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Novel Capsular Aggregates from Flexible Tripodal Triureas with C_s Symmetry

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Abstract: Tris(2- and 3-ureidobenzyl)amines with C_s symmetry self-assemble in solution forming mixtures of regioisomeric capsular aggregates, one chiral and one centrosymmetric. Under certain conditions, a predominance of the centrosymmetric regioisomer is found before the equilibrium, *i.e.* a mixture close to the statistical ratio of both species, is reached. In the solid state, there is a preference for the centrosymmetric capsules. Molecular models of both regioisomeric aggregates have been built and analyzed for comparison. Guests inside capsules formed by self-assembly of desymmetrized tris(3-ureidobenzyl)amines feel different magnetic environments depending on whether they are inside a chiral or an achiral regioisomeric container. Of special significance are the experiments with a "*highly flexible*" triurea endowed with an ureidopropylic arm, which self-assembles with the same efficiency as the more rigid tris(ureidobenzyl)amines.

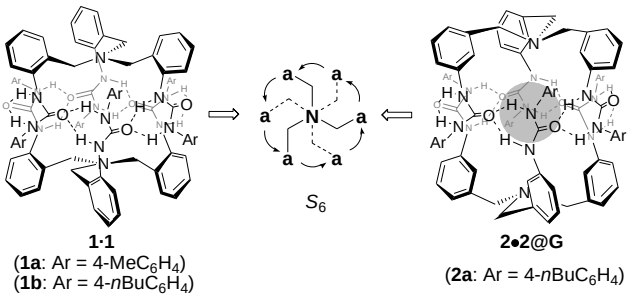
Keywords: Supramolecular chemistry• Hydrogen bonding • Self-assembling capsules •Ureas• Self-assembly

Introduction

The ability of molecules to spontaneously generate order through self-assembly is one of the most attractive phenomena investigated in the last decade.[1, 2] The design of self-assembling systems with potential applications needs a profound knowledge of the rules that govern supramolecular chemistry.[3] Organizational rigidity has been frequently appealed for the design of efficient supramolecular assemblies to minimize entropy losses.[4] However, that the efficiency of molecular recognition processes suffers less than generally assumed from the presence of single bonds has been proved in supramolecular systems based on hydrogen bonds[5, 6] or electrostatic interactions.[7]

In recent years much attention has been paid to self-assembled capsules, nanoscale structures made up of several synthetic subunits and connected through noncovalent interactions.[8-10] These systems exhibis the key properties of selective guest recognition and reversible encapsulation.[11] A range of capsules have been constructed from modules with rigid and preformed concave geometries such as resorcarenes,[12, 13] calixarenes[14, 15] and calixpyrroles.[16, 17]

Tris(2- and 3-ureidobenzyl)amines **1** and **2** have proved to be useful scaffolds in supramolecular chemistry despite their flexibility. They form capsular dimeric aggregates held together by a seam of six hydrogen-bonded urea groups (Figure 1).[18] Whereas assemblies **1·1** exist as *solvent free* capsular aggregates,[19, 20] **2·2** are able to encapsulate guests of appropriate size and shape.[21, 22] The tribenzylamine core provides a high degree of flexibility to triureas **1** and **2**, which adopt averaged C_{3v} symmetry in competitive solvents with hydrogen bonds. In non-competitive solvents, aggregates **1·1** or **2·2** are formed by assembly of two self-complementary and enantiomeric tripods of C_3 symmetry offset by 60º each other, resulting in a global achiral S_6 symmetry for the supermolecule (self-discrimination).



1·1
(**1a**: Ar = 4-MeC_6H_4)
(**1b**: Ar = 4-$nBuC_6H_4$)

2•2@G
(**2a**: Ar = 4-$nBuC_6H_4$)

Figure 1. Structure and schematic representation of capsular aggregates **1·1** and

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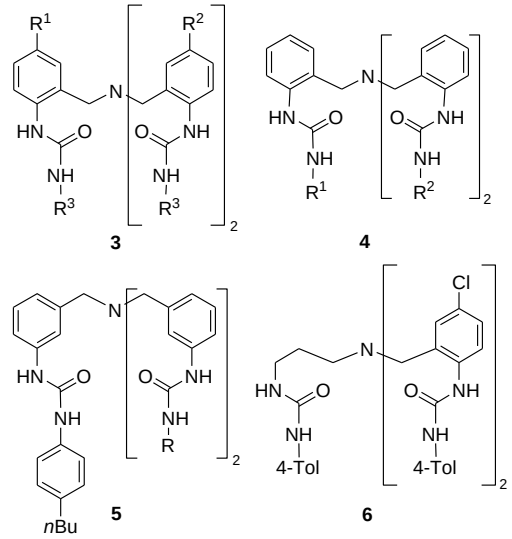
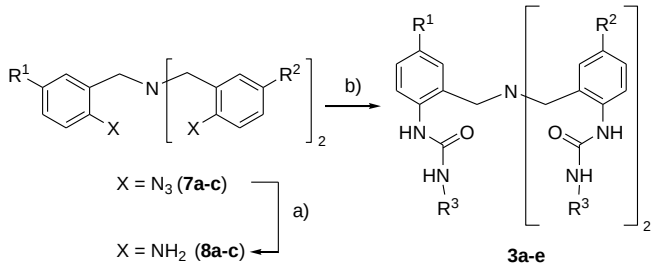
2 · 2 formed by self-assembly of tris(2- and 3-ureidobenzyl)amines **1** and **2**.

Although more complex systems are known, capsular aggregates **1 · 1** or **2 · 2** are attractive and challenging due to their special geometry. Moreover, the modular structure of the tribenzylamine skeleton has a great potential for modification. The sequential construction "arm to arm" of the tertiary amine core would provide access to new triureas of C_s symmetry varying both, the pendant ureido positions[20] and the substitution at the tribenzylamine skeleton. Moreover, triureas with branches even more flexible would be easily available. Herein we present a detailed study of the self-assembly of desymmetrized tris(2- and 3-ureidobenzyl)amines **3-5**. New capsules derived from the assembly of **5·5** have been characterised in solution and the solid state. Of special significance is the self-assembly of the highly flexible supramolecular tecton **6** endowed with an ureidopropylic arm. The formation of regioisomeric aggregates from triureas **3-6** has also been examined.



Results and Discussion

Tris(2-ureidobenzyl)amines **3a-e**, differentially substituted at one of the arylic groups of the tribenzylamine skeleton, were synthesized from the key triazides **7a-c** (Scheme 1, Table 1). Intermediate azides **7** were prepared by following a synthetic route previously reported by our group.[23]



Scheme 1. General procedure for the synthesis of triureas **3**. Reagents and reaction conditions: a) LAH, Et_2O, 0→20 °C, 6 h; b) R^3NCO, CH_2Cl_2, 20 °C, 18 h (R^1, R^2 and R^3 in Table 1).

Tris(2-ureidobenzyl)amines **3** feature overall C_s symmetries in competitive solvents, and thus are not chiral. Figure 2a shows the exchange equilibrium by inverting the rotation sense of the propeller of the tribenzylamine skeleton in C_s-symmetric triureas. Accordingly, ^{1}H-, ^{13}C{^{1}H}-, and ^{19}F{^{1}H}-NMR spectra of triureas **3a-e** measured in [D$_6$]DMSO exhibit the expected resonances for C_s-symmetric monomers. The spectra display two sets of signals in a 2:1 ratio corresponding to the two differentially substituted branches of the tripodal molecules. This pattern is clearly evident in Figure 3a, where the high-frequency region of the ^{1}H NMR spectrum of **3b** shows the resonances for the NH's bearing the R^3 groups (full spectrum of **3a** included in the Supporting Information).

Table 1. Synthesis of triamines **8** and triureas **3**.

Entry	Compound	R^1	R^2	R^3	Yield
1	**8a**	H	Me	-	92[a]
2	**8b**	Me	H	-	61[a]
3	**8c**	Cl	H	-	76[a]
4	**3a**	H	Me	4-MeC$_6$H$_4$	84[b]
5	**3b**	H	Me	4-CF$_3$C$_6$H$_4$	92[b]
6	**3c**	Me	H	4-MeC$_6$H$_4$	81[b]
7	**3d**	Cl	H	4-MeC$_6$H$_4$	71[b]
8	**3e**	Cl	H	4- CF$_3$C$_6$H$_4$	73[b]

[a] After chromatography. [b] Precipitated from the reaction mixture.

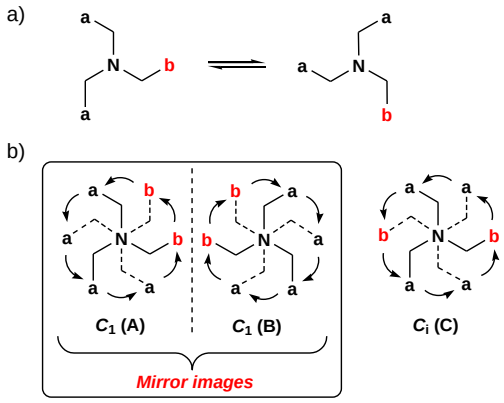


Figure 2. Schematic representation of: a) the exchange equilibrium between the two enantiomeric conformations of a triurea with C_s symmetry by inverting the rotation sense of the propeller; b) the three putative dimeric aggregates derived from the assembly of C_s-symmetric triureas (the arrows symbolize the directionality of the belt of hydrogen bonds).

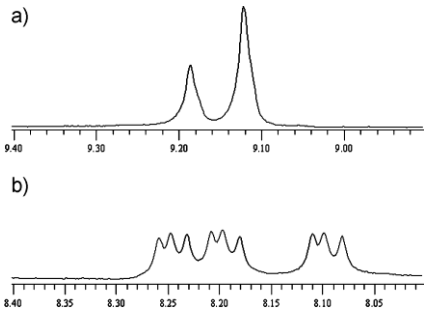


Figure 3. High-frequency regions of the ^{1}H NMR spectra of **3b** (300 MHz, 20 °C) in: a) [D$_6$]DMSO and b) $CDCl_3$, where the NH's bearing the pendant R^3 groups resonate.

The self-assembly of **3a-e** was subsequently investigated in a non-competitive solvent such as $CDCl_3$ (20-40 mM). The ^1H NMR spectra of **3a-e** in $CDCl_3$ are very complex compared to those of **3a-e** measured in [D6]DMSO and to those of the C_{3v}-symmetric triureas **1** and **2** in the same halogenated solvent (Supporting Information). In spite of their complexity, the diagnostic features for the dimeric aggregates **3·3** can be clearly distinguished: a) shifts to higher frequencies for the resonances of the NH protons respect to those of diphenylurea used as reference,[24] and b) anisotropic effects for the protons of the pendant aromatic groups and the methylenic protons of the $(ArCH_2)_3N$ fragments. The resonances for the monomeric species are not observed at the measured concentrations. The complexity of the spectra of **3** may due not only to the loss of symmetry by formation of dimeric assemblies **3·3** but also to the presence of two regioisomeric species: one enantiomeric pair of C_1 symmetry, labelled as **A** and **B** in Figure 4, and one C_i-symmetric species, labelled **C** (Figure 4). Aggregates **A** and **B** are schematically represented in Figure 2b and they feature supramolecular chirality.[25-27] Since separated signals for the two regioisomers are observed, their interconversion by a dissociation/recombination process may be slow on the NMR time scale. The relative proportion of the two regioisomers was determined by analyzing the resonances of the NH's bearing the pendant substituents R^3 appearing in the region of 7.8-8.3 ppm. Nine signals of similar area are observed in this region of the spectra, as illustrated for **3b** in Figure 3b. Six singlets were attributed to the chiral regioisomer and three singlets to the *meso* aggregate, the three assemblies being present in statistical ratio (33:33:33). An analogous conclusion can be drawn for the self-assembly of **3a** and **3c-d** although the corresponding high-frequency regions of their NMR spectra display more significant overlap. The self-assembly of **3b** and **3e** was further analyzed by $^{19}F\{^1H\}$-NMR spectroscopy. By analogous reasoning, the statistical ratio of C_1- and C_i-symmetric regioisomers should give rise to nine signals of equal integration, as in fact is observed in the region around -62.6 ppm for **3e**.

