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# Study of the Inclusion Complexes of $\beta$-Cyclodextrin with the Sodium Salt of Trisulfonated Triphenylphosphine

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**Abstract.** The formation of inclusion complexes between the sodium salt of trisulfonated triphenylphosphine and $\beta$-cyclodextrin has been investigated at two temperatures by high field nuclear magnetic resonance, electrospray mass and UV-vis spectroscopies. At 268 K, titration experiments and Job's method suggest that the major species in solution is a 1 : 1 inclusion complex. The molecular geometry of this inclusion complex was studied using the ROESY NMR technique complemented by molecular modelling. All these methods converged towards the structure attained by inserting one aromatic ring into the hydrophobic cavity of the host from the side of the secondary hydroxyls. At 298 K, a higher proportion of 2 : 1 and 3 : 1 complexes induces strong alterations of the NMR signals, preventing an easy and reliable determination of association constants. Nevertheless, an apparent association constant can be determined from UV-vis data by assuming a 1 : 1 equilibrium. The geometry of the 2 : 1 and 3 : 1 complexes is also briefly discussed from ROESY NMR experiments.

**Key words:** inclusion complex, $\beta$-cyclodextrin, trisulfonated triphenylphosphine, NMR spectroscopy, electrospray mass spectroscopy, UV-vis spectroscopy, molecular modelling.

## 1. Introduction

Native cyclodextrins (CDs) are cyclic oligosaccharides composed of six($\alpha$-), seven($\beta$-), or eight($\gamma$-) $\alpha$-1,4-linked D-glucopyranose residues (Scheme 1). They form inclusion complexes with a wide range of molecules and thus find numerous applications [1]. In particular, the importance of $\beta$-CDs in transition-metal catalyzed reactions in two-phase systems has rapidly grown in recent years [2]. Indeed, owing to a subtle molecular recognition process between the organic substrate

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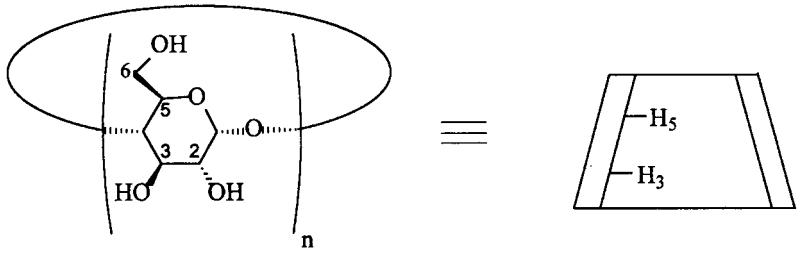
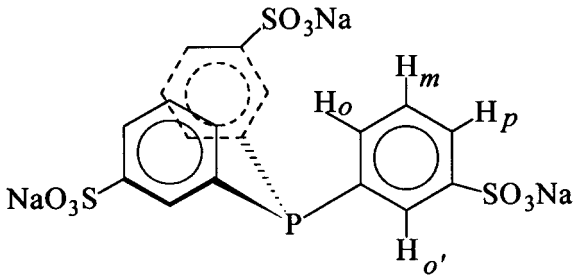



n = 6 α-cyclodextrin
n = 7 β-cyclodextrin
n = 8 γ-cyclodextrin

*Scheme 1.* Schematic representation of the shape of $\alpha$-, $\beta$- and $\gamma$-CD. The protons H-3 and H-5 are situated inside the host cavity, whereas protons H-1, H-2 and H-4 point outwards.




*Scheme 2.* Representation of the sodium salt of trisulfonated triphenylphosphine (TPPTS). Protons of only one aromatic ring have been annotated (H-m, H-p, H-o′ and H-o).

and the host cavity of CD, these compounds make it possible to improve greatly the catalytic activity [3–9] and to achieve substrate selective catalytic reactions which cannot be performed with conventional transition metal catalysts [10, 11]. One of the most used ligand in two-phase media involving CDs as inverse phase transfer catalysts is the sodium salt of the trisulfonated triphenylphosphine (P(*m*-$C_6H_4SO_3Na)_3$; TPPTS – scheme 2) [12–15]. Indeed, this ligand is a non-detergent, highly water soluble, non-toxic and easily synthesized from bulk available and inexpensive triphenylphosphine [16–19]. Recently, we have reported that TPPTS can form inclusion complexes with $\beta$-CD [20] and that this inclusion process could probably explain the selectivity decrease observed during the rhodium catalyzed hydroformylation of olefins [21].

In order to get a better insight into the selectivity decrease and to optimize the catalytic properties of the $\beta$-CD, a systematic characterization of the TPPTS/$\beta$-CD complexes has been undertaken. Indeed, the full determination of the inclusion complex, i.e., the stoichiometry, the association constant and the geometry was not achieved in our previous work [20]. The present study was performed using high field NMR and UV-vis spectroscopies at 268 and 298 K. The intermolecular proximity and the orientation of the TPPTS in the host cavity of $\beta$-CD were invest-

igated with the aid of two-dimensional rotating frame experiments (2D-ROESY) that provide the most reliable information about the relative inter proton distances in CD complexes [22–25]. Force field molecular modelling was also used to derive a realistic model for the TPPTS/$\beta$-CD complex.

## 2. Experimental

### 2.1. MATERIALS

The sodium salt of the trisulfonated triphenylphosphine (TPPTS) was synthesized as reported by Gärtner *et al*. [26] and was recrystallized in a mixture of methanol and water. $\beta$-CD was purchased from Aldrich and was carefully dried before use. $D_2O$ (99.95% isotopic purity) was obtained from Merck.

### 2.2. MEASUREMENTS

The NMR and UV experiments at 268 K were performed on liquid solutions. In order to avoid solidification of TPPTS/$\beta$-CD solutions at this temperature, the samples were filtered on a 0.45 $\mu$m pore size membrane filter tip (MILLIPORE) before analysis.

The $^1$H NMR spectra were recorded at 600.13 and 300.13 MHz on Bruker Avance DMX and DRX spectrometers, respectively. The probe temperature was set at 268 or 298 $\pm$ 0.1 K using a Bruker BVT 2000 variable temperature unit. Chemical shifts are given in parts per million (ppm) relative to trimethylsilyl-3-propionic acid-$d_4$-2,2,3,3 sodium salt (98% atom D) in $D_2O$ using internal capillary. The 2D-ROESY experiments were run on the 600 MHz instrument using the software supplied by Bruker. Mixing times for ROESY experiments were set at 300 ms. Spectra were acquired with 1024 $\times$ 256 complex points and transformed after zero filling to 2 $\times$ 1 k and multiplication with $\pi/4$ shifted squared sine in both dimensions. The resolution was 2.9–11.7 Hz/point in F2 and F1, respectively

UV-vis spectroscopy was performed on a Perkin Elmer Lambda 2S spectrometer. The cell used was placed in a cuvette holder and the temperature was kept constant at 268 or 298 K $\pm$ 0.1 by means of a thermostated bath. The TPPTS concentration was fixed at either 0.1 mM or 1 mM.

