

-Electronic Supporting Information (ESI)-

*Highly Diastereoselective Self-Assembly of Chiral
Tris(m-ureidobenzyl)amino Capsules*

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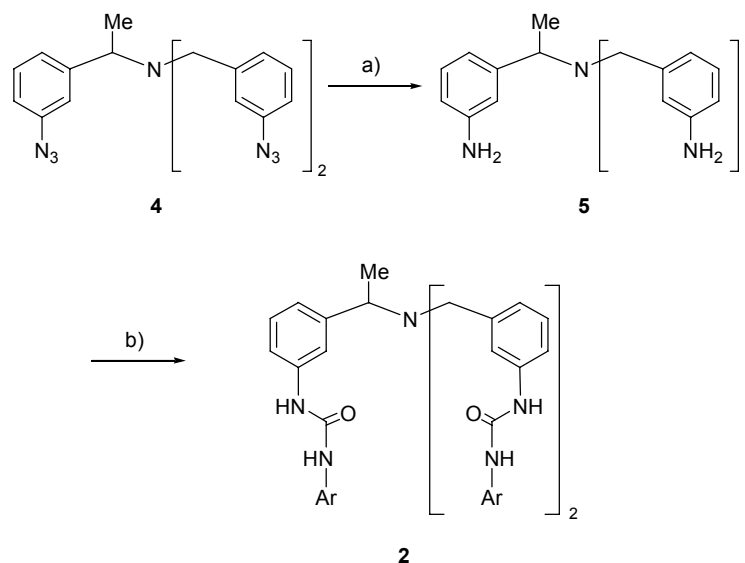
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General. Melting points are not corrected. IR spectra were recorded as nujol emulsions or neat. ^1H -NMR spectra were recorded at 300 or 400 MHz. ^{13}C -NMR spectra were measured at 50 or 75 MHz. The chemical shifts are expressed in ppm, relative to TMS δ 0.00 ppm for ^1H , while the chemical shifts for ^{13}C are reported relative to the resonances of CDCl_3 (δ 77.1 ppm) or $\text{DMSO}-d_6$ (δ 39.5 ppm). Mass spectra were recorded on the EI or ESI mode. The ESI-MS were measured from 1 mM CHCl_3 solutions (plus 1% of AcOH) of the corresponding triurea.

Crystallography Report. The instruments, software and procedures used for data collection, structure solution and refinement were the following: Bruker APEX CCD Diffractometer with Bede Microsource; Data collection and integration: SMART V5.625 (Bruker, 2001) and 'SAINT+ NT V6.22 (Bruker, 2001)' Solution and Refinement 'SHELXS-97' and 'SHELXL-97' (G. M. Sheldrick, University of Goettingen, 1997). Disorder of the butyl chains was modelled in terms of two alternate positions with a common, refined fractional occupancy summed to 1.0. The guest molecules were badly disordered and a model based on the apparent shape of the electron density was adopted. This model lacked H atoms.

Synthesis of the Tris(*m*-ureidobenzyl)amines 2a-c

The triureas **2a-c** were prepared in a two-step sequence by starting from the triazide **4**¹ (Scheme S1). The yields of every step are included in Table S1.



Scheme S1. General procedure for the synthesis of the triureas **2**. a) LiAlH_4 (LAH), Et_2O , 20 °C, 4 h. b) ArNCO , CH_2Cl_2 , 20 °C, 18 h.

Table S1. Synthesis of the triamine 5, and the triureas 2.

Entry	Compound	Ar	Yield (%)
1	5	-	44
2	2a	<i>p</i> -MeC ₆ H ₄	96
3	2b	<i>p</i> -BuC ₆ H ₄	68
4	2c	<i>p</i> -CF ₃ C ₆ H ₄	54

