"Self-assembled Structures Based on Functionalized Calix[4]arenes and Calix[8]arenes"

„Selbstorganisierte Strukturen basierend auf funktionalisierten Calix[4]- und Calix[8]arenen"

Dissertation

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"Doktor der Naturwissenschaften"

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Contents

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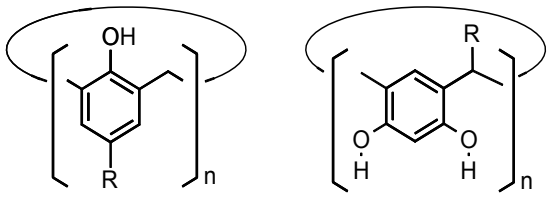
Chapter 1

The basics of calixarene chemistry

1.1 Introduction and definitions

The condensation of *p*-*tert*-butylphenol and formaldehyde leads in one step and good yields to macrocycles, in which, depending on the reaction conditions, four, six or eight phenol units are connected by methylene bridges.[1] The cup-like shape of the most stable conformation of the cyclic tetramer has inspired the name "calix[n]arene" for all oligomers with the general formula **I**. In Latin and Greek "calix" means "chalice." The part "[n]arene" was added to indicate the kind (arene) and the number (n) of units forming the macrocycle.



I **II**

Cyclic oligomers with other aromatic units and/or bridges have been also included in the family of calixarenes.[2] From those compounds the oligomers **II** composed of resorcinol units are called "resorcarenes" or "calixresorcinols".

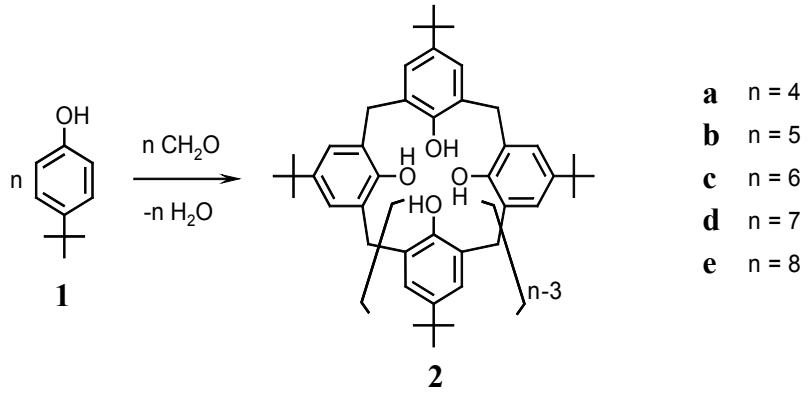
1.2 Syntheses of calixarenes

1.2.1 "Classical" calixarenes (calixphenols)

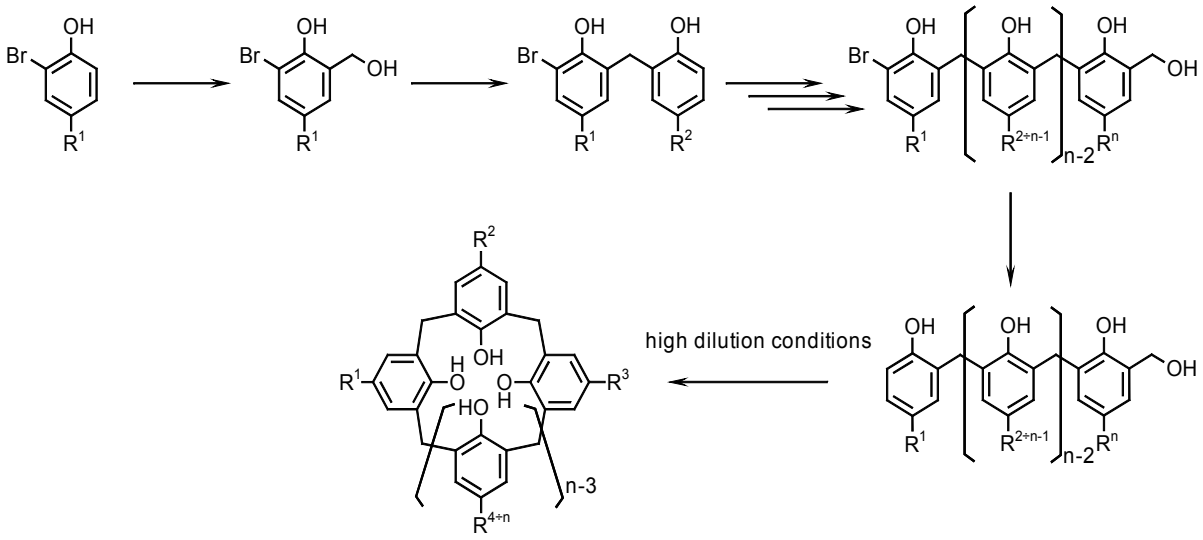
The presence of cyclic oligomers among the products of the base-induced condensation of *p*-alkylphenols with formaldehyde was found in the 1940s by Zinke.[3] However, the remarkable acceleration of the development of calixarene chemistry started only in the middle of the 1970s. In these years Gutsche and his co-workers[4] reviewed the previous results and developed convenient procedures (Scheme 1) for the single-step synthesis of the three "major" cyclic oligomers (calixarenes **2a,c,e**) in 50-85% yield[5] and the two minor oligomers (calixarenes **2b,d**) in 11-17% yield[6]. Like in the synthesis of Zinke alkali-catalysis was used to induce the condensation.

The selectivity of the formation of "major" *p-tert*-butylcalix[n]arenes is attributed to kinetic (n = 8), thermodynamic (n = 4) control or to template effect of the potassium cation (n = 6).

Unfortunately, the procedures optimized for *p-tert*-butylphenol **1** turned out to be not so effective with most of the other phenols (except *p-tert*-octylphenol). Usually their condensation led to mixtures which are difficult to separate. Thus, for the most studied *p*-alkylphenols the attempts to tune the reaction conditions were not so successful, like in the case of *p-tert*-butylphenol.[7]



Scheme 1. One-pot synthesis of calixarenes **2a-e** starting from *tert*-butylphenol **1**.



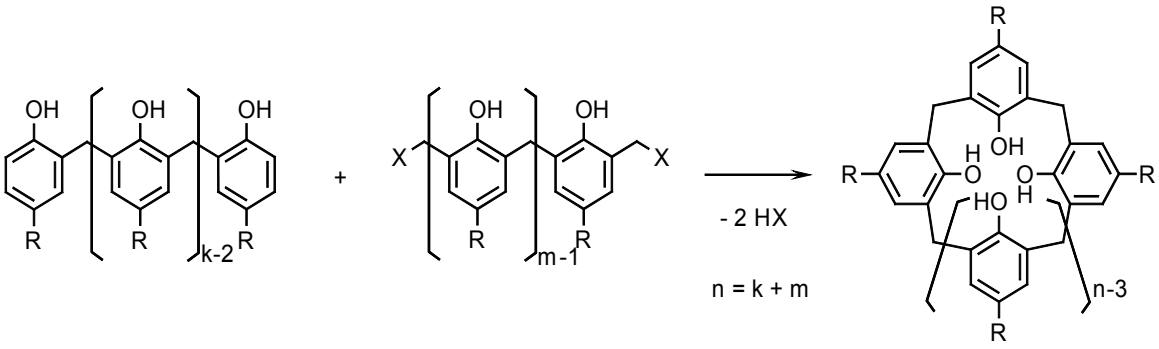
Scheme 2. Synthesis of calixarenes by stepwise strategy. R = alkyl.

