

FULL PAPER

## Host-Guest Chemistry and Chemical Sensors: FT-IR-Analysis and Spectra Simulation of $\text{CDCl}_3$ Inclusion

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**Abstract** Host-guest principles are put into action advantageously by cyclodextrins that give remarkable sensor responses to halogenated hydrocarbons on mass-sensitive devices such as QMB (quartz micro balance) and SAW (surface acoustic wave) resonators. Modifications of the structure can tune the compound to different analytes and molecular modeling allows us to understand and predict specific host-guest interactions. The FT-IR analysis of  $\text{CDCl}_3$ , incorporated into a partially methylated cyclodextrine, yields an astonishingly strong band shift of about  $50 \text{ cm}^{-1}$  to lower wave numbers, in contrast to the permethylated product that shows a displaced band of  $10 \text{ cm}^{-1}$  for the C-D stretching vibration. The explanation can be given by semiempirical methods and force field calculations. Two  $\text{CDCl}_3$  binding sites are revealed, one being a multicentered inclusion ( $\tilde{\nu} \sim 2195 \text{ cm}^{-1}$ ) of  $\text{CDCl}_3$  at the upper rim of the  $\beta$ -cyclodextrine cone, whereas the other is incorporated within the cavity ( $\tilde{\nu} \sim 2240 \text{ cm}^{-1}$ ).

**Keywords** Host-guest chemistry, FT-IR, Force field and semiempirical calculations, Chemical sensors

### Introduction

Host-guest interactions can be exploited in the design of chemical sensors.[1] Especially supramolecular chemistry can be utilized for sensor technology with compounds like cyclodextrine, paracyclophanes and calixarenes that are capable of forming molecular cavities to include analytes because of the high preorganization of these structures. It is possible to customize these guest molecules for different hosts and influence their chemical properties by varying the size of the hollow or subunit arrangements, which is of in-

terest for both experimental results and their understanding with the help of computational chemistry. Besides separations in gas chromatography with high stereoselectivity, cyclodextrines[2,3] are already used in analytical chemistry for mass-sensitive detection principles. The hydrophilic hydroxyl groups at the upper and the lower rim of the  $\beta$ -cyclodextrine cavity affect the cross sensitivity to water, which makes it very difficult to use them as sensor materials. This problem can be solved by methylation or silylation of the hydroxyl groups of the host molecule.[4] Such derivatives can be applied for mass-sensitive measurements to QMB[5,6] or SAW[7] devices based on piezoelectric crystals.[2,8] To gain a better insight into host-guest geometry and particularly into the orientation and inclusion of the analyte in cyclodextrine, it is essential to determine the ef-

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fects of the host-guest interactions. The C-D-stretching vibration of deuteriochloroform is well suited since the bands of the host molecule do not interfere in the same spectral range. This vibrational label has been used as a conformational probe for the orientation of the nitrogen atoms in 1, (k+2) diazabicyclo[k.k.k]alkanes.[9] Based on semiempirical methods (MM3, MOPAC)[10,11] computational chemistry is applied to improve the understanding of the mechanism of the observed frequency shift in  $\text{CDCl}_3$ -host interactions. Mass-sensitive and optical measurements determine the specific sensor characteristics of the layer used.

## Experimental

### Chemicals

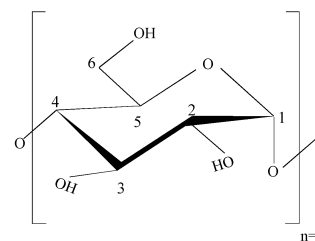
The compounds investigated are the permethylated  $\beta$ -cyclodextrin  $\text{TM}\beta\text{CD}$  and the  $\text{TM}\beta\text{CD}/\text{OH}$ , which contains only very few hydroxyl groups. These two products have been synthesized by methylation of dry  $\beta$ -cyclodextrin using iodomethane/sodium hydride. The final recrystallization from cyclohexane separates the pure methylated compound  $\text{TM}\beta\text{CD}$  from the product containing one hydroxyl group  $\text{TM}\beta\text{CD}-\text{OH}$  that corresponds to a methylation degree of 95%, experimentally verified by  $^1\text{H-NMR}$ . Position 3 (Scheme 1) of the glucose unit is most difficult to methylate[12] because of internal H-bonding between the neighboring hydroxyl groups at C-atoms 2 and 3. Thus,  $\text{TM}\beta\text{CD}-\text{OH}$  is mainly a  $\beta$ -cyclodextrin with one remaining hydroxyl group at C(3).

