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Molecules with New Topologies Derived from Hydrogen-Bonded Dimers of Tetraurea Calix[4]arenes

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Abstract: Tetraurea calix[4]arenes **2** have been synthesized in which two adjacent aryl urea residues are connected to a loop by an aliphatic chain -O-$(CH_2)_n$-O-. The remaining urea residues have a bulky 3,5-di-*tert*-butylphenyl residue and an ω-alkenyloxyphenyl residue. Since this bulky residue cannot pass through the loop, only one homodimer (**2·2**) is formed in apolar solvents, for steric reasons, in which the two alkenyl residues penetrate the two macrocyclic loops. Covalent connection of these alkenyl groups by olefin metathesis followed by hydrogenation creates compounds **3**, which consist of molecules with hitherto unknown topology. Their molecular structure was confirmed by ^{1}H NMR spectroscopy and ESIMS, and for one example by single-crystal X-ray analysis.

Keywords: calixarenes · dimers · knots · macrocycles · topology

Introduction

The preparation of topologically nontrivial molecules is primarily an intellectual challenge.[1] Their controlled synthesis usually requires a suitable prearrangement of the molecular building blocks to ensure their correct covalent connection.[2] The dimerization of calix[4]arenes substituted with four urea residues at the wide rim[3,4] may be used to arrange functional groups attached to these urea residues in well-defined positions.[5] In this way controlled intramolecular reactions between these functions are possible.

We obtained multimacrocyclic molecules from heterodimers with a tetratosyl urea group through a metathesis reaction between the alkenyl groups (followed by hydrogenation of the double bonds).[6,7] Fourfold [2]rotaxanes are formed for shorter loops.[8] The exclusive heterodimerization of bis- or tetraloop tetraureas with tetra- or octaalkenyl ureas was successfully used to prepare bis[2]catenanes,[9] bis[3]catenanes, or even cyclic[8]catenanes.[10]

Alternatively, bis[2]catenanes can be prepared by metathesis of homodimers formed by bisalkenyl monoloop ureas **1** (Figure 1).[9] Starting with a monoloop ($n=8$; see Scheme 1 for n and p nomenclature) bisalkenyl ($p=6$) compound it was possible to synthesize a bis[2]catenane in which two loops of different sizes were attached to each calix[4]arene, whereas for longer alkenyl residues ($p=9$) a pure compound could not be isolated from the reaction mixture, although the reaction product clearly had the expected molar mass according to ESIMS.

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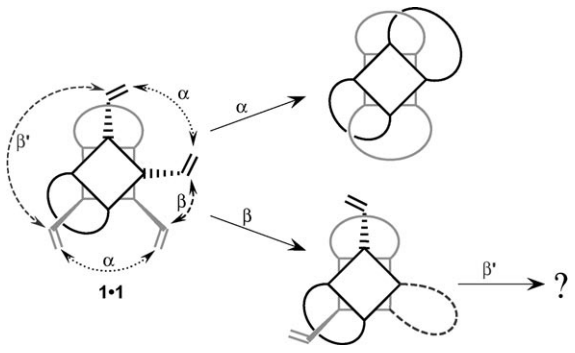


Figure 1. Synthesis of bis[2]catenanes by metathesis of homodimers **1·1** ($2\times\alpha$ connections). Possible side reactions through β and subsequent β′ connections are also shown.

To obtain bis[2]catenanes, alkenyl groups attached to the same calixarene must be connected by the metathesis reaction (α connections). In principle, connections between alkenyl groups attached to different calixarenes are also possible (β connections), at least when these groups are in adjacent positions in the dimer.[11] Such a β connection would leave two "isolated" alkenyl groups that could be connected in a second step to form a product isomeric to the expected bis[2]catenane (Figure 1). Since the separation of these isomers can be difficult, we were primarily interested to see if the connection of remote alkenyl residues within the dimer (β′ connection) is possible at all.

Results and Discussion

To check, if alkenyl groups of different calixarenes can be covalently linked by metathesis within a dimer when they are not in adjacent positions, we prepared monoloop compounds **2** with one alkenyl urea (of different lengths) and one bulky urea residue (Figure 2). These compounds should

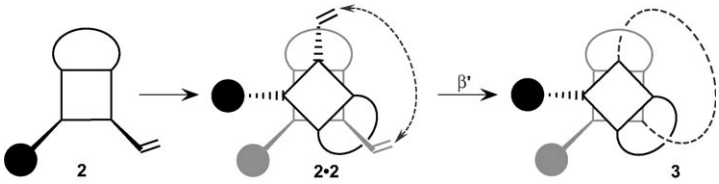


Figure 2. Dimerization of tetraurea **2** and metathesis reaction (followed by hydrogenation) of the alkenyl residues within the dimer **2•2** (=β′ connection).

form only one homodimer because, for steric reasons, the loops cannot overlap and the bulky residue cannot penetrate the loop.[12] Thus, if an intramolecular metathesis reaction is possible for such a dimer, the product **3** must contain the discussed β′ connection.

Compounds **2** were synthesized in four steps starting with the bis-BOC protected tetraamine **4**,[13] as shown in Scheme 1: Cyclization with an activated bisurethane[14] under dilution led to the formation of macrocyclic diureas (60–80%), which were quantitatively deprotected. Diamines **5a**,**b** were first monoacylated with the activated urethane **7a** to introduce the bulky urea residue (47–52% of **6a**,**b**). Finally the alkenyl urea residue was introduced analogously by acylation with **7b**,**c** in the last step to give **2b**,**d** in 60–80% yield. Alternatively, the alkenyl group was introduced first by acylation of **5a**,**b** with active ester **7b** (44–59% of **6c**,**d**) followed by acylation with **7a** in the second step to give **2a**,**c** in yields of 58–80%. No clear advantage was found for one of these two possible pathways.

