An infrared study of host–guest association in solution by substituted resorcinarene cavitands. Part I. Structural aspects of halide complexation by a tetraurea cavitand

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Complexation of chloride, bromide and iodide ion was investigated for a resorcinarene cavitand substituted on its upper rim with four *N*-(*o*-nitrophenoxy-*n*-octyl)ureido groups. Association in chloroform takes place solely *via* hydrogen bonding by the urea moieties, and is monitored well by infrared spectroscopy. Association constants are high, about 10^4 M^{-1}, and a small preference for chloride over bromide and iodide is observed.

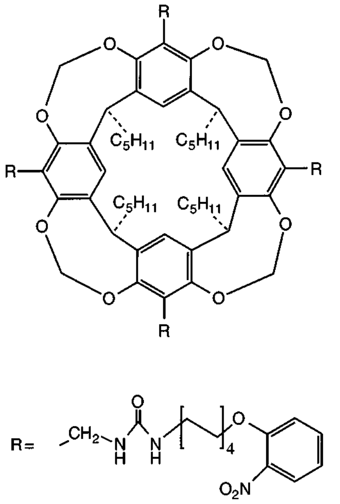
Upon binding of the anion, the array of weak intramolecular bonds is disrupted and replaced by hydrogen bonds towards the halide lone pairs. No significant reorganisation of the urea *o*-nitrophenoxy-*n*-octyl substituents was found, which suggests a re-ordering of the urea groups only upon binding. Co-operation of the bonding moieties is observed in the complexation of halide ions as a result of pre-organisation of the urea groups on the upper rim of the resorcinarene cavitand by weak hydrogen bonding interactions.

1. Introduction

Hydrogen bonding plays an important role in molecular recognition and selective association processes of neutral compounds as well as ionic species.[1] It has been shown that urea moieties are strong hydrogen bond donors, and complexation of anions solely through hydrogen bonding by these structural units has been reported for several types of anions.[2–5]

Urea-substituted calixarenes have been investigated for complexation of ionic species. Although a co-operative effect in complexation is observed if more than one urea moiety is present at the calixarene, still the efficiency is lower than expected due to hydrogen bonding of the side chains within the structure.[6–8] Recently, synthetically well accessible resorcinarene cavitands were reported, composed of four bridged aromatic units,[9] that are suitable for a wide range of further functionalisation with hydrogen bonding moieties.[10–12] Therefore, new types of interesting receptors have become available, which can give useful insights in recognition processes and anion transport.[13]

Complexation and membrane transport of halide ions by new neutral urea-functionalised resorcinarene cavitand anion ligands was investigated recently by Boerrigter *et al.*,[13] and a method for the determination of the association constant and stoichiometry was reported by Nissink *et al.*[14] In this study, the complexation of halide anions by a functionalised cavitand is investigated. The cavitand, tetrakis[*N*′-(*o*-nitrophenoxy-*n*-octyl)ureidomethyl]cavitand (NPOE),[13] has four urea moieties on its upper rim, substituted with *o*-nitrophenoxy-*n*-octyl groups to improve its solubility in chloroform. Association with halide is achieved through hydrogen bonding by ureido groups within the cavitand, as was indicated by ^{1}H NMR experiments.[13] Although the sensorial potentials of vibrational modes in general, and the XH stretching modes (X = O,N) in particular, have been shown to be very useful in the analysis of binding phenomena[15–17] in host–guest chemistry, IR spectroscopy is not widely applied. Therefore, we initiated an infrared study to shed some light on the structural and associative properties of the above-mentioned cavitand. In addition to this, MM2-optimisation and a comparison of solid-state data were used to evaluate the spatial characteristics of the binding site.



NPOE

2. Experimental

Materials

The urea ligand NPOE (tetrakis[*N*′-(*o*-nitrophenoxy-*n*-octyl)-ureidomethyl]cavitand) was prepared according to literature procedures.[13] Tetra-*n*-butylammonium halide salts (TBA-X, X = Cl, Br, I) (Aldrich, p.a.) were used as received. Ethanol-free chloroform, was prepared by treating the solvent (Merck, p.a.) with alumina and was used within 6 h.

Infrared spectroscopy

Infrared spectra were recorded on a Perkin-Elmer System 2000 Spectrometer equipped with a DTGS detector and a sample shuttle. Scanning conditions: resolution 4 cm^{-1}, number of scans 16, medium Norton–Beer apodisation. All experiments were performed at room temperature.