### Measuring procedure

Mass-sensitive measurements were performed with AT-cut QMB resonators with gold electrodes on each side (5.5 mm in diameter) operating in the thickness shear mode with a fundamental frequency of 10 MHz. A dual line chip enabled the parallel recording of a sensor and an uncoated reference line to eliminate instabilities caused by pressure or temperature fluctuations. A gas mixing apparatus was used to set solvent vapor concentrations and resonance frequencies were measured with a Keithley 775 A frequency counter and transferred via an IEC bus to a personal computer and subtracted digitally.

Spectra in solution and gas phase were measured with a Perkin-Elmer FT-IR spectrometer system 2000 equipped with gas and liquid cells. For the measurements, the thin films were exposed to  $\text{CDCl}_3$  in a temperature controlled cell with  $\text{CaF}_2$  or  $\text{NaCl}$  windows. All measurements were taken at a temperature of 20 °C. The inner surface of one of the  $\text{CaF}_2$ -windows was coated with a 5  $\mu\text{m}$  film of  $\text{TM}\beta\text{CD}$  or  $\text{TM}\beta\text{CD}-\text{OH}$ . The length of the gas cell was 1 mm, spectra were taken with 20 coadded scans with a resolution of 2  $\text{cm}^{-1}$ . The background taken was the coated substrate with 0% r. H. The desired concentration of the solvent analyte and relative

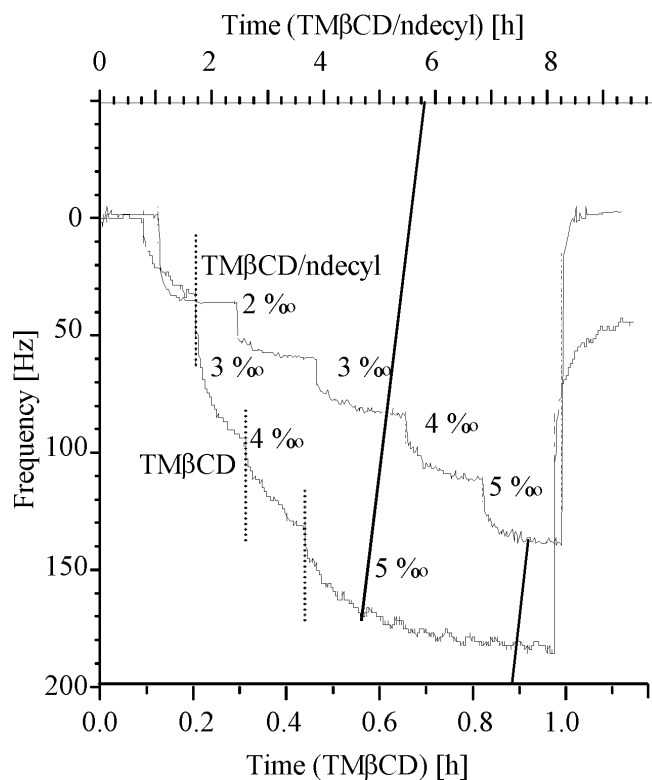
**Scheme 1** In the cross-section of the  $\beta$ -cyclodextrine cavity represents two opposite glucose units



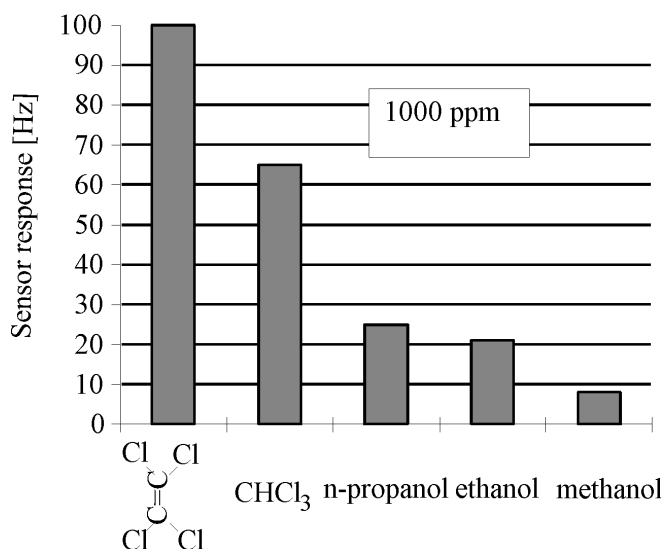
humidity were adjusted with mass flow controllers (Tylan FC-260).