Electrospray mass spectrometry experiments were performed on a Micromass Quattro II. The TPPTS was dissolved in a 50 : 50 mixture of water and acetonitrile containing ammonium acetate (0.06 mM) to obtain a concentration of 20 pmol/$\mu$l. The solution was introduced through the fused silica inlet capillary at a flow rate of 3 $\mu$l/min. The ion spray needle potential was set at 3100 V. In order to investigate the effects of higher orifice potentials on the fragmentation of the parent ions, the orifice potential was varied between 10 and 90 V. The temperature of the interface was set at 80 °C. Positive ion detection mode was used and the calibration was performed with polypropylene glycol.

### 2.3. CALCULATION OF ASSOCIATION CONSTANTS

The *meta*-proton of the TPPTS was used for the determination of the association constant as no spectral overlap impedes a reliable determination of the chemical shift. Assuming a 1 : 1 inclusion mechanism, the observed chemical shift of this proton ($\delta_{OBS}$) and the complex concentration [COMP] are described as follows:

$$\delta_{OBS} = (\delta_{TPPTS} * [TPPTS] + \delta_{COMP} * [COMP])/[TPPTS]_T, \quad (1)$$

$$[COMP] = -\frac{1}{2}\left[\left(\frac{1}{K_f} + [CD]_T + [TPPTS]_T\right)^2 - 4[CD]_T * [TPPTS]_T\right]^{1/2} + \frac{1}{2}\left(\frac{1}{K_f} + [CD]_T + [TPPTS]_T\right), \quad (2)$$

where $K_f$ and T stand for formation constant and total, respectively. For a given value of $K_f$, [COMP] is known and $\delta_{COMP}$ may be calculated from (1) for each $[CD]_T$. Standard deviation over $\delta_{COMP}$ is minimized relative to $K_f$ to obtain the 1 : 1 association constant [27].

A similar algorithmic treatment was used to calculate a 1 : 1 association constant from UV-vis data. The algorithmic treatment was applied to first derivatives of UV spectra, so that no effect from the refractive index relative to $\beta$-CD was observed. The association constant was also determined by applying a spectral displacement method with methyl-orange (MO) in its basic form. 1 : 1 Equilibria between MO, $\beta$-CD and TPPTS are described as follows:

$$(\beta\text{-CD/MO}) + \text{TPPTS} \rightleftharpoons \beta\text{-CD} + \text{TPPTS} + \text{MO} \leftrightharpoons (\beta\text{-CD/TPPTS}) + \text{MO}.$$

While concentrations of MO and $\beta$-CD are kept constant, the addition of TPPTS implies an absorbance increase, proportional to the expulsion of MO from the $\beta$-CD cavity. The formation constant of $\beta$-CD/TPPTS can therefore be deduced from this absorbance difference. An algorithmic method was used for data treatment. Its principle consists in the calculation of the concentrations of the complexes, by considering the two equilibria successively in an iterative way [27]. Spectra were recorded between 520–530 nm for a MO concentration fixed at 0.1 mM. This wavelength range corresponds to the optimal spectral variation between the free and complexed forms of MO, thus leading to an increased precision of the calculated formation constant.

### 2.4. MOLECULAR MODELLING

Simulations were carried out using CAChe [28], integrating MM3 force field. All energy minimisations were performed by using successively steepest descent, conjugate gradient and the Newton–Raphson algorithm, with final convergence fixed

to 0.001 kJ/mol. The $\beta$-CD initial structure was obtained from a crystallographic study from Harata [29]. The benzyl alcohol and water molecules described in the Harata study were removed and the macrocycle was then relaxed by energy minimisation. Since the modelling of the ionic form of the TPPTS requires special parameterisation, the docking of the acidic form of the phosphine was then realised in order to estimate the steric complementarity between host and guest. Each inclusion mode of the acidic form of TPPTS has been investigated by moving this guest along a vector perpendicular to the mean plane of the CD linkage oxygens $O_4$, with a 0.2 Å increment. Each structure was fully energy minimized.

## 3. Results and Discussion

### 3.1. STUDY AT 268 K

The evidence of an inclusion process between TPPTS and $\beta$-CD and the determination of the stoichiometry were provided by the continuous variation technique [30]. A series of samples containing variable ratios of $\beta$-CD and TPPTS was prepared keeping the total concentration of species constant (10 mM in the present case). The NMR spectra of the samples are presented in Figure 1.

Each spectrum denotes chemical shift variations for the guest protons as well as for most of the host protons. The largest differences in the chemical shifts for the $\beta$-CD protons are observed for the protons situated *inside* the hydrophobic cavity (H-3 and H-5). This observation proves the reality of an inclusion process. Indeed, when external interaction phenomena occur between a CD and a guest molecule, no variation of chemical shifts for these inner protons is observed [22]. Under the present conditions, only shifts of these signals were observed and no new peak which could be assigned to the pure complex appeared. This observation implies that the complexation is a dynamic process, the included TPPTS being in exchange between free and bound states. Job's plots that supply the stoichiometry of the inclusion complex [30, 31] were derived from the corresponding $^1$H NMR spectra and are presented in Figure 2 for selected protons from $\beta$-CD and TPPTS.

All plots show a maximum at r = 0.5 and highly symmetrical shapes, suggesting that a 1 : 1 complex is formed [30, 31]. The plot of the chemical shift of the TPPTS *meta*-proton as a function of the CD/TPPTS molar ratio is also consistent with a 1 : 1 stoichiometry. Indeed, the chemical shift values increase linearly up to a ratio equal to 1 and level off markedly beyond this ratio (Figure 3).

These NMR data fit well with a 1 : 1 equilibrium and an association constant of 12000 $M^{-1}$ $\pm$10% can be calculated (see experimental). The effect of $\beta$-CD on the UV-vis spectra of TPPTS was also quantitatively investigated by holding the concentration of the TPPTS constant at 0.1 mM and by varying the cyclodextrin concentration up to 10 mM. The spectral variation upon complexation is described in Figure 4, which shows a bathochromic shift of the $\lambda_{max}$ from 261.3 nm to 262.5 nm.