Bis(3-aminobenzyl)[1-(3-aminophenyl)ethyl]amine (5). A solution of bis(3-azidobenzyl)[1-(3-azidophenyl)ethyl]amine (**4**) (0.45 g, 1.18 mmol) in anhydrous Et₂O (10 mL) was slowly added to a suspension of LAH (0.13 g, 3.53 mmol) in the same solvent (10 mL) at 20 °C and under a nitrogen-gas atmosphere. Then, the reaction mixture was stirred at the same temperature for 4 h. After cooling down to 0 °C, 10% aqueous NaOH (10 mL) was slowly added and the resulting suspension was filtered through a pad of celite and subsequently washed with Et₂O (3 × 5 mL). The aqueous phase was extracted with CH₂Cl₂ (3 × 10 mL) and the combined organic extracts were dried over anhydrous MgSO₄. After removal of the solvent under reduced pressure the crude product was purified by silica-gel chromatography eluting first with 10:1 AcOEt/hexane and subsequently with AcOEt (*R_f* = 0.15 in 10:1 AcOEt/hexane) to give **5** as a yellow oil (44%); $\nu_{\max}(\text{neat})/\text{cm}^{-1}$ 3415 (vs), 3341 (vs), 3205 (vs), 1633 (vs), 1602 (vs), 1588 (vs), 1489 (vs), 871 (s), 790 (vs) and 696 (vs); δ_{H} (300 MHz; CDCl₃; Me₄Si) 1.37 (3 H, d, *J* = 7.0 Hz), 3.37 (2 H, d, *J* = 14.0 Hz), 3.53 (2 H, d, *J* = 14.0 Hz), 3.44-3.70 (6 H, br s), 3.86 (1 H, q, *J* = 7.0 Hz), 6.51-6.58 (3 H, m), 6.71-6.73 (3 H, m), 6.79 (3 H, d, *J* = 7.5 Hz), 7.07 (2 H, t, *J* = 7.7 Hz) and 7.11 (1 H, t, *J* = 7.7 Hz); δ_{C} (75 MHz; CDCl₃) 14.6 (q), 53.7 (t), 56.4 (d), 113.5 (d), 115.0 (d), 115.4 (d), 118.7 (d), 119.1 (d), 128.7 (d), 129.0 (d), 141.9 (s), 144.0 (s), 146.0 (s) and 146.3 (s); *m/z* (MS-EI): 347 (M⁺ + 1, 2), 346 (M⁺, 2), 331 (17), 240 (65), 226 (32), 211 (24), 121 (38), 120 (42), 107 (39), 106 (100); *m/z* (HRMS-EI): 346.2177 (M⁺, C₂₂H₂₆N₄ requires 346.2158).

General procedure for the synthesis of the triureas 2. The corresponding isocyanate (0.87 mmol) was added to a solution of the triamine **5** (0.10 g, 0.29 mmol) in anhydrous CH₂Cl₂ (10 mL) and the reaction mixture was stirred at 20 °C under a nitrogen-gas atmosphere for 18 h. After removal of the solvent under reduced pressure, the crude product was washed with Et₂O (2 mL), filtered and dried under vacuum. The resulting solid was subsequently purified by recrystallization.

