Synthesis and Characterization of Tetraurea Derivatives of Calix[4]arenes

Synthese und Charakterisierung von Tetraharnstoff Derivaten des Calix[4]arens

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Yuliya Rudzevich
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1. CALIXARENES AND THEIR DERIVATIVES

1. 1. Introduction

In recent years calixarene chemistry developed in many directions. Calixarenes are widely used for instance in such different fields like the construction of sensors, for ion transport phenomena and as enzyme models. The rapid and broad development is explained by the ease by which larger amounts of *tert*-butyl calixarenes can be made. The single-step condensation of *p*-*tert*-butylphenol with formaldehyde under alkaline conditions affords cyclic oligomers, in which the number of the phenolic units connected *via* methylene bridges, depends on the reaction conditions (Figure 1). This easy synthesis, however, was not recognised in former time by Zinke, who discovered in the 1940s the property of *p*-alkylphenols to form cyclic oligomers in a similar way[1]. Eventually in the 1970s Gutsche and co-workers were able to look at this synthesis from a different viewpoint and to improve Zinke's procedure. From that time each of the three main calix[n]arenes, where n = 4, 6, 8, became available in good and reproducible yields[2].

The name "calixarenes" was given to this class of compounds by C. D. Gutsche since the conformation of the tetra- and pentamer looks like an ancient Greek vase, known as "calix crater". The number "n" indicates the number of phenolic units within the macrocycle.

In the present chapter a short introduction to the world of calixarenes will be presented.

1. 2. Synthesis, Properties, Modifications

1. 2. 1. Synthesis and Nomenclature of Calixarenes

Up to now calix[n]arenes with n = 4 - 8[3] (Figure 1) are available in multigram quantities, while other members of calixarene family with n ≤ 20 have been isolated from the mixtures chromatographically. Especially well established procedures exist for the preparation of the "major" calixarenes with n = 4, 6, 8. The condensation of *p*-*tert*-butylphenol with HCHO in the presence of NaOH leads either to calix[4]- or to calix[8]arene as products of thermodynamic or kinetic control of the reaction respectively. For the synthesis of calix[6]arene KOH is usually used as a base since a template effect of the K^+ cation is assumed. However these syntheses work well only with *p*-*tert*-butylphenol, while reactions with other p-alkyl phenols lead to mixtures, which are difficult to separate.

In the systematic nomenclature the name “calixarene” is used to designate only the basic macrocyclic framework and the substituents are usually indicated additionally. Thus the systematic name for a calix[4]arene consisting of *tert*-butylphenol units is 5,11,17,23-tetra-*tert*-butylcalix[4]arene-25,26,27,28-tetrol, but it is too complicated for the everyday use. Therefore it was simplified and “*p-tert*-butylcalix[4]arene” is the trivial name usually applied for this macrocycle. For other calix[n]arenes the same rule is accepted.

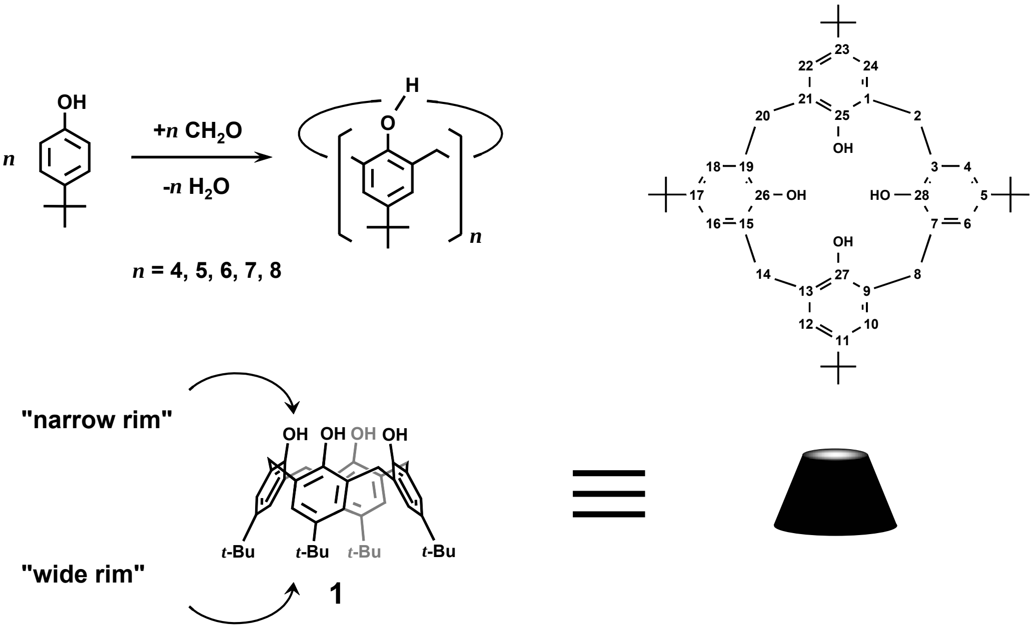


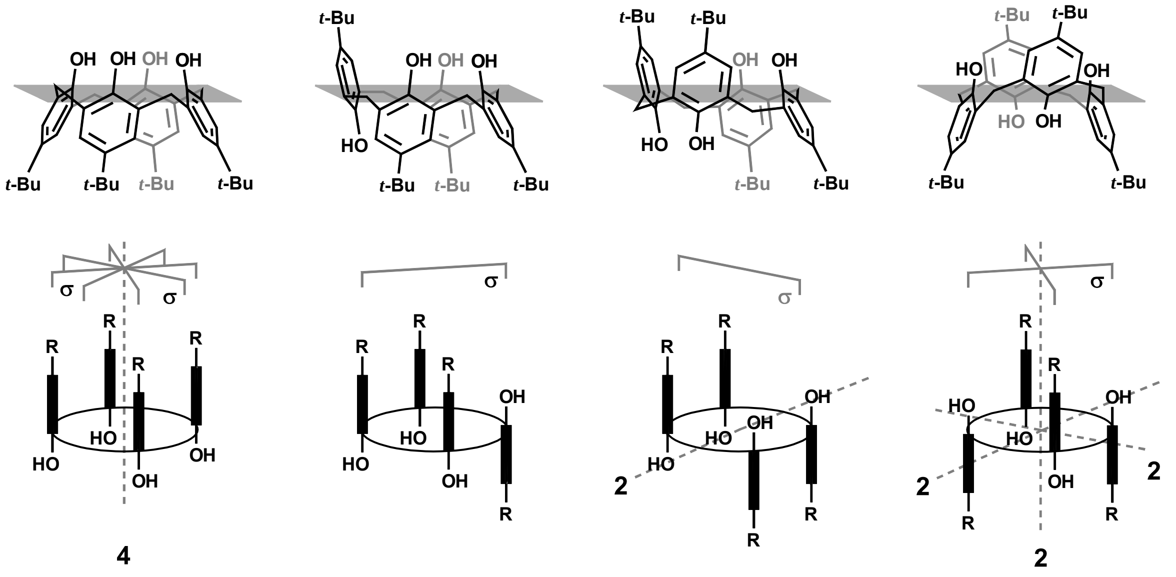
Figure 1. Synthesis, nomenclature and sketchy drawing of calix[4]arenes.

To determine the “rims” of the calixarene formed by phenolic hydroxy groups and the groups in the *p*-position the definitions “narrow” (“lower”) and “wide” (“upper”) rim respectively were introduced.

1. 2. 2. Conformational Properties

In general, the conformation of calix[4]arenes (or their derivatives) is analyzed in terms of the “up” or “down” orientations of the phenolic rings relative to the mean macrocyclic plane defined by the four methylene ($ArCH_2Ar$) carbons. Four basic conformations can be distinguished, which were named by Gutsche *cone*, *partial cone*, *1,2-alternate*, and *1,3-alternate* (Figure 2). They have C_{4v}, C_s, C_{2h} and D_{2d} symmetry respectively. In the *cone* conformer all four phenolic rings are oriented in the same direction, while in the *partial cone* one of them is inverted. In *1,2-* or *1,3*-alternates two adjacent or opposite rings are inverted.

Frequently the actual molecules possess conformations and symmetries slightly different from those depicted in the Figure 2. For example, in *cone* conformers often two opposite aromatic rings are almost parallel and the other two are turned outside.



cone C_{4v} *partial cone* C_s *1,2-alternate* C_{2h} *1,3-alternate* D_{2d}

Figure 2. Conformations of the *p*-*tert*-butylcalix[4]arene.

The parent calix[4]arene in solution and in the solid state is usually found in the *cone* conformation stabilized by a circular array of hydrogen bonds between the four phenolic OH groups. However this compound is conformationally flexible and interconversion between two identical *cone* conformations occurs (Figure 3). In this process, phenolic units rotate around the Ar–CH$_2$–Ar bonds in the way, that the OH groups pass through the cavity annulus.

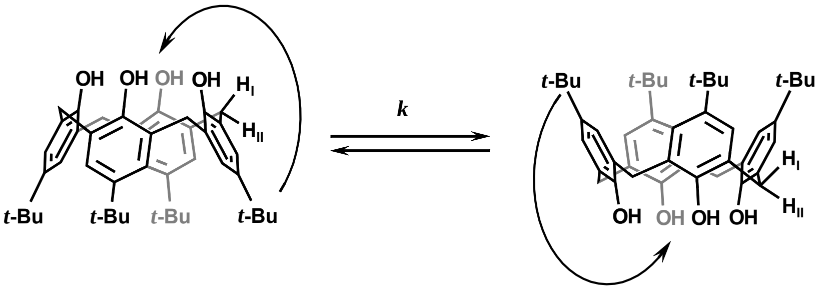


Figure 3. *Cone*-to-*cone* ring inversion.

The conformational mobility of calixarenes can be restricted by bridging of phenolic units (biscrown ethers, see chapter II) or by the introduction of O-alkyl groups, larger than ethoxy[4], which are not able to pass through the annulus of the macrocycle. Methoxy groups are still rather small and provide for tetramethoxy and tetrahydroxy calix[4]arenes a similar flexibility. However, due to the absence of hydrogen bonding, the *partial cone* conformer is the most stable and the three other conformers are also found at 243 K[5].

1. 2. 3. Chemical Modifications of the Calix[4]arenes

There are two main places to modify a calixarene, which may be addressed independently: the phenolic hydroxy groups (substitution on the narrow rim) and the *p*-positions to the OH-groups (substitution on the wide rim). This property of calixarene offers a possibility to introduce different functional groups pointing in opposite directions, what was successfully used for various purposes (for example to build larger structures). Already introduced functional groups can be further modified by subsequent reactions.

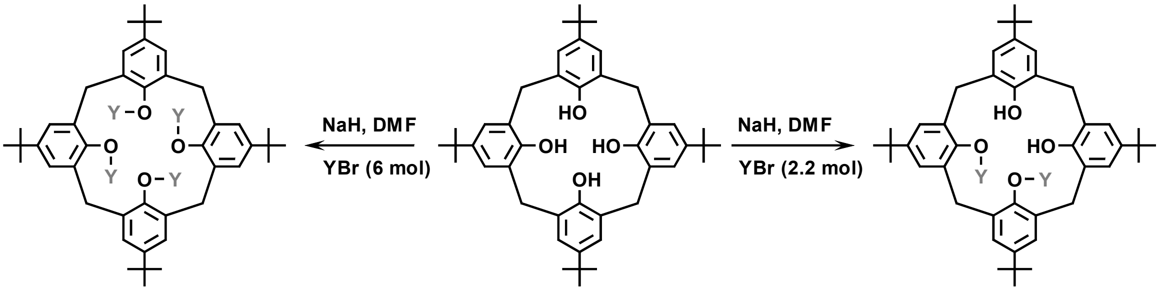
Reactions may also occur at the methylene bridges or affect the aromatic system of the phenolic units (oxidation, hydrogenation).

1. 2. 3. 1. Substitution at the narrow rim (O-alkylation)

The alkylation (or acylation) of the phenolic OH groups is one of the easiest reactions in calixarene chemistry. But this simple reaction has a very important meaning – a huge variety of the functional groups can be introduced into the calixarene *via* alkylation with appropriate reagents.

Partial or exhaustive substitution could be carried out depending on the reaction conditions (solvent, base, temperature), quantity and reactivity of reagents. For example alkylation of calixarenes with alkyl bromides in the presence of the strong base (NaH in DMF/THF) leads to tetraethers if both reagents are taken in excess and *1,2*-diethers if the alkyl bromide is taken in a stoichiometric amount (Scheme 1). Milder conditions (Na_2CO_3, CH_3CN) are usually applied for the synthesis of *1,3*-disubstituted calixarenes.

When two or more residues have to be introduced the formation of stereoisomers must be considered. Thus, the ether groups can be pointing into the same (*syn*) or into different (*anti*) directions with respect to each other. Such an orientation should not be mixed up with the conformation of the calixarene. For example in *1,3*-diethers the remaining OH groups can freely pass through the annulus and therefore the molecule is still conformationally flexible. Thus one should distinguish between the relative orientation of the residues and the actual conformation of a compound.

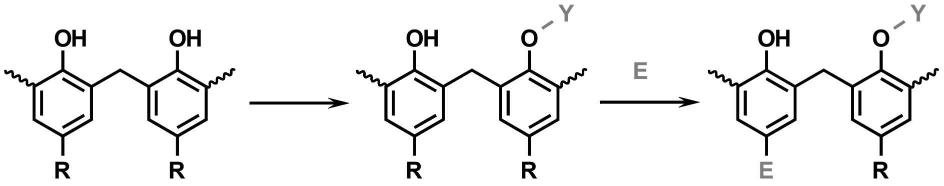


Scheme 1. Substitution at the narrow rim.

1. 2. 3. 2. Substitution at the wide rim

Numerous reactions were performed on the wide rim of calixarenes. One of the most important exhaustive modifications is the cleavage of the *tert*-butyl groups by reaction with $AlCl_3$ in toluene in the presence of phenol.[6] It results in free *p*-positions which are now available for all kinds of electrophilic substitution reactions which are possible with phenols. Among them nitration, bromination (or iodination), sulphonation, bromomethylation, aminomethylation, formylation, acylation and coupling with diazonium salts could be mentioned.

Partial substitutions (or *ipso*-substitutions) could be accomplished in a statistical way using appropriate reaction conditions or selectively on the basis of the different reactivity between phenol and phenol ether or ester units. This means, that the selectivity pattern of the *O*-alkylation (*O*-acylation) reactions on the narrow rim may be successfully transferred to the wide rim (Scheme 2).



Scheme 2. Schematic representation of the principle of selectivity transfer from the narrow to the wide rim.

The principle of such reactions can be explained on a simple example – the nitration or *ipso*-nitration. Carrying out the statistical reaction of *ipso*-nitration mononitro-tri-*tert*-butyl derivatives (R_1 = NO_2, R_2-R_4 = *t*-Bu) of tetraethers could be obtained in good yields under appropriate conditions. While the two dinitro- and the trinitro derivatives have to be isolated chromatographically from the mixtures of products. In contrast to this the dinitrophenol derivatives were obtained in yields up to 75 % *via* selective *ipso*-nitration of 1,3-diethers.[7] The *ipso-attack* at the methylene bridges was found as a side reaction.

Further partial modifications (bromination, formylation ect.) could be made analogously.

1. 2. 4. Multiple Calixarenes

Calixarenes are easily (and often selectively) functionalized and therefore they can be combined in various ways to larger molecules containing more than one calixarene substructure. Three possibilities exist to join calixarenes: *via* the narrow rims, the wide rims and the so called “head-to-tail” connection between wide and narrow rims.[8] The main types of double calixarenes connected by two bridges are shown in Figure 4.

The actual method of coupling depends on the desired product. Different amide-bridged bis-calix[4]arenes connected *via* a single bridge between the narrow rims were prepared either by reacting the triether monoacid (monoamine) with α,ω-diamines (acids, alokohols) or by direct alkylation with difunctional reagents.[9] For the preparation of double bridged calixarenes reactions with difunctional reagents are more appropriate due to the preferred formation of *syn*-1,3-diethers or 1,3-diesters. Among double calix[4]arenes with four bridges tetra ethylene-bridged compounds (X = CH_2CH_2) should be mentioned. They are obtained in about 50 % yields by the reaction of the tetrakis(tosyloxyethoxy) *p-tert*-butylcalix[4]arene with the parent p-*tert*-butylcalix[4]arene in the presence of K_2CO_3, were the K^+-ion obviously acts as a template.[10] A connection *via* four bridges at the wide rim is less satisfactory, probably due to the flexibility of calix[4]arenes.

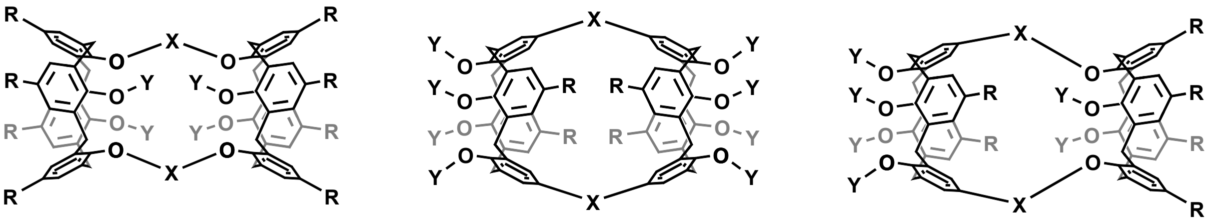


Figure 4. The main types of double calixarenes.

For the connection of calixarenes on the wide rim following groups are most frequently used: formyl (CHO, and its reduction and oxidation products CH_2OH, COOH), amino (available by reduction of the nitro group), hydroxyl and halogen (Br, I).

Linear, branched and cyclic oligomers were also prepared combining the principles listed above. Several main examples are shown in Figures 6 and 7.

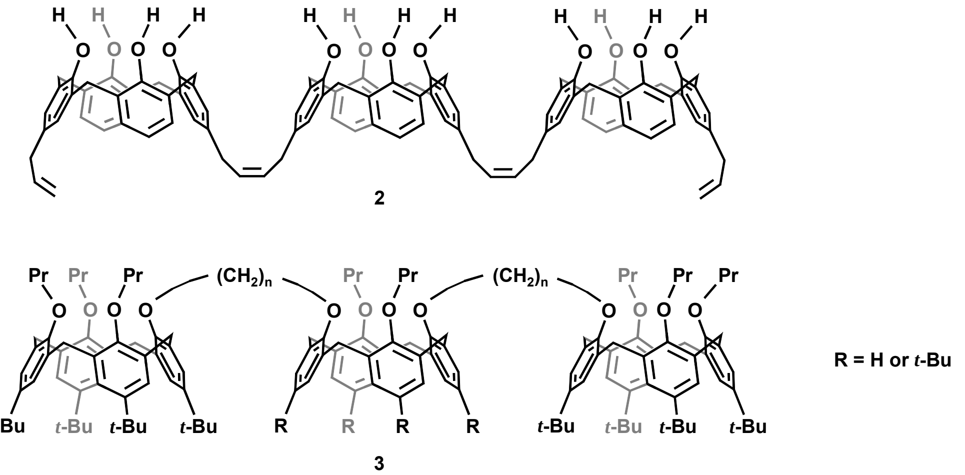


Figure 5. Linear oligomers on the base of the calix[4]arenes.

Intermolecular metathesis of the 1,3-*p*-allyl calix[4]arene (Grubbs' catalyst, benzene) led to the linear trimer **2** isolated in 20% yield (Figure 5).[11] Compound **3** was made in two steps. *O*-Alkylation of a tripropyl ether with excess of an α,ω-dibromoalkane followed by reaction with 1,3-di-propyl ether (R = H, *t-Bu*) led to desired product in 27-53 % yield.[12]

For the synthesis of branched oligomers different types of spacers could be used (Figure 6). For example 1,3,5-Benzenetricarboxylic acid[13] or a calixarene in the *cone*[12] or 1,3-*alternate*[14] conformation itself.

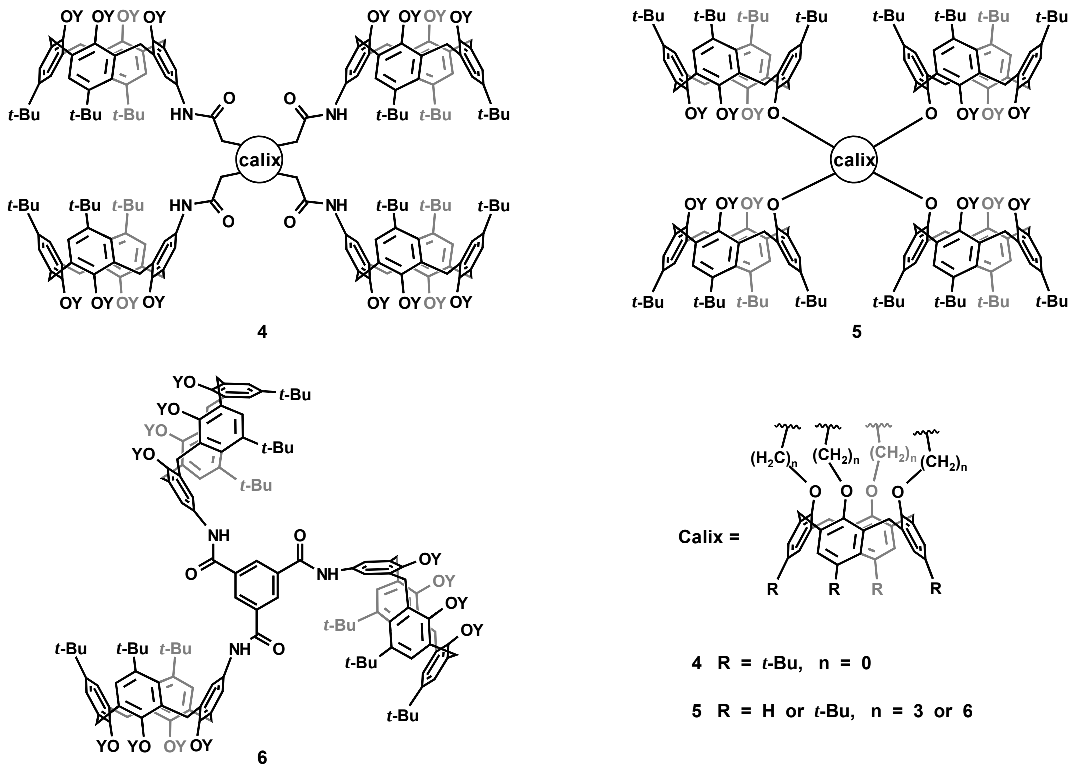
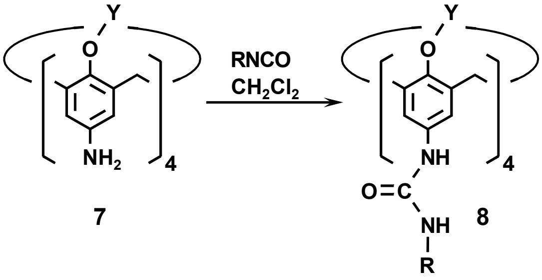


Figure 6. Branched molecules.

1. 3. Self-Assembly

1. 3. 1. Dimers Based on a Cyclic Array of Hydrogen-Bonded Urea Functions

Self-organization is found as a general principle in nature and remains one of the current topics of interest in supramolecular chemistry. A wide variety of biological systems consist of rather simple subunits which are held together *via* noncovalent interactions. Indeed, self-assembly gives some advantages in comparison to the construction of larger molecules by covalent connection of appropriate building blocks. Reversibility of the hydrogen bonds, facile formation of the end product and synthetic economy – these are the main features of self-assembly.[15]



Scheme 3. Synthesis of tetraurea calix[4]arenes

Various examples of self-complementary molecules which are able to form dimers, oligomers and large well defined aggregates have been described. In the last 10 years calix[4]arenes have filled up the number of these compounds. Calixarenes **8** bearing four urea functions on the wide rim are easily synthesized by reaction of the corresponding *p*-amino-derivatives with isocyanates (Scheme 3). They form hydrogen-bonded capsules in apolar, aprotic solvents in the presence of a suitable guest (Figure 7). The urea functions, four from each calixarene, assume a “head-to-tail” arrangement and form a circle of eight hydrogen bonded urea groups.

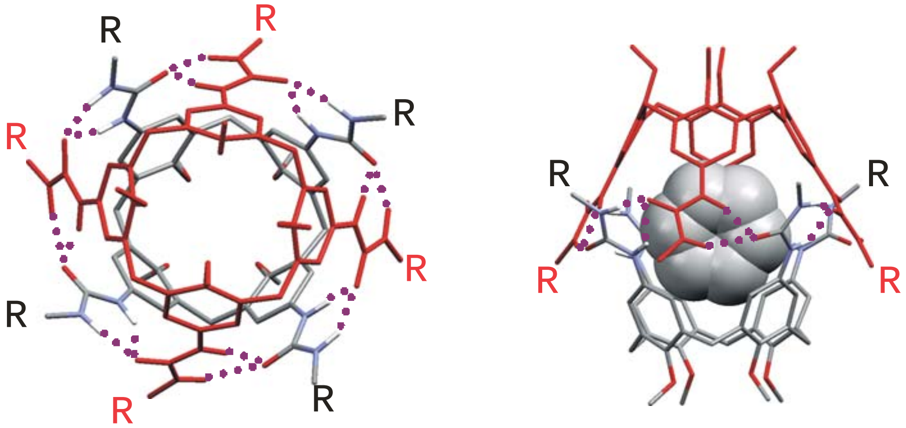


Figure 7. Schematic representation of a calix[4]arene urea dimer (side- and top views); hydrogen bonds are represented by dashed lines.

The first indication of such assemblies was found in the ^{1}H NMR spectra of tetraurea derivatives in apolar solvents. While in DMSO-d_6 one singlet for the aromatic protons (~6.8

ppm) and two closely disposed singlets for the NH protons (~8.35 and 8.21 ppm) were found, as it was expected for the C_{4v} symmetrical pattern (Figure 8), the signals for the NH protons were separated by 2.35 ppm (~9.41/7.05 ppm) in $CDCl_3$ and, more surprising, the Ar-H protons of the calixarene part appeared as two strongly separated doublets (~7.62 and ~5.88 ppm) with a coupling constant of 2.1 Hz, typical for protons in meta-position. This picture shows, that all four phenolic rings are identical, whereas the two Ar-H protons of a single ring are different. The obtained ^{1}H NMR spectrum could be easily explained by ***intra***molecular hydrogen bonds of type A (Figure 8), but molecular models speak against this version. The distances between two adjacent C(O) and NH functions are too large to form such hydrogen bonds.

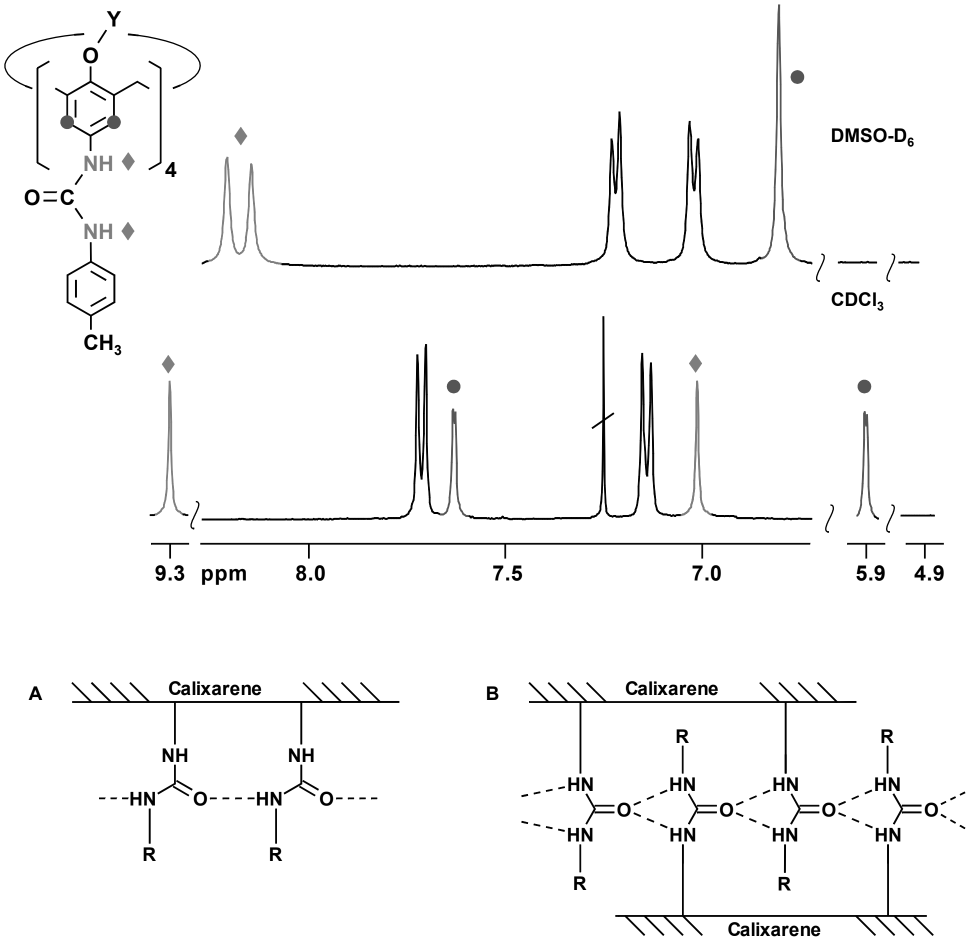


Figure 8. Sections of the ^{1}H NMR spectra of tetratolyl urea calix[4]arene as monomer in DMSO-d_6 (a) and as a homodimer in $CDCl_3$ (b) and schematic representation of the hydrogen bonding pattern.

The crucial explanation was given by Rebek. He suggested the self-assembly of two calixarenes *via* their wide rims (assuming ***inter***molecular hydrogen bonding of type B)[16] and he was able to prove this showing the inclusion of solvent molecules (guests) inside the formed cavity. For example in mixed solvent systems two obviously different assemblies were observed. And in case, when fluorobenzene was used as a potential guest, the peak of the encapsulated guest (~5.4 ppm upfield shifted from the free fluorobenzene) was observed in the ^{19}F NMR.

A completely different proof of the dimeric nature of the capsule was provided by Böhmer et al. Having in mind, that two different ureas A and B form dimers AA and BB in apolar solvents he supposed, that in their mixture the signals of heterodimer AB also should be present.[17] As expected, the ^{1}H NMR spectrum of the mixture of two different ureas in polar solvents, like DMSO-d_6 or THF-d_8, appears as a superimposition of the spectra of the two pure compounds, while in aprotic, apolar solvents, like $CDCl_3$ or C_6D_6, new signals, corresponding neither to one of the homodimers (nor to one of monomers) were observed simultaneously with the signals of the dimers AA and BB (Figure 9). Obviously these signals belong to the mixed dimer AB. This was an additional strong indication of the dimerization.

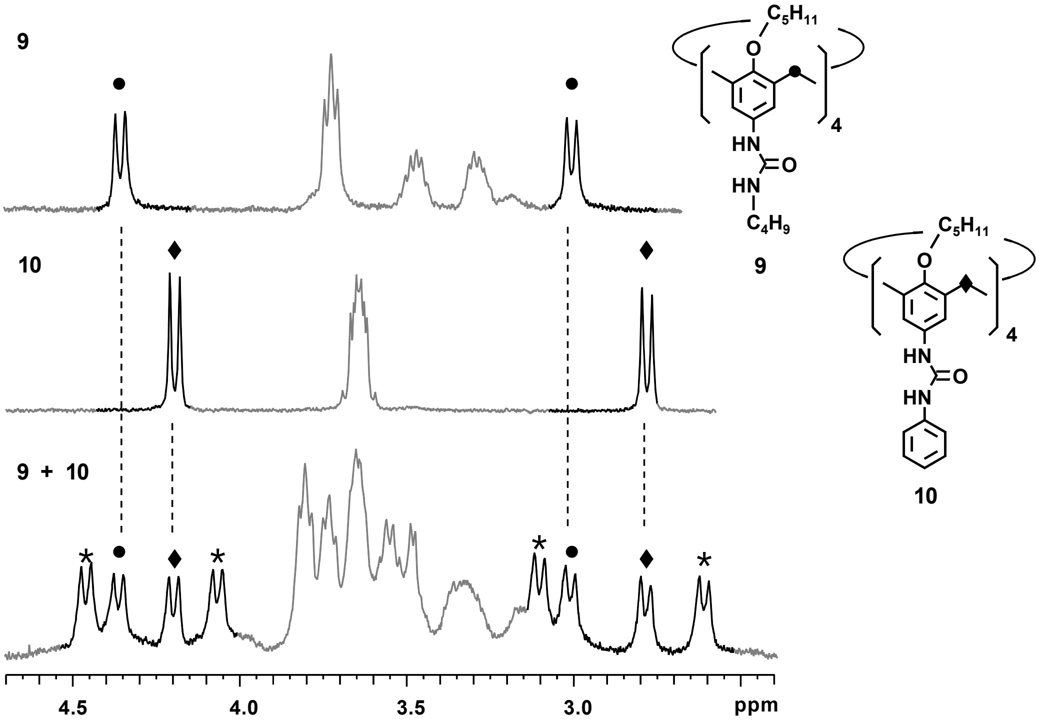


Figure 9. Sections of the ^{1}H NMR spectra of **9**, **10** and of the mixture **9+10** in the ratio 1:1. The new signals for ArCH$_2$Ar protons are marked with an asterisk.

Later, the crystal structure with the clearly defined hydrogen bonds unambiguously confirmed the existence of a dimer in the crystalline state (Figure 10).[18] The two calixarenes are held together by 16 hydrogen bonds between NH and C=O functions. ^{1}H NMR spectra suggest a stronger hydrogen bond for NH attached to R than for NH attached to the calixarene, which was confirmed for capsules with benzene as a guest by a shorter N···O distance in the crystalline state. Since both parts of the capsule are turned by 45° around the common axis with respect to each other the dimer has (dynamic) S_8-symmetry in solution.

The association is strong enough to exclude the simultaneous observation of the monomeric and dimeric form under the usual conditions. Such dimers reversibly encapsulate smaller molecules under slow exchange with respect to the NMR time scale and the kinetic stability of the capsules depends on included guest and the solvent. The solvent itself (C_6H_6, C_6H_{12}, $CHCl_3$, 1,4-difluorobenzene) or suitably sized organic cations (tetraethylammonium, tropylium) could be taken as good guests for the dimers.

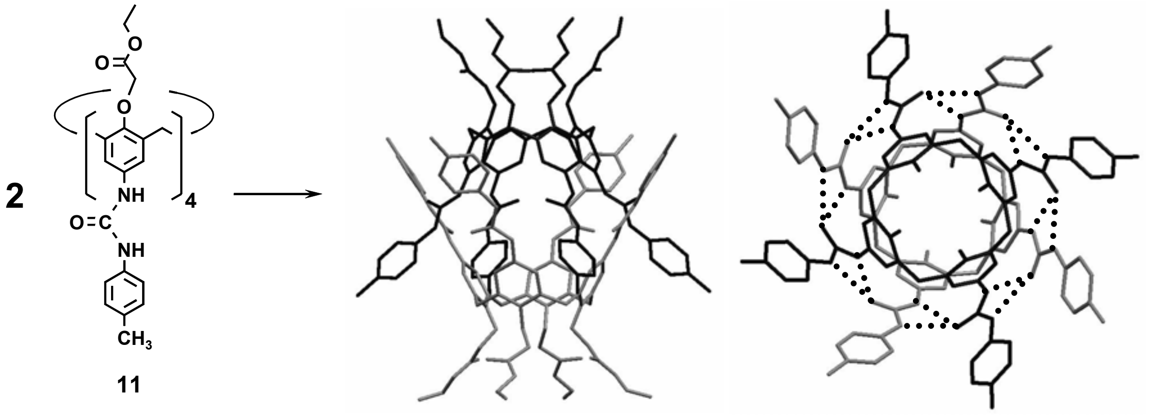
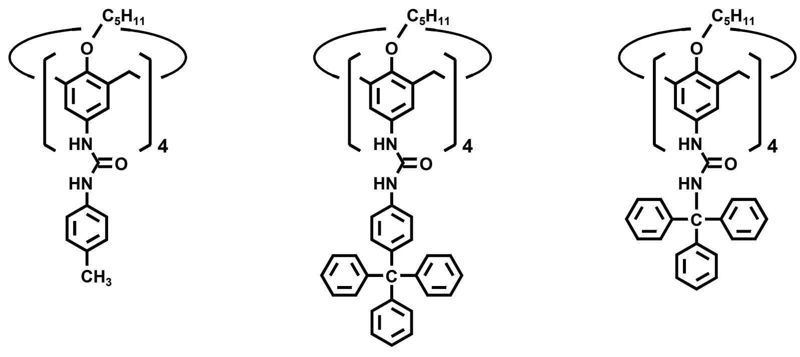


Figure 10. X-ray structure of the dimer (crystals were obtained from benzene).

Although capsules are kinetically stable on the NMR time scale, their dissociation/recombination occurs within seconds with the rate constants of k=0.26 s^{-1}. The kinetic stability of such capsules was increased by introducing bulky urea substituents on the wide rim.[19] From the tetraurea derivatives shown in Figure 11 only compound **14** does not form homodimers in benzene and all of them form heterodimers with each other. Remarkably a 1:1 mixture of **13** and **14** shows nearly exclusively the presence of the heterodimers **13•14**. Evidently the heterodimer formation is favoured over the situation where the homodimer **13•13** and an undefined assembly are present in the mixture.



12 13 14

Figure 11. Tetraurea derivatives of calix[4]arene.

A comparison of the half-life times for **12•12** (ca. 1 s),[20] **12•14** (130 min), and **13•14** (60 h) shows that the steric crowding by the residues R plays a very important role for the kinetic stability of these dimers in benzene. But nevertheless the driving force of dimerization is still the hydrogen bonding between two tetraureas, since the capsule is rapidly destroyed by the addition of DMSO.

As described above the combination of two tetraurea derivatives resulted in a mixture of two homodimers and heterodimer in statistical ratio (1_{homo}:2_{hetero}:1_{homo}). Surprisingly the heterodimer is formed exclusively when aryl and arylsulfonyl ureas are mixed together in the ratio 1:1 (Figure 12).[21] While the reasons for this preference remain unknown this fact became a new step on the way to larger assemblies based on calixarene dimers (which will be described later). The heterodimeric capsule has C_{4v} symmetry and become chiral (C_4-symmetric) by the directionality of the hydrogen bonded belt.

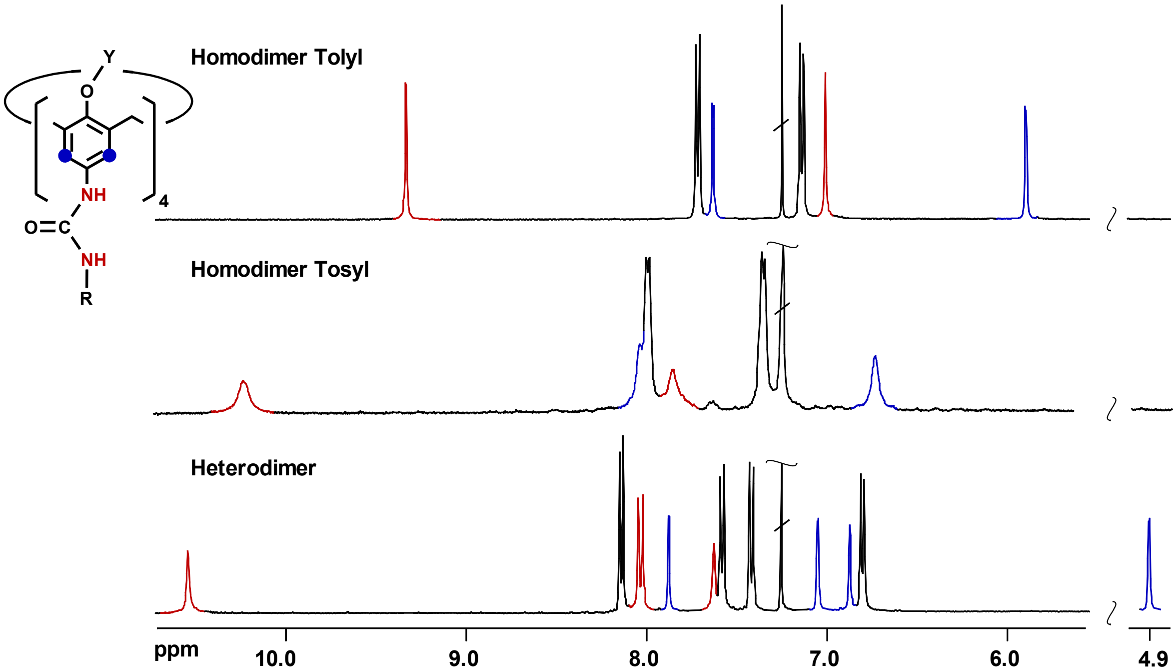
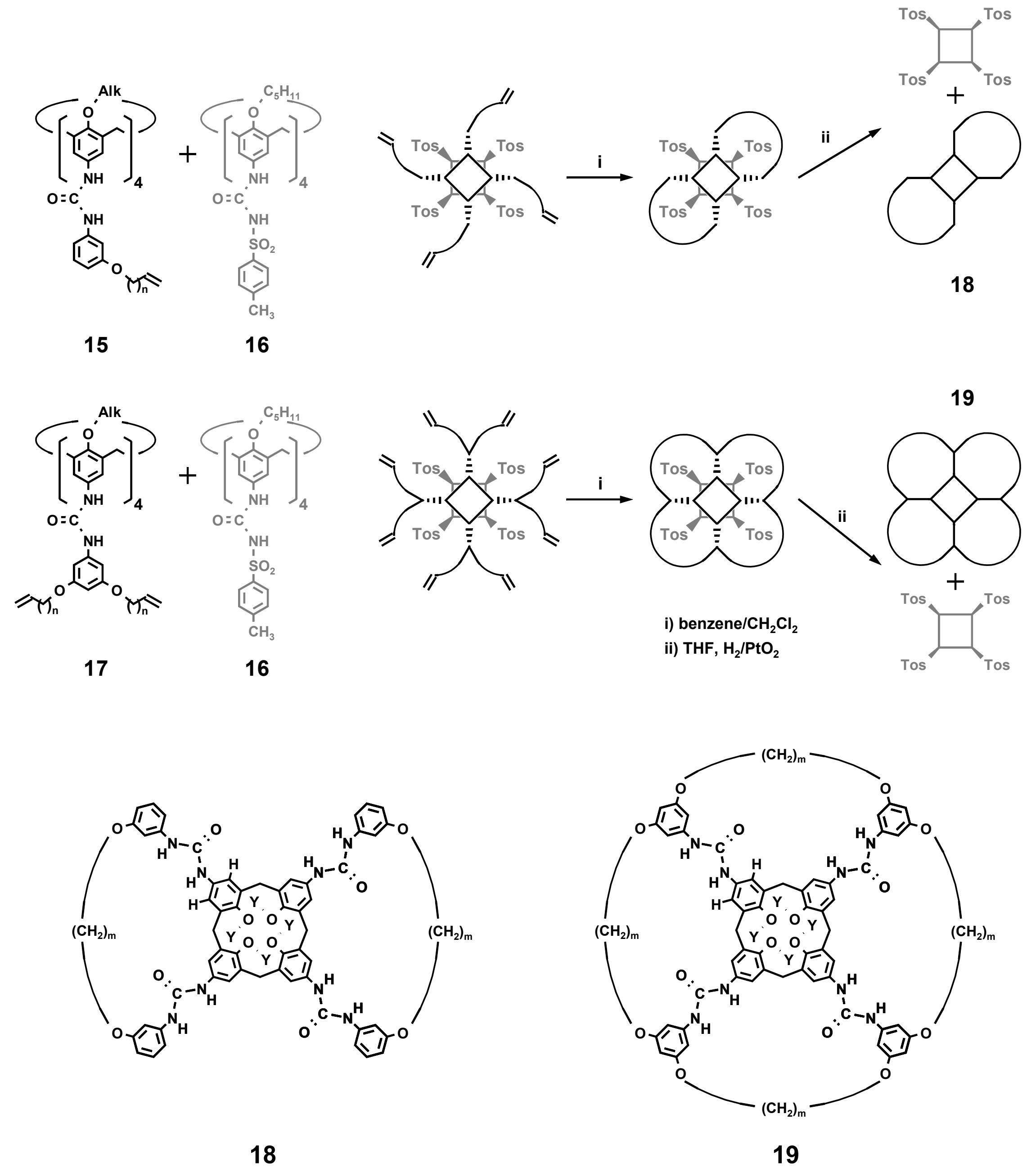


Figure 12. Homo and hetero heterodimerization of tetraurea calix[4]arenes.

Selective heterodimerization of aryl/sulfonyl tetraurea calix[4]arenes has been effectively used to synthesize multimacrocycles (Scheme 4), which in turn heterodimerize with the various "noncyclic" tetraurea calix[4]arenes exclusively.[22] This is due to the fact, that the homodimerization of the bis(tetra)-loop-containing compounds is not possible, because this would lead to a sterically unfavourable overlap of the loops.



Scheme 4. Template synthesis of bis- and tetraloop tetraurea.

The mentioned macrocycles were prepared from tetraurea derivatives **15** or **17** bearing four or eight ω-alkenyl groups *via* metathesis reaction (with Grubbs' catalyst) under high-dilution conditions. In this synthesis the tetratosyl urea **16** was used as a template which forms exclusively a heterodimer with arylureas. In such a dimer the opposite urea residues R are effectively separated and the transcavity bridging (Figure 13) is no longer possible. Now the desired macrocycle in which adjacent phenolic units are connected should be the only product of intramolecular reaction. After metathesis followed by hydrogenation the dimer can be easily destroyed by hydrogen bond breaking solvents and the reaction product (multimacrocyclic derivative) can be separated from the template and isolated by column chromatography. Indeed compounds of type **18** and **19** were obtained in yields up to 65 %, while all attempts to obtain tetraloop derivatives in the absence of **16** were unsuccessful.

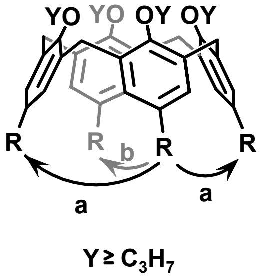
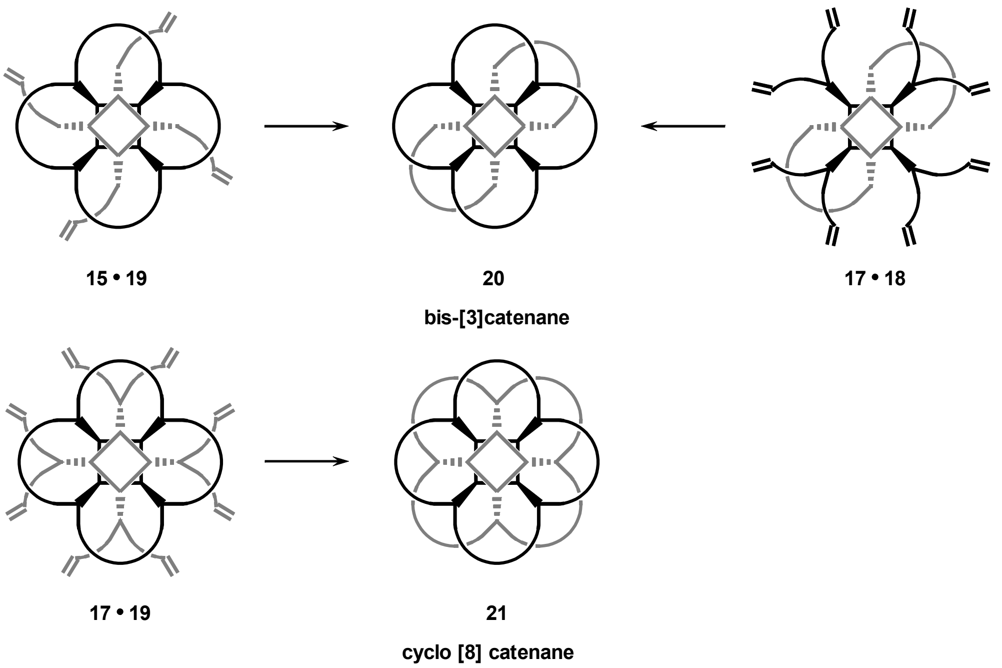


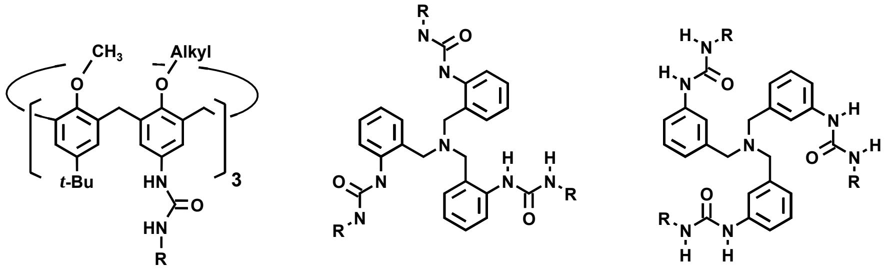
Figure 13. Possible intramolecular connections: *a - for adjacent units* and *b – transcavity connection* of residues R.

The selective dimerization between "tetraloop" and "open chain" tetraureas was used also for the preparation of more sophisticated structures like catenanes (Scheme 5).[23] Thus a solution of, for example, a 1:1 mixture of **15** and **19** contains only the heterodimer **15•19**. Heterodimers **17•18** and **17•19** were obtained analogously. Metathesis reaction of such heterodimers followed by reduction leads to the single reaction products **20** or **21** in more than 50 % yield.



Scheme 5. Strategies to Synthesize Multiple Catenanes.

Dimers without inclusion of guests were also found for triureas derived from calix[6]arenes **22**[24] or *o*-substituted tribenzylamines **23** (Figure 14).[25] However capsules formed by *m*-substituted tribenzylamine derivatives **24** are able to encapsulate dichloromethane because of their larger internal cavity,[26] which was confirmed by X-ray analysis. Chloroform and benzene were also tested as potential guests. In contrast to CH_2Cl_2 in both cases mixtures of empty and filled capsules were observed in solution.



22 **23** **24**

Figure 14. Triurea derivatives able to form dimers.

Unexpectedly, well defined assemblies/capsules were not observed for calix[5]arenes, although a variety of guests were offered as templates.[27]

The formation of a completely different and more sophisticated assembly was found for calix[4]arene **25**, substituted at the wide rim with one acetamide and three *p*-tolylurea functions. It assumes a C_1-symmetrical conformation in apolar solvents which is not compatible with the usual capsule. In the crystalline state, four molecules of **25**, adopting a pinched cone conformation, assemble into a quasi S_4-symmetrical tetramer stabilized by a (cyclic) array of 24 NH···O=C hydrogen bonds and four NH···π interactions (Figure 15).[28]

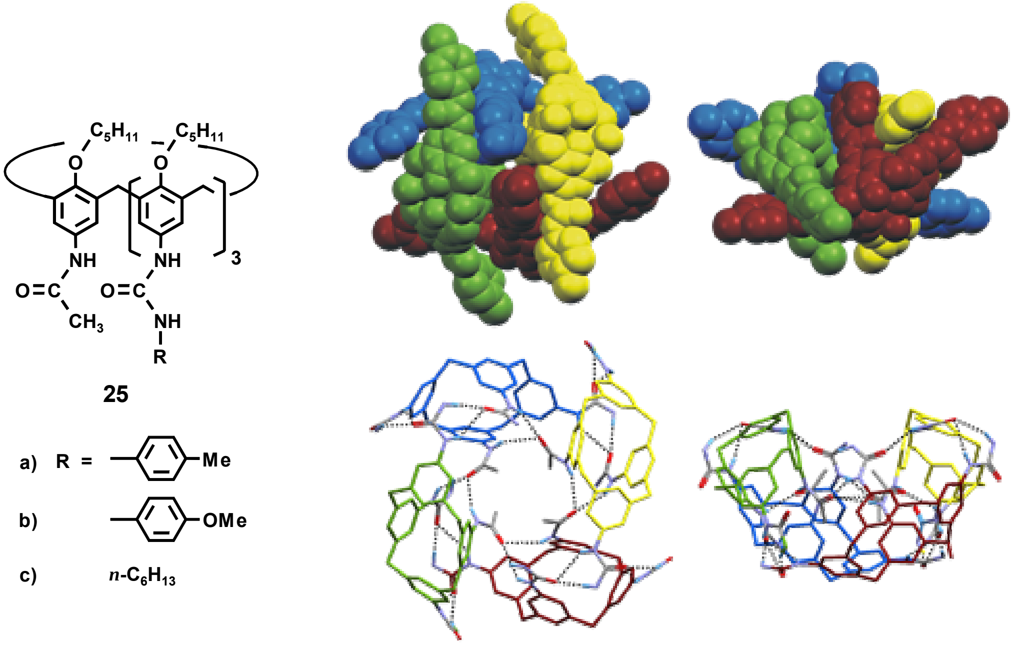


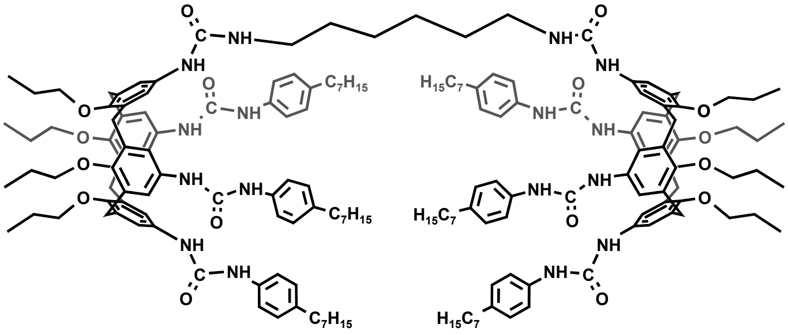
Figure 15. Single-crystal X-ray structure of **25a**: Space-filling representation of the tetramer, pentyl chains are omitted (top); stick representation of the tetramer pentyl chains and *p*-tolyl fragments are omitted for clarity; hydrogen bonds are shown in dashed lines (bottom); the S_4 axis is perpendicular to the drawing plane (left).

1. 3. 2. Self-Assembly of the Multiple Tetraurea Calix[4]arenes

1. 3. 2. 1. Connection of the units via wide rim

Self-assembly properties of bis-tetraureacalix[4]arenes composed from two calixarenes covalently attached *via* their wide (urea residues are pointing towards each other) or narrow (urea residues are pointing away from each other) rims were also studied.

For the upper rim connection the hexamethylene tether was used as a spacer. The double calixarene **26** shown in Figure 16 was prepared and characterized using ^{1}H NMR spectroscopy and ESI-MS spectrometry.[29]



26

Figure 16. Double tetraurea calix[4]arene with upper rim connection.

It was shown that in apolar, aprotic solvent the equilibrium between monomeric and dimeric state of the molecule is shifted towards the intramolecular dimer, while no evidence for intermolecular dimerization or oligo(poly)merization was found (Figure 17). The formation of heterodimeric assemblies of the double calixarene with other aryl substituted ureas at comparable concentrations was not observed, but it could be forced to heterodimerize with excess of arylsulfonyl ureas.

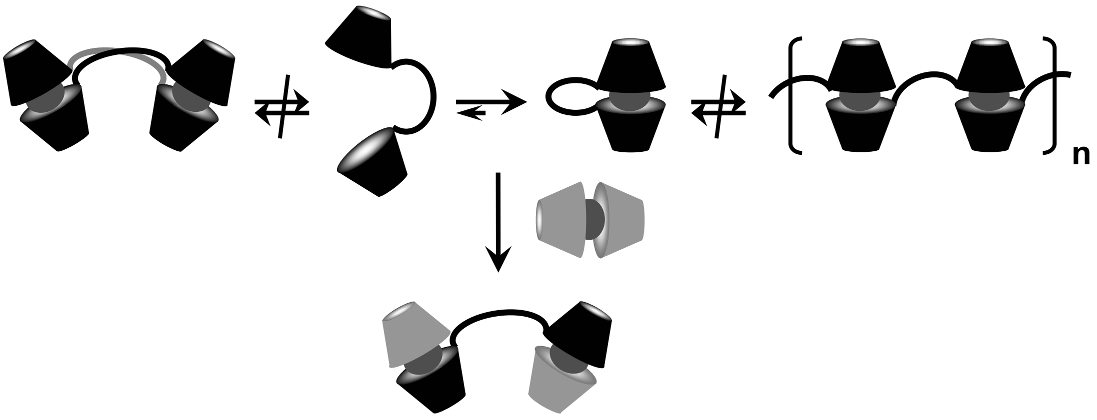
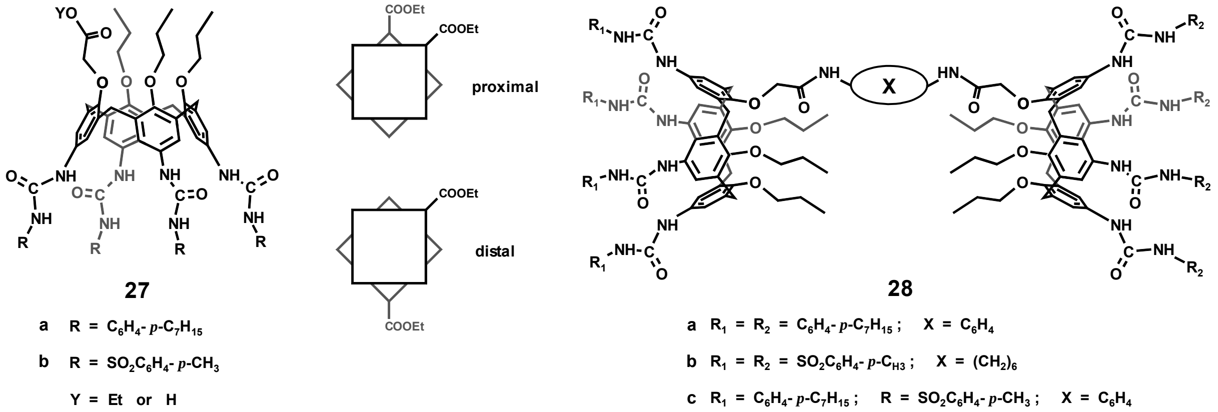


Figure 17. Self-assembly of the double calixarene **26**.

1. 3. 2. 2. Connection of the units via narrow rim

Tetraurea calix[4]arenes monofunctionalized at the narrow rim were also prepared.[30] These compounds (**27**) form capsules and show all of the expected spectroscopic characteristics. Two regioisomers with distal and proximal location of functional groups in the dimer exist in solution (Figure 18). This means that for all 8 NH protons (downfield shifted or strong bonded) in each isomer 16 signals could be found in ^{1}H NMR spectra. They appear within a range of 0.1 ppm.



27

a $R = C_6H_4\text{-}p\text{-}C_7H_{15}$

b $R = SO_2C_6H_4\text{-}p\text{-}CH_3$

$Y = Et$ or H

28

a $R_1 = R_2 = C_6H_4\text{-}p\text{-}C_7H_{15}$; $X = C_6H_4$

b $R_1 = R_2 = SO_2C_6H_4\text{-}p\text{-}C_{H3}$; $X = (CH_2)_6$

c $R_1 = C_6H_4\text{-}p\text{-}C_7H_{15}$; $R = SO_2C_6H_4\text{-}p\text{-}CH_3$; $X = C_6H_4$

Figure 18. The basic units of the polymeric capsules.

Covalent connection of two calixarenes *via* their narrow rims affords building blocks **28**, which form polymeric capsules in apolar solvents (Figure 19 and 20). The polymeric assemblies show broadened NMR spectra. This happens because the number of different capsules is enormous: each capsule can be formed as a proximal or distal regioisomer, the circular array of ureas can be arranged in a clockwise or counterclockwise sense, and every site is in a slightly different magnetic environment along the polymer chain. But the positions of the resonances matched very closely those of simple dimeric capsules. Addition of guests different from the solvent results in the emergence of new signals for capsules filled with this guest.

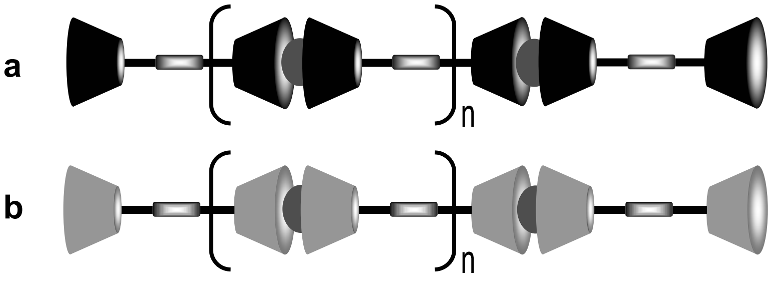
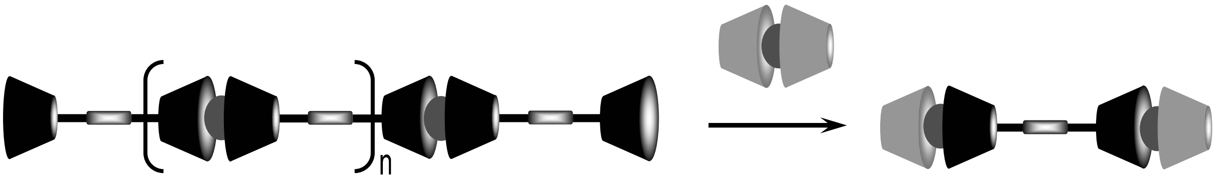


Figure 19. Schematic representation of linear polymeric capsules based on tetratolyl (a) and tetratosyl (b) double calixarenes.

Finally, the polycap rapidly broke down to a dumbbell-shaped assembly when treated with an excess of the simple dimeric capsule. The dumbbell featured a sharply resolved ^{1}H NMR spectrum that showed all of the expected resonances.



The information offered by the aryl urea-arylsulfonyl urea heterodimerization was used for programmed, or “smart” polymers (Figure 20).[13] As told above, calixarenes **28a** and **28b** form linear polycaps in organic solvents. Representative ^{1}H NMR spectra show the -NH protons (close to the residue R) of each clustered around 9.4 and 10.2 ppm, respectively. The heterodimerization tendency of aryl and arylsulfonyl ureas predicts that a combination of **28a** and **28b** should lead to polycaps of alternating subunits. Indeed, only –NH resonances from the arylsulfonyl urea interaction are observed in the ^{1}H NMR spectrum around 10.6 ppm. Likewise, the self-complementary derivative, **28c** polymerizes “head-to-tail” with alternating aryl urea and arylsulfonyl urea rims.

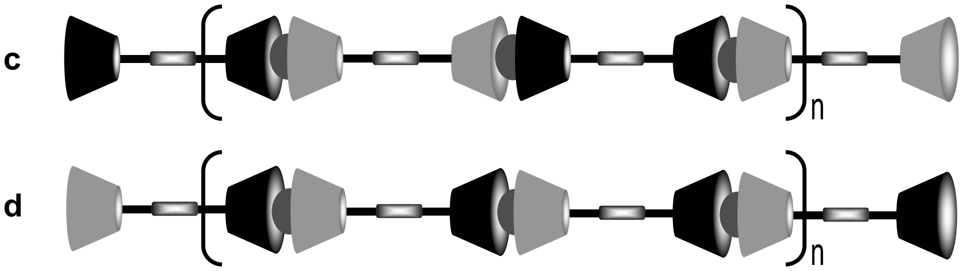
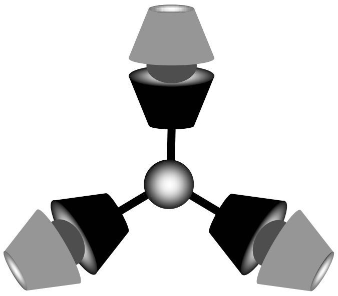


Figure 20. “Smart polymers”.

More complicated systems follow in two-dimensional assemblies. Triple calixarene based on a spacer derived from a symmetrical 1,3,5-trisubstituted benzene was prepared. Addition of $CDCl_3$ to this compound produces an uncharacterized insoluble gel, presumably through the formation of cross-linked polycaps. In contact with aromatic solvents such as benzene and *p*-xylene, it exists as an insoluble powder. Nonetheless, addition of 3 mol of tetratosyl urea calix[4]arene to the gel in $CDCl_3$ yields a homogeneous solution, and the capped derivative **29** emerges as the only species detectable by ^{1}H NMR. Again the characteristic four signals for the downfield shifted

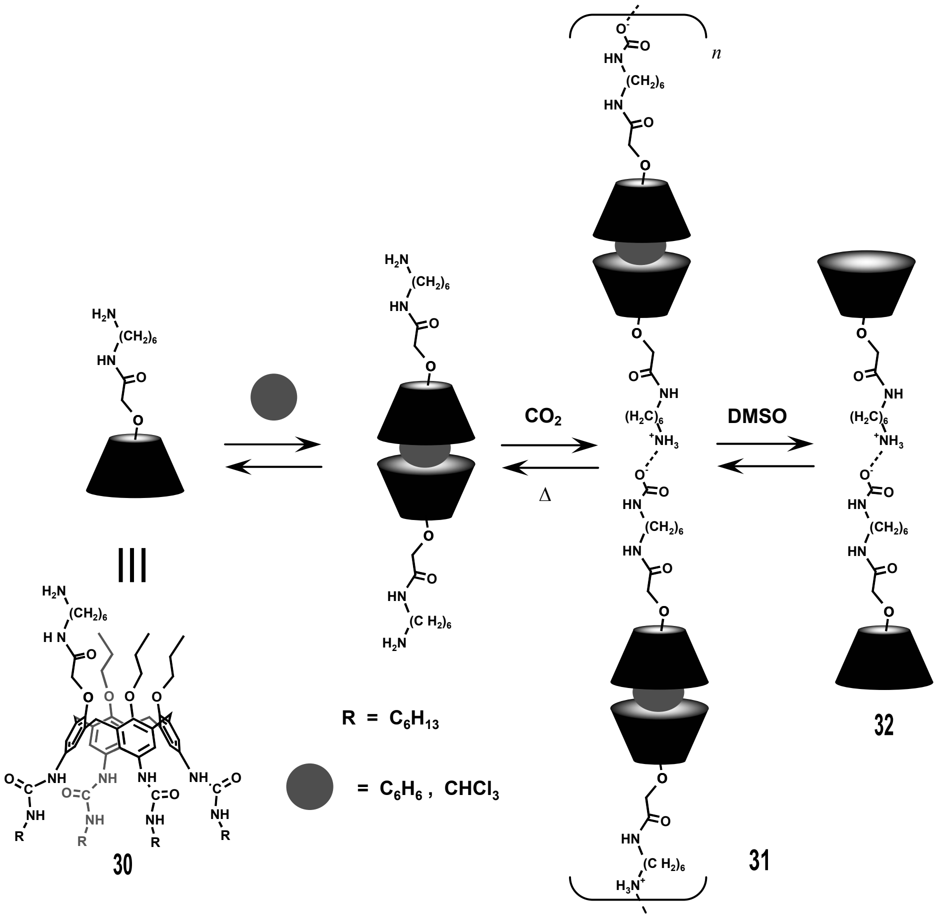


29

-NH protons of the cap are observed. This is one of complicatest assemblies on the base of calix[4]arenes prepared to a date.

Supramolecular, reversibly formed polymers consisting of self-assembled capsules have been constructed also through the chemical fixation of CO_2 and hydrogen bonding.[31] For this purpose tetraurea calix[4]arene **27a** bearing one carboxylic group on the narrow rim was transferred into monoamine **30** *via* reaction with 1,6-diaminohexane. As expected, **30** dimerizes in apolar solvents. During the bubbling of CO_2 through a solution of **30•30** in benzene carbamate-based polymer **31** precipitates. Now the initially formed capsules are held together by salt bridges (carbamates) $CH_2N^+H_3 \ldots O_2C(O)NHCH_2$ (Scheme 6).

Presumably, one molecule of an amine reacts with CO_2 to form the corresponding carbamic acid. It is highly unstable and rapidly transfers the acidic proton to the second amine molecule, thus producing a relatively stable carbamate salt. Formation of the carbamate bridges was confirmed by NMR spectroscopy in DMSO, were the calixarene capsules completely dissociate and only the salt **32** can be found. This salt can be destroyed upon heating during several hours at ~ 100 °C. So polymeric assembly **31** can be demolished either by changing the solvent polarity or the temperature.



Scheme 6. Self-assembled polymers constructed through the chemical fixation of CO_2 and hydrogen bonding.

1. 4. Goal

Interest in supramolecular polymers has been stimulated to a great extent by the impressive progress made in supramolecular chemistry in general and in the field of synthetic, self-assembling molecules in particular.

When the covalent bonds that keep together the monomeric units in a macromolecule are replaced by highly directional noncovalent interactions, supramolecular polymers are obtained. Although hydrogen bonds between neutral organic molecules are not among the strongest noncovalent interactions, they hold a prominent place in supramolecular chemistry because of their directionality and versatility.

Using a directionally complementary couple (A-B) or a self-complementary unit (A-A) it is possible to create almost all known structures of polymers, including linear homo- and copolymers, cross-linked networks, and even branched structures in the case of complementary couples.

Such couples (A-A or A-B) can be also formed by calixarenes. For this purpose the two tetraurea calix[4]arenes, bearing appropriate functional groups, must be connected *via* their narrow or wide rims. The most simple way is the connection *via* **one tether**. To introduce a single functional group suitable for further modification selective functionalization of calixarenes must be performed. The synthesis of such building blocks may become rather sophisticated.

In general the number of supramolecular polymers based on multiple hydrogen-bonded units is relatively small because of the increased synthetic efforts required for the synthesis of the monomers. Only several polymers were prepared on the basis of calixarenes. As shown by Rebek, covalent connection of **two** tetraurea calix[4]arenes at their **narrow** rims affords molecules, which form linear polymers in apolar solvents (See Chapter I, p. 17). In these molecules two tetraurea units are preoriented for such polymerization by short spacers (xylylenediamine), which keep the tetraureas pointing away from each other. The ability of the tetratolyl (A) and tetratosyl (B) ureas to form exclusively heterodimers was effectively used for the formation of polymers with alternating sequence of the units. Up to the moment bis-calixarenes, connected *via* the longer and flexible spacers were not studied at all. To investigate the self-assembly properties of such rather flexible units we planed to connect two calixarenes *via* (long) PEG spacers. In this case formation of cyclic structures as well linear polymers is possible. We suppose to study the influence of concentration and solvent(guest) on dimerization.

In contrast, coupling of **two** calixarenes at their **wide** rim by a hexamethylene bridge leads to the formation of unimolecular capsule (See Chapter I, p. 16). Oligo- or polymeric species have not been detected. Hitherto this is the only example of the self-assembled bis-tetraurea calix[4]arene with the upper rim connection of the units, although such attachment *via* suitable spacers offers new possibilities to create supramolecular structures. For example if the chosen spacer does not allow the intramolecular dimerization the formation of unimolecular capsule is excluded. Keeping two tetraurea derivatives more or less parallel to each other the cyclic oligomer shown in Figure 21 should be one of the possible products of self-assembly. Synthesis of the such building block will be one of the topics of our work (for more details see Chapter IV).

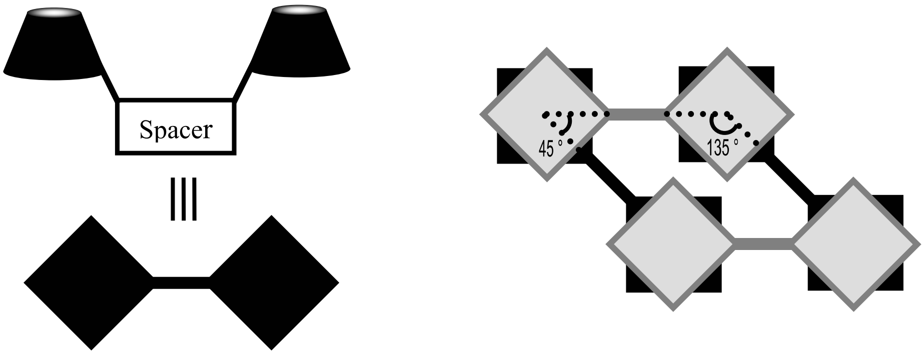


Figure 21. Possible self-assembly of bis-tetraurea calix[4]arene. Two calixarenes are connected via their upper rims.

More then two calixarenes can also be connected together. Depending on the spacer and the units attached together this connection can lead to cross-linked polymers (Figure 22a) or well-defined dendritic structures (Figure 22b). The first example can be obtained *via* self-assembly of the molecules possessing three (or more) tetraurea calixarenes of the same type (tetratolyl urea). To obtain this supramolecular structure no selective dimerization is required. More sophisticated building blocks must be prepared for the synthesis of dendritic structure *via* self-assembly. Here we have to prepare and connect together several types of tetraurea units which form exclusively only certain dimers. In other words the molecules in solution should obey a self-sorting principle. For example if calixarene A can form only homodimers, while calixarenes B and C form only heterodimers, but not with A, and the unit D does not form any dimers we can obtain a well-defined dendrimer as shown in Figure 22b. This is just a simple example, which illustrates the general idea of our research. In more details we describe these studies in the chapter V.

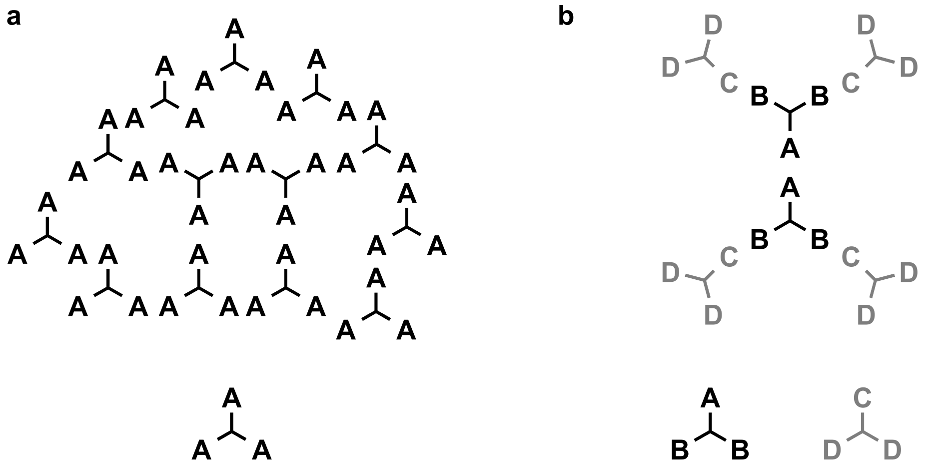


Figure 22. Sketchy drawing of the cross linked polymers (a) and well-defined dendritic assemblies (b).

Summarizing the ideas discussed above four main topics of the present work can be distinguished:

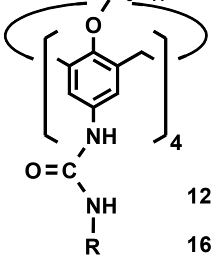
1) Being engaged with the single molecules bearing several urea functions we will try to get a better understanding of the driving forces of (hetero). Since heterodimerization will play an important role in our studies the tetratolyl and tetratosyl derivatives should be investigated. As models for these studies we have chosen two types of calix[4]arenes, subsequently functionalized by urea functions: rigid – biscrown and flexible – tetrapentoxy calix[4]arenes (see Chapter II).
2) The synthesis of tetraurea calix[4]arenes (**units**) bearing one or more functional groups at the narrow rim have to be developed (Chapter III, IV).
3) These units will be used to synthesize different types of multiple tetraurea calixarenes (**building blocks** for supramolecular structures). The self-assembly properties of the building blocks will be investigated (if necessary in collaboration with other groups) (Chapter III, IV).
4) Self-sorting processes, expressed by the exclusive formation of heterodimers or the complete absence of heterodimers will be used to design well-organized dendritic structures (See Chapter V).

