Cyclic tetraureas with variable flexibility – synthesis, crystal structures and properties†

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Macrocyclic molecules containing several amide or urea functions may serve as anion receptors. We describe the synthesis of 32-membered macrocycles, in which four rigid xanthene units (X) and/or diphenyl ether units (D) as flexible analogues are linked *via* urea groups. All six possible combinations of these units (XXXX, XXXD, XXDD, XDXD, XDDD and DDDD) were synthesized and two examples were characterised by single-crystal X-ray analyses (DDDD and two structures for XXXD). Both macrocycles showed distinct differences in their overall conformation and consequently in their hydrogen-bonding pattern. Hydrogen-bonded solvent molecules are found for both compounds and intramolecular hydrogen bonds for the two structures of XXXD, but surprisingly no direct intermolecular hydrogen bonds between the macrocyclic tetraurea molecules. The interaction with various anions was studied by ^{1}H NMR spectroscopy. Stability constants for all tetramers were determined by UV spectroscopy for complexes with chloride, bromide, acetate and dihydrogenphosphate in acetonitrile–THF (3 : 1). The strongest binding was found for XXXD and acetate ($\log\beta = 7.4 \pm 0.2$), the weakest for XXXX and acetate ($\log\beta = 5.1 \pm 0.5$). MD simulations in chloroform and acetonitrile boxes show that all molecules except DDDD adopt very similar conformations characterized by an up–down–up–down arrangement of the spacer groups. Clustered solvation shells of acetonitrile molecules around XXXX and DDDD suggest their preorganization for spherical/planar and tetrahedral/bidentate anions, respectively, which in turn was corroborated by simulation of the corresponding complexes with chloride and dihydrogenphosphate.

Introduction

In spite of all the progress made during recent decade(s), the search for novel anion receptors is still a field of current interest.[1] Efficient ligands for a common anion such as nitrate are rare,[2–4] although nitric acid or nitrates are frequently used in technical processes (for instance as explosives or fertilizers), or appear in the environment as pollutants. Many of the synthetic ligands synthesized so far contain pyrrole,[5] amide[6] or urea functions,[4,7] arranged as podands[8] or incorporated in a cyclic[4,9,10] or bicyclic[2,10] skeleton. (Thio)urea groups have the ability to form two hydrogen bonds to the same acceptor (*e.g.* a carbonyl oxygen).[11] Thus, the appropriate/suitable arrangement of three urea groups in a macrocyclic molecule should lead to host molecules for the planar nitrate or similar anions.[12]

We have recently reported the synthesis and the properties of cyclic triurea molecules in which the three urea groups are connected *via* rigid xanthene (X) or flexible diphenyl ether (D) fragments.[13] Unfortunately the affinity towards nitrate, predicted on the basis of MD-simulations, was low for all four combinations of X and D. On the other hand, a cyclic hexamer (XXDXXD) revealed an unusual and completely unexpected affinity towards chloride anions.[14] The formation of the hexamer is strongly favored by chloride, and the 2 : 1 complex is the only well defined species identified in solution by NMR and characterised by a crystal structure.

With this background we extended our studies on cyclic ureas composed of xanthene and diphenyl ether units. We now describe the whole series of six cyclic tetraureas available by combination of "flexibility" (expressed by the D-units) and "rigidity" (introduced by the X-units), addressing in this way the interplay between rigidity and flexibility of the skeleton in a more detailed manner.

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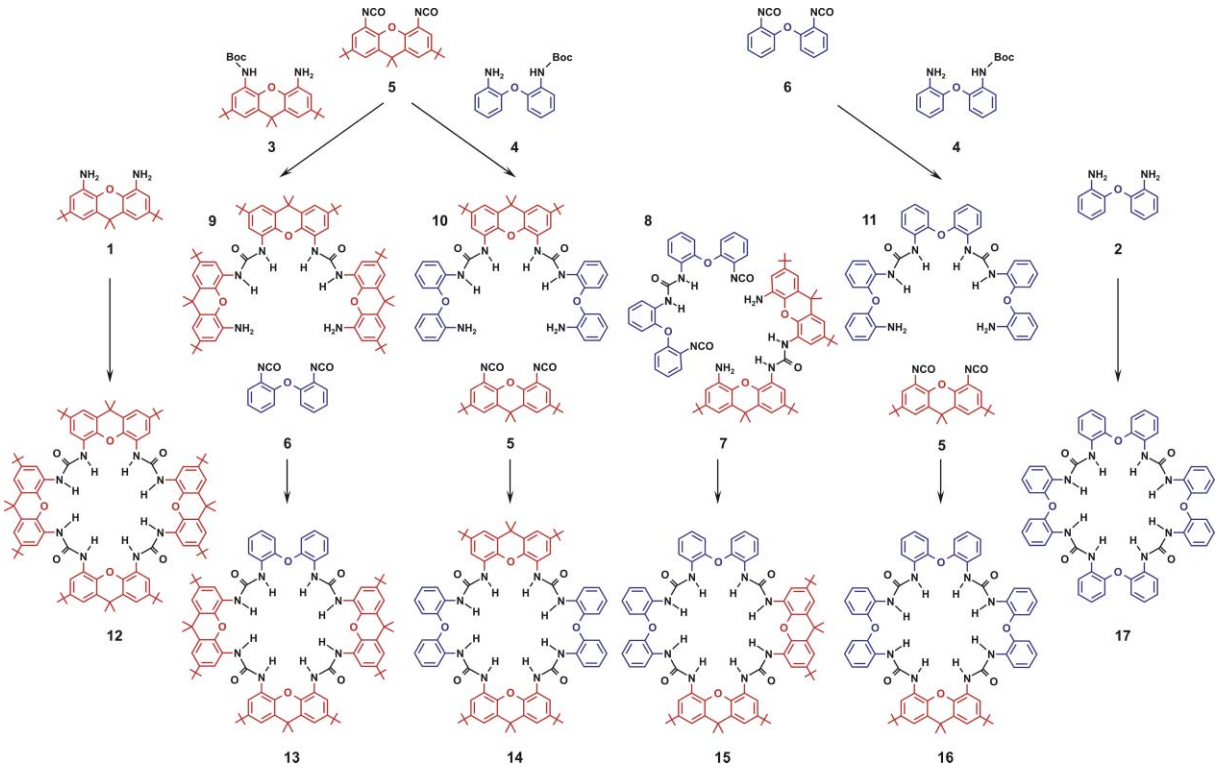

Scheme 1 Synthesis of cyclic tetraureas and their precursors.

Results and discussion

Syntheses

The known 2,7-di-*tert*-butyl-9,9-dimethyl-4,5-diaminoxanthene **1** was chosen as a building block (X-unit) for the synthesis of macrocycles, since it is easily prepared from the commercially available dicarboxylic acid.[15] This xanthene-derived spacer has already been used in some simple open-chain urea-based anion receptors which demonstrated promising results.[16] In addition to the rigid xanthene units, the diphenyl ether derivative **2** (D-unit) was used as the more flexible unit, which could be also prepared following relatively simple procedures.[17] The synthesis of their mono-Boc protected derivatives **3** and **4**, of the diisocyanates **5** and **6** and of the dimers **7** and **8** has been described before.[13]

There are various possibilities or strategies for the preparation of tetramers depending on their composition. According to the number and size of the D- or X-fragments combined in the cyclisation step, they may be distinguished as 4×1 (or $2 \times 1 + 2 \times 1$), 2 + 2 and 3 + 1 condensations. The direct condensation of monomeric diamine units **1** or **2** with 4-nitrophenyl chloroformate (4×1) was used for the synthesis of **12** (XXXX) and **17** (DDDD). Other possibilities, such as the 4×1 reaction of a mono-isocyanate or the $2 \times 1 + 2 \times 1$ reaction of a bis-isocyanate **5** or **6** with the diamine **1** or **2**, were not checked. A 2 + 2 reaction between **7** and **8** was used for the synthesis of **15** (XXDD), as suggested by its structure. All other cyclisations followed the 3 + 1 principle, using the monomeric bis-isocyanates **5** and **6** and the linear trimers **9**, **10**, and **11**, which in their turn were prepared by reaction of **5** and **6** with the mono-Boc protected compounds **3** and **4**, followed by deprotection. These cyclisation reactions and the syntheses of novel intermediates are summarized in Scheme 1.

The direct cyclisation of diamines **1** and **2** using 4-nitrophenyl chloroformate as a bifunctional reagent may lead to a variety of cyclic oligomers. Usually the reaction mixture contains in addition also linear oligomers. Nevertheless, conditions were found ($CHCl_3$ as solvent, addition of the reagent over 10 h, followed by the addition of *N*-diisopropylethylamine, 4 h at r. t.) under which the pure cyclic tetramer **12** precipitates as a white solid from the mixture in 15% yield; **17** crystallized from a concentrated solution in ethyl acetate in yields as high as 58%. From the cyclisation reaction of D-diamine **2**, a "cyclic mono-urea"[18] and a cyclic di-urea[19] were also isolated. Cyclic trimers, however, were not detected in significant quantity for either system.