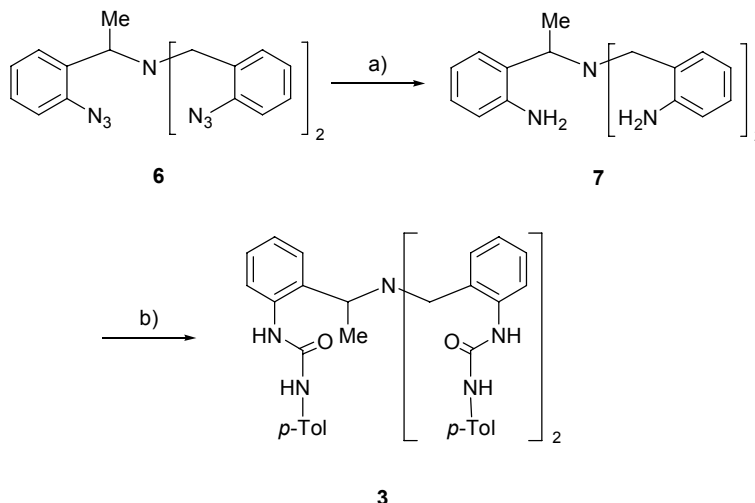
Bis{3-[*N'*-(4-methylphenyl)ureido]benzyl}{ α -methyl-3-[*N'*-(4-methylphenyl)ureido]benzyl}amine (2a). mp 204-206 °C (from CHCl₃/Et₂O); 96%; ν_{\max} (nujol)/cm⁻¹ 3374 (vs), 3298 (vs), 1666 (vs), 1661 (vs), 1604 (vs), 1557 (vs), 1316 (s), 1247 (s), 821 (m), 778 (m), 736 (m) and 700 (s); δ_{H} (300 MHz; DMSO-*d*₆; Me₄Si) 1.40 (3 H, d, *J* = 6.8 Hz), 2.21 (9 H, s), 3.35 (2 H, d, *J* = 14.1 Hz), 3.59 (2 H, d, *J* = 14.1 Hz), 3.81 (1 H, q, *J* = 6.8 Hz), 7.04-7.06 (9 H, m), 7.20-7.40 (12 H, m), 7.47 (3 H, s), 8.49 (3 H, s), 8.56 (2 H, s) and 8.59 (1 H, s); δ_{C} (50 MHz; DMSO-*d*₆) 14.4 (q), 20.3 (q), 53.1 (t), 56.0 (d), 116.6 (d), 117.6 (d), 118.2 (d), 121.4 (d), 121.7 (d), 128.3 (d), 128.6 (d), 129.1 (d), 130.5 (s), 137.1 (s), 139.5 (s), 139.7 (s), 140.6 (s), 142.8 (s), 152.5 (s) and 152.6 (s); found C, 73.72; H, 6.22; N, 13.13. Calc. for C₄₆H₄₇N₇O₃: C, 74.07; H, 6.35; N, 13.14%.

Bis{3-[*N'*-(4-butylphenyl)ureido]benzyl}{ α -methyl-3-[*N'*-(4-butylphenyl)ureido]benzyl}amine (2b). mp 159-163 °C (colourless prisms from CHCl₃/Et₂O); 68%; ν_{\max} (nujol)/cm⁻¹ 3363 (m), 3307 (m), 1662 (s), 1603 (vs), 1552 (vs), 1513 (m), 1411 (w), 1316 (s), 1303 (m), 1246 (s), 1220 (w), 896 (w), 836 (w) and 698 (w); δ_{H} (300 MHz; DMSO-*d*₆; Me₄Si) 0.87 (9 H, t, *J* = 7.2 Hz), 1.27 (6 H, sext, *J* = 7.5 Hz), 1.39 (3 H, d, *J* = 6.9 Hz), 1.49 (6 H, quint, *J* = 7.8 Hz), 2.48 (6 H, t, *J* = 7.2 Hz), 3.35 (2 H, d, *J* = 14.1 Hz), 3.58 (2 H, d, *J* = 14.1 Hz), 3.80 (1 H, q, *J* = 6.9 Hz), 6.99-7.05 (9 H, m), 7.19-7.35 (12 H, m), 7.49 (3 H, s), 8.50 (3 H, s), 8.57 (2 H, s) and 8.59 (1 H, s); δ_{C} (75 MHz; DMSO-*d*₆) 13.7 (q), 14.4 (q), 21.7 (t), 33.2 (t), 34.1 (t), 53.1 (t), 56.1 (d), 116.6 (d), 117.7 (d), 118.2 (d), 118.3 (d), 121.3 (d), 121.7 (d), 128.4 (d), 128.6 (d), 135.6 (s), 137.3 (s), 139.6 (s), 139.8 (s), 140.6 (s), 142.9 (s), 152.5 (s) and 152.6 (s); found C, 74.97; H, 7.83; N, 11.31. Calc. for C₅₅H₆₅N₇O₃•0.5 H₂O: C, 74.97; H, 7.55; N, 11.13%.