The single-step synthesis of calixarenes gives a possibility to prepare only macrocycles having equal substituents (usually *p*-*tert*-butyl) in *para*-positions of the phenolic units. To synthesize calix[*n*]arenes with *n* different ring-substituents within the same molecule stepwise synthesis was developed (Scheme 2).[8]

The synthesis strategy is as follows:

- protection of one *ortho* position in a *p*-alkylphenol (by bromination);
- preparation of linear oligomers by an appropriate sequence of hydroxymethylation and condensation;
- deprotection;
- cyclization of the oligomers under high dilution conditions.

Various calix[4]arenes were also synthesized by 3 + 1 and 2 + 2 fragment condensation catalyzed by $TiCl_4$ in 25-30% yield[9] (Scheme 3). For the preparation of larger calixarenes these conditions are less successful because of side reactions (for example, cleavage of methylene bridges). Nevertheless, some calix[5]- and calix[6]arenes have been prepared by this procedure.[10] This strategy was successfully applied to prepare calix[4]- and calix[5]arenes with different substituents at their bridges.[10,11]



Scheme 3. Synthesis of calix[n]arenes by fragment condensation "k + m". X = Br, OH.

1.2.2 Resorcarenes (calixresorcinols)

Resorcarenes of general formula **II** have been synthesized by condensation of resorcinol with different aldehydes (except formaldehyde) under acidic conditions. Normally this condensation leads to cyclic tetramers in high yields.[12] However, for each aldehyde optimization of the reaction conditions is required. As catalyst hydrochloric acid is usually used.[13]

Different arrangements of R substituents at -CHR- bridges create four stereoisomers (Fig. 1). For simplification of their distinction the macrocycle is considered as "plane" with residues R pointing to one or the other side of this plane. One of the residues R should be

taken as reference (*r*) and the positions of other residues are called *cis* (*c*) or *trans* (*t*). The most frequently observed isomers are *rccc* and *rctt*. Synthetic procedures can be often modified to produce the *rccc* isomer exclusively.

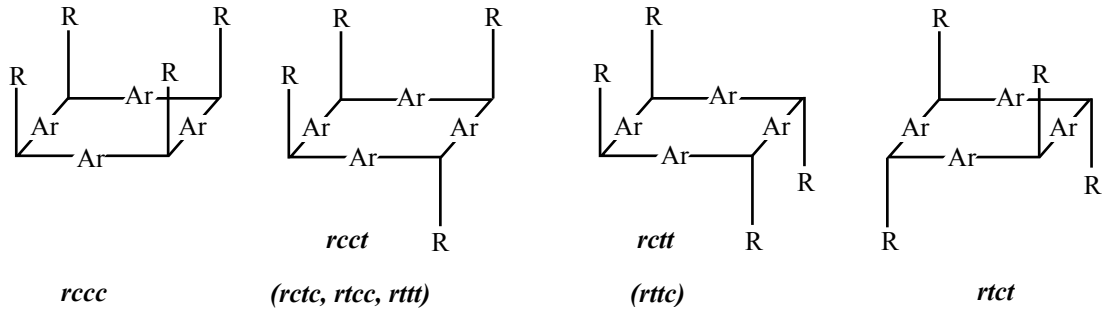


Figure 1. Schematic representation of the different stereoisomers of resorcarenes.

1.3 Classification of calixarenes and their stereoisomers

1.3.1 Nomenclature

The name of the compounds of this type according to IUPAC nomenclature is very long and complicated. That is why a trivial name "calixarene" which includes a cyclic skeleton formed by phenyl rings and methylene bridges (hydroxy groups and *tert*-butyls are counted as substituents) is so wide-spread in the literature in spite of its incorrectness to the larger members of this family (the shape of the cyclic hexamer and larger oligomers is not anymore a chalice-like).

The numbering of carbon atoms in calixarene skeleton (Fig. 2) serves to indicate the exact position of a substituent. For example, the systematic name for the cyclic tetramer derived from *p-tert*-butylphenol is 5,11,17,23-tetra-*tert*-butylcalix[4]arene-25,26,27,28-tetrol. But often a shorter name is used when it is clear that all *para*-positions of the phenolic units are substituted with the same groups: for example, "*p-tert*-butylcalix[4]arene" (four *tert*-butyl groups), "*p-tert*-butylcalix[8]arene" (eight *tert*-butyl groups).

In the literature also the single phenolic units of calixarenes are often called by numbers 1, 2, 3, 4... or by letters A, B, C, D...

The crater-like representation of calix[4]arene gave birth to the terms "upper rim" and "lower rim" to describe transformations done at the hydroxyl groups (*lower rim*) or at the *para*-positions of the phenolic units (*upper rim*). It was objectively criticized using the argument that this nomenclature is depended on how a calixarene formula is drawn (what is a

matter of taste or necessarity in the case of multicalixarenes). Thus, it was suggested to use instead of the terms mentioned above the terms "*narrow rim*" (for the *lower rim*) and "*wide rim*" (fot the *upper rim*) (Fig. 3a). Currently both classifications are in use.

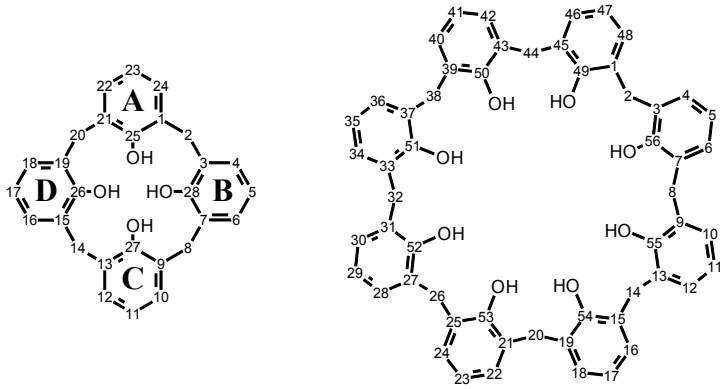


Figure 2. The numbering scheme of carbon atoms in the calixarene skeleton (for cyclic tetramer and octamer).

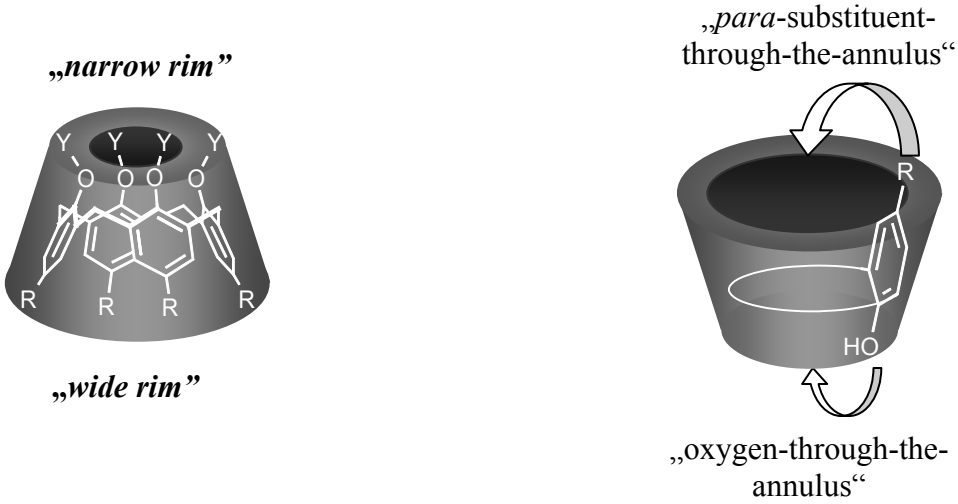
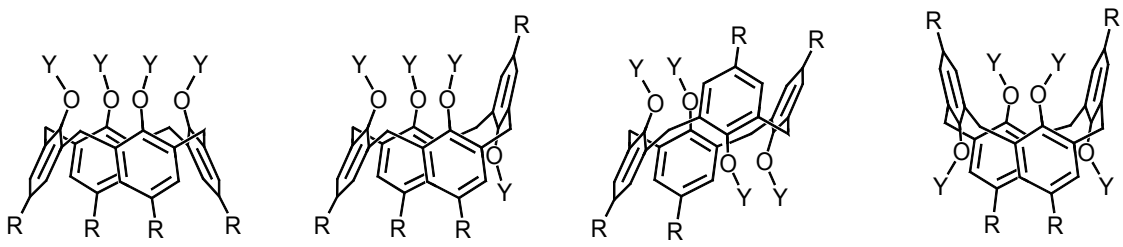


Figure 3. a) Classification of calixarene rims. b) The pathways of inversion of phenolic units in calixarene molecule.



cone ***partial cone*** ***1,2-alternate*** ***1,3-alternate***

Figure 4. The basic conformations of calix[4]arenes.

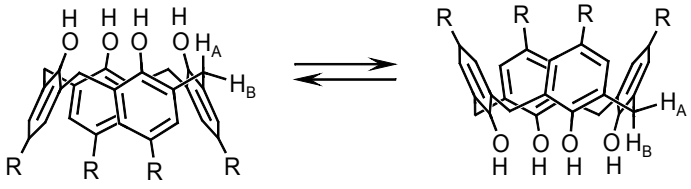
1.3.2 Conformational properties of calixarenes

The flexibility of calixarenes allows a free rotation of their phenolic units around the σ-bonds to the methylene bridges. In the case of calix[4]arenes only the „oxygen-through-the-annulus“ rotation is possible (Fig. 3b). The phenolic units of larger calixarenes (for example, calix[8]arene) can pass through the annulus in two ways: via the „oxygen-through-“ or „*para*-substituent-through-the-annulus“ passages (even when the *para*-substituent R is *t*-Bu).

The four main conformations assumed by calix[4]arene are named *cone*, *partial cone*, *1,2-alternate* and *1,3-alternate*[14] (Fig. 4).

The parent tetrahydroxy calix[4]arenes are found only in the *cone* conformation, which is stabilized by an array of intramolecular hydrogen bonds formed between the OH groups. As a consequence, the protons of the methylene bridges (-CH_2-) are fixed in the different environment. Thus, the signals of axial (H_A) and equatorial protons (H_B) (Scheme 4) appeared at low temperature in ^{1}H NMR spectrum in chloroform-d_1 as a pair of doublets. At higher temperatures hydrogen bonds are broken and the phenolic units rotate rapidly through the plane of methylene bridges. This leads to fast change of the environment for H_A and H_B protons, which is reflected in coalescence of their doublets into one singlet. The energy barrier $\Delta G^{\neq}$ for the interconversion between two identical *cone* conformations in chloroform-d_1 has been determined by variable temperature ^{1}H NMR studies. For calix[4]arenes with different *p*-substituents it lies between 14.6 and 15.7 kcal·mol^{-1}. Similar signals for the methylene protons (a pair of doublets or a singlet) were found in the ^{1}H NMR spectra of calix[5]- and calix[8]arenes. In case of calix[5]arenes these doublets are attributed to the time-averaged *cone* conformation. While in the spectra of calix[8]arenes the analogous doublets are present due to the "pleated loop" conformation with regular up and down arrangement of the Ar-CH_2-Ar units (in detail discussed in Chapter 6.1).

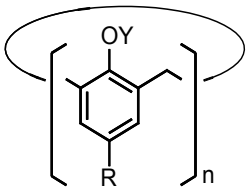
The inversion of phenolic rings in calix[n]arenes can be blocked by the attachment of the large residues Y to the phenolic oxygens or by intramolecular bridging.



Scheme 4. *Cone*-to-*cone* inversion of calix[4]arenes.

1.4 Modification of calixarenes (calixphenols) at the *narrow rim*

1.4.1 Complete conversions

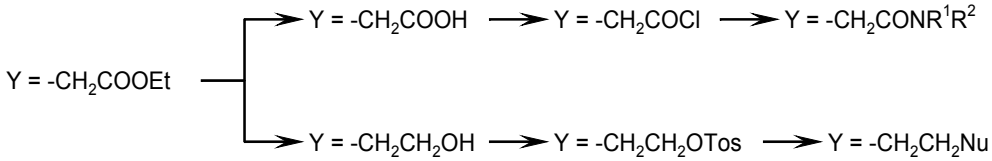


Ia

Calix[n]arenes bearing various *p*-substituents R can be easily exhaustively *O*-alkylated or *O*-acylated to produce ethers or esters with the general formula **Ia**.

Reaction of **I** with a strong base (NaH) in DMF in the presence of an excess of alkylating reagent usually leads to complete *O*-alkylation of calix[n]arenes.[15] In some cases an increased temperature is required. More reactive reagents such as allyl bromide, benzyl or picolyl chloride (or bromide) or bromoacetates can be introduced using carbonates as base in refluxing acetone or acetonitrile.

Functional groups attached via ether links to the narrow rim can be further modified. One of the early examples is the -CH_2COOEt group, which was used for the introduction of many residues by re-esterification or acylation (Scheme 5). Another possibility is the reduction of the ester groups followed by tosylation and substitution by various nucleophiles (= Nu).



Scheme 5. An example for the modification of functional groups attached to calixarenes via ether links.

Exhaustive *O*-acylation of calixarenes is less frequently used and studied than *O*-alkylation.

As already mentioned, calix[4]arenes can be fixed in one of four main conformations (Fig. 4) by introduction of *O*-alkyl or *O*-acyl groups of an appropriate size. This is true for all Y equal or larger than propyl and for ester groups larger than acetyl. The formation of a certain stereoisomer depends mainly on

- the reaction conditions (base, solvent, temperature),
- the residue Y to be attached,
- the substituents R in *p*-positions of the phenolic units.

A template effect of the metal cation (from the used base) influences considerably the ratio of the conformers produced. Usually sodium cations drive tetra-*O*-alkylation to the formation of the *cone* isomer exclusively. Hence, in the presence of NaH in DMF solution at room temperature calix[4]arenes can be completely *O*-alkylated with alkylhalides or tosylates

yielding the product fixed in the *cone* conformation.[16] Sodium carbonate is often used to obtain the *cone* conformer by *O*-alkylation with more reactive reagents such as bromo- or chloroacetates.

Larger alkali ions, like potassium and caesium, favour the formation of *partial cone* and *1,3-alternate* isomers. The *1,2-alternate* isomer is less frequently formed.

Also partially *O*-alkylated compounds (see next subchapter) can be exhaustively *O*-alkylated to introduce different groups to the narrow rim. In these cases the stereochemical result depends on the sequence of *O*-alkylation steps.

1.4.2 Partial conversions of calix[4]arenes

Mono-*O*-alkylation of calix[4]arenes has been achieved using 1.1 mole of weak base (K_2CO_3 in acetonitrile or CsF in DMF) and 1.1 mole of alkylating reagent.[16] Another pathway to mono-ethers is selective cleavage of ether groups from more easily available di- or tetraethers by 1 or 3 mole of trimethylsilyl iodide.[17]

The functionalization of only two hydroxy groups in calix[4]arenes may lead to two regioisomers (1,2 or AB and 1,3 or AC) and for sufficiently large residues Y two conformational isomers (*syn*/*anti*) for each case (Fig. 5a).

The selective *syn*-1,3-*O*-difunctionalization of calix[4]arenes has been achieved in the presence of a weak base (sodium or potassium carbonate) under reflux in acetonitrile or acetone in high yields.[18] It allows synthesis of 1,3-diethers or -esters with identical residues Y or with different residues (Y^1,Y^2), if a mono-*O*-substituted derivative is subjected to these conditions. Such selectivity can be explained by the formation of the intermediate monoanion of the corresponding monoether which is stabilized by two hydrogen bonds formed with the adjacent hydroxy groups (Fig. 5b).

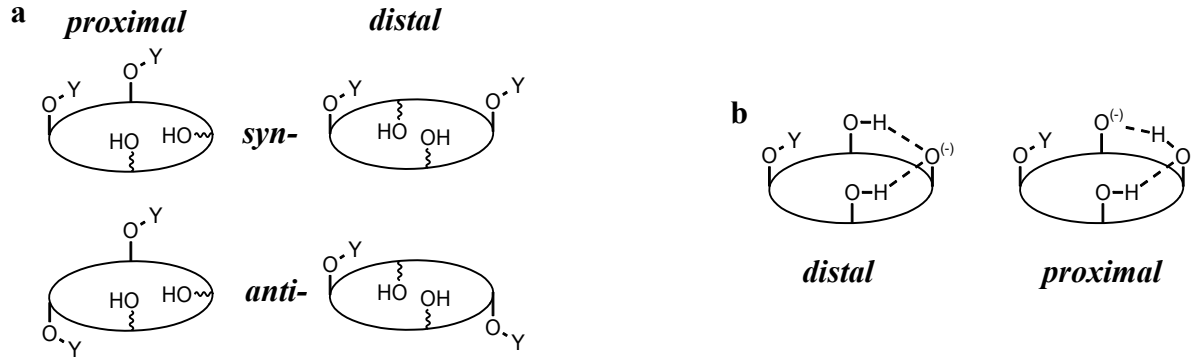


Figure 5. Schematic representation of possible a) regioisomers of di-*O*-fuctionalized calix[4]arenes and their conformational isomers; b) intermediate monoanions.

However, 1,2-products must be statistically favoured. Thus, in the presence of an excess of a strong base (NaH in DMF/THF) and 2.2 mole of alkylating reagent 1,2-diethers are synthesized. In these conditions di- or even trianion are "intermediates". Although the selectivity for the formation of 1,2 diethers is less pronounced than for 1,3-derivatives, different *syn*-1,2-diethers were obtained by direct alkylation in yields up to 90% in special cases.[16,19] Recently an easy access to 1,2-ethers was found by selective protection of two adjacent oxygens by a disiloxane bridge.[20]

1.4.3 Introduction of the bridges at the narrow rim of calix[4]arenes

The narrow rim of calix[4]arene can be bridged with difunctional reagents. This could be achieved by direct *O*-alkylation with ditosylates (under the conditions used for selective di-*O*-functionalization), which is frequently used for the preparation of various 1,2- and 1,3-calix[4]crowns (Fig. 6a).[21]

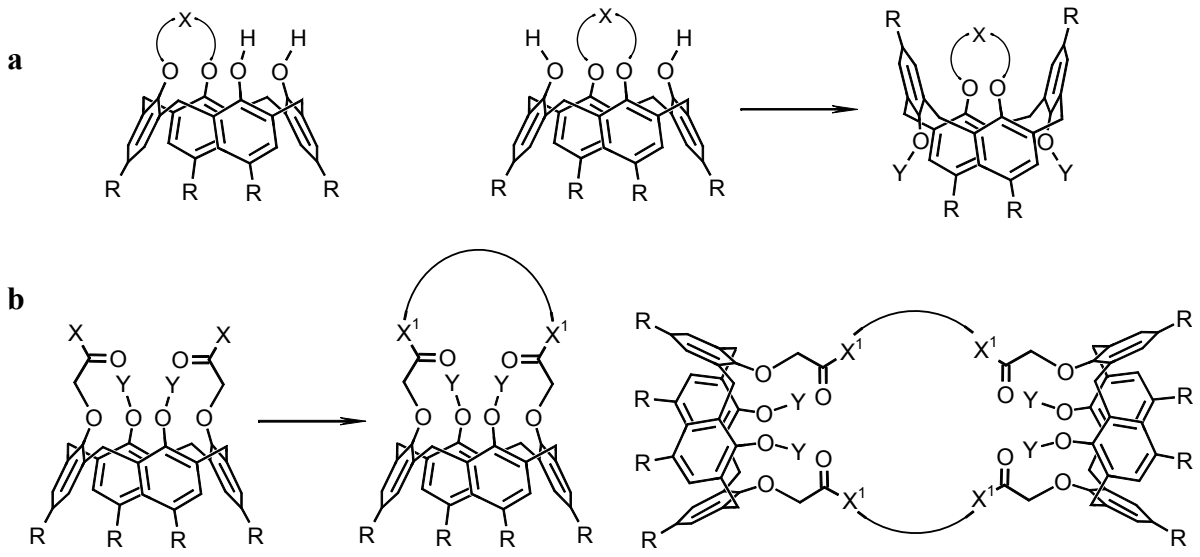


Figure 6. Selected examples of bridged calix[4]arenes (R = H or *t*-Bu). a) X = -(CH_2CH_2-O-CH_2CH_2)$_n$-, Y = alkyl; b) X = OEt, OH, Cl; X^1 = -NH-, Y = H or alkyl.

The bridged dihydroxy derivatives can be further alkylated by monofunctional or difunctional reagents (introduction of the second bridge) leading to the exhaustively alkylated products, which in the second case are doubly-bridged calixarenes (or *bis*-crowns, if the linkages are -(CH_2CH_2-O-CH_2CH_2)$_n$-). Depending on the reaction conditions the products could be obtained in the *cone* or *1,3-alternate* conformation.

Another pathway is a bridging of the calix[4]arenes by difunctional reagents via two functional groups X already attached to the phenolic oxygens at 1,2- or 1,3-positions by *O*-alkylation. For instance, calix[4]arenes with -CH_2COOEt (also as acid or acid chloride) groups attached to the oxygens in 1,3-positions were used for acylation of diamines leading to intramolecularly and in some cases intermolecularly bridged products (Fig. 6b).[22]

1.5 Modification of calix[n]arenes at the *wide rim*

1.5.1 Complete substitution

Since the one-pot synthesis of calixarenes works best with *p-tert*-butylphenol, often *p-tert*-butylcalixarenes are the starting materials for the preparation of appropriately functionalized calixarenes. *t*-Butyl groups can be easily removed from *para*-positions of calixarenes by *trans*-butylation with $AlCl_3$ in toluene,[23] which is used here as a solvent and as an acceptor. The free *para*-positions of phenolic units have been functionalized via electrophilic substitution or rearrangements.[15] Sulphonation, nitration, bromination (or iodination), bromomethylation, aminomethylation, formylation, acylation of calixarenes and their coupling with diazonium salts have been described.

Also *ipso*-substitution of *p-tert*-butyls on calixarenes has been elaborated (*ipso*-sulfonation,[24] *ipso*-acetylation,[25] *ipso*-nitration[26]).

However, there are still numerous gaps, which partially have been filled out only during the last years. For example, the octabromination and octaiodination of the free *para*-positions of phenolic units of calix[8]arene were unknown until 2002, when also for the first time Sonogashira cross-coupling of the octaiodo derivative have been published.[27, 28]

1.5.2 Selectivity transfer from the narrow to the wide rim

Phenols have higher reactivity than their ethers and esters. Thus, the substituition pattern achieved by the partial *O*-alkylation (*O*-acylation) (Section 1.4.2) can be transferred from the narrow rim to the wide rim.

Selective partial *ipso*-substitution (including de-*tert*-butylation), electrophilic substitution or rearrangements have been realized under mild reaction conditions.[15] In this way calix[n]arenes bearing different functions at the wide rim have been synthesized (Fig. 7).

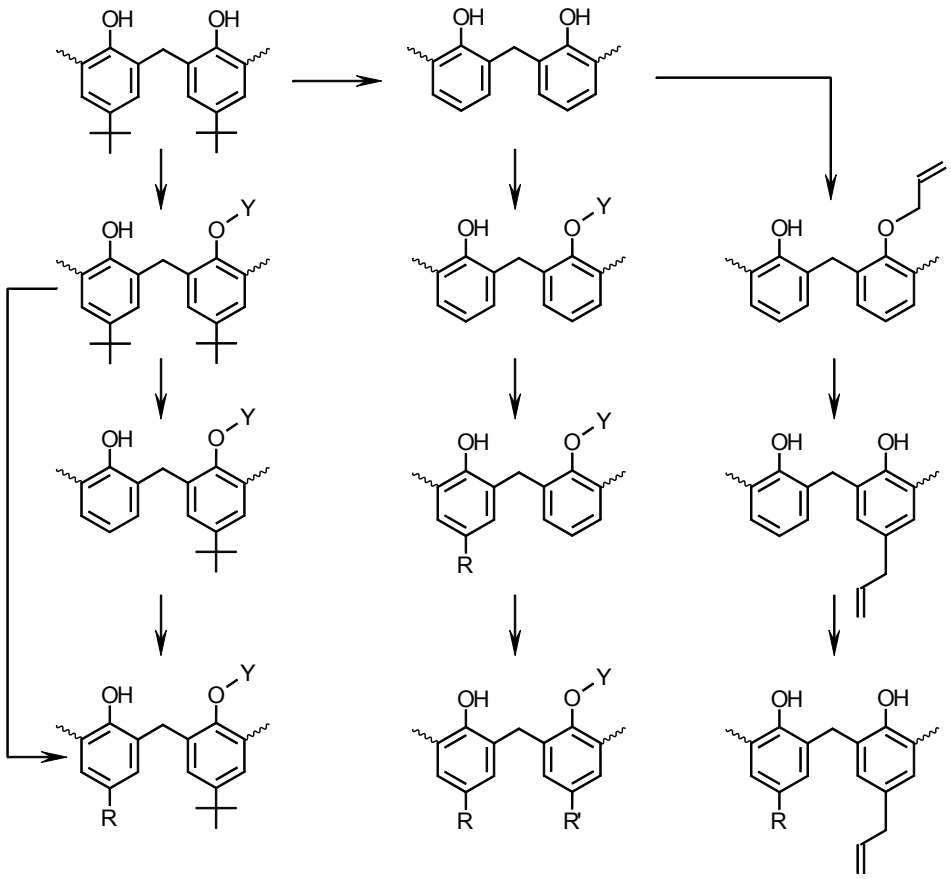


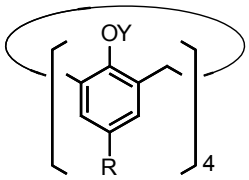
Figure 7. Schematic representation of the selectivity transfer from the narrow to the wide rim for two units of calix[n]arene.[1b,c]

1.5.3 Modification of substituents

Substituents introduced at the wide rim by electrophilic substitution can be replaced or modified by further reactions. Here is shown only a short overview of modifications, which were realized for calix[4]arenes (illustrated in Scheme 6).[15]

p-Nitro groups of **Ia** (R = NO_2) can be reduced by catalytic hydrogenation,[29] by hydrazine[30] or by Sn(II) yielding tetraamine **Ia** (R = NH_2).[31] Acylation of *p*-tetraamino calixarenes has led to various amides (R = NH-C(O)-R^1) and ureas (R = NH-C(O)-NH-R^1). The tetraureas can be also obtained via the isocyanate **Ia** (R = N=C=O). Reaction of tetraamine with aldehydes produces the Schiff-bases **Ia** (R = N=C-R^1).[29]

Calix[4]arene Schiff-bases are also available by the reaction of tetra-*p*-formyl derivative **Ia** (R = C(O)H) with amines.[32] Formyl groups can be also oxydized to the corresponding carboxylic groups **Ia** (R = C(O)OH)[33] or reduced to **Ia** (R = CH_2OH).[30a,34] *p*-Stilbene derivatives **Ia** (R = C(CN)=CH-Ar) are accessible from tetraaldehyde by Wittig-Horner reaction.[35]



Ia

Y = Alk or OH

R = NO_2	→ NH_2	→ NH-R^1
		→ NH-C(O)-R^1
		→ NH-C(O)-NH-R^1
		→ N=C-R^1
		→ N=C=O
R = C(O)H	→ C=N-R^1	
	→ CH=CH-Ar	
	→ CH_2-OH	
	→ C(O)OH	
R = $CH_2(NR^1)_2$	→ CH_2-C≡N	→ CH_2-C(O)OH
		→ CH_2-CH_2-NH_2
		→ $C(R^2)_2$-CN
		→ C(CN)=CH-Ar
R = I or Br	→ Phthalimide	→ NH_2
	→ Li	→ $B(OH)_2$→ Ar or OH
	→ C≡C-Ar	

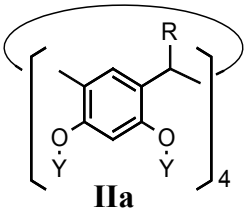
Scheme 6. Modifications of substituents at the wide rim realized for calix[4]arenes.

Aminomethyl groups **Ia** (R = $CH_2(NR^1)_2$) introduced by Mannich reaction with secondary amines,[36] can be quarternized and substituted by nucleophiles (for example, Nu = CN) to give **Ia** (R = CH_2Nu) products. Hydrolysis of the cyanomethyl derivatives[36] yields CH_2-C(O)OH groups.[37] Reduction of **Ia** (R = CN) leads to the product with R = -CH_2-CH_2-NH_2.[36]

Coupling of calixarenes **Ia** (R = I) with phthalimide followed by hydrazinolysis is an alternative strategy to tetraamino derivatives.[38] Complete lithiation of calixarenes **Ia** (R = Br) is possible by an excess of BuLi (-78°C).[39] Treatment of the compounds **Ia** (R = Li) with different electrophiles leads to derivatives with various *p*-substituents, for instance, tetraboronic acids (which can be followed by Suzuki coupling with iodoarenes or by oxidation to produce *p*-hydroxy derivatives).[39a,40] The calixarenes **Ia** (R = Br or I) can be also coupled with arylboronic acids.[41] C-C couplings were also achieved by Heck,[42] Negishi and Stille[15] reactions.

Chloromethylated calix[4]arenes **Ib** (R = Cl) can be reduced or alkylated giving *p*-methyl[43] (R = H) and *p*-ethyl compounds[43a] **Ib** (R = CH_3) respectively. Treatment of **Ib** (R = Cl) with amines yields derivatives **Ib** (R = $N(R^1)_2$).[43a] Reaction of **Ib** (R = Cl) with aromatic compounds in the presence of BF_3 gives *p*-arylmethyl calixarenes.[43a] Ether groups can be introduced by reaction of **Ib** (R = Cl) with R^1ONa.[44]

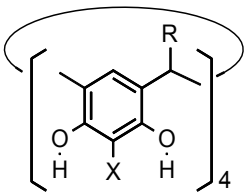
1.6 Modification of resorcarenes



IIa

Hydroxy groups of calixresorcinols (*rccc*, *rcct*, *rctt*) can be completely esterified or alkylated to obtain the corresponding octa-*O*-esters (for example, Y = C(O)-Alk, C(O)-Ar,[45] $P(O)Ar_2$,[46] PAr_2,[47] $S(O)_2$-Ar,[48] $SiMe_3$[49]) or octa-*O*-ethers (Y = Me to Bu,[50] CH_2COOEt[51]).

The octa-*O*-substituted *rccc*-resorcarenes **IIa** (Y = CH_2COOEt) are versatile starting compounds for further derivatization. They can be hydrolyzed to the octaacids (Y = CH_2COOH). The reduction of **IIa** (Y = CH_2COOEt) with $LiAlH_4$ leads to the octol **IIa** (Y = CH_2CH_2OH), which has been converted to the octaphthalimide by Mitsunobu reaction (phthalimide / diethylazodicarboxylate / PPh_3). Hydrazinolysis of phthalimide functions resulted in the corresponding octaamine **IIa** (Y = $CH_2CH_2NH_2$).[52]

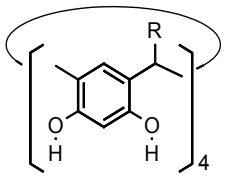


IIb

The 2-positions (between hydroxy groups) of resorcarenes may undergo electrophilic substitution,[53] such as bromination,[54] coupling with diazonium salts[55] and Mannich-type reactions. Aminomethylation of the resorcarenes **II** with secondary amines gives the corresponding tetraamines **IIb** (X = $CH_2NR^1R^2$).[56]

Functional groups could be incorporated at the bridges of resorcarenes **II** via acid-catalysed condensation of resorcinol with the appropriately functionalized aldehydes. In this way hydroxy-, alkoxy-, aryldiazo, sulphonyl- and $B(OH)_2$ groups, halogens and double bonds have been introduced.[1c] These functions have been used for further modification of the resorcarenes.

For example, the sulfide derivatives **II** (R = $(CH_2)_{10}$-S-$(CH_2)_9$-CH_3) have been synthesized via *anti*-Markovnikoff addition of thiols to the double bonds of the resorcarene **II** (R = $(CH_2)_8$-CH=CH_2) (hydroxy groups were protected beforehand by acylation and deprotected after the addition reaction).[57] This sulfide compound and its derivatives were shown to form self-assembled monolayers on gold surfaces (see in Chapter 3.1).



II

R =

$p\text{-}C_6H_4\text{-}B(OH)_2$

$(CH_2)_8\text{-}CH{=}CH_2$

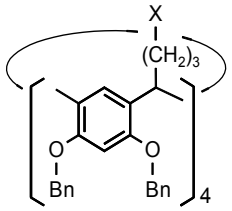
$(CH_2)_{10}\text{-}S\text{-}(CH_2)_9\text{-}CH_3$

$(CH_2)_{10}\text{-}SH$

$(CH_2)_3\text{-}OH$

$(CH_2)_3\text{-}NH_2$

$(CH_2)_3\text{-}Cl$



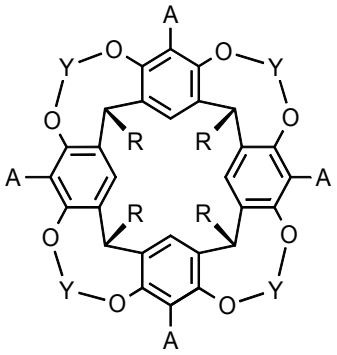
IId

X =

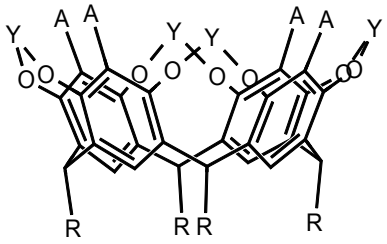
OH

N_3

NHBoc



≡



III

A = H, Br, Me

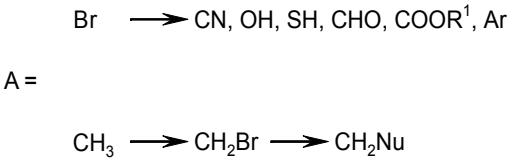
R = Alk

The selective benzylation (K_2CO_3, NaI) of the phenolic hydroxy groups in **II** (R = $(CH_2)_3$-OH) led to the derivative **IId** (X = OH), which after acylation with methane sulfonychloride followed by reaction with NaN_3 gave the tetraiazide **IId** (X = N_3). Subsequent hydrogenation (Raney-Ni) and acylation with Boc-anhydride resulted in *N*-protected amine **IId** (X = NHBoc), which gave after cleavage of benzyl and Boc-groups the tetraamine **II** (R = $(CH_2)_3$-NH_2).[58]

Intramolecular connection of the adjacent hydroxy groups in neighbouring resorcinol units via suitable bridges leads to rigidified bowl-shaped molecules **III**, which were named "cavitands" (derived from "cavity").[59]

A methylene bridge is most frequently used for the cavitands. It could be easily introduced in resorc[4]arenes **II** by alkylation with CH_2BrCl in yields up to 65%.[60] The cavity of these compounds can be extended by attachment of aromatic units to the A positions of **III** via Suzuki coupling (when A = Br).[61]

Tetracyano,[62] -hydroxy, -thio, -formyl and -COOR derivatives have been obtained starting from **III** (A = Br).[63]



The methyl groups in the A positions can be easily brominated with NBS[64] and bromines can be further substituted by a variety of nucleophiles.[65]

1.7 Self-assembly

"Self-assembly is the autonomous organization of components into patterns or structures without human intervention. Self-assembling processes are common throughout nature and technology. They involve components from the molecular (crystals) to the planetary (weather systems) scale and many different kinds of interactions. The concept of self-assembly is used increasingly in many disciplines, with a different flavour and emphasis in each."[66]

Self-assembly can be classified as static or dynamic. Static self-assembly involves systems that are at global or local equilibrium and do not dissipate energy. In static self-assembly, formation of the ordered structure may require energy, but once it is formed, it is stable. Examples for static self-assembling systems are liquid crystals[67], globular proteins and self-assembled monolayers.[68] In dynamic self-assembly, the interactions responsible for the formation of structures or patterns between components only occur if the system is dissipating energy. An example for dynamic system is bacterial colonies.[69]

Molecular self-assembly involves reversible noncovalent or weak covalent interactions such as van der Waals, electrostatic and hydrophobic interaction, hydrogen and coordination bonds, π-π-interactions. In the nature are various examples of complex systems constructed from small simple building blocks, which are kept together only by such weak interactions.[70]

Two types of self-assembly may be distinguished, intramolecular and intermolecular. Intramolecular self-assembling molecules are often complex polymers which are able to organize from the random coil conformation into a well-defined stable structure (secondary and tertiary structure). An example of intramolecular self-assembly is protein folding.[70] Intermolecular self-assembly is the ability of molecules to form well-organized structures due to reversible noncovalent bonding. A simple example is the formation of a micelle by surfactant molecules in solution.

Development of highly organized complex chemical systems from synthetically available components, which are bound by noncovalent interactions, is a target of supramolecular chemistry.[71]

Since self-assembly can be also a manufacturing method used to construct complex objects at the nanometer-scale, supramolecular chemistry contributes to the development of nanotechnology.[72] It is referred to as a "bottom-up" manufacturing technique, as compared to lithography being a "top-down" technique.

1.8 Literature and comments

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Chapter 2

Tetraurea calix[4]arenes bearing pyridyl/carboxyl functions at the wide rim

2.1 Dimerization of calix[4]arene derivatives

A variety of basic modifications of the parent calixarenes has been already described[1] (see also Chapter 1). These modifications allowed synthesis of building blocks which self-assemble into highly-ordered supramolecular structures.[2] In this chapter only selected examples of calix[4]arenes and resorc[4]arenes tetra-functionalized at the narrow or wide rim and their dimerization via hydrogen bonding will be discussed.

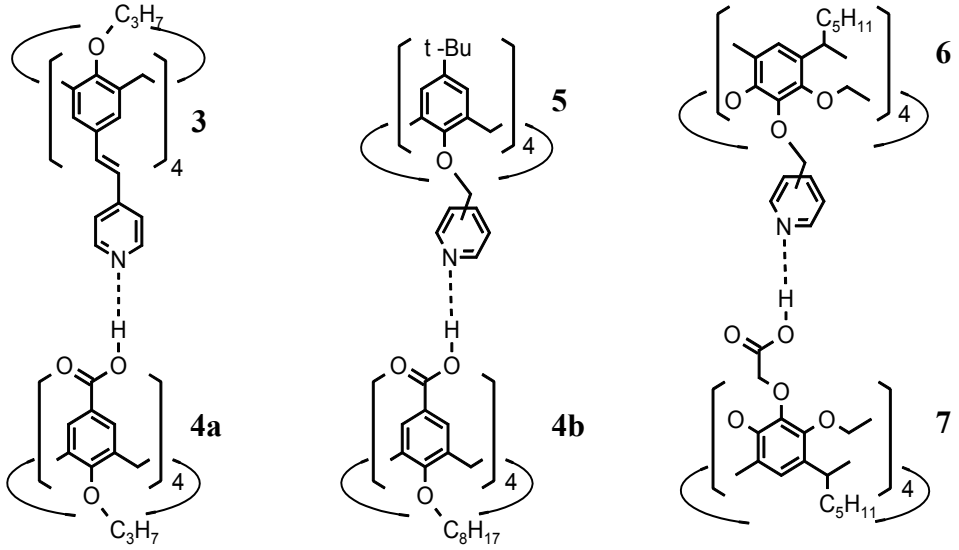


Figure 1. Hydrogen bonded heterodimers based on carboxyl-pyridyl combination.

A complementary pair formed by carboxylic groups (hydrogen bond donor) and pyridine residues (acceptor) was one of the first motives used to create self-organized dimeric structures based on calixarenes.

The tetraacid **4a** which is insoluble itself in $CDCl_3$ was extracted by tetrapyridyl derivative **3** (Fig. 1) into $CDCl_3$ solution in the ratio 1:1.[3] This was the first indication for a 1:1 interaction between the molecules. Obviously four functions from one molecule bind four

partner-functions of another molecule. However the ^{1}H NMR-spectrum of **3** in the presence of tetraacid **4a** did not show significant changes and the signal for the carboxylic protons remained broad. The proof for the existence of the dimer **3**·**4a** was achieved by vapour-pressure osmometry experiments (VPO) where the found molecular weight was in agreement with a heterodimer structure.

In the same way calix[4]arenes **5** containing four pyridine units (*m*- or *p*-) at their narrow rim bind the tetraacid **4b** and carry it into $CDCl_3$ solution in the ratio 1:1.[4] The formation of heterodimers **5**·**4b** was again proved by VPO. Remarkably the *o*-pyridine derivative **5** does not behave like its *m*- and *p*-pyridyl analogues and does not solubilize the tetraacid.

Similar heterotopic structures were designed from resorc[4]arenes **6** and **7** and confirmed in the same way.[5] In all cases the encapsulation of guest molecules was not observed.

The phenomenon of self-assembly of tetraureacalix[4]arenes **8** (R = Ar, Alk; Y = Alk) in apolar solvents into dimeric capsules in which two calixarene counterparts are bound by a belt of 16 hydrogen bonds (as shown in Fig. 2b) was discovered first by Rebek *et al*.[6]

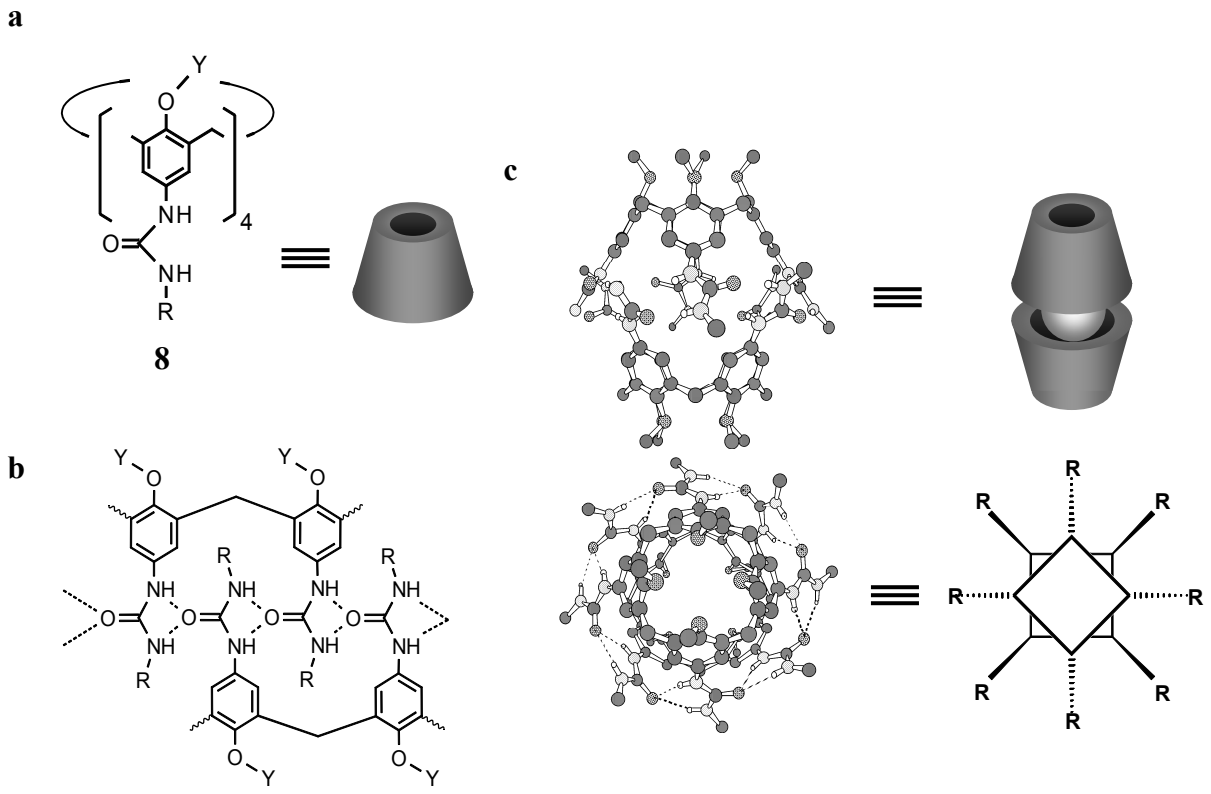
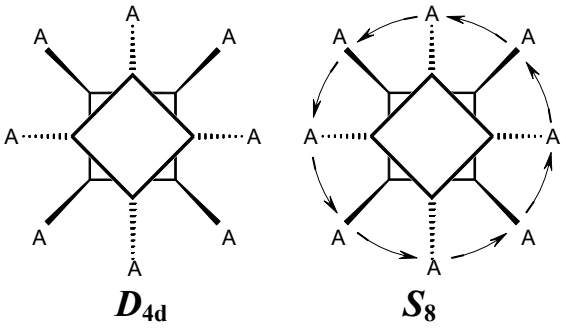


Figure 2. a) General formula of tetraureacalix[4]arenes **8** (R = Ar, Alk; Y = Alk). b) Schematic representation of hydrogen bonding in dimers of **8**. c) The X-ray structure of **8** (R = *p*-tolyl; Y = $CH_2C(O)OEt$) (side and top view) and a schematic presentation of the tetraurea dimer.

The ^{1}H NMR-spectrum of tetraurea **8** in DMSO-d_6 (Fig. 3a) displays only one singlet for the aromatic protons of calixarene skeleton and corresponds to a time averaged C_{4v}-symmetrical molecule. When ^{1}H NMR-spectrum of tetraureas is recorded in apolar solvents like $CDCl_3$ or C_6D_6, a set of two *m*-coupled doublets appears for the aromatic protons of the calixarene skeleton (Fig. 3b) and one the signals for NH protons is downfield shifted (what is usually a sign of strong hydrogen bonding). These are the first indications of dimerization of tetraureacalix[4]arenes, by which the splitting of the signals in ^{1}H NMR-spectrum is caused.



In the dimer the calixarenes are turned by 45° in respect to each other. The dimer without directionality of the hydrogen bonds has D_{4d} symmetry. If the directionality of the hydrogen bonded belt is taken into account, each of the calixarene counterparts in the dimer becomes chiral (C_4-symmetry). Therefore, the whole assembly formed by two pairs of enantiomers has S_8 symmetry and is achiral. The dimeric structure of tetraureacalix[4]arenes suggested by Rebek was found also in the solid state by single crystal X-ray analysis (Fig. 2c).[7]

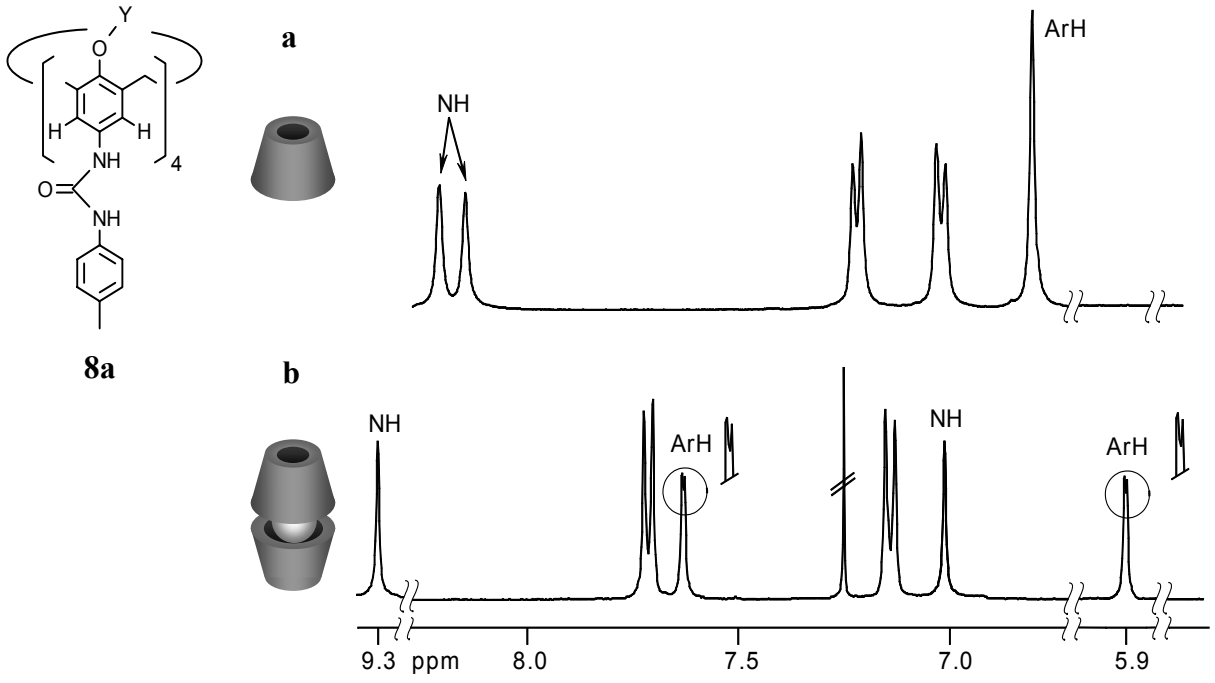
