

## Conformational isomerism and self-association of calixarene building blocks in non-polar solution studied by Fourier transform infrared spectrometry

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Received 21 January 1995

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### Abstract

In order to establish the conformational equilibrium of calix[6]arene derivatives, a series of phenolic building blocks differing in chain length (oligomers) have been studied in solution by Fourier transform infrared spectrometry (FT-IR). Different intramolecular OH...X interactions have been established in the calixarene building blocks, i.e. OH... $\pi$ , OH...OH, OH...OCH<sub>3</sub> and a bifurcated OH...OH/OCH<sub>3</sub> or OH...OH/OH one. Concentration-dependent measurements show that the “biphenol” and “triphenol” oligomers form cyclic dimers even at very low concentration (< 10<sup>-5</sup> M). The presence of a molecular conformation where the terminal hydroxyl groups form part of a linear (cooperative) H-bond seems to promote cyclic self-association. Comparing *p*-tert-butylcalix[4]arene with *p*-tert-butylcalix[6]arene reveals that fixation of the skeleton strengthens the circular H-bond. Intramolecular OH...OCH<sub>3</sub> or OH... $\pi$  interaction prevents the formation of associates for the building blocks with only one terminal OH group at relatively high concentration (> 10<sup>-2</sup> M). Preliminary MM3 calculations were performed to support conformational assignment.

**Keywords:** Phenols; Calixarenes; Hydrogen bonding, bifurcated; Cyclic dimers; Self-association; Dimerisation; Infrared spectrometry

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### 1. Introduction

Calixarenes are macrocyclic phenolic compounds which have been recognised as a potential group of enzyme mimics [1]. The possibility to vary cavity size and site activity by functionalisation allows the creation of selective receptor cavities of biochemical interest. These macrocyclic compounds are also in-

creasingly employed as building blocks for molecules used in the complexation of cations, anions and neutral molecules [1–3]. Ring sizes ranging from 4 to 10 aromatic residues are synthesised by base-induced condensation of the appropriate *para*-substituted phenols and formaldehyde [1].

Earlier Conforth et al. [4] pointed out that the smallest member of the series, calix[4]arene, can exist in four extreme conformations viz. the “cone”, “partial-cone”, “1,2-alternate” and “1,3-alternate”. The structural flexibility of these molecules is an-

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other reason for the increasing popularity of this class of compounds.

X-ray crystallographic studies [5,6] of unsubstituted calix[4]arenes provide unequivocal evidence that these compounds exist in the cone conformation in the solid state. This conformational preference is due to the hydroxyl groups which in a cooperative organisation form very strong intra-molecular hydrogen bonds, as reflected by the very low frequency of the OH stretching band. Recently we reported [7] on the conformational distribution of partially methylated *p*-*tert*-butylcalix[4]arenes in non-polar solvents studied by Fourier transform infrared (FT-IR) and nuclear magnetic resonance (NMR) spectrometry. Also the molecular conformation of *anti* and *syn* 27,28-diethoxy-*p*-*tert*-butylcalix[4]arene in the solid phase and in solution [8] has been verified with the help of the sensoric value of the OH stretching vibration. In these papers we correlated absorption bands, measured at different frequencies, with different types of hydrogen bonds: OH...OH (cooperative and isolated), OH...OMe and OH... $\pi$ .

As reported by Gutsche and Bauer [9] the calix[6]arenes can exist in eight “up-down” conformations and numerous intermediate ones with one or more of the aryl groups pointing outward from the average molecular plane. In the solid state a distorted cone structure has been observed by X-ray diffraction studies [10], with the *tert*-butyl groups outside the macro-ring and the six phenolic oxygens pointing towards the interior. Space-filling (Corey–Pauling–Koltun) molecular models suggest that the conformational flexibility of calixarenes increases with ring size. However, temperature-dependent  $^1\text{H}$  NMR measurements [11–13] have shown that this is not necessarily the case for calix[4]arene and calix[8]arene, as they behave almost identical in non-polar solvents. In contrast, calix[5]arenes, calix[6]arenes and calix[7]arenes, as well as the oxacalixarenes, appear to be more flexible.

In continuation to our previous spectroscopic results with respect to partially methylated calix[4]arenes we decided to study the conformational flexibility of larger macrocyclic compounds in non-polar solution. Earlier Cairns and Eglinton [14] suggested that the *ortho*–*ortho* methylene bridged di- and tri-phenolic compounds adopt cyclic configurations when forming dimers, similar to calixarenes.

On the absence of *ortho*-substituents, intramolecular OH...OH bonding is dominant at very low concentrations, but superseded by dimerisation at higher concentrations [15].

We studied the conformational equilibrium and self-association of linear oligomers and *p*-*tert*-butylcalix[4]- and calix[6]arene at different concentrations in non-polar solution. Assuming transferability of spectral characteristics of the OH stretching band data, correlated with structural features, a reliable assignment of absorption bands to conformers and rotamers including their relative presence could be made. As the hydroxyl functionality is known to be most sensitive in infrared, attention was focused on the region 3700–3000  $\text{cm}^{-1}$ .

In addition to the assignment this study also provides insight into structural features affecting the OH stretching band parameters, i.e. position and bandshape.

## 2. Experimental

### Compounds

The compounds **0**, **I**, **III**, **VIII** and **IX** were obtained commercially with a purity > 99%. Compound **II** and **IV**–**VII** were synthesised, chromatographically purified and checked with  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR and fast-atom bombardment mass (FAB-MS) spectrometry. Compound **VII** was prepared according to a literature procedure [16]. The procedures for the synthesis and characterisation of the compounds **II** and **IV**, **V** and **VI** will be described elsewhere [17].

### Infrared spectra

All IR spectra were run on a Perkin Elmer 2000 FT-IR spectrometer equipped with a deuterated triglycine sulphate (DTGS) detector. Scanning conditions: resolution 2 and 4  $\text{cm}^{-1}$ , apodization medium, number of scans 200–400. Galactic GRAMS 386 software was been applied for resolution enhancement and curve-fit techniques.

To avoid the formation of associates the concentrations were in the range of  $10^{-5}$ – $10^{-3}$  M. To study self-association the concentration ranges were strongly dependent on the component. The path-length of the liquid cells was 2, 10 and 50 mm for



Table 1  
Substituents of the aromatic nuclei (see Fig. 1)

Compound	<i>n</i>	R	X <sub>1</sub>	X <sub>2</sub>	X <sub>3</sub>
I	0	H	OH	–	H
II	0	H	OH	–	OMe
III	0	H	OH	–	OH
IV	1	<i>t</i> -Bu	OMe	OH	OMe
V	1	<i>t</i> -Bu	OMe	OMe	OH
VI	1	<i>t</i> -Bu	OH	OMe	OH
VII	1	<i>t</i> -Bu	OH	OH	OH

*t*-Bu = *tert*-butyl; Me = methyl.

different dilutions. All measurements were carried out at ambient temperature and ratioed against background; residual water vapour had been removed by interactive subtraction. All compounds were mea-

sured in CCl<sub>4</sub> and the compounds III, VII, *p*-*tert*-butylcalix[4]arene and *p*-*tert*-butylcalix[6]arene also in CS<sub>2</sub>.

The absorption coefficient  $a_i$  was calculated based on the integrated area by using the equation  $A_i = a_i bc$ , with  $b$  the path length (cm),  $c$  the concentration (mol l<sup>-1</sup>) and  $a_i$  the integrated area (cm mmol<sup>-1</sup>).

Additionally variable-temperature measurements on pure liquid II in the range 328–117 K were performed while the compounds I and III were also measured in the solid state (KBr pellets).

#### MM3 calculations

Calculations of local optimised H-bond geometries were carried out with the MM3(92) program.