Bis{3-[*N'*-(4-trifluoromethylphenyl)ureido]benzyl}{ α -methyl-3-[*N'*-(4-trifluoromethylphenyl)ureido]benzyl}amine (2c). mp 207-210 °C (colourless prisms); this compound could not be recrystallized due to its high insolubility; 54%; ν_{\max} (nujol)/cm⁻¹ 3325 (m), 1668 (vs), 1605 (vs), 1567 (vs), 1411 (w), 1325 (vs), 1254 (m), 1165 (m), 1120 (s), 1071 (s), 1015 (w), 845 (w), 778 (w), 722 (w) and 698 (w); δ_{H} (300 MHz; DMSO-*d*₆; Me₄Si) 1.41 (3 H, d, *J* = 6.8 Hz), 3.37 (2 H, d, *J* = 14.1 Hz), 3.61 (2 H, d, *J* = 14.1 Hz), 3.82 (1 H, q, *J* = 6.8 Hz), 7.07-7.11 (3 H, m), 7.22-7.29 (3 H, m), 7.32-7.39 (3 H, m), 7.54-7.57 (9 H, m), 7.63 (6 H, d, *J* = 8.7 Hz), 8.74 (2 H, s), 8.76 (1 H, s) and 9.05 (3 H, s); δ_{C} (75 MHz; DMSO-*d*₆) 14.4 (q), 53.1 (t), 56.2 (d), 117.0 (d), 117.7 (d), 118.1 (d), 118.6 (d), 121.7 (q, *J* = 31.5 Hz) (s), 121.8 (d), 122.3 (d), 124.5 (q, *J* = 269.5 Hz) (s), 126.0 (q, *J* = 3.6 Hz) (d), 128.4 (d), 128.7 (d), 139.1 (s), 139.3 (s), 140.7 (s), 143.0 (s), 143.4 (s), 152.3 (s) and 152.3 (s); δ_{F} (188 MHz; DMSO-*d*₆) -60.4 (s); found C, 60.72; H, 4.10; N, 10.79. Calc. for C₄₆H₃₈F₉N₇O₃: C, 60.86; H, 4.22; N, 10.80%.

Synthesis of the Triurea **3**

The triurea **3** was prepared in a two-step sequence by starting from the triazide **6**² (Scheme S2).



Scheme S2. Synthesis of the triurea **3**. a) LAH, Et₂O, 20 °C, 4 h. b) *p*-MeC₆H₄NCO, CH₂Cl₂, 20 °C→reflux, 20 h.

Bis(2-aminobenzyl)[1-(2-aminophenyl)ethyl]amine (7). A solution of bis(2-azidobenzyl)[1-(2-azidophenyl)ethyl]amine (**6**) (0.22 g, 0.52 mmol) in anhydrous Et₂O (10 mL) was slowly added to a suspension of LAH (0.06 g, 1.56 mmol) in the same solvent (20 mL) at 20 °C under a nitrogen-gas atmosphere. Then, the reaction mixture was stirred at the same temperature for 4 h more. After cooling at 0 °C, 10% aqueous NaOH (5 mL) was added. The resulting suspension was filtered over a pad of celite and subsequently washed with Et₂O (3 × 5 mL). The aqueous phase was extracted with CH₂Cl₂ (3 × 10 mL) and the combined organic extracts were dried with anhydrous MgSO₄. After removal of the solvent under reduced pressure, the crude product was purified by silica-gel chromatography eluting with 2:1 hexane/AcOEt (*R_f* = 0.28); mp 177-181 °C (from CH₂Cl₂/Et₂O); 75%; $\nu_{\max}(\text{nujol})/\text{cm}^{-1}$ 3435 (vs), 3348 (vs), 1624 (vs), 1618 (vs), 1612 (vs), 1283 (s), 1112 (s), 1055 (m), 936 (m), 750 (vs) and 732 (s); δ_{H} (300 MHz; CDCl₃; Me₄Si) 1.49 (3 H, d, *J* = 6.8 Hz), 3.31 (2 H, d, *J* = 13.1 Hz), 3.65 (6 H, br s), 3.84 (2 H, d, *J* = 13.1 Hz), 4.14 (1 H, q, *J* = 6.8 Hz), 6.51-6.56 (3 H, m), 6.68 (2 H, td, *J* = 7.4 and 1.3 Hz), 6.74 (1 H, td, *J* = 7.5 and 1.1 Hz), 7.03-7.10 (5 H, m) and 7.27 (1 H, dd, *J* = 7.8 and 1.2 Hz); δ_{C} (75 MHz; CDCl₃) 7.0 (q), 51.0 (t), 51.2 (d), 115.6 (d), 116.0 (d), 117.8 (d), 117.9 (d), 122.0 (s), 126.0 (s), 128.0 (d), 128.4 (d), 129.0 (d), 132.0 (d), 145.5 (s) and 145.8 (s); *m/z* (MS-EI): 347 (M⁺ + 1,