The following general procedure was used to prepare the trimeric diamines: the diisocyanate **5** or **6** (for X or D) was reacted with the stoichiometric quantity of the respective monoprotected derivative **3** or **4** in CH_2Cl_2 at r.t. for 10–18 h. The crude product was directly deprotected with trifluoroacetic acid and the desired products **9**, **10** and **11** were obtained after neutralisation of the excess acid in yields of 60–94%.

For the preparation of the cyclic tetramers **13** and **14** (XXXD and XDXD), the trimeric diamines **9** and **10** were reacted with the respective diisocyanates **6** and **5** in dichloromethane. The pure compounds were isolated with yields of 69 and 55%. In case of the more flexible **16** (XDDD), the cyclisation under these conditions produced significant amounts of byproducts, which made the isolation of the pure tetramer difficult or impossible. To avoid the unwanted association *via* hydrogen bonding, the reaction was performed finally in acetonitrile.

Table 1 Characterisation of the conformation in the crystal by interplanar angles (°) between aromatic rings (first four columns) and between urea groups (N–C(O)–N) and the adjacent aromatic units (last four columns)

Compound	Ph_1/Ph_2	Ph_3/Ph_4	Ph_5/Ph_6	Ph_7/Ph_8	Ph_2–Ur–Ph_3	Ph_4–Ur–Ph_5	Ph_6–Ur–Ph_7	Ph_8–Ur–Ph_1
13·2CH_3CN (XXXD)	12.0 X	29.5 X	5.7 X	71.7 D	24.0/13.1 X–X	52.6/20.0 X–X	5.6/25.8 X–D	62.9/53.8 D–X
13·5EtOH (XXXD)	9.7 X	41.9 X	7.1 X	74.5 D	10.6/12.8 X–X	64.8/41.1 X–X	10.7/9.2 X–D	64.8/53.9 D–X
17·5THF (DDDD)[a]	81.3	74.8	80.2	76.5	13.2/22.4	17.4/14.8	11.0/10.6	12.2/18.9

[a] Values for one of the two crystallographically independent molecules with very similar shape.

Moreover, tetrabutylammonium chloride was added to the solution of diamine **11** (one mole per mole of the diamine) as an additional acceptor for hydrogen bonds. These conditions finally allowed to isolate the desired compound **16** with 25% yield. The tetramer **15** was formed by the reaction of the dimeric diisocyanate **8** with the diamine **7** in dichloromethane and could be isolated in yields up to 45%.

Crystal structures

The structures of two tetraureas **13** (XXXD) and **17** (DDDD) were confirmed by single-crystal X-ray analysis. The conformation of the two molecules **13** and **17** is entirely different, with small differences being found for **13** when it was crystallized from different solvents. Table 1 contains a comparison on the basis of interplanar angles between the aromatic planes and the plane based on N–C(O)–N atoms of the urea.

Suitable crystals of **17** were obtained by slow evaporation of its solution in THF. The asymmetric unit has two molecules of the tetramer **17** and ten THF molecules. In each case four THF molecules are bound by the four urea groups of each tetramer. Neither intramolecular hydrogen bonds within a tetramer nor intermolecular hydrogen bonds (tetramer-to-tetramer) are present. The remaining two THF molecules are located between tetramer molecules, obviously filling gaps in the crystal lattice.

Each tetramer molecule is folded into a compact "box" with THF molecules lying between the aromatic rings of the opposite sides of this box. This conformation, with alternate urea functions pointing in opposite directions, is somehow reminiscent of a calix[4]arene in the 1,3-alternate conformation.

The urea groups are nearly coplanar with the neighbouring aromatic rings, while the angles between the planes of the aromatic rings in each diphenyl ether unit are in the range of 75–81° (Table 1). The box-like conformation is possible due to this flexibility of these units. The crystal cell contains two molecules (I, II) with slightly different geometry. Therefore, there are two pairs of distances between two opposite urea carbons (N–C(O)–N): 7.443/7.458 Å (I) and 7.802/7.428 Å (II), as well as between opposite diphenyl ether oxygens (9.095/8.152 Å (I) and 8.539/8.848 Å (II)). The arrows in Fig. 1 illustrate the deviation from an entirely symmetrical square.

In the crystal lattice the molecules of **17** are arranged in sheets parallel to the *a*–*c*-plane. Adjacent sheets are shifted towards each other and the molecules are neither directly aligned within a sheet, nor exactly stapled to columns perpendicular to the sheets. The packing is illustrated by Fig. 2.

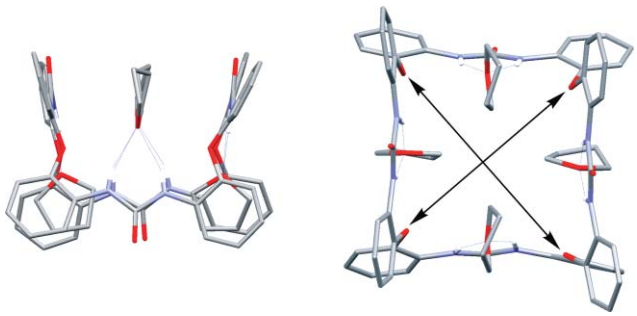

Fig. 1 Molecular conformation of **17**, seen from two different directions. Intermolecular hydrogen bonds are indicated by thin dashed lines. Black arrows between ether oxygens illustrate the distortion of the square-like conformation.

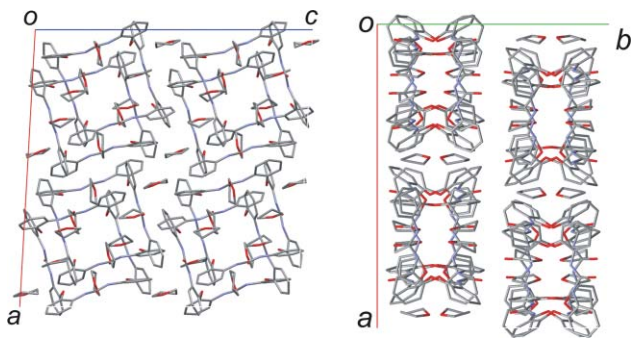

Fig. 2 Packing diagram of **17**, seen from two directions; left: along the *b*-axis; right: along the *c*-axis.

Single crystals for **13** (XXXD) were obtained by slow evaporation from a solution in dichloromethane–acetonitrile (**13**·2CH_3CN) and from a solution in dichloromethane–ethanol (**13**·5EtOH). The conformations of **13** in both crystal structures are very similar as shown by the root-mean-square deviation (rmsd) of 0.47 Å for all heavy atoms excluding the *tert*-butyl and the methyl groups (see Fig. 3). In contrast to **17** (DDDD), which forms hydrogen bonds exclusively to the solvent, the molecular conformation of **13** is mainly determined by intramolecular hydrogen bonds between pairs of adjacent urea groups This requires the folding of the macrocycle shown in Fig. 3. Additionally, the urea groups form hydrogen bonds to the solvent, alternately acting as donor (NH groups) and acceptor (C=O groups). The systems of hydrogen bonds are illustrated in Fig. 4.

Although the molecular conformations of **13** are similar (Fig. 3), the pattern of hydrogen bonds of the four urea functions is quite different for **13**·2CH_3CN and **13**·5EtOH (see Fig 4). This must be

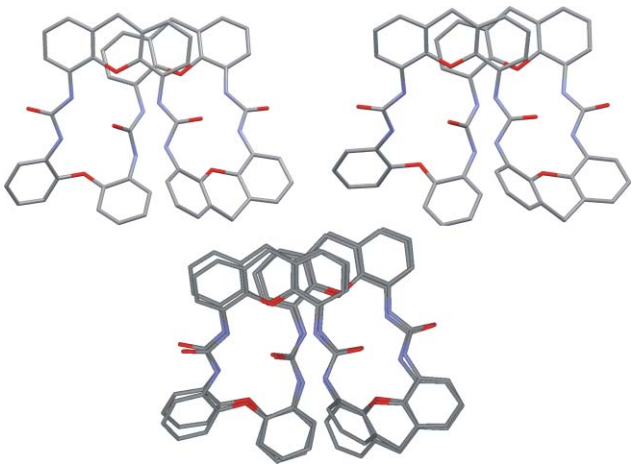

Fig. 3 Superimposition of the molecular skeletons from the two different X-ray structures of the tetramer **13** (**13**·2CH_3CN on the left, **13**·5EtOH on the right). Hydrogen atoms, methyl and *tert*-butyl groups, as well as solvent molecules, are omitted for clarity.