The structure of compounds **2** was confirmed by ESIMS and ^{1}H NMR spectroscopy in [D$_6$]DMSO or [D$_8$]THF. Since the molecules are fixed in the cone conformation, they are chiral (C_1 symmetry) and this chirality can be demonstrated by the splitting of signals after addition of Pirkles reagent. It is worth noting that the dimerization of **2** can occur stereoselectively only between molecules of the same enantiomer. Hence, the dimer has "structurally" C_2 symmetry, which is reduced to C_1 symmetry by the directionality of the hydrogen-bonded belt.[15]

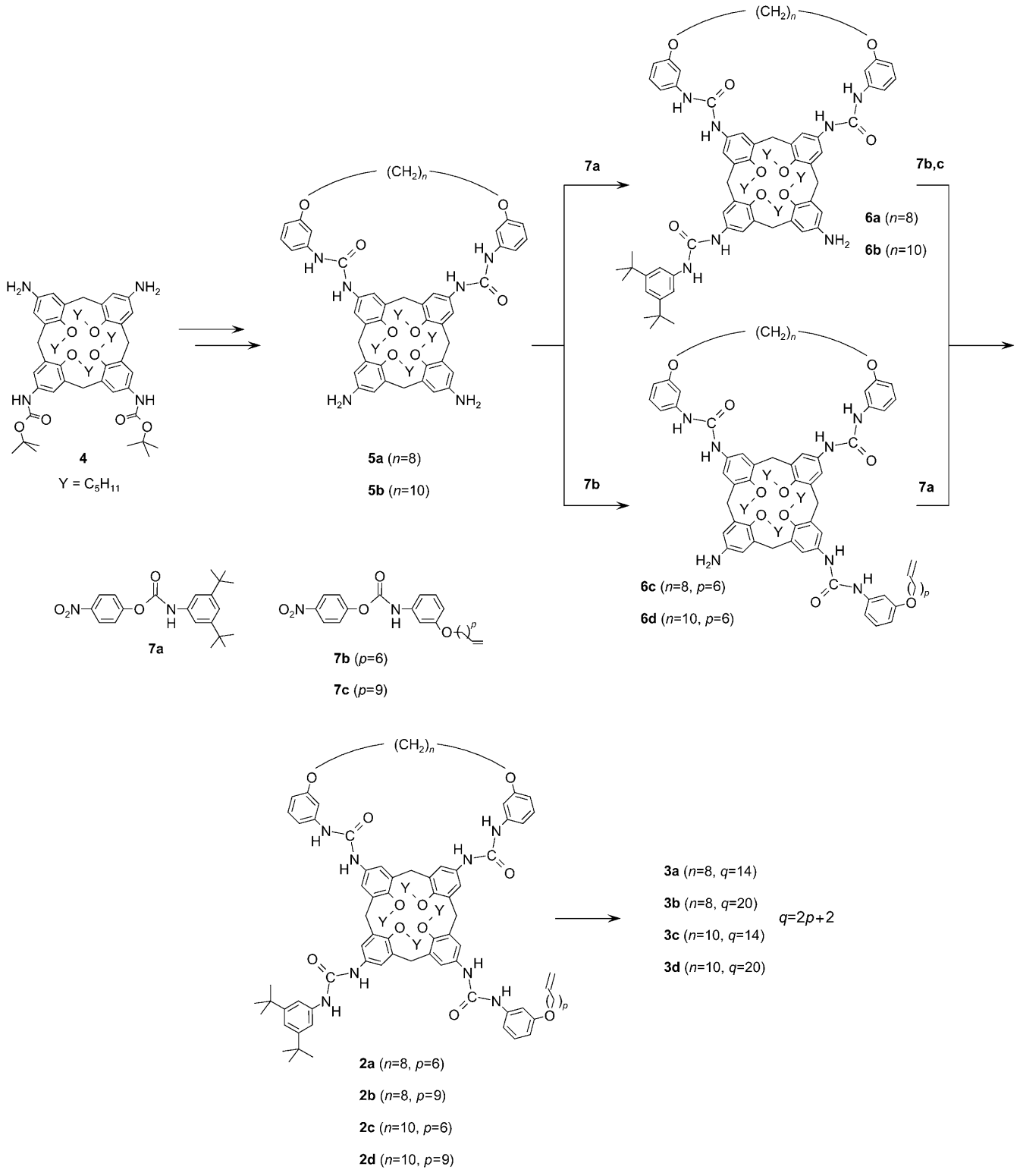
^{1}H NMR spectra in $CDCl_3$ or [D$_6$]benzene are in agreement with the formation of a single dimer **2•2** with C_1 symmetry. They show for instance (in **2d** for example) eight signals for the NH$_\alpha$ protons at $\delta = 10.06$–9.90 ppm (two are overlapped), eight doublets with *meta* coupling in the $\delta =$ 6.41–6.24 ppm region, which have the corresponding signals at $\delta = 8.25$–8.0 ppm (eight signals were found in the Cosy spectra, but four of them are overlapped). The aromatic protons of the bulky residue appear as two doublets ($\delta =$ 8.33 and 8.26 ppm) and two broad triplets ($\delta = 7.29$ and 7.23 ppm). Also the two singlets for *tert*-butyl groups at $\delta =$ 1.35 and 1.32 ppm demonstrate that the two 3,5-di-*tert*-butylphenyl residues are different in the C_1-symmetrical dimer.[16]