97), 334 (19), 333 (44), 226 (100), 209 (98), 119 (99) and 77 (99); found C, 75.30; H, 7.56; N, 16.03. Calc. for $C_{22}H_{26}N_4 \cdot 0.25 H_2O$: C, 75.29; H, 7.61; N, 15.96%.

Bis{2-[N'-(4-methylphenyl)ureido]benzyl}{ α -methyl-2-[N'-(4-methylphenyl)ureido]benzyl}amine (3). *p*-Methylphenyl isocyanate (0.12 g, 0.87 mmol) was added to a solution of the triamine **7** (0.10 g, 0.29 mmol) in anhydrous CH_2Cl_2 (5 mL). The reaction mixture was stirred at 20 °C under a nitrogen-gas atmosphere for 18 h and subsequently under reflux for 2 h more. After removal of the solvent under reduced pressure, the crude product was washed with Et_2O (2 mL), filtered and dried under vacuum. The resulting solid was subsequently purified by recrystallization; mp 164-168 °C (colourless prisms from $CHCl_3/Et_2O$); 72%; $\nu_{max}(nujol)/cm^{-1}$ 3316 (s), 1651 (vs), 1602 (vs), 1548 (vs), 1512 (vs), 1314 (s), 1292 (s), 1237 (vs), 814 (m) and 754 (m); δ_H (300 MHz; $DMSO-d_6$; Me_4Si) 1.45 (3 H, d, $J = 6.8$ Hz), 2.24 (9 H, s), 3.61 (2 H, d, $J = 15.0$ Hz), 3.64 (2 H, d, $J = 15.0$ Hz), 4.26 (1 H, q, $J = 6.8$ Hz), 6.89 (2 H, t, $J = 7.5$ Hz), 6.99-7.16 (10 H, m), 7.29-7.43 (10 H, m), 7.57-7.60 (2 H, m), 7.70 (1 H, s), 7.80 (2 H, s), 8.52 (1 H, s) and 8.64 (2 H, s); δ_C (75 MHz; $DMSO-d_6$) 13.4 (q), 20.3 (q), 50.6 (t), 53.5 (d), 118.26 (d), 118.32 (d), 123.6 (d), 124.1 (d), 124.3 (d), 125.9 (d), 126.8 (d), 127.1 (d), 127.7 (d), 129.0 (d), 129.5 (d), 130.37 (s), 130.44 (s), 130.9 (s), 135.4 (s), 136.5 (s), 136.8 (s), 137.10 (s), 137.14 (s), 153.2 (s) and 153.8 (s); found C, 73.73; H, 6.46; N, 13.27. Calc. for $C_{46}H_{47}N_7O_3$: C, 74.07; H, 6.35; N, 13.14%.