Table 2  
Spectral data of calixarenes and building blocks measured in CCl<sub>4</sub> solution

No.	Name	Free	Pseudo-free	OH...π	OH...OH	OH...OCH <sub>3</sub>	Bifurcated H-bond	Dimers
0	3,5-Dimethylphenol	3613	–	–	–	–	–	–
I	2-Benzylphenol	3611	–	3567	–	–	–	–
II	2-(2-Methoxybenzyl)phenol	3613	–	3549 <sup>a</sup>	–	3425	–	–
III	2-(2-Hydroxybenzyl)phenol	3611 <sup>a</sup> 3612 <sup>b</sup>	3602 3602 <sup>b</sup>	3542 <sup>a</sup> 3543 <sup>b</sup>	3472 3472 <sup>b</sup>	–	–	3345 3335 <sup>c</sup>
IV	4-(1,1-Dimethylethyl)-2,6-bis[5(1,1-dimethylethyl)-2-hydroxybenzyl]phenol	–	–	–	–	3428	–	–
V	4-(1,1-Dimethylethyl)-2-[5-(1,1-dimethylethyl)-2-hydroxybenzyl]-1-methoxy-6-[5(1,1-dimethylethyl)-2-methoxybenzyl]benzene	3612	–	3524 <sup>a</sup> 3513 <sup>d</sup>	–	3430 <sup>b</sup>	3358 OH... (OCH <sub>3</sub> ,OCH <sub>3</sub> )	–
VI	4-(1,1-Dimethylethyl)-2,6-bis[5-(1,1-dimethylethyl)-2-hydroxybenzyl]-1-methoxybenzene	3612	–	3524 <sup>a,d</sup> 3572 <sup>b</sup> 3532 <sup>b</sup>	–	3428 <sup>a</sup>	3372 OH... (OH,OCH <sub>3</sub> )	–
VII	4-(1,1-Dimethylethyl)-2,6-bis[2-hydroxy-5(1,1-dimethylethyl)benzyl]phenol	3610 <sup>a</sup>	3596	3533 <sup>a,d</sup>	3422 <sup>d</sup> 3387 <sup>a,d</sup>	–	3387 <sup>a,d</sup>	3210 3215 <sup>c</sup>
VIII	<i>p</i> - <i>tert</i> -Butylcalix[4]arene				3138 3191 <sup>c</sup>			
IX	<i>p</i> - <i>tert</i> -Butylcalix[6]arene				3150 3165 <sup>c</sup>			

<sup>a</sup> Data obtained by Fourier self deconvolution.

<sup>b</sup> Curve fitting results.

<sup>c</sup> Measurement in CS<sub>2</sub> solution.

<sup>d</sup> Data obtained via second derivative.

### 3. Results and discussion

As a start we selected a series of small linear oligomers (Fig. 1) with different numbers of phenolic residues. We measured the infrared spectra of the compounds listed in Table 1 (I–VII), a reference standard compound 3,5-dimethylphenol (**0**) and also *p*-*tert*-butylcalix[4]arene (VIII) and *p*-*tert*-butylcalix[6]arene (IX). The spectral data presented in the Tables 2–5 were obtained from non-polar solutions measured at different concentrations.

We have chosen to discuss spectral information in relation with molecular structure starting with phenol followed by an increasing number of aromatic residues in the approach to the calixarenes.

#### 3.1. Phenols (**0**)

The smallest compound of these building blocks consists of one aromatic residue. As a starting reference compound 3,5-dimethylphenol was selected. The absence of *ortho* substituents allows a straightforward comparison with free terminal hydroxyls in the linear oligomers. In symmetrically di-*ortho*-substituted phenols, (e.g. 2,6-di-*tert*-butyl) solute–solute and solute–solvent interaction is sterically prohibited by the bulky *tert*-butyl groups, and an appreciable shift to higher wavenumbers is observed [18]. In mono-*ortho*-substituted phenols ( $R_2 \neq R_6$ ), shifts are observed for the “*cis*” isomer compared to the “*trans*” configuration due to the considerable repulsive steric interaction of the aliphatic *ortho* substituent, and therefore the equilibrium is in favour of the *trans* isomer (2-methylphenol in  $\text{CCl}_4$ ;  $\nu_{\text{max}}$  at  $3613.5 \text{ cm}^{-1}$  with a halfband width (HBW) of  $17.8 \text{ cm}^{-1}$ , slightly asymmetric to higher wavenumbers.

The spectrum of phenol in dilute  $\text{CCl}_4$  solution

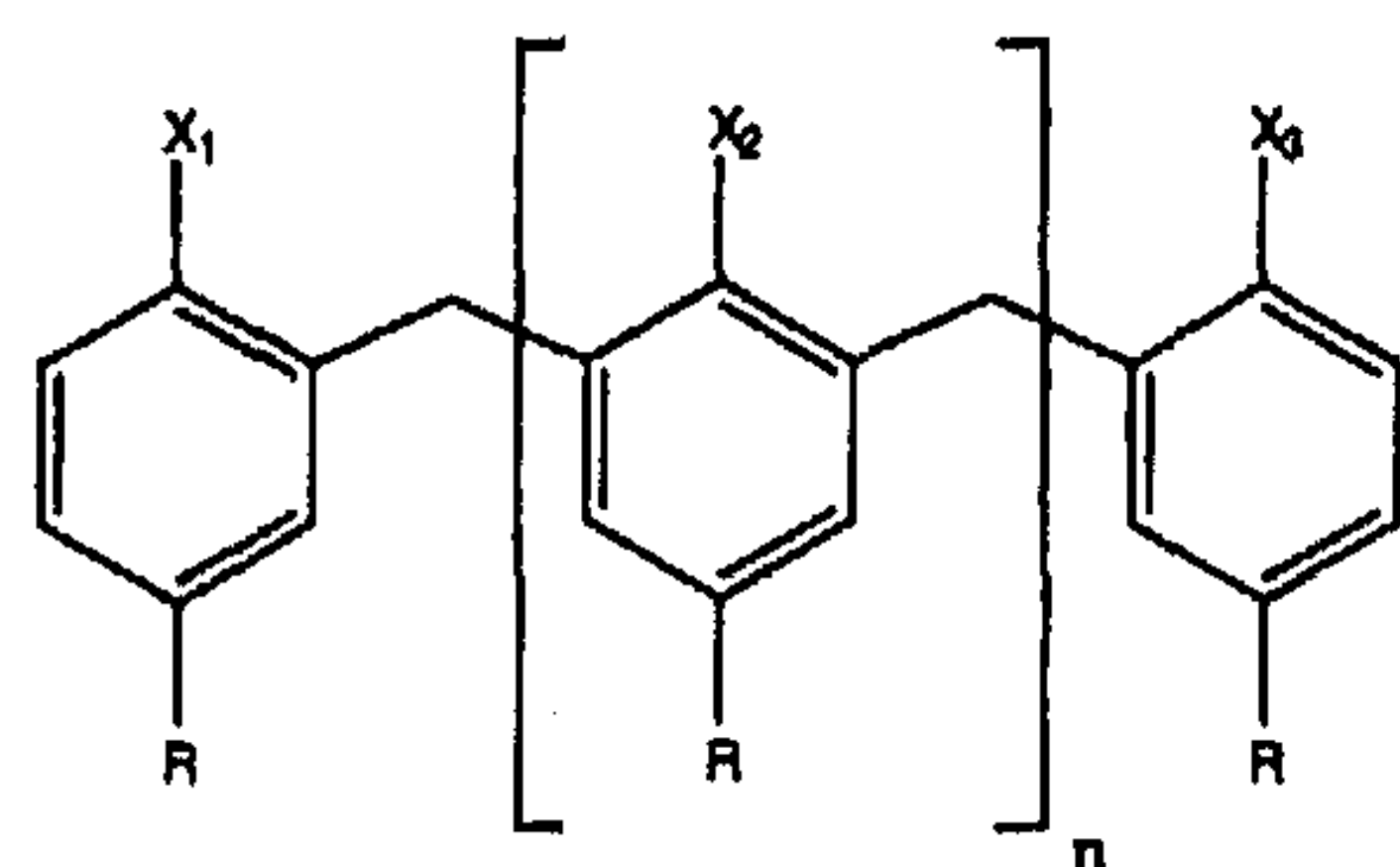


Fig. 1. Molecular structure of the compounds listed in Table 1.

Table 3

OH band data of pure compounds

2-Benzylphenol (I)	2-(2-Methoxybenzyl) phenol (II)	2-(2-Hydroxybenzyl) phenol (III)
(3538)	3270 sh	3250 sh
(3400 sh)	3385	3317
3293	3520 sh	3402 sh
3373 sh		

Liquid data between brackets from Ref. [23].

shows a symmetric OH stretching vibration band at  $3612.5 \text{ cm}^{-1}$  [19]. The *meta* alkyl substituents of the reference compound (**0**) hardly affect the stretching vibration of the hydroxyl ( $\nu_{\text{max}} = 3613.0 \text{ cm}^{-1}$  and  $\text{HBW} = 16.0 \text{ cm}^{-1}$ ).

