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Dimeric Self-Assembling Capsules Derived from the Highly Flexible Tribenzylamine Skeleton†

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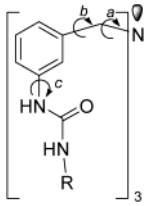
Tris(*m*-ureidobenzyl)amines dimerize both in solid state and in solution to give molecular capsules which are able to encapsulate small molecules. The self-assembly was confirmed by crystal X-ray analysis and NMR spectroscopy. The X-ray structure showed the encapsulation of one molecule of CH_2Cl_2. This new type of capsules presents a propeller-like topology and a belt of six hydrogen-bonded ureas. Encapsulation studies in solution and heterodimerization processes are also disclosed.

Introduction

The fascinating world of the molecule-within-molecule complexes (molecular capsules) is one of the most attractive fields in supramolecular chemistry, not only because of the need of significant creativity to design the final target but because of their great number of direct applications.[1] If these applications are to expand, the accessibility of the capsules, especially with regard to more diverse shapes, must improve. In particular, self-assembling capsules are formed by self-complementary units held together by reversible noncovalent interactions, of which hydrogen bonding is the favorite by virtue of its directionality, specificity, and biological relevance.[2] These self-complementary units are generally based on conformationally restricted systems such as calixarenes,[3] resorcinarenes,[4] or glycoluryl[5] derivatives.

In a previous communication,[6] we reported on the self-assembly of tris(*o*-ureidobenzyl)amines. These tris(ureas) associate forming dimeric aggregates in which two monomers interact by intercalation of their arms, forming a belt of six hydrogen-bonded ureas. Crystal X-ray analysis showed that the dimers exist as "empty" capsules probably due to their small internal cavities. This pattern of self-assembly is well-known for the poliureidocalixarenes studied by Rebek,[7] Böhmer,[8] and de Mendoza.[9] However, a particular value of our new type of capsules is that no guest is needed for the nucleation of the assembly, in stark contrast to the ureidocalixarenes capsules previously described.

Following our investigations directed toward the design of new self-assembling capsules based on the tribenzylamine skeleton, we decided to synthesize the structurally related tris(*m*-ureidobenzyl)amines. We took into account that tris(*m*-ureidobenzyl)amines have all the structural and functional features necessary for self-assembly like their *ortho* counterparts, but they should form dimers with larger internal cavities. Both types of subunit *ortho* and *meta* share a highly flexible skeleton. Thus, at least twelve rotations per dimer considering bonds *a* and *b* (eighteen taking into account bonds *a*, *b*, and *c*) and the inversion of the pivotal nitrogen atom must be restricted in the assemblies.



Results and Discussion

The readily available tris(*m*-azidobenzyl)amine[10] **1** (Scheme 1) was converted into the tris(amine) **2** by reduction with $LiAlH_4$ (LAH) in 74% of yield. Tris(*m*-

† Dedicated to Professor Waldemar Adam on the occasion of his 65th birthday.

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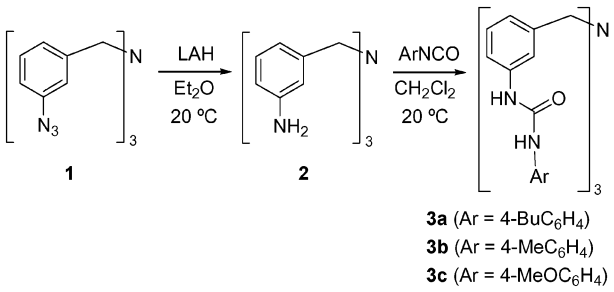
SCHEME 1



ureidobenzyl)amines **3a**−**c** were obtained from **2** by treatment with the corresponding isocyanate in yields ranging 89−98%.

As it was expected, the single-crystal X-ray analysis[11,12] of the tris(urea) **3a** showed the existence of a hydrogen-bonded dimer entangled by a belt of six hydrogen-bonded ureas in a head-to-tail manner (Figure 1), analogously to the structurally related tris(*o*-ureidobenzyl)amines.[6] In agreement with our initial predictions, the dimer is large enough to include in its cavity an ordered molecule of CH_2Cl_2 (the distance between the two pivotal nitrogen atoms in the dimer is 9.671/9.896 Å (two independent pairs), significantly larger than the *ortho* analogue: 5.511 Å[6]). There are two unique capsules in the crystal lattice and each half is related to the other half by a near-perfect inversion symmetry (broken by the guest molecules themselves and one *n*-butyl side chain in one capsule and implying the space group is actually P1[12]). Such guest ordering within an essentially symmetric capsule is remarkable and implies a degree of guest−guest interactions from one capsule to the next.