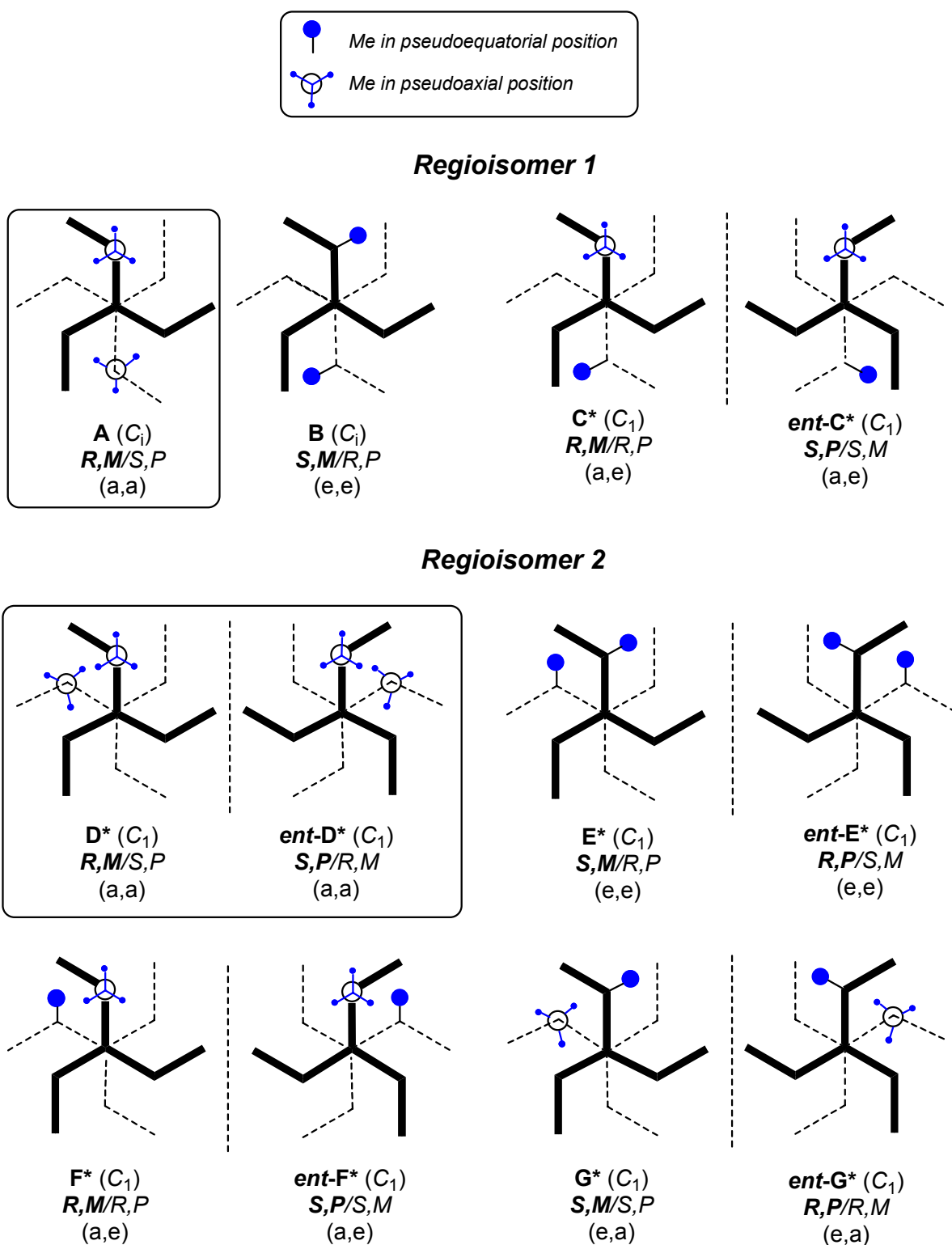


Figure S1. Symmetry properties of the chiral tris(*m*-ureidobenzyl)amines **2**. Regioisomer 1 may exist as three diastereoisomers, two of them are centrosymmetric (**A** and **B**) and one is chiral (the pair of enantiomers **C*** and **ent-C***). Regioisomer 2 may

exist as four chiral diastereoisomers (the four pairs of enantiomers: **D***/*ent*-**D***, **E***/*ent*-**E***, **F***/*ent*-**F*** and **G***/*ent*-**G***).

