FT-Raman Spectra of 2-, 3-, and 4-Chlorostyrene Molecules Included in Cyclodextrins

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Abstract

FT-Raman spectra of 2-, 3-, and 4-chlorostyrene included in α-cyclodextrin (CD), glycerol ether α-CD, β-CD, sulfated β-CD, and glycerol ether β-CD were recorded. In the inclusion complexes, the area of the vinyl ν(C=C) band decreased remarkably, whereas the area of the phenyl ν(C=C) band increased compared to those of liquid 2-, 3-, and 4-chlorostyrene, respectively. From the results, the inclusion structures of 2-, 3-, and 4-chlorostyrene were discussed.

Introduction

Cyclodextrins (CDs) are cyclic natural oligomers connecting six, seven, and eight glucose units via α-(1,4)-linkages, which are called α-, β-, and γ-cyclodextrins, respectively. Schematically, the shape of CDs can be presented as a truncated cone with six, seven, and eight primary hydroxyl groups attached to the smaller opening cone while the remaining twelve, fourteen, and sixteen secondary hydroxyl groups are located on the larger opening of the cone [1, 2].

As a consequence of these structural features, CDs are capable of forming inclusion complexes, even with molecules significantly larger than their cavities, as long as at least some part of the guest can penetrate into the cavity [3, 4]. CDs are known to be good models for enzymatic action, combining the cage effects with the conformational control of the guest molecule. Their stereoselective action, especially of α- and β-CDs, offers new possibilities in particular for pharmaceutical application, e.g., enhancement of the bioavailability of certain drugs [5–10]. CDs also present several advantages in other areas, such as food, cosmetics, industrials and agrochemistry [11–13], especially owing to their capacity to protect the guest molecules against oxidation, light-induced reaction and loss by evaporation. Additionally, they usually enhance the solubility of poorly soluble or even insoluble compounds.

In a previous study, the inclusion complexes of *m*- and *p*-nitrophenol in β-cyclodextrins were studied using Raman spectroscopy in solution. It was found that the intensity of the vibration peaks of C–O and C–N at 1284 and 856 cm^{-1} of *p*-nitrophenol increased remarkably in the presence of a cyclodextrin modified with epichlorohydrin [14]. On the other hand, the inclusion complexes of cyclodextrins in aqueous solution have usually been researched using spec-

trometry such as fluorimetry, phosphorimetry, NMR spectroscopy, chromatography, etc. [15]. However, little has been reported about the inclusion complexes of cyclodextrins in the solid state using FT-Raman spectroscopy.

In this study, the solid state inclusion complexes of 2-, 3-, and 4-chlorostyrene with cyclodextrins was prepared by freeze-drying, and then recorded by FT-Raman spectroscopy. Based on these results, the inclusion structures are discussed.

Experimental

Materials

α- and β-Cyclodextrin (CD), sulfated β-CD and 2-, 3-, and 4-chlorostyrene were obtained from Aldrich Co. All the other chemicals were reagent grade and used without further purification. Scheme 1 shows the structure of the host compounds used in this study.

Preparation of inclusion complexes

Scheme 2 shows the preparation of the inclusion complexes and the structure of the guest molecules. The inclusion complexes were prepared by mixing 2-, 3-, and 4-chlorostyrene and cyclodextrins in aqueous solution, respectively. This led immediately to the formation of white precipitates which were separated by centrifugation and freeze-dried. The glycerol ether α- and β-CD used in this study were prepared earlier [14].

FT-Raman spectroscopy experiments

The NIR Fourier transform (FT) Raman spectra were recorded with a Bruker FT-106 Raman module, equipped with a
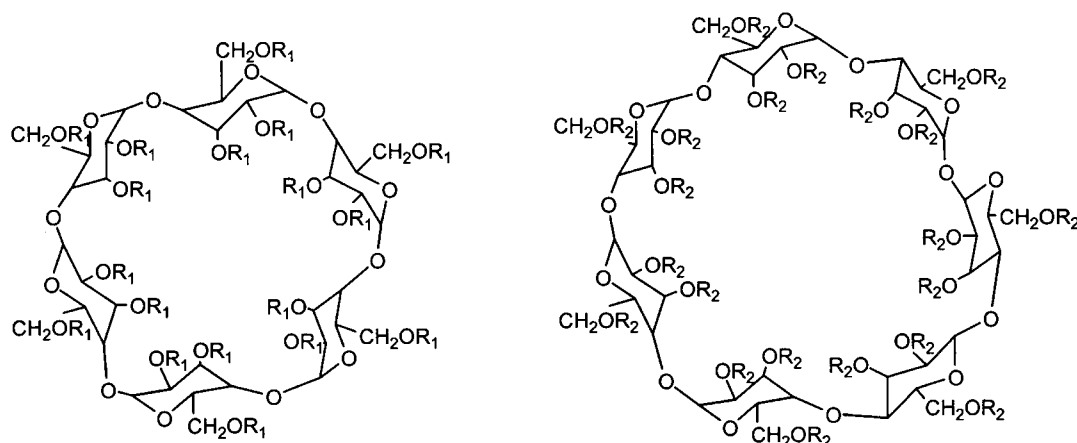
Scheme 1. Structure of the host compounds used in this study.