From the integrated area of the free OH stretching vibration of compound **0**, the value  $a_i$  has been calculated ( $a_i = 4069.1 \text{ cm mmol}^{-1}$ ). We assume that  $a_i$  is transferable to similar phenolic rotamers and can be used to determine the equilibrium ratio in compound I.

#### 3.2. Linear biphenolic oligomers (I–III)

The spectra of the compounds I–III measured in  $\text{CCl}_4$  solution at different concentrations are displayed in Fig. 2a–c.

The spectrum of highly diluted I shows two band maxima in the OH stretching region at  $3611$  and  $3567 \text{ cm}^{-1}$  to be assigned to free OH and  $\text{OH} \cdots \pi$ , respectively (see Table 2). In this compound the formation of an internal  $\text{OH} \cdots \pi$  interaction can only be realised if the molecule adopts a sterically somewhat unfavourable structure. The hydroxyl group must be rotated, at least partly, out of the plane of the aromatic nucleus. The subsequent loss of resonance energy is compensated for by the H-bond energy [20].

Based on the integrated area calculated for the free OH (after curve fitting) and using the reference value  $a_i$  of compound **0**, the ratio  $\text{OH}_{\text{free}}:\text{OH} \cdots \pi$  in solution has been determined to be approximately 3:1.

On substitution of a methoxyl group at the 2'-position of the neighbouring aromatic ring the intensity of the free hydroxyl band decreases drastically

Table 4  
Spectral data obtained from measurement in CS<sub>2</sub> solution

No.	Name	Free	Pseudo-free	OH... $\pi$	OH...OH	Dimers
III	2-(2-Hydroxybenzyl)phenol	3592 <sup>a</sup>	3580	3534 <sup>b</sup>	3466	3335 <sup>a</sup>
VII	4-(1,1-Dimethylethyl)-2,6-bis [2-hydroxy-5(1,1-dimethyl- ethyl)benzyl]phenol	3589 <sup>b</sup>	3572	3525 <sup>b</sup>	3419 <sup>a</sup> 3380 <sup>a</sup>	3215

<sup>a</sup> Data obtained by Fourier self deconvolution.

<sup>b</sup> Data obtained via second derivative.

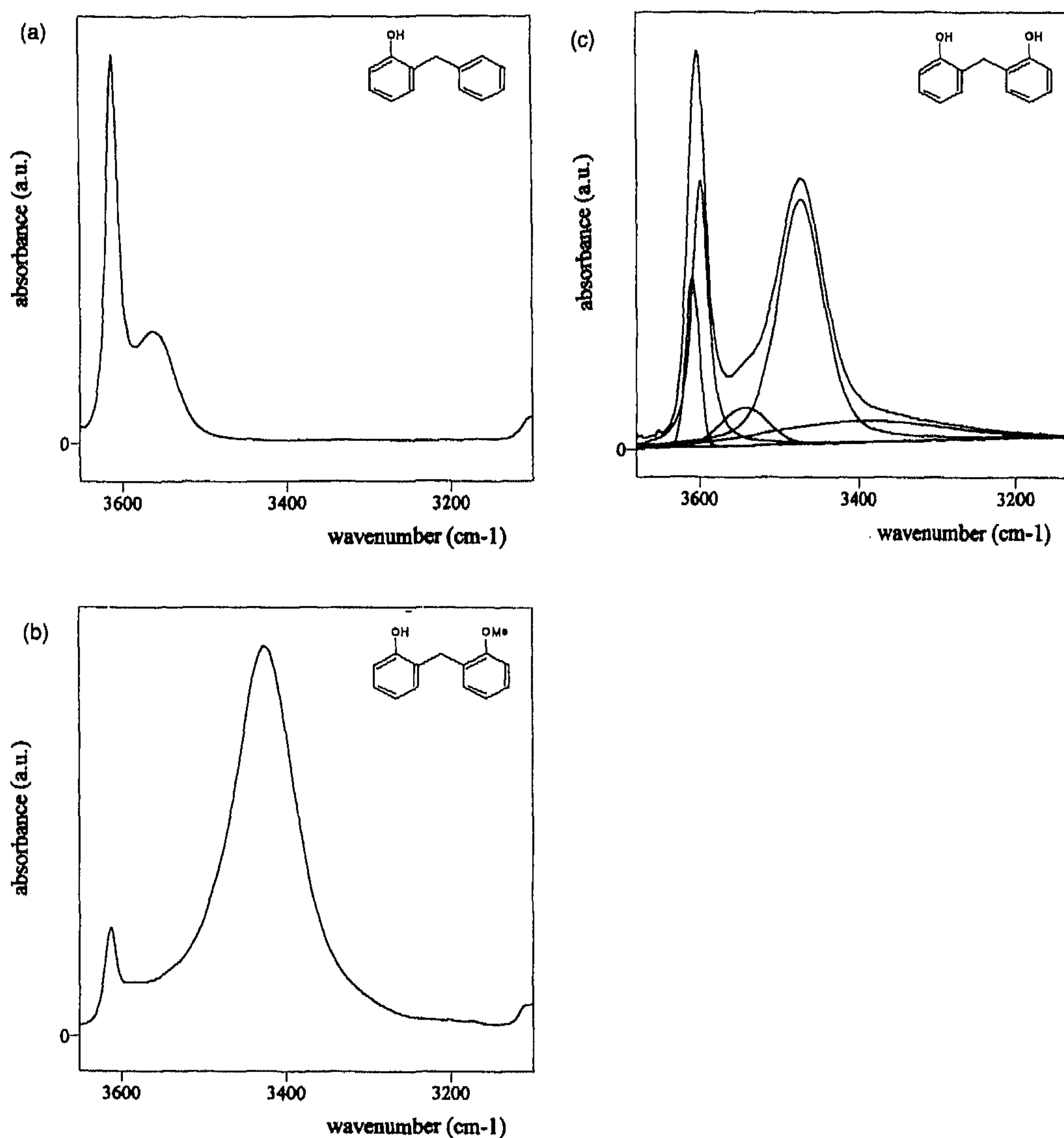


Fig. 2. OH stretching region of (a) compound I, (b) compound II and (c) compound III in dilute CCl<sub>4</sub> solution. Curve-fitting results are included for compound III.



Table 5  
Spectral shifts ( $\text{cm}^{-1}$ ) between cyclic dimers and calixarenes

Compound	$\Delta\nu$		$\Delta\nu_{\text{CCl}_4} - \Delta\nu_{\text{CS}_2}$
	$\text{CCl}_4$	$\text{CS}_2$	
III–VIII	207	144	63
VII–IX	60	50	10

(Fig. 2b, compound II) and apparently the intramolecular  $\text{OH} \cdots \text{OMe}$  hydrogen bond dominates. After resolution enhancement a band of minor intensity at  $3549 \text{ cm}^{-1}$  shows up which must be assigned to an  $\text{OH} \cdots \pi$  conformer.

The OH stretching region of compound III in dilute  $\text{CCl}_4$  solution (Fig. 2c, Table 2) shows two distinct maxima,  $3602$  and  $3472 \text{ cm}^{-1}$ , and a shoulder at  $3542 \text{ cm}^{-1}$ . The band at  $3602 \text{ cm}^{-1}$  is red-shifted by  $11 \text{ cm}^{-1}$  compared to the reference, free phenol. A detailed analysis of this band by curve fitting reveals the presence of two components: one at  $3602 \text{ cm}^{-1}$  due to the pseudo-free OH, acting as an acceptor only, and one at  $3611 \text{ cm}^{-1}$  due to a completely free hydroxyl. Like in compound II the  $3472 \text{ cm}^{-1}$  band, assigned to the intramolecular  $\text{OH} \cdots \text{O}$  hydrogen bond, dominates. Also the presence of  $\text{OH} \cdots \pi$  interaction can be recognised in the spectrum at  $3542 \text{ cm}^{-1}$ , be it with a lower intensity. MM3 calculations indicate that the “double” interacting conformer (Fig. 3) is more stable than the conformer with one  $\text{OH} \cdots \pi$  interaction. The intensity of the broad band at  $3345 \text{ cm}^{-1}$  is highly concentration dependent and will therefore be discussed in Section 3.4.

### 3.3. Linear triphenolic oligomers (IV–VII)

On the approach to calix[6]arenes the analysis of linear oligomers consisting of three phenolic residues is an essential one if intermolecular association is considered, as cyclic dimerisation may yield flexible calix[6]arene-type intermediates in one step.