Solid state spectra were recorded as KBr pellets (Merck, Uvasol). Solutions were measured in cells with KBr, NaCl or CaF_2 windows and path length 0.5, 1 or 2 mm.

Sampling

Spectra were recorded of freshly prepared solutions in water- and ethanol-free chloroform for host NPOE with tetra-*n*-butylammonium halide salts as guests, with host fractions covering the range 0.1–0.9 and a constant total molar content (<1 mM). At least 5 samples were prepared.

Sampling is performed such that the sum of initial (weighed-in) host and guest concentration is constant, and the stoichiometry of the reaction is obtained from a plot of complex concentration *vs*. initial host fraction, a so-called Job-plot.[18] No interfering interactions of the counterion with the host were observed in ^{31}P NMR measurements of related tetra-*n*-alkylphosphonium salts. At the highest concentrations applied for the cavitand (~0.6 mM), no self association of the host was observed in the IR spectra.

Association constants

Data analysis was performed by using an algorithm described elsewhere.[14] In order to calculate the association constant, the ureide NH stretching vibrations were used as a probe. A concentration profile for the complex was obtained by multivariate regression of the NH stretching region, followed by an additional correction. This profile was fitted with models of 1-to-*n* and *n*-to-1 ($n = 1$–4) stoichiometry, finally yielding the association constant and association order of the reaction.

We estimate the error of association constants to be ±10%.

Qualitative analysis by application of multivariate regression

Information on binding behaviour of the host was obtained by subjecting a series of spectra to regression analysis (Partial Least Squares-1) as described elsewhere.[14] On selecting a wavenumber range for regression analysis that contains mainly host and complex features, one expects that regression as a function of initial host fraction yields two factors that contribute to the sample spectra. The first factor described a spectral component linearly related to the initial host fraction. The residual spectral contribution, not linearly correlated to the initial host fraction is accounted for in the second (and higher) factors,[19,20] and is, in the underlying case, due to association of host and guest in the sample solutions and noise.

When spectral changes due to association are significant, the second factor accounts for non-linear spectral deviations caused by formation of the host–guest complex. The scores obtained for the above-mentioned factors reflect the trends in concentrations of the host (score for factor 1) and the complex (score for factor 2). The corresponding factors can be used to obtain a qualitative indication of spectral changes due to the presence of host and complex in the sample solutions.[14] Scores and factors solved by the regression technique should be used with care and results should always be checked, as in regions where guest spectral contributions are to be expected, interpretation is not straightforward.

Table 1 Structural information for *N*,*N*′-disubstituted urea–halide contacts from crystal data. No iodide–*N*-alkylamide contacts were found. Mean distances are given. The number of contacts found is given in parentheses

trans-*N*,*N*′-Dialkyl-substituted urea–chloride contact		
N–Cl	3.16 Å	Cl^- is in the N–CO–N′ plane, anion centred between nitrogen atoms (2)
N′–Cl	3.25 Å	
N–N′	2.26 Å	
Unsubstituted urea–bromide contact (1)		
N–Br	3.53 Å	Br^- is in the N–CO–N′ plane, anion centred between nitrogen atoms (1)
N′–Br	3.60 Å	
N–N′	2.28 Å	
N–Br	3.6 Å	Br^- across the NH_2 group (6)
trans-*N*-Alkyl-substituted amide–chloride contact		
N–Cl	3.2 Å	Linear NH···Cl bond, in-plane (5)
trans-*N*-Alkyl-substituted amide–bromide contact		
N–Br	3.4 Å	Linear NH···Br bond, in-plane (4)
trans-*N*-Aryl-substituted amide–iodide contact		
N–I	3.7 Å	Linear NH···I bond, in-plane (4)

Data treatment

Regression analysis (Partial Least-Squares-1) was performed using GRAMS PLS software.[21] The built-in baseline correction was applied in all cases.

Curve fitting analysis was performed using the GRAMS software package.[21] Band positions, widths, intensities and shape were left free on optimisation. Consistency of fit of the solutions was ensured by processing several spectra from a sample series.

Structure optimisation

MM2-level structure optimisation was performed using the Apple Macintosh Chem3D package.[22]

3. Results and discussion

3.1 Structural analysis

Several crystal structures are known for substituted resorcinarenes, but no halide inclusion complexes have been reported yet for urea substituted cavitands. For a *N*,*N*′-disubstituted urea, two urea–chloride contacts (within the same crystal structure[23]) are found in the Crystallographic Structural Database. In these contacts, bridging is exerted by both NH units, in the plane of the urea moiety. Distances can be found in Table 1.