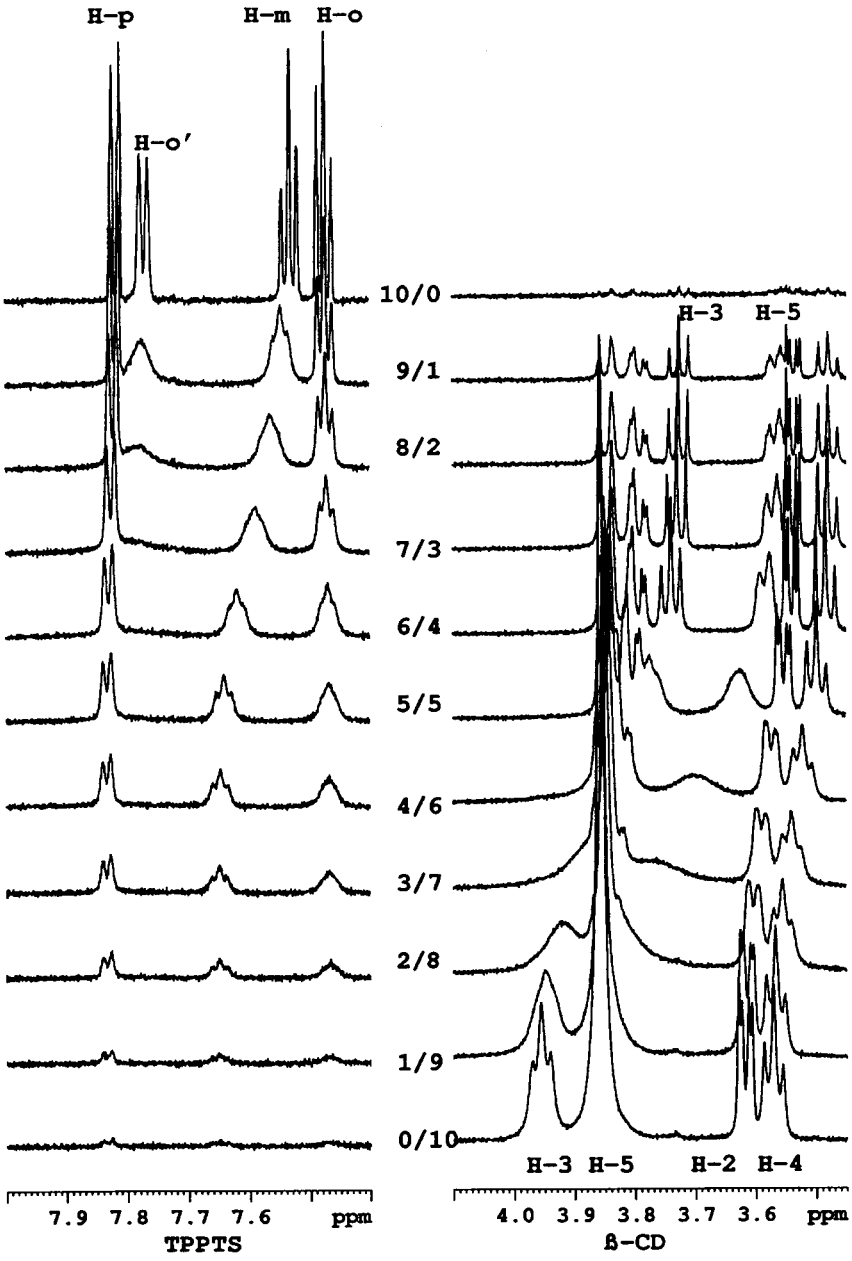



*Figure 1.* Partial 600 MHz $^1$H NMR spectra of TPPTS/$\beta$-CD mixtures in $D_2O$ at 268 K. The total concentration of species is 10 mM. The TPPTS to $\beta$-CD ratios are given between the two sets of spectra.

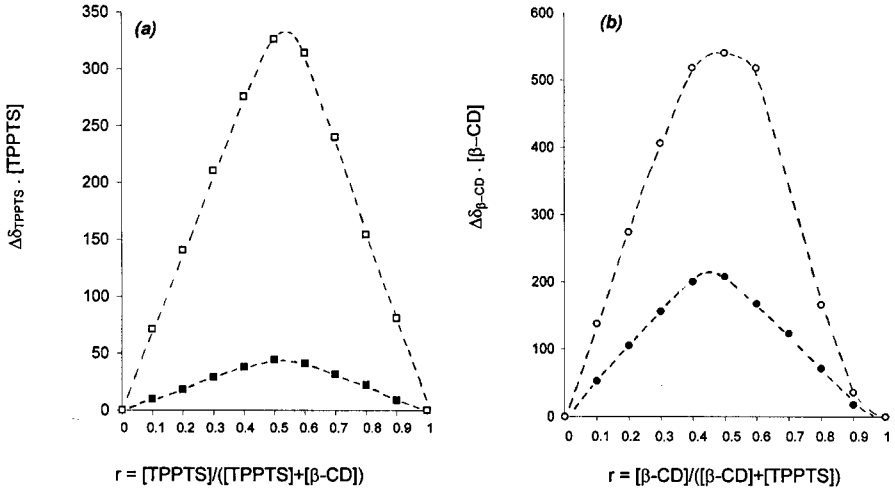



*Figure 2.* Continuous variation plots (Job's plots) derived from experimental data of Figure 1 for selected protons (a) of TPPTS (H-m: □; H-p: ■) and (b) of $\beta$-CD (H-1: ●; H-3: ○). For the H-3 proton, the experimental datum relative to the ratio 0.7 cannot be determined due to the spectral overlap between the H-6 and H-3 protons.

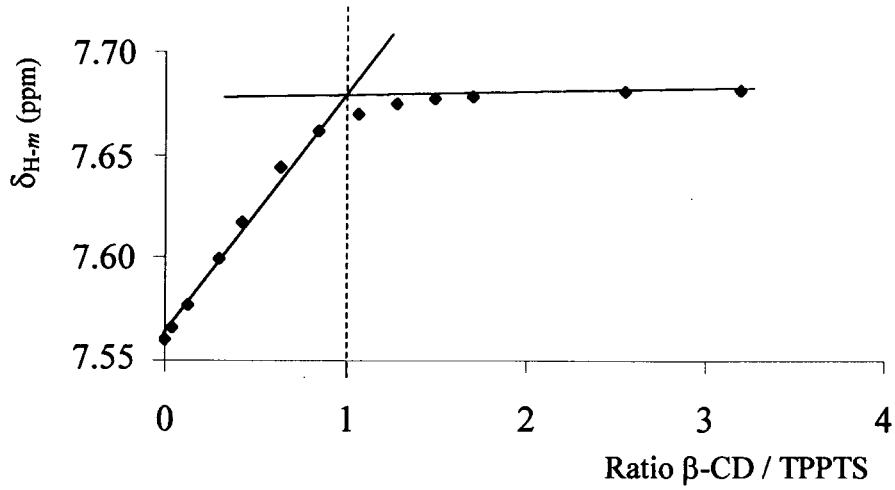



*Figure 3.* Graph of the chemical shifts of the TPPTS *meta*-proton (ppm) as a function of the $\beta$-CD/TPPTS mole ratio in aqueous solution. The TPPTS concentration was fixed at 2 mM.

The UV-vis data were in agreement with a 1 : 1 equilibrium and led to an association constant of 3100 $M^{-1}$ $\pm$10%. The lack of agreement observed between the association constant value derived by NMR spectroscopy and that obtained by UV measurements is rather surprising and will be discussed further.