In compound IV the phenolic group is positioned between two methoxy acceptors. The solution spectrum shows only one band at  $3428 \text{ cm}^{-1}$  (Fig. 4a), which obviously has to be assigned to the intramolecular  $\text{OH} \cdots \text{OMe}$  interaction. The frequency of this band corresponds to the appropriate

band of the similar hydrogen bond in compound II (Table 2) and thus supports the assignment.

In compound V the terminal OH group has the possibility to interact with the neighbouring ether functionality like in compound II and IV. The spectrum taken from this sample in dilute solution shows the presence of two bands and a shoulder (Fig. 4b). The dominant band at  $3358 \text{ cm}^{-1}$  has to be assigned to strong internal hydrogen bonding as it is independent of concentration. The red-shift of  $70 \text{ cm}^{-1}$  of this band with respect to the  $\text{O}-\text{H} \cdots \text{O}$  bands of compounds IV and II points to a somewhat different H-bond geometry. An analysis with Dreiding models shows that the formation of a bifurcated hydrogen bond with both the terminal and the adjacent  $\text{OCH}_3$  group is possible. MM3 calculations revealed that the conformation depicted in Fig. 5 has a local energy minimum; the calculated donor–acceptor  $\text{H} \cdots \text{O}$  distances are  $2.342 \text{ \AA}$  and  $2.495 \text{ \AA}$  for the adjacent and next neighbour  $\text{OCH}_3$  group, respectively. Rotational freedom of the phenolic rings also allows the formation of conformations stabilised by  $\text{O}-\text{H} \cdots \text{OCH}_3$  alone ( $3430 \text{ cm}^{-1}$ ),  $\text{OH} \cdots \pi$  hydrogen bonding at  $3524 \text{ cm}^{-1}$  and a minor contribution of free OH (Table 2), which is visualised by curve fitting.

Compound VI shows two maxima at  $3612$  and  $3372 \text{ cm}^{-1}$  and one shoulder at about  $3525 \text{ cm}^{-1}$ . Resolution enhancement brings about the presence of an additional lower intensity band at  $3428 \text{ cm}^{-1}$  (Fig. 4c, Table 2). Optimised H-bond energies are obtained if the lone pair orbitals of the ether oxygen acceptor are oriented in the direction of the OH vector, an almost linear  $\text{O}-\text{H} \cdots \text{O}$  bond being most favourable. This angle dependency prohibits the methoxyl group to act as a “bifurcated” acceptor for both terminal hydroxyls in this compound. Dreiding

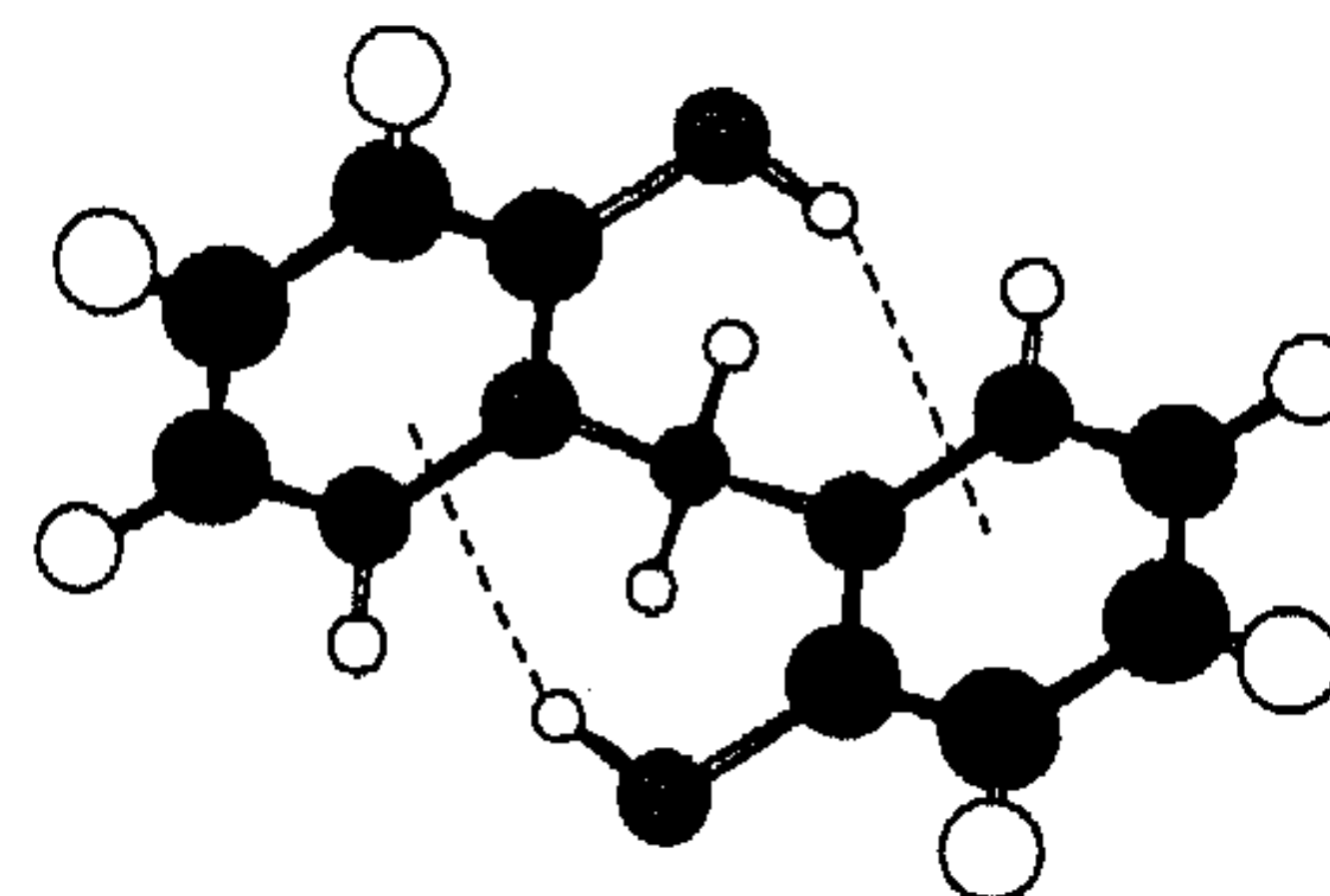


Fig. 3. Possible double  $\text{OH} \cdots \pi$  conformation of compound III.

models show that the formation of a bifurcated hydrogen bond between one of the OH groups and both the residual terminal OH and neighbouring OCH<sub>3</sub> group is possible. The main absorption at 3372 cm<sup>-1</sup> is assigned to this bifurcated hydrogen bond, like for compound V, though its red-shift appears to be slightly less. Support for the correctness of this assignment comes from a comparison with the internal OH...OCH<sub>3</sub> hydrogen bond in compound II and the OH...OH bond in compound III, for which

a larger red shift (47 cm<sup>-1</sup>) has been observed for the OH...ether interaction. The difference of 14 cm<sup>-1</sup> between the bands assigned to the same conformers of the compounds V and VI, i.e. the bifurcated H-bonded ones, can be explained by the difference in the acceptor sites, ether/ether and hydroxyl/ether, respectively. The weak band at 3428 cm<sup>-1</sup> is assigned to the "single" intramolecular OH...OCH<sub>3</sub> interaction, which nicely corresponds with the frequency of this conformer in II and IV.