Unfortunately, no data are found for *N*,*N*′-disubstituted ureas with bromide. For unsubstituted urea, several contacts emerge. In these cases the same behaviour is observed as described for the two chloride contacts, but also a cluster of anions within bonding range is found at positions opposite to the NH_2 groups, indicating that bonding to the urea moiety does not always need to be symmetric.

To gain insight in bonding through one of the NH groups solely, information was gathered on amide–halide contacts (Table 1). Data on these contacts are more abundant than for urea and distances found are remarkably similar to the urea–halide contact distances. The main difference from the urea contacts is that in all cases, the amide NH–halide bonds are near-to-linear.

Data for purine- and pyrimidine-NH···Cl hydrogen bonding indicate H···Cl distances of $2.04\ Å < d < 2.39\ Å$, with a mean of 2.13 Å.[24] This distance is well in accordance with the data observed for both the urea-NH···Cl and amide-NH···Cl contacts. An interesting characteristic found for the

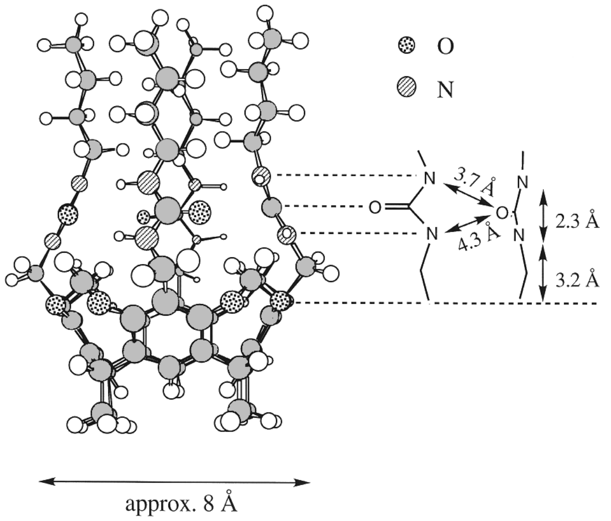


Fig. 1 Representation of MM2 optimised NPOE. The *o*-nitrophenoxy-*n*-octyl substituents of the urea moieties are mimicked by shorter *o*-nitrophenoxy-*n*-butyl chains; the lower rim pentyl chains of the cavitand are replaced by methyl groups. A schematic representation of the two rightmost substituents is depicted on the right. Data were obtained from the optimised cavitand structure.

hydrogen-bonded chloride anion is that in general the spread of bond lengths is relatively narrow in the solid state, compared to other donor–acceptor systems.[24]

A model cavitand structure was optimised by MM2[22] to obtain information on the geometry of the cavitand. The optimised structure is displayed in Fig. 1. Distances for the resorcinarene backbone thus obtained are comparable to crystal-structure data for a related substituted cavitand compound.[25] From crystal-structural data, we expect that the urea moieties bind with both NH groups in a bifurcated way at a distance of approximately 2.2 Å, resulting in a strong interaction. As can be seen, the cavity formed by the four urea groups leaves ample space for the halide to be bonded in this void (Fig. 1). Binding of the halide ion by more than one urea moiety is possible, taking into account that a chloride ion is known to be either three- or four-co-ordinated and that no strong directional properties have been observed for the anion as an acceptor in hydrogen bonding.[24]

3.2 Infrared spectroscopy

3.2.1 NPOE and tetrabutylammonium chloride. Spectra for series of mixtures of NPOE and halide salts in chloroform are presented in Fig. 2a–c. Hydrogen bond formation is clearly visible for NPOE and tetrabutylammonium chloride, bromide and iodide, even in the millimolar range shown here. At these concentrations (0.6 mM and lower), no evidence of self-association was found for solutions of pure NPOE. A spectrum of NPOE in chloroform is displayed in Fig. 3a (top spectrum), and a tentative assignment of characteristic bands is given in Table 2.

