Self-Assembly of Tris(2-ureidobenzyl)amines: A New Type of Capped, Capsule-Like Dimeric Aggregates Derived from a Highly Flexible Skeleton

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Abstract: A set of tris(2-ureidobenzyl)-amines **3** was prepared and their dimerization processes thoroughly investigated. In spite of their inherent flexibility, tris(ureas) **3** form dimeric aggregates both in the solid state and in solution. Evidence for the existence of these dimeric species was provided by a combination of techniques (X-ray analysis, NMR and IR spectroscopy, and ESI-MS). The association constants and thermodynamic parameters for the dimerization processes of selected tris(ureas) were determined and show that they are enthalpically driven. Heterodimerization experiments in solution reveal a high degree of self-recognition or narcissistic self-sorting. On the other hand, desymmetrized tris(ureas) derived from **3** self-assemble with modest regioselectivities depending on the terminal substituent of every urea functionality.

Keywords: dimerization · hydrogen bonds · molecular recognition · self-assembly · ureas

Introduction

Complementarity and preorganization are key concepts in supramolecular chemistry.[1] Thus, for several units to self-assemble they have to possess binding sites with the correct electronic character (polarity, hydrogen bond donor/acceptor ability, hardness or softness, etc.) to complement each other. Furthermore, if these units do not undergo a significant conformational reorganization upon self-assembling they are said to be preorganized. In this case, the entropic penalty associated with the loss of degrees of freedom of the individual subunits upon self-association is minimized. This is the reason why in most cases self-assembling subunits are based on conformationally restricted systems.

The tribenzylamine unit provides an excellent scaffold for supramolecular chemistry in spite of its flexibility. Nine rotations per subunit (i.e., around bonds *a*–*c* in Figure 1) and inversion of the pivotal nitrogen atom must be restricted in assemblies incorporating rigid tribenzylamine subunits.

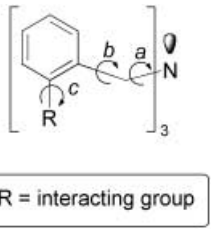

Figure 1. Tribenzylamine functionalized at the 2-position. Letters *a*, *b*, and *c* represent the bond rotations which would be restricted in a tripod–tripod assembly.

Nevertheless, tribenzylamines properly functionalized at every arm assemble with other tripodal subunits as recently described in the literature.[2] Thus, chiral macrobicyclic triphosphazides and triphosphazenes have been prepared by tripod–tripod coupling of tris(2- and 3-azidobenzyl)amines with 1,1,1-[tris(diphenylphosphino)methyl]ethane. Based on this success, our investigations have been aimed at the synthesis of self-assembling capsules containing the tribenzylamine moiety in which each arm of this tripodal molecule is

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Supporting information for this article is available on the WWW under http://www.chemeurj.org or from the author, including 2D ROESY spectra for tris(ureas) **3a**, **3d**, and **3g** and ^{1}H NMR spectra in $CDCl_3$ for tris(ureas) **6a–c**.

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endowed with secondary urea groups, which are excellent for hydrogen bonding interactions.[3]

To our delight, tris(2-ureidobenzyl)amines associate in solution and in the solid state to give dimeric aggregates.[4] These dimers are composed of two enantiomeric units associated through their urea residues (Figure 2). The interacting

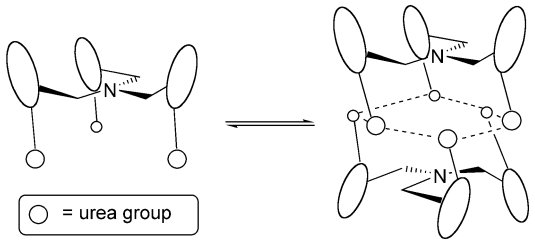
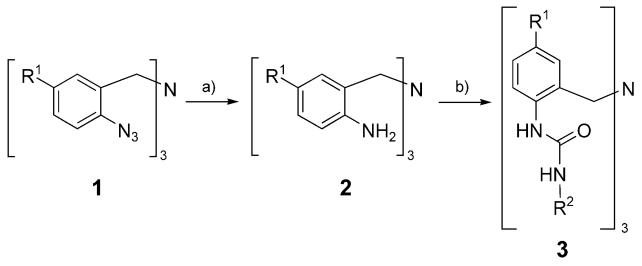


Figure 2. Schematic view of the self-assembly between two tris(2-ureidobenzyl)amine subunits showing the belt of hydrogen-bonded ureas.

urea functionalities form a belt of 12 hydrogen bonds, a rather singular motif that has only been previously observed by Rebek Jr. et al.,[5] Böhmer et al.,[6] and de Mendoza et al.[7] for ureidocalix[4]- and -[6]arenes. Herein we present a full study of these self-assembling systems which includes complete characterization of the dimeric aggregates in the solid state and solution, the determination of thermodynamic parameters for the dimerization process, the formation of heterodimeric species, and the study of the regioselectivity in the self-assembly of tris(ureas) lacking C_{3v} symmetry.

Results and Discussion

Synthesis: The readily available tris(2-azidobenzyl)amines **1**[2b] (Scheme 1) were converted into the tris(amines) **2** in good yields by two alternative methods: A) reduction with



Scheme 1. Synthesis of tris(ureas) **3**. a) Method A: LAH, Et_2O, 20 °C, 4 h or method B: i) PMe_3, THF, 0 °C, 20 min; ii) THF/H_2O, 20 °C, 18 h; b) R^2NCO, solvent, temperature (see Table 1).

$LiAlH_4$ (LAH) or B) sequential treatment with PMe_3 and tetrahydrofuran (THF)/H_2O (Table 1). Tris(2-ureidobenzyl)-amines **3a**–**m** were obtained from **2** in 58–91% yield by treatment with the corresponding isocyanate. The data included in Table 1 highlight several factors: in particular, the more sterically encumbered the terminal substituent at the ureido functionality (e.g., aromatic 2,6-disubstitution or secondary carbons next to the terminal nitrogen atom of the

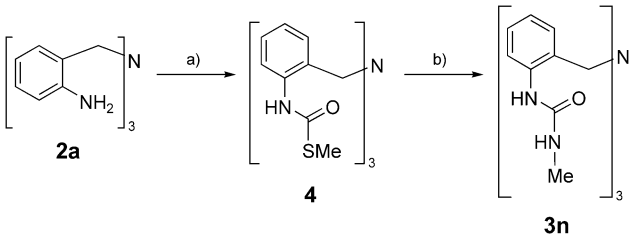
Table 1. Synthesis of tris(amines) **2** and tris(ureas) **3**.

Entry	Compound	R^1	R^2	Solvent	T [°C]	Yield [%]
1	**2a**	H	–	–	–	75[a](90)[b]
2	**2b**	Me	–	–	–	73[a]
3	**3a**	H	4-MeC_6H_4	CH_2Cl_2	20	87
4	**3b**	Me	4-MeC_6H_4	CH_2Cl_2	20	87
5	**3c**	H	4-$nBuC_6H_4$	CH_2Cl_2	20	77
6	**3d**	Me	4-$nBuC_6H_4$	CH_2Cl_2	20	77
7	**3e**	H	4-$MeOC_6H_4$	CH_2Cl_2	20	86
8	**3f**	H	4-$CF_3C_6H_4$	CH_2Cl_2	20	89
9	**3g**	H	Bn	$CHCl_3$	reflux	81
10	**3h**	Me	Bn	$CHCl_3$	reflux	91
11	**3i**	H	CH_2=$CHCH_2$	$CHCl_3$	reflux	58
12	**3j**	Me	*n*Pr	$CHCl_3$	reflux	80
13	**3k**	Me	(*S*)-Ph(Me)CH	$CHCl_3$	reflux	62
14	**3l**	Me	*i*Pr	DMF	80	64
15	**3m**	H	2,6-$Me_2C_6H_3$	DMF	80	77

[a] By method A. [b] By method B.

ureido functionality), the more drastic the reaction conditions that were required regardless of the reactivity of the corresponding isocyanate.

The synthesis of the tris(urea) **3n** was conducted in a two-step synthetic sequence[8] by starting from the tris(amine) **2a** (Scheme 2). Thus, treatment of **2a** with 1,1,1,3,3,3-hexa-



Scheme 2. Synthesis of the tris(urea) **3n**. a) i) HMDS, *n*BuLi, DMDTC, THF, −78→20 °C, 6 h; b) $MeNH_2$, MeOH, reflux, 15 h.

methyldisilazane (HMDS) and *S*,*S*-dimethyldithiocarbonate (DMDTC) led to the tris(thiocarbamate) **4**, which was then allowed to react with $MeNH_2$ to give the tris(urea) **3n** with three pendant *N*-methylureido groups.

Solid-state structure of 3d:[9] Diffraction-quality crystals of the tris(urea) **3d** were obtained by recrystallization from CH_2Cl_2/Et_2O. The single-crystal X-ray analysis revealed the existence of two independent dimeric aggregates **3d**·**3d** in the crystal lattice with slightly different shapes, one of which is shown in Figure 3.

As found in a previous example,[4] the dimers are formed by two C_3-symmetric enantiomeric tripods turned 60° with respect to each other and encircled by a belt of six hydrogen-bonded ureas. This arrangement results in S_6 symmetry for the dimeric core. The conformationally restricted tribenzylamine skeleton adopts a propeller-like conformation, which can be visualized from the view along the C_3 axis (Figure 3a).

Notably, the formation of the aggregate is accompanied by a chiral self-discrimination event, since one enantiomeric tripod recognizes its mirror image. Very few examples of such self-discrimination have been described thus far.[10]

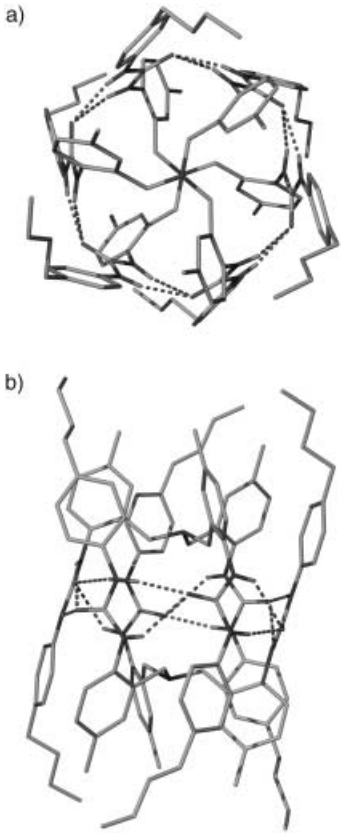


Figure 3. Top (a) and side view (b) of the dimeric structure **3d·3d**. The belt of hydrogen-bonded urea moieties is indicated by dotted lines.

Table 2. Crystallographic data for **3d·3d**.

Parameter	Value
empirical formula	$C_{58}H_{71}Cl_2N_7O_3$
formula weight	985.12
T [K]	100(2)
wavelength [Å]	0.71073
crystal system	trigonal
space group	$R\bar{3}$
a [Å]	21.256(3)
b [Å]	21.256(3)
c [Å]	42.469(7)
α [°]	90
β [°]	90
γ [°]	120
V [Å^3]	16617(4)
Z	12
ρ [g cm^{-3}]	1.181
μ [mm^{-1}]	0.166
F(000)	6312
crystal size [mm^3]	0.50×0.40×0.30
θ range [°]	2.64–25.00
h	−25 to 22
k	−25 to 24
l	−50 to 44
reflections collected	25372
unique reflections	6496
R(int)	0.0976
no. of parameters	408
no. of restraints	0
$R1$ ($I>2\sigma$(I))	0.0666
$\omega R2$ ($I>2\sigma$(I))	0.1542
$R1$ (all data)	0.1036
$\omega R2$ (all data)	0.1700
$\Delta\rho$[e Å^{-3}]	0.269/−0.234

The diaryl urea units of every arm are far from planarity with approximate interplanar angles of 46.4–46.6°/48.8–49.0° between the two aryl rings. The X-ray structure of **3d·3d** (Table 2) also shows weak edge-to-face π-stacking interactions between the aromatic rings of the tribenzylamine skeleton and the pendant aromatic rings from the other subunit.

Interestingly, the urea-type hydrogen bonds are very different with the distance N···O=C (2.84–2.89 Å) for the urea nitrogen atoms bearing the pendant 4-butylphenyl substituents being rather shorter than the distance N···O=C (3.12–3.20 Å) for the urea nitrogen atoms attached to the tribenzylamine skeleton. In contrast to the new dimer **3d·3d**, the previously described X-ray structure of **3g·3g** (Figure 4a) has a more symmetrical belt of hydrogen bonds with distances of 2.90–3.02 Å (Figure 4b).[4]

These differences in the arrangement of the hydrogen bond network between **3d·3d** and **3g·3g** and the lack of π-stacking interactions in **3g·3g** could explain important differences in their respective behavior in solution (see below).

A detailed inspection of both crystal structures reveals that the success of the dimerization process seems to be determined by a subtle interplay of conformational features: the propeller-like topology around the pivotal nitrogen atoms of the tripodal moieties, the tilt of the 1,2-disubstituted arene rings in relation to the C_3 axis passing through those nitrogen atoms, and the dihedral angles between the mean planes of the urea cores with respect to their adjacent arene rings. The consonance of these structural fragments provides the unique conformation shown in Figures 3 and 4a which allows the effective interdigitation of the urea units. Any appreciable change in some of these fragments would render the dimerization process less favorable by destroying the optimal alignment of the 12 hydrogen bonds within the urea belt. This factor may account for the high degree of narcissistic self-sorting shown by these aggregates in solution (see below).

Dimers **3d·3d** form capsule-like aggregates with an internal cavity. The distance between the two pivotal nitrogen atoms in **3d·3d** (5.911/6.307 Å) relative to **3g·3g** (5.511 Å) implies a slightly larger cavity in the former although no guest was found inside.

Behavior in solution of tris(ureas) 3a–j and 3n: These tris(ureas) self-assemble in solution in solvents that provide no competitive hydrogen bonding (e.g., $CDCl_3$, CD_2Cl_2, and benzene) to give dimers linked by 12 hydrogen bonds of similar geometry to those depicted in the X-ray structures. Evidence for these self-assembling processes was provided by a combination of different experiments (i.e., ^{1}H and ^{13}C NMR data recorded in different solvents, 2D ROESY experiments, IR spectroscopy, and ESI-MS measurements). Furthermore, encapsulation experiments and heterodimerization processes have been investigated.

^{1}H and ^{13}C NMR data: For all tris(ureas) the number and pattern of the ^{1}H NMR signals in polar competitive hydro-

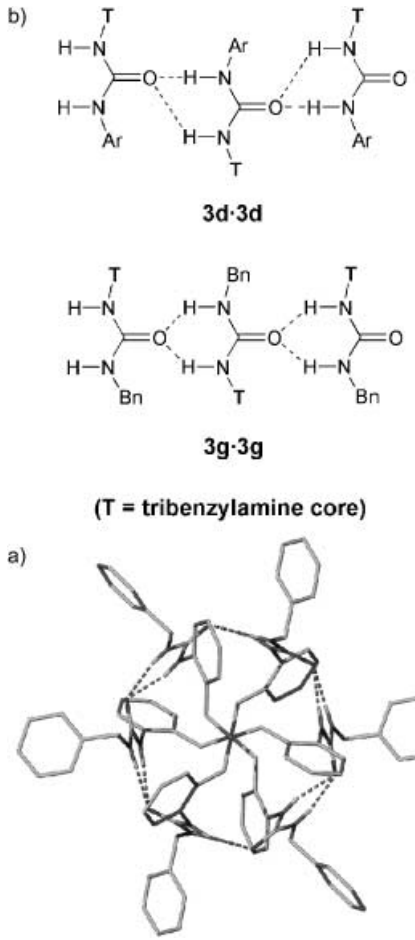


Figure 4. a) Top view of the dimeric structure **3g·3g**. The belt of hydrogen-bonded urea moieties is indicated by dotted lines. b) Comparison of the pattern of the hydrogen bonding network for **3d·3d** and **3g·3g** based on the crystallographic data.

gen-bonding solvents such as [D_6]DMSO and [D_4]methanol corresponded to those expected for monomers of averaged C_{3v} symmetry (Figures 5a and 6a). The most representative signal was that for the methylenic protons of the $(ArCH_2)_3N$ fragment: a singlet at $\delta = 3.43$–3.64 ppm.

However, a completely different picture was observed in noncompetitive solvents such as $CDCl_3$. Thus, two sets of signals emerged corresponding to two species of different symmetry. The ratio in which both species were present in $CDCl_3$ depends on the substituent R^2 to a great extent. While for tris(ureas) **3a–f** and **3n** only the signals attributed to the less symmetric species were apparent (Figure 5b), the spectra for the tris(*N*-alkyl)ureas **3g–j** were interpreted as corresponding to equilibrium mixtures of both compounds (Figure 6c). The more symmetric species, assigned to the monomer when it was detected, featured the expected pattern consistent with an averaged C_{3v} symmetry. The chemical shifts for nearly all this set of signals (except for the NH protons) were very similar to those measured in [D_6]DMSO (Figures 6a and c). On the other hand, the less symmetrical species typically revealed the splitting of the singlet corresponding to the methylenic protons of the $(ArCH_2)_3N$ fragment into two doublets ($J = 14.5$–15.9 Hz) (Figures 5b and 6c).