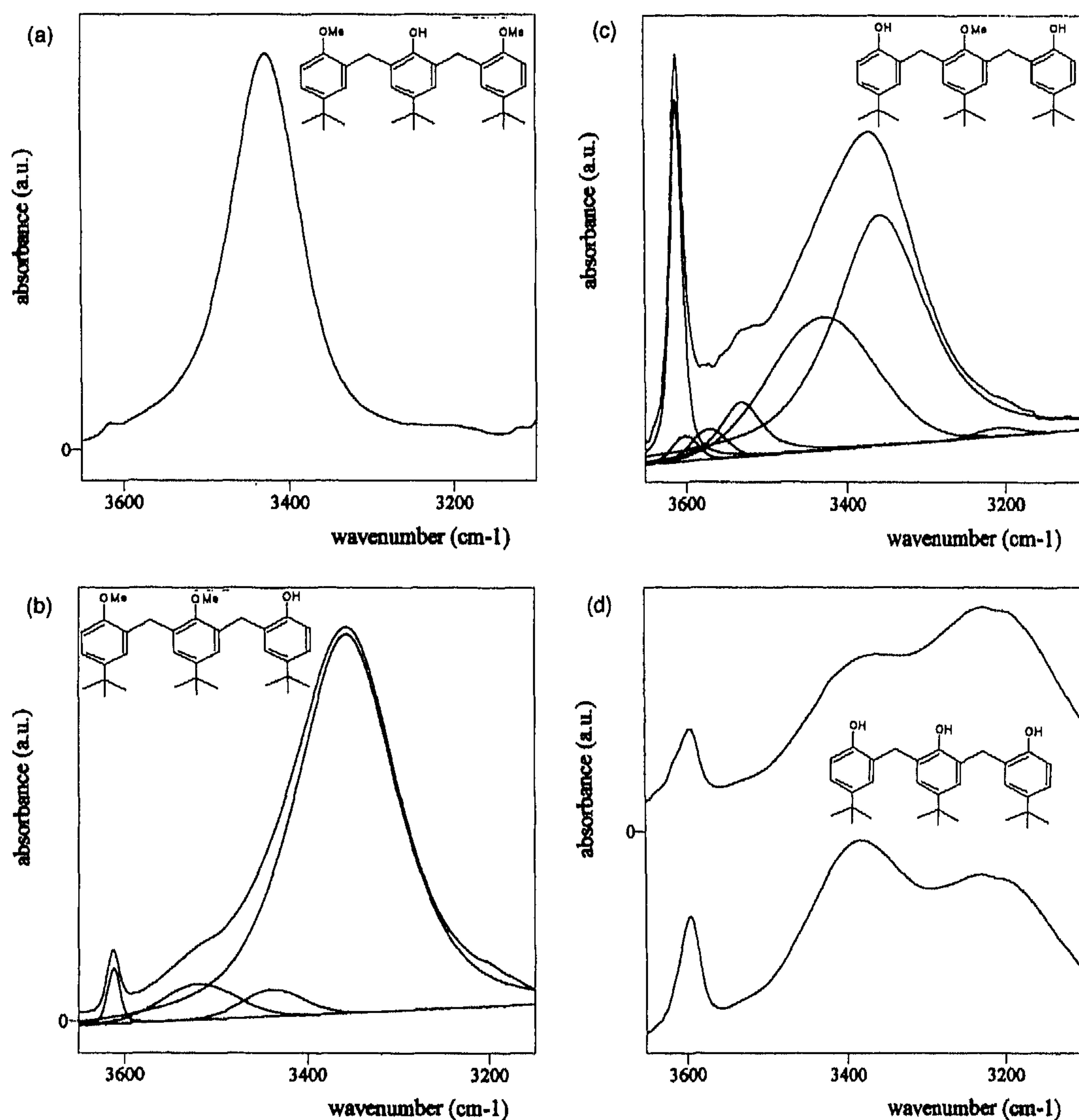


Fig. 4. OH stretching region of the compounds (a) IV, (b) V, (c) VI and (d) VII in CCl<sub>4</sub> solution. The concentration in the spectra of compound VII is 10<sup>-5</sup> M (top) and 10<sup>-3</sup> M (bottom), respectively. Curve-fitting results are included.



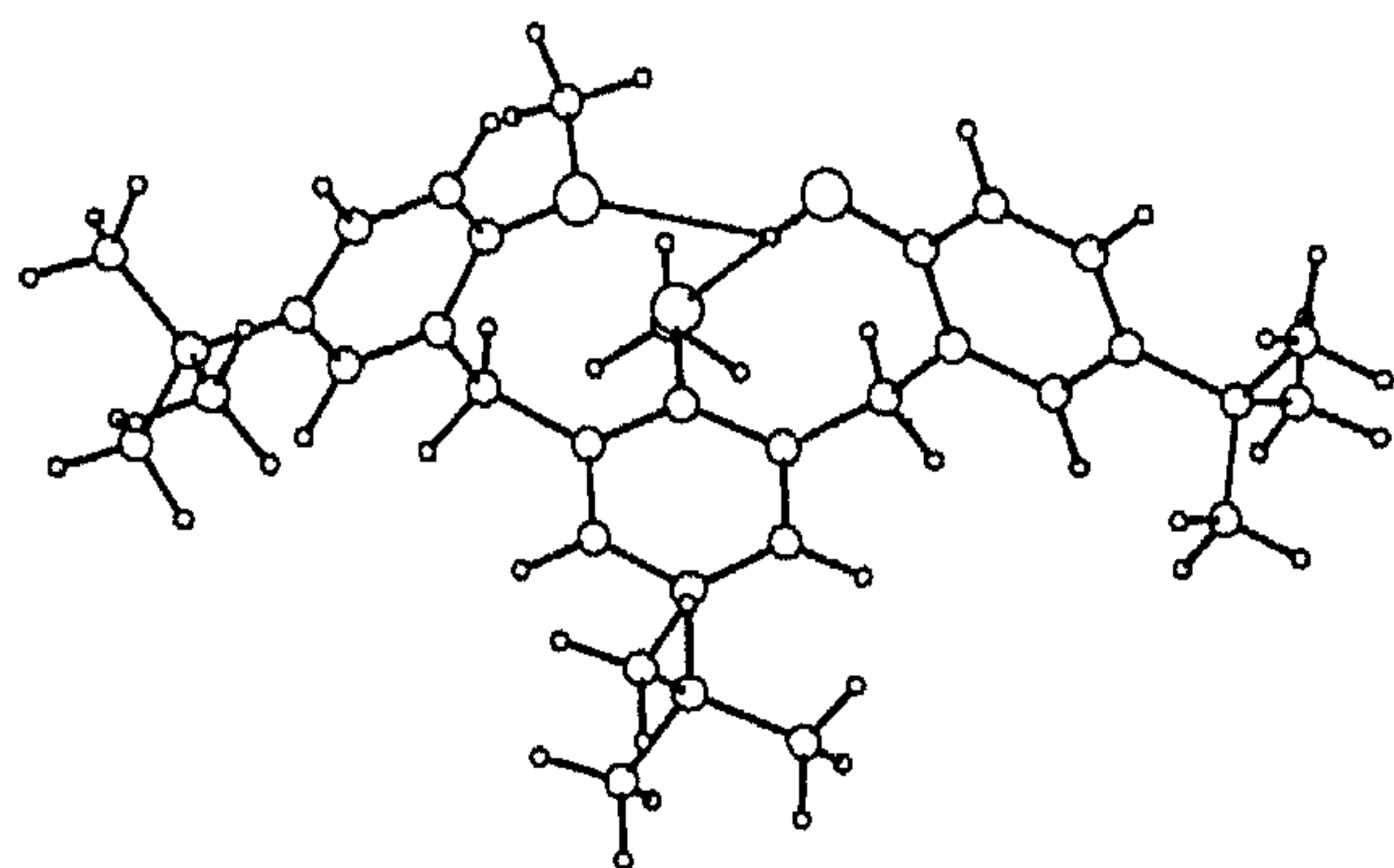


Fig. 5. Pluton plot of MM3 calculated bifurcated H-bond structure of V.

Once the intramolecular H-bond with the adjacent methoxyl group is formed the residual phenolic group at the terminal position is “free”, which explains the absorption band at  $3612\text{ cm}^{-1}$  and also the presence of an OH interaction with the aromatic ring ( $3524\text{ cm}^{-1}$ ). Obviously better curve-fit results are obtained when two different  $\text{OH} \cdots \pi$  species are allowed at respectively  $3572$  and  $3532\text{ cm}^{-1}$  (Fig. 4c).

