An infrared study of host–guest association in solution by substituted resorcinarene cavitands. Part II.[1] Comparison of halide complexation by tetrathiourea cavitands and a simple thiourea

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Binding of halide has been studied for two thioureido-substituted resorcin[4]arenes and a model compound, with special attention to the NH stretching region and the bonding behaviour. Mathematical techniques such as curve fitting, Fourier self-deconvolution and Partial Least Squares analysis have been applied to investigate the characteristics of bonding, and the results are correlated with information obtained from a steric analysis.

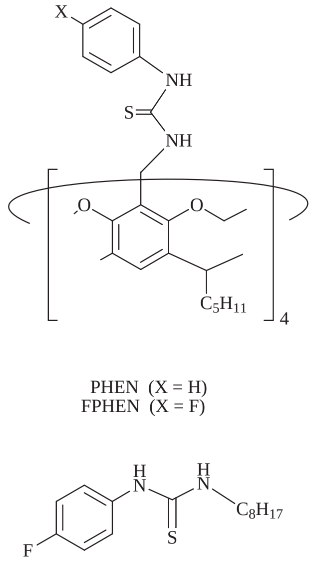
It is shown that association of the halide guest takes place *via* hydrogen bonding between halide ions and thioureido moieties solely for all ligands. Compared to a simple thiourea compound, pre-organisation of the thioureide side-chains on the upper rim by intramolecular bonding enhances the capability of association by a factor of 10 to 100.

An analogy is found between complexation of a halide anion in the cavitands and complexation of an iodide anion by the model compound. This suggests that within the cavitand, chloride, bromide and iodide are all complexed by at least two thioureido moieties, whereas a simple thiourea binds chloride and bromide in a 1-to-1 fashion, and iodide in a 2-to-1 fashion.

Introduction

Molecular recognition processes in which hydrogen bonding plays an important role have been reported for neutral as well as ionic species.[2] An example is the complexation of anions by urea[3] and thiourea moieties.[4] Urea-substituted calixarenes have been investigated for association with ionic species. Although a cooperative effect in complexation has been observed when more than one urea moiety is present on the calixarene, still the efficiency appears to be lower than expected due to hydrogen bonding of the side-chains within the structure.[5–7] Recently, synthetically well accessible resorcinarenes composed of four bridged aromatic units[8] have been reported.[9]

Boerrigter *et al.*[10] reported on the complexation and membrane transport of halide ions by new neutral urea-functionalised resorcinarene cavitand anion ligands. Functionalisation of the rigid carcerand structure with thioureide moieties opens a way to develop interesting new receptors applicable in supported liquid membranes for selective separations.[10] A method to determine the association constant and stoichiometry was proposed by Nissink *et al.*[11] In Part I,[1] halide complexation by a tetraureide-substituted compound was described. Here, we present a comparative infrared spectroscopic study of complexation of halide through hydrogen bonding by two thioureide-functionalised methylene-bridged resorcin[4]arene anion ligands PHEN and FPHEN (Scheme 1).[10] These cavitands associate with halide anions more strongly than the ureide-substituted resorcinarene compound[1,10] as a result of the difference in acidity of the thiourea hydrogens compared to the urea ones.[12] Results are compared with those for a simple thiourea, OFP (Scheme 1).



PHEN (X = H)
FPHEN (X = F)

OFP

Scheme 1

Infrared spectroscopy has been applied, as the sensorial potential of the XH stretching modes (X = O, N) has been shown to be very useful in the analysis of binding phenomena.[13–15] The NH stretching vibrations and related vibrations of the amide moiety are studied in detail to shed some light on the hydrogen-bonding behaviour of the above-mentioned ligands. Results are correlated with those obtained by a steric analysis.

Experimental

Materials

The thiourea ligands PHEN, FPHEN and OFP were prepared according to literature procedures.[10] Tetra-*n*-butylammonium halide salts (TBA–X, with X = I, Br, Cl) (Aldrich, *p.a.*, used as received) were applied as guests. Ethanol-free chloroform was freshly prepared by treating chloroform (Merck, *p.a.*) with neutral aluminum oxide. The solvent was stored on molecular sieves and used within 6 h.

Infrared spectroscopy and sampling

For a description of the experimental conditions we refer to Part I.[1] No interfering interactions of the tetra-*n*-alkylammonium counterion with the host were observed in ^{31}P NMR measurements of the corresponding phosphonium 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

Association constants were determined according to an algorithm described elsewhere.[11] In order to calculate the association constant, the thioureide NH stretching vibrations were used as a probe. The concentration profile for the complex obtained using the algorithm was fitted with models of 1-to-*n* and *n*-to-1 (*n* = 1, 2, 3, 4) stoichiometry in order to obtain the association constant and association order of the reaction.

Qualitative analysis

Information on the bonding behaviour of the host was obtained by subjecting a series of spectra to regression analysis (Partial Least Squares-1). Details are described elsewhere.[1,11] Subjecting a wavenumber-region containing mainly features of host and complex to regression as a function of initial host fraction, one expects this to yield two factors that contribute significantly to the sample spectra. The first factor and score describe a component linear with host fraction. The residual spectral contribution is accounted for in the second (and higher) factors and scores and is in the underlying case a result of association of host and guest in the sample solutions (and noise).[16,17]

Data analysis

Curve fitting analyses were performed using the GRAMS software package.[18] Band position, -width, -intensity and -shape (Gaussian–Lorentzian mix) were left free on optimisation. Fits were produced for different initial parameters that were close to probable solutions; in the case of multiple fit solutions, the error given by the program was used to compare the results. The number of bands was limited to the minimal amount that would yield a satisfactory residual spectrum without anomalies. When possible, Fourier Self Deconvolution (FSD) was applied to determine the number of bands. Consistency of the fitting solutions was further checked by processing several spectra from a sample series. FSD was performed using GRAMS.