The ^{1}H NMR data for the less symmetrical species are consistent with the hydrogen-bonded dimeric aggregates of S_6 symmetry revealed by the crystal structures of **3d·3d** and **3g·3g** (Scheme 3 and Figures 3 and 4a).

Notably, all these equilibria could be shifted toward the monomer by: 1) decreasing the concentration of the tris(ureas), 2) increasing the temperature (Figure 6b,c), and 3) by addition of competitive hydrogen-bonding solvents such as [D_6]DMSO.

The shift to lower field of the signals for the NH groups supports the engagement of the urea functionalities in an ordered, extensively hydrogen-bonded system in solution when compared to a reference urea (Scheme 4). Notably, the chemical shifts of these protons remained concentration-independent in the range 10.0–0.3 mM. In contrast, the ^{1}H NMR spectra of most ureas (e.g., diphenyl urea) are highly concentration-dependent.[11]

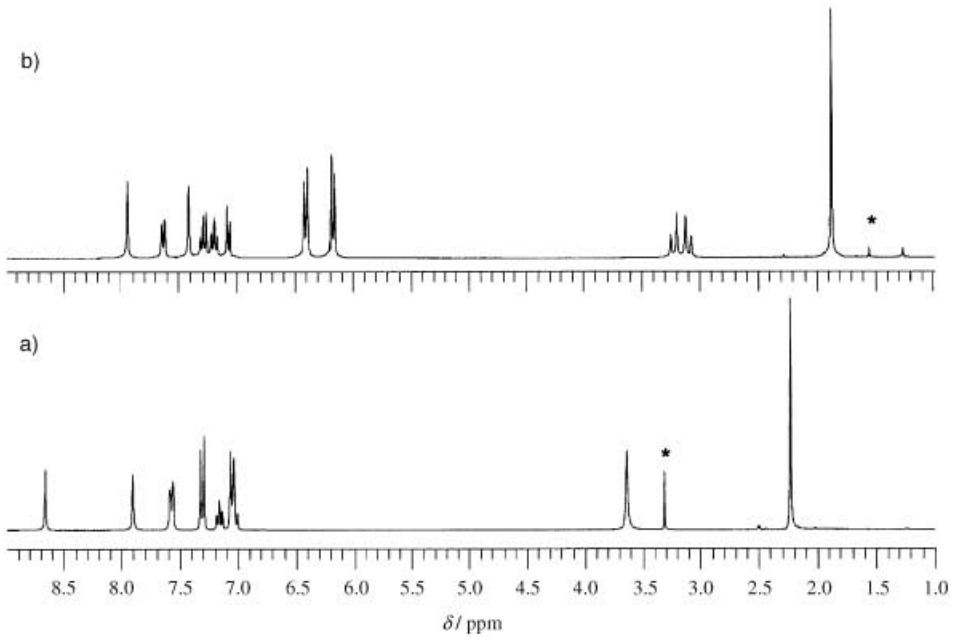


Figure 5. ^{1}H NMR spectra (300 MHz) of **3a** a) in [D_6]DMSO and b) in $CDCl_3$ at 296 K; asterisks label the signals for residual water.

The upfield shifts observed for the methylenic protons next to the pivotal nitrogen atom and for those located at the terminal substituents of the urea functionalities in the dimeric tris(ureas) **3a–f** (schematically represented by **3d·3d** in Scheme 5) were even more informative. These results reflected the mutual anisotropy experienced by the tribenzylamine

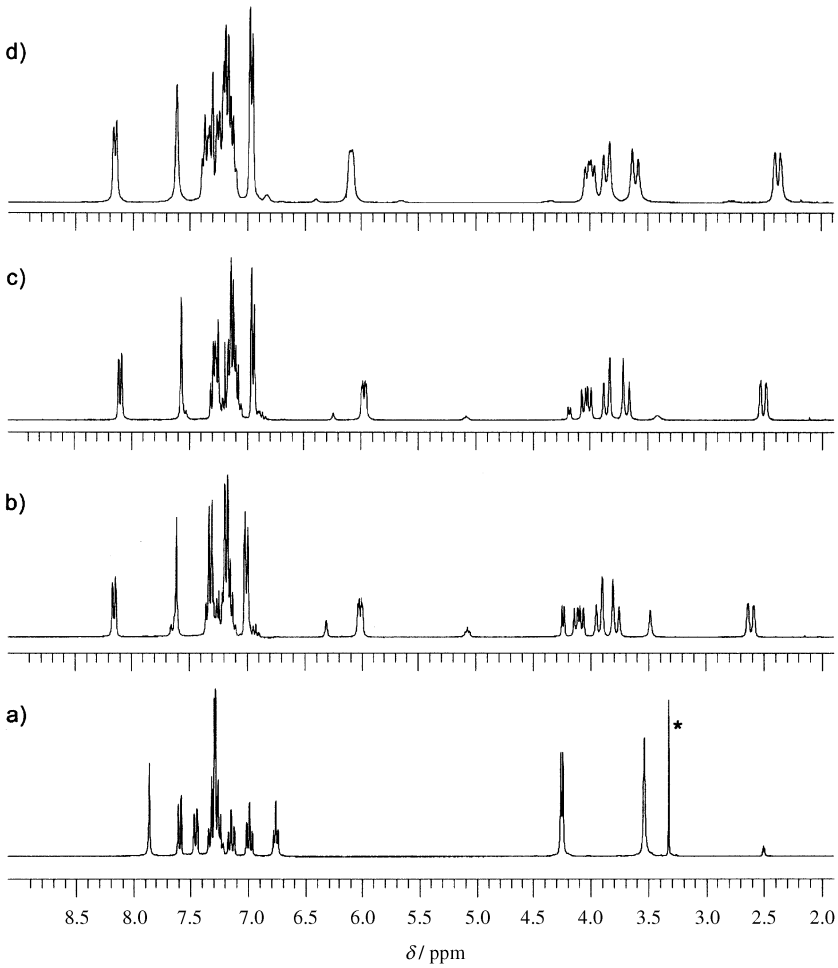
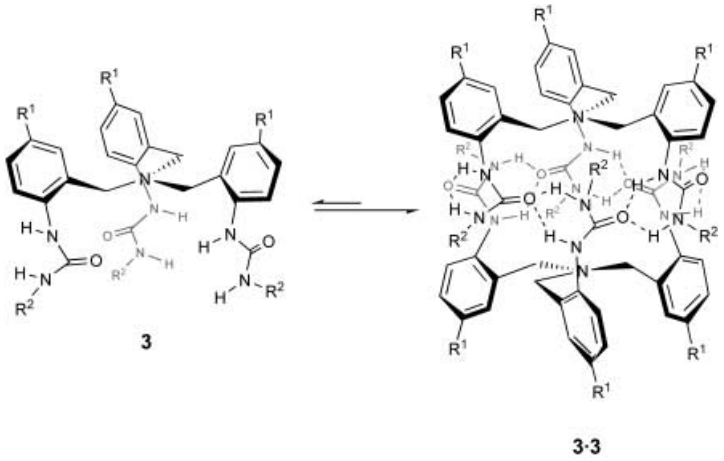
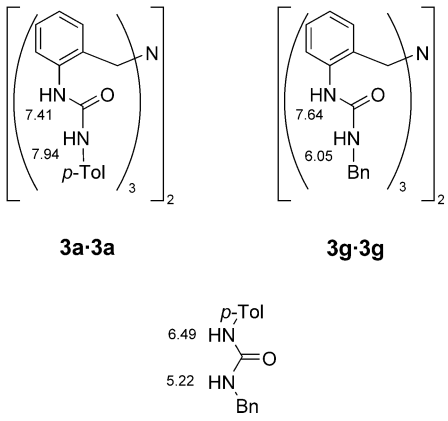


Figure 6. ^{1}H NMR spectra (300 MHz) of **3g** a) in [D_6]DMSO at 296 K; in $CDCl_3$ at b) 323 K, c) 296 K, and d) 213 K; asterisk labels the signal for residual water.



Scheme 3. Self-association of tris(ureas) **3** in solution of noncompetitive hydrogen-bonding solvents.

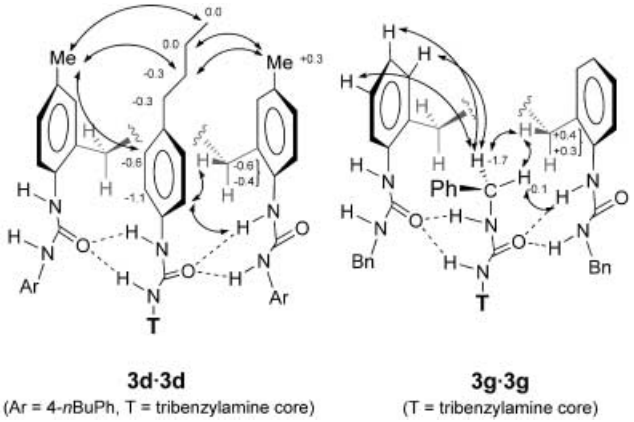


Scheme 4. Chemical shifts ($CDCl_3$) for the NH resonances in **3a·3a** and **3g·3g** compared to a reference urea.

unit and the pendant aromatic substituents owing to the intercalation of the six arms in the dimeric structure.

In contrast, the methylenic protons next to the pivotal nitrogen atom in dimeric tris(ureido)amines **3g–j** (schematically represented by **3g·3g** in Scheme 5), although inequivalent, did not display upfield shifts presumably as a result of lacking this peculiar arrangement of intercalating aromatic rings.

The appearance of rather different δ values ($\Delta\delta =$ 1.6 ppm) for the resonances owing to the two methylenic protons of the pendant alkyl groups ($R^2 = CH_2R$) was also



Scheme 5. Chemical shift differences (ppm) between the dimer and the corresponding monomer for selected protons in **3d·3d** and **3g·3g** (CH_2N_{piv} not unequivocally assigned). Arrows indicate important NOE contacts from a 2D ROESY spectrum (600 MHz).

noticeable in the spectra of dimeric aggregates of tris(ureas) **3g–j**. The aromatic rings of the tribenzylamine skeleton provide the anisotropic environment that determines the shielding of only one of these benzylic protons. This proton was assigned as that appearing at lower δ values and the assignment was confirmed on the basis of the ROE contacts between the signal due to this proton and those corresponding to the tribenzylamine aryl protons (see structure **3g·3g** in Scheme 5). These cross peaks were not observed for the other benzylic proton.

The ^{13}C NMR spectra of **3g–j** measured in $CDCl_3$ also revealed the involvement of the urea carbonyl groups as hydrogen bond acceptors in the dimeric aggregates. Their δ values ($\delta = 157.7$–158.3 ppm) appeared downfield relative to those in the corresponding monomers ($\delta = 154.9$–155.2 ppm).

To provide semiquantitative data on the relative stability of the dimers, $CDCl_3$ solutions were titrated with [D_6]DMSO until the dimeric species signals were no longer visible (Table 3). The dimeric assemblies of *N*-aryl-substituted tris(ureas) **3a**, **3c**, and **3d** are therefore more stable than those of the *N*-alkyl-substituted **3g**, **3h**, and **3j**.

Table 3. Volume of [D_6]DMSO required to totally shift the equilibrium towards the monomeric species.

Entry	Urea	R^1	R^2	% [D_6]DMSO[a,b]
1	**3a**	H	4-MeC_6H_4	50
2	**3c**	H	4-*n*BuC_6H_4	50
3	**3d**	Me	4-*n*BuC_6H_4	51
4	**3g**	H	Bn	30
5	**3h**	Me	Bn	27
6	**3j**	Me	*n*Pr	31

[a] With respect to the volume of $CDCl_3$. [b] [D_6]DMSO was added to a solution of $CDCl_3$ until the monomer/dimer ratio was $\geq$95:5 (200 MHz or 300 MHz) in the ^1H NMR spectra.

2D ROESY experiments: Two-dimensional ROESY experiments in $CDCl_3$ and [D_6]DMSO were employed to obtain structural details of aggregates **3a·3a**, **3d·3d**, and **3g·3g** in solution (see Supporting Information). The most significant NOE contacts are illustrated in Scheme 5 and nicely support the formation of a dimeric aggregate in $CDCl_3$. The most revealing cross peaks were those relating the tribenzylamine core with the pendant urea protons. These nuclei are too far apart in the monomeric structure to allow these cross peaks to be assigned to intramolecular NOE contacts. Notably, they were not present in the spectra measured in [D_6]DMSO.

All the protons involved in NOE contacts were examined in the corresponding X-ray structures (**3d·3d** and **3g·3g**) and have interatomic distances below 3.5 Å. This fact provides an additional proof that the geometry of the dimers in the solid state remains in solution.

IR measurements: Another telltale sign of the engagement of the NH groups in hydrogen bonding was provided by the FTIR spectra of **3a** (13.7 mM) and **3g** (16.4 mM) in $CHCl_3$ solution. The spectra showed exclusively the hydrogen-bonded NH stretching band at 3317–3327 cm^{-1} (non-hydrogen-bonded NH stretches usually appear as a weak and sharp band above 3400 cm^{-1}).[12]

ESI-MS spectra: Although mass spectrometry only reflects the properties of gas-phase species, the correlation between gas phase and solution is often reliable for ESI-MS, and consequently this method has recently been used to analyze solution-phase aggregation processes.[13]

The dimeric assemblies of tris(ureas) **3a**, **3g**, and **3h** were detected by ESI-MS experiments. The spectra measured in $CHCl_3$ had base peaks for the respective protonated monomers and the corresponding molecular ions for the protonated dimers **3a·3a** (*m*/*z* 1463), **3g·3g** (*m*/*z* 1464), and **3h·3h** (*m*/*z* 1547) albeit with very low intensities (Figure 7). These low abundances may be explained by taking into account that the use of solvents that do not compete for hydrogen bonds in ESI-MS usually requires an ion-labeling step (e.g., Na^+/crown ether complexes,[14] anions,[15] and metal[16] or quaternary ammonium[17] cations), which is not the case here; with our dimers, protons provide the charge needed for ESI-MS detection.

On the other hand, the combination of two monomers can produce three structurally different dimeric aggregates (two homodimers and one heterodimer) with three different masses. An equimolar solution of **3g** and **3h** afforded a nearly statistical mixture (1:2:1) of the three species **3g·3g**, **3h·3h**, and **3g·3h** detected in the ESI-MS spectra by their respective protonated molecular ions. These findings almost exactly parallel those observed by NMR experiments (see below).

All these results make it difficult to distinguish between the formation of dimeric capsule-like aggregates or other unspecific associations in the gas phase. Nevertheless, it seems unlikely that the capsule-like structure, which according to the NMR experiments is present in solution, is transformed into a nonspecific aggregate during the electrospray process; however, this possibility cannot be excluded.

Encapsulation behavior: Usually, the addition of a suitable guest, often a solvent molecule, of complementary size and

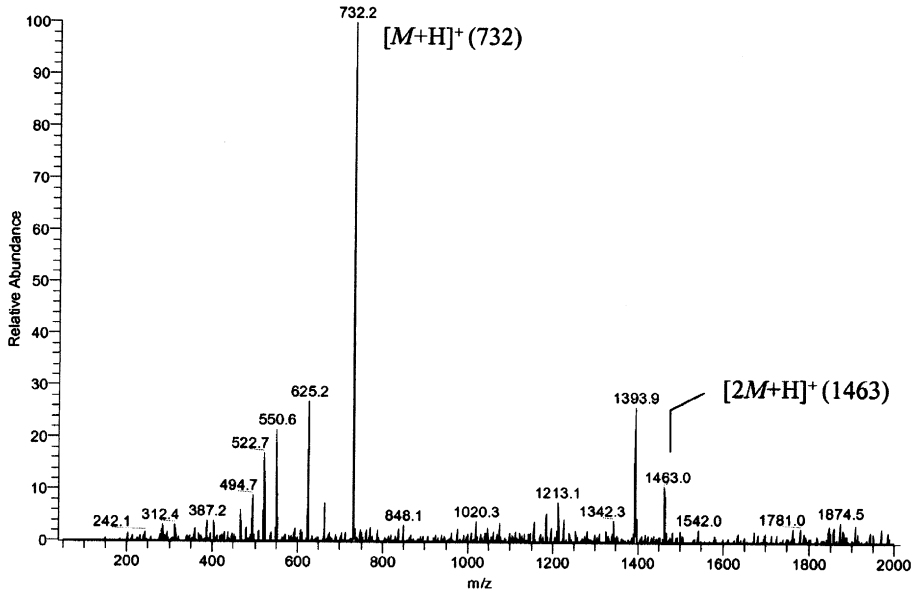


Figure 7. ESI mass spectrum of a $CHCl_3$ solution of **3a**.

shape favors the formation of discrete aggregates by acting as a template.[18]

In our case, encapsulation studies of small organic molecules such as MeI and CH_2Cl_2, which are good guests for tris(3-ureidobenzyl)amines,[19] were performed for **3a·3a**. After dissolving the sample in $CDCl_3$, an excess of the guest was added and the ^{1}H NMR spectrum was recorded at 20 and −60 °C. Unfortunately, the spectra did not show any change relative to those measured without the guest. Furthermore, no signal for an encapsulated molecule was found confirming that no species occupied the interior of the cavity. These findings agree with the results revealed by the X-ray structures (see above) and may be explained as resulting from the small dimensions of the cavity.

