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Vibrational Raman Optical Activity of Cyclodextrins

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Abstract: Vibrational Raman optical activity spectra of aqueous solutions of α-, β- and γ-D-cyclodextrin in the range 700-1500 cm^{-1} are reported. As well as showing features characteristic of D-glucose, the ROA spectra all show remarkably intense features between 890 and 960 cm^{-1} originating in coupled C(1)-H deformations and glycosidic C-O stretches delocalized around the cyclodextrin ring and which reflect the stereochemistry of the glycosidic links.

Vibrational optical activity measurements on chiral molecules can provide much new stereochemical information because a vibrational spectrum contains bands associated with every part of the molecule.[1] Vibrational optical activity in typical chiral molecules in the disordered phase was first observed using the Raman optical activity (ROA) technique, which measures a small difference in the Raman-scattered intensity in right and left circularly polarized incident light.[2,3] Until recently, lack of sensitivity has restricted ROA studies to favourable samples such as neat liquids;[4,5] but a major breakthrough in ROA instrumentation based on the use of a backscattering geometry[6,7] together with a cooled CCD detector[8] has now rendered a much wider range of samples accessible to such studies. This communication reports ROA spectra of cyclodextrins in aqueous solution which indicate that this technique has great potential for stereochemical studies of these and other polysaccharides.

Most carbohydrates are not well suited to conventional electronic circular dichroism (ECD) measurements, which are restricted to the long-wavelength tails of the first ECD bands;[9] nonetheless, some useful information about conformations of cyclodextrins has been obtained in this way.[10] Vibrational optical activity spectra of simple carbohydrates obtained using ROA's sibling technique of vibrational circular dichroism (VCD) have been reported,[11] but no VCD spectra of cyclodextrins have so far been published.

The ROA spectra were recorded using the Glasgow multichannel instrument[12] modified for backscattering[6,7] and CCD detection.[8] The cyclodextrin samples were purchased from Aldrich and Fluka and studied as near-saturated solutions, in water for α- and γ-D-cyclodextrin, and in 1N NaOH for β-D-cyclodextrin in order to boost the solubility. The ROA measurements were made using a focused 500 mW argon-ion laser beam with a spectral resolution (FWHH) of ~ 8 cm^{-1}. All the ROA spectra were acquired for 2 hours.

The ROA spectra of α-, β- and γ-D-cyclodextrin are shown in Figs. 1-3 respectively. The ROA spectra of D-glucose, D-maltose and D-maltotriose, to be published elsewhere as part of

a preliminary survey of ROA spectra of a range of carbohydrates,[13] are of central importance in discussing the cyclodextrin results. Thus all three cyclodextrin ROA spectra show a negative-positive couplet centred at ~ 1340 cm^{-1} that also appears in D-glucose (at slightly lower frequency) where it has been associated with deformations of the CH_2OH group; and all three show an ROA 'fingerprint' between ~ 980 and 1170 cm^{-1} similar to that in glucose and associated with ring C-O and C-C stretching together with C-O-H and C-C-H bending which is characteristic of the pattern of OH ring substituents. The most striking cyclodextrin ROA features are the enormous positive-negative couplets between ~ 890 and 960 cm^{-1}: no similar features appear in D-glucose, but they appear with much less intensity in D-maltose and D-maltotriose where they have been associated with modes involving contributions from the anomeric C(1)-H deformations and the glycosidic C-O-C stretch.

The general appearance of the three cyclodextrin ROA spectra is itself quite revealing. Thus the ROA features of β-D-cyclodextrin (as predominantly monoanion in base[14]) show sharp structure, especially in the couplet centred at ~ 1340 cm^{-1}: the same characteristics are seen in the ROA spectrum of D-maltose,[13] and may reflect a similar restriction of conformational possibilities in β-cyclodextrin and maltose. The ROA features of γ-D-cyclodextrin are generally broader and much less structured than those of β-D-cyclodextrin (anion), and are remarkably similar to those of D-maltotriose,[13] indicating that γ-cyclodextrin might have a similar increase in conformational possibilities to maltotriose on account of the larger ring.

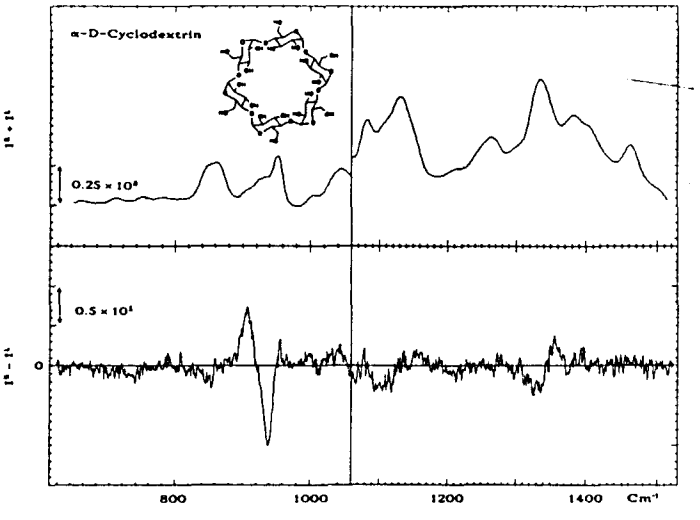

Figure 1. The backscattered Raman ($I^R + I^L$) and ROA ($I^R - I^L$) spectra of α-D-cyclodextrin in water.