### Force-field and semiempirical calculations

Force-field calculations[13,14] of the structures were performed with the HyperChem 5.1[15] modeling software on a pentium computer to preoptimize the geometries of the molecules and generate the input coordinates for MOPAC V6[16,17]. To shorten calculation-time when optimizing big structures, the files were transferred to a RISC workstation (HP 9000/715-80) and were calculated with the MM3/92

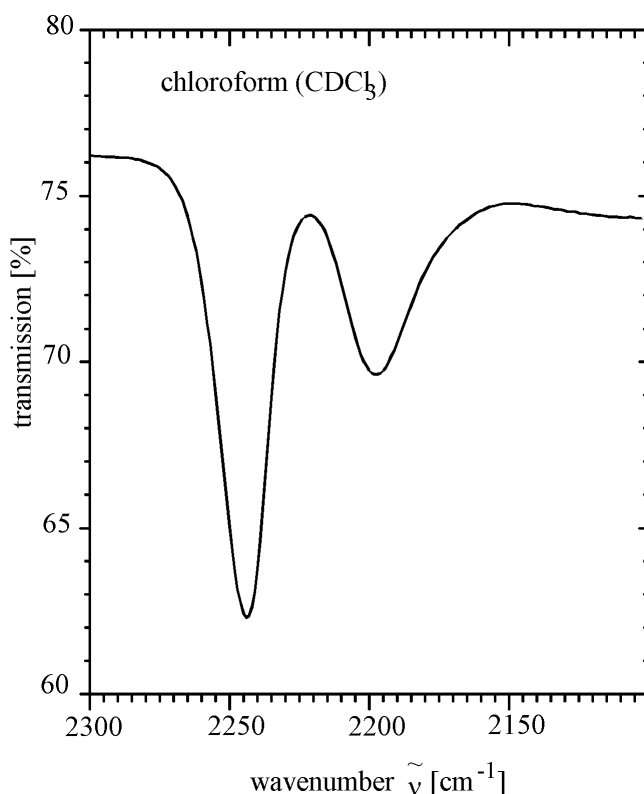


**Figure 1** Sensor responses of a 10 MHz QMB coated with a 100 nm  $\text{TM}\beta\text{CD}$  and a  $\text{TM}\beta\text{CD}/\text{ndecyl}$  layer to chloroform at 20 °C,  $\text{RH} = 30\%$



**Figure 2** Sensor responses of a 10 MHz QMB coated with a 220 nm TM $\beta$ CD layer to different solvents at 20 °C, RH = 30 %

version of Allinger's molecular modelling program.[18] Afterwards these output files were transferred back to the PC to obtain the internal distances and angles. Since HyperChem allows the input of crystallographic data, an X-ray structure of  $\beta$ -cyclodextrine was used as an initial model. The methylated structure was optimized by keeping the ring structure fixed and optimizing the alkyl chains and afterwards *vice versa*. This was repeated until no further changes occurred. The partially methylated cyclodextrine (TM $\beta$ CD-OH) was generated by the calculation of seven different conformers, each of them having a different methoxy group changed to OH. The conformer with the lowest energy was chosen for the interaction with chloroform. With this method a specific interaction of CCl<sub>3</sub> and TM $\beta$ CD-OH could be made plausible. Final optimizations of the structure and calculations of the force matrix and vibrational spectrum were performed with semiempirical methods using the MOPAC V6 program with PM3 parameters on the workstation. Since the complete arrangement is too complex for the semiempirical calculation, a Z-matrix of a moiety of this complex was developed. Thus, only a fraction of the whole structure was optimized and for this purpose two glucose units were separated and saturated with hydroxyl groups. The mutual angle of these rings was set fixed to simulate the arrangement in the cone. No other rigid units were defined. Optimizations of the structures of the host and guest were performed separately. When adding the guest molecule to the host, the guest molecule was held fixed, while the host was optimized in the host-guest complex. Afterwards the host was held fixed and the guest was optimized. This was repeated until no changes occurred. The vibrational spectra were obtained with the FORCE command of the PM3 method.