Behavior in solution of tris(ureas) 3k–m: As mentioned above, the nature of the pendant substituent at the urea functionality decisively influences the ratio of monomer/dimer present in $CDCl_3$ solutions. Thus, for tris(*N*-arylureidobenzyl)amines **3a–f** and tris(*N*-methylureidobenzyl)amine **3n** the monomer was present in tiny concentrations. In contrast, for tris(*N*-alkylureidobenzyl)amines **3g–j** the monomer/dimer ratio was higher. Consistent with the same trend, tris(ureas) **3k–m** (Table 1) do not form dimeric aggregates in solution at all. Their ^{1}H NMR spectra only have signals for a species of averaged C_{3v} symmetry at chemical shifts rather similar to those measured in competitive solvents such as [D_6]DMSO which were assigned to the corresponding monomers. This fact confirms that sterically encumbered R^2 residues make the dimerization process unfavorable.

For the particular case of the enantiomerically enriched tris(urea) (*S*)-**3k**, the formation of both the homochiral species (*S*)-**3k**·(*S*)-**3k** and the heterochiral species (*S*)-**3k**·(*R*)-**3k** was tested with negative results.

Determination of the thermodynamic parameters of the dimerization process: Since the association–dissociation rates for the respective monomers and dimers were slow on the NMR time scale, the populations of both species were determined by integration of their respective peaks in the ^{1}H NMR spectra. This provided a convenient means of determining the association constants at different temperatures.[20] The values of $\Delta G°$, $\Delta H°$, and $\Delta S°$ were obtained for the dimerization equilibria of tris(ureas) **3a**, **3g**, and **3h** (Table 4) from the corresponding van't Hoff plots (Figure 8).

These values indicate the large and compensating effects operating in the dimerization processes, since they are enthalpically favorable and entropically very unfavorable. The negative enthalpic component may be the result of the stabilizing interactions between the six urea functionalities by hydrogen bonding. Likewise, the high negative $\Delta S°$ values measured must account for the reduction of conformational freedom during dimerization.

Table 4. Association constants and thermodynamic parameters for the dimerization of tris(ureas) **3a**, **3g**, and **3h** in $CDCl_3$.

Entry	Dimer	K_{ass}[a] [M^{-1}]	$\Delta G°$ [kJ mol^{-1}]	$\Delta H°$ [kJ mol^{-1}]	$\Delta S°$ [J mol^{-1} K^{-1}]
1	**3a·3a**	91200	−28.3	−49.3	−70.6
2	**3g·3g**	4000	−20.6	−74.9	−182.2
3	**3h·3h**	1000	−17.1	−64.0	−157.6

[a] At 298 K.

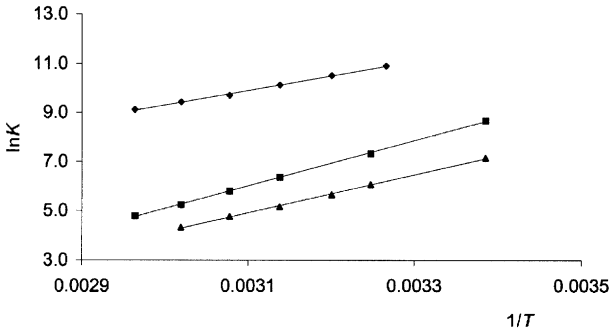


Figure 8. Van't Hoff plots ($r^2 > 0.996$) for the association processes of tris(ureas) **3a** (◆), **3g** (■), and **3h** (▲) in $CDCl_3$ over the temperature range 295–337 K.

Notably, this loss of freedom is rather acute for **3g·3g** ($\Delta S° = -182.2$) compared to **3a·3a** ($\Delta S° = -70.6$) which may be related to two facts: 1) a more ordered hydrogen bond network of **3g·3g** compared to **3a·3a**[21] (Figure 4b) revealed by the X-ray structures, and 2) a less significant loss of con-

formational freedom on going from monomer **3a** to dimer **3a·3a** than in the case of formation of **3g·3g**, since **3a** is more preorganized owing to conjugation between the urea and the pendant aryl groups.

Additionally, the more symmetrical belt of **3g·3g** comprises twelve strong hydrogen bonds compared to six strong and six weak hydrogen bonds for **3a·3a**. This fact is consequently reflected by a more negative value of $\Delta H°$ (−74.9 versus −49.3) for the former. Notably, the weak π-stacking interactions present in **3a·3a** and the higher acidity of their urea hydrogen atoms do not compensate this effect (the same arguments may be applied to **3h·3h**).

Heterodimerization processes: The combination of two monomers can produce three structurally different dimeric aggregates (two homodimers and one heterodimer). These processes have frequently been used to verify dimerization of tetraureido[4]calixarenes in solution[6a,c] and the gas phase.[17c]

The formation of the corresponding heteromeric assemblies between tris(ureas) **3a**, **3d**, **3f**, **3g**, and **3h** was investigated by ^{1}H NMR spectroscopy. Since these tris(ureas) are self-complementary, it would be reasonable to expect that they would also complement each other. The formation of hybrid aggregates was induced by dissolving equimolar quantities of two different tris(ureas) in $CDCl_3$.

As depicted in Table 5, the nature of the terminal substituent at the urea functionality determines the degree of heterodimerization, in parallel to what we have previously observed in the corresponding homodimerization processes. The hybrid species was formed in a statistical ratio only when these pendant substituents were identical (**3g·3h**).

Table 5. Percentage [%] of heterodimerization between tris(ureas) **3a**, **3d**, **3f**, **3g**, and **3h** in $CDCl_3$.[a]

	3a	**3d**	**3f**[b]	**3g**	**3h**
3a		27	61	5	9
3d			80	5	7
3f				12	31
3g					51
3h					

[a] Calculated according to the equation: [AB]×100/([AB]+[AA]+[BB]). [b] Measured in $C_2D_2Cl_4$.

Surprisingly, the change of a 4-tolyl (**3a**) by a 4-butylphenyl (**3d**) terminal substituent led to a two-fold decrease in the percentage of heterodimerization with respect to the statistical ratio (27% versus 50%). Finally, mixtures of aryl/benzyl-substituted tris(ureas) (**3a·3g**, **3d·3g**, **3a·3h**, or **3d·3h**) showed less than 9% of heterodimerization. The degree of heterodimerization was independent of the solvent (similar percentages of heterodimerization were found in [D_8]toluene and $C_2D_2Cl_4$).

On the basis of all these results, tris(2-ureidobenzyl)amines can be considered to behave with a high degree of self-recognition or narcissistic self-sorting. This is not a very common phenomenon and is defined as the high-fidelity recognition of self from nonself.[22]

The association constants for the formation of three heterodimeric assemblies (Table 6) were calculated by using equations described by Cram.[20]

Table 6. Association constants for the formation of homodimeric and heterodimeric assemblies of tris(ureas) **3a**, **3g**, and **3h**.

Entry	Assemblies	K_{ass} [a,b]
1	**3a·3a**	91200
2	**3g·3g**	4000
3	**3h·3h**	1000
4	**3a·3g**	2200
5	**3a·3h**	2100
6	**3g·3h**	7900

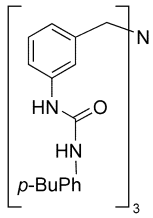
[a] M^{-1}. [b] Calculated at 298 K.

Isaacs and co-workers[22] have investigated theoretically the variables that affect the fidelity of self-sorting processes: one is how large the difference between the equilibrium constants for homomeric versus heteromeric aggregation is sufficient to drive narcissistic self-sorting. They found that a 10-fold difference in favor of the homomeric aggregate is more than enough, although these studies were conducted by fixing the values for the equilibrium constants of both homodimeric assemblies to be $10^6\,M^{-1}$.

Thus, for the system comprising monomers **3a** and **3g**, homodimers **3a·3a** (K_{ass} = 91200) and **3g·3g** (K_{ass} = 4000) and the heterodimer **3a·3g** (K_{ass} = 2200), we found the following distribution of molar fractions: χ_{3a3a} = 0.94 (χ_{3a} = 0.02 and χ_{3a3g} = 0.04) and χ_{3g3g} = 0.87 (χ_{3g} = 0.09 and χ_{3a3g} = 0.04). These values reveal that the respective homodimeric assemblies are the major species and confirm the findings described by Isaacs for species which present narcissistic self-sorting behavior (slight differences may be due to the fact that both homodimeric association constants are not equal). Analogous results were found for **3a·3h** (χ_{3a3a} = 0.90, χ_{3a} = 0.02, χ_{3h3h} = 0.71, χ_{3h} = 0.21, and χ_{3a3h} = 0.08).

As an exception, heterodimers formed with tris(urea) **3f** (the experiments were conducted in $C_2D_2Cl_4$ as a result of insolubility in $CDCl_3$) displayed high levels of heterodimerization; in other words, these heterodimeric assemblies showed higher stabilities compared to the rest of the heterodimers investigated in Table 5. These findings may be rationalized in terms of the increased acidity of the 4-trifluorophenyl-substituted urea NH protons which complements the relative basicity of the tris(ureas) **3a**, **3d**, **3g**, and **3h**. As has been previously established,[23] the strong dependence of hydrogen bonding on electron distribution provides a facile means of controlling the strength of this interaction through substituent effects.

Finally, we investigated if tris(2- and 3-ureidobenzyl)amines were complementary, since the 3-isomers also form dimeric species of analogous structure in $CDCl_3$ solution.[19] Thus, we tried the heterodimerization of **3a** or **3g** with the tris(3-ureidobenzyl)amine **5**. However, the respective hybrid species were detected in 18% and 0%, respectively, thus showing again the high tendency of tris(2-ureidobenzyl)amines to narcissistic self-aggregation.



5

Self-assembly of desymmetrized tris(2-ureidobenzyl)amines 6: As mentioned above, monomeric tris(2-ureidobenzyl)-amines adopt C_{3v} symmetry in solution, which is reduced to C_3 when they are integrated into the dimeric assembly. Interdigitation of the six arms of the two tripods converts the C_3 axis of each monomer to an overall S_6 axis for the dimer.

Although dimeric assemblies of tris(ureas) **3** are achiral, their geometry offers the possibility to achieve chirality in the assemblies, for instance by the dimerization of tris(ureas) with different substituents in each arm. In the particular case of two identical arms and a different one (C_s symmetry for the monomer), three different assemblies may be formed: two enantiomeric dimers of C_1 symmetry (**A** and **B** in Figure 9) and another dimeric assembly of C_i symmetry

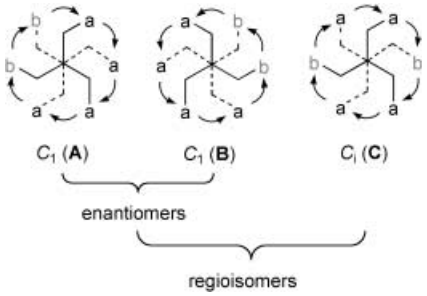
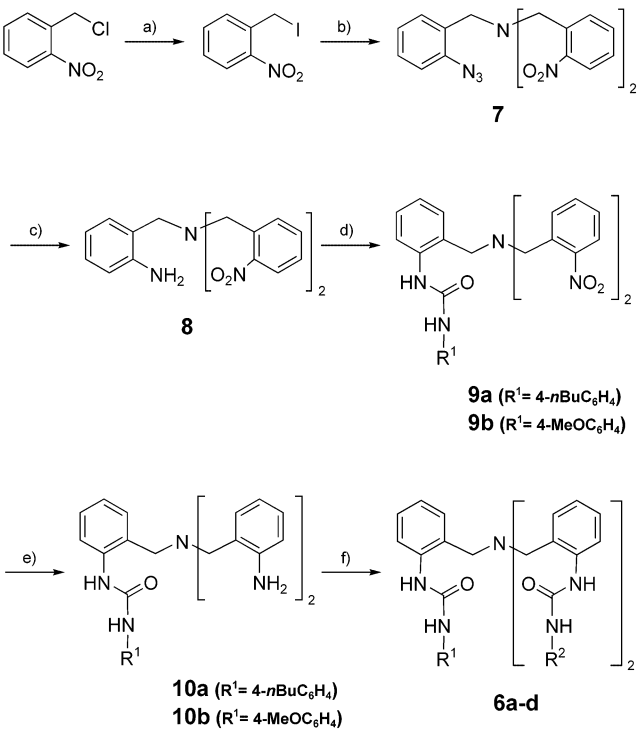


Figure 9. Schematic representation of the symmetry properties of tris(ureas) **6** consisting of two similar and one different terminal substituent of the urea functionality (the directionality of the belt of hydrogen bonds is symbolized by arrows).

(**C**), which is regioisomeric with the other two. The chirality featured by dimers **A/B** is supramolecular, since it is due only to the mutual arrangement of the two tris(ureas) in the dimer.[24]

Taking into account these preliminary considerations, desymmetrized tris(ureas) **6** were prepared as depicted in Scheme 6. Based on previous results found for tris(ureas) with C_{3v} symmetry, we anticipated that the regioselection should be more pronounced for different terminal residues than for different substituents at the tribenzylamine core. The preparation started with the treatment of 2-nitrobenzylchloride with NaI to give the corresponding iodide (96% yield), which was then treated with 2-azidobenzylamine in the presence of Na_2CO_3 to yield the tertiary amine **7** (91%). The formation of the corresponding iminophosphorane by reaction of **7** with trimethylphosphane followed by hydrolysis in THF/H_2O led to the amine **8** (67–90%). After reaction



Scheme 6. Reagents and reaction conditions for the synthesis of tris(ureas) **6**. a) NaI, acetone, 20°C, 20 h; b) 2-azidobenzylamine, Na_2CO_3, CH_3CN, reflux, 24 h; c) i) PMe_3, THF, 0°C, 30 min; ii) H_2O/THF, 20°C, 20 h; d) R^1NCO, CH_2Cl_2, 20°C, 24 h; e) H_2, PtO_2, THF, 20°C, 18–22 h; f) R^2NCO, CH_2Cl_2, 20°C, 16–18 h.

with an isocyanate the tribenzylamines **9a** and **9b** were isolated in 98% yield. Compounds **6a–d** were obtained from **9a**,**b** by sequential catalytic hydrogenation (**10a**: 74%; **10b**: 84%) and treatment with the corresponding isocyanate (Table 7).

The self-assembly of **6a–c** in $CDCl_3$ solutions was investigated (**6d** was highly insoluble in $CDCl_3$ or $C_2D_2Cl_4$). Regioisomers **A/B** and **C** interconvert by dissociation and recombination of the two subunits. Since this dissociation–recombination process is slow on the NMR time scale, the ratio of both regioisomeric species **A/B** and **C** present in the equilibrium could be determined by integration of selected signals (resonances of terminal NHs). As depicted in Table 7, the ratio of both regioisomers was only slightly influenced by the electronic nature of the terminal residue attached to the urea functionality.

Since a 66:33 ratio of regioisomers corresponds to a statistical distribution of **A**, **B**, and **C** (33:33:33), some degree of

Table 7. Yields[%] and regioselectivities in the association process of tris(ureas) **6**.

Entry	Urea	R^1	R^2	Yield[%]	**A/B**:**C**[a]
1	**6a**	4-nBuC_6H_4	4-$CF_3C_6H_4$	43	57:43
2	**6b**	4-nBuC_6H_4	4-FC_6H_4	90	66:34
3	**6c**	4-$CH_3OC_6H_4$	4-$CF_3C_6H_4$	44	60:40
4	**6d**	4-$CH_3OC_6H_4$	4-FC_6H_4	91	–[b]

[a] Determined by integration of selected signals in their ^1H NMR spectra (400 MHz); error ±5% of the stated value. [b] Value could not be determined as a result of the insolubility of **6d** in $CDCl_3$ and $C_2D_2Cl_4$.

regioselection was only found for **6a** and **6c** in favor of the C_i regioisomer (**C**) (entries 1 and 3; Table 7). In contrast to the desymmetrized tetraurea calix[4]arenes described by Böhmer and co-workers, no influence in the regioisomeric distribution was observed by changing the solvent from $CDCl_3$ to $C_2D_2Cl_4$ or [D_8]toluene.[24]

Interestingly, when a sample of **6a** obtained by slow evaporation of a $CDCl_3$ solution was redissolved in the same solvent and its ^{1}H NMR spectrum immediately recorded, it showed a 36:64 ratio of C_1:C_i regioisomers (see Supporting Information)! After one day, the mixture of regioisomers equilibrated and reached a similar ratio to that shown in Table 7 (the results in Table 7 were achieved by recording the spectra under equilibrium conditions, that is, 15 min after being dissolved in $CDCl_3$). This interesting result seems to be an indication of a clear predominance of the C_i regioisomer of **6a** in the solid state. Unfortunately we did not succeed in growing single crystals of tris(urea) **6a** suitable for X-ray determination. Efforts are currently underway in our laboratories to investigate this phenomenon in more depth.

