Hydrogen bonding in dimers of tritolyl and tritosylurea derivatives of triphenylmethanes†

Yuliya Rudzevich,[a] Valentyn Rudzevich,‡[a] Dieter Schollmeyer,[b] Iris Thondorf[c] and Volker Böhmer*[a]

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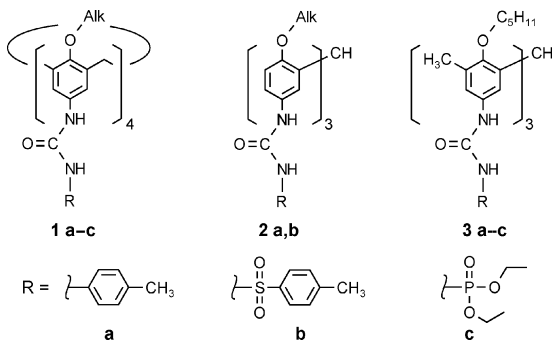
The crystal structure of the homodimer formed by the tritolylurea **3a** proves the existence of a belt of six bifurcated hydrogen bonds between both NH and the O=C groups of the adjacent urea residues. For the tritosylurea **3b**, four additional three-center hydrogen bonds, also involving the SO_2 oxygen, are found in the crystalline state. Molecular dynamics simulations in a chloroform box confirm these patterns of the hydrogen bonds and the resulting elongation of the dimer **3b**·**3b** in comparison to **3a**·**3a**. The calculated complexation energies for the three dimeric combinations are nearly identical in agreement with the simultaneous formation of heterodimer **3a**·**3b** in a mixture of **3a** and **3b**.

Introduction

The key factor for the dimerisation of calix[4]arene derivatives **1**, substituted at their wide rim by four urea functions, is the formation of a belt of intermolecular hydrogen bonds between their urea functions.[1] The structure of these dimeric capsules, initially deduced from their ^{1}H NMR spectra,[2] was confirmed for the solid state by several X-ray structures.[3] This dimerisation is not only interesting for the inclusion of guests.[4] It has been used also to build up larger polymeric structures *via* self-assembly processes.[5] In this regard, it is of great importance that tetraaryl (**1a**) and tetraarylsulfonylurea derivatives (**1b**) combine exclusively to heterodimers in a stoichiometric mixture, although both form homodimers when dissolved alone.[6] This serendipitous observation was the basis for the construction of alternating (∼A–AB–BA–A∼) or directional (∼A–BA–BA–B∼) polymers from "monomeric" bis-tetraurea units (A–A/B–B or A–B), in which two calix[4]arenes are covalently linked *via* their narrow rim.[7] It also enabled the construction of well-defined structures with three[7] or four[8] dimeric/capsular substructures, as well as the self-assembly of structurally uniform dendrimers[9] with molar masses up to 25 000. Tetraarylsulfonylureas **1b** have been successfully used also as template in the synthesis of bis- or tetraloop tetraureas by metathesis,[10] since four or eight alkenyl groups attached to a tetraarylurea **1** are perfectly prearranged for their intramolecular connection within its heterodimer with a tetratosylurea **1b**.

In spite of its frequent use, the reason for this pronounced selectivity, which is not found for alkyl as opposed to arylureas, is not exactly known. A favorable combination of the increased acidity of –SO_2–NH– and the basicity of the urea carbonyl group has been tentatively suggested, but the different geometry of the two urea groups seems to be also important. The two X-ray structures reported for tosylureas reveal that the O=S=O oxygen can also act as a hydrogen bond acceptor.[11] Numerous attempts to obtain single crystals of a homodimer **1b**·**1b** or even of a heterodimer **1a**·**1b** failed so far. Recently, we could show[12,13] that triarylurea derivatives of triphenylmethanes **2a** form hydrogen bonded dimers, as well as their tosylurea counterparts **2b**. Heterodimers **2a**·**2b** are also observed in this case, though not exclusively.



We were able, however, to obtain single crystals from homodimers of a similar triurea **3a**·**3a** and **3b**·**3b**, which are described subsequently, and discussed together with MD-simulations on these systems. The dimerisation studies were extended also to further triureas of type **3**.

Results and discussion

Synthesis and dimerisation

Triurea derivatives **3a**–**c** were prepared as usual by reaction of the corresponding triamine[14] with the respective isocyanates.

In contrast to the analogous calix[4]arenes, the 1 : 1 mixture of **3a** and **3b** did not lead to the exclusive formation of the heterodimer **3a**·**3b** in apolar solvents (chloroform, dichloromethane, tetrachloroethane, benzene), but to a mixture of the two homodimers

[a]*Abteilung Lehramt Chemie, Fachbereich Chemie, Pharmazie und Geowissenschaften, Johannes Gutenberg-Universität Mainz, Duesbergweg 10-14, D-55099, Mainz, Germany. E-mail: vboehmer@uni-mainz.de*
[b]*Institut für Organische Chemie, Johannes Gutenberg-Universität Mainz, Duesbergweg 10-14, D-55099, Mainz, Germany*
[c]*Fachbereich Biochemie/Biotechnologie, Institut für Biochemie, Martin-Luther-Universität Halle-Wittenberg, Kurt-Mothes-Str. 3, D-06099, Halle, Germany*

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‡ Permanent address: Institute of Organic Chemistry, NAS of Ukraine, Murmanska str. 5, 02094, Kyiv-94, Ukraine

and the heterodimer in a (nearly statistical) ratio 1 : 1 : 1 (Fig. 1). See the ESI for full NMR data.†