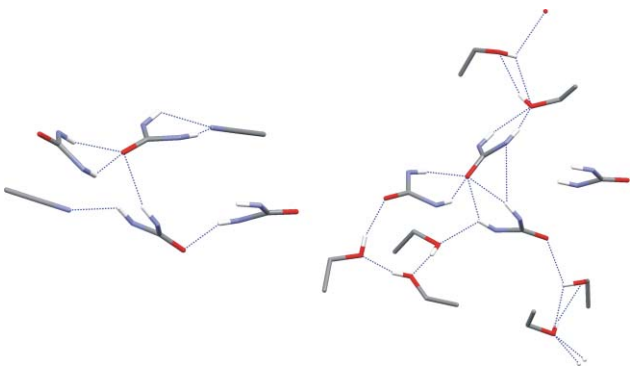

Fig. 4 Hydrogen-bonded arrays formed by the urea groups of **13** in the crystal. Left: **13**·2CH_3CN; right: **13**·5EtOH.

due to the different hydrogen-bonding abilities of the two solvents. While acetonitrile is an acceptor of hydrogen bonds by its nitrogen atom, ethanol is able both to accept and to donate hydrogen bonds. Thus, ethanol forms a hydrogen-bonded network which interconnects the tetramer molecules in the lattice.[20] Remarkably, direct intermolecular hydrogen bonds between the tetraurea macrocycles are not observed again. This has already been found for cyclic triureas built from xanthene and diphenyl units,[13] but it is even more surprising for the more flexible cyclic tetraureas, especially since intermolecular hydrogen bonds are often found for diaryl ureas.[21] The different molecular arrangement is illustrated by the packing diagrams in Fig. 5.

NMR studies

Distinct changes of the ^{1}H NMR spectrum are usually observed upon addition of a tetrabutylammonium salt to the solution of a tetramer. Usual responses comprise a sharpening or broadening of the whole spectrum, as well as more or less pronounced up- or downfield shifts of single signals, where those for the urea protons are most strongly affected. Since we deal with compounds which tend very strongly to intra- and intermolecular hydrogen bonding, we are forced to use polar, hydrogen-bond-breaking NMR solvents

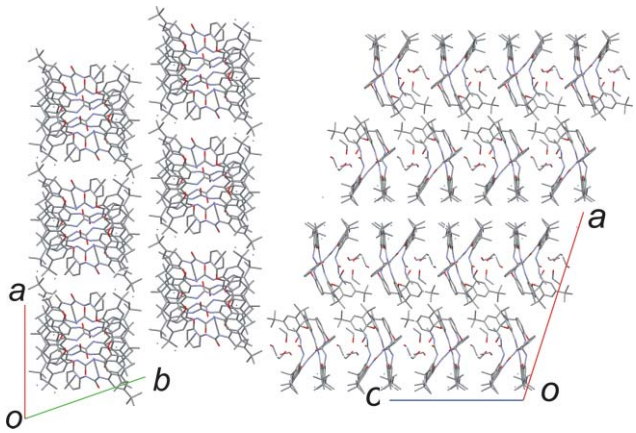

Fig. 5 Crystal cells of two different crystalline samples of the tetramer **13** (left: **13**·2CH_3CN, seen along the *c*-axis; right: **13**·5EtOH seen along the *b*-axis). Hydrogen atoms are omitted for clarity.

to obtain sharp, interpretable spectra under normal conditions. The best results were achieved with DMSO-d_6, although two of the six tetraureas were not soluble at r.t., and in the other cases we were not always able to obtain interpretable spectra.

The following tetrabutylammonium salts were checked with the tetramers: chloride, bromide, iodide, nitrate, hydrogensulfate, dihydrogenphosphate and acetate.

Tetramer 12 (XXXX). At normal temperature the compound is either completely insoluble or at least insufficiently soluble in the majority of organic solvents. However, a sharp spectrum was obtained at 120 °C in DMSO-d_6, which contains signals corresponding to the expected time-averaged D_{4h} symmetry (*t*Bu/Me/ArH/ArH/NH = 9 : 3 : 1 : 1 : 1). The addition of more than twofold excess of tetrabutylammonium (= TBA) chloride leads to a strong downfield shift of the urea signal from 8.66 ppm to 9.69 ppm, while other signals are (nearly) not affected. The shift is less pronounced for dihydrogenphosphate (0.39 ppm), acetate (0.27 ppm), bromide (0.19 ppm) and other anions (<0.1 ppm).

Tetramer 13 (XXXD). The compound is less affected by the solubility issues mentioned above, but also insufficiently soluble in DMSO up to 80 °C. Even though it is soluble in other solvents (*e.g.* THF or chloroform), the spectra are broad and insignificant. However, the spectrum sharpens drastically upon addition of selected tetrabutylammonium salts. The example shown in Fig. 6, obtained with TBA chloride, clearly reveals the expected dynamic C_{2v} symmetry.

With TBA acetate and bromide the sharpening is far less significant, obviously due to weaker interactions with the anion, while entirely broadened spectra were obtained with the other anions checked.

Tetramer 14 (XDXD). The compound is soluble in DMSO-d_6 and produces a well resolved spectrum which reflects the time-averaged D_{2h} symmetry. It contains two signals for the urea protons, two for aromatic protons of the xanthene skeleton, four for the aromatic protons of the diphenyl units, a singlet for the methyl protons and a singlet for the *tert*-butyl groups.

The spectrum remains sharp upon addition of halides and the downfield shifts for signals observed upon addition of TBA bromide and chloride are more pronounced for the latter. The

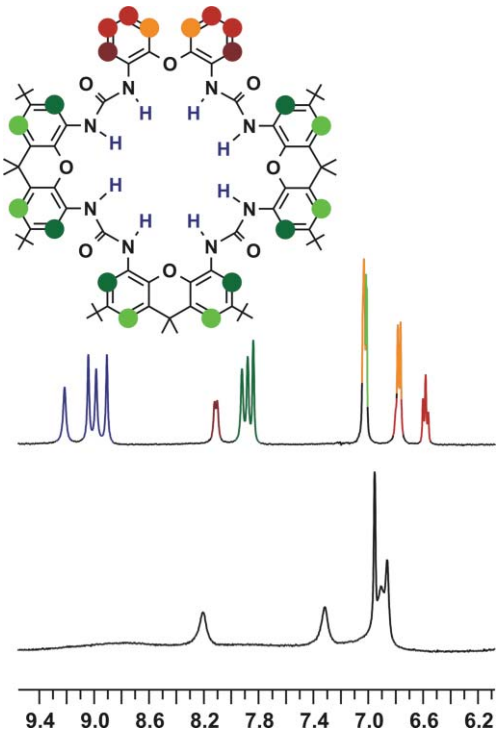

Fig. 6 Top: the low-field part of the spectrum of the tetramer **13** in THF-d_8 in the presence of excess of TBA chloride; bottom: without salt.

addition of acetate, hydrogensulfate and dihydrogenphosphate led to completely broadened and unclear spectra, while nitrate and iodide showed no effect.

Tetramer 15 (XXDD). The different sequence of X and D units in the skeleton of **15** (time averaged C_{2v}-symmetry) compared to **14** led to strong changes in the NMR behaviour of the compound. The tetramer does not produce sharp spectra in DMSO-d_6 with the exception of the mixture with TBA chloride (Fig. 7), although the interaction with other anions (first of all hydrogensulfate, dihydrogenphosphate and acetate) is evident from downfield shifts of several signals.

Tetramer 16 (XDDD). Although not entirely sharp, the spectrum of **16** in DMSO-d_6 at room temperature is well resolved and this is also true for the spectra in the presence of anions. Among the anions studied, chloride, acetate and especially dihydrogenphosphate cause pronounced downfield shifts (up to 1.5 ppm), while bromide and hydrogensulfate only slightly change the shape of the signals. Iodide and nitrate have no visible effect.

The evidently strong influence caused by the addition of the non-spherical (!) anions dihydrogenphosphate and acetate in comparison to the usually more effective chloride and bromide is especially intriguing. Obviously, the more flexible skeleton of XDDD is also more responsive to the different geometrical requirements of the guests.