Olefin metathesis with dimers **2•2** followed by hydrogenation led to a single reaction product, **3b**,**d** in the case of **2b**,**d**, which was isolated in 40 and 57% yield, respectively, after the usual chromatographic work up. The yield drops to 15–20% for compounds **3a**,**b** with the shorter loop and the crude product contains several byproducts. In the case of **3b**,**d**, ESI mass spectra were measured for samples dissolved in chloroform/methanol (2:1) and peaks corresponding to $[M+2\mathrm{Na}]^{2+}$ (**3b**) and $[M+\mathrm{H}+\mathrm{Na}]^{2+}$ (**3d**) were observed with the highest (99–100%) abundance. For compounds **3a**,**c**, samples prepared in a similar way gave spectra in which the peaks could not be interpreted. Clear ESI mass spectra were obtained, however, when the samples were dissolved in chloroform and tetraethylammonium tetrafluoroborate was added. In these cases only the peaks corresponding to $[M+\mathrm{Et_4N}]^+$ were found with 100% abundance.[17] At this point it is important to notice that the encapsulation of the cation took place in minutes and no peak corresponding to a solvent containing capsule was detected.

^{1}H NMR spectra (Figure 3) reveal the expected C_1 symmetry (no symmetry element), showing for instance eight low-field signals for NH$_\alpha$ of the urea groups and eight pairs of *m*-coupled doublets for the aromatic protons of the calixarene parts, which are completely resolved for the low-field part.

All these results prove that the envisaged β′ connection was in fact achieved in all cases.

Many early attempts to confirm the complicated connectivities in compounds **3** by crystallography failed. Although several single crystals were grown from **3d**, it was impossible to solve their structure by X-ray analysis. Since heavy atoms often facilitate the determination of the structure, we started the synthesis of compound(s) in which bromine atoms replace the *tert*-butyl groups as the bulky residues. Unfortunately the bromine atoms are too small to ensure a selective dimerization, at least in combination with a loop of $n = 10$. After a crystal structure was eventually obtained for **3d** these studies were not continued.



Scheme 1. Synthesis of monoloop compounds **2a**–**d**.

Crystal structure: After numerous attempts with various crystals the structure of **3d** could be finally solved. Crystals were obtained by slow evaporation of a solution in chloroform/acetonitrile. Two crystallographically independent molecules (**I**, **II**) were found, in which both calixarene parts form a hydrogen-bonded capsule. They differ mainly by the conformation of the aliphatic $(CH_2)_{10}$ chains connecting two adjacent phenylurea groups (**a**, **b**) within each calixarene part (**A** ,**B**) and the $(CH_2)_{20}$ chain connecting the two calixarene parts (via **c**). The capsule includes two acetonitrile

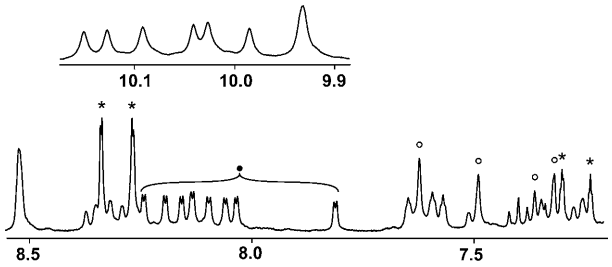


Figure 3. Sections of the ^{1}H NMR-spectrum of **3b** in C_6D_6. Top: aryl NH. Bottom: calix NH protons (○), aromatic protons of the calixarene skeleton (●), and aromatic protons of the 3,5-di-*tert*-butylphenyl groups (*) are indicated and the rest of the signals are the *meta*-substituted phenolic rings of the loops.

molecules in a roughly antiparallel orientation. Five chloroform and five acetonitrile molecules are additionally incorporated into the crystal lattice. The molecular conformation of molecule **I** is shown in Figure 4a and the packing of molecules **I** and **II** is shown in Figure 4b.

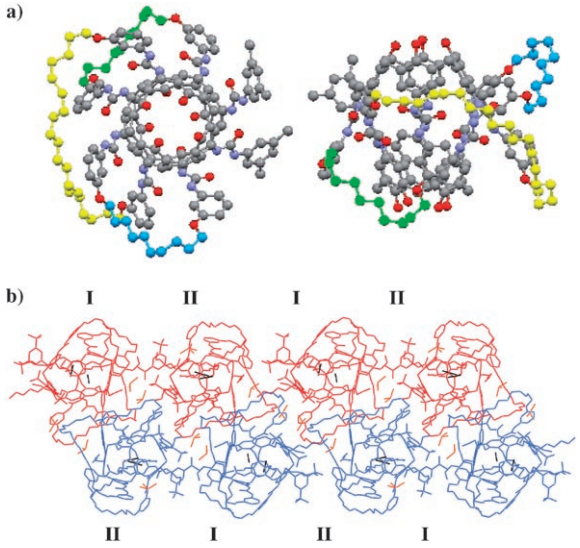


Figure 4. a) Molecular conformation of **3d** (molecule **I**) seen from the top (left) and from the side (right). Hydrogen atoms are omitted for clarity. Loops connecting adjacent urea groups within a calixarene are green and blue; the chain connecting the two calixarenes is yellow. b) Packing of **3d** in the crystal lattice, as seen along the *a* axis. The two crystallographically independent molecules are indicated by **I** and **II**.