Every capsule is formed by two enantiomeric tripods turned 59−61° with respect to each other resulting on an approximate S_6 symmetry for the dimeric core. Observed along the C_3 axis the dimer shows its peculiar propeller-like topology. The distance N···O═C (2.88−3.00 Å) for the urea nitrogen atoms bearing the pendant 4-(*n*-butyl)phenyl substituents is shorter than the distance N···O═C (3.03−3.38 Å) for the urea nitrogen atoms attached to the tribenzylamine skeleton, implying a rather unsymmetric six-membered hydrogen bonded ring, also unlike the *ortho* analogue.[6] All these data turned to be especially valuable due to the fact that only a very few number of self-assembling capsules have been characterized in solid state by X-ray analysis.

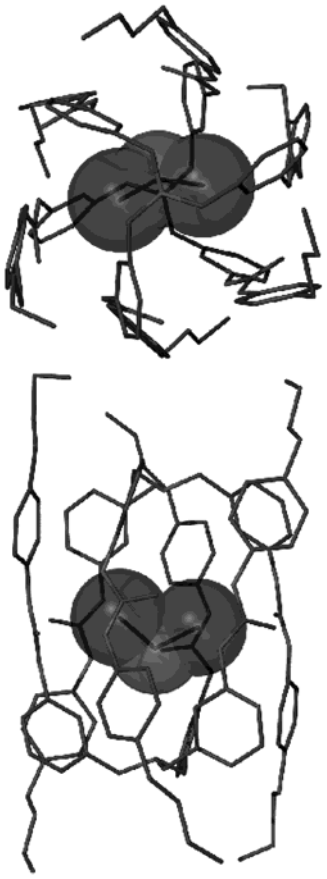


FIGURE 1. Crystal structure of the tris(urea) dimer **3a**·**3a** (top and axial view) showing the self-assembling capsule with one enclosed molecule of CH_2Cl_2.

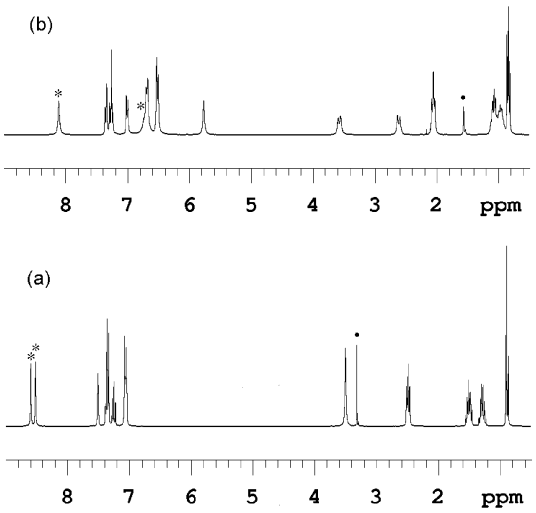


FIGURE 2. (a) ^{1}H NMR spectrum (300 MHz) of the tris(urea) **3a** measured in DMSO-d_6; (b) ^{1}H NMR spectrum (300 MHz) measured in $CDCl_3$ showing the dimer **3a**·**3a**; (●) signal for residual water; (*) peaks corresponding to NH resonances

In regard to the solution behavior of tris(ureas) **3a**−**c**, they showed dramatic differences in their ^{1}H NMR spectra when recorded in $CDCl_3$, CD_2Cl_2, and C_6D_6 compared to the competitive solvent DMSO-d_6 (Figure 2). While the spectra of **3a**−**c** in DMSO-d_6 displayed the expected patterns for the monomers **3** (Figure 2a) con-

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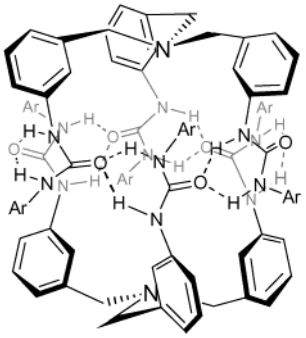
(11) Diffraction quality crystals were obtained from **3a** by recrystallization from CH_2Cl_2/Et_2O.