For compound VII, with three hydroxyl groups, the formation of H-bond stabilised conformers has increased. CNDO/2 calculations by Inuzuka [22] indicate that compound VII has two stable conformations: a *cis* and a *trans* one. This notation refers to the position of both terminal aromatic moieties with respect to the middle phenolic nucleus, i.e. *trans* when opposite to each other and *cis* when both groups are at the same side. Both conformations are stabilised by intramolecular hydrogen bonds in which all three OH groups participate, chain cooperativity of the type  $\text{O}_1\text{--H}_1 \cdots \text{O}_2\text{--H}_2 \cdots \text{O}_3\text{--H}_3$ . The *trans* conformer has been calculated to be energetically the most stable one [22]. Focusing on the spectroscopic data in the OH stretching region and the appropriate data obtained after resolution enhancement and second derivative (see Table 2) leaves two different interpretations. First, the bands at  $3387\text{ cm}^{-1}$  and  $3422\text{ cm}^{-1}$  can be assigned to (i) the cooperative hydrogen bond  $\cdots \text{O}_2\text{--H}_2 \cdots \text{O}_3$  and (ii) to the terminal  $\text{O--H}_1 \cdots \text{O}_2$  bond, respectively, in agreement with the CNDO/2 results. Secondly, the band at  $3387\text{ cm}^{-1}$  is assigned to a bifurcated H-bond with  $\text{O}_2\text{H}$  and  $\text{O}_3\text{H}$  as acceptors. In contrast

to Inuzuka [22] MM3 calculations have shown that the *cis* conformer is energetically more stable than the *trans* one. The “bifurcated” *cis* conformation represents a local energy minimum (like in Fig. 5). The latter assignment is only valid if the molecular structure is predominantly in the *cis* conformation. The band at  $3422\text{ cm}^{-1}$  is assigned to  $\cdots \text{O}_2\text{--H}_2 \cdots \text{O}_3$ , the red-shift of this band ( $50\text{ cm}^{-1}$ ), compared to the similar conformation in compound III, is due to the donating  $\text{O}_1\text{H}_1$  group to  $\text{O}_2$ , i.e. cooperativity. The broad concentration-dependent band at about  $3300\text{ cm}^{-1}$  (Fig. 4d) will be discussed in Section 3.4.

The “free” OH band around  $3600\text{ cm}^{-1}$  is composed of two signals: an intense one to be assigned to  $\text{O}_3\text{--H}_3$ , which is pseudo-free because the oxygen acts as an acceptor, and a weaker one at  $3610\text{ cm}^{-1}$  to be attributed to the “real” free OH. The contribution of the latter is small, because of the fact that conformers with free hydroxyls are less stable than the intramolecularly bonded ones. As follows from the shoulder at  $3533\text{ cm}^{-1}$ , these molecules can also adopt conformations in which one or more hydroxyl groups associate with the aromatic  $\pi$ -system.

### 3.4. Self-association

As the geometry of molecular associates is of initial importance for (condensation) reactions, it is noteworthy to know the geometric arrangement in molecular clusters in solution [1]. Infrared spectra of solutions measured at increased concentration yield information on intermolecular association mechanisms at a time scale down to  $10^{-12}\text{ s}$ .

#### Compound I

As expected the intensity of the bands assigned to free and  $\text{OH} \cdots \pi$  interaction decreases with increasing concentration. A complex band at low frequency,  $3450\text{--}3300\text{ cm}^{-1}$ , shows up indicating that linear  $\text{OH} \cdots \text{O}$  hydrogen bonds of different types are being formed, e.g. dimer, trimer, etc. When measured as a liquid (melt) [23] the dominant absorption band is observed at  $3538\text{ cm}^{-1}$  certainly pointing to  $\text{OH} \cdots \pi$  interaction. The frequency red-shift of this band ( $29\text{ cm}^{-1}$  compared to the solution data listed in Table 2) originates from dielectric bulk solvent effects. In the solid state a broad



band at  $3293\text{ cm}^{-1}$  with a shoulder at  $3373\text{ cm}^{-1}$  is observed. This splitting might be due to polymorphism or a crystalline impurity; neither residual  $\text{OH} \cdots \pi$  nor free OH is observed (Table 3).

### Compound II

As appears the OH stretching region is affected only at high concentrations  $> 10^{-2}\text{ M}$ . The red-shift and band broadening then obtained originate from dielectric effects (solution) and not from switching of intra- to intermolecular H-bonding. We believe that apart from attractive  $\text{H} \cdots \text{O}$  interactions also repulsive  $\text{O} \cdots \text{O}$  lone pair interactions play a role. This hypothesis is supported by variable-temperature measurements of compound II as a pure liquid measured in the range 300–117 K, which shows that the intramolecular  $\text{OH} \cdots \text{OCH}_3$  remains dominant. The intensity of the shoulder, assigned to  $\text{OH} \cdots \pi$  interaction at ambient temperature, decreases upon cooling, while another absorption at lower wavenumber shows up. The low wavenumber of this band suggests that the OH groups are involved in some cooperative H-bond. Taking into account the relative intensity this phenomenon is energetically unfavourable compared to the intramolecular  $\text{OH} \cdots \text{OCH}_3$  bond.

### Compound III

Even at very low concentrations ( $< 10^{-4}\text{ M}$ ) compound III shows a broad band, at  $3345\text{ cm}^{-1}$ , which can only be assigned to a dimer. Cairns and Eglinton [14] suggested that relatively unstrained closed rings of hydrogen bonds are possible for this compound. Difference spectroscopy provides evidence for this mechanism as on interactive subtraction the residual spectra of self-associates no longer show a free, i.e. terminal hydroxyl. Indeed dimer cyclisation is energetically most favourable due to H-bond cooperativity and two extreme conformations are displayed in Fig. 6.

The spectrum of the solid [23] (not displayed here) shows a broad complex band (Table 3) with three different types of  $\text{OH} \cdots \text{O}$  hydrogen bonds, most likely due to polymorphic crystallisation. Casiraghi et al. [21] reported that in the solid state, the molecules of III are joined in zig-zag polymer chains running along by  $\text{O} \cdots \text{O}$  hydrogen bonds whereas the contacts between the chains are consistent with

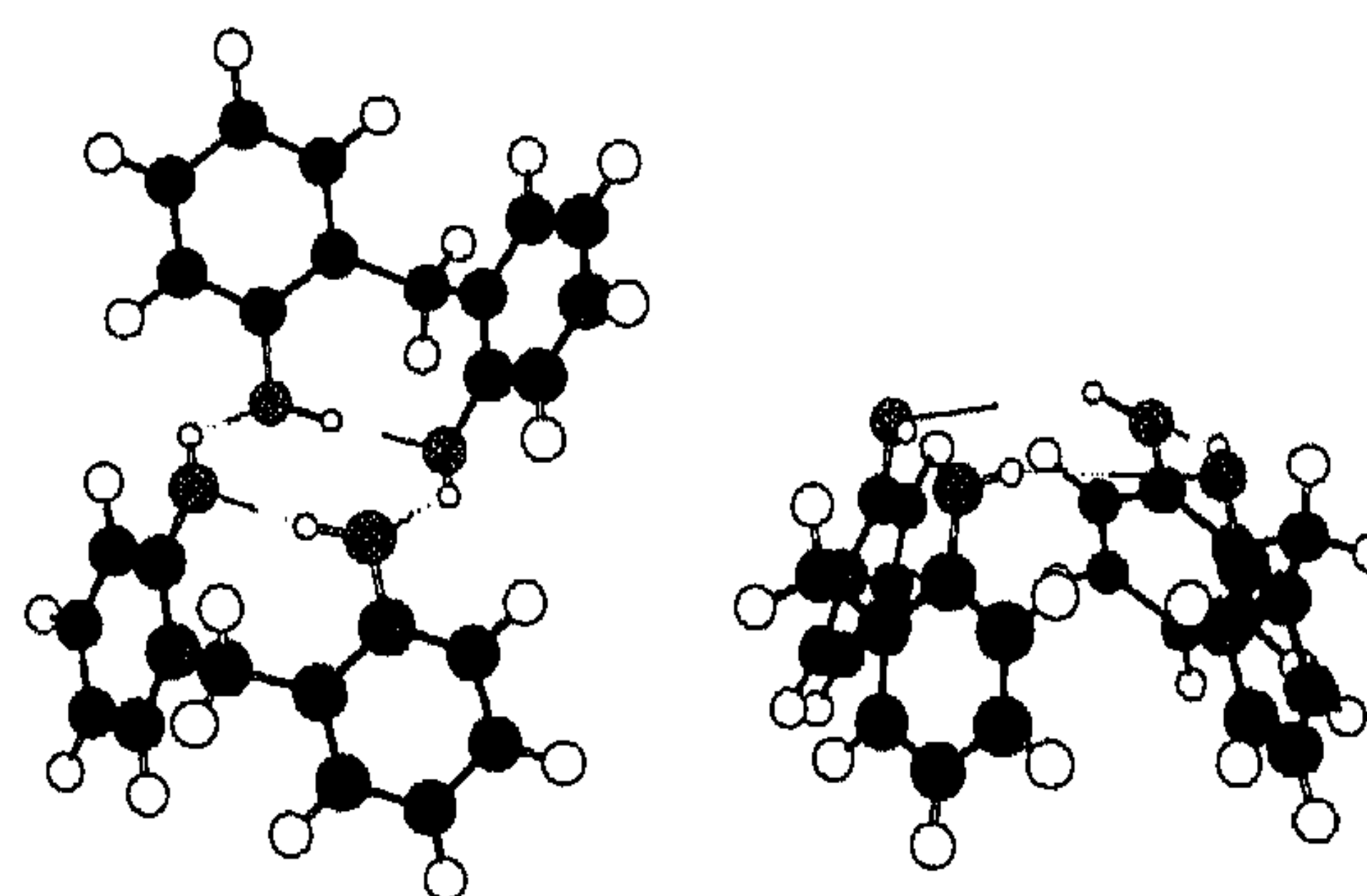


Fig. 6. (a) “trans” (alternate) and (b) “cis” (cone) configuration of the cyclic dimer of III.