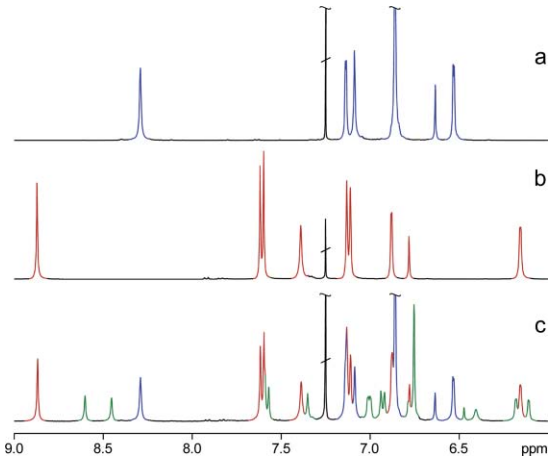
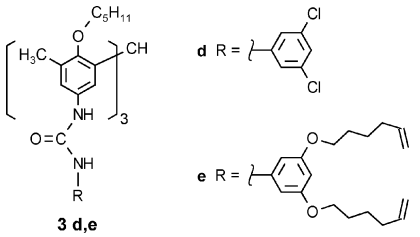


Fig. 1 Sections of the ^{1}H NMR spectra (400 MHz, $CDCl_3$) of **3a** (a), **3b** (b) and of their stoichiometric mixture (c). The signals for the heterodimer are shown in green.

The phosphorylurea derivative **3c** was synthesized to complete the picture, since the corresponding tetraurea **1c** formed exlusively heterodimers **1a**·**1c**, although neither homodimers **1c**·**1c** nor heterodimers **1b**·**1c** were observed. In the case of the triureas, however, no dimerisation at all was found for **3c**.

No heterodimerisation was observed for the 3,5-*m*-substituted derivatives **3d**,**e**, even not with a tenfold excess of the tritosylurea **3b**, although homodimers are readily and quantitatively formed. This makes the initially-intended synthesis of multi-macrocycles *via* intramolecular olefin metathesis of **3e** impossible, which it was easily performed in the case of tetraurea calix[4]arenes.



Crystal structures

Single crystals of **3a** and **3b** were obtained by slow diffusion of hexane into a solution in chloroform.§ Although the space group is different (*C*2/*c* for **3a**, *P*1- for **3b**), both form similar hydrogen bonded dimers in which the two molecules are related by a centre of symmetry (Fig. 2).

The shape of the triphenyl methane skeleton shows stronger deviations from a threefold symmetry for **3b** than for **3a**, as revealed by stronger deviations from a regular triangle for the phenolic oxygens and the methyl carbons. This is compensated by stronger differences between the dihedral angles of the three phenyl rings, and the triangle of the nitrogen atoms attached to trityl is (necessarily) close to "regular" (compare Table 1).

Both dimers are held together by a closed belt of intermolecular hydrogen bonds between the (sulfonyl)urea of the opposite molecules (Fig. 2). For **3a**, bifurcated hydrogen bonds between C=O as acceptor and both NH as donor are found, like in dimers of tetraurea calix[4]arenes. However, in contrast to the calixarenes, the hydrogen bond formed by the tolyl–NH is weaker, as evidenced by a longer NH···O and N···O distance. The angle between

§ CCDC reference numbers 614133–614134. For crystallographic data in CIF format see DOI: 10.1039/b609707c

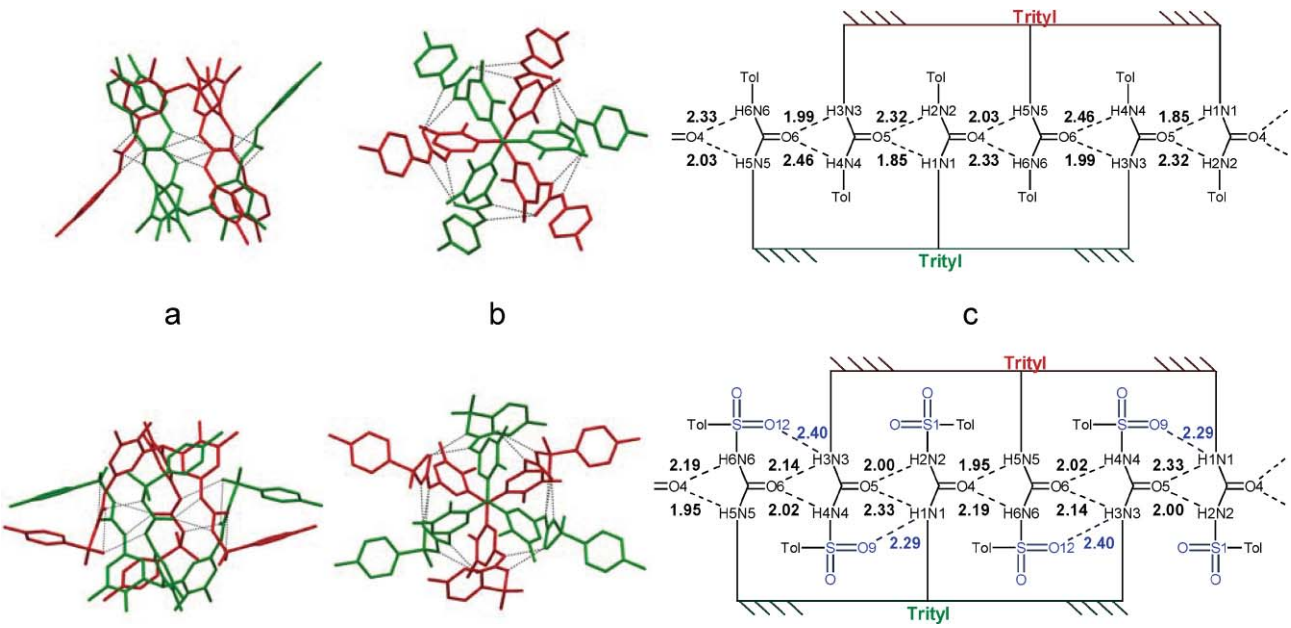


Fig. 2 Molecular conformation of dimers **3a**·**3a** (top) and **3b**·**3b** (bottom), seen from the side (a) and from the top (b) and schematic description of the hydrogen bonding systems (c) (distances NH···O=C and NH···O=S in Å). Hydrogen atoms and pentyl substituents are omitted for clarity. Top views are obtained from the side views by 90° rotation around a horizontal axis.