The first crystal structure described for a hydrogen-bonded dimer of a tetraurea calix[4]arene[18] shows a molecule with a fourfold axis.[19] Such a fourfold symmetry is impossible for the present molecule **3d**, but the shape of the capsules itself, without the connecting aliphatic chains is rather similar, as shown by the values compared in Table 1.[20] The distance between the centers of the two reference planes defined by the carbon atoms of the calixarene methylene bridges is nearly identical for **I** and **II** (10.226/10.217 Å), but significantly larger (by 0.438 Å) than in the tetraester capsule.[18] A significant distortion and a slight difference of both capsules is indicated by the interplanar angle for the best planes through the phenolic oxygen atoms (7.4 and 9.5°) and the carbon atoms of the methylene bridges (3.2/5.5°), whereas the cyclic belt of hydrogen bonds requires nearly parallel planes (1.4/2.9°) for the carbonyl carbons.

Table 1. Comparison of some characteristic crystallographic data.

Dimer	**I**[a]	**II**[a]	Tetraester[18]
planes of calix O atoms			
distance between centers [Å]	12.819	12.818	12.487
angle [°]	7.4	9.5	0.0
planes of methylene C atoms			
distance between centers [Å]	10.226	10.217	9.784
angle [°]	3.2	5.5	0.0
planes of carbonyl C atoms			
distance between centers [Å]	1.422	1.375	1.100
angle [°]	1.4	2.9	0.0
calixarene A[b]			
O–O distance diagonal [Å]	4.944	5.025	4.376
	3.963	3.855	
angle calix-phenyl plane/	64.9[c]	58.6[c]	62.4
reference plane [°]	57.1[c]	72.1[c]	
	63.4	69.8	
	70.8[d]	56.0[d]	
calixarene B[b]			
O–O distance diagonal [Å]	4.951	4.899	4.469
	3.878	4.211	
angle calix-phenyl plane/	62.0[c]	66.5[c]	64.1
reference plane [°]	70.9[c]	67.5[c]	
	68.5	68.0	
	54.2[d]	56.8[d]	

[a] Two crystallographically independent molecules. [b] Two calixarene parts per molecule. [c] Adjacent phenyl rings connected by the loop. [d] Phenyl ring with the voluminous residue.

The distortion of the single calix[4]arenes may be characterized by the diagonal distances of the phenolic oxygen atoms, which differ by 0.981 and 1.073 Å for both calixarenes forming capsule **I** and by 1.17 and 0.688 Å for those of **II**. They are also indicated by the inclination angles of the aromatic planes of the calixarene, which range from 54.2 to 72.1°. However, these slight distortions are not (necessarily) caused by the aliphatic chains within and between the calix[4]arenes, which contain many *anti* and *gauche* conformations characteristic for an unstrained aliphatic chain.

The crystal structure reveals a rather "relaxed" situation despite the different phenyl substituents attached to the four urea groups. Probably the difference of the four phenolic units is not pronounced enough, to entirely prevent the incorporation of the molecules under (slightly) different orientations in the crystal lattice. Such a disorder, obtained for instance by rotation around the axis of the dimeric capsule, would explain the difficulties in solving the structure that we initially faced.

Conclusion

Molecules **3** show an interesting and, to the best of our knowledge, unprecedented topology that can be explained by the "transformations" shown in Figure 5.

First the nonconnected urea arms can be omitted and the calixarene macrocycles may be reduced to a point because they are not involved in catenation. Further deformations finally lead to a topological representation that may be described as follows: Two rings with an attached axle form a "double" rotaxane by mutual penetration. Additionally the open ends of the axles are connected to a macrocycle. Thus, the molecule combines structural elements of rotaxanes and catenanes and shows in addition some similarities to knots. To the best of our knowledge, such a topology has not yet been described and synthetically realized.

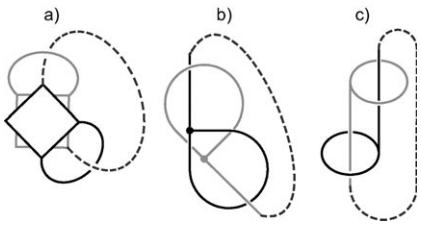


Figure 5. Illustration of the topology of molecules **3** by graphical simplifications: a) omission of the bulky "open ended" urea residue; b) "shrinkage" of the calixarene to a point; and c) graphical rearrangement.

Experimental Section

General: DMF (peptide synthesis grade) was purchased from Acros, the Grubbs catalyst (first generation) from Strem and deuterated solvents from Deutero GmbH. All reactions were carried out under nitrogen. Column chromatography was performed with silica gel (Merck, 0.040–0.063 mm). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX400 Avance Instrument at 400 and 100.6 MHz, respectively. Chemical shifts were calibrated to the residual signal of the deuterated solvent. Mass spectra were obtained on a Finnigan MAT 8230 spectrometer.

Syntheses: Compounds **4**,[12] **5**, and **7b**,**c** were prepared as described previously.[19] The active urethane **7d** was synthesized in three steps and is reported in the Supporting Information. For compounds **6**, **2**, and **3**, representative examples are described herein, together with ^{1}H NMR and MS data. The remaining compounds and all ^{13}C NMR data are included in the Supporting Information.

General procedure for the synthesis of the compound **6**: A solution of active urethane **7** (0.84 mmol) in DMF (peptide synthesis grade, 25 mL) was added dropwise (5 mL h^{-1}) to a solution of diamine **5** (0.7 mmol) and diisopropylethylamine (1 mL) in DMF (200 mL). The reaction mixture was stirred for an additional hour and then the solvent was evaporated. The dry residue was dissolved in dichloromethane and washed with a solution of K_2CO_3 until the water phase remained colorless. After drying over $MgSO_4$, the solvent was evaporated and the product was purified by column chromatography (silica gel, THF or ethyl acetate/hexane mixture as the eluent). The product was used in the next step after being analyzed by MS.