In order to obtain information on the geometry and orientation of the guest in the cavity, two-dimensional rotating-frame NOE experiments (ROESY) have been performed. In ROESY experiments, dipolar interactions between protons at

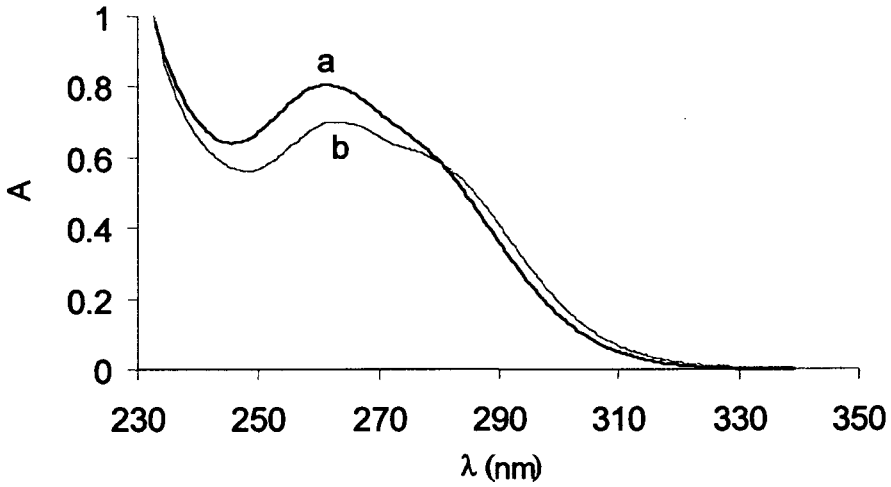



*Figure 4.* UV spectra of TPPTS (0.1 mM) in the absence (a) and in the presence of $\beta$-CD (10 mM), (b) at 268 K.

a distance less than 3–4 Å are detected as cross-peaks in a bi-dimensional map, indicating the reality of the inclusion and the portion of the guest situated in the torus cavity [22, 23]. Figure 5 displays a partial contour plot of the 2D-ROESY spectrum of a mixture of TPPTS and $\beta$-CD.

All cross-peaks are indicative of the presence of a least one aromatic ring in the hydrophobic cavity. Indeed, strong dipolar interactions between H-3 and the *meta*- and *ortho*-protons of the TPPTS and between H-5 and the *para*- and *meta*-protons of TPPTS are observed. As no cross-peak between the protons of TPPTS and the H-6 proton of $\beta$-CD is observed, the inclusion occurs undoubtedly by the secondary side of $\beta$-CD. The fact that the *para*-proton and the *ortho*-proton of the TPPTS show only a strong interaction with the H-5 and H-3 protons respectively, suggest that at least one sulfonate group is located at the primary side of the $\beta$-CD during the inclusion process. As these data do not allow us to propose easily a geometry for the inclusion complex, in particular the number of aromatic rings included in the cavity, the geometry determination was complemented by a molecular modelling study.

Scheme 3 describes the six inclusion modes which have been investigated for the complexation simulations.

The docking of the TPPTS acid through the $\beta$-CD shows that no real inclusion phenomena could arise from modes 1 to 4. Indeed, steric crowding is observed before any moiety of the TPPTS could interact with the $\beta$-CD cavity. In contrast, for modes 5 and 6, one of the phenyl groups may penetrate into the macrocycle cavity, so that favourable van der Waals interactions take place between the two species. Furthermore, it has to be emphasized that more stable conformations are obtained if the inclusion occurs by the secondary side of the $\beta$-CD (mode 5) rather

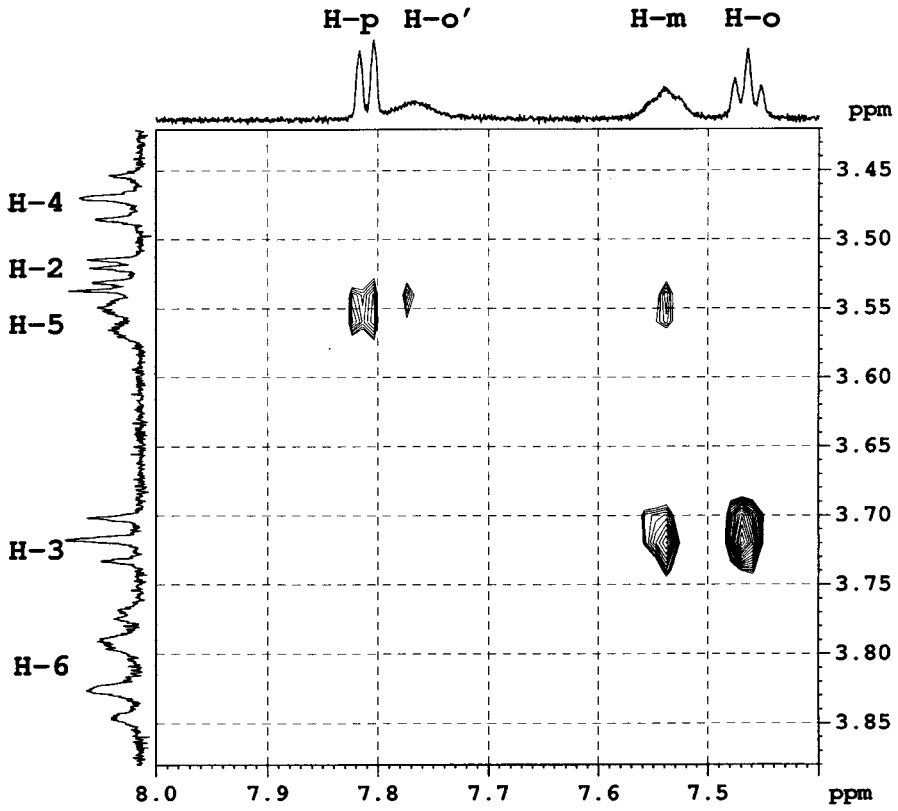
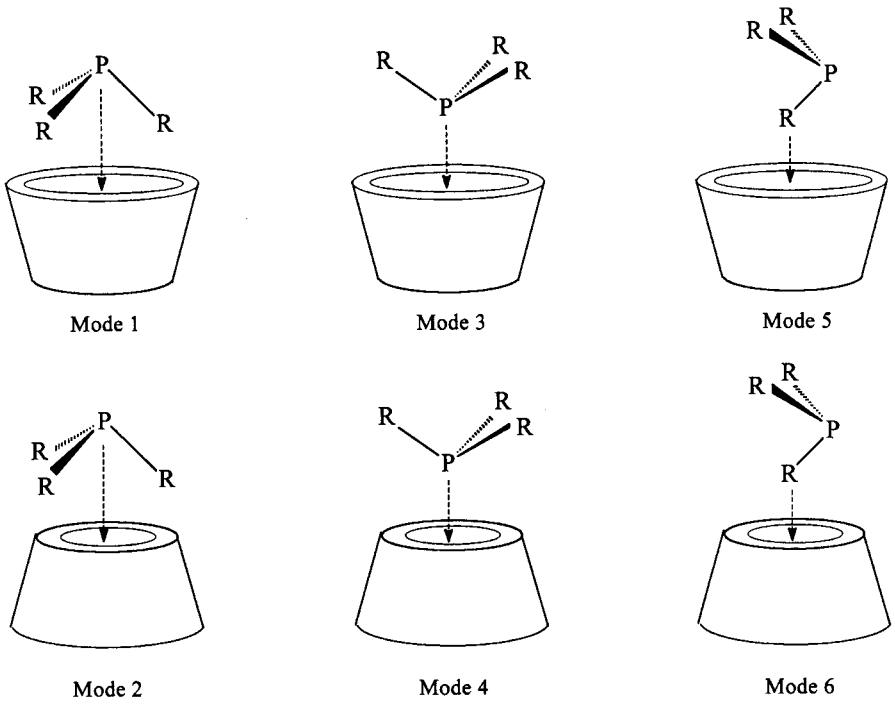



*Figure 5.* Partial contour plot of the ROESY spectrum of a solution containing $\beta$-CD (1 mM) and TPPTS (6 mM) in $D_2O$ at 600 MHz and 268 K with 300 ms mixing time.

than by the primary side (mode 6): the wider rim afforded by the secondary side results in a better fit of $\beta$-CD with the two phenyl groups which remain outside the cavity. Such a result is consistent with the fact that no cross peak between the aromatic protons and the H-6 protons of $\beta$-CD has been observed in the 2D-ROESY spectrum. Figure 6 represents the most stable structure calculated for the 1 : 1 complex.