2. DIMERIZATION OF TOLYL- AND TOSYLUREA DERIVATIVES OF FLEXIBLE AND RIGID CALIX[4]ARENES

2. 1. Introduction

It is now well established that tetraurea derivatives of calix[4]arenes form dimeric capsules in apolar, aprotic solvents. In chloroform or benzene these are held together by a seam of hydrogen bonds between the urea functions attached to the wide rim. The inclusion of a suitable guest, often the solvent, is a necessary condition for this dimerization. The dimeric structure, initially proposed on the basis of ^{1}H NMR spectra,[16] has been confirmed subsequently by several X-ray structures,[18,32] and for cationic guests by mass spectroscopy.[33]

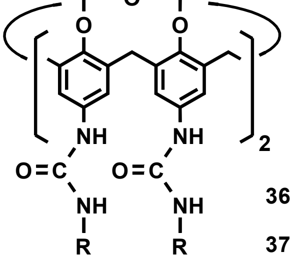
If two tetraurea derivatives of type **I**, where R may be alkyl or aryl are mixed in a suitable solvent the two possible homodimers and the heterodimer are usually formed in a (more or less) statistical ratio of 1:2:1. This formation of heterodimers could be considered as a strong and unambiguous proof of the dimerization.[17] Unexpected, and still not understood in detail, was the observation, that a mixture of the tolyl urea **12** with tetra tosyl urea **16** of type **I** contained only the heterodimer **12**•G•**16**, if **12** and **16** are present in stoichiometric amounts, accompanied inevitably by the respective homodimer, if one of the tetraureas is present in excess.[21] This exclusive formation of heterodimers was successfully used to control the structure of larger assemblies or to proof the ability of the multiple tetraurea calix[4]arenes to form heterodimers.[13,30]



12 R = Tolyl

16 R = Tosyl

I



36 R = Tolyl

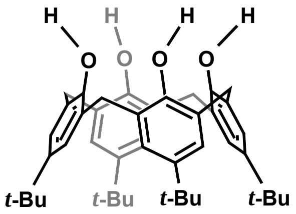
37 R = Tosyl

II

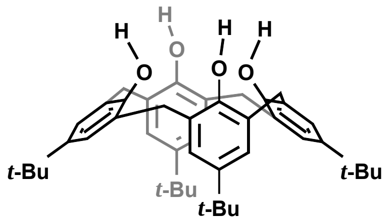
Since subsequently we want to deal with such systems it is highly important to get a better understanding of the factors which control the homo- or heterodimerization. Under "factors" we understand not only the external ones, like solvent or temperature, but also how the changes in chemical structure of calixarenes taking part in the dimerization can influence this process. Being engaged with the single calixarenes (before we switch to the multiple tetraurea derivatives) we wanted to study these factors in more details.

2. 2. Rigid and Flexible Calix[4]arenes

As described above the calixarenes can be fixed in the cone conformation by *O*-alkyl groups larger then ethoxy. This conformation is necessary or must be assumed for the dimerization since all urea functions must be oriented in the same direction. Nevertheless such fixation is quite relative. Usually the single molecules adopt a so called “pinched cone” conformation and possess C_{2v} symmetry. On average the ^{1}H NMR spectra of such derivatives do not reveal this symmetry. Thus, for example, only one signal for the aromatic protons of the calixarene skeleton is usually observed instead of two expected for C_{2v} symmetrical unit. The apparent C_{4v} symmetry expressed by the NMR could be explained with the rapid interconversion of two identical C_{2v} symmetrical “pinched cones”. We will call this type of calixarenes “flexible”. Forming a dimer flexible calixarenes adopt the ideal “cone” conformation (the most suitable for the dimers) and became C_{4v} symmetrical.



Ideal Cone



Pinched Cone

Connection of adjacent oxygens at the narrow rim by two diethyleneglycol tethers leads to a more rigid calixarene skeleton. Now the monomeric unit is already found in the “cone” conformation with a nearly C_{4v} symmetrical shape, as it was shown by several X-ray structures.[34] Thus, in monomeric state and as the dimers, calixarenes of this type -“rigid calixarenes”- possess the “cone” conformation.

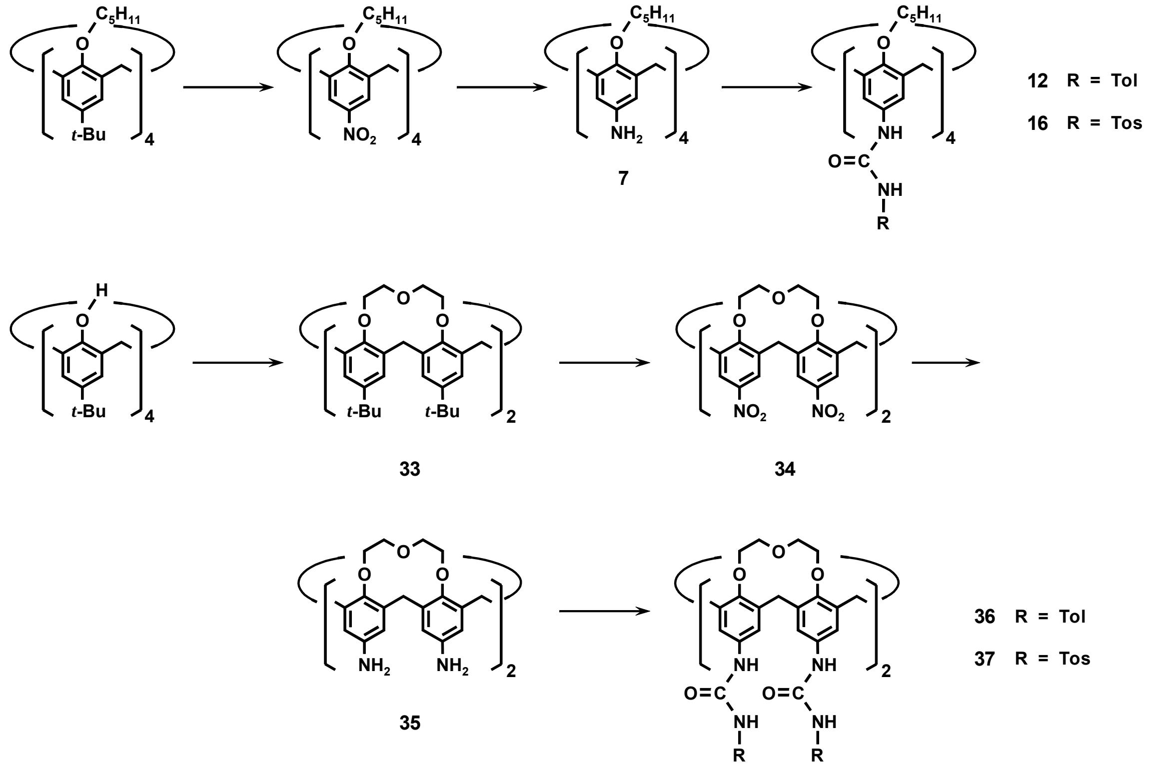
In our group it was recently shown that such a rigidification of the calix[4]arene skeleton (tetraureas of type **II**) led to remarkable changes of their properties. There is, for instance, a strong increase of the thermodynamic stability of homodimers **36•36** (Scheme 7), formed by rigid tolyl urea, which tolerate larger amounts (roughly four times) of DMSO than the analogous dimers **12•12**, formed by flexible tolyl ureas.[35] The kinetic stability expressed by the rate of guest exchange[36] is higher as well.

Rather unexpected was the observation that **12** and **36** obviously do not form heterodimers. A mixture of both tetraureas in $CDCl_3$ contains only the two homodimers **12•12** and **36•36**.

This observation raises the question, which of the two tendencies would be more pronounced, the well-known formation of heterodimers between tolyl and tosyl ureas, or the absence of heterodimers in a mixture of a flexible and rigid calixarenes? In other words, with the compounds discussed so far, are heterodimers form exclusively in a mixture of **16** and **36** or not? To obtain a complete answer on this question, which might be important for the selective construction of supramolecular assemblies via reversible bonds, we included also the tetra-tosyl urea **37**, derived from the rigidified calix[4]arene**.**

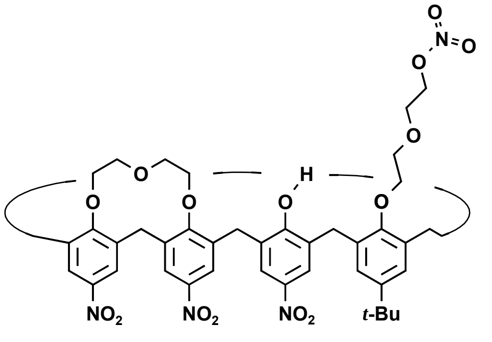
2. 3. Synthesis

The target compounds have been synthesized from the parent calix[4]arene *via* consecutive alkylation, *ipso*-nitration, hydrogenation and following reaction with tolyl or tosyl isocyanates (Scheme 7). All reactions with the flexible calixarenes were made according the well elaborated procedures, described in the literature. Although the synthesis of the compound **33** was also reported earlier,[37] the reaction conditions still had to be adjusted. Thus in accordance to the literature the slurry of parent calixarene **1**, NaH and diethylene glycol ditosylate in DMF was stirred at room temperature during 4 hours. Then the solvent was removed in vacuum, the residue was treated with HCl and extracted with ethyl acetate. The column separation afforded the pure product in 30 % yield. In contrast to the described procedure the temperature and the duration of reaction were considerably increased. Only after stirring during 4 days at 70 °C the TLC control showed only one main spot corresponding to the desired product, while several spots including the starting calix[4]arene were observed before. After that the solvent was removed in vacuum. The residue was treated with water and then dissolved in acetone to remove the rests of parent calixarene and some of insoluble by-products. After recrystallization from $CHCl_3/CH_3CN$ the pure product was obtained in 65-70 % yield. Thus, we could obtain calix[4]arene **33** without column chromatography and improve the yield.



Scheme 7. Synthesis of the tetraurea derivatives of calix[4]arenes.

Due to the limited solubility of **33** the reaction of *ipso*-nitration is carried out in boiling acetic acid and affords tetranitro compound **34** in relatively low yield (30–40%).[38] In general, the product precipitates from the reaction mixture directly in analytically pure form. But repeating the *ipso*-nitration of **33** numerous times we established, that when the volume of solvent is too big, very often precipitation does not occur. Optimizing the reaction conditions we have found that the highest yields were observed when the starting material was divided and reacted in several small portions (0.2–0.4 g) and the volume of the solvent was not larger than 7-10 mL. Moreover, if precipitation itself did not occur, the reaction mixture should be deluted with water and the subsequent recrystallization of the residue from CH_3CN or THF lead to the same yield of the product.



38

The latter observation led us to carry out the reaction under conditions usually used for the *ipso*-nitration of calixarenes (CH_2Cl_2, HNO_3, CH_3COOH, 2 hours). The ^1H NMR spectrum recorded for the reaction mixture (after the organic layer was washed with water and evaporated) showed that the mixture contained approximately 60-70 % of the desired compound **34**. The rest of the signals could not be interpreted. TLC control showed two main spots. Simple treatment of the reaction mixture with THF afforded the tetranitro compound in 45-50 % yield. Acetonitrile could be considered as an alternative solvent, but the purity of the product is less satisfactory in this case. Thus we could elaborate a better procedure for *ipso*-nitration of the rigid calixarene and improve the yield.

Among the side products by-product **38** having one ethyleneglycol bridge broken (the second spot on TLC) is usually formed in approximately 15 % yield and was separated from the reaction mixture by column chromatography. The structure of this compound was established on the basis of ^{1}H NMR, ^{13}C, ^{13}C{^{1}H}, ^{1}H-^{13}C HMBC and 2D COSY experiments and proved by MASS spectrometry.

The reduction of **34** was carried out using hydrazine and Raney nickel. However the reaction was continued until only the spot corresponding to the desired tetraamine was observed on TLC, the product was isolated with the surprisingly low yield (25%). Thus it was assumed that the main part of compound left on the nickel surface. To destroy the complex the catalyst was washed with 10 M water solution of ammoniac and the product was extracted with chloroform. Finally the tetraamino compound was isolated with 70 % yield.

The reaction of **35** with tolyl isocyanate was accomplished without complications. But the reaction with tosyl isocyanate seemed not to work properly. After recrystallization of the crude product from $CHCl_3$/MeOH (the compound was dissolved in a small amount of dichloromethane and methanol was added until the precipitate appeared, then the sample was heated to get a clear solution again and left to cool slowly) the products of partial substitution were observed in the spectrum. Therefore the reaction time and excess of the tosyl isocyanate were increased, but the outcome of the reaction remained the same. Hence we have concluded, that either the reaction could not be accomplished or the product is partially destroyed during recrystallization. To find out the reason the spectrum of the crude product was recorded and only the mixture of desired tetratosyl urea and the rests of isocyanate were detected. But after recrystallization the products of the partial substitution were observed again. Why could this happen? Could the tosyl urea be hydrolyzed by heating with MeOH? Thus after the reaction was finished the solvent was concentrated to approximately 1 ml and the product was just precipitated with methanol. The one additional reprecipitation (no heating) lead to the pure tetratosyl derivative. So one can conclude that the tosyl urea derivatives are not stable in the proton donating solvents at higher temperatures. This observation was also confirmed by the spectra of compound **16** in DMSO. The amount of water present in this solvent was sufficient to destroy urea groups at 50-75°C, while in tetrachloroethane at the same temperature they were not affected.

2. 4. Dimerization

As expected, all four tetraureas (**12**, **16**, **36**, **37**) form homodimers in $CDCl_3$ solutions containing only a single calixarene as evidenced by clear ^{1}H NMR spectra with. Surprisingly, both tetratosyl ureas **16** and **37** form homodimers also in CD_2Cl_2, where the spectrum of **12** shows only broad and uninterpretable bands. Broadening of signals is also observed for **36** in CD_2Cl_2 but the chemical shifts are in accordance with those of the homodimer **36•36** in $CDCl_3$ (Figure 23).

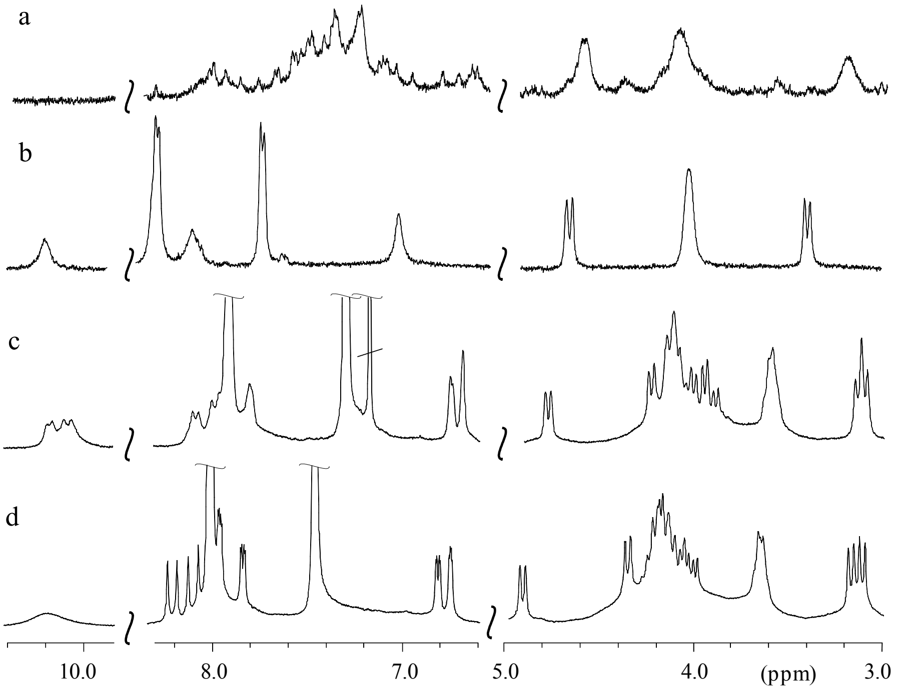


Figure 23. Selected ^{1}H NMR spectra (400 MHz, 25 °C) of tetraureas: irregular aggregates of **12** in CD_2Cl_2 (a); homodimer **16•16** in CD_2Cl_2 (b); homodimer **37•37** in $CDCl_3$ (c); homodimer **37•37** in CD_2Cl_2 (d).

To study the formation of heterodimers either the single calixarenes were dissolved in $CDCl_3$ or in CD_2Cl_2 (at c = 3.08 mM) and equimolar amounts of the two solutions (containing the respective homodimers) were mixed or the mixture of two calixarenes was dissolved in appropriate solvent and spectra were recorded. Deutero benzene was not used for the dimerization studies due to the limited solubility of the components.

The NMR spectra shown in Figure 24 clearly display that the two homodimers are present in the mixture of **12** with the corresponding tetra tolyl urea **36**, derived from the rigidified calix[4]arene. Even the addition of excess of **12** to the solution did not shift the equilibrium towards the formation of a heterodimer and no new signals appeared. This result can be tentatively explained on an entropic basis, since the internal mobility of a dimer/capsule formed by **36** (homo- or heterodimer) is much more restricted than that of a homodimer of **12**. Thus, the formation of heterodimers **12•**G**•36** would be entropically less advantageous than the exclusive formation of homodimers **12•**G**•12**, and **36•**G**•36**. No changes occur and no additional signals were observed in the mixture after longer times (1 month).

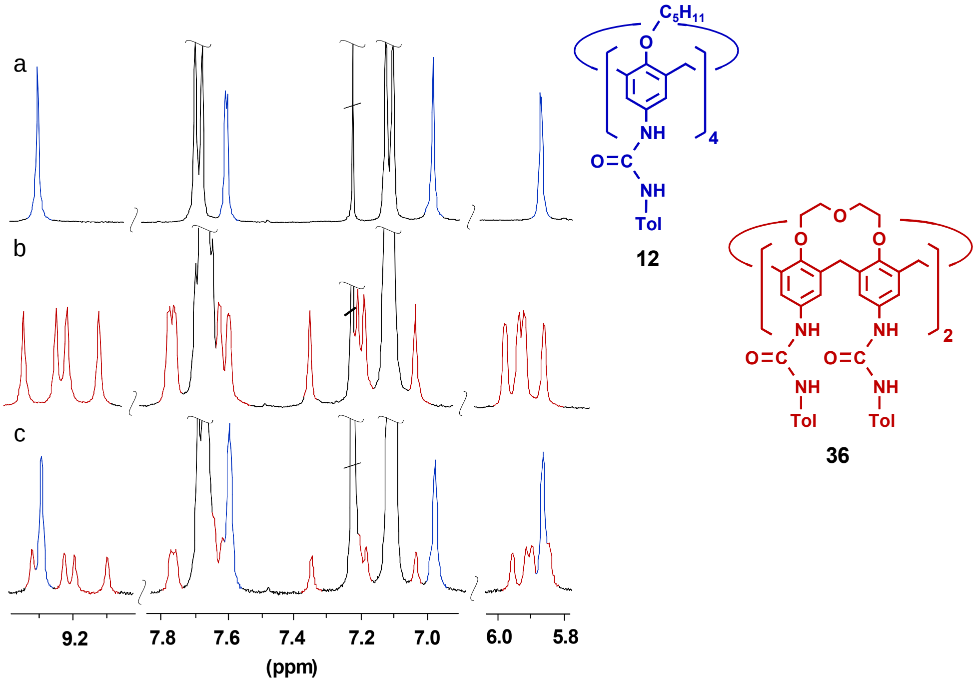


Figure 24. Sections of the ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C) spectra of: homodimer **12•12** (a); homodimer **36•36** (b); mixture of **12** and **36** in the ratio 1:1 (c).

On the first glance in those cases, where rigid calixarenes **36** and **37** were involved, the measurements resulted either in superimposition of the spectra of two possible homodimers or in very complicated sets of the signals. The latter after more detailed analysis were attributed to the mixtures of the two homodimers and probably heterodimer. Only in the case when compounds **12** and **16** were mixed together a clear heterodimer was immediately observed. After one weak for the selected mixtures the spectra were recorded again. Surprisingly they were simplified and the signals corresponding to the homodimers disappeared. So, if the resulting assemblies are the target heterodimers which sets of signals should be expected?

In general one can judge about dimerization from the aromatic part of the spectrum. Usually in appropriate solvents the Ar*H* protons of the calixarene skeleton appear as two strongly separated *meta*-coupled doublets. Moreover due to the hydrogen bonding the N*H* protons are also separated more then by 2 ppm. Thus the most obvious part of the spectrum of such a dimer is the region between 6 and 10 ppm. Unfortunately in some cases due to the low symmetry of the capsule it can happen, that there are to many signals in the aromatic part of the spectrum. Then one can see if self-assembly occurs or not looking at the signals in the region at about 10 ppm, where the N*H* protons forming the stronger hydrogen bonds appear. But this part alone cannot be considered as an unambiguous proof of dimerization. It is also possible to get some additional information about the dimer from the ArCH_2Ar proton's region. But in our studies the signals of this part are usually so overlapped, that they could be assigned only using two dimensional spectroscopy.

Two identical calixarenes possessing C_{4v} symmetry, produce a homodimeric capsule that is S_8-symmetric and achiral (**12•12**, **16•16**). The situation is different for heterodimers (capsules composed from two different units), which are C_{4v}-symmetric (**12•16**) and become C_4-symmetric and chiral by the directionality of the hydrogen bonded belt (Figure 25).

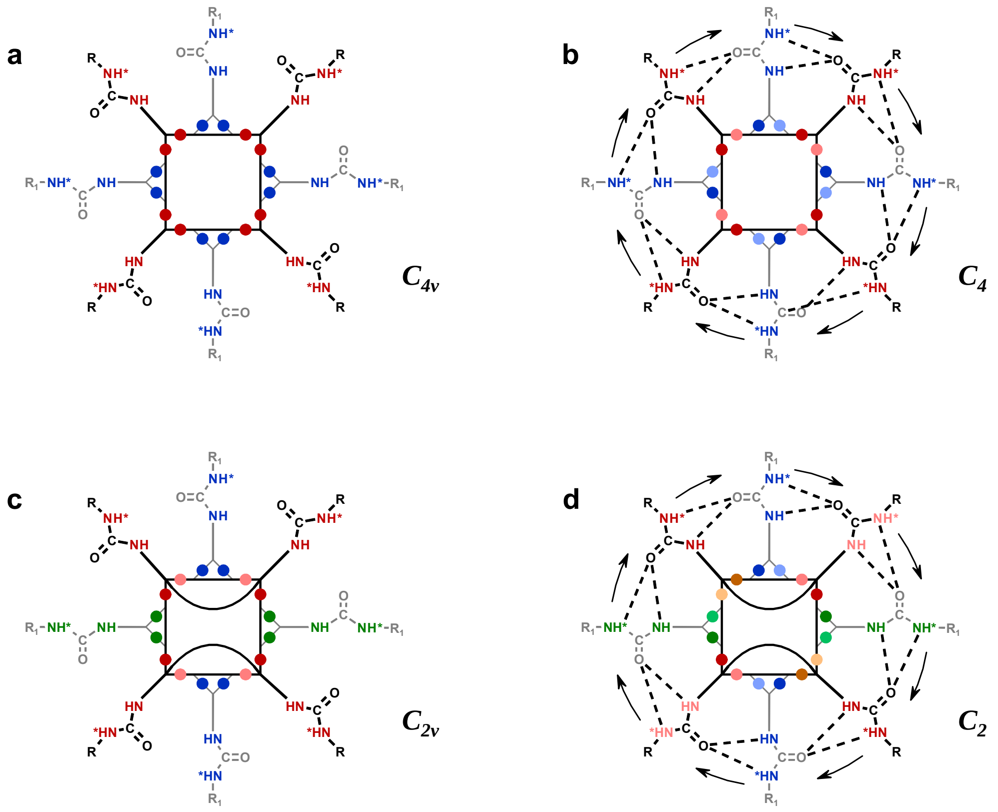


Figure 25. Schematic representation of the heterodimers 12•37 and 16•36. The directionality of hydrogen bonded belt is indicated by arrows. Aromatic protons of the calixarene skeleton are indicated by circles. The different protons are shown in different colors.

A lower symmetry is expected for the dimers, where calixarenes rigidified by two short ethyleneglycol bridges (**36**, **37**) are involved. The single biscrown calix[4]arene has C_{2v} symmetry, like a calixarene consisting of two different phenolic units in alternating sequence (ABAB). However, the symmetry planes intersect opposite methylene bridges and not opposite phenolic units. A homodimer **36•36** or **37•37** thus has D_2-symmetry, which is reduced to C_2 by the directionality of the hydrogen bonded belt. With or without directionality, they form only ***one*** pair of enantiomers, since the chirality is caused by the combination of the two calixarenes and not by this directionality. In combination with a flexible calixarene a C_{2v}-symmetric heterodimer (**12•37**, **16•36**) is formed. And again the symmetry is reduced to C_2 by the directionality of the hydrogen bonded belt.

Thus the expected set of characteristic signals for heterodimer **12•16** should consist of four singlets for N*H* protons (two from each calixarene) and four pairs of *meta*-coupled doublets for Ar*H* (the aromatic protons of the given phenolic unit differ by the directionality of hydrogen bonding belt), while for heterodimers **12•37** and **16•36** the amount of the signals is doubled.

Indeed in those cases, where heterodimers were formed, the expected pattern of the signals has been observed. Unfortunately the *meta*-coupled doublets for the aromatic protons are not always recognized from the ^{1}H NMR and two dimensional experiments had to be performed.

Let us concentrate on the detailed analysis of the heterodimer **16•36** in CD_2Cl_2 as an example. First using COSY-experiments we could distinguish between the signals of N*H* and Ar*H* protons. The two dimensional spectrum shows four cross peaks corresponding to the aromatic protons of calixarene rings and two cross peaks corresponding to the protons of tolyl and tosyl residues (Figure 26). In ^{1}H NMR spectrum they emerge as seven (red, two signals overlapped) and four (black) signals respectively (Figure 27a). The remaining six signals correspond to the N*H* protons.

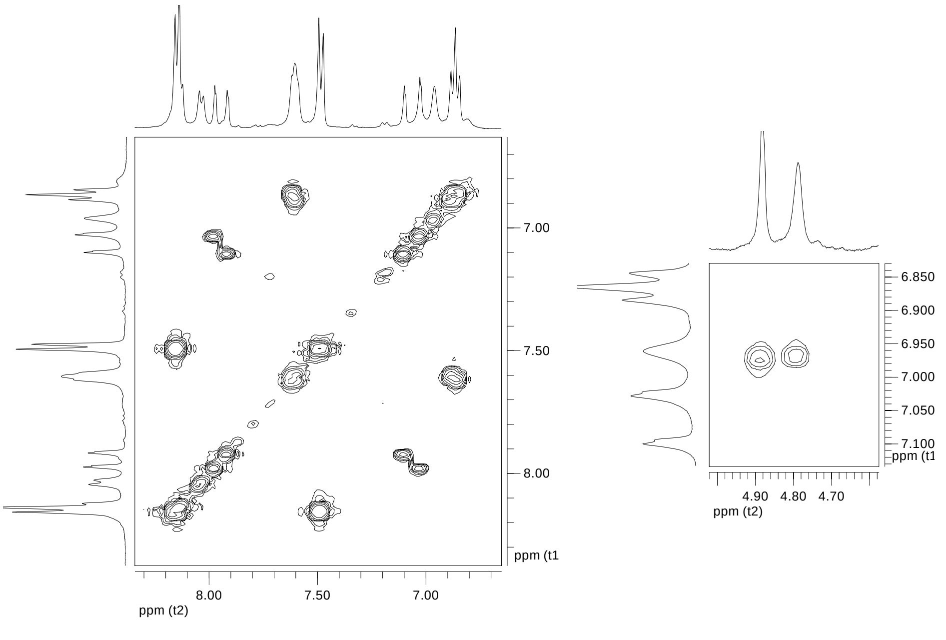


Figure 26. Sections of the COSY-gs spectrum of the dimer **16•36**.

In accordance to our expectations the two signals for N*H* protons are lacking. Being guided by integration we assumed that one of them is overlapped with the Tolyl-Ar*H* at 8.14 ppm and another one with the group of signals at 7.1-6.9 ppm.

Low temperature measurements were performed as an attempt to see all eight N*H* protons simultaneously. Unfortunately the appearance of the desired signals in the expected region was accompanied by an overlapping of the former visible signals (Figure 27b).

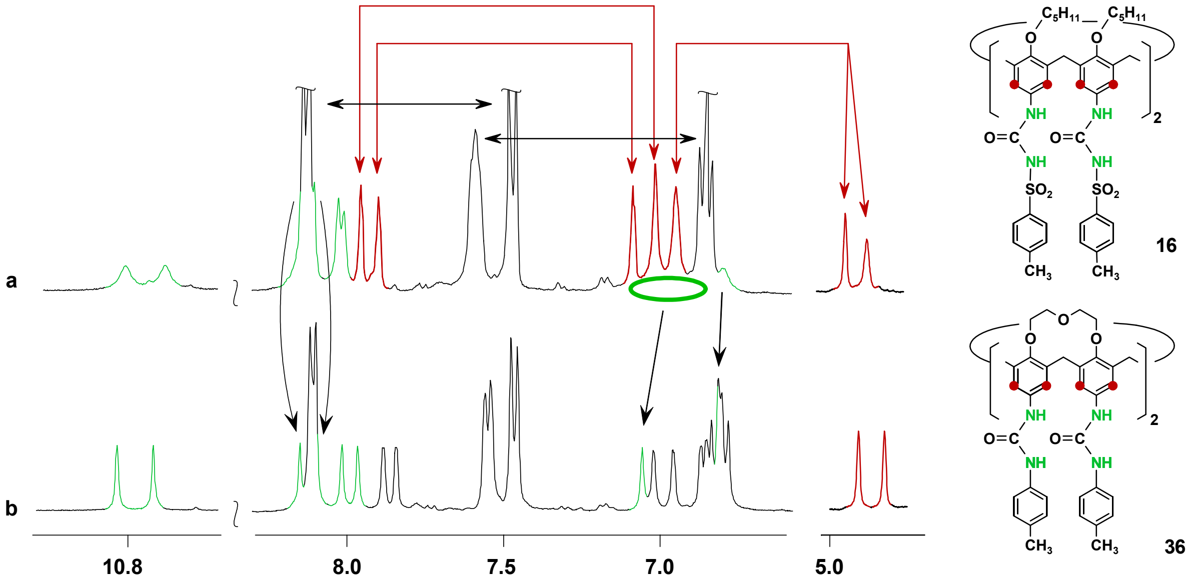


Figure 27. Sections of the ^{1}H NMR (400 MHz, CD_2Cl_2) spectra of heterodimer **16•36** at room temperature (a) and at -20°C (b).

In the aliphatic region of the ^{1}H NMR spectrum eight doublets are found for the methylene bridges together with one and two singlets for the CH_3 protons of tolyl and tosyl residues respectively (Figure 28). Thus the observed picture is found to be totally in accordance to the expected one.

The additional information obtained from TOCSY and NOESY correlations allow to attribute all signals in the spectrum (Figure 28). To simplify the assignment all visible signals were numbered. Finally for clarity the signals corresponding to the tetratosyl urea are shown in black and those of the tolyl derivative in gray.

The COSY spectrum shows that H9 is coupled with H8 and H10 with H11. This means that each pair of protons (H8-H9 and H10-H11) belong to the same aromatic ring of calixarene skeleton.

In turn, H8 gives a NOESY cross-peak to H11, and both H8 and H11 correlate with the closest methylene protons H27 of the bridges. The relations between methylene protons

H27 and H18 were established using COSY correlations. Thus the two described aromatic rings are connected *via* methylene bridge possessing the protons H27 and H18 and belong to the same calixarene.

The OCH_2 protons H24 were assigned to the diethyleneglycol bridges using COSY experiments (no cross peaks with the aliphatic part of the spectrum were found). In turn H24 gives NOEs to H18. Therefore all signals discussed so far belong to the rigid tetratolyl urea.

Following this methodology, all the protons of the aromatic rings of the calixarene skeleton, the OCH_2 and the methylene bridges were identified for both calixarenes. The resonances of methyl groups of the *p*-phenyl fragments were assigned through NOE and TOCSY signals to the *ortho*-protons which, in turn, give COSY cross-peaks to the *meta*-Ar*H*.

Unfortunately we experienced some difficulties to attribute *p*-phenyl fragments to tolyl or tosyl group and to assign all NH protons only on the base of 1D and 2D NMR. For example the resonances of N*H*-5 and N*H*-5’ show TOCSY cross-peaks to ^{1}H NMR signals of Ar*H*-11 and Ar*H*-9 (calixarene skeleton) respectively, while N*H*-6 and N*H*-7 correlate with Ar*H*-12,14 of *p*-phenyl groups. But there was no TOCSY correlation between N*H*-5 and N*H*-6 found. Meantime N*H*-5 shows NOESY cross-peaks to N*H*-1 and N*H*-6. So there is no unambiguous proof that described calixarene skeleton and *p*-phenyl groups belong to the same molecule.

In contrast N*H*-1 (N*H*-2) gives TOSCY peaks only to N*H*-17(N*H*-9’), but not to calixarene skeleton or to *p*-phenyl groups. However, NOEs between N*H*-17 and Ar*H*-19, N*H*-9’ and Ar*H*-20 were found. In consequence we can suppose that latter NH signals belong to the flexible calixarene (tetratosyl urea).

Looking for an additional information we prepared the model heterodimer using tosyl urea **16** and the *p*-methoxy phenyl urea (typ I, R = *p*-C_6H_4OMe), instead of the *p*-tolyl derivative **12**. We expected that the signal of ArOCH_3 protons will be down-field shifted with respect to the signal of ArCH_3 protons in tolyl urea, while the signal of ArCH_3 group in tosyl urea will remain on it’s place. In this way we supposed to distinguish between aryl and sulfonyl groups. Indeed we have established, that ^{1}H NMR signals Ar*H*-12,14, Ar*H*-13,15 and ArCH_3-31 belong to the tolyl urea and therefore to the rigid calixarene **36**, what is in good agreement with all arguments discussed above. The remaining signals were attributed to the tosyl residue.

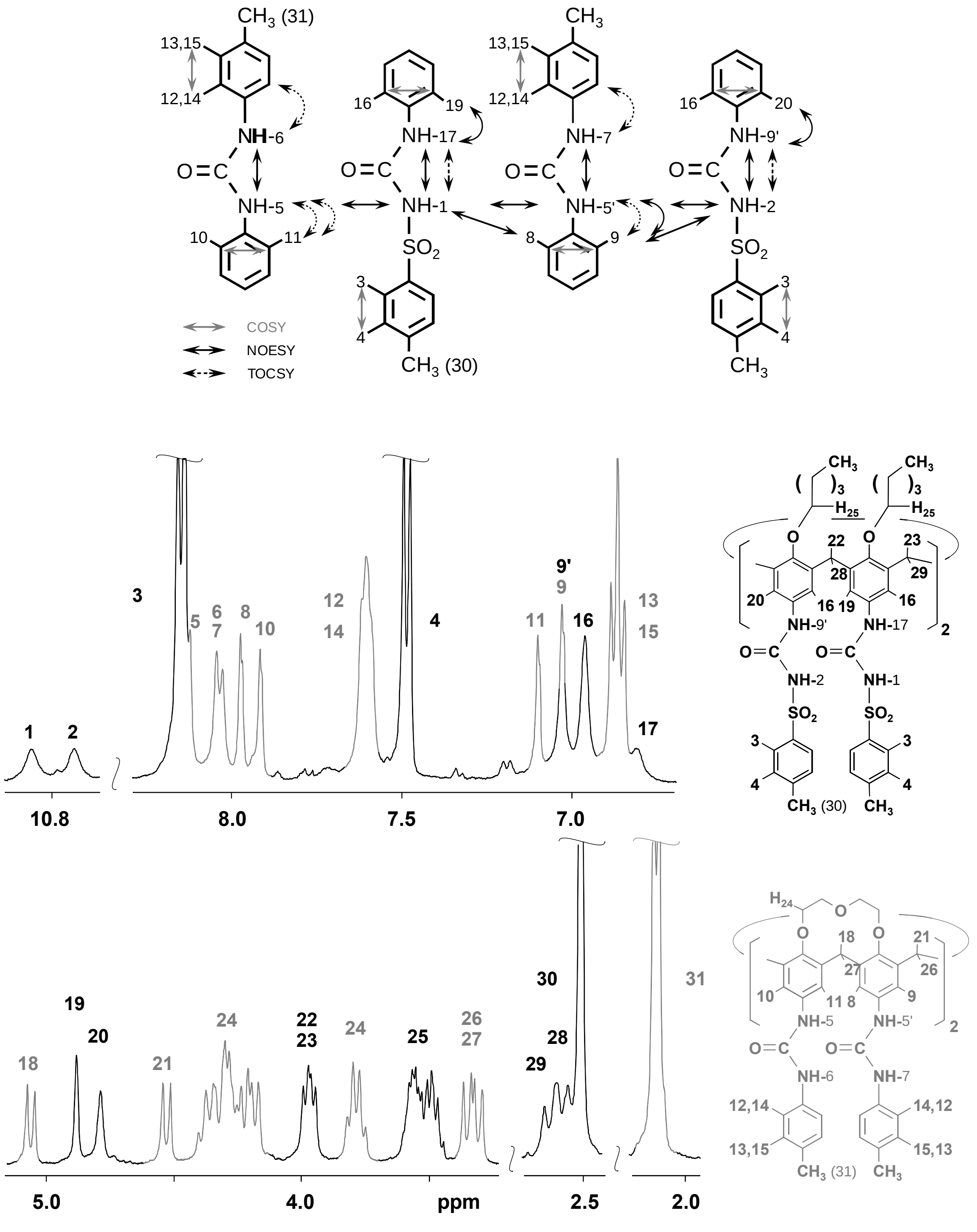


Figure 28. ^{1}H NMR (400 MHz, CD_2Cl_2) spectrum of the heterodimer **16•36** with assignment of all the peaks.

Heterodimers **36•37** are C_2-symmetric already by the combination of the two calixarenes. The directionality of the H-bonded belt is added now as an independent element of chirality (this is the case only in heterodimers) and ***two*** diastereomeric pairs of enantiomers (C_2-symmetry) are expected, as demonstrated schematically in Figure 29. Indeed, these are observed in the ^{1}H NMR spectra.

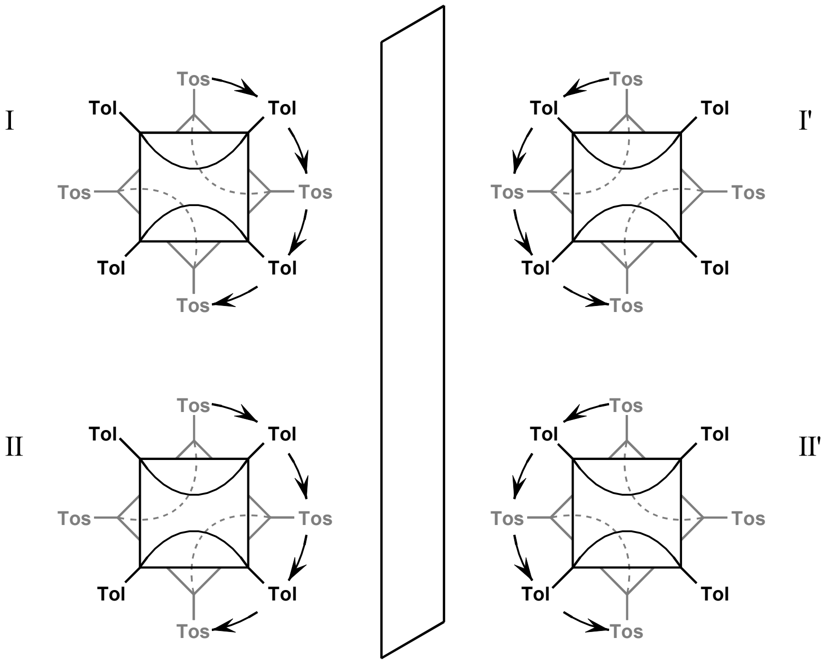


Figure 29. Schematic representation of the possible stereoisomers of heterodimers **36•37**. The directionality of the hydrogen bonded belt is indicated by arrows. Without directionality **I** and **II'** are identical as well as **II** and **I'**.

Finally for all possible combinations in both solvents the spectra were recorded immediately, after 3 h, 20 h and one week. In those cases, where heterodimers with the rigid calixarenes **33** and **37** were formed, this formation was slow. After 3 h usually about 50% conversion was observed. The reaction was complete in all cases after 20 h (see Figure 30), and no further changes were noticed in the spectra after one week.

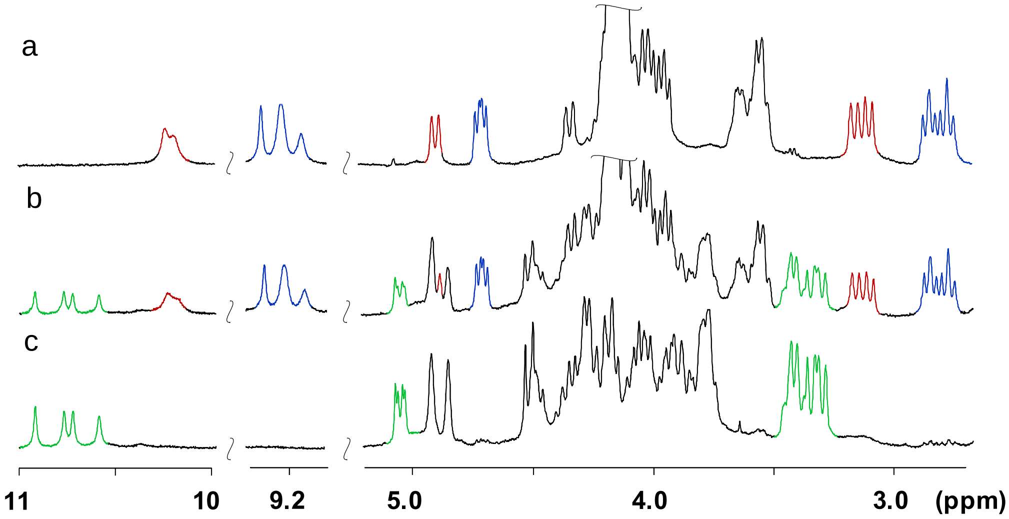


Figure 30. Formation of heterodimers of **36** and **37** in CD_2Cl_2. ^1H NMR spectra (400 MHz, 25 °C) were recorded immediately after mixing (a); 3 h after mixing (b); 20 h after mixing (c).

Table 1 summarizes the results obtained for all combinations of **12**, **16**, **36** and **37** and both solvents after the equilibrium was reached. They can be rationalized by considering two factors:

a) The combination of a flexible with a rigid calixarenes disfavors the formation of heterodimers. For entries I) and II) this is the only factor and heterodimers are not observed for tolyl as well as tosyl ureas in both solvents.

b) The combination of tolyl with tosyl ureas favors the exclusive formation of heterodimers. This is the only factor in entries III) and IV) and it is working for rigid as well as flexible calixarenes in CD_2Cl_2. The situation is less clear for $CDCl_3$ where the heterodimer is formed for flexible ureas but **not** for the rigid ones. Thus we have the interesting situation (entry IV), that the dimerization can be « switched » between hetero (CD_2Cl_2) and homo ($CDCl_3$) by the solvent, or (perhaps better) by the guest, since most probably the/a solvent molecule is included as guest.

In entries V) and VI) both effects are present. And in CD_2Cl_2 the situation is clear, the tendency of tosyl/tolyl residues to induce the formation of heterodimers is dominant for both combinations. In $CDCl_3$ however, in agreement with entry IV) the « tosyl/tolyl » effect is less pronounced than the « flexible/rigid » effect, and heterodimers are not formed in entry VI). This may be due to **3**, the compound present in both entries IV) and VI).

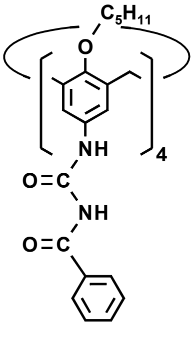
Table 1 Dimerization experiments between tetraurea calix[4]arenes **1**–**4**.

Entry	Mixture	**$CDCl_3$**		**CD_2Cl_2**	
		Equilibrium state picture	Determining factor	Equilibrium state picture	Determining factor
I	**12** (Tol, F) + **36** (Tol, R)	–	S	–[a]	S
II	**16** (Tos, F) + **37** (Tos, R)	–	S	–	S
III	**12** (Tol, F) + **16** (Tos, F)	+	H	+	H
IV	**36** (Tol, R) + **37** (Tos, R)	–	H	+	H
V	**12** (Tol, F) + **37** (Tos, R)	+	H > S	+	H > S
VI	**36** (Tol, R) + **16** (Tos, F)	–	H < S	+	H > S

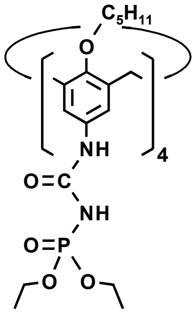
+ indicates the exclusive formation of the heterodimer; **-** means that only the two homodimers are present; **(-)** stands for an irregular assembly; the factor which disfavors the formation of heterodimers is designated by S (entropic factor); the factor which favors the formation of heterodimers is designated by H (enthalpic factor).

Although this is not yet a detailed explanation, it is a self-consistent, general picture. In accordance to all observations the mixing of **12•**G**•37** and **16•**G**•36** heterodimers together does not lead to any changes in the spectra during 3 days.

2. 5. Tetrabenzoyl and Tetraphosphoryl Ureas

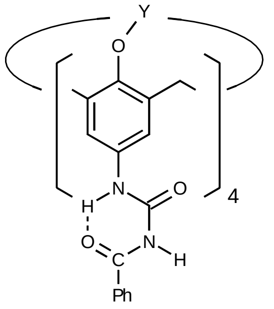


39



40

As described above, the tetratosyl and tetratolyl ureas form exclusively heterodimers. This can be tentatively explained by assuming that the SO_2 groups are also involved in the hydrogen bonding. Searching for similar examples benzoyl **39** and phosphoryl **40**[1] ureas were also examined. They were prepared from tetraamino calix[4]are **7** *via* reactions with corresponding isocyanates. Rather unexpected the tetraurea **39** was not able to form neither homo- nor heterodimers with aryl or sulfonyl ureas. The capsule formation could not be initiated by different solvents (guests) offered for dimerization. The formation of undefined structures (usually found in similar cases) in apolar solvents was also not observed. The spectra in $CDCl_3$ or $C_2D_2Cl_4$ (at room temperature and under heating) clearly represent that the benzoyl urea **39** is present in the monomeric state. This could mean that the acceptor group attached to the urea functions somehow hinders not only the dimerization but also the hydrogen bonding formation (what is difficult to believe). As an alternative explanation the formation of intramolecular hydrogen bonds could be considered.



The tetraurea **40** also does not form homodimers. However it makes exclusively heterodimers with the tetratolyl urea **12** (Figure 31) but not with the tetratosyl derivative **16**. The structure of the dimer was proved by NMR spectroscopy. Dimerization occurs slowly in time. In chloroform at room temperature it takes approximately 1-2 days until the heterodimer is completely formed. Other solvents could not be used for the studies because of the limited solubility of **40**.

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[1] Compound 40 was kindly given by Dr. V. Brusko.

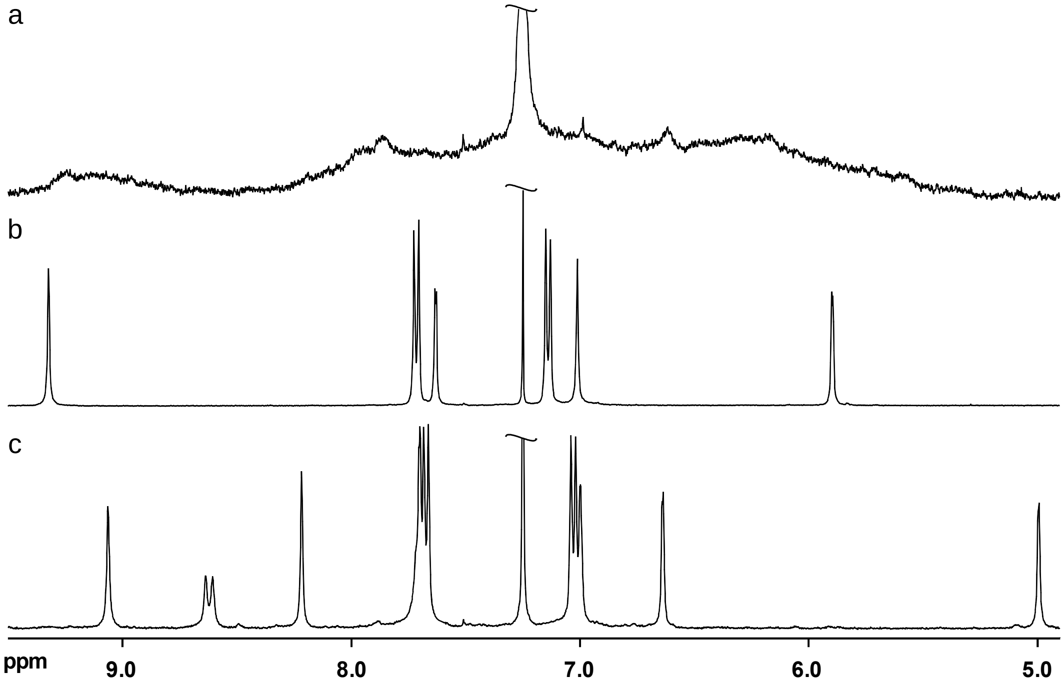


Figure 31. Sections of the ^{1}H NMR spectra (400 MHz, 25 °C, $CDCl_3$) of tetraphosphoryl urea **40** (a); tetratolyl urea **12** (b); the mixture of tetraureas **40** and **12** in the ratio 1:1 after one day (c).

2. 6. Conclusions

Wide rim tetratolyl (**1**, **3**) and tetratosyl (**2**, **4**) ureas with a more flexible calix[4]arene tetrapentylether (**1**, **2**) or a rigidified biscrown-3 ether derivative (**3**, **4**) as basic skeleton form homodimers in apolar solvents such as $CDCl_3$. For mixtures of two tetraureas there is the additional possibility to form heterodimers. Very subtle enthalpic and entropic contributions involving also the solvent (and guest) are obviously responsible for the exclusive formation of either homo- or heterodimers in stoichiometric (1:1) mixtures. This may be concluded from the observation that for two pairs (**3**/**2** and **3**/**4**) the self-assembly switches from hetero- to homodimers when going from CD_2Cl_2 to $CDCl_3$. The tetraphosphoryl urea could be used instead of tetratosyl derivative for the selective heterodimerization, but the slow kinetics and solubility problems make it less interesting, than the tosyl urea. Tetrabenzoyl urea can not be used in dimerization studies at all.

2. 7. Experimental Part

All solvents were of analytical quality (p. a.) and were used without additional purification. All solvents for NMR were purchased from Deutero GmbH. All ^{1}H NMR spectra were recorded on a Bruker Avance DRX 400 or Bruker 200 spectrometers at 400 and 200

MHz, respectively, and ^{13}C NMR on a Bruker Avance DRX 400 at 100 MHz using the solvent signals as internal reference. Mass spectra were recorded with a Finnigan MAT 8230 instrument. The melting points were not corrected.

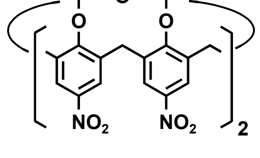
Starting tetraamino tetrapentoxy calix[4]arene **7**[39] and biscrown calix[4]arenes **33**, **35**[40] were synthesized in accordance with the published procedures, *p*-phenylmethoxy tetraurea was given by Dr. M. O. Vysotsky.

Tetranitro calix[4]arene 34

A) Calix[4]arene **33**[*] (0.40 g, 0.5 mmol) was placed in a 50 ml flask and dissolved in boiling acetic acid (6.60 ml) and fuming nitric acid (2.70 ml) was immediately added to the boiling solution. The solution was vigorously stirred for 0.5 h at room temperature. A product started to precipitate 2 minutes after the nitric acid was added. The precipitate was filtered off, washed with water (5x10ml) and methanol (2x5ml). Calix[4]arene **34** (0.14g, 36%) was obtained as a light yellow powder.

B) Calix[4]arene **33** (2.00 g, 2.5 mmol) was dissolved in CH_2Cl_2 (50 ml) and acetic acid (10 ml) was added. The solution was cooled down to the 0°C. After that fuming nitric acid (12 ml) was added slowly to keep the temperature of the reaction mixture about 0°C. The solution was vigorously stirred for 2 h. During this time the temperature of the reaction mixture increased to room temperature. The reaction mixture was diluted with water (30 ml), the organic layer was separated, washed with water (5x30 ml), dried over $MgSO_4$ and filtered. The filtrate was evaporated and treated with THF (or CH_3CN). The precipitate was filtered off yielding calix[4]arene **34** (0.85 g, 45 %) as a yellow powder. mp > 280°C decompose;

The mother liquid was evaporated and the residue was subjected to the chromatographic separation (THF/Hexane = 1/1). Compound **38** (0.3 g, 15 %) was obtained as pale yellow powder; mp 145-147 °C;



34 ^{1}H NMR (200 MHz, DMSO-d$_6$), δ: 8.33 (s, 4H Ar*H*), 8.32 (s, 4H Ar*H*), 5.05 (d, 2H, $^2J = 11.7$ Hz, ArC*H*$_2$Ar), 4.50 (d, 2H, $^2J = 11.7$ Hz, ArC*H*$_2$Ar), 4.41-4.20 (m, 12H, OC*H*$_2$), 3.82-3.69 (m, 8H, ArC*H*$_2$Ar and OC*H*$_2$).

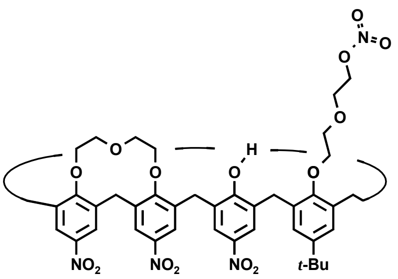
38 ^{1}H NMR (400 MHz, CDCl$_3$), δ:

8.33 (d, 1H, $^4J = 2.7$ Hz, Ar*H*), 8.30 (d, 1H, $^4J = 2.7$ Hz, Ar*H*), 8.19 (d, 1H, $^4J = 2.7$ Hz, Ar*H*), 8.13 (d, 1H, $^4J = 2.7$ Hz, Ar*H*), 7.81 (d, 1H, $^4J = 2.7$ Hz, Ar*H*), 7.60 (d, 1H, $^4J = 2.7$ Hz, Ar*H*), 7.49 (m, 2H, Ar*H*), 7.25 (s, 1H, O*H*), 5.51 (d, 1H, $^2J = 12.5$ Hz, ArC*H*$_2$Ar),

---

[*] It is important to work with small amounts of calix[4]arene to have best yields of compound.

5.43 (d, 1H, $^2J = 12.5$ Hz, ArCH_2Ar), 5.40 (d, 1H, $^2J = 12.5$ Hz, ArCH_2Ar), 4.70 (d, 1H, $^2J = 16.0$ Hz, ArCH_2Ar), 4.67 (d, 1H, $^2J = 16.0$ Hz, ArCH_2Ar), 4.41-4.35 (m, 2H, OCH_2), 4.31-4.27 (m, 2H, OCH_2), 4.10-3.93 (m, 4H, OCH_2), 3.89-3.91 (m, 2H, OCH_2), 3.77 (d, 1H, $^2J = 16.0$ Hz, ArCH_2Ar), 3.72 (d, 1H, $^2J = 16.0$ Hz, ArCH_2Ar), 3.56 (d, 1H, $^2J = 12.5$ Hz, ArCH_2Ar), 3.44-3.33 (m, 6H, OCH_2), 1.38 (s, 9H, C(CH_3)$_3$).



MS(FD) *m/z* (%) 817.2 (100) [M$^+$].

General procedure for the synthesis of 16 and 39

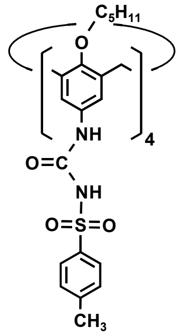
The tetraamine **7** (0.65 mmol) was dissolved in CH$_2$Cl$_2$ (10 ml) and the isocyanate (3.92 mmol) was added to the solution. The reaction mixture was stirred 16 h at room temperature and MeOH (20 ml) was added to the reaction mixture. The precipitate was filtered, washed with MeOH (3x10 ml).

Tetratosylurea calix[4]arene 16

Calix[4]arene **16** (77 %) was obtained as a white powder; mp 216-218°C;

^{1}H NMR (400 MHz, DMSO-d$_6$), δ: 10.17 (s, 4H, NH), 8.42 (s, 4H, NH), 7.79 (d, 8H, $^3J = 7.8$ Hz, ArH_{Tos}), 7.42 (d, 8H, $^3J = 7.8$ Hz, ArH_{Tos}), 6.60 (s, 8H, ArH), 4.20 (d, 4H, $^2J = 12.5$ Hz, ArCH_2Ar), 3.71 (t, 8H, J = 7.0 Hz, OCH_2), 3.01 (d, 4H, $^2J = 12.5$ Hz, ArCH_2Ar), 2.40 (s, 12H, ArCH_3), 1.80 (br s, 8H, CH_2), 1.31 (br s, 16H, CH_2), 0.87 (t, 12H, J = 6.4 Hz, CH$_2$CH_3);

^{1}H NMR (400 MHz, CD$_2$Cl$_2$, integration is given for a dimeric species), δ: 10.11 (s, 8H, NH), 7.95 (m, 24H, ArH, ArH_{Tos}), 7.76 (s, 8H, NH), 7.39 (d, 16H, $^3J = 7.8$ Hz, ArH_{Tos}), 6.67 (s, 8H, ArH), 4.34 (d, 4H, $^2J = 11.7$ Hz, ArCH_2Ar), 3.71 (br s, 16H, OCH_2), 4.34 (d, 8H, $^2J = 11.7$ Hz, ArCH_2Ar), 2.41 (s, 24H, ArCH_3), 1.90 (br s, 16H, CH_2), 1.32-1.20 (m, 32H, CH_2), 0.87 (t, 24H, $^3J = 6.8$ Hz, CH$_2$CH_3).

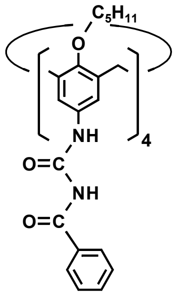


MS(ESI) *m/z* (%) 1575.7 (100) [M$^+$Na].

Tetrabenzoylurea calix[4]arene 39

Calix[4]arene **39** (80 %) was obtained as a white powder; mp 249-251°C;

^{1}H NMR (400 MHz, DMSO-d$_6$), δ: 10.66 (s, 4H, N*H*), 10.39 (s, 4H, N*H*), 7.83 (d, 8H, ^3J = 7.8 Hz, *o*-ArH_{Ph}), 7.50 (d, 4H, ^3J = 7.8 Hz, *p*-ArH_{Ph}), 7.32 (d, 8H, ^3J = 7.8 Hz, *m*-ArH_{Ph}), 6.91 (s, 8H, Ar*H*), 4.37 (d, 4H, ^2J = 13.3 Hz, ArCH_2Ar), 3.86 (t, 8H, ^3J = 7.0 Hz, OCH_2), 3.21 (d, 4H, ^2J = 13.3 Hz, ArCH_2Ar), 1.90 (br s, 8H, CH_2), 1.41 (br s, 16H, CH_2), 0.94 (m, 12H, CH_3);



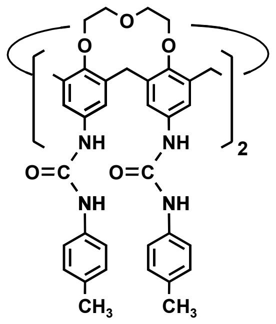
^{1}H NMR (400 MHz, $C_2D_2Cl_4$, 75 °C), δ: 10.24 (s, 4H, N*H*), 9.30 (s, 4H, N*H*), 7.86 (d, 8H, ^3J = 7.8 Hz, *o*-ArH_{Ph}), 4.43 (m, 4H, *p*-ArH_{Ph}), 7.30 (m, 8H, *m*-ArH_{Ph}), 6.92 (s, 8H, Ar*H*), 4.55 (d, 4H, ^2J = 13.3 Hz, ArCH_2Ar), 4.01 (t, 8H, ^2J = 7.0 Hz, OCH_2), 3.20 (d, 4H, ^2J = 13.3 Hz, ArCH_2Ar), 2.00 (br s, 8H, CH_2), 1.51 (br s, 16H, CH_2), 1.04 (m, 12H, CH_3);

MS(ESI) *m/z* (%) 1375.5 (100) [M$^+$Na].

General procedure for the synthesis of 36 and 37

Tetraamine **35** (0.54 mmol) was dissolved in dichloromethane (40ml) and isocyanate (6.53 mmol) was added to the solution. The reaction mixture was stirred for 16 h at room temperature.

Tetratolylurea-calix[4]arene 36



Methanol was added and a white precipitate formed was filtered off, washed with methanol (3 x 10 mL) and was crystallised additionally from a chloroform/methanol mixture yielding a white crystalline compound (60%); mp > 300°C decompose;

^{1}H NMR (400 MHz, DMSO-d$_6$) δ 8.42 (s, 4H, N*H*), 8.17 (s, 4H, N*H*), 7.25 (d, 8H, ^3J = 8.3 Hz, ArH_{Tol}), 7.10 (s, 4H, Ar*H*), 7.08 (s, 4H, Ar*H*), 7.03 (d, 8H, ^3J = 8.3 Hz, ArH_{Tol}), 4.92 (d, 2H, ^2J = 11.7 Hz, ArCH_2Ar), 4.41 (d, 2H, ^2J = 11.7Hz, ArCH_2Ar), 4.20-4.13 (m, 12H, OCH_2), 3.19 (d, 2H, ^2J = 11.7 Hz, ArCH_2Ar), 3.64–3.58 (m, 4H, OCH_2), 2.92 (d, 2H, ^2J = 11.7Hz, ArCH_2Ar), 2.21 (s, 12H ArCH_3);

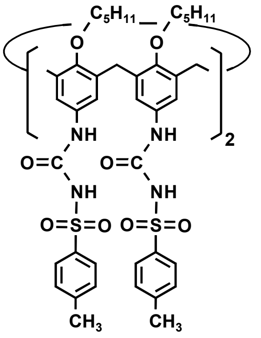
^{1}H NMR (400 MHz, $CDCl_3$, integration is given for a dimeric species): δ 9.35 (s, 2H, N*H*), 9.26 (s, 2H, N*H*), 9.22 (s, 2H, N*H*), 9.13 (s, 2H, N*H*), 7.80 (d, 2H, ^4J = 2.0 Hz, Ar*H*), 7.78 (d, 2H, ^4J = 2.0 Hz, Ar*H*), 7.72-7.67 (m, 16H, ArH_{Tol}), 7.64 (d, 2H, ^4J = 2.0 Hz, Ar*H*), 7.61 (d, 2H, ^4J = 2.0 Hz, Ar*H*), 7.37 (s, 2H, N*H*), 7.23 (s, 2H, N*H*), 7.21 (s, 2H, N*H*), 7.14 (d, 16H, ^3J = 7.6 Hz, ArH_{Tol}), 7.06 (s, 2H, N*H*), 5.98 (d, 2H, ^4J = 2.0 Hz, Ar*H*), 5.94 (d, 2H, ^4J = 2.0 Hz, Ar*H*), 5.92 (d, 2H, ^4J = 2.0 Hz, Ar*H*), 5.86 (d, 2H, ^4J = 2.0 Hz, Ar*H*), 4.69 (d, 2H, ^2J =

11.8 Hz, ArC*H*$_2$Ar), 4.67 (d, 2H, ^2J = 11.8 Hz, ArC*H*$_2$Ar), 4.20-3.94 (m, 28H, ArC*H*$_2$Ar, OC*H*$_2$), 3.65-3.57 (m, 8H, OC*H*$_2$), 2.88-2.77 (m, 8H, ArC*H*$_2$Ar), 2.26 (s, 24H, ArC*H*$_3$);

MS(ESI) *m/z* (%) 1179.5 (100) [M$^+$Na].

Tetratosylurea calix[4]arene 37

The solvent was removed at reduced pressure and Et$_2$O (30 ml) was added. The crude product was filtered, washed with Et$_2$O (3x 15ml), MeOH (1x5 ml) and precipitated from CHCl$_3$/MeOH. The calix[4]arene **37** (0.35 g, 46 %) was obtained as a light yellow powder; mp > 206°C decompose;



^{1}H NMR (200 MHz, DMSO-d$_6$), δ: 10.47 (br s, 4H, N*H*), 8.44 (s, 4H, N*H*), 7.82 (d, 8H, ^3J = 7.80 Hz, Ar*H*$_{\text{Tos}}$), 7.41 (d, 8H, ^3J = 7.80 Hz, Ar*H*$_{\text{Tos}}$), 6.90 (s, 8H, Ar*H*), 4.80 (d, 2H, ^2J = 12.2 Hz, ArC*H*$_2$Ar), 4.31-4.12 (m, 14H, ArC*H*$_2$Ar, OC*H*$_2$), 3.61-3.35 (m, 4H, OC*H*$_2$), 3.15-3.12 (d, 2H, ^2J = 12.2 Hz, ArC*H*$_2$Ar), 2.39 (s, 12H, ArC*H*$_3$).

^{1}H NMR (400 MHz, CD$_2$Cl$_2$, integration is given for a dimeric species), δ: 10.20 (br s, 8H, N*H*), 8.24 (s, 2H, N*H*), 8.19 (s, 2H, N*H*), 8.13 (s, 2H, N*H*), 8.07 (s, 2H, N*H*), 8.02 (d, 8H, ^3J = 8.2 Hz, Ar*H*$_{\text{Tos}}$), 8.01 (d, 8H, ^3J = 8.2 Hz, Ar*H*$_{\text{Tos}}$), 7.97 (d, 2H, ^4J = 2.4 Hz, Ar*H*), 7.95 (d, 2H, ^4J = 2.4 Hz, Ar*H*), 7.85 (d, 2H, ^4J = 2.4 Hz, Ar*H*), 7.83 (d, 2H, ^4J = 2.4 Hz, Ar*H*), 7.46 (d, 16H, ^3J = 8.2 Hz, Ar*H*$_{\text{Tos}}$), 6.82 (d, 2H, ^4J = 2.4 Hz, Ar*H*), 6.80 (d, 2H, ^4J = 2.4 Hz, Ar*H*), 6.75 (d, 2H, ^4J = 2.4 Hz, Ar*H*), 6.74 (d, 2H, ^4J = 2.4 Hz, Ar*H*), 4.92 (d, 4H, ^2J = 11.6 Hz, ArC*H*$_2$Ar), 4.36 (d, 4H, ^2J = 11.6 Hz, ArC*H*$_2$Ar), 4.23-3.98 (m, 24H, OC*H*$_2$), 3.67-3.63 (m, 8H, OC*H*$_2$), 3.17 (d, 4H, ^2J = 11.6 Hz, ArC*H*$_2$Ar), 3.12 (d, 4H, ^2J = 11.6 Hz, ArC*H*$_2$Ar), 2.48 (s,12, ArC*H*$_3$), 2.47 (s, 12H, ArC*H*$_3$).

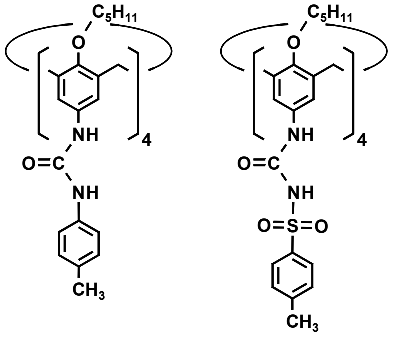
MS(ESI) *m/z* (%) 1435.5 (100) [M$^+$Na].

Heterodimerization

In a typical experiment tetraurea calix[4]arenes **12** (4.32 μmol) and **16** (4.32 μmol) were mixted together, dichlormethane-d$_2$ (0.7 mL) was added and the solution formed (sometimes with the help of ultrasonic bath) was transferred in a NMR tube and ^{1}H NMR spectra were recorded. All other heterodimeres were prepared analogously. ^{1}H NMR spectra of the heterodimers are given bellow.

Heterodimer 12•16

^{1}H NMR (400 MHz, CD_2Cl_2), δ:



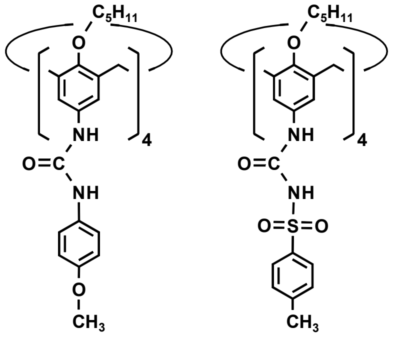
N*H*: 10.81 (s, 4H), 8.04 (s, 4H), 7.96 (s, 4H), 6.91 (br s, 4H); **Ar*H***$_{\mathbf{Tos}}$: 8.14 (d, 8H, $^3J = 8.2$ Hz), 7.48 (d, 8H, $^3J = 8.2$ Hz); **Ar*H***$_{\mathbf{Tol}}$: 7.60 (d, 8H, $^3J = 7.7$ Hz), 6.87 (d, 8H, $^3J = 7.7$ Hz); **Ar*H***$_{\mathbf{cal}}$: 7.88 (s, 4H), 7.01 (s, 4H), 6.96 (s, 4H), 4.86 (s, 4H); **ArC*H*$_2$Ar**: 4.58 (d, 4H, $^2J = 11.7$ Hz), next 4H are overlapped with multiplet at 4.00-3.89, 3.33 (d, 4H, $^2J = 11.7$ Hz), 2.59 (d, 4H, $^2J = 11.7$ Hz); **OC*H*$_2$**: 4.00-3.89 (m, 12H (from them 4H belong to **ArC*H*$_2$Ar**)), 3.60-3.45 (m, 8H); **ArC*H*$_3$** $_{\mathbf{Tos}}$: 2.50 (s, 12H); **ArC*H*$_3$** $_{\mathbf{Tol}}$: 2.08 (s, 12H); **C*H*$_2$**: 1.83-1.72 (m, 8H), 1.60-1.19 (m, 40H); **CH$_2$C*H*$_3$**: 0.99 (t, 12H, $^3J = 7.2$ Hz), 0.90 (t, 12H, $^3J = 7.2$ Hz).

^{1}H NMR (400 MHz, $CDCl_3$), δ:

N*H*: 10.52 (s, 4H), 8.04 (s, 4H), 8.02 (s, 4H), 7.62 (s, 4H); **Ar*H***$_{\mathbf{Tos}}$: 8.14 (d, 8H, $^3J = 8.2$ Hz), 7.48 (d, 8H, $^3J = 8.2$ Hz); **Ar*H***$_{\mathbf{Tol}}$: 7.57 (d, 8H, $^3J = 8.3$ Hz), 6.79 (d, 8H, $^3J = 8.3$ Hz); **Ar*H***$_{\mathbf{cal}}$: 7.86 (d, 4H, $^4J = 2.3$ Hz), 7.04 (d, 4H, $^4J = 2.3$ Hz), 6.87 (d, 4H, $^4J = 2.3$ Hz), 4.89 (d, 4H, $^4J = 2.3$ Hz); **ArC*H*$_2$Ar**: 4.54 (d, 4H, $^2J = 11.7$ Hz), 3.91 (d, 4H, $^2J = 11.7$ Hz), 3.37 (d, 4H, $^2J = 11.7$ Hz), 2.52 (d, 4H, $^2J = 11.7$ Hz); **OC*H*$_2$**: 3.95-3.84 (m, 8H), 3.53-3.40 (m, 8H); **ArC*H*$_3$** $_{\mathbf{Tos}}$: 2.48 (s, 12H); **ArC*H*$_3$** $_{\mathbf{Tol}}$: 2.05 (s, 12H); **C*H*$_2$**: 1.72-1.68 (m, 8H), 1.45-1.12 (m, 40H), **CH$_2$C*H*$_3$:** 0.97 (t, 12H, $^3J = 7.0$ Hz), 0.88 (t, 12H, $^3J = 7.0$ Hz).

Heterodimer (*p*-phenylmethoxy tetraurea)•16

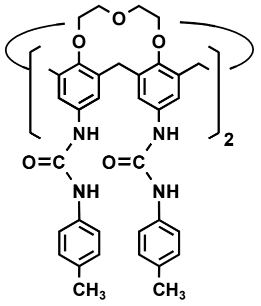
^{1}H NMR (400 MHz, $CDCl_3$), δ:

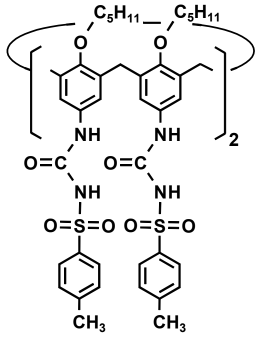


N*H*: 10.51 (s, 4H), 8.13 (s, 4H), 7.97 (s, 4H), 7.62 (s, 4H); **Ar*H***$_{\mathbf{Tos}}$: 8.14 (d, 8H, $^3J = 7.8$ Hz), 7.41 (d, 8H, $^3J = 7.8$ Hz); **Ar*H***$_{\mathbf{Tol}}$: 7.60 (d, 8H, $^3J = 7.8$ Hz), 6.55 (d, 8H, $^3J = 7.8$ Hz); **Ar*H***$_{\mathbf{cal}}$: 7.85 (s, 4H), 7.04 (s, 4H), 6.90 (s, 4H), 4.99 (s, 4H); **ArCH$_2$Ar**: 4.53 (d, 4H, $^2J = 11.2$ Hz), 3.94 (d, 4H, $^2J = 11.2$ Hz), 3.36 (d, 4H, $^2J = 11.2$ Hz), 2.56 (d, 4H, $^2J = 11.2$ Hz); **OC*H*$_2$**: 3.89-3.83 (m, 8H), 3.51-3.44 (m, 8H); **ArOC*H*$_3$** $_{\mathbf{Tol}}$: 3.55 (s, 12H); **ArC*H*$_3$**: 2.46 (s, 12H); **C*H*$_2$**: 2.08 (br s, 8H), 1.74 (br s, 8H), 1.40-1.21 (m, 72H), **CH$_2$C*H*$_3$**: 0.89 (br s, 24H).