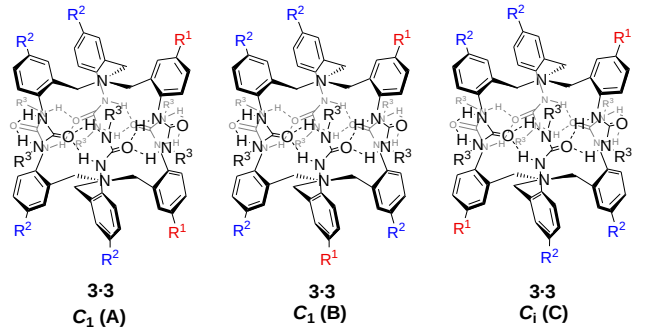


Figure 4. Structure of the three isomeric aggregates of C_1 and C_i symmetry of **3·3** labelled as **A**, **B** and **C** (R^1, R^2 and R^3 shown in Table 1).

As we previously reported,[20] triureas **4a-c** (**4a**: R^1 = 4-*n*BuC_6H_4, R^2 = 4-$CF_3C_6H_4$; **4b**: R^1 = 4-*n*BuC_6H_4, R^2 = 4-FC_6H_4; **4c**: R^1 = 4-$MeOC_6H_4$, R^2 = 4-$CF_3C_6H_4$), differentially substituted at one of the pendant aryl groups, are easily available from a common intermediate. Taking into account that a 66:33 ratio of C_1- and C_i-symmetric regioisomers corresponds to the statistical arrangement, **4a** (57:43) and **4c** (60:40) display some degree of selectivity in favour of the C_i dimeric species **4a·4a** and **4c·4c**. The ^1H NMR spectra of triureas **4b** and **4c** remain invariant over time. Conversely, when a sample of **4a** obtained by slow evaporation of a $CDCl_3$ solution was redissolved in the same solvent and its ^1H NMR spectrum immediately recorded, it showed a 36:64 ratio of C_1- and C_i-symmetric regioisomers! After some minutes (~20), the mixture of species equilibrated reaching a 57:43 ratio. After five days a value close to the statistical ratio was reached (Table 2).[20] This result seems to be an indication of a predominance of the centrosymmetric dimer in the solid state.

Table 2. Ratio of C_1- and C_i-symmetric regioisomers of **4a·4a** over time.

Entry	Time[a]	C_1:C_i [b]
1	1 min	36:64
2	20 min	57:43
3	2 d	59:41
4	5 d	62:38

[a] From the preparation of the sample ($CDCl_3$, 20 °C) until the spectrum was measured. [b] Determined by integration of selected signals in their ^1H NMR spectra (400 MHz); error ±5% of the stated value.

In order to evaluate subtle differences in the structures of both regioisomeric aggregates **4a·4a**, we used the program MacroModel® 8.1 (AMBER* force field) to build the two molecular models. The results from the molecular modelling conducted in gas phase and chloroform led to similar structures (Figure 5).

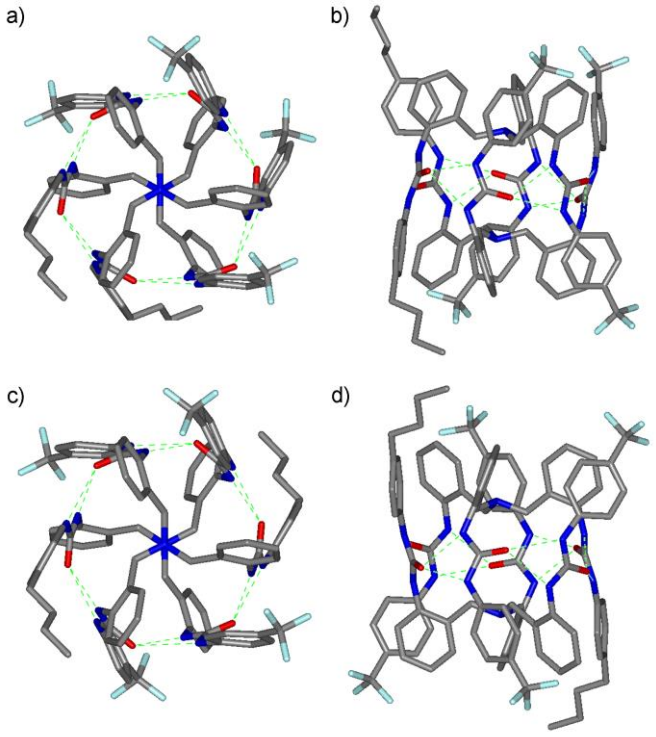
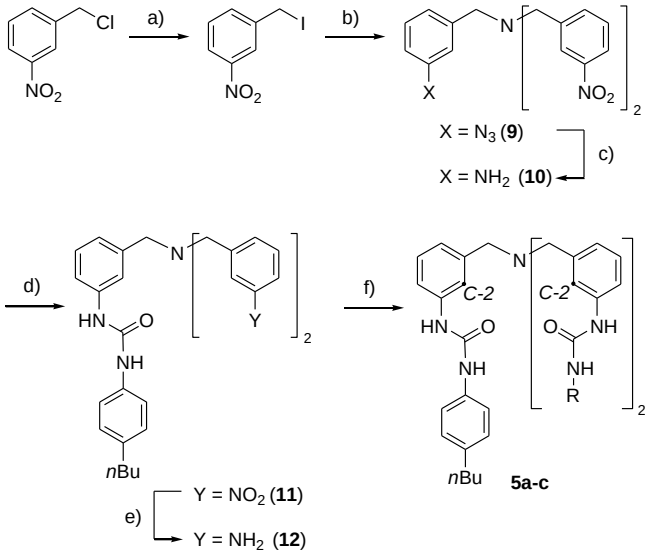


Figure 5. Minimum energy structures of **4a·4a** calculated in chloroform. Top (a) and side (b) views of the chiral regioisomer. Top (c) and side (d) views of the centrosymmetric regioisomer. The belt of hydrogen-bonded urea moieties is indicated by dotted lines.

A detailed analysis of the two energy-minimized structures reveals that there are no significant differences. The belt of hydrogen-bonded ureas is very symmetric with distances N…O=C (2.84-2.89 Å) for the urea nitrogen atoms bearing the pendant aromatic substituents being very similar to the distances N···O=C

(2.82 – 2.88 Å) for the urea nitrogen atoms attached to the tribenzylamine skeleton. The separation between the two pivotal nitrogen atoms is almost coincident being 5.18 Å and 5.22 Å for the chiral and the centrosymmetric regioisomer, respectively. The structural resemblance of both dimeric suprastructures would explain their similar stability and thus, the statistical ratio observed in solution.

The synthesis of the tris(3-ureidobenzyl)amines **5a-c**, differentiated in the pendant substituents, is depicted in Scheme 2. The treatment of 3-nitrobenzylchloride with NaI led to the corresponding iodide (99% yield), which was then allowed to react with 3-azidobenzylamine in the presence of Na_2CO_3 yielding the tertiary amine **9** (57%). The formation of the corresponding iminophosphorane by reaction of **9** with trimethylphosphine followed by hydrolysis in THF/H_2O led to the amine **10** (96%). Tribenzylamine **11** was isolated in 97% yield after the reaction of **10** with 4-*n*-butylphenyl isocyanate. Compounds **5a-c** were obtained from **11** by sequential catalytic hydrogenation (75%) and reaction with the corresponding isocyanate (Table 3).



Scheme 2. Reagents and reaction conditions for the synthesis of triureas **5a-c**: a) NaI, acetone, 20 °C, 20 h; b) 3-azidobenzylamine, Na_2CO_3, MeCN, reflux, 24 h; c) i) PMe_3, THF, 0 °C, 30 min, ii) H_2O/THF, 20 °C, 16 h; d) 4-*n*BuC_6H_4NCO, CH_2Cl_2, 20 °C, 24 h; e) H_2, PtO_2, THF, 20 °C, 16 h; f) RNCO, solvent, temperature, 24 h (Table 3).

Table 3. Reaction conditions and yields (%) for the synthesis of triureas **5a-c**.

Entry	Compound	R	Solvent	T (ºC)	Yield (%)
1	**5a**	4-$CF_3C_6H_4$	CH_2Cl_2	20	72
2	**5b**	4-$MeOC_6H_4$	CH_2Cl_2	20	92
3	**5c**	Bn	$CHCl_3$	reflux	80

Subsequently, the self-assembly of triureas **5a-c** in $CDCl_3$ was tested. The complexity and line-width of the signals once more indicate the presence of a mixture of species. Whereas the spectrum of **5c** is too complex to extract any conclusion, the ^{1}H NMR spectra of **5a-b** possess typical signatures of tribenzylamine-derived capsules (Figure 6).[21, 22] Large shifts to lower frequencies were observed for the signals of the protons of the pendant aromatic substituents as well as the protons located at the C-2 position of the tribenzylamine skeleton (marked in Scheme 2), the latter ones shifted as much as 2 ppm to lower frequencies. Thus, whereas protons at C-2 resonate at 7.5 ppm in [D_6]DMSO, they appear as broad signals at 5.7-5.9 ppm in the halogenated solvent. The benzylic protons of the $(ArCH_2)_3N$ fragment resonate as two multiplets at δ = 2.6-2.7 and δ = 3.2-3.6 ppm. Finally, the broad signals around 7.9-8.6 ppm were assigned, as in capsules **2•2**, to the ureido NH protons bearing the pendant aromatic groups. The dimeric assembly **5a•5a** was also detected by ESI-MS experiments. The spectrum measured in $CHCl_3$ shows the corresponding molecular ion of the protonated dimer at *m*/*z* = 1764 (Supporting Information).

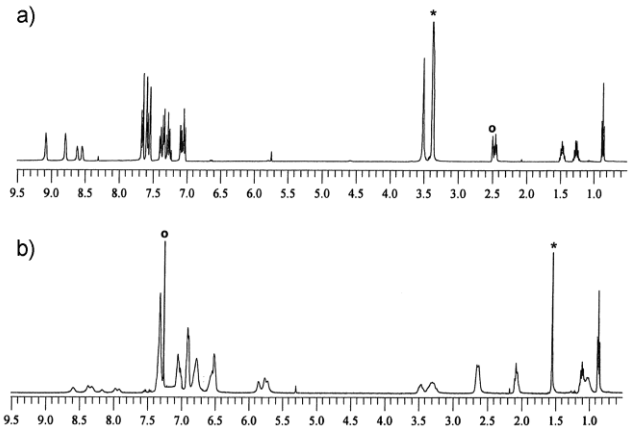


Figure 6. ^{1}H NMR spectra (400 MHz, 25 °C) of **5a** in: a) [D_6]DMSO and b) $CDCl_3$; (*) water and (º) signal for the residual peak of the solvent.