(12) Crystallographic data for **3a**·CH_2Cl_2·**3a**: Formula $C_{54.5}H_{64}ClN_7O_3$, triclinic crystal, space group P1, a = 14.6398(5), b = 15.8871(5), c = 22.5512(7) Å, α = 90.280(2), β = 91.939(2), γ = 112.538(2)°. T = 120(2) K, U = 4840.8(3) Å^3, D_c 1.236 mg m^{-3}, 20540 independent reflections used in refinement, 2360 parameters, $R1$ ($I > 2\sigma(I)$) = 0.0622, $\omega R2$ (all data) 0.1599. CCDC 172793. The possibility that the crystal might be the more common *P*-1 was investigated. The centric solution obtained (two-half capsules) resulted in disorder to one of the sidearms and both guest species which is absent in P1.

sistent with averaged C_{3v} symmetries, only a less symmetric species, assigned to the dimeric aggregates **3·3** was observed on changing the solvent to $CDCl_3$, CD_2Cl_2, or C_6D_6. No indication of the monomer was observed in all these solvents (Figure 2b).

The dimeric species featured two well-separated doublets assigned to the diastereotopic methylenic protons of the $(ArCH_2)_3N$ fragment (J_{gem} = 10.5−11.7 Hz in $CDCl_3$), instead of the singlet observed for the same nuclei in DMSO-d_6. The signals assigned to the NH protons (6.67−6.76 and 8.07−8.11 ppm) in $CDCl_3$ appeared significantly sharp and also shifted to lower field when compared to the reference compound *N*-(4-butylphenyl)-*N*′-(4-methylphenyl) urea (δ = 6.65 ppm). The significant differences in the δ values for both NH protons in **3·3** indicate that the two hydrogen bonds are rather different in strength, in agreement with that observed in the X-ray structure. Additionally, the involvement of the urea carbonyl groups as hydrogen bonding acceptors was supported by the δ values of their carbon atoms in the ^{13}C NMR spectra. These signals were shifted to downfield in $CDCl_3$ ($\Delta\delta$ = 2.6−2.8 ppm) compared to the spectra recorded in DMSO-d_6 (only $\Delta\delta$ = 1.2 ppm was found for the reference urea). Indeed, FT-IR of **3a** (12.6 mM) in $CHCl_3$ solutions revealed typical hydrogen-bonded NH-stretching bands at 3318 cm^{-1}. All these data pointed out to a highly ordered, hydrogen-bonded structure (**3·3**) for compounds **3a**−**c** in noncompetitive solvents which perfectly fits with the conformation found in the solid state.



3•3

Further comparisons on the ^1H NMR spectra of the dimer **3a·3a** ($CDCl_3$) and the monomer **3a** (DMSO-d_6) strongly support that the conformation shown by the X-ray structure in solid-state persists in solution (Figure 3). Large shifts[13] to upfield were observed for the pendant aryl protons (−0.54, −0.68 ppm), the protons at the *n*-butyl chain placed nearest to the aromatic ring (−0.43, −0.54 ppm), and the protons at the tribenzylamine skeleton which are directed to the internal cavity (−1.73 ppm). These shifts may be rationalized in terms of the shielding effect between the aromatic rings from the tribenzylamine skeleton and the pendant aromatic substituents placed alternatively due to the interpenetration of the six arms in the dimeric structure. Finally, ROE contacts were detected from a ROESY experiment (cf. Supporting Information) with **3a·3a** ($CDCl_3$) that are only possible in a dimer but not in a monomer (Figure 3).

(13) Since a few signals are overlapped these differences are approximated.