Heterodimer 36•37

^{1}H NMR (400 MHz, CD$_2$Cl$_2$), δ:

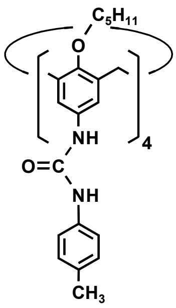


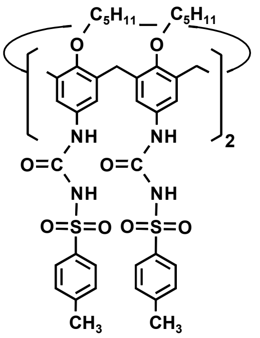


N*H*: 10.93 (s, 1H), 10.78 (s, 1H), 10.73 (s, 1H), 10.60 (s, 1H), next 4H are overlapped with doublet at 8.16, 8.11 (s, 2H), 8.07 (s, 2H), 7.23 (s, 1H), 7.22 (s, 1H), 7.07 (s, 1H), 7.07-7.01 (br s, 1H); **Ar*H***$_{\mathbf{Tos}}$: 8.16 (d, 12H (from them 4H belong to **N*H***), ^3J = 8.3 Hz,), 7.50 (d, 4H, ^3J = 8.3 Hz), 7.49 (d, 4H, ^3J = 8.3 Hz); **Ar*H***$_{\mathbf{Tol}}$: 7.67-7.61 (m, 8H), 6.93 (d, 4H, ^3J = 8.3 Hz), 6.90 (d, 4H, ^3J = 8.3 Hz); **Ar*H***$_{\mathbf{cal}}$: 8.02 (d, 1H, ^4J = 2.4 Hz), 7.99 (d, 1H, ^4J = 2.4 Hz), 7.95 (d, 1H, ^4J = 2.4 Hz), 7.92 (d, 1H, ^4J = 2.4 Hz), 7.18 (s, 1H), 7.17 (s, 1H), 7.12 (d, 1H, ^4J = 2.4 Hz), 7.11 (d, 1H, ^4J = 2.4 Hz), 7.05 (d, 1H, ^4J = 2.4 Hz), 7.02 (d, 1H, ^4J = 2.4 Hz), 7.01 (s, 1H), 6.99 (s, 1H), 4.95 (s, 2H), 4.88 (s, 2H); **ArC*H*$_2$Ar**: 5.09 (d, 1H, ^2J = 11.7 Hz), 5.07 (d, 1H, ^2J = 11.7 Hz), 4.55 (d, 2H, ^2J = 11.7 Hz), next 4H are overlapped with multiplet at 4.49-3.78, 3.37 (d, 2H, ^2J = 11.7 Hz), 3.43 (d, 2H, ^2J = 11.7 Hz), 2.76-2.52 (m, 4H); **OC*H*$_2$**: 4.49-3.78 (m, 32H (from them 4H belong to **ArC*H*$_2$Ar**)), 3.49-3.41 (m, 4H); **ArC*H*$_3$** $_{\mathbf{Tos}}$: 2.52 (s, 12H); **ArC*H*$_3$** $_{\mathbf{Tol}}$: 2.12 (s, 12H).

Heterodimer 12•37

^{1}H NMR (400 MHz, CD$_2$Cl$_2$), δ:





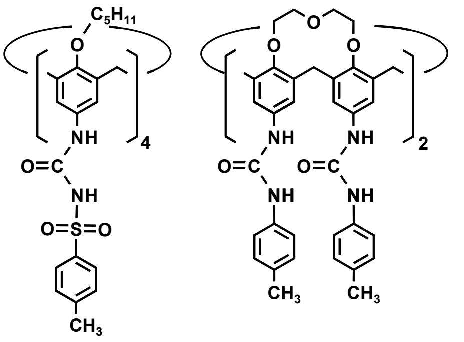
N*H* 10.91 (br s, 2H), 10.68 (br s, 2H), 8.09 (s, 4H), 7.99 (s, 2H), 7.96 (s, 2H), 7.09 (br s, 2H), 6.95-6.90 (br s, 2H); **Ar*H***$_{\mathbf{Tos}}$: 8.14 (d, 8H, ^3J = 8.3 Hz), 7.48 (d, 8H, ^3J = 8.3 Hz); **Ar*H***$_{\mathbf{Tol}}$: 7.64 (d, 4H, ^3J = 8.3 Hz), 7.61 (d, 4H, ^3J = 8.3 Hz), 6.93 (d, 4H, ^3J = 8.3 Hz), 6.90 (d, 4H, ^3J = 8.3 Hz); **Ar*H***$_{\mathbf{cal}}$: 7.91 (d, 2H, ^4J = 1.9 Hz), 7.88 (d, 2H, ^4J = 1.9 Hz), 7.16 (s, 2H), 7.02 (d, 2H ^4J = 1.9 Hz), 6.99 (s, 4H), 4.96 (s, 2H), 4.93 (d, 2H, ^4J = 1.9 Hz); **ArC*H*$_2$Ar**: 4.60 (d, 2H, ^2J = 11.7 Hz), 4.59 (d, 2H, ^2J = 11.7 Hz), 4.51 (d, 2H, ^2J = 11.7 Hz), next 2H are overlapped with multiplet at 4.12-3.82, 3.35 (d, 2H, ^2J = 11.7 Hz), 3.34 (d, 2H, ^2J = 11.7 Hz), 2.64 (d, 2H, ^2J = 11.7 Hz), 2.57 (d, 2H, ^2J = 11.7 Hz); **OC*H*$_2$**: 4.12-3.82 (m, 22H (from them 2H belong to **ArC*H*$_2$Ar**)), 3.48-3.40 (m, 4H); **ArC*H*$_3$** $_{\mathbf{Tos}}$: 2.51 (s, 12H); **ArC*H*$_3$** $_{\mathbf{Tol}}$: 2.12 (s, 12H); **C*H*$_2$**: 1.51-1.40 (m, 24H); **CH$_2$C*H*$_3$**: 1.02-0.98 (m, 12H).

^{1}H NMR (400 MHz, CDCl$_3$), δ:

N*H*: 10.54 (s, 2H), 10.29 (s, 2H), 8.08 (s, 2H), 8.06 (s, 2H), 8.05 (s, 2H), 8.00 (s, 2H), 7.84 (s, 2H), 7.76 (s, 2H); **Ar*H*$_{Tos}$**: 8.13 (d, 8H, $^3J = 8.3$ Hz), 7.41 (d, 8H, $^3J = 8.3$ Hz); **Ar*H*$_{Tol}$**: 7.59 (d, 4H, $^3J = 8.3$ Hz), 7.56 (d, 4H, $^3J = 8.3$ Hz), 6.83 (d, 4H, $^3J = 8.3$ Hz), 6.81 (d, 4H, $^3J = 8.3$ Hz); **Ar*H*$_{cal}$**: 7.86 (s, 4H), 7.04 (s, 4H), 7.00 (s, 2H), 6.90 (s, 2H), 5.04 (s, 2H), 4.92 (s, 2H); **ArC*H*$_2$Ar**: 4.55 (d, 2H, $^2J = 11.7$ Hz), 4.54 (d, 2H, $^2J = 11.7$ Hz), 4.42 (d, 2H, $^2J = 11.7$ Hz), next 2H are overlapped with multiplet at 4.12-3.78, 3.37 (d, 2H, $^2J = 11.7$ Hz), 3.36 (d, 2H, $^2J = 11.7$ Hz), 2.57 (d, 2H, $^2J = 11.7$ Hz), 2.52 (d, 2H, $^2J = 11.7$ Hz); **OC*H*$_2$**: 4.12-3.78 (m, 22H (from them 2H belong to **ArC*H*$_2$Ar**)), 3.48-3.42 (m, 4H); **ArC*H*$_3$ $_{Tos}$**: 2.46 (s, 12H); **ArC*H*$_3$ $_{Tol}$**: 2.06 (s, 12H); **C*H*$_2$**: 1.50-1.36 (m, 24H); **CH$_2$C*H*$_3$**: 1.01-0.96 (m, 12H).

Heterodimer 16•36

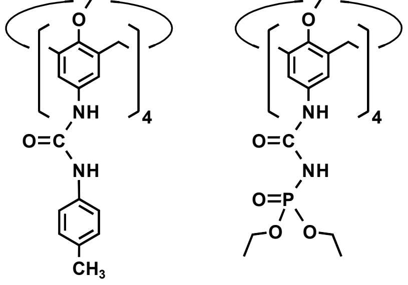
^{1}H NMR (400 MHz, CD$_2$Cl$_2$), δ:



N*H*: 10.86 (s, 2H), 10.73 (s, 2H), 8.12 (s, 4H), 8.04 (s, 2H), 8.03 (s, 2H), 7.10-6.95 (br s, 2H), 6.81 (br s, 2H); **Ar*H*$_{Tos}$**: 8.14 (d, 8H, $^3J = 7.7$ Hz), 7.48 (d, 8H, $^3J = 7.7$ Hz); **Ar*H*$_{Tol}$**: 7.61 (br s, 8H), 7.87 (d, 4H, $^3J = 8.0$ Hz), 6.85 (d, 4H, $^3J = 8.0$ Hz); **Ar*H*$_{cal}$**: 7.97 (d, 2H, $^4J = 1.9$ Hz), 7.92 (d, 2H, $^4J = 1.9$ Hz), 7.10 (d, 2H, $^4J = 1.9$ Hz), 7.03 (d, 2H, $^4J = 1.9$ Hz), 6.96 (s, 4H), 4.88 (s, 2H), 4.79 (s, 2H); **ArC*H*$_2$Ar**: 5.05 (d, 2H, $^2J = 11.6$ Hz), 4.53 (d, 2H, $^2J = 11.6$ Hz), 3.98 (d, 2H, $^2J = 11.1$ Hz), 3.95 (d, 2H, $^2J = 11.1$ Hz), 3.34 (d, 2H, $^2J = 11.6$ Hz), 3.31 (d, 2H, $^2J = 11.6$ Hz), 2.59 (d, 2H, $^2J = 11.1$ Hz), 2.52 (d, 2H, $^2J = 11.1$ Hz); **OC*H*$_2$**: 4.40-4.17 (m, 12H), 3.82-3.75 (m, 4H), 3.56-3.46 (m, 8H); **ArC*H*$_3$ $_{Tos}$**: 2.50 (s, 12H); **ArC*H*$_3$ $_{Tol}$**: 2.09 (s, 6H), 2.07 (s, 6H); **C*H*$_2$**: 1.79-1.74 (m, 8H), 1.34-1.23 (m, 16H); **CH$_2$C*H*$_3$**: 1.89 (t, 6H, $^3J = 9.7$ Hz), 0.90 (t, 6H, $^3J = 9.7$ Hz).

Heterodimer 12•40

^{1}H NMR (400 MHz, CD$_2$Cl$_2$), δ:



N*H*: 9.06 (s, 4H), 8.60 (d, 4H, J = 12.3 Hz), 8.22 (s, 4H), next 4H are overlapped with multiplet at 7.86-7.66; **Ar*H*$_{Tol}$**: 7.86-7.66 (m, 16H, (from them 4H belong to **NH** and 4H to **Ar*H***), 7.03 (d, 4H, $^3J = 8.3$ Hz); **Ar*H*$_{cal}$**: 4H are overlapped with multiplet at 7.86-7.66, 7.00 (d, 4H, $^{4}J = 2.0$ Hz), 6.64 (d, 4H, $^{4}J = 2.0$ Hz), 5.00 (d, 4H, $^{4}J = 2.0$ Hz); **ArC*H*₂Ar**: 4.47 (d, 4H, $^{2}J = 11.7$ Hz), 4.00 (d, 4H, $^{2}J = 11.7$ Hz), 3.09 (d, 4H, $^{2}J = 11.7$ Hz), 2.62 (d, 4H, $^{2}J = 11.7$ Hz); **OCH_2CH_3**: 4.44-4.37 (m, 16H); **OCH_2CH_2**: 3.85-3.79 (m, 8H), 3.63-3.48 (m, 8H); **$ArCH_{3\,Tol}$**: 2.13 (s, 12H); **CH_2**: 2.08-2.01 (m, 8H), 1.87-1.77 (m, 8H), 1.44-1.24 (m, 32H); **OCH_2CH_3**: 1.52 (t, 6H, $^{3}J = 7.1$ Hz), **CH_2CH_3**: 0.97 (t, 6H, $^{3}J = 7.4$ Hz), 0.93 (t, 6H, $^{3}J = 7.4$ Hz).

3. MULTIPLE TETRAUREA CALIX[4]ARENES (CONNECTION *VIA* THE NARROW RIM)

3. 1. Introduction

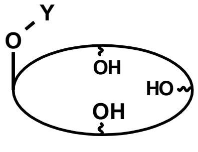
As discussed above two or more calixarenes can be covalently connected *via* their narrow or wide rims. Such a connection of tetraurea derivatives *via* a single spacer leads to the formation of self-assembled linear oligo(poly)mers in the first case[30] and the unimolecular capsule in the second case.[29] It should be possible to use the dimerization of tetraurea calix[4]arenes, to build up not only linear polymers *via* self-assembly, but also macrocyclic and definitely branched molecules including dendritic structures. This would require oligomers in which tetraurea calix[4]arenes or similar self-complementary units are covalently linked.

As the first step in this direction tetraurea calix[4]arenes bearing one (or more) functional groups at the narrow (wide) rim, should be prepared. Further covalent connection of these tetraurea units will give appropriate building blocks. Their self-assembly finally should afford the desired objects. Characterisation of the mechanic stability of the dimer using AFM methods has also been planed (in collaboration with other groups).

In the present chapter we are dealing with the synthesis of tetraurea calix[4]arenes bearing one or two functional groups at the narrow rim. This synthesis requires the selective *O*-alkylation of the calixarene or it's derivatives and therefore first we have to describe several main aspects of *O*-alkylation.

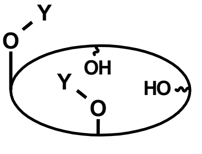
3. 2. *O*-Alkylation of calix[4]arenes

Partial or exhaustive substitution could be carried out depending on the quantity and reactivity of reagents and the reaction conditions. When two or more ether residues have to be introduced the formation of regio- and/or stereoisomers must be also considered.

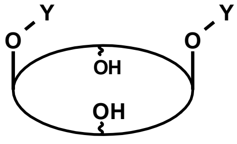


mono

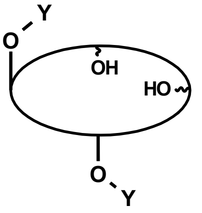
Monoethers of calix[4]arenes are usually prepared using 0.6 mol K_2CO_3 in CH_3CN or 1.2 mol CsF in DMF as a base, high dilution and an excess of the alkylating agent.[41] In the more rare cases other combinations of bases (alkali metal hydrides,[42] $Ba(OH)_2$,[42,43] $NaOCH_3$,[44] and bis-(butyltin)oxide) have been used. Unfortunately in most cases the monoethers are not the only products of these reactions and must be separated from other partially substituted byproducts. As alternative way for synthesis of monoethers the suitable protection of appropriate OH groups (with the ethers[45], silylethers[46] or esters[6a,47]) followed by alkylation and subsequent deprotection could be offered.



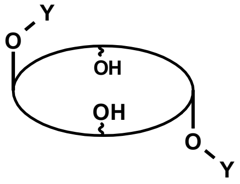
1,2 ***syn***



1,3 ***syn***



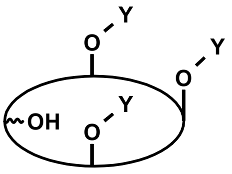
1,2 ***anti***



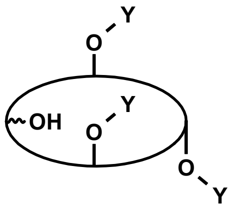
1,3 ***anti***

Functionalization of two OH groups may lead to the formation of two regioisomers (1,2- or 1,3-substituted calixarene). The introduced residues can be found in *syn* or *anti* orientation to each other. In contrast to the monoethers *syn*-1,3-derivatives are usually formed selectively. They are easily synthesized in refluxing acetone or acetonitrile using 2.2 mol of K_2CO_3 or Na_2CO_3 as a base in one step with the same[48] or in two steps with different[49] residues. The easy synthesis of 1,3-difunctionalisated calixarenes is explained with the preferable formation of the distal anion of the monoether which is stabilized by two intramolecular hydrogen bonds and by steric reasons. Almost all known *anti*-1,3-isomers were obtained by more sophisticated ways.

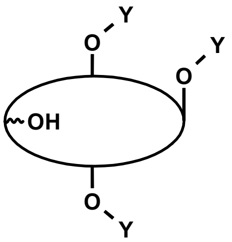
For synthesis of 1,2-diethers an excess of the strong base (NaH in DMF/THF) is usually required. It provides the formation of di-anion of the intermediate monoether, in which two opposite hydroxyl groups are deprotonated. The extent of alkylation is usually controlled by the amount of the alkylating agent.



syn-syn



anti-syn



syn-anti

For the tri-*O*-substituted derivatives (with the same residue R) three stereoisomers are possible: *syn-syn*, *anti-syn* and *syn-anti*.

Direct alkylation of the parent calix[4]arene leading to the *syn-syn*-triethers can be made using CaH_2[50] or excess of $BaO/Ba(OH)_2$[51] in DMF. *Anti-syn* and *syn-anti*-isomers have been prepared starting with the monobenzyl ether[52], which could be cleaved after the exhaustive alkylation. The formation of a certain stereoisomer strongly depends on the reaction conditions.

Mixed tri-ethers also could be obtained in several steps starting from the mono- or di-substituted precursors.

Four stereoisomers (*cone*, *partial cone*, *1,2-* and *1,3-alternates*) (Figure 2) may by formed during the tetra-*O*-alkylation of calix[4]arene. The main factors influencing the stereochemical result of the reaction are the alkylation conditions: solvent, base, temperature. Usually the formation of the *cone* isomer is favoured in the presence of Na^+ cations. Therefore Na_2CO_3 and NaH are mostly used for the alkylation. The choice of the base depends on the reactivity of alkylating agents. Na_2CO_3 in acetone or acetonitrile is often applied in combination with rather reactive bromo-or chloro-acetates, -acetamides or –ketones, while NaH in DMF or THF/DMF is the standard for alkylbromides, -iodides or tosylates.

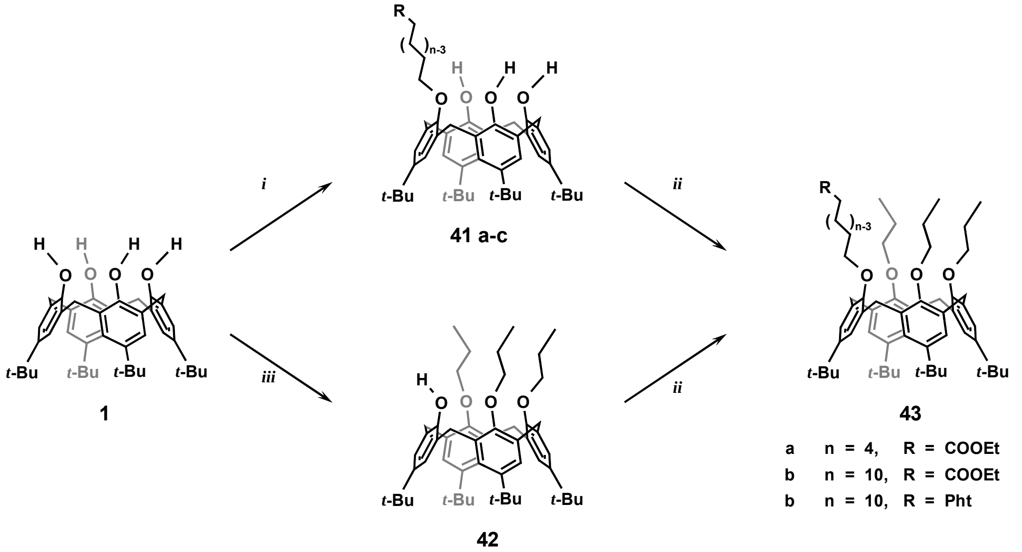
When the *partial cone*[53,54] or *1,3-alternate*[55] conformers are desired larger alkali cations (K^+, Cs^+) should be used. Often mixtures of conformers are formed during the reaction and their separation requires chromatographic techniques. The *1,2-alternate* isomer is the most difficult to obtain[56]. For example tetrapropyl ether in *1,2-alternate* conformation was obtained *via* alkylation of *syn*-1,3-dibenzylether with PrI, cleavage of the benzyl groups in the partial cone isomer and further alkylation of the *anti*-1,3-dipropylether thus obtained with propylbromide (Cs_2CO_3/DMF/70°C).[57]

Tetraethers with different ether groups were also synthesised. Exhaustive alkylation of mono-[58], di-[59] and tri-[13] O-substituted calixarenes under appropriate conditions affords the target tetraethers in desired conformations.

3. 3. Synthesis of Tetraurea Calix[4]arenes Bearing One Functional Group at the Narrow Rim

Calixarenes, bearing one amino or carboxylic and three alkyl (usually propyl) groups at the narrow rim have been prepared as it is shown in the Schemes 6-8.

Two different ways, leading to compound **43**, should be considered here (Scheme 8):



Scheme 8. Synthesis of the calixarenes bearing one functional group at the narrow rim. i) PrBr, BaO/$Ba(OH)_2$, DMF; ii) $Br(CH_2)_nR$, NaH, DMF; iii) $Br(CH_2)_nR$, K_2CO_3, CH_3CN.

I) monoalkylation[41] of the calixarene **1** with an alkyl bromide possessing the target functional group protected in a suitable way (in our case the phthalimide or ester function) affords the compound **41**.

In order to suppress the usual formation of *1,3*-disubstituted calixarenes as by-products modifications of the general procedure of monoalkylation (0.6 mol of K_2CO_3, 1 mol of RBr, 1 mol of calixarene) were made on this step. The calixarene **1** has been taken in slight excess (10-15%) in relation to the alkylating agent and to K_2CO_3. The alkylation was carried out under high dilution (the concentration of calixarene - 10 g/l). It was expected that after the reaction is finished the excess of calixarene **1** could be easily filtered off after treatment of the crude product with acetone or acetonitrile. The parent calixarene is insoluble in these solvents, while almost all products are. Indeed the reaction mixture contains only starting materials and the desired compound **41**. Usually after two weeks the alkyl bromide was not reacted completely. Probably due to the low concentrations of the reagents the full conversion of RBr can not be achieved during reasonable reaction times.

Unfortunately all attempts to achieve a full conversion of alkylating agent and having simultaneously only mono substituted calixarene as the product were unsuccessful. Change of the solvent, temperature or duration of reaction did not lead to a significant difference in results. So, in cases of products, which are oily the separation by column chromatography was necessary. Exhaustive alkylation of **41** with n-PrBr finally leads to tetrasubstituted compounds **43** with yields of about 55-65 % (overall about 36%).

There are several points on which attention should be paid:

a) during the exhaustive alkylation of the calixarene bearing an ester function at the narrow rim a transesterification COOEt → COOPr may occur. In this case in ^{1}H NMR spectrum instead of one resonance for OCH_2 protons two signals appear within 0.05 ppm of each other. The same is true for the signal of $O(CH_2)_nCH_3$ group. Reesterification was easily made by refluxing of the mixture of esters for 3 hours in EtOH in the presence of the acid catalyst;

b) after exhaustive alkylation the excess of sodium hydride should be destroyed by addition of acetic acid, since the direct dilution of DMF solution with water leads to the cleavage of the protecting group (phthalimide or ester function).

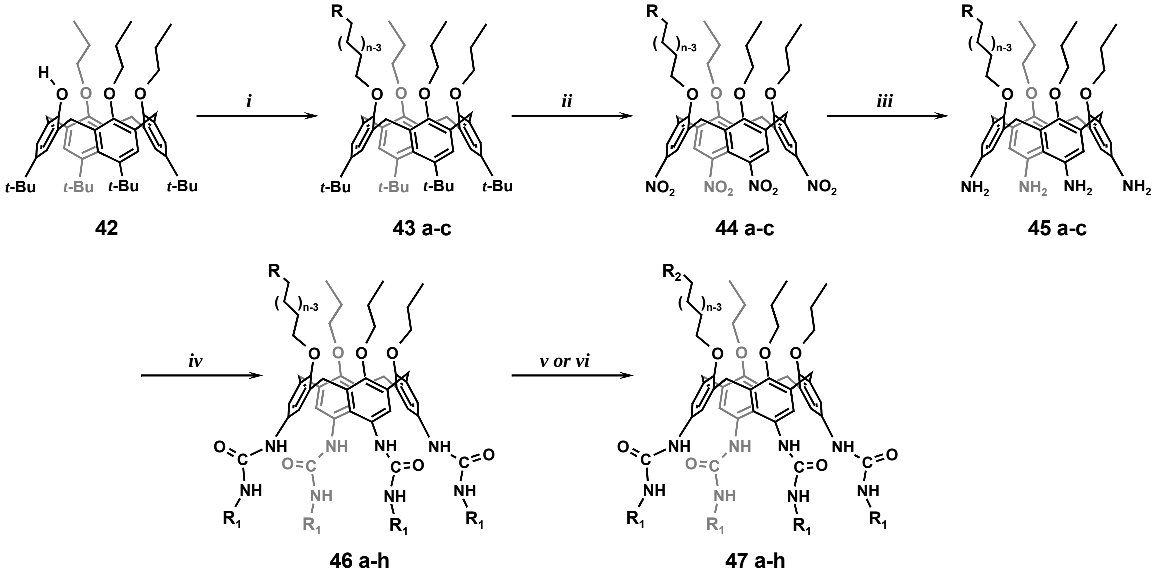
II) tripropylation of the calixarene **1** using $BaO/Ba(OH)_2$ in DMF, followed by alkylation of **42** with desired bromide also results in tetraethers **43**. The product could be crystallized from CH_3CN. In cases of oily compounds the excess of the bromide could be simply washed out (extracted) with the mentioned solvent. Other solvents were tested as alternative to acetonitrile, but a better one was not found. So, tetraethers **43** were obtained with rather good yields (about 65% overall) and did not require a purification by column chromatography.

After analysis of the results described above the second route has been chosen for further synthesis due to better yields and easier separation of the products.

The complete route to the target compounds is shown in the Scheme 9. The calix[4]arenes possessing phthalimide or ester functions were obtained *via* consecutive tripropylation and exhaustive alkylation with corresponding alkylbromide. The general procedures for *ipso*-nitration (using CH_3COOH and fuming HNO_3), hydrogenation (in the presence of Raney nickel) and reaction with isocyanates are applicable to all cases described here. However, although reactions like the hydrogenation of nitro groups usually should proceed quantitatively in some cases we met difficulties exactly in this step. The reduction did not took place at all or proceeded very slowly. After 24 hours the main spot on TLC still corresponded to the starting nitro compound. We have tried to change the solvent used for the reduction, to increase the temperature, to use more catalyst or to add an extra amount of catalyst during hydrogenation. Unfortunately all these manipulations did not help to reduce the starting material. According to the observations poisoning of the catalyst was conjectured and we assumed, that the starting material contains a poison. Although ^{1}H NMR spectra did not show any impurities, on TLC we observed the small amount of pale-brown spot, which could be separated chromatographically or mainly disappear after recrystallization from methanol. But we were not able to crystallize all nitro compounds from this solvent. Some of them we got as a powder only after treatment with hexane. And quite often exactly in these cases we had the problems with the reduction. Thus the nitro derivatives, containing the pale-brown spot were filtered through the short silicagel column and reduction was attempted again. Now hydrogenation proceeded without any complications although in some cases the temperature had to be increased. Alternatively, solution of the nitro compound must be stirred with Raney nickel during 1 hour and then the poisoned catalyst has to be changed completely.

At the last step deprotection of the corresponding functional group (carboxylic or amino) should be made. Hydrolysis of ester function in the presence of NaOH proceeds clean and does not affect tolyl urea groups at the wide rim of calixarene. Compounds **47a,c,e-h** were made in this way. However these conditions are not suitable for tosyl ureas, which are obviously hydrolysed. Thus, a milder base must be used to obtain the desired tetratosyl calix[4]arenes with the acid function at the narrow rim. Therefore in these cases NaOH was replaced by LiOH and the compounds **47b,d** were obtained with rather good yields (60-80%).

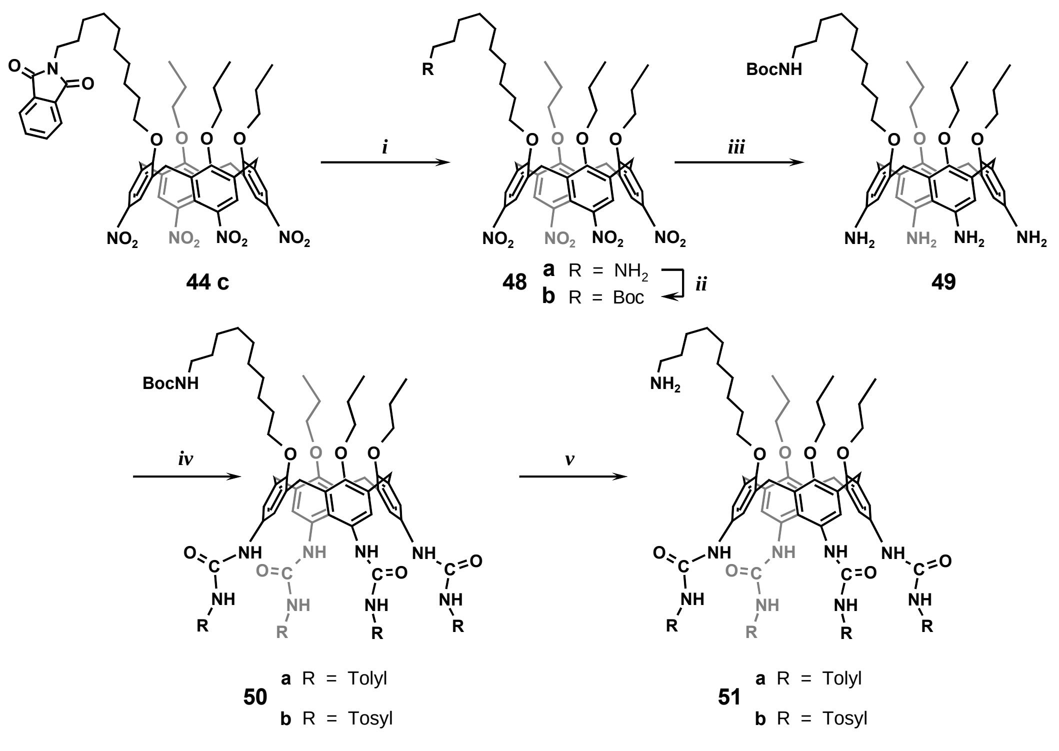
Unfortunately the cleavage of the phthalimide function appears to be more difficult. All attempts to accomplish deprotection using hydrazine led to partial cleavage of urea functions. Neither tolyl, nor tosyl ureas survived during the reaction. Therefore another amino protecting group had to be chosen.



	n	R	R_1	R_2	Yield
43a	4	COOEt	—	—	98%
43b	10	COOEt	—	—	80%
43c	10	Pht	—	—	50-90%
44a	4	COOEt	—	—	85%
44b	10	COOEt	—	—	65%
44c	10	Pht	—	—	65-75%
45a	4	COOEt	—	—	65%
45b	10	COOEt	—	—	60%
45c	10	Pht	—	—	85%
46a	4	COOEt	Tol	—	95%
46b	4	COOEt	Tos	—	80%
46c	10	COOEt	Tol	—	95%
46d	10	COOEt	Tos	—	80%
46e	10	COOEt	$PhOC_{10}H_{21}$	—	80%
46f	10	COOEt	C_5H_{11}	—	65%
46g	10	COOEt	$C_{12}H_{25}$	—	85%
46h	10	Pht	Tol	—	85%
47a	4	—	Tol	COOH	65-90%
47b	4	—	Tos	COOH	60%
47c	10	—	Tol	COOH	90%
47d	10	—	Tos	COOH	80%
47e	10	—	$PhOC_{10}H_{21}$	COOH	70%
47f	10	—	C_5H_{11}	COOH	70%
47g	10	—	$C_{12}H_{25}$	COOH	85%
47h	10	—	Tol	NH_2	—

Scheme 9. Synthesis of tetraurea calixarenes bearing one functional group at the narrow rim. i) $Br(CH_2)_nR$, NaH, DMF; ii) CH_3COOH, HNO_3, CH_2Cl_2; iii) Raney-nickel, THF or toluene; iv) R_1NCO, CH_2Cl_2; v) MeOH(or LiOH)/H_2O/NaOH, THF; vi) N_2H_4, EtOH;

The *tert*-butoxy carbonyl group (Boc) was selected from the set of protecting groups. It is inert towards catalytic hydrogenation, could be cleaved under acidic conditions at room temperature and is comparatively cheap. However, since the Boc-group does not survive the conditions used for *ipso*-nitration it must be introduced after this step. Thus, we came back to the compound **44c** and phthalimide deprotection followed by reaction with Boc-anhydride was carried out. After this change of the protecting group reduction of nitro groups and further reaction of resulting tetraamine **49** with tolyl and tosyl isocyanates were accomplished with good yields (Scheme 10).



Scheme 10. Synthesis of the tetraurea calixarenes bearing one amino on the narrow rim. i) N_2H_4, EtOH; ii) Boc_2O, $CHCl_3$; iii) Raney nickel, toluene; iv) RNCO, CH_2Cl_2; iv) CF_3COOH, CH_2Cl_2.

After that, Boc protection was easily removed with CF_3COOH/CH_2Cl_2 from the aliphatic chain of calixarene **50a**, bearing tolyl urea functions at the wide rim. Unfortunately for calixarene **50b** these conditions were not convenient. Tosyl ureas do not survive again. Thus in the future trifluoroacetamide protection has to be also considered.

All of the prepared compounds (with protected functional groups) are able to form homo and heterodimers in the appropriate solvents.

3. 4. Mechanic Stability of the Dimeric Capsule

It was planned to study the mechanical stability of the dimeric capsule with the help of dynamic Atomic Force Microscopy (in collaboration with the group of Prof. Janshoff). The practical approach is the following: from one side the tetraurea calix[4]arenes bearing the sulfur function at the narrow rim should be fixed on the gold surface. From other side a single tetraurea derivative must be attached to the cantilever. Going down with the cantilever the single tetraurea should find a partner to form a dimer. Usually dimerization occurs within seconds. Then the cantilever has to be pulled up (Figure 32) and the force necessary to destroy the dimer (to break the hydrogen bonds) must be measured.

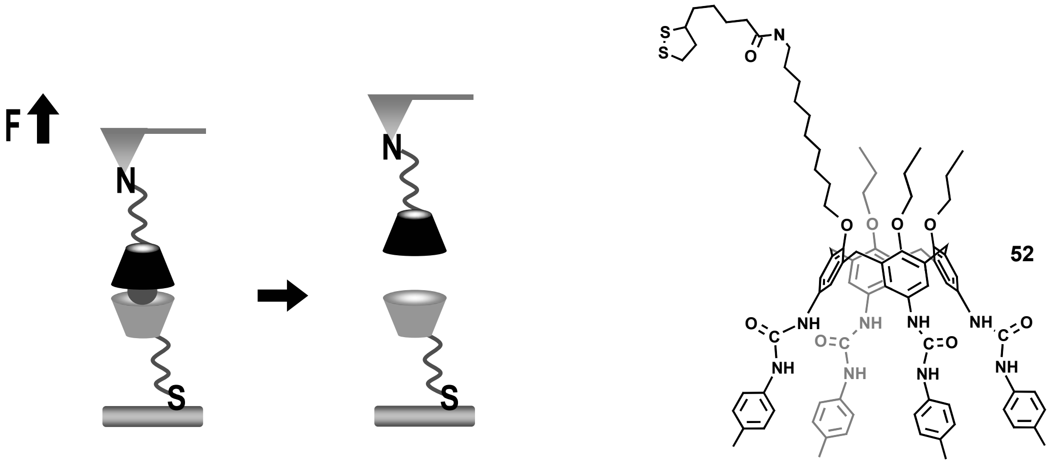


Figure 32. “Stretching” of a single capsule.

Thus tetraurea derivative **52** (Figure 32) was made *via* reaction of calixarene **51a** with lipoic acid in the presence of DCC. The ability of this compound to form dimers was examined and it was given for investigations to Prof. Janshoff. Unfortunately, due to technical reasons these studies had to be postponed. Meanwhile we are able to prepare a better model for these studies, which are planned for the near future.

The given instance has one considerable disadvantage – a disruption of the capsule occurs only one time per stretched molecule. Thus one can not always be sure, that all events observed during the measurements correspond to the dissociation of the dimer. Moreover the possibility of the molecules attached to the gold surface to dimerize have also to be considered. The described model can be improved by combination of several tetraurea derivatives within one molecule. Then working with the single unit we should observe the dissociation of the capsule several times. This gives more confidence that the observed events are the correct ones.

One of the possible models is shown in the Figure 33a. Here the tetraurea derivatives are connected within oligomeric chain (for example *via* oligo-condensation of the corresponding aminoacid). In the ideal case such arrangement would allow the formation of desired intermolecular capsules, requested for the measurements. Unfortunately for this example the intermolecular cross-linking can not be avoided.

The problem could be easily solved by synthesis of oligomers *via* coupling of catenanes (for example of type **21**), which are now easily available. The present model (Figure 33b) ensure the desired intramolecular dimerization of tetraurea derivatives. After the capsule is destroyed the two calixarene units are still kept together by the catenane chains.

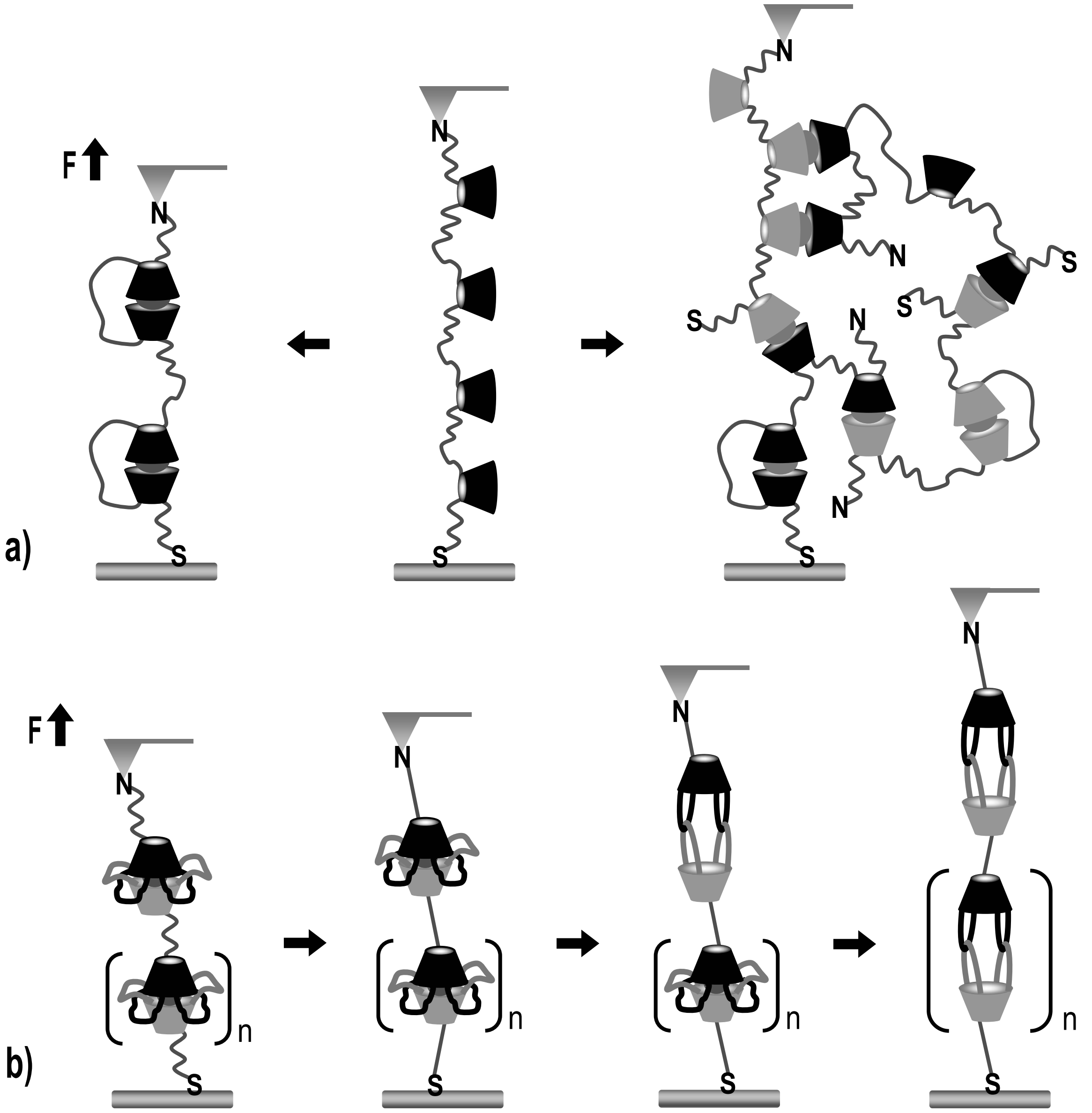


Figure 33. Mechanic stability of the capsules: tension of a molecule containing several tetraurea calix[4]arenes (a); tension of a molecule containing several multi-catenanes (no intermolecular dimerization) (b). The loops are drawn just to indicate the catenane structure. The number of the loops in actual catenanes can be two or four per calixarene.

For the synthesis of appropriate compound unsymmetrical multi-catenanes bearing a -COOH group at the narrow rim of one calixarene and a -NH_2 group at the narrow rim of the second one have to be prepared and subsequently covalently linked to oligomeric amides. The free amino and carboxylic groups of the obtained oligoamide should be reacted with lipoic acid and with *α,ω*-diamine respectively to get the two different functions on both ends of oligomer. This will provide the fixation of the oligomer on the cantilever and on the gold.

3. 5. Bis-Tetraurea Calix[4]arenes

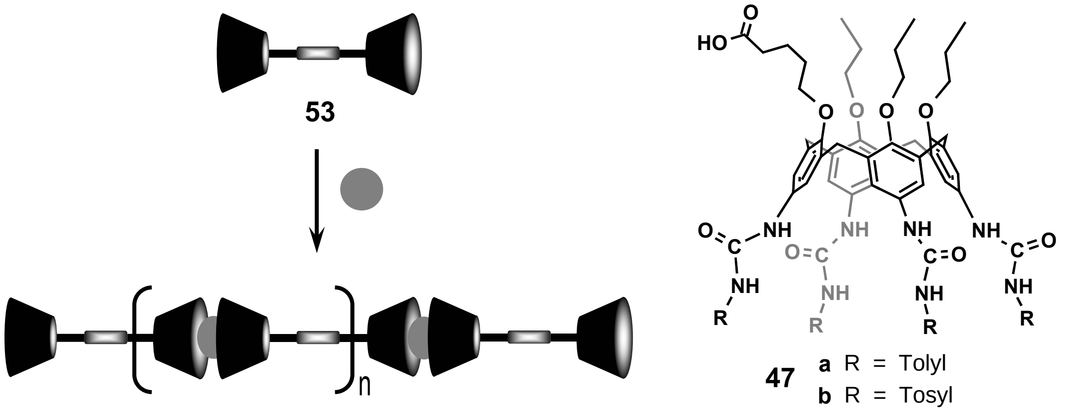


Figure 34. Self-assembly of bis-calixarene.

Linear polymers could be considered as the simplest case of the polymeric structures on the base of calixarenes which we would like to build. The calixarenes of type **53** will be used as building blocks for such self-assembled polymers (Figure 34). Analogous molecules (building blocks) containing two tetraurea calix[4]arenes connected *via* short chains were already described by the group of Rebek. In their case the chain was chosen in the way to prevent the intramolecular dimerization. This possibility can not be excluded in our studies while we planned to use longer spacers, for example PEG, between urea units.

The compounds **47a,b** were send to Lausanne, Switzerland, for further synthesis of bis-calixarenes of type **53,** which will be prepared *via* condensation of tetraurea derivatives **47a,b** with the linear polyethyleneglycol having amino functions at the both ends.

3. 6. Tetrakis – Tetraurea Calix[4]arenes

More then two tetraurea calixarenes, bearing one functional group at the narrow rim, also could be combined in one molecule. The number of units depends on the core to which they will be covalently attached. In other words choosing the central molecule we set the number of urea derivatives which will be covalently connected. In contrast to described bis-calixarenes, which should form linear polymers in appropriate solvents, self-assembly of multiple calixarenes could result in cross-linked polymers. As example molecule possessing four tetraurea units is schematically drawn on Figure 35.

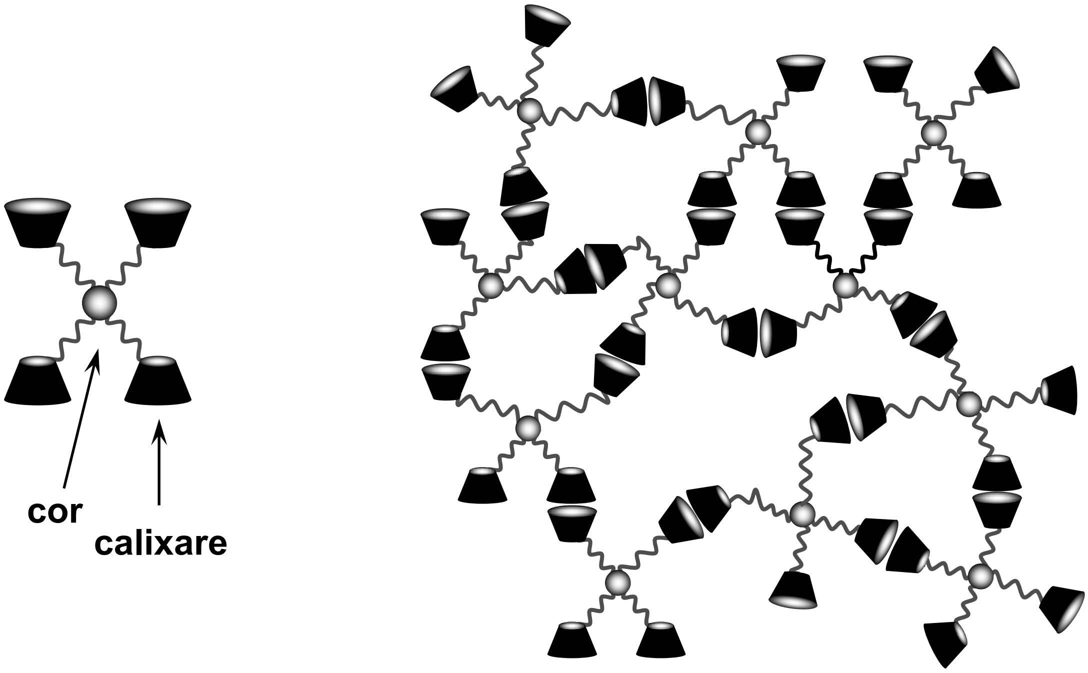
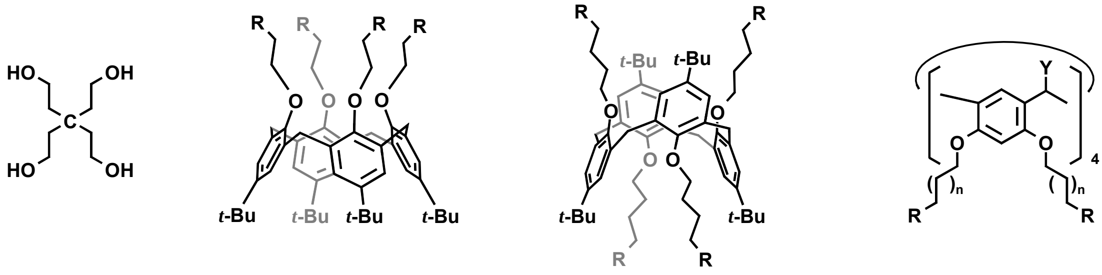


Figure 35. Self-assembly of tetrakis-tetraurea calix[4]arene.

Searching for the central unit several molecules allowing to combine up to eight tetraurea derivatives together (some of them are shown on the Figure 36) were considered. The preference was given to calixarenes.



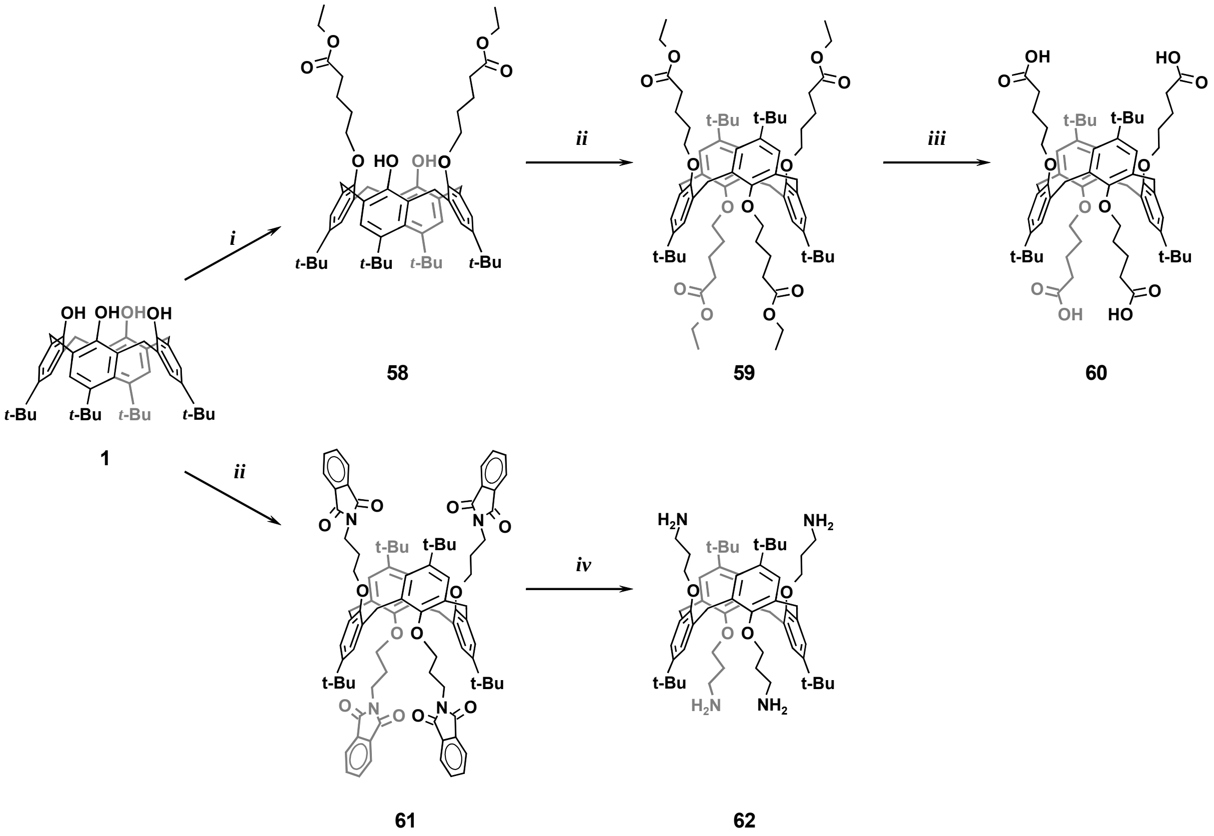
54 55 56 57

R = NH_2 or COOEt
Y = Alkyl

Figure 36. Examples of the possible central units for the multiple calixarenes.

Actually, it is not necessary to have a calixarene as a core, but being engaged with those for a long time and having good knowledge of their chemistry we have chosen namely calixarenes for our purposes. Moreover a calix[4]arene, for instance, can be fixed in four different conformations. This property can also be used to orient urea derivatives in different directions and thus to get so called star-like molecules. For this purpose we have selected a *1,3-alternate* conformer as a core for the multiple calixarenes.

Now, having in mind, that tetraurea calix[4]arenes bearing amino or acid functions at the narrow rim are already available, we can choose the residues to fix the central calixarene in *1,3-alternate* conformation and in the same time to introduce the respective functional groups necessary for further modifications. From synthetic point of view it would be suitable to make connections *via* amide groups. Therefore calixarenes **60** and **62** were prepared as it is shown in the Scheme 11.



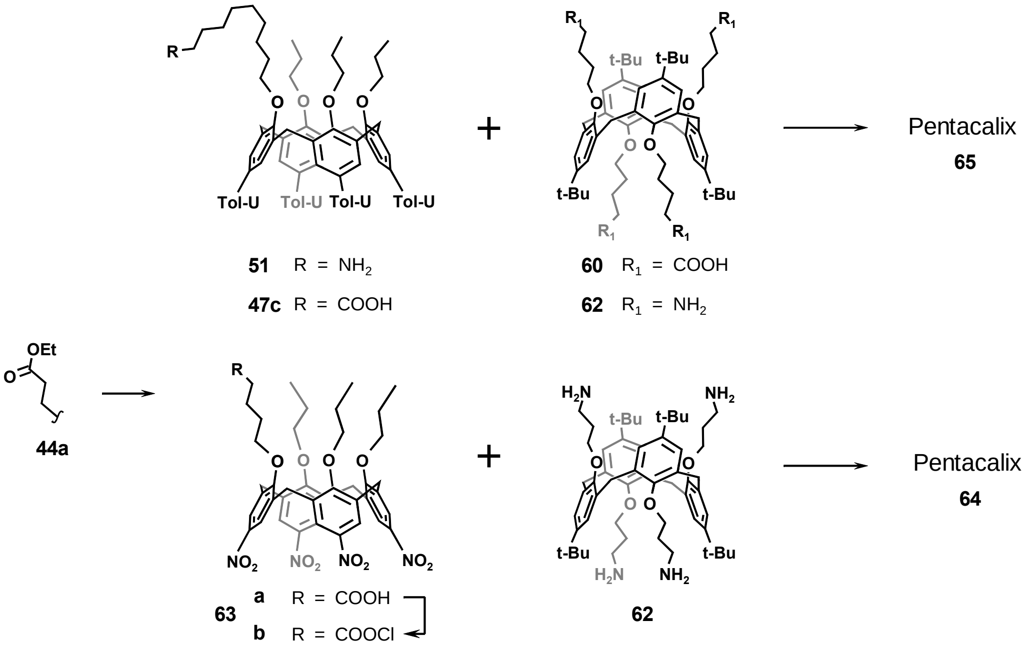
Scheme 11. Synthesis of the calix[4]arene possessing *1,3-alternate* conformation. i) K_2CO_3, CH_3CN, $Br(CH_2)_4COOEt$, ii) Cs_2CO_3, THF or CH_3CN, $Br(CH_2)_nR$; iii) $MeOH/H_2O/NaOH$, THF; iv) N_2H_4, EtOH.

In general a calixarene derivative in the *1,3-alternate* conformation could be prepared in one step (direct tetraalkylation) or in two steps (*via* consecutive 1,3-di and then exhaustive alkylation). The crucial step – the inversion of the two phenolic units – occurs during the exhaustive alkylation of the *1,3*-substituted derivative. Both possibilities were examined for the synthesis of compounds **59** and **61**. The number of steps towards desired products (two for **59** and one for **61**, Scheme 11) was chosen on the basis of the yields obtained. Cleavages of ester and phthalimide functions were carried out without any problems using NaOH and N_2H_4 respectively.

Finally four equivalents of tetraurea calix[4]arene must be attached to the core. Since the teratolyl derivative bearing one amino function at the narrow rim was already prepared, we have used namely this compound in reaction with *1,3-alternate* **60** possessing four carboxylic groups (Scheme 12).

Unfortunately several attempts to accomplish the covalent connection using DCC (in THF or DMF) were unsuccessful – usually the conversion was not complete. Due to the limited solubility of the components it was not possible to use other solvents. The reaction cannot be really followed by TLC, which causes the additional difficulties, because the mixture of products (after several tetraurea units are attached to the core) looks either as one very broad spot evenly distributed along the TLC plate or as one spot at the start. The best result using DCC was achieved in THF under reflux during 2 (or more) days. The formation of product was clearly detected by ^{1}H NMR, but the further purification did not afford the clean penta-calixarene.

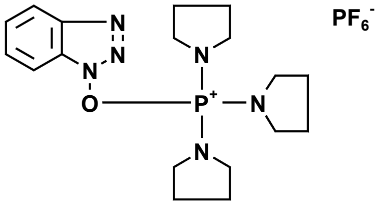
We have also tried to convert tetra carboxylic acid **60** in tetra chloranhydride *via* reaction with oxalyl chloride and react it with compound **51**. These conditions resulted in mixture of polymers insoluble in any solvent. Probably the N*H* protons from the urea residues took part in the reaction.



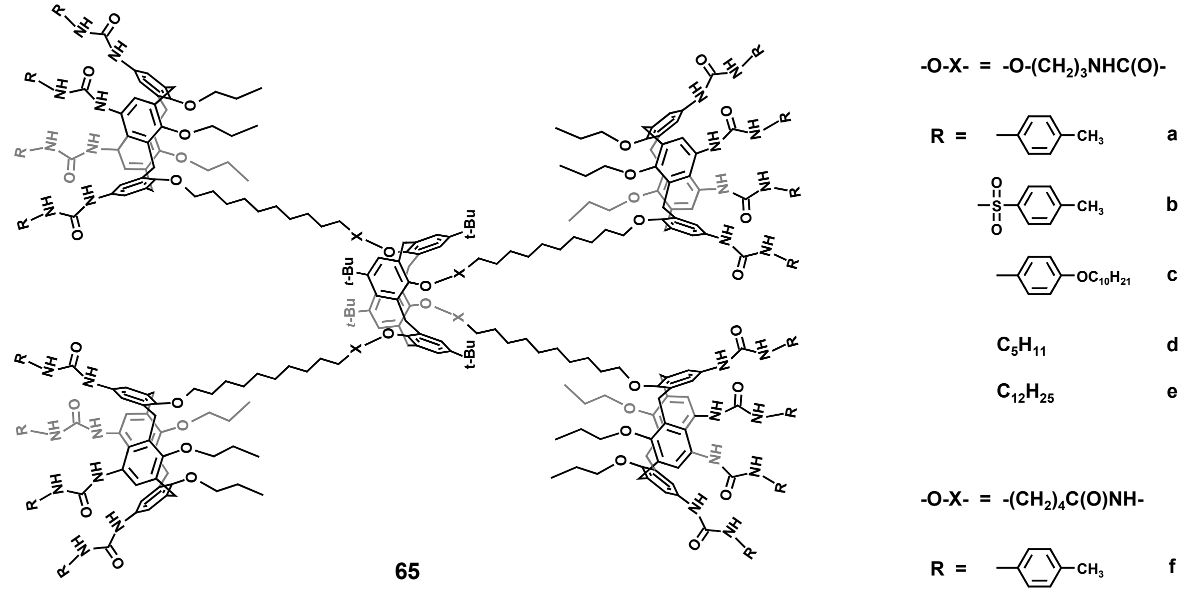
Scheme 12. Synthetic strategies towards penta-calixarenes.

It would be also possible to prepare a chloranhydride from calixarene, bearing carboxylic function at the narrow rim and four nitro groups at the wide rim, and react it with *1,3-alternate* **62**. Subsequent reduction of the product followed by reaction with isocyanate should lead to the target tetrakis-tetraurea derivative. So far we were not sure that the latter attempt will lead to satisfactory results we decided to carry out a kind of model reaction, using instead of calixarene **44b** tetranitro derivative **44a** possessing shorter alkyl chains. This deviation is explained by more easy synthesis (or better to say purification) of compounds with the short chains. Therefore chloranhydride **63b**, obtained in two steps, was reacted with *1,3-alternate* **62** and penta-calixarene **64** was obtained in 80 % yield.

Unfortunately all attempts to reduce the mentioned multiple calixarene (16 NO_2 groups within one molecule) were unsuccessful. The hydrogenation using Pd/C or Raney-Nickel at room temperature under heating was incomplete. The reduction with $N_2H_4 \times H_2O$ lead to the partial cleavage of -NHC(O)- bonds.



Thus we came back to the former idea to connect calixarenes already bearing urea functions. Now instead of DCC the peptide coupling reagent PyBOP (1-Benzotriazolyloxy-tripyrrolidinophosphonium hexafluorophosphate) was used. The two steps of reaction were carried out in situ: the appropriate calixarene bearing carboxylic functions was dissolved in DMF and reacted with PyBOP, then the solution of amino derivative and Et_3N in DMF was added and the reaction was continued for approximately 12~24 hours, what usually afforded the penta-calixarenes **65** in up to 80% yields.



65

Multiple calixarene **65a**, bearing four tetratolyl urea units, was obtained as the first example. Although the integration is correct, the number of some signals observed in the aromatic part of the ^{1}H NMR spectrum in DMSO-d_6, differs from the expected one. Thus we observe:

- 4 singlets for N*H*-urea protons (three pairs of singlets in the ratio 1:2:1 expected) – overall 32 protons;
- one signal for amide N*H* (one expected) – 4 protons;
- two multiplets for Ar*H* of tolyl groups (three pairs of doublets in the ratio 1:2:1 could be expected) – each 32 protons;
- one singlet for Ar*H* protons of the calixarene skeleton found in *1,3-alternate* conformation (one expected) – 8 protons,
- two singlets for Ar*H* protons of the calixarene skeleton found in cone conformation (four signals (two singlets and two doublets) expected) – overall 32 protons.

All the differences in the number of the signals concern only the calixarene bearing the urea functions and possessing C_s-symmetry (for starting calixarene **47c** the similar picture is observed). Such a picture could be explained with the pinched cone conformation of the mentioned unit if it does not feel the difference between the substituents at the narrow rim.

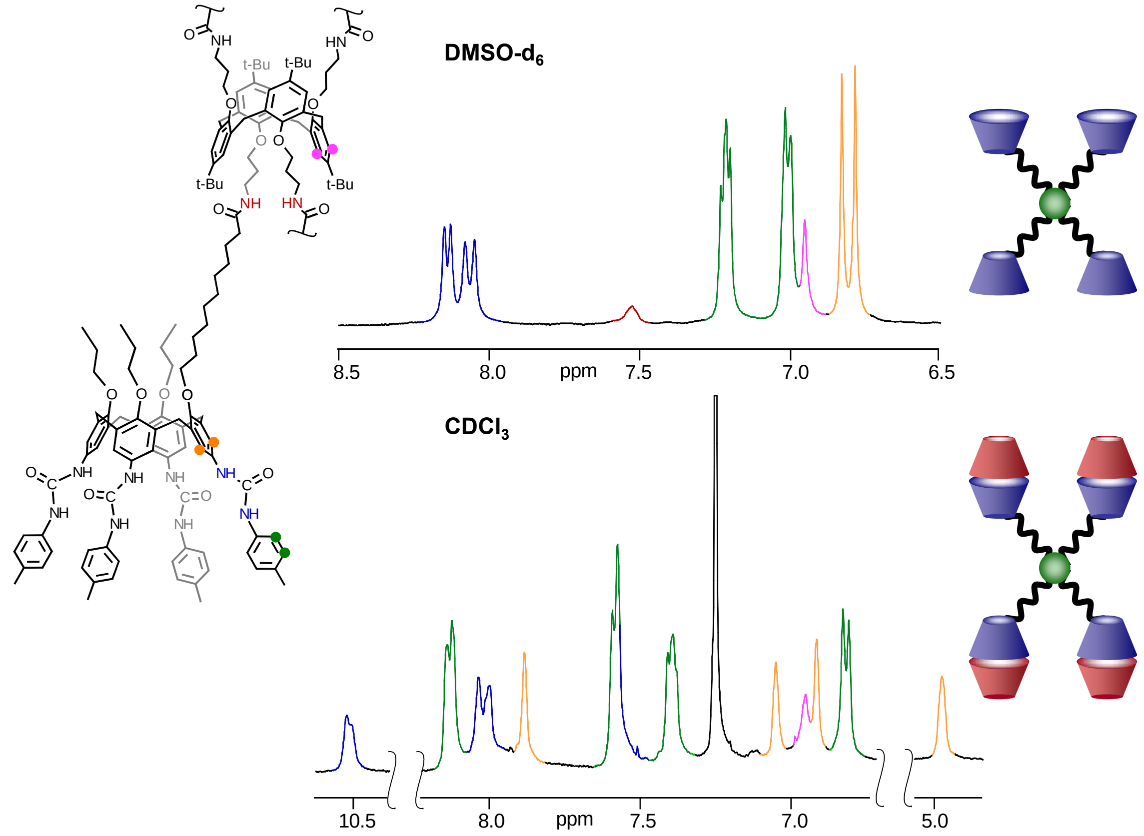


Figure 37. Calixarene **65a** in monomeric and as a tetrakis-heterodimer state.

Penta-calixarene **65f** was prepared analogously starting with tetratolyl urea **51**, bearing the amino function at the narrow rim, and *1,3-alternate* **60**, possessing four carboxylic groups. As it was expected, compounds **65a** and **65f** have very similar properties. But the synthesis of the latter one is less advantageous, because the preparation of calixarene **51** requires more steps, then those needed for **47b**, since the amino protecting group must be changed during the reaction sequence. Therefore the first strategy towards penta-calixarenes was applied subsequently.

In benzene or chloroform compound **65a** has limited solubility, which is not sufficient to record ^{1}H NMR spectrum in this solvents. We were able to get the clear solution of **65a** in $CHCl_3$ only in the presence of 4 equivalents of tetratosyl urea **16**. Usually formation of the tetrakis-heterodimer is complete within one day (due to the low solubility of components). The ^{1}H NMR shows three signals for N*H* protons of the heterodimer, while the last one is overlapped with the multiplet for Ar*H* protons of tolyl rings (Figure 37) and four signals for Ar*H* protons of tetraurea calixarene skeleton. The chemical shifts are totally in accordance with those from the tolyl-tosyl heterodimer.

Thus there is no doubt about the purity of the penta-calixarene compounds (according to the ^{1}H NMR spectra in DMSO) and in their ability to form dimers (proofed by heterodimerization experiments).

Light scattering experiments were performed to get an additional proof of the formation of self-assemblies. The results are shown in the Table 2.

Table 2. Results of the light scattering.

	Assembly/Compound	**Solvent**	**Rh, nm**
I	**12** (tetratolyl urea)	DMSO	~0.93
II	**12•16** (heterodimer tolyl-tosyl)	$CHCl_3$	1.1
III	**65a** (penta-calixarene)	DMSO	2.2
IV	**65a•16** (tetrakis-heterodimer)	$CHCl_3$	2.4

Let us assume, that the molecules have more or less spherical shape. Then operating with obtained hydrodynamic radii we can compare the sizes (volumes) of the particles. Knowing that the volume of the spherical unit is proportional to r^3, the ratio V_{II}/V_I could be simple calculated as the quotient of r_{II}^3/r_I^3.

It is obvious, that the radius of the particle corresponding to single unit should be smaller then the radius of the particle, corresponding to a dimeric assembly. Indeed the data obtained by light scattering are in agreement with this statement: $r_{II}>r_I$ and $r_{IV}>r_{III}$. In the same time the expected ratio r_{II}/r_I should be less then two, because during dimerization the partial overlapping of subunits occurs (Figure 38). Thus, taking in account the X-Ray structure of the capsule, one could expect that the radius r_{II} of the dimer is equal approximately $1.4r_I$ of monomer.

In case of described penta-calix[4]arene the ratio r_{IV}/r_{III} (assembly/single unit) must be even less then 1.4, since the size of the particle should not be strongly influenced by assembly with comparatively small units (Figure 38).

The ratios r_{II}/r_I (V_{II}/V_I) and r_{IV}/r_{III} (V_{IV}/V_{III}) calculated on the base of the light scattering experiments are equal to ~ 1.18 (1.64) and 1.09 (1.30) respectively, what is really correlates with the expectations and thus gives an additional evidence of self-assembly.

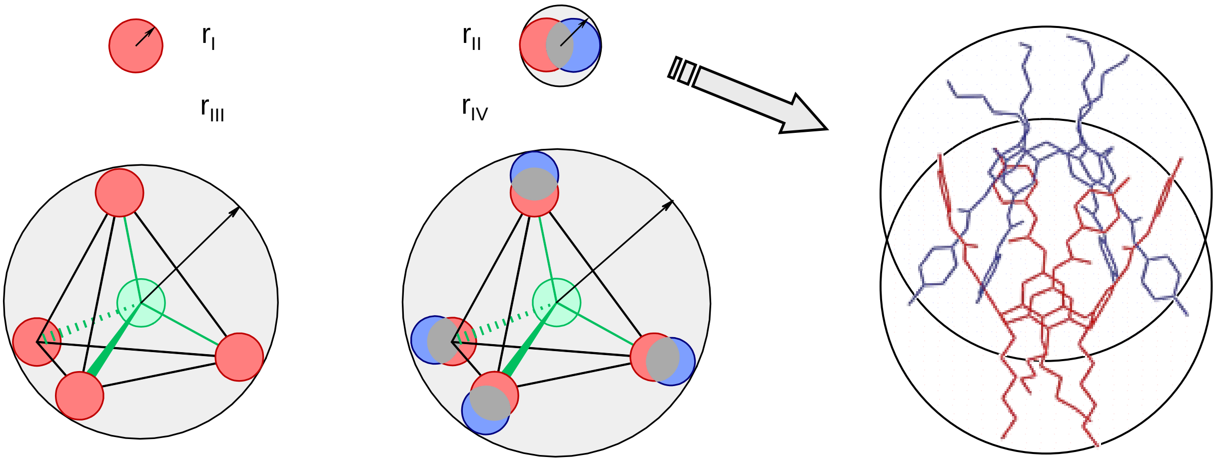


Figure 38. Graphical interpretation of the results obtained by light scattering.

Since it was possible to dissolve the compound **65a** in apolar solvents only with the help of tetratosyl urea **16**, the penta-calixarene **65b**, bearing the tosyl urea functions, was prepared. The purity of compound was controlled by ^{1}H NMR in DMSO-d_6. We were expecting to get cross-linked polymers with alternating sequence of the units. Unfortunately compound **65b** appeared to be insoluble in all solvents suitable for dimerization neither alone nor after addition of 4 equivalents or excess of tetratolyl urea calix[4]arene **12**.

To improve the solubility of urea derivatives in apolar solvents lipophilic residues should be introduced either at the narrow rim during the alkylation or at the wide rim modifying the urea functions. Since to change the alkyl residues we should come back to the parent calixarene each time (6 steps), it is more reasonable to introduce different urea functions starting from the tetraamine **49** *via* reactions with respective isocyanates. Therefore calixarenes **65c**, **65d** and **65e** were prepared and the purity of compounds was proved by ^{1}H NMR. The addition of chloroform to the samples affords clear solutions only in cases of **65c** and **65e**, but the ^{1}H NMR spectra do not show any well defined structures for both of them (what is not entirely unexpected).

To find out the sizes of aggregates for **65c,e** in chloroform the dynamic light scattering experiments were performed. In both cases the obtained hydrodynamic radii are ~5 - 6 nm. This means that we are dealing not with the expected entropically favoured cross linked polymers, for which hydrodynamic radius of the particle should be considerably larger, but with the mixture of well-defined oligomeric structures. From the ratio $V_{assembly}/V_{single\ unit} = 5^3/2.2^3 \approx 12$ one can estimate that up to 12 molecules could be assembled together.

Attempting to provide an additional evidence for the assembly process atomic force microscopy experiments were performed (M. Janke, group of Prof. Janshoff). Results of the measurements are found to be in good correlation to those, obtained by light scattering. Typically the particles are about 15-25 nm wide. But still some additional measurements must be done. Figure 39 shows the AFM image of self-organized penta-calixarene **65c**. The sample was prepared by spin-casting of a 0,01 mg/ml solution of compound in chloroform on highly oriented pyrolytic graphite.

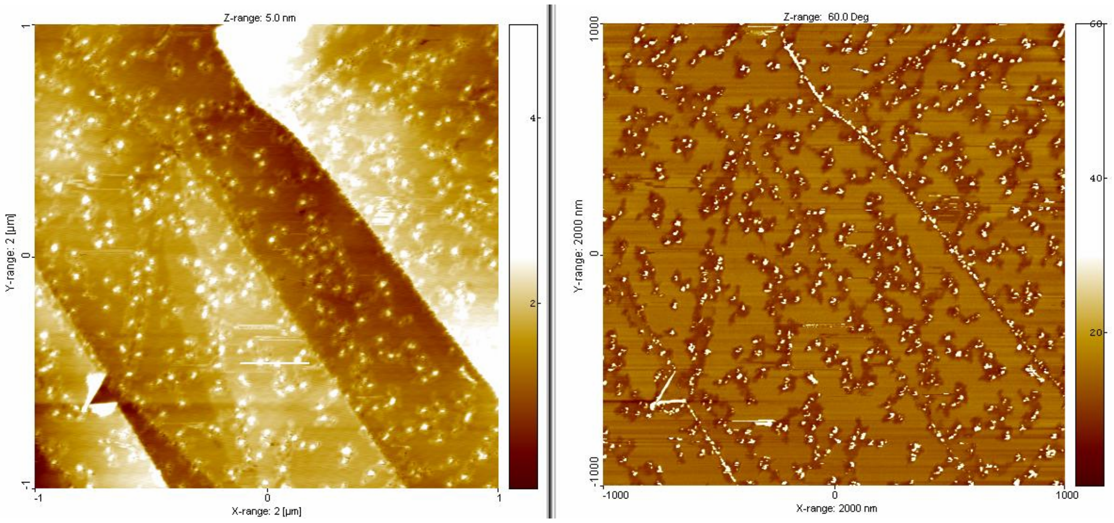


Figure 39. AFM image (TappingMode) of penta-calixarene **65c**; height image (left) and phase image (right).

Assembly, shown in Figure 40, represents one of the possible interpretations of the self-assembled structure with hydrodynamic radius ~ 5 nm. However this is only an assumption, up to the moment we have not enough information to give more convincing explanations. The study of this type of compounds is still not finished.

As discussed above the single penta-calixarene has a tetrahedral arrangement of the tetraurea parts, what is caused by the structure of the central molecule – calixarene in *1,3-alternate* conformation. In other words the tetraurea calix[4]arenes are disposed more or less at the corners of a tetrahedron. Due to the flexibility of the core and the alkyl chains the tetrahedron is not necessary regular.

In general each tetraurea calix[4]arene in appropriate solvents should be satisfied by forming a dimer. If this would be true also in our case, it can be fulfilled by the formation of a cyclic oligomer (Figure 40).

To explain the principle of it's formation we assume, that the number of penta-calixarenes involved is equal six. In accordance to our calculations it may be ≤ 12, but CPK models suggest, that the structures composed from five or less molecules are rather tensed and therefore less favoured. Thus six is the smallest reasonable number, but assemblies with a different number of molecules can be formed analogously.

In the assembly each penta-calixarene is arranged in the way that it's tetraurea parts **I** are placed in the drawing plane and altogether form a regular hexagon. Dimerization of these residues afford a cyclic array with the number of capsules equal to the number of units involved. The tetraurea parts **II** and **III**, situated over and under the drawing plane respectively, form two other imaginary circles. Thus all the tetraurea residues are involved in the assembly process.

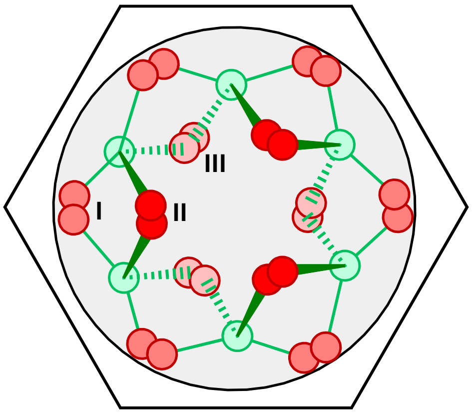
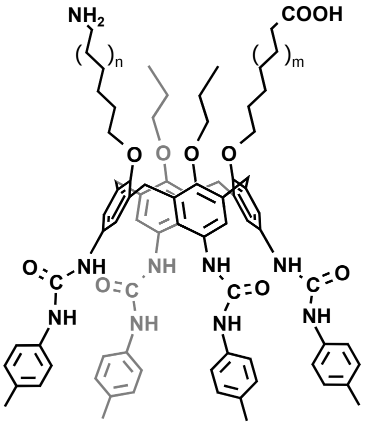


Figure 40. Sketchy drawing of assumed structure formed *via* self-assembly of six penta-calixarenes **65**.

3. 7. Synthesis of Tetraurea Calix[4]arenes Bearing Two Functional Groups at the Narrow Rim

The ability to control the conformational structure of polymeric molecules is one of the main keys to produce materials with optimized properties. The conformation of a polymeric chain in solution strongly depends on several parameters: the chemical structure of the polymer (for example the length and flexibility of linkages between the repeating units), the concentration, the solvent, the temperature.

The structural units within the molecule may be connected in various ways. Linear polymers are the simplest of all, however branched, star-like, cyclic or knotted structures are also widely studied. Design and synthesis of polymers and investigation of their conformational properties remains actual in our time.



66

The synthetic methods of peptide chemistry may be used for the preparation of linear oligomers from calixarene **66**. The prefabricated oligomers could be subsequently connected *via* appropriate polymeric segments, what may be considered as one of the ways to prepare block-copolymers (Figure 41).