For chloride association, a broad band emerges at 3320 cm^{-1}, displaced from the non-ligating-NH vibrations by 120 cm^{-1}. For the pure host, these NH^{free} bands are found at 3446 and 3426 cm^{-1} (shoulder), as determined from the second derivative and curve-fitting. The co-operative effect of the four bonding urea units at the upper rim of the cavitand induces an association constant that is significantly higher than for chloride complexation by a single disubstituted urea. An association constant of 8.6×10^4 M^{-1} for 1-to-1 complexation with chloride ion was derived from infrared data for NPOE,[14] whereas ^1H NMR measurements indicate that for a single urea model compound the association constant is about 1000 M^{-1}.[26]

A set of spectra for host fractions in the range 0.1–0.9 was subjected to PLS-1 regression analysis as a function of the initial host fraction. The spectral regions and results for analysis of the NPOE···Cl set are depicted in Fig. 3a (factors) and 3b (scores). Factor 1 (Fig. 3a, middle) strongly resembles the host spectrum (Fig. 3a, top) and the plot of the score of factor 1 (Fig. 3b, left) shows an almost linear dependency of this spectral contribution and the weighed-in amount of host.

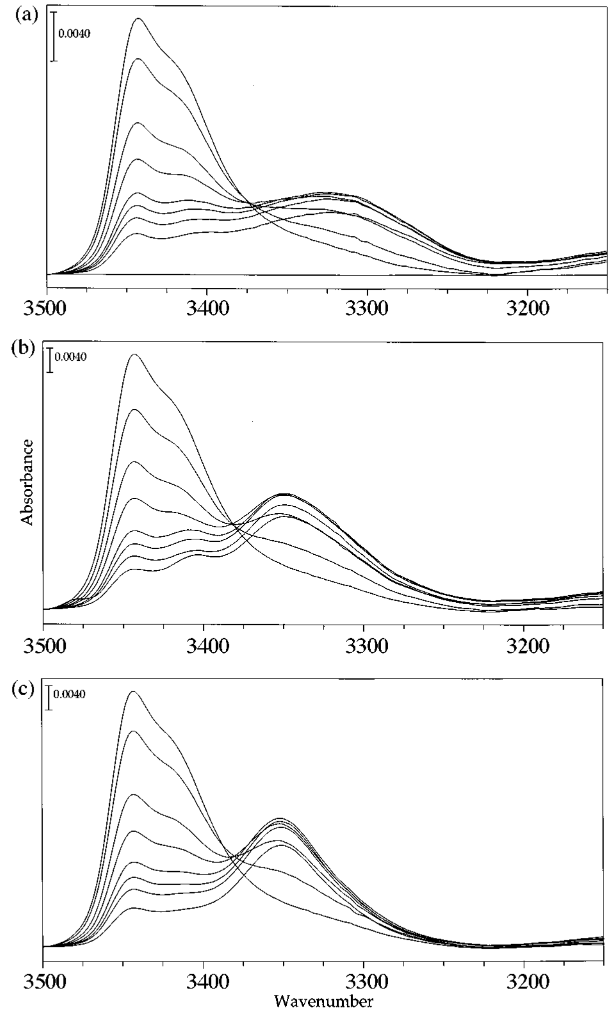


Fig. 2 NH stretching region for host NPOE with guest tetrabutylammonium halide (pure host spectrum, concentration 0.5 mM, and samples at host fractions in the 0.9–0.1 range). (a) Guest TBA-Cl; (b) Guest TBA-Br; (c) Guest TBA-I.

The score of factor 2 (Fig. 3b, right) can be regarded as a Job's plot, and 1-to-1 complexation is indicated by the maximum at an initial host fraction of 0.5. Factor 2 itself reflects the spectral changes that must be added to the contribution of factor 1 in order to approximate a mixture spectrum for increasing concentrations of the complex. This means that negative bands must be interpreted as a decrease of the band intensity, and positive bands must be regarded as band increases induced by complexation of halide. A closer inspection of factor 2 reveals the most influential changes: a decrease of the 1539 cm^{-1} band in the host spectrum and introduction of new bands at 1560 and 1661 cm^{-1}. The latter is about 20% narrower than the original one present in the NPOE host spectrum.