Ge detector cooled by liquid nitrogen, connected to a Bruker FT-IR 66 interferometer. To excite the Raman spectra, a continuous wave diode-pumped Nd:YAG laser with radiation of wavelength 1064 nm (9398.4 cm^{-1}) was used. In all cases, the laser power was 300 mW and the spectral resolution 2 cm^{-1}.

Results and discussion

The phenyl C=C and vinyl C=C stretching modes of the guest molecules were observed in the 1550–1680 cm^{-1} region of the FT-Raman spectra. Furthermore, these regions were recorded without any interfering bands of the cyclodextrins. The 2950–3150 cm^{-1} region of the guest molecules contain νCH bands. In some cases, the vCH region displays band shifts on complexation with cyclodextrins [15]. Therefore, two regions, 1550–1680 cm^{-1} and 2950–3150 cm^{-1}, of chlorostyrene included in cyclodextrin were used.

Inclusion complex of 2-chlorostyrene

Figure 1 shows the FT-Raman spectra of 2-chlorostyrene in the 1550–1680 cm^{-1} and 2950–3150 cm^{-1} regions at room temperature. Liquid 2-chlorostyrene gives the phenyl ν(C=C) band at 1593 cm^{-1} and the vinyl ν(C=C) band at 1628 cm^{-1}, respectively. The area of the vinyl ν(C=C) band of 2-chlorostyrene in the CD complexes decreased remarkably, whereas the area of the phenyl ν(C=C) band increased compared to that of liquid 2-chlorostyrene. The Full Width at Half Maximum (FWHM) intensity increased compared to that of liquid 2-chlorostyrene except for the glycerol ether α-CD complex (see Table 1).
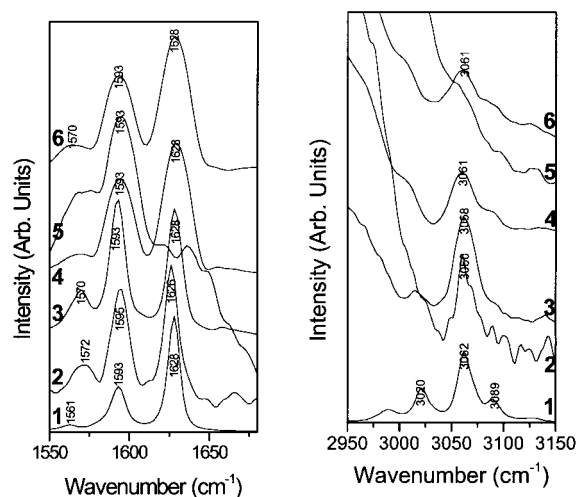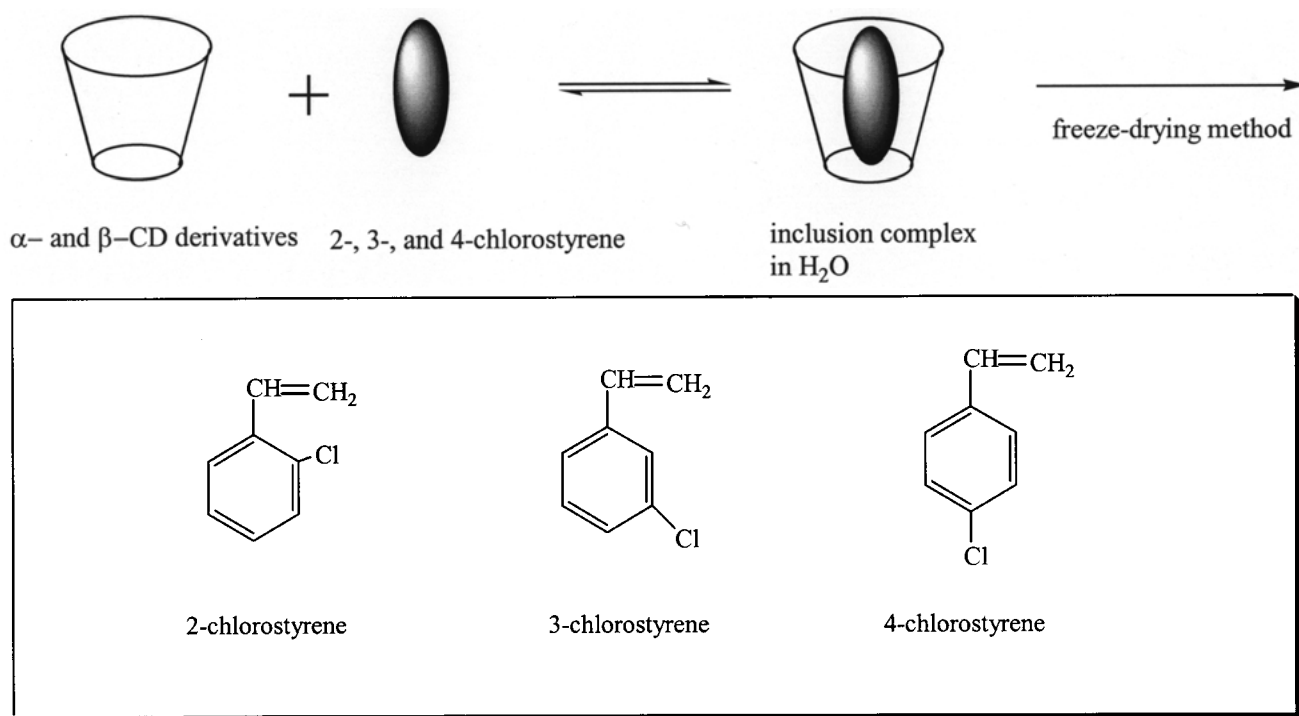