Conclusion

Tris(2-ureidobenzyl)amines **3** proved to be avid self-assemblers in spite of their inherent flexibility, since they form dimeric aggregates both in the solid state and solution in a variety of noncompetitive solvents. Evidence for these dimeric species, which are capped, capsule-like aggregates in which the six hydrogen-bonded urea functionalities form a belt around the equator of the molecule, was provided by a combination of several techniques (X-ray analysis, NMR and IR spectroscopy, and ESI-MS). Association constants and thermodynamic parameters for the dimerization processes of selected tris(ureas) reveal that they are enthalpically driven although the size of the terminal substituent is decisive in the stability of the dimeric species. Tris(2-ureidobenzyl)amines **3** also present a high degree of narcissistic self-sorting as shown by the investigation of heterodimerization processes. Finally, the assembly of desymmetrized tris(ureas) **6** afforded modest regioselectivities which depend on the electronic nature of the terminal substituent at the ureido functionality.

Experimental Section

Single-crystal X-ray analysis of 3d: Crystallographic measurements were carried out at 100 K. The structure was solved by using SHELXS-97[25] and developed via alternating least-squares cycles and difference Fourier synthesis (SHELXL-97[25]) with the aid of the program XSeed.[26] Inspection of the difference Fourier map revealed the presence of a highly disordered molecule of CH_2Cl_2 occupying a total of 2315 Å^3 per unit cell. This was treated by using the SQUEEZE procedure.[27]

General: ^{1}H and ^{13}C NMR spectra were measured on a Bruker AC 200 (^{1}H: 200 MHz, ^{13}C: 50 MHz), Varian Unity-300 (^{1}H: 300 MHz, ^{13}C: 75 MHz), or Bruker Advance 400 (^{1}H: 401 MHz, ^{13}C: 101 MHz) spectrophotometer with TMS ($\delta = 0.00$ ppm) or the solvent residual peak as internal standards. IR spectra were recorded on an FTIR Nicolet Impact 400 infrared spectrophotometer, and melting points were taken on a Reichert apparatus and are uncorrected.

S,*S*-Dimethyl dithiocarbonate (DMDTC) was prepared according to a reported procedure.[28]

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

General procedure for the synthesis of tris(2-aminobenzyl)amines 2:

Method A: The corresponding tris(azide) **1**[2b] (2.03 mmol) was dissolved in freshly distilled Et_2O (10 mL) and slowly added to a suspension of $LiAlH_4$ (0.23 g, 6.09 mmol) in the same solvent (30 mL) at 0 °C under N_2. The mixture was stirred at this temperature for 0.5 h, warmed to 20 °C, and stirred for 4 h more. The reaction mixture was then cooled to 0 °C and treated with 10% aqueous NaOH (5 mL). After filtration over a pad of Celite, the ethereal phase was separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined extracts were dried over $MgSO_4$, the solvent was evaporated (30 °C/75 Torr), and the residue was purified by silica gel chromatography.

Method B: PMe_3 in THF (1.0 M, 7.24 mL, 7.24 mmol) was slowly added at 0 °C to a solution of the corresponding tris(azide) **1** (2.14 mmol) in freshly distilled THF (30 mL) under N_2. The reaction mixture was then stirred at this temperature until the band corresponding to the azide functionality (around 2100 cm^{-1}) disappeared from its IR spectrum (20 min approximately). At this time a white precipitate corresponding to the phosphazene was apparent in the mixture. THF (80 mL) and H_2O (15 mL) were then added and the reaction mixture was stirred at 20 °C for 18 h. After removal of the organic solvent (30 °C/75 Torr), H_2O (50 mL) was added and the aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL). The combined extracts were dried over $MgSO_4$, the solvent was evaporated (30 °C/75 Torr), and the residue was purified by silica gel chromatography.

Tris(2-aminobenzyl)amine (2a): The title compound was prepared according to methods A and B in 75% and 90% yield, respectively. Purification by silica gel chromatography, eluted first with 5:1 Et_2O/hexanes and subsequently with Et_2O ($R_f = 0.46$ in 5:1 Et_2O/hexanes) afforded **2a** as colorless prisms (an analytical sample was obtained by recrystallization from 1:4 CH_2Cl_2/Et_2O). M.p. 195–206 °C; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 3.46$ (s, 6H), 3.85 (s, 6H), 6.56 (dd, ^3J(H,H) = 8.4 Hz, ^4J(H,H) = 1.1 Hz, 3H), 6.67 (td, ^3J(H,H) = 7.3 Hz, ^4J(H,H) = 0.8 Hz, 3H), 7.03–7.11 ppm (m, 6H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): $\delta = 57.1$ (t), 115.5 (d), 117.8 (d), 121.8 (s), 128.9 (d), 132.0 (d), 145.6 ppm (s); IR (Nujol): $\tilde{\nu} = 3463$ (NH), 3428 (NH), 3350 cm^{-1} (NH); MS (70 eV, EI): *m*/*z* (%): 332 (4) [M^+], 106 (100); elemental analysis calcd (%) for $C_{21}H_{24}N_4$ (332.5): C 75.87, H 7.28, N 16.85; found: C 75.42, H 7.39; N 16.94.

Tris(2-amino-5-methylbenzyl)amine (2b): The title compound was prepared in 73% yield according to method A. Purification by silica gel chromatography, eluted first with 5:1 Et_2O/hexanes and subsequently with Et_2O ($R_f = 0.41$ in 5:1 Et_2O/hexanes), afforded **2b** as colorless prisms (an analytical sample was obtained by recrystallization from 2:1 CH_2Cl_2/Et_2O). M.p. 230–236 °C; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 2.20$ (s, 9H), 3.41 (s, 6H), 3.80 (s, 6H), 6.46 (d, ^3J(H,H) = 8.5 Hz, 3H), 6.84–6.87 ppm (m, 6H); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): $\delta = 20.4$ (q), 57.1 (t), 115.7 (d), 122.1 (s), 126.8 (s), 129.4 (d), 132.6 (d), 143.1 ppm (s); IR (Nujol): $\tilde{\nu} = 3461$ (NH), 3367 cm^{-1} (NH); MS (70 eV, EI): *m*/*z* (%): 374 (20) [M^+], 120 (100); elemental analysis calcd (%) for $C_{24}H_{30}N_4$ (374.5): C 76.97, H 8.07, N 14.96; found: C 76.75, H 8.35, N 15.13.

General procedure for the synthesis of tris(ureas) 3a–f: The corresponding tris(amine) **2** (0.30 mmol) was dissolved in dry CH_2Cl_2 (5 mL) and the isocyanate (0.90 mmol) was added under N_2. After stirring at 20 °C for 18 h the solvent was removed (30 °C/75 Torr) and Et_2O (5 mL) was added. The white solid was filtered and dried under vacuum. Further purification was conducted by recrystallization from the appropriate mixture of solvents.

Tris{2-[*N*′-(4-methylphenyl)ureido]benzyl}amine (3a): The title compound was prepared in 87% yield according to the general procedure to afford **3a** as colorless prisms (an analytical sample was obtained by recrystallization from 1:1 $CHCl_3$/Et_2O). M.p. 234–236 °C; ^{1}H NMR (300 MHz, [D_6]DMSO, 25 °C, TMS, only monomer was observed): $\delta =$ 2.23 (s, 9H), 3.64 (s, 6H), 7.01–7.06 (m, 9H), 7.16 (td, ^3J(H,H) = 7.5 Hz,

^4J(H,H) = 0.9 Hz, 3H), 7.31 (d, ^3J(H,H) = 8.1 Hz, 6H), 7.56–7.59 (m, 6H), 7.90 (s, 3H), 8.66 ppm (s, 3H); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS, only dimer was observed): δ = 1.87 (s, 18H), 3.09 (d, ^2J(H,H) = 14.7 Hz, 6H), 3.22 (d, ^2J(H,H) = 14.7 Hz, 6H), 6.17 (d, ^3J(H,H) = 8.4 Hz, 12H), 6.40 (d, ^3J(H,H) = 8.4 Hz, 12H), 7.07 (d, ^3J(H,H) = 7.8 Hz, 6H), 7.19 (t, ^3J(H,H) = 7.4 Hz, 6H), 7.28 (t, ^3J(H,H) = 7.4 Hz, 6H), 7.41 (s, 6H), 7.63 (d, ^3J(H,H) = 7.5 Hz, 6H), 7.94 ppm (s, 6H); ^{13}C NMR (50 MHz, [D$_6$]DMSO, 25 °C): δ = 20.3 (q), 54.4 (t), 118.3 (2 × d), 123.7 (d), 123.8 (d), 127.1 (d), 128.6 (d), 129.1 (2 × d), 130.0 (s), 130.6 (s), 137.0 (s), 137.1 (s), 153.1 ppm (s); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 20.3 (q), 53.4 (t), 117.9 (2 × d), 126.2 (d), 126.5 (d), 128.3 (d), 128.6 (d), 128.9 (2 × d), 131.3 (s), 134.7 (s), 135.4 (s), 136.5 (s), 155.9 ppm (s); IR (Nujol): $\tilde{\nu}$ = 3322 (NH), 1655 cm^{-1} (C=O); IR ($CHCl_3$, 13.7 mM): $\tilde{\nu}$ = 3317 (NH), 1658 cm^{-1} (C=O); MS (FAB$^+$): *m*/*z* (%): 754 (45) [*M*$^+$+Na], 732 (42) [*M*$^+$+1], 239 (95), 132 (61); elemental analysis calcd (%) for $C_{45}H_{45}N_7O_3$ (731.9): C 73.85, H 6.20, N 13.40; found: C 73.83, H 6.37, N 13.53.

Tris{5-methyl-2-[*N*′-(4-methylphenyl)ureido]benzyl}amine (3b): The title compound was prepared in 87% yield according to the general procedure to afford **3b** as colorless prisms. M.p. 270–272 °C; ^{1}H NMR (300 MHz, [D$_6$]DMSO, 25 °C, TMS, only monomer was observed): δ = 2.10 (s, 9H), 2.21 (s, 9H), 3.58 (s, 6H), 6.90 (dd, ^3J(H,H) = 8.1 Hz, ^4J(H,H) = 1.8 Hz, 3H), 7.02 (d, ^3J(H,H) = 8.3 Hz, 6H), 7.12 (s, 3H), 7.28 (d, ^3J(H,H) = 8.3 Hz, 6H), 7.33 (d, ^3J(H,H) = 8.1 Hz, 3H), 7.87 (s, 3H), 8.59 ppm (s, 3H); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS, a 82:18 mixture of dimer and monomer was observed): δ(dimer) = 1.89 (s, 18H), 2.47 (s, 18H), 3.00 (d, ^2J(H,H) = 14.5 Hz, 6H), 3.16 (d, ^2J(H,H) = 14.5 Hz, 6H), 6.20 (d, ^3J(H,H) = 8.3 Hz, 12H), 6.38 (d, ^3J(H,H) = 8.3 Hz, 12H), 6.93 (d, ^3J(H,H) = 7.7 Hz, 6H), 7.00 (d, ^3J(H,H) = 7.7 Hz, 6H), 7.36 (s, 6H), 7.42 (s, 6H), 7.86 ppm (s, 6H); δ(monomer) = 2.27 (s, 18H), 3.49 (s, 6H), 6.77 (s, 3H), 7.13 ppm (d, ^3J(H,H) = 8.1 Hz, 6H), the rest of the signals are overlapped with those corresponding to the dimer; ^{13}C NMR (50 MHz, [D$_6$]DMSO, 25 °C): δ = 20.3 (2 × q), 55.0 (t), 118.4 (2 × d), 123.9 (d), 127.8 (d), 129.0 (2 × d), 129.9 (s), 130.2 (d), 130.4 (s), 132.5 (s), 134.7 (s), 137.2 (s), 153.4 ppm (s); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, only dimer was observed since the signals for the monomer were too weak): δ = 20.2 (q), 21.5 (q), 53.2 (t), 118.0 (2 × d), 127.1 (d), 128.4 (d), 128.6 (2 × d), 129.0 (d), 131.1 (s), 132.1 (s), 135.3 (s), 135.5 (s), 136.3 (s), 156.0 ppm (s); IR (Nujol): $\tilde{\nu}$ = 3318 (NH), 1660 cm^{-1} (C=O); elemental analysis calcd (%) for $C_{48}H_{51}N_7O_3$ (774.0): C 74.49, H 6.64, N 12.67; found: C 74.41, H 6.75, N 12.74.

Tris{2-[*N*′-(4-butylphenyl)ureido]benzyl}amine (3c): The title compound was prepared in 77% yield according to the general procedure to afford **3c** as colorless prisms (an analytical sample was obtained by recrystallization from 1:1 $CHCl_3$/Et_2O). M.p. 227–231 °C; ^{1}H NMR (300 MHz, [D$_6$]DMSO, 25 °C, TMS, only monomer was observed): δ = 0.89 (t, ^3J(H,H) = 7.2 Hz, 9H), 1.29 (m, ^3J(H,H) = 7.3 Hz, 6H), 1.51 (m, ^3J(H,H) = 7.5 Hz, 6H), 2.50 (t, ^3J(H,H) = 7.7 Hz, 6H), 3.64 (s, 6H), 7.01–7.06 (m, 9H), 7.16 (t, ^3J(H,H) = 7.4 Hz, 3H), 7.31 (d, ^3J(H,H) = 8.7 Hz, 6H), 7.55–7.58 (m, 6H), 7.90 (s, 3H), 8.66 ppm (s, 3H); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS, only dimer was observed): δ = 0.90–0.95 (m, 18H), 1.17–1.22 (m, 24H), 2.13 (t, ^3J(H,H) = 7.2 Hz, 12H), 3.11 (d, ^2J(H,H) = 15.0 Hz, 6H), 3.22 (d, ^2J(H,H) = 15.0 Hz, 6H), 6.17 (d, ^3J(H,H) = 8.4 Hz, 12H), 6.41 (d, ^3J(H,H) = 8.4 Hz, 12H), 7.13 (dd, ^3J(H,H) = 7.7 Hz, ^4J(H,H) = 1.4 Hz, 6H), 7.20 (td, ^3J(H,H) = 7.4 Hz, ^4J(H,H) = 1.3 Hz, 6H), 7.26 (td, ^3J(H,H) = 7.4 Hz, ^4J(H,H) = 1.7 Hz, 6H), 7.37 (s, 6H), 7.64 (d, ^3J(H,H) = 7.5 Hz, 6H), 8.05 ppm (s, 6H); ^{13}C NMR (75 MHz, [D$_6$]DMSO, 25 °C): δ = 13.8 (q), 21.7 (t), 33.2 (t), 34.1 (t), 54.4 (t), 118.3 (2 × d), 123.7(d), 123.9 (d), 127.1 (d), 128.4 (2 × d), 128.7 (d), 130.0 (s), 135.6 (s), 137.1 (s), 137.3 (s), 153.1 ppm (s); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 14.1 (q), 22.4 (t), 33.6 (t), 34.6 (t), 53.2 (t), 117.7 (2 × d), 126.58 (d), 126.63 (d), 127.9 (d), 128.2 (2 × d), 128.9 (d), 134.6 (s), 135.5 (s), 136.4 (s), 136.6 (s), 155.9 ppm (s); IR (Nujol): $\tilde{\nu}$ = 3317 (NH), 1658 cm^{-1} (C=O); MS (FAB$^+$): *m*/*z* (%): 858 (35) [*M*$^+$+1], 281 (100); elemental analysis calcd (%) for $C_{54}H_{63}N_7O_3$ (858.1): C 75.58, H 7.40, N 11.43; found: C 75.39, H 7.64, N 11.56.

Tris{5-methyl-2-[*N*′-(4-butylphenyl)ureido]benzyl}amine (3d): The title compound was prepared in 77% yield according to the general procedure to afford **3d** as colorless prisms (an analytical sample was obtained by recrystallization from 1:2 $CHCl_3$/Et_2O). M.p. 252–254 °C; ^{1}H NMR (300 MHz, [D$_6$]DMSO, 25 °C, TMS, only monomer was observed): δ = 0.89 (t, ^3J(H,H) = 7.4 Hz, 9H), 1.28 (m, ^3J(H,H) = 7.4 Hz, 6H), 1.51 (m, ^3J(H,H) = 7.5 Hz, 6H), 2.10 (s, 9H), 2.49 (t, ^3J(H,H) = 7.4 Hz, 6H), 3.59 (s, 6H), 6.90 (d, ^3J(H,H) = 8.1 Hz, 3H), 7.02 (d, ^3J(H,H) = 8.7 Hz, 6H), 7.11 (s, 3H), 7.28–7.33 (m, 9H), 7.87 (s, 3H), 8.59 ppm (s, 3H); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS, only dimer was observed): δ = 0.90–0.95 (m, 18H), 1.23–1.24 (m, 24H), 2.15 (m, 12H), 2.44 (s, 18H), 3.04 (d, ^2J(H,H) = 14.9 Hz, 6H), 3.16 (d, ^2J(H,H) = 14.9 Hz, 6H), 6.24 (d, ^3J(H,H) = 8.4 Hz, 12H), 6.42 (d, ^3J(H,H) = 8.4 Hz, 12H), 7.00 (s, 12H), 7.29 (s, 6H), 7.43 (s, 6H), 8.03 ppm (s, 6H); ^{13}C NMR (50 MHz, [D$_6$]DMSO, 25 °C): δ = 13.8 (q), 20.5 (q), 21.7 (t), 33.3 (t), 34.2 (t), 55.3 (t), 118.5 (2 × d), 124.1(d), 127.9 (d), 128.4 (2 × d), 130.1 (s), 130.4 (d), 132.6 (s), 134.7 (s), 135.6 (s), 137.5 (s), 153.5 ppm (s); ^{13}C NMR (50 MHz, $CDCl_3$, 25 °C): δ = 14.0 (q), 21.6 (q), 22.4 (t), 33.4 (t), 34.5 (t), 53.1 (t), 117.7 (2 × d), 127.3 (d), 127.9 (2 × d), 128.5 (d), 128.6 (d), 132.1 (s), 135.5 (s), 135.7 (s), 136.1 (s), 136.4 (s), 156.0 ppm (s); IR (Nujol): $\tilde{\nu}$ = 3352 (NH), 3291 (NH), 1661 cm^{-1} (C=O); MS (FAB$^+$): *m*/*z* (%): 900 (19) [*M*$^+$+1], 295 (100), 219 (30); elemental analysis calcd (%) for $C_{57}H_{69}N_7O_3$ (900.2): C 76.05, H 7.73, N 10.89; found: C 75.76, H 7.93, N 11.04.