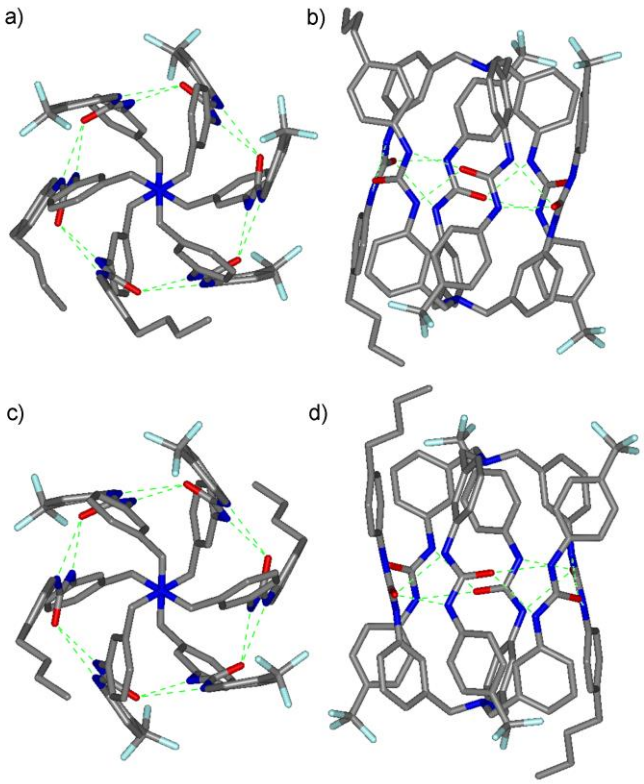


Figure 7. Minimum energy structures of **5a·5a** calculated in gas phase. Top (a) and side (b) views of the chiral regioisomer. Top (c) and side (d) views of the centrosymmetric regioisomer. The belt of hydrogen-bonded urea moieties is indicated by dotted lines.

Molecular models of both regioisomeric aggregates **5a · 5a** (Figure 7) were computed in both gas phase and chloroform by using MacroModel® 8.1 (AMBER* force field). The two energy-minimized structures reveal no significant differences. The separations between the two pivotal nitrogen atoms are 10.11 Å and 10.12 Å for the chiral and the centrosymmetric species, respectively. The distances N…O=C (2.77 – 2.79 Å) for the urea nitrogen atoms bearing the pendant aromatic substituents are slightly shorter than the distances N…O=C (2.90 – 3.00 Å) for the urea nitrogen atoms attached to the tribenzylamine skeleton.

The regioselectivity in the self-assembly of triureas **5a** and **5b** was examined by analyzing the region where the NH protons bearing the terminal substituents resonate. Nevertheless, the broadness and overlap of these signals hampered this analysis. The spectrum of **5a** in $CDCl_3$ recorded at -10 ºC and -60 ºC and measured in toluene-d_8 also at low temperatures, did not provide a better resolution. The resonances were resolved as nine peaks by using CD_2Cl_2 as solvent, where the capsule **5a·5a@CD$_2$Cl$_2$** exists (Supporting Information). The observed ratio for C_1- and C_i-symmetric regioisomers was 62:38, very close to the statistical distribution.

Tris(3-ureidobenzyl)amines **2** (Figure 1) form dimeric aggregates whose cavities are able to encapsulate guests of appropriate shape and size.[21, 22] The resemblance of the spectra of triureas **5** with those of triureas **2** in $CDCl_3$ suggests the presence of capsules **5•5@CDCl$_3$**. In a preceding work we demonstrated that dimeric aggregates **2·2** are excellent containers for MeI, CH_2Cl_2 and $MeNO_2$.[22] At -15 ºC, the ^{1}H NMR spectra of **5a** in the presence of an excess of MeI, CH_2Cl_2 and $MeNO_2$, show the resonances for the capsules **5a•5a@MeI**, **5a•5a@CH$_2$Cl$_2$**, **5a•5a@MeNO$_2$** as well as the encapsulated guests, shifted 0.3-0.4 ppm to lower frequencies with respect to those of the free ones. The high-frequency regions of the ^{1}H NMR spectra support a distribution of regioisomers close to statistical (Figure 8, left) which indicates that the presence of these guests inside the cavity may not influence the regioselectivity of the self-assembly process.[27] Interestingly, the spectra reveal two different resonances for MeI and $MeNO_2$ inside **5a•5a**, with slightly different chemical shifts in a 2:1 ratio (Figures 8a and 8c, right). The most intense signals were assigned to the guests inside the chiral capsules, since they exists as a 50:50 mixture of two enantiomers, and the less intense to the guest inside the achiral one. Clearly, the guests feel a different magnetic environment depending on whether they are inside the chiral container or the achiral one.

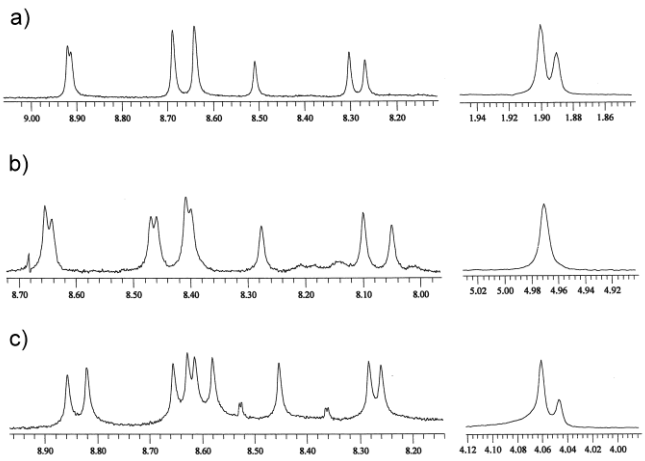


Figure 8. Selected regions of the ^{1}H NMR spectra (400 MHz, $CDCl_3$, -15 °C) of: a) **5a·5a@MeI**, b) **5a·5a@CH$_2$Cl$_2$** and c) **5a·5a@MeNO$_2$**, where the NH's bearing the pendant aryl groups (left part) and the encapsulated guest (right part) resonate.

We succeeded in growing single crystals of **5a** suitable for X-ray analysis ($CHCl_3$/*n*-pentane). The structure comprises two independent molecules **5a·5a** each forming a unique capsule by symmetry as we have described previously (Figure 9).[21, 28] The belt of hydrogen-bonded ureas is rather symmetrical as expected from the computed structures ranging the distances N…O=C from 2.86 to 3.09 Å. Inside the capsule, a disordered molecule of *n*-pentane was found as the guest species. Notably, the crystal shows the exclusive presence of the C_i regioisomeric capsule. The preference for the centrosymmetric arrangement in the solid state suggests that crystal packing forces must play a significant role.[28, 29]

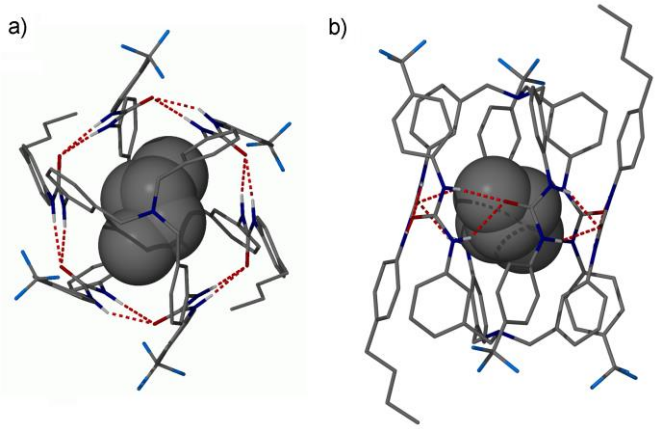
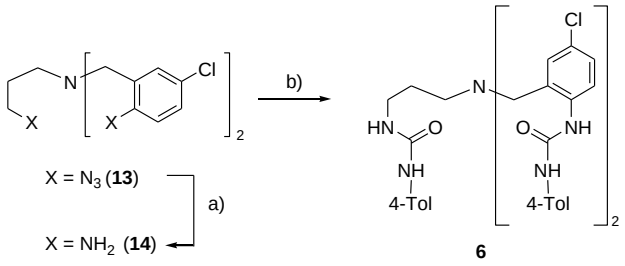


Figure 9. X-ray structure of **5a·5a@*n*-pentane**: a) top and b) side view. The belt of hydrogen-bonded urea moieties is indicated by dotted lines. A molecule of pentane is located inside the cavity.

Intrigued by the self-assembly abilities of more flexible triureas, we designed triurea **6** with an ureido-branch of a completely different nature. By virtue of its ureidopropylic arm triurea **6** possesses a "*superflexible*" skeleton. Rigid molecules have been frequently designed to minimize the entropy losses and favour their self-assembly processes.[4] However, the presence of flexible regions is less of a disadvantage than previously supposed, since single bonds can better accommodate strain.[3, 5, 6] The synthesis of **6** was conducted from the triazide **13**[30] by reduction to the triamine **14** and subsequent reaction with 4-methylphenyl isocyanate (Scheme 3).



Scheme 3. Synthesis of triamine **14** and triurea **6**. Reagents and reaction conditions: a) i) PMe_3, THF, 0 °C, 5 h, ii) H_2O/THF, 20 °C, 18 h; b) 4-MeC_6H_4NCO, $CHCl_3$, 20 °C, 20 h.

The pattern of signals of **6** in its ^{1}H NMR spectrum measured in [D$_6$]DMSO is consistent with the presence of an averaged C_s symmetric monomer (Figure 10a). However, a more complex picture is present in $CDCl_3$. The ^{1}H NMR spectrum of **6** in this solvent reveals a high number of sharp signals, discarding the presence of oligomeric associations (Figure 10b). The spectrum was interpreted as due to an equilibrium mixture of two C_1- and C_i-symmetric regioisomers (Figure 11). The resonances appearing around 7.5-8.5 ppm were assigned to the NH's bearing the pendant aromatic groups. Additionally, the signals resonating around 6.10-7.00 ppm were attributed to the arylic protons of the pendant 4-methylphenyl groups and those appearing at 1.89-2.28 ppm to the methyl protons of the same fragments. The lack of a singlet around 3.6 ppm points to an undetectable amount of monomeric species at this concentration (40 mM). The dimeric assembly **6•6** was also detected by ESI-MS experiments. The spectrum measured in $CHCl_3$ shows the corresponding molecular ion of the protonated dimer at m/z = 1505 (Supporting Information).

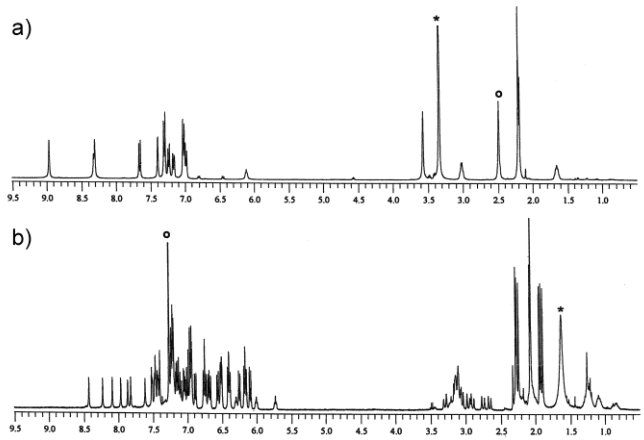


Figure 10. ^{1}H NMR spectra (400 MHz, 25 °C) of **6** in: a) [D$_6$]DMSO and b) $CDCl_3$; (*) water and (°) signal for the residual peak of the solvent.