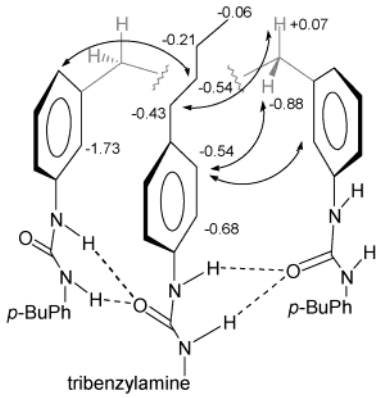


FIGURE 3. Schematic representation of the dimer **3a·3a** in which some chemical shifts differences (^1H NMR spectra) respect to the same signals for the monomer **3a** are reflected. The most significant observed ROE effects are also represented

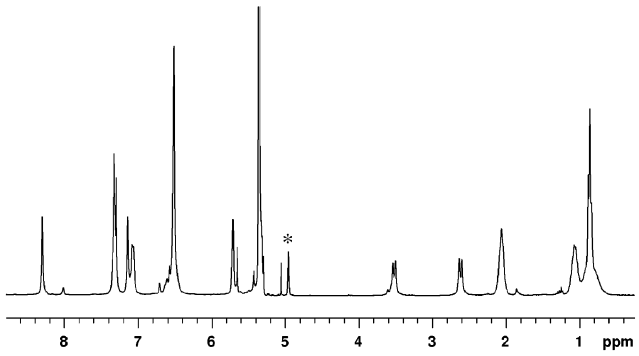


FIGURE 4. ^1H NMR spectra (−60 °C; 300 MHz) of **3a·3a** after addition of CH_2Cl_2 in $CDCl_3$; (encapsulated CH_2Cl_2 is indicated by *).

The dimeric assembly of **3b** was further detected by ESI-MS[14] experiments. The spectrum measured in $CHCl_3$ showed the corresponding molecular ion for the protonated dimer **3b·3b** (1464.7).

Encapsulation studies in solution were performed with **3a**. After dissolving the sample (10.8 mg) in $CDCl_3$ (0.6 mL) and adding CH_2Cl_2 (30 μL), the ^1H NMR spectrum (300 MHz) was recorded at room temperature but only the signal of "nonencapsulated" CH_2Cl_2 (δ = 5.30 ppm) was observed, besides those corresponding to the capsule which showed only minor changes in their chemical shifts. Interestingly, on cooling to −60 °C a new signal appeared at δ = 4.96 ppm, integrating in a 1:1 ratio with those of the dimeric capsule, which was attributed to encapsulated CH_2Cl_2 (Figure 4). At room temperature the exchange rate between free and encapsulated CH_2Cl_2 should be fast on the NMR time scale leading to a time-averaged spectrum.

Further addition of CD_2Cl_2 (30 μL) to the same sample led to a half-decreasing of the intensity for the signal at 4.96 ppm when the ^1H NMR spectrum was measured under the same conditions (i.e. −60 °C). This may be

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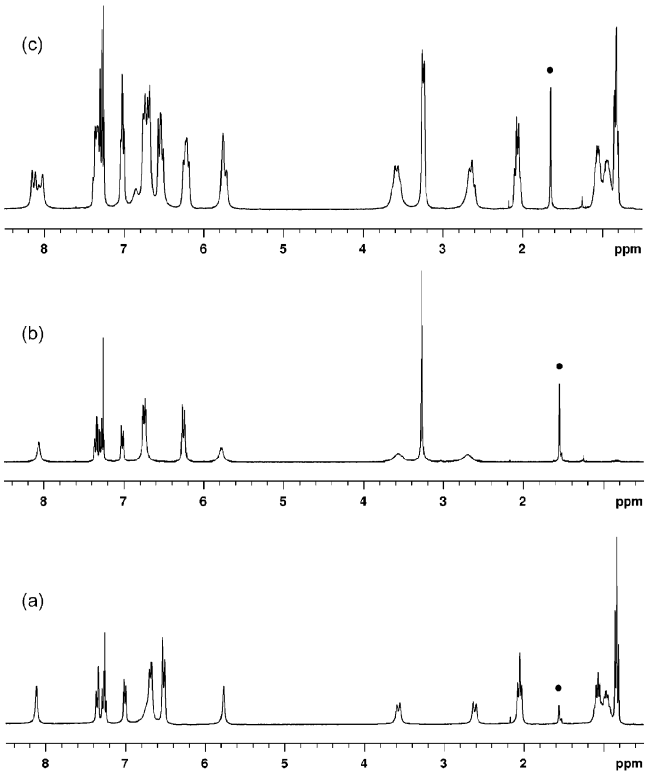


FIGURE 5. (a) ^{1}H NMR (300 MHz) spectrum of **3a·3a** in $CDCl_3$; (b) ^{1}H NMR spectrum of **3c·3c** in $CDCl_3$; (c) ^{1}H NMR spectrum of an equimolecular mixture of tris(ureas) **3a** and **3c** showing the 2:1:1 mixture of hetero- and homodimers respectively; (●) signal for residual water.