**Figure 3** FT-IR-spectrum of CDCl<sub>3</sub>: a 10  $\mu$ m film of partially methylated  $\beta$ -cyclodextrine (TM $\beta$ CD-OH) in a vapor of CDCl<sub>3</sub>. Spectra were taken with 20 scans with a resolution of 2 cm<sup>-1</sup>

## Results

According to mass-sensitive experiments using QMB devices, thin films of TM $\beta$ CD and TM $\beta$ CD-OH absorb CDCl<sub>3</sub> from the gas phase. Figure 1 shows these sensor responses of 10 MHz QMBs coated with TM $\beta$ CD and its derivative with a n-decyl chain bound *via* ether bridges. A linear dependency between concentration and mass-sensitive effect is observed for both and the effect is fully reversible. Both layers are approximately 100 nm thick and since TM $\beta$ CD forms a very compact layer, the sensor response is rather sluggish and slow and reacts on a time scale that is larger by a factor of ten. The n-decyl spacer loosens up the layer and diffusion to deeper parts of the layer is more easily possible, so retention times are down to a few minutes. The overall effect for the TM $\beta$ CD/n-decyl layer is smaller. A possible explanation for this could be that some of the alkyl chains block the entrance of some of the cavities, so the number of accessible guest molecules is smaller. Figure 2 gives sensor responses of a 10 MHz QMB coated with TM $\beta$ CD to some solvents with different donor-acceptor properties and polarizability. The largest effects are obtained for perchloroethylene and chloroform. Due to the

**Table 1** Calculated frequencies of  $\text{CDCl}_3$  compared with experimental values. Calculations were performed using all implemented parameters of the different semiempirical methods of MOPAC V6

vibrations of $\text{CDCl}_3$	exp. [ $\text{cm}^{-1}$ ]	MNDO [ $\text{cm}^{-1}$ ]	MINDO/3 [ $\text{cm}^{-1}$ ]	AM1 [ $\text{cm}^{-1}$ ]	PM3 [ $\text{cm}^{-1}$ ]
$\nu(\text{C-Cl})$ -stretching, sym., $a_1$	651	739	608	685	623
$\nu(\text{C-Cl})$ -stretching, asym., e	742	829	649	773	645
$\nu(\text{C-D})$ -rocking, asym., e	913	1021	926	898	847
$\nu(\text{C-D})$ -stretching, $a_1$	2258	2394	2557	2199	2168

**Table 2** Calculated C-D-stretching frequencies, relative absorption coefficients and values of  $\text{CDCl}_3$  bond length and order compared with experimental values. Semiempirical calculations were performed with MOPAC 6, PM3

solvent	$\Delta\tilde{\nu}$ [ $\text{cm}^{-1}$ ] exp. [a]	$\Delta\tilde{\nu}$ [ $\text{cm}^{-1}$ ] calc.	$\Delta A$ exp. [b]	$\Delta A$ calc.	calc. bond length [ $\text{\AA}$ ]	calc. bond order
$\text{CDCl}_3$ pure	0	0	1	1	1.1114	0.9644
THF	-9	-10	3.8	4	1.1134	0.9579
methanol	-8	-12	4	3.8	1.1129	0.9597
triethylamine	-76	-66	11	10	1.1266	0.9340

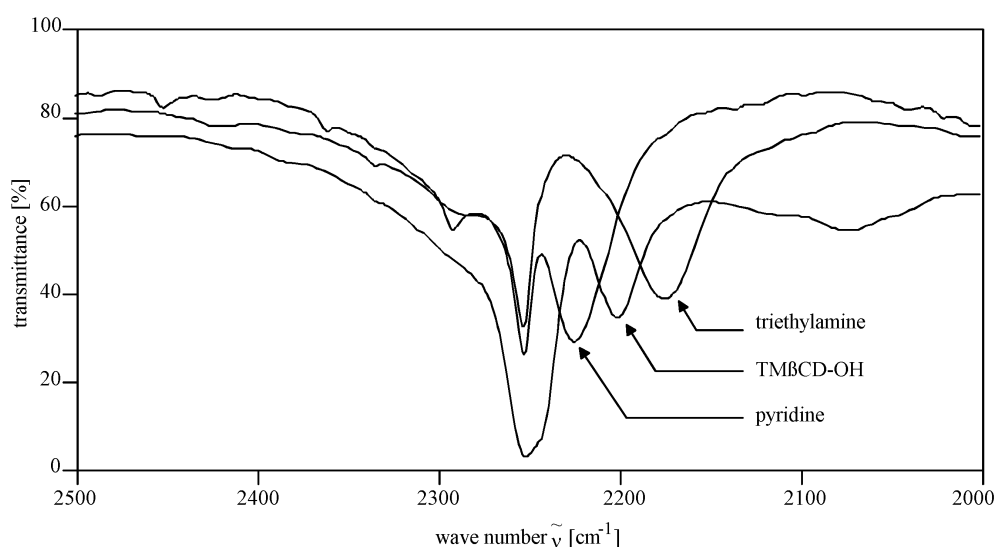
[a]  $\Delta\tilde{\nu}$ : frequency shift compared with pure  $\text{CDCl}_3$ ,  $\Delta\tilde{\nu} = \tilde{\nu} - \tilde{\nu}_0$  including sign