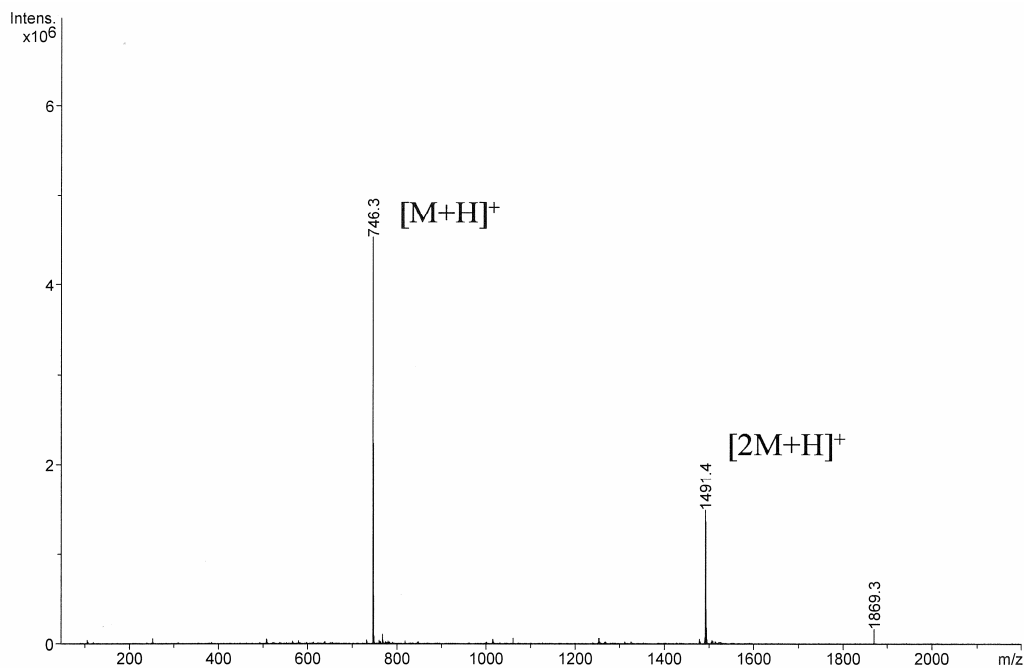


Figure S2. ESI-MS (CHCl₃; 1% AcOH) of the triurea **2a**.

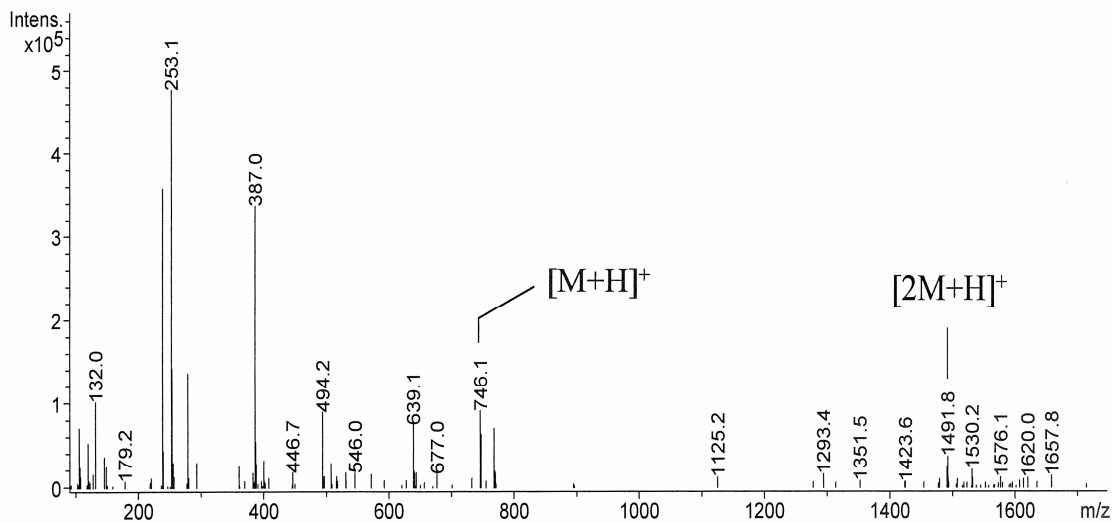


Figure S3. ESI-MS (CHCl₃; 1% AcOH) of the triurea **3**.