Tetramer 17 (DDDD). This compound produces sharp spectra corresponding to the dynamic D_{4h} symmetry under all conditions. It contains one urea singlet and four signals for the aromatic protons of the diphenyl ether unit. Interestingly, addition of bromide and chloride causes no visible effect at all, while it is

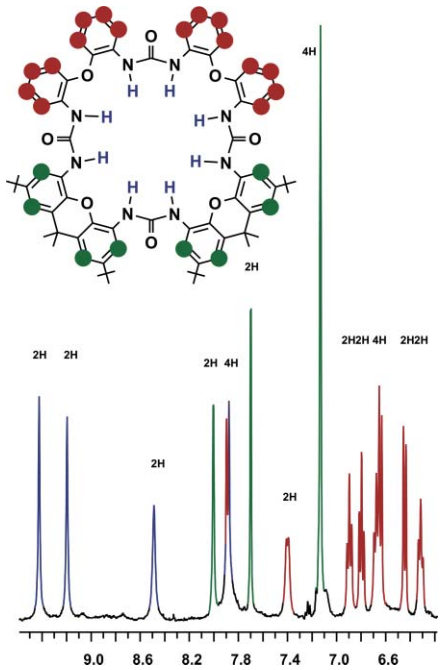

Fig. 7 The ^{1}H NMR spectrum of the solution of tetramer **15** mixed with TBA chloride (DMSO-d_6, 25 °C).

quite pronounced in the case of dihydrogenphosphate and acetate (Fig. 8).

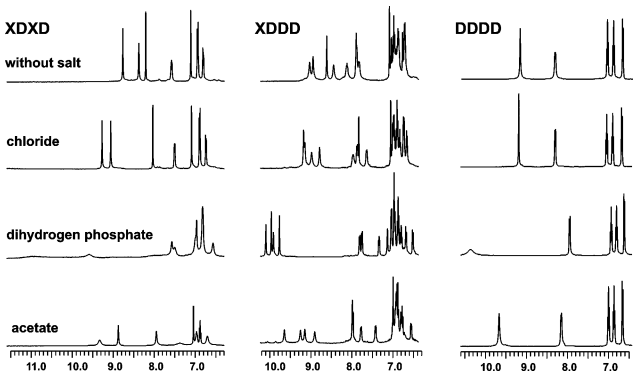

Fig. 8 Interaction of the tetramers **14**, **16** and **17** with selected anions (DMSO-d_6, 25 °C, $c = 0.1$ mM).

For the side-by-side comparison we have used conditions under which all tetramers produce sharp NMR spectra with and without the anion. This is possible in the highly polar DMSO-d_6 at 120 °C for all tetramers, where comparative measurements were performed. TBA chloride was chosen as the salt for these studies. A combined view of the NMR spectra of all tetramers is presented in Fig. 9.

The compounds show various responses to the addition of chloride, which are difficult to place in a row. In all cases more or less significant downfield shifts of the urea proton signals were observed, while the signals of the aromatic protons (especially those with a neighbouring urea group) shift most frequently upfield.

Two main conclusions can be drawn:

1. The observed downfield shift for the signals for the urea protons decreases with increasing flexibility of the skeleton;

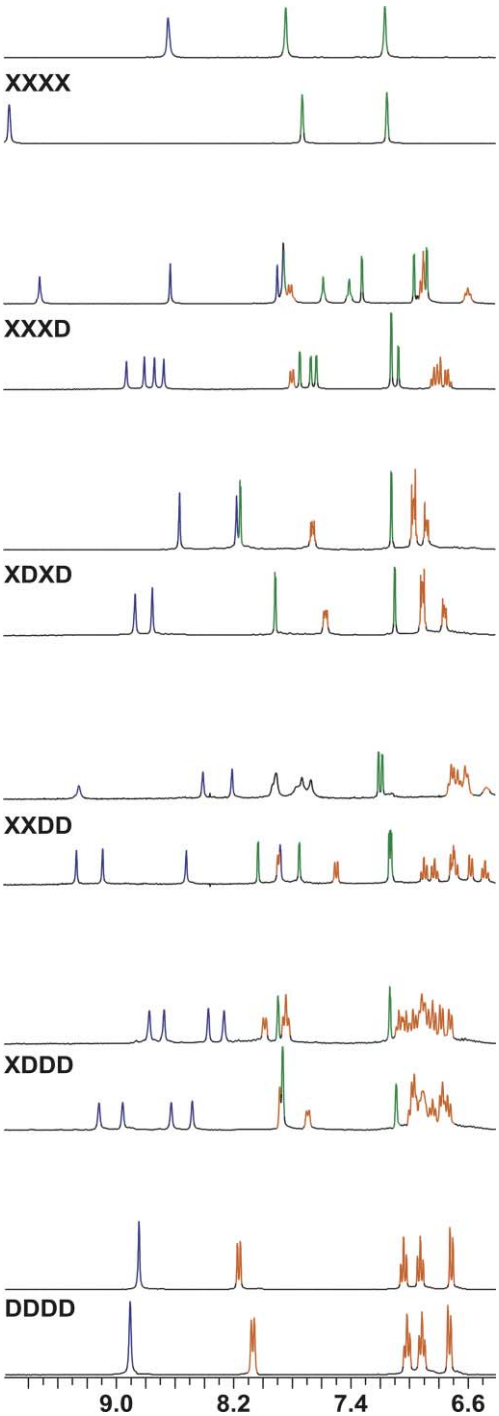

Fig. 9 Summarized view of the ^{1}H NMR spectra of all tetramers at 120 °C in DMSO-d_6 without (above) and with TBA chloride (below). Colors: blue for urea protons, green for aromatic protons of xanthene, brown for the protons of the diphenyl ether unit.

2. Addition of chloride to XXXD and XXDD leads to significant changes even in the order of the urea signals. Relatively strong shifts are also observed for the aromatic protons. Such pronounced variations of the magnetic environment unambiguously indicate conformational changes. The variations may be caused by the involvement of urea protons in the binding of a chloride instead of their participation in intramolecular hydrogen bonding.

Complexation studies

The interactions between the six tetramers and TBA chloride, bromide, acetate and dihydrogenphosphate have been studied by UV absorption spectrophotometry (for exact conditions see the Experimental section). In general, the spectral changes induced by acetate and dihydrogenphosphate are more distinct than those observed with spherical chloride and bromide.

The spectrophotometric titration of the tetramer **16** (XDDD) by acetate is shown in Fig. 10 as an example. No spectral changes occurred for **17** (DDDD) with chloride and with all ligands except **14** (XDXD) upon addition of bromide. This seems to be consistent with the fact that the NMR spectra show smaller shifts with increasing flexibility of the ligands.

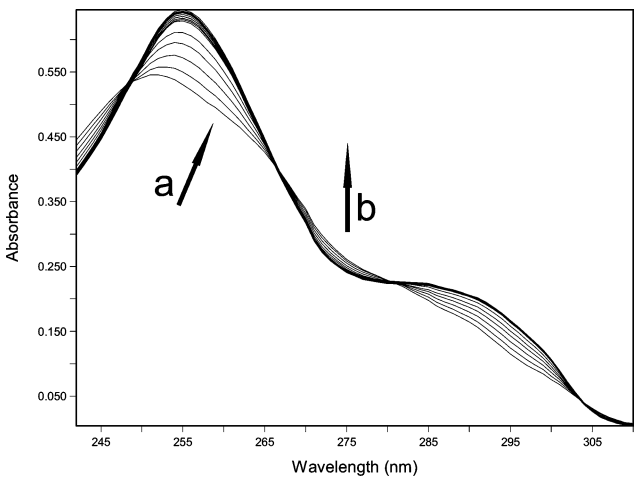

Fig. 10 Changes in the UV spectra of tetramer **16** (XDDD) upon addition of acetate ($C_L = 6.4 \times 10^{-6}$ M, $0 \leq C_A/C_L \leq 3$). The arrows indicate: a) the spectrum of **16**; b) increasing amounts of acetate.

Stability constants which could be obtained from the UV spectra are given in Table 2. The following trends can be observed:

(a) Ligands **13** (XXXD), **15** (XXDD), **16** (XDDD) and **17** (DDDD) form exclusively 1 : 1 complexes with all the anions studied. For **14** (XDXD) mainly 1 : 2 (anion:ligand) complexes were found, accompanied in the case of acetate and dihydrogenphosphate by 1 : 1 complexes. A small positive cooperative effect is observed for the formation of the biligand complex in the former case. The more rigid macrocycle **12** (XXXX) forms 1 : 1 complexes with acetate, chloride and dihydrogenphosphate and an additional 2 : 1 species with the last two anions. No positive cooperative effect is found; the stability constant is lower for the second complexation step than for the 1 : 1 complexes. For instance, $\log \beta = 6.34$ for the 1 : 1 chloride complex, whereas the stepwise stability constant for the corresponding 2 : 1 complex (which can be derived from the data in Table 2) is $\log K_2 = 5.16$.

(b) The ligand **12** (XXXX) prefers the spherical chloride anion while all other macrocycles show the highest stability constants for the multidentate acetate and dihydrogenphosphate. Selectivity for acetate, although not very pronounced, was observed for **13** (XXXD), **15** (XXDD) and **16** (XDDD), whereas **14** (XDXD) and **17** (DDDD) exhibit a comparable affinity for acetate and dihydrogenphosphate.