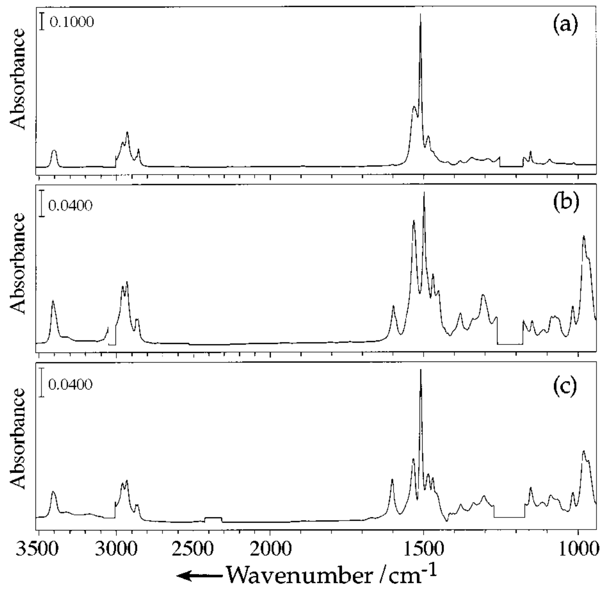


Fig. 1 Spectra of (a) OFP (5.6 mM), (b) PHEN (0.5 mM), (c) FPHEN (0.5 mM) in chloroform.

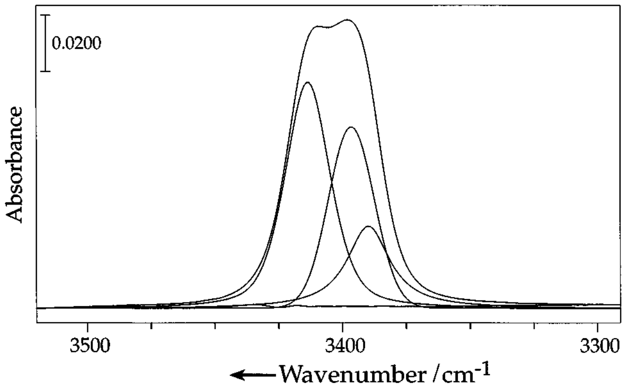


Fig. 2 Fitted bands in the NH stretching region for host OFP.

Steric analysis

Crystallographic data were extracted from the Cambridge Crystallographic Structural Database. MM2 optimisations were performed on an Apple Macintosh computer using Chem3D software.[19]

Results and discussion

We studied the complexation of the three aforementioned hosts with chloride, bromide and iodide anions. Results obtained by IR spectroscopy of unassociated as well as associated hosts are reported below, and are discussed, while the outcome of a steric analysis is also given.

Anion complexation

Host OFP. The spectrum of OFP in a solution of chloroform is presented in Fig. 1(a) and a tentative assignment in Table 1. The non-bonded NH stretching of OFP is seen as a relatively narrow feature centred at 3400 cm^{-1}. Both FSD[20] and curve fit analysis reveal that this band consists of at least three bands, centred at 3414 (21),† 3396 (21) and 3391 (20) cm^{-1} (Fig. 2). As substituted thiourea compounds bear a strong analogy to substituted thioamides and amides, we assign the former to $\nu_{\text{NH-aryl}}$ of the NH moiety at the aryl side and the latter two to $\nu_{\text{NH-alkyl}}$[21] of the different rotamers of the alkyl chain, in

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† Full bandwidth at half height (FWHH) in parentheses.

Table 1 Characteristic band maxima in the infrared spectra of solutions of the hosts OFP, PHEN and FPHEN in chloroform (OFP < 6 mM, cavitands < 1 mM) together with a tentative assignment (data in cm^{-1})

OFP[a]	PHEN[a]	FPHEN[a]	Assignment
3414	3413	3413	ν_{NH} aryl side
3396	3389sh	3392sh	ν_{NH} benzyl side
3389	3328	3324	ν_{NH} intramolecularly bonded
		3171	Combination band amide I–amide II
2959	2959	2960	ν_{CH_3} as.
2930	2932	2933	ν_{CH_2} as.
2872	2872	2873	ν_{CH_3} s.
2857	2861	2861	ν_{CH_2} s.
1531	1532	1533	$\delta_{NH} + \nu_{CN}$ (amide II)
1510	1499	1509	Aromatic semicircle stretch {19a} (subst.)
1485	1487sh	1485	δ_{CH_3} as.
1456w	1470	1470	CH_3,CH_2 deform.
	1452		Aromatic C–C stretching {19b} (subst.)
1382	1380	1380	δ_{CH_3} s.
	1340	1338	Amide III
1292			?
	1307	1304	OCHO wag?
1154			CC stretch *n*-alkane
	1149	1153	CC stretch, ν_{COCOC} doublet
	1144	1148	CC stretch, ν_{COCOC} doublet
1093	1087	1089	δ_{CH} in plane bending (subst.) {2}?
	1075		δ_{CH} in plane bending (subst.) {18b}
	1065	1069	$\nu_{C=S}$
1015	1018	1017	δ_{CH} in plane bending (subst.) {18a}
	982	982	Cavitand/substituent ring breathing mode?
	967	968	Cavitand ring breathing mode?

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

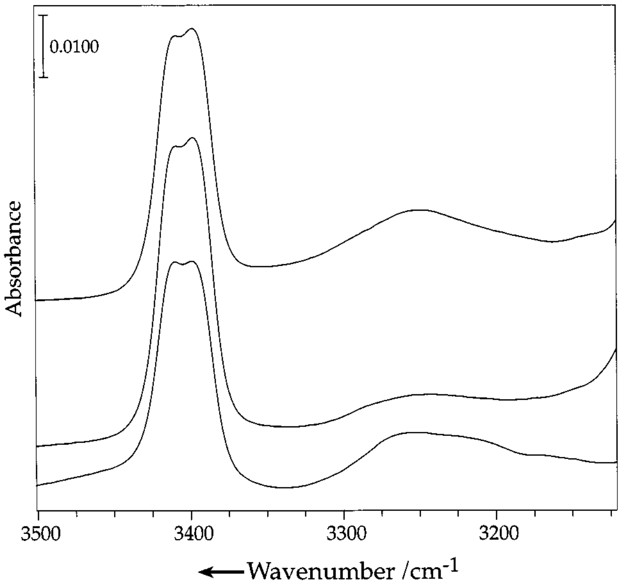

Fig. 3 NH stretching region for host OFP with tetrabutylammonium halide as guest (mol fraction 0.5): (top) guest TBA–Cl (initial host concentration 5.6 mM); (middle) guest TBA–Br (initial host concentration 5.6 mM); (bottom) guest TBA–I (initial host concentration 3.0 mM).

which the β-carbon atom is *trans* or *gauche* to the NH group.[22] No significant amount of *trans*-to-*cis* isomerisation of the thiourea moiety is expected for steric reasons.