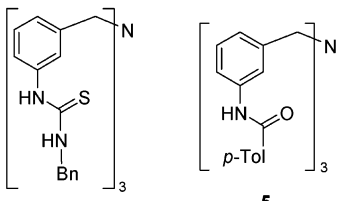
rationalized by the fact that in this case 50% of the capsules include CH_2Cl_2 and the other 50% CD_2Cl_2 which cannot be observed in the ^{1}H NMR spectrum.

The encapsulation of CH_2Cl_2 and $CHCl_3$ by using $C_2D_2Cl_4$ as solvent was also tested. In this case, the peak corresponding to encapsulated CH_2Cl_2 was found at $\delta =$ 4.95 ppm when the spectrum was measured at −30 °C (300 MHz). For $CHCl_3$ the signal attributable to the encapsulated guest was assigned at $\delta = 6.80$ ppm (−30 °C; 300 MHz) although it was partially overlapped with other signals in the aromatic region of the spectrum (further addition of $CDCl_3$ led to a decreasing of this signal). For CH_2Cl_2, only the signals for the filled capsule were found. On the contrary, the spectrum showed two sets of signals in approximately 1:1 ratio when $CHCl_3$ was used as guest. These two sets of signals were assigned to filled and empty capsule and reflect that $CHCl_3$ is not as good guest as CH_2Cl_2 is.

Finally, encapsulation studies were conducted to elucidate whether C_6H_6 could be included inside tris(*m*-ureidobenzyl)amine dimers. However, no changes were observed in the ^{1}H NMR spectrum after addition of C_6H_6 to a solution of **3a** in $CDCl_3$ (30 °C and −60 °C) which indicates that $CDCl_3$ was preferably encapsulated. That the encapsulation of C_6H_6 is also possible was confirmed from the ^{1}H NMR spectrum of **3a** in a 1:1 mixture of $C_6D_6/C_2D_2Cl_6$. The spectrum (−30 °C) showed a mixture of two sets of signals (approximately in 1:1 ratio) assigned to the empty capsule and the capsule with enclosed C_6D_6.

The formation of heterodimers by the combination of two homodimeric species is a well-known phenomenon for ureidocalixarenes.[8] In our case, the ^{1}H NMR spectrum of an equimolecular mixture of **3a** and **3c** revealed the appearance of signals attributable to the heterodimer **3a·3c**, besides those of homodimers **3a·3a** and **3c·3c**. In this experiment the regions of the aryl-NH protons (8.00−8.20 ppm) and of the methoxy substituents (3.20−3.30 ppm) were especially informative (Figure 5). Thus, four NH singlets appeared (1:1:1:1 relative intensities), two of them due to the homodimers **3a·3a** (8.12 ppm) and **3c·3c** (8.07 ppm) and the other two to both aryl-NH protons of the heterodimer **3a·3c** (8.02, 8.16 ppm). Similarly, two singlets of nearly the same intensity appeared, corresponding to both methoxy groups in the homodimer **3c·3c** (3.26 ppm) and in the heterodimer **3a·3c** (3.23 ppm). The relative intensities revealed a nearly statistical mixture of the three aggregates (2:1:1 for the heterodimer and both homodimers respectively).

Thiourea and amide functionalities are known to behave as good hydrogen bond donors and acceptors,[15] hence both functionalities are also candidates to construct molecules that self-assemble by hydrogen-bonding. For comparison, the behavior in solution of the tris(*m*-thioureidobenzyl)amine **4** and the tris(*m*-amidobenzyl)-amine **5** was tested. Unfortunately, neither tris(thiourea) **4** nor tris(amide) **5** self-assemble in $CDCl_3$ since the expected patterns for the corresponding monomers with C_{3v} symmetries were found in their respective ^{1}H NMR spectra.