Tris{2-[*N*′-(4-methoxyphenyl)ureido]benzyl}amine (3e): The title compound was prepared in 86% yield according to the general procedure to afford **3e** as colorless prisms. M.p. 221–222 °C; ^{1}H NMR (200 MHz, [D$_6$]DMSO, 25 °C, TMS, only monomer was observed): δ = 3.63 (s, 6H), 3.70 (s, 9H), 6.84 (d, ^3J(H,H) = 8.8 Hz, 6H), 7.02 (t, ^3J(H,H) = 7.3 Hz, 3H), 7.16 (t, ^3J(H,H) = 7.3 Hz, 3H), 7.32 (d, ^3J(H,H) = 8.8 Hz, 6H), 7.53–7.59 (m, 6H), 7.89 (s, 3H), 8.61 ppm (s, 3H); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS, an 83:17 mixture of dimer and monomer was observed): δ(dimer) = 3.12 (d, ^2J(H,H) = 14.7 Hz, 6H), 3.25 (d, ^2J(H,H) = 14.7 Hz, 6H), 3.47 (s, 18H), 6.15–6.24 (m, 24H), 7.10 (d, ^3J(H,H) = 7.8 Hz, 6H), 7.20 (td, ^3J(H,H) = 7.8 Hz, ^4J(H,H) = 1.2 Hz, 6H), 7.26–7.33 (m, 6H), 7.39 (s, 6H), 7.66 (d, ^3J(H,H) = 7.2 Hz, 6H), 7.90 ppm (s, 6H); δ(monomer) = 3.58 (s, 6H), 3.76 (s, 9H), 6.77 ppm (d, ^3J(H,H) = 9.0 Hz, 6H), the rest of the signals are overlapped with those corresponding to the dimer; ^{13}C NMR (50 MHz, [D$_6$]DMSO, 25 °C): δ = 54.3 (t), 55.1 (q), 113.9 (2 × d), 120.0 (2 × d), 123.5 (d), 123.7 (d), 127.1 (d), 128.7 (d), 129.8 (s), 132.7 (s), 137.7 (s), 153.2 (s), 154.4 ppm (s); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, only dimer was observed since the signals for the monomer were too weak): δ = 53.4 (t), 55.2 (q), 113.6 (2 × d), 119.2 (2 × d), 126.6 (d), 126.7 (d), 128.2 (d), 128.5 (d), 131.2 (s), 134.8 (s), 136.4 (s), 155.8 (s), 155.9 ppm (s); IR (Nujol): $\tilde{\nu}$ = 3320 (NH), 1657 cm^{-1} (C=O); elemental analysis calcd (%) for $C_{45}H_{45}N_7O_6$ (779.9): C 69.30, H 5.82, N 12.57; found: C 68.91, H 5.88, N 12.56.

Tris(2-{*N*′-[4-(trifluoromethyl)phenyl]ureido}benzyl)amine (3f): The title compound was prepared in 89% yield according to the general procedure to afford **3f** as colorless prisms. M.p. 258–260 °C; ^{1}H NMR (300 MHz, [D$_6$]DMSO, 25 °C, TMS, only monomer was observed): δ = 3.63 (s, 6H), 7.05 (t, ^3J(H,H) = 7.5 Hz, 3H), 7.15 (t, ^3J(H,H) = 7.7 Hz, 3H), 7.52 (d, ^3J(H,H) = 7.5 Hz, 3H), 7.56–7.62 (m, 15H), 8.09 (s, 3H), 9.18 ppm (s, 3H); ^{1}H NMR (300 MHz, $C_2D_2Cl_4$, 25 °C, TMS, only dimer was observed): δ = 2.93 (d, ^2J(H,H) = 14.7 Hz, 6H), 3.15 (d, ^2J(H,H) = 14.7 Hz, 6H), 6.28 (d, ^3J(H,H) = 8.4 Hz, 12H), 6.83 (d, ^3J(H,H) = 8.4 Hz, 12H), 7.16 (d, ^3J(H,H) = 7.2 Hz, 6H), 7.30 (t, ^3J(H,H) = 7.5 Hz, 6H), 7.38 (t, ^3J(H,H) = 7.2 Hz, 6H), 7.57–7.60 (m, 12H), 8.11 ppm (s, 6H); ^{13}C NMR (75 MHz, [D$_6$]DMSO, 25 °C): δ = 54.3 (t), 117.8 (2 × d), 121.7 (q, ^2J(C,F) = 31.8 Hz), 124.3 (d), 124.4 (d), 124.5 (q, ^1J(C,F) = 269.5 Hz), 126.0 (2 × d), 127.2 (d), 128.8 (d), 130.8 (s), 136.5 (s), 143.5 (s), 152.9 ppm (s); ^{13}C NMR (75 MHz, $C_2D_2Cl_4$, 25 °C): δ = 53.0 (t), 117.2 (2 × d), 123.5 (q, ^1J(C,F) = 269.5 Hz), 123.9 (q, ^2J(C,F) = 32.8 Hz), 125.5 (2 × d), 127.4 (2 × d), 127.8 (d), 128.6 (d), 133.2 (s), 135.3 (s), 140.4 (s), 155.3 ppm (s); IR (Nujol): $\tilde{\nu}$ = 3331 (NH), 1667 cm^{-1} (C=O); elemental analysis calcd (%) for $C_{45}H_{36}F_9N_7O_3$ (893.8): C 60.47, H 4.06, N 10.97; found: C 60.20, H 4.13, N 10.94.

General procedure for the synthesis of tris(ureas) 3g–k: The corresponding tris(amine) **2** (0.30 mmol) was dissolved in dry $CHCl_3$ (5 mL) and the isocyanate (0.90 mmol) was added under N_2. After stirring at reflux for 18 h the solvent was removed (30 °C/75 Torr) and Et_2O (5 mL) was added. The white solid was filtered and dried under vacuum. Further purification was conducted by recrystallization from the appropriate mixture of solvents (except for **3j**).

Tris{2-[*N*′-(benzyl)ureido]benzyl}amine (3g): The title compound was prepared in 81% yield according to the general procedure to afford **3g** as colorless prisms (an analytical sample was obtained by recrystallization from 1:3 $CHCl_3$/Et_2O). M.p. 205–207 °C; ^{1}H NMR (200 MHz, [D$_6$]DMSO,

25 °C, TMS, only monomer was observed): $\delta = 3.53$ (s, 6H), 4.25 (d, $^3J(H,H) = 5.7$ Hz, 6H), 6.77 (t, $^3J(H,H) = 5.7$ Hz, 3H), 6.98 (t, $^3J(H,H) = 7.3$ Hz, 3H), 7.15 (t, $^3J(H,H) = 7.7$ Hz, 3H), 7.23–7.36 (m, 15H), 7.46 (d, $^3J(H,H) = 7.3$ Hz, 3H), 7.60 (d, $^3J(H,H) = 7.9$ Hz, 3H), 7.87 ppm (s, 3H); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS, 84:16 mixture of dimer and monomer was observed): δ(dimer) = 2.60 (dd, $^2J(H,H) = 15.4$ Hz, $^3J(H,H) = 3.0$ Hz, 6H), 3.78 (d, $^2J(H,H) = 15.8$ Hz, 6H), 3.94 (d, $^2J(H,H) = 15.8$ Hz, 6H), 4.12 (dd, $^2J(H,H) = 15.4$ Hz, $^3J(H,H) = 9.1$ Hz, 6H), 6.05 (dd, $^3J(H,H) = 9.1$ Hz, $^3J(H,H) = 3.0$ Hz, 6H), 7.03 (dd, $^3J(H,H) = 7.4$ Hz, $^4J(H,H) = 1.5$ Hz, 12H), 7.15–7.39 (m, 36H), 7.64 (s, 6H), 8.18 ppm (d, $^3J(H,H) = 7.8$ Hz, 6H); δ(monomer) = 3.50 (s, 6H), 4.26 (d, $^3J(H,H) = 5.8$ Hz, 6H), 5.12 (t, $^3J(H,H) = 5.8$ Hz, 3H), 6.31 ppm (s, 3H), the rest of the signals are overlapped with those corresponding to the dimer; ^{13}C NMR (75 MHz, [D$_6$]DMSO, 25 °C): $\delta = 43.0$ (t), 54.3 (t), 122.85 (d), 122.91 (d), 126.7 (d), 127.07 (d), 127.13 (2×d), 128.2 (2×d), 128.8 (d+s), 137.9 (s), 140.1 (s), 155.5 ppm (s); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ(dimer) = 42.8 (t), 53.8 (t), 126.6 (d), 126.79 (d), 126.80 (d), 127.0 (2×d), 127.2 (d), 128.2 (2×d), 129.0 (d), 135.1 (s), 136.2 (s), 139.3 (s), 158.2 ppm (s); δ(monomer) = 44.2 (t), 56.5 (t), 122.3 (d), 123.2 (d), 125.8 (s), 127.3 (d), 128.0 (2×d), 128.5 (2×d), 129.4 (d), 132.3 (d), 137.8 (s), 138.8 (s), 155.0 ppm (s); IR (Nujol): $\tilde{\nu} = 3334$ (NH), 3265 (NH), 1643 cm^{-1} (C=O); IR ($CHCl_3$, 16.4 mM): $\tilde{\nu} = 3327$ (NH), 1647 cm^{-1} (C=O); MS (FAB$^+$): *m*/*z* (%): 732 (25) [M^++1], 731 (49) [M^+], 220 (100), 132 (41); elemental analysis calcd (%) for $C_{45}H_{45}N_7O_3$ (731.9): C 73.85, H 6.20, N 13.40; found: C 73.65, H 6.30, N 13.49.

Tris{5-methyl-2-[*N*′-(benzyl)ureido]benzyl}amine (3h): The title compound was prepared in 91% yield according to the general procedure to afford **3h** as colorless prisms (an analytical sample was obtained by recrystallization from 1:3 $CHCl_3$/Et_2O). M.p. 219–222 °C; ^{1}H NMR (300 MHz, [D$_6$]DMSO, 25 °C, TMS, only monomer was observed): $\delta =$ 2.18 (s, 9H), 3.49 (s, 6H), 4.22 (d, $^3J(H,H) = 6.0$ Hz, 6H), 6.60 (t, $^3J(H,H) = 6.0$ Hz, 3H), 6.93 (d, $^3J(H,H) = 8.1$ Hz, 3H), 7.07 (d, $^3J(H,H) =$ 1.2 Hz, 3H), 7.22–7.31 (m, 15H), 7.39 (d, $^3J(H,H) = 8.4$ Hz, 3H), 7.79 ppm (s, 3H); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS, a 70:30 mixture of dimer and monomer was observed): δ(dimer) = 2.44 (s, 18H), 2.54 (dd, $^2J(H,H) = 15.5$ Hz, $^3J(H,H) = 3.4$ Hz, 6H), 3.66 (d, $^2J(H,H) = 15.6$ Hz, 6H), 3.89 (d, $^2J(H,H) = 15.6$ Hz, 6H), 4.15 (dd, $^2J(H,H) = 15.5$ Hz, $^3J(H,H) = 9.4$ Hz, 6H), 6.02 (dd, $^3J(H,H) = 9.4$ Hz, $^3J(H,H) = 3.4$ Hz, 6H), 6.92–7.03 (m, 18H), 7.11–7.34 (m, 24H), 7.61 (s, 6H), 7.92 ppm (s, 6H); δ(monomer) = 2.19 (s, 9H), 3.44 (s, 6H), 4.24 (d, $^3J(H,H) = 5.8$ Hz, 6H), 5.01 (t, $^3J(H,H) = 5.8$ Hz, 3H), 6.22 (s, 3H), 6.76 (dd, $^3J(H,H) = 8.3$ Hz, $^4J(H,H) = 1.8$ Hz, 3H), 7.52 ppm (d, $^3J(H,H) = 8.3$ Hz, 3H), the rest of the signals are overlapped with those corresponding to the dimer; ^{13}C NMR (75 MHz, [D$_6$]DMSO, 25 °C): $\delta = 20.4$ (q), 43.0 (t), 54.7 (t), 123.2 (d), 126.6 (d), 127.1 (2×d), 127.9 (d), 128.1 (2×d), 128.9 (s), 130.5 (d), 131.8 (s), 135.4 (s), 140.1 (s), 155.8 ppm (s); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ(dimer) = 21.7 (q), 42.7 (t), 53.9 (t), 126.7 (3×d), 127.0 (d), 127.8 (d), 128.2 (2×d), 128.8 (d), 133.5 (s), 135.0 (s), 135.9 (s), 139.5 (s), 158.3 ppm (s); δ(monomer) = 20.6 (q), 44.1 (t), 56.5 (t), 122.2 (d), 125.8 (d), 127.2 (d), 128.0 (2×d), 128.5 (2×d), 129.9 (d), 132.7 (s), 132.8 (s), 135.2 (s), 139.0 (s), 155.0 ppm (s); IR (Nujol): $\tilde{\nu} = 3338$ (NH), 3252 (NH), 1650 (C=O), 1645 cm^{-1} (C=O); MS (FAB$^+$): *m*/*z* (%): 774 (17) [M^++1], 773 (29) [M^+], 233 (51), 123 (100); elemental analysis calcd (%) for $C_{48}H_{51}N_7O_3$ (774.0): C 74.49, H 6.64, N 12.67; found: C 74.20, H 7.03, N 12.67.

Tris{2-[*N*′-(2-propenyl)ureido]benzyl}amine (3i): The title compound was prepared in 58% yield according to the general procedure to afford **3i** as colorless prisms. M.p. 249–252 °C; ^{1}H NMR (200 MHz, [D$_6$]DMSO, 25 °C, TMS, only monomer was observed): $\delta = 3.53$ (s, 6H), 3.69 (t, $^3J(H,H) =$ 5.3 Hz, 6H), 5.07 (dd, $^3J(H,H) = 10.3$ Hz, $^2J(H,H) = 1.6$ Hz, 3H), 5.16 (dd, $^3J(H,H) = 17.4$ Hz, $^2J(H,H) = 1.6$ Hz, 3H), 5.84 (ddt, $^3J(H,H) = 17.4$ Hz, $^3J(H,H) = 10.3$ Hz, $^3J(H,H) = 5.3$ Hz, 3H), 6.40 (t, $^3J(H,H) = 5.3$ Hz, 3H), 7.02 (t, $^3J(H,H) = 7.1$ Hz, 3H), 7.18 (t, $^3J(H,H) = 7.3$ Hz, 3H), 7.47 (d, $^3J(H,H) = 6.8$ Hz, 3H), 7.58 (d, $^3J(H,H) = 7.7$ Hz, 3H), 7.78 ppm (s, 3H); ^{1}H NMR (300 MHz, $C_2D_2Cl_4$, 25 °C, TMS, a 77:23 mixture of dimer and monomer was observed): δ(dimer) = 2.17–2.23 (m, 6H), 3.32–3.36 (m, 6H), 3.56 (d, $^2J(H,H) = 15.8$ Hz, 6H), 3.73 (d, $^2J(H,H) = 15.8$ Hz, 6H), 4.80 (d, $^3J(H,H) = 10.2$ Hz, 6H), 4.90 (d, $^3J(H,H) = 17.1$ Hz, 6H), 5.30–5.43 (m, 6H), 5.53 (dd, $^3J(H,H) = 8.1$ Hz, $^3J(H,H) = 3.6$ Hz, 6H), 7.29–7.35 (m, 18H), 7.43 (s, 6H), 8.04 ppm (d, $^3J(H,H) = 7.2$ Hz, 6H); δ(monomer) = 3.53 (s, 6H), 3.88 (t, $^3J(H,H) = 5.0$ Hz, 6H), 5.12–5.19 (m, 9H), 5.79 (ddt, $^3J(H,H) = 17.1$ Hz, $^3J(H,H) = 10.2$ Hz, $^3J(H,H) = 5.0$ Hz, 6H), 6.35 (s, 3H), 7.07 (t, $^3J(H,H) = 7.5$ Hz, 3H), 7.73 ppm (d, $^3J(H,H) =$ 7.5 Hz, 3H), the rest of the signals are overlapped with those corresponding to the dimer; ^{13}C NMR (50 MHz, [D$_6$]DMSO, 25 °C): $\delta = 41.7$ (t), 54.3 (t), 114.8 (t), 123.0 (2×d), 127.1 (d), 128.7 (d), 128.9 (s), 136.1 (d), 137.8 (s), 155.3 ppm (s); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ(dimer) = 41.6 (t), 53.5 (t), 115.2 (t), 126.46 (d), 126.50 (d), 126.8 (d), 128.5 (d), 134.7 (s), 134.8 (d), 135.6 (s), 157.7 ppm (s); δ(monomer) = 42.3(t), 56.2 (t), 115.8 (t), 122.7 (d), 123.4 (d), 126.4 (s), 129.1 (d), 132.2 (d), 134.6 (d), 137.5 (s), 154.9 ppm (s); IR (Nujol): $\tilde{\nu} = 3357$ (NH), 3248 (NH), 1651 (C=O), 1643 cm^{-1} (C=O); elemental analysis calcd (%) for $C_{33}H_{39}N_7O_3$ (581.7): C 68.14, H 6.76, N 16.86; found: C 67.74, H 6.69, N 17.11.