[b]  $\Delta A$ : proportion of the absorbance  $A$  relative to the absorbance  $A_0$  of pure  $\text{CDCl}_3$ ,  $\Delta A = A / A_0$

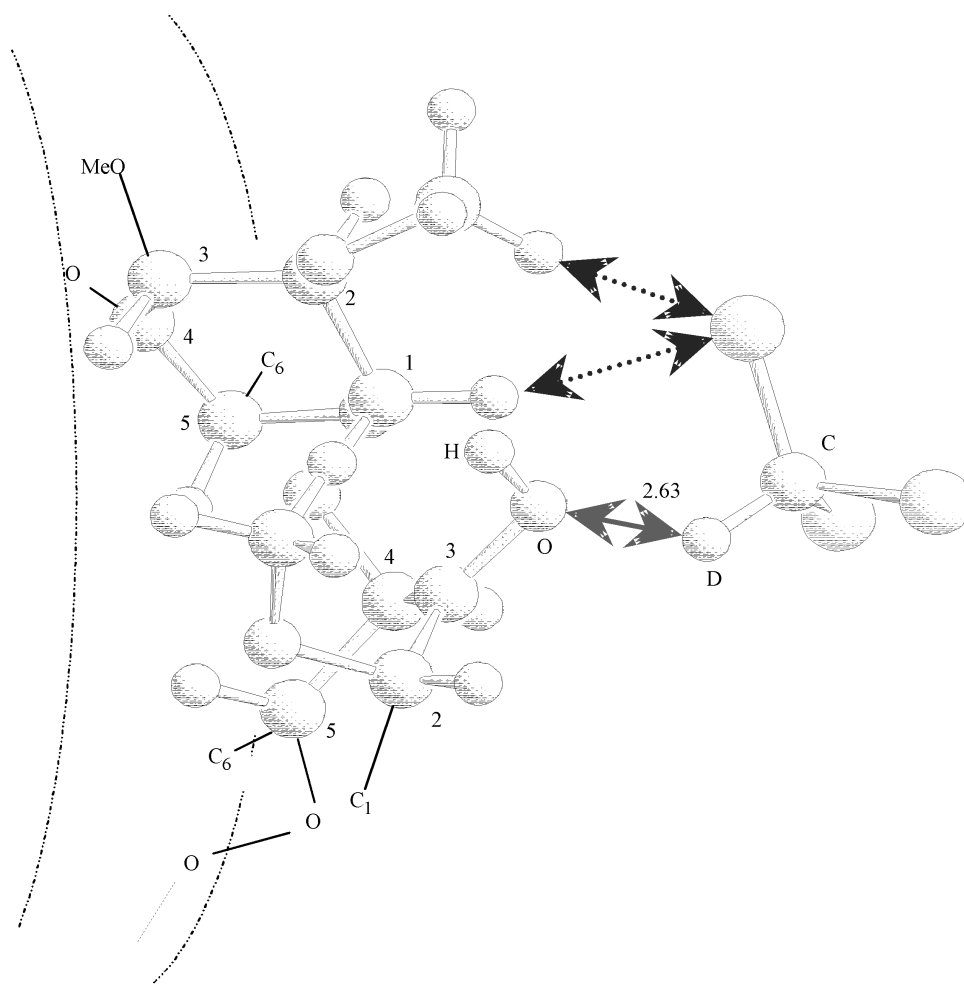
high number of oxygen atoms on the inner walls of the cavity, the cyclodextrine possess donor properties and polarizability and are therefore very suitable for the detection of halogenated solvent vapors with chlorine atoms. Permethylation of the OH-groups inverts the polarity of the compound into hydrophobic and generates a cavity that is still capable of strong interactions in the interior. Since the methyl group is very small, the cavity is not closed by permethylation, but some deformations occur. The alkylations increases the height of the cone, widens the upper rim and

tightens the under rim of the cavity with a very much reduced water cross sensitivity.[2]