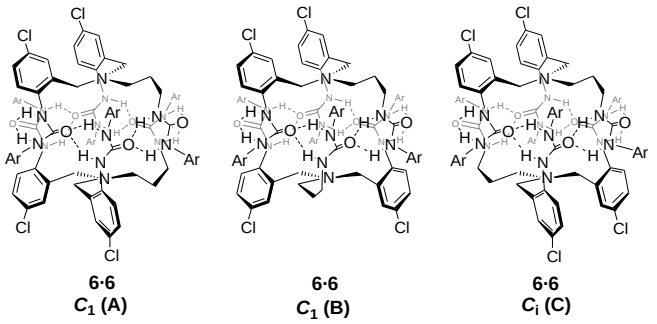


Figure 11. Structure of the three isomeric aggregates of C_1 and C_i symmetry of **6 · 6** labelled as **A**, **B** and **C** (Ar = 4-$CH_3C_6H_4$).

The appearance of nine signals with a similar integration in the high-frequency region of the ^{1}H-NMR spectrum of **6** ($CDCl_3$) would be in agreement with the presence of the two regioisomeric aggregates in 66:33 (statistical) ratio (Figure 11). In fact, this is the overall picture although only seven signals are clearly visible, the two missing resonances may be overlapped by the aromatic region (Figure 12a). The analysis of the region between 1.86-2.30 ppm is even more revealing (Figure 12b). Thus, the spectrum displays eight singlets, one of them of double intensity, for the resonances of the methyl groups of the pendant 4-methylphenyl substituents. Compared to the resonances of the C_{3v}-symmetric aggregates **1 · 1** the resonances attributed to these protons are spread out of a wider region. This fact can be rationalized on the basis of a more different environment experienced by the six methyl groups within **6 · 6** depending on their location, *i.e.* either between two ureidobenzylic branches or between one ureidopropylic and one ureidobenzylic arms (Figure 11).

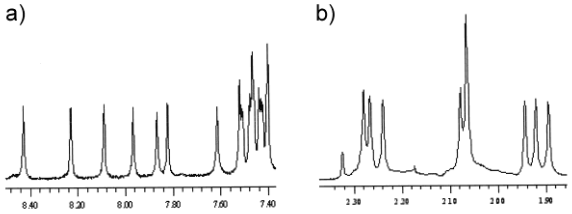


Figure 12. Selected regions of the ^{1}H NMR spectrum (400 MHz, $CDCl_3$, 25 °C) of the triurea **6** where: a) the NH's bearing the pendant aryl groups and b) the methyl groups of the 4-methylphenyl substituents resonate.

Conclusions

Flexible tris(2- and 3-ureidobenzyl)amines with C_s symmetry are synthetically accessible and able to self-assemble forming capsular dimeric aggregates. In solution, the dimeric aggregates exist as a mixture of regioisomers, one chiral and one centrosymmetric. Under certain conditions, the predominance of the centrosymmetric dimers is observed before the equilibrium, *i.e.* a distribution close to the statistical ratio of both regioisomers, is reached. Computed molecular models point to the two regioisomeric structures having similar stability. Interestingly, the guests inside capsules derived from desymmetrized tris(3-ureidobenzyl)amines feel different magnetic environments depending on whether they are inside a chiral or an achiral container. Moreover, there is a preference for the centrosymmetric capsule in the solid state, probably due to crystal packing effects. Finally, a "*superflexible*" triurea endowed with an ureidopropylic arm has the ability to self-assemble with the same efficiency as the tris(ureidobenzyl)amines do. These results further authenticate the use of tris(ureidobenzyl)amines and their derivatives as versatile frameworks for the rational design of more sophisticated supramolecular systems in a foreseeable future.

Experimental Section

General: ^{1}H and ^{13}C NMR spectra were measured on Bruker AC 200 (^{1}H: 200 MHz, ^{13}C: 50 MHz), Varian Unity-300 (^{1}H: 300 MHz, ^{13}C: 75 MHz), Bruker AVANCE 300 (^{1}H: 300 MHz, ^{13}C: 75 MHz) and Bruker AVANCE 400 (^{1}H: 400 MHz, ^{13}C: 101 MHz) spectrometers with TMS (δ 0.00 ppm) or the solvent residual peak as internal standards. IR spectra were recorded on a FT-IR Nicolet Impact 400 infrared spectrometer and melting points were taken on a Reichert apparatus and are not corrected.

All molecular mechanics calculations were carried out using the AMBER* force field as implemented within Maestro/MacroModel® 8.1. Standard potentials and atomic charges, as provided by the AMBER* force field, were employed without modifications. AMBER* and OPLAA force fields produce essentially the same results in related structures. Calculations were initially performed under vacuum and then in chloroform solution (GB/SA solvation model). Most complex structures were virtually identical under both conditions. Energy minimizations were conducted over 500 iterations on a Silicon Graphics Computer. Minimized structures were then subjected to conformational searches with 5000-step Monte Carlo multiple minimum simulations. All conformations within 15 kJ mol^{-1} of the computed global minimum were stored and the representative lowest-energy structure was analysed.

CAUTION: Azido compounds may represent an explosion hazard when being concentrated under vacuum or stored neat. A safety shield and appropriate handling procedures are recommended.

Preparation of tris(2-ureidobenzyl)amines 3

Synthesis of triazides 7a-c. The synthesis of triazides **7a-b** has been previously reported.[23]

Bis(2-azidobenzyl)(2-azido-5-chlorobenzyl)amine (7c). A solution of 2-azido-5-chlorobenzyl iodide[23] (0.75 g, 2.6 mmol) in dry dioxane (15 mL) was slowly added to a solution of bis(2-azidobenzyl)amine[23] (0.71 g, 2.6 mmol) in the same solvent (30 mL). Then, the reaction mixture was stirred under reflux for 5 h. After cooling, a solution of triethylamine (0.52 g, 3.1 mmol) in dry dioxane (2 mL) was added and the stirring was maintained for 2 h more. The solvent was removed under reduced pressure and the residue purified by silica-gel chromatography eluting with 13:1 hexanes/Et_2O (R_f = 0.82) to afford **7c** (68% yield) as colorless prisms (an analytical sample was obtained by recrystallization from 1:1 Et_2O/*n*-hexane). M.p. 83-85 °C; ^{1}H NMR (200 MHz, $CDCl_3$, 20 °C, TMS): δ = 3.51 (s, 2H), 3.56 (s, 4H), 7.00 (d, ^3J(H,H) = 8.4 Hz, 1H), 7.07-7.19 (m, 4H), 7.22-7.31 (m, 3H), 7.48-7.56 (m, 2H), 7.65 ppm (d, ^4J(H,H) = 2.6 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$, 20 °C): δ = 52.6 (t), 53.2 (2×t), 118.1 (2×d), 119.1 (d), 124.7 (2×d), 127.9 (d), 128.3 (2×d), 130.2 (s), 130.3 (d), 130.4 (2×s), 130.6 (2×d), 132.7 (s), 136.7 (s), 138.5 ppm (2×s); IR (Nujol): $\tilde{\nu}$= 2126 (vs), 2090 (vs), 1581 (m), 1487 (vs), 1407 (w), 1284 (s), 1151 (m), 1114 (m), 980 (w), 900 (w), 816 (w), 800 (w), 756 (m) cm^{-1}; MS (70 eV, EI): *m/z* (%): 446 (1) [M^++2], 444 (3) [M^+], 256 (21), 241 (11), 222 (23), 221 (32), 220 (27), 206 (13), 205 (13), 193 (17), 165 (14), 137 (15), 118 (16), 106 (30), 104 (80), 102 (55), 91 (22), 89 (37), 77 (100); elemental analysis calcd (%) for $C_{21}H_{17}ClN_{10}$ (444.9): C 56.70, H 3.85, N 31.48; found: C 56.38, H 3.92, N 31.08.

General procedure for the synthesis of triamines 8a-c. The corresponding triazide **7a-c** (2.3 mmol) was dissolved in freshly distilled Et_2O (30 mL) and slowly added to a suspension of $LiAlH_4$ (0.26 g; 6.9 mmol) in the same solvent (40 mL) at 0 °C under N_2. The mixture was stirred at this temperature for 1 h, warmed to 20 °C, and further stirred for 5 h. Then, the reaction mixture was cooled to 0 °C and treated with 10% aqueous NaOH (10 mL). After filtration over a pad of celite, which was subsequently washed with Et_2O (2×25 mL), the ethereal phase was separated and the aqueous phase extracted with CH_2Cl_2 (3×20 mL). The combined extracts were dried over $MgSO_4$, the solvent evaporated under reduced pressure and the residue was purified by silica-gel chromatography.

Bis(2-amino-5-methylbenzyl)(2-aminobenzyl)amine (8a). The crude product was eluted with 1:2 AcOEt/hexanes (R_f = 0.24) to afford **8a** (92% yield) as colorless prisms (an analytical sample was obtained by recrystallization from 1:1 Et_2O/*n*-pentane). M.p. 187-189 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = 2.20 (s, 6H), 3.42 (s, 4H), 3.45 (s, 2H), 3.79 (br s, 6H), 6.46-6.49 (m, 2H), 6.55 (dd, ^3J(H,H) = 8.4 Hz, ^4J(H,H) = 0.9 Hz, 1H), 6.66 (td, ^3J(H,H) = 7.4 Hz, ^4J(H,H) = 1.0 Hz, 1H), 6.86-6.88 (m, 4H), 7.03-7.08 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, 20 °C): δ = 20.4 (2×q), 57.1 (3×t), 115.5 (d), 115.7 (2×d), 117.8 (d), 121.98 (s), 122.03 (2×s), 126.9 (2×s), 128.9 (d), 129.4 (2×d), 132.0 (d), 132.6 (2×d), 143.1 (2×s), 145.7 ppm (s); IR (Nujol): $\tilde{\nu}$= 3456 (vs), 3368 (vs), 1620 (s), 1582 (m), 1504 (vs), 1315 (s), 1293 (s), 1249 (w), 1155 (m), 1098 (s), 1007 (w), 963 (m), 825 (s), 750 (s) cm^{-1}; MS (70 eV, EI): *m/z* (%): 360 (3) [M^+], 254 (12), 241 (5), 240 (29), 238 (7), 237 (10), 224 (5), 223 (15), 135 (17), 134 (5), 121 (17), 120 (100), 107 (8), 106 (48), 91 (11), 79 (5), 77 (13); elemental analysis calcd (%) for $C_{23}H_{28}N_4 \cdot 0.25H_2O$ (360.5): C 75.68, H 7.87, N 15.35; found: C 75.82, H 7.98, N 15.46.

Bis(2-aminobenzyl)(2-amino-5-methylbenzyl)amine (8b). The crude product was eluted with 1:1 AcOEt/hexanes (R_f = 0.39) to afford **8b** (61% yield) as colorless prisms (an analytical sample was obtained by recrystallization from 4:1 Et_2O/*n*-hexane). M.p. 191-195 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = 2.21 (s, 3H), 3.43 (s, 2H), 3.46 (s, 4H), 3.92 (br s, 6H), 6.49 (d, ^3J(H,H) = 8.4 Hz, 1H), 6.56 (dd, ^3J(H,H) = 8.1 Hz, ^4J(H,H) = 1.2 Hz, 2H), 6.67 (td, ^3J(H,H) = 7.5 Hz, ^4J(H,H) = 1.1 Hz, 2H), 6.86-6.88 (m, 2H), 7.03-7.09 ppm (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, 20 °C): δ = 20.4 (q), 57.1 (3×t), 115.5 (2×d), 115.7 (d), 117.8 (2×d), 121.9 (2×s), 122.0 (s), 126.9 (s), 128.9 (2×d), 129.4 (d), 132.0 (2×d), 132.6 (d), 143.0 (s), 145.6 ppm (2×s); IR (Nujol): $\tilde{\nu}$= 3446 (s), 3347 (s), 1618 (s), 1579 (m), 1506 (s), 1494 (vs), 1311 (s), 1285 (m), 1155 (m), 1098 (w), 958 (m), 750 (vs) cm^{-1}; MS (70 eV, EI): *m/z* (%): 346 (8) [M^+], 240 (49), 226 (54), 223 (64), 209 (61), 135 (54), 120 (100), 106 (97); elemental analysis calcd (%) for $C_{22}H_{26}N_4 \cdot 0.75H_2O$ (346.5): C 73.40, H 7.70, N 15.56; found: C 73.72, H 7.56, N 15.73.