6a: Yield = 52 %; ESIMS: *m*/*z* (%): 1398.9 (100) $[M+Na]^+$.

General procedure for the synthesis of the compound **2**: A solution of **6** in THF, the corresponding active urethane **7** (in a molar ratio of 1:1) and diisopropylethylamine (1 mL) was heated at reflux for 12 h. The reaction mixture was diluted with dichloromethane and washed with a solution of K_2CO_3 until the water phase remained colorless. After drying over $MgSO_4$, the solvent was evaporated and the product was crystallized from chloroform/methanol. If the product was not yet pure it was further purified by column chromatography (THF or ethyl acetate/hexane mixture as the eluent).

2a: Yield = 58 %; ^{1}H NMR ([D$_6$]DMSO, 400 MHz, 25 °C): δ = 8.34 (s, 1H; N**H**), 8.26 (s, 1H; N**H**), 8.23 (s, 1H; N**H**), 8.22 (s, 1H; N**H**), 8.12 (s, 1H; N**H**), 8.07 (s, 1H; N**H**), 8.02 (s, 1H; N**H**), 8.01 (s, 1H; N**H**), 7.17 (brt, 1H; Ar_{meta}-**H**), 7.12 (brd, 2H; Ar-**H**), 7.09 (brt, 1H; Ar_{meta}-**H**), 7.03 (d, 1H; $^4J \approx 1.5$ Hz, Ar_{calix}-**H**), 7.00–6.96 (3m, 3H; Ar_{meta}-**H**), 6.90 (m, 2H; Ar_{calix}-**H** + Ar-**H**), 6.84 (brs, 1H; Ar_{calix}-**H**), 6.76 (brs, 1H; Ar_{calix}-**H**), 6.73 (brs, 1H; Ar_{calix}-**H**), 6.67 (dd, 1H; $^3J = 8.2$ Hz, $^4J \approx 1.0$ Hz, Ar_{meta}-**H**), 6.48–6.45 (m, 4H; 2 Ar_{calix}-**H** + 2 Ar_{meta}-**H**), 6.42–6.38 (m, 5H; Ar_{calix}-**H** + 4 Ar_{meta}-**H**), 5.74–5.67 (m, 1H, =C-**H**), 4.93–4.83 (m, 2H, =C-**H**$_2$), 4.27 (d, 4H; $^2J = 11.44$ Hz, Ar-C**H**$_2$-Ar_{ax}), 3.85–3.72 (m, 12H; -OC**H**$_2$), 3.08–3.00 (m, 4H; Ar-C**H**$_2$-Ar_{eq}), 1.93 (m, 2H; -C**H**$_2$-), 1.83 (m, 10H; -C**H**$_2$-), 1.59 (m, 4H; -C**H**$_2$-), 1.36–1.30 (m, 16H; -C**H**$_2$-), 1.26–1.24 (m, 4H; -C**H**$_2$-), 1.16(s, 18H; *t*Bu) 0.87 ppm (t, $^3J = 5.6$ Hz, 12H; -C**H**$_3$); ESIMS: *m*/*z* (%): 1645.01 (100) $[M+Na]^+$.