We assign the 1354 cm^{-1} band in the host spectrum to the symmetric aryl–NO_2 stretching.[27] The antisymmetric stretching at 1530 cm^{-1} overlaps with the amide II band of the urea group. As in factor 2, no bands are observed in the 1360–1300 cm^{-1} region, we conclude that the surroundings of the nitro group present on the *o*-nitrophenoxy-*n*-octyl substituent remain fairly constant on complexation of halide. Therefore, the antisymmetric aryl–NO_2 stretching (expected in the 1580–1530 cm^{-1} region) does not appear in factor 2 either. The band

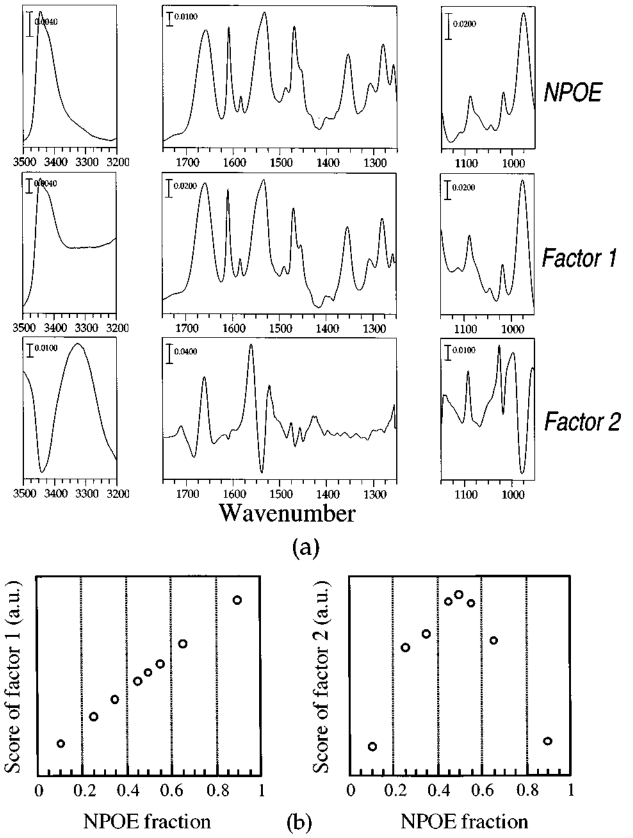


Fig. 3 (a) Host spectrum (top), and factors 1 (middle) and 2 (bottom) obtained after multivariate regression of the NPOE/tetrabutylammonium chloride set. (b) Scores for factors 1 (left) and 2 (right) as obtained by PLS-1.

Table 2 Most characteristic band maxima observed in the IR spectrum of a solution of host NPOE in chloroform (1 mg ml^{-1}) and a tentative assignment (all data in cm^{-1})

NPOE[a]	Assignment[b]
3447	ν_{NH} aryl side
3412	ν_{NH} benzyl side
3360	ν_{NH}, intra-bonded
3170	Combination band amide I/amide II
2958	ν_{CH_3} as.
2932	ν_{CH_2} as.
2873	ν_{CH_3} s.
2858	ν_{CH_2} s.
1667sh	$\nu_{C=O}$, (amide I)
1653	$\nu_{C=O}$, (amide I), hydrogen bonded
1609	Aromatic quadrant stretching,
1602	*o*-Nitrophenyl ring
1550	$\delta_{NH} + \nu_{CN}$ (amide II), hydrogen bonded
1527	$\delta_{NH} + \nu_{CN}$ (amide II)
1488	δ_{CH_3} as.
1469, 1453	CH_3,CH_2 def.
1354	Amide III
1307	OCHO wagging?
1280	ν_{NO_2} s.
1165	CC stretching *n*-alkane
1149	CC stretching, ν_{COCOC} doublet,
1088	δ_{CH} in-plane bending (subst.) {2}?
1071	δ_{CH} in-plane bending (subst.) {18b}
1018	δ_{CH} in-plane bending (subst.) {18a}
975	δ_{CH} out-of-plane wagging (subst.)? Cavitand ring breathing mode?

[a] Positions of overlapping bands determined by second derivative and curve-fitting. [b] s. symmetric; as. antisymmetric; w. weak; sh. shoulder; def. deformation; subst. phenyl or *p*-fluorophenyl substituent on ureido moiety; { } Wilson mode number for aromatic ring vibrations.

at 1560 cm^{-1} in factor 2 and the negative contribution at 1531 cm^{-1} indicate an increase and decrease, respectively, of the intensities of bands at these positions. These features are attributed to the occurrence of a new hydrogen-bonded[28] amide II type band found at 1555 cm^{-1} in the mixture spectra on complexation of halide. The original amide II-type band of non-associated NPOE is found at 1528 cm^{-1}, with a shoulder at 1546 cm^{-1} indicating intramolecular hydrogen bonding of the amide moieties to some extent.