Complexation of chloride and bromide by OFP. On complexation of thiourea host OFP with a chloride ion, a second, broad spectral feature emerges at a wavenumber of 3251 cm^{-1}, red-shifted by 155 cm^{-1} from the original NH stretching vibration (Fig. 3, top). Both the frequency and width of this peak (FWHH 144 cm^{-1}) indicate hydrogen bonding with the chloride anion.

On association, the shape of the free NH stretch band does not alter, apart from the effect of superposition of the broad feature at 3251 cm^{-1}. This indicates that no free NH moiety is left on hydrogen bonding, which is analogous with the observed bidentate association of urea compounds with halide in the solid state.[1] Fitted bands are shown in Fig. 4(a). An analysis of the infrared data revealed a 1-to-1 complexation order and an association constant of 2.2×10^3 l mol^{-1} for the association with chloride ion;[11] the constant determined by NMR was 2.0×10^3 l mol^{-1}.[10]

The NH stretching vibrations (Fig. 3, middle) for OFP on complexation with a bromide ion are found at 3413, 3397, 3390 cm^{-1} (free ν_{NH} vibrations) and 3254 cm^{-1} ($\nu_{NH\text{-bonded}}$) [Fig. 4(b)]. Bromide complexation appears to be similar to chloride complexation, although the extinction coefficient for the complex is smaller due to the softer[23] accepting properties of the bromide ion. The bonded NH feature at 3254 cm^{-1} is narrower (FWHH 103 cm^{-1}) than the corresponding band observed for the chloride complexation, probably indicating that the bromide ion fits better into the ligand's binding site.

An analysis of the IR-data shows that the complexation order for bromide is 1-to-1 and the association constant is slightly higher than for the chloride association, *viz*. 8.6×10^3 l mol^{-1}. From the similarity in association constant, the red-shift, and the observation that one band emerges upon complexation, we conclude that bonding for the chloride and bromide atoms is bidentate and comparable in strength.

Iodide complexation by OFP. The bonded-NH region proves to be slightly more complex for the association of OFP with iodide than for association with chloride or bromide (Fig. 3, bottom). A curve fit analysis [Fig. 4(c)] reveals that the non-bonded NH stretching band is best fitted by three bands at positions 3415, 3400 and 3391 cm^{-1}. Intensities and widths differ from those observed for complexation of chloride and bromide ion [*cf.* Fig. 4(a),(b)]. At least two bands are required, centred at 3262 and 3209 cm^{-1}, to fit the hydrogen bond feature in the spectrum. Half band widths associated with these bands are 68 and 57 cm^{-1}. An analysis of the infrared data reveals a complexation of 2 hosts to 1 guest, with an association constant of 1.6×10^3 l^2 mol^{-2}.

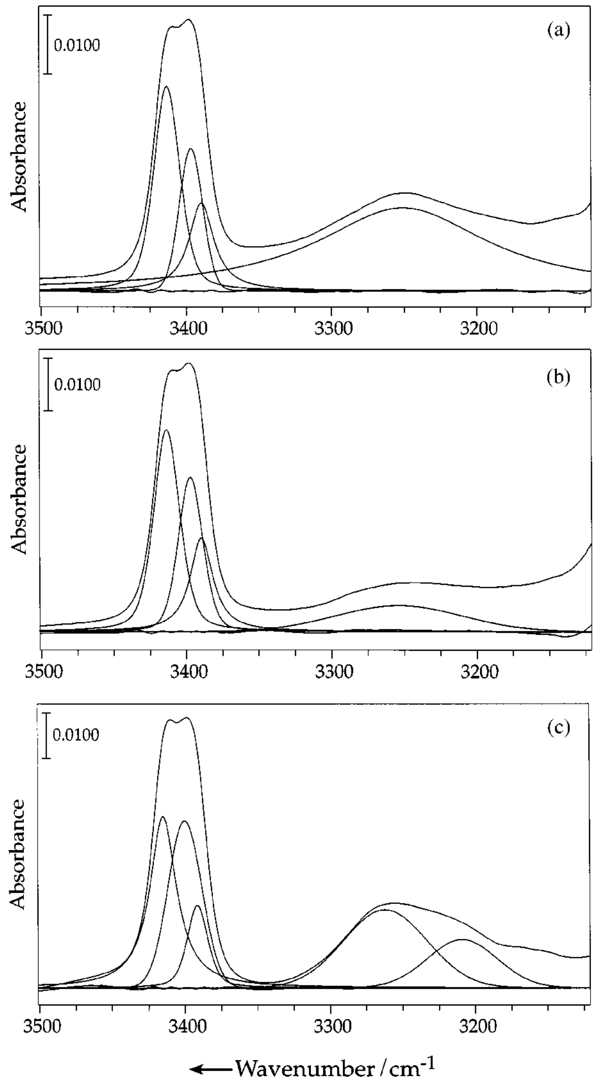

Fig. 4 Fitted bands in the NH stretching region for host OFP complexed with halide. (a) OFP and chloride (host fraction 0.5), with bands at 3413 (21), 3396 (19), 3389 (21) and 3251 (144) cm^{-1}; (b) OFP and bromide (host fraction 0.5), with bands at 3413 (21), 3397 (20), 3390 (19) and 3254 (103) cm^{-1}; (c) OFP and iodide (host fraction 0.1), with bands at 3415 (22), 3400 (27), 3391 (17), 3262 (68) and 3209 (57) cm^{-1}. To account for the CH stretching at the right side of the spectral window, a band was added in all cases. This band has been omitted for clarity.