2b: Yield = 58 %; ^{1}H NMR ([D$_6$]benzene, 400 MHz, 60 °C): δ = 9.92 (s, 1H; N**H**), 9.88 (s, 1H; N**H**), 9.86 (s, 3H; N**H**), 9.84 (s, 1H; N**H**), 9.72 (s, 2H; N**H**), 9.69 (s, 2H; N**H**), 8.39 (brs, 2H; Ar_{meta}-**H**), 8.23 (brd, 2H; Ar-**H**), 8.23–8.21 (m, 2H; Ar_{meta}-**H**), 8.19 (m, 3H; Ar-**H** + Ar_{calix}-**H** + Ar_{calix}-**H**), 8.11 (brt, 1H; Ar_{meta}-**H**), 8.09 (d, $^4J = 1.8$ Hz, 1H; Ar_{calix}-**H**), 8.05 (brt, 1H; Ar_{meta}-**H**), 8.03 (d, $^4J = 2.6$ Hz, 1H; Ar_{calix}-**H**), 8.02 (d, $^4J = 2.6$ Hz, 1H; Ar_{calix}-**H**), 7.96 (brs, 2H; Ar_{calix}-**H**), 7.92 (d, $^4J = 1.8$ Hz, 1H; Ar_{calix}-**H**), 7.61 (m, 2H; Ar_{meta}-**H** + Ar_{meta}-**H**), 7.55 (brt, 1H; Ar_{meta}-**H**), 7.53 (s, 1H; N**H**), 7.49 and 7.47 (brdd, $^3J = 8.1$ Hz, 1H; Ar_{meta}-**H**), 7.46 (s, 1H; N**H**), 7.36 (m, 2H; Ar_{meta}-**H**), 7.29 (brs, 1H; Ar-**H**), 7.27 (s, 1H; N**H**), 7.24 (brs, 1H; Ar-**H**), 7.24 (m, 2H; Ar_{meta}-**H** + N**H**), 7.22 (t, $^3J = 8.2$ Hz, 1H; Ar_{meta}-**H**), 7.07 (t, $^3J = 7.8$ Hz, 1H; Ar_{meta}-**H**), 7.03 (t, 1H; $^3J = 8.2$ Hz, Ar_{meta}-**H**), 6.75–6.69 (m, 4H; 2 Ar_{meta}-**H** + 2 N**H**), 6.62–6.55 (m, 5H; 4 Ar_{meta}-**H** + N**H**), 6.39 (d, $^4J = 2.0$ Hz, 1H; Ar_{calix}-**H**), 6.33 (m, 2H; Ar_{calix}-**H**), 6.31 (d, $^4J = 2.0$ Hz, 1H; Ar_{calix}-**H**), 6.29 (m, 2H; Ar_{calix}-**H**), 6.19 (d, $^4J = 2.0$ Hz, 1H; Ar_{calix}-**H**), 6.04 (d, $^4J = 2.0$ Hz, 1H; Ar_{calix}-**H**), 5.85–5.75 (m, 2H; =C-**H**), 5.05–4.95 (m, 4H; =C-**H**$_2$), 4.63 (d, $^2J = 12.0$ Hz, 1H; Ar-C**H**$_2$-Ar_{ax}), 4.57 (d, $^2J = 12.0$ Hz, 2H; Ar-C**H**$_2$-Ar_{ax}), 4.55 (d, $^2J = 10.6$ Hz, 1H; Ar-C**H**$_2$-Ar_{ax}), 4.53 (d, $^2J = 12.3$ Hz, 1H; Ar-C**H**$_2$-Ar_{ax}), 4.48 (d, $^2J = 11.2$ Hz, 1H; Ar-C**H**$_2$-Ar_{ax}), 4.46 (d, $^2J = 11.7$ Hz, 1H; Ar-C**H**$_2$-Ar_{ax}), 4.45 (d, $^2J = 10.9$ Hz, 1H; Ar-C**H**$_2$-Ar_{ax}), 4.25–3.10 (2×m, 4H; -OC**H**$_2$), 3.9–3.75 (m, 24H; -OC**H**$_2$), 3.30 (d, $^2J = 11.7$ Hz, 1H; Ar-C**H**$_2$-Ar_{eq}), 3.25 (d, $^2J = 11.7$ Hz, 1H; Ar-C**H**$_2$-Ar_{eq}), 3.24 (d, $^2J = 11.7$ Hz, 1H; Ar-C**H**$_2$-Ar_{eq}), 3.22 (d, $^2J = 12.0$ Hz, 1H; Ar-C**H**$_2$-Ar_{eq}), 3.15 (d, $^2J = 11.7$ Hz, 1H; Ar-C**H**$_2$-Ar_{eq}), 3.13 (d, $^2J = 11.7$ Hz, 1H; Ar-C**H**$_2$-Ar_{eq}), 3.06 (d, $^2J = 12.0$ Hz, 1H; Ar-C**H**$_2$-Ar_{eq}), 3.01 (d, $^2J = 12.3$ Hz, 1H; Ar-C**H**$_2$-Ar_{eq}), 2.1–1.2 (5×m, 106H; -C**H**$_2$-), 1.36 (s, 18H; *t*Bu), 1.34 (s, 18H; *t*Bu), 1.0–0.91 ppm (m, 24H; -C**H**$_3$).

2c: Yield = 80 %; ESIMS: *m*/*z* (%): 1673.16 (100) $[M+Na]^+$.

2d: Yield = 60 %; ESIMS: *m*/*z* (%): 1715.04 (100) $[M+Na]^+$, 1693.07 (46) $[M+H^+]$.

General procedure for the synthesis of **3**: A 0.5 mmol solution of **2** in benzene was heated at 60 °C for 2–6 h and the formation of the homodimer was confirmed by NMR spectroscopy measurements. After cooling at room temperature the reaction mixture was purged with nitrogen for 30 min and a solution of the Grubbs catalyst (0.15 mmol/double bond) in benzene (5 mL) was added in one portion. The reaction mixture was stirred at room temperature for two days. The catalyst was destroyed by adding triethylamine (1 mL) and additional stirring for 30 min. The reaction mixture was concentrated at low pressure and hydrogenated in the presence of platinum dioxide. After filtration and evaporation the crude product was purified by column chromatography (THF/hexane mixture as the eluent). The pure compound was obtained after crystallization from THF/methanol.

3a: M.p. > 270 °C decomposition without melting; yield = 18 %; ^{1}H NMR ([D$_6$]benzene, 400 MHz, 25 and 60 °C): very broad and insignificant; ESIMS (complex with $(C_2H_5)_4N^+PF_6^-$): *m*/*z* (%): 3348.61 (100) $[M+Et_4N]^+$.