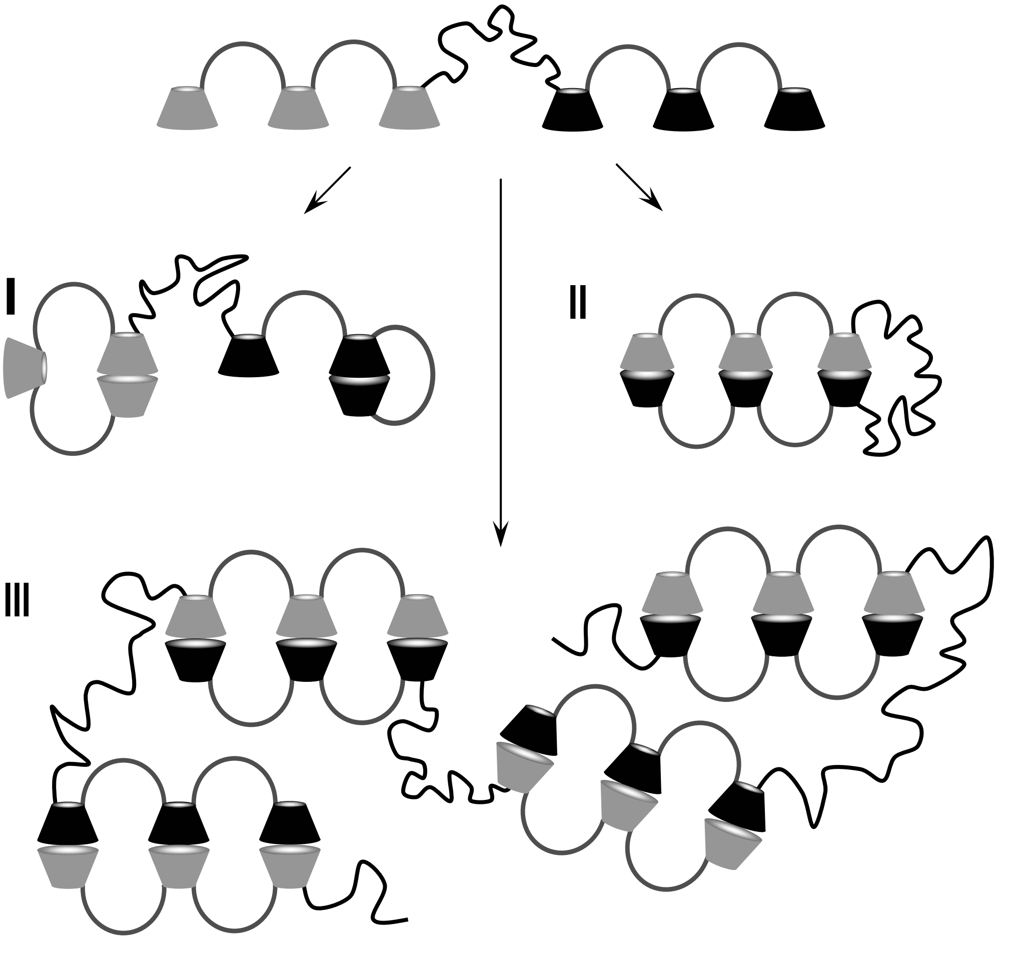


Figure 41. Several examples of possible intra- and intermolecular dimerization in polymers *via* heterodimerization.

In solution situations I and II (intramolecular hydrogen bonding), and III (intermolecular assembly) could be assumed. In case of block copolymers, constructed from tetraurea derivatives with the strong tendency for heterodimerization the situations II and III should be more pronounced and probably the result will depend on the concentration. Actually all described situations are only several main examples of possible assemblies. We also do not exclude the formation of cyclic or two dimensional structures. AFM and light scattering methods should help us in the analysis of the future results. The solid phase synthesis also allows to prepare molecules with the programmed sequence of the building blocks, but we were not really thinking to accomplish such synthesis within this PhD thesis.

The length of the spacer between calixarenes should fulfil the following requirements:

- at least two adjacent calixarenes should not dimerize (Figure 42a);
- the dimerization of two calixarenes should not disturb the self-assembly of the two adjacent units (Figure 42b), but should allow it (Figure 42c).

So the spacer should be neither too long nor too short.

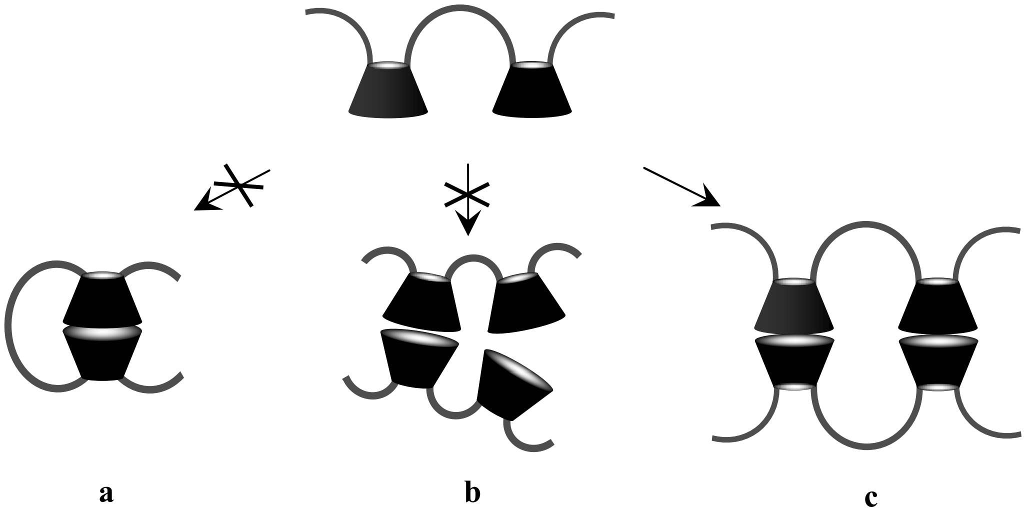


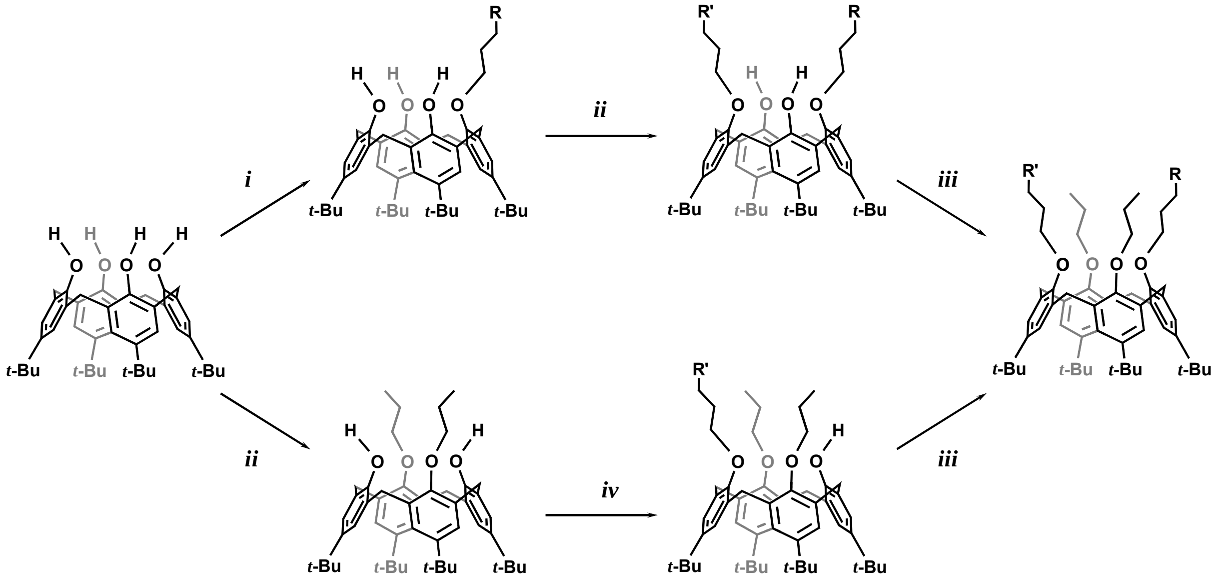
Figure 42. The optimal length of the spacer between calixarenes.

CPK models suggest, that the number **n** of CH_2 fragments in the chain between two tetraurea units, should be in the range of $20 \leq \mathbf{n} \leq 40$. The necessary distance finally will be provided by connection of the resulting aminoacid *via* respective spacers.

It is obvious that the required amino and carboxylic functional groups can be introduced using appropriately protected ω-bromoalkylamine and ethyl ester of ω-bromoalkylcarboxylic acid respectively. Among numerous amino protecting groups which were considered, there were no examples which would survive during the whole multi-step synthesis. Therefore protection must be changed appropriately during the reaction sequence. For our purposes ethyl ester of 5-bromopentanoic acid and 7-bromoheptanitrile (as a precursor for the amino function) were chosen. In general, two ways leading to the desired tetraethers are possible (Scheme 13). Each way consists of three steps:

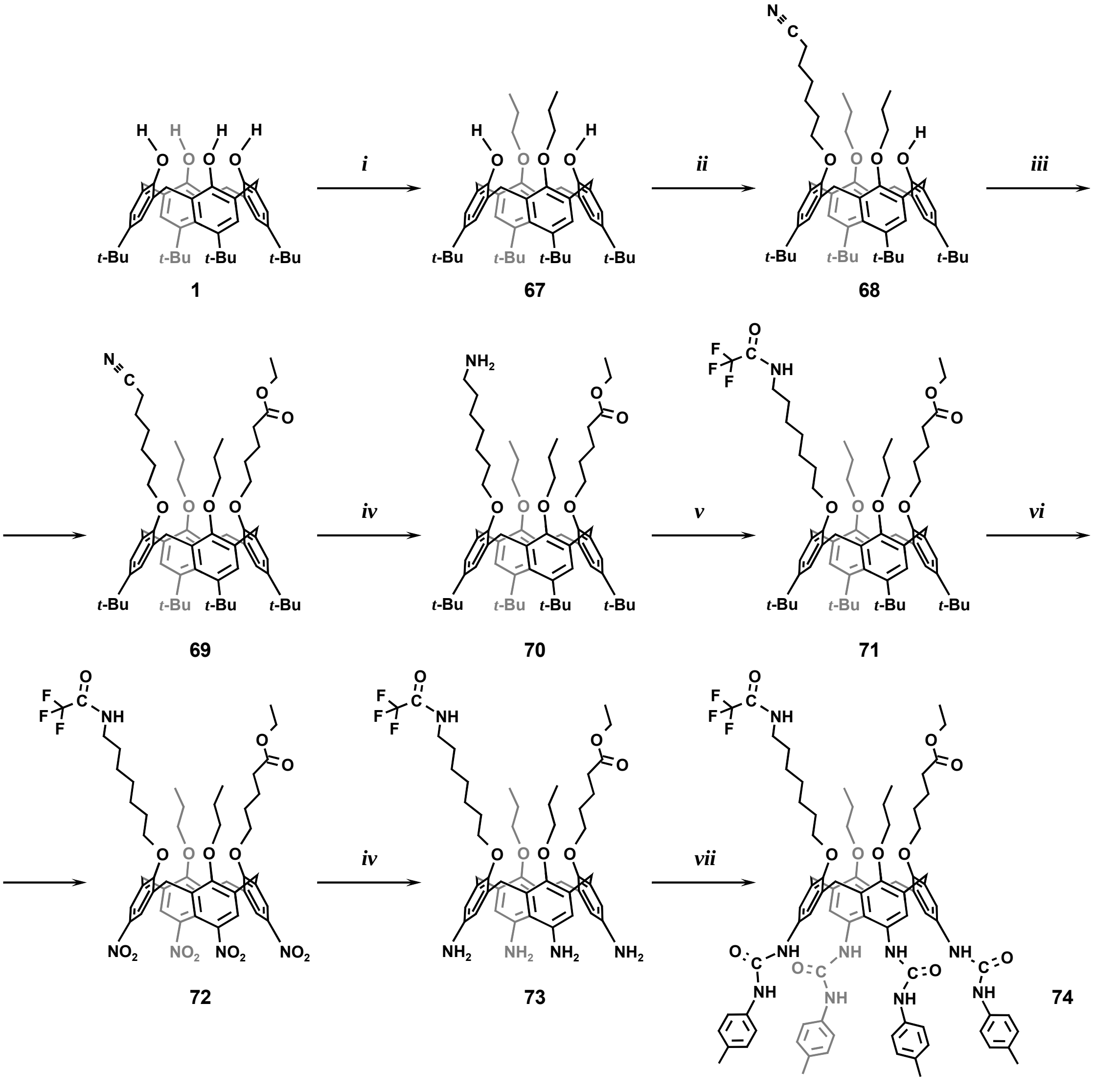
- the functional groups could be introduced during the first two steps *via* selective monoalkylation, followed by a second *O*-alkylation in the distal position. In the last step of exhaustive alkylation ether residues bearing no functional groups will be introduced;
- introduction of the functional groups occurs in the second and third step, after alkylation in *1,3* positions with alkyl bromide.

As discussed above the synthetic routes comprising the step of monoalkylation are not desired since it is almost impossible to avoid the formation of the side product – *1,3*-substituted compound, which leads to column separation and not so high yields. Thus, in principle, the second way (consecutive *1,3*-, tri- and finally exhaustive alkylation) would be more suitable.



Scheme 13. Strategies of synthesis of calix[4]arenes bearing two different functional groups on the narrow rim; i) 0.6 mol K_2CO_3, CH_3CN or acetone; ii) 2.2 mol K_2CO_3, CH_3CN; iii) NaH, DMF; iv) BaO, $Ba(OH)_2$, DMF.

The synthetic route affording compound **74** is shown in the Scheme 14. The stepwise *O*-alkylation was carried out in accordance to the general procedures described above. Direct *1,3*-alkylation was done using propyl bromide to keep the *cone* conformation of the tetrasubstituted product (groups larger then ethoxy must be used). The third group was introduced using the conditions of direct tri alkylation - BaO and $Ba(OH)_2$ in DMF because, according to the literature, this conditions are optimal to obtain the product with *syn-syn* arrangement of alkyl residues. After recrystallization from acetonitrile compound **68** was obtained in a 70 % yield. Other conditions (1 mol of NaH in DMF or 1.5 mol of K_2CO_3 in refluxing acetone with an excess of alkylating agent) might be also considered. The exhaustive alkylation with 5-bromopentanoic acid afforded desired tetraether **69**.



Scheme 14. Synthesis of calixarene bearing amino and carboxylic acid functions at the narrow rim using 7-bromoheptanitrile and ester of 5-bromopentanoic acid; i) PrBr, K_2CO_3, CH_3CN; ii) $Br(CH_2)_6CN$, BaO, $Ba(OH)_2$, DMF, 60°C; iii) $Br(CH_2)_4COOEt$, NaH, DMF; iv) Raney-Nickel, H_2, toluene, 40°C; v) $(CF_3CO)_2O$, $CHCl_3$; vi) HNO_3, CH_3COOH, CH_2Cl_2; vii)TolNCO, CH_2Cl_2.

As discussed above the nitrile group must be transferred into amino function. We must reduce it before the *ipso*-nitration will be carried out to avoid a selective hydrogenation of CN in the presence of NO_2 groups. In general reduction of CN occurs in the water/ethanol solution of sodium hydroxide, what will afford the cleavage of the ester function. Most probably the subsequent reesterification would not make any problem, but attempting to avoid this simple step we have tried catalytic hydrogenation under heating without any base. In this way the calixarene **70** was obtained in 90% yield.

In the next step the new amino protecting group must be introduced. For this purpose the *tert*-butoxycarbonyl and trifluoroacetamide groups have been considered. Since Boc protection is cleaved under acidic conditions, it may be removed it in the presence of ester function (and *vice versa*). This is the advantage of Boc protection. But unfortunately it will not survive the *ipso*-nitration conditions. Moreover the tosyl urea functions are usually hydrolyzed during the Boc deprotection. Therefore we have chosen the trifluoroacetamide group, which is labile to basic hydrolysis. Due to the literature it is easily cleaved by LiOH – the condition that preserves tosyl ureas.

The new protection was introduced by acylation of the amine with $(CF_3CO)_2O$ in chloroform (some drops of NEt_3 also could be added). The trifluoroacetamide function in ^{13}C NMR gave typical signals at δ, ppm: 157.23 (q, J= 37 Hz, $C(O)CF_3$) and 115.52 (q, J = 287 Hz, $C(O)CF_3$) (Figure 43). In ^1H NMR the strong downfield shifting of the signal corresponding to $CH_2NHC(O)CF_3$ was observed.

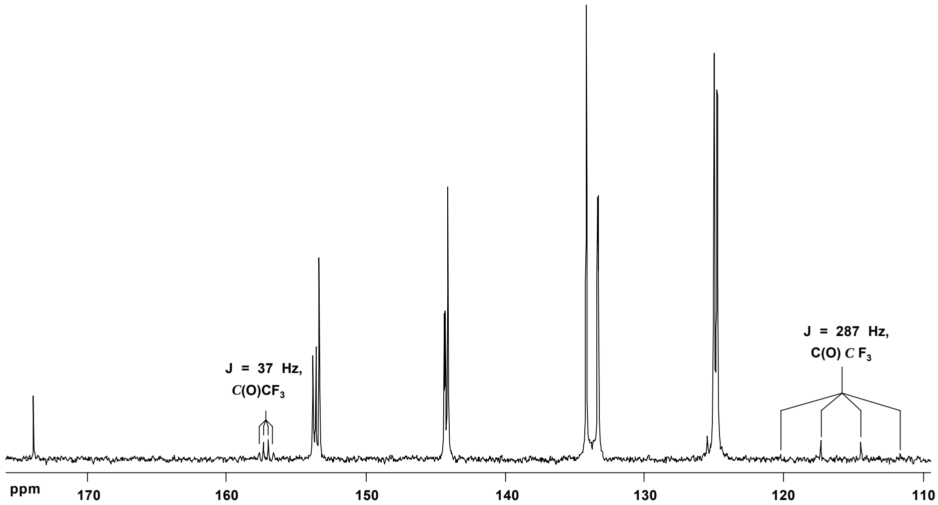
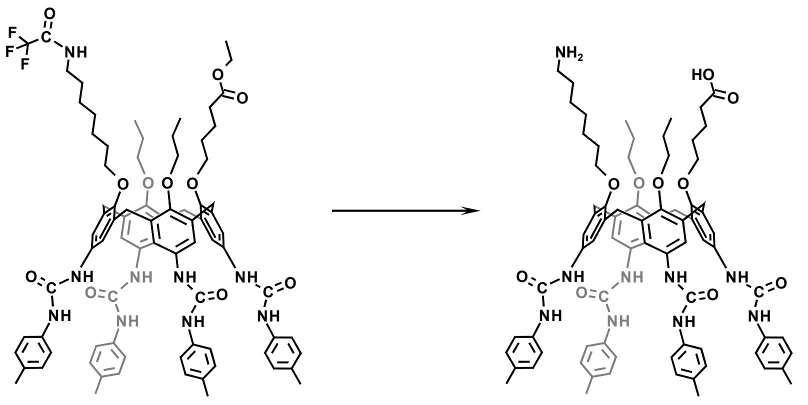


Figure 43. Section of the ^{13}C NMR of calixarene **71** in chloroform.

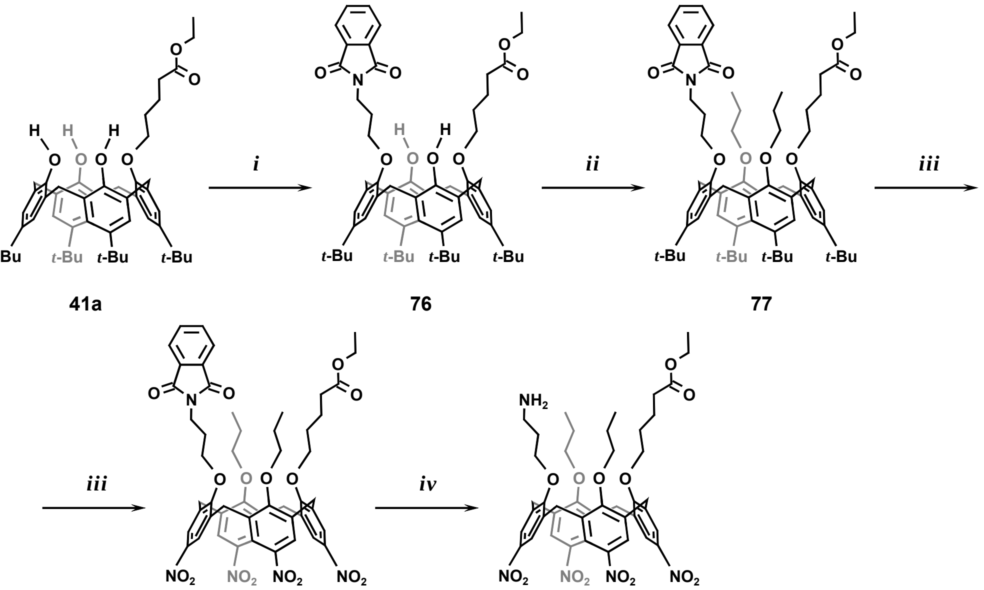
Ipso-nitration of **75** followed by consecutive reduction and reaction with tolyl isocyanate afforded the target tetraurea calix[4]arene **78**, bearing protected amino and carboxylic functions. The ability of described compound to form homodimers was examined by ^1H NMR in chloroform and additionally proved by COSY-gs spectrum. The 5 fold excess of NaOH was used for simultaneous hydrolysis of the both protecting groups and the target aminoacid was obtained in a 85% yield (Scheme 15).



74 **75**

Scheme 15. Deprotection of amino and carboxylic groups.

We have also tried to elaborate another method of synthesis of the target aminoacid using N-(3-bromopropyl)-**phthalimide** instead of 7-bromohepta**nitrile** (Scheme 16). The sequence of *O*-alkylation in this method differ from the previous one. Neither phthalimide nor ester functions do not survive the alkylation with BaO/Ba$(OH)_2$ and were introduced *via* consecutive mono and second dialkylation in the distal position. The exhaustive alkylation of **76** with propyl bromide led to compound **77**.



41a **76** **77**

78 **79**

Scheme 16. Synthesis of calixarene bearing amino and carboxylic acid functions at the narrow rim using N-(3-bromopropyl)-phthalimide and ester of 5-bromopentanoic acid; i) $Br(CH_2)_3Phth$, K_2CO_3, CH_3CN; ii) PrBr, NaH, DMF; iii) HNO_3, CH_3COOH, CH_2Cl_2; iv)2 mol N2H4 × H2O.

Ipso-nitration of **77** afforded tetranitro calix[4]arene **78** with the yield about 80%. In this step the amino protective group mast be changed. To preserve the ester function we have attempted to cleave the phthalimide group using hydrochloric acid (according to one of the general procedures). Unfortunately we could not obtain any satisfactory result. Usually desired reaction did not occur at all. Thus, in spite of the probability of side reactions of N_2H_4 with ester (formation of hydrazides), we have tried the selective deprotection of amino group using 2 fold excesses of hydrazine (small amount in comparison to those given in literature[60]). The cleavage was accomplished successfully, but the yield was rather low - 35%. The good solution of the problem would be simultaneous cleavage of the phthalimide and ester function using NaOH and their subsequent protection in a suitable way. However, this method was not developed to the very end because the synthesis described above was accomplished faster.

3. 8. Conclusions

Procedures for multi-step syntheses of tetraurea calix[4]arenes bearing one or two functional groups at the narrow rim were elaborated. The ability of all of them to form dimers was confirmed by ^1H NMR spectroscopy.

Tetraureas **47c-f** and **51a** were used for the synthesis of penta-calixarenes of type **65**. The purity of multiple calixarenes was proved by ^1H MNR spectra in DMSO-d_6 and their self-assembly properties were studied in apolar solvents. Due to the limited solubility of compounds up to now we were using only $CDCl_3$ for the studies. In the mentioned solvent tetrakis-tetratolyl ureas **65a,f** itself are not soluble, but only in the presence of 4 equivalents of tosyl urea. In this case, as expected, the tetrakis-heterodimers emerge as the only species detectable by ^1H NMR and could be characterized. In contrast, tetrakis-tetratosyl urea **65b** remains insoluble even in combination with 4 equivalents (or excess) of tetratolyl urea. Up to the moment solubility is one of the main problems for the self-assembling systems. To overcome this problem we have prepared the penta-calixarene **65c**, which is easily soluble in chloroform, but the spectrum is very broad. The addition of 4 equivalents of tetratosyl urea afforded the formation of heterodimer. Since the exclusive heterodimerization occurs only between aryl and sulfonyl ureas this method of characterization is not eligible for tetrakis-tetraalkyl ureas. Thus among compounds **65d,e** only **65e** is soluble in chloroform and it’s spectrum is also broad.

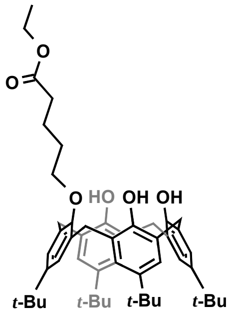
The light scattering experiments (Karl Fischer, Mainz) were performed for penta-calixarene **65a** in DMSO-d_6 solution, for tetrakis-heterodimer **65a•16** and **65c,e** dissolved in chloroform. The hydrodynamic radii of the units are equal 2.2, 2.4, 5 and 5.2 nm respectively. The AFM measurements (Matthias Janke, Mainz) performed for compound **65c** also show the formation of particles about 15-25 nm wide. However the results are still not understood in details, the penta-calixarenes in apolar solvent do not form the expected cross-linked polymers, but form the mixture of oligomeric (probably cyclic) structures. Due to our calculations on the basis of light scattering experiments up to 12 molecules can be assembled together.

3. 9. Experimental Part

calix[4]arene 41a

A slurry of calix[4]arene **1** (2.00 g, 3.08 mmol), K_2CO_3 (0.26 g, 1.85 mmol) and ethyl ester of 5-bromopentanoic acid (1.94 g (1.45 ml), 9.24 mmol) in CH_3CN (100 ml) was refluxed for 48 h. The insoluble inorganic salts were filtered off and the solvent was removed in vacuum. The residue was recrystallized from $CHCl_3$/MeOH. Calix[4]arene **41a** was obtained as a white powder (1.3 g, 54 %); mp 216-218°C;

^{1}H NMR (200MHz, $CDCl_3$), δ: 10.15 (s, 1H, O*H*), 9.54 (s, 2H, O*H*), 7.07-6.97 (m, 8H, Ar*H*), 4.36-4.09 (m, 8H, ArC*H*$_2$Ar, OC*H*$_2$CH$_2$, OC*H*$_2$CH$_3$), 3.43 (d, 2H, $^{2}J = 12.7$ Hz, ArC*H*$_2$Ar), 3.41 (d, 2H, $^{2}J = 12.7$ Hz, ArC*H*$_2$Ar), 2.52 (t, 2H, $^{3}J = 6.8$ Hz, C(O)C*H*$_2$), 2.24-2.15 (m, 2H, CH$_2$), 2.07-1.96 (m, 2H, C*H*$_2$), 1.28 (t, 3H, $^{3}J = 6.8$ Hz, O CH$_2$C*H*$_3$), 1.21 (s, 9H, C(C*H*$_3$)$_3$), 1.20 (s, 18H, C(C*H*$_3$)$_3$), 1.82 (s, 9H, C(C*H*$_3$)$_3$);



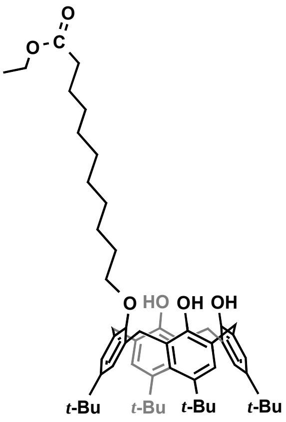
^{13}C NMR (100MHz, $CDCl_3$), δ: 173.35, 149.27, 148.47, 148.17, 147.75, 143.63, 143.12, 133.46, 128.33, 128.08, 127.61, 126.46, 125.95, 125.76, 125.70, 125.65, 60.44, 34.24, 34.01, 33.01, 32.25, 31.49, 31.25, 29.27, 21.46, 14.28;

MS(FD) *m/z* (%) 777.8 (100) [M^{+}].

General procedure for synthesis of 41b,c.

A slurry of calix[4]arene **1** (2.30 mmol), K_2CO_3 (0.50 mmol) and alkylating agent (2.20 mmol) in CH_3CN was refluxed for 4 days. The excess of K_2CO_3 was filtered off and the solvent was removed in vacuum. The residue was treated with acetone and unreacted calix[4]arene was filtered off. The filtrate was evaporated in vacuum. The crude product was purified by column chromatography.

calix[4]arene 41b



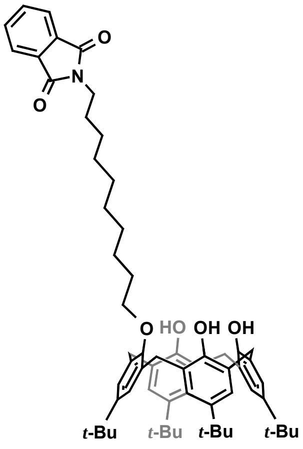
Alkylating agent - ethyl-(ω-bromododecanoate). THF : Hexane = 1 : 10 was used as eluent for column chromatography. Calixarene **41b** was obtained as a yellow oil (55 %).

^{1}H NMR (200MHz, $CDCl_3$), δ: 10. 19 (s, 1H, OH), 9.60 (s, 2H, OH), 7.08-6.97 (m, 8H, ArH), 4.34 (d, 2H, $^2J = 13.2$ Hz, $\mathrm{ArC}H_2\mathrm{Ar}$), 4.26 (d, 2H, $^2J = 13.2$ Hz, $\mathrm{ArC}H_2\mathrm{Ar}$), 4.15-4.05 (m, 4H, $\mathrm{OC}H_2\mathrm{CH_3}$, $\mathrm{OC}H_2$), 3.45-3.36 (m, 4H, $\mathrm{ArC}H_2\mathrm{Ar}$), 2.28 (t, 2H, $^3J = 7.6$ Hz, $\mathrm{C(O)C}H_2$), 2.18-2.09 (m, 2H, $\mathrm{C}H_2$), 1.61 (m, 4H, $\mathrm{C}H_2$), 1.34-1.23 (m, 10H, $\mathrm{C}H_2$), 1.20-1.17 (m, 39H, $\mathrm{OCH_2C}H_3$, $\mathrm{C(C}H_3)_3$);

^{13}C NMR (100MHz, $CDCl_3$), δ: 173.85, 149.39, 148.44, 148.00, 147.73, 143.58, 143.05, 133.51, 128.31, 128.13, 127.64, 126.32, 125.66, 125.63, 125.57, 77.24, 70.74, 60.08, 38.10, 33.87, 33.02, 32.26, 31.50, 31.27, 29.77, 29.46, 29.41, 29.15, 28.60, 26.85, 25.84, 14. 16;

MS(FD) *m/z* (%) 861.0 (100) [M^+].

calix[4]arene 41c



Alkylating agent - *N*-(ω-bromododecyl)phthalimide-anoate. THF : Hexane = 1:8 was used as eluent for column chromatography. Calixarene **41c** was obtained as a white powder (55 %); mp 200-202°C;

^{1}H NMR (200MHz, $CDCl_3$), δ: 10.19 (s, 1H, OH), 9.59 (s, 2H, OH), 7.85-7.80 (m, 2H, $\mathrm{Ar}H_{\mathrm{pht}}$), 7.70-7.66 (m, 2H, $\mathrm{Ar}H_{\mathrm{pht}}$), 7.07-6.97 (m, 8H, Ar$H$), 4.33 (d, 2H, $^2J = 12.7$ Hz, $\mathrm{ArC}H_2\mathrm{Ar}$), 4.25 (d, 2H, $^2J = 12.7$ Hz, $\mathrm{ArC}H_2\mathrm{Ar}$), 4.10 (t, 2H, $^3J = 6.8$ Hz, $\mathrm{OC}H_2$), 3.66 (t, 2H, $^3J = 7.3$ Hz, $\mathrm{NC}H_2$), 3.43 (d, 2H, $^2J = 12.7$ Hz, $\mathrm{ArC}H_2\mathrm{Ar}$), 3.41 (d, 2H, $^2J = 12.7$ Hz, $\mathrm{ArC}H_2\mathrm{Ar}$), 2.15-2.06 (m, 2H, $\mathrm{C}H_2$), 1.77-1.50 (m, 4H, $\mathrm{C}H_2$), 1.35-1.18 (m, 10H, $\mathrm{C}H_2$), 1.20 (s, 9H, $\mathrm{C(C}H_3)_3$), 1.19 (s, 18H, $\mathrm{C(C}H_3)_3$), 1.18 (s, 9H, $\mathrm{C(C}H_3)_3$);

^{13}C NMR (100MHz, $CDCl_3$), δ: 168.44, 149.42, 148.49, 147.98, 147.79, 143.54, 143.03, 133.77, 133.52, 132.17, 128.32, 128.16, 127.66, 126.37, 125.93, 125.68, 125.62, 123.10, 77.27, 38.06, 33.89, 33.02, 32.27, 31.49, 31.25, 29.79, 29.46, 29.41, 29.16, 28.60, 26.87, 25.83;

MS(FD) *m/z* (%) 934.3 (100) [M^+].

The general procedure for synthesis of 43

Method A

A slurry of calix[4]arene **41** (3.21 mmol) and NaH (0.62 g, 25.70 mmol) in DMF (100 ml) was stirred at room temperature for 1 h. Then propyl bromide (25.70 mmol) was added and the stirring was continued for 72 h. After that acetic acid was added to neutralize the excess of NaH. The solvents were removed in vacuum and the residue was dissolved in chloroform, washed with water and dried over $MgSO_4$. Then the solvent was evaporated and calix[4]arene **43** (65 %-70 %) was obtained as a yellow oil.

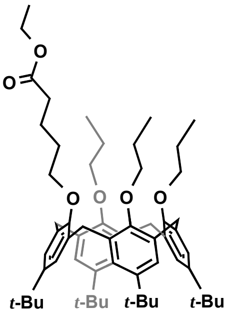
Method B

A suspension of calix[4]arene **42** (3.87 mmol) and NaH (5.03 mmol) in DMF (90 ml) was stirred for 1 h at room temperature and then alkylating agent (5.03 mmol) was added. The stirring was continued for 72 h and then acetic acid was added to neutralize the excess of NaH. After that water (120 ml) was added.

calixarene 43a

Alkylating agent - 5-bromopentanoic acid

Precipitate was filtered off, washed with water (3x40 ml) and dried. The crude product was dissolved in $CHCl_3$ (100 ml), washed with water, dried over $MgSO_4$ and filtered. The filtrate was evaporated and the residue was recrystallized from CH_3CN. Calix[4]arene **43a** was obtained as a white powder (98 %); mp 74-76°C;



^{1}H NMR (400MHz, $CDCl_3$), δ: 6.77 (s, 4H, Ar*H*), 6.75 (s, 4H, Ar*H*), 4.39 (d, 2H, ^2J = 12.5 Hz, ArC*H*$_2$Ar), 4.37 (d, 2H, ^2J = 12.5 Hz, ArC*H*$_2$Ar), 4.14 (q, 2H, ^3J = 7.0 Hz, OC*H*$_2$CH$_3$), 3.86 (t, 2H, ^3J = 7.4 Hz, OC*H*$_2$), 3.82-3.77 (m, 6H, OC*H*$_2$CH$_2$), 3.10 (d, 4H, ^2J = 12.5 Hz, ArC*H*$_2$Ar), 2.38 (t, 2H, ^3J = 7.4 Hz, C(O)C*H*$_2$), 2.06-1.96 (m, 8H, C*H*$_2$), 1.82-1.71 (m, 2H, C*H*$_2$), 1.26 (t, 3H, ^3J = 7.0 Hz, OCH$_2$C*H*$_3$), 1.07 (s, 18H, C(C*H*$_3$)$_3$), 1.05 (s, 18H, C(C*H*$_3$)$_3$), 0.98 (t, 9H, ^3J = 7.3 Hz, CH$_2$C*H*$_3$);

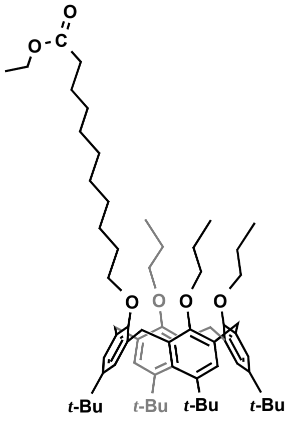
^{13}C NMR (100MHz, $CDCl_3$), δ: 173.56, 153.65, 144.33, 144.19, 133.85, 133.78, 133.70, 124.90, 74.64, 60.25, 34.42, 33.81, 31.48, 31.10, 29.72, 23.35, 21.72, 14.28, 10.34;

MS(FD) *m/z* (%) 902.9 (100) [M$^+$].

calixarene 43b

Alkylating agent - ethyl-(ω-bromododecanoate)

The product was extracted from the milky suspension with $CHCl_3$ (3 x 30ml). Then the chloroform layer was separated, dried over $MgSO_4$ and evaporated to dryness. The residue was treated 3 times with CH_3CN to extract the alkylating agent from the oil. The residue was dried in vacuum of an oil pump. Calix[4]arene **43a** was obtained as a yellow oil (80 %).



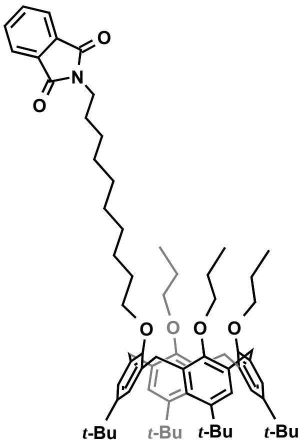
^{1}H NMR (400MHz, $CDCl_3$), δ: 6.76 (s, 8H, ArH), 4.40 (d, 4H, ^2J = 12.7 Hz, ArCH_2Ar), 4.11 (q, 2H, ^3J = 7.3 Hz, OCH_2CH$_3$), 3.83-3.79 (m, 8H, OCH_2CH$_2$), 3.10 (d, 4H, ^2J = 12.7 Hz, ArCH_2Ar), 2.28 (t, 2H, ^3J = 7.3 Hz, C(O)CH_2), 2.03-1.99 (m, 8H, CH_2), 1.37-1.24 (m, 14H, CH_2), 1.24 (t, 3H, ^3J = 7.3 Hz, OCH$_2$CH_3), 1.07 (s, 36H, C(CH_3)$_3$), 0.99 (t, 9H, ^3J = 7.3 Hz, CH$_2$CH_3);

^{13}C NMR (100MHz, $CDCl_3$), δ: 173.83, 153.81, 153.73, 144.11, 133.83, 124.86, 76.96, 75.42, 60.11, 34.38, 33.80, 31.48, 31.09, 30.26, 29.80, 29.52, 29.30, 29.18, 26.26, 25.01, 23.33, 23.28, 14.26, 10.36;

MS(FD) *m/z* (%) 988.4 (100) [M$^+$].

calix[4]arene 43c

Alkylating agent - *N*-(ω-bromododecyl)phthalimideanoate



Oil was formed. The solvents were poured off and the residue was dissolved in chloroform (100 ml), washed with water, dried over $MgSO_4$ and filtered. The filtrate was evaporated. Calix[4]arene **4c** was either purified by column chromatography (THF:Hexane = 1:10) and obtained as a yellow oil (90 %) or by treatment with CH_3CN (as for **4b**) (50%);

^{1}H NMR (200MHz, $CDCl_3$), δ: 7.85-7.82 (m, 2H, ArH_{pht}), 7.71-7.67 (m, 2H, ArH_{pht}), 6.77 (s, 8H, ArH), 4.41 (d, 4H, ^2J = 12.2 Hz, ArCH_2Ar), 3.84-3.77 (m, 8H, OCH_2), 3.68 (t, 2H, ^3J = 7.3 Hz, NCH_2), 3.11 (d, 4H, ^2J = 12.2 Hz, ArCH_2Ar), 2.07-1.95 (m, 8H, CH_2), 1.70-1.66 (m, 2H, CH_2), 1.34 (br s, 12H, CH_2), 1.08 (s, 36H, C(CH_3)$_3$), 0.99 (t, 9H, ^3J = 7.3 Hz, CH_3);

^{13}C NMR (100MHz, $CDCl_3$), δ: 168.42, 153.78, 153.71, 153.66, 144.08, 133.78, 132.18, 124.83, 123.11, 77.20, 76.93, 76.68, 75.39, 38.06, 33.77, 31.45, 31.05, 30.22, 29.77, 29.74, 29.53, 29.21, 28.61, 26.89, 26.21, 23.29, 23.24, 10.32, 10.28;

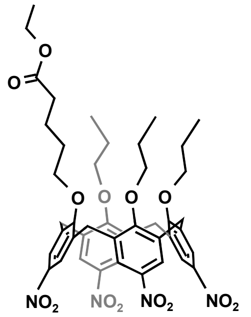
MS(FD) *m/z* (%) 1061.3 (100) [M$^+$].

The general procedure for synthesis of 44

Calix[4]arene **43** (2.44 mmol) was dissolved in CH_2Cl_2 (50 ml) and acetic acid (3.7 ml) was added. The solution was vigorously stirred and fuming HNO_3 (3 ml) was added. The solution became dark immediately and stirring was continued for approximately 2 h at room temperature. The reaction mixture was diluted with water (40 ml). Organic layer was separated, washed with water (5x25 ml), dried over $MgSO_4$ and filtered.

calix[4]arene 44a

The filtrate was concentrated to approximately 10-15 ml and the product was precipitated with methanol. Calix[4]arene **44a** (85 %) was obtained as a yellow powder; mp 230-232°C;



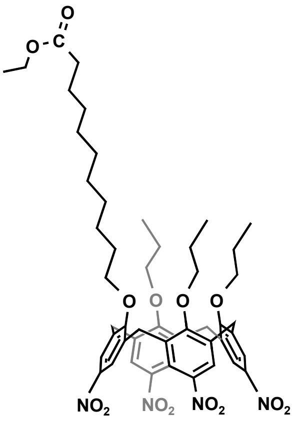
^{1}H NMR (400MHz, $CDCl_3$), δ: 7.60 (s, 4H, Ar*H*), 7.52 (s, 4H, Ar*H*), 4.51 (d, 2H, ^2J = 14.1 Hz, ArC*H*$_2$Ar), 4.49 (d, 2H, ^2J = 14.1 Hz, ArC*H*$_2$Ar), 4.13 (q, 2H, ^3J = 6.8 Hz, OC*H*$_2$CH$_3$), 4.00-3.91 (m, 8H, OC*H*$_2$CH$_2$), 3.40 (d, 4H, ^2J = 14.1 Hz, ArC*H*$_2$Ar), 2.37 (t, 2H, ^3J = 7.3 Hz, C(O)C*H*$_2$), 1.93-1.84 (m, 8H, C*H*$_2$), 1.77-1.69 (m, 2H, C*H*$_2$), 1.25 (t, 3H, ^3J = 6.8 Hz, OCH$_2$C*H*$_3$), 1.04-0.97 (m, 9H, CH$_2$C*H*$_3$);

^{13}C NMR (100MHz, $CDCl_3$), δ: 172.83, 161.73, 161.55, 161.38, 142.88, 135.50, 135.42, 135.28, 124.07, 123.93, 77.72, 75.60, 60.46, 33.83, 31.12, 29.51, 23.24, 21.29, 14.23, 10.17, 10.06;

MS(FD) *m/z* (%) 858.5 (100) [M$^+$].

calix[4]arene 44b

The filtrate was evaporated and residue was treated with methanol. Precipitate was filtered off yielding calix[4]arene **44b** (65 %) as a yellow powder; mp 145-147°C;



^{1}H NMR (400MHz, $CDCl_3$), δ: 7.56 (s, 8H, Ar*H*), 4.51 (d, 4H, ^2J = 13.7 Hz, ArC*H*$_2$Ar), 4.10 (q, 2H, ^3J = 7.0 Hz, OC*H*$_2$CH$_3$), 3.99-3.92 (m, 8H, OC*H*$_2$CH$_2$), 3.39 (d, 4H, ^2J = 13.7 Hz, ArC*H*$_2$Ar), 2.27 (t, 2H, ^3J = 7.4 Hz, C(O)C*H*$_2$), 1.95-1.86 (m, 8H , C*H*$_2$), 1.60-1.51 (m, 2H, C*H*$_2$), 1.34-1.25 (m, 12H, C*H*$_2$), 1.24 (t, 3H, ^3J = 7.0 Hz, OCH$_2$C*H*$_3$), 1.00 (t, 9H, ^3J = 7.4 Hz, CH$_2$C*H*$_3$);

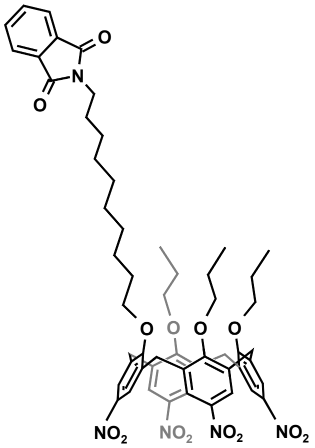
^{13}C NMR (100MHz, $CDCl_3$), δ: 173.80, 161.68, 142.78, 135.40, 123.92, 77.68, 76.22, 60.13, 34.27, 31.06, 30.06, 29.55, 29.50, 29.32, 29.18, 29.05, 25.88, 24.87, 23.21, 14.19, 10.10;

MS(FD) *m/z* (%) 944.0 (100) [M$^+$].

calix[4]arene 44c

The filtrate was evaporated and residue was treated with methanol. Precipitate was filtered off yielding calix[4]arene **44c** (65-75 %) as a yellow powder; mp 127-129°C;

^{1}H NMR (200MHz, CDCl$_3$), δ: 7.85-7.82 (m, 2H, Ar*H*$_{pht}$), 7.71-7.69 (m, 2H, Ar*H*$_{pht}$), 7.55 (s, 8H, Ar*H*), 4.50 (d, 4H, ^2J = 14.1 Hz, ArC*H*$_2$Ar), 4.00-3.90 (m, 8H, OC*H*$_2$), 3.65 (t, 2H, ^3J = 7.3 Hz, NC*H*$_2$), 3.39 (d, 4H, ^2J = 14.1 Hz, ArC*H*$_2$Ar), 1.94-1.84 (m, 8H, C*H*$_2$), 1.63 (br s, 2H, C*H*$_2$), 1.29 (br s, 12H, C*H*$_2$), 1.00 (t, 9H, ^3J = 7.3 Hz, CH$_2$C*H*$_3$);



^{13}C NMR (100MHz, CDCl$_3$), δ: 168.47, 161.65, 142.89, 135.39, 133.90, 132.13, 124.00, 123.14, 77.70, 76.23, 37.99, 31.55, 31.11, 30 .08, 29.53, 29.48, 29.36, 29.09, 28.55, 26.80, 25.88, 23.24, 22.62, 14.08, 10.14;

MS(FD) *m/z* (%) 1015.7 (100) [M$^+$].

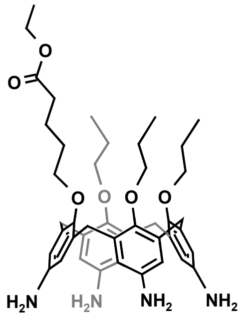
The general procedure for synthesis of 45

Calix[4]arene **44** (1.16 mmol) was dissolved in the mixture of toluene/ethanol (25 ml/ 5ml) (for **44a** THF was used instead of THF) and hydrogenated during 14 h at room temperature in the presence of the Raney-nickel. The progress of reaction was monitored by TLC in THF. After reaction is finished the catalyst was filtered off and washed with THF (2x10 ml). The combined organic layers were evaporated under reduced pressure.

calix[4]arene 45a

The residue was treated with hexane and precipitate was filtered off. Calix[4]arene **5** (65 %) was obtained as a brown powder; mp > 170-172°C decompose;

^{1}H NMR (200MHz, CDCl$_3$), δ: 6.04 (s, 8H, Ar*H*), 4.29 (d, 2H, ^2J = 13.2 Hz, ArC*H*$_2$Ar), 4.26 (d, 2H, ^2J = 13.2 Hz, ArC*H*$_2$Ar), 4.12 (q, 2H, ^3J = 6.8 Hz, OC*H*$_2$CH$_3$), 3.77-3.66 (m, 8H, OC*H*$_2$CH$_2$), 2.90 (d, 4H, ^2J = 13.2 Hz, ArC*H*$_2$Ar), 2.73 (br s, 8H, N*H*$_2$), 2.33 (t, 2H, ^3J = 7.3 Hz, C(O)C*H*$_2$), 1.89-1.70 (m, 10H, C*H*$_2$), 1.24 (t, 3H, ^3J = 6.8 Hz, OCH$_2$C*H*$_3$), 0.93 (t, 9H, ^3J = 7.3 Hz, CH$_2$C*H*$_3$);

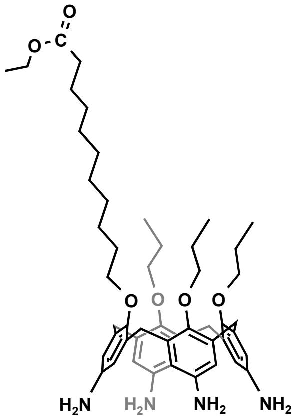


^{13}C NMR (100MHz, CDCl$_3$), δ: 173.49, 150.10, 149.96, 140.16, 140.01, 135.64, 115.86, 76.68, 74.31, 60.20, 34.33, 31.12, 29.53, 23.12, 21.68, 14.23, 10.34;

MS(FD) *m/z* (%) 738.7 (100) [M$^+$].

calix[4]arene 45b

The residue was crystallized from CH_3CN. Calix[4]arene **45b** (60 %) was obtained as a brown powder; mp 150-152°C;



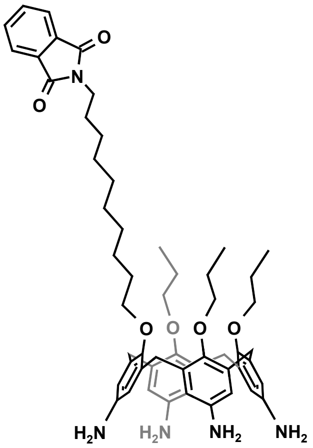
^1H NMR (400MHz, $CDCl_3$), δ: 6.07 (s, 4H, Ar*H*), 6.05 (s, 4H, Ar*H*), 4.28 (d, 4H, $^2J = 13.2$ Hz, ArC*H*$_2$Ar), 4.11 (q, 2H, $^3J = 6.8$ Hz, OC*H*$_2$CH$_3$), 3.73-3.68 (m, 8H, OC*H*$_2$CH$_2$), 3.26 (br s, 8H, N*H*$_2$), 2.90 (d, 4H, $^2J = 13.2$ Hz, ArC*H*$_2$Ar), 2.27 (t, 2H, $^3J = 7.3$ Hz, C(O)C*H*$_2$), 1.87-1.80 (m, 8H, C*H*$_2$), 1.64-1.58 (m, 2H, C*H*$_2$), 1.32-1.24 (m, 12H, C*H*$_2$), 1.24 (t, 3H, $^3J = 6.8$ Hz, OCH$_2$C*H*$_3$), 0.93 (t, 9H, $^3J = 7.3$ Hz, CH$_2$C*H*$_3$);

^{13}C NMR (100MHz, $CDCl_3$), δ: 173.90, 150.17, 140.09, 135.71, 135.61, 115.83, 76.68, 75.05, 60.13, 34.39, 31.14, 30.09, 29.72, 29.48, 29.27, 29.16, 26.23, 25.00, 23.11, 14.25, 10.35;

MS(FD) *m/z* (%) 822.7 (100) [M$^+$].

calix[4]arene 45c

Calix[4]arene **45c** (0.38 g, 85 %) was obtained as a brown powder; mp >180°C decompose;



^1H NMR (200MHz, $CDCl_3$), δ: 7.84-7.81 (m, 2H, Ar*H*$_{pht}$), 7.71-7.68 (m, 2H, Ar*H*$_{pht}$), 6.05 (s, 4H, Ar*H*), 6.03 (s, 4H, Ar*H*), 4.29 (d, 4H, $^2J = 13.2$ Hz, ArC*H*$_2$Ar), 3.74-3.62 (m, 10H, OCH$_2$, NC*H*$_2$), 2.90 (d, 4H, $^2J = 13.2$ Hz, ArC*H*$_2$Ar), 1.90-1.79 (m, 8H, C*H*$_2$), 1.69-1.63 (m, 2H, C*H*$_2$), 1.29 (br s, 12H, C*H*$_2$), 0.93 (t, 9H, $^3J = 7.3$ Hz, CH$_2$C*H*$_3$);

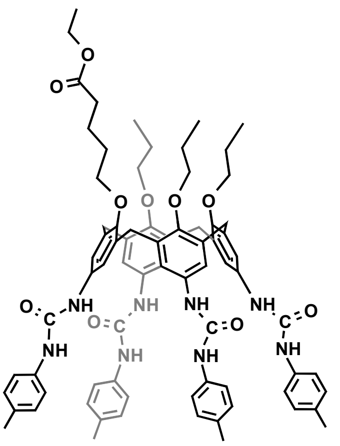
MS(FD) *m/z* (%) 896.1 (100) [M$^+$].

The general procedure for synthesis of 46a-d,f-h

The tetraamine **45** (0.65 mmol) was dissolved in CH_2Cl_2 (25 ml) and corresponding isocyanate (5.24 mmol) was added to the solution. The reaction mixture was stirred for 6h.

calix[4]arene 46a

MeOH (30 ml) was added to the solution. The mixture was concentrated to ~15 ml and precipitate was filtered, washed with MeOH and dried on the air. Calix[4]arene **7a** (95 %) was obtained as a white powder; mp > 290°C decompose;

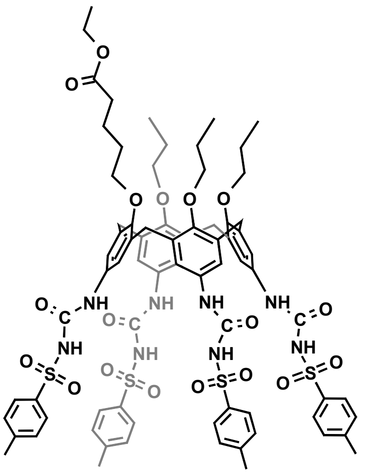


^{1}H NMR (300MHz, DMSO-d$_6$), δ: 8.22 (s, 4H, N*H*), 8.16 (s, 4H, N*H*), 7.22 (d, 8H, ^3J = 8.3 Hz, Ar*H*$_{\text{Tol}}$), 7.02 (d, 8H, ^3J = 8.3 Hz, Ar*H*$_{\text{Tol}}$), 6.81 (s, 4H, Ar*H*), 6.80 (s, 4H, Ar*H*), 4.34 (d, 2H, ^2J = 12.6 Hz, ArC*H*$_2$Ar), 4.31 (d, 2H, ^2J = 12.6 Hz, ArC*H*$_2$Ar), 4.07 (q, 2H, ^3J = 7.0 Hz, OC*H*$_2$CH$_3$), 3.84-3.74 (m, 8H, OC*H*$_2$CH$_2$), 3.10 (d, 4H, ^2J = 12.6 Hz, ArC*H*$_2$Ar), 2.37 (t, 2H, ^3J = 7.0 Hz, C(O)C*H*$_2$), 2.21 (s, 12H, ArC*H*$_3$), 1.96-1.85 (m, 8H, C*H*$_2$), 1.73-1.65 (m, 2H, C*H*$_2$), 1.19 (t, 3H, ^3J = 7.0 Hz, OCH$_2$C*H*$_3$), 1.00-0.94 (m, 9H, CH$_2$C*H*$_3$);

^{13}C NMR (100MHz, CDCl$_3$), δ: 172.55, 152.41, 150.93, 137.21, 134.27, 133.42, 130.18, 128.99, 118.11, 117.95, 76.40, 74.30, 59.64, 33.47, 30.58, 28.96, 22.63, 21.19, 20.23, 14.05, 10.10;

MS(MALDI TOF) *m/z* 1295.2 [M$^+$Na].

calix[4]arene 46b



Reaction mixture was concentrated to 3 ml. Then MeOH was added, precipitate was filtered off and washed with MeOH. Calix[4]arene **7b** (80 %) was obtained as a white powder; mp 225-227°C;

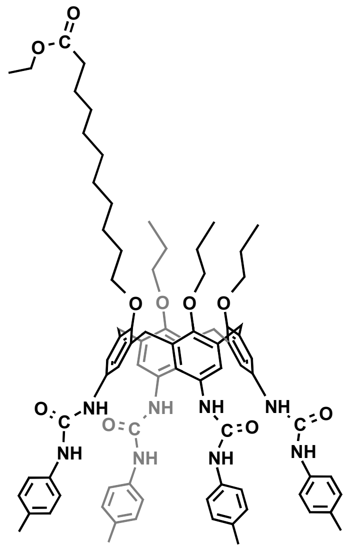
^{1}H NMR (300MHz, DMSO-d$_6$), δ: 10.19 (s, 4H, N*H*), 8.43 (s, 4H, N*H*), 7.82 (d, 8H, ^3J = 8.4 Hz, Ar*H*$_{\text{Tos}}$), 7.42 (d, 8H, ^3J = 8.4 Hz, Ar*H*$_{\text{Tos}}$), 6.61 (s, 4H, Ar*H*), 6.60 (s, 4H, Ar*H*), 4.21 (d, 2H, ^2J = 12.5 Hz, ArC*H*$_2$Ar), 4.18 (d, 2H, ^2J = 12.5 Hz, ArC*H*$_2$Ar), 4.02 (q, 2H, ^3J = 7.0 Hz, OC*H*$_2$CH$_3$), 3.74-3.64 (m, 8H, OC*H*$_2$CH$_2$), 3.10 (d, 4H, ^2J = 12.5 Hz, ArC*H*$_2$Ar), 2.40 (s, 12H, ArC*H*$_3$), 2.31 (t, 2H, ^3J = 7.4 Hz, C(O)C*H*$_2$), 1.86-1.74 (m, 8H, C*H*$_2$), 1.65-1.55 (m, 2H, C*H*$_2$), 1.16 (t, 3H, ^3J = 7.0 Hz, OCH$_2$C*H*$_3$), 0.92-0.86 (m, 9H, CH$_2$C*H*$_3$);

^{13}C NMR (100MHz, CDCl$_3$), δ: 172.45, 151.85, 151.80, 148.89, 143.69, 137.05, 134.29, 131.62, 129.38, 127.35, 118.87, 76.31, 74.23, 59.59, 33.33, 30.22, 28.80, 22.48, 21.05, 20.96, 13.98, 9.97;

MS ESI: mass peak was not observed due to decomposition

calix[4]arene 46c

The working up procedure as for **46a**. Calix[4]arene **46c** (95 %) was obtained as a light brown powder; mp 193-195°C;



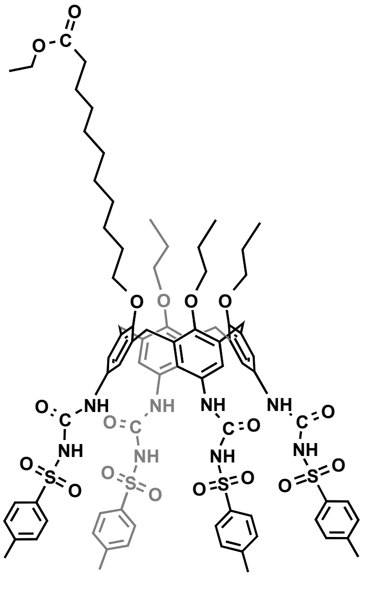
^{1}H NMR (400MHz, DMSO-d$_6$), δ: 8.22 (s, 2H, N*H*), 8.19 (s, 2H, N*H*), 8.17 (s, 2H, N*H*), 8.13 (s, 2H, N*H*), 7.23-7.19 (m, 8H, ArH_{Tol}), 7.02 (d, 8H, ^3J = 6.9 Hz, ArH_{Tol}), 6.81 (s, 4H, Ar*H*), 6.75 (s, 4H, Ar*H*), 4.33 (d, 4H, ^2J = 12.7 Hz, ArCH_2Ar), 4.04 (q, 2H, ^3J = 6.8 Hz, OCH_2CH$_3$), 3.82-3.75 (m, 8H, OCH_2CH$_2$), 3.10 (d, 4H, ^2J = 12.7 Hz, ArCH_2Ar), 2.26 (t, 2H, ^3J = 6.8 Hz, C(O)CH_2), 2.21 (s, 12H, ArCH_3), 1.96-1.85 (m, 8H, CH_2), 1.52-1.35 (m, 14H, CH_2), 1.17 (t, 3H, ^3J = 6.8 Hz, OCH$_2$CH_3), 0.96 (t, 9H, ^3J = 7.3 Hz, CH$_2$CH_3);

^{13}C NMR (100MHz, CDCl$_3$), δ: 172.75, 152.39, 151.05, 150.90, 150.84, 137.19, 134.39, 134.14, 133.42, 133.35, 130.14, 128.96, 118.08, 117.91, 76.43, 76.27, 74.78, 59.50, 33.40, 30.55, 29.47, 29.02, 28.92, 28.77, 28.54, 28.32, 25.58, 24.37, 22.67, 22.56, 20.21, 14.01, 10.16, 10.03;

MS(ESI) *m/z* (%) 1377.9 (100) [M$^+$Na].

calix[4]arene 46d

The working up procedure as for **46b**. Calix[4]arene **46d** (80 %) was obtained as a white powder; mp 211-213°C;



^{1}H NMR (400MHz, DMSO-d$_6$), δ: 10.18 (s, 4H, N*H*), 8.44 (s, 2H, N*H*), 8.40 (s, 2H, N*H*), 7.82 (d, 4H, ^3J = 8.2 Hz, ArH_{Tos}), 7.81 (d, 4H, ^3J = 8.2 Hz, ArH_{Tos}), 7.43 (d, 8H, ^3J = 8.2 Hz, ArH_{Tos}), 6.64 (s, 4H, Ar*H*), 6.58 (s, 4H, Ar*H*), 4.21 (d, 4H, ^2J = 12.9 Hz, ArCH_2Ar), 4.03 (q, 2H, ^3J = 7.0 Hz, OCH_2CH$_3$), 3.72-3.64 (m, 8H, OCH_2CH$_2$), 3.02 (d, 4H, ^2J = 12.9 Hz, ArCH_2Ar), 2.40 (s, 12H, ArCH_3), 2.24 (t, 2H, ^3J = 7.0 Hz, C(O)CH_2), 1.82-1.77 (m, 8H, CH_2), 1.46 (br s, 2H, CH_2), 1.27-1.21 (m, 12H, CH_2), 1.12 (t, 3H, ^3J = 7.0 Hz, OCH$_2$CH_3), 0.89-0.84 (m, 9H, CH$_2$CH_3);

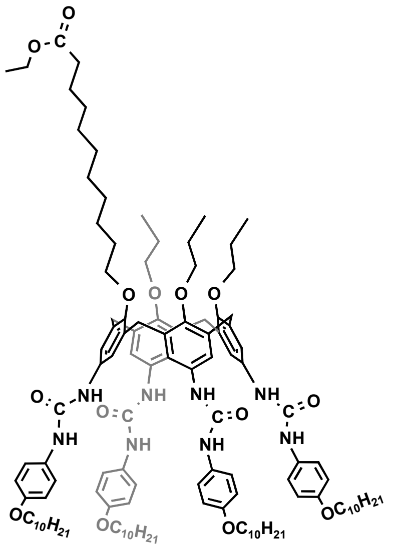
^{13}C NMR (100MHz, DMSO-d$_6$), δ: 173.27, 152.53, 152.34, 149.48, 144.21, 137.65, 134.97, 134.73, 132.16, 129.92, 127.89, 126.07, 119.43, 76.89, 76.74, 75.26, 60.03, 33.93, 31.14, 30.77, 29.88, 29.47, 29.40, 29.24, 29.04, 28.83, 26.00, 24.88, 23.09, 22.99, 21.51, 14.55, 10.58, 10.48;

MS(ESI) *m/z* (%) 1633.7 (100) [M$^+$Na].

calix[4]arene 46e

The tetraamine **45** (0.16 g, 0.20 mmol) was dissolved in THF (25 ml) and corresponding active urethane (0.35 g, 0.84 mmol) and Et_3N (0.2 ml) were added to the solution. The reaction mixture was refluxed for 12h, cooled down and then methanol was added. The precipitate was filtered off and washed with Et_2O. Calixarene **46e** (0.30 g, 79 %) was obtained as white powder; mp 162-164°C;

^{1}H NMR (400MHz, DMSO-d$_6$, 75°C), δ: 7.92 (s, 2H, N*H*), 7.91 (s, 2H, N*H*), 7.88 (s, 2H, N*H*), 7.86 (s, 2H, N*H*), 7.22 (d, 4H, ^3J = 9.0 Hz, Ar*H*$_{\mathrm{Ph}}$), 7.21 (d, 4H, ^3J = 9.0 Hz, Ar*H*$_{\mathrm{Ph}}$), 6.84-6.77 (m, 16H, Ar*H*$_{\mathrm{Ph}}$, Ar*H*), 4.40 (d, 4H, ^2J = 12.9 Hz, ArC*H*$_2$Ar), 4.07 (q, 2H, ^3J = 7.1 Hz, OC*H*$_2$CH$_3$), 3.95-3.82 (m, 16H, OC*H*$_2$), 3.10 (d, 4H, ^2J = 12.9 Hz, ArC*H*$_2$Ar), 2.26 (t, 2H, ^3J = 7.2 Hz, C(O)C*H*$_2$), 1.96-1.87 (m, 8H, C*H*$_2$), 1.72-1.65 (m, 8H, C*H*$_2$), 1.60-1.55 (m, 2H, C*H*$_2$), 1.43-1.38 (m, 8H, C*H*$_2$), 1.29 (br s, 60H, C*H*$_2$), 1.19 (t, 3H, ^3J = 7.1 Hz, OCH$_2$C*H*$_3$), 1.03-0.98 (m, 9H, (CH$_2$)$_2$C*H*$_3$), 0.89-0.86 (m, 12H, O(CH$_2$)$_9$C*H*$_3$);



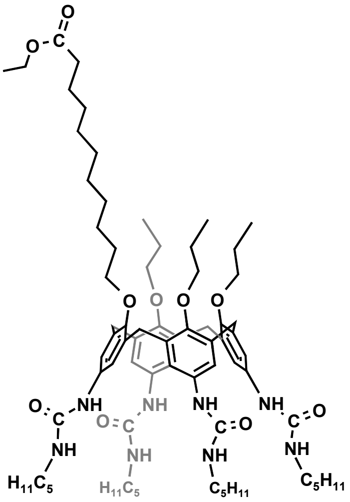
^{13}H NMR (400MHz, DMSO-d$_6$, 75°C), δ: 172.25, 153.44, 152.23, 150.74, 150.65, 133.83, 133.68, 133.04, 132.51, 119.70, 119.47, 118.07, 114.34, 75.81, 75.70, 74.13, 67.57, 58.86, 33.10, 30.61, 30.32, 28.95, 28.43, 28.30, 28.26, 28.12, 27.95, 25.14, 24.91, 23.87, 22.09, 22.03, 21.34, 13.44, 13.08, 9.58, 9.53;

MS(ESI) *m/z* (%) 1947.2 (19) [M$^+$Na].

calix[4]arene 46f

MeOH was added to the solution. The mixture of solvents was evaporated, the residue was treated with hexane and the precipitate was filtered off. Calix[4]arene **46f** (65 %) was obtained as a white powder; mp 230-232°C;

^{1}H NMR (400MHz, DMSO-d$_6$, 100°C), δ: 7.91 (s, 2H, N*H*), 7.88 (s, 2H, N*H*), 6.73 (s, 4H, Ar*H*), 6.68 (s, 4H, Ar*H*), 5.80-5.74 (m, 4H, N*H*), 4.28 (d, 4H, ^2J = 11.0 Hz, ArC*H*$_2$Ar),



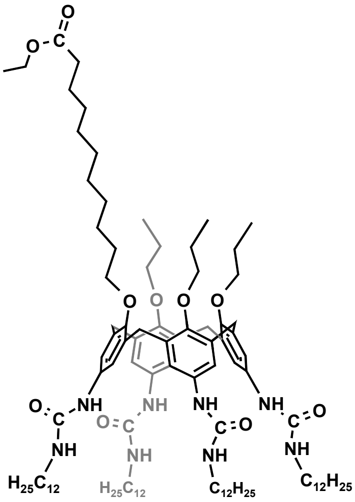
4.03 (q, 2H, ^3J = 7.0 Hz, OCH_2CH$_3$), 3.76-3.70 (m, 8H, OCH_2CH$_2$), 3.01-2.98 (m, 12H, ArCH_2Ar, NCH_2), 2.25 (t, 2H, ^3J = 7.2 Hz, C(O)CH_2), 1.91-1.85 (m, 8H, CH_2), 1.54-1.51 (m, 2H, CH_2), 1.36-1.27 (m, 36H, CH_2), 1.16 (t, 3H, ^3J = 7.0 Hz, OCH$_2$CH_3), 0.97-0.91 (m, 9H, (CH$_2$)$_2$CH_3), 0.88-0.85 (m, 12H, (CH$_2$)$_{11}$CH_3);

^{13}C NMR (100MHz, DMSO-d$_6$, 100°C), δ: 172.68, 155.07, 150.48, 150.33, 150.29, 134.11, 134.02, 133.87, 117.84, 76.34, 76.18, 74.70, 59.47, 38.85, 33.39, 30.60, 29.42, 29.02, 28.91, 28.75, 28.50, 28.30, 25.57, 24.34, 22.60, 22.49, 21.77, 13.98, 13.81, 10.11, 9.98;

MS(ESI) *m/z* (%) 1297.9 (100) [M$^+$Na].

calix[4]arene 46g

The product was precipitated directly from the reaction mixture with CH$_3$CN, washed with two times with CH$_3$CN and dried on the air. Calix[4]arene **46h** (85 %) was obtained as a yellow powder; mp 193-195°C;



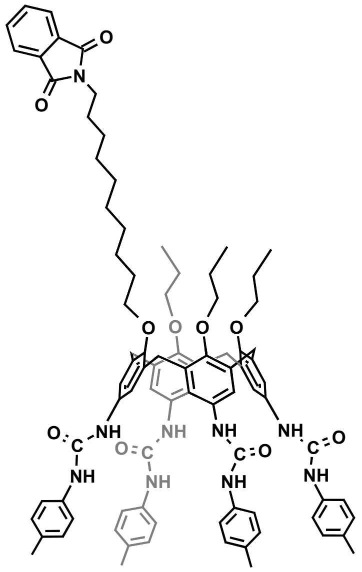
^{1}H NMR (400MHz, DMSO-d$_6$, 100°C), δ: 7.50 (m, 4H, NH), 6.71 (s, 4H, ArH), 6.69 (s, 4H, ArH), 5.55 (m, 4H, NH), 4.37 (d, 4H, ^2J = 12.9 Hz, ArCH_2Ar), 4.08 (q, 2H, ^3J = 7.0 Hz, OCH_2CH$_3$), 3.87-3.80 (m, 8H, OCH_2CH$_2$), 3.07-3.01 (m, 12H, ArCH_2Ar, NCH_2), 2.26 (t, 2H, ^3J = 7.2 Hz, C(O)CH_2), 1.93-1.84 (m, 8H, CH_2), 1.61-1.56 (m, 2H, CH_2), 1.42 (m, 8H, CH_2), 1.27 (m, 84H, CH_2), 1.20 (t, 3H, ^3J = 7.0 Hz, OCH$_2$CH_3), 1.01-0.97 (m, 9H, (CH$_2$)$_2$CH_3), 0.90-0.87 (m, 12H, (CH$_2$)$_{11}$CH_3);

^{13}C NMR (100MHz, DMSO-d$_6$, 100°C), δ: 171.80, 154.72, 150.26, 133.48, 133.38, 118.11, 75.51, 75.42, 73.82, 58.63, 38.64, 32.99, 30.45, 30.28, 29.28, 28.76, 28.20, 28.01, 27.80, 27.67, 25.71, 25.00, 23.71, 21.86, 21.80, 21.13, 13.21, 12.76, 9.34;

MS(ESI) *m/z* (%) 1691.4 (100) [M$^+$Na].

calix[4]arene 46h

MeOH (30 ml) was added to the solution. The solvents were evaporated. The crude product was precipitated from CHCl$_3$/Hexane and then from CHCl$_3$/MeOH. Calix[4]arene **46h** (85 %) was obtained as a yellow powder; mp 75-177°C;



^{1}H NMR (200MHz, DMSO-d$_6$), δ: 8.24 (s, 2H, N*H*), 8.21 (s, 2H, N*H*), 8.18 (s, 2H, N*H*), 8.16 (s, 2H, N*H*), 7.85-7.82 (m, 4H, Ar*H*$_{pht}$), 7.22 (d, 4H, ^3J = 8.3 Hz, Ar*H*$_{Tol}$), 7.21 (d, 4H, ^3J = 8.3 Hz, Ar*H*$_{Tol}$), 7.02 (d, 8H, ^3J = 8.3 Hz, Ar*H*$_{Tol}$), 6.84 (s, 4H, Ar*H*), 6.77 (s, 4H, Ar*H*), 4.33 (d, 4H, ^2J = 13.2 Hz, ArC*H*$_2$Ar), 3.80-3.70 (m, 8H, OC*H*$_2$), 3.56 (t, 2H, ^3J = 6.8 Hz, NC*H*$_2$), 3.10 (d, 4H, ^2J = 13.2 Hz, ArC*H*$_2$Ar), 2.21 (s, 12H, ArC*H*$_3$), 1.95-1.84 (m, 8H, C*H*$_2$), 1.61-1.56 (m, 2H, C*H*$_2$), 1.29 (br s, 12H, C*H*$_2$), 0.99-0.92 (m, 9H, CH$_2$C*H*$_3$);

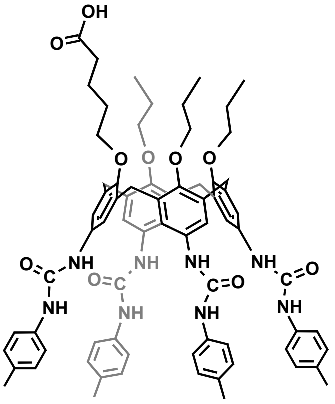
^{13}C NMR (100MHz, DMSO-d$_6$), δ: 168.37, 152.94, 151.60, 151.39, 137.74, 134.94, 134.80, 134.67, 133.99, 133.89, 132.05, 130.69, 129.51, 123.41, 118.63, 118.46, 76.96, 76.80, 75.32, 37.83, 31.90, 29.98, 29.52, 29.40, 29.31, 28.99, 28.34, 26.68, 26.07, 23.20, 23.09, 20.76, 10.69, 10.57;

MS(FD) *m/z* (%) 1428.6 (5.6) [M$^+$].