If the sensor material TM $\beta$ CD-OH is applied to a  $\text{CaF}_2$  substrate, the sensor effect to  $\text{CDCl}_3$  can be followed by FT-IR as described. In the spectra two bands of the C-D stretching vibration can be observed. The major band is shifted about  $10 \text{ cm}^{-1}$  to lower wave numbers (at  $2195 \text{ cm}^{-1}$ ) compared to free deuteriochloroform. An additional broader band shows a very appreciable dislocation of about  $50 \text{ cm}^{-1}$  (to  $2243 \text{ cm}^{-1}$ , see Figure 3). When permethylated cyclodextrins are stud-

**Figure 4** FT-IR spectrum of  $1.8 \text{ mol/l CDCl}_3$  in  $\text{CCl}_4$  after addition of  $21 \text{ mmol/l}$  partially methylated  $\beta$ -cyclodextrine (TM $\beta$ CD-OH),  $0.25 \text{ mol/l}$  triethylamine and  $0.4 \text{ mol/l}$  pyridine. Spectra were taken in a  $\text{CaF}_2$ -cell ( $d = 1 \text{ mm}$ ) with 20 scans and a resolution of  $2 \text{ cm}^{-1}$ 

**Figure 5** Scheme of the final estimated complex between  $\text{CDCl}_3$  and  $\text{TM}\beta\text{CD-OH}$ . Calculations were performed with MOPAC V6 with PM3 parameters



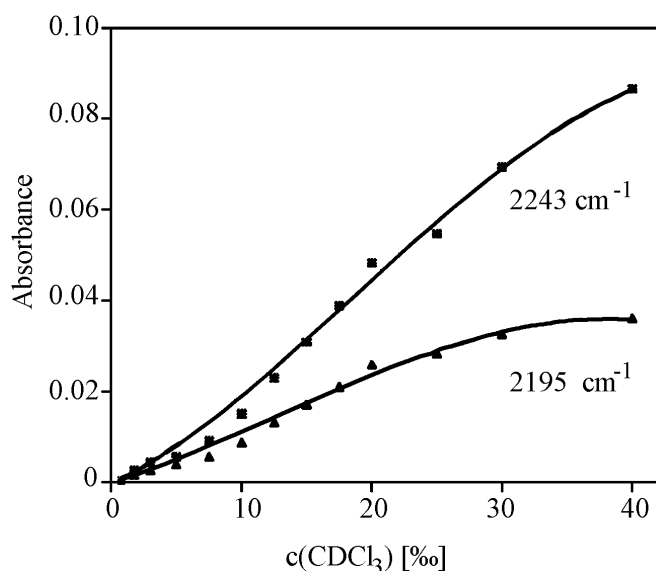
ied, this second significant band shift change is not observed. In  $\text{CCl}_4$  as solvent with  $\text{CDCl}_3$  and  $\text{TM}\beta\text{CD-OH}$  this effect is also shown. By adding analytes with ether or alcohol functionalities to the  $\text{CDCl}_3$  solutions instead of  $\text{TM}\beta\text{CD-OH}$ , the shift is by about  $10\text{ cm}^{-1}$ . Nitrogen containing donors such as triethylamine, however, can force an experimentally measured frequency shift of up to  $90\text{ cm}^{-1}$  to lower wave numbers. Figure 4 shows FT-IR spectra of  $\text{CDCl}_3$  in  $\text{CCl}_4$  after addition of  $\text{TM}\beta\text{CD-OH}$ , triethylamine and pyridine.

To elucidate the nature of the band shift, model calculations were performed. The C-D vibration frequencies of  $\text{CDCl}_3$  were calculated using all implemented parameters of MOPAC V6. Different semiempirical methods were used and Table 1 shows that PM3 gives the best results compared to the experiments. Differences could be due to anharmonicity of large amplitudes and to coupling between vibrational modes that is not accounted for in the computational model. Having found that PM3 works best, in a second step calculations of complexes between  $\text{CDCl}_3$  and single solvent molecules were performed to interpret experimental FT-IR spectra. Table 2 gives a comparison of measured and calculated data of the C-D stretching frequencies and their relative absorbances. Although the absolute values of the results in Table 1 show an offset, the frequency shifts for the com-

plexes of different solvents with  $\text{CDCl}_3$  compared with the pure  $\text{CDCl}_3$  in Table 2 are very close to the experimental data.