3b: M.p. > 250 °C decomposition without melting; yield = 57 %; ^{1}H NMR ([D$_6$]benzene, 400 MHz, 25 °C): δ = 10.14 (s, 1H; N**H**), 10.12 (s, 1H; N**H**), 10.08 (s, 1H; N**H**), 10.03 (s, 1H; N**H**), 10.02 (s, 1H; N**H**), 9.98 (s, 1H; N**H**), 9.92 (s, 2H; N**H**), 8.52 (brs, 3H; Ar$_{meta}$-**H**), 8.36 and 8.34 (br dd, ^3J = 8.2 Hz, 2H; Ar$_{meta}$-**H**), 8.33 (d, ^4J = 1.6 Hz, 2H; Ar-**H**), 8.33 and 8.31 (br dd, ^3J = 8.2 Hz, 2H; Ar$_{meta}$-**H**), 8.33 and 8.31 (br dd, ^3J = 8.2, ^4J = 1.4 Hz, 2H; Ar$_{meta}$-**H**), 8.28 and 8.26 (br dd, 2H; ^3J = 8.2 Hz, ^4J = 1.4 Hz, Ar$_{meta}$-**H**), 8.26 (d, 2H; ^4J = 1.6 Hz, Ar-**H**), 8.23 (d, ^4J = 2.3 Hz, 1H; Ar$_{calix}$-**H**), 8.19 (d, ^4J = 2.5 Hz, 1H; Ar$_{calix}$-**H**), 8.15 (d, ^4J = 2.5 Hz, 1H; Ar$_{calix}$-**H**), 8.13 (d, ^4J = 2.5 Hz, 1H; Ar$_{calix}$-**H**), 8.09 (d, ^4J = 2.5 Hz, 1H; Ar$_{calix}$-**H**), 8.05 (d, ^4J = 2.3 Hz, 1H; Ar$_{calix}$-**H**), 8.03 (d, ^4J = 2.3 Hz, 1H; Ar$_{calix}$-**H**), 7.80 (d, ^4J = 2.3 Hz, 1H; Ar$_{calix}$-**H**), 7.64 (t, ^4J = 1.8 Hz, 1H; Ar$_{meta}$-**H**), 7.62 (s, 2H; N**H**), 7.59 (t, ^4J = 1.7 Hz, 1H; Ar$_{meta}$-**H**), 7.56 (t, ^4J = 1.8 Hz, 1H; Ar$_{meta}$-**H**), 7.50 and 7.48 (br dd, ^3J = 8.1 Hz, 1H; Ar$_{meta}$-**H**), 7.48 (s, 1H; N**H**), 7.39 (t, ^3J = 8.1 Hz, 1H; Ar$_{meta}$-**H**), 7.36 (s, 1H; N**H**), 7.310 (t, ^3J = 8.1 Hz, 1H; Ar$_{meta}$-**H**), 7.316 (s, 1H; N**H**), 7.27 (t, ^4J = 1.5 Hz, 1H; Ar-**H**), 7.27 and 7.25 (br dd, ^3J = 8.2 Hz, 1H; Ar$_{meta}$-**H**), 7.23 (t, ^4J = 1.6 Hz, 1H; Ar-**H**), 7.12 (t, ^3J = 8.2 Hz, 1H; Ar$_{meta}$-**H**), 7.08 (t, ^3J = 6.3 Hz, 1H; Ar$_{meta}$-**H**), 7.01 (t, ^3J = 8.2 Hz, 1H; Ar$_{meta}$-**H**), 6.99 (t, ^3J = 8.1 Hz, 1H; Ar$_{meta}$-**H**), 6.88 (s, 1H; N**H**), 6.68 and 6.66 (dd, ^3J = 8.2, ^4J = 1.8 Hz, 1H; Ar$_{meta}$-**H**), 6.78 and 6.76 (dd, ^3J = 8.4, ^4J = 1.6 Hz, 1H; Ar$_{meta}$-**H**), 6.70 (m, 1H; Ar$_{meta}$-**H**), 6.67 and 6.65 (dd, ^3J = 8.2, $^4J \approx 2$ Hz, 1H; Ar$_{meta}$-**H**), 6.65 and 6.63 (dd, ^3J = 8.2, $^4J \approx 2$ Hz, 1H; Ar$_{meta}$-**H**), 6.60 (s, 1H; N**H**), 6.59 and 6.57 (dd, ^3J = 8.2, ^4J = 2.1 Hz, 1H; Ar$_{meta}$-**H**), 6.41 (d, ^4J = 2.5 Hz, 1H; Ar$_{calix}$-**H**), 6.32 (m, 4H; Ar$_{calix}$-**H**), 6.24 (d, ^4J = 2.5 Hz, 1H; Ar$_{calix}$-**H**), 6.21 (d, ^4J = 2.3 Hz, 1H; Ar$_{calix}$-**H**), 6.01 (d, ^4J = 2.5 Hz, 1H; Ar$_{calix}$-**H**), 4.59–4.40 (m, 8H; Ar-C**H**$_2$-Ar$_{ax}$), 4.3–3.50 (four m, 28H; -OC**H**$_2$), 3.28–3.07 (m, 8H; Ar-C**H**$_2$-Ar$_{eq}$), 2.1–1.9 (m, 16H; -C**H**$_2$-), 1.8–1.7 (m, 6H; -C**H**$_2$-), 1.5–1.1 (m, 80H; -C**H**$_2$-), 1.37 (s, 18H; *t*Bu), 1.32 (s, 18H; *t*Bu), 1.0–0.91 ppm (m, 12H; -C**H**$_3$); ESIMS: *m*/*z* (%): 1674.02 (100) $[M+2Na]^{2+}$, 3324.94 (61) $[M+Na]^+$.

3c: M.p. > 270 °C decomposition without melting; yield = 15 %; ^{1}H NMR ([D$_6$]benzene, 400 MHz, 25 and 60 °C): very broad and insignificant; ESIMS (complex of the molecule with $C_8H_{20}NPF_6$): *m*/*z* (%): 3404.65 (100) $[M+Et_4N]^+$.