The general procedure for synthesis of 47

A solution of NaOH (4.6 mmol) in the mixture of MeOH/H$_2$O (6 ml/2 ml) was added to the solution of calixarene **7** (0.46 mmol) in THF (30 ml). The reaction mixture was stirred 6 h at room temperature and acetic acid was added to neutralize the excess of NaOH. The reaction mixture was concentrated to ~5-10 ml and then water was added.

calix[4]arene 47a



The precipitate was filtered off, washed with MeOH (5 ml) and calix[4]arene **47a** (65-90 %) was obtained as a white powder; mp > 230°C decompose;

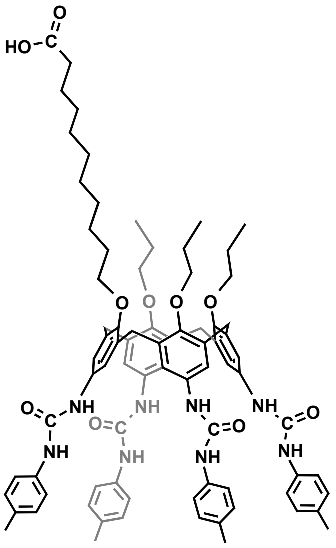
^{1}H NMR (400MHz, DMSO-d$_6$), δ: 12.07 (s, 1H, COO*H*), 8.22 (s, 4H, N*H*), 8.16 (s, 4H, N*H*), 7.22 (d, 8H, ^3J = 8.2 Hz, Ar*H*$_{Tol}$), 7.02 (d, 8H, ^3J = 8.2 Hz, Ar*H*$_{Tol}$), 6.81 (s, 4H, Ar*H*), 6.80 (s, 4H, Ar*H*), 4.34 (d, 2H, ^2J = 12.6 Hz, ArC*H*$_2$Ar), 4. 32 (d, 2H, ^2J = 12.6 Hz, ArC*H*$_2$Ar), 3.82-3.72 (m, 8H, OC*H*$_2$), 3.10 (d, 4H, ^2J = 12.6 Hz, ArC*H*$_2$Ar), 2.30 (t, 2H, ^3J = 7.4 Hz, C(O)C*H*$_2$), 2.21 (s, 12H, ArC*H*$_3$), 1.96-1.85 (m, 8H, C*H*$_2$), 1.73-1.65 (m, 2H, C*H*$_2$), 0.97 (t, 9H, ^3J = 7.4 Hz, CH$_2$C*H*$_3$);

^{13}C NMR (100MHz, DMSO-d$_6$), δ: 174.15, 152.42, 150.95, 137.20, 134.28, 133.40, 130.18, 128.98, 118.13, 117.95, 76.42, 74.40, 33.62, 30.58, 29.07, 22.64, 21.20, 20.23, 10.13.

MS(MALDI TOF) *m/z* 1267.4 [M$^+$].

calix[4]arene 47c

The oil was formed. Then the water was diluted with MeOH and the mixture was left for 30 min in the ultrasonic bath. The precipitate was filtered off, washed with MeOH (5 ml) and dried on the air. Calix[4]arene **47c** (90 %) was obtained as a white powder; mp > 190°C decompose;



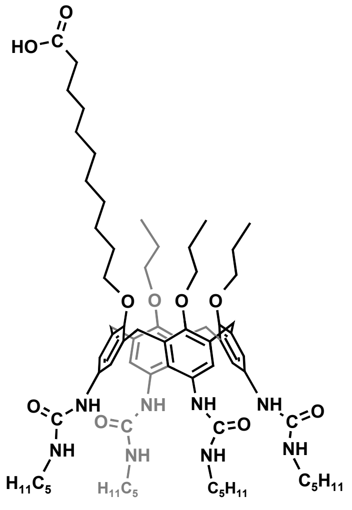
^{1}H NMR (400MHz, DMSO-d$_6$), δ: 12.07 (s, 1H, COO*H*), 8.22 (s, 2H, N*H*), 8.19 (s, 2H, N*H*), 8.16 (s, 2H, N*H*), 8.12 (s, 2H, N*H*), 7.23-7.19 (m, 8H, Ar*H*$_{\mathrm{Tol}}$), 7.02 (d, 8H, ^3J = 6.9 Hz, Ar*H*$_{\mathrm{Tol}}$), 6.84 (s, 4H, Ar*H*), 6.77 (s, 4H, Ar*H*), 4.33 (d, 4H, ^2J = 12.6 Hz, ArC*H*$_2$Ar), 3.82-3.71 (m, 8H, OC*H*$_2$), 3.10 (d, 4H, ^2J = 12.6 Hz, ArC*H*$_2$Ar), 2.21 (s, 12H, ArC*H*$_3$), 2.18 (t, 2H, ^3J = 7.2 Hz, C(O)C*H*$_2$), 1.96-1.85 (m, 8H, C*H*$_2$), 1.49-1.25 (m, 14H, C*H*$_2$), 1.00-0.95 (m, 9H, CH$_2$C*H*$_3$);

^{13}C NMR (100MHz, DMSO-d$_6$), δ: 174.86, 152.90, 157.57, 151.37, 137.71, 134.90, 134.64, 133.93, 133.86, 130.64, 129.46, 118.63, 118.41, 7693, 7678, 7529, 3407, 3368, 3106, 2999, 2950, 2917, 2898, 2610, 2493, 2318, 2072, 1068, 1054;

MS(ESI) *m/z* (%) 1349.8 (100) [M$^+$Na].

calix[4]arene 47f

The precipitate was filtered off and washed with acetone. Calix[4]arene **47f** (70 %) was obtained as a light beige powder; mp 199-201°C;

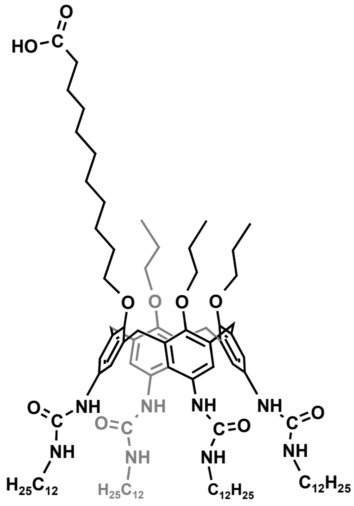


^{1}H NMR (400MHz, DMSO-d$_6$), δ: 7.92 (s, 2H, N*H*), 7.88 (s, 2H, N*H*), 6.73 (s, 4H, Ar*H*), 6.67 (s, 4H, Ar*H*), 5.79-5.75 (m, 4H, N*H*), 4.28 (d, 4H, ^2J = 12.1 Hz, ArC*H*$_2$Ar), 3.77-3.69 (m, 8H, OC*H*$_2$CH$_2$), 3.01-2.97 (m, 12H, ArC*H*$_2$Ar, NHC*H*$_2$), 2.18 (t, 2H, ^3J = 7.8 Hz, C(O)C*H*$_2$), 1.91-1.86 (m, 8H, C*H*$_2$), 1.49-1.25 (m, 38H, C*H*$_2$), 0.97-0.92 (m, 9H, (CH$_2$)$_2$C*H*$_3$), 0.88-0.85 (m, 12H, (CH$_2$)$_{11}$C*H*$_3$);

^{13}C NMR (100MHz, DMSO-d$_6$), δ: 174.36, 155.09, 150.52, 150.36, 150.31, 134.16, 134.02, 133.87, 117.86, 76.3976.20, 74.73, 39.44, 33.57, 30.63, 29.44, 29.05, 28.97, 28.83, 28.65, 28.51, 25.59, 24.42, 22.63, 22.51, 21.79, 13.85, 10.16, 10.02;

MS(ESI) *m/z* (%) 1269.9 (100) [M$^+$Na].

calix[4]arene 47g



The precipitate was filtered off and washed with acetone. Calix[4]arene **47g** (85 %) was obtained as a light beige powder; mp 158-160°C;

^{1}H NMR (400MHz, DMSO-d$_6$), δ: 7.68 (s, 2H, N*H*), 7.66 (s, 2H, N*H*), 6.71 (s, 4H, Ar*H*), 6.68 (s, 4H, Ar*H*), 5.67 (m, 4H, N*H*), 4.33 (d, 4H, ^2J = 12.9 Hz, ArCH_2Ar), 3.84-3.76 (m, 8H, OCH_2CH$_2$), 3.02 (m, 12H, ArCH_2Ar, NHCH_2), 2.18 (t, 2H, ^3J = 7.2 Hz, C(O)CH_2), 1.91-1.85 (m, 8H, CH_2), 1.53 (m, 2H, CH_2), 1.40 (m, 8H, CH_2), 1.27 (m, 84H, CH_2), 0.99-0.94 (m, 9H, (CH$_2$)$_2$CH_3), 0.89-0.85 (m, 12H, (CH$_2$)$_{11}$CH_3);

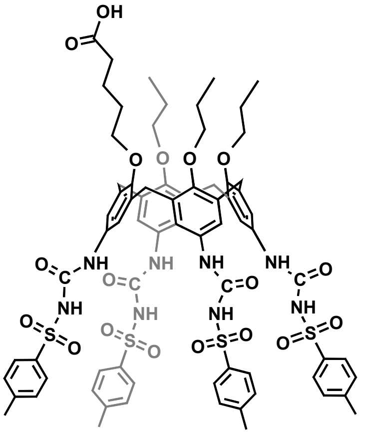
^{13}C NMR (100MHz, DMSO-d$_6$), δ: 174.67, 155.50, 151.30, 151.22, 134.65, 134.50, 118.92, 76.76, 76.44, 75.05, 39.66, 34.45, 31.66, 31.37, 30.27, 29.94, 29.41, 29.27, 29.21, 29.10, 29.03, 26.87, 26.15, 25.07, 23.08, 23.01, 22.38, 14.11, 10.61, 10.54;

MS(ESI) *m/z* (%) 1663.3 (100) [M$^+$Na].

The general procedure for synthesis of 47b,d

A solution of LiOHxH$_2$O (2.56 mmol) in the mixture of MeOH/H$_2$O (8.5 ml/2.5 ml) was added to the solution of calixarene **7** (0.41 mmol) in THF (25 ml). The reaction mixture was stirred for 12 h and acetic acid was added to neutralize the excess of LiOH.

calix[4]arene 47b



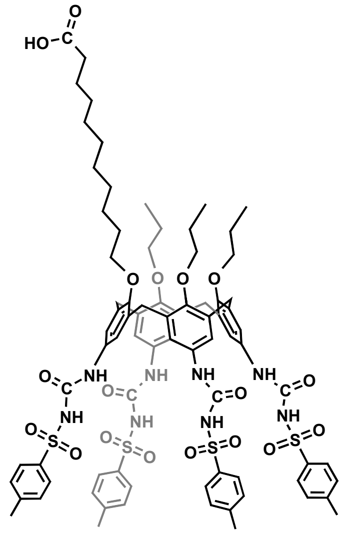
CHCl$_3$ (40 ml) and H$_2$O (40 ml) were added to the solution, organic layer was separated, washed with water (2x15 ml) and solvents were evaporated. The residue was diluted with water. The precipitate was filtered off and washed with MeOH (5 ml). Calix[4]arene **47b** (60 %) was obtained as a white powder; mp 217-219°C;

^{1}H NMR (400MHz, DMSO-d$_6$), δ: 12.00 (br s, 1H, COO*H*), 10.13 (br s, 4H, N*H*), 8.42 (s, 4H, N*H*), 7.82 (d, 8H, $^3J = 8.2$ Hz, ArH_{Tos}), 7.42 (d, 8H, $^3J = 8.2$ Hz, ArH_{Tos}), 6.61 (s, 4H, Ar*H*), 6.60 (s, 4H, Ar*H*), 4.20 (d, 4H, $^2J = 12.9$ Hz, ArCH_2Ar), 3.72-3.67 (m, 8H, OCH_2), 3.02 (d, 4H, $^2J = 12.9$ Hz, ArCH_2Ar), 2.40 (s, 12H, ArCH_3), 2.31 (t, 2H, $^3J = 7.1$ Hz, C(O)CH_2), 1.83-1.77 (m, 8H, CH_2), 1.62-1.55 (m, 2H, CH_2), 0.89 (t, 9H, $^3J = 7.1$ Hz, CH_2CH_3);

calix[4]arene 47d

The reaction mixture was concentrated to ~5ml and the product was precipitated with water and dried on the air. Calix[4]arene **47d** (80 %) was obtained as a white powder; mp > 230°C decompose;

^{1}H NMR (400MHz, DMSO-d_6), δ: 11.95 (br s, 1H, COO*H*), 10.15 (s, 4H, N*H*), 8.43 (s, 2H, N*H*), 8.39 (s, 2H, N*H*), 7.82 (d, 4H, $^3J = 7.8$ Hz, ArH_{Tos}), 7.81 (d, 4H, $^3J = 7.8$ Hz, ArH_{Tos}), 7.42 (d, 8H, $^3J = 7.8$ Hz, ArH_{Tos}), 6.64 (s, 4H, Ar*H*), 6.57 (s, 4H, Ar*H*), 4.21 (d, 4H, $^2J = 12.9$ Hz, ArCH_2Ar), 3.72-3.64 (m, 8H, OCH_2), 3.02 (d, 4H, $^2J = 12.9$ Hz, ArCH_2Ar), 2.40 (s, 12H, ArCH_3), 2.16 (t, 2H, $^3J = 7.4$ Hz, C(O)CH_2), 1.83 -1.77 (m, 8H, CH_2), 1.46 (br s, 2H, CH_2), 1.27-1.21 (m, 12H, CH_2), 0.92-0.86 (m, 9H, CH_2CH_3);

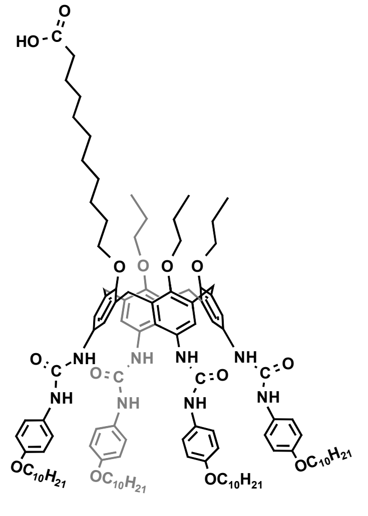


^{13}C NMR (100MHz, DMSO-d_6), δ: 174.36, 151.73, 151.67, 149.59, 143.33, 137.57, 134.39, 134.13, 131.94, 131.84, 129.27, 127.31, 118.86, 76.32, 76.16, 74.69, 33.55, 30.26, 29.35, 28.96, 28.92, 28.78, 28.62, 28.43, 25.48, 24.39, 22.56, 22.45, 20.96, 10.07, 9.94;

MS(ESI) *m/z* (%) 1605.7 (9) [M^+Na], 1408.72 (13) [M^+-Et-Tos+Na], 1211.68 (3) [M^+-Et-2Tos+Na], 1015.67 (100) [M^+-Et-3Tos+Na].

calix[4]arene 47e

The precipitate was filtered off, washed with MeOH and calix[4]arene **47e** (70 %) was obtained as a white powder; mp 171-173°C;



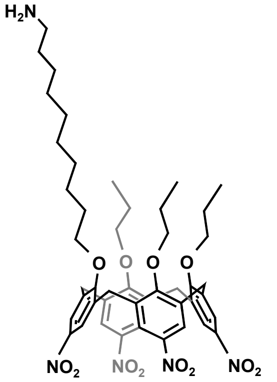
^{1}H NMR (400MHz, DMSO-d_6, 75°C), δ: 8.01 (br s, 4H, N*H*), 7.95 (br s, 4H, N*H*), 7.23 (m, 8H, ArH_{Ph}), 6.78 (m, 16H, ArH_{Ph}, Ar*H*), 4.39 (d, 4 H, $^2J = 12.5$ Hz, ArCH_2Ar), 3.90 (m, 16H, OCH_2), 3.10 (d, 4H, $^2J = 12.5$ Hz, ArCH_2Ar), 1.19 (m, 2H, C(O)CH_2), 1.90 (m, 8H, CH_2), 1.68 (m, 8H, CH_2), 1.55 (m, 2H, CH_2), 1.28 (m, 68H, CH_2), 1.00 (m, 9H, $(CH_2)_2CH_3$), 0.87 (m, 12H, $O(CH_2)_9CH_3$);

^{13}H NMR (400MHz, DMSO-d_6, 75°C), δ: 173.80, 153.37, 152.24, 150.71, 150.62, 133.82, 133.67, 133.04, 132.55, 119.64, 119.41, 118.08, 114.29, 75.80, 75.69, 67.51, 33.48, 30.62, 30.31, 28.96, 28.41, 28.26, 28.12, 27.97, 25.14, 24.92, 24.08, 22.10, 21.35, 13.09, 9.60, 9.53;

MS(ESI) *m/z* (%) 1919.1 (54) [M^+Na].

calix[4]arene 48a

Calix[4]arene **44c** (2.00 g, 1.96 mmol) was dissolved in EtOH (80 ml) and hydrazine monohydrate (18.67 g (18.13 ml), 0.36 mol) was added. The solution was refluxed for 4 h and concentrated to 50 ml. The product started to precipitate and solution was cooled down to 30°C. Precipitate was filtered off, washed with water (3x10 ml) and ethanol (2x10 ml) and dried. Monoamine **48a** (1.30 g, 75%) was obtained as a orange powder; mp 227-229°C;



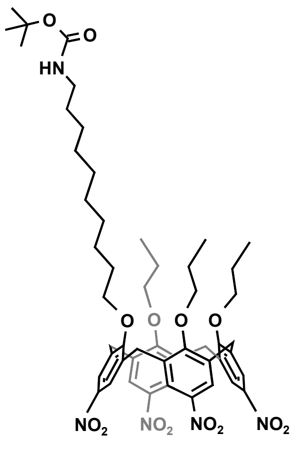
^{1}H NMR (400MHz, $CDCl_3$), δ: 7.57 (s, 4H, ArH), 7.55 (s, 4H, ArH), 4.51 (d, 4H, $^2J = 14.2$ Hz, ArCH_2Ar), 3.99-3.92 (m, 8H, OCH_2), 3.39 (d, 4H, $^2J = 14.2$ Hz, ArCH_2Ar), 2.68 (t, 2H, $^3J = 6.8$ Hz, NH_2CH_2), 1.92-1.87 (m, 8H, CH_2), 1.58 (br s, 2H, NH_2), 1.43-1.29 (br s, 14H, CH_2), 1.01 (t, 9H, $^3J = 7.3$ Hz, CH_2CH_3);

^{13}C NMR (100MHz, $CDCl_3$), δ: 161.61, 161.60, 142.88, 135.39, 135.37, 124.02, 123.99, 77.69, 76.22, 42.09, 33.45, 31.11, 30.09, 29.61, 29.53, 29.43, 26.86, 25.92, 23.23, 23.21, 10.33;

MS(FD) *m/z* (%) 886.9 (54.8) [M^+], 1771 (100) [$2M^+$].

calix[4]arene 48b

Calix[4]arene **48a** (1.30 g, 1.47 mmol) was dissolved in $CHCl_3$ (50 ml) and Boc-anhydride (0.42 g, 1.91 mmol) was added. The solution was refluxed for 8 h, concentrated to 5 ml and hexane (25 ml) was added. The precipitate was filtered off, washed with hexane and dried. Calix[4]arene **48b** (1.29 g, 89 %) was obtained as a yellow powder; mp 105-107°C;



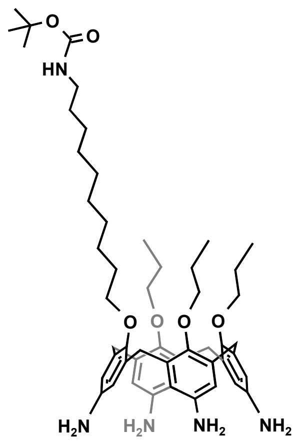
^{1}H NMR (400MHz, $CDCl_3$), δ: 7.57 (s, 4H, ArH), 7.56 (s, 4H, ArH), 4.52 (br s, 1H, NH), 4.52 (d, 2H, $^2J = 14.2$ Hz, ArCH_2Ar), 4.50 (d, 2H, $^2J = 14.2$ Hz, ArCH_2Ar), 3.99-3.92 (m, 8H, OCH_2), 3.39 (d, 4H, ^2J = 14.2 Hz, ArCH_2Ar), 3.10-3.06 (m, 2 H, NHCH_2), 1.93-1.86 (m, 8H, CH_2), 1.44-1.28 (m, 14H, CH_2), 1.43 (s, 9H, OC(CH_3)$_3$), 1.01 (t, 9H, ^3J = 7.4 Hz, CH$_2$CH_3);

^{13}C NMR (100MHz, CDCl$_3$), δ: 161.67, 161.65, 161.61, 142.90, 135.38, 124.02, 77.70, 76.23, 40.62, 31.12, 30.10, 29.60, 29.54, 29.50, 29.22, 28.41, 27.41, 26.76, 25.93, 23.25, 23.22, 10.15, 10.13;

MS(FD) *m/z* (%) 886.9 (100) [M$^+$-Boc]

calix[4]arene 49.

Calix[4]arene **48b** (1g, 1.01 mmol) was dissolved in the mixture of toluene/ethanol (25 ml/ 5ml) and hydrogenated during 14 h at 40°C in the presence of the Raney-nickel. The progress of reaction was monitored by TLC in THF. After reaction is finished the catalyst was filtered off and washed with THF (2x10 ml). The combined organic layers were evaporated under reduced pressure. Calix[4]arene **49** (0.87 g, 98 %) was obtained as a brown powder; mp 115-117°C;



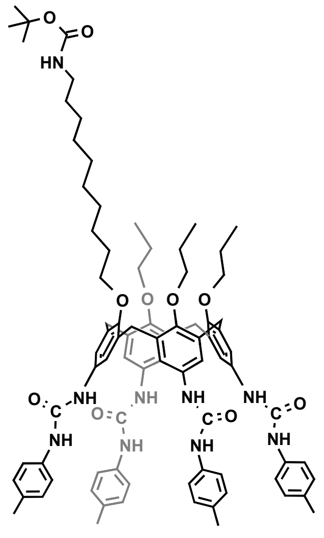
^{1}H NMR (400MHz, CDCl$_3$), δ: 6.06 (s, 4H, ArH), 6.03 (s, 4H, ArH), 4.47 (br s, 1H, NH), 4.30 (d, 4H, ^2J = 13.2 Hz, ArCH_2Ar), 3.77-3.68 (m, 8H, OCH_2), 3.10-3.06 (m, 2H, NHCH_2), 2.90 (d, 4H, ^2J = 13.2 Hz, ArCH_2Ar), 2.71 (br s, 8H, NH_2), 1.88-1.82 (m, 8H, CH_2), 1.43 (s, 9H, OC(CH_3)$_3$), 1.33 (s, 4H, CH_2), 1.28 (s, 10H, CH_2), 0.94 (t, 9H, ^3J = 7.3 Hz, CH$_2$CH_3);

^{13}C NMR (100MHz, CDCl$_3$), δ: 155.98, 150.15, 140.18, 135.72, 135.57, 115.79, 76.68, 75.02, 40.65, 31.15, 30.08, 29.69, 29.56, 29.30, 28.42, 26.82, 26.20, 23.11, 10.36;

MS(FD) *m/z* (%) 865.9 (100) [M$^+$].

calix[4]arene 50a

See procedure for synthesis of **46c** Calix[4]arene **50a** (87 %) was obtained as a yellow powder; mp > 247°C decompose;



^{1}H NMR (400MHz, DMSO-d$_6$), δ: 8.22 (s, 2H, NH), 8.19 (s, 2H, NH), 8.16 (s, 2H, NH), 8.12 (s, 2H, NH), 7.22 (d, 4H, ^3J = 7.3 Hz, ArH_{Tol}), 7.20 (d, 4H, ^3J = 7.3 Hz, ArH_{Tol}), 7.02 (d, 8H, ^3J = 7.3 Hz, ArH_{Tol}), 6.84 (s, 4H, ArH), 6.78 (s, 4H, ArH), 6.71 (s, 1H, NHBoc), 4.34 (d, 4H, ^2J = 11.7 Hz, ArCH_2Ar), 3.81-3.75 (m, 8H, OCH_2), 3.10 (d, 4H,

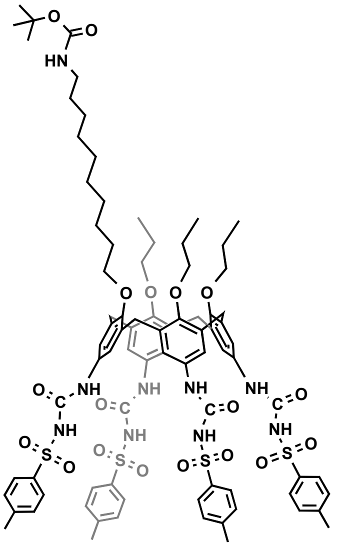
^{2}J = 11.7 Hz, ArCH_2Ar), 2.90-2.87 (m, 2H, NHCH_2), 2.21 (s, 12H, ArCH_3), 1.95-1.86 (m, 8H, CH_2), 1.40-1.26 (m, 23H, CH_2, OC(CH_3)$_3$), 1.01-0.95 (m, 9H, CH$_2$CH_3);

^{13}C NMR (100MHz, DMSO-d$_6$), δ: 155.47, 152.40, 151.07, 150.92, 150.86, 137.21, 134.40, 134.15, 133.45, 133.37, 130.18, 128.98, 118.10, 117.93, 77.13, 76.44, 76.29, 74.80, 30.56, 29.50, 29.40, 29.10, 28.99, 28.65, 28.16, 26.18, 25.62, 22.68, 22.57, 20.22, 10.17, 10.04;

calix[4]arene 50b

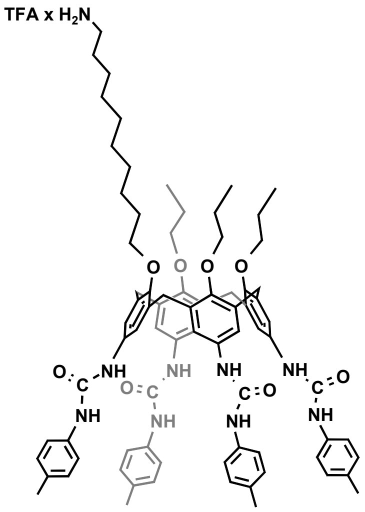
See procedure for synthesis of **46c** Calix[4]arene **50b** (60 %) having 10 % of urethane was obtained as a yellow powder;

^{1}H NMR (400MHz, DMSO-d$_6$), δ: 10.19 (s, 2H, N*H*), 10.15 (s, 2H, N*H*), 8.43 (s, 2H, N*H*), 8.39 (s, 2H, N*H*), 7.82 (d, 4H, ^{3}J = 7.8 Hz, ArH_{Tos}), 7.81 (d, 4H, ^{3}J = 7.8 Hz, ArH_{Tos}), 7.42 (d, 8H, ^{3}J = 7.8 Hz, ArH_{Tos}), 6.71 (s, 1H, N*H*Boc), 6.64 (s, 4H, Ar*H*), 6.57 (s, 4H, Ar*H*), 4.20 (d, 4H, ^{2}J = 12.7 Hz, ArCH_2Ar), 3.71-3.65 (m, 8H, OCH_2), 3.01 (d, 4H, ^{2}J = 12.7 Hz, ArCH_2Ar), 2.89-2.84 (m, 2H, NHCH_2), 2.40 (s, 12H, ArCH_3), 1.80 (m, 8H, CH_2), 1.35 (s, 9H, OC(CH_3)$_3$), 1.43-1.26 (m, 23H, CH_2, OC(CH_3)$_3$), 1.40-1.26 (m, 14H, CH_2, OC(CH_3)$_3$), 0.92-0.87 (m, 9H, CH$_2$CH_3);



MS(MALDI TOF) *m/z* 1656.0 [M$^+$].

calix[4]arene 51a x **TFA**.



The tetratolylurea **50a** (0.30 g, 0.21 mmol) was dissolved in CH$_2$Cl$_2$ (15 ml) and trifluoroacetic acid (15 ml) was added to the solution. The reaction mixture was stirred for 2 h at room temperature and evaporated to dryness. The Et$_2$O (15 ml) was added and precipitate was filtered off. Calix[4]arene **51a** (0.27 g, 89 %) was obtained as a yellow powder; mp > 247°C decompose;

^{1}H NMR (400MHz, DMSO-d$_6$), δ: 8.31 (s, 2H, N*H*), 8.28 (s, 2H, N*H*), 8.24 (s, 2H, N*H*), 8.20 (s, 2H, N*H*), 7.68 (br s, 3H, NH_3^+), 7.22 (m, 8H, ArH_{Tol}), 7.01 (m, 8H, ArH_{Tol}), 6.83 (s, 4H, Ar*H*), 6.80 (s, 2H, Ar*H*), 6.78 (s, 2H, Ar*H*), 4.34 (d, 4H, ^{2}J = 12.5 Hz, ArCH_2Ar), 3.81-3.75 (m, 8H, OCH_2), 3.10 (d, 4H, $^2J = 12.5$ Hz, ArC*H*$_2$Ar), 2.81-2.75 (m, 2H, NH$_2$C*H*$_2$), 2.21 (s, 12H, ArC*H*$_3$), 1.97-1.89 (m, 8H, C*H*$_2$), 1.52-1.28 (m, 14H, C*H*$_2$), 1.01-0.95 (m, 9H, CH$_2$C*H*$_3$);

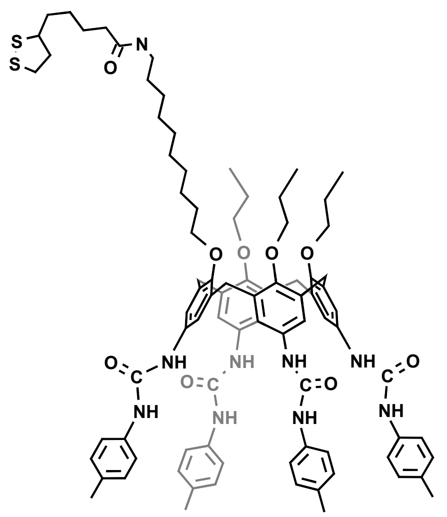
^{13}C NMR (100MHz, DMSO-d$_6$), δ: 158.32 (q, $^2J_{CF} = 32$ Hz), 152.43, 151.05, 150.88, 137.22, 134.37, 134.17, 133.46, 133.42, 130.17, 128.98, 118.14 117.94, 76.42, 76.28, 74.77, 30.58, 29.50, 29.07, 28.98, 28.81, 28.48, 26.94, 25.74, 25.63, 22.69, 22.59, 20.23, 10.21, 10.09;

MS(ESI) *m/z* (%) 1322.7 (100) [M$^+$-TFA+Na].

calix[4]arene 52

The tetratolylurea **51a** (0.23 g, 0.16 mmol) was dissolved in THF (20 ml) and several drops of Et$_3$N were added. The solution was stirred at room temperature during 1 h and fresh prepared α-lipoic acide anhydride (0.13 g, 0.33 mmol) was added. (Preparation of anhydride: the α-lipoic acid (0.14 g, 0.68 mmol) and DCC (0.07 g, 0.34 mmol) were dissolved in benzene (1 ml), stirred for 1h and precipitate formed was filtered off. The filtrate was added to tolylurea). The reaction mixture was stirre d during 14 h at room temperature and evaporated to dryness (do not heat more than 50°C). The crude product was precipitated from CHCl$_3$/CH$_3$CN. The calix[4]arene **52** (0.15 g, 63 %) was obtained as a yellow powder; mp > 50°C decompose;

^{1}H NMR (200MHz, DMSO-d$_6$), δ: 8.24 (s, 2H, N*H*), 8.21 (s, 2H, N*H*), 8.18 (s, 2H, N*H*), 8.14 (s, 2H, N*H*), 7.72 (br s, 1H, CH$_2$C(O)N*H*), 7.21 (d, 4H, $^3J = 8.3$ Hz, Ar*H*$_{Tol}$), 7.20 (d, 4H, $^3J = 8.3$ Hz, Ar*H*$_{Tol}$), 7.00 (d, 8H, $^3J = 8.3$ Hz, Ar*H*$_{Tol}$), 6.82 (s, 4H, Ar*H*), 6.76 (s, 4H, Ar*H*), 4.32 (d, 4H, $^2J = 12.2$ Hz, ArC*H*$_2$Ar), 3.80-3.75 (m, 8H, OC*H*$_2$), 3.65-3.55 (m, 2H, C*H*$_2$), 3.13-2.98 (m, 8H, ArC*H*$_2$Ar, CH$_2$), 2.43-2.34 (m, 1H, C*H*$_{(cycle)}$), 2.20 (s, 12H, ArC*H*$_3$), 2.06-1.82 (m, 8H, C*H*$_2$), 1.63-1.27 (m, 22H, C*H*$_2$), 1.01-0.94 (m, 9H, CH$_2$C*H*$_3$);

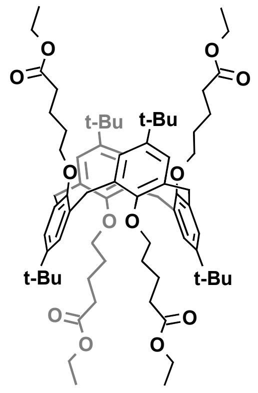


^{1}H NMR (400MHz, CDCl$_3$, integration is given for a dimeric species), δ: 9.31 (s, 8H, N*H*), 7.71 (d, 16H, $^3J = 7.8$ Hz, Ar*H*$_{Tol}$), 7.62 (s, 8H, Ar*H*), 7.14 (d, 16H, $^3J = 7.8$ Hz, Ar*H*$_{Tol}$), 7.00 (s, 8H, N*H*), 5.89 (s, 8H, Ar*H*), 4.28 (br s, 2H, N*H*), 4.21 (d, 8H, $^2J = 11.6$ Hz, ArC*H*$_2$Ar), 3.63 (br s, 20H, OC*H*$_2$, C(O)C*H*$_2$), 3.31-3.07 (m, 12H, C*H*$_2$), 2.82 (d, 8H, $^2J = 11.6$ Hz, ArC*H*$_2$Ar), 2.44-2.37 (m, 2H, C*H*), 2.26 (s, 24H, ArC*H*$_3$), 2.16 (br s, 12H, C*H*$_2$), 1.87 (br s, 12H, C*H*$_2$), 1.64 (br s, 8H, C*H*$_2$), 1.46 (br s, 8H, C*H*$_2$), 1.15-1.13 (m, 16H, C*H*$_2$), 0.91 (t, 18H, $^3J = 7.2$ Hz, CH$_2$C*H*$_3$);

MS(MALDI TOF) *m/z* 1487.1 [M$^+$].

calix[4]arene 59

Calix[4]arene **58** (1.00 g, 1.10 mmol) was dissolved in CH$_3$CN (100 ml) and Cs$_2$CO$_3$ (5.40 g, 16.57 mmol) was added to the solution. The mixture was refluxed for 0.5 h and ethyl 5-bromovalerate (3.50 g, 16.57 mmol) was added to the suspension. The refluxing was continued during 6 days. Then the solvent was evaporated and chloroform (100 ml) was added to the residue. Organic layer was washed with 1N HCl, water, dried over MgSO$_4$ and filtered. The filtrate was evaporated and the crude product was crystallized from CH$_3$CN. Calix[4]arene **59** was obtained as a white powder (0.53 g, 42 %); mp 209-211°C;



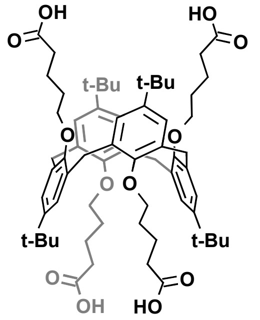
^{1}H NMR (200MHz, CDCl$_3$), δ: 6.93 (s, 8H, Ar*H*), 4.15 (q, 8H, $^3J = 7.3$ Hz, OC*H*$_2$CH$_3$), 3.69 (s, 8H, ArC*H*$_2$Ar), 3.40 (t, 8H, $^3J = 7.8$ Hz, OC*H*$_2$CH$_2$), 2.21 (t, 8H, $^3J = 8.30$ Hz, C(O)C*H*$_2$), 1.55-1.43 (m, 8H, C*H*$_2$), 1.31-1.21 (m, 56H, CH$_2$, OCH$_2$C*H*$_3$, C(C*H*$_3$)$_3$);

^{13}C NMR (100MHz, CDCl$_3$), δ: 173.35, 154.55, 143.43, 132.99, 126.16, 70.25, 60.25, 38.77, 34.12, 33.84, 31.66, 29.24, 21.34, 14.23;

MS(FD) *m/z* (%) 1160.6 (100) [M$^+$].

calix[4]arene 60

A solution of NaOH (0.25 g, 6.25 mmol) in MeOH (6 ml) and H$_2$O (2 ml) was added to the solution of calixarene **59** (0.45 g, 0.39 mmol) in THF (30 ml). The reaction mixture was stirred 12 h at room temperature. After that 1N HCl (5 ml) was added to neutralize the excess of NaOH. Then reaction mixture was concentrated to ~10 ml under reduced pressure and the mixture of CHCl$_3$/THF = 2:1 (40 ml) was added. The solution was washed with brine (3x15 ml), dried over MgSO$_4$, filtered and solvent was evaporated. Calix[4]arene **60** (0.39 g, 95 %) was obtained as a white powder; mp 280-282°C;



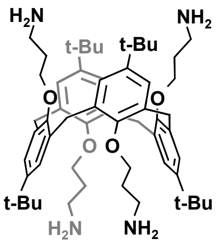
^{1}H NMR (400MHz, CDCl$_3$), δ: 11.98 (s, 4H, COO*H*), 6.94 (s, 8H, Ar*H*), 3.71 (s, 8H, ArC*H*$_2$Ar), 3.40 (t, 8H, $^3J = 7.4$ Hz, OC*H*$_2$), 2.06 (t, 8H, $^3J = 7.8$ Hz, C(O)C*H*$_2$), 1.37-1.32 (m, 8H, C*H*$_2$), 1.22 (s, 36H, C(C*H*$_3$)$_3$), 1.17-1.07 (m, 8H, C*H*$_2$);

^{13}C NMR (100MHz, $CDCl_3$), δ: 174.60, 154.68, 143.14, 133.23, 125.90, 69.86, 38.60, 34.06, 33.98, 31.85, 28.98, 21.36;

MS(FD) *m/z* (%) 1048.6 (100) [M^+].

calix[4]arene 62

Calix[4]arene **61** (0.62 g, 0.44 mmol) and hydrazine monohydrate (7.21 g (7 ml), 144 mmol) were refluxed in EtOH (45 ml) during 4h. After that reaction mixture was concentrated to ~10 ml and water (30 ml) was added to the solution. Precipitate was filtered off, washed with water and dried. Calix[4]arene **62** (0.32 g, 100 %) was obtained as a white powder; mp > 246°C decompose;



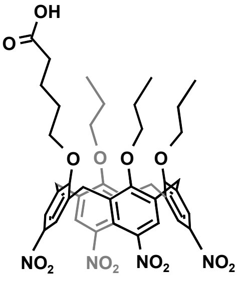
^{1}H NMR (400MHz, $CDCl_3$), δ: 6.99 (s, 8H, Ar*H*), 3.80 (s , 8H, ArC*H*$_2$Ar), 3.45 (s, 8H, OC*H*$_2$), 2.50 (s, 8H, NH_2C*H*$_2$), 1.52-1.38 (ws, 16H, N*H*$_2$, C*H*$_2$), 1.30 (s, 18H, C(C*H*$_3$)$_3$), 1.29 (s, 18H, C(C*H*$_3$)$_3$);

^{13}C NMR (100MHz, $CDCl_3$), δ: 154.94, 143.78, 133.02, 125.93, 68.80, 39.48, 39.21, 33.96, 33.21, 31.67;

MS(FD) *m/z* (%) 877.8 (100) [M^+].

calix[4]arene 63a

See general procedure of synthesis of **47**. Calix[4]arene **63a** (100 %) was obtained as a white powder; mp 251-253°C;



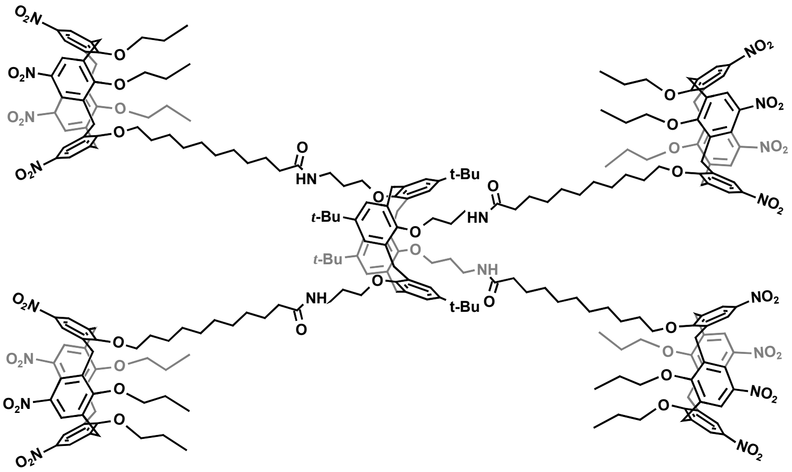
^{1}H NMR (400MHz, DMSO-d_6), δ: 12.11 (br s, 1H, COO*H*), 7.67 (s, 4H, Ar*H*), 7.62 (s, 4H, Ar*H*), 4.37 (d, 4H, $^2J = 13.7$ Hz, ArC*H*$_2$Ar), 3.98 (m, 8H, OC*H*$_2$), 3.69 (d, 4H, $^2J = 13.7$ Hz, ArC*H*$_2$Ar), 2.29 (t, 2H, $^3J = 7.1$ Hz, C(O)C*H*$_2$), 1.90-1.83 (m, 8 H, C*H*$_2$), 1.68-1.61 (m, 2H, C*H*$_2$), 0.99-0.95 (m, 9H, C*H*$_3$);

^{13}C NMR (100MHz, DMSO-d_6), δ: 174.55, 162.35, 162.23, 142.46, 136.14, 124.22, 124.12, 77.63, 75.77, 33.84, 30.21, 29.56, 23.25, 21.42, 10.39;

MS(FD) *m/z* (%) 831.7 (100) [M^+].

penta-calix[4]arene 64

Calixarene **63a** (0.1 g, 0.12 mmol) was dissolved in THF (10 ml) and oxalyl chloride (0.03 g (0.02 ml), 0.24 mmol) was added to the solution. The reaction mixture was stirred for 2 h at 60 °C and then solvent was evaporated under reduced pressure. The residue diluted with 10



ml of dry toluene and the solvent was evaporated again. The crude product **63b** was dried for 1 h in the vacuum (50 mm/Hg) at 60 °C. After that the solution of calixarene **62** (0.023 g, 0.027 mmol) and Et$_3$N in THF (10 ml) was added to **63b** and reaction mixture was stirred for 12 h at room temperature. After that the solvent was evaporated under reduced pressure, the residue was dissolved in CHCl$_3$ and precipitated with MeOH. The precipitate was washed with water (3 times), MeOH and reprecipitated from CHCl$_3$/MeOH. Penta-calixarene **64** was obtained as a yellow powder; mp > 300°C decompose;

^{1}H NMR (400MHz, DMSO-d$_6$), δ: 7.67-7.71 (m, 36H, Ar*H*, N*H*), 6.92 (s, 8H, Ar*H*$_{\mathrm{alt}}$), 4.37-4.33 (m, 16H, ArC*H*$_2$Ar), 3.97-3.92 (m, 32H, OC*H*$_2$), 3.71-3.63 (m, 24H, ArC*H*$_2$Ar, ArC*H*$_2$Ar$_{\mathrm{alt}}$), 3.31 (br s, 8H, OC*H*$_{2\mathrm{alt}}$), 2.97 (br s, 8H, C*H*$_2$NH), 2.14 (m, 8H, C(O)C*H*$_2$), 1.84 (m, 32H, C*H*$_2$), 1.63 (m, 6H, C*H*$_2$), 1.41 (m, 6H, C*H*$_2$), 1.26-1.14 (m, 4H, C*H*$_2$), 1.14, (s, 36H, C(C*H*$_3$)$_3$), 0.98-0.92 (m, 9H, C*H*$_3$).

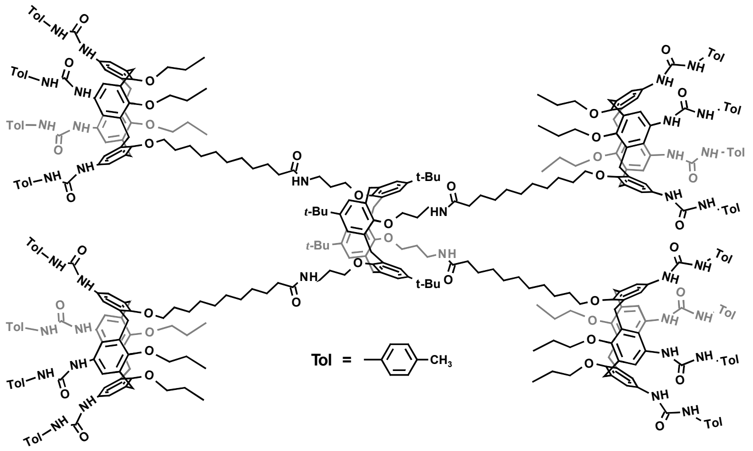
The general procedure for synthesis of penta-calix[4]arene 65

The acid **47c-g** (0.069 mmol) and PyBOP (0.069 mmol) were dissolved in DMF for peptide synthesis grade (2 ml). The solution was stirred 1 h at room temperature and then amine **62** (0.017 mmol) and triethylamine (0.15 mmol) in DMF (1 ml) were added. The stirring was continued for 12 h at room temperature and 2 h at 30°C. After that the reaction mixture was diluted with water (7 ml), the precipitate was filtered off, washed with MeOH and dried.

penta-calix[4]arene 65a

The product was additionally washed with chloroform. Calix[4]arene **65a** (62 %) was obtained as a white powder; mp > 335°C decompose;

^{1}H NMR (400MHz, DMSO-d$_6$), δ: 8.22 (s, 8H, N*H*), 8.19 (s, 8H, N*H*), 8.16 (s, 8H, N*H*), 8.13 (s, 8H, N*H*), 7.65 (s, 4H, N*H*), 7.21 (m, 32H, Ar*H*$_{\mathrm{Tol}}$), 7.01 (m, 32H, Ar*H*$_{\mathrm{Tol}}$), 6.94 (s, 8H, Ar*H*$_{\mathrm{alt}}$), 6.83 (s, 16H, Ar*H*), 6.78 (s, 16 H, Ar*H*), 4.3 1 (br s, 16H, ArC*H*$_2$Ar), 3.73 (br s, 40H, OC*H*$_2$, ArC*H*$_2$Ar$_{\mathrm{(alt)}}$), 3.20 (br s, 8H, OC*H*$_{2\ \mathrm{alt}}$), 3.09 (br s, 16H, ArC*H*$_2$Ar), 2.90 (br s, 8H, NHCH_2), 2.21 (s, 48H, ArCH_3), 2.05 (br s, 8H, C(O)CH_2), 1.91 (br s, 32H, CH_2), 1.49 (br s, 8H, CH_2), 1.36-1.27 (m, 56H, CH_2), 1.19 (s, 36H, C(CH_3)$_3$), 0.94 (br s, 36H, CH$_2$CH_3).



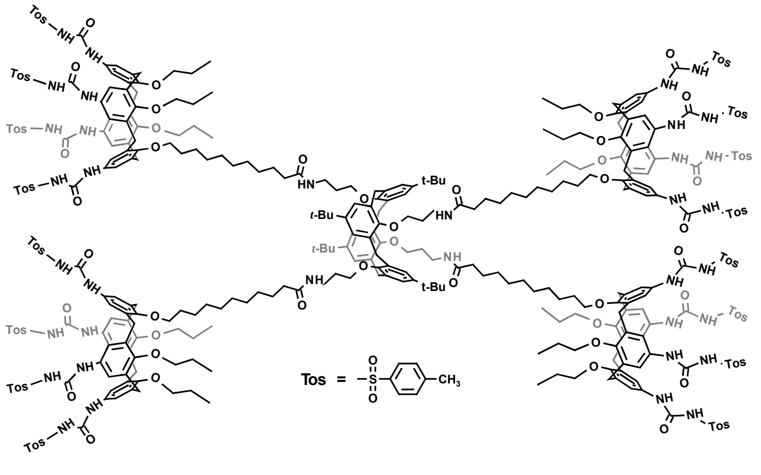
tetrakis heterodimer 65a•16$_4$

^{1}H NMR (400MHz, CDCl$_3$), δ: **N*H***: 10.52 (s, 16H), 8.03 (s, 16H), 8.02 (s, 16H), 7.62 (s, 16H); **Ar*H*$_{\text{Tos}}$**: 8.12 (m, 32H), 7.39 (m, 32H); **Ar*H*$_{\text{Tol}}$**: 7.57 (d, 32H, $^3J = 7.9$ Hz), 6.79 (d, 32H, $^3J = 7.9$ Hz); **Ar*H*$_{\text{cal}}$**: 7.87 (s, 16H), 7.04 (s, 16H), 6.86 (s, 16H), 4.88 (s, 16H); **Ar*H*$_{\text{1,3alt}}$**: 6.94 (s, 8H); **ArC*H*$_2$Ar**: 4.54 (d, 16H, $^2J = 11.2$ Hz), next 16H are overlapped with broad signal at 3.88, next 16H are overlapped with multiplet at 3.68-3.34, 2.53-2.42 (m, 16H); **ArC*H*$_2$Ar$_{\text{1,3alt}}$**: 8H are overlapped with broad signal at 3.88; **OC*H*$_2$**: 3.88 (br s, 56H (from them 32H belong to described group), 3.68-3.34 (m, 48H (from them 32H belong to described group)); **OCH$_{2(1,3\text{ alt})}$**: 3.19 (br s, 8H); **NHC*H*$_2$**: 2.93 (br s, 8H); **C(O)C*H*$_2$**: 8H are overlapped with singlet at 2.05; **ArC*H*$_{3\text{Tos}}$**: 2.48 (s, 48H); **ArC*H*$_{3\text{Tol}}$**: 2.05 (s, 56H (from them 48H belong to described group); **C*H*$_2$**: 1.64 (br s, 100H), 1.32-1.21 (m, 92H); **C(C*H*$_3$)$_3$:** 1.23 (s, 36H); **CH$_2$C*H*$_3$**: 1.00 (t, 36H, $^3J = 7.3$ Hz), 0.88 (t, 48H, $^3J = 7.3$ Hz).

penta-calix[4]arene 65b

Calix[4]arene **65b** (70 %) was obtained as a white powder; mp>270°C decompose;

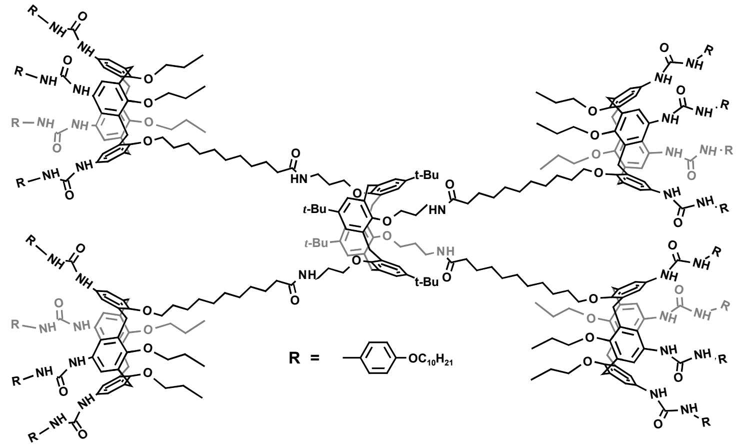
^{1}H NMR (400MHz, DMSO-d$_6$, 50°C), δ: 7.91 (s, 16H, NH), 7.75 (m, 32H, ArH_{Tos}), 7.51 (br s, 4 H, NH), 7.20 (m, 32H, ArH_{Tos}), 6.95-6.88 (m, 40H, ArH_{alt}, ArH), 4.24 (br s, 16H, ArCH_2Ar), 3.68 (br s, 40H, OCH_2, ArCH_2Ar$_{\text{alt}}$), 3.20 (under the sygnal of water, 8H,



OC*H*$_{2\,\text{alt}}$), 2.93-2.86 (m, 24H, ArC*H*$_2$Ar, NHC*H*$_2$), 2.34 (s, 48H, ArC*H*$_3$), 2.04 (br s, 8H, C(O)C*H*$_2$), 1.87 (br s, 32H, C*H*$_2$), 1.48-1.26 (m, 64H, C*H*$_2$), 1.19 (s, 36H, C(C*H*$_3$)$_3$), 0.93 (m, 36H, CH$_2$C*H*$_3$).

penta-calix[4]arene 65c

Then washed with Et$_2$O. Calix[4]arene **9c** (80 %) was obtained as a white powder; mp>240°C decompose;



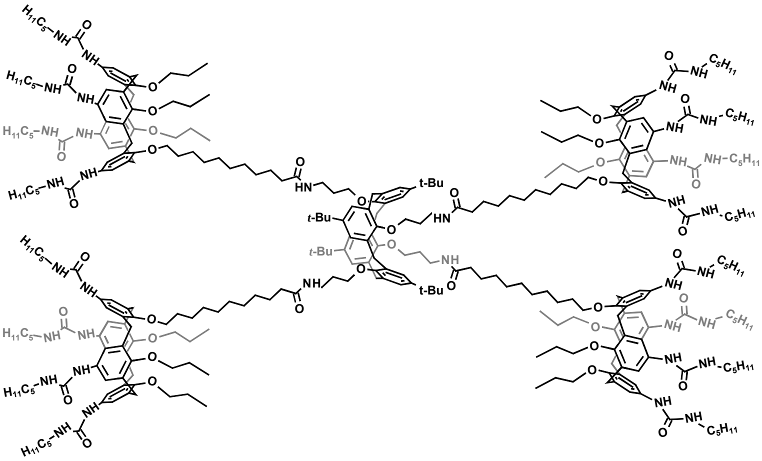
^{1}H NMR (400MHz, DMSO-d$_6$, 100 °C), δ: 7.87 (s, 16H, N*H*), 7.82 (s, 16H, N*H*), 7.23-7.20 (m, 32H, Ar*H*$_{\text{Tol}}$), 7.20 (br s, 4H, N*H*), 6.97 (s, 8H, Ar*H*$_{\text{alt}}$), 6.81-6.76 (br s, 64H, Ar*H*$_{\text{Tol}}$, Ar*H*), 4.04 (d, 16H, ^2J = 12.1 Hz, ArC*H*$_2$Ar), 3.91-3.81 (m, 64H, OC*H*$_2$), 3.67 (s, 8H, ArC*H*$_2$Ar$_{\text{alt}}$), 3.41 (br s, 8H, OC*H*$_{2\,\text{alt}}$), 3.09 (d, 16H, ^2J = 12.1 Hz, ArC*H*$_2$Ar), 3.02 (br s, 8H, NHC*H*$_2$), 2.07 (br s, 8H, C(O)C*H*$_2$), 1.92-1.88 (m, 32H, C*H*$_2$), 1.68 (br s, 32H, C*H*$_2$), 1.53 (m, 16H, C*H*$_2$), 1.41-1.29 (m, 272H, C*H*$_2$), 1.23 (s, 36H, C(C*H*$_3$)$_3$), 0.99 (br s, 36H, (CH$_2$)$_2$C*H*$_3$), 0.94 (br s, 48H, O(CH$_2$)$_9$C*H*$_3$).

tetrakis heterodimer 65c•16$_4$

^{1}H NMR (400MHz, CDCl$_3$), δ: **N*H***: 10.54 (s, 8H), 10.51 (s, 8H), 7.95 (s, 32H), next 16H are overlapped with multiplet at 7.58; **Ar*H*$_{\text{Tos}}$**: 8.13 (d, 32H, ^3J = 7.4 Hz), 7.39 (br s, 32H); **Ar*H*$_{\text{Tol}}$**: 7.58 (m, 48H, from them 32H belong to described group), 6.54 (d, 32H, ^3J = 7.8 Hz); **Ar*H*$_{\text{cal}}$**: 7.86 (s, 16H), 7.03 (s, 16H), 6.89 (s, 16H), 5.01 (s, 16H); **Ar*H*$_{1,3\text{alt}}$**: 6.95 (s, 8H); **ArC*H*$_2$Ar**: 4.55 (d, 16H, ^2J = 11.0 Hz), next 16H are overlapped with multiplet at 3.95-3.80, 3.36 (d, 16H, ^2J = 11.0 Hz), 2.57 (d, 16H, ^2J = 11.0 Hz); **ArC*H*$_2$Ar$_{1,3\text{alt}}$**: 8H are overlapped with multiplet at 3.95-3.80; **OC*H*$_2$**: 3.95-3.80 (m, 56H (from them 32H belong to described group), 3.68-3.62 (m, 32H), 3.47-3.44 (m, 32H); **OCH$_{2\,1,3\text{alt}}$**: 3.17 (br s, 8H); **NHC*H*$_2$**: 2.93 (br s, 8H); **C(O)C*H*$_2$**: 2.15 (br s, 8H); **ArC*H*$_{3\text{Tos}}$**: 2.46 (s, 48H); **C*H*$_2$**: 2.04 (br s, 24H), 1.76 (br s, 32H), 1.60 (br s, 64H), 1.26 (br s, 364H (from them 328H belong to described group)); **C(CH_3)$_3$**: 36H are overlapped with broad signal at 1.26; **CH_2CH_3**: 1.01 (t, 36H, ^3J = 6.7 Hz), 0.91-0.86 (m, 96H).

penta-calix[4]arene 65d

Calix[4]arene **65d** (70 %) was obtained as a white powder; mp 196-198°C;

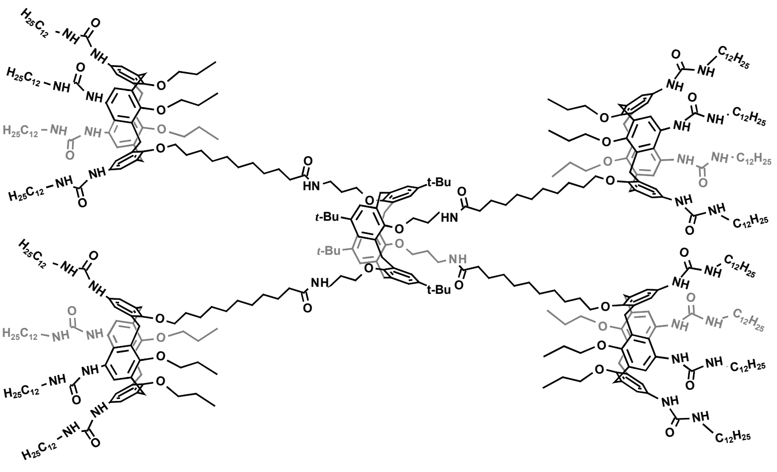


^{1}H NMR (400MHz, DMSO-d_6, 75 °C), δ: 7.65-7.63 (m, 16H, NH), 7.32 (br s, 4H, NH), 6.96 (s, 8H, ArH_{alt}), 6.71 (s, 16H, ArH), 6.68 (s, 16H, ArH), 5.63-5.62 (m, 16H, NH), 4.33 (d, 16H, ^2J = 12.1 Hz, ArCH_2Ar), 3.81-3.76 (m, 32H, OCH_2), 3.67 (s, 8H, ArCH_2Ar$_{alt}$), 3.38 (m, 8H, OC$H_{2\,alt}$), 3.01 (m, 56H, ArCH_2Ar, C(O)NHCH_2, NHCH_2), 2.07 (t, ^3J = 7.0 Hz, 8H, C(O)CH_2), 2.06-1.86 (m, 32H, CH_2), 1.52 (m, 16H, CH_2), 1.41-1.28 (m, 144H, CH_2), 1.22 (s, 36H, C(CH_3)$_3$), 0.96 (m, 36H, (CH$_2$)$_2$CH_3), 0.87 (m, 48H, (CH$_2$)$_4$CH_3).

Penta-calix[4]arene 65e

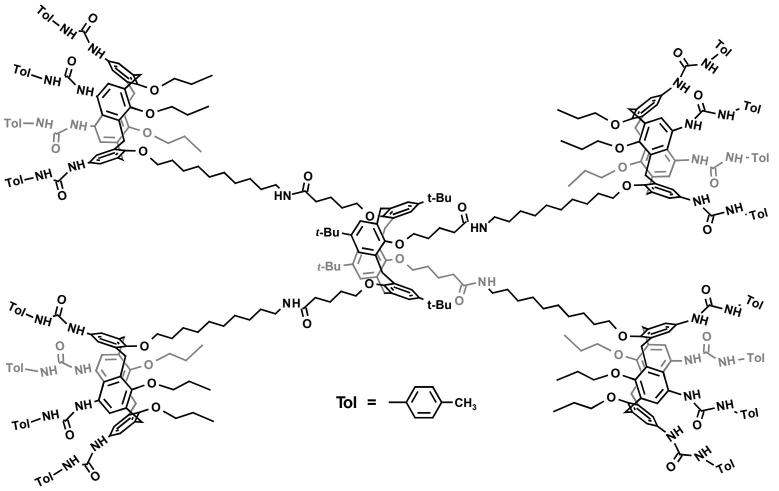
Calix[4]arene **65e** (66 %) was obtained as a white powder; mp 180-183°C;

^{1}H NMR (400MHz, DMSO-d_6, 100 °C), δ: 7.47 (br s, 16H, NH), 7.09 (br s, 4H, NH), 6.98 (s, 8H, ArH_{alt}), 6.70-6.68 (m, 32H, ArH), 5.55 (br s, 16H, NH), 4.36 (d, 16H, ^2J = 12.1 Hz, ArCH_2Ar), 3.83-3.80 (m, 32H, OCH_2), 3.69 (s, 8H, ArCH_2Ar$_{alt}$), 3.44 (m, 8H, OC$H_{2\,alt}$), 3.04 (m, 56H, ArCH_2Ar, C(O)NHCH_2, NHCH_2), 2.07 (t, ^3J = 7.4 Hz, 8H, C(O)CH_2), 1.88-1.76 (m, 32H, CH_2), 1.54 (m, 16H, CH_2), 1.41-1.28 (m, 368H, CH_2), 1.24 (s, 36H, C(CH_3)$_3$), 0.98 (m, 36H, (CH$_2$)$_2$CH_3), 0.88 (m, 48H, (CH$_2$)$_{11}$CH_3).



Penta-calix[4]arene 65f

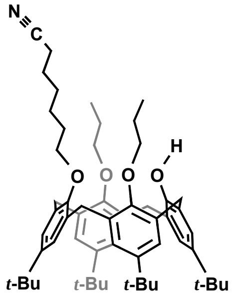
Calix[4]arene **65f** (73 %) was obtained as a white powder; mp > 270°C decompose;



^{1}H NMR (400MHz, DMSO-d$_6$), δ: 8.22 (s, 8H, N*H*), 8.19 (s, 8H, N*H*), 8.15 (s, 8H, N*H*), 8.12 (s, 8H, N*H*), 7.70 (s, 4H, N*H*), 7.21 (m, 32H, Ar*H*$_{\mathrm{Tol}}$), 7 .01 (m, 32H, Ar*H*$_{\mathrm{Tol}}$), 6.90 (s, 8H, Ar*H*$_{\mathrm{alt}}$), 6.83 (s, 16H, Ar*H*), 6.78 (s, 16H, Ar*H*), 4.33 (br s, 16H, ArC*H*$_2$Ar), 3.76 (br s, 32H, OC*H*$_2$) 3.64 (br s, 8H, ArC*H*$_2$Ar$_{\mathrm{alt}}$), 3.20 (br s, 8H, OC*H*$_{2\ \mathrm{alt}}$), 3.06 (m, 24H, ArC*H*$_2$Ar, NHC*H*$_2$), 2.20 (s, 48H, ArC*H*$_3$), 2.05 (br s, 8H, C(O)C*H*$_2$), 1.91 (br s, 32H, C*H*$_2$), 1.37-1.25 (m, 72H, C*H*$_2$), 1.19 (s, 36H, C(C*H*$_3$)$_3$), 0.96 (br s, 36H, CH$_2$C*H*$_3$).

calix[4]arene 68

Calix[4]arene **67** (4.00 g, 5.46 mmol) was dissolved in hot DMF (70 ml) and after that the Ba(OH)$_2$x8H$_2$O (4.00 g, 12.68 mmol), the BaO (3.75 g, 24.46 mmol) and the 7-bromoheptanitrile (3.12 g (2.46 ml), 16.39 mmol) were added. Reaction mixture was stirred overnight at 60°C. The suspension was diluted with water (50 ml) and extracted with CHCl$_3$ (4x25 ml). Chloroform layer was separated, washed with 1M HCl (2x25 ml), water, dried over MgSO$_4$ and filtered. The filtrate was concentrated to ~10 ml and yellow oil was formed. After that MeOH (200 ml) was added and evaporated till the crystals appeared. This mixture was left overnight in a freezer (-14°C) and filtered. The filtration afforded **68** (3.2 g, 70 %) as a white powder; mp 123-125°C;



^{1}H NMR (400MHz, CDCl$_3$), δ: 7.13 (s, 2H, Ar*H*), 7.05 (s, 2H, Ar*H*), 6.50 (s, 2H, Ar*H*), 6.49 (s, 2H, Ar*H*), 5.59 (s, 1H, O*H*), 4.34 (d, 2H, $^2J = 12.9$ Hz, ArC*H*$_2$Ar), 4.31 (d, 2H, $^2J = 12.9$ Hz, ArC*H*$_2$Ar), 3.89 (t, 2H, $^3J = 7.9$ Hz, OC*H*$_2$CH$_2$), 3.80-3.70 (m, 4H, OC*H*$_2$CH$_2$), 3.22 (d, 2H, $^2J = 12.9$ Hz, ArC*H*$_2$Ar), 3.17 (d, 2H, $^2J = 12.9$ Hz, ArC*H*$_2$Ar), 2.38 (t, 2H, $^3J = 7.3$ Hz, C*H*$_2$CN), 2.38-2.29 (m, 2H, C*H*$_2$), 1.98-1.81 (m, 4H, C*H*$_2$), 1.79-1.72 (m, 2H, C*H*$_2$), 1.63-1.55 (m, 2H, C*H*$_2$), 1.45-1.38 (m, 2H, C*H*$_2$), 1.33 (s, 9H, C(C*H*$_3$)$_3$), 1.32 (s, 9H, C(C*H*$_3$)$_3$), 1.09 (t, 6H, $^3J = 7.3$ Hz, CH$_2$C*H*$_3$), 0.81 (s, 18H, C(C*H*$_3$)$_3$);

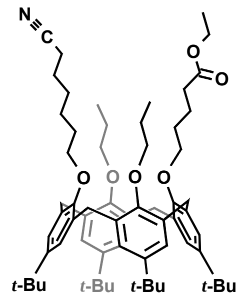
^{13}C NMR (100MHz, $CDCl_3$), δ: 153.89, 151.66, 150.71, 145.65, 145.07, 141.44, 135.99, 132.12, 131.79, 129.41, 125.66, 125.02, 124.80, 124.66, 119.78, 77.83, 74.44, 34.14, 33.85, 33.65, 31.77, 31.70, 31.31, 31.06, 29.01, 28.91, 25.70, 25.23, 23.50, 17.20, 10.94;

MS(FD) *m/z* (%) 842.8 (100) [M^+].

calix[4]arene 69

A slurry of calix[4]arene **68** (7.40 g, 8.78 mmol) and NaH (0.32 g, 13.18 mmol) in DMF (200 ml) was stirred for 1 h at room temperature and then ethyl ester of 5-bromopentanoic acid (2.73 g (2.07 ml), 13.18 mmol) was added. The stirring was continued for 1 day. During this period the progress of reaction was controlled by TLC (THF/Hexane = 1/10). After reaction was complete acetic acid (25 ml) was added to the reaction mixture. Solution almost immediately reduced it's color. Then DMF was evaporated to dryness. The residue was diluted with water and extracted with chloroform (2x40 ml). The organic layer was washed with water (3x200 ml), dried over $MgSO_4$ and filtered. The filtrate was evaporated. After that MeOH (50 ml) was added and the oil was formed. This mixture was putted in refrigerator (1°C) and after 2 h MeOH was decanted and new portion of MeOH (30 ml) was added to the oil. The flask was putted in refrigerator (4°C) again and after 8 h the oil was crystallized. The precipitate was filtered off and washed with methanol. It affords calixarene **69** (6.4 g, 75 %) as a light yellow powder; mp 106-108°C;

^{1}H NMR (400MHz, $CDCl_3$), δ: 6.76 (s, ArH, 8H), 4.36 (d, 2H, ^{2}J = 12.5 Hz, ArCH_2Ar), 4.34 (d, 2H, ^{2}J = 12.5 Hz, ArCH_2Ar), 4.14 (q, 2H, ^{3}J = 7.4 Hz, OC$H_2$$CH_3$), 3.88-3.77 (m, 8H, OC$H_2$$CH_2$), 3.10 (d, 4H, ^{2}J = 12.5, ArCH_2Ar), 2.40-2.35 (m, 4H, CH_2), 2.02-1.97 (m, 8H, CH_2), 1.79-1.67 (m, 4H, CH_2), 1.58-1.41 (m, 4H, CH_2), 1.25 (t, 3H, ^{3}J = 7.0 Hz, OCH_2CH_3), 1.06 (s, 36H, C(CH_3)$_3$), 0.99 (t, 6H, ^{3}J = 7.4 Hz, CH_2CH_3);

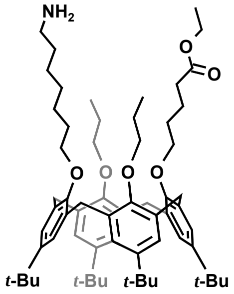


^{13}C NMR (100MHz, $CDCl_3$), δ: 174.98, 153.59, 144.33, 144.25, 133.73, 124.91, 74.84, 74.56, 60.26, 34.37, 33.79, 31.43, 31.06, 29.92, 29.67, 28.88, 25.57, 25.50, 23.37, 21.68, 17.13, 14.26, 10.36;

MS(FD) *m/z* (%) 969.8 (100) [M^+].

calix[4]arene 70

Calix[4]arene **69** (1.13 g, 1.16 mmol) was dissolved in toluene (40 ml) and hydrogenated during 10 h at 40°C in the presence of the Raney-nickel*. Then catalyst was filtered off and the solvent was removed in vacuum. Product **70** was purified by column chromatography (THF/Hexane=1/3, followed by THF) and obtained as a yellow oil (1.13 g, 75 %);

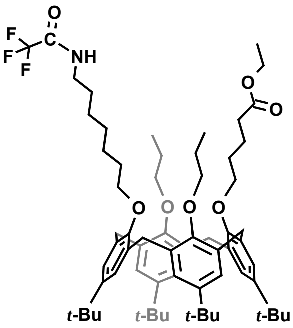


^{1}H NMR (300MHz, CDCl$_3$); δ: 6.78 (s, 4H, Ar*H*), 6.74 (s, 4H, Ar*H*), 4.39 (d, 2H, ^2J = 12.5 Hz, ArC*H*$_2$Ar), 4.37 (d, 2H, ^2J = 12.5 Hz, ArC*H*$_2$Ar), 4.13 (q, 2H, ^3J = 7.4 Hz, OC*H*$_2$CH$_3$), 3.89-3.78 (m, 8H, OC*H*$_2$CH$_2$), 3.1 0 (d, 4H, ^2J = 12.5, ArC*H*$_2$Ar), 2.72 (t, 2H, ^3J = 7.4 Hz, NH$_2$C*H*$_2$), 2.38 (t, 2H, ^3J = 7.4 Hz, C(O)C*H*$_2$), 2.07-1.97 (m, 8H, C*H*$_2$), 1.78-1.70 (m, 2H, C*H*$_2$), 1.52-1.47 (m, 2H, C*H*$_2$), 1.39 (s, 6H, C*H*$_2$), 1.25 (t, 3H, ^3J = 7.4 Hz, OCH$_2$C*H*$_3$), 1.07 (s, 18H, C(C*H*$_3$)$_3$), 1.05 (s, 18H, C(C*H*$_3$)$_3$), 0.98 (t, 6H, ^3J = 7.4 Hz, CH$_2$C*H*$_3$);

MS(FD) *m/z* (%) 973.8 (100) [M$^+$].

calix[4]arene 71

Calix[4]arene **70** (4.0 g, 4.11 mmol) was dissolved in THF (60 ml) and trifluoroacetic acid anhydride (1.72 g (1.16 ml), 8.21 mmol) was added to the solution. The reaction mixture was stirred at room temperature for 2 h. The solvent was removed in vacuum. The crude product was chromatographed on SiO$_2$ (THF/Hexane=1/1) and compound **71** (3.51 g, 80 %) was obtained as a yellow oil;



^{1}H NMR (300MHz, CDCl$_3$), δ: 6.84 (s, 4H, Ar*H*), 6.80 (br s, 1H, N*H*), 6.69 (s, 4H, Ar*H*), 4.37 (d, 4H, ^2J = 12.5 Hz, ArC*H*$_2$Ar), 4.13 (q, 2H, ^3J = 7.0 Hz, OC*H*$_2$CH$_3$), 3.92 (t, 2H, ^3J = 7.4 Hz, OC*H*$_2$CH$_2$), 3.85 (t, 2H, ^3J = 7.4 Hz, OC*H*$_2$CH$_2$), 3.76 (t, 4H, ^3J = 7.4 Hz, OC*H*$_2$CH$_2$), 3.38 (d × t, 2H, ^3J = 7.0 Hz, ^3J = 7.0 Hz, NHC*H*$_2$), 3.10 (d, 4H, ^2J = 12.5, ArC*H*$_2$Ar), 2.38 (t, 2H, ^3J = 7.4 Hz, C(O)C*H*$_2$), 2.04-1.91 (m, 8H, C*H*$_2$), 1.75-1.70 (m, 2H, C*H*$_2$), 1.67-1.59 (m, 2H, C*H*$_2$), 1.43 (s, 6H, C*H*$_2$), 1.26 (t, 3H, ^3J = 7.0 Hz, OCH$_2$C*H*$_3$), 1.12 (s, 18H, C(C*H*$_3$)$_3$), 1.01 (s, 18H, C(C*H*$_3$)$_3$), 0.98 (t, 6H, ^3J = 7.4 Hz, CH$_2$C*H*$_3$)*[†];

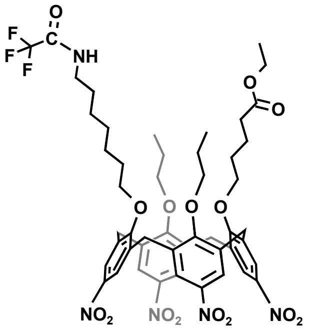
^{13}C NMR (100MHz, CDCl$_3$), δ: 173.83, 157.23 (q, $^2J_{CF}$ = 37 Hz, *C*(O)CF$_3$), 153.83, 153.63, 153.39, 144.43, 144.35, 144.15, 134.17, 133.36, 133.29, 125.00, 124.80, 124.76, 115.52 (q, $^1J_{CF}$ = 287 Hz, C(O)*C*F$_3$), 77.03, 75.10, 74.33, 67.93, 60.37, 39.95, 34.50, 33.84, 33.73, 31.49, 31.38, 31.08, 31.05, 30.31, 30.13, 29.61, 29.47, 28.95, 26.84, 25.99, 23.42, 21.70, 14.19, 10.46;

MS(FD) *m/z* (%) 1071.0 (100) [M$^+$].