In conclusion, we have reported a key for accessing a new class of self-assembling capsules based on the tribenzylamine skeleton. They present as particular features: (a) high flexibility of the corresponding monomers, (b) a propeller-like topology, and (c) a belt of six hydrogen-bonded ureas. Investigations directed to the synthesis of new structural variations for modulating the size of the internal cavities are in progress in our laboratories.

Experimental Section

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

Tris(3-aminobenzyl)amine 2. The tris(azide) **1** (2.00 g, 4.9 mmol) was dissolved in freshly distilled Et_2O (20 mL) and slowly added to a suspension of LAH (0.56 g, 14.6 mmol) in the same solvent (50 mL) at 0 °C and under a nitrogen-gas atmosphere. The mixture was stirred at this temperature for 0.5 h, warmed to 20 °C, and stirred for 4 h more. Then, the reaction mixture was cooled to 0 °C and treated with 10% aqueous KOH (100 mL). After filtration over a pad of Celite, the ethereal phase was separated and the aqueous phase

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extracted with CH_2Cl_2 (4 × 50 mL). The combined organic extracts were dried ($MgSO_4$), the solvent was evaporated (20 °C/75 Torr), and the residue was purified by silica gel chromatography eluting first with AcOEt and subsequently with 10:1 AcOEt/MeOH (R_f = 0.36, AcOEt), 74% yield. An analytical sample was obtained by recrystallization from 1:1 Et_2O/petroleum ether. Colorless prisms, mp 140−141 °C; IR (Nujol) ν: 3411 (NH), 3336 (NH), 3210 (NH) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 3.47 (s, 6 H), 3.62 (br s, 6 H), 6.55 (dd, J = 7.7 Hz, J = 1.5 Hz, 3 H), 6.74 (s, 3 H), 6.80 (d, J = 7.6 Hz, 3 H), 7.09 (t, J = 7.7 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 57.9 (t), 113.6 (d), 115.4 (d), 119.1 (d), 129.0 (d), 141.0 (s), 146.3 (s); Anal. Found: C, 74.68; H, 7.44; N, 16.70%. Calcd for $C_{21}H_{24}N_4 \cdot 0.25\ H_2O$: C, 74.86; H, 7.33; N, 16.63%. EI-MS: m/z:333 ($M^+ + 1$, 9), 332 (M^+, 20), 226 (99), 106 (100).

General Procedure for the Synthesis of the Tris(ureas) 3a−c. The tris(amine) **2** (0.05 g, 0.15 mmol) was dissolved in dry CH_2Cl_2 (3 mL) and the appropriate isocyanate (0.45 mmol) was slowly added at 0 °C under a nitrogen-gas atmosphere. After stirring at 20 °C for 18 h, the solvent was removed (20 °C/75 Torr) and Et_2O (3 mL) was added. The white solid was filtered off and dried under vacuum.

Tris{3-[*N*′-(4-butylphenyl)ureido]benzyl}amine (3a): 89% yield. Colorless prisms (from 1:1 $CHCl_3/Et_2O$), mp 185−208 °C; IR (Nujol) ν: 3317 (NH), 1660 (C═O) cm^{-1}; ^1H NMR (DMSO-d_6, 300 MHz): δ 0.89 (t, J = 7.2 Hz, 9 H), 1.28 (m, J = 7.3 Hz, 6 H), 1.51 (m, J = 7.5 Hz, 6 H), 2.48 (t, J = 7.7 Hz, 6 H), 3.50 (s, 6 H), 7.04−7.08 (m, 9 H), 7.25 (t, J = 7.7 Hz, 3 H), 7.33−7.39 (m, 9 H), 7.50 (s, 3 H), 8.52 (s, 3 H), 8.59 (s, 3H); ^1H NMR ($CDCl_3$, 300 MHz): δ 0.83 (t, J = 7.1 Hz, 18 H), 0.97 (m, 12 H), 1.07 (m, 12 H), 2.05 (t, J = 7.7 Hz, 12 H), 2.62 (d, J = 11.4 Hz, 6 H), 3.57 (d, J = 11.7 Hz, 6 H), 5.77 (s, 6 H), 6.52 (d, J = 8.1 Hz, 12 H), 6.67−6.70 (m, 18 H), 7.00 (d, J = 7.2 Hz, 6 H), 7.27 (t, J = 7.7 Hz, 6 H), 7.35 (d, J = 8.1 Hz, 6 H), 8.11 (s, 6H); ^{13}C NMR (DMSO-d_6, 50 MHz): δ 13.7 (q), 21.6 (t), 33.2 (t), 34.1 (t), 57.1 (t), 116.7 (d), 118.3 (3×d), 121.9 (d), 128.4 (2×d), 128.6 (d), 135.6 (s), 137.3 (s), 139.7 (s), 139.8 (s), 152.5 (s); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 14.1 (q), 22.4 (t), 33.5 (t), 34.7 (t), 58.3 (t), 118.1 (2×d), 125.7 (2×d), 127.2 (2×d), 128.4 (2×d), 136.5 (s), 136.7 (s), 136.9 (s), 139.7 (s), 155.3 (s); Anal. Found: C, 75.35; H, 7.67; N, 11.72%. Calcd for $C_{54}H_{63}N_7O_3$ (858.1): C, 75.58; H, 7.40; N, 11.43%.