Tris{5-methyl-2-[*N*′-(propyl)ureido]benzyl}amine (3j): The title compound was prepared according to the above general procedure. However, after removal of the solvent from the reaction mixture, the crude product was purified by silica gel chromatography eluting with 1:2 AcOEt/hexanes ($R_f = 0.18$) to afford **3j** in 80% yield. An analytical sample (colorless prisms) was obtained by recrystallization from 1:3 $CHCl_3$/Et_2O. M.p. 234–236 °C; ^{1}H NMR (300 MHz, [D$_6$]DMSO, 25 °C, TMS, only monomer was observed): $\delta = 0.84$ (t, $^3J(H,H) = 7.5$ Hz, 9H), 1.40 (m, $^3J(H,H) = 7.1$ Hz, 6H), 2.21 (s, 9H), 2.95 (q, $^3J(H,H) = 6.2$ Hz, 6H), 3.43 (s, 6H), 6.07 (t, $^3J(H,H) = 5.4$ Hz, 3H), 6.97 (d, $^3J(H,H) = 8.3$ Hz, 3H), 7.05 (s, 3H), 7.37 (d, $^3J(H,H) = 8.3$ Hz, 3H), 7.49 ppm (s, 3H); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS, 80:20 mixture of dimer and monomer was observed): δ(dimer) = 0.66 (t, $^3J(H,H) = 7.4$ Hz, 18H), 1.01–1.14 (m, 12H), 1.39–1.51 (m, 6H), 2.38 (s, 18H), 2.76–2.88 (m, 6H), 3.47 (d, $^2J(H,H) = 15.9$ Hz, 6H), 3.68 (d, $^2J(H,H) = 15.9$ Hz, 6H), 5.47 (dd, $^3J(H,H) = 9.0$ Hz, $^3J(H,H) = 2.7$ Hz, 6H), 7.06 (d, $^3J(H,H) = 8.1$ Hz, 6H), 7.20 (d, $^3J(H,H) =$ 8.1 Hz, 6H), 7.38 (s, 6H), 7.77 ppm (s, 6H); δ(monomer) = 0.90 (t, $^3J(H,H) = 7.5$ Hz, 9H), 2.29 (s, 9H), 3.06 (m, 6H), 4.76 (t, $^3J(H,H) =$ 6.2 Hz, 3H), 6.22 (s, 3H), 7.82 ppm (d, $^3J(H,H) = 8.1$ Hz, 3H), the rest of the signals are overlapped with those corresponding to the dimer; ^{13}C NMR (75 MHz, [D$_6$]DMSO, 25 °C): $\delta = 11.3$ (q), 20.4 (q), 22.8 (t), 41.1 (t), 55.1 (t), 123.3 (d), 128.0 (d), 128.7 (s), 130.9 (d), 131.6 (s), 135.6 (s), 155.8 ppm (s); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ(dimer) = 11.2 (q), 21.5 (q), 23.7 (t), 41.0 (t), 53.7 (t), 126.9 (d), 127.4 (d), 128.6 (d), 133.5 (s), 135.1 (s), 135.7 (s), 158.2 ppm (s); δ(monomer) = 11.3 (q), 20.6 (q), 23.1 (t), 42.0 (t), 56.7 (t), 121.7 (d), 125.3 (s), 129.9 (d), 132.5 (s), 132.9 (d), 135.4 (s), 155.2 ppm (s); IR (Nujol): $\tilde{\nu} = 3357$ (NH), 3258 (NH), 1645 cm^{-1} (C=O); elemental analysis calcd (%) for $C_{36}H_{51}N_7O_3$ (629.9): C 68.65, H 8.16, N 15.57; found: C 68.58, H 8.42, N 15.58.

Tris{5-methyl-2-[*N*′-(1-phenylethyl)ureido]benzyl}amine (3k): The title compound was prepared in 62% yield according to the general procedure to afford **3k** as colorless prisms (an analytical sample was obtained by recrystallization from 1:1 CH_2Cl_2/Et_2O). M.p. 235–238 °C; $[\alpha]_D^{25} = -32.96$ ($c = 0.2$ in $CHCl_3$) for the reaction with (*S*)-α-methylbenzyl isocyanate; ^{1}H NMR (300 MHz, [D$_6$]DMSO, 25 °C, TMS, only monomer was observed): $\delta = 1.27$ (d, $^3J(H,H) = 6.8$ Hz, 9H), 2.22 (s, 9H), 3.14 (d, $^2J(H,H) = 12.8$ Hz, 3H), 3.73 (d, $^2J(H,H) = 12.8$ Hz, 3H), 4.72 (m, $^3J(H,H) = 6.8$ Hz, 3H), 6.53 (d, $^3J(H,H) = 6.8$ Hz, 3H), 6.92 (d, $^3J(H,H) =$ 8.1 Hz, 3H), 7.10 (s, 3H), 7.17–7.22 (m, 9H), 7.25–7.30 (m, 9H), 7.47 ppm (s, 3H); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS, only monomer was observed): $\delta = 1.35$ (d, $^3J(H,H) = 4.5$ Hz, 9H), 2.22 (s, 9H), 3.37 (brs, 6H), 4.73 (brs, 3H), 5.34 (brs, 3H), 6.47 (brs, 3H), 6.84 (d, $^3J(H,H) = 7.8$ Hz, 3H), 6.95 (s, 3H), 7.20–7.29 (m, 15H), 7.39 ppm (brs, 3H); ^{13}C NMR (75 MHz, [D$_6$]DMSO, 25 °C): $\delta = 20.4$ (q), 22.9 (q), 49.0 (d), 55.6 (t), 123.7 (d), 125.6 (2×d), 126.4 (d), 128.1 (2×d), 128.2 (d), 128.6 (s), 131.3 (d), 131.7 (s), 135.4 (s), 145.3 (s), 155.1 ppm (s); IR (Nujol): $\tilde{\nu} = 3406$ (NH), 3333 (NH), 3221 (NH), 1699 (C=O), 1647 cm^{-1} (C=O); elemental analysis calcd (%) for $C_{51}H_{57}N_7O_3$ (816.1): C 75.06, H 7.04, N 12.02; found: C 74.83, H 6.99, N 12.11.

Tris{5-methyl-2-[*N*′-(1-methylethyl)ureido]benzyl}amine (3l): A mixture of tris(amine) **2b** (0.10 g, 0.27 mmol) and isopropyl isocyanate (0.14 g, 1.60 mmol) was dissolved in dry DMF (10 mL) under N_2 and stirred at 80 °C for 18 h. After cooling, the reaction mixture was poured in H_2O (20 mL) and extracted with CH_2Cl_2 (3×10 mL). The combined organic extracts were washed with H_2O (3×20 mL) and dried over $MgSO_4$. The solvent was then removed (30 °C/75 Torr) and the crude product was purified by silica gel chromatography eluting with 1:1 AcOEt/hexanes ($R_f =$ 0.41) to afford **3l** in 64% yield. An analytical sample (colorless prisms) was obtained by recrystallization from 1:3 $CHCl_3$/Et_2O. M.p. 228–229 °C;

^{1}H NMR (300 MHz, [D$_6$]DMSO, 25 °C, TMS, only monomer was observed): δ = 1.04 (d, ^3J(H,H) = 6.3 Hz, 18H), 2.22 (s, 9H), 3.40 (s, 6H), 3.68 (m, ^3J(H,H) = 6.7 Hz, 3H), 5.97 (d, ^3J(H,H) = 7.5 Hz, 3H), 7.00 (d, ^3J(H,H) = 8.1 Hz, 3H), 7.06 (s, 3H), 7.29 (s, 3H), 7.38 ppm (d, ^3J(H,H) = 8.1 Hz, 3H); ^{1}H NMR (300 MHz, CDCl$_3$, 25 °C, TMS, only monomer was observed): δ = 1.13 (d, ^3J(H,H) = 6.6 Hz, 18H), 2.28 (s, 9H), 3.43 (s, 6H), 3.86 (m, ^3J(H,H) = 6.7 Hz, 3H), 4.76 (d, ^3J(H,H) = 7.2 Hz, 3H), 6.36 (s, 3H), 6.99 (s, 3H), 7.08 (d, ^3J(H,H) = 8.1 Hz, 3H), 7.84 ppm (d, ^3J(H,H) = 8.1 Hz, 3H); ^{13}C NMR (75 MHz, CDCl$_3$, 25 °C): δ = 20.6 (q), 22.8 (2 × q), 42.2 (d), 56.9 (t), 122.1 (d), 125.2 (s), 129.8 (d), 132.3 (s), 132.8 (d), 135.2 (s), 154.4 ppm (s); IR (Nujol): $\tilde{\nu}$ = 3384 (NH), 3375 (NH), 3265 (NH), 1699 (C=O), 1660 cm^{-1} (C=O); elemental analysis calcd (%) for $C_{36}H_{51}N_7O_3$ (629.9): C 68.65, H 8.16, N 15.57; found: C 68.39, H 8.30, N 15.71.

Tris{2-[*N*′-(2,6-dimethylphenyl)ureido]benzyl}amine (3m): A mixture of tris(2-aminobenzyl)amine (**2a**) (0.13 g, 0.39 mmol) and 2,6-dimethylphenyl isocyanate (0.17 g, 1.18 mmol) was dissolved in dry DMF (15 mL) under N_2 and stirred at 80 °C for 10 h. After cooling, the reaction mixture was poured in H_2O (40 mL) and the white solid was filtered, washed with H_2O and subsequently with Et_2O to afford **3m** as colorless prisms in 77% yield. M.p. 246–248 °C; ^{1}H NMR (300 MHz, [D$_6$]DMSO, 25 °C, TMS, only monomer was observed): δ = 2.22 (s, 18H), 3.67 (s, 6H), 7.06 (m, 12H), 7.20 (t, ^3J(H,H) = 7.5 Hz, 3H), 7.54 (m, 3H), 7.64 (d, ^3J(H,H) = 8.1 Hz, 3H), 7.89 (s, 3H), 8.16 ppm (s, 3H); ^{1}H NMR (300 MHz, CDCl$_3$, 25 °C, TMS, only monomer was observed): δ = 2.09 (s, 18H), 3.64 (s, 6H), 6.24 (br s, 3H), 7.01–7.15 (m, 15H), 7.22–7.25 (m, 6H), 7.62 ppm (br s, 3H); ^{13}C NMR (75 MHz, [D$_6$]DMSO, 25 °C): δ = 18.2 (2 × q), 54.2 (t), 123.2 (d), 123.4 (d), 126.0 (d), 127.0 (d), 127.7 (2 × d), 128.4 (d), 129.5 (s), 135.3 (s), 135.6 (2 × s), 137.7 (s), 153.6 ppm (s); IR (Nujol): $\tilde{\nu}$ = 3273 (NH), 1634 cm^{-1} (C=O); MS (FAB$^+$): *m*/*z* (%): 774 (30) [M^++1], 253 (100), 132 (29); elemental analysis calcd (%) for $C_{48}H_{51}N_7O_3$ (774.0): C 74.49, H 6.64, N 12.67; found: C 74.19, H 6.95, N 12.57.

Tris[2-(methylthiocarbonylamino)benzyl]amine (4): *n*BuLi (1.6 M, 3.5 mL, 5.41 mmol) in hexane was added to a solution of tris(2-aminobenzyl)amine (**2a**) (0.30 g, 0.90 mmol) and hexamethyldisilazane (0.44 g, 2.71 mmol) in THF (10 mL) at −78 °C under N_2. The solution was stirred at −78 °C for 0.5 h, followed by addition of a solution of DMDTC (0.33 g, 2.71 mmol) in THF (5 mL). The solution was then allowed to react at 20 °C for 6 h. The reaction was quenched by pouring into ice–water. The crude product was extracted with CH_2Cl_2 (3 × 10 mL), washed with brine (3 × 10 mL), and dried over $MgSO_4$. After removal of the solvent (30 °C/75 Torr), Et_2O (15 mL) was added and the white solid was filtered and dried under vacuum to afford **4** in 99% yield as colorless prisms. M.p. 152–154 °C; ^{1}H NMR (200 MHz, CDCl$_3$, 25 °C, TMS): δ = 2.33 (s, 9H), 3.49 (s, 6H), 7.08–7.33 (m, 9H), 7.81–7.87 ppm (m, 6H); ^{13}C NMR (50 MHz, CDCl$_3$, 25 °C): δ = 12.8 (q), 57.2 (t), 124.1 (d), 125.3 (d), 127.7 (s), 129.0 (d), 131.5 (d), 136.5 (s), 167.4 ppm (s); IR (Nujol): $\tilde{\nu}$ = 3285 (NH), 1658 cm^{-1} (C=O); MS (FAB$^+$): *m*/*z* (%): 555 (20) [M^++1], 507 (37), 132 (100).

Tris[2-(*N*′-methylureido)benzyl]amine (3n): $MeNH_2$ (3.26 mmol, 0.31 g, 33 wt% in EtOH) was added to a solution of the tris(thiocarbamate) **4** in hot MeOH (25 mL) and the reaction mixture was stirred at reflux for 15 h. After removal of the solvent (30 °C/75 Torr) Et_2O (5 mL) was added. The white solid was filtered, washed with MeOH (3 × 2 mL), and dried under vacuum to afford **3n** as colorless prisms in 78% yield. M.p. 266–268 °C; ^{1}H NMR (401 MHz, [D$_6$]DMSO, 25 °C, TMS, only monomer was observed): δ = 2.58 (d, ^3J(H,H) = 4.5 Hz, 9H), 3.48 (s, 6H), 6.13 (q, ^3J(H,H) = 4.5 Hz, 3H), 7.00 (td, ^3J(H,H) = 7.5 Hz, ^4J(H,H) = 1.0 Hz, 3H), 7.16 (td, ^3J(H,H) = 7.7 Hz, ^4J(H,H) = 1.1 Hz, 3H), 7.40 (dd, ^3J(H,H) = 7.1 Hz, ^4J(H,H) = 0.9 Hz, 3H), 7.51 (dd, ^3J(H,H) = 8.0 Hz, ^4J(H,H) = 0.7 Hz, 3H), 7.72 ppm (s, 3H); ^{1}H NMR (401 MHz, $C_2D_2Cl_4$, 25 °C, TMS, only dimer was observed): δ = 1.85 (d, ^3J(H,H) = 4.5 Hz, 18H), 3.50 (d, ^2J(H,H) = 15.8 Hz, 6H), 3.68 (d, ^2J(H,H) = 15.8 Hz, 6H), 5.33 (q, ^3J(H,H) = 4.5 Hz, 6H), 7.25–7.29 (m, 18H), 7.43 (s, 6H), 7.98–8.00 ppm (m, 6H); ^{13}C NMR (101 MHz, [D$_6$]DMSO, 25 °C): δ = 26.3 (q), 54.3 (t), 123.0 (d), 123.3 (d), 127.1 (d), 129.2 (d), 129.3 (s), 138.0 (s), 156.2 ppm (s); ^{13}C NMR (101 MHz, $C_2D_2Cl_4$, 25 °C): δ = 26.2 (q), 53.4 (t), 126.4 (d), 126.5 (d), 126.7 (d), 128.6 (d), 134.7 (s), 135.5 (s), 158.3 ppm (s); IR (Nujol): $\tilde{\nu}$ = 3379 (NH), 3252 (NH), 1646 cm^{-1} (C=O); MS (FAB$^+$): *m*/*z* (%): 504 (20) [M^++1], 163 (83); elemental analysis calcd (%) for $C_{27}H_{33}N_7O_3$ (503.6): C 64.40, H 6.60, N 19.47; found: C 64.08, H 6.43, N 19.81.

2-Nitrobenzyl iodide: NaI (0.44 g, 2.90 mmol) was added to a solution of 2-nitrobenzyl chloride (0.25 g, 1.45 mmol) in dry acetone (5 mL) and the reaction mixture was stirred at 20 °C for 20 h. The solid was then filtered and washed with cold acetone (5 × 5 mL). The filtrate was collected, the solvent removed (30 °C/75 Torr), and the residue purified by silica gel chromatography eluting with 1:9 AcOEt/hexanes (R_f = 0.49) to afford the title compound as yellow prisms in 96% yield. M.p. 74–75 °C (lit.: 73–75 °C);[29] ^{1}H NMR (300 MHz, CDCl$_3$, 25 °C, TMS): δ = 4.79 (s, 2H), 7.41–7.59 (m, 3H), 8.03 ppm (d, ^3J(H,H) = 7.8 Hz, 1H); IR (Nujol): $\tilde{\nu}$ = 1520 (NO_2), 1340 (NO_2), 1171, 793, 759, 696 cm^{-1}.