The assumption that the mode of hydrogen bonding is altered completely is endorsed by the observation that a new band appears for the C=O stretching vibration at a slightly higher position (1661 cm^{-1}). A small increase in wavenumber as well as band width caused by a change in hydrogen bonding is not very likely, as this would cause a shift to a lower rather than to a higher wavenumber.[28] The change in the C=O stretching vibration of the urea is ascribed therefore to induced electronic effects as a result of hydrogen bonding of the neighbouring NH units and to differences in the surroundings of the C=O group possibly caused by a conformational change of the urea moiety.

3.2.2 NPOE and tetrabutylammonium bromide. Association of bromide with host NPOE occurs in a 1-to-1 manner comparable to chloride complexation with an association constant of 1.3 × 10^4 M^{-1}. A band for the hydrogen-bonded NH moiety is seen at 3349 cm^{-1}, shifted from the non-bonded NH stretching bands by ~100 cm^{-1} (Fig. 2b). Regression analysis (not shown) reveals that the amide II band is affected most, in a way similar to the complexation of chloride. A positive contribution in the second factor at 1553 cm^{-1} is observed, accounting for the band that emerges at 1549 cm^{-1} in mixture spectra on complexation of bromide. This band is 6 cm^{-1} lower than the corresponding amide II band observed for chloride complexation, indicating a weaker hydrogen bond. A second positive contribution is found in the C=O stretching region at 1663 cm^{-1}. There is no evidence for disorder of the *o*-nitrophenoxy-*n*-octyl substituents.

3.2.3 NPOE and tetrabutylammonium iodide. Analysis of the complexation of iodide anion by NPOE reveals a behaviour more similar to bromide complexation than to chloride complexation. A band due to hydrogen-bonding emerges at 3351 cm^{-1} (Fig. 2c). An analysis of the infrared data set shows that the complexation stoichiometry again is 1-to-1 (association constant: 1.4 × 10^4 M^{-1}). A band emerging at 1549 cm^{-1} is seen in the sample spectra. Regression analysis (not shown) suggests formation of bands at 1663 cm^{-1} and 1552 cm^{-1}, as a result of complexation of iodide by the urea moieties.

Again the orientation of the ligating side-chains does not change very much on association, as no distinct spectral changes indicative of side group disorder are observed.

3.3 Halide bonding by NPOE

The results from regression analysis clearly show that binding of the halide ion is accomplished by means of the urea moieties. If we assume similar modes of binding for chloride, bromide and iodide, the shifts of the NH···X stretching bands with respect to the non-bonded NH stretching bands indicate that the strength of hydrogen bonding decreases in the order Cl > Br > I. This is in agreement with the order of binding strength observed for hydrogen bonding of halide by methanol.[29] Also, the half band widths of the bonded-NH features decrease in the same order, possibly as a result of a decrease in translational freedom of the anion when bonded.

There is no indication that the orientation of the *o*-nitrophenoxy-*n*-octyl substituents changes drastically on complexation. The CH out-of-plane wagging (*ortho*-substituted ring) of the side chain is observed at 978 cm^{-1} and does not shift on