Figure 1. FT-Raman spectra of 2-chlorostyrene in the 1550–1680 and 2950–3150 cm^{-1} regions at room temperature. **1** liquid 2-chlorostyrene; **2** α-CD inclusion complex; **3** glycerol ether α-CD inclusion complex; **4** β-CD inclusion complex; **5** sulfated β-CD inclusion complex; **6** glycerol ether β-CD inclusion complex.

In the 2950–3150 cm^{-1} region, liquid 2-chlorostyrene gives three prominent bands at 3020, 3062, and 3089 cm^{-1} due to νCH=, ring νCH, and asymmetric ν=CH, respectively. The ring νCH peak of the inclusion complexes shifted to lower wavenumber than that of liquid 2-chlorostyrene.

Table 1 shows the properties of the ν(C=C) band and the ring νCH band of the 2-chlorostyrene-cyclodextrin complex. The area ratio of the phenyl/vinyl band of liquid 2-chlorostyrene was *ca.* 0.55. The area ratio of the phenyl/vinyl peak of the α-CD, glycerol ether α-CD complex, β-CD and glycerol ether β-CD complexes were *ca* 1.36, 1.36, 0.81, and 1.13, respectively. The area ratio of the

Scheme 2. Inclusion complex of 2-, 3-, and 4-chlorostyrene with α- and β-CD derivatives.
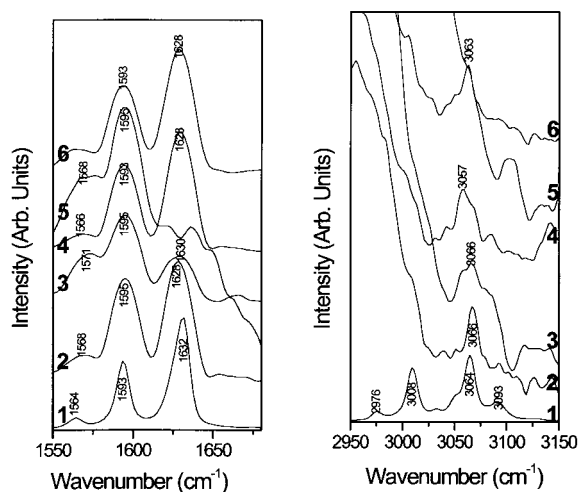

Figure 2. FT-Raman spectra of 3-chlorostyrene in the 1550–1680 and 2950–3150 cm^{-1} regions at room temperature. **1** liquid 3-chlorostyrene; **2** α-CD inclusion complex; **3** glycerol ether α-CD inclusion complex; **4** β-CD inclusion complex; **5** sulfated β-CD inclusion complex; **6** glycerol ether β-CD inclusion complex.