The enormous glycosidic couplets seen in all three cyclodextrin ROA spectra between ~ 890 and 960 cm^{-1} have dimensionless ROA intensities $\Delta = (I^R - I^L)/(I^R + I^L)$ of several parts in 10^2, which is an order of magnitude larger than the largest Δ-values usually encountered. The fact that the Δ-values of the similar glycosidic ROA feature in maltose and maltotriose have more typical magnitudes, with those of maltotriose roughly double those of maltose, is

evidence that these large cyclodextrin ROA couplets originate in coupled vibrational modes of the glycosidic links delocalized around the cyclodextrin ring. In fact Raman bands in this region have been assigned previously to skeletal ring modes involving the glycosidic bonds:[15,16] but only the bands at 949 cm^{-1} in α-cyclodextrin and 945 cm^{-1} in β-cyclodextrin (and by analogy that at 945 cm^{-1} in γ-cyclodextrin) were explicitly associated with a

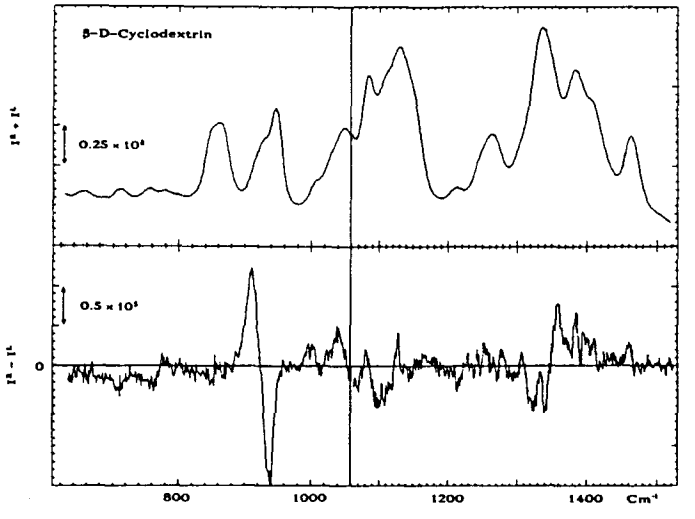

Figure 2. The backscattered Raman and ROA spectra of β-D-cyclodextrin in 1N NaOH.

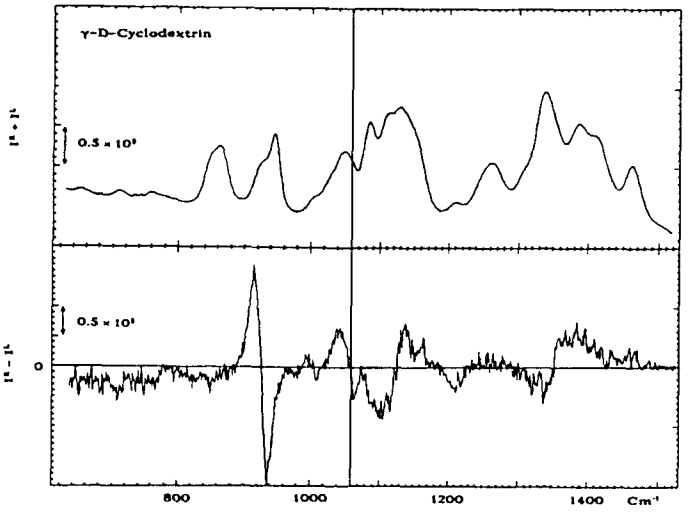

Figure 3. The backscattered Raman and ROA spectra of γ-D-cyclodextrin in water.

delocalized ring mode;[15] yet close inspection of our ROA spectra reveals that the negative parts of the glycosidic ROA couplets are not in fact associated with these particular bands

but are at slightly lower frequency. We therefore conclude that, in all three cyclodextrins, there are at least two overlapping bands on the low-frequency side of the previously-assigned delocalized ring mode that are also delocalized around the cyclodextrin ring.

We have also measured ROA spectra of aqueous solutions of α-D-cyclodextrin containing the guest molecules sodium benzoate and the two enantiomers of phenylalanine. While they are generally very similar to the spectra shown here, there are some small but significant local differences which may reflect a transformation from a 'tense' to a more symmetrical 'relaxed' conformation corresponding to the model of Saenger et al.[17]

Instrumental improvements are now in hand which should provide an order of magnitude increase in speed of the measurements. This will enable quantitative differences in ROA features to be measured when different guests are incorporated, thereby providing a completely new source of information on the details of conformational changes associated with the accommodation of different guests in cyclodextrins in aqueous solution.

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