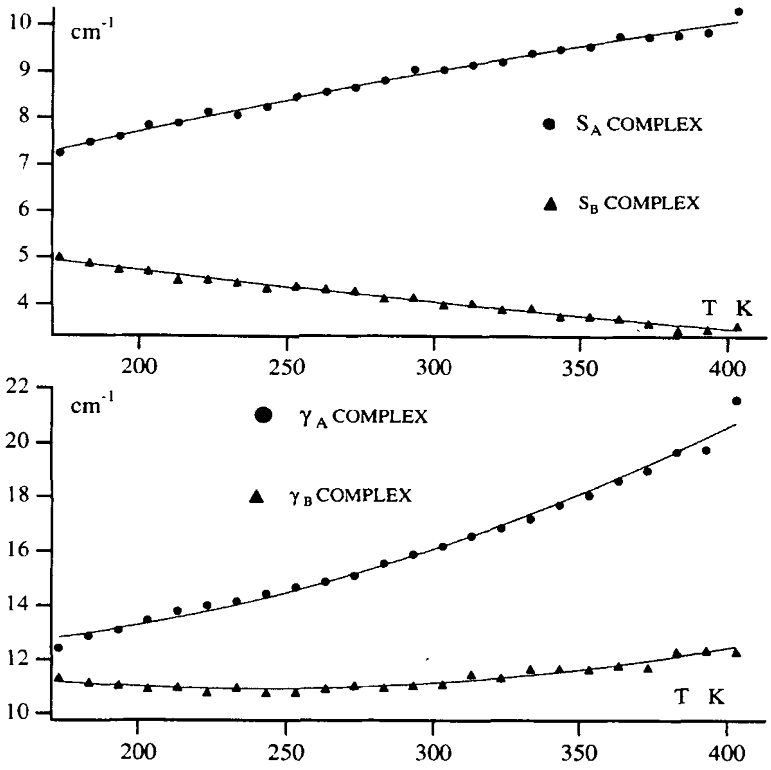


Figure 8. Strength and half-width of the two components of the carbonyl stretching peak versus temperature in complex hydroquinone diacetate in β-cyclodextrin.

It is important to note that we used the area of the band and not the peak height. For a Lorentzian profile the peak is related to the strength S and the width γ by :

$$I_{peak} = \frac{S}{\pi \gamma}$$

The peak intensity has no direct significance because it reflects variations of the strength and the half-width of the peak.

The width of the B peak remains quite constant over the temperature range, Figure 7, while the width of the A peak shows a regular increase from lower to higher temperature. It is not easy to give a correct explanation of this behaviour for a vibrational peak of such a heavy molecule.

We observe only that A is a polar conformer and it is well known that the half-width of a peak is very sensitive to the dipole moment of the molecule.

When this compound is complexed, the wavenumbers are not modified, but the intensity profile changes (Figure 6). The B peak has a reduced peak intensity. The

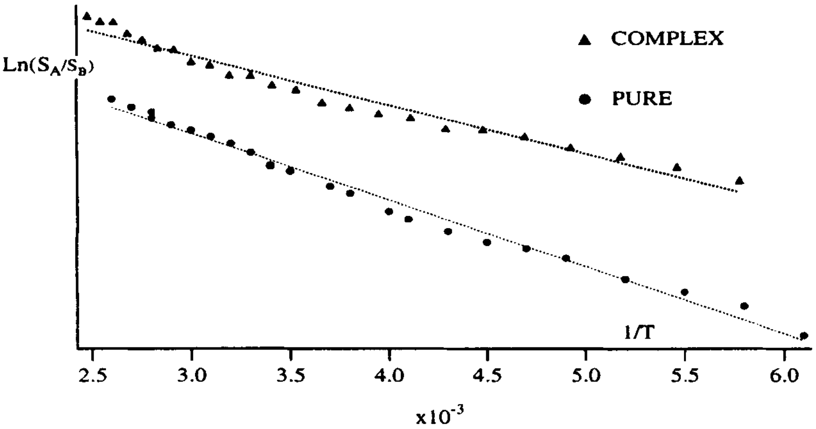


Figure 9. Fit of the curves ln(SA/SB) versus 1/T for pure hydroquinone diacetate and complexed compound in β-cyclodextrin.