A possible explanation for the occurrence of at least two hydrogen-bonded NH stretching vibrations is that bonding to the NH moieties is no longer symmetric due to steric incongruity of the anion to a single thioureide unit. This will result in different hydrogen bonds for each NH. However, the red-shift of the broad band observed at 3262 cm^{-1} is similar to that for the bromide and iodide.

On the other hand, the strong red-shift of approx. 200 cm^{-1} of the second band possibly indicates formation of a single, strong, linear NH$\cdots$I bond. The differences observed in the free-NH region endorse this view, as on formation of a linear bond, one of the NH moieties is left non-bonded. We therefore tentatively assign the bands at 3262 cm^{-1} to a bidentate S=C(NH)$_2\cdots$I contact similar to the contact found in the binding of chloride and bromide, and we ascribe the band at 3209 cm^{-1} to a strong unidentate NH$\cdots$I contact. Apparently, for the chloride and bromide ions the bidentate bond is favoured over the unidentate one.

Hosts PHEN and FPHEN. The spectra of hosts PHEN and FPHEN are shown in Fig. 1(b) and (c), and an assignment of the bands is given in Table 1. Due to the electron-withdrawing effect of the fluorine atom in the *para* position to the thioureido moiety, the acidity of the NH group has increased. Yet only slight changes are observed in the spectra for the vibrations of the thioureido moiety and no significant shifts are noted for the resorcinarene cavitand backbone vibrations, so similar orientations of the side-chains are expected.

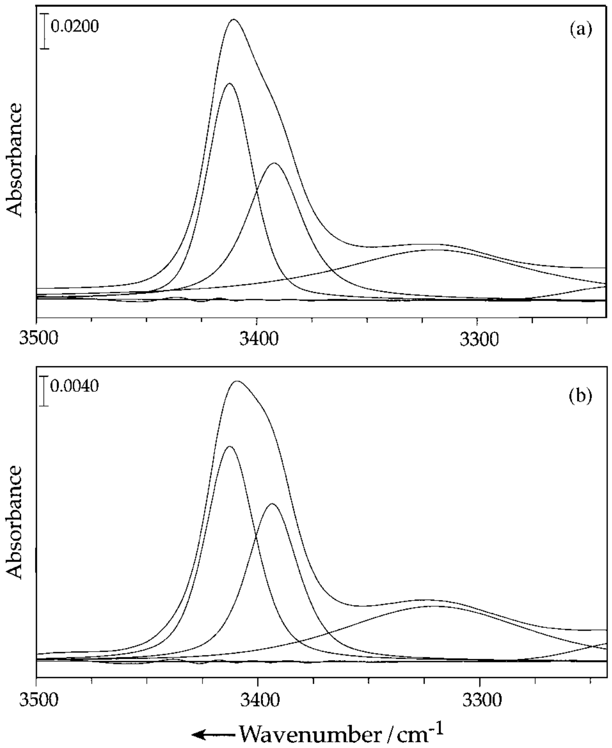

Fig. 5 Band fits for the NH stretching regions of unassociated hosts PHEN and FPHEN. (a) PHEN 3412 (24), 3392 (30) and 3319 (112) cm^{-1}; (b) FPHEN 3412 (27), 3393 (27) and 3320 (98) cm^{-1}. The rightmost band accounts for an overtone outside the region and is omitted from the list. No intermolecular association is observed at the concentrations used.

A band fit for the NH stretching region of both hosts is shown in Fig. 5(a),(b). Results for PHEN and FPHEN are similar. The non-bonded NH region is fitted well by two bands at 3412 and 3393 cm^{-1}, which we assign to NH stretching vibrations of the (fluoro)phenyl-NH and benzyl-side NH groups, respectively. Compared to PHEN, the intensity of the 3393 cm^{-1} band of FPHEN is slightly enhanced.

Given the form of the cavitand, two conformations are possible for the benzylic NH group on its rim, *viz.* pointing either towards, or outwards from, the cavity. Only one band is detected for the benzylic NH and this indicates that the orientation of the thiourea moieties in the cavitand is rather rigid. The broad band at 3320 cm^{-1} does not disappear on dilution and hence it has to be ascribed to an intramolecularly bonded thiourea NH group. This leads us to the conclusion that an array of $>$NH$\cdots$S=C$<$ hydrogen bonds is formed, which pre-organises the thioureide units on the upper rim of the resorcinarene backbone.

Complexation of chloride and bromide by PHEN. For host PHEN, broad bands emerge in the presence of chloride at 3279 and 3202 cm^{-1} (band widths 101 and 80 cm^{-1}, respectively), which we ascribe to hydrogen-bonded NH$\cdots$Cl groups. The free-NH bands decrease in intensity. An association constant of 1.5×10^5 l mol^{-1} is found for a 1-to-1 complex. Fig. 6(a) shows the NH region for a mixture of host and tetrabutylammonium chloride at a host fraction of 0.5. Clearly, the intramolecular bonding pattern is broken on complexation.