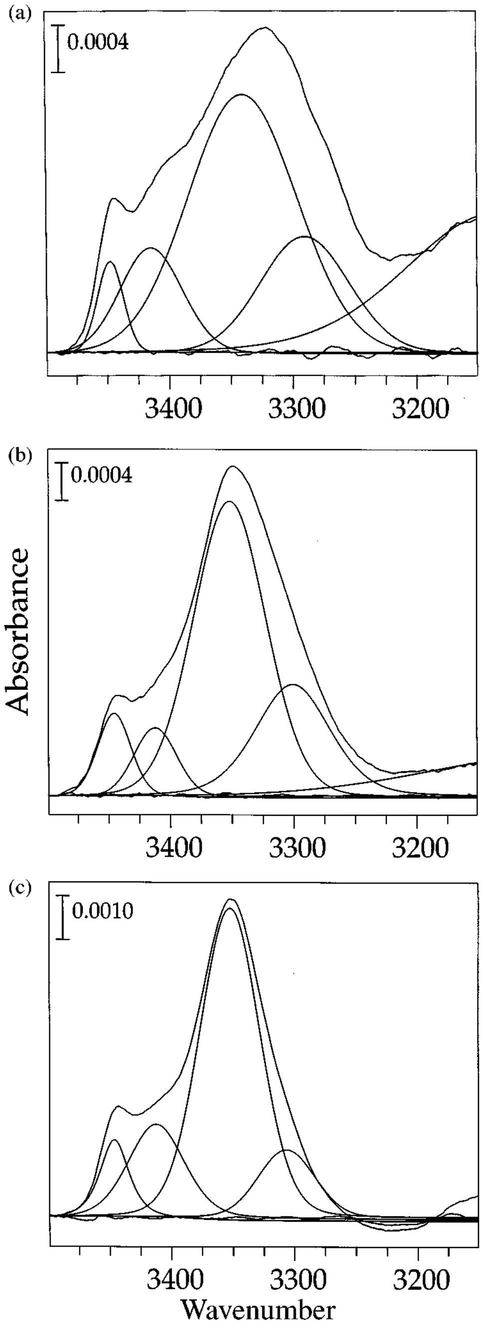


Fig. 4 Fitted bands for the NH region (HBWs are given in parentheses). (a) NPOE/Chloride at host fraction 0.15. Fitted bands: 3447 (25), 3415 (60), 3340 (103) and 3290 cm^{-1} (83). (b) NPOE/Bromide at host fraction 0.15. Fitted bands: 3446 (32), 3412 (40), 3352 (70) and 3301 cm^{-1} (72). (c) NPOE/Iodide at host fraction 0.3. Fitted bands: 3446 (29), 3412 (54), 3353 (58) and 3307 cm^{-1} (54). Bands below 3200 (not listed) were inserted to account for baseline effects due to CH stretching absorptions. The total concentration of host and guest together was 0.5 mM.

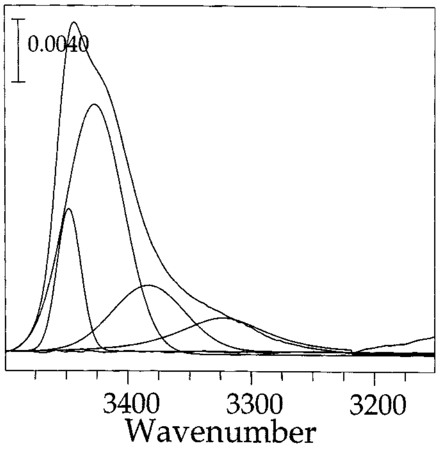


Fig. 5 Fitted bands for the NH region of host NPOE at 0.5 mM (HBWs are given in parentheses). Fitted bands: 3448 (23), 3426 (55), 3381 (69) and 3323 cm^{-1} (86). One band was added to account for the CH stretch absorption tail on the right side of the spectrum (not shown).

complexation. Also, a band at 1282 cm^{-1}, tentatively assigned to the aryl CO stretching of the side chain, does not change significantly. No changes are observed in the nitro-group vibrations.

Curve-fitting analyses were performed for the bands in the NH-stretching region. Band fits for chloride, bromide and iodide complexation at low host fractions are displayed in Fig. 4a–c. The high-wavenumber NH$^{\text{free}}$ part of the spectrum could be fitted well in all cases by two bands. The band shape for the NH$^{\text{bonded}}$ stretching vibration could not be described satisfactorily with one single band, but a good fit was obtained with two bands. As the intensities of the bands are too high for overtones, we assign these pairs to bonded alkylic and benzylic NH moieties. This view is endorsed by the fact that the host NH moieties are found at different positions in the ^{1}H NMR spectrum,[30] and it is clear therefore that the donating properties of both ureido NH groups are not identical.

The ν(NH···Cl) vibrations were fitted by bands at 3340 (HBW 103) and 3290 cm^{-1} (HBW 83); ν(NH···Br) by bands at 3352 (HBW 70) and 3301 cm^{-1} (HBW 72); ν(NH···I) by bands at 3353 (HBW 58) and 3307 cm^{-1} (HBW 54). The largest difference in wavenumber between the fitted NH$^{\text{bonded}}$ stretching bands and the NH$^{\text{free}}$ stretching bands is observed for chloride, followed by bromide and iodide. Association of bromide and iodide results in a similar complex, as can be deduced from the positions of the corresponding NH$^{\text{bonded}}$ peaks, but clear differences are seen in intensities and halfband widths for both species (see Fig. 4b,c).