Such an inclusion, which corresponds to mode 5, implies that the sulfonic group is deeply included in the $\beta$-CD cavity and faces the primary hydroxyls. In addition, the main part of the phenyl ring is included and spatial proximity less than 4 Å is observed between the following atoms: *ortho*-proton and H-3, *meta*-proton and H-3, *ortho'*-proton and H-5, *meta*-proton and H-5, *para*-proton and H-5. Thus, the simulated structure is in good agreement with the experimental interactions observed in the 2D-ROESY spectrum.




*Scheme 3.* Schematic representation showing the orientations of the $\beta$-CD and TPPTS used in this work to determine the most stable structure for a 1 : 1 inclusion complex.

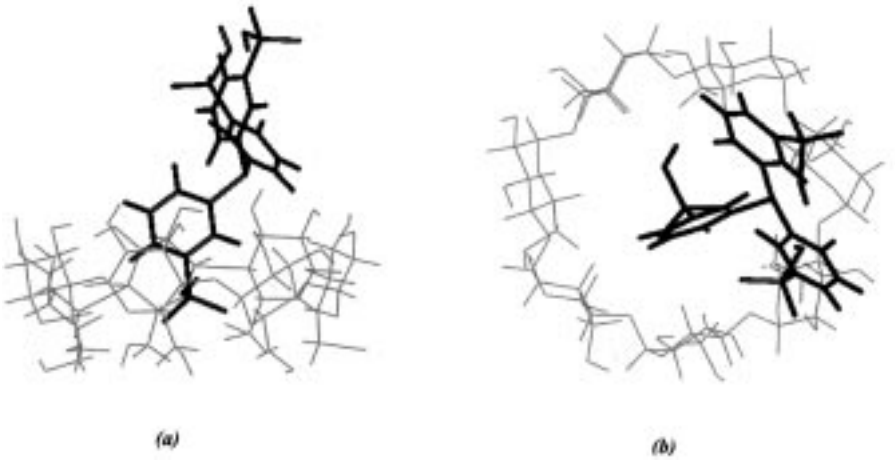



*Figure 6.* Side view (a) and top-view (b) of the computer generated structures of the 1 : 1 inclusion complex of TPPTS with $\beta$-CD. Hydrogens atoms have been removed for clarity.

### 3.2. STUDY AT 298 K

The inclusion process at 298 K was investigated as previously described at 268 K. A series of samples containing variable ratios of $\beta$-CD and TPPTS was prepared keeping the total concentration of species constant (10 mM in the present case). The NMR spectra of the samples are presented in Figure 7.

The large upfield shifts experienced by protons H-3 and H-5 prove that an inclusion process occurs at 298 K. However, an intriguing alteration of the NMR signals of TPPTS and $\beta$-CD protons has been observed for molar ratios between 4.25/5.75 and 7/3. This alteration was also clearly evidenced on the anomeric protons of the $\beta$-CD (Figure 8).

At this point, it must be mentioned that these experiments have been carried out several times and that the spectra were reproducible. Therefore, it can be concluded that the NMR signal alteration is not due to some artifacts. Attempts to simulate such a phenomenon in the case of a genuine 1 : 1 equilibrium between the $\beta$-CD and TPPTS have failed, thus suggesting that the alteration cannot be attributed to the dynamics of a 1 : 1 equilibrium. Similarly, attempts to derive a stoichiometry by Job's method was unsuccessful. Indeed, different stoichiometries can be derived depending on the proton considered and the plots show unsymmetrical shapes (Figure 9).

Interestingly, the alteration of NMR signals is much less marked when the NMR spectra are recorded at lower frequency, i.e., 300.13 MHz (Figure 10).

However, no relevant information about the stoichiometry can be obtained once again from these spectra. The above results led us to assume the existence of different complexes in solution. This assumption was fully supported by mass spectrometry experiments.

Although the soft electrospray ionization mass spectrometry method requires a dissolving medium for the $\beta$-CD/TPPTS complexes different to pure water, this method was preferred to other mass spectrometry methods. Indeed, electrospray ionization mass spectrometry preserves the integrity of weak supramolecular associations in the phase gas [32–34]. Figure 11 shows the electrospray mass spectrum of a 1 : 1 mixture of TPPTS and $\beta$-CD recorded in the positive mode at different orifice potentials.

It must be noticed that measurements made on different preparations of the same 1 : 1 TPPTS/$\beta$-CD mixture provided reliable and reproducible spectra. In both spectra, the peaks relative to $\beta$-CD adducts are clearly detected, namely $[\beta\text{-CD} + \text{Na}]^+$ (*m/z* 1157; relative abundance: 100%); $[(\beta\text{-CD})_4 + 3\text{Na}]^{3+}$ (*m/z* 1534; 14.77%); $[(\beta\text{-CD})_3 + 2\text{Na}]^{2+}$ (*m/z* 1724; 37.1%) and $[(\beta\text{-CD})_5 + 3\text{Na}]^{3+}$ (*m/z* 1911; 7.2%) [34]. Besides the peak corresponding to the expected 1 : 1 inclusion complex (sodium adduct of the $\beta$-CD: $[\beta\text{-CD} + \text{TPPTS} + 2\text{Na}]^{2+}$; *m/z* 874; 85.9%), the mass spectrum at a 10 V orifice potential exhibited two peaks at *m/z* 1440.6 (24.4%) and 1345.1 (18.1%) which were assigned to adducts of the ternary complexes formed by two $\beta$-CD molecules and one TPPTS molecule (ion parent: $[(\beta\text{-CD})_2 + \text{TPPTS}$