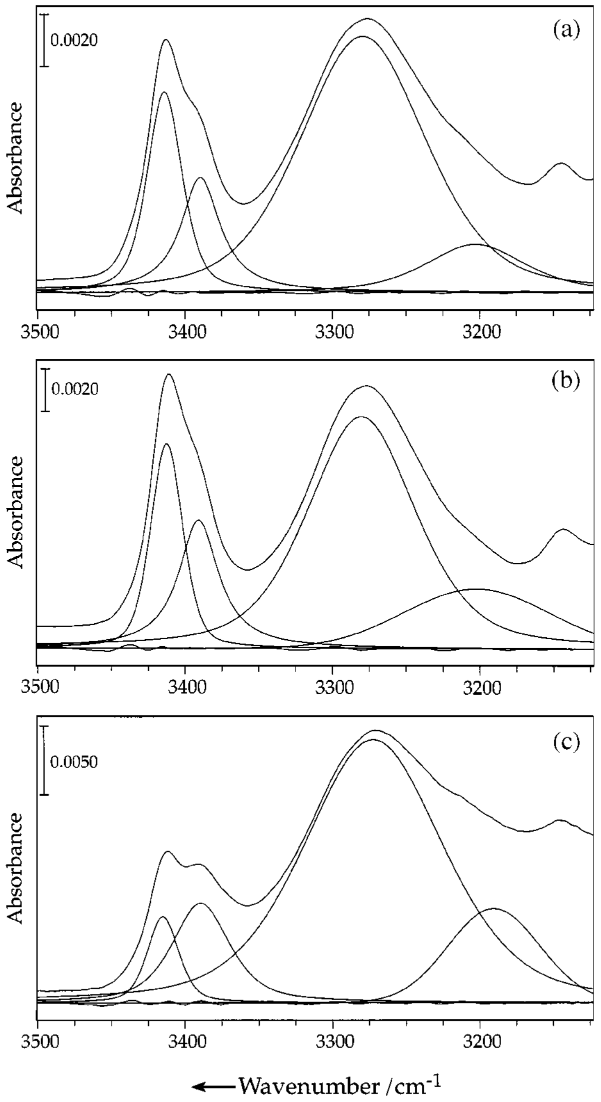

Fig. 6 Fitted bands in the NH region for PHEN complexed with halide (mol fraction 0.5). (a) PHEN and chloride, with bands at 3413 (28), 3389 (32), 3279 (101) and 3202 (80) cm^{-1}; (b) PHEN and bromide, with bands at 3412 (26), 3391 (32), 3280 (87) and 3202 (115) cm^{-1}; (c) PHEN and iodide, with bands at 3415 (25), 3389 (46), 3272 (112) and 3190 (73) cm^{-1}. In all cases a band was added to account for the CH stretching at the right side of the spectral window. This band and the fitted overtone at 3144 cm^{-1} have been omitted for clarity.

The spectral changes that occur in the NH stretching and fingerprint regions on complexation of anions are presented in Fig. 7(a). Spectra are depicted for host fractions in the range 0.2–0.9. A qualitative analysis of the spectral changes on complexation was performed by applying PLS-1 as a function of the initial host concentrations. A model was obtained with two factors, displayed in Fig. 7(b) and (c). Factor 2 comprises a correction on the spectral contribution of the host on complexation and therefore accounts mainly for the spectral changes induced by host–guest association in solution. This is also indicated by the calculated scores for factor 2 that resemble a Job's plot for 1-to-1 complexation (Fig. 8). Spectral interference of the guest is minimal and is therefore ignored.

The main spectral changes in the second factor are a negative change in intensity in the free ν_{NH} region and a positive one around 3276 cm^{-1}. Combined with the formation of a band at 1542 cm^{-1}, a decrease in intensity of the amide-II-type band at 1530 cm^{-1}, and enhancement of the amide-III-type band at 1348 cm^{-1} [*cf.* Fig. 7(a) and Fig. 7(c)], this is strong evidence for hydrogen bonding of the halide by the thiourea-NH moieties. In the region 1100–1000 cm^{-1}, small changes are observed for bands assigned to the substituent ring vibrations, possibly due to some reorganisation of the phenyl units.

The complexation of the bromide anion by PHEN is in line with that observed for chloride. The association constant for bromide is found to be 1.2 × 10^{4} l mol^{-1}, for a 1-to-1 complex.[10] A band fit analysis for the NH stretching region [Fig. 6(b)] reveals peak positions similar to that of chloride, *viz.* 3280 and 3202 cm^{-1} for the bonded NH stretching modes. A PLS-1 qualitative analysis discloses that, upon association with the bromide, a band emerges at 1560 cm^{-1}, again indicating hydrogen bonding by the thioureido moieties.

Complexation of iodide by PHEN. The complexation of the iodide anion by PHEN differs only marginally from the chloride one. The association constant determined from infrared data is 1.0 × 10^{4} l mol^{-1}, indicating 1-to-1 complexation. This clearly differs from the 2-to-1 complexation that is found for complexation of iodide by OFP. The bonded-NH bands at 3272 and 3190 cm^{-1} [Fig. 6(c)] are red-shifted slightly more than in the case of chloride and bromide. In addition to the effects observed for the association of bromide and chloride, a relative intensity increase and broadening of the band from 32 to 46 cm^{-1} is noticed for the band at 3389 cm^{-1}, which we assign to the stretching of the urea NH at the benzylic side. A PLS-1 analysis reveals that, as for bromide, a band is formed at 1560 cm^{-1} for the iodide. Again, this indicates hydrogen bonding by the NH moieties.

Complexation of chloride, bromide and iodide by FPHEN. The influence of the electron-withdrawing fluorine substituent at the *para*-position of the ring is reflected in the association constants for FPHEN, which are found to be about a factor of 10 higher with respect to PHEN, *viz.* >2 × 10^{5} and 1.8 × 10^{5} for Cl and Br, respectively.[10] The behaviour of the host FPHEN is largely in line with that of PHEN. Fits of the NH stretching region are shown in Fig. 9 for mixtures at a host fraction of 0.5. The fits display a high degree of similarity for chloride, bromide and iodide association. A complex band emerges at 3280 cm^{-1} on complexation, which is fitted well by two bands at 3279 (FWHH ~87) and 3215 cm^{-1} (FWHH ~52) for both chloride and bromide, and at 3282 (FWHH 72) and 3222 cm^{-1} (FWHH 52) for iodide.

Halide bonding by thiourea hosts

A closer inspection of the NH stretching region reveals that for the cavitand hosts only two bands appear in the region 3460–3360, whereas OFP has three bands in this region. As the extra band in the spectra of OFP is most likely due to a rotamer, this indicates that the orientation of the thiourea moieties in the cavitands is rather rigid. In addition, intramolecular bonding is observed for both resorcinarenes, endorsing the view of a fixed conformation held by an array of H-bonds.

Binding of the halide ion takes place *via* the NH moieties of the thiourea groups for all hosts. This follows from an analysis of the ν_{NH} band profile and the results from regression analysis. The overall structure changes drastically upon complexation as the intramolecular bonding pattern of the unassociated host is destroyed. Furthermore, small changes in the ring modes point to a re-orientation of the *p*-fluorophenyl-urea counterparts.