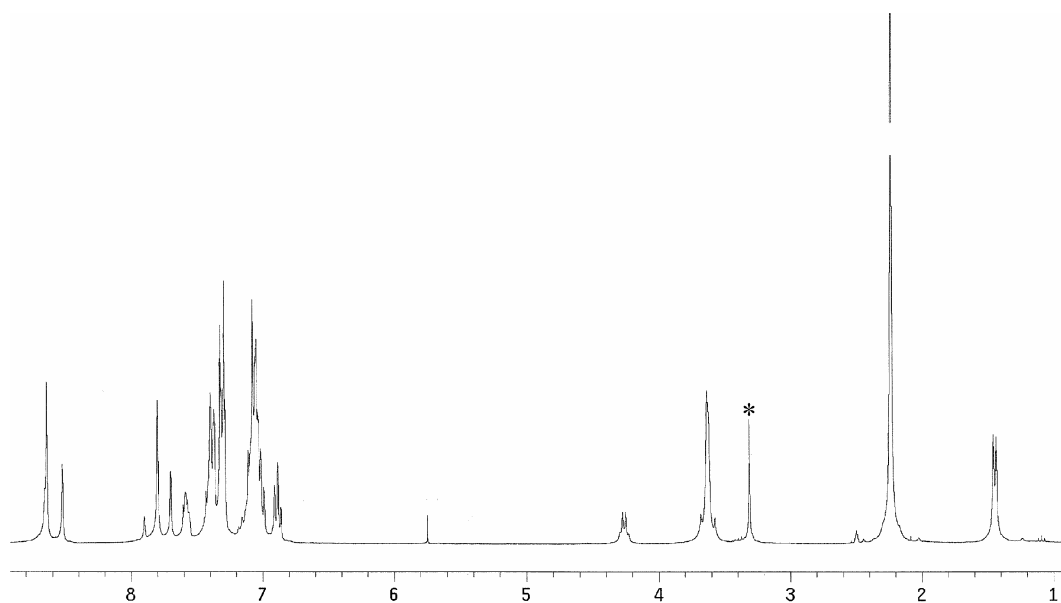


Figure S4. ^1H NMR spectrum (300 MHz, 25 °C) of the triurea **3** in $\text{DMSO-}d_6$. The signal from water has been labelled with an asterisk.

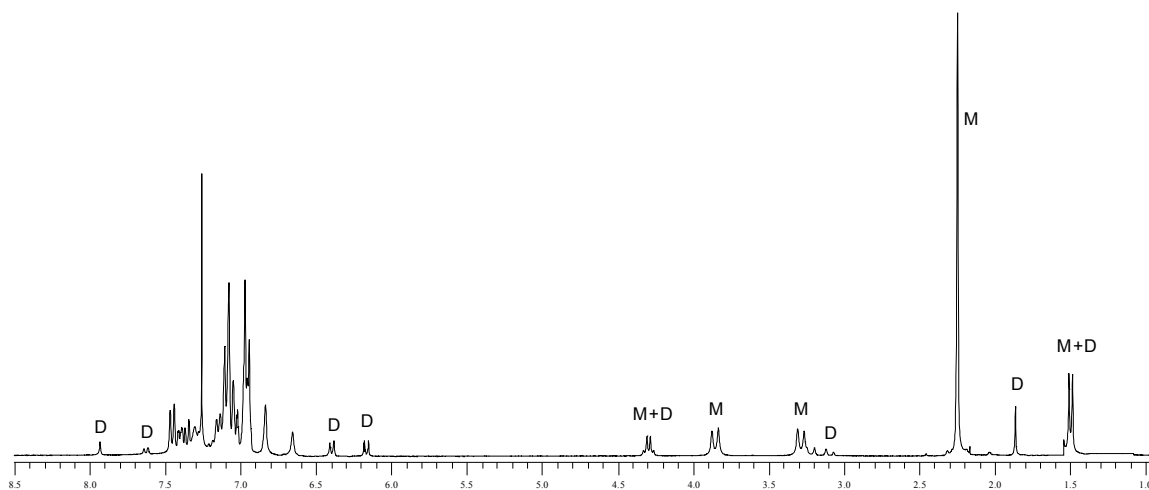


Figure S5. ^1H NMR spectrum (300 MHz, 25 °C) of the triurea **3** in CDCl_3 (the signals attributed to the monomer and dimer species have been labelled with **M** and **D**, respectively).

1. Alajarin, M.; López-Leonardo, C.; Vidal, A.; Berná, J.; Steed, J. W. *Angew. Chem. Int. Ed.* **2002**, *41*, 1205-1208.
2. Alajarin, M.; López-Lázaro, A.; Vidal, A.; Berná, J. *Chem. Eur. J.* **1998**, *4*, 2558-2570.