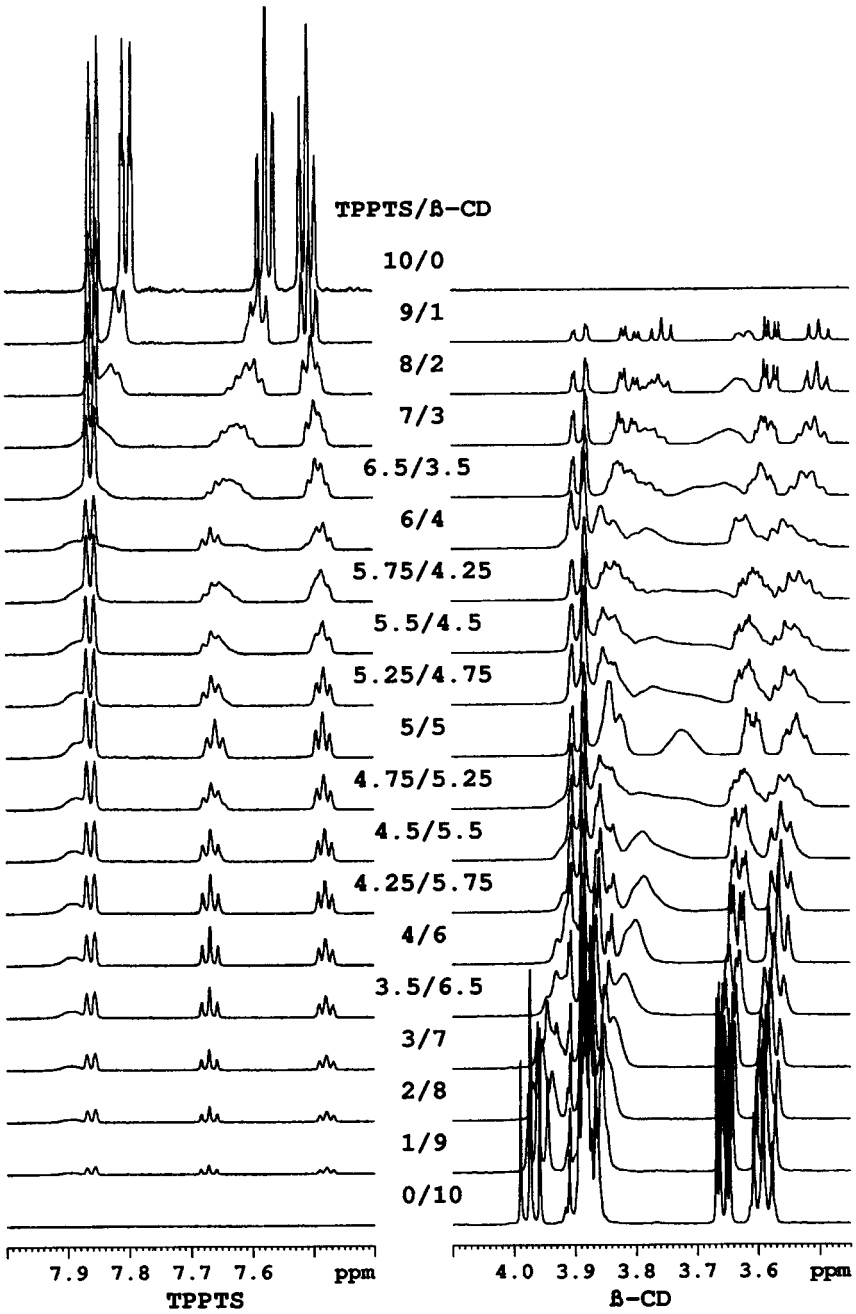



*Figure 7.* Partial 600 MHz $^1$H NMR spectra of TPPTS/$\beta$-CD mixtures in $D_2O$ at 298 K. The total concentration of species is 10 mM. The TPPTS to $\beta$-CD ratios are given between the two sets of spectra.

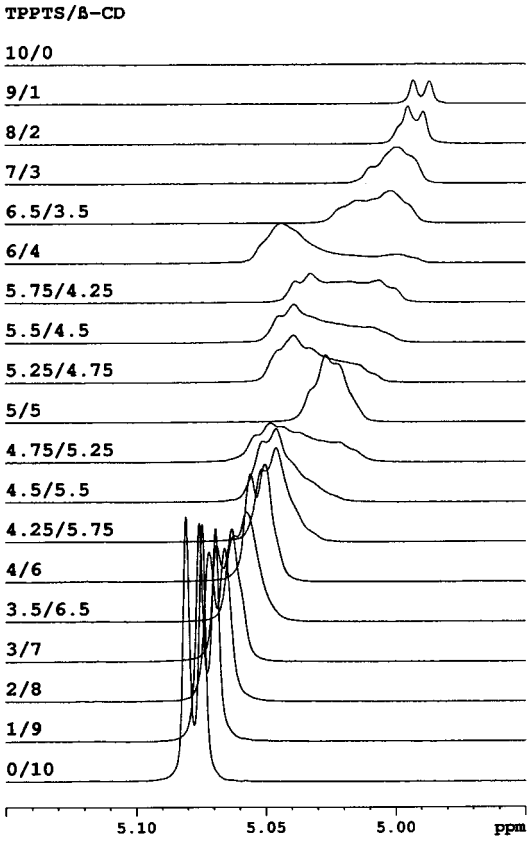



*Figure 8.* 600 MHz $^1$H NMR spectra of the H-1 proton of $\beta$-CD for different TPPTS/$\beta$-CD mixtures in $D_2O$ at 298 K. The total concentration of species is 10 mM. The TPPTS to $\beta$-CD ratios are given on the left of the spectra.

+ $NH_4$ +Na]$^{2+}$) and a quaternary complex formed by three $\beta$-CD molecules and one TPPTS molecule (ion parent: [($\beta$-CD)$_3$ + TPPTS + K + Na + H]$^{3+}$). The ions belonging to the two latter complexed species exhibited a much lower intensity with respect to that relative to the 1 : 1 complex, thus suggesting a lower degree of complexation. The fact that the 3 : 1 species has disappeared at 60 V while the 2 : 1 species is still present at this voltage (22% relative abundance – Figure 11c) indicates clearly that in the 3 : 1 complex one $\beta$-CD is very weakly bound to the complex.

Reliable determination of the $K_{2:1}$ and $K_{3:1}$ association constants by computer fitting of the NMR data obtained at 298 K was also impossible due to the strong alterations of the NMR signals. The fact that the proportion of 2 : 1 and 3 : 1 complexes probably differs from one temperature to another can explain why a 1 : 1 stoichiometry can be determined by the Job plot at 268K. Indeed, if the 1 : 1 complex proportion is higher at lower temperature, less perturbations from com-