[†] Under 1.01 (s, C(CH$_3$)$_3$, 18H)

calix[4]arene 72

Calix[4]arene **71** (3.5 g, 3.18 mmol) was dissolved in CH_2Cl_2 (65 ml) and acetic acid (6 ml) was added. The solution was intensively stirred and the fuming HNO_3 (5 ml) was added. The solution became dark immediately and stirring was continued for approximately 2 h at room temperature. The reaction mixture was diluted with water (40 ml). Organic layer was separated, washed with water (5x25 ml), dried over $MgSO_4$ and filtered. The filtrate was concentrated to ~5 ml and precipitated with hexane. Calix[4]arene **72** (2.2 g, 66 %) was obtained as a orange powder; mp 73-75°C;



^{1}H NMR (300MHz, $CDCl_3$), δ: 7.57 (s, 4H, Ar*H*), 7.54 (s, 4H, Ar*H*), 6.57 (br s, 1H, N*H*), 4.49 (d, 4H, ^2J = 14.0 Hz, ArC*H*$_2$Ar), 4.12 (q, 2H, ^3J = 7.0 Hz, OC*H*$_2$CH$_3$), 4.03-3.91 (m, 8H, OC*H*$_2$CH$_2$), 3.42-3.33 (m, 6H, NHC*H*$_2$, ArC*H*$_2$Ar), 2.36 (t, 2H, ^3J = 7.4 Hz, C(O)C*H*$_2$), 1.94-1.83 (m, 10H, C*H*$_2$), 1.76-1.69 (m, 2H, C*H*$_2$), 1.65 -1.59 (m, 2H, C*H*$_2$), 1.38 (s, 4H, C*H*$_2$), 1.24 (t, 3H, ^3J = 7.0 Hz, OCH$_2$C*H*$_3$), 1.01 (t, 6H, ^3J = 7.4 Hz, CH$_2$C*H*$_3$);

^{13}C NMR (100MHz, $CDCl_3$), δ: 172.98, 161.58, 161.38, 157.95 (q, $^2J_{CF}$ = 36 Hz), 142.92, 142.84, 135.40, 135.34, 135.27, 123.97, 116.11 (q, $^1J_{CF}$ = 287 Hz), 77.70, 76.04, 75.47, 60.51, 39.75, 33.86, 31.08, 29.95, 29.45, 29.05, 28.82, 26.57, 25.69, 23.24, 21.26, 14.17, 10.12;

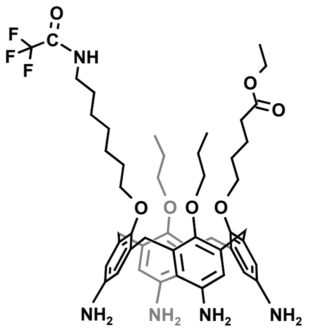
MS(FD) *m/z* (%) 1025.4 (100) [M$^+$].

calix[4]arene 73

Calix[4]arene **72** (2.10 g, 2.05 mmol) was dissolved in the mixture of THF/toluene = 1/1 (70 ml) and hydrogenated during 16 h at room temperature in the presence of the Raney-nickel. Then the catalyst was filtered off and washed with THF (2x10 ml). The combined organic layers were concentrated to ~5 ml in vacuum and 25 ml of hexane was added. Calix[4]arene **73** (1.67 g, 90 %) was obtained as a brown powder; mp 103-105°C;

^{1}H NMR (400MHz, $CDCl_3$), δ: 6.92 (s, 1H, N*H*), 6.12 (s, 4H, Ar*H*), 5.95 (s, 4H, Ar*H*), 4.27 (d, 2H, ^2J = 13.2 Hz, ArC*H*$_2$Ar), 4.25 (d, 2H, ^2J = 13.2 Hz, ArC*H*$_2$Ar), 4.12 (q, 2H, ^3J = 7.0 Hz, OC*H*$_2$CH$_3$), 3.82-3.76 (m, 4H, OC*H*$_2$CH$_2$), 3.67 (t, 4H, ^3J = 7.3 Hz, OC*H*$_2$CH$_2$), 3.35-3.30 (m, 2H, NHC*H*$_2$), 3.04 (br s, 8H, N*H*), 2.90 (d, 4H, ^2J = 13.2 Hz, ArC*H*$_2$Ar), 2.33 (t, 2H, ^3J = 7.6 Hz, C(O)C*H*$_2$), 1.85-1.80 (m, 8H, C*H*$_2$), 1.75-1.67 (m, 2H , C*H*$_2$), 1.65-1.58

(m, 2 H, CH_2), 1.36 (s, 6H, CH_2), 1.24 (t, 3H, $^3J = 7.0$ Hz, OCH_2CH_3), 0.96 (t, 6H, $^3J = 7.3$ Hz, CH_2CH_3);



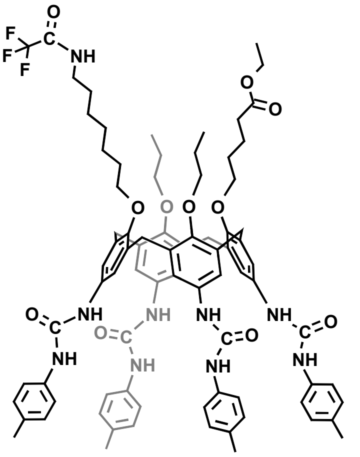
^{13}C NMR (100MHz, $CDCl_3$), δ: 173.75, 157.16 (q, $^2J_{CF} = 36$ Hz), 150.12, 149.90, 149.69, 140.39, 140.26, 135.96, 135.07, 116.11 (q, $^1J_{CF} = 286$ Hz), 115.76, 115.64, 76.70, 74.69, 74.14, 60.30, 39.94, 34.41, 31.12, 29.85, 29.43, 29.19, 28.75, 26.70, 25.87, 23.20, 21.65, 14.16, 10.49;

MS(FD) *m/z* (%) 906.4 (100) [M^+].

calix[4]arene 74

The tetraamine **73** (1.6 g, 1.77 mmol) was dissolved in CH_2Cl_2 (20 ml) and tolyl isocyanate (1.4 g (1.31 ml), 10.59 mmol) was added to the solution. The reaction mixture was stirred during 6h and MeOH (30 ml) was added. The mixture was concentrated to ~15 ml and precipitate was filtered off. The calix[4]arene **74** (1.80 g, 71 %) was obtained as a yellow powder; mp 184-186°C;

^{1}H NMR (400MHz, DMSO-d_6), δ: 9.38 (s, 1H, $NHCH_2$), 8.21 (s, 4H, NH), 8.15 (s, 2H, NH), 8.14 (s, 2H, NH), 7.22 (d, 8H, $^3J = 7.3$ Hz, ArH_{Tol}), 7.02 (d, 8H, $^3J = 7.3$ Hz, ArH_{Tol}), 6.81 (s, 4H, ArH), 6.80 (s, 4H, ArH), 4.32 (d, 4H, $^2J = 11.5$ Hz, $ArCH_2Ar$), 4.06 (q, 2H, $^3J = 7.0$ Hz, OCH_2CH_3), 3.82-3.74 (m, 8H, OCH_2CH_2), 3.19 (d × t, 2H, $^3J = 6.5$ Hz, $^3J = 6.5$ Hz, $NHCH_2$), 3.10 (d, 4H, $^2J = 11.5$ Hz, $ArCH_2Ar$), 2.37 (t, 2H, $^3J = 7.4$ Hz, $C(O)CH_2$), 2.21 (s, 12H, $ArCH_3$), 1.93-1.88 (m, 8H, CH_2), 1.73-1.67 (m, 2H, CH_2), 1.65-1.57 (m, 2H, CH_2), 1.40-1.41 (m, 6H, CH_2), 1.18 (t, 3H, $^3J = 7.0$ Hz, OCH_2CH_3), 0.97 (t, 6H, $^3J = 7.4$ Hz, CH_2CH_3);



^{1}H NMR (400MHz, $CDCl_3$, integration is given for a dimeric species), δ: 9.34 (s, 4H, NH), 9.28 (s, 4H, NH), 7.71 (m, 16H, ArH_{Tol}), 7.66 (s, 4H, ArH), 7.59 (s, 4H, ArH), 7.14 (m, 16H, ArH_{Tol}), 7.02 (s, 4H, NH), 7.00 (s, 4H, NH), 6.62 (s, 2H, $NHCH_2$), 5.91 (s, 4H, ArH), 5.87 (s, 4H, ArH), 4.21-4.11 (m, 12H, $ArCH_2Ar$, OCH_2CH_3), 3.76-3.58 (m, 16H, OCH_2CH_2), 3.40-3.35 (m, 4H, $NHCH_2$), 2.83 (d, 4H, $^2J = 11.4$ Hz, $ArCH_2Ar$), 2.80 (d, 4H, $^2J = 11.4$ Hz, $ArCH_2Ar$), 2.34 (t, 4H, $^3J = 7.8$ Hz, $C(O)CH_2$), 2.26 (s, 24H, $ArCH_3$), 2.00-1.89 (m, 8H, CH_2), 1.87-1.77 (m, 8H, CH_2), 1.71-1.60 (m, 12H, CH_2), 1.40-1.32 (m, 8H, CH_2), 1.26 (t, 6H, $^3J = 7.0$ Hz, OCH_2CH_3), 0.90 (t, 12H, $^3J = 7.6$ Hz, CH_2CH_3);

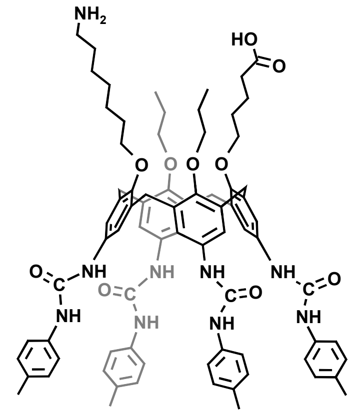
^{13}C NMR (100MHz, DMSO-d$_6$), δ: 173.00, 156.54 (q, $^{2}J_{\mathrm{CF}} = 36$ Hz), 152.90, 151.43, 151.32, 137.70, 134.75, 133.91, 130.66, 129.47, 118.60, 118.43, 116.41 (q, $^{1}J_{\mathrm{CF}} = 288$ Hz), 76.89, 75.24, 74.71, 60.10, 33.96, 31.08, 30.04, 29.44, 29.30, 28.67, 26.76, 26.10, 23.14, 21.69, 20.72, 14.50, 10.57;

MS (ESI) m/z 1481.7 (100) [M^{+}2Na], 741.8 (21) [M^{2+}Na].

calix[4]arene 75

A solution of NaOH (0.42 g, 10.4 mmol) in MeOH (15 ml) and H_2O (5 ml) was added to the solution of calixarene **74** (1.50 g, 1.04 mmol) in THF (20 ml). The reaction mixture was stirred 6 h at room temperature (after 2 h precipitate appeared) and acetic acid (10 ml) was added to neutralize the excess of NaOH. Then water (25 ml) was added to the solution and the product was extracted with $CHCl_3$/THF one time. The organic layer was separated and concentrated to ~5 ml. After that MeOH (10 ml) was added to the suspension. The precipitate was filtered off and calix[4]arene **75** (1.16 g, 85 %) was obtained as a white powder; mp>300°C decompose;

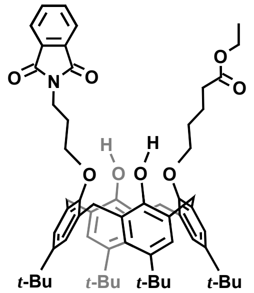
^{1}H NMR (400MHz, DMSO-d$_6$), δ: 8.51 (s, 1H, N*H*), 8,49 (s, 1H, N*H*), 8.45 (s, 2H, N*H*), 8.35 (s, 1H, N*H*), 8.33 (s, 1H, N*H*), 8.28 (s, 2H, N*H*), 7.24 (d, 4H, $^{3}J = 8.2$ Hz, $\mathrm{Ar}H_{\mathrm{Tol}}$), 7.22 (d, 4H, $^{3}J = 8.2$ Hz, $\mathrm{Ar}H_{\mathrm{Tol}}$), 7.01 (d, 4H, $^{3}J = 8.2$ Hz, $\mathrm{Ar}H_{\mathrm{Tol}}$), 6.99 (d, 4H, $^{3}J = 8.2$ Hz, $\mathrm{Ar}H_{\mathrm{Tol}}$), 6.80 (s, 4H, Ar*H*), 6.74 (s, 2H, Ar*H*), 6.72 (s, 2H, Ar*H*), 4.33 (d, 4H, $^{2}J = 11.5$ Hz, $\mathrm{ArC}H_2\mathrm{Ar}$), 3.84 (br s, 4H, $\mathrm{OC}H_2$), 3.75 (br s, 4H, $\mathrm{OC}H_2$), 3.09 (d, 4H, $^{2}J = 11.5$ Hz, $\mathrm{ArC}H_2\mathrm{Ar}$), 2.76 (t, 2H, $^{3}J = 7.0$ Hz, $\mathrm{NH_2C}H_2$), 2.26 (t, 2H, $^{3}J = 7.4$ Hz, $\mathrm{C(O)C}H_2$), 2.21 (s, 12H, $\mathrm{ArC}H_3$), 1.92-1.87 (m, 8H, $\mathrm{C}H_2$), 1.64 (br s, 2H, $\mathrm{C}H_2$), 1.56 (br s, 2H, $\mathrm{C}H_2$), 1.37 (br s, 6H, $\mathrm{C}H_2$), 0.99 (t, 6H, $^{3}J = 7.0$ Hz, $\mathrm{CH_2C}H_3$);



^{13}C NMR (100MHz, $CDCl_3$), δ: 177.18, 152.66, 152.52, 151.37, 151.27, 150.62, 135.57, 137.50, 134.97, 134.93, 133.63, 133.47, 133.37, 133.23, 129.81, 129.70, 128.88, 128.79, 118.35, 117.89, 117.74, 76.44, 74.61, 74.42, 38.98, 37.83, 30.63, 29.71, 29.34, 28.63, 27.89, 25.83, 25.11, 22.88, 22.79, 20.20, 10.47.

calix[4]arene 76

The mixture of calix[4]arene **41a** (4.00 g, 5.15 mmol), K_2CO_3 (0.85 g, 6.15 mmol) and N-(3-bromopropyl)-phthalimide (1.66 g, 6.15 mmol) in CH_3CN (50 ml) was refluxed for 14 h. The rest of K_2CO_3 was filtered off and solvent was removed in vacuum. The residue was precipitated from CH_2Cl_2/MeOH (could be also crystallized from the mentioned solvents). Calix[4]arene **76** was obtained as a white powder (3.5 g, 71 %); mp 151-153°C;



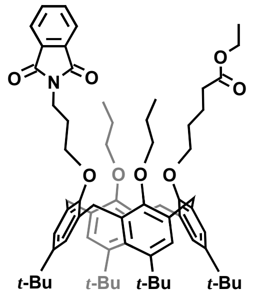
^{1}H NMR (400MHz, $CDCl_3$), δ: 7.86-7.83 (m, 2H, ArH_{pht}), 7.70-7.68 (m, 2H, ArH_{pht}), 7.45 (s, 2H, OH), 7.03 (s, 4H, ArH), 6.80 (s, 2H, ArH), 6.78 (s, 2H, ArH), 4.28 (d, 2H, $^2J = 12.7$ Hz, ArCH_2Ar), 4.26 (d, 2H, $^2J = 12.7$ Hz, ArCH_2Ar), 4.11-4.04 (m, 6H, OCH_2CH$_2$, OCH_2CH$_3$), 3.99 (t, 2H, $^3J = 6.8$ Hz, NCH_2), 3.30 (d, 2H, $^2J = 12.7$ Hz, ArCH_2Ar), 3.29 (d, 2H, $^2J = 12.7$ Hz, ArCH_2Ar), 2.46 (t, 2H, $^3J =$ 6.8 Hz, C(O)CH_2), 2.40 (quintet, 2H, $^3J = 6.8$ Hz, CH_2), 2.10-2.04 (m, 2H, CH_2), 2.01- 1.96 (m, 2H, CH_2), 1.27 (s, 18H, C(CH_3)$_3$), 1.21 (t, 3H, $^3J = 6.8$ Hz, OCH$_2$CH_3), 0.96 (s, 9H, C(CH_3)$_3$), 0.94 (s, 9H, C(CH_3)$_3$);

^{13}C NMR (100MHz, $CDCl_3$), δ: 173.52, 168.23, 150.69, 149.83, 146.84, 146.75, 141.34, 133.88, 132.60, 132.17, 127.75, 125.52, 125.46, 125.04, 123.23, 76.09, 74.05, 60.18, 35.44, 33.97, 33.92, 33.80, 31.69, 31.01, 29.41, 21.63, 14.22;

MS(FD) *m/z* (%) 963.8 (100) [M$^+$].

calix[4]arene 77

Calix[4]arene **76** (1.00 g, 1.04 mmol) was dissolved in DMF (20 ml) and NaH (75 mg, 3.11 mmol) was added to the solution. The suspension was stirred during 1 h and then propyl bromide (0.38 g (0.28 ml), 3.11 mmol) was added. The stirring was continued for 48 h at room temperature and for 2 h at 50°C. After that AcOH (2 ml) was added to neutralize the excess of NaH and the solvent was removed in vacuum. The residue was washes with water (5x15 ml) and dried. The traces of the propyl ester (reesterification) were detected in the ^{1}H NMR spectrum. The mixture of esters was dissolved in EtOH (50 ml) and catalytic amount of H_2SO_4 was added. Solution was refluxed during 3 h and concentrated to ~5-10 ml. After that water (25 ml) was added and precipitate was filtered off, washed with water (5x10 ml) and dried. Calixarene **77** (0.74 g, 75 %) was obtained as a yellow powder; mp 87-89°C;



^{1}H NMR (400MHz, $CDCl_3$), δ: 7.87-7.85 (m, 2H, ArH_{pht}), 7.72-7.70 (m, 2H, ArH_{pht}), 6.85 (s, 2H, ArH), 6.83 (s, 2H, ArH), 6.67 (d, 2H, $^4J = 2.3$ Hz, ArH), 6.65 (d, 2H, $^4J = 2.3$ Hz, ArH), 4.38 (d, 2H, $^2J = 12.5$ Hz, ArCH_2Ar), 4.35 (d, 2H, $^2J = 12.5$ Hz, ArCH_2Ar), 4.13 (q, 2H, $^3J = 7.0$ Hz, OCH_2CH$_3$), 3.99-3.90 (m, 4H, OCH_2CH$_2$), 3 .84 (t, 2H, $^3J = 7.0$ Hz, NCH_2), 3.77-3.73 (m, 4H, OCH_2CH$_2$), 3.10 (d, 4H, ^2J

= 12.5 Hz, ArCH_2Ar), 2.48 (quintet, 2H, ^3J = 7.0 Hz, CH_2), 2.38 (t, 2H, ^3J = 7.0 Hz, C(O)CH_2), 2.05-1.89 (m, 6H, CH_2), 1.72 (quintet, 2H, ^3J = 7.0 Hz, CH_2), 1.25 (t, 3H, ^3J = 7.0 Hz, OCH$_2$CH_3), 1.14 (s, 9H, C(CH_3)$_3$), 1.13 (s, 9H, C(CH_3)$_3$), 0.99 (s, 18H, C(CH_3)$_3$), 0.95 (t, 6H, ^3J = 7.0 Hz, CH$_2$CH_3);

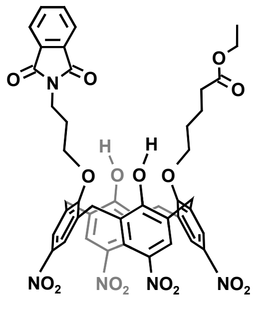
^{13}C NMR (100MHz, CDCl$_3$), δ: 173.61, 168.26, 153.89, 153.57, 153.30, 144.68, 144.39, 144.13, 134.36, 134.27, 133.88, 133.24, 132.24, 125.09, 124.78, 123.21, 77.17, 74.71, 72.45, 60.20, 35.53, 34.40, 33.89, 33.75, 31.53, 31.38, 31.18, 31.08, 29.68, 23.45, 21.62, 14.29, 10.43;

MS(FD) *m/z* (%) 1147.6 (100) [M$^+$].

calix[4]arene 78

Calix[4]arene **77** (0.6 g, 0.59 mmol) was dissolved in CH$_2$Cl$_2$ (20 ml) and acetic acid (0.9 ml) was added. The solution was vigorously stirred and fuming HNO$_3$ (0.75 ml) was added. The solution became dark immediately and stirring was continued for approximately 2 h at room temperature. The reaction mixture was diluted with water (40 ml). The organic layer was separated, washed with water (5x25 ml), dried over MgSO$_4$, filtered and evaporated. Calix[4]arene **78** (0.5 g, 85 %) was obtained as a orange powder; mp 157-159°C;

^{1}H NMR (400MHz, CDCl$_3$), δ: 7.86-7.83 (m, 2H, ArH_{pht}), 7.75-7.73 (m, 2H, ArH_{pht}), 7.59 (s, 4H, ArH), 7.51 (s, 2H, ArH), 7.48 (s, 2H, ArH), 4.51 (d, 2H, ^2J = 14.0 Hz, ArCH_2Ar), 4.49 (d, 2H, ^2J = 14.0 Hz, ArCH_2Ar), 4.14-3.96 (m, 10H, OCH_2CH$_2$, OCH_2CH$_3$), 3.84 (t, 2H, ^3J = 7.2 Hz, NCH_2), 3.40 (d, 4H, ^2J = 14.0 Hz, ArCH_2Ar), 2.37 (t, 2H, ^3J = 7.2 Hz, C(O)CH_2), 2.26 (quintet, 2H, ^3J = 7.2 Hz, CH_2), 1.91-1.84 (m, 6H, CH_2), 1.78-1.72 (m, 2H, CH_2), 1.23 (t, 3H, ^3J = 7.2 Hz, OCH$_2$CH_3), 1.97 (t, 6H, ^3J = 7.2 Hz, CH$_2$CH_3);



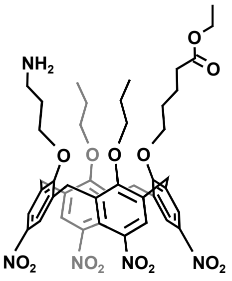
^{13}C NMR (100MHz, CDCl$_3$), δ: 172.90, 168.17, 161.72, 161.38, 161.20, 143.04, 142.96, 142.86, 135.44, 135.30, 134.28, 131.90, 124.14, 124.00, 123.95, 123.37, 77.85, 75.70, 73.44, 60.44, 34.89, 33.80, 31.20, 31.13, 29.57, 29.52, 23.31, 21.28, 14.25, 10.09;

MS(FD) *m/z* (%) 1004.2 (43.9) [M$^+$].

calix[4]arene 79

Calix[4]arene **78** (0.20 g, 0.20 mmol) and hydrazine monohydrate (0.05 g (0.05 ml), 1.00 mmol) were refluxed in EtOH (40 ml) during 2 h. After that precipitate was filtered off (from the hot solvent), washed with water and dried. Calix[4]arene **79** (55 mg, 32 %) was obtained as a yellow powder; mp 227-229°C;

^{1}H NMR (300MHz, $CDCl_3$), δ: 7.65 (s, 4H, Ar*H*), 7.46 (s, 2H, Ar*H*), 7.45 (s, 2H, Ar*H*), 4.50 (d, 2H, ^2J = 14.0 Hz, ArCH_2Ar), 4.49 (d, 2H, ^2J = 14.0 Hz, ArCH_2Ar), 4.17-3.94 (m, 10H, OCH_2CH_2, OCH_2CH_3), 3.40 (d, 4H, ^2J = 14.0 Hz, ArCH_2Ar), 2.89 (t, 2H, ^3J = 7.0 Hz, NH_2CH_2), 2.38 (t, 2H, ^3J = 7.4 Hz, C(O)CH_2), 2.06-2.01 (m, 2H, CH_2), 1.90-1.74 (m, 10H, CH_2, NH_2), 1.25 (t, 3H, ^3J = 7.0 Hz, OCH_2CH_3), 0.98 (t, 3H, ^3J = 7.4 Hz, CH_2CH_3);



^{13}C NMR (100MHz, $CDCl_3$), δ: 172.91, 161.87. 161.37, 161.29, 142.82, 135.59, 135.19, 124.17, 123.81, 77.07, 75.67, 74.02, 60.46, 38.73, 33.77, 33.47, 31.12, 29.50, 23.23, 21.27, 14.23, 10.04;

MS(FD) *m/z* (%) 874.5 (74.2) [M^+].

4. MULTIPLE TETRAUREA CALIX[4]ARENES (CONNECTION *VIA* THE WIDE RIM)

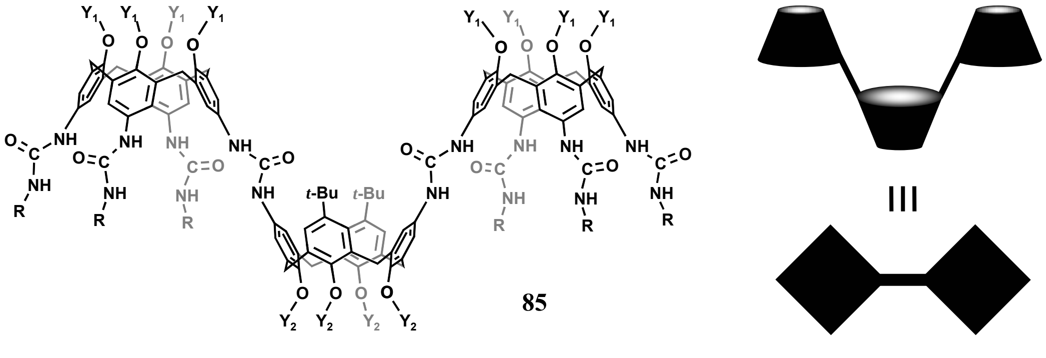
4. 1. Introduction

As already shown, suitably connected tetraurea calix[4]arenes are able to form well-defined self-assembled supramolecular structures. In the previous chapter we have discussed the synthesis and the properties of such units, covalently connected *via* the narrow rims. In contrast to these studies, which were concentrated more on the synthesis of building blocks for linear and cross-linked polymers, in present chapter we are dealing with molecules designed in a way to make the formation of cyclic oligomers *via* self-assembly possible. Now connection of the calixarenes will be made *via* their wide rims.

4. 2. Possible Organization in Cyclic Oligomers

A desired building block for such a supramolecular structure could be prepared by the connection of two calixarenes at the wide rims *via* a rather rigid spacer, which keeps molecules on the same level, more or less parallel to each other and do not allow the intramolecular dimerization. Thus we obtain a molecule in which all urea functions are oriented in the same direction.

A calixarene fixed in the *cone* conformation (bearing no urea groups) could be used as a spacer that provides the desired orientation. The general formula of the target building block and its sketchy drawing are shown in Figure 44.



85

Figure 44. General formula of the triple calixarene.

The dimerization of this system should make the formation of two cyclic oligomers possible:

- a diamond-shaped tetramer (Figure 45e);
- a regular octamer (Figure 45f).

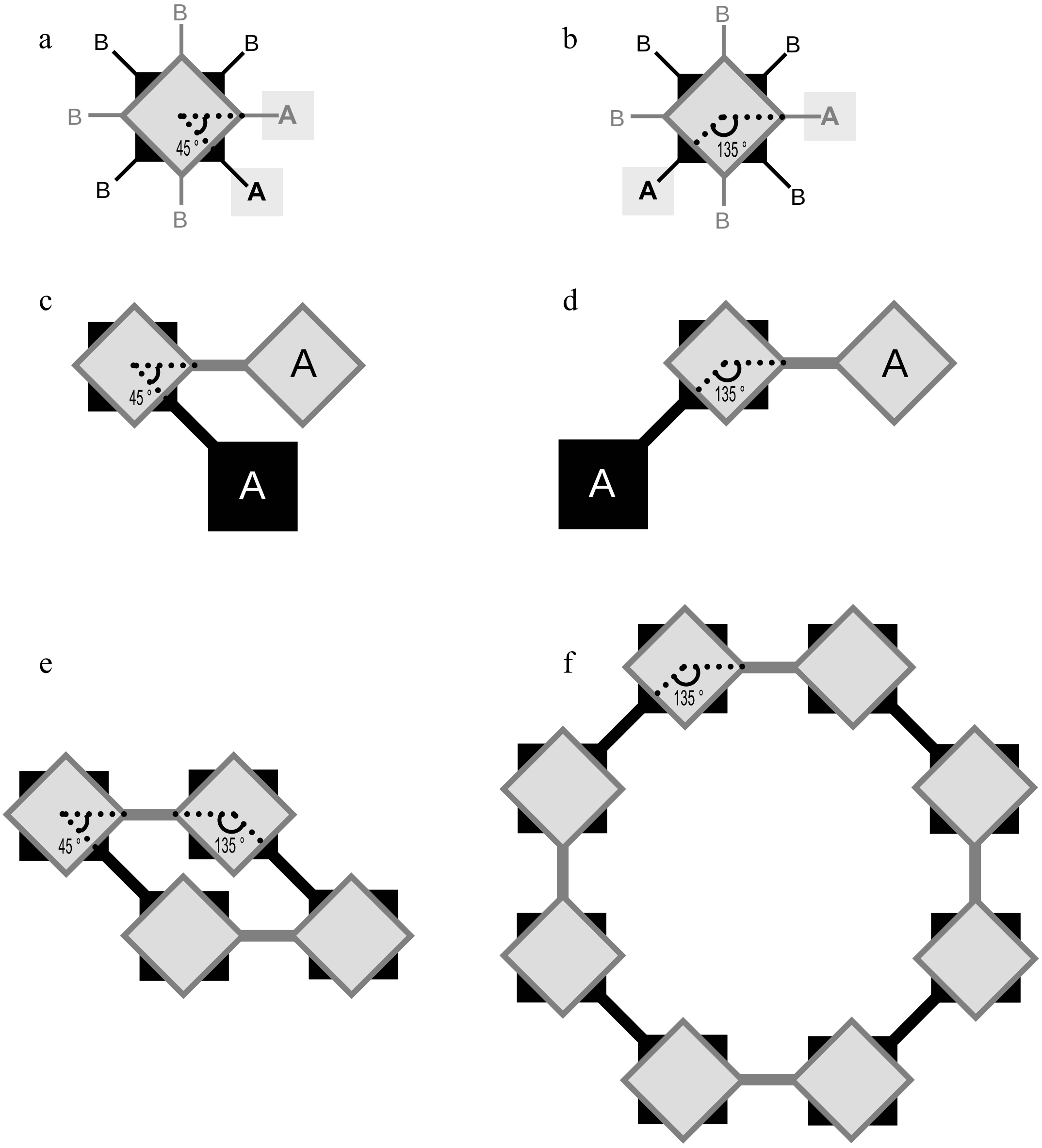


Figure 45. Possible organization of **85** in cyclic tetramer (left) and octamer (right). The different colours were used only to distinguish between units depicted above and below the drawing plane.

The reasons for such an association are very simple. In general two tetraurea units in the dimer are turned by 45° around the common axis with respect to each other. Urea derivatives of ABBB type, where three substituents are equal and one is different, form two regioisomers with proximal and distal arrangement of the residues A. This means, that in the capsule the angles formed by the residues A are equal to 45° and 135° respectively (Figure 45a,b).

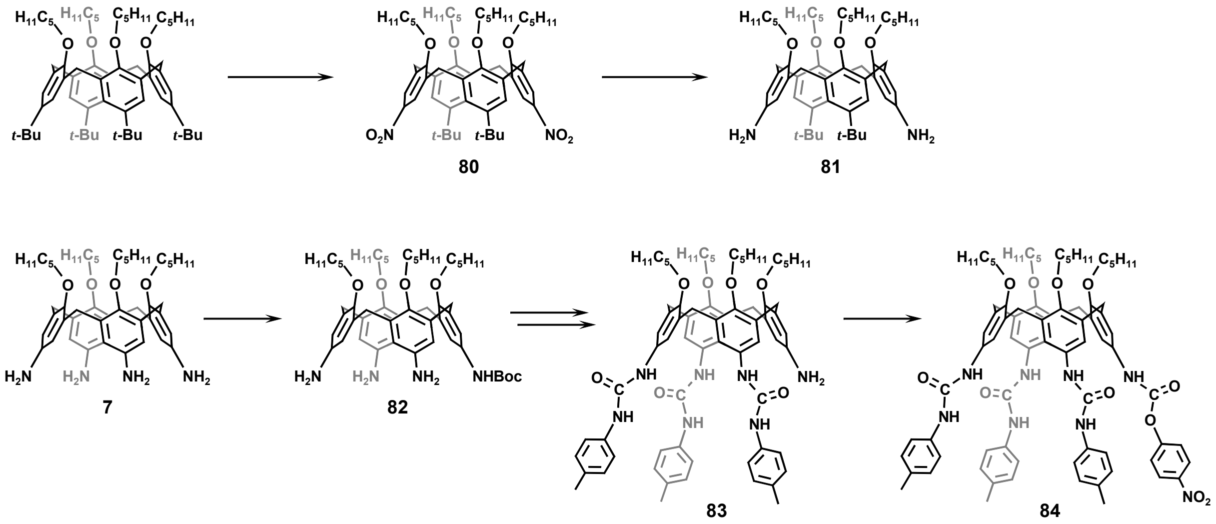
In the building block, composed of two tetraurea derivatives connected *via* spacer, each calixarene can be considered as tetraurea of ABBB type. It possess the residue A - the second calixarene attached by the spacer, and three residues B - the simple aryl ureas. Dimerization of only two bis-calixarenes affords the intermediate assemblies shown in Figure 45c,e. These assemblies should grow by subsequent dimerization and either cyclic structures or polymers can be formed.

Since the formation of the polymeric structures is entropically less favourable and all tetraurea calix[4]arenes in solution usually must be satisfied by dimerization we guess that formation of well defined cyclic structures will be more probable in comparison to the linear ones.

Thus the cyclic tetramer should be formed if both calixarenes in the dimer turned by 45° and 135° to each other alternatingly and the octahedral octamer if they are regularly turned by 135°.

4. 3. Synthesis and ^{1}H NMR Analysis

The synthesis of calixarene **81**, which was used as the spacer, was performed in accordance with well elaborated procedures.[61] Partial *ipso*-nitration of the tetrapentoxy calix[4]arene, followed by catalytic hydrogenation afforded compound **81** (Scheme 17a).



Scheme 17. Synthesis of building blocks for bis-tetraurea calix[4]arene.

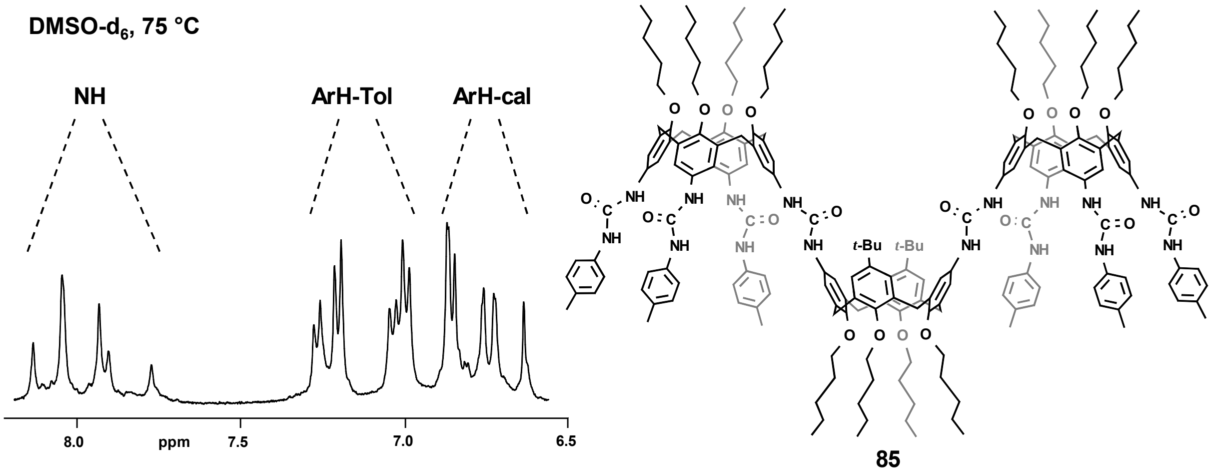
Tritolyl urea **83** was prepared as described by Böhmer at al.[60] *via* consecutive mono-Boc protection of tetraamino calixarene **7**, reaction of the remaining amino groups with tolyl isocyanate and cleavage of the Boc group. Reaction of tritolyl urea **83** with *p*-nitrophenyl chloroformate gave the active urethane **84** in 80% yield (Scheme 17b).

Bis-tetraurea calixarene **85** was prepared *via* reaction of 1,3-diamino calixarene **81** and active urethane **84** in $CHCl_3$/THF in the presence of triethylamine (or Hünig base). The recrystallization of the reaction mixture from CH_2Cl_2/methanol afforded the pure product in 35% yield. The ^{1}H MNR and ESI-MS spectra of the compound are in agreement with the proposed structure. The most obvious part of the spectrum is shown in Figure 46. According to the C_S symmetry of tetraurea calix[4]arene (ABBB-type) and the C_{2V} symmetry of the calixarene-spacer (ABAB-type) and thus the C_{2V} symmetry of the whole molecule we expect to see:

- 6 singlets for NH protons (in the ratio 1:1:1:1:2:2);
- two pairs of doublets for aromatic protons of tolyl ureas (in the ratio 1:2)
- 6 signals for aromatic protons of both calixarene skeletons (all equivalent).

Indeed we observe:

- 5 singlets for NH protons in the ratio 1:3:2:1:1, what means that two signals are overlapping;
- two pairs of doublets for ArH of tolyl ureas;
- 5 signals for ArH protons of both calixarene skeletons in the ratio 2:1:1:1:1 – again overlapping of the two signals occurs. In principle here we should observe 4 singlets and two meta-coupled doublets, but probably the resolution is not sufficient.



85

Figure 46. Section of the ^{1}H NMR spectrum of bis-tetraurea calix[4]arene **85** in DMSO-d$_6$.

Among apolar solvents, suitable for dimerization, compound **85** is good soluble only in $CDCl_3$, but the ^{1}H NMR in this solvent is very broad and unresolved (Figure 47a). In the presence of two equivalents of tetratosyl urea **16** this compound forms bis-heterodimer. The whole spectrum of assembly is rather complicated because the different directionality of hydrogen bonding belt can make the two dimers within one molecule different. In combination with two equivalents of tetratolyl urea **12** formation of the bis-heterodimer was not observed in different solvents.

In the presence of tetraethylammonium salt the guest inside the capsule (usually the solvent molecule) is replaced by the cationic guest. Moreover the methyl group of the encapsulated Et_4N^+ ion gives one up-field shifted signal at approximately -1.8 ppm, what provides the obvious evidence of dimerization.[62] Therefore the ^{1}H NMR spectrum in $CDCl_3$ of the mixture of **85** and Et_4N^+ PF_6^- in the ratio 1:1 was recorded (Figure 47b). Indeed we could observe the signal of included cation at -1.55 ppm – the prove of dimerization. The integration of the guest signal suggests that approximately 40 % of the tetraethylammonium cation is encapsulated. Probably the remaining amount of the cation is included into the open cavity of monomeric tetraurea. Since the chemical shifts of the "encapsulated" and "included" Et_4N^+ could be different, the resonances of the latter may be covered by other signals.

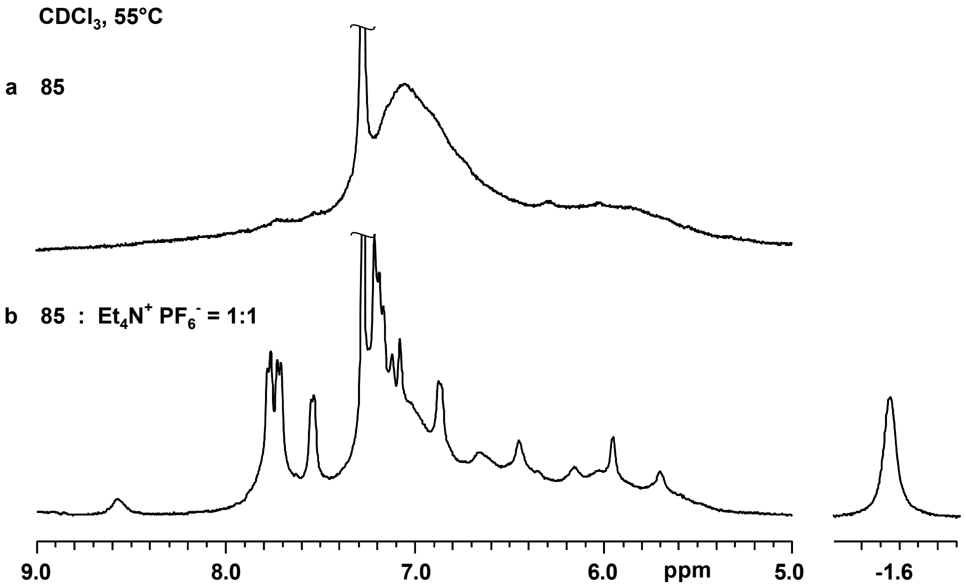


Figure 47. The sections of the ^{1}H NMR spectra in $CDCl_3$ of **85** (a) and the mixture of **85**: Et_4N^+ PF_6^- = 1:1 (b).

In solvents like benzene or toluene compound **85** has only a limited solubility at room temperature, but it is soluble under heating. Therefore all the spectra in these solvents were recorded at 77°C. In contrast to the chloroform solution, in C_6D_6 we could observe sharp signals and the low-field shifted signals of NH protons, which obviously take part in dimerization (Figure 48). In toluene as the solvent and the guest) any indication of dimerization was not found.

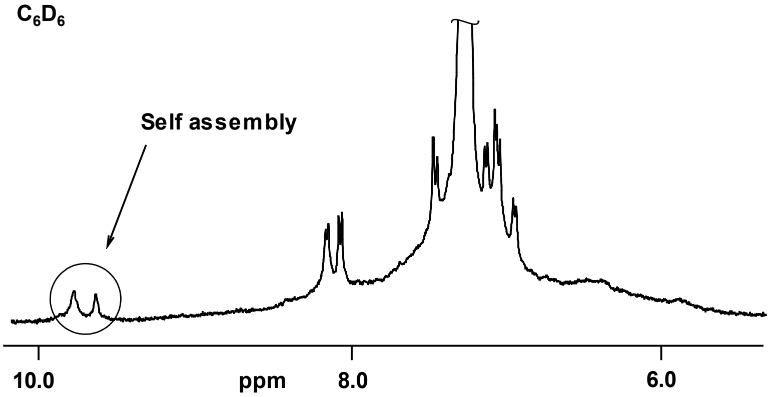


Figure 48. The section of the spectrum of **85** in C_6D_6.

The solubility of **85** in cyclohexane-d_{12} is not enough to record a spectrum. The addition of 1,4-difluorobenzene (which is found to be a good guest) to all solutions did not really influence(improve) dimerization.

Up to the moment we were not able to demonstrate the formation of the well-defined aggregates, but all the possibilities are still not exhausted. For example, while the self-assembly of **85** into the cyclic octamer in principle may be too complicated, the formation of the tetramer can be hampered due to the close distance between the “spacer” and the tetraurea calixarenes. This distance can be increased by the introduction of acetylene bridges as shown in Figure 49 or a totally different spacer (instead of the calixarene) can be also considered.

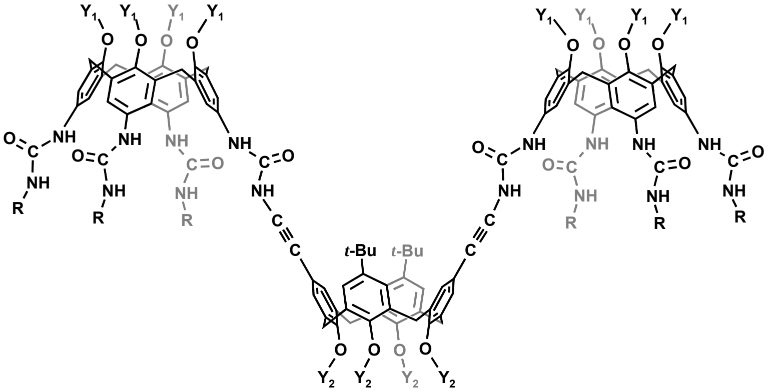


Figure 49. Bis-tetraurea triple calixarene, possessing acetylene bridges.

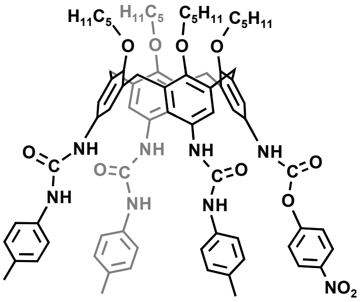
4. 4. Conclusions

One example of a bis-tetraurea triple calix[4]arene has been prepared and the structure of the compound was proved by ^{1}H NMR spectroscopy and ESI MS spectrometry. The self-assembly properties of this compound were also studied by ^{1}H NMR. Although up to the moment the formation of well-defined self-assembled structures was not detected, we could prove the general ability of bis-tetraurea triple calixarene **85** to self-assemble. Among the offered guests (solvents and tetraethyl ammonium cation) benzene and tetraethyl ammonium are found to be the most appropriate to provide evidence for dimerization. The solubility of **85** still has to be improved by the introduction of other urea residues or other substituents instead of *tert*-butyl groups.

4. 5. Experimental Part

calix[4]arene 84

The solution of tritolyl urea **83** (0.2 g, 0.39 mmol) and *p*-nitrophenyl chloroformate (0.23 g, 1.16 mmol) in THF was refluxed for 24 h and then the solvent was evaporated. The residue was treated with CH3CN, the precipitate was filtered off and calixarene **84** was obtained in 80 % yield; mp>190°C decompose;

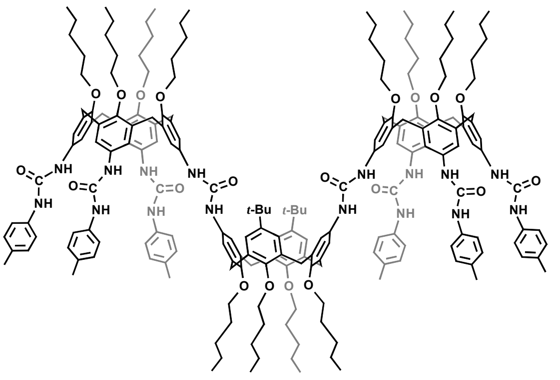


^{1}H NMR (400MHz, DMSO-d$_6$), δ: 9.95 (s, 1H, NH), 8.28 (s, 2H, NH), 8.22 (s, 1H, NH), 8.20 (s, 1H, NH), 8.16 (s, 2H, NH), 7.37 (d, 2H, $^3J = 8.5$ Hz, ArH), 7.25-7.21 (m, 6H, ArH), 7.02-7.00 (m, 8H, ArH), 6.94 (s, 2H, ArH_{calix}), 6.79 (s, 4H, ArH_{calix}), 6.75 (s, 2H, ArH_{calix}), 4.36-4.32 (m, 4H, ArCH_2Ar), 3.82 (m, 8H, OCH_2), 3.10 (d, 4H, $^2J = 12.6$ Hz, ArCH_2Ar), 2.21 (s, 9H, ArCH_3), 1.90 (m, 8H, CH_2), 1.39 (m, 16H, CH_2), 0.93 (br s, 12H, CH$_2$CH_3);

triple-calix[4]arene 85

The solution of active urethane **84** (0.20 g, 0.15 mmol), diamine **81** (0.06 g, 0.07 mmol) and triethylamine (0.15 ml) in THF (DMF) was refluxed (stirred at 50 °C) for 72h. After that acetonitrile (water) was added and the precipitate was filtered off and washed with MeOH three times. The crude product was precipitated from CH$_2$Cl$_2$/MeOH twice and triple-calixarene **85** was obtained in 35% yield; mp > 300°C decompose;

^{1}H NMR (400MHz, DMSO-d$_6$, 75°C), δ: 8.13 (s, 1H, NH), 8.04 (s, 3H, NH), 7.93 (s, 2H, NH), 7.90 (s, 1H, NH), 7.77 (s, 1H, NH), 7.26 (d, 2H, ^3J = 8.2 Hz, ArH_{Tol}), 7.20 (d, 4H, ^3J = 8.2 Hz, ArH_{Tol}), 7.03 (d, 2H, ^3J = 8.2 Hz, ArH_{Tol}), 6.99 (d, 4H, ^3J = 8.2 Hz, ArH_{Tol}), 6.86 (s, 4H, ArH), 6.85 (s, 4H, ArH), 6.84 (s, 4H, ArH), 6.75 (s, 4H, ArH), 6.72 (s, 4H, ArH), 6.63 (s, 4H, ArH), 4.39-4.32 (m, 12H, ArCH_2Ar), 3.91-3.75 (m, 24H, OCH_2), 3.12 (m, 12H, ArCH_2Ar), 2.22 (s, 3H, ArCH_3), 2.20 (s, 6H, ArCH_3), 1.90 (m, 24H, CH_2), 1.40 (m, 48H, CH_2), 0.94 (br s, 36H, CH$_2$CH_3);

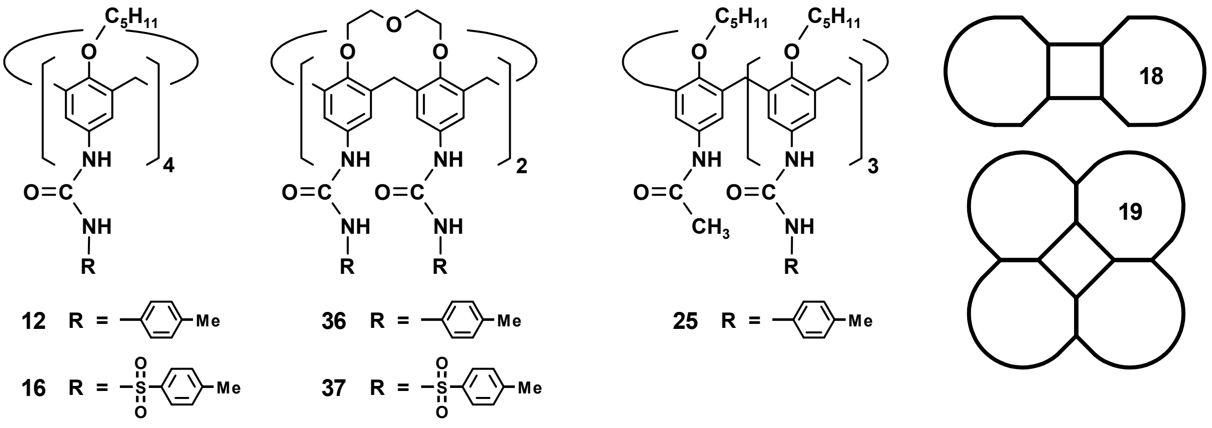


MS(ESI): *m/z* (%) = 3229.0 (6.5) [M$^+$], 1614.9 (23.6) [M^{2+}].

5. TOWARDS STRUCTURALY UNIFORM SELF-ASSEMBLED DENDRIMERS

5. 1. Introduction

In the previous chapters we have explained, that calix[4]arenes substituted at their wide rim by urea groups form dimers in apolar, aprotic solvents in the presence of a suitable guest (often a solvent molecule). The two calixarenes are held together by a seam of hydrogen bonds between urea functions. If two different aryl or alkyl ureas are mixed together two possible homodimers and a heterodimer are usually formed in more or less statistical ratio.[17] However, the stoichiometric mixture of the two flexible tetratolyl and tetratosyl ureas **12** and **16** affords only the heterodimeric assembly **12•16**.[21] We could also show that for the same combination of the analogous rigid tetraureas **36** and **37** the outcome of dimerization can be influenced by the solvent. In $CDCl_3$ for instance the latter mixture results in two homodimers **36•36** and **37•37**, while in CD_2Cl_2 only the heterodimer **36•37** is observed.



Another interesting example for the selective formation of heterodimers is the combination of open chain (**12**) and bis-or tetraloop tetraurea derivatives (**18**, **19**).[23,63] In apolar solvents **18** or **19** can not homodimerize due to the sterically unfavorable overlapping of the loops, however both require a partner. In the presence of stoichiometric amount of tetratolylurea derivative **12** they form heterodimers **12•18** or **12•19** exclusively, since the tolyl urea groups of **12** can easily pass through the loops of **18** or **19**. Only in this way all urea functions of both calixarenes can be involved in the usual hydrogen bonding belt. Selectivities such as these represent one of the topics of our interest.

As described in chapter I (p. 15) the replacement of one of the urea groups attached to the calixarene core by an acetamide function (calixarene **25**) leads to a tetrameric assembly with a totally different hydrogen bonding pattern.

Four acetamide groups are situated in the middle of the tetramer and connected through a cycle of four NH···C=O hydrogen bonds (Figure 50).[28] Each amide carbonyl oxygen (for example green) forms a second hydrogen bond with the calix-attached urea NH at ring **II** of a second calixarene (red), while the tolyl-attached NH of the same urea fragment is involved in NH···π interactions with the aryl ring **IV**. The carbonyl oxygen at ring **II** and both urea NH-groups at ring **III** (red) form four hydrogen bonds with the urea fragment at ring **I** of the third calixarene (blue). The oxygen of C=O group at the ring **III** (red) is not involved in the hydrogen bonding.‡

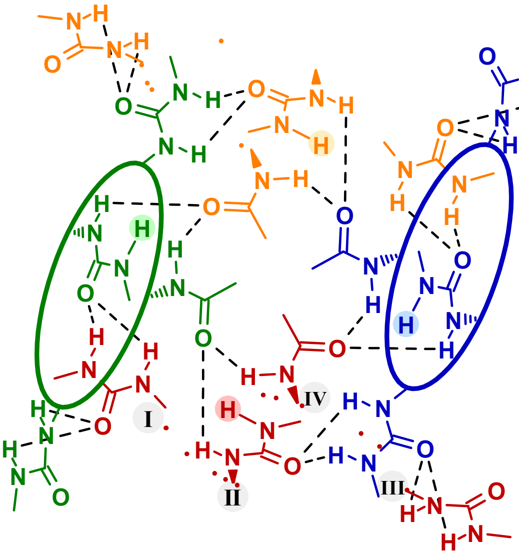


Figure 50. Schematic drawing of the hydrogen bonding pattern found in the crystal structure of **25**. Ellipses denote the wider rim of the calixarene subunits; they are drawn in bold lines when they lie above the plane of the acetamide carbonyl groups (with their substituents pointing away from the viewer), while dashed lines indicate that they are below this area and the substituents are pointing upwards. Hydrogen bonds are represented with dashed black lines. Hydrogens involved in NH···π interactions are shown in circles coloured in respective colours.

Extensive NMR studies revealed similar structures in apolar solvents such as $CDCl_3$ or C_6D_6 for calixacetamide **25**. The formation of these tetramers in solution is critically dependent on the size of the amide fragment. Propionamide, butyramide, and *p*-tolylamide form only ill-defined aggregates, due to the steric crowding inside the tetrameric assembly.

In the presence of tetraethylammonium salts compound **25** forms the "usual" dimeric capsule, incorporating a single ammonium cation. Only one of two possible regioisomeric dimers is formed, in which both acetamide groups are surrounded by two urea residues.

The presence of the tetratolyl urea **12** (in stoichiometric amount or in excess) does not intervene with the formation of the tetramer and vice versa, what is extremely important for our further studies.

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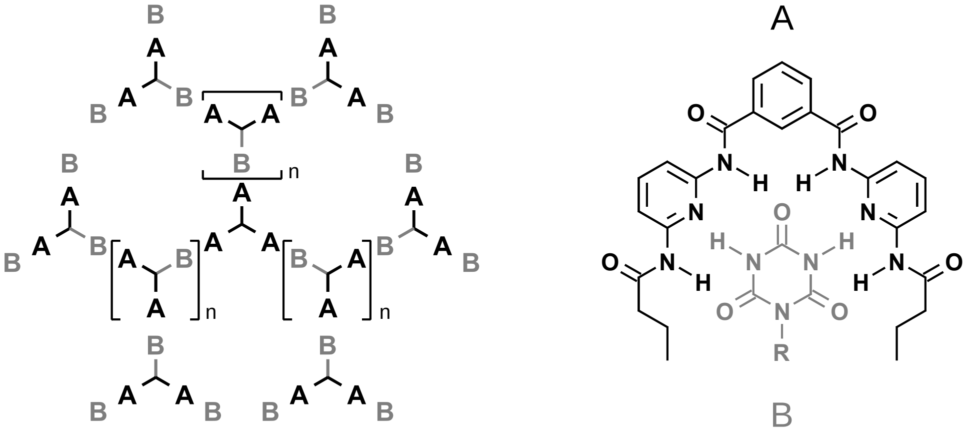
‡ The Figure 50 was reproduced from that published in ref. 4.

The described examples give remarkable evidence of how self-assembly in solution can be strongly dependent on subtle structural factors and of how the formation of dimeric capsules can be induced by the presence of an appropriate guest. These fascinating properties could be used to build up well-defined dendritic structures *via* self-assembly of the appropriate calixarenes covalently connected *via* their narrow rims.

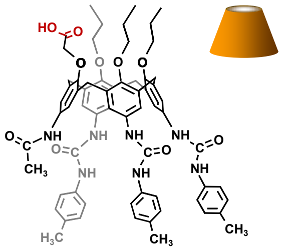
5. 2. Possible Formation of the Dendritic Assembly

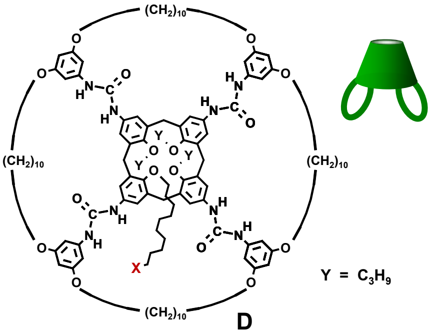
Various attempts to obtain dendrimers *via* self-assembly have been reported. Among them we concentrate on hydrogen bonded assemblies. In most examples two or more covalently linked dendrons are held together by complementary hydrogen bonding motifs just in the core.[64] Only recently a first approach was published in which the whole dendritic assembly was built up, shell by shell, in a self assembly process.[65] It was based on a single complementary pair of hydrogen bonding motifs -**A** and **B**- forming an -**A•B**- assembly. Self-assembled dendrimers are formed by mixing a tripodal core $\mathbf{A_3}$ with a branched linker $\mathbf{BA}_2$ and a capping unit **B** in the required ratio.



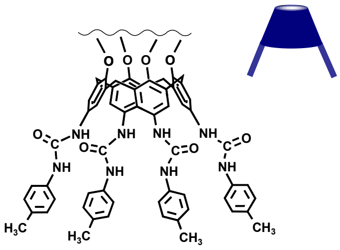
However, in such system it cannot be guaranteed that the tripodal core $\mathbf{A_3}$ combines only with the **B** site of the linker and that the capping **B** combines only with the **A** sites of the linker (in the outer shell). “Wrong” combinations, e.g. of **B** with $\mathbf{A_3}$ are also possible, and the ratio of the three compounds only determines the average size of a mixture consisting of structurally different assemblies.

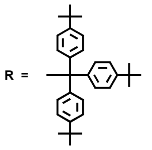
On the basis of our knowledge (observations) about selective dimerization of tri- or tetraurea calix[4]arenes (**units**) we intended to build up dendritic architectures which are uniform in ***size*** and ***structure*** *via* self-assembly of the covalently connected oligourea units (**building blocks**). The first approach towards desired dendrimers is shown in Figure 51.


C

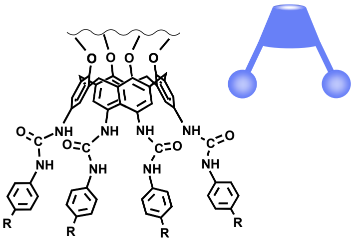


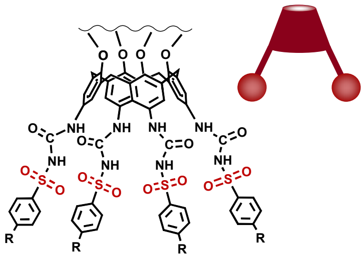
D


E



X = NH_2 or COOH


F


G

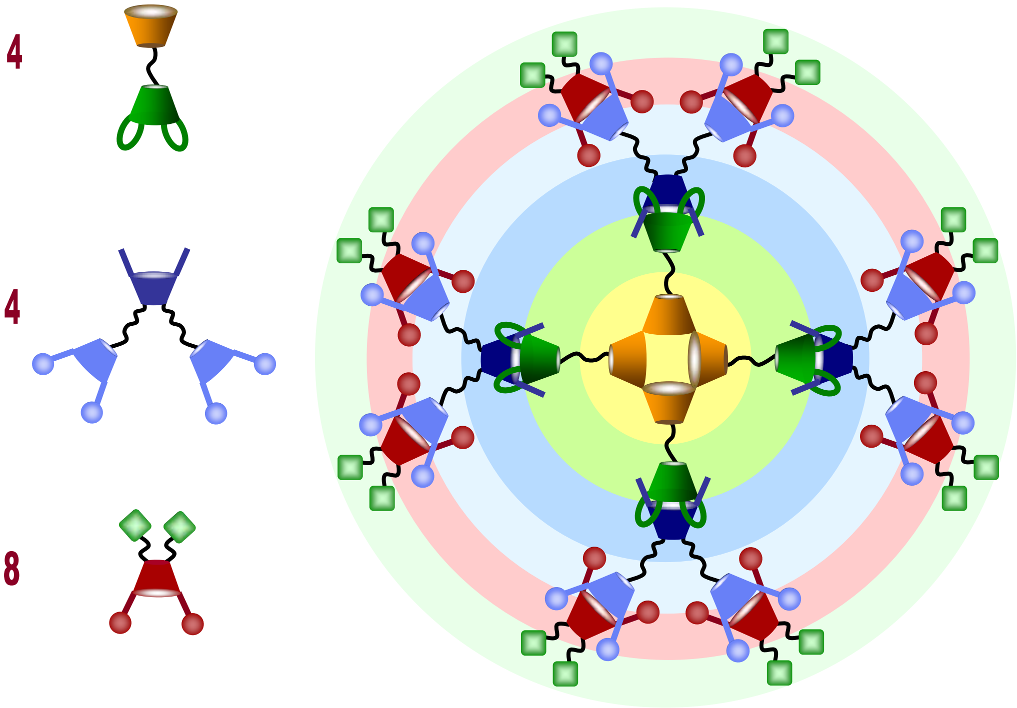


Figure 51. An example of formation of dendritic structure *via* selective di- or tetramerization of urea derivatives of calix[4]arenes. The green square indicates, that calixarene G can contain other functional groups (two or four) e.g. dyes.

The envisaged combination of the calixarene units within the building blocks is based on the following reasons. As explained above in apolar solvents the tritolyl urea momoacetamide **C** forms tetramer (orange). The tetramerization cannot be disturbed by tetratolyl ureas and therefore should not be disturbed by tetraloop derivative **D** - just a variation of a tetratolyl urea. **D** (green) can not homodimerize, but needs a partner. Among the rest of the units only tetratolyl urea the **E** (dark blue) can be the partner, because the voluminous tritylphenyl urea groups of the units **F** (light blue) and **G** (red) can not pass through the loops of **D** to form the dimers. Thus the green layer should dimerize with the dark blue one. In the next step the homodimerization of the units **F** (light blue) can lead to the cross linked structures, which should be avoided by addition of the arylsulfonyl tetraurea **G**, because aryl and arylsulfonyl ureas form heterodimers exclusively.

Thus when all building blocks are mixed together in the ratio 4:4:8 the dendritic structure shown in Figure 51 should be formed.

5. 3. Synthesis of Tri-and Tetraurea Units

5. 3. 1. Preparation of the Mono-Acetamide Calix[4]arene

At the beginning NMR spectroscopy will be the main method of analysis of envisaged self-assembled structures. Therefore the spectra of the units which will take part in the dimerization should be as simple as possible spectra. This means that oligourea calixarenes should posses at least the highest possible symmetry.

The first unit which has to be prepared for our purpose is the calixacetamide bearing one carboxylic group at the narrow rim. This group is required for the linking of **95** (Scheme 18) to unit tetraloop compound (related syntheses will be described below).

To get a simple tetrameric assembly (simmilar to that formed by monoacetamide **25**) the amide group mast be introduced in the aromatic ring bearing the ester function (Figure 52, left) or in the opposite one (Figure 52, right).

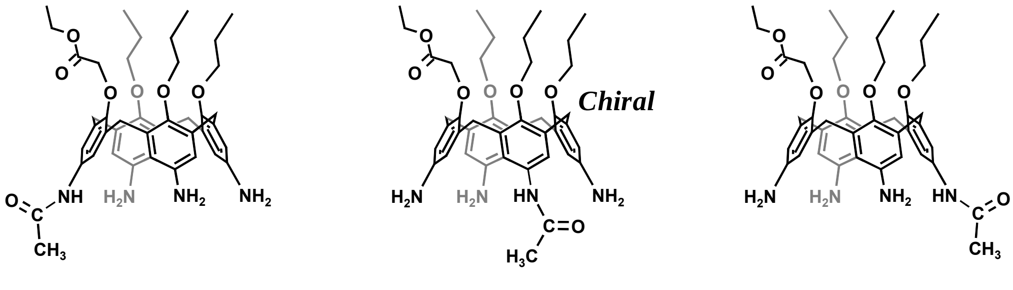
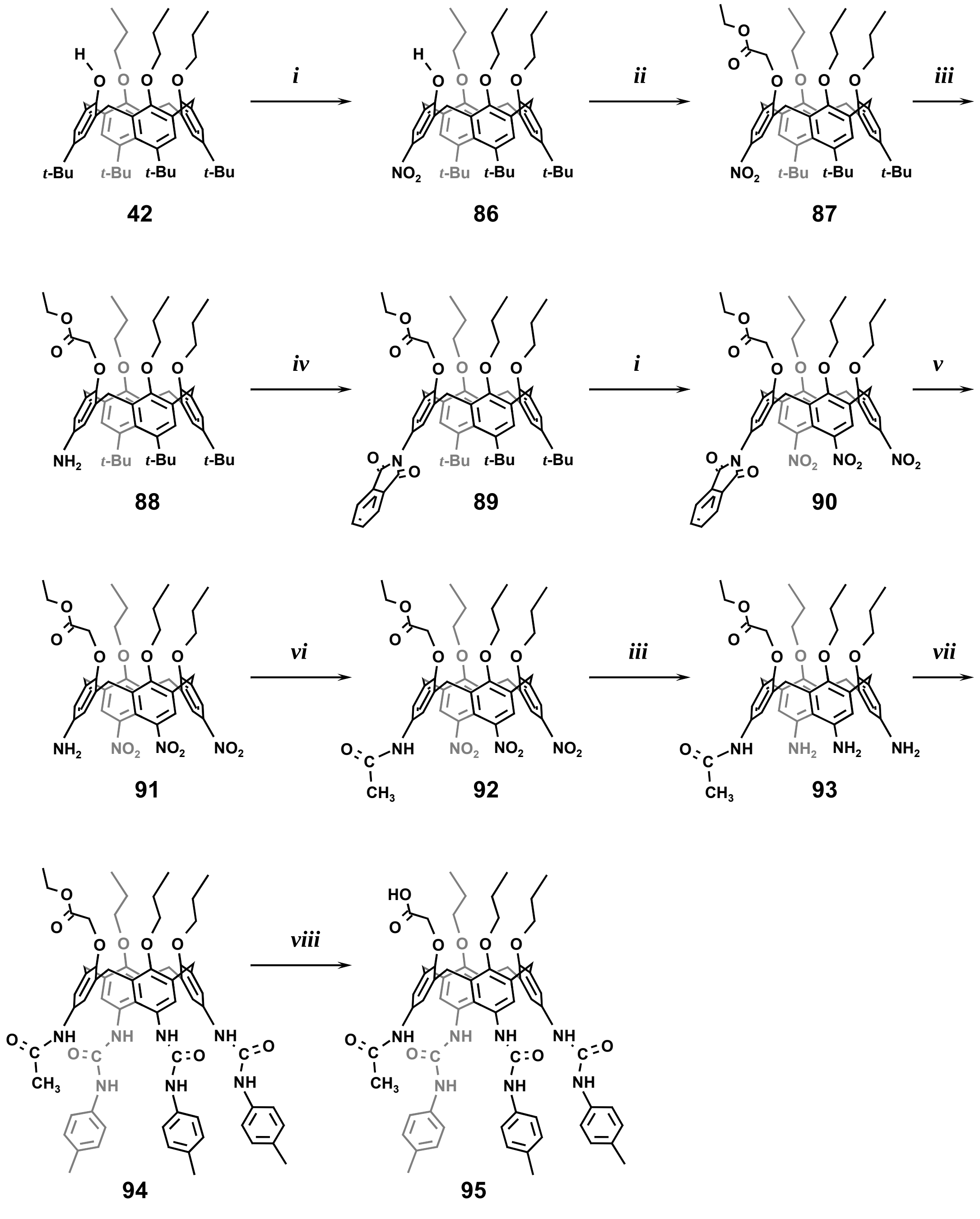


Figure 52. Possible regioisomers of mono-acetamide, possessing one functional group at the narrow rim.

The simple reaction of corresponding tetraamine with, for example, one equivalent of the acetyl chloride in the best case will result in the mixture of three regioisomers, one of which is chiral (Figure 52). In addition di-and triacetamides also will be formed. Therefore another strategy to synthesise target compound was chosen. Since the synthesis of the monoacetamide shown in Figure 52 left is much easier, this isomer will be prepared. The full synthetic rout is shown in Scheme 18.



Scheme 18. Synthetic route towards tritolyl urea monoacetamide **95**. i) CH_3COOH, HNO_3, CH_2Cl_2; ii) $BrCH_2COOEt$, Na_2CO_3, CH_3CN; iii) Raney-nickel, H_2, toluene/EtOH; iv) phthalic anhydride, $(CH_3CO)_2Zn$, pyridine; v) HCl, toluene/EtOH; vi) $(CH_3CO)_2O$, $CHCl_3$; vii) TolNCO, CH_2Cl_2; viii) NaOH/H_2O, THF/DMF.

The selective *ipso*-nitration of the known tripropyl ether **42**, followed by exhaustive alkylation with bromoethylacetate afforded calixarene **87**. Due to the low nucleophilicity of the *p*-nitrophenol ring it was advantageous to use such reactive alkylating agent as bromoethylacetate, since ω-alkylbromides with the longer alkyl are less active.

The nitro group can be easily reduced and then acylated. But, as described in the literature,[66] the subsequent *ipso*-nitration of the remaining *tert*-butyl phenolic rings leads to the product, in which the *ortho*-position of the N-acylamino group is also substituted. Recently it was shown, that the phthalimido protection of the amino groups allows to carry out the ipso-nitration in a desired manner.[67] Thus monoamine **88** was reacted with phthalic acid anhydride using $(CH_3CO)_2Zn$ in pyridine. Then compound **89** was easily *ipso*-nitrated and phthalimide was subsequently cleaved with the 3-fold excess of hydrochloric acid. Reaction of the monoamine **91** with the acetic acid anhydride in chloroform afforded calixacetamide **92**, in which the ester function at the narrow rim and the amide group at the wide rime were introduced into the same phenolic ring. Finally consecutive reduction of the remaining nitro groups, reaction with tolyl isocyanate and hydrolysis of the ester function afforded the target calixarene **95**.

The ability of compound **94** to form a tetramer was proved by ^1H (Figure 53) and COSY-gs NMR spectra.

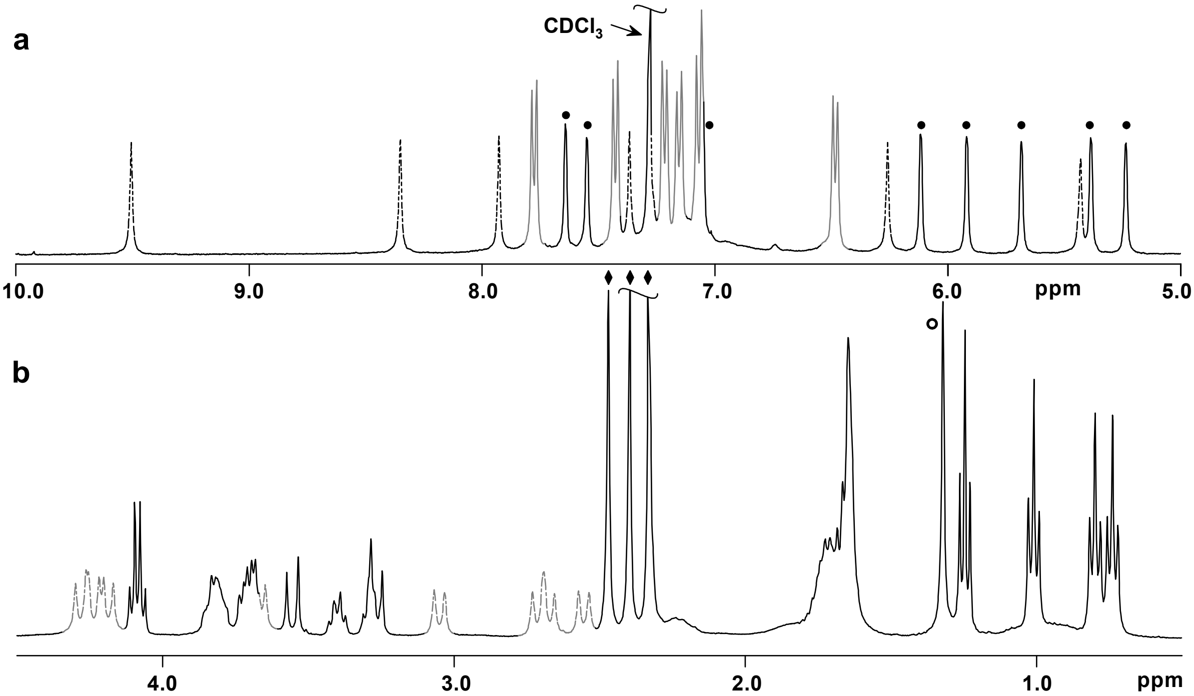
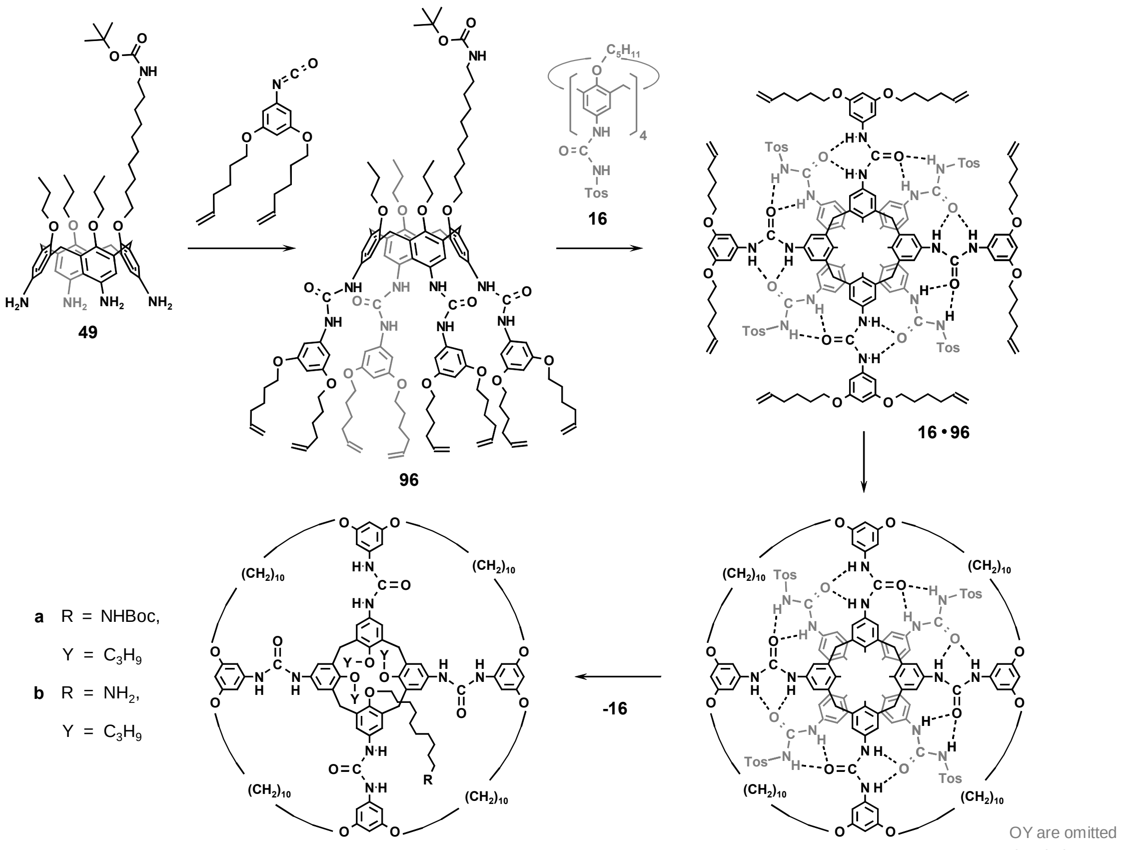


Figure 53. The ^1H NMR spectrum of **94** in $CDCl_3$ (400 MHz, 25 °C): a) aromatic and NH signals: ArH of calixarene skeleton are marked with ●, ArH of tolyl groups are shown in grey, NH signals are shown by dotted lines; b) aliphatic signals: $ArCH_2Ar$ protons are shown by grey dotted lines, $ArCH_3$ protons are marked with ♦, $C(O)CH_3$ protons are marked with ○.