Bis(2-aminobenzyl)(2-amino-5-chlorobenzyl)amine (8c). The crude product was eluted with 2:3 AcOEt/hexanes (R_f = 0.59) to afford **8c** (76% yield) as colorless prisms (an analytical sample was obtained by recrystallization from 1:1 Et_2O/*n*-hexane). M.p. 128-135 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 20 °C, TMS): δ = 3.39 (s, 2H), 3.43 (s, 4H), 3.85 (br s, 6H), 6.46 (d, ^3J(H,H) = 8.4 Hz, 1H), 6.56 (d, ^3J(H,H) = 7.8 Hz, 2H), 6.67 (td, ^3J(H,H) = 7.5 Hz, ^4J(H,H) = 1.2 Hz, 2H), 6.99-7.09 ppm (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, 20 °C): δ = 56.8 (t), 57.1 (2×t), 115.6 (2×d), 116.5 (d), 118.0 (2×d), 121.6 (2×s), 122.1 (s), 123.4 (s), 128.6 (d), 129.0 (2×d), 131.3 (d), 132.0 (2×d), 144.3 (s), 145.5 ppm (2×s); IR (Nujol): $\tilde{\nu}$ = 3411 (vs), 3335 (vs), 1622 (s), 1583 (m), 1495 (vs), 1421 (m), 1314 (m), 1293 (m), 1277 (m), 1098 (m), 1061 (w), 966 (w), 817 (w), 760 (s) cm^{-1}; MS (70 eV, EI): *m/z* (%): 366 (2) [M^+], 262 (8), 260 (27), 243 (15), 226 (20), 209 (12), 155 (11), 140 (30), 121 (54), 106 (100), 103 (18), 93 (6), 79 (17), 78 (11), 76 (43); elemental analysis calcd (%) for $C_{21}H_{23}ClN_4$ (366.9): C 68.75, H 6.32, N 15.27; found: C 68.32, H 6.83, N 15.35.

General procedure for the synthesis of triureas 3a-e. To a solution of the corresponding triamine **8** (0.30 mmol) in dry CH_2Cl_2 (8 mL) the corresponding isocyanate (0.90 mmol) was added under N_2. After stirring at 20 °C for 18 h the solvent was removed under reduced pressure and the residue triturated with Et_2O (5 mL). The white solid was filtered and dried under vacuum. Further purification was carried out by recrystallization.

Bis{5-methyl-2-[*N′*-(4-methylphenyl)ureido]benzyl}{2-[*N′*-(4-methylphenyl)ureido]benzyl}amine (3a): 84% yield; colorless prisms (from 1:1 $CHCl_3$/Et_2O). M.p. 234-236 °C; ^{1}H NMR (300 MHz, [D_6]DMSO, 20 °C): δ = 2.13 (s, 6H), 2.21 (s, 9H), 3.59 (s, 6H), 6.91-6.97 (m, 3H), 7.01-7.04 (m, 6H), 7.12 (t, ^3J(H,H) = 7.2 Hz, 1H), 7.19 (s, 2H), 7.26-7.31 (m, 6H), 7.34 (d, ^3J(H,H) = 8.1 Hz, 2H), 7.43 (d, ^3J(H,H) = 7.2 Hz, 1H), 7.54 (d, ^3J(H,H) = 8.1 Hz, 1H), 7.83 (s, 2H), 7.98 (s, 1H), 8.60 (s, 2H), 8.66 ppm (s, 1H); ^{13}C NMR (50 MHz, [D_6]DMSO, 20 °C): δ = 20.4 (q), 20.6 (q), 54.8 (t), 118.3 (d), 123.2 (d), 123.4 (d), 124.3 (d), 127.1 (d), 127.8 (d), 129.1 (d), 129.5 (s), 129.9 (d), 130.2 (s), 130.5 (s), 132.8 (s), 134.5 (s), 137.2 (s), 137.3 (s), 153.0 (s), 153.4 ppm (s); IR (Nujol): $\tilde{\nu}$= 3319 (s), 1665 (vs), 1607 (vs), 1557 (vs), 1516 (s), 1316 (m), 1287 (m), 1244 (m), 1208 (m), 819 (s), 746 (w), 721 (w), 695 (w) cm^{-1}; elemental analysis calcd (%) for $C_{47}H_{49}N_7O_3$ (760.0): C 74.28, H 6.50, N 12.90; found: C 73.91, H 6.84, N 12.99.

Bis{5-methyl-2-[*N′*-(4-trifluoromethylphenyl)ureido]benzyl}{2-[*N′*-(4-trifluoromethylphenyl)ureido]benzyl}amine (3b): 92% yield, colorless prisms (from 1:1 $CHCl_3$/Et_2O). M.p. 248-251 °C; ^{1}H NMR (300 MHz, [D_6]DMSO, 20 °C): δ = 2.11 (s, 6H), 3.61 (s, 6H), 6.90 (dd, ^3J(H,H) = 8.1 Hz, ^4J(H,H) = 1.5 Hz, 2H), 6.96 (t, ^3J(H,H) = 7.2 Hz, 1H), 7.11 (t, ^3J(H,H) = 7.2 Hz, 1H), 7.20 (s, 2H), 7.31 (d, ^3J(H,H) = 8.4 Hz, 2H), 7.43 (d, ^3J(H,H) = 7.2 Hz, 1H), 7.50 (d, ^3J(H,H) = 7.2 Hz, 1H), 7.53-7.62 (m, 12H), 8.01 (s, 2H), 8.16 (s, 1H), 9.12 (s, 2H), 9.18 ppm (s, 1H); ^{13}C NMR (75 MHz, [D_6]DMSO, 20 °C): δ = 20.4 (q), 54.7 (t), 117.9 (d), 121.6 (q, ^2J(C,F) = 31.6 Hz) (s), 123.8 (d), 123.9 (d), 124.5 (q, ^1J(C,F) = 269.5 Hz) (s), 124.8 (d), 125.9 (q, ^3J(C,F) = 3.6 Hz) (d), 127.2 (d), 127.8 (d), 129.3 (d), 130.1 (d), 130.3 (s), 130.9 (s), 133.4 (s), 134.0 (s), 136.8 (s), 143.5 (s), 152.8 (s), 153.2 ppm (s); ^{19}F NMR (188 MHz, [D_6]DMSO, 20 °C): δ = - 59.8 ppm; IR (Nujol): $\tilde{\nu}$= 3329 (s), 1666 (vs), 1605 (vs), 1563 (vs), 1410 (w), 1325 (vs), 1249 (m), 1168 (s), 1125 (vs), 1068 (s), 850 (m), 833 (w) cm^{-1}; elemental analysis calcd (%) for $C_{47}H_{40}F_9N_7O_3$ (921.9): C 61.24, H 4.37, N 10.64; found: C 61.17, H 4.47, N 10.68.

Bis{2-[*N′*-(4-methylphenyl)ureido]benzyl}{5-methyl-2-[*N′*-(4-methylphenyl)ureido]benzyl}amine (3c): 81% yield; colorless prisms (from 1:1 $CHCl_3$/Et_2O). M.p. 235-237 °C; ^{1}H NMR (300 MHz, [D_6]DMSO, 20 °C): δ = 2.16 (s, 3H), 2.22 (s, 9H), 3.61 (s, 6H), 6.92-7.17 (m, 12H), 7.28-7.30 (m, 6H), 7.37 (d, ^3J(H,H) = 8.1 Hz, 1H), 7.50 (d, ^3J(H,H) = 7.8 Hz, 2H), 7.53-7.56 (m, 2H), 7.79 (s, 1H), 7.92 (s, 2H), 8.59 (s, 1H), 8.65 ppm (s, 2H); ^{13}C NMR (75 MHz, [D_6]DMSO, 20 °C): δ = 20.3 (q), 20.6 (q), 54.5 (t), 54.6 (t), 118.3 (d), 123.5 (d), 123.6 (d), 124.4 (d), 127.0 (d), 127.7 (d), 128.8 (d), 129.0 (d), 129.6 (d), 129.8 (s), 129.9 (s), 130.3 (s), 130.4 (s), 130.5 (s), 132.8 (s), 134.4 (s), 137.1 (s), 153.0 (s), 153.4 ppm (s); IR (Nujol): $\tilde{\nu}$= 3322 (vs), 1655 (vs), 1601 (vs), 1564 (vs), 1313 (m), 1233 (m), 977 (w), 940 (w), 817 (m), 744 (m), 715 (m), 689 (m) cm^{-1}; elemental analysis calcd (%) for $C_{46}H_{47}N_7O_3$ (745.9): C 74.07, H 6.35, N 13.14; found: C 74.38, H 6.49, N 13.29.

Bis{2-[*N′*-(4-methylphenyl)ureido]benzyl}{5-chloro-2-[*N′*-(4-methylphenyl)ureido]benzyl}amine (3d): 71% yield; colorless prisms (from 1:1 $CHCl_3$/Et_2O). M.p. 226-230 °C; ^{1}H NMR (300 MHz, [D_6]DMSO, 20 °C): δ = 2.21 (s, 9H), 3.62 (s, 2H), 3.65 (s, 4H), 7.02-7.06 (m, 8H), 7.13-7.21 (m, 3H), 7.26-7.30 (m, 6H), 7.53-7.61 (m, 6H), 7.92 (s, 2H), 7.94 (s, 1H), 8.67 ppm (s, 3H); ^{13}C NMR (50 MHz, [D_6]DMSO, 20 °C): δ = 20.4 (q), 54.1 (t), 54.4 (t), 118.3 (d), 118.4 (d), 123.7 (d), 123.8 (d), 124.8 (d), 126.9 (d), 127.1 (d), 127.4 (s), 127.6 (d), 128.0 (d), 129.2 (d), 129.8 (s), 130.6 (s), 130.8 (s), 131.9 (s), 136.0 (s), 137.0 (s), 137.2 (s), 152.7 (s), 153.1 ppm (s); IR (Nujol): $\tilde{\nu}$= 3328 (s), 1660 (vs), 1604 (vs), 1563 (vs), 1514 (s), 1313 (m), 1239 (m), 1113 (w), 973 (w), 818 (m), 749 (m) cm^{-1}; elemental analysis calcd (%) for $C_{45}H_{44}ClN_7O_3$ (766.3): C 70.53, H 5.79, N 12.79; found: C 70.36, H 6.12, N 12.83.