Table 2 Overall stability constants ($\log\beta \pm \sigma$) of the complexes formed by the tetramers with chloride, bromide, acetate and dihydrogenphosphate (counterion: Bu_4N^+) in acetonitrile–THF (3 : 1) mixture

	Ligands					
Anions	**12** (XXXX)	**13** (XXXD)	**14** (XDXD)	**15** (XXDD)	**16** (XDDD)	**17** (DDDD)
Cl^-	6.34 ± 0.05 (AL)	6.4 ± 0.3 (AL)	—	5.44 ± 0.05 (AL)	5.4 ± 0.3 (AL)	—[a]
	11.5 ± 0.6 (A_2L)	—	10.30 ± 0.01(AL_2)	—	—	—
Br^-	—[a]	—[a]	9.2 ± 0.3 (AL_2)	—[a]	—[a]	—[a]
OAc^-	5.1 ± 0.5 (AL)	7.4 ± 0.2 (AL)	6.8 ± 0.3 (AL)	6.4 ± 0.1 (AL)	6.4 ± 0.4 (AL)	5.2 ± 0.5 (AL)
	—	—	12.89 ± 0.01 (AL_2)	—	—	—
$H_2PO_4^-$	5.6 ± 0.3 (AL)	5.3 ± 0.2 (AL)	6.3 ± 0.1 (AL)	5.53 ± 0.06 (AL)	6.1 ± 0.1 (AL)	5.8 ± 0.4 (AL)
	9.5 ± 0.2 (A_2L)	—	13.0 ± 0.2 (AL_2)	—	—	—

[a] Spectral variations too small.

(c) The more rigid ligands **12** (XXXX) and **13** (XXXD) form the most stable 1 : 1 chloride complexes, which is consistent with the shift values observed by NMR spectroscopy. For acetate the introduction of one flexible diphenyl ether unit in the rigid ligand **12** (XXXX) leads to an important increase of stability of the complex (from 5.1 to 7.4 log units), and the stability decreases again when two or more of these units are present in the ligand. With dihydrogenphosphate, **14** (XDXD) forms the most stable 1 : 1 complex. Notably, the sequence of the different spacers seems to have a decisive influence, as shown by the different stabilities of the 1 : 1 complex with **14** (XDXD) ($\log\beta = 6.3$) and with **15** (XXDD) ($\log\beta = 5.53$). Such a variation is not observed with acetate, for which the complexes with both ligands have a similar stability.

Molecular dynamics simulations

Molecular dynamics (MD) simulations were carried out to explore structure and dynamics of the tetramers as well as their preorganization for the complexation of anions. In order to investigate the influence of solvent polarity and intermolecular hydrogen bonding on the conformation of the tetramers, we used boxes of acetonitrile (the solvent used for the determination of stability constants) and chloroform, respectively.

A priori, we did not expect the tetramers to adopt single, preferred conformations during the MD simulations due to the putative high flexibility of their 32-membered macrocyclic ring system. However, as illustrated by the average structures in Fig. 11, five of the six tetramers (the exception being DDDD (**17**), see below) adopt on average very similar conformations in the two solvents used for the simulations.[22] In this preferred conformation the bridging xanthene and diphenyl ether units arrange in an up–down–up–down fashion while the urea functions form a belt in the middle. This enables intramolecular hydrogen bonding between the urea groups as well as $\pi\cdots\pi$ stacking interactions of the aromatic ring systems. The tetramer **12**, however, adopts the up–down–up–down conformation without forming these stabilizing intramolecular interactions. Instead, all the urea protons point to the center of the macrocycle where on average 3.2 acetonitrile molecules are captured in the cavity by intermolecular $NH\cdots N$ hydrogen bonding (Fig. 12a). A similar clustered solvation shell was obtained for the DDDD tetramer **17** in acetonitrile solution (Fig. 12b). Its average structure closely resembles the X-ray structure (rmsd value for the heavy atoms 0.37 Å) but is different from the conformations of the other tetramers. In the case of **17** the up–down arrangement is caused by an interplanar angle of about 90° between the aromatic rings of the diphenyl ether units, while in all other structures it is caused by the more or less parallel arrangement of opposite urea units required by the xanthene building blocks.

The pronounced complexation of acetonitrile molecules by the urea groups of **12** and **17** (for a comparison with a statistically distributed solvation shell see Fig. 12c) suggests that both macrocycles should be preorganized for the complexation of suitably sized anions. Because of the different spatial arrangement of the ligating urea functions (Fig. 11) we hypothesized that the XXXX tetramer **12** should prefer spherical or planar anions while the DDDD tetramer **17** could recognize tetrahedral anions.

To test this assumption we performed MD simulations of the complexes with TBA chloride and TBA dihydrogenphosphate in acetonitrile solution.[23] The average structures of the simulations in acetonitrile illustrated in Fig. 13 show the complexation of the anions by a network of hydrogen bonds to the urea groups. On average, 7.5 to 8.6 hydrogen bonds exist between the macrocycle and the anion (Table 3). A comparison of the structures of free and complexed macrocycles in Figs. 11 and 13 reveals that **12** is indeed preorganized for chloride and **17** for dihydrogenphosphate, respectively. The macrocycles have to undergo only minor conformational changes upon complexation of the anion, which is also reflected in the small energy contributions necessary for their reorganization (Table 3). A closer inspection of the interaction and complexation energies listed in Table 3 suggests that for both macrocycles the complexation of chloride is energetically more favourable than the complexation of dihydrogenphosphate, although the complexation energies differ only slightly in the case of **17**. Here, the highly attractive interactions between the macrocycle and the chloride anion are in part counterbalanced by a high reorganization energy due to a complete change of the conformation (Fig. 13). It is interesting to note that dihydrogenphosphate is bound to **17** only *via* its nonprotonated oxygen atoms while the hydroxyl oxygen atoms form no hydrogen bonds to the macrocycle. This suggests that **17** should be a good receptor for bidentate anions such as carboxylate.

Conclusion

Six tetraurea macrocycles involving flexible and rigid spacers have been synthesised and characterised by NMR spectroscopy

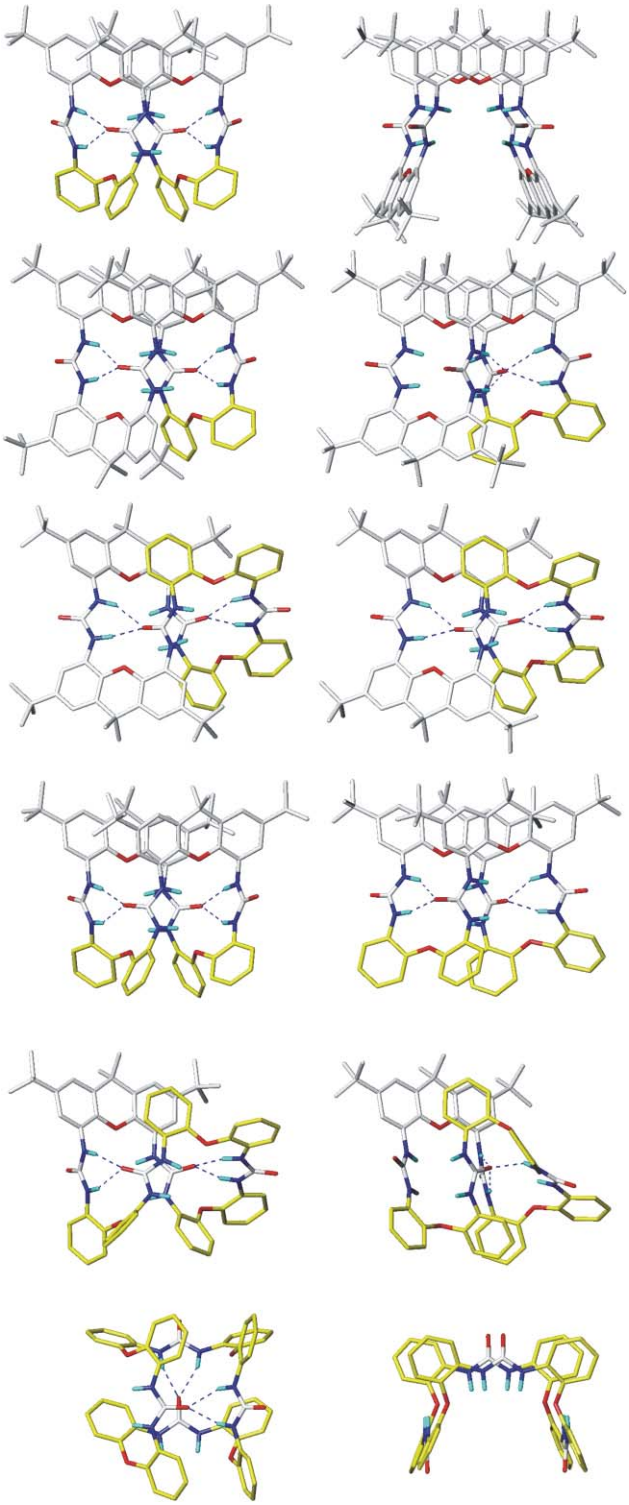

Fig. 11 Minimized average structures from the MD simulations in chloroform (left column) and acetonitrile (right column) for the macrocycles **12–17** (from top to bottom). Nonpolar hydrogen atoms have been omitted, and the carbon atoms of the diphenyl ether units are colored in yellow.