Table 1 Selected geometrical parameters for the molecules **3a** and **3b**

Parameter	**3a**	**3b**
Angles in the triangles of, (deg)		
Phenyl oxygens	62.98, 57.24, 59.79	60.28, 66.53, 53.18
Methyl carbons attached to trityl	61.05, 57.32, 61.63	60.81, 64.17, 55.01
Nitrogens attached to trityl	58.47, 58.96, 62.56	58.93, 61.88, 59.19
Nitrogens attached to tolyl or tosyl	59.27, 59.48, 61.24	61.15, 60.95, 57.91
Interplanar angles of, (deg)[a]		
{Aryl}/{Aryl}	82.13, 78.40, 78.31	78.57, 88.85, 77.08
{Aryl}/attached {Urea}	49.85, 51.00, 56.51	53.80, 50.13, 61.66
{Urea}/H-bonded {Urea}′	80.10, 70.39, 77.92	72.65, 78.88, 63.07
Distances between planes, (Å)		
Carbons substituted by urea	4.095	4.934
Nitrogens attached to trityl	1.651	2.490
Urea oxygens	−0.036	0.573
Nitrogens attached to tolyl or tosyl	−2.452	−1.777

[a] {Aryl}—best planes through the carbons of the trityl phenyl rings; {Urea}—best planes through N–CO–N groups.

hydrogen bonded urea groups (best plane through two N, C and O) is in the range of 70–80° for **3a** while it was 84° for a dimer of a tetraurea calix[4]arene (**1a** with Y = CH_2COOEt).[3] A stronger difference is found for the angles between aromatic planes of the trityl skeleton and the urea attached to it. They are 8–9° for **1a** and 50–57° for **3a**.

For **3b** the situation is slightly more complex. All C=O groups are acceptors for such bifurcated hydrogen bonds, and in two cases (O5, O6) the more acidic tosyl–NH forms the stronger hydrogen bond according to the shorter distance, while for O4 the trityl–NH is the stronger bound. In the former two cases the trityl–NH is involved in three-centered hydrogen bonds involving also the oxygen (O9, O12) of the adjacent SO_2 group as acceptor. The sulfonyl group of S1 is not involved in hydrogen bonding (Fig. 2). This is expressed already by a torsion angle S1–N2–C9–O4 = −33° (compared to −11 and 2° for the two other groups), which turns it away from the corresponding urea function. Similar to **3a** the angles between hydrogen bonded urea groups are 63–79° for **3b** and those between urea and aryl planes 50–62°.

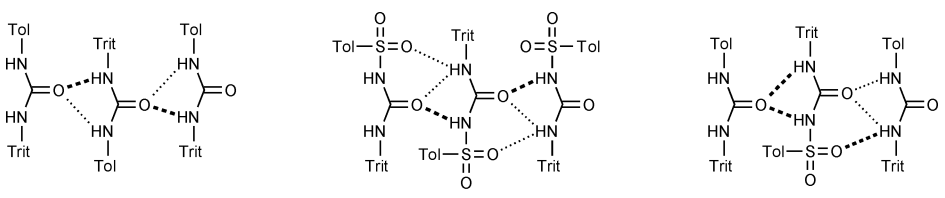
The difference in the hydrogen bonding, involving also the SO_2-groups in **3b**, leads to a significant elongation of the dimer. The distance between the methin carbon atoms is 8.13 Å in **3a** *vs* 9.03 Å in **3b**. Similarly the enlargement can be expressed by the distance between various reference planes (carbons substituted by urea, urea nitrogens (N1, N3, N5 and N2, N4, N6) or oxygens (O4, O5, O6), see Table 1.

Molecular dynamics simulations

MD simulations using the Amber7 program were performed for the homodimers **3a**·**3a** and **3b**·**3b** as well as for the heterodimer **3a**·**3b** in a box of chloroform molecules. In all starting structures the monomers were arranged to form a bifurcated hydrogen bonding pattern involving only the urea groups. This structure persisted on the MD timescale for **3a**·**3a**. The dimers with tosyl units rearranged to form hydrogen bonding patterns different from the starting one during the first nanoseconds of the simulation.

In principle, 12 bifurcated hydrogen bonds could be formed in **3a**·**3a**, 18 in **3b**·**3b** (bifurcated, three centered) and 15 in **3a**·**3b** (compare Scheme 1). Averaging over the simulation time revealed that 8.7, 12.1 and 9.8 hydrogen bonds were present in **3a**·**3a**, **3b**·**3b** and **3a**·**3b**, respectively, albeit with different strengths and different occupancies (*cf.*, Table 2). Like in the crystal, in the homodimer **3a**·**3a** the trityl–NH formed stronger hydrogen bonds than the NH attached to the tolyl rings. Generally, the structure averaged over the 9 ns MD simulations very closely resembles the X-ray structure (rms deviation of the heavy atoms of the trityl units and the urea functions 0.25 Å).

In contrast, the homodimer **3b**·**3b** was characterized by a strong hydrogen bond between the tosyl–NH and the carbonyl oxygen of the adjacent urea group ($d_{NH\cdots O} = 2.01$ Å) which is present in 87% of the snapshots. Weaker hydrogen bonds were formed between the trityl–NH and the C=O and S=O groups which in turn were also less frequently detected during the simulations (55 and 57% of all snapshots, respectively). This observed hydrogen bonding pattern (schematically shown in Scheme 1) is commensurate with the overall picture provided by the X-ray structure of **3b**·**3b** (superposition of the heavy atoms of the trityl residues and the urea functions of the X-ray structure and the average MD structure yielded a rms deviation of 0.29 Å). The involvement of the tosyl–NH protons in the strongest hydrogen bond and the formation of a NH ··· O=S hydrogen bond are the reasons for the enlargement of



Scheme 1 Hydrogen bonding pattern of the dimers observed in the MD simulations. Strong hydrogen bonds are labelled by thick dashed lines.