3d: M.p. > 265 °C decomposition without melting; yield = 37 %; ^{1}H NMR ([D$_6$]benzene, 400 MHz, 25 °C): δ = 10.13 (s, 1H; N**H**), 10.06 (s, 1H; N**H**), 10.05 (s, 1H; N**H**), 10.03 (s, 1H; N**H**), 10.00 (s, 1H; N**H**), 9.97 (s, 1H; N**H**), 9.95 (s, 1H; N**H**), 9.92 (s, 1H; N**H**), 8.50 (brs, 2H; Ar$_{meta}$-**H**), 8.44 (brs, 1H; Ar$_{meta}$-**H**), 8.38 and 8.36 (br dd, ^3J = 8.2 Hz, 2H; Ar$_{meta}$-**H**), 8.30 (d, ^4J = 1.5 Hz, 2H; Ar-**H**), 8.26 (d, ^4J = 1.3 Hz, 2H; Ar-**H**), 8.26 and 8.24 (br dd, ^3J = 8.2 Hz, 2H; Ar$_{meta}$-**H**), 8.19 (d, ^4J = 2.3 Hz, 1H; Ar$_{calix}$-**H**), 8.18 (d, ^4J = 2.3 Hz, 1H; Ar$_{calix}$-**H**), 8.16 (d, ^4J = 2.0 Hz, 1H; Ar$_{calix}$-**H**), 8.13 (d, ^4J = 2.2 Hz, 1H; Ar$_{calix}$-**H**), 8.09 (d, ^4J = 2.5 Hz, 1H; Ar$_{calix}$-**H**), 8.08 (d, ^4J = 2.5 Hz, 1H; Ar$_{calix}$-**H**), 8.06 (d, ^4J = 2.2 Hz, 1H; Ar$_{calix}$-**H**), 7.90 (d, ^4J = 2.3 Hz, 1H; Ar$_{calix}$-**H**), 7.62 (s, 1H; N**H**), 7.60 (brs, 2H; Ar$_{meta}$-**H**), 7.57 (m, 2H; N**H** + Ar$_{meta}$-**H**), 7.53 (brs, 1H; Ar$_{meta}$-**H**), 7.50 and 7.48 (br dd, ^3J = 8.1 Hz, 2H; Ar$_{meta}$-**H**), 7.40 (s, 1H; N**H**), 7.38 (t, ^3J = 8.3 Hz, 1H; Ar$_{meta}$-**H**), 7.35 (s, 1H; N**H**), 7.27 (m, 2H; Ar$_{meta}$-**H** + Ar-**H**), 7.26 (t, ^3J = 8.1 Hz, 1H; Ar$_{meta}$-**H**), 7.23 (m, 2H; N**H** + Ar-**H**), 7.11 (t, ^3J = 8.1 Hz, 1H; Ar$_{meta}$-**H**), 7.08 (brs, 1H; Ar$_{meta}$-**H**), 7.05 (s, 1H; N**H**), 7.04 (s, 1H; N**H**), 7.01 (t, ^3J = 8.2 Hz, 1H; Ar$_{meta}$-**H**), 6.98 (t, ^3J = 8.4 Hz, 1H; Ar$_{meta}$-**H**), 6.79 (s, 1H; N**H**), 6.73–6.71 (m, 3H; Ar$_{meta}$-**H**), 6.66 and 6.64 (dd, ^3J = 8.2, ^4J = 1.7 Hz, 1H; Ar$_{meta}$-**H**), 6.57 and 6.55 (dd, ^3J = 8.2, ^4J = 2.0 Hz, 1H; Ar$_{meta}$-**H**), 6.56 and 6.54 (dd, ^3J = 7.9, ^4J = 2.0 Hz, 1H; Ar$_{meta}$-**H**), 6.38 (d, ^4J = 2.0 Hz, 1H; Ar$_{calix}$-**H**), 6.35 (d, ^4J = 2.3 Hz, 1H; Ar$_{calix}$-**H**), 6.32 (m, 4H; Ar$_{calix}$-**H**), 6.26 (d, ^4J = 2.2 Hz, 1H; Ar$_{calix}$-**H**), 6.19 (d, ^4J = 2.2 Hz, 1H; Ar$_{calix}$-**H**), 4.54–4.41 (m, 8H; Ar-C**H**$_2$-Ar$_{ax}$), 4.00–3.52 (m, 28H; -OC**H**$_2$), 3.36–3.18 (m, 8H; Ar-C**H**$_2$-Ar$_{eq}$), 2.1–1.9 (m, 16H; -C**H**$_2$-), 1.72–1.63 (m, 6H; -C**H**$_2$-), 1.5–0.9 (m, 88H; -C**H**$_2$-), 1.35 (s, 18H; *t*Bu), 1.31 (s, 18H; *t*Bu), 0.99–0.92 ppm (m, 12H; -C**H**$_3$); ESIMS: *m*/*z* (%): 1691.06 (100) $[M+H+Na]^{2+}$, 1680.07 (99) $[M+2H]^{2+}$, 1702.06 (30) $[M+2Na]^{2+}$.

X-ray structure analysis: $2(C_{208}H_{282}N_{16}O_{22})\cdot 5\,CHCl_3\cdot 5\,C_2H_3N$; M_r = 3759.55; triclinic; space group $P\bar{1}$; a = 20.2740(4), b = 28.4843(6), c = 40.4609(10) Å; α = 77.373(2), β = 88.180(2), γ = 72.699(2)°; V = 21755.2(8) Å^3; Z = 4; colorless block-shaped crystal; STOE-IPDS-II two-circle diffractometer; T = 173 K; Mo$_{K\alpha}$ radiation; 2θ range = 2.82–51.38°; 416706 reflections collected; 81625 independent reflections (R_{int} = 0.0949); empirical absorption correction (MULABS);[21] structure solution with SHELXS-90;[22] refinement on F^2 with SHELXL-97;[23] $R1$-[$I > 2\sigma(I)$] = 0.1495; GOF = 1.596. The methylene chains were refined with restraints of 1.50(1) Å for 1–2 and 2.45(1) Å for 1–3 distances. The disordered aromatic ring was refined with restraints of 1.40(1) Å for 1–2 and 2.45(1) Å for 1–3 distances.

CCDC-689511 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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Please note: Minor changes have been made to Scheme 1 in this publication in *Chemistry—A European Journal* Early View. The Editor.