explanation of this phenomenon is not exactly the same as put forward for terephthalaldehyde. The cyclodextrin host always has an action of a screen protecting the guest from all neighbours, but it creates a new potential acting on the guest. Nevertheless, this potential energy is not the same on the two acetate groups due to steric considerations. It is reasonable to expect that the acetate inside the host has only one conformation, which is the A conformation, while the other acetate group is governed by a two minima potential which are not necessarily the same as in the pure compound. The observed profile is the sum of the contributions of the two acetate groups. The strength of the components are $S_A+S^*_A$ and $S_B+S^*_B$, the star being related to the group inside the host.

The lack of symmetry between the two acetate groups does not allow the direct use of a Boltzmann law. Nevertheless, if we assume that within the cyclodextrin cavity we have only the A conformation, S^*_A is constant, and $S^*_B \approx 0$, we can draw a convenient curve. Figure 9 shows that the plot of $\ln(S_A/S_B)$ versus 1/T gives a peak whose slope is:

$$\Delta E^*hc/k = 208.83.$$

A last comment concerns the half-width of the peaks. Conformer B has a width ranging from 12 to 20 cm^{-1} while conformer A has a width ranging from 10.5 to 12 cm^{-1}. It is established that the potential energy acting on the molecule is responsible for the half-width of an absorption peak, but it is difficult to understand this phenomenon.

We carried out the same experiments on a mixture of cyclodextrin and hydroquinone diacetate. The results are very similar to those obtained with the pure compound. Nevertheless we measured an energy: $\Delta E^*hc/k = 224.81$. This difference may be an indication of the partial formation of solid state particles in the mixture.

It appears interesting to note an extra peak at 1737 cm^{-1} (Figure 6) on the recordings corresponding to the complexed molecule. This peak does not exist on the recordings corresponding to the mixture. It is very significant at low temperature and disappears at higher temperature. It may be the result of some intermolecular bonding such as hydrogen bonding between the hydroxyl of the cyclodextrin and carbonyl group of one acetate group.

CONCLUSION

This study by IR spectroscopy gives new information about the mechanism of inclusion. The effect of temperature shows that the host molecule appears like a screen isolating the guest compound from neighbours. The guest molecule may be compared to a solid solution and the action of temperature widens the observed peak at the limit of expulsion of the complex. On the other hand, the host is able to create non homogeneous potential sufficient to force the molecule into some rotational conformation. This new conformation may be the same as in a liquid or diluted state, like in terephthalaldehyde, or may be different as for hydroquinone diacetate.

EXPERIMENTAL

a. Synthesis of inclusion compounds: The CD-complexes are easily obtained using the following procedure: a saturated solution of cyclodextrin in water or a mixture of ethanol/water of 10 g of cyclodextrin in 100 mL of solvent is heated to 60 °C. The solution is maintained for 3 h at 60 °C with vigorous stirring. The guest compound is then added slowly in the correct proportions. The mixture is maintained under fast stirring for 3 h and is then slowly cooled resulting in crystallisation of the complex.[19]

b. Spectroscopy. The spectra were recorded with an IFS 66 Bruker Fourier Transform Infrared spectrometer. The KBr beamsplitter limited the spectral range to 6000 cm^{-1} to 400 cm^{-1} using a conventional DTGS detector. The limit of resolution was 1 cm^{-1}. In the solid state, the samples were obtained by pressing into a KBr pellet. To overcome pressure effects on the complexes, some recordings were made using a Diffuse Reflectance System (Graseby/Specac Corporation). In order to observe compounds in solution, a horizontal ATR was used (Graseby/Specac Corporation).

Temperature effect measurements were achieved using a variable temperature cell (Graseby/Specac Corporation) connected to an automatic temperature controller. The system is convenient for recording spectra from liquid nitrogen temperature (-180 °C) up to 200 °C. The KBr pellet holder is installed in a vacuum jacket. This system is convenient for studying solid state samples in a KBr pellet. The phase transition was studied directly in the KBr pellet, but strong diffusion occurs at a temperature above the melting point, and evidence of vaporisation was observed.

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