Table 2 Average geometric parameters obtained from the MD simulations (all distances in Å)

Parameter	**3a·3a**	**3b·3b**	**3a·3b**
General			
Number of H-bonds[a]	8.7	12.1	9.8
$d_{C\cdots C}$[b]	8.05 ± 0.28	9.25 ± 0.26	9.46 ± 0.33
r_{gyr}[c]	4.59 ± 0.07	4.50 ± 0.07	4.43 ± 0.08
$d_{O\cdots O}$[d]	4.22 ± 0.24	4.18 ± 0.22	4.15 ± 0.25
$d_{CO\cdots CO}$[e]	4.47 ± 0.21	4.39 ± 0.21	4.11 ± 0.25
			4.60 ± 0.15
Trityl NH · · · O=C			
$d_{NH\cdots O}$	1.98 ± 0.21	2.48 ± 0.50	1.97 ± 0.18[g]
			3.30 ± 0.67[h]
Observed[f]	88%	55%	96%[g]/10%[h]
Tol or Tos NH · · · O=C			
$d_{NH\cdots O}$	2.41 ± 0.35	2.01 ± 0.24	2.05 ± 0.19[g]
			2.46 ± 0.40[h]
Observed	57%	87%	90%[g]/30%[h]
Trityl NH · · · O=S			
$d_{NH\cdots O}$		2.39 ± 0.42	2.11 ± 0.68
Observed		57%	75%
Tol NH · · · O=S			
$d_{NH\cdots O}$		3.81 ± 0.57	3.10 ± 0.93
Observed		3%	25%

[a] Number of H-bonds between the monomeric units, distance and angle criterion 2.75 Å and 135°, respectively. [b] Distance of the methine carbon atoms. [c] Radius of gyration of the carbonyl groups. [d] Intramolecular distance of the ether oxygen atoms. [e] Intermolecular distance of adjacent carbonyl carbon atoms. [f] Percentage of the snapshots in which this H-bond was observed. [g] Tritosylurea. [h] Tritolylurea.

the dimer along the axis defined by the two methine carbons (the S_3 axis) by more than 1 Å compared to the dimer **3a·3a** (Table 2).

In the heterodimer **3a·3b** the tosylureas formed strong bifurcated hydrogen bonds ($d_{NH\cdots O}$ = 1.98/2.05 Å, occupancy 96 and 90%, respectively). In contrast to **3b·3b**, the O=S group is also involved in a strong hydrogen bond ($d_{NH\cdots O}$ = 2.11 Å, occupancy 75%) to the trityl–NH while the tolyl–NH formed weaker hydrogen bonds to O=C (Scheme 1). In 25% of all snapshots even a hydrogen bond is formed between the tolyl–NH and O=S (not shown in Scheme 1). As a consequence of this hydrogen bonding pattern the dimer **3a·3b** exhibits an even larger extension along the S_3 axis as **3b·3b** (Table 2).

It is interesting to note that the dimers **3a·3a** and **3a·3b** experience an additional stabilization by intermolecular CH · · · π contacts between the methyl groups attached to the trityl residues and the adjacent tolyl rings (average distances between the methyl carbon and the centroid of the aromatic ring 3.94 and 4.58 Å, respectively)[15] while this arrangement is not possible for the tosyl residues due to their bent structure.

Judging from the number and strengths of hydrogen bonds per monomeric unit the formation of the heterodimer should be slightly favoured over the two homodimers (ΔE_i = −236.0 kcal mol^{-1} *vs* −228.3 kcal mol^{-1}, *cf.* Table 3). However, the monomeric units are slightly more strained in **3a·3b** and the difference of the complexation energies (ΔE_c = −93.4 kcal mol^{-1} *vs* −92.7 kcal mol^{-1}) is insignificant. This is in agreement with the simultaneous formation of homo- and heterodimers from a mixture of **3a** and **3b**.

Conclusions

Like the tetratolylurea calix[4]arene dimers **1a·1a** the tritolylurea dimers **3a·3a** are held together by bifurcated hydrogen bonds between NH– and O=C-groups. However, the crystal structure of **3a·3a** reveals small geometrical differences (distances, interplanar angles aryl–urea and urea–urea). The crystal structure of **3b·3b** proves that three-center hydrogen bonds involving the SO_2-groups are additionally formed in the tritosylurea dimers. Molecular dynamics simulations for both dimers are in close agreement with these results, predicting also correctly the elongation of the dimer, due to the different hydrogen bonding pattern. They do not suggest significant differences for the complexation energies of the three possible dimeric combinations **3a·3a**, **3a·3b** and **3b·3b** which again is in agreement with the simultaneous observation of homo- and heterodimers.

It is reasonable to assume that analogous patterns with a combination of bifurcated and three center hydrogen bonds are present in tetraurea dimers involving the tetratosylurea **1b**. Due to geometrical differences between the calix[4]arene and the trityl skeleton they may lead to an energy gain for the heterodimer **1a·1b** which then would explain its exclusive formation in a stoichiometric mixture of **1a** and **1b**.

Experimental

Synthesis of compounds

Melting points are uncorrected. ^{1}H, ^{13}C and ^{31}P nuclear magnetic resonance spectra were recorded on a Bruker Avance DRX 400 spectrometer at 400, 100.6 and 162 MHz, respectively. Chemical shifts were reported in δ units (ppm) with reference to the residual solvent peaks, and J values are given in Hz. Decoupling and DEPT experiments confirmed the assignments of the signals. ESI mass spectra were recorded on a Waters/Micromass QTof Ultima 3 mass spectrometer. All solvents were HPLC grade and used without further purification. The isocyanates were purchased from Aldrich or Acros.