In the aromatic region 21 signals can be observed, from which six *ortho*-coupled doublets correspond to the aromatic protons of the tolyl residues. The eight *meta*-coupled doublets were distinguished with the help of COSY-gs and attributed to the aromatic protons of calixarene rings. The remaining six singlets were attributed to the NH protons of the urea and amide residues, while one singlet is covered by the signal of the solvent. In the aliphatic part of the spectrum eight doublets for the methylene bridges, three singlets for the tolyl CH_3 protons and one signal for amide CH_3 are found. The whole spectrum of **94** in $CDCl_3$ is very similar to that of compound **25**, described in the literature.[28]

5. 3. 2. Synthesis of the Tetraloop Compound

As explained above in the next step towards dendritic structure we envisaged to synthesise bis- or tetraloop tetraurea calix[4]arenes (which do not form homodimers) bearing one functional group at the narrow rim. Since the tetraloop compound possess higher symmetry, it would be more advantageous for spectroscopic reasons. Moreover bisloop calixarene monosubstituted at the narrow rim is chiral and thus its heterodimerization will result in the mixture of diastereomers, what is not desired. Therefore the tetraloop **97b** was prepared as shown in Scheme 19.



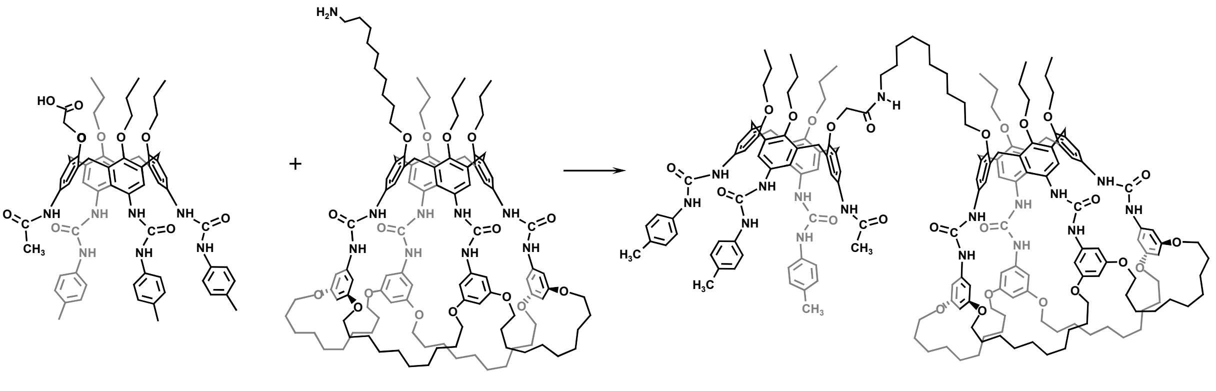
Scheme 19. Synthesis of tetraloop compound bearing one amino group at the narrow rim.

The tetraamine **49** was reacted with the appropriate freshly prepared isocyanate and calixarene **96** was obtained in 68% yield.

Usually macrocyclic compounds are synthesized under high dilution conditions. But high dilution conditions alone can suppress the undesired **inter**molecular reactions, but not wrong **intra**molecular connections. The problem was solved by use of selective heterodimerization between aryl and arylsulfonyl ureas.[22] The tetratosyl urea **16** was used as a template to prevent the transcavity bridging. Therefore the heterodimer **16•96** was prepared and the metathesis reaction was carried out under high dilution conditions (CH_2Cl_2, 0.1×10^{-3} mol/l). After the reaction is finished the Grubb's catalyst was destroyed with triethylamine and the remaining double bonds were hydrogenated in the presence of PdO_2. The reaction mixture was passed through the column to remove **16** and to get pure tetraloop compound **97a** in 70% yield. Deprotection finally afforded the target amino compound **97b**.

5. 4. Bis-Calixarenes: Syntheses and Self-Assembly Properties

The coupling of the monoacid **95** and monoamine **97a** using PyBOP in DMF afforded the first building block for the intended dendrimer (bis-calixarene **98)** in 85 % yield (Scheme 20).



95 **97b** **98**

Scheme 20. Synthesis of bis-calixarene **98**.

The aromatic part of ^{1}H NMR spectrum of **98** recorded in DMSO at room temperature (Figure 54) shows:

- one signal for the acetamide N*H*;
- the set of signals for the urea and amide N*H* (at 75 °C the amide N*H* can be observed separately);
- two doublets for the Ar*H* protons of the tolyl residues in the ratio 1:2, while the other two are overlapped with one of the singlets for C*H* protons of the calixarene skeleton of **95**;
- the three singlets for the remaining C*H* protons of the same calixarene skeleton;

- the rest of the signals correspond to the aromatic protons of calixarene **97b**.

  The whole spectrum is in accordance with the proposed structure.

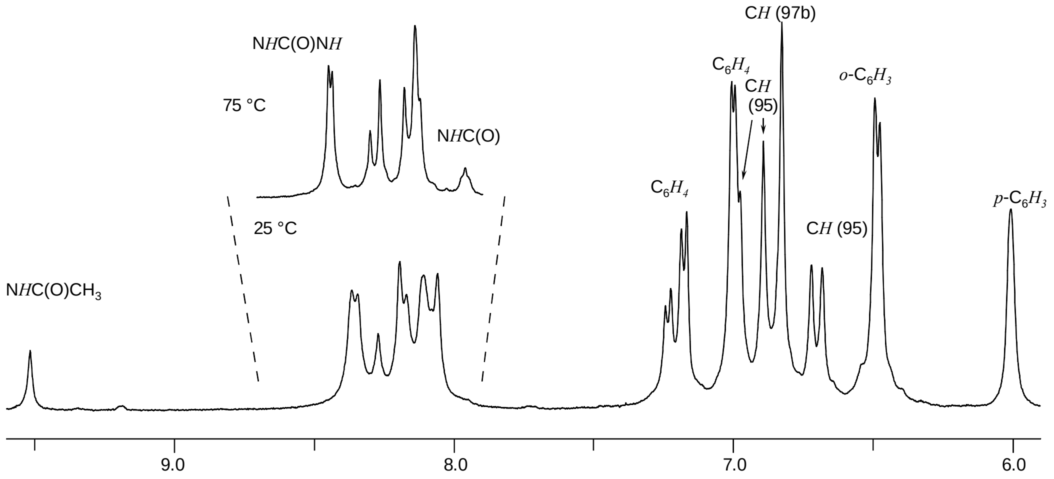
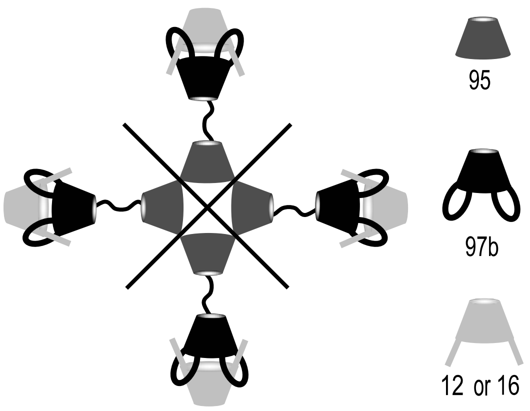


Figure 54. The sections of the ^{1}H NMR spectra of **98** in DMSO.

Now we already can examine the formation of the first two shells of envisaged dendritic structure. For this purpose the calixarene **98** was mixed with the tetratolyl urea **12** in the ratio 1:1 in $CDCl_3$ and the ^{1}H NMR spectrum of the mixture was recorded. Surprisingly we could not observe any evidence of the correct assembly. The signals corresponding to the tetrameric structure were almost absent, while among the rest of the signals, those corresponding to homodimer **12•12** were detected. After one week the spectrum was measured once again and the same picture was observed.



On the basis of these observations we assumed, that heterodimer tolyl/loop is formed not exclusively and the remaining without partner tetraloop-end disturbs tetramerization of monoacetamide. This result was totally unexpected and reasons for this were not clear.

Since tolyl and tosyl derivatives have strong tendency to form heterodimeric capsule, we have tried to improve the situation *via* selective dimerization of tetraloop-end of **98** with tosyl urea **16**. But in the ^{1}H NMR spectrum of the 1:1 mixture of **98** and **16** in $CDCl_3$ a very complicated set of signals has been observed instead of the expected one. In the NH region of the spectrum resonances corresponding to tosyl/tosyl and tosyl/loop dimeric capsules were detected. Among the remaining NH signals those corresponding to the tetramer were not found. This means that the acetamide-end of bis-calixarene **98** is involved in undesired assembly, which is present in both mixtures **98 / 12** and **98 / 16**. But which?

Looking for the answer to this question we have recorded the spectrum of building block **98** alone in $CDCl_3$ without the addition of the capping unit **12** or **16**. We supposed to see the signals of the tetramer and the broad peaks corresponding to the tetraloop compound. Unexpectedly we observed a set of slightly broadened signals (Figure 55c), which most probably must be attributed to assembly present in the mixtures of **98 / 12** (Figure 55a) and **98 / 16** (Figure 55b). The small differences in the shape of the signals could be explained by the presence of other assemblies in the mixture.

Then calixarenes **94** and **97b** (not connected to each other) were mixed together and formation of heterodimer **94•97b** have been observed. Thus, however tritolyl urea monoacetamide **94** do not form homo- or heterodimeric capsules with "open chain" tetraureas (even with tosyl derivatives) if solvents are used as guests, it formed heterodimer with the tetraloop compound. These observations show how the small changes in the structure of molecules can strongly influence an outcome of dimerization.

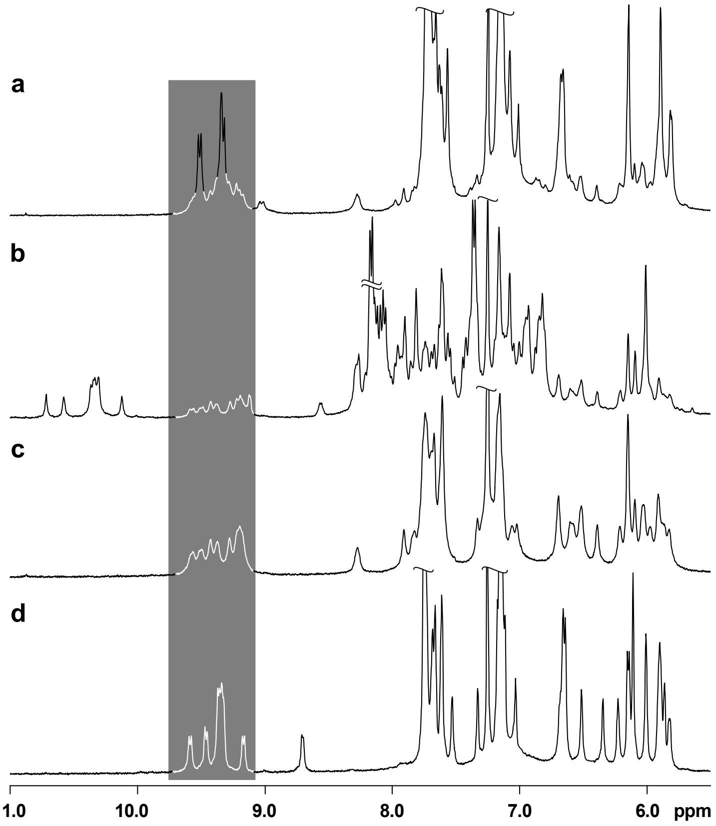
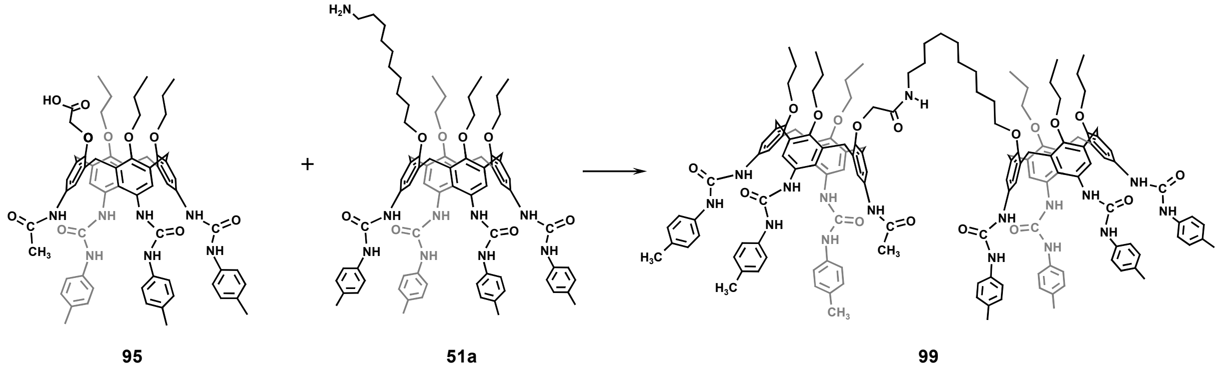


Figure 55. The sections of the ^1H NMR spectra in $CDCl_3$ of a 1:1 mixture of bis-calixarene **98** and tetratolyl urea **12** (a); 1:1 mixture of bis-calixarene **98** and tetratosyl urea **16** (b); bis-calixarene **98** (c); 1:1 mixture of tetraloop **97b** and tritolyl urea monoacetamide **94**.

It is also important to note, that among all assemblies detected in the spectra we never found the signals of tetramer. This observation rises a question: can the acetamide-end of bis-calixarene in principle form a tetramer or not? To examine this possibility we have prepared the model bis-calixarene **99** (Scheme 21). In contrast to the previous example, the homodimerization of tetratolylurea-end of **99** is possible and thus the formation of cross-linked structures can not be excluded. To prevent this calixarene **99** has to be mixed in the ratio 1:1 with tetratosyl urea.



Scheme 21. Synthesis of bis-calixarene **99**.

Before we have started the synthesis of **99** we have performed the model experiment which shows that the stoichiometric mixture of tritolyl urea momoacetamide **25**, tetratolyl urea **12** and tetratosyl urea **16** affords the mixture of tetramer and heterodimer exclusively (Figure 56), however the self-assembly occurs rather slowly (30 min) and even can be followed by ^{1}H NMR.

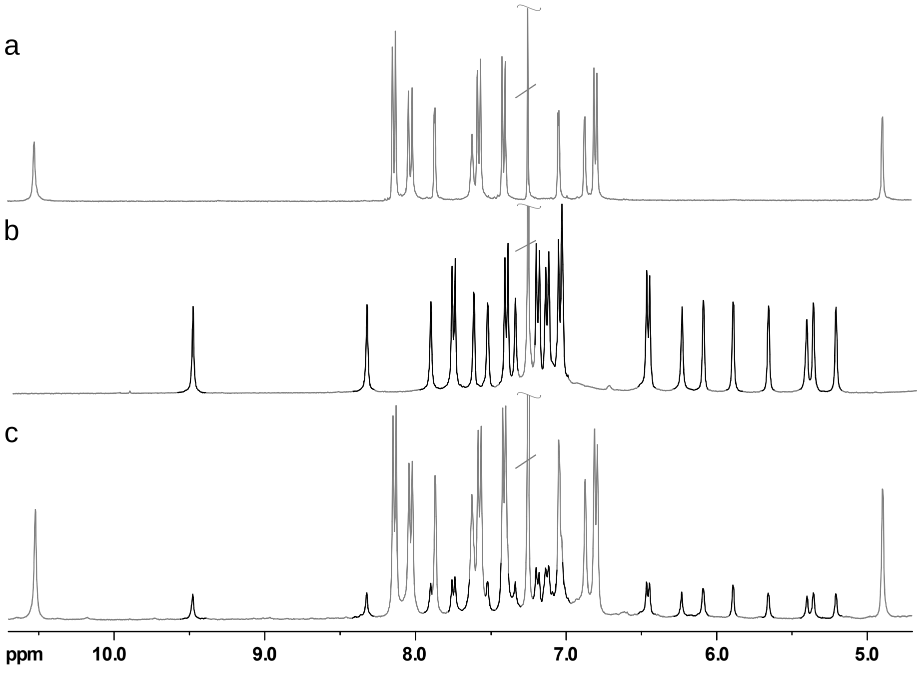


Figure 56. The section of the ^{1}H NMR spectra in $CDCl_3$ of the mixture of **12** and **16** in the ratio 1:1 (a), tritolyl urea monoacetamide **25** (b) and mixture of **12**, **16** and **25** (c).

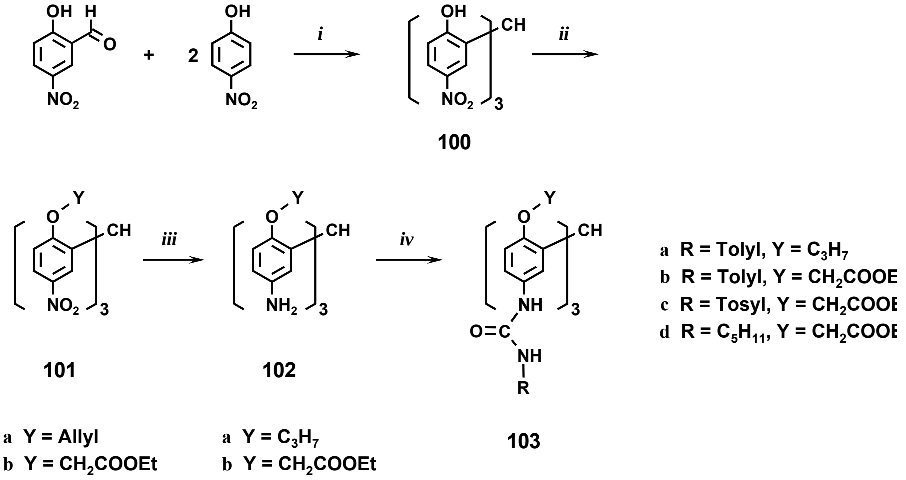
When **99** was dissolved in $CDCl_3$ alone the main signals in the spectrum were attributed to the homodimer tolyl/tolyl. The rest of the signals are broad and probably corresponds to undefined assemblies. In the 1:1 mixture of **99** and **16** the signals of tetramer have not been observed again, while resonances of tolyl/tosyl heterodimer were present. The only reasonable explanation of this fact can be given by the short alkyl spacer, connecting the two calixarenes. This means that the distance separating tolyl- and acetamide-ends is too short to allow tetramerization of monoacetamide. Now we are working in direction of the prolongation of the spacer.

Summarizing the results discussed above two main things should be outlined:

- in the mixture of tetratolyl urea **12** and **94** only homodimer **12•12** and tetramer **94**$_4$ are present. In contrast (and totally unexpected), the tetraloop derivatives **97** and tritolyl urea monoacetamide **94** form exclusively heterodimer **97•94**.
- in bis-calixarenes of type **99** the dimerization of the tetratolyl urea-end does not allow the mono-acetamide-end to form tetramer. Most probably this happens since the spacer between the two calixarene units is too short.

5. 5. Triphenylmethanes as a Core for Dendritic Structure

Meantime in our group was developed a simple synthesis for tri-(2-alkoxy-5-aminophenyl)methanes, which is indicated in Scheme 1.[*] Acid catalyzed condensation of 2-hydroxy-5-nitro-benzaldehyde with four moles excess of *p*-nitrophenol leads to **100** (89%)[68] which can be subsequently *O*-alkylated with reactive alkylhalogenides and then reduced giving amino triphenylmethanes **102**.



Scheme 22. Synthesis of the target triureas; i) H_2SO_4, 155 °C; ii) YBr, K_2CO_3, acetone; iii) Raney-Ni, H_2; iv) RNCO, CH_2Cl_2.

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[*] Compounds 100-102 were prepared by Dr. V. Rudzevich

Having in mind, that urea derivatives of triphenylmethanes also could be used as a core for the dendritic assembly (instead of tritolylurea monoacetamide) we have prepared triureas **103** from amines **102** by reaction with the respective isocyanates and examined their ability to form dimers.

The ^{1}H NMR spectra of **103** in DMSO-d_6 demonstrate the expected pattern of a molecule with (dynamic) C_{3V}-symmetry (Figure 57a), showing for instance one singlet for the enantiotopic –O-CH_2-protons in **103b**. In solvents such as $CDCl_3$, $C_2D_2Cl_4$ or benzene this signal splits into a pair of doublets ($\Delta\delta$ = 1.1 ppm) with geminal coupling (J = 16 Hz) (Figure 57b) indicating that these CH_2 protons experience now a chiral environment rendering them diastereotopic. All aromatic protons of the triphenylmethanes skeleton are up-field shifted (the strongest shift is observed for the *m*-Ar*H* marked in blue). The strong splitting of the two N*H*-singlets suggests that one of the N*H*-groups forms a hydrogen bond, and the whole spectrum is in agreement with a C_3-symmetrical conformation, e.g. in a kinetically stable dimer with S_3-symmetry.

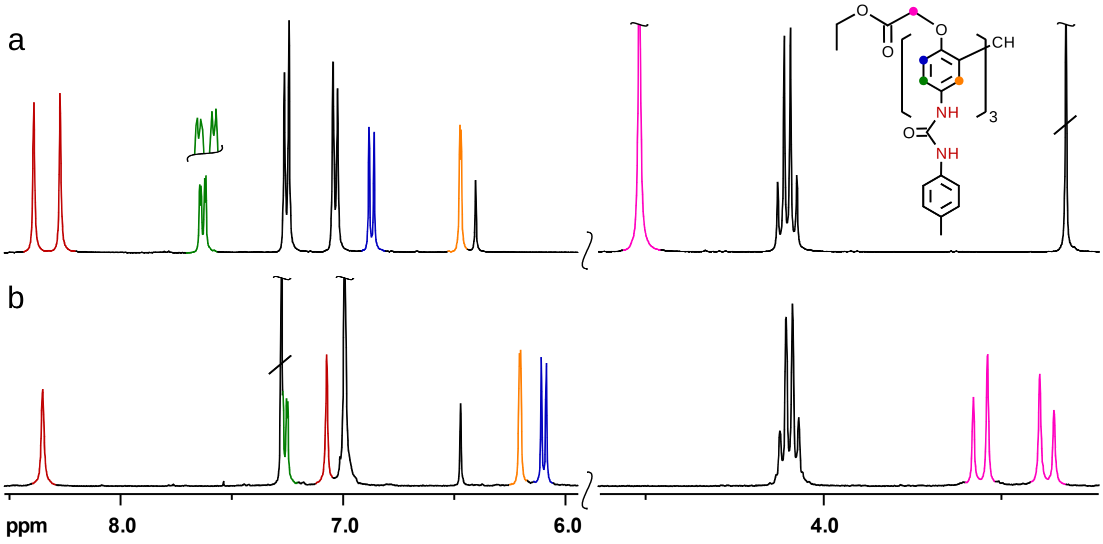


Figure 57. Sections of the ^{1}H NMR spectra (400 MHz) of **103b** in DMSO-d_6 (a) and in $CDCl_3$ (b).

Dimerization was unambigously proved by the formation of heterodimers in 1:1 mixtures of two triureas **103a** and **103b**. While the spectrum of such a mixture in DMSO-d_6 consists of a superimposition of the two single spectra, in $C_2D_2Cl_4$ an additional double set of signals corresponds to the heterodimer as demonstrated in Figure 58. Simultaneously the formation of a larger assembly is excluded by this still simple spectrum. In contrast to tetraurea derivatives of calixarenes, the stoichiometric mixture of tritolyl urea **103b** and tritosyl urea **103c** also leads to the formation of all possible dimers.

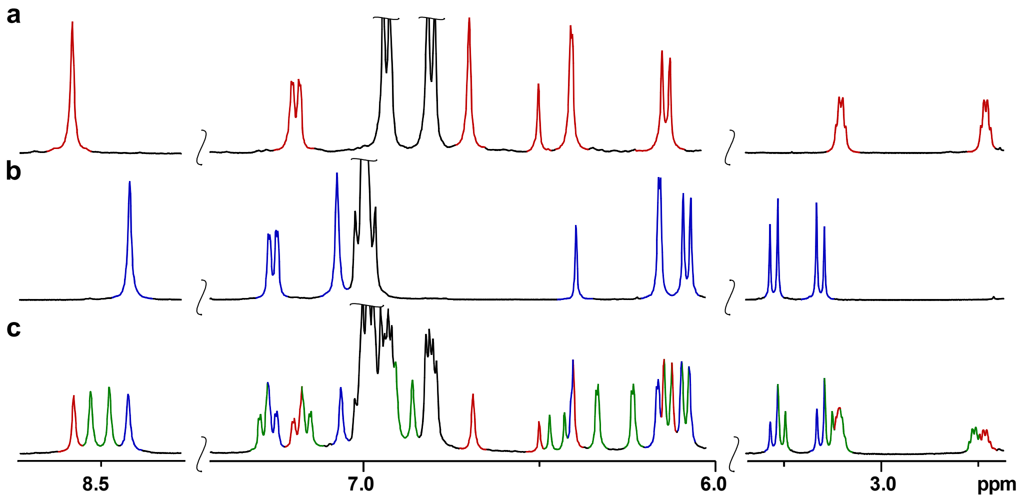


Figure 58. Sections of the ^{1}H NMR spectra (400 MHz) in $C_2D_2Cl_4$ of **103a** (a), **103b** (b) and 1:1 mixtures of **103a** and **103b** (c). The additional set of signals (corresponding to heterodimer) is shown in green.

While tetraurea calix[4]arenes do not show any peaks of dimers in their mass spectra, the dimerization of triurea triphenylmethanes was demonstrated as well by ESI-MS. A mixture of **103b** and **103d** shows the peak for the heterodimer with 100% abundance, the two peaks for the homodimers with ~30-35% and the peaks for the single molecules with 25-100% (all peaks with one Na^+) (Figure 59). It is unclear, if this is due to a greater stability of dimers **103•103** or to their lower mass in comparison to **8•8**. Titration experiments show that dimers **103•103** are present up to 9 % DMSO-d_6 in a $C_2D_2Cl_4$ solution, what is comparable to dimeric capsules of calix[4]arenes **36** while dimers of **12** are less stable.[35]

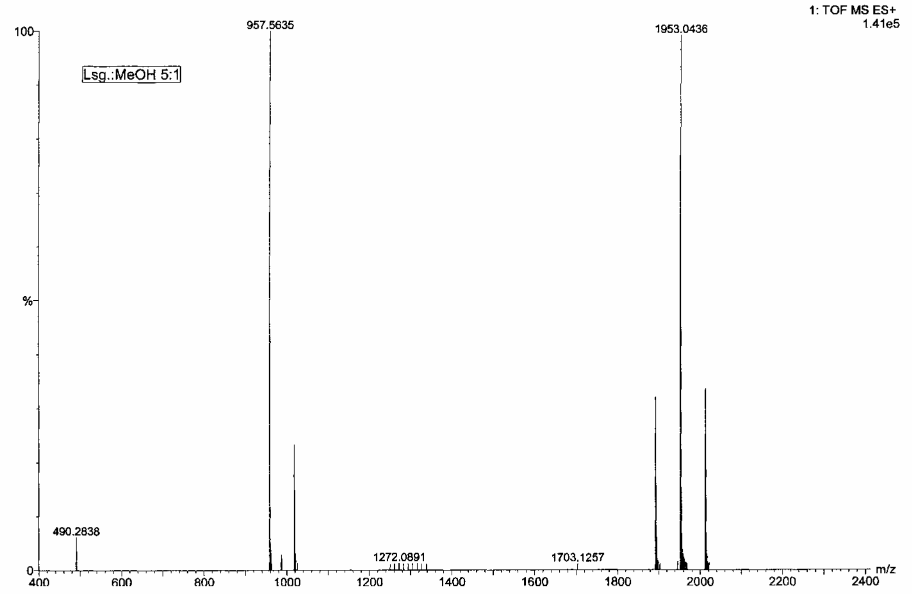


Figure 59. ESI-MS of the mixture of **103b** and **103d** in $CHCl_3$/MeOH = 5/1.

The structure of the dimer was also proved by X-Ray analysis (Figure 60). The dimer is composed of two crystallographically independent triphenylmethanes, which resemble a three-bladed propeller. The two parts of the capsule are kept together by twelve hydrodgen bonds. In contrast to calixarenes, here the hydrogen bonds formed by NH attached to the triphenylmethane core are stronger than those formed by NH attached to the tolyl residues. The respective N···O distances 2.85/2.90 and 3.07/3.28 Å found in crystalline state are in accordance to information given by ^{1}H NMR in solution.

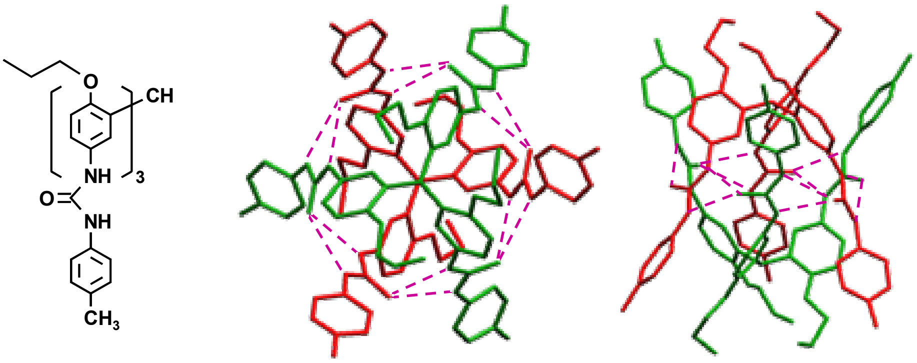


Figure 60. X-Ray structure of the homodimer **103a•103a**.

As expected, ^{1}H NMR spectra of the solutions of **103** and **12** in $CDCl_3$ show only the presence of both homodimers. Since also **12** and the more rigid **36** do not form heterodimers[35] a mixture of all three urea derivatives (**12**, **36**, **103b**) contains only the three possible homodimers (Figure 61). Selectivities such as these are very important for building up well defined dendritic structures *via* self-assembly processes from molecules containing two (or more) tri- and/or tetraurea units.

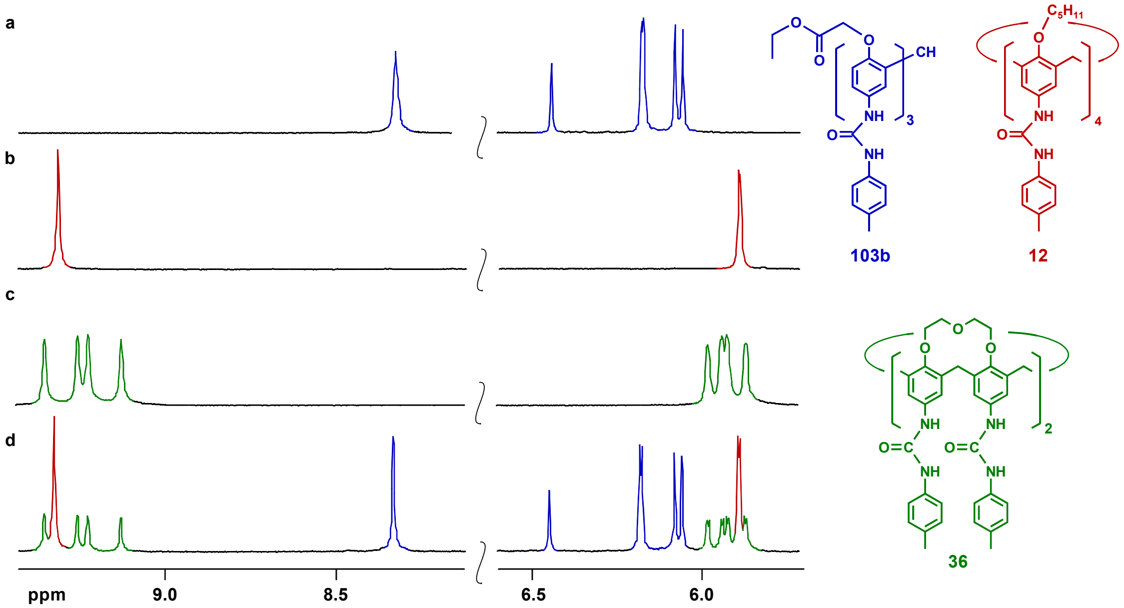


Figure 61. Sections of the ^{1}H NMR spectra (400 MHz) of **103b** (a)**,** **12** (b), **36** (c) and of their stoichiometric mixture (d) in $CDCl_3$.

5. 6. Second Approach Towards Dendritic Structures

Triurea triphenylmethanes possessing three functional groups at the “narrow rim” (for example **103b**) can be used in construction of a first self-assembled shell of dendrimers. Thus, if we take instead of the tritolyl urea monoacetamide calix[4]arene **95** tritolyl urea triphenylmethane, the dendritic assemblies shown in Figure 62 should be formed. In general the principle of self-assembly of the units towards dendrimer is similar to that described above.

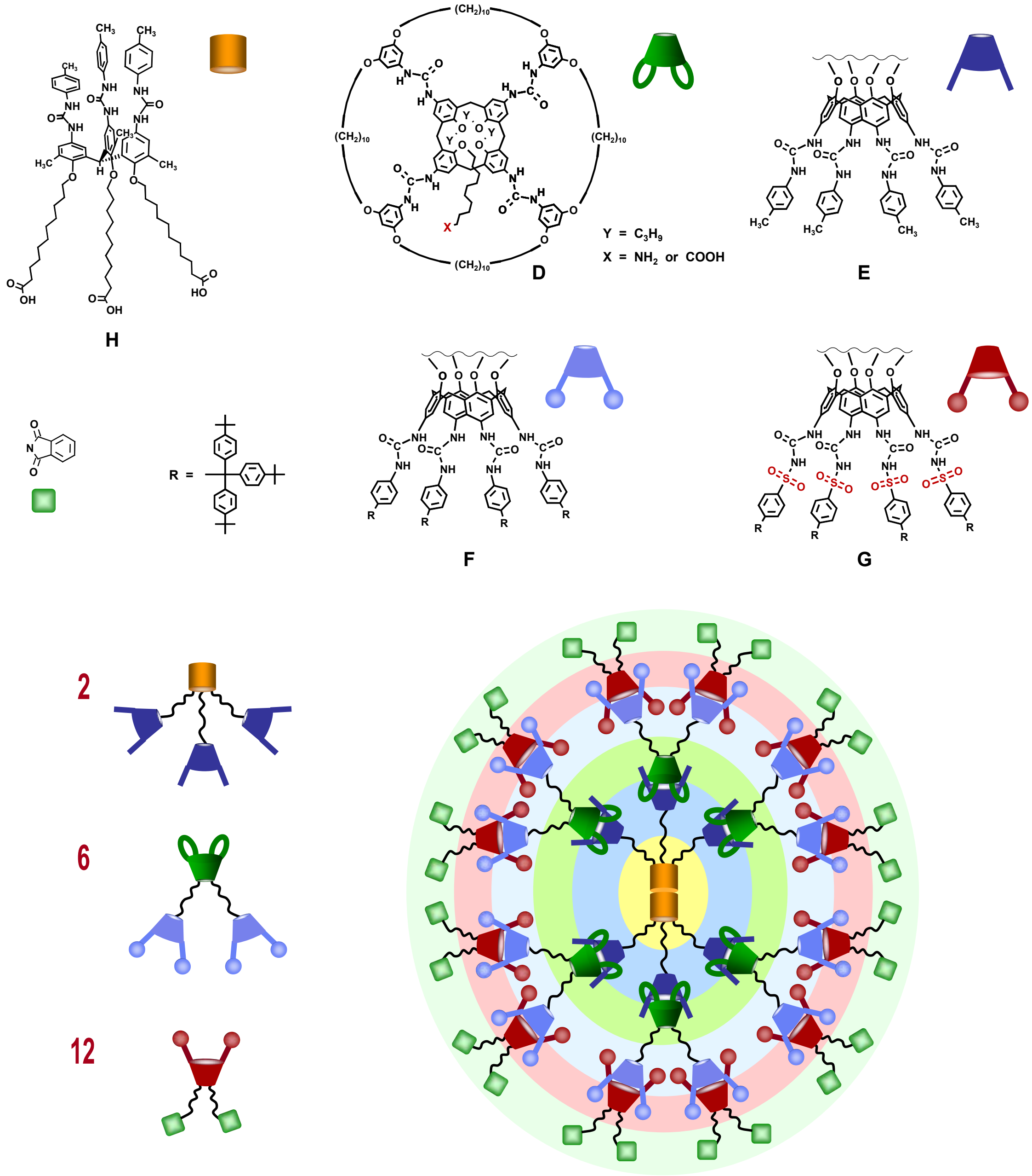


Figure 62. The second strategy for the formation of dendritic structure *via* selective self-assembly of tetraurea calix[4]arenes and triurea triphenylmethanes.

The tritolyl urea **H** (orange) form homodimers in apolar solvents. This process does not affect the dimerization of any tetraurea calix[4]arenes and vice versa. Thus the formation of homodimer **H•H** is the only existing possibility for unit **H**.

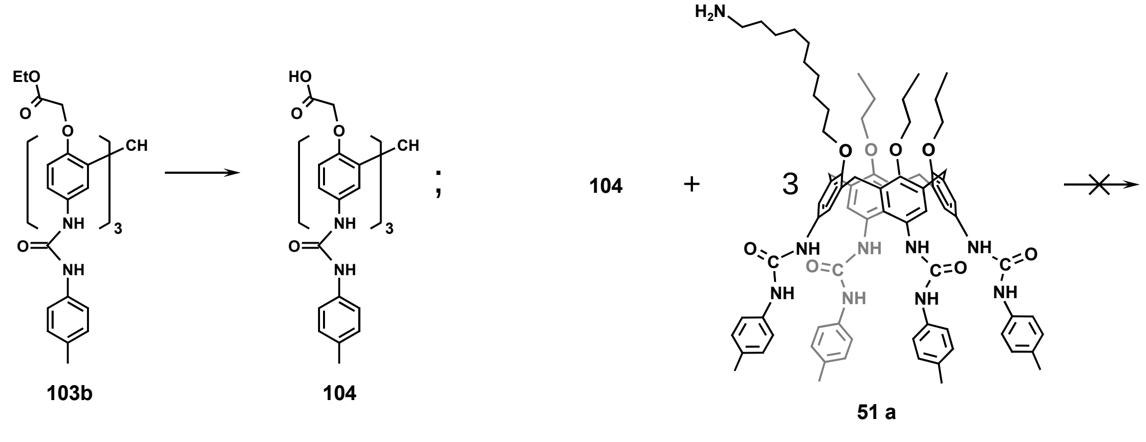
Unit **D** can only heterodimerize. From the remaining units **E**, **F** and **G** (which can form homo- or heterodimers) only tetratolyl urea **E** can be accepted as a partner for **D**. The units **F** and **G** possess tritylphenyl groups, which are not able to pass trough the loops to form a capsule with **D**, but have strong tendency to heterodimerize with each other.

Two or four phthalimides will be attached to the unit **G** as potential functional groups useful for the attachment of further calixarene molecules or dyes.

Thus when all six units will be combined within three building blocks **HE$_3$**, **DF$_2$**, **GPht$_n$** and all building blocks will be mixed together in the ratio 2:6:12 respectively the dendritic structure shown in Figure 62 should be formed.

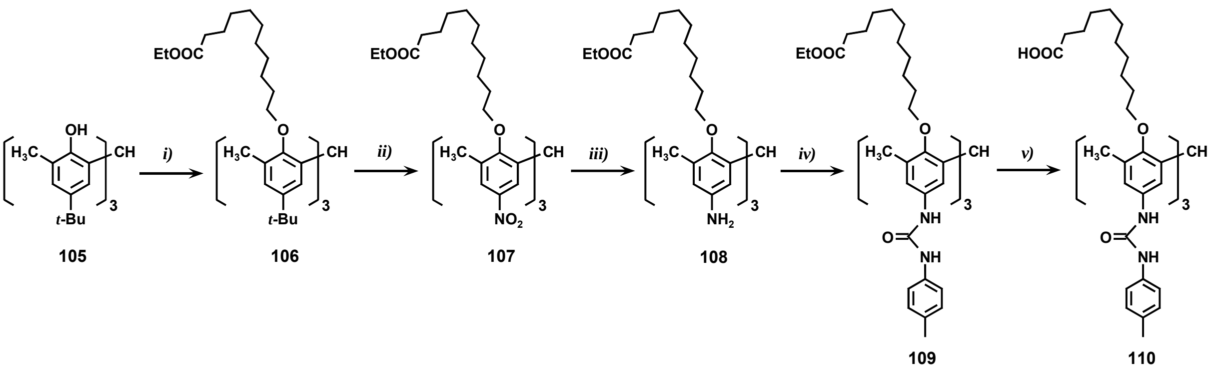
5. 7. Synthesis of the first building block and ^{1}H NMR analysis

To prepare the first building block the ester functions of triurea **103b** were hydrolyzed and the triacid **104** was reacted with three moles of tetratolyl urea **51a**. Unfortunately it was not possible to accomplish the reaction and introduce all tree molecules off **51a**, but maximum two. Most probably such outcome of reaction could be explained by the steric problems due to the short alkyl chains of **104**. In principle, these chains can be prolonged by reaction with corresponding aminoacid, but then undesired additional signals can appear in the ArH/NH region of the spectrum. Therefore we have decided to prepare triphenylmethane, initially bearing three longer chains at the "narrow rim". The synthesis of such unit is shown in Scheme 24.



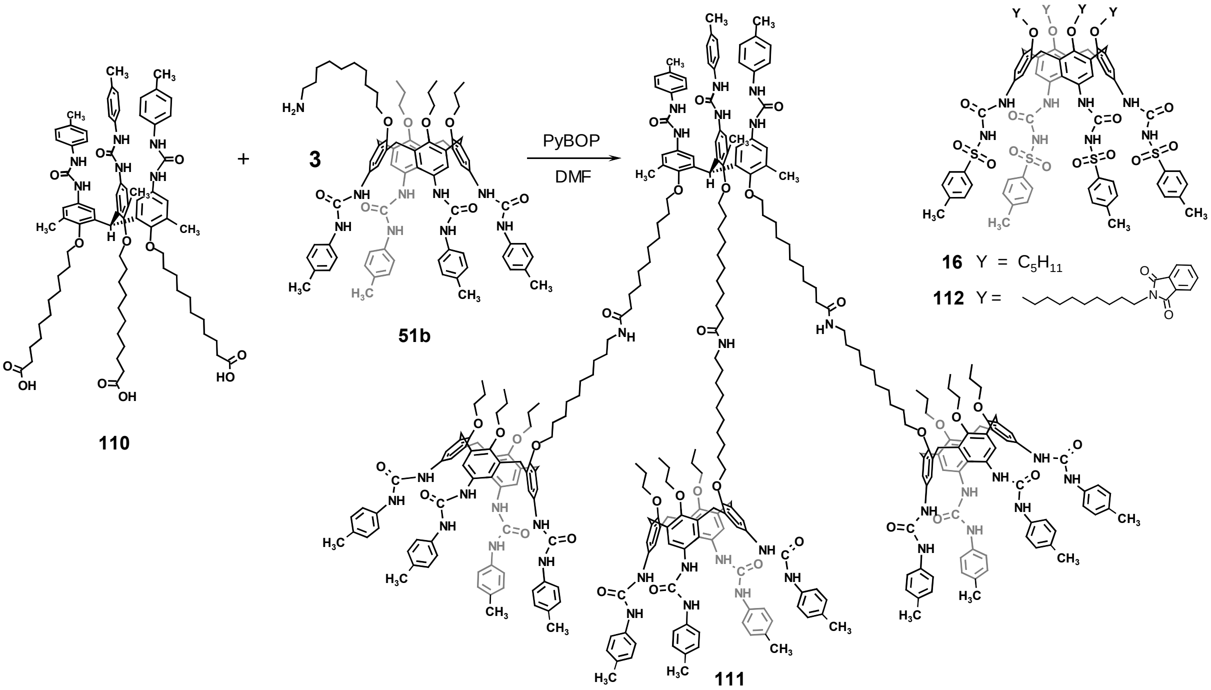
Scheme 23. Towards first building block of dendritic structure.

To simplify the spectral characteristics of the final compound we have started with triphenylmethane, bearing methyl group in one *meta* position and to have a possibility to introduce the long alkyl chains the *tert*-butyl group in the other one. All the steps of this multi-step reaction were carried out analogously to the calixarenes.



Scheme 24. Synthesis of triphenylmethane, bearing long alkyl chains at the narrow rim. i) $Br(CH_2)_{10}COOEt$, NaH, DMF; ii) CH_3COOH, HNO_3, CH_2Cl_2; iii) Raney-nickel, H_2 toluene/EtOH; iv) TolNCO, CH_2Cl_2; v) NaOH/H_2O, THF/DMF.

The coupling of triurea triphenylmethane **110** with three tetratolyl urea units **51a** using PyBOP afforded the central building block **111** (Scheme 25). The structure of the product was proved by ^{1}H NMR spectroscopy and ESI MS spectrometry. A tetratosyl urea **112** bearing four phthalimide residues at the narrow rim was prepared in the usual way, by reaction of the respective wide rim tetraamine with tosylisocyanate.



Scheme 25. Synthesis of the central building block **111**.

Under conditions suitable for the dimerization of the oligourea motifs, e.g. in $CDCl_3$ as solvent, **111** is not soluble. This fact could be explained by formation of cross-linked structures *via* homodimerization of tetratolyl urea units. The building block **111** can be solubilized by the addition of tetratosyl ureas **16, 112** or tetraloop compound **19** (**D** in Figure 62). Only if all tetraurea units **51a** are involved in heterodimerisation, the dendritic architectures shown in Figure 63 are formed.

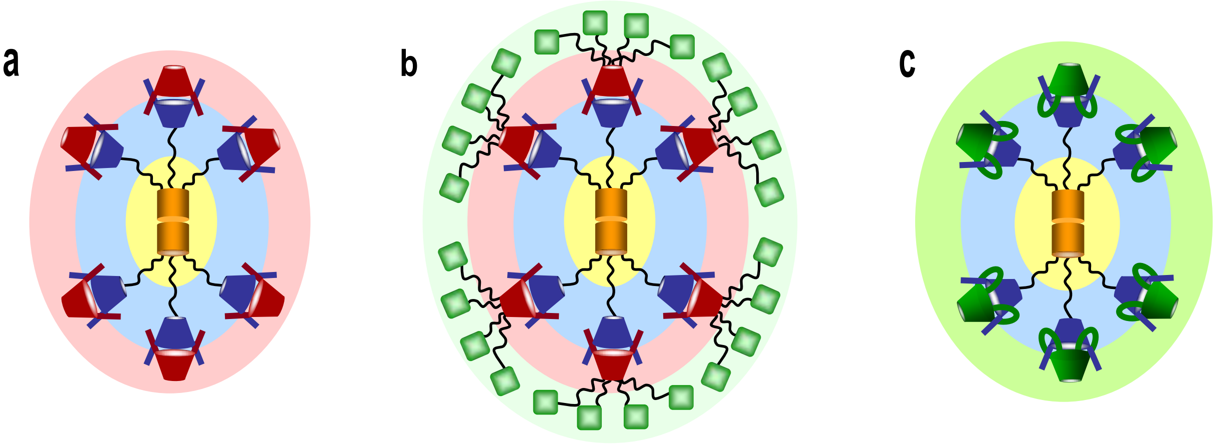


Figure 63. Schematic representation of the dendritic assemblies $\mathbf{111_2{\bullet}16_6}$ (a), $\mathbf{111_2{\bullet}112_6}$ (b), $\mathbf{111_2{\bullet}19_6}$ (c).

A typical ^1H NMR spectrum of the dendritic assembly is shown in Figure 64c. It contains all spectroscopic elements expected for a $\mathbf{111_2{\bullet}16_6}$ assembly, which was prepared by mixing of **111** and **16** in the ratio 1:3 in $C_2D_2Cl_4$: signals for the homodimer **111•111** and much stronger of course signals for the heterodimer **51a•16**. No additional peaks or broad signals were detected. For comparison the spectra of triphenylmethane **109** and heterodimer **12•16** in the same solvent are also shown in Figure 63a,b respectively. Other solvents were not examined due to the limited solubility of **111**.

Considering the fact that each dimeric capsule formed by tetraurea calix[4]arenes contains one solvent molecule as guest[16,36a] these assemblies consist of 14 molecules with a total molecular mass of ~20 700, ~25 800 and ~22 900 g/mol respectively. This explains also the light broadening of peaks in ^1H NMR at room temperature.

Thus the programmed formation of the self-assembled aggregate (the first step towards larger dendritic structure) finally was achieved. Up to the moment this is the first example of a self-assembled dendrimer, which is **uniform in size and structure**.

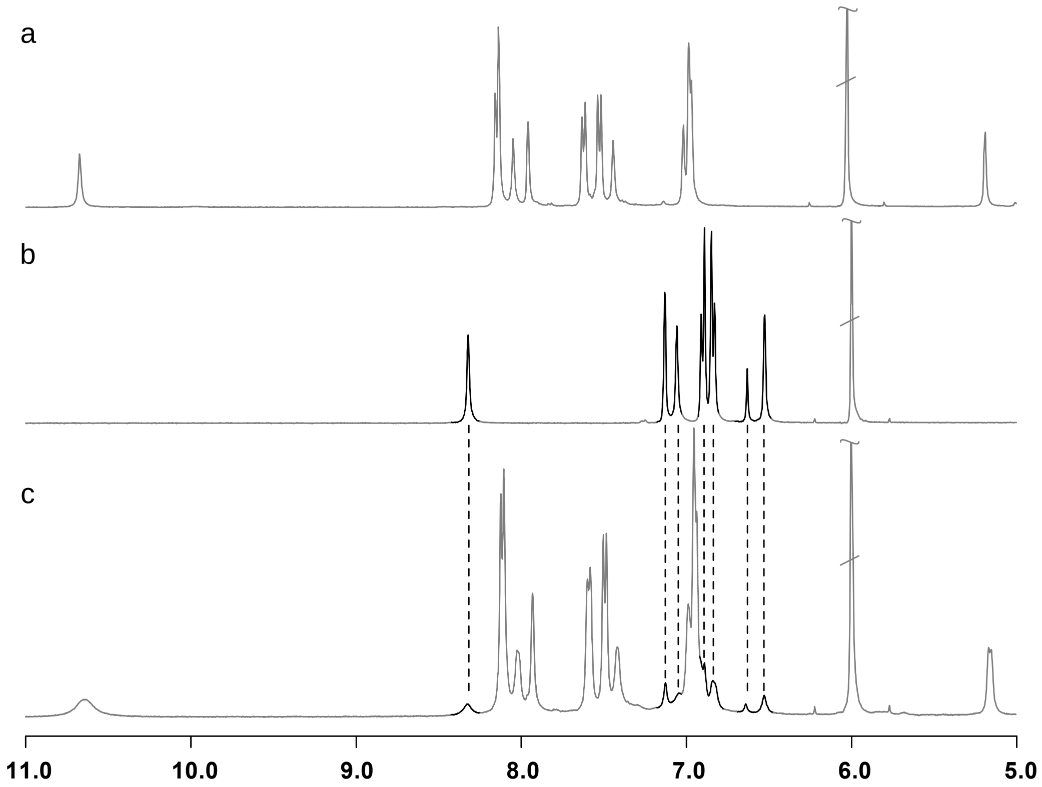


Figure 64. The section of the spectra in TCE of triphenylmethane **109** (a), heterodimer **12•16** (b), and dendritic structure **111₂•16₆** (c).

Now we are elaborating the synthesis of the next building block for envisaged dendritic architecture.

5. 8. Conclusions

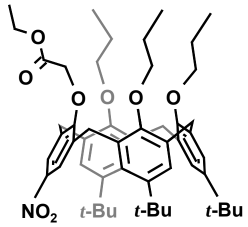
As a first step towards self-assembled dendrimers the multi-step synthesis of tritolyl urea monoacetamide **95**, bearing one carboxylic group at the narrow rim has been developed. To keep the symmetry of the original tritolyl urea monoacetamide **25** (and thus of it's tetrameric assembly) the ester function was introduced in the *para*-position to acetamido group. Subsequent reaction of **95** with the tetratolyl ureas **98** or **51a** affords bis-calixarenes **98** and **99** respectively. These compounds had to be used as central units of the dendritic assemblies. But, in contrast to our expectations, in apolar solvents the calix-acetamide part of bis-calixarene does not form a tetramer. It could be tentatively explained by the short alkyl spacer connecting two calixarenes. Therefore the dimerization of the tetratolyl urea-end of bis-calixarene makes tetramerization impossible.

An alternative strategy towards dendritic assemblies is based on the dimerization of tritolyl urea derivatives of triphenylmethanes, which were prepared analogously to tetraurea calix[4]arenes. The dimerization was evidenced by ^{1}H NMR spectroscopy and unambiguously proved by X-Ray analysis. The reaction of triurea triphenylmethane **110** with three equivalents of **51a** affords a multiple unit **111**, which is able to form the desired self-assembled structure in combination with 3 equivalents of tetratosyl ureas **16**, **112** or tetraloop tetraurea **19**.

5. 9. Experimental Part

calix[4]arene 87

A mixture of calix[4]arene **86** (4.30 g, 5.63 mmol), Na$_2$CO$_3$ (0.063 g, 0.59 mmol) and ethyl bromoacetate (0.098 g (0.065 ml), 0.59 mmol) was refluxed during 4 days in CH$_3$CN (50 ml). The progress of the reaction was controlled by TLC (THF/Hexane=1/10). When the reaction is finished the colour of the mixture is changed from bright orange to the pale yellow. After that the sodium salts Na$_2$CO$_3$ was filtered out from the hot reaction mixture and washed with chloroform on the filter paper. Then the solvent was removed in vacuum. The residue was dissolved in MeOH/Acetone=5/1 (30 ml) and water (30 ml) was added to the solution. The turbid water layer was decanted and MeOH (20 ml) was added again. The flask was left in an ultrasonic bath for 1 h and then the formed precipitate was filtered off and dried. Calixarene **87** (3.78 g, 79 %) was obtained as a white powder; mp 195-197°C;



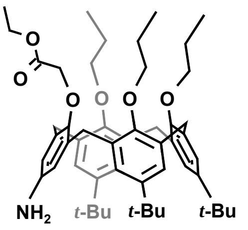
^{1}H NMR (400MHz, CDCl$_3$), δ: 7.42 (s, 2H, ArH), 7.05 (d, 2H, $^4J = 2.3$ Hz, ArH), 6.98 (d, 2H, $^4J = 2.3$ Hz, ArH), 6.40 (s, 2H, ArH), 4.66 (s, 2H, C(O)CH_2), 4.57 (d, 2H, $^2J = 12.9$ Hz, ArCH_2Ar), 4.43 (d, 2H, $^4J = 12.9$ Hz, ArCH_2Ar), 4.24 (q, 2H, $^3J = 7.4$ Hz, OCH_2CH$_3$), 4.06-3.99 (m, 2H, OCH_2), 3.92-3.85 (m, 2H, OCH_2), 3.73 (t, 2H, $^3J = 7.4$ Hz, OCH_2), 3.24 (d, 2H, $^2J = 12.9$ Hz, ArCH_2Ar), 3.17 (d, 2H, $^2J = 12.9$ Hz, ArCH_2Ar), 2.05-1.89 (m, 6H, CH_2), 1.31 (t, 3H, $^3J = 7.4$ Hz, OCH$_2$CH_3), 1.27 (s, 18H, C(CH_3)$_3$), 1.08 (t, 3H, $^3J = 7.4$ Hz, CH$_2$CH_3), 0.95 (t, 6H, $^3J = 7.4$ Hz, CH$_2$CH_3), 0.77 (s, 18H, C(CH_3)$_3$);

^{13}C NMR (100MHz, CDCl$_3$), δ: 168.94, 160.06, 154.39, 153.01, 145.27, 144.54, 142.85, 135.43, 133.21, 132.52, 126.54, 124.97, 124.67, 123.44, 77.16, 76.77, 71.30, 61.00, 34.06, 33.31, 31.59, 31.10, 30.88, 23.58, 23.10, 14.21, 10.70, 10.08;

MS(FD) *m/z* (%) 851.2 (100) [M$^+$].

calix[4]arene 88

Calix[4]arene **87** (3.2 g, 3.76 mmol) was dissolved in toluene (20 ml) and EtOH (20 ml) and hydrogenated during 8 h at room temperature in the presence of the Raney-nickel. After that the catalyst was filtered off and washed with toluene (2x10 ml). The combined organic layers were evaporated under reduced pressure. The rest of toluene was removed by simultaneous evaporation with methanol (2x20 ml). After that MeOH (20 ml) was added to the residue and flask was left in the ultrasonic bath for 10 minutes. The formed precipitate was filtered off and dried. Calix[4]arene **88** (2.84 g, 92 %) was obtained as a white powder; mp 174-176°C;



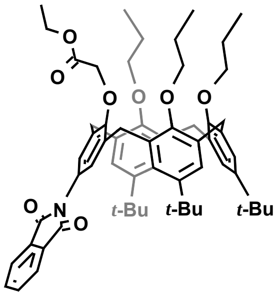
^{1}H NMR (400MHz, CDCl$_3$), δ: 7.02 (d, 2H, $^4J = 2.3$ Hz, ArH), 6.93 (d, 2H, $^4J = 2.3$ Hz, ArH), 6.38 (s, 2H, ArH), 5.78 (s, 2H, ArH), 4.45 (d, 2H, $^2J = 12.5$ Hz, ArCH_2Ar), 4.43 (s, 2H, C(O)CH_2), 4.23 (q, 2H, $^3J = 7.0$ Hz, OCH_2CH$_3$), 3.95 (t, 4H, $^3J = 7.4$ Hz, OCH_2), 3.73 (t, 2H, $^3J = 7.4$ Hz, OCH_2), 3.13 (d, 2H, $^2J = 12.5$ Hz, ArCH_2Ar), 3.03 (d, 2H, $^2J = 12.5$ Hz, ArCH_2Ar), 2.89 (br s, 2H, NH_2), 2.05-1.89 (m, 6H, CH_2), 1.31 (t, 3H, $^3J = 7.0$ Hz, OCH$_2$CH_3), 1.27 (s, 18H, C(CH_3)$_3$), 1.08 (t, 3H, $^3J = 7.4$ Hz, CH$_2$CH_3), 0.92 (t, 6H, $^3J = 7.4$ Hz, CH$_2$CH_3), 0.85 (s, 18H, C(CH_3)$_3$);

^{13}C NMR (100MHz, CDCl$_3$), δ: 169.84, 154.79, 153.18, 148.11, 144.28, 143.83, 140.35, 135.41, 134.69, 134.01, 132.67, 125.69, 125.07, 124.58, 115.02, 76.62, 71.95, 60.49, 33.97, 33.53, 31.66, 31.38, 31.19, 31.06, 23.55, 23.00, 14.27, 10.71, 10.07;

MS(FD) *m/z* (%) 820.8 (100) [M$^+$].

calix[4]arene 89

A mixture of calixarene **88** (2.36 g, 2.88 mmol), zinc acetate (1.05 g, 5.75 mmol) and phthalic anhydride (0.85 g, 5.75 mmol) was refluxed in pyridine (25 ml) during 3 days. After that water (30 ml) was added to the suspension and precipitate was filtered off, washed with 1N HCl (3x10 ml), water (5x15 ml) and methanol (3x10 ml). After drying on the air calixarene **89** (2.00 g, 73 %) was obtained as a cream coloured powder; mp 207-209°C;



^{1}H NMR (400MHz, CDCl$_3$), δ: 7.92-7.90 (m, 2H, ArH_{pht}), 7.75-7.73 (m, 2H, ArH_{pht}), 7.10 (s, 2H, ArH), 6.94 (s, 2H, ArH), 6.63-6.62 (m, 4H, ArH), 5.00 (s, 2H, C(O)CH_2), 4.70 (d, 2H, $^2J = 12.9$ Hz, ArCH_2Ar), 4.42 (d, 2H, $^2J = 12.5$ Hz, ArCH_2Ar), 4.21 (q, 2H, $^3J = 7.2$ Hz, OCH_2CH$_3$), 3.87 (t, 2H, $^3J = 7.8$ Hz, OCH_2), 3.77-3.72 (m, 4H, OCH_2), 3.24 (d, 2H, $^2J = 12.9$ Hz, ArCH_2Ar), 3.14 (d, 2H, $^2J = 12.5$ Hz, ArCH_2Ar), 2.14-1.88 (m, 2H , CH_2), 1.97-1.88 (m, 4H, CH_2), 1.29 (t, 3H,

$^3J = 7.2$ Hz, OCH$_2$C*H*$_3$), 1.17 (s, 18H, C(C*H*$_3$)$_3$), 1.02 (t, 6H, $^3J = 7.4$ Hz, CH$_2$C*H*$_3$), 0.99 (t, 3H, $^3J = 7.4$ Hz, CH$_2$C*H*$_3$), 0.97 (s, 18H, C(C*H*$_3$)$_3$);

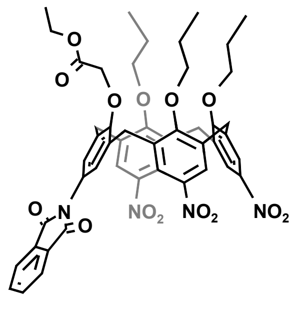
^{13}C NMR (100MHz, CDCl$_3$), δ: 170.56, 167.21, 155.13, 154.17, 153.25, 144.71, 144.56, 136.04, 134.92, 134.03, 132.82, 131.99, 131.83, 126.14, 125.98, 125.35, 125.10, 124.85, 123.46, 77.35, 76.86, 70.35, 60.36, 33.92, 33.77, 31.75, 31.50, 31.35, 31.03, 23.47, 23.37, 14.23, 10.56, 10.15;

MS(FD) *m/z* (%) 950.8 (100) [M$^+$].

calix[4]arene 90

Calix[4]arene **89** (2.6 g, 2.74 mmol) was dissolved in CH$_2$Cl$_2$ (260 ml) and acetic acid (7.8 ml) was added. The solution was vigorously stirred and fuming HNO$_3$ (3.6 ml) was added. The solution became dark immediately and stirring was continued for approximately 1 h at room temperature. The reaction mixture was diluted with water (50 ml). Organic layer was separated, washed with water (5x50 ml), dried over MgSO$_4$ and filtered. The filtrate was concentrated to dryness and methanol (20 ml) was added to the residue. The flask was left in the ultrasonic bath for 20 minutes and precipitate formed was filtered off. Calix[4]arene **90** (2.23 g, 89 %) was obtained as a cream colored powder; mp 227-229°C;

^{1}H NMR (400MHz, CDCl$_3$), δ: 7.85-7.83 (m, 2H, Ar*H*$_{\mathrm{pht}}$), 7.79 (d, 2H, $^4J = 2.4$ Hz, Ar*H*), 7.77 (d, 2H, $^4J = 2.4$ Hz, Ar*H*), 7.72-7.70 (m, 2H, Ar*H*$_{\mathrm{pht}}$), 7.47 (s, 2H, Ar*H*), 6.63 (s, 2H, Ar*H*), 4.68 (d, 2H, $^2J = 13.7$ Hz, ArC*H*$_2$Ar), 4.54 (d, 2H, $^2J =$ 13.7 Hz, ArC*H*$_2$Ar), 4.54 (s, 2H, OC*H*$_2$), 4.26 (q, 2H, $^3J = 7.2$ Hz, OC*H*$_2$CH$_3$), 4.21-4.14 (m, 2H, OC*H*$_2$), 4.0 9-4.03 (m, 2H, OC*H*$_2$), 3.84 (t, 2H, $^3J = 7.2$ Hz, OC*H*$_2$), 3.40 (d, 2H, $^2J = 13.7$ Hz, ArC*H*$_2$Ar), 3.38 (d, 2H, $^2J = 13.7$ Hz, ArC*H*$_2$Ar), 2.00-1.87 (m, 6H, C*H*$_2$), 1.32 (t, 3H, $^3J = 7.2$ Hz, OCH$_2$C*H*$_3$), 1.04 (t, 3H, $^3J = 7.2$ Hz, CH$_2$C*H*$_3$), 0.99 (t, 6H, $^3J = 7.2$ Hz, CH$_2$C*H*$_3$);

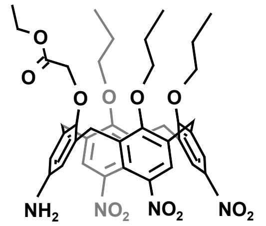


^{13}C NMR (100MHz, CDCl$_3$), δ: 168.73, 166.62, 162.34, 160.99, 154.31, 143.60, 142.82, 136.43, 135.52, 134.35, 134.25, 133.46, 131.52, 127.32, 126.64, 124.59, 124.17, 124.03, 123.73, 77.91, 77.61, 71.69, 61.11, 31.27, 31.12, 23.34, 23.15, 14.28, 10.29, 10.07;

MS(FD) *m/z* (%) 917.6 (100) [M$^+$].

calix[4]arene 91

Hydrochloric acid$_{37\%}$ (10 ml) was added to the solution of calix[4]arene **90** (1.00 g, 1.11 mmol) in EtOH (30 ml) and toluene (25 ml). The turbid reaction mixture was refluxed until the clear solution was formed (approximately 4 days) and then concentrated to ~20 ml. After that toluene (10 ml) was added to the residue and the excess of HCl was neutralized using 1N solution of $NaHCO_3$. The organic layer was washed with water (20 ml), dried over $MgSO_4$ and the solvent was removed under reduced pressure. The rest of toluene was removed by simultaneous evaporation with methanol (3x10 ml). After that MeOH (50 ml) was added to the residue and flask was left in the ultrasonic bath for 30 minutes. The precipitate formed was filtered off, dried and passed through the short silicagel column (ethyl acetate). Calix[4]arene **91** (0.62 g, 72 %) was obtained as a pale brown powder; mp 221-223°C;



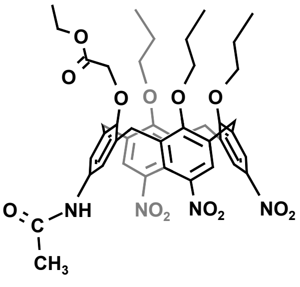
^1H NMR (400MHz, $CDCl_3$), δ: 7.81 (s, 4H, Ar*H*), 7.29 (s, 2H, Ar*H*), 5.63 (s, 2H, Ar*H*), 4.54 (d, 2H, $^2J = 14.1$ Hz, ArC*H*$_2$Ar), 4.51 (d, 2H, $^2J = 14.1$ Hz, ArC*H*$_2$Ar), 4.37 (s, 2H, OC*H*$_2$), 4.22 (q, 2H, $^3J = 7.1$ Hz, OC*H*$_2$CH$_3$), 4.18-4.12 (m, 2H, OC*H*$_2$), 3.99-3.93 (m, 2H, OC*H*$_2$), 3.86 (t, 2H, $^3J = 7.4$ Hz, OC*H*$_2$), 3.36 (d, 2H, $^2J = 14.1$ Hz, ArC*H*$_2$Ar), 3.19 (d, 2H, $^2J = 14.1$ Hz, ArC*H*$_2$Ar), 1.92-1.83 (m, 6H, C*H*$_2$), 1.29 (t, 3H, $^3J = 7.1$ Hz, OCH$_2$C*H*$_3$), 1.06 (t, 3H, $^3J = 7.4$ Hz, CH$_2$C*H*$_3$), 0.94 (t, 6H, $^3J = 7.4$ Hz, CH$_2$C*H*$_3$);

^{13}C NMR (100MHz, $CDCl_3$), δ: 169.10, 162.88, 161.40, 147.64, 142.55, 142.45, 142.38, 137.30, 135.76, 134.98, 133.16, 124.66, 123.68, 123.58, 114.66, 77.62, 77.50, 71.68, 60.79, 31.17, 31.07, 23.31, 23.16, 14.21, 10.31, 9.98;

MS(FD) *m/z* (%) 787.2 (100) [M^+].

calix[4]arene 92

Calix[4]arene **91** (1.5 g, 1.91 mmol) was dissolved in $CHCl_3$ (10 ml) and acetic acid anhydride (20 ml) was added. The solution was stirred for 10 h and chloroform (30 ml) was added to the reaction mixture. The excess of anhydride mainly was neutralized using 1N solution of $NaHCO_3$. The rest of anhydride (~1-2 ml) was evaporated with ethanol. The residue was treated with EtOH/H_2O (10/20 ml). The precipitate formed was filtered off. Calix[4]arene **92** (1.20 g, 76 %) was obtained as a brown powder; mp 173-175°C;



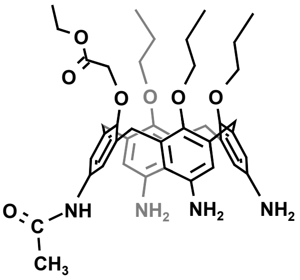
^1H NMR (400MHz, $CDCl_3$), δ: 7.86 (s, 2H, Ar*H*), 7.85 (s, 2H, Ar*H*), 7.20 (s, 2H, Ar*H*), 6.63 (s, 1H, N*H*), 6.42 (s, 2H, Ar*H*), 4.56 (d, 2H, $^2J = 14.5$ Hz, ArC*H*$_2$Ar), 4.52 (d, 2H, $^2J = 14.5$ Hz, ArC*H*$_2$Ar), 4.40 (s, 2H, OC*H*$_2$), 4.23 (q, 2H, $^3J = 7.2$ Hz, OC*H*$_2$CH$_3$), 4.18-4.11 (m, 2H, OC*H*$_2$), 4.02-3.95 (m, 2H, OC*H*$_2$), 3.85 (t, 2H, $^3J = 7.4$ Hz, OC*H*$_2$), 3.36 (d, 2H, $^2J = 14.5$ Hz, ArC*H*$_2$Ar), 3.32 (d, 2H, ^{2}J = 14.5 Hz, ArCH_2Ar), 2.01 (s, 3H, C(O)CH_3), 1.94-1.83 (m, 6H, CH_2), 1.30 (t, 3H, ^{3}J = 7.2 Hz, OCH$_2$CH_3), 1.07 (t, 3H, ^{3}J = 7.4 Hz, CH$_2$CH_3), 0.94 (t, 6H, ^{3}J = 7.4 Hz, CH$_2$CH_3);

^{13}C NMR (100MHz, CDCl$_3$), δ: 168.76, 168.41, 162.70, 161.46, 151.56, 142.53, 136.98, 135.80, 135.08, 133.42, 133.17, 124.71, 123.86, 123.54, 120.49, 77.64, 77.56, 71.48, 60.94, 31.15, 31.04, 24.00, 23.28, 23.11, 14.18, 10.29, 9.94;

MS(FD) *m/z* (%) 829.5 (100) [M$^+$].

calix[4]arene 93

Calix[4]arene **92** (1.05 g, 1.27 mmol) was dissolved in toluene (15 ml) and ethanol (15 ml) and hydrogenated during 18 h at room temperature in the presence of the Raney-nickel. The progress of reaction was monitored by TLC in THF. After that the catalyst was filtered off and washed with toluene (2x10 ml). The combined organic layers were evaporated under reduced pressure. Calix[4]arene **93** (0.78 g, 83 %) was obtained as a brown powder; mp > 190°C - decompose;



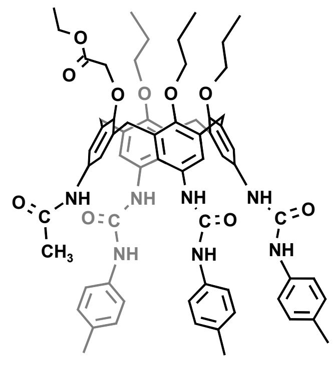
^{1}H NMR (400MHz, THF-d$_8$), δ: 8.68 (s, 1H, NH), 6.87 (s, 2H, ArH), 6.02 (s, 2H, ArH), 5.81 (s, 2H, ArH), 5.79 (s, 2H, ArH), 4.60 (s, 2H, OCH_2), 4.54 (d, 2H, ^{2}J = 13.3 Hz, ArCH_2Ar), 4.28 (d, 2H, ^{2}J = 13.3 Hz, ArCH_2Ar), 4.13 (q, 2H, ^{3}J = 7.1 Hz, OCH_2CH$_3$), 3.75-3.60 (m, 12H, OCH_2, NH_2), 2.94 (d, 2H, ^{2}J = 13.3 Hz, ArCH_2Ar), 2.80 (d, 2H, ^{2}J = 13.3 Hz, ArCH_2Ar), 1.90 (s, 3H, C(O)CH_3), 1.87-1.83 (m, 6H, CH_2), 1.23 (t, 3H, ^{3}J = 7.1 Hz, OCH$_2$CH_3), 0.97 (t, 6H, ^{3}J = 7.6 Hz, CH$_2$CH_3), 0.93 (t, 3H, ^{3}J = 7.6 Hz, CH$_2$CH_3);

^{13}C NMR (100MHz, THF-d$_8$), δ: 170.40, 167.39, 153.49, 150.09, 149.40, 143.47, 142.92, 136.61, 136.35, 135.60, 135.15, 134.71, 121.40, 115.56, 77.43, 71.43, 60.49, 32.42, 32.08, 23.99, 23.86, 14.61, 10.97, 10.71;

MS(FD) *m/z* (%) 739.4 (100) [M$^+$].

calix[4]arene 94

Calix[4]arene **93** (0.72 g, 0.97 mmol) was dissolved in CH$_2$Cl$_2$ (10 ml) and tolyl isocyanate (1.04 g (0.97 ml), 7.80 mmol) was added to the solution. The reaction mixture was stirred for 6h and MeOH (30 ml) was added. The solvents were removed in vacuum and the residue was treated methanol. The precipitate was filtered and dried. The calix[4]arene **94** (0.71 g, 65 %) was obtained as a white powder; mp > 240°C - decompose;



^{1}H NMR (400MHz, DMSO-d$_6$), δ: 9.61 (s, 1H, N*H*C(O)CH$_3$), 8.34 (s, 1H, N*H*), 8.26 (s, 1H, N*H*), 8.13 (s, 2H, N*H*), 8.02 (s, 2H, N*H*), 7.29 (d, 2H, ^3J = 8.2 Hz, Ar*H*$_{\mathrm{Tol}}$), 7.17 (d, 4H, ^3J = 8.2 Hz, Ar*H*$_{\mathrm{Tol}}$), 7.12 (s, 2H, Ar*H*), 7.05 (d, 2H, ^3J = 8.2 Hz, Ar*H*$_{\mathrm{Tol}}$), 7.01 (d, 4H, ^3J = 8.2 Hz, Ar*H*$_{\mathrm{Tol}}$), 6.98 (s, 2H, Ar*H*), 6.62 (s, 2H, Ar*H*), 6.59 (s, 2H, Ar*H*), 4.75 (s, 2H, OC*H*$_2$), 4.55 (d, 2H, ^2J = 12.9 Hz, ArC*H*$_2$Ar), 4.33 (d, 2H, ^2J = 12.9 Hz, ArC*H*$_2$Ar), 4.14 (q, 2H, ^3J = 7.6 Hz, OC*H*$_2$CH$_3$), 3.82-3.67 (m, 6H, OC*H*$_2$), 3.10 (d, 2H, ^2J = 12.9 Hz, ArC*H*$_2$Ar), 3.09 (d, 2H, ^2J = 12.9 Hz, ArC*H*$_2$Ar), 2.22 (s, 3H, ArC*H*$_3$), 2.21 (s, 6H, ArC*H*$_3$), 1.94 (s, 3H, C(O)C*H*$_3$), 1.88-1.83 (m, 6H, C*H*$_2$), 1.23 (t, 3H, ^3J = 7.6 Hz, OCH$_2$C*H*$_3$), 0.99 (t, 6H, ^3J = 7.4 Hz, CH$_2$C*H*$_3$), 0.93 (t, 3H, ^3J = 7.4 Hz, CH$_2$C*H*$_3$);