Van der Waals interaction radii. In this case vibrational coupling, in-phase and out-of-phase, may give rise to splitting of the OH stretching band.

### Compound VII

The concentration-dependent band at  $3210\text{ cm}^{-1}$  is assigned to association, more in particular to dimerisation. The extreme low frequency of this band indicates that the hydroxyl groups are involved in a strong cooperative hydrogen bond system. Like in compound III, the formation of cyclic dimers is favoured [14]. In our opinion a monomer in the *cis* conformer, or even better with a bifurcated H-bond, allows the straightforward formation of a cyclic dimer. From a structural point of view these cyclic dimers show a strong similarity with calix[6]arenes, be it with more flexibility. Further dilutions were performed in order to get rid of this band, but even at  $10^{-5}\text{ M}$ , self-association is still present. Without breaking the cyclic H-bond the high flexibility of these dimers allows many possible geometric arrangements in solution, which explains the large bandwidth. Like in III (Fig. 6) two different conformations can be adopted.

### Compounds IV, V and VI

In contrast to the compounds VII and III no intermolecular association species have been detected in the OH stretching region at a concentration of  $< 10^{-2}\text{ M}$ . This must be due to the presence of intramolecular H-bonds being preferred to intermolecular association.

#### 4. Calixarenes

We have previously reported on the presence of an Evans' hole in the spectra of calix[4]arene and derivatives [7]. This interfering feature seems to show up in *p*-*tert*-butylcalix[6]arene and compound VII too. We believe that the intensity drop at approximately  $3215\text{ cm}^{-1}$  in the broad OH band is due to perturbations between a broad fundamental and a sharp overtone [24]; this spectral feature is neither sensitive to solvent nor to concentration.

In addition to the calixarene building blocks we have analysed the spectra of *p*-*tert*-butylcalix[4]arene (VIII) and *p*-*tert*-butylcalix[6]arene (IX) both in  $\text{CCl}_4$  and  $\text{CS}_2$ . The spectra of  $\text{CCl}_4$  solution are shown in Figs. 7 and 8 and the band maxima and shifts are listed in the Tables 2 and 5. The existence of the cone conformation for calix[4]arene in solution has been established [1,7] and for calix[8]arene experimental evidence was found for a pleated-loop hydrogen bond array. The hydroxyl groups in the cone conformation form a very strong cooperative cyclic hydrogen bond and this interaction is known to stabilise the conformation. The spectral data in the OH stretching region support this proposal. A broad band at low wavenumbers is observed for ca-

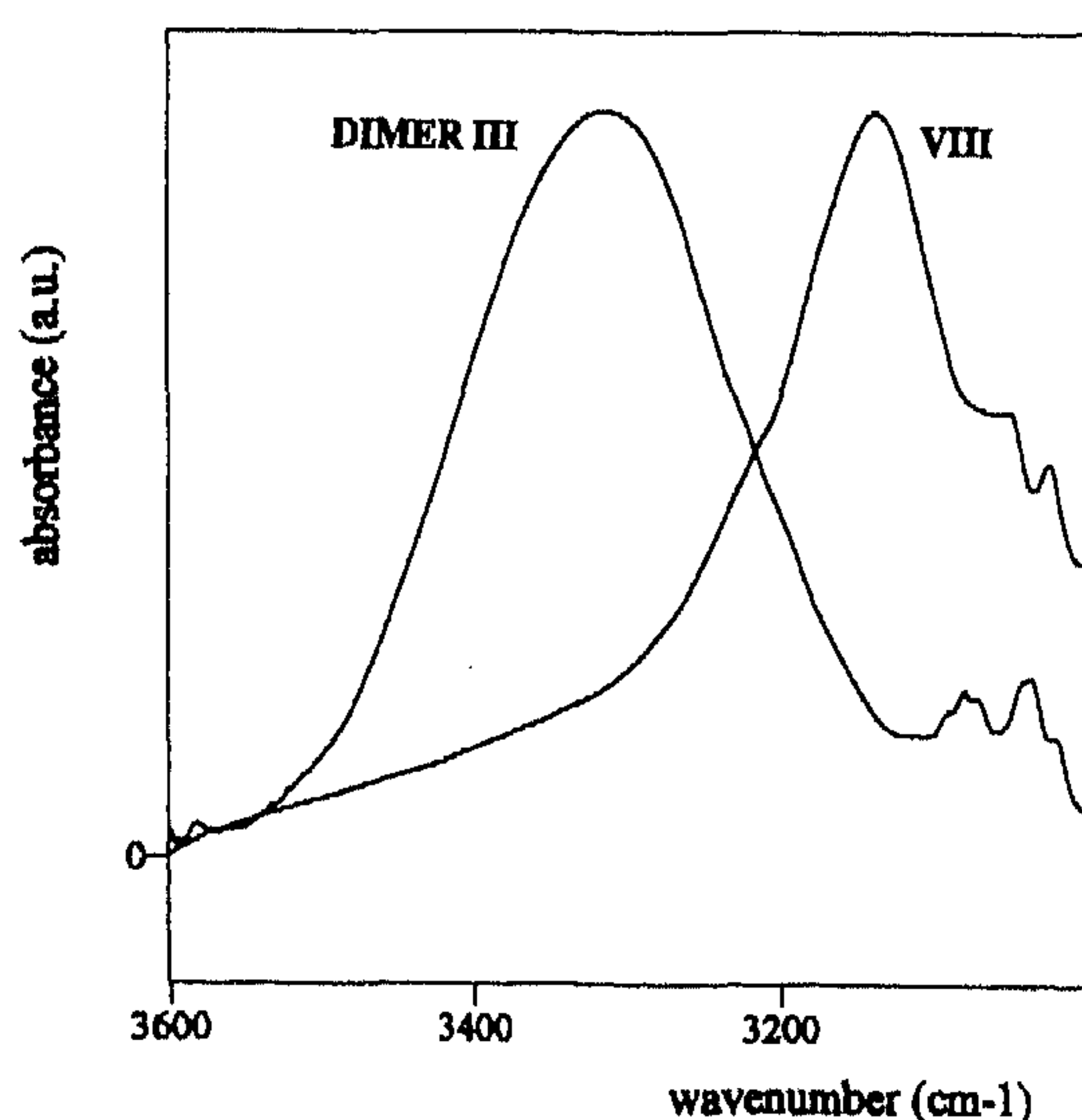


Fig. 7. Dimer OH band of III (after spectral subtraction) and original OH band of VIII in  $\text{CCl}_4$  solution.