Based on X-ray structure[19]  $\text{TM}\beta\text{CD}$  and several conformers of  $\text{TM}\beta\text{CD-OH}$  were calculated using the MM3 force field program. These calculations show that the free hydroxyl group is located at the broader end of the cone and is orientated to the outside. The optimized structure yields a stabilization by  $7.7\text{ kcal}\cdot\text{mol}^{-1}$  in comparison to  $14.2\text{ kcal}\cdot\text{mol}^{-1}$  of a chloroform situated in the cone. The semiempirical calculation of the moiety containing only two glucose units indicates a dipole-dipole interaction between the hydroxyl group and the C-D-bonding. Furthermore, the complex is stabilized by van der Waals interactions between the chlorine and a methoxy group of the cyclodextrine. Figure 5 shows the calculated structure of the complexes between  $\text{CDCl}_3$  and  $\text{TM}\beta\text{CD-OH}$ . This final geometry exhibits a calculated frequency shift of  $36\text{ cm}^{-1}$  (about  $50\text{ cm}^{-1}$  experimental) and a relative absorption coefficient of 0.783 compared to 0.284 of the pure  $\text{CDCl}_3$ .

To determine the amount of incorporated  $\text{CDCl}_3$ , saturation experiments were performed. Figure 6 shows the absorbances of two C-D-stretching vibrations (Figure 3) due to an exposure of  $\text{TM}\beta\text{CD-OH}$  to  $\text{CDCl}_3$  gas. As can be seen,



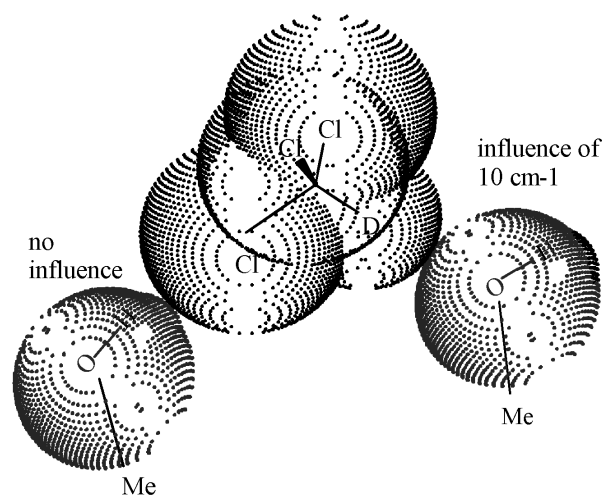
**Figure 6** Absorbance of the two C-D-stretching vibrations of  $\text{CDCl}_3$  incorporated in  $\text{TM}\beta\text{CD-OH}$  as a function of  $c(\text{CDCl}_3)$ . NaCl-cell ( $d = 1 \text{ mm}$ ), coated on both sides ( $\sim 5 \mu\text{m}$ ) with  $\text{TM}\beta\text{CD-OH}$ ,  $20^\circ\text{C}$ ,  $\text{RH} = 0\%$ , spectra were taken with 20 scans and a resolution of  $2 \text{ cm}^{-1}$

the absorbance at  $\tilde{\nu} = 2195 \text{ cm}^{-1}$  shows saturation behavior above 3%  $\text{CDCl}_3$  in the state of saturation, whereas the absorbance of the stronger shifted band  $\tilde{\nu} = 2243 \text{ cm}^{-1}$  increases monotonously.

## Discussion

The mass-sensitive measurements proved incorporation of chloroform into the cyclodextrine compounds. Obviously more  $\text{CDCl}_3$  is incorporated by the layers than cavities are available. The FT-IR spectra presented clearly indicate that different binding sites for  $\text{CDCl}_3$  in  $\text{TM}\beta\text{CD-OH}$  exist. The plateau of the absorbance at  $2195 \text{ cm}^{-1}$  proves specific interaction and the building of stoichiometric complexes, while the continuous increase of the absorbance at  $2243 \text{ cm}^{-1}$  indicates that interstitial sites must also be considered. To expound this phenomenon, calculations were made by varying the distance between the two centers. As shown in Figure 7, polar interactions of  $\text{CDCl}_3$  with methanol were studied. The formation of a hydrogen binding between the chlorine atom in  $\text{CDCl}_3$  and the  $-\text{OH}$  of methanol shows obviously no effect. The oxygen donor atom of methanol forms a hydrogen bond to the "D" of  $\text{CDCl}_3$  that gives a frequency shift of only  $10 \text{ cm}^{-1}$ .