Table 3 Average energy components[a] for the dimers of **3a** and **3b**

Dimer	E_1	E_2	ΔE_i	ΔE_s	ΔE_c
3a·3a	−145.5 ± 7.3	−145.4 ± 7.3	−94.8 ± 3.4	−385.6 ± 10.6	−41.5 ± 9.3
3b·3b	−419.6 ± 8.3	−419.3 ± 8.4	−133.5 ± 7.6	−972.5 ± 10.5	−51.2 ± 9.4
3a·3b	−144.5 ± 7.3	−417.4 ± 8.4	−118.0 ± 6.2	−679.9 ± 11.1	−46.7 ± 8.0

[a] E_1, E_2: energies of the two monomeric units within the assembly, the energies of the free monomeric units are E_{3a} = 151.3 ± 7.6 kcal mol^{-1}, E_{3b} = 435.1 ± 7.9 kcal mol^{-1}; E_i: interaction energy between the two monomeric units; E_s: steric energy of the assembly = $E_1 + E_2 + E_i$; E_c: complexation energy per monomeric unit = 0.5 × (E_s–$E_{1,free}$–$E_{2,free}$).

Tris(2-pentoxy-3-methyl-5-*p*-tolylureidophenyl)methane (3a). Tolyl isocyanate (0.4 g, 3.05 mmol) was added to the solution of tris(2-pentoxy-3-methyl-5-aminophenyl)methane[14] (0.3 g, 0.51 mmol) in methylene chloride (10 mL). The reaction mixture was diluted with methanol (30 mL) after stirring for 12 h. The formed precipitate was filtered off and dried on the air to give compound **3a** (0.46 g, 91%) as a white powder. Mp = 290–293 °C (decomposition); ^{1}H NMR (400 MHz, DMSO-d$_6$), δ: 0.87 (9H, t, $^3J = 7$ Hz, CH_2CH_3), 1.27 (12H, m, CH_2), 1.59 (6H, m, CH_2), 2.20 (9H, s, $ArCH_3$), 2.21 (9H, s, $ArCH_3$), 3.41 (6H, br s, OCH_2), 6.41 (3H, d, $^4J = 2.3$ Hz, Ar*H*), 6.45 (1H, s, Ar_3CH), 7.04 (6H, d, $^3J = 8.2$ Hz, ArH_{Tol}), 7.26 (6H, d, $^3J = 8.2$ Hz, ArH_{Tol}), 7.58 (3H, d, $^4J = 2.3$ Hz, Ar*H*), 8.26 (3H, s, N*H*), 8.41 (3H, s, N*H*); ^{13}C{^{1}H} NMR (100.6 MHz, DMSO-d$_6$), δ: 13.8 (CH_2CH_3), 16.4 ($ArCH_3$), 20.2 ($ArCH_3$), 22.1 (CH_2), 27.6 (CH_2), 29.3 (CH_2), 37.2 (Ar_3CH), 71.9 (OCH_2), 117.2 (CH_{Ar}), 118.0 (CH_{Tol}), 118.9 (CH_{Ar}), 129.0 (CH_{Tol}), 130.4 (C_{Ar}), 130.7 (C_{Ar}), 134.6 (C_{Ar}), 137.0 (C_{Ar}), 137.3 (C_{Ar}), 149.9 (C_{Ar}), 152.3 (*C*(O)); *m/z* (ESI) 1011.6 (100%) [M + Na]$^+$, calc. 1012.31.

Dimer 3a·3a. ^{1}H NMR (400 MHz, $CDCl_3$), δ: 0.82 (9H, t, $^3J = 7$ Hz, CH_2CH_3), 0.9–1.2 (12H, m, CH_2), 1.35 (6H, m, CH_2), 1.77 (9H, s, $ArCH_3$), 2.18 (9H, s, $ArCH_3$), 2.29 (3H, m, OCH_2), 2.46 (3H, m, OCH_2), 6.53 (3H, d, $^4J = 2.4$ Hz, Ar*H*), 6.63 (1H, s, Ar_3CH), 6.86 (12H, s, ArH_{Tol}), 7.09 (3H, s, N*H*), 7.14 (3H, d, $^4J = 2.4$ Hz, Ar*H*), 8.29 (3H, s, N*H*); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$), δ: 14.1 (CH_2CH_3), 16.7 ($ArCH_3$), 20.6 ($ArCH_3$), 22.5 (CH_2), 28.0 (CH_2), 29.4 (CH_2), 35.5 (Ar_3CH), 71.8 (OCH_2), 120.8 (CH_{Tol}), 122.8 (CH_{Ar}), 126.2 (CH_{Ar}), 129.2 (CH_{Tol}), 131.6 (C_{Ar}), 132.3 (C_{Ar}), 132.5 (C_{Ar}), 135.5 (C_{Ar}), 137.6 (C_{Ar}), 152.9 (C_{Ar}), 156.4 (*C*(O)).