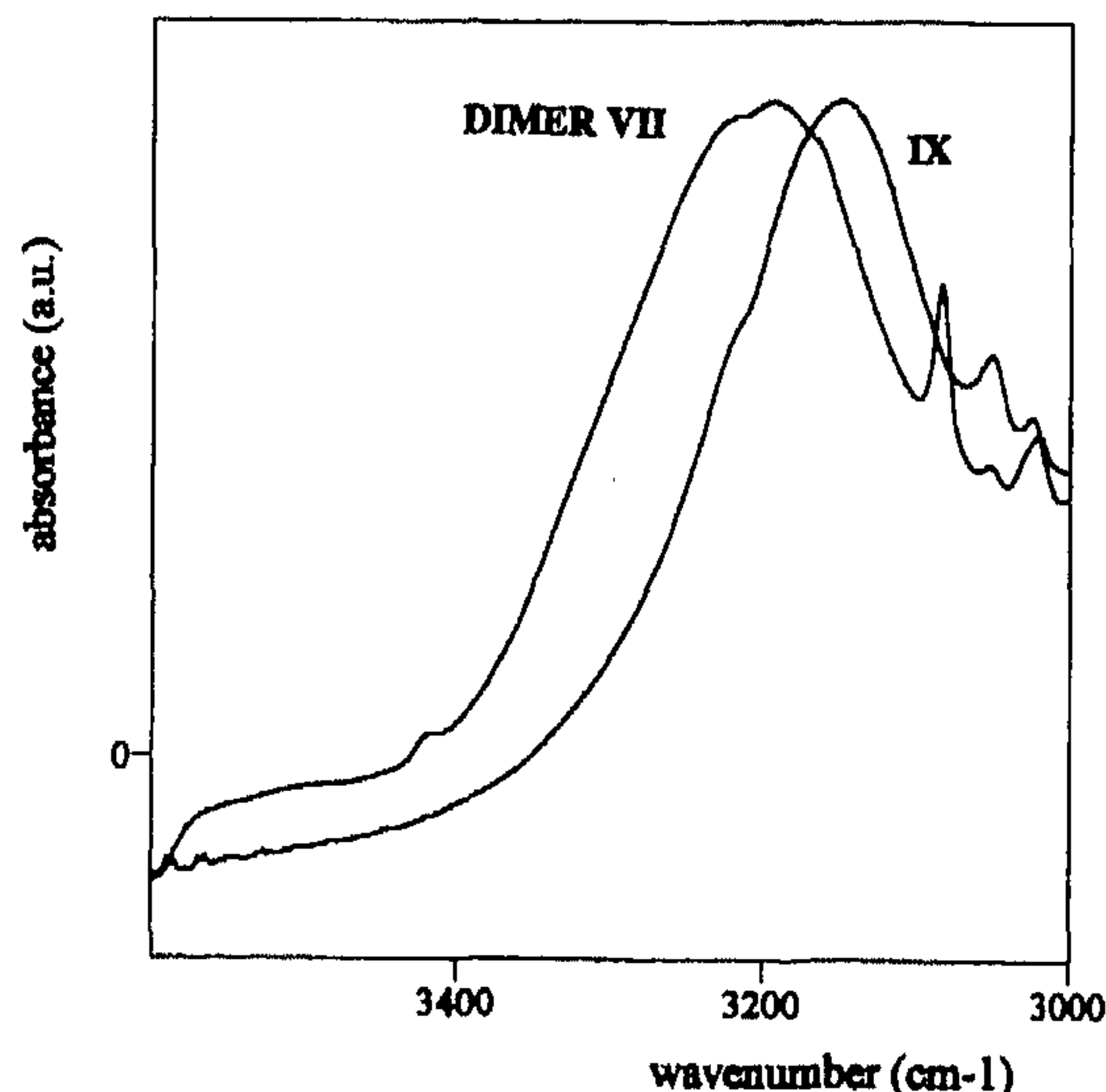


Fig. 8. Dimer OH band of VII (after spectral subtraction) and original OH band of IX in  $\text{CCl}_4$  solution.

lixarenes, the shape and position of this band depending on the number of phenolic residues of the molecule [25,26]. Also the effect of concentration variation is hardly observed, which confirms that each isolated molecule has no free (terminal) hydroxyl left to form intermolecular associates. Even in the crystal phase the cooperative intramolecular H-bond is the driving force for the cone conformation of calix[4]arene [7].

In order to compare the dimers of compounds III and VII with the monomers of *p*-*tert*-butylcalix[4]arene and *p*-*tert*-butylcalix[6]arene, respectively, the samples were measured in  $\text{CCl}_4$  and  $\text{CS}_2$ . The bands reflecting self-association of compounds III and VII were obtained by interactively subtracting two spectra taken at different concentrations (Figs. 7 and 8).

The frequency difference between the dimer band of III and the monomer band of VIII (Table 5) is 207 and  $144\text{ cm}^{-1}$  for  $\text{CCl}_4$  and  $\text{CS}_2$ , respectively. The frequency difference between the cyclic dimers which are formed in non-polar solution and the appropriate calixarene can be explained in terms of conformational flexibility (Fig. 6). Compound III has enough orientational freedom to allow the formation of different geometries between the extreme



“cone” and “alternate” conformations without interruption of the circular H-bond. The larger HBW value, compared to the rigid calix structure, very well explains the flexibility of the dimers in solution. The average position of the hydrogen atoms acting as donors varies with the mobility of the molecules, and therefore the band becomes broader. We assume that on the average the freedom of the system weakens the intermolecular  $\cdots \text{OH} \cdots \text{OH} \cdots$  interaction despite the fact that these are involved in a cooperative cyclic system. In **VIII** the mobility of the system is reduced but it has been shown that this structure is very sensitive to different solvents [7].

The wavenumber shift of the band maximum due to solvent variation, i.e. the solvent shift value ( $\nu_{\text{CCl}_4} - \nu_{\text{CS}_2}$ ), of the dimer band of **III** is small ( $+10 \text{ cm}^{-1}$ ) compared to the shift of **VIII** ( $-53 \text{ cm}^{-1}$ ). In continuation to our previous results [7] of the solvent effect on the geometry of the cone conformation in (partly) methylated *p*-*tert*-butylcalix[4]arenes we propose that the configuration of the cone is altered by this inclusion, most likely  $\text{CS}_2$ . As appears from the frequency shift the hydrogen bonds of **VIII** become weaker in  $\text{CS}_2$ . On the other hand, the flexibility of the dimers of compound **III** do not seem to be that solvent sensitive. The flexibility of dimer **III** allows solvent molecules to enter the cavity and does not form cavities attractive or selective to solvent molecules. Apparently the solvent shift of more “open” or “flatter” dimer structure is the result of a dielectric solvent effect.

The compounds **VII** and **IX** behave in a similar way. Compared to **III** the band maximum of the dimer is strongly red-shifted, which points to improved cooperativity due to fixation of the three aromatic residues in each monomer. The spectra show a smaller frequency difference between the dimer band of **VII** and the monomer of **IX** (Table 5), 60 and  $50 \text{ cm}^{-1}$ , respectively, for  $\text{CCl}_4$  and  $\text{CS}_2$ . The solvent shift ( $\nu_{\text{CCl}_4} - \nu_{\text{CS}_2}$ ) is small, 5 and  $15 \text{ cm}^{-1}$ , most likely due to dielectric solvent effect. It confirms that both solvents can freely enter into the annulus without causing considerable cone distortion. The effect of the solvent is mainly a bulk (dielectric) effect not disrupting the cooperative H-bond in these flexible molecules or molecular clusters.

The results of this study will be used to verify the conformational equilibrium of partly methylated *p*-*tert*-butylcalix[6]arene derivatives. Advanced calculations on these compounds are in progress.

## 5. Conclusions

Different conformers are energetically stabilised by various types of hydrogen bonds, viz.  $\text{OH} \cdots \pi$ ,  $\text{OH} \cdots \text{OH}$ ,  $\text{OH} \cdots \text{OCH}_3$ , bifurcated  $\text{OH} \cdots \text{O/O}$  and cooperative  $\cdots \text{OH} \cdots \text{OH} \cdots \text{OH}$  chains. The transferability of spectral data related to molecular H-bond structures has been shown to be an excellent tool to establish the presence of different types of conformers in this series of phenols. The presence of two terminal hydroxyl groups in a building block, both being involved in an intramolecular cooperative H-bond, seems to be a structural condition to promote the formation of stable cyclic dimers in solution.

An increase in the ring size facilitates optimal geometric alignment of H-bonds and thus stimulates the cooperativity of the H-bond in cyclic dimers as well as in calixarenes.

Increase in the flexibility, in cyclic dimers of **III** and **VII**, results in a decrease in the H-bond strength, in fact the average H-bond ( $\text{O} \cdots \text{O}$ ) distances slightly increase. The increase in the HBW is related to random disorder of the H-bonding proton.

The effect of (small) solvent molecules ( $\text{CCl}_4$  or  $\text{CS}_2$ ) on the band maximum is strongest in a rigid calix[4]arene with a relatively small cavity in the cone conformation.

## Acknowledgements

The research described in this paper was partly supported by the Netherlands Foundation for Chemical Research (SON) with financial aid from the Netherlands Organisation for Scientific Research (NWO). Dr. L. Kroon-Batenburg and M. Langoor are kindly acknowledged for their assistance in performing MM3 calculations.

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