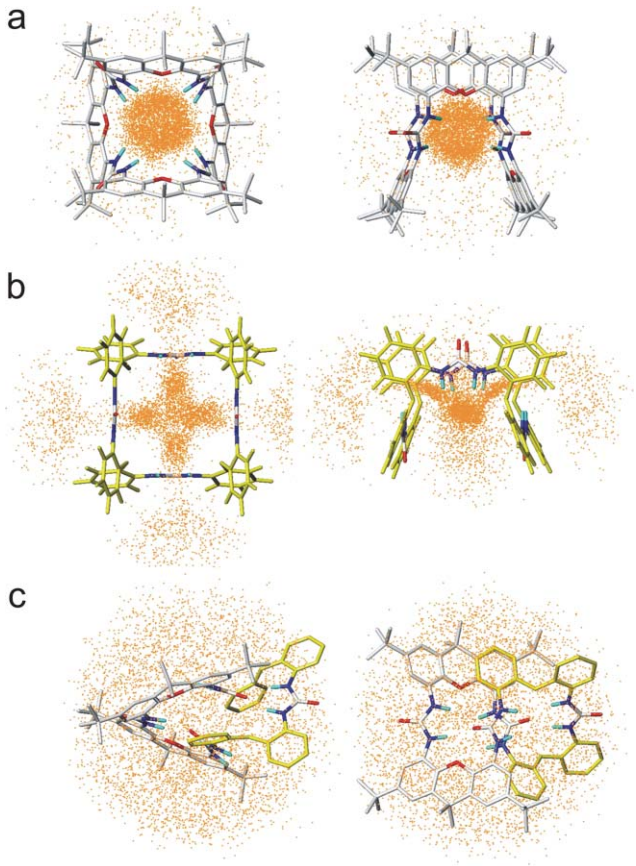

Fig. 12 Distribution of the nitrogen atoms of the twelve closest acetonitrile molecules around the empty receptors **12** (a), **17** (b) and **15** (c) during the 10 ns MD simulation, seen from two different directions. The carbon atoms of the diphenyl ether units are colored in yellow.

and partly by single-crystal X-ray spectroscopy. Their complexes with different spherical, planar and bidentate anions have been investigated by NMR spectroscopy, UV spectrophotometry and in part by MD simulations. Despite unexpected solubility problems it could be established that all macrocycles act as anion receptors, although with different affinity and selectivity. In general, no complexes were observed with iodide and nitrate and only weak interactions were found for bromide. This may be attributed to the nonplanar, box-like conformation of the macrocycles (observed in the MD simulations and corroborated by the X-ray analyses of two examples), which spans a cavity that is too small for the larger halide anions. For nitrate the discrepancy between the number of donating and accepting sites seems to be the excluding factor for complexation. Among the complexed anions, chloride seems to prefer the more rigid macrocycles while acetate and dihydrogenphosphate are best complexed by ligands combining both flexible and rigid elements.

Experimental

All solvents were of analytical quality (p. a.) and were used without additional purification. Deuterated solvents for NMR were purchased from Deutero GmbH. ^{1}H NMR spectra were recorded on a Bruker Avance DRX 400 spectrometer at 400 MHz using the solvent signals as an internal reference. Mass spectra were recorded with a Finnigan MAT 8230 instrument. The melting points are not corrected.

Table 3 Selected average energies (kcal mol^{-1}) and geometrical parameters for the complexes of **12** and **17** with chloride and dihydrogenphosphate

	12 (XXXX)		**17** (DDDD)	
	Cl^-	$H_2PO_4^-$	Cl^-	$H_2PO_4^-$
Interaction energy MC $\cdots$ X^- [a]	−126.8	−102.1	−146.7	−113.3
Interaction energy MC $\cdots$ TBA^+	−7.7	0.0	−1.8	−2.5
Interaction energy $TBA^+ \cdots X^-$	−14.9	−0.4	−5.1	−7.4
Sum of the interaction energies	−149.4	−102.5	−153.7	−123.2
Steric energy $MC_{complex}$	243.4	243.3	−71.8	−88.0
Steric energy MC_{free}	247.2	247.2	−100.0	−100.0
Reorganization energy $MC_{free} \rightarrow MC_{complex}$	−3.8	−3.9	28.2	12.0
Complexation energy $\Sigma E_{complex} - \Sigma E_{free}$	−128.8	−91.5	−101.8	−95.4
Number of hydrogen bonds MC $\cdots$ X^-	7.5	8.6	7.7	7.6
Average NH $\cdots$ X^- distance [b]	2.16	2.82	2.11	3.07

[a] MC: macrocycle. [b] For dihydrogenphosphate the NH $\cdots$ P distances were chosen.

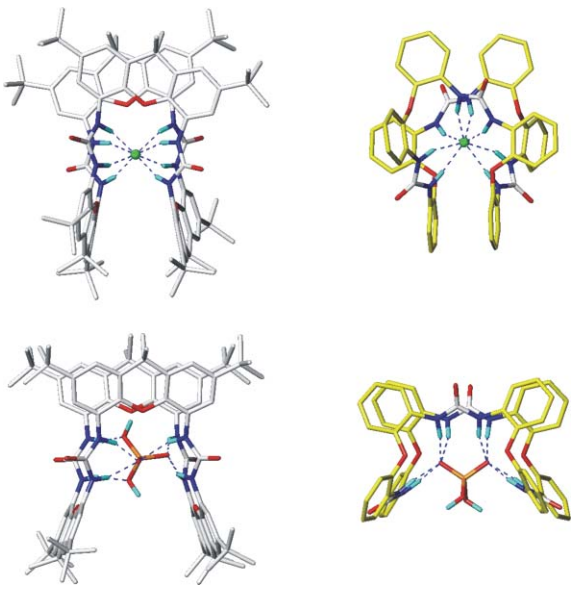

Fig. 13 Minimized average structures of the complexes of **12** (left) and **17** (right) with chloride (top) and dihydrogenphosphate (bottom) in acetonitrile. Nonpolar hydrogen atoms have been omitted, and the carbon atoms of the diphenyl ether units are colored in yellow.

Diamine 9 (XXX)

A solution of diisocyanate **5** (1.0 g, 2.5 mmol) in dichloromethane (90 cm^3) was added dropwise over 30 min to a stirred solution of the mono-BOC-protected amine **3** (2.23 g, 5 mmol) in dichloromethane (90 cm^3) under nitrogen. After 18 h of stirring the solvent was removed under reduced pressure and the residual sticky solid was triturated with acetonitrile (20 cm^3). The solid was filtered off and washed with acetonitrile (2 × 10 cm^3) yielding the protected trimeric diamine as a light-yellow powder (2.38 g, 1.81 mmol). The compound was dissolved in dichloromethane (50 cm^3), and trifluoroacetic acid (30 cm^3) was added to the stirred solution cooled in an ice bath. The reaction mixture was allowed to warm up to room temperature over the next 3 h and slowly poured into a 5 N solution of sodium carbonate (400 cm^3). The pH was controlled to be 9–10. The organic layer was separated and the water layer was washed with dichloromethane (2 × 50 cm^3). The combined dichloromethane solutions were dried over $MgSO_4$, and evaporated. The crude product was triturated with 20 cm^3 acetonitrile and the solid was filtered off yielding the trimeric diamine **9** (1.68 mg, 60%) as a white powder; mp >360 °C (decomp.); δ_H (400 MHz, DMSO-d_6): 8.79 (2 H, s, N*H*), 8.74 (2 H, s, N*H*), 8.08 (2 H, d, *J* 2.0, Ar*H*), 7.97 (2 H, d, *J* 2.0, Ar*H*), 7.20 (2 H, d, *J* 2.0, Ar*H*), 7.13 (2 H, d, *J* 2.0, Ar*H*), 6.62 (2 H, d, *J* 2.0, Ar*H*), 6.26 (2 H, d, *J* 1.6, Ar*H*), 4.83 (4 H, s, NH_2), 1.66 (6 H, s, CH_3), 1.50 (12 H, s, CH_3), 1.32 (18 H, s, *tBu*), 1.27 (18 H, s, *tBu*), 1.15 (18 H, s, *tBu*); *m*/*z* (ESI) 1132.4 [M^+ + Na, 100%].