As the band shapes for the hydrogen bond feature in the NH stretching region were different for chloride, bromide and iodide complexation, a curve fit analysis was performed. Generally, the results for the iodide differ slightly from those for the chloride and bromide. In our opinion this effect arises from steric influences because of the increased size of the iodide anion, and the 'softer' nature of the electrostatic interactions with this ion.

On complexation of OFP with chloride or bromide anion, only one band shows up in the spectra, whereas the iodide–OFP

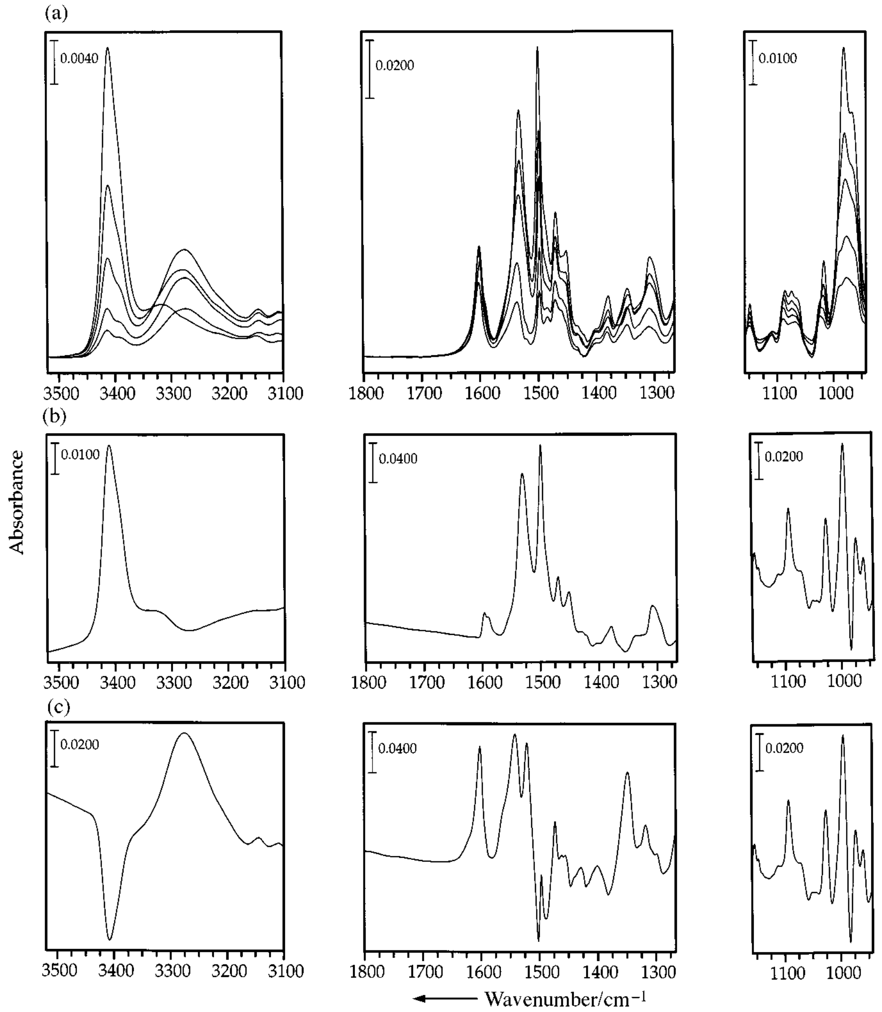

Fig. 7 (a) Association of PHEN and tetrabutylammonium chloride. Spectral regions are shown for host fractions 0.2, 0.3, 0.5, 0.6 and 0.9. (b) Factor 1 and (c) factor 2 obtained from PLS-1 analysis of the series shown above.

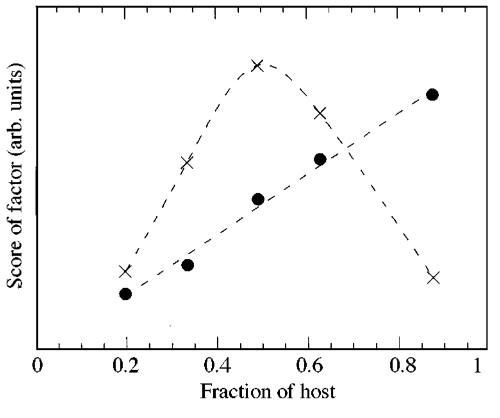

Fig. 8 Scores calculated for the series of spectra depicted in Fig. 7. Score 1 (●) and score 2 (×). Scores are plotted on arbitrary scales. Fitted lines only serve as a guide to the eye.

associate gives rise to two bands, attributed to two hydrogen bonded ν_{NH} bands. In the latter case, two OFP molecules were found to ligate one anion. The cavitand–halide association process gives rise to two bands in all cases of halide complexation, and the positions of the bands are remarkably similar. Bands for PHEN are found at 3280 and 3202 cm^{-1} (slightly more red-shifted for iodide) and the bands for FPHEN at 3277 and 3215 cm^{-1}. A difference shows up in the band widths: in the case of PHEN, a width of approximately 100 cm^{-1} is found for the band profile whereas it is 10–15% narrower for FPHEN, indicating a more rigid fixation of the anions.

The fit for the cavitands is remarkably similar to that observed for the second-order OFP–iodide association, where two bands show up at 3262 and 3209 cm^{-1}. The second feature is red-shifted by 45 cm^{-1} with respect to the 'first order band' found for the OFP–Cl/Br associates and probably due to a short unidentate NH$\cdots$iodide contact, which opens a way to a linear, and therefore stronger, H-bond.

From this observation we conclude that halide bonding in the cavitand is exerted *via* at least two types of hydrogen bonding, in analogy with the second-order complexation of iodide by OFP.