Tris(2-pentoxy-3-methyl-5-*p*-tolylsulfonylureidophenyl)methane (3b). Tosyl isocyanate (0.6 g, 3.05 mmol) was added to the solution of tris(2-pentoxy-3-methyl-5-aminophenyl)methane (0.3 g, 0.51 mmol) in methylene chloride (10 mL). The reaction mixture was diluted with methanol (30 mL) after stirring for 12 h. The solvents were removed at room temperature under reduced pressure and the residue was treated with hexane (20 mL). After removing hexane the rest was treated with methanol (10 ml) and formed precipitate was filtered off, washed with methanol and dried on the air to give compound **3b** (0.42 g, 70%) as a white powder. Mp = 243–246 °C (decomposition); ^{1}H NMR (400 MHz, DMSO-d$_6$), δ: 0.81 (9H, t, $^3J = 7$ Hz, CH_2CH_3), 1.20 (12H, m, CH_2), 1.50 (6H, m, CH_2), 2.11 (9H, s, $ArCH_3$), 2.38 (9H, s, $ArCH_3$), 3.29 (6H, br s, OCH_2), 6.30 (3H, d, $^4J = 2.4$ Hz, Ar*H*), 6.34 (1H, s, Ar_3CH), 7.33 (3H, d, $^4J = 2.4$ Hz, Ar*H*), 7.39 (6H, d, $^3J = 8$ Hz, ArH_{Tos}), 7.81 (6H, d, $^3J = 8$ Hz, ArH_{Tos}), 8.66 (3H, s, N*H*), 10.21 (3H, br s, N*H*); ^{13}C{^{1}H} NMR (100.6 MHz, DMSO-d$_6$), δ: 13.8 (CH_2CH_3), 16.2 ($ArCH_3$), 20.9 ($ArCH_3$), 22.0 (CH_2), 27.5 (CH_2), 29.2 (CH_2), 37.0 (Ar_3CH), 71.8 (OCH_2), 117.9 (CH_{Ar}), 119.5 (CH_{Ar}), 127.4 (CH_{Tos}), 129.3 (CH_{Tos}), 130.9 (C_{Ar}), 132.9 (C_{Ar}), 136.9 (C_{Ar}), 137.1 (C_{Ar}), 143.7 (C_{Ar}), 148.8 (C_{Ar}), 150.7 (*C*(O)); *m/z* (ESI) 1203.7 (100%) [M + Na]$^+$, 2385.4 (82) [2M + Na]$^+$, calc. 1204.50.

Dimer 3b·3b. ^{1}H NMR (400 MHz, $CDCl_3$), δ: 0.84 (9H, t, $^3J = 7$ Hz, CH_2CH_3), 1.27 (12H, m, CH_2), 1.59 (6H, m, CH_2), 2.24 (9H, s, $ArCH_3$), 2.36 (9H, s, $ArCH_3$), 3.14 (3H, d × t, $^2J = 9$ Hz, $^3J = 6.7$ Hz, OCH_2), 3.80 (3H, d × t, $^2J = 9$ Hz, $^3J = 6.7$ Hz, OCH_2), 6.16 (3H, d, $^4J = 2$ Hz, Ar*H*), 6.78 (1H, s, Ar_3CH), 6.88 (3H, d, $^4J = 2$ Hz, Ar*H*), 7.12 (6H, d, $^3J = 8.2$ Hz, ArH_{Tos}), 7.39 (3H, s, N*H*), 7.61 (6H, d, $^3J = 8.2$ Hz, ArH_{Tos}), 8.87 (3H, s, N*H*); ^{13}C NMR (100.6 MHz, $CDCl_3$), δ: 14.1 (CH_2CH_3), 16.8 ($ArCH_3$), 21.6 ($ArCH_3$), 22.7 (CH_2), 28.2 (CH_2), 29.9 (CH_2), 36.5 (Ar_3CH), 72.4 (OCH_2), 124.2 (CH_{Ar}), 127.8 (CH_{Ar}), 128.0 (CH_{Tos}), 129.0 (C_{Ar}), 129.4 (CH_{Tos}), 133.3 (C_{Ar}), 136.5 (C_{Ar}), 136.9 (C_{Ar}), 144.0 (C_{Ar}), 152.9 (C_{Ar}), 154.2 (*C*(O)).

Tris(2-pentoxy-3-methyl-5-diethoxyphosphorylcarbamoylphenyl)-methane (3c). Diethoxyphosphinyl isocyanate (0.46 g, 2.54 mmol) was added to the solution of tris(2-pentoxy-3-methyl-5-aminophenyl)methane (0.25 g, 0.42 mmol) in methylene chloride (10 mL). The reaction mixture was diluted with methanol (10 mL) after stirring for 12 h. The solvents were removed at room temperature under reduced pressure and the residue was crystallized from methanol (5 mL) at −14 °C. The mother solution was removed by syringe, diethyl ester (15 mL) was added to the crystals, them were filtered off, washed with diethyl ester and dried on the air to give compound **3c** (0.265 g, 55%) as a white powder. Mp = 211–213 °C (decomposition); ^{1}H NMR (400 MHz, DMSO-d$_6$), δ: 0.86 (9H, t, $^3J = 7$ Hz, CH_2CH_3), 1.24 (30H, m, CH_2 and $POCH_2CH_3$), 1.56 (6H, m, CH_2), 2.18 (9H, s, $ArCH_3$), 3.37 (6H, br s, $ArOCH_2$), 4.03 (6H, m, $POCH_2$), 6.39 (3H, d, $^4J = 2.6$ Hz, Ar*H*), 6.43 (1H, s, Ar_3CH), 7.43 (3H, d, $^4J = 2.6$ Hz, Ar*H*), 7.84 (3H, d, $^2J_{PH} = 8.6$ Hz, PN*H*), 8.63 (3H, s, ArN*H*); ^{13}C{^{1}H} NMR (100.6 MHz, DMSO-d$_6$), δ: 13.8 (s, CH_2CH_3), 15.9 (d, $^3J_{PC} = 6.8$ Hz, $POCH_2CH_3$), 16.3 (s, $ArCH_3$), 22.0 (s, CH_2), 27.6 (s, CH_2), 29.3 (s, CH_2), 37.1 (s, Ar_3CH), 62.8 (d, $^2J_{PC} = 5.4$ Hz, $POCH_2CH_3$), 71.9 (s, OCH_2), 117.6 (s, CH_{Ar}), 119.3 (s, CH_{Ar}), 131.0 (s, C_{Ar}), 133.6 (s, C_{Ar}), 137.2 (s, C_{Ar}), 150.5 (s, C_{Ar}), 151.3 (d, $^2J_{PC} = 2.7$ Hz, *C*(O)); ^{31}P{^{1}H} NMR (162 MHz, DMSO-d$_6$), δ: −0.51 (s). Only broad signals were observed in the ^{1}H spectrum in $CDCl_3$ and CD_2Cl_2. *m/z* (ESI) 1127.6 (4%) [M]$^+$, 1149.5 (100%) [M + Na]$^+$, calc. 1127.21.