Bis(2-nitrobenzyl)(2-azidobenzyl)amine (7): 2-Azidobenzylamine (1.60 g, 10.8 mmol) and 2-nitrobenzyl iodide (5.68 g, 21.6 mmol) in dry acetonitrile (2 and 5 mL, respectively) were added to a suspension of Na_2CO_3 (6.58 g, 62.1 mmol) in the same solvent (10 mL) and the reaction mixture was stirred at reflux for 24 h. After cooling, the inorganic salts were filtered and washed with cold acetonitrile (5 × 5 mL). The filtrate was collected, the solvent removed (30 °C/75 Torr), and the residue was purified by silica gel chromatography eluting with 1:9 AcOEt/hexanes (R_f = 0.21) to afford **7** as a yellow oil in 91% yield. ^{1}H NMR (200 MHz, CDCl$_3$, 25 °C, TMS): δ = 3.55 (s, 2H), 3.91 (s, 4H), 7.04–7.11 (m, 2H), 7.22–7.37 (m, 4H), 7.51 (td, ^3J(H,H) = 7.5 Hz, ^4J(H,H) = 1.3 Hz, 2H), 7.65 (dd, ^3J(H,H) = 7.7 Hz, ^4J(H,H) = 1.1 Hz, 2H), 7.78 ppm (dd, ^3J(H,H) = 8.0 Hz, ^4J(H,H) = 1.3 Hz, 2H); ^{13}C NMR (50 MHz, CDCl$_3$, 25 °C): δ = 54.2 (t), 55.6 (2 × t), 118.1 (d), 124.3 (2 × d), 124.6 (d), 127.9 (2 × d), 128.6 (s), 128.9 (d), 131.0 (2 × d), 131.4 (d), 132.6 (2 × d), 134.1 (2 × s), 138.9 (s), 149.6 ppm (2 × s); IR (neat): $\tilde{\nu}$ = 2131 (N_3), 1531 (NO_2), 1522, 1342 cm^{-1} (NO_2); MS (70 eV, EI): *m*/*z* (%): 420 (40) [M^++2], 419 (43) [M^++1], 418 (11) [M^+], 286 (66), 105 (100); elemental analysis calcd (%) for $C_{21}H_{18}N_6O_4$ (418.4): C 60.28, H 4.34, N 20.09; found: C 60.01, H 4.50, N 20.45.

Bis(2-nitrobenzyl)(2-aminobenzyl)amine (8): PMe_3 in toluene (1.0 M, 11.7 mL, 11.7 mmol) was slowly added at 0 °C to a solution of **7** (4.10 g, 9.8 mmol) in freshly distilled THF (30 mL) under N_2. The reaction mixture was then stirred at this temperature for 20–30 min. H_2O (15 mL) was added and the reaction mixture was stirred at 20 °C for a further 20 h. After removal of the organic solvent (30 °C/75 Torr), H_2O (40 mL) was added and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined extracts were dried over $MgSO_4$, the solvent evaporated (30 °C/75 Torr), and the residue purified by silica gel chromatography eluting with 1:4 AcOEt/hexanes (R_f = 0.16) to afford **8** (67–90% yield) as yellow prisms (an analytical sample was obtained by recrystallization from 1:4 CHCl$_3$/Et$_2$O). M.p. 96–99 °C; ^{1}H NMR (200 MHz, CDCl$_3$, 25 °C, TMS): δ = 3.55 (s, 2H), 3.85 (s, 4H), 4.13 (s, 2H), 6.53–6.65 (m, 2H), 6.98–7.06 (m, 2H), 7.22–7.31 (m, 2H), 7.37–7.48 (m, 4H), 7.66 ppm (dd, ^3J(H,H) = 8.1 Hz, ^4J(H,H) = 1.0 Hz, 2H); ^{13}C NMR (50 MHz, CDCl$_3$, 25 °C): δ = 56.3 (2 × t), 59.4 (t), 115.6 (d), 117.8 (d), 121.4 (s), 124.2 (2 × d), 128.2 (2 × d), 128.9 (d), 131.2 (d), 132.0 (2 × d), 132.6 (2 × d), 133.4 (2 × s), 146.5 (s), 149.7 ppm (2 × s); IR (Nujol): $\tilde{\nu}$ = 3486 (NH), 3390 (NH), 1623, 1522 (NO_2), 1340 cm^{-1} (NO_2); MS (70 eV, EI): *m*/*z* (%): 393 (42) [M^++1], 375 (39), 286 (47), 257 (82), 120 (100); HRMS (EI): *m*/*z*: calcd for $C_{21}H_{20}N_4O_4$: 392.148455, found 392.148647.

Bis(2-nitrobenzyl){2-[*N*′-(4-butylphenyl)ureido]benzyl}amine (9a): 4-Butylphenyl isocyanate (0.22 g, 1.3 mmol) was added to a solution of **8** (0.50 g, 1.3 mmol) in dry CH_2Cl_2 (35 mL) under N_2. After stirring at 20 °C for 24 h the solvent was removed (30 °C/75 Torr) and the residue was purified by silica gel chromatography eluting with 1:4 AcOEt/hexanes (R_f = 0.21) to afford **9a** (98% yield) as yellow prisms (an analytical sample was obtained by recrystallization from 1:3 CHCl$_3$/Et$_2$O). M.p. 68–70 °C; ^{1}H NMR (401 MHz, CDCl$_3$, 25 °C, TMS): δ = 0.93 (t, ^3J(H,H) = 7.3 Hz, 3H), 1.36 (m, ^3J(H,H) = 7.4 Hz, 2H), 1.56–1.63 (m, 2H), 2.59 (t, ^3J(H,H) = 7.7 Hz, 2H), 3.74 (s, 2H), 3.94 (s, 4H), 6.90 (td, ^3J(H,H) = 7.4 Hz, ^4J(H,H) = 0.9 Hz, 1H), 7.10–7.24 (m, 8H), 7.38 (td, ^3J(H,H) = 7.5 Hz, ^4J(H,H) = 1.1 Hz, 2H), 7.52 (d, ^3J(H,H) = 8.4 Hz, 2H), 7.60 (dd, ^3J(H,H) = 8.1 Hz, ^4J(H,H) = 1.0 Hz, 2H), 7.72 (s, 1H), 7.83 (s, 1H), 8.00 ppm (d, ^3J(H,H) = 8.1 Hz, 1H); ^{13}C NMR (101 MHz, CDCl$_3$, 25 °C): δ = 14.0 (q), 22.4 (t), 33.9 (t), 35.1 (t), 57.6 (2 × t), 61.4 (t), 119.3 (2 × d), 121.6 (d), 122.6 (d), 124.5 (2 × d), 125.1 (s), 128.4 (2 × d), 128.9 (2 × d), 129.1 (d), 131.0 (d), 132.1 (2 × d), 133.4 (2 × d), 133.5 (2 × s), 137.0 (s), 137.4 (s), 138.7 (s), 148.8 (2 × s), 152.7 ppm (s); IR (Nujol): $\tilde{\nu}$ = 3384 (NH), 1702 (C=O), 1593, 1528 (NO_2), 1345 cm^{-1} (NO_2); MS (FAB$^+$): *m*/*z*

(%): 568 (65) [$M^+ + 1$], 567 (11) [M^+], 281 (92), 279 (42), 106 (100); elemental analysis calcd (%) for $C_{32}H_{33}N_5O_5$ (567.7): C 67.71, H 5.86, N 12.34; found: C 67.36, H 5.90, N 12.41.

Bis(2-nitrobenzyl){2-[*N'*-(4-methoxyphenyl)ureido]benzyl}amine (9b): 4-Methoxyphenyl isocyanate (0.19 g, 1.3 mmol) was added to a solution of **8** (0.50 g, 1.3 mmol) in dry CH_2Cl_2 (35 mL) under N_2. After stirring at 20 °C for 24 h the solvent was removed (30 °C/75 Torr) and the residue was purified by silica gel chromatography eluting first with 3:7 and subsequently with 1:1 AcOEt/hexanes (R_f = 0.24 in 3:7 AcOEt/hexanes) to afford **9b** (98% yield) as colorless prisms (an analytical sample was obtained by recrystallization from 1:3 CH_2Cl_2/Et_2O). M.p. 170–172 °C; ^{1}H NMR (300 MHz, [D$_6$]DMSO, 25 °C): δ = 3.62 (s, 2H), 3.70 (s, 3H), 3.86 (s, 4H), 6.87 (d, ^3J(H,H) = 9.3 Hz, 2H), 7.03 (t, ^3J(H,H) = 7.2 Hz, 1H), 7.18 (t, ^3J(H,H) = 7.2 Hz, 1H), 7.35–7.44 (m, 5H), 7.55–7.62 (m, 3H), 7.75 (d, ^3J(H,H) = 7.5 Hz, 2H), 7.83 (d, ^3J(H,H) = 7.8 Hz, 2H), 7.92 (s, 1H), 8.62 ppm (s, 1H); ^{13}C NMR (75 MHz, [D$_6$]DMSO, 25 °C): δ = 54.5 (2×t), 54.8 (t), 55.1 (q), 114.0 (2×d), 120.1 (2×d), 123.1 (d), 123.4 (d), 124.1 (2×d), 127.3 (d), 128.3 (2×d), 129.0 (d), 129.2 (s), 130.6 (2×d), 132.8 (s), 132.9 (2×d + 2×s), 137.5 (s), 149.1 (2×s), 153.0 (s), 154.5 ppm (s); IR (Nujol): $\tilde{\nu}$ = 3386 (NH), 3329 (NH), 1706 (C=O), 1651, 1531 (NO_2), 1349 cm^{-1} (NO_2); MS (FAB$^+$): *m/z* (%): 542 (100) [$M^+ + 1$], 407 (41), 255 (92), 132 (82); elemental analysis calcd (%) for $C_{29}H_{27}N_5O_6$ (541.6): C 64.32, H 5.03, N 12.93; found: C 64.29, H 4.91, N 12.99.

Bis(2-aminobenzyl){2-[*N'*-(4-butylphenyl)ureido]benzyl}amine (10a): PtO_2 (0.28 g, 1.2 mmol) was added to a solution of **9a** (0.59 g, 1.0 mmol) in freshly distilled THF (35 mL) and the reaction mixture was stirred at 20 °C for 22 h under H_2. After filtration over a pad of Celite, the solvent was removed (30 °C/75 Torr) and Et_2O (5 mL) was added. The white solid was filtered, dried under vacuum, and purified by silica gel chromatography eluting with 1:3 AcOEt/hexanes (R_f = 0.46) to afford **10a** (74% yield) as colorless prisms (an analytical sample was obtained by recrystallization from 1:3 $CHCl_3$/Et_2O). M.p. 94–96 °C; ^{1}H NMR (401 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.93 (t, ^3J(H,H) = 7.3 Hz, 3H), 1.36 (m, ^3J(H,H) = 7.4 Hz, 2H), 1.55–1.63 (m, 2H), 2.58 (t, ^3J(H,H) = 7.7 Hz, 2H), 3.45 (s, 4H), 3.55 (s, 2H), 3.88 (s, 4H), 6.66 (d, ^3J(H,H) = 7.8 Hz, 2H), 6.76 (t, ^3J(H,H) = 7.3 Hz, 2H), 6.94 (t, ^3J(H,H) = 7.1 Hz, 1H), 7.08–7.17 (m, 7H), 7.25–7.28 (m, 1H), 7.39 (d, ^3J(H,H) = 8.3 Hz, 2H), 8.19 (d, ^3J(H,H) = 8.1 Hz, 1H), 8.31 (s, 1H), 8.62 ppm (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ = 14.1 (q), 22.4 (t), 33.9 (t), 35.1 (t), 57.0 (2×t), 58.4 (t), 116.8 (2×d), 119.39 (2×d), 119.43 (2×d), 120.7 (d), 122.1 (2×s), 122.2 (d), 124.9 (s), 128.9 (2×d), 129.0 (d), 129.5 (2×d), 131.1 (d), 132.5 (2×d), 137.1 (s), 137.3 (s), 138.4 (s), 144.4 (2×s), 152.9 ppm (s); IR (Nujol): $\tilde{\nu}$ = 3375 (NH), 3318 (NH), 3252 (NH), 1692 cm^{-1} (C=O); MS (FAB$^+$): *m/z* (%): 508 (14) [$M^+ + 1$], 403 (10), 279 (16), 106 (100); elemental analysis calcd (%) for $C_{32}H_{37}N_5O$ (507.7): C 75.71, H 7.35, N 13.79; found: C 75.34, H 7.57, N 13.83.

Bis(2-aminobenzyl){2-[*N'*-(4-methoxyphenyl)ureido]benzyl}amine (10b): PtO_2 (0.29 g, 1.3 mmol) was added to a solution of **9b** (0.58 g, 1.1 mmol) in freshly distilled THF (35 mL) and the reaction mixture was stirred at 20 °C for 18 h under H_2. After filtration over a pad of Celite, the solvent was removed (30 °C/75 Torr) and Et_2O (5 mL) was added. The white solid was filtered, dried under vacuum, and purified by silica gel chromatography eluting first with 1:3 and subsequently with 1:1 AcOEt/hexanes (R_f = 0.21 in 1:3 AcOEt/hexanes) to afford **10b** (84% yield) as colorless prisms (an analytical sample was obtained by recrystallization from 1:1 $CHCl_3$/Et_2O). M.p. 199–201 °C; ^{1}H NMR (401 MHz, $CDCl_3$, 25 °C, TMS): δ = 3.47 (s, 4H), 3.57 (s, 2H), 3.80 (s, 3H), 3.87 (s, 4H), 6.66 (d, ^3J(H,H) = 7.7 Hz, 2H), 6.76 (td, ^3J(H,H) = 7.4 Hz, ^4J(H,H) = 1.0 Hz, 2H), 6.88 (d, ^3J(H,H) = 9.0 Hz, 2H), 6.95 (td, ^3J(H,H) = 7.4 Hz, ^4J(H,H) = 1.1 Hz, 1H), 7.08–7.12 (m, 4H), 7.17 (dd, ^3J(H,H) = 7.5 Hz, ^4J(H,H) = 1.3 Hz, 1H), 7.25–7.29 (m, 1H), 7.37 (d, ^3J(H,H) = 9.0 Hz, 2H), 8.17 (dd, ^3J(H,H) = 8.2 Hz, ^4J(H,H) = 0.8 Hz, 1H), 8.26 (s, 1H), 8.40 ppm (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ = 55.6 (q), 57.0 (2×t), 58.4 (t), 114.3 (2×d), 116.8 (2×d), 119.5 (2×d), 120.8 (d), 121.4 (2×d), 122.16 (2×s), 122.24 (d), 125.0 (s), 129.0 (d), 129.5 (2×d), 131.1 (d), 132.56 (s), 132.57 (2×d), 138.5 (s), 144.5 (2×s), 153.1 (s), 155.5 ppm (s); IR (Nujol): $\tilde{\nu}$ = 3379 (NH), 3306 (NH), 3272 (NH), 1688 cm^{-1} (C=O); MS (FAB$^+$): *m/z* (%): 482 (31) [$M^+ + 1$], 375 (16), 253 (23), 106 (100); elemental analysis calcd (%) for $C_{29}H_{31}N_5O_2$ (481.6): C 72.33, H 6.49, N 14.54; found: C 72.35, H 6.10, N 14.68.

Bis(2-{*N'*-[4-(trifluoromethyl)phenyl]ureido}benzyl){2-[*N'*-(4-butylphenyl)-ureido]benzyl}amine (6a): 4-Trifluoromethylphenyl isocyanate (0.09 g, 0.48 mmol) was added to a solution of **10a** (0.12 g, 0.24 mmol) in dry CH_2Cl_2 (8 mL) under N_2. After stirring at 20 °C for 16 h the solvent was removed (30 °C/75 Torr) and Et_2O (5 mL) was added. The white solid was filtered and dried under vacuum to afford **6a** (43% yield) as colorless prisms (an analytical sample was obtained by recrystallization from 1:3 $CHCl_3$/*n*-pentane). M.p. 243–247 °C; ^{1}H NMR (200 MHz, [D$_6$]DMSO, 25 °C): δ = 0.83 (t, ^3J(H,H) = 7.1 Hz, 3H), 1.23 (m, ^3J(H,H) = 7.2 Hz, 2H), 1.46 (m, ^3J(H,H) = 7.1 Hz, 2H), 2.45 (m, 2H), 3.60 (s, 6H), 6.98–7.16 (m, 8H), 7.28 (d, ^3J(H,H) = 8.0 Hz, 2H), 7.52–7.56 (m, 14H), 7.92 (s, 1H), 8.04 (s, 2H), 8.64 (s, 1H), 9.15 ppm (s, 2H); ^{13}C NMR (50 MHz, [D$_6$]DMSO, 25 °C): δ = 13.8, 21.7, 33.3, 34.2, 54.3, 117.8, 118.4, 121.7 (2×q, ^2J(C,F) = 31.9 Hz), 123.9, 124.2, 124.3, 124.6 (2×q, ^1J(C,F) = 270.8 Hz), 126.1 (4×dq, ^3J(C,F) = 3.7 Hz), 127.2, 128.5, 128.7, 130.3, 130.6, 135.7, 136.6, 137.0, 137.3, 143.5, 152.8, 153.3 ppm (four signals are overlapped); ^{19}F NMR (188 MHz, [D$_6$]DMSO, 25 °C): δ = −59.6 ppm; IR (Nujol): $\tilde{\nu}$ = 3331 (NH), 1667 cm^{-1} (C=O); MS (FAB$^+$): *m/z* (%): 882 (53) [$M^+ + 1$], 293 (48), 281 (34), 132 (100); 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 64.97, H 5.51, N 10.97.