Bis{2-[*N′*-(4-trifluoromethylphenyl)ureido]benzyl}{5-chloro-2-[*N′*-(4-trifluoromethylphenyl)ureido]benzyl}amine (3e): 73% yield; colorless prisms (from 1:1 $CHCl_3$/Et_2O). M.p. 248-251 °C; ^{1}H NMR (300 MHz, [D_6]DMSO, 20 °C): δ = 3.62 (s, 2H), 3.66 (s, 4H), 7.05 (td, ^3J(H,H) = 7.5 Hz, ^4J(H,H) = 0.9 Hz, 2H), 7.12-7.19 (m, 3H), 7.51-7.61 (m, 18H), 8.12 (s, 3H), 9.19 ppm (s, 3H); ^{13}C NMR (50 MHz, [D_6]DMSO, 20 °C): δ = 53.9 (t), 54.4 (t), 117.9 (d), 121.7 (q, ^2J(C,F) = 31.7 Hz) (s), 121.8 (q, ^2J(C,F) = 31.7 Hz) (s), 124.3 (d), 124.4 (d), 124.6 (q, ^1J(C,F) = 269.2 Hz) (s), 125.4 (d), 126.0 (q, ^3J(C,F) = 3.5 Hz) (d), 127.0 (d), 127.3 (d), 127.9 (d), 128.1 (s),

128.5 (d), 130.6 (s), 132.8 (s), 135.5 (s), 136.6 (s), 143.3 (q, ^5J(C,F) = 1.1 Hz) (s), 143.5 (q, ^5J(C,F) = 1.2 Hz) (s), 152.6 (s), 152.9 ppm (s); ^{19}F NMR (188 MHz, [D$_6$]DMSO, 20 °C): δ = -59.81, -59.78 ppm; IR (Nujol): $\tilde{\nu}$= 3329 (s), 1668 (vs), 1602 (s), 1558 (vs), 1409 (m), 1328 (vs), 1238 (m), 1184 (m), 1164 (s), 1115 (vs), 1071 (s), 1017 (w), 848 (m), 833 (w), 751 (w), 715 (w) cm^{-1}; elemental analysis calcd (%) for $C_{45}H_{35}ClF_9N_7O_3$ (928.2): C 58.23, H 3.80, N 10.56; found: C 58.41, H 4.15, N 10.72.

Preparation of tris(3-ureidobenzyl)amines 5

3-Nitrobenzyl ioide. NaI (9.61 g, 64.2 mmol) was added to a solution of 3-nitrobenzyl chloride (5.50 g, 32.1 mmol) in dry acetone (50 mL) and the reaction mixture was stirred at 20 °C for 20 h. The solid was filtered and washed with cold acetone (5×20 mL). The solvent was removed under reduced pressure and the residue purified by silica-gel chromatography eluting with 1:9 AcOEt/hexanes (R_f = 0.45) to afford 3-nitrobenzyl iodide (99% yield) as yellow prisms. M.p. 84-85 °C (lit. 84-86 °C);[31] ^{1}H NMR (200 MHz, CDCl$_3$, 20 °C, TMS): δ = 4.50 (s, 2H), 7.49 (t, ^3J(H,H) = 8.0 Hz, 1H), 7.71 (dt, ^3J(H,H) = 7.7 Hz, ^4J(H,H) = 1.3 Hz, 1H), 8.11 (ddd, ^3J(H,H) = 8.2 Hz, ^4J(H,H) = 2.2 Hz, ^4J(H,H) = 1.0 Hz, 1H), 8.23 ppm (t, ^3J(H,H) = 2.0 Hz, 1H); IR (Nujol): $\tilde{\nu}$= 1516 (vs), 1352 (vs), 1313 (s), 1097 (w), 1070 (w), 906 (w), 816 (m), 739 (m), 685 (s), 672 (m) cm^{-1}.

Bis(3-nitrobenzyl)(3-azidobenzyl)amine (9). To a suspension of Na_2CO_3 (1.77 g, 16.7 mmol) in dry acetonitrile (10 mL) 3-azidobenzylamine[30] (0.43 g, 2.9 mmol) and 3-nitrobenzyl iodide (1.53 g, 5.8 mmol) were subsequently added in the same solvent (2 and 5 mL respectively) and the reaction mixture stirred under reflux for 24 h and under N_2. After cooling, the inorganic salts were filtered and washed with cold acetonitrile (4×10 mL). The filtrate was collected, the solvent removed and the residue purified by silica-gel chromatography eluting with 1:13 EtOAc/hexanes (R_f = 0.11) to afford **9** (57% yield) as colorless prisms (an analytical sample was obtained by recrystallization from 1:3 CH_2Cl_2/Et_2O). M.p. 105-108 °C; ^{1}H NMR (200 MHz, CDCl$_3$, 20 °C, TMS): δ = 3.60 (s, 2H), 3.69 (s, 4H), 6.93 (ddd, ^3J(H,H) = 7.8 Hz, ^4J(H,H) = 2.2 Hz, ^4J(H,H) = 1.0 Hz, 1H), 7.03 (s, 1H), 7.17 (d, ^3J(H,H) = 7.7 Hz, 1H), 7.34 (t, ^3J(H,H) = 7.7 Hz, 1H), 7.52 (t, ^3J(H,H) = 7.9 Hz, 2H), 7.74 (d, ^3J(H,H) = 7.6 Hz, 2H), 8.11 (ddd, ^3J(H,H) = 8.1 Hz, ^4J(H,H) = 2.2 Hz, ^4J(H,H) = 1.0 Hz, 2H), 8.22 ppm (s, 2H); ^{13}C NMR (50 MHz, CDCl$_3$, 20 °C): δ = 57.5 (2×t), 58.0 (t), 118.1 (d), 119.2 (d), 122.5 (2×d), 123.5 (2×d), 125.2 (d), 129.6 (2×d), 130.1 (d), 134.7 (2×d), 140.36 (s), 140.38 (s), 141.0 (2×s), 148.4 ppm (2×s); IR (Nujol): $\tilde{\nu}$= 2110 (vs), 1586 (w), 1531 (vs), 1348 (vs), 1282 (s), 1245 (w), 1199 (w), 1163 (w), 1126 (w), 1080 (w), 974 (w), 877 (w), 820 (w), 809 (m), 791 (w), 740 (s); MS (70 eV, EI): *m/z* (%): 418 (28) [M^+], 391 (30), 390 (72), 373 (42), 284 (54), 268 (43), 254 (53), 165 (24), 163 (25), 151 (27), 121 (24), 120 (51), 107 (89), 105 (38), 104 (53), 89 (93), 77 (56); elemental analysis calcd (%) for $C_{21}H_{18}N_6O_4$ (418.4): C 60.28, H 4.34, N 20.09; found: C 60.22, H 4.47, N 20.18.

Bis(3-nitrobenzyl)(3-aminobenzyl)amine (10): PMe_3 in toluene (1.0 M; 3.6 mL; 3.6 mmol) was slowly added at 0 °C to a solution of **9** (1.00 g; 2.4 mmol) in freshly distilled THF (30 mL) under N_2. The reaction mixture was then stirred at this temperature for 30 min. Then, H_2O (15 mL) was added and the reaction mixture stirred at 20 °C for 16 h. After removal of the organic solvent, H_2O (20 mL) was added and the aqueous phase extracted with CH_2Cl_2 (3×20 mL). The combined extracts were dried over $MgSO_4$, the solvent evaporated under reduced pressure and the residue purified by silica-gel chromatography eluting with 1:1 AcOEt/hexanes (R_f = 0.39); 96% yield (yellow oil); ^{1}H NMR (200 MHz, CDCl$_3$, 20 °C, TMS): δ = 3.50 (s, 2H), 3.67 (s, 4H), 3.74 (br s, 2H), 6.59 (d, ^3J(H,H) = 7.2 Hz, 1H), 6.72 (s, 1H), 6.76 (d, ^3J(H,H) = 8.6 Hz, 1H), 7.14 (t, ^3J(H,H) = 7.6 Hz, 1H), 7.49 (t, ^3J(H,H) = 8.0 Hz, 2H), 7.73 (d, ^3J(H,H) = 7.6 Hz, 2H), 8.08 (d, ^3J(H,H) = 7.2 Hz, 2H), 8.24 ppm (br s, 2H); ^{13}C NMR (50 MHz, CDCl$_3$, 20 °C): δ = 57.4 (2×t), 58.4 (t), 114.3 (d), 115.3 (d), 119.0 (d), 122.3 (2×d), 123.5 (2×d), 129.4 (2×d), 129.5 (d), 134.7 (2×d), 139.4 (s), 141.4 (2×s), 146.8 (s), 148.3 ppm (2×s); IR (Neat): $\tilde{\nu}$= 3465 (s), 3387 (s), 1622 (s), 1533 (vs), 1351 (vs), 1320 (m), 1297 (m), 1245 (w), 1162 (w), 1124 (w), 981 (w), 873 (w), 806 (m), 790 (w), 735 (s), 697 (s), 674 (s) cm^{-1}; MS (70 eV, EI): *m/z* (%): 393 (36) [M^++1], 392 (47) [M^+], 136 (79), 120 (28), 108 (71), 107 (97), 106 (100), 90 (83), 89 (57), 79 (53), 78 (40), 77 (49); elemental analysis calcd (%) for $C_{21}H_{20}N_4O_4$ (392.4): C 64.28, H 5.14, N 14.28; found: C 64.63, H 5.50, N 14.44.

Bis(3-nitrobenzyl){3-[*N*′-(4-butylphenyl)ureido]benzyl}amine (11). To a solution of **10** (0.66 g; 1.67 mmol) in dry CH_2Cl_2 (20 mL) 4-*n*-butylphenyl isocyanate (0.30 g; 1.67 mmol) was added under N_2. After stirring at 20 °C for 24 h the solvent was removed under reduced pressure and the residue purified by silica-gel chromatography eluting with 3:7 AcOEt/hexanes (R_f = 0.11); 97% yield; colorless prisms (an analytical sample was obtained by recrystallization from 1:1 CH_2Cl_2/Et_2O). M.p. 132-133 °C; ^{1}H NMR (401 MHz, CDCl$_3$, 20 °C, TMS): δ = 0.87 (t, ^3J(H,H) = 7.3 Hz, 3H), 1.27 (sext, ^3J(H,H) = 7.3 Hz, 2H), 1.46 (quint, ^3J(H,H) = 7.2 Hz, 2H), 2.44 (t, ^3J(H,H) = 7.6 Hz, 2H), 3.39 (s, 2H), 3.52 (s, 4H), 6.95-6.99 (m, 4H), 7.09-7.13 (m, 3H), 7.40 (t, ^3J(H,H) = 7.9 Hz, 2H), 7.44 (s, 1H), 7.55 (s, 1H), 7.63 (d, ^3J(H,H) = 7.6 Hz, 2H), 7.68 (s, 1H), 8.00 (dd, ^3J(H,H) = 8.0 Hz, ^4J(H,H) = 1.4 Hz, 2H), 8.13 ppm (s, 2H); ^{13}C NMR (101 MHz, CDCl$_3$, 20 °C): δ = 14.0 (q), 22.3 (t), 33.6 (t), 35.0 (t), 57.2 (2×t), 58.2 (t), 119.1 (d), 120.6 (d), 121.1 (2×d), 122.3 (2×d), 123.4 (2×d), 123.6 (d), 129.0 (2×d), 129.2 (d), 129.4 (2×d), 134.8 (2×d), 135.5 (s), 138.70 (s), 138.74 (s), 139.2 (s), 141.3 (2×s), 148.3 (2×s), 154.2 ppm (s); IR (Nujol): $\tilde{\nu}$= 3323 (s), 1656 (s), 1596 (s), 1530 (vs), 1351 (vs), 1311 (s), 1242 (s), 1218 (s), 1165 (m), 1126 (m), 1082 (m), 973 (w), 893 (w), 804 (w), 741 (s) cm^{-1}; MS (FAB$^+$): *m/z* (%): 568 (100) [M^++1], 567 (46) [M^+], 566 (65), 550 (44), 281 (43), 221 (31), 149 (46), 147 (80), 133 (45), 132 (95), 120 (47), 109 (63); elemental analysis calcd (%) for $C_{32}H_{33}N_5O_5$ (567.7): C 67.71, H 5.86, N 12.34; found: C 67.76, H 5.94, N 12.46.