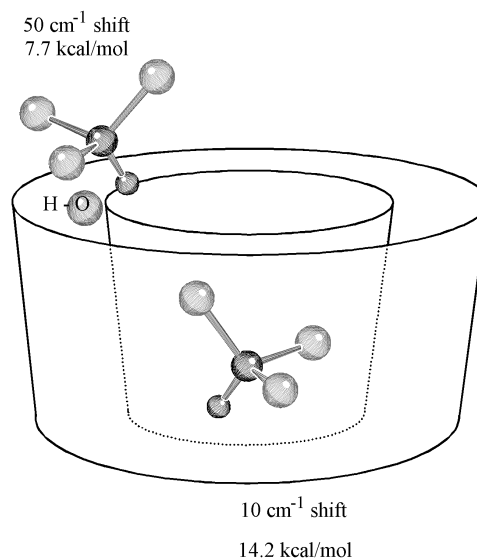
The experimental comparison of the complexes of deuteriochloroform and the two different  $\beta$ -cyclodextrine derivatives indicates that the single free hydroxyl group is essential in the complex interaction of the strongly shifted vibration band observed. This finding corresponds to both the measured experimental data and the calculated vibrations.



**Figure 7** Two different interaction possibilities between  $\text{CDCl}_3$  and hydroxyl groups. Prediction of a polar interaction between  $\text{CDCl}_3$  and a hydroxyl-function. Calculations were performed with MOPAC V6/PM3

The addition of dipole-dipole interaction and two van der Waals bindings, as shown in Figure 5, influences the C-D-bond.

According to the fact that the major band at  $2243 \text{ cm}^{-1}$  can be observed in both derivatives, this frequency shift is



**Figure 8** Semiempirical calculation of the structure of the complexes of  $\text{TM}\beta\text{CD-OH}$  with  $\text{CDCl}_3$  for the two observed IR-absorptions using PM3 parameters of MOPAC V6. To increase clarity, several atoms of the calculated structure are not depicted

caused by the insertion of a chloroform molecule into the cone forming a host-guest complex. The final structure shows the normal host-guest complex inside the cone that is applied in mass-sensitive devices. One deuteriochloroform molecule is situated inside the cone with a strong van der Waals interaction to the hydrophobic walls of the  $\beta$ -cyclodextrine. This highly stabilized complex is responsible for the sensitivity of methylated  $\beta$ -cyclodextrine in mass recording experiments with QMB and SAW.

Obviously calculations and measurements of the frequency  $\tilde{\nu}$  of the C-D vibration of  $\text{CDCl}_3$  and methanol in the liquid phase do not lead to the observed frequency shift of  $50 \text{ cm}^{-1}$ . The strong frequency shift is only observed by TMBCD-OH and is caused by a complexation of the multicenter bond at the upper rim where the hydroxyl group is situated. Figure 8 shows semiempirical calculation of the structure of the complexes of TMBCD-OH with  $\text{CDCl}_3$  for the two observed IR-absorptions. A sufficient effect can only be found if the  $\text{CDCl}_3$  participates in a multicentered bonding, which perhaps could lead to minor changes in the lengths of the O - D - C bond resulting in a change of the force constant. Hereby the three center bindings fix the  $\text{CDCl}_3$  molecule at the surface of the upper rim, which extends the  $\text{CDCl}_3$  molecule, so that the C-D-bond is elongated and the C-D-band is shifted to lower energy. This effect can be simulated with semiempirical calculations so that the scheme given in Figure 8 is a good estimate of the structure giving the FT-IR bands of Figure 3.

## Conclusions

This computational study demonstrates the application of molecular modeling to provide meaningful structural information on the host-guest interactions of cyclodextrine and chloroform. In this way computational chemistry helps to obtain a better understanding of what happens during the inclusion process and it is even possible to visualize the three dimensional structures of the host-guest interactions and to predict interaction energies for the inclusion of the analyte. This saves time and money consuming synthesis and makes molecular modeling a great tool for the design of sophisticated chemical sensitive layers.

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