Tris(2-pentoxy-3-methyl-5-(3,5-dichlorophenyl)ureidophenyl)-methane (3d). was synthesized as described for **3a**, yield is 85%, white powder. Mp = 293–295 °C (decomposition); ^{1}H NMR (400 MHz, DMSO-d$_6$), δ: 0.86 (9H, t, $^3J = 7$ Hz, CH_2CH_3), 1.26 (12H, m, CH_2), 1.58 (6H, m, CH_2), 2.20 (9H, s, $ArCH_3$), 3.40 (6H, br s, OCH_2), 6.46 (1H, s, Ar_3CH), 6.47 (3H, d, $^4J = 2.4$ Hz, Ar*H*), 7.11 (3H, m, $Ar_{Cl}H$), 7.46 (6H, d, $^4J = 1.6$ Hz, $Ar_{Cl}H$), 7.54 (3H, d, $^4J = 2.4$ Hz, Ar*H*), 8.68 (3H, s, N*H*), 8.73 (3H, s, N*H*); ^{13}C{^{1}H} NMR (100.6 MHz, DMSO-d$_6$), δ: 13.8 (CH_2CH_3), 16.3 ($ArCH_3$), 22.1 (CH_2), 27.6 (CH_2), 29.3 (CH_2), 37.2 (Ar_3CH), 71.9 (OCH_2), 116.0 (CH_{Ar}), 117.8 (CH_{Ar}), 119.4 (CH_{Ar}), 120.6 (CH_{Ar}), 130.9 (C_{Ar}), 133.9 (C_{Ar}), 134.0 (C_{Ar}), 137.3 (C_{Ar}), 142.1 (C_{Ar}), 150.3 (C_{Ar}), 151.9 (*C*(O)); *m/z* (ESI) 1153.6 (24%) [M]$^+$, 1175.5 (100) [M + Na]$^+$, 2308.1 (6) [2M]$^+$, calc. 1153.91.

Dimer 3d·3d. ^{1}H NMR (400 MHz, $CDCl_3$), δ: 0.84 (9H, t, $^3J = 7$ Hz, CH_2CH_3), 0.95–1.25 (12H, m, CH_2), 1.42 (6H, m, CH_2), 1.94 (9H, s, $ArCH_3$), 2.38 (3H, m, OCH_2), 2.61 (3H, m, OCH_2), 6.51 (3H, d, $^4J = 2.3$ Hz, Ar*H*), 6.72 (1H, s, Ar_3CH), 6.92 (3H, m, $Ar_{Cl}H$), 6.96 (6H, d, $^4J = 2$ Hz, $Ar_{Cl}H$), 7.06 (3H, s, N*H*), 7.15 (3H, d, $^4J = 2.3$ Hz, Ar*H*), 8.28 (3H, s, N*H*); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$), δ: 14.1 (CH_2CH_3), 16.8 ($ArCH_3$), 22.6 (CH_2), 27.9 (CH_2), 29.5 (CH_2), 35.2 (Ar_3CH), 72.2 (OCH_2), 118.1 (CH_{Ar}), 122.6 (CH_{Ar}), 123.1 (CH_{Ar}), 126.3 (CH_{Ar}), 130.8 (C_{Ar}),

133.2 (C_{Ar}), 135.1 (C_{Ar}), 137.7 (C_{Ar}), 139.9 (C_{Ar}), 153.7 (C_{Ar}), 155.6 (C(O)).

Tris(2-pentoxy-3-methyl-5-(3,5-dihex-5-enyloxyphenyl)ureidophenyl)methane (3e). A solution of 3,5-di(hex-5-enyloxy)benzoic acid (1.34 g, 4.21 mmol), DPPA (1.18 g, 0.93 ml, 4.28 mmol) and Et_3N (0.43 g, 0.6 ml, 4.28 mmol) in toluene (90 mL) was stirred at 70 °C for 6 h under nitrogen atmosphere. After that tris(2-pentoxy-3-methyl-5-aminophenyl)methane (0.41 g, 0.70 mmol) was added to the solution and stirring was continued during 11 h at the same conditions. Then the solvent was removed under reduced pressure, hexane (100 mL) was added to the residue (oil) and it was left in an ultrasonic bath for 15 min. Then hexane was decanted and the crude product was crystallized from Et_2O–methanol to give **3e** (0.87 g, 81%) as a white powder. Mp = 246–248 °C (decomposition); ^{1}H NMR (400 MHz, DMSO-d_6), δ: 0.87 (9H, t, ^3J = 7 Hz, CH_2CH_3), 1.28 (12H, m, CH_2), 1.46 (12H, m, CH_2), 1.63 (18H, m, CH_2), 2.05 (12H, d × t, ^3J = 7 Hz, ^3J = 7 Hz, $CH_2CH{=}CH_2$), 2.20 (9H, s, $ArCH_3$), 3.41 (6H, br s, OCH_2), 3.87 (12H, t, ^3J = 6.6 Hz, OCH_2), 4.97 (12H, m, $CH{=}CH_2$), 5.80 (6H, m, $CH{=}CH_2$), 6.07 (3H, br s, p-$Ar_{OR}H$), 6.42 (3H, d, ^4J = 2 Hz, ArH), 6.45 (1H, s, Ar_3CH), 6.57 (6H, d, ^4J = 1.8 Hz, o-$Ar_{OR}H$), 7.56 (3H, d, ^4J = 2 Hz, ArH), 8.32 (3H, s, NH), 8.44 (3H, s, NH); ^{13}C{^{1}H} NMR (100.6 MHz, DMSO-d_6), δ: 13.8 (CH_2CH_3), 16.3 ($ArCH_3$), 22.1 (CH_2), 24.6 (CH_2), 27.6 (CH_2), 28.0 (CH_2), 29.3 (CH_2), 32.7 (CH_2), 37.2 (Ar_3CH), 67.0 (OCH_2), 71.9 (OCH_2), 94.5 (CH_{Ar}), 96.7 (CH_{Ar}), 114.7 ($CH{=}CH_2$), 117.4 (CH_{Ar}), 118.9 (CH_{Ar}), 130.8 (C_{Ar}), 134.4 (C_{Ar}), 137.2 (C_{Ar}), 138.4 ($CH{=}CH_2$), 141.2 (C_{Ar}), 149.9 (C_{Ar}), 152.1 (C(O)), 159.8 (C_{Ar}); m/z (ESI) 1537.3 (87%) $[M]^+$, 1559.3 (85) $[M + Na]^+$, 3073.6 (35) $[2M]^+$, calc. 1536.12.