Bis{2-[*N'*-(4-fluorophenyl)ureido]benzyl}{2-[*N'*-(4-butylphenyl)ureido]-benzyl}amine (6b): 4-Fluorophenyl isocyanate (0.07 g, 0.48 mmol) was added to a solution of **10a** (0.12 g, 0.24 mmol) in dry CH_2Cl_2 (8 mL) under N_2. After stirring at 20 °C for 16 h the solvent was removed (30 °C/75 Torr) and Et_2O (5 mL) was added. The white solid was filtered and dried under vacuum to afford **6b** (90% yield) as colorless prisms (an analytical sample was obtained by recrystallization from 1:1 $CHCl_3$/Et_2O). M.p. 229–231 °C; ^{1}H NMR (200 MHz, [D$_6$]DMSO, 25 °C): δ = 0.84 (t, ^3J(H,H) = 7.1 Hz, 3H), 1.24 (m, ^3J(H,H) = 7.2 Hz, 2H), 1.47 (m, ^3J(H,H) = 7.3 Hz, 2H), 2.45 (t, ^3J(H,H) = 7.2 Hz, 2H), 3.61 (s, 6H), 7.00–7.16 (m, 12H), 7.30 (d, ^3J(H,H) = 8.2 Hz, 2H), 7.37–7.44 (m, 4H), 7.51–7.55 (m, 6H), 7.92 (s, 3H), 8.66 (s, 1H), 8.80 ppm (s, 2H); ^{13}C NMR (50 MHz, [D$_6$]DMSO, 25 °C): δ = 13.8, 21.7, 33.3, 34.2, 54.4, 115.3 (4×dd, ^2J(C,F) = 22.2 Hz), 118.3, 119.9 (4×dd, ^3J(C,F) = 7.7 Hz), 123.8, 123.9, 124.0, 127.1, 128.5, 128.6, 130.1, 130.2, 135.7, 136.1 (2×d, ^4J(C,F) = 2.3 Hz), 136.9, 137.1, 137.4, 153.15, 153.17, 157.3 ppm (2×d, ^1J(C,F) = 238.1 Hz) (four signals are overlapped); ^{19}F NMR (188 MHz, [D$_6$]DMSO, 25 °C): δ = −121.8 ppm; IR (Nujol): $\tilde{\nu}$ = 3320 (NH), 1654 cm^{-1} (C=O); MS (FAB$^+$): *m/z* (%): 782 (16) [$M^+ + 1$], 243 (17); elemental analysis calcd (%) for $C_{46}H_{45}F_2N_7O_3$ (781.9): C 70.66, H 5.80, N 12.54; found: C 70.27, H 6.20, N 12.58.

Bis(2-{*N'*-[4-(trifluoromethyl)phenyl]ureido}benzyl){2-[*N'*-(4-methoxy-phenyl)ureido]benzyl}amine (6c): 4-Trifluoromethylphenyl isocyanate (0.09 g. 0.50 mmol) was added to a solution of **10b** (0.12 g; 0.25 mmol) in dry CH_2Cl_2 (15 mL) under N_2. After stirring at 20 °C for 16 h the solvent was removed (30 °C/75 Torr) and Et_2O (5 mL) was added. The white solid was filtered and dried under vacuum to afford **6c** (44% yield) as colorless prisms (an analytical sample was obtained by recrystallization from 1:3 $CHCl_3$/Et_2O). M.p. 227–232 °C; ^{1}H NMR (300 MHz, [D$_6$]DMSO, 25 °C): δ = 3.66 (s, 6H), 3.69 (s, 3H), 6.85 (d, ^3J(H,H) = 8.7 Hz, 2H), 7.00–7.20 (m, 6H), 7.35 (d, ^3J(H,H) = 8.7 Hz, 2H), 7.54–7.65 (m, 14H), 7.94 (s, 1H), 8.10 (s, 2H), 8.63 (s, 1H), 9.21 ppm (s, 2H); ^{13}C NMR (75 MHz, [D$_6$]DMSO, 25 °C): δ = 54.5, 54.6, 55.2, 114.0, 117.9, 120.3, 121.8 (2×q, ^2J(C,F) = 32.0 Hz), 123.9, 124.3, 124.5, 124.6 (2×q, ^1J(C,F) = 271.0 Hz), 126.0 (4×dq, ^3J(C,F) = 3.0 Hz), 127.3, 129.25, 129.34, 130.5, 130.8, 132.7, 136.7, 137.2, 143.5, 153.0, 153.7, 154.6 ppm (two signals are overlapped); ^{19}F NMR (188 MHz, [D$_6$]DMSO, 25 °C): δ = −59.8 ppm; IR (Nujol): $\tilde{\nu}$ = 3327 (NH), 1666 cm^{-1} (C=O); MS (FAB$^+$): *m/z* (%): 856 (46) [$M^+ + 1$], 293 (52), 255 (46), 131 (100); elemental analysis calcd (%) for $C_{45}H_{39}F_6N_7O_4$ (855.8): C 63.15, H 4.59, N 11.46; found: C 62.77, H 4.89, N 11.45.

Bis{2-[*N'*-(4-fluorophenyl)ureido]benzyl}{2-[*N'*-(4-methoxyphenyl)urei-do]benzyl}amine (6d): 4-Fluorophenyl isocyanate (0.07 g, 0.50 mmol) was added to a solution of **10b** (0.12 g, 0.25 mmol) in dry CH_2Cl_2 (8 mL) under N_2. After stirring at 20 °C for 18 h the solvent was removed (30 °C/75 Torr) and Et_2O (5 mL) was added. The white solid was filtered and dried under vacuum to afford **6d** (91% yield) as colorless prisms. M.p. 246–254 °C; ^{1}H NMR (401 MHz, [D$_6$]DMSO, 25 °C): δ = 3.60 (s, 6H), 3.69 (s, 3H), 6.82 (d, ^3J(H,H) = 9.1 Hz, 2H), 6.97–7.16 (m, 10H), 7.30 (d, ^3J(H,H) = 9.0 Hz, 2H), 7.38–7.41 (m, 4H), 7.48–7.51 (m, 6H), 7.85 (s,

1H), 7.90 (s, 2H), 8.55 (s, 1H), 8.76 ppm (s, 2H); ^{13}C NMR (101 MHz, [D$_6$]DMSO, 25°C): δ = 54.5, 54.6, 55.2, 114.0, 115.2 (4×dd, ^2J(C,F) = 22.2 Hz), 120.0 (4×dd, ^3J(C,F) = 7.6 Hz), 120.2, 123.8, 124.0, 124.2, 124.3, 127.2, 129.2, 130.2, 130.4, 132.7, 136.1 (2×d, ^4J(C,F) = 2.1 Hz), 137.0, 137.2, 153.3, 153.5, 154.5, 157.3 ppm (2×d, ^1J(C,F) = 238.1 Hz) (two signals are overlapped); ^{19}F NMR (188 MHz, [D$_6$]DMSO, 25°C): δ = −121.1 ppm; IR (Nujol): $\tilde{\nu}$ = 3321 (NH), 1657 cm^{-1} (C=O); MS (FAB$^+$): *m*/*z* (%): 756 (10) [*M*$^+$+1], 255 (37), 243 (53), 132 (100); elemental analysis calcd (%) for $C_{43}H_{39}F_2N_7O_4 \times 0.5\,H_2O$ (784.8): C 67.53, H 5.27, N 12.82; found: C 66.98, H 5.42, N 12.69.

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[1] J.-M. Lehn, *Supramolecular Chemistry: Concepts and Perspectives*, VCH, Weinheim, **1995**, pp. 11–13.

[2] a) M. Alajarín, P. Molina, A. López-Lázaro, C. Foces-Foces, *Angew. Chem.* **1997**, *109*, 147–150; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 67–70; b) M. Alajarín, A. López-Lázaro, A. Vidal, J. Berná, *Chem. Eur. J.* **1998**, *4*, 2558–2570; c) M. Alajarín, A. Vidal, C. López-Leonardo, J. Berná, M. C. Ramírez de Arellano, *Tetrahedron Lett.* **1998**, *39*, 7807–7810; d) M. Alajarín, C. López-Leonardo, A. Vidal, J. Berná, J. W. Steed, *Angew. Chem.* **2002**, *114*, 1253–1256; *Angew. Chem. Int. Ed.* **2002**, *41*, 1205–1208.

[3] a) M. C. Etter, Z. Urbañczyk-Lipkowska, M. Zia-Ebrahimi, T. W. Panunto, *J. Am. Chem. Soc.* **1990**, *112*, 8415–8426; b) X. Zhao, Y.-L. Chang, F. W. Fowler, J. W. Lauher, *J. Am. Chem. Soc.* **1990**, *112*, 6627–6634; c) J. S. Nowick, V. Antonovich, G. Noronha, J. W. Ziller, *J. Org. Chem.* **1995**, *60*, 1888–1890; d) J. J. Kane, R.-F. Liao, J. W. Lauher, F. W. Fowler, *J. Am. Chem. Soc.* **1995**, *117*, 12003–12004; e) Y. Tobe, S. Sasaki, M. Mizuno, K. Hirose, K. Naemura, *J. Org. Chem.* **1998**, *63*, 7481–7489; f) S. Pulacchini, I. Abrahams, J. Eames, M. Watkinson, *Supramol. Chem.* **2002**, *14*, 353–357.

[4] M. Alajarín, A. López-Lázaro, A. Pastor, P. D. Prince, J. W. Steed, R. Arakawa, *Chem. Commun.* **2001**, 169–170.

[5] a) B. C. Hamann, K. D. Shimizu, J. Rebek, Jr. *Angew. Chem.* **1996**, *108*, 1425–1427; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1326–1329; b) R. K. Castellano, B. H. Kim, J. Rebek, Jr. *J. Am. Chem. Soc.* **1997**, *119*, 12671–12672; c) R. K. Castellano, C. Nuckolls, J. Rebek, Jr. *J. Am. Chem. Soc.* **1999**, *121*, 11156–11163; d) J. Rebek, Jr. *Chem. Commun.* **2000**, 637–643.

[6] a) O. Mogck, V. Böhmer, W. Vogt, *Tetrahedron* **1996**, *52*, 8489–8496; b) M. O. Vysotsky, V. Böhmer, *Org. Lett.* **2000**, *2*, 3571–3574; c) M. O. Vysotsky, I. Thondorf, V. Böhmer, *Angew. Chem.* **2000**, *112*, 1309–1312; *Angew. Chem. Int. Ed.* **2000**, *39*, 1264–1267; d) M. O. Vysotsky, A. Pop, F. Broda, I. Thondorf, V. Böhmer, *Chem. Eur. J.* **2001**, *7*, 4403–4410.

[7] a) J. J. González, R. Ferdani, E. Albertini, J. M. Blasco, A. Arduini, A. Pochini, P. Prados, J. de Mendoza, *Chem. Eur. J.* **2000**, *6*, 73–80; b) A. M. Rincón, P. Prados, J. de Mendoza, *J. Am. Chem. Soc.* **2001**, *123*, 3493–3498.

[8] a) J.-L. Lai, M.-k. Leung, G. H. Lee, *J. Org. Chem.* **1996**, *61*, 8364–8365; b) C.-F. Liao, J.-L. Lai, J.-A. Chen, H.-T. Chen, H.-L. Cheng, G.-R. Her, J.-K. Su, Y. Wang, G. H. Lee, M.-K. Leung, *J. Org. Chem.* **2001**, *66*, 2566–2571.

[9] CCDC-219431 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44)1223-1336-1033; or e-mail: deposit@ccdc.cam.ac.uk).

[10] a) M. Kitamura, S. Okada, S. Suga, R. Noyori, *J. Am. Chem. Soc.* **1989**, *111*, 4028–4036; b) T. W. Kim, M. S. Lah, J.-I. Hong, *Chem. Commun.* **2001**, 743–744; c) Z. Zhong, A. Ikeda, S. Shinkai, S. Sakamoto, K. Yamaguchi, *Org. Lett.* **2001**, *3*, 1085–1087; d) C. G. Claessens, T. Torres, *J. Am. Chem. Soc.* **2002**, *124*, 14522–14523; e) I. Alkorta, J. Elguero, *J. Am. Chem. Soc.* **2002**, *124*, 1488–1493.

[11] a) K. D. Shimizu, J. Rebek, Jr. *Proc. Natl. Acad. Sci. USA* **1995**, *92*, 12403–12407; b) R. K. Castellano, D. M. Rudkevich, J. Rebek, Jr. *J. Am. Chem. Soc.* **1996**, *118*, 10002–10003.

[12] a) J. Scheerder, R. H. Vreekamp, J. F. J. Engbersen, W. Verboom, J. P. M. van Duynhoven, D. N. Reinhoudt, *J. Org. Chem.* **1996**, *61*, 3476–3481; b) J. Dormann, A. Ruoff, J. Schatz, M. O. Vysotsky, V. Böhmer, *J. Chem. Soc. Perkin Trans. 2* **2002**, 83–87.

[13] a) M. Scherer, J. L. Sessler, M. Moini, A. Gebauer, V. Lynch, *Chem. Eur. J.* **1998**, *4*, 152–158; b) S. A. Hofstadler, R. H. Griffey, *Chem. Rev.* **2001**, *101*, 377–390.

[14] K. C. Russell, E. Leize, A. Van Dorsselaer, J.-M. Lehn, *Angew. Chem.* **1995**, *107*, 244–248; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 209–213.

[15] X. Cheng, Q. Gao, R. D. Smith, E. E. Simanek, M. Mammen, G. M. Whitesides, *J. Org. Chem.* **1996**, *61*, 2204–2206.

[16] a) K. A. Jolliffe, M. Crego Calama, R. Fokkens, N. M. M. Nibbering, P. Timmerman, D. N. Reindhoudt, *Angew. Chem.* **1998**, *110*, 1294–1297; *Angew. Chem. Int. Ed.* **1998**, *37*, 1247–1251; b) P. Timmerman, K. A. Jolliffe, M. Crego Calama, J.-L. Weidmann, L. J. Prins, F. Cardullo, B. H. M. Snellink-Ruël, R. H. Fokkens, N. M. M. Nibbering, S. Shinkai, D. N. Reindhoudt, *Chem. Eur. J.* **2000**, *6*, 4104–4115.

[17] a) C. A. Schalley, J. M. Rivera, T. Martín, J. Santamaría, G. Siuzdak, J. Rebek, Jr. *Eur. J. Org. Chem.* **1999**, 1325–1331; b) C. A. Schalley, T. Martín, U. Obst, J. Rebek, Jr. *J. Am. Chem. Soc.* **1999**, *121*, 2133–2138; c) C. A. Schalley, R. K. Castellano, M. S. Brody, D. M. Rudkevich, G. Siuzdak, J. Rebek, Jr. *J. Am. Chem. Soc.* **1999**, *121*, 4568–4579.

[18] a) R. S. Meissner, J. Rebek, Jr. J. de Mendoza, *Science* **1995**, *270*, 1485–1488; b) R. Meissner, X. Garcias, S. Mecozzi, J. Rebek, Jr. *J. Am. Chem. Soc.* **1997**, *119*, 77–85.

[19] M. Alajarín, A. Pastor, R.-A. Orenes, J. W. Steed, *J. Org. Chem.* **2002**, *67*, 7091–7095.

[20] D. J. Cram, H.-J. Choi, J. A. Bryant, C. B. Knobler, *J. Am. Chem. Soc.* **1992**, *114*, 7748–7765.

[21] The values obtained for the X-ray structure of **3d·3d** were extrapolated to the dimer **3a·3a**.

[22] a) A. Wu, A. Chakraborty, J. C. Fettinger, R. A. Flowers II, L. Isaacs, *Angew. Chem.* **2002**, *114*, 4200–4203; *Angew. Chem. Int. Ed.* **2002**, *41*, 4028–4031; b) A. Wu, L. Isaacs, *J. Am. Chem. Soc.* **2003**, *125*, 4831–4835.

[23] G. Cooke, V. M. Rotello, *Chem. Soc. Rev.* **2002**, *31*, 275–286.

[24] A. Pop, M. O. Vysotsky, M. Saadioui, V. Böhmer, *Chem. Commun.* **2003**, 1124–1125.

[25] G. M. Sheldrick, SHELXL-97, Program for the Solution of Crystal Structures, University of Göttingen, Göttingen (Germany), **1997**.

[26] L. J. Barbour, XSeed, Program of the Manipulation and Display of Crystallographic Models, University of Missouri (Columbia), **1999**.

[27] P. v. d. Sluis, A. L. Spek, *Acta Crystallogr.* **1990**, *A46*, 194.

[28] M.-k. Leung, J.-L. Lai, K.-H. Lau, H.-h. Yu, H.-J. Hsiao, *J. Org. Chem.* **1996**, *61*, 4175–4179.

[29] G. H. Daub, R. N. Castle, *J. Org. Chem.* **1954**, *19*, 1571–1574.

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