Steric analysis

Several crystal structures of resorcinarene cavitands are known, but no inclusion complexes have been reported for the thiourea substituted cavitands yet. Furthermore, no thiourea–halide contacts were found in the Cambridge Crystal Structural Database. A search for amide–halide contacts revealed that linear bonds were formed with lengths $d(N\cdots Cl) < d(N\cdots Br) < d(N\cdots I)$, and that a strong analogy exists between the few urea–halide contacts present and these amide–halide contacts.[1]

One might expect, therefore, that a thiourea–halide contact will be similar to a thioamide–halide contact, on going from chloride to bromide and iodide. Unfortunately, only one thioamide–chloride contact was found. The nitrogen–chloride atom distance for this contact is similar to that of the amide–chloride, *viz.* 3.18 Å, and the angle N–H–Cl is 141°. The chloride atom is almost in the plane of the thioamide moiety

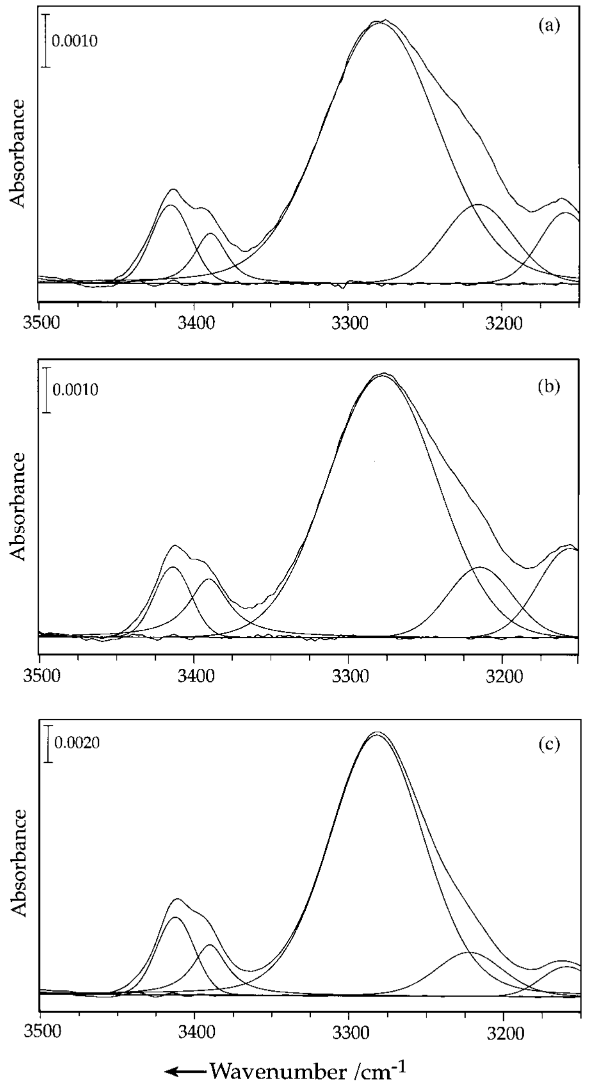

Fig. 9 Fitted bands in the NH stretching region for host FPHEN complexed with halide (mol fraction 0.5). (a) FPHEN and chloride, with bands at 3415 (30), 3389 (25), 3278 (89) and 3215 (54) cm^{-1}; (b) FPHEN and bromide, with bands at 3413 (28), 3390 (31), 3277 (84) and 3214 (50) cm^{-1}; (c) FPHEN and iodide, with bands at 3412 (29), 3390 (26), 3282 (72) and 3222 (52) cm^{-1}. The rightmost band accounts for an overtone band at 3157 cm^{-1} and is not listed.

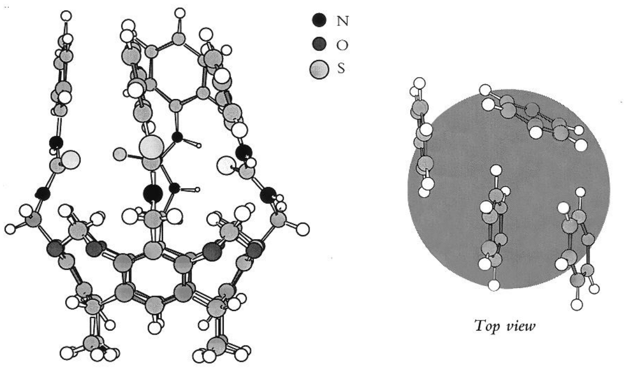

Fig. 10 MM2-optimised structure for model cavitand PHEN. A schematic top view is depicted on the right.

(deviation from the plane: 29°), possibly due to steric effects. Yet we assume that thioamide and thiourea bonds are very similar when compared to normal amides and ureas, although bond distances might be slightly shorter due to the higher acidity of the NH protons.

The MM2-optimised structure with the lowest energy is shown in Fig. 10 for a model of compound PHEN. Cavitand sizes of the ‘backbone’ derived from steric optimisation of the cavitand correspond well with crystallographic data of a similar compound.[24] Distances for the N···S=C contacts seem quite long (approx. 3.8 and 4.7 Å), but they may be overestimated by the MM2 model. In dimers of tetraurea calix[4]arenes similar arrays of eight intermolecularly hydrogen bonded urea units have been found, that also feature different N···O=C distances, *viz.* 2.85 and 3.13 Å for the NH donors within the same ureide moiety.[25]

The optimisation shows clearly that π–π stacking interactions between the substituent rings in the cavitand result in an arc of weak H-bonds, leaving one of the thioureido moieties free, and that ample space is present within the molecule for binding of a guest. The breaking of the circular intramolecular array by one unit as a result of stacking of the aromatic rings is typical and has not been observed in earlier calculations of a cavitand derivative with *o*-nitrophenoxy-*n*-octyl side-chains fixed to the ureido moieties.[1] In that case, a circular bonding pattern is present, and association coefficients with halide are approximately one order of magnitude lower.[1] The high association constants of PHEN and FPHEN most likely arise from the pre-organisation of the upper-rim substituents, in which one of the thioureido moieties is easily made free to bind the halide, without competition from intramolecular bonds.