Dimer 3e·3e. ^{1}H NMR (400 MHz, $CDCl_3$), δ: 0.85 (9H, t, ^3J = 7 Hz, CH_2CH_3), 1.20 (12H, m, CH_2), 1.43 (18H, m, CH_2), 1.62 (12H, m, CH_2), 1.73 (9H, s, $ArCH_3$), 2.06 (12H, d × t, ^3J = 7 Hz, ^3J = 7 Hz, $CH_2CH{=}CH_2$), 2.49 (3H, m, OCH_2), 2.66 (3H, m, OCH_2), 3.42 (6H, m, OCH_2), 3.67 (6H, m, OCH_2), 4.97 (12H, m, $CH{=}CH_2$), 5.78 (6H, m, $CH{=}CH_2$), 6.04 (3H, t, ^4J = 2 Hz, p-$Ar_{OR}H$), 6.10 (6H, d, ^4J = 2 Hz, o-$Ar_{OR}H$), 6.46 (3H, d, ^4J = 2.5 Hz, ArH), 6.63 (1H, s, Ar_3CH), 7.06 (3H, d, ^4J = 2.5 Hz, ArH), 7.21 (3H, s, NH), 8.41 (3H, s, NH); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$), δ: 14.0 (CH_2CH_3), 16.5 ($ArCH_3$), 22.7 (CH_2), 25.4 (CH_2), 28.0 (CH_2), 28.6 (CH_2), 29.7 (CH_2), 33.5 (CH_2), 35.6 (Ar_3CH), 67.4 (OCH_2), 72.0 (OCH_2), 97.6 (CH_{Ar}), 99.7 (CH_{Ar}), 114.7 ($CH{=}CH_2$), 122.5 (CH_{Ar}), 126.0 (CH_{Ar}), 131.4 (C_{Ar}), 132.8 (C_{Ar}), 137.7 (C_{Ar}), 138.4 ($CH{=}CH_2$), 139.0 (C_{Ar}), 153.0 (C_{Ar}), 156.3 (C(O)), 160.2 (C_{Ar}).

Single-crystal X-ray diffraction

Intensity data for **3a** were collected on an Enraf Nonius CAD4 diffractometer with Cu Kα radiation (graphite monochromator) at 193 K or on KAPPA CCD with Mo Kα at 120 K for **3b**. The structures were solved using SIR2002[16] and refined with SHELX97.[17] All non-hydrogen atoms were refined anisotropically with C–H hydrogen atoms generated at idealized positions and refined as riding atoms. Hydrogen atoms important for potential hydrogen bonds could be located in differential Fourier maps. The refinement converged at $R1 = 0.1020$ for **3a** and $R1 = 0.0912$ for **3b**. The position of the solvent molecule (chloroform) in crystals of **3a** and **3b** is highly disordered.

Crystal data for 3a. $C_{61}H_{76}N_6O_6$*1/2$CHCl_3$, M = 1097.92, monoclinic, a = 34.004(4) Å, b = 15.738(3) Å, c = 26.894(4) Å, β = 122.233(5)°, V = 12175(3) Å^3, T = 193 K, space group C2/c (no. 15), Z = 8, μ(Cu Kα) = 1.170 mm^{-1}, 11539 reflections measured, 11539 reflections unique which were used in all calculations.

Crystal data for 3b. $C_{61}H_{76}N_6O_{12}S_3$*2$CHCl_3$, M = 1420.23, triclinic, a = 14.3620(6) Å, b = 14.7300(6) Å, c = 18.9930(6) Å, α = 67.8510(10)°, β = 70.2640(10)°, γ = 80.3860(10)°, V = 3499.3(2) Å^3, T = 120 K, space group P-1 (No.2), Z = 2, μ(Mo Kα) = 0.397 mm^{-1}, 62249 reflections measured, 11692 reflections unique (R_{int} = 0.1462) which were used in all calculations.

Molecular dynamics simulations

Computational methods. All molecular dynamics simulations were performed using the AMBER 7 software package and the *gaff* parameter set.[18] The initial geometry of all models was obtained by manual construction. Charges were derived following the standard RESP procedure from a 6–31G* electrostatic potential calculated with the GAMESS program and the assemblies were transferred into the LEaP format.[19,20] Subsequently, a rectangular box of chloroform molecules (approximately 14 Å solvent layer thickness on each side) was added. The solvated structures were subjected to 5000 steps of minimization followed by a 30 ps belly dynamics (300 K, 1 bar, 1 fs timestep) for solvent relaxation and by a 100 ps equilibration period. Subsequently, MD simulations were performed in a NTP (300 K, 1 bar) ensemble for 9 ns using a 1 fs time step. Constant temperature and pressure conditions were achieved by the weak coupling algorithm and isotropic position scaling. Temperature and pressure coupling times of 0.5 and 1.0 ps, respectively, and the experimental compressibility value of 100 × 10^{-6} bar^{-1} for chloroform were used. Bonds containing hydrogen atoms were constrained to their equilibrium length using the SHAKE algorithm. Snapshots were recorded every 2 ps. The free monomeric units were subjected to a MD simulation of 3 ns using the conditions as described above. For analysis purposes the trajectories were averaged over 9 ns for **3a**·**3a**, over the last 8 ns for **3b**·**3b** and over the last 6.4 ns for **3a**·**3b**.

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