Diamine 10 (DXD)

A solution of the monoprotected diamine **4** (215 mg, 0.716 mmol) in dichloromethane (10 cm^3) was added to the solution of diisocyanate **5** (145 mg, 0.358 mmol) in dichloromethane (10 cm^3). After 12 h of stirring under nitrogen the solvent was removed under reduced pressure yielding BOC-protected trimeric diamine as a light-brown glass-like solid. The crude diurea (360 mg, 0.358 mmol) was dissolved in dichloromethane (10 cm^3), cooled in an ice bath and then trifluoroacetic acid (10 cm^3) was added. The mixture was allowed to warm up to room temperature over the next 4 h, with stirring. The reaction was stopped by pouring the mixture slowly into a 5 N solution of sodium carbonate (100 cm^3). The pH of the solution was controlled to be 9–10. The organic layer was separated, the aqueous layer was washed with dichloromethane (2 × 25 cm^3), and the combined organic phase was dried over $MgSO_4$. The solvent was removed under reduced pressure yielding diamine **10** (0.272 g, 94%) as a brown powder; mp > 190 °C (decomp.); δ_H (400 MHz, DMSO-d_6): 8.91 (2 H, s, N*H*), 8.67 (2 H, s, N*H*), 8.19 (2 H, d, *J* 2.3, ArH_{xan}), 7.86–7.80 (2 H, m, ArH_{diph}), 7.14 (2 H, d, *J* 2.3, ArH_{xan}), 7.00–6.92 (4 H, m, ArH_{diph}), 6.86 (2 H, ddd, ^3J 8.0, ^3J 7.0, ^4J 1.6, ArH_{diph}), 6.71 (2 H, dd, ^3J 8.0, ^4J 1.4, ArH_{diph}), 6.63 (dd, 2 H, ^3J 7.8, ^4J 1.2, ArH_{diph}), 6.53–6.47 (2 H, m, ArH_{diph}), 6.34 (2 H, ddd, ^3J 7.6, ^3J 7.6, ^4J 1.4, ArH_{diph}), 4.89 (4 H, s, NH_2), 1.62 (6 H, s, CH_3), 1.30 (18 H, s, *tBu*); *m*/*z* (ESI) 827.6 [M^+ + Na, 100%].

Diamine 11 (DDD)

This was prepared as described for **10**. Diisocyanate **6** (329 mg, 1.3 mmol) and the monoprotected diamine **4** (300 mg, 2.6 mmol) yielded the dimeric diamine **11** (510 mg, 60%) as a brownish powder; mp 185 °C; δ_H (400 MHz, DMSO-d_6): 9.23 (2 H, s, N*H*), 9.17 (2 H, s, N*H*), 8.29 (2 H, dd, ^3J 8.2, ^4J 1.2, Ar*H*), 8.15 (2 H,

dd, ^3J 8.2, ^4J 1.6, Ar*H*), 7.10 (2 H, ddd, ^3J 7.8, ^4J 1.6, Ar*H*), 7.00–6.83 (8 H, m, Ar*H*), 6.81–6.72 (6 H, m, Ar*H*), 6.57–6.50 (4 H, m, Ar*H*), 4.92 (4 H, s, NH_2). *m/z* (ESI) 675.7 [M^+ + Na, 100%].

Tetramer 12 (XXXX)

Solutions of the diamine **1** (124 mg, 0.35 mmol) and 4-nitrophenyl chloroformate (71 mg, 0.35 mmol) in $CHCl_3$ (50 cm^3 each) were simultaneously added dropwise with stirring over 10 h into a flask containing 100 cm^3 of chloroform. The solvent was removed *in vacuo* and a solution of *N*-ethyldiisopropylamine (46 mg, 0.35 mmol) in THF (50 cm^3) was added. Stirring was continued for the next 4 h. A white solid appeared in the reaction mixture, which was filtered off and identified as the cyclic tetramer **12** (33 mg, 15%); mp >320 °C (decomp.); δ_H (400 MHz, DMSO-d_6, 120 °C): 8.67 (8 H, s, N*H*), 7.87 (8 H, s, Ar*H*), 7.19 (8 H, s, Ar*H*), 1.65 (24 H, s, CH_3), 1.38 (72 H, s, *tBu*); *m/z* (FD) 1514.9 [M^+, 100%].

Tetramer 13 (XXXD)

Solutions of the diisocyanate **6** (40 mg, 0.158 mmol) in dichloromethane (10 cm^3) and the diamine **9** (176 mg, 0.158 mmol) in dichloromethane (10 cm^3) were simultaneously added dropwise with stirring over 10 min to a flask containing dichloromethane (20 cm^3). After 18 h at room temperature the solvent was removed under reduced pressure and the crude product was triturated with acetonitrile (15 cm^3). The solid was filtered off yielding the tetramer **13** (148 mg, 68%) as a white powder; mp >270 °C (decomp.); δ_H (400 MHz, DMSO-d_6, 120 °C): 9.52 (2 H, s, N*H*), 8.63 (2 H, s, N*H*), 7.90 (2 H, s, N*H*), 7.86 (4 H, s, ArH_{xan}, N*H*), 7.82 (2 H, d, *J* 7.4, ArH_{diph}), 7.59 (2 H, s, ArH_{xan}), 7.42 (2 H, s, ArH_{xan}), 7.33 (2 H, d, *J* 2.3, ArH_{xan}), 6.97 (2 H, d, *J* 2.3, ArH_{xan}), 6.91–6.88 (4 H, m, ArH_{diph}), 6.87 (2 H, d, *J* 2.0, ArH_{xan}), 6.60 (2 H, t, ArH_{diph}), 1.76 (6 H, s, CH_3), 1.38 (6 H, s, CH_3), 1.33 (18 H, s, *tBu*), 1.12 (18 H, s, *tBu*), 1.11 (18 H, s, *tBu*); *m/z* (FD) 1362.6 [M^+, 100%].

Tetramer 14 (XDXD)

Solutions of the diisocyanate **5** (85 mg, 0.21 mmol) in dichloromethane (25 cm^3) and diamine **10** (170 mg, 0.21 mmol) in dichloromethane (25 cm^3) were simultaneously added dropwise under nitrogen over 30 min to a flask containing dichloromethane (25 cm^3). After 8 h of stirring the solvent was removed under reduced pressure. The crude product was triturated with boiling acetonitrile (15 cm^3). After 1 h a beige solid appeared and was filtered off. The tetramer **14** (140 mg, 55%) was obtained as a light-beige powder; mp >235 °C (decomp.); δ_H (400 MHz, DMSO-d_6): 8.78 (4 H, s, N*H*), 8.39 (4 H, s, N*H*), 8.22 (4 H, d, *J* 2.0, ArH_{xan}), 7.60 (4 H, m, ArH_{diph}), 7.13 (4 H, d, *J* 2.0, ArH_{xan}), 7.00–6.92 (8 H, m, ArH_{diph}), 6.86–6.79 (4 H, m, ArH_{diph}), 1.59 (12 H, s, CH_3), 1.28 (36 H, s, *tBu*); *m/z* (ESI) 1231.8 [M^+ + Na, 100%].

Tetramer 15 (XXDD)

Solutions of the diisocyanate **8** (100 mg, 0.21 mmol) in dichloromethane (25 cm^3) and the dimeric diamine **7** (153 mg, 0.21 mmol) in dichloromethane (25 cm^3) were simultaneously added dropwise under nitrogen over 30 min to a flask containing dichloromethane (20 cm^3). After 18 h of stirring the solvent was removed under reduced pressure. The crude product was triturated with acetonitrile (15 cm^3) to furnish the tetramer **15** (104 mg, 41%) as a white powder; mp >260 °C (decomp.); δ_H (400 MHz, DMSO-d_6, 120 °C): 9.25 (2 H, s, N*H*), 8.40 (2 H, s, N*H*), 8.21 (2 H, s, N*H*), 7.97–7.59 (10 H, br.m, N*H*, ArH_{diph}, ArH_{xan}), 7.21 (2 H, d, *J* 2.0, ArH_{xan}), 7.18 (2 H, d, *J* 2.0, ArH_{xan}), 6.75–6.42 (12 H, br.m, ArH_{diph}), 1.65 (12 H, s, CH_3), 1.31 (18 H, s, *tBu*), 1.29 (18 H, s, *tBu*); *m/z* (ESI) 1231.9 [M^+ + Na, 100%].