Bis(3-aminobenzyl){3-[*N*'-(4-butylphenyl)ureido]benzyl}amine (12): To a solution of **11** (0.82 g; 1.5 mmol) in freshly distilled THF (25 mL), PtO_2 (0.40 g; 1.8 mmol) was added and the reaction mixture stirred at 20 °C for 16 h under H_2. After filtration over a pad of celite, which was further washed with THF (2×5 mL), the solvent was removed under reduced pressure and the residue was purified by silica-gel chromatography eluting with 4:1 AcOEt/hexanes (R_f = 0.34); 75% yield; colorless prisms (an analytical sample was obtained by recrystallization from 1:3 $CHCl_3$/*n*-pentane). M.p. 150-151 °C; ^{1}H NMR (401 MHz, CDCl$_3$, 20 °C, TMS): δ = 0.88 (t, ^3J(H,H) = 7.3 Hz, 3H), 1.27 (sext, ^3J(H,H) = 7.4 Hz, 2H), 1.48 (quint, ^3J(H,H) = 7.7 Hz, 2H), 2.45 (t, ^3J(H,H) = 7.4 Hz, 2H), 3.37 (s, 6H), 3.51 (br s, 4H), 6.47 (d, ^3J(H,H) = 7.5 Hz, 2H), 6.71 (d, ^3J(H,H) = 7.5 Hz, 2H), 6.75 (s, 2H), 6.94-7.10 (m, 9H), 7.40-7.47 (m, 2H), 7.54 ppm (br s, 1H); ^{13}C NMR (101 MHz, CDCl$_3$, 20 °C): δ = 14.0 (q), 22.4 (t), 33.7 (t), 35.0 (t), 57.6 (t), 57.8 (2×t), 113.9 (2×d), 115.7 (2×d), 118.8 (d), 119.3 (2×d), 120.7 (d), 120.9 (2×d), 123.8 (d), 128.7 (d), 128.9 (2×d), 129.0 (2×d), 135.8 (s), 138.4 (2×s), 140.8 (s), 140.9 (2×s), 146.4 (2×s), 154.2 ppm (s); IR (Nujol): $\tilde{\nu}$= 3350 (vs), 3204 (vs), 1665 (s), 1599 (vs), 1550 (vs), 1515 (vs), 1314 (s), 1248 (s), 1167 (m), 1123 (w), 873 (w), 784 (m), 701 (m) cm^{-1}; MS (FAB$^+$): *m/z* (%): 508 (97) [M^++1], 506 (59), 401 (84), 281 (33), 221 (40), 211 (59), 207 (44), 147 (100), 133 (55), 132 (68), 121 (47), 120 (48), 109 (61); elemental analysis calcd (%) for $C_{32}H_{37}N_5O$ (507.7): C 75.71, H 7.35, N 13.79; found: C 75.45, H 7.70, N 13.88.

General procedure for the synthesis of triureas 5a-b. To a solution of **12** (0.28 g; 0.55 mmol) in dry CH_2Cl_2 (10 mL) the corresponding isocyanate (1.10 mmol) was added under N_2. After stirring at 20 °C for 24 h, the solvent was removed under reduced pressure and Et_2O (5 mL) was added. The white solid was filtered and dried under vacuum.

Bis{3-[*N*′-(4-trifluoromethylphenyl)ureido]benzyl}{3-[*N*′-(4-butylphenyl)ureido]benzyl}amine (5a): 72% yield; colorless prisms (an analytical sample was obtained by recrystallization from 1:3 $CHCl_3$/*n*-pentane). M.p. 179-181 °C; ^{1}H NMR (401 MHz, [D$_6$]DMSO, 20 °C): δ = 0.86 (t, ^3J(H,H) = 7.3 Hz, 3H), 1.25 (sext, ^3J(H,H) = 7.3 Hz, 2H), 1.47 (quint, ^3J(H,H) = 7.5 Hz, 2H), 2.45 (t, ^3J(H,H) = 7.5 Hz, 2H), 3.50 (s, 6H), 7.02-7.09 (m, 5H), 7.23-7.29 (m, 3H), 7.32-7.35 (m, 3H), 7.38 (d, ^3J(H,H) = 8.0 Hz, 2H), 7.54 (s, 3H), 7.58 (d, ^3J(H,H) = 8.7 Hz, 4H), 7.62 (d, ^3J(H,H) = 8.6 Hz, 4H), 8.54 (s, 1H), 8.61 (s, 1H), 8.79 (s, 2H), 9.08 ppm (s, 2H); ^{13}C NMR (101 MHz, [D$_6$]DMSO, 20 °C): δ = 13.7 (q), 21.7 (t), 33.2 (t), 34.1 (t), 57.0 (t), 57.1 (t), 116.8 (d), 117.1 (d), 117.8 (d), 118.26 (d), 118.33 (d), 118.7 (d), 121.7 (q, ^2J(C,F) = 32.1 Hz) (s), 121.9 (d), 122.4 (d), 124.5 (q, ^1J(C,F) = 269.4 Hz) (s), 126.0 (q, ^3J(C,F) = 3.7 Hz) (d), 128.5 (d), 128.7 (d), 135.7 (s), 137.3 (s), 139.3 (s), 139.7 (s), 139.8 (s), 143.5 (s), 152.2 (s), 152.6 ppm (s); IR (Nujol): $\tilde{\nu}$= 3329 (s), 1668 (vs), 1608 (vs), 1565 (vs), 1488 (m), 1415 (m), 1331 (vs), 1251 (s), 1165 (s), 1118 (vs), 1076 (s), 853 (m), 778 (w), 703 (m) cm^{-1}; MS (FAB$^+$): *m/z* (%): 882 (74) [M^++1], 881 (34) [M^+], 880 (63), 600 (27), 588 (32), 294 (26), 293 (100), 237 (26); elemental analysis calcd (%) for $C_{48}H_{45}F_6N_7O_3$ (881.9): C 65.37, H 5.14, N 11.12; found: C 64.91, H 5.13, N 11.11.

Bis{3-[*N*′-(4-methoxyphenyl)ureido]benzyl}{3-[*N*′-(4-butylphenyl)ureido]benzyl}amine (5b): 92% yield; colorless prisms (an analytical sample was obtained by recrystallization from 10:1 $CHCl_3$/Et_2O). M.p. 141-146 °C; ^{1}H NMR (401 MHz, [D$_6$]DMSO, 20 °C): δ = 0.89 (t, ^3J(H,H) = 7.2 Hz, 3H), 1.29 (sext, ^3J(H,H) = 7.4 Hz, 2H), 1.50 (quint, ^3J(H,H) = 7.2 Hz, 2H), 2.49 (t, ^3J(H,H) = 7.5 Hz, 2H), 3.51 (s, 6H), 3.70 (s, 6H), 6.86 (d, ^3J(H,H) = 6.8 Hz, 4H), 7.06-7.08 (m, 5H), 7.25-7.28 (m, 3H), 7.36-7.38 (m, 9H), 7.50-7.52 (m, 3H), 8.47 (s, 2H), 8.56 (s, 1H), 8.60 (s, 2H), 8.64 ppm (s, 1H); ^{13}C NMR (101 MHz, [D$_6$]DMSO, 20 °C): δ = 13.8 (q), 21.7 (t), 33.3 (t), 34.2 (t), 55.1 (q), 57.1 (t), 114.0 (d), 116.8 (d), 118.3 (d), 120.0 (d), 121.8 (d), 121.9 (d), 128.5 (d), 128.7 (d), 132.7 (s), 135.7 (s), 137.3 (s), 139.7 (s), 139.8 (s), 139.9 (s), 152.6 (s), 152.7 (s), 154.4 ppm (s); IR (Nujol): $\tilde{\nu}$= 3326 (s), 1654 (vs), 1606 (vs), 1555 (vs), 1511 (vs), 1489 (vs), 1311 (s), 1247 (vs), 1181 (m), 1113 (w), 1036 (w), 834 (m), 780 (w), 700 (m) cm^{-1}; MS (FAB$^+$): *m/z* (%): 806 (42) [M^++1], 805 (20) [M^+], 804 (33), 550 (21), 255 (45), 237 (28), 133 (22), 132 (100), 124 (37), 123 (78), 122 (32), 120 (20); elemental analysis calcd (%) for $C_{48}H_{51}N_7O_5$ (806.0): C 71.53, H 6.38, N 12.17; found: C 71.90, H 6.42, N 12.47.

Bis{3-[*N*′-(benzyl)ureido]benzyl}{3-[*N*′-(4-butylphenyl)ureido]benzyl}amine (5c). To a solution of **12** (0.10 g; 0.20 mmol) in dry $CHCl_3$ (10 mL) benzyl isocyanate (0.05 g; 0.40 mmol) was added under N_2. After stirring under reflux for 24 h the solvent was removed under reduced pressure and *n*-pentane (5 mL) was added. The white solid was filtered and dried under vacuum to give **5c** in 80% yield; colorless prisms (an analytical sample was obtained by recrystallization from 1:1 acetone/*n*-pentane). M.p. 155-158 °C; ^{1}H NMR (401 MHz, [D$_6$]DMSO, 20 °C): δ = 0.88 (t, ^3J(H,H) = 7.2 Hz, 3H), 1.28 (sext, ^3J(H,H) = 7.2 Hz, 2H), 1.50 (quint, ^3J(H,H) = 7.2 Hz, 2H), 2.45 (br s, 2H), 3.43 (s, 6H), 4.28 (d, ^3J(H,H) = 5.5 Hz, 4H), 6.57 (t, ^3J(H,H) = 6.0 Hz, 2H), 6.97-7.08 (m, 5H), 7.12-

7.41 (m, 22H), 8.54 (s, 2H), 8.60 ppm (s, 1H); ^{13}C NMR (75 MHz, [D$_6$]DMSO, 20 °C): δ = 13.8 (q), 21.7 (t), 33.3 (t), 34.2 (t), 42.7 (t), 57.05 (t), 57.13 (t), 116.4 (d), 116.7 (d), 118.0 (d), 118.3 (d), 121.3 (d), 121.9 (d), 126.7 (d), 127.0 (d), 127.1 (d), 128.3 (d), 128.5 (d), 128.6 (d), 135.7 (s), 137.3 (s), 139.6 (s), 139.8 (s), 140.3 (s), 140.4 (s), 152.6 (s), 155.2 ppm (s); IR (Nujol): $\tilde{\nu}$= 3312 (s), 1647 (vs), 1606 (s), 1552 (vs), 1490 (s), 1315 (s), 1239 (s), 1131 (w), 1083 (w), 888 (w), 784 (w), 696 (s) cm^{-1}; MS (FAB$^+$): *m/z* (%): 774 (100) [M^++1], 773 (29) [M^+], 772 (50), 534 (42), 492 (26), 147 (26), 132 (78), 108 (23); elemental analysis calcd (%) for $C_{48}H_{51}N_7O_3$ (774.0): C 74.49, H 6.64, N 12.67; found: C 74.70, H 6.71, N 12.77.