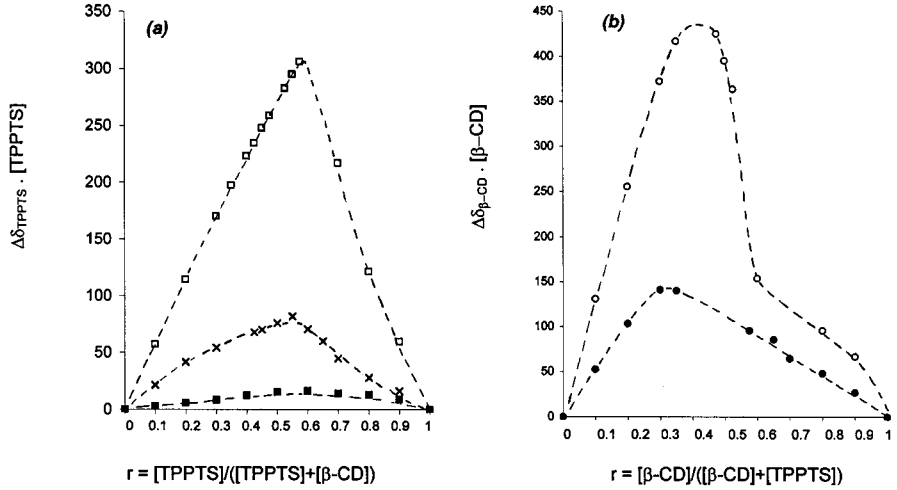



*Figure 9.* Continuous variation plots (Job's plots) derived from experimental data of Figure 7 for selected protons (a) of TPPTS (H-m: □; H-p: ■; H-o: ×) and (b) of $\beta$-CD (H-1: ●; H-3: ○). For the H-3 proton, the experimental datum relative to the ratio 0.7 cannot be determined due to the spectral overlap between H-6 and H-3 protons.

plexes of higher stoichiometry are intended to occur at 268K, so that the chemical shift variations are mainly due to the 1 : 1 equilibrium. On the other hand, small interferences of such complexes on the NMR spectra recorded at this temperature cannot be totally excluded, and the association constant values calculated at 268 K by NMR and UV-vis have to be carefully considered. This might explain the bad agreement observed between the association constant derived by these two techniques at 268 K.

Surprisingly, it is interesting to note that a titration of a TPPTS solution by the $\beta$-CD followed by UV-vis spectroscopy enables determination of an association constant at 298 K. Indeed, UV-vis data collected at this temperature with a 10 mm cell at a TPPTS concentration of 0.1 mM fit well with a 1 : 1 equilibrium and an association constant of 1200 $M^{-1} \pm 10\%$ was found. This value was also confirmed by carrying out UV-vis measurements with a 1mm cell at a TPPTS concentration of 1 mM. The independence between the estimated association constant and the TPPTS concentration indicates that a very good agreement exists between the UV-vis data and a 1 : 1 equilibrium. The fact that such an agreement is obtained for UV-vis data, while no association constant may be calculated on the basis of NMR, might be explained not only by the low proportion of 2 : 1 and 3 : 1 complexes relative to the 1 : 1 complex but also by *(i)* similar molar absorptivity coefficients for the various inclusion complexes; *(ii)* the lower resolution of UV-vis spectroscopy relative to NMR spectroscopy.

These assertions are also confirmed by the results obtained with a spectral displacement method with methyl orange, since an association constant equal to

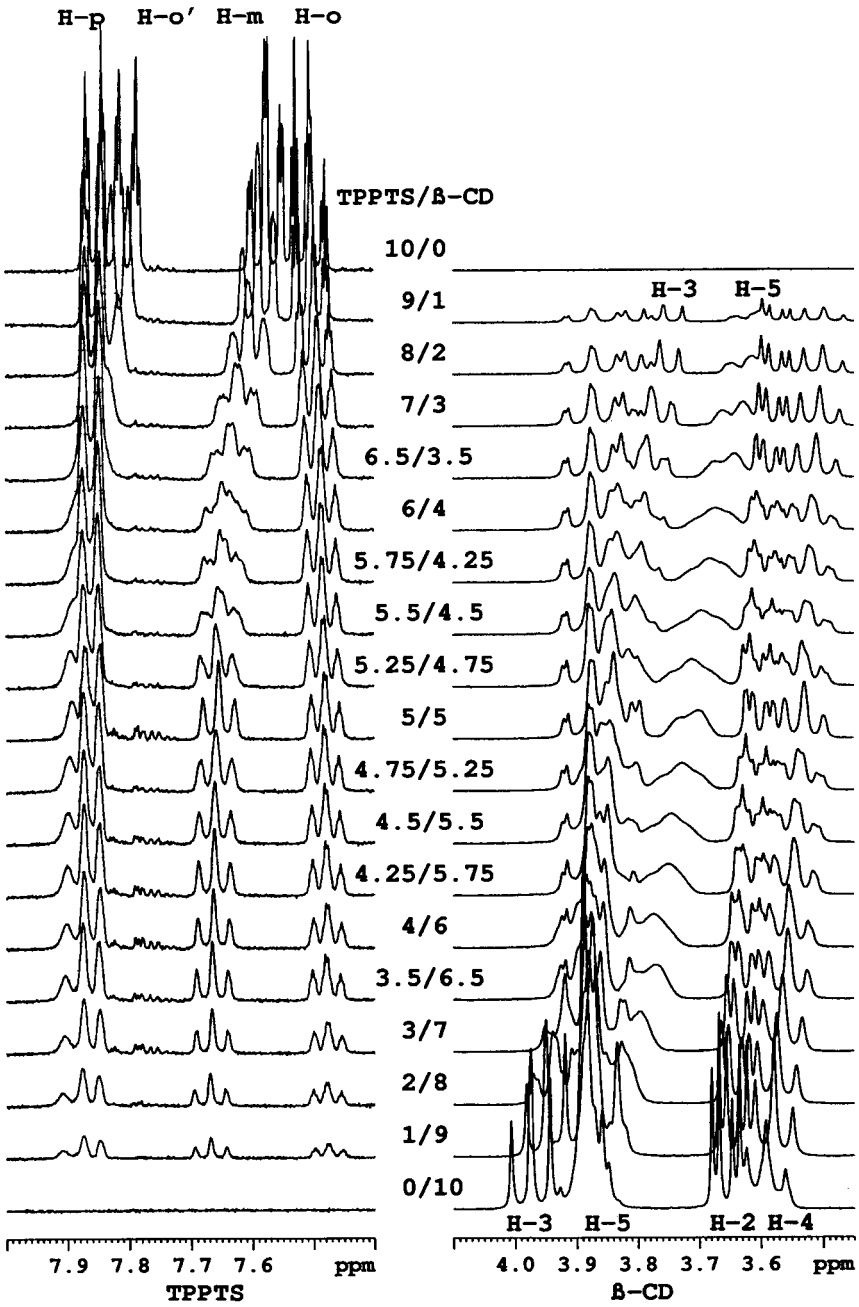



*Figure 10.* Partial 300 MHz $^1$H NMR spectra of TPPTS/$\beta$-CD mixtures in $D_2O$ at 298 K. The total concentration of species is 10 mM. The TPPTS to $\beta$-CD ratios are given between the two sets of spectra.