Conclusions

Both PHEN and FPHEN associate with halide anions *via* hydrogen bonding between halide ions and thioureido moieties solely, similar to complexation of these guests by a ureide-substituted cavitand (see Part I[1]). From a comparison of the binding behaviour of PHEN and FPHEN on the one hand and OFP on the other hand it follows that complexation of the halide ions in these cavitands is very similar to complexation of iodide by the model compound OFP. This leads us to the conclusion that in the cavitands, binding takes place in a ‘forced’ stoichiometry of at least two thioureide moieties to one halide, leading to a strong association of the cavitand with the anion.

Pre-organisation of the thioureide side-chains on the upper rim of a cavitand by intramolecular bonding strongly determines their availability to the association process. For the more flexible calix[4]arene derivatives, relatively low association constants have been observed as a result of a strong hydrogen bonding network between the ligating units.[10] An improvement by a factor of 10 to 100 is seen in our case when comparing the resorcinarene hosts to a simple thiourea compound.

The intramolecular bonding pattern does not extend through the whole molecule, but leaves free one thioureido unit to bind the guest, unhindered by intramolecular bonding with the other units. This is unlike the pattern of hydrogen bonding observed for the ureide-substituted host studied in Part I, that featured a circular array of hydrogen bonds. The strong complexation of halide observed for PHEN and FPHEN can be explained by taking into account the increased acidity of the $S{=}C(NH_2)_2$ units compared to their oxo pendant, and, in addition, the loose arrangement of the binding moieties on the resorcinarene rim as a result of a stacking of the phenyl rings of the substituent.

References

1 Part I. J. W. M. Nissink, H. Boerrigter, W. Verboom, D. N. Reinhoudt and J. H. van der Maas, *J. Chem. Soc.*, *Perkin Trans. 2*, 1998, 2541.

2 B. Dietrich, J. Guilhem, J.-M. Lehn, C. Pascard and E. Sonveaux, *Helv. Chim. Acta*, 1984, **67**, 91.

3 A. Allerhand and P. von Ragué Schleyer, *J. Am. Chem. Soc.*, 1963, **85**, 1233.

4 S. Nishizawa, P. Bühlmann, M. Iwao and Y. Umezawa, *Tetrahedron Lett.*, 1995, **36**, 6483.

5 J. Scheerder, M. Fochi, J. F. J. Engbersen and D. N. Reinhoudt, *J. Org. Chem.*, 1994, **59**, 7815.

6 J. Scheerder, J. P. M. v. Duynhoven, J. F. J. Engbersen and D. N. Reinhoudt, *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 1090.

7 J. Scheerder, J. F. J. Engbersen, A. Casnati, R. Ungaro and D. N. Reinhoudt, *J. Org. Chem.*, 1995, **60**, 6448.

8 For reviews see: D. J. Cram and J. M. Cram, *Container molecules and their guests*, The Royal Society of Chemistry, Cambridge, 1994; P. Timmerman, W. Verboom and D. N. Reinhoudt, *Tetrahedron*, 1996, **52**, 2663.

9 T. N. Sorrel and F. C. Pigge, *J. Org. Chem.*, 1993, **58**, 784; K. Kim and K. Paek, *Bull. Korean Chem. Soc.*, 1993, **14**, 659; H. Boerrigter, W. Verboom and D. N. Reinhoudt, *J. Org. Chem.*, 1997, **62**, 7148.

10 H. Boerrigter, L. Grave, J. W. M. Nissink, L. A. J. Christoffels, J. H. van der Maas, W. Verboom, F. de Jong and D. N. Reinhoudt, *J. Org. Chem.*, 1998, **63**, 4174.

11 J. W. M. Nissink, H. Boerrigter, W. Verboom, D. N. Reinhoudt and J. H. van der Maas, *J. Chem. Soc., Perkin Trans. 2*, 1998, **7**, 1671.

12 E. Bordwell, D. J. Algrim and J. A. Harrelson, *J. Am. Chem. Soc.*, 1988, **110**, 5093.

13 E. T. G. Lutz and J. H. van der Maas, *J. Mol. Struct.*, 1997, **436–437**, 213.

14 E. T. G. Lutz, J. Jacob and J. H. van der Maas, *Vib. Spectrosc.*, 1996, **12**, 197.

15 E. T. G. Lutz, G. Astarloa, J. H. van der Maas, R. G. Janssen, W. Verboom and D. N. Reinhoudt, *Vib. Spectrosc.*, 1995, **10**, 29.

16 R. M. Dyson, S. Kaderly, G. A. Lawrance, M. Maeder and A. D. Zuberbühler, *Anal. Chim. Acta*, 1997, **353**, 381.

17 M. Kubista, R. Sjöback and B. Albinsson, *Anal. Chem.*, 1993, **65**, 994.

18 GRAMS Research for System 2000 FTIR, Version 3.01b and Add-on Application PLSPlus Version 2.1G, Galactic Industries, Salem, NH, 1993.

19 CSC Chem3D, Cambridge Scientific Computing, Inc., Cambridge, MA, 1991.

20 Deconvolution was performed with a gamma of 2.62 and 49% Fourier smoothing. Peaks were observed at 3413 and 3393 cm^{-1}, and a distinct shoulder at 3398 cm^{-1}.

21 D. Lin-Vien, N. B. Colthup, W. G. Fateley and J. G. Grasselli, *The Handbook of Infrared and Raman Characteristic Frequencies of Organic Molecules*, Academic Press Ltd., London, 1991.

22 I. D. Campbell, G. Eglinton and R. A. Raphael, *J. Chem. Soc.* (*B*), 1968, 338.

23 R. G. Pearson, *J. Am. Chem. Soc.*, 1963, **85**, 3533.

24 W. Xu, J. P. Rourke, J. J. Vittal and R. J. Puddephatt, *J. Chem. Soc., Chem. Commun.*, 1993, 145.

25 O. Mogck, E. F. Paulus, V. Böhmer, I. Thondorf and W. Vogt, *Chem. Commun.*, 1996, 2533. See also: O. Mogck, V. Böhmer and W. Vogt, *Tetrahedron*, 1996, **52**, 8489; B. C. Hamann, K. D. Shimizu and J. C. Rebek, Jr., *Angew. Chem., Int. Ed. Engl.*, 1996, **35**, 1326.

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