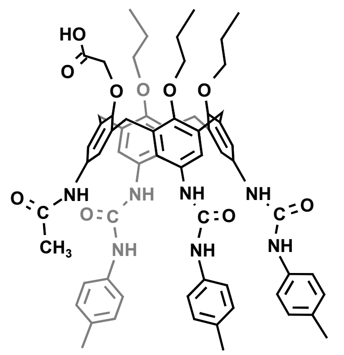
^{1}H NMR (400MHz, CDCl$_3$), δ: 9.48 (s, 1H, N*H*), 8.32 (s, 1H, N*H*C(O)CH$_3$), 7.90 (s, 1H, N*H*), 7.75 (d, 2H, ^3J = 8.2 Hz, Ar*H*$_{\mathrm{Tol}}$), 7.61 (s, 1H, Ar*H*), 7.52 (s, 1H, Ar*H*), 7.40 (d, 2H, ^3J = 8.2 Hz, Ar*H*$_{\mathrm{Tol}}$), 7.25 (s, 1H, N*H*), 7.18 (d, 2H, ^3J = 8.2 Hz, Ar*H*$_{\mathrm{Tol}}$), 7.12 (d, 2H, ^3J = 8.2 Hz, Ar*H*$_{\mathrm{Tol}}$), 7.04 (d, 2H, ^3J = 8.2 Hz, Ar*H*$_{\mathrm{Tol}}$), 7.04 (s, 1H, Ar*H*), 6.45 (d, 2H, ^3J = 8.2 Hz, Ar*H*$_{\mathrm{Tol}}$), 6.23 (s, 1H, N*H*), 6.09 (s, 1H, Ar*H*), 5.89 (s, 1H, Ar*H*), 5.66 (s, 1H, Ar*H*), 5.40 (s, 1H, N*H*), 5.36 (s, 1H, Ar*H*), 5.21 (s, 1H, Ar*H*), 4.25 (d, 1H, ^2J = 14.5 Hz, ArC*H*$_2$Ar), 4.21 (d, 1H, ^2J = 14.5 Hz, ArC*H*$_2$Ar), 4.16 (d, 1H, ^2J = 14.5 Hz, ArC*H*$_2$Ar), 4.06 (q, 2H, ^3J = 7.2 Hz, OC*H*$_2$CH$_3$), 3.85-3.75 (m, 2H, OC*H*$_2$), 3.71-3.65 (m, 3H, OC*H*$_2$, ArC*H*$_2$Ar), 3.53 (d, 1H, ^2J = 15.3 Hz, ArC*H*$_2$Ar), 3.43-3.37 (m, 1H, OC*H*$_2$), 3.31-3.24 (m, 1H, OC*H*$_2$), 3.24 (d, 1H, ^2J = 15.3 Hz, ArC*H*$_2$Ar), 3.02 (d, 1H, ^2J = 14.5 Hz, ArC*H*$_2$Ar), 2.68 (d, 1H, ^2J = 14.5 Hz, ArC*H*$_2$Ar), 2.64 (d, 1H, ^2J = 14.5 Hz, ArC*H*$_2$Ar), 2.52 (d, 1H, ^2J = 14.5 Hz, ArC*H*$_2$Ar), 2.44 (s, 3H, ArC*H*$_3$), 2.37 (s, 3H, ArC*H*$_3$), 2.30 (s, 3H, ArC*H*$_3$), 1.70-1.60 (m, 6H, C*H*$_2$), 1.60 (s, 3H, C(O)C*H*$_3$), 1.22 (t, 3H, ^3J = 7.2 Hz, OCH$_2$C*H*$_3$), 0.97 (t, 3H, ^3J = 7.4 Hz, CH$_2$C*H*$_3$), 0.77 (t, 3H, ^3J = 7.4 Hz, CH$_2$C*H*$_3$), 0.71 (t, 3H, ^3J = 7.4 Hz, CH$_2$C*H*$_3$);

^{13}C NMR (100MHz, DMSO-d$_6$), δ: 169.73, 167.56, 152.42, 152.32, 151.30, 150.61, 137.18, 134.98, 134.61, 133.68, 133.57, 133.40, 133.29, 130.24, 130.10, 129.02, 128.93, 119.18, 118.18, 117.98, 117.86, 76.59, 76.35, 70.39, 59.87, 31.06, 30.50, 23.75, 22.61, 20.21, 13.95, 10.31, 9.89;

MS(ESI) *m/z* (%) 1160.5 (100) [M$^+$Na].

calix[4]arene 95

A 3N water solution of NaOH (2 ml) was added to the solution of calixarene **94** (0.6g, 0.53mmol) in THF/DMF (20/7 ml). The reaction mixture was stirred 12 h at room



temperature and acetic acid (5 ml) was added to neutralize the excess of NaOH. The solution was concentrated to ~15 ml and water (35 ml) was added. The precipitate was filtered off and dried on the air leading the calix[4]arene **95** (0.57 g, 98%) as a white powder; mp > 260°C decompose;

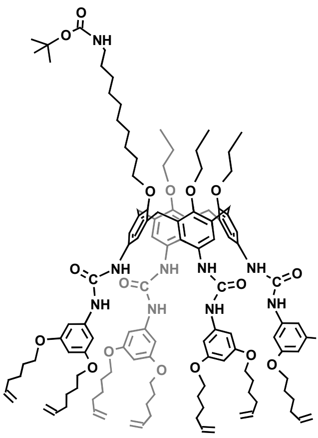
^{1}H NMR (400MHz, DMSO-d$_6$/CD$_3$COOD (10%)), δ: 8.25 (s, 1H, N*H*C(O)CH$_3$), 7.24 (d, 2H, $^{3}J = 8.2$ Hz, Ar*H*$_{\mathrm{Tol}}$), 7.16 (d, 4H, $^{3}J = 8.2$ Hz, Ar*H*$_{\mathrm{Tol}}$), 7.15 (s, 2H, Ar*H*), 7.00 (d, 2H, $^{3}J = 8.2$ Hz, Ar*H*$_{\mathrm{Tol}}$), 6.99 (d, 4H, $^{3}J = 8.2$ Hz, Ar*H*$_{\mathrm{Tol}}$), 6.98 (s, 2H, Ar*H*), 6.65 (d, 2H, $^{4}J = 2.0$ Hz, Ar*H*), 6.59 (d, 2H, $^{4}J = 2.0$ Hz, Ar*H*), 4.63 (s, 2H, OC*H*$_2$), 4.47 (d, 2H, $^{2}J = 12.9$ Hz, ArC*H*$_2$Ar), 4.32 (d, 2H, $^{2}J = 12.9$ Hz, ArC*H*$_2$Ar), 3.80 (t, 2H, $^{3}J = 7.6$ Hz, OC*H*$_2$), 3.82-3.67 (m, 4H, OC*H*$_2$), 3.08 (d, 2H, $^{2}J = 12.9$ Hz, ArC*H*$_2$Ar), 3.07 (d, 2H, $^{2}J = 12.9$ Hz, ArC*H*$_2$Ar), 2.25 (s, 3H, ArC*H*$_3$), 2.19 (s, 6H, ArC*H*$_3$), 1.94 (s, 3H, C(O)C*H*$_3$), 1.88-1.85 (m, 6H, C*H*$_2$), 0.93 (t, 6H, $^{3}J = 7.4$ Hz, CH$_2$C*H*$_3$), 0.84 (t, 3H, $^{3}J = 7.4$ Hz, CH$_2$C*H*$_3$);

^{13}C NMR (100MHz, DMSO-d$_6$), δ: 171.24, 168.09, 152.79, 152.68, 151.58, 151.44, 150.76, 137.48, 135.48, 135.09, 134.22, 133.91, 133.76, 130.72, 130.62, 129.40, 129.32, 119.66, 118.58, 118.34, 118.25, 77.26, 76.95, 70.75, 67.30, 31.38, 30.86, 25.40, 23.96, 22.93, 20.46, 10.52, 10.17;

MS(ESI) *m/z* (%) 1132.5 (100) [M^{+}Na].

calix[4]arene 96

A solution of 3,5-(4'-pentenyloxy)benzoic acid (1.5g, 4.7mmol), DPPA (1.41g, 1.11ml, 5.18mmol) and Et$_3$N (0.52g, 0.73ml, 5.18mmol) in toluene (100 ml) was stirred at 70°C for 6 h under nitrogen atmosphere. After that compound **42** (0.68g, 0.79mmol) was added to the solution and stirring was continued during 4h at the same conditions. Then the solvent was evaporated under reduced pressure and the rest of toluene was removed by simultaneous evaporation with methanol (3x10ml). The residue was diluted with MeOH (20ml) and left in ultrasonic bath for 30 minutes. The precipitate formed was filtered off and passed through the silicagel column (ethyl acetate/hexane=1/8). Calix[4]arene **96** (1.15g, 68%) was obtained as a white powder; mp > 230°C decompose;



^{1}H NMR (400MHz, THF-d$_8$), δ: 7.52 (s, 2H, N*H*), 7.51 (s, 2H, N*H*), 7.45 (s, 4H, N*H*), 6.82 (s, 4H, Ar*H*), 6.80

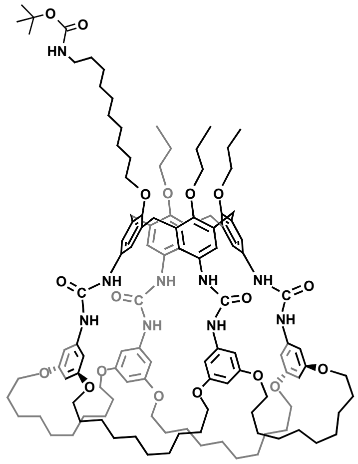
(s, 4H, Ar*H*), 6.58 (s, 8H, Ar*H*), 6.03 (s, 4H, Ar*H*), 5.93 (s, 1H, N*H*Boc), 5.86-5.76 (m, 8H, C*H*=CH$_2$), 5.02-4.90 (m, 8H, CH=C*H*$_2$), 4.44 (d, 4H, ^2J = 13.3 Hz, ArC*H*$_2$Ar), 3.85-3.80 (m, 24H, OC*H*$_2$), 3.08 (d, 4H, ^2J = 13.3 Hz, ArC*H*$_2$Ar), 3.02 (q, 2H, ^3J = 6.5 Hz, NHC*H*$_2$), 2.12-2.06 (m, 16H, C*H*$_2$), 1.98-1.92 (m, 8H, C*H*$_2$), 1.74-1.68 (m, 16H, C*H*$_2$), 1.56-1.49 (m, 16H, C*H*$_2$), 1.44-1.29 (m, 14H, C*H*$_2$), 1.40 (s, 9H, OC(C*H*$_3$)$_3$), 1.02 (t, ^3J = 7.4 Hz, 9H, CH$_2$C*H*$_3$);

^{13}C NMR (100MHz, THF-d$_8$), δ: 161.41, 153.09, 152.73, 142.81, 139.47, 135.92, 135.86, 134.92, 119.20, 114.93, 97.55, 95.62, 77.54, 75.88, 68.12, 41.24, 34.41, 32.09, 31.15, 30.75, 30.66, 30.41, 29.77, 28.75, 27.85, 27.27, 26.36, 24.15, 10.89;

MS(ESI) *m/z* (%) 2150.4 (100) [M$^+$Na].

calix[4]arene 97a

The mixture of tetraurea **96** (0.2 g, 0.094 mmol) and tetratosylurea **16** (0.146 g, 0.094 mmol) in benzene (25 ml) was stirred for 12 h at room temperature and then diluted to 1 L with dichloromethane. After that the nitrogen was blown through the solution during 2 h and the Grubbs's catalyst (0.015 g, 0.019 mmol) was added. The progress of reaction was controlled by TLC (THF/Hexane = 2/3). After 2 days the solvent was evaporated to dryness and the residue was filtered through the short column (SiO$_2$, THF/Hexane). The white stuff was dissolved in THF (25 ml) and hydrogenated during 6 h at room temperature in the presence of the Pt$_2$O (40 mg). Then the catalyst was filtered off and the solvent was removed in vacuum. The product was purified by the column chromatography (THF/Hexane = 1/3) to give the calixarene **97a** (0.13 g, 68 %) as a white powder; mp > 260°C decompose;

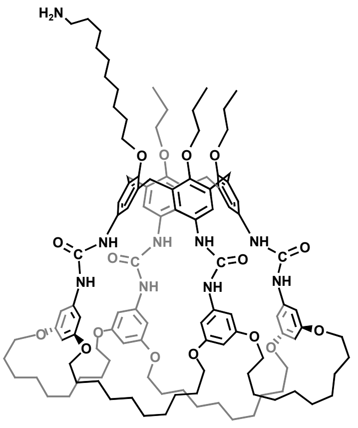


^{1}H NMR (400MHz, THF-d$_8$), δ: 7.53 (s, 8H, N*H*), 6.91 (s, 4H, Ar*H*), 6.90 (s, 4H, Ar*H*), 6.58 (s, 8H, Ar*H*), 6.01 (s, 4H, Ar*H*), 5.94 (s, 1H, N*H*Boc), 4.45 (d, 4H, ^2J = 12.5 Hz, ArC*H*$_2$Ar), 3.88-3.82 (m, 24H, OC*H*$_2$), 3.09 (d, 4H, ^2J = 12.5 Hz, ArC*H*$_2$Ar), 3.02 (q, 2H, ^3J = 6.5 Hz, NHC*H*$_2$), 2.03-1.97 (m, 8H, C*H*$_2$), 1.72-1.66 (m, 16H, C*H*$_2$), 1.42-1.30 (m, 71H, CH$_2$, OC(CH$_3$)$_3$), 1.01-0.95 (m, 9H, CH$_2$C*H*$_3$);

MS(ESI) *m/z* (%) 2046.1 (100) [M$^+$Na].

calix[4]arene 97b

The urea **97a** (0.33 g, 0.16 mmol) was dissolved in CH_2Cl_2 (20 ml) and trifluoroacetic acid (10 ml) was added to the solution. The reaction mixture was stirred at room temperature for 2 h and evaporated to dryness. The Et_2O (20 ml) was added and precipitate was filtered off. The calix[4]arene **97b** (0.32 g, 97 %) was obtained as a grey powder; mp > 270°C decompose;



^{1}H NMR (400MHz, DMSO-d$_6$), δ: 8.43 (s, 2H, N*H*), 8.41 (s, 2H, N*H*), 8.22 (s, 2H, N*H*), 8.17 (s, 2H, N*H*), 7.63 (br s, 3H, NH_3^+), 6.92 (s, 4H, Ar*H*), 6.87-6.85 (m, 4H, Ar*H*), 6.52 (s, 4H, Ar*H*), 6.51-6.49 (m, 4H, Ar*H*), 6.04 (s, 4H, Ar*H*), 4.32 (d, 4H, $^2J = 11.7$ Hz, ArCH_2Ar), 3.83-3.74 (m, 24H, OCH_2), 3.11 (d, 4H, $^2J = 11.7$ Hz, ArCH_2Ar), 2.76 (q, 2H, $^3J = 6.5$ Hz, NHCH_2), 1.97-1.92 (m, 8H, CH_2), 1.64-1.26 (m, 78H, CH_2), 1.01-0.95 (m, 9H, CH$_2$CH_3);

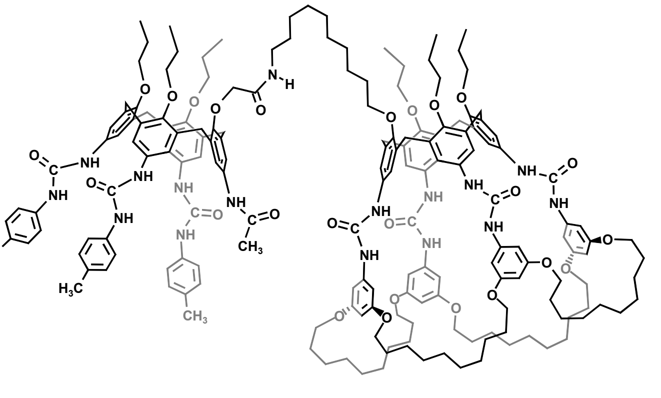
MS(ESI) *m/z* (%) 1924.3 (100) [M$^+$Na-TFA].

General procedure for synthesis of bis-calix[4]arenes

The acid **95** (0.147 mmol) and PyBOP (0.147 mmol) were dissolved in DMF for peptide synthesis grade (4 ml). The solution was stirred 1 h at room temperature and then amine **97b** (**51a**) (0.123 mmol) and triethylamine (0.3ml) in DMF (2 ml) were added. The stirring was continued for 24 h at room temperature. After that the reaction mixture was diluted with water (15 ml), the precipitate was filtered off, washed with MeOH (4x5 ml) and dried.

bis-calix[4]arene 98

Compound **98** (85 %) was obtained as a white powder; mp > 278°C decompose;

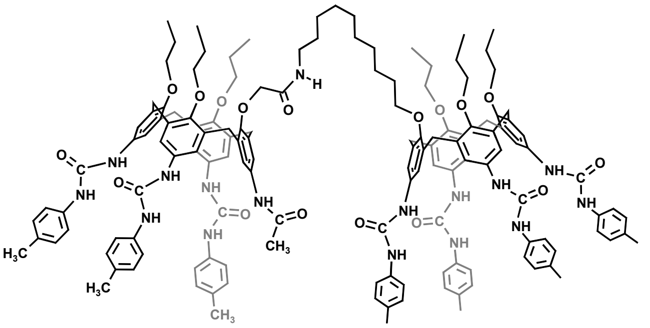


^{1}H NMR (400MHz, DMSO-d$_6$), δ: 9.54 (s, 1H, N*H*C(O)CH$_3$), 8.40-8.09 (m, 15H, N$H_{(urea)}$, CH$_2$C(O)N*H*), 7.26 (d, 2H, $^3J = 7.8$ Hz, ArH_{Tol}), 7.21 (d, 4H, $^3J = 7.8$ Hz, ArH_{Tol}), 7.04-7.01 (m, 8H, Ar$H_{(Tol)}$, Ar*H*), 6.92 (s, 2H, Ar*H*), 6.86 (s, 8H, Ar*H*), 6.75 (s, 2H, Ar*H*), 6.71 (s, 2H, Ar*H*), 6.52 (s, 4H, Ar*H*), 6.51 (s, 4H, Ar*H*), 6.04 (s, 4H, Ar*H*), 4.42 (m, 10H, OCH_2, ArCH_2Ar), 3.85-3.75 (m, 30H, OCH_2), 3.32 (br s, 2H, NHC*H*$_2$), 3.14-3.12 (m, 8H, ArC*H*$_2$Ar), 2.21 (s, 9H, ArC*H*$_3$), 1.95-1.80 (m, 15H, C*H*$_2$, C(O)C*H*$_3$), 1.63 (br s, 16H, C*H*$_2$), 1.35 (br s, 32H, C*H*$_2$), 1.25 (br s, 32H, C*H*$_2$), 1.00-0.90 (m, 18H, CH$_2$C*H*$_3$);

MS(ESI) *m/z* (%) 3038.6 (5) [M$^+$Na].

bis-calix[4]arene 99

Compound **99** (0.315 g, 80 %) was obtained as a white powder; mp>280°C decompose;



^{1}H NMR (400MHz, DMSO-d$_6$), δ: 9.55 (s, 1H, N*H*C(O)CH$_3$), 8.30-8.09 (m, 15H, N*H*$_{urea}$, CH$_2$C(O)N*H*), 7.22 (br s, 12H, Ar*H*$_{Tol}$), 7.02 (d, 16H, Ar*H*$_{Tol}$), 6.84-6.71 (m, 16H, Ar*H*), 4.41-4.32 (m, 10H, OC*H*$_2$, ArC*H*$_2$Ar), 3.80-3.75 (m, 14H, OC*H*$_2$), 3.26 (br s, 2H, NHC*H*$_2$), 3.11 (br s, 8H, ArC*H*$_2$Ar), 2.21 (s, 21H, ArC*H*$_3$), 1.90-1.82 (m, 17H, C*H*$_2$, C(O)C*H*$_3$), 1.56 (br s, 2H, C*H*$_2$), 1.34 (br s, 12H, C*H*$_2$), 0.98-0.92 (m, 18H, CH$_2$C*H*$_3$);

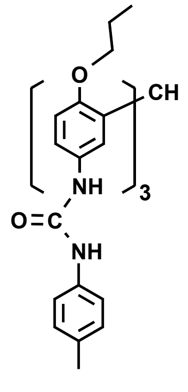
MS(ESI) *m/z* (%) 2414.1 (3) [M$^+$Na], 1218.07 (79) [M^{2+}Na].

General procedure of the synthesis of triphenylmethanes 103

The tetraamine **102** (0.42 mmol) was dissolved in CH$_2$Cl$_2$ (15 ml) and corresponding isocyanate (2.52 mmol) was added to the solution. The reaction mixture was stirred for 6h.

triphenylmethane 103a

MeOH (30 ml) was added to the solution. Precipitate was filtered off and washed with MeOH. Calix[4]arene **103a** (57 %) was obtained as a white powder; mp > 300°C;



^{1}H NMR (400 MHz, DMSO-d$_6$), δ: 8.31 (s, 3H, N*H*), 8.23 (s, 3H, N*H*), 7.59 (d × d, 3H, ^3J = 9.0 Hz, ^4J = 2.4 Hz, *p*-Ar*H*), 7.22 (d, 6H, ^3J = 8.6 Hz, Ar*H*$_{Tol}$), 7.00 (d, 6H, ^3J = 8.6 Hz, Ar*H*$_{Tol}$), 6.84 (d, 3H, ^3J = 9.0 Hz, *m*-A r*H*), 6.41 (s, 1H, Ar$_3$C *H*), 6.40 (d, 3H, ^4J = 2.4 Hz, *o*-Ar*H*), 3.74 (t, 6H, ^3J = 7.0 Hz, OC*H*$_2$), 2.21 (s, 9H, ArC*H*$_3$), 1.55-1.47 (m, 6H, C*H*$_2$), 0.78 (t, 9H, ^3J = 7.0 Hz, OCH$_2$C*H*$_3$);

^{1}H NMR (400 MHz, CDCl$_3$, integration is given for a dimeric species), δ: 8.43 (s, 6H, N*H*), 7.20 (d × d, 6H, ^3J = 8.6 Hz, ^4J = 2.4 Hz, *p*-Ar*H*), 6.90 (d, 12H, ^3J = 8.6 Hz, Ar*H*$_{Tol}$), 6.85 (d, 12H, ^3J = 8.6 Hz, Ar*H*$_{Tol}$), 6.78 (s, 6H, N*H*), 6.45 (s, 2H, Ar$_3$C*H*), 6.36

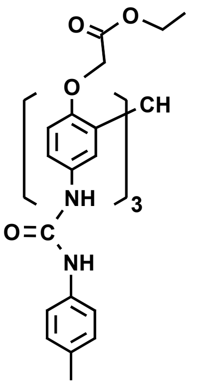
(d, 6H, ^4J = 2.4 Hz, *o*-Ar*H*), 6.12 (d, 6H, ^3J = 8.6 Hz, *m*-Ar*H*), 3.20-3.15 (m, 6H, OC*H*$_2$), 2.51-2.45 (m, 6H, OC*H*$_2$), 2.19 (s, 18H, ArC*H*$_3$), 1.35-1.24 (m, 12H, C*H*$_2$), 0.65 (t, 18H, ^3J = 7.4 Hz, OCH$_2$C*H*$_3$);

^{13}C NMR (400 MHz, DMSO-d$_6$), δ: 152.48 (s, *C*(O)), 151.44 (s, *C*$_{\text{Ar}}$), 137.15 (s, *C*$_{\text{Ar}}$), 132.58 (s, *C*$_{\text{Ar}}$), 132.12 (s, *C*$_{\text{Ar}}$), 130.24 (s, *C*$_{\text{Ar}}$), 129.02 (s, *C*H$_{\text{Tol}}$), 119.41 (s, *C*H$_{\text{Ar}}$), 117.94 (s, *C*H$_{\text{Tol}}$), 116.84 (s, *C*H$_{\text{Ar}}$), 112.40 (s, *C*H$_{\text{Ar}}$), 69.55 (s, O*C*H$_2$), 36.27 (s, Ar$_3$*C*H), 22.19 (s, *C*H$_2$), 20.20 (s, *C*H$_{3\text{Tol}}$), 10.21 (s, CH$_2$CH$_3$);

MS (FD) m/z (%) 863.7 (25) [MH$^+$].

triphenylmethane 103b

The working up procedure as for **103a**; yield 77%, mp 267-269°C;



^{1}H NMR (400 MHz, DMSO-d$_6$), δ: 8.39 (s, 3H, N*H*), 8.27 (s, 3H, N*H*), 7.63 (d × d, 3H, ^3J = 9.0 Hz, ^4J = 2.3 Hz, *p*-Ar*H*), 7.25 (d, 6H, ^3J = 8.2 Hz, Ar*H*$_{\text{Tol}}$), 7.03 (d, 6H, ^{3}J = 8.2 Hz, Ar*H*$_{\text{Tol}}$), 6.87 (d, 3H, ^{3}J = 9.0 Hz, *m*-Ar*H*), 6.47 (d, 3H, ^4J = 2.3 Hz, *o*-Ar*H*), 6.40 (s, 1H, Ar$_3$C*H*), 4.52 (s, 6H, C(O)C*H*$_2$), 4.10 (q, 6H, ^3J = 7.0 Hz, OC*H*$_2$CH$_3$), 2.21 (s, 9H, ArC*H*$_3$), 1.16 (t, 9H, ^3J = 7.0 Hz, OCH$_2$C*H*$_3$);

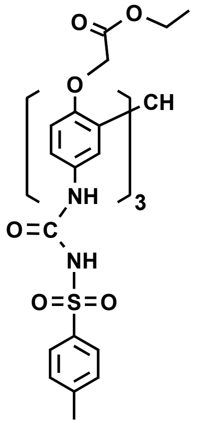
^{1}H NMR (400 MHz, CDCl$_3$, integration is given for a dimeric species), δ: 8.32 (s, 6H, N*H*), 7.23 (d × d, 6H, ^3J = 9.0 Hz, ^4J = 2.0 Hz, *p*-Ar*H*), 7.04 (s, 6H, N*H*), 6.96 (s, 24H, Ar*H*$_{\text{Tol}}$), 6.44 (s, 2H, Ar$_3$C*H*), 6.18 (d, 6H, ^4J = 2.0 Hz, *o*-Ar*H*), 6.07 (d, 6H, ^3J = 9.0 Hz, *m*-Ar*H*), 4.07 (q, 12H, ^3J = 7.0 Hz, OC*H*$_2$CH$_3$), 3.53 (d, 6H, ^2J = 16.0 Hz, C(O)C*H*$_2$), 3.34 (d, 6H, ^2J = 16.0 Hz, C(O)C*H*$_2$), 2.23 (s, 18H, ArC*H*$_3$), 1.16 (t, 18H, ^3J = 7.0 Hz, OCH$_2$C*H*$_3$);

^{1}H NMR (400 MHz, CD$_2$Cl$_4$, integration is given for a dimeric species), δ: 8.32 (s, 6H, N*H*), 7.26 (d × d, 6H, ^3J = 9.0 Hz, ^4J = 2.0 Hz, *p*-Ar*H*), 7.08 (s, 6H, N*H*), 7.00 (m, 24H, Ar*H*$_{\text{Tol}}$), 6.40 (s, 2H, Ar$_3$C*H*), 6.16 (d, 6H, ^4J = 2.0 Hz, *o*-Ar*H*), 6.08 (d, 6H, ^3J = 9.0 Hz, *m*-Ar*H*), 4.08 (m, 12H, OC*H*$_2$CH$_3$), 3.55 (d, 6H, ^2J = 16.0 Hz, C(O)C*H*$_2$), 3.31 (d, 6H, ^2J = 16.0 Hz, C(O)C*H*$_2$), 2.27 (s, 18H, ArC*H*$_3$), 1,19 (t, 18H, ^3J = 7.0 Hz, OCH$_2$C*H*$_3$);

^{13}C NMR (400 MHz, DMSO-d$_6$), δ: 168.77 (s, *C*(O)), 152.45 (s, *C*(O)), 150.65 (s, *C*$_{\text{Ar}}$), 137.07 (s, *C*$_{\text{Ar}}$), 133.37 (s, *C*$_{\text{Ar}}$), 132.64 (s, *C*$_{\text{Ar}}$), 130.32 (s, *C*$_{\text{Ar}}$), 129.02 (s, *C*H$_{\text{Tol}}$), 119.53 (s, *C*H$_{\text{Ar}}$), 117.99 (s, *C*H$_{\text{Tol}}$), 116.97 (s, *C*H$_{\text{Ar}}$), 113.99 (s, *C*H$_{\text{Ar}}$), 66.45 (s, C(O)*C*H$_2$), 60.28 (s, O*C*H$_2$CH$_3$), 36.86 (s, Ar$_3$*C*H), 20.20 (s, *C*H$_{3\text{Tol}}$), 13.87 (s, OCH$_2$*C*H$_3$);

MS (FD) m/z (%) 996.1 (100) [MH$^+$], 1993.4 (28) [2MH$^+$].

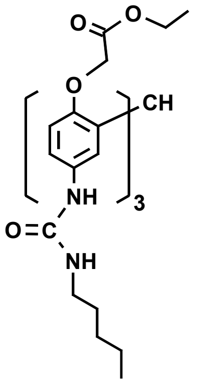
triphenylmethane 103c



The solvent was evaporated and the residue was treated with Et_2O. Calixarene **103c** (55%) was obtained as a white powder;

^{1}H NMR (400 MHz, DMSO-d_6), δ: 10.22 (br s, 3H, N*H*), 8.60 (s, 3H, N*H*), 7.80 (d, 6H, ^3J = 7,8 Hz, ArH_{Tos}), 7.30-7.40 (m, 9H, *p*-Ar*H*, ArH_{Tos}), 6.78 (d, 3H, ^3J = 9.0 Hz, *m*-Ar*H*), 6.33 (d, 3H, ^4J = 2.0 Hz, *o*-Ar*H*), 6.27 (s, 1H, Ar_3CH), 4.46 (s, 6H, C(O)CH_2), 4.03 (q, 6H, ^3J = 7.0 Hz, OCH_2CH$_3$), 2.38 (s, 9H, ArCH_3), 1.09 (t, 9H, ^3J = 7.0 Hz, OCH$_2$CH_3).

triphenylmethane 103d



The solvent was concentrated to 3-5ml and hexane was added to the solution. Calixarene **103d** (77%) was obtained as a white powder; mp 225-227°C

^{1}H NMR (400 MHz, DMSO-d_6), δ: 8.12 (s, 3H, ArN*H*), 7,55 (d × d, 3H, ^3J = 8.6 Hz, ^4J = 2.0 Hz, *p*-Ar*H*), 6.79 (d, 3H, ^3J = 8,6 Hz, *m*-Ar*H*), 6.36 (d, 3H, ^4J = 2.0 Hz, *o*-Ar*H*), 6.34 (s, 1H, Ar_3CH), 5.84 (t, 3H, ^3J = 5.7 Hz, N*H*CH$_2$), 4.45 (s, 6H, OCH_2C(O)), 4.09 (q, 6H, ^3J = 7.0 Hz, OCH_2CH$_3$), 3.00 (q, 6H, ^{3}J = 6.4 Hz, NCH_2), 1.30-1.40 (m, 6H, CH_2), 1.20-1.30 (m, 12H, CH_2CH_2), 1.16 (t, 9H, ^3J = 7.0 Hz, OCH$_2$CH_3), 0.86 (t, 9H, ^3J = 7 Hz, (CH$_2$)$_4$CH_3);

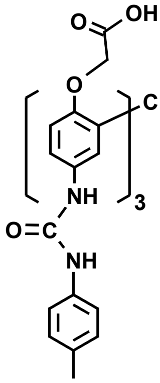
^{1}H NMR (400 MHz, $CDCl_3$, integration is given for a dimeric species), δ: 7.60 (br s, 6H, ArN*H*), 7.24 (d, 6H, ^3J = 8.6 Hz, *p*-Ar*H*), 6.80 (d, 6H, ^3J = 8.6 Hz, *m*-Ar*H*), 6.77 (s, 2H, Ar_3CH), 6.14 (s, 6H, *o*-Ar*H*), 5.72 (br s, 6H, N*H*CH$_2$), 4.50 (s, 12H, OCH_2C(O)), 4.19 (m, 12H, OCH_2CH$_3$), 3.00 (m, 6H, NHCH_2), 2.07 (m, 6H, NHCH_2), 1.10-1.30 (m, 54H, CH_2, OCH$_2$CH_3), 0.82 (t, 18H, ^3J = 7.0 Hz, (CH$_2$)$_4$CH_3);

^{13}C NMR (100 MHz, DMSO-d_6), δ: 168.84 (s, OCH$_2$*C*(O)), 155.11 (s, NH*C*(O)NH), 150.12 (s, C_{Ar}), 134.30 (s, C_{Ar}), 132.77 (s, C_{Ar}), 118.95 (s, CH_{Ar}), 116.35 (s, CH_{Ar}), 114.15 (s, CH_{Ar}), 66.63 (s, O*C*H$_2$C(O)), 60.21 (s, O*C*H$_2$CH$_3$), 38.77 (s, NH*C*H$_2$), 36.67 (s, Ar$_3$*C*H), 29.36 (s, *C*H$_2$), 28.44 (s, *C*H$_2$), 21.74 (s, *C*H$_2$), 13.84 (s, *C*H$_3$), 13.82 (s, *C*H$_3$);

MS (FD) m/z (%) 936.2 (100) [MH$^+$], 1873.7 (69) [2MH$^+$].

triphenylmethane 104

A solution of NaOH (0.15 g, 0.15 mmol) in the mixture of MeOH/H_2O (6 ml/2 ml) was added to the solution of triphenylmethane **109** (0.06 g, 1.50 mmol) in THF (15 ml). The reaction mixture was stirred 6 h at room temperature and acetic acid was added to neutralize the excess of NaOH. The reaction mixture was concentrated to ~5 ml and then water was added. The precipitate was filtered off and washed with acetone. Triphenylmethane **110** (75 mg, 55 %) was obtained as a white powder; mp>270°C decompose;

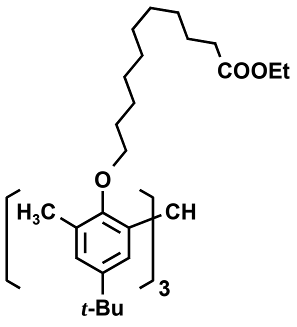


^{1}H NMR (400 MHz, DMSO-d_6), δ: 8.38 (s, 3H, N*H*), 8.27 (s, 3H, N*H*), 7.62 (d, 3H, ^3J = 9.0 Hz, *p*-Ar*H*), 7.25 (d, 6H, ^3J = 7.8 Hz, ArH_{Tol}), 7.03 (d, 6H, ^{3}J = 7.8 Hz, ArH_{Tol}), 6.85 (d, 3H, ^{3}J = 9.0 Hz, *m*-Ar*H*), 6.46 (s, 3H, *o*-Ar*H*), 6.42 (s, 1H, Ar_3CH), 4.42 (s, 6H, C(O)CH_2), 2.21 (s, 9H, ArCH_3);

^{13}C NMR (400 MHz, DMSO-d_6), δ: 170.42 (s, *C*(O)), 152.43 (s, *C*(O)), 150.94 (s, C_{Ar}), 137.07 (s, C_{Ar}), 133.15 (s, C_{Ar}), 132.76 (s, C_{Ar}), 130.27 (s, C_{Ar}), 129.01 (s, CH_{Tol}), 119.54 (s, CH_{Ar}), 117.96 (s, CH_{Tol}), 116.93 (s, CH_{Ar}), 114.03 (s, CH_{Ar}), 66.42 (s, C(O)CH_2), 36.76 (s, Ar_3CH), 20.18 (s, CH_{3Tol});

triphenylmethane 106

A slurry of triphenylmethane **105** (1 g, 1.99 mmol) and NaH (0.24 g, 9.95 mmol) in DMF (40 ml) was stirred at room temperature for 1 h. Then ethyl-(ω-bromododecanoate) (2.92 g, 9.95 mmol) was added and stirring was continued for 72 h. After that acetic acid (0.5 ml) was added to neutralize the excess of NaH. The reaction mixture was diluted with water and the product was extracted with chloroform (2 x 50 ml). The organic layer was washed with water, dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The residue was crystallized from methanol (10 ml) at -14 °C two times (at room temperature the product is oil). Compound **106** (2.0 g, 77 %) was obtained as yellow oil;



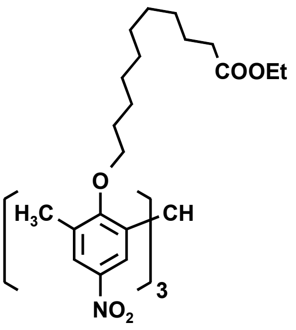
^{1}H NMR (400 MHz, $CDCl_3$), δ: 6.93 (d, 3H, ^4J = 2.4 Hz, Ar*H*), 6.82 (d, 3H, ^4J = 2.4 Hz, Ar*H*), 6.60 (s, 1H, Ar_3CH), 4.11 (q, 6H, ^3J = 7.0 Hz, OCH_2CH_3), 3.36 (t, 6H, ^3J = 7.0 Hz, OCH_2CH_2), 2,27 (t, 6H, ^3J = 7.5 Hz, C(O)CH_2), 2.20 (s, 9H, ArCH_3), 1.63-1.58 (m, 12H, CH_2), 1,27 (br s, 36H, CH_2), 1.23 (t, 9H, ^3J = 7.0 Hz, OCH_2CH_3), 1.13 (s, 27H, C$(CH_3)_3$);

^{13}C NMR (400 MHz, CDCl$_3$), δ: 173.79 (s, *C*(O)), 153.41 (s, *C*$_{Ar}$), 144.72 (s, *C*$_{Ar}$), 136.70 (s, *C*$_{Ar}$), 129.64 (s, *C*$_{Ar}$), 125.81 (s, *C*H$_{Ar}$), 125.40 (s, *C*H$_{Ar}$), 72.40 (s, O*C*H$_2$), 60.07 (s, O*C*H$_2$CH$_3$), 37.49 (s, Ar$_3$*C*H), 34.36 (s, C(O)*C*H$_2$), 34.03 (s, *C*(CH$_3$)$_3$), 31.38 (s, C(*C*H$_3$)$_3$), 30.17 (s, *C*H$_2$), 29.66 (s, *C*H$_2$), 29.62 (s, *C*H$_2$), 29.48 (s, *C*H$_2$), 29.31 (s, *C*H$_2$), 29.18 (s, *C*H$_2$), 26.01 (s, *C*H$_2$), 24.99 (s, *C*H$_2$), 16.79 (s, Ar*C*H$_3$), 14.22 (s, OCH$_2$*C*H$_3$);

MS(FD) *m/z* (%) 1141.3 (100) [M$^+$H].

triphenylmethane 107

Triphenylmethane **106** (1.90 g, 1.67 mmol) was dissolved in CH$_2$Cl$_2$ (50 ml) and acetic acid (6 ml) was added. The solution was vigorously stirred and fuming HNO$_3$ (4 ml) was added. Stirring was continued for approximately 2 h at room temperature. The reaction mixture was diluted with water (40 ml). Organic layer was separated, washed with water (4x20 ml), dried over MgSO$_4$ and filtered. The filtrate was evaporated and the residue was crystallized from acetone (10 ml) at -14 °C. Compound 107 was obtained as light yellow crystalls; mp = 77-79 °C;



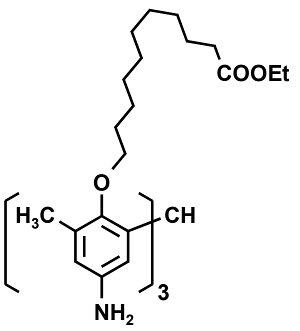
^{1}H NMR (400 MHz, CDCl$_3$), δ: 8.04 (d, 3H, ^4J = 2.7 Hz, Ar*H*), 7.55 (d, 3H, ^4J = 2.7 Hz, Ar*H*), 6.61 (s, 1H, Ar$_3$C*H*), 4.10 (q, 6H, J = 7.0 Hz, OC*H*$_2$CH$_3$), 3.47 (t, 6H, ^3J = 7.0 Hz, OC*H*$_2$CH$_2$), 2.35 (s, 9H, ArC*H*$_3$), 2.26 (t, 6H, ^3J = 7.6 Hz, C(O)C*H*$_2$), 1.65-1.54 (m, 12H, C*H*$_2$), 1.30-1.15 (m, 45H, OCH$_2$C*H*$_3$, C*H*$_2$);

^{13}C NMR (400 MHz, CDCl$_3$), δ: 173.73 (s, *C*(O)), 161.02 (s, *C*$_{Ar}$), 143.36 (s, *C*$_{Ar}$), 136.79 (s, *C*$_{Ar}$), 132.96 (s, *C*$_{Ar}$), 126.31 (s, *C*H$_{Ar}$), 122.75 (s, *C* H$_{Ar}$), 73.26 (s, O*C*H$_2$CH$_2$), 60.10 (s, O*C*H$_2$CH$_3$), 38.64 (s, Ar$_3$*C*H), 34.27 (s, C(O)*C*H$_2$), 29.99 (s, *C*H$_2$), 29.51 (s, *C*H$_2$), 29.46 (s, *C*H$_2$), 29.38 (s, *C*H$_2$), 29.25 (s, *C*H$_2$), 29.10 (s, *C*H$_2$), 25.76 (s, *C*H$_2$), 24.90 (s, *C*H$_2$), 17.09 (s, Ar*C*H$_3$), 14.20 (s, OCH$_2$*C*H$_3$);

MS (FD) m/z 1107.9 (100) [MH$^+$].

triphenylmethane 108

Triphenylmethane **107** (1.00 g, 0.90 mmol) was dissolved in the mixture of toluene/ethanol (20 ml/ 20ml) and hydrogenated during 14 h at room temperature in the presence of the Raney-nickel. The progress of reaction was monitored by TLC in THF. After reaction is finished the catalyst was filtered off and washed with THF (2x10 ml). The combined organic layers were evaporated under reduced pressure to give the pure product **108** (0.80 g, 87 %) as a pale oily mass;



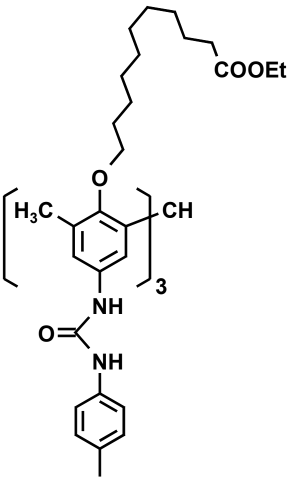
^{1}H NMR (400 MHz, CDCl$_3$), δ: 6.39 (s, 1H, Ar$_3$C*H*), 6.30 (d, 3H, ^4J = 2.7 Hz, Ar*H*), 6.16 (d, 3H, ^4J = 2.7 Hz, Ar*H*), 4.10 (q, 6H, ^3J = 7.0 Hz, OC*H*$_2$CH$_3$), 3.35 (t, 6H, ^3J = 7.0 Hz, OC*H*$_2$CH$_2$), 3.15 (br s, 6H, N*H*$_2$), 2.27 (t, 6H, ^3J = 7.6 Hz, C(O)C*H*$_2$), 2.12 (s, 9H, ArC*H*$_3$), 1.65-1.55 (m, 12H, C*H*$_2$), 1.30-1.15 (m, 45H, OCH$_2$C*H*$_3$, C*H*$_2$);

^{13}C NMR (400 MHz, CDCl$_3$), δ: 173.81 (s, *C*(O)), 148.59 (s, *C*$_{\mathrm{Ar}}$), 141.11 (s, *C*$_{\mathrm{Ar}}$), 138.44 (s, *C*$_{\mathrm{Ar}}$), 131.52 (s, *C*$_{\mathrm{Ar}}$), 115.72 (s, *C*H$_{\mathrm{Ar}}$), 115.36 (s, *C*H$_{\mathrm{Ar}}$), 72.58 (s, O*C*H$_2$CH$_2$), 60.08 (s, O*C*H$_2$CH$_3$), 37.59 (s, Ar$_3$*C*H), 34.35 (s, C(O)*C*H$_2$), 30.17 (s, *C*H$_2$), 29.67 (s, *C*H$_2$), 29.64 (s, *C*H$_2$), 29.47 (s, *C*H$_2$), 29.29 (s, *C*H$_2$), 29.17 (s, *C*H$_2$), 26.01 (s, *C*H$_2$), 24.97 (s, *C*H$_2$), 16.48 (s, Ar*C*H$_3$), 14.22 (s, OCH$_2$*C*H$_3$);

MS (FD) m/z 1018.0 (100) [MH$^+$].

triphenylmethane 109

The triamine **108** (0.45 g, 0.44 mmol), was dissolved in CH$_2$Cl$_2$ (15 ml) and tolyl isocyanate (0.35 g (0.33 ml), 2.66 mmol) was added to the solution. The reaction mixture was stirred for 6h and then the solvent was evaporated. The residue was crystallized from Et$_2$O/MeOH by slow evaporation of Et$_2$O yielding triurea **109** (0.44 g, 70 %) as white oily mass;



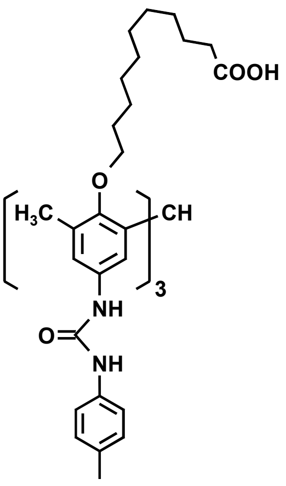
^{1}H NMR (400 MHz, DMSO-d$_6$), δ: 8.40 (s, 3H, N*H*), 8.26 (s, 3H, N*H*), 7.58 (d, 3H, ^4J = 2.4 Hz, Ar*H*), 7.26 (d, 6H, ^3J = 8.6 Hz, Ar*H*$_{\mathrm{Tol}}$), 7.03 (d, 6H, ^3J = 8.6 Hz, Ar*H*$_{\mathrm{Tol}}$), 6.43 (s, 1H, Ar$_3$C*H*), 6.39 (d, 3H, ^4J = 2.4 Hz, Ar*H*), 4.03 (q, 6H, ^3J = 7.2 Hz, OC*H*$_2$CH$_3$), 3.40 (br s, 6H, OC*H*$_2$CH$_2$), 2.24 (t, 6H, ^3J = 7.4 Hz, C(O)C*H*$_2$), 2.21 (s, 9H, ArC*H*$_{3\,\mathrm{Tol}}$), 2.12 (s, 9H, ArC*H*$_3$), 1.59-1.49 (m, 12H, C*H*$_2$), 1.24 (m, 36H, C*H*$_2$), 1.16 (t, 9H, ^3J = 7.2 Hz, OCH$_2$C*H*$_3$);

^{1}H NMR (400 MHz, CDCl$_3$), δ: 8.28 (s, N*H*, 3H), 7.13 (d, 3H, ^4J = 2.4 Hz, Ar*H*), 7.10 (s, 1H, N*H*), 6.86 (s, 12H, Ar*H*$_{\mathrm{Tol}}$), 6.61 (s, 1H, Ar$_3$C*H*), 6.51 (d, 3H, ^4J = 2.4 Hz, Ar*H*), 4.11 (q, 6H, ^3J = 7.2 Hz, OC*H*$_2$CH$_3$), 2.48-2.43 (m, 3H, OC*H*$_2$CH$_2$), 2.28-2.24 (m, 3H, OC*H*$_2$CH$_2$), 2.27 (t, 6H, ^3J = 7.6 Hz, C(O)C*H*$_2$), 2.21 (s, 9H, ArC*H*$_{3\,\mathrm{Tol}}$), 1.76 (s, 9H, ArC*H*$_3$), 1.63-1.56 (m, 6H, C*H*$_2$), 1.34-1.17 (m, 45H, OCH$_2$C*H*$_3$, C*H*$_2$), 1.10-0.94 (m, 12H, C*H*$_2$);

^{13}C NMR (400 MHz, DMSO-d$_6$), δ: 172.61, 152.34, 149.87, 137.25, 137.03, 134.65, 130.69, 130.36, 129.02, 118.92, 117.99, 117.27, 71.94, 59.47, 37.21, 33.42, 29.71, 29.11, 29.06, 28.87, 28.71, 28.42, 25.49, 24.39, 20.19, 16.36, 13.98.

MS (FD) or (ESI) decomposed.

triphenylmethane 110



A solution of NaOH (0.4 g, 0.28 mmol) in the mixture of MeOH/H_2O (10 ml/4 ml) was added to the solution of triphenylmethane **109** (0.12 g, 2.80 mmol) in THF (10 ml). The reaction mixture was stirred 6 h at room temperature and acetic acid was added to neutralize the excess of NaOH. The reaction mixture was concentrated to ~5 ml and then water was added. The precipitate was filtered off and washed with acetone. Triphenylmethane **110** (0.36 g, 95 %) was obtained as a white powder; mp 206-208°C;

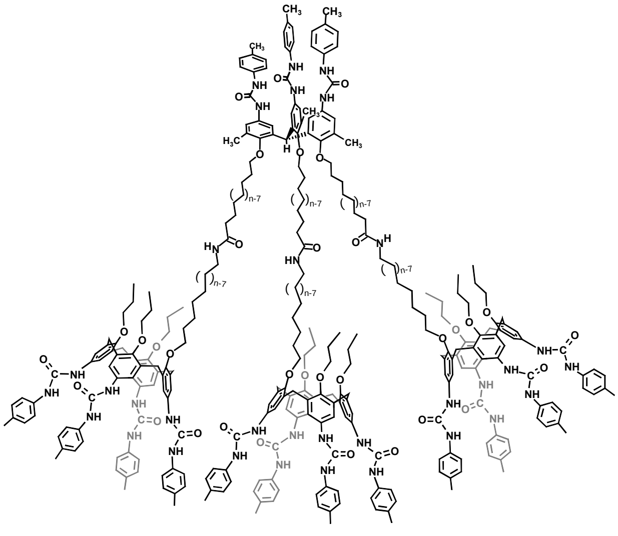
^{1}H NMR (400 MHz, DMSO-d_6), δ: 8.40 (s, 3H, N*H*), 8.26 (s, 3H, NH), 7.57 (d, 3H, ^4J = 2.0 Hz, Ar*H*), 7.25 (d, 6H, ^3J = 8.2 Hz, ArH_{Tol}), 7.03 (d, 6H, ^3J = 8.2 Hz, ArH_{Tol}), 6.42 (s, 1H, Ar_3CH), 6.39 (d, 3H, ^4J = 2.0 Hz, Ar*H*), 3.38 (br s, 6H, OCH_2CH_2), 2.21 (s, 9H, $ArCH_{3\,Tol}$), 2.19 (s, 9H, $ArCH_3$), 2.17 (t, 6H, ^3J = 7.4 Hz, C(O)CH_2), 1.57 (m, 6H, CH_2), 1.48 (m, 6H, CH_2), 1.24 (br s, 36H, CH_2);

MS (ESI) m/z 1353.8 (100) [M^+Na].

Multiple unit 111

The acid **110** (37 mg, 0.028 mmol) and PyBOP (47 mg, 0.087 mmol) were dissolved in DMF for peptide synthesis grade (3 ml) and the solution amine **51b** (113 mg, 0.087 mmol) and triethylamine (0.05 ml) in DMF (3 ml) were added. The stirring was continued for 12 h at room temperature and 12 h at 40°C. After that the reaction mixture was diluted with brine, and the product was extracted with $CHCl_3$/THF. The organic layer was separated, evaporated and the residue was treated with MeOH. The precipitate was filtered off, washed with MeOH and dried on the air. Compound **111** (33%) was obtained as a light yellow powder; mp > 210 decompose;

^{1}H NMR (400 MHz, DMSO-d_6, 75°C), δ: 8.18-7.92 (m, 30H, N*H*C(O)N*H*), 7.53 (s, 3H, ArH_{TPhM}), 7.29 (br s, 3H,



N*H*C(O)CH$_2$), 7.26-7.21 (m, 30H, ArH_{Tol}), 7.02 (br s, 30H, ArH_{Tol}), 6.82 (s, 12H, ArH_{calix}), 6.80 (s, 12H, ArH_{calix}), 6.48 (s, 4H, Ar$_3$C*H*, ArH_{TPhM}), 4.40 (d, 12H, ^2J = 12.5 Hz, ArCH_2Ar), 3.87-3.83 (m, 24H, OCH_2), 3.44 (br s, 6H, OCH_2), 3.10 (d, 12H, ^2J = 12.5 Hz, ArCH_2Ar), 3.04 (m, 6H, NHCH_2), 2.23 (s, 9H, ArC$H_{3\,\mathrm{Tol}}$, ArCH_3), 2.05 (t, 6H, ^3J = 7.0 Hz, C(O)CH_2), 1.93-1.88 (m, 18H, CH_2), 1.58-1.26 (m, 94H, CH_2), 1.00 (br s, 27H, CH_3);

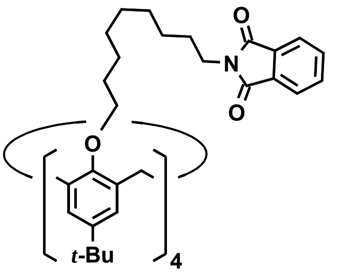
MS (ESI) m/z 5198.7 (1) [M$^+$Na].

Self-assembly 111$_2$•16$_3$

^{1}H NMR (400 MHz, $C_2D_2Cl_4$), δ: 10.64 (br s, 24H, N*H*C(O)NH_{calix}), 8.32 (br s, 6H, N*H*C(O)NH_{TPhM}), 8.11 (d, 48H, ^3J = 7.8 Hz, ArH_{Tos}), 8.10 (br s, 24H, N*H*C(O)NH_{calix}), 8.03 (br s, 24H, N*H*C(O)NH_{calix}), 7.93 (s, 24H, ArH_{calix}), 7.59 (m, 48H, Ar$H_{\mathrm{Tol\text{-}calix}}$), 7.49 (d, 48H, ^3J = 7.8 Hz, ArH_{Tos}), 7.42 (br s, 24H, N*H*C(O)NH_{calix}), 7.13 (s, 6H, ArH_{TPhM}), 7.05 (br s, 6H, N*H*C(O)NH_{TPhM}), 6.99 (s, 24H, ArH_{calix}), 6.95 (br s, 78H, Ar$H_{\mathrm{Tol\text{-}calix}}$, Ar$H_{\mathrm{calix}}$, N*H*C(O)CH$_2$), 6.89 (br s, 12H, Ar$H_{\mathrm{Tol\text{-}TPhM}}$), 6.84 (br s, 12H, Ar$H_{\mathrm{Tol\text{-}TPhM}}$), 6.64 (s, 2H, Ar$_3$C*H*), 6.53 (s, 6H, Ar$H_{\mathrm{TPhM}}$), 5.17 (s, 12H, Ar$H_{\mathrm{calix}}$), 5.16 (s, 12H, Ar$H_{\mathrm{calix}}$), 4.55 (d, 24H, ^2J = 11.0 Hz, ArCH_2Ar), 4.05 (d, 24H, ^2J = 11.0 Hz, ArCH_2Ar), 3.95-3.85 (m, 48H, OC$H_{2\,\mathrm{calix}}$), 3.56 (br s, 48H, OC$H_{2\,\mathrm{calix}}$), 3.38 (d, 24H, ^2J = 11.0 Hz, ArCH_2Ar), 3.22 (br s, 12H, NHCH_2), 2.66 (d, 24H, ^2J = 11.0 Hz, ArCH_2Ar), 2.53 (s, 72H, ArC$H_{3\,\mathrm{Tos}}$), 2.44 (m, 6H, OC$H_{2\text{-}\mathrm{TPhM}}$), 2.32 (m, 12H, C(O)C$H_2$), 2.21 (s, 18H, ArC$H_{3\,\mathrm{Tol\text{-}TPhM}}$), 2.16 (s, 72H, ArC$H_{3\,\mathrm{Tol\text{-}calix}}$), 2.05 (br s, 72H C$H_2$), 1.83 (br s, 88H C$H_2$), 1.78 (s, 18H, ArC$H_{3\,\mathrm{TPhM}}$), 1.61 (br s, 28H C$H_2$), 1.43-1.25 (m, 184H, C$H_2$), 0.91 (m, 60H, OC$H_{2\text{-}\mathrm{TPhM}}$, O(C$H_2$)$_2CH_3$), 0.91 (t, 72H, ^3J = 7.0 Hz, O(CH_2)$_4$CH_3).

Tetratosyl urea 112

Step 1



A slurry of calixarene **1** (2 g, 3.08 mmol) and NaH (0.44 g, 18.5 mmol) in DMF (60 ml) was stirred at room temperature for 1 h. Then *N*-(ω-bromododecyl)phthalimideanoate (6.77 g, 18.5 mmol) was added and stirring was continued for 4 days. After that acetic acid (1 ml) was added to neutralize the excess of NaH. The reaction mixture was diluted with water and the product was extracted with chloroform (2 x 50 ml). The organic layer was washed with water, dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography in CH_2Cl_2 followed by MeOH. The product (3.85 g, 70 %) was obtained as yellow oil;

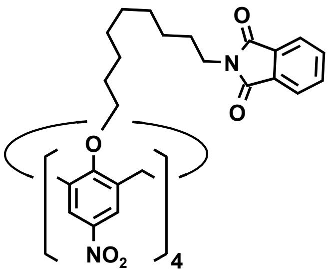
^{1}H NMR (400MHz, $CDCl_3$), δ: 7.81-7.79 (m, 8H, ArH_{pht}), 7.67-7.65 (m, 8H, ArH_{pht}), 6.75 (s, 8H, Ar*H*), 4.37 (d, 4H, ^2J = 12.7 Hz, ArCH_2Ar), 3. 81 (t, 8H, ^2J = 7.5 Hz, OCH_2), 3.64 (t, 8H, ^3J = 7.3 Hz, NCH_2), 3.08 (d, 4H, ^2J = 12.7 Hz, ArCH_2Ar), 1.97 (m, 8H, CH_2), 1.64 (m, 8H, CH_2), 1.30 (br s, 48H, CH_2), 1.06 (s, 36H, C(CH_3)$_3$);

^{13}C NMR (100MHz, $CDCl_3$), δ: 168.35, 153.74, 144.03, 133.81, 133.73, 132.18, 124.80, 123,07, 75.34, 38.03, 32.75, 21.44, 31.08, 30.29, 29.88, 29.61, 29.27, 28.62, 26.92, 26.24.

MS(FD) *m/z* (%) 1789.6 (100) [M$^+$].

Step 2

The tetraalkylphthalimide calixarene (1.90 g, 1.06 mmol) was dissolved in CH_2Cl_2 (60 ml) and acetic acid (6 ml) was added. The solution was vigorously stirred and fuming HNO_3 (4 ml) was added. Stirring was continued for approximately 2 h at room temperature. The reaction mixture was diluted with water (50 ml). Organic layer was separated, washed with water (4x20 ml), dried over $MgSO_4$ and filtered. The filtrate was evaporated and the residue was washed with MeOH, then with Et_2O and dried in vacuum of an oil pump. The product (1.40 g, 76 %) was obtained as light yellow glass; mp 60°C;



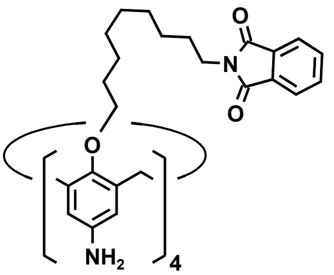
^{1}H NMR (400MHz, $CDCl_3$), δ: 7.81-7.79 (m, 8H, ArH_{pht}), 7.69-7.67 (m, 8H, ArH_{pht}), 7.56 (s, 8H, Ar*H*), 4.49 (d, 4H, ^2J = 14.0 Hz, ArCH_2Ar), 3.96 (t, 8H, ^2J = 7.5 Hz, OCH_2), 3.63 (t, 8H, ^3J = 7.5 Hz, NCH_2), 3.39 (d, 4H, ^2J = 14.0 Hz, ArCH_2Ar), 1.85 (m, 8H, CH_2), 1.63 (m, 8H, CH_2), 1.30 (m, 48H, CH_2);

^{13}C NMR (100MHz, $CDCl_3$), δ: 168.37, 161.65, 142.86, 135.38, 133.85, 132.11, 124.00, 123.09, 76.18, 37.94, 31.13, 30.11, 29.60, 29.54, 29.41, 29.11, 28.54, 26.81, 25.91;

MS(FD) *m/z* (%) 1745.7 (16) [M$^+$].

Step 3

Tetranitro calix[4]arene (1.30 g, 0.74 mmol) was dissolved in toluene/ethanol (50 ml) and hydrogenated during 14 h at room temperature in the presence of the Raney-nickel. The progress of reaction was monitored by TLC in THF. After reaction is finished the catalyst was filtered off and washed with THF (2x10 ml). The combined organic layers were evaporated under reduced pressure to give the pure product (0.80 g, 87 %) as a pale glass mass;



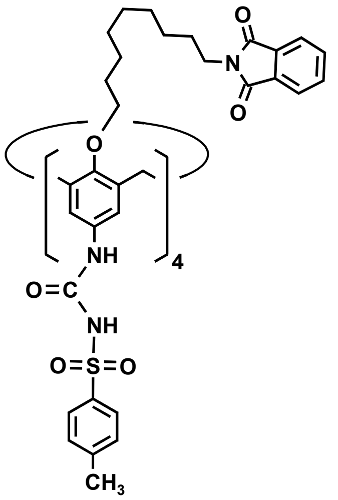
^{1}H NMR (400MHz, CDCl$_3$), δ: 7.81-7.78 (m, 8H, Ar*H*$_{pht}$), 7.67-7.65 (m, 8H, Ar*H*$_{pht}$), 6.05 (s, 8H, Ar*H*), 4.26 (d, 4H, ^2J = 12.7 Hz, ArC*H*$_2$Ar), 3.71 (t, 8H, ^2J = 7.5 Hz, OC*H*$_2$), 3.63 (t, 8H, ^3J = 7.5 Hz, NC*H*$_2$), 3.50 (m, 8H, N*H*$_2$), 2.88 (d, 4H, ^2J = 12.7 Hz, ArC*H*$_2$Ar), 1.79 (m, 8H, C*H*$_2$), 1.63 (m, 8H, C*H*$_2$), 1.29 (m, 48H, C*H*$_2$);

^{13}C NMR (100MHz, CDCl$_3$), δ: 168.34, 150.32, 139.58, 135.72, 133.73, 132.16, 123.06, 116.01, 74.97, 38.02, 31.13, 30.28, 30.07, 29.76, 29.56, 29.23, 28.61, 26.91, 26.19;

MS(FD) *m/z* (%) 1625.7 (100) [M$^+$].

Step 4

The tetraamino calix[4]arene (0.50 g, 0.31 mmol), was dissolved in CH$_2$Cl$_2$ (25 ml) and tolyl isocyanate (0.48 g (0.37 ml), 2.46 mmol) was added to the solution. The reaction mixture was stirred for 6h. The prduct was precipitated from CH$_2$Cl$_2$/MeOH yielding tetratosyl urea **112** (0.50 g, 68 %) as pale grey powder; mp 190-192°C



^{1}H NMR (400MHz, DMSO-d$_6$), δ: 10.17 (s, 4H, NH), 8.41 (s, 4H, NH), 7.82 (d, 8H, ^2J = 7.5 Hz, ArH$_{Tos}$), 7.72 (s, 16H, Ar*H*$_{pht}$), 7.41 (d, 8H, ^2J = 7.5 Hz, ArH$_{Tos}$), 6.60 (s, 8H, Ar*H*), 4.15 (d, 4H, ^2J = 11.0 Hz, ArC*H*$_2$Ar), 3.64 (br s, 8H, OC*H*$_2$), 3.46 (br s, 8H, NC*H*$_2$), 2.98 (d, 4H, ^2J = 11.0 Hz, ArC*H*$_2$Ar), 2.38 (s, 12H, ArCH$_3$), 1.73 (m, 8H, C*H*$_2$), 1.48 (m, 8H, C*H*$_2$), 1.16 (m, 48H, C*H*$_2$);

^{13}C NMR (100MHz, CDCl$_3$), δ: 167.59, 151.84, 148.86, 143.67, 137.05, 134.30, 134.09, 131.61, 131.37, 129.36, 127.35, 122.70, 118.84, 74.74, 37.16, 30.18, 29.58, 29.29, 29.18, 28.92, 28.53, 27.79, 26.17, 25.73, 20.94.

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SUMMARY

Wide rim tetraurea calix[4]arenes form hydrogen bonded dimeric capsules in apolar solvents in the presence of a suitable guest (often a solvent molecule), which must be included in the cavity. The monomeric and dimeric form are never observed simultaneously under usual conditions. In general the combination of two different alkyl or aryl tetraurea derivatives results in the mixture of two homodimers and a heterodimer, however, only the heterodimeric species is observed in the 1:1 mixture of aryl and tosyl ureas. Up to the moment the reasons for this exclusive dimerization are not entirely understood. To get a better idea of this selectivity the heterodimerization was studied in more details. Among very subtle factors influencing the result of dimerization the solvent and the flexibility of calixarene skeleton are most significant. For the first time it was shown that in some cases the self-assembly can be switched from hetero- to homodimers by changing the solvent. The tetraphosphoryl urea can be used instead of the tosyl derivative in heterodimerization studies.

The (hetero)dimerization of oligourea calix[4]arenes (**units**) was used to construct larger structures *via* self-assembly of multiple calixarenes (**building blocks**) containing two (or more) covalently connected units. Among these self-assembled structures linear or branched polymers, cyclic oligomers and well-organized dendrimers were envisaged.

The synthesis of the building blocks requires the preparation of calix[4]arene units possessing one (or more) functional group (for instance amino- or carboxylic functions) at the narrow or wide rim. In general the synthetic route towards a single unit comprises from six to eleven steps depending on the target product. These steps usually include the consecutive alkylation, (selective) *ipso*-nitration, catalytic hydrogenation, reaction with isocyanate and deprotection of the functional group. The ability of all the units to self-assemble was proved by ^{1}H NMR spectroscopy.

Finally the oligourea units were covalently connected either directly or *via* suitable spacers within appropriate building blocks using amide bonds. Self-assembly properties of such building blocks were investigated.

In general the formation of a certain assembly strongly depends on the design of the building blocks.

To construct cyclic oligomers *via* self-assembly a bis-tetraurea triple calix[4]arene has been prepared. In this building block two tetraurea units were linked at their wide rims *via* a central calixarene-spacer, which prevents the intramolecular dimerization. The ability of the triple-calixarene to form dimers was evidenced by its heterodimerization with tetratosyl urea.

Although up to the moment the formation of well-defined self-assembled structures was not detected, we could show that the "homodimerization" of this building block occurs in benzene and in chloroform in the presence of tetraethyl ammonium salts.

To obtain cross-linked polymers *via* self-assembly tetrakis-tetraurea penta-calixarenes were prepared. The coupling of four tetraurea units with the calixarene-core in the *1,3-alternate* conformation was done in DMF using PyBOP in up to 80% yield. The confirmation of the structure of penta-calix[4]arenes is mainly based on clear ^{1}H NMR spectra and for tetrakis-tetraarylureas also discussed in connection with heterodimerization studies. Not entirely unexpected the ^{1}H NMR spectra of such building blocks, which are soluble in $CDCl_3$ do not show any well defined structures. Light scattering experiments evidenced the formation of oligomeric (probably cyclic) assemblies, but not of cross-linked structures.

We have also attempted to build up *via* self-assembly dendritic architectures which are uniform in size and structure.

Here the triurea triphenylmethanes, which were synthesised for the first time, were used as an additional self-complementary hydrogen bonding motif. The triurea derivatives dimerize only with each other. This process does not affect the dimerization of any tetraurea calix[4]arenes and vice versa.

The developed strategies comprise the synthesis of three building blocks, which when mixed together should afford the desired dendritic assemblies. The combination of calixarenes or alternative oligourea units within building blocks is based on the principles of selective dimerization and self-sorting of urea derivatives in solution.

The two shells of the envisaged dendritic architecture were self-assembled by combination of the first building block with three different capping units. In this way dendrimers with the total molecular masses of up to ~23 000 g/mol were obtained. Up to the moment these are the first examples of **self-assembled** dendrimers, which are **uniform in size and structure**.

ZUSAMMENFASSUNG

Calix[4]arene, die am weiten Rand durch vier Harnstoffreste substituiert sind, bilden in unpolaren Lösungsmitteln über Wasserstoffbrücken gebundene dimere Kapseln. Ein geeigneter Gast wird dabei in den gebildeten Hohlraum eingeschlossen. Das Monomer und Dimer werden unter üblichen Bedingungen nie nebeneinander beobachtet. Im allgemeinen enthält eine 1:1 Mischung von zwei verschiedenen Alkyl- oder Aryl-Tetraharnstoff-Derivaten die jeweiligen Homodimere und das Heterodimer. In der entsprechenden Mischung von Aryl- und Tosyl-Harnstoffen liegt jedoch nur das Heterodimer vor. Die Gründe für diese ausschließliche Bildung von Heterodimeren sind noch nicht im Detail verstanden. Um ein besseres Verständnis von dieser Selektivität zu bekommen, wurde die Heterodimerisierung detaillierter untersucht. Unter den sehr subtilen Faktoren, die das Resultat der Dimerisierung beeinflussen, sind das Lösungsmittel und die Flexibilität des Calixaren-Gerüstes am bedeutendsten. Zum ersten Mal wurde gezeigt, daß in einigen Fällen die Selbstorganisation zu Homo- und Heterodimeren abhängig von dem Lösungsmittel geschaltet werden kann. Auch Tetraphosphoryl-Harnstoffe können statt der Tosyl-Derivate zur Bildung von Heterodimeren benutzt werden.

Die (Hetero)Dimerisierung von Oligoharnstoff-Derivaten des Calix[4]arens (**Einheiten**) wurde benutzt, um gezielt größere Strukturen durch Selbstorganisation von Mehrfachcalixarenen (**Bausteinen**), die zwei (oder mehr) kovalent verknüpfte Einheiten enthalten, aufzubauen. Als selbstorganisierte Strukturen wurden lineare oder vernetzte Polymere, zyklische Oligomere und definierte Dendrimere angestrebt.

Der Aufbau von Bausteinen erfordert zunächst die Synthese von Calix[4]aren-Einheiten mit einer oder mehreren funktionellen Gruppen (zum Beispiel Amino- oder Carboxyl Funktionen) am engen Rand. Insgesamt umfaßt die Synthesestrategie sechs bis elf Stufen abhängig von dem Zielprodukt. Unter diesen Stufen sind die schrittweise Alkylierung, die (selektive) *ipso*-Nitrierung, katalytische Hydrierung, Reaktion mit Isocyanat und Abspaltung der Schutzgruppe. Die Fähigkeit von allen Einheiten zur Dimerisierung wurde durch ^{1}H NMR Spektroskopie bewiesen.

Schließlich wurden die Tetraharnstoff-Einheiten entweder direkt oder durch passende „Spacer“ kovalent miteinander verknüpft. Normalerweise erfolgt die Verknüpfung über Amid-Bindungen. Auf diese Weise wurden verschiedene Mehrfachcalixarene dargestellt und Untersuchungen zur Selbstorganisation dieser Bausteine durchgeführt.

Die Bildung eines bestimmten Assoziatiats hängt stark vom Design des Bausteins ab.

Um zyklische Oligomere durch Selbstorganisation zu erhalten, wurde ein Bis-tetraharnstoff eines dreifachen Calix[4]arens synthetisiert. In diesem Baustein sind drei Calixarene so miteinander verknüpft, daß die beiden Tetraharnstoff-Strukturen durch das mittlere Calixaren als „Spacer“ an einer intramolekularen Dimerisierung gehindert werden. Die Fähigkeit des Bausteins zur Dimerisierung wurde durch die Bildung von Heterodimeren mit einem Tetratosylharnstoff bewiesen. Obwohl definierte cyclische Oligomere noch nicht sicher nachgewiesen werden konnten, wurde die „Homodimerisierung“ des dreifachen Calixarens in Benzol oder in Chloroform mit Tetraäthylammonium Kationen als Gast beobachtet.

Um vernetzte Polymere durch Selbstorganisation zu bekommen, wurden mehrere Pentacalix[4]arene mit vierfacher Tetraharnstoffstuktur dargestellt. Die Verknüpfung von Tetraharnstoff-Einheiten mit einem Kerncalixaren in der 1,3-alternate Konformation gelingt in DMF mit PyBOP in bis zu 80 % Ausbeute. Die Struktur von Pentacalix[4]arenen wurde hauptsächlich durch ^{1}H NMR Spektroskopie nachgewiesen und in einigen Fällen auch im Zusammenhang mit der Heterodimerisierung diskutiert. Nicht ganz unerwartet zeigen die ^{1}H NMR Spektren der oben genannten Bausteine, die in $CDCl_3$ löslich sind, keine gut definierten Strukturen. Die Untersuchungen des Assoziationsverhaltens durch (dynamische) Lichtstreuung bewiesen die Bildung von Oligomeren (vermutlich zyklischen), aber nicht von vernetzte Polymeren.

Wir haben auch versucht, dendritische Aggregate, die in der Größe und in der Struktur einheitlich sind, durch Selbstorganisation aufzubauen.

Hier wurden Triharnstofftriphenylmethan-Derivate, die zum ersten Mal synthetisiert wurden, als zusätzliches selbstkomplementäres Wasserstoffbrückenmotiv benutzt. Triharnstoff-Einheiten dimerisieren nur untereinander und stören weder die Dimerisierung von Tetraharnstoffen, noch wird ihre Dimerisierung dadurch gestört.

Die entwickelten Strategien umfassen die Synthese von drei Bausteinen. Aus ihrer Mischung sollte sich durch Selbstorganisation ein einheitliches Dendrimer bilden. Das Bauprinzip beruht auf der selektiven Dimerisierung und Selbstsortierung der Oligoharnstoff-Einheiten in der Lösung.

Die zwei Schalen des geplanten Dendrimers wurden durch die Selbstorganisation von den Kernbaustein mit drei verschiedenen Endstücken aufgebaut. Auf diese Weise wurden Dendrimere mit Molmassen bis zu ~23 000 g/mol dargestellt. Im Moment sind die oben genanten Aggregate die ersten Beispiele von selbstorganisierten Dendrimeren, die in der Größe und in der Struktur einheitlich sind.

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"Enhanced Thermodynamic and Kynetic Stability of Calix[4]arene Dimers Locked in the Cone Conformation"
M. O. Vysotsky, O. Mogck, Y. Rudzevich, A. Shivanyuk, V. Böhmer, M. S. Brody, Y. L. Cho, D. M. Rudkevich, J. Rebek, Jr.
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"Preferred Dimerization of Tetra-Tolyl- and Tetra-Tosylurea Derivatives of Flexible and Rigidified Calix[4]arenes"
Y. Rudzevich, M. O. Vysotsky, V. Böhmer, M. S. Brody, J. Rebek, Jr., F. Broda, I. Thondorf
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"Self-Assembly of Programmed Building Blocks into Structurally Uniform Dendrimers"
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