Tris{3-[*N*′-(4-methylphenyl)ureido]benzyl}amine (3b): 98% yield. Colorless prisms (from 4:1 $CHCl_3/Et_2O$), mp 193−195 °C; IR (Nujol) ν: 3374 (NH), 3292 (NH), 1664 (C═O) cm^{-1}; ^1H NMR (DMSO-d_6, 200 MHz): δ 2.21 (s, 9 H), 3.49 (s, 6 H), 7.03−7.07 (m, 9 H), 7.25 (t, J = 7.9 Hz, 3 H), 7.31−7.39 (m, 9 H), 7.47 (s, 3 H), 8.52 (s, 3 H), 8.60 (s, 3H); ^1H NMR ($CDCl_3$, 300 MHz): δ 1.71 (s, 18 H), 2.65 (d, J = 10.5 Hz, 6 H), 3.55 (d, J = 10.5 Hz, 6 H), 5.72 (s, 6 H), 6.47 (d, J = 8.1 Hz, 12 H), 6.68−6.71 (m, 18 H), 7.02 (d, J = 6.6 Hz, 6 H), 7.27 (t, J = 7.7 Hz, 6 H), 7.34 (d, J = 8.1 Hz, 6 H), 8.08 (s, 6 H); ^{13}C NMR (DMSO-d_6, 50 MHz): δ 20.3 (q), 57.1 (t), 116.8 (d), 118.2 (3×d), 121.9 (d), 128.7 (d), 129.2 (2×d), 130.5 (s), 137.1 (s), 139.7 (s), 139.8 (s), 152.5 (s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 20.1 (q), 58.4 (t), 118.0 (2×d), 125.6 (2×d), 126.9 (d), 127.2 (d), 129.1 (2×d), 131.5 (s), 136.5 (s), 137.0 (s), 139.8 (s), 155.3 (s); Anal. Found: C, 73.71; H, 6.35; N, 13.47%. Calcd for $C_{45}H_{45}N_7O_3$ (731.9): C, 73.85; H, 6.20; N, 13.40%.

Tris{3-[*N*′-(4-methoxyphenyl)ureido]benzyl}amine (3c): 98% yield. Colorless prisms (from 1:1 $CHCl_3/Et_2O$), mp 145−245 °C; IR (Nujol) ν: 3314 (NH), 1659 (C═O) cm^{-1}; ^1H NMR (DMSO-d_6, 300 MHz): δ 3.49 (s, 6 H), 3.69 (s, 9 H), 6.84 (d, J = 9.0 Hz, 6 H), 7.04 (d, J = 7.5 Hz, 3 H), 7.24 (t, J = 7.7 Hz, 3 H), 7.32−7.38 (m, 9 H), 7.46 (s, 3 H), 8.42 (s, 3 H), 8.55 (s, 3H); ^1H NMR ($CDCl_3$, 300 MHz): δ 2.70 (br s, 6 H), 3.27 (s, 18 H), 3.57 (br s, 6 H), 5.78 (s, 6 H), 6.25 (d, J = 8.7 Hz, 12 H), 6.73−6.76 (m, 18 H), 7.02 (d, J = 7.2 Hz, 6 H), 7.28 (t, J = 7.8 Hz, 6 H), 7.35 (d, J = 7.8 Hz, 6 H), 8.07 (s, 6 H); ^{13}C NMR (DMSO-d_6, 50 MHz): δ 55.1 (q), 57.1 (t), 114.0 (2×d), 116.7 (d), 118.3 (d), 120.0 (2×d), 121.8 (d), 128.7 (d), 132.7 (s), 139.7 (s), 139.9 (s), 152.7 (s), 154.4 (s); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 55.3 (q), 58.5 (t), 114.2 (2×d), 119.3 (2×d), 125.5 (2×d), 127.0 (d), 127.4 (d), 132.4 (s), 137.2 (s), 140.1 (s), 154.7 (s), 155.3 (s); Anal. Found: C, 69.08; H, 5.98; N, 12.77%. Calcd for $C_{45}H_{45}N_7O_6$ (779.9): C, 69.30; H, 5.82; N, 12.57%.