Tetramer 16 (XDDD)

The diamine **11** (100 mg, 0.15 mmol) and tetrabutylammonium chloride (43 mg, 0.15 mmol) were dissolved in acetonitrile (25 cm^3). A solution of the diisocyanate **5** (62 mg, 0.15 mmol) in acetonitrile (10 cm^3) was added dropwise under nitrogen over 1 h to the stirred diamine solution. After 12 h the solvent was removed under reduced pressure and the crude product was dissolved in ethyl acetate (10 cm^3). The solution was washed three times with 10 cm^3 water to remove the chloride. The organic layer was dried with $MgSO_4$. Then hexane (50 cm^3) was added to the solution and the beige precipitate was filtered off yielding the tetramer **16** (41 mg, 25%); mp >220 °C (decomp.); δ_H (400 MHz, DMSO-d_6, 120 °C): 8.78 (2 H, s, N*H*), 8.68 (2 H, s, N*H*), 8.38 (2 H, s, N*H*), 8.27 (2 H, s, N*H*), 8.00 (2 H, d, *J* 8.2, ArH_{diph}), 7.90 (2 H, s, ArH_{xan}), 7.85 (4 H, t, *J* 8.0, ArH_{diph}), 7.14 (2 H, d, *J* 2.0, ArH_{xan}), 7.12–6.82 (14 H, m, ArH_{diph}), 6.79 (2 H, d, *J* 7.8, ArH_{diph}), 6.74 (2 H, d, *J* 7.8, ArH_{diph}), 1.61 (6 H, s, CH_3), 1.30 (18 H, s, *tBu*); *m/z* (ESI) 1079.5 [M^+ + Na, 100%].

Tetramer 17 (DDDD)

Solutions of the diamine **2** (500 mg, 2.5 mmol) in ethyl acetate (50 cm^3) and 4-nitrophenyl chloroformate (503 mg, 2.5 mmol) in ethyl acetate (50 cm^3) were simultaneously added dropwise over 10 h (nitrogen, stirring) to a flask containing ethyl acetate (100 cm^3). A white precipitate appeared in the reaction mixture. Then the solution of *N*-diisopropylethylamine (323 mg, 2.5 mmol) in ethyl acetate (25 cm^3) was added dropwise over 2 h. The reaction mixture was stirred for 12 h. The white precipitate (112 mg, 20%) was filtered off, and identified as the cyclic tetramer. The liquid was filtered through silica gel (100 g), which was then washed with ethyl acetate (3 × 60 cm^3). The eluent was concentrated to 10 cm^3 and then left for 12 h in an open 250 cm^3 flask. The tetramer **17** (330 mg, 58%) was obtained as a colorless crystals; mp >215 °C (decomp.); δ_H (400 MHz, DMSO-d_6): 9.19 (8 H, s, N*H*), 8.34 (8 H, d, *J* 7.4, Ar*H*), 7.06 (8 H, t, *J* 7.6, Ar*H*), 6.91 (8 H, t, *J* 7.4, Ar*H*), 6.69 (8 H, d, *J* 7.6, Ar*H*); *m/z* (ESI) 927.1 [M^+ + Na, 100%].

UV spectrophotometry

The apparent overall stability constants β were determined in a mixture of acetonitrile and THF (3 : 1 v/v) by absorption spectrophotometry as previously described.[13] The spectra were recorded between 230 and 320 nm with a VARIAN (Cary 3) spectrophotometer using quartz cells (Hellma) with an optical path length of 1 cm. The concentration of the ligands was *ca.* 5×10^{-6} M. The various anions studied were used as tetrabutylammonium salts : Bu_4NCl (Fluka, ≥97%), Bu_4NBr (Fluka, ≥99%), Bu_4NOAc (Aldrich, ≥97%), and $Bu_4NH_2PO_4$ (Fluka, ≥97%)). No background electrolyte was added to the solutions because of (i)

Table 4 Summary of crystallographic data

	13 (XXXD)	**13** (XXXD)	**17** (DDDD)
Chemical formula	$C_{85}H_{100}N_8O_8 \cdot 2CH_3CN$	$C_{85}H_{100}N_8O_8 \cdot 5C_2H_5OH$	$C_{52}H_{40}N_8O_8 \cdot 5C_4H_8O$
CCDC ref. numbers	687874	687875	687873
M	1443.84	1592.07	1265.44
Crystal system	Triclinic	Monoclinic	Monoclinic
Space group	$P\bar{1}$	$P2_1/c$	$P2_1/c$
a/Å	14.9282(13)	29.7280(13)	25.808(2)
b/Å	18.9297(17)	16.1350(5)	19.667(2)
c/Å	19.2836(16)	20.0431(9)	25.792(2)
α/°	61.351(6)	90	90
β/°	86.758(7)	107.696(3)	93.206(7)
γ/°	71.553(7)	90	90
V/Å^3	4506.7(7)	9159.0(6)	13071(2)
Z	2	4	8
T/K	173(2)	173(2)	100(2)
Reflections	47861	73886	112990
Unique reflections	16476	16079	24137
R_{int}	0.0586	0.0710	0.1890
$wR(F^2)$, all data	0.3104	0.2593	0.0915

the insolubility of most inert salts in the solvent and (ii) the very small ligand and anion concentrations used. The anion-to-ligand ratios which were reached at the end of the titrations were in the range 1.5–13. The spectral changes were interpreted using the program SPECFIT.[24] The values of the stability constants given in Table 2 are the average of at least 3 experiments and the precision corresponds to the standard deviation of these mean values.

Molecular dynamics simulation

All molecular dynamics simulations were performed using the AMBER 9 software package and the *gaff* parameter set.[25] The initial geometry of the macrocycles was obtained either by manual construction with an all-*trans* arrangement of the urea amide groups, by converting other tetramer structures into the desired structure or from the X-ray structures of **13** and **17**. Charges (see ESI† and ref. 13) were derived following the standard RESP procedure[26] from a 6-31G* electrostatic potential calculated with the Gaussian98 program,[27] and the molecule structures were transferred into the LEaP format. Subsequently, a rectangular box of chloroform or acetonitrile molecules, respectively (approximately 14 Å solvent layer thickness on each side) was added. For the chloroform solvent model, the corresponding parameters[28] of AMBER 7, and for the acetonitrile model the parameters by Kollman *et al.*[29] were used. Missing parameters for the ca–oh bond length, the ca–ca–oh and ca–oh–ho bond angles, as well as the X–ca–oh–X and ca–ca–c–oh dihedral angles were adopted from the AMBER 7 *parm98* parameter set. The missing parameter for ca–c3–ca was taken from Kirchhoff *et al.*[30] The solvated structures were subjected to 5000 steps of minimisation followed by a 30 ps belly dynamics (300 K, 1 bar, 1 fs timestep) for solvent relaxation and a 100 ps equilibration period. Subsequently, MD simulations were performed in a NTP (300 K, 1 bar) ensemble for 10 ns using a 1 fs time step. Constant temperature and pressure conditions were achieved by the weak coupling algorithm and isotropic position scaling. Temperature and pressure coupling times of 0.5 ps and 1.0 ps, respectively, and the experimental compressibility values of 100×10^{-6} bar^{-1} for chloroform and of 87.1×10^{-6} bar^{-1} for acetonitrile were used. The particle mesh Ewald (PME) method[31] was applied to treat long-range electrostatic interactions, and the van der Waals interactions were truncated by using a cut-off value of 12 Å. Bonds containing hydrogen atoms were constrained to their equilibrium length using the SHAKE algorithm. Snapshots were recorded every 2 ps.

Geometric and energetic analyses of the trajectories were carried out with the carnal and anal modules of AMBER 7. Graphical analysis of the results was performed with the SYBYL program.[32]

Single-crystal X-ray diffraction

Data were collected on a STOE-IPDS-II two-circle diffractometer employing graphite-monochromated MoKα radiation (0.71073 Å). Data reduction was performed with the X-Area software.[33] Structures were solved by direct methods with SHELXS-90[34] and refined by full-matrix least-squares techniques with SHELXL-97.[34]

All non-H atoms were refined with anisotropic displacement parameters. Hydrogens were included at calculated positions and allowed to ride on their parent atoms. Two *t*-butyl groups of $C_{85}H_{100}N_8O_8 \cdot 2CH_3CN$ are disordered over two positions with a ratio of the site occupation factors of 0.55(2)/0.45(2) and 0.51(1)/49(1), respectively. In one of them the C–C distances were restrained to 1.50(3) Å. One t-butyl group of $C_{85}H_{100}N_8O_8 \cdot 5C_2H_5OH$ is disordered over two positions with a ratio of the site occupation factors of 0.566(9)/0.434(9). The corresponding C–C bond lengths were restrained to 1.500(5) Å and the non-bonding 1–3 C–C distances were restrained to 2.5(1) Å.

Crystallographic data are summarised in Table 4.

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References and notes

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