Preparation of the triurea 6

Preparation of bis(2-amino-5-chlorobenzyl)(3-aminopropyl)amine (14). PMe_3 in THF (1.0 M; 3.5 mL; 3.5 mmol) was slowly added at 0 °C to a solution of **13**[30] (0.23 g; 0.5 mmol) in freshly distilled THF (20 mL) under N_2. The reaction mixture was then stirred at this temperature for 5 h. Then, H_2O (18 mL) was added and the reaction mixture was stirred at 20 °C for 18 h. After that, more H_2O (50 mL) was added and the aqueous phase extracted with CH_2Cl_2 (3×50 mL). The combined extracts were dried over $MgSO_4$, the solvent evaporated under reduced pressure, and the residue purified by silica-gel chromatography eluting with 9:1 EtOH/NH_3(aq) (R_f = 0.40); 98% yield. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$, 20 °C, TMS): δ = 1.67 (quint, ^3J(H,H) = 6.7 Hz, 2H), 2.44 (t, ^3J(H,H) = 6.9 Hz, 2H), 2.61 (t, ^3J(H,H) = 6.7 Hz, 2H), 3.41 (s, 4H), 4.20 (br s, 6H), 6.52 (d, ^3J(H,H) = 8.3 Hz, 2H), 6.98-7.03 ppm (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$, 20 °C): δ = 29.8 (t), 40.3 (t), 51.7 (t), 57.3 (t), 116.7 (d), 122.3 (s), 123.8 (s), 128.5 (d), 130.9 (d), 144.5 (s); IR (Neat): $\tilde{\nu}$= 3449 (s), 3341 (s), 3206 (s), 1622 (vs), 1425 (s), 1293 (s), 1211 (m), 1152 (m), 1118 (m), 911 (m), 882 (m), 821 (m), 738 (s) cm^{-1}.

Preparation of bis{5-chloro-2-[*N′*-(4-methylphenyl)ureido]benzyl}{3-[*N′*-(4-methylphenyl)ureido]propyl}amine (6). To a solution of **14** (0.06 g; 0.16 mmol) in dry $CHCl_3$ (15 mL) 4-methylphenyl isocyanate (0.06g; 0.48 mmol) was added under N_2. After stirring at 20 °C for 20 h the solvent was removed under reduced pressure and Et_2O (2 mL) was added. The white solid was filtered and dried under vacuum. The corresponding triurea was purified by recrystallization from 2:1 $CHCl_3$/Et_2O. Yield: 77%; M.p. 218-220 °C; ^{1}H NMR (400 MHz, [D$_6$]DMSO, 20 °C): δ = 1.65 (quint, ^3J(H,H) = 6.1 Hz, 2H), 2.19 (s, 3H), 2.21 (s, 6H), 2.49 (m, 2H), 3.01 (q, ^3J(H,H) = 5.9 Hz, 2H), 3.57 (s, 4H), 6.11 (t, ^3J(H,H) = 6.0 Hz, 1H), 6.97-7.03 (m, 6H), 7.16 (dd, ^3J(H,H) = 8.6 Hz, ^4J(H,H) = 2.1 Hz, 2H), 7.23 (d, ^3J(H,H) = 8.2 Hz, 2H), 7.29 (d, ^3J(H,H) = 8.2 Hz, 4H), 7.39 (d, ^4J(H,H) = 1.9 Hz, 2H), 7.65 (d, ^3J(H,H) = 8.7 Hz, 2H), 8.31 (s, 2H), 8.32 (s, 1H), 8.96 (s, 2H); ^{13}C NMR (100 MHz, [D$_6$]DMSO, 20 °C): δ = 20.35 (q), 20.39 (q), 26.4 (t), 37.4 (t), 51.9 (t), 54.4 (t), 118.0 (d), 118.8 (d), 124.3 (d), 127.0 (s), 127.1 (d), 129.0 (d), 129.1 (d), 129.8 (s), 130.8 (s), 131.5 (s), 136.7 (s), 137.1 (s), 137.9 (s), 152.9 (s), 155.6 (s); IR (Nujol): $\tilde{\nu}$= 3340 (s), 1656 (vs), 1599 (vs), 1555 (s), 1514 (s), 1410 (w), 1318 (m), 1289 (m), 1247 (m), 1184 (w), 1116 (w), 823 (m) cm^{-1}; MS (FAB$^+$): *m/z* (%): 754 (21) [M^++3], 753 (15) [M^++2], 752 (27) [M^++1], 373 (17), 308 (28), 290 (18), 275 (26), 274 (21), 273 (79), 271 (34), 266 (17), 241 (30), 219 (26); HRMS (EI): m/z: 752.2883 [M^++H]. Calcd for $C_{41}H_{44}Cl_2N_7O_3$: 752.2877.

Instruments, software and procedures used for data collection, structure solution and refinement of the crystal structure of 5a. $C_{53}H_{57.5}Cl_{1.5}F_6N_7O_3$, M = 1007.74, 0.17 × 0.11 × 0.10 mm^3, triclinic, space group P-1 (No. 2), a = 14.7822(6), b = 18.1191(7), c = 18.4515(7) Å, α = 94.795(2), β = 93.989(2), γ = 98.372(2)°, V = 4855.5(3) Å^3, Z = 4, D_c = 1.379 g/cm^3, F_{000} = 2112, Bruker SMART 1000, MoKα radiation, λ = 0.71073 Å, T = 120(1)K, $2\theta_{max}$ = 46.6°, 25611 reflections collected, 13904 unique (R_{int} = 0.0758). The structure was solved and refined using the programs SHELXS-97[32] and SHELXL-97[32] respectively. The program X-Seed[33] was used as an interface to the SHELX programs and to prepare the figures. Final *GooF* = 0.865, *R1* = 0.0861, *wR2* = 0.2201, *R* indices based on 5164 reflections with I >2σ(I) (refinement on F^2), 1227 parameters, 0 restraints. Lp and absorption corrections applied, μ = 0.182 mm^{-1}. CCDC 813383.

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[1] D. Philp, J. F. Stoddart, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1154-1196.
[2] J.-M. Lehn, *Chem. Soc. Rev.* **2007**, *36*, 151-160.
[3] H.-J. Schneider, *Angew. Chem. Int. Ed.* **2009**, *48*, 3924-3977.
[4] J. K. M. Sanders, *Chem. Eur. J.* **1998**, *4*, 1378-1383.
[5] F. Eblinger, H.-J. Schneider, *Angew. Chem. Int. Ed.* **1998**, *37*, 826-828.
[6] T. Grawe, T. Schrader, R. Zadmard, A. Kraft, *J. Org. Chem.* **2002**, *67*, 3755-3763.
[7] M. A. Hossain, H.-J. Schneider, *Chem. Eur. J.* **1999**, *5*, 1284-1290.
[8] M. M. Conn, J. Rebek Jr., *Chem. Rev.* **1997**, *97*, 1647-1668.
[9] T. S. Koblenz, J. Wassenaar, J. N. H. Reek, *Chem. Soc. Rev.* **2008**, *37*, 247-262.
[10] J. Rebek Jr., *Acc. Chem. Res.* **2009**, *42*, 1660-1668.
[11] F. Hof, S. L. Craig, C. Nuckolls, J. Rebek Jr., *Angew. Chem Int. Ed.* **2002**, *41*, 1488-1508.
[12] L. R. MacGillivray, J. L. Atwood, *Nature* **1997**, *389*, 469-472.
[13] M. R. Ams, D. Ajami, S. L. Craig, J.-S. Yang, J. Rebek Jr., *J. Am. Chem. Soc.* **2009**, *131*, 13190-13191.
[14] J. Rebek Jr., *Chem. Commun.* **2000**, 637-643.
[15] V. Rudzevich, Y. Rudzevich, V. Böhmer, *Synlett* **2009**, 1887-1904.
[16] P. Ballester, G. Gil-Ramirez, *Proc. Natl. Acad. Sci. USA* **2009**, *106*, 10455-10459.
[17] G. Gil-Ramírez, M. Chas, P. Ballester, *J. Am. Chem. Soc.* **2010**, *132*, 2520-2521.
[18] M. Alajarin, R.-A. Orenes, J. W. Steed, A. Pastor, *Chem. Commun.* **2010**, *46*, 1394-1403.
[19] M. Alajarin, A. Lopez-Lazaro, A. Pastor, P. D. Prince, J. W. Steed, R. Arakawa, *Chem. Commun.* **2001**, 169-170.
[20] M. Alajarin, A. Pastor, R.-A. Orenes, J. W. Steed, R. Arakawa, *Chem. Eur. J.* **2004**, *10*, 1383-1397.
[21] M. Alajarin, A. Pastor, R.-A. Orenes, J. W. Steed, *J. Org. Chem.* **2002**, *67*, 7091-7095.
[22] M. Alajarin, A. Pastor, R.-A. Orenes, E. Martinez-Viviente, H. Rüegger, P. S. Pregosin, *Chem. Eur. J.* **2007**, *13*, 1559-1569.
[23] M. Alajarin, A. Lopez-Lazaro, A. Vidal, J. Berna, *Chem. Eur. J.* **1998**, *4*, 2558-2570.
[24] L. J. Prins, D. N. Reinhoudt, P. Timmerman, *Angew. Chem. Int. Ed.* **2001**, *40*, 2382-2426.
[25] G. A. Hembury, V. V. Borovkov, Y. Inoue, *Chem. Rev.* **2008**, *108*, 1-73.
[26] M. A. Mateos-Timoneda, M. Crego-Calama, D. N. Reinhoudt, *Chem. Soc. Rev.* **2004**, *33*, 363-372.
[27] A. Pop, M. O. Vysotsky, M. Saadioui, V. Böhmer, *Chem. Commun.* **2003**, 1124-1125.
[28] M. Alajarin, A. Pastor, R.-A. Orenes, A. E. Goeta, J. W. Steed, *Chem. Commun.* **2008**, 3992-3994.
[29] J. Rebek Jr., *Angew. Chem. Int. Ed.* **2005**, *44*, 2068-2078.
[30] M. Alajarin, C. Lopez-Leonardo, J. Berna, *Tetrahedron* **2006**, *62*, 6190-6202.
[31] J. M. Aizpurua, B. Lecea, C. Palomo, *Can. J. Chem.* **1986**, *64*, 2342-2347.
[32] G. M. Sheldrick, *Acta Crystallogr., Sect. A* **2008**, *64*, 112-122.
[33] L. J. Barbour, *J. Supramol. Chem.* **2001**, *1*, 189-191.

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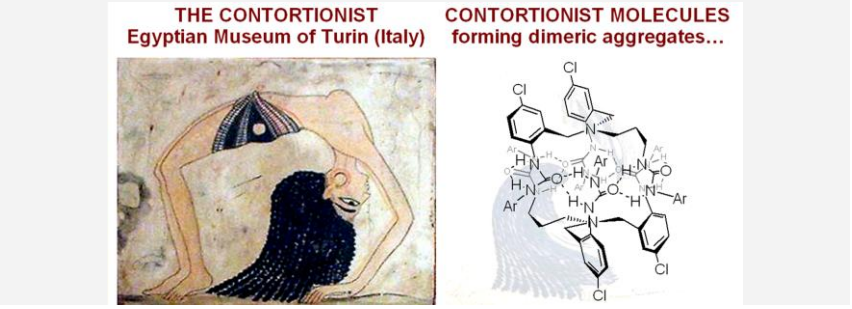
Entry for the Table of Contents

Contortionist molecules forming robust capsular aggregates!

Mateo Alajarin, Raul-Angel Orenes, Judith A. K. Howard, Elinor C. Spencer, Jonathan W. Steed and Aurelia Pastor**……..… Page – Page

Novel Capsular Aggregates from Flexible Tripodal Triureas with C_s Symmetry



"*Flexible*" tris(2- and 3-ureidobenzyl)amines with C_s symmetry self-assemble forming mixtures of regioisomeric capsular aggregates. Of special significance is the efficient self-assembly of a "*highly flexible*" triurea endowed with an ureidopropylic arm.