Tris{3-[*N*′-(benzyl)thioureido]benzyl}amine (4). The tris(amine) **2** (0.15 g, 0.45 mmol) was dissolved in dry $CHCl_3$ (10 mL), and benzyl isothiocyanate (0.20 g, 1.36 mmol) was added. After stirring under reflux for 20 h, the solvent was removed (20 °C/75 Torr) and the residue was purified by recrystallization from 1:1 CH_2Cl_2/Et_2O, 72% yield. Colorless prisms, mp 96−99 °C; IR (Nujol) ν: 3379 (NH), 3217 (NH) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 3.49 (s, 6 H), 4.80 (d, J = 5.2 Hz, 6 H), 6.47 (br s, 3 H), 7.11−7.30 (m, 27 H), 9.04 (s, 3 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 49.1 (t), 57.8 (t), 123.1 (d), 124.6 (d), 127.0 (d), 127.6 (3×d), 128.7 (2×d), 129.7 (d), 136.8 (s), 137.3 (s), 141.5 (s), 180.2 (s); Anal. Found: C, 68.64; H, 6.12; N, 12.59%. Calcd for $C_{45}H_{45}N_7S_3 \cdot 0.50\ H_2O$: C, 68.50; H, 5.88; N, 12.43%.

Tris[3-(4-methylbenzamido)benzyl]amine (5). The tris(amine) **2** (0.15 g, 0.45 mmol) and triethylamine (0.14 g, 1.36 mmol) were dissolved in dry CH_2Cl_2 (15 mL). After cooling to 0 °C, a solution of 4-methylbenzoyl chloride (0. 21 g, 1.36 mmol) in the same solvent (8 mL) was slowly added. The reaction mixture was warmed to 20 °C and stirred at this temperature for 20 h. Then, the mixture was washed with saturated aqueous $NaHCO_3$ solution (15 mL) and the organic phase was dried with $MgSO_4$. After removal of the solvent (20 °C/75 Torr), the residue was purified by silica gel chromatography eluting with 2:3 AcOEt/hexanes (R_f = 0.36), 95% yield. An analytical sample was obtained by recrystallization from 1:1 CH_2Cl_2/Et_2O. Colorless prisms, mp 210−215 °C; IR (Nujol) ν: 3325 (NH), 1658 (C═O), 1652 (C═O) cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 2.34 (s, 9 H), 3.63 (s, 6H), 6.97 (d, J = 7.8 Hz, 6 H), 7.06 (d, J = 7.5 Hz, 3 H), 7.26 (t, J = 7.8 Hz, 3 H), 7.61−7.64 (m, 9 H), 8.12 (br s, 3 H), 8.30 (s, 3 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 21.4 (q), 57.4 (t), 118.8 (d), 120.8 (d), 124.7 (d), 127.3 (2×d), 128.7 (d), 129.2 (2×d), 132.5 (s), 138.5 (s), 140.9 (s), 141.7 (s), 166.2 (s); Anal. Found: C, 77.29; H, 6.60; N, 8.06%. Calcd for $C_{45}H_{42}N_4O_3 \cdot 0.50\ H_2O$: C, 77.67; H, 6.23; N, 8.05%.

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Supporting Information Available: ROESY spectrum of the tris(urea) **3a** in $CDCl_3$ (600 MHz). This material is available free of charge via the Internet at http://pubs.acs.org.

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