Figure 3. FT-Raman spectra of 4-chlorostyrene in the 1550–1680 and 2950–3150 cm^{-1} regions at room temperature. **1** liquid 4-chlorostyrene; **2** α-CD inclusion complex; **3** glycerol ether α-CD inclusion complex; **4** β-CD inclusion complex; **5** sulfated β-CD inclusion complex; **6** glycerol ether β-CD inclusion complex.

2-chlorostyrene peak included in CDs increased compared to that of pure 2-chlorostyrene. On the other hand, the full width at half maximum (FWHM) intensity of the ν(C=C) band in the inclusion complex increased compared to that of liquid 2-chlorostyrene.

There are two possibilities for 2-chlorostyrene insertion: (i) with the vinyl group inserted in the cavity or (ii) with both substituents pointing outside. A third possibility with the halogen atom inserted in the hydrophobic cavity seems unreasonable, since it is a general rule that CD cavities in-

cluded preferentially the most hydrophobic moieties of the guest molecule (e.g., the aromatic ring) [16].

Inclusion complex of 3-chlorostyrene

Figure 2 shows the FT-Raman spectra of 3-chlorostyrene in the 1550–1680 cm^{-1} and 2950–3150 cm^{-1} regions at room temperature. Liquid 3-chlorostyrene gives the phenyl ν(C=C) band at 1593 cm^{-1} and the vinyl ν(C=C) band at 1632 cm^{-1}. The area of the vinyl ν(C=C) band of

Table 1. Properties of the ν(C=C) and ring νCH bands of the 2-chlorostyrene-CD complexes

| | Individual area (%) | | Area ratio of phenyl/vinyl | FWHM of νC=C (cm^{-1})[a] | | Ring νCH (cm^{-1}) | Raman shift of ring νCH (cm^{-1})[b] |
	Phenyl	Vinyl		Phenyl	Vinyl		
2-Chlorostyrene	35.5	64.5	0.55	12.1	8.3	3062	0.0
Inclusion complex of α-CD	57.6	42.4	1.36	13.8	10.8	3060	−2.0
Inclusion complex of glycerol ether α-CD	57.9	42.1	1.36	11.6	10.8	3058	−4.0
Inclusion complex of β-CD	44.8	55.2	0.81	14.2	11.3	3061	−1.0
Inclusion complex of sulfated β-CD	_c	_c	_c	23.3	_c	–	–
Inclusion complex of glycerol ether β-CD	53.0	47.0	1.13	12.5	12.5	3061	−1.0

[a] The FWHM denotes the Full Width at Half Maximum Intensity.
[b] Raman shift = inclusion complex – liquid 2-chlorostyrene.
[c] The data cannot be calculated.

Table 2. Properties of the ν(C=C) and ring νCH bands of the 3-chlorostyrene-CD complexes

| | Individual area (%) | | Area ratio of phenyl/vinyl | FWHM of νC=C (cm^{-1})[a] | | Ring νCH (cm^{-1}) | Raman shift of ring νCH (cm^{-1})[b] |
	Phenyl	Vinyl		Phenyl	Vinyl		
3-Chlorostyrene	32.3	67.7	0.48	10.8	11.6	3064	0.0
Inclusion complex of α-CD	47.8	52.2	0.92	20.8	20.0	3066	2.0
Inclusion complex of glycerol ether α-CD	72.7	37.3	1.95	25.0	23.3	3066	2.0
Inclusion complex of β-CD	44.4	55.6	0.80	22.5	20.0	3057	−7.0
Inclusion complex of sulfated β-CD	_c	_c	_c	23.3	_c	–	–
Inclusion complex of glycerol ether β-CD	45.5	54.5	0.83	22.5	22.5	3063	−1.0

[a] The FWHM denotes the Full Width at Half Maximum Intensity.
[b] Raman shift = inclusion complex – liquid 3-chlorostyrene.
[c] The data cannot be calculated.

3-chlorostyrene in the CD complexes decreased remarkably, whereas the area of a phenyl ν(C=C) band increased compared to that of liquid 3-chlorostyrene (see Table 2).