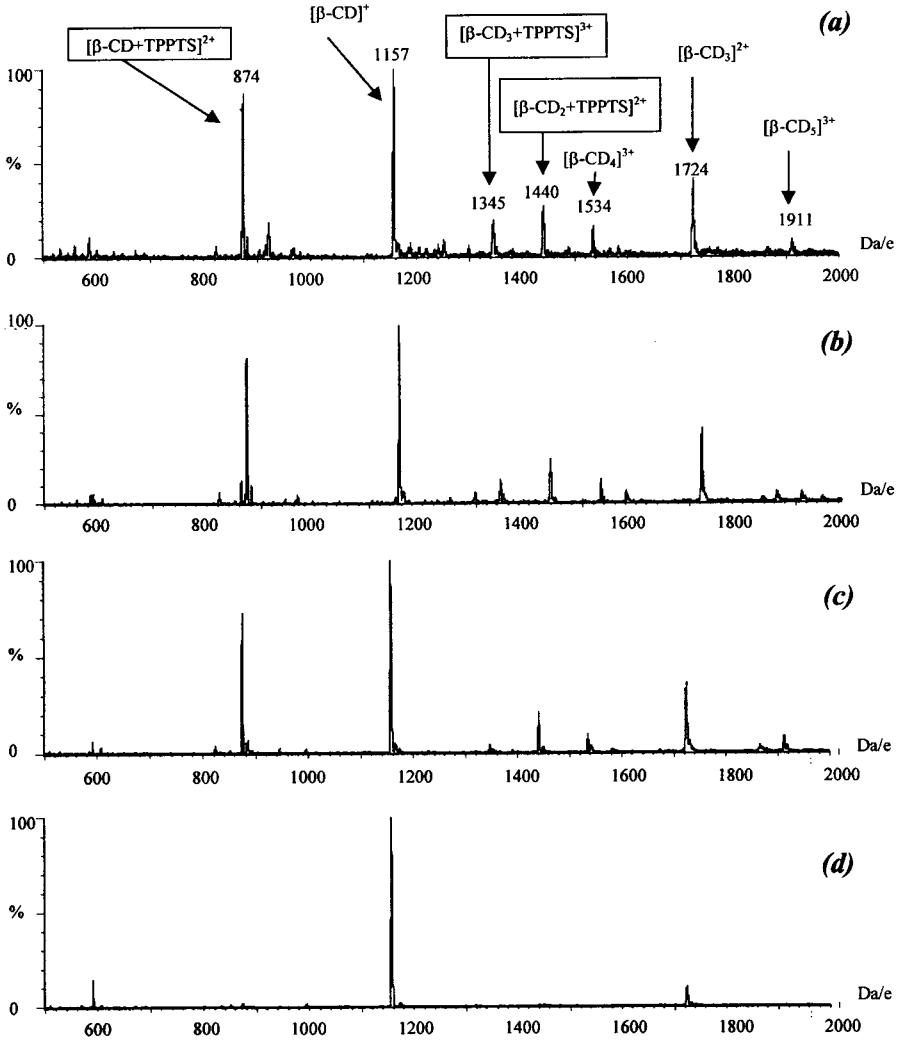



*Figure 11.* Electrospray mass spectrum of a 1 : 1 mixture of TPPTS and $\beta$-CD recorded in the positive mode at different orifice potentials. (a) 10 V, (b) 30 V, (c) 60 V and (d) 90 V.

1300 $M^{-1} \pm$ 10% has been estimated (for a TPPTS concentration of 0.6 mM and a $\beta$-CD concentration of 0.5 mM – Figure 12).

Indeed, such a method is not dependent on the spectral characteristics of TPPTS and TPPTS complexes, and relies only on the calculation of the $\beta$-CD concentration which is involved in the TPPTS complexation. Thus, this method leads to the estimation of an overall affinity value. In consequence, the association constant derived by the spectral displacement method may agree with another method if the 1 : 1 inclusion compound is present in large excess, and if the spectral characteristics of the different complexes are similar. Therefore, the agreement existing

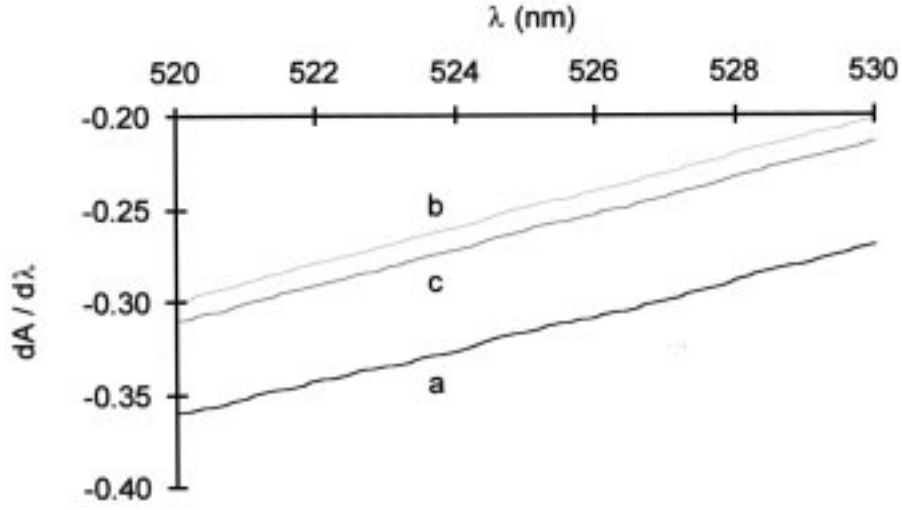



*Figure 12.* First derivatives of the absorption spectra for solutions containing (a) methyl-orange (0.1 mM); (b) methyl-orange (0.1 mM) and $\beta$-CD (0.5 mM); (c) methyl-orange (0.1 mM), $\beta$-CD (0.5 mM) and TPPTS (0.6 mM).

between the spectral displacement method and the UV-vis measurements emphasizes the predominance of the 1 : 1 equilibrium and the validity of the association constant estimated by optical methods.

2D ROESY experiments on a solution of $\beta$-CD and TPPTS have also been performed at 298 K. The ROESY spectra obtained at 298 K exhibited the same cross peaks to those obtained at 268 K. This may be due to the low concentration of 2 : 1 and 3 : 1 complexes relative to the 1 : 1 complex and/or to the nature of the 2 : 1 and 3 : 1 complexes. Indeed, from molecular models, it appears clearly that high steric hindrances in the 2 : 1 and 3 : 1 complexes impede the deep inclusion of phenyl groups into two or three CD cavities. Thus, it is reasonable to postulate that only one of the aromatic rings of the TPPTS is deeply included in a CD cavity and that the other aromatic rings are very partially included inside the cavity of other cyclodextrins. In such complexes, the aromatic rings which are not deeply included should not result in supplementary cross-peaks in the ROESY spectra. Further molecular modelling is currently under way in our laboratories to study thoroughly the geometry of these complexes.

## 4. Conclusion

This work has demonstrated that TPPTS can bind to $\beta$-CD to form 1 : 1; 2 : 1 and 3 : 1 complexes. Although the full determination of the geometry of all complexes has not been achieved, it appears clearly that the phosphorus atom of TPPTS is located near the secondary hydroxyl side of the CD. Such a result suggests that the phosphorus is not available to complex the water soluble organometallic catalyst

used in biphasic catalysis and, consequently, that the $\beta$-CD cannot act as a second-sphere ligand for the TPPTS/ transition-metal complexes. However, by trapping the ligand, $\beta$-CD can modify the equilibrium between the different catalytic species. The synthesis of chemically modified CDs that do not form inclusion complexes with TPPTS is currently under way in our laboratory.

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