The NH region of the neat host (Fig. 5) features a bonded-NH band due to intramolecular bonding of the urea groups. A band fit of this region yields two bands, located at higher wavenumbers than those observed on complexation, *viz.* 3381 (HBW 69 cm^{-1}) and 3323 cm^{-1} (HBW 86 cm^{-1}). Although the MM2-optimised structure is only an estimate of the actual situation, results are perfectly in agreement with infrared observations. From Fig. 1 it is clear than an intramolecular pre-organisation of the urea moieties is possible. However, MM2-optimised bonding distances NH···O=C are approximately 3 Å (upper NH) and 3.7 Å (lower NH), indicating that bonds are weak, as normal distances for NH···O=C are about 2 Å.[24] The presence of both NH$^{\text{free}}$ and NH$^{\text{bonded}}$ bands in the infrared spectra suggests that the array of bonds is not very stable, but that a dynamic equilibrium exists between fully and partially intra-bonded species.

From the disappearance of the NH stretching bands of the host assigned to intramolecular bonds (3381 and 3323 cm^{-1}), we conclude that the original intramolecular bonding pattern of urea moieties is largely destroyed on complexation with a halide. Spectral changes indicating either disorder in the octyl chains, or a change in the environment of the nitro groups are absent. Therefore, it is not likely that the orientation of the *o*-nitrophenoxy-*n*-octyl side-chains changes very much on association. When bonding of the halide takes place within the cavitand, one expects that only a re-orientation of the ureido groups is necessary to accommodate the anion.

The fitting of the NH···X (X = Cl, Br, I) band profile by two broad bands can be explained by attributing them to the vibrations of two hydrogen-bonded NH donors. Extinction coefficients for these vibrations rise in the order I ~ Br > Cl. The ratio of areas of these bands changes on going from iodide to chloride, which indicates that either hydrogen bonds are not equal in number for both NH donors within one urea, or that two geometrically different urea–halide bonds occur. The observation from crystal data that hydrogen bonding by a ureido moiety in the solid state is exerted, both symmetrically by two donor NH groups, as well as by one single donor, does not exclude one of these possibilities.

In addition, different bands may also be observed as a result of bonding of the halide by more than one ureide within the complex. Chloride has been found to be three- or four-coordinated in bonding. The ligands of four-coordinated chloride ions appear to be in an approximate tetrahedral conformation.[24] Here, in a sterically efficient association with more than one ligating group, not all moieties will bind in similar geometries with respect to the halide ion, and consequently this leads to formation of different hydrogen bonds. This is probably the most plausible explanation for the occurrence of more than one band for bonded NH.

The fact that tris-substituted ligands gave association constants ten times lower than the tetrakis-substituted carcerands[13] endorses the view that binding of the guest takes place within the cavity formed by the ureas rather than at the outside, and that a co-operative ligating process of the urea moieties is responsible for association. This view is supported by the decrease of the band width in the order HBW(Cl) > HBW(Br) > HBW(I), which can be ascribed to a restriction of the translational freedom of the anion when encapsulated by ligating groups. This librational freedom can be linked directly to the size of the anion, which follows the order Cl < Br < I, and is expected to be smallest for the largest anion. Recently, encapsulation of the halide within a cage of four urea moieties has been reported by Jagessar *et al.* for a similar neutral host system based on porphyrin.[5]

4. Conclusions

Infrared spectroscopy in combination with multivariate regression offers a versatile method for the analysis of association phenomena. The complexation of halide by resorcinarene cavitand NPOE appears to be similar for chloride, bromide and iodide. Complexation stoichiometry is 1 host to 1 guest molecule in all cases. The association constants are high, and a small preference of the host for chloride over bromide and iodide is observed.

Compared to a simple urea ligand, the halide-bonding properties of cavitand NPOE are improved considerably, due to the co-operative, entropy-lowering effect of the four ligating *N*-(*o*-nitrophenoxy-*n*-octyl)ureido units positioned in a rather rigid way on the resorcinarene upper rim. The observation that tris-substituted analogues bind the anions less well, suggests that binding takes place within the cavity. The infrared spectroscopic analysis of the binding process endorses this view, and shows that upon binding, the intramolecular array of hydrogen bonds is disturbed significantly, without influencing the *o*-nitrophenoxy-*n*-octyl substituent orientation. The fact that the array of intramolecular bonds is very weak and easily disturbed, is probably a prerequisite for the efficient encapsulation of the halide anion.

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