Three prominent bands of liquid 3-chlorostyrene were also observed at 3008, 3064, and 3093 cm^{-1} due to νCH=, ring νCH, and asymmetric ν=CH, respectively. The ring νCH peak of the α- and glycerol ether α-CD inclusion complex shifted to a higher wavenumber than that of liquid 3-chlorostyrene, whereas the β-CD and glycerol ether β-CD inclusion complexes shifted to a lower wavenumber (see Table 2).

Table 2 shows the properties of the ν(C=C) and νCH bands of the 3-chlorostyrene-cyclodextrin complexes. The relative area ratio of the phenyl/vinyl peaks of liquid 3-chlorostyrene, the α-CD, glycerol ether α-CD, and glycerol ether β-CD complexes were *ca.* 0.48, 0.92, 1.95, 0.80, and 0.83, respectively. The relative area ratio of 3-chlorostyrene included in CDs increased compared to that of liquid 3-chlorostyrene. The FWHM intensity of the inclusion complex also increased compared to that of liquid 3-chlorostyrene.

Concerning 3-chlorostyrene, there are two possibilities for the guest insertion: (i) with the vinyl group inserted in the cavity or (ii) with both substituents pointing outside. Ribero-Claro *et al.* [15] studied substituted styrene molecules such as 3-bromostyrene, 3-nitrostyrene, and 3-methoxystyrene included in cyclodextrin. They suggested that bromine atoms insertion in the hydrophobic cavity is unlikely.

Inclusion complex of 4-chlorostyrene

Figure 3 shows the FT-Raman spectra of 4-chlorostyrene in the 1550–1680 cm^{-1} and 2950–3150 cm^{-1} regions at room temperature. Liquid 4-chlorostyrene gives the phenyl ν(C=C) band at 1595 cm^{-1} and the vinyl ν(C=C) band at 1632 cm^{-1}. The area of the vinyl ν(C=C) peak of 4-chlorostyrene in the CD complexes decreased remarkably, whereas the area of a phenyl ν(C=C) peak increased compared to that of liquid 3-chlorostyrene.

Three prominent bands of liquid 4-chlorostyrene were observed at 3008, 3064, and 3093 cm^{-1} due to νCH=, ring νCH, and asymmetric ν=CH, respectively. The ring νCH peak of the α-CD and glycerol α-CD complexes shifted to a higher wavenumber than that of pure 4-chlorostyrene, whereas the β-CD and glycerol ether β-CD inclusion complexes shifted to a lower wavenumber (see Table 3).

Table 3 shows the properties of the ν(C=C) and ring νCH bands of the 4-chlorostyrene-cyclodextrin complexes. The relative area ratio of the phenyl/vinyl peaks of liquid 4-chlorostyrene, α-CD complex, glycerol ether α-CD complex, β-CD complex, and glycerol ether β-CD complex were *ca.* 0.74, 1.02, 2.30, 0.95, and 0.90, respectively. The relative area ratio of 4-chlorostyrene included in CDs was greater than that of liquid 4-chlorostyrene. The FWHM intensity of the inclusion complex increased compared to that of pure 4-chlorostyrene.

Concerning 4-chlorostyrene, once again two reasonable orientations of the guest molecule are possible: (i) with the vinyl group or (ii) with the halogen substituent in the cavity.

Table 3. Properties of the ν(C=C) and ring νCH bands of the 4-chlorostyrene-CD complexes

| | Individual area (%) | | Area ratio of phenyl/vinyl | FWHM of νC=C (cm^{-1})[a] | | Ring νCH (cm^{-1}) | Raman shift of ring νCH (cm^{-1})[b] |
	phenyl	vinyl		phenyl	vinyl		
4-Chlorostyrene	42.6	57.4	0.74	20.8	9.2	3064	0.0
Inclusion complex of α-CD	50.6	49.4	1.02	22.5	11.3	3066	2.0
Inclusion complex of glycerol ether α-CD	69.6	30.4	2.30	25.8	21.6	3066	2.0
Inclusion complex of β-CD	48.7	51.3	0.95	24.2	19.2	3057	−7.0
Inclusion complex of sulfated β-CD	_[c]	_[c]	_[c]	_[c]	22.1	−	−
Inclusion complex of glycerol ether β-CD	47.5	52.5	0.90	20.4	10.0	3063	−1.0

[a] The FWHM denotes the Full Width at Half Maximum Intensity.
[b] Raman shift = inclusion complex – liquid 3-chlorostyrene.
[c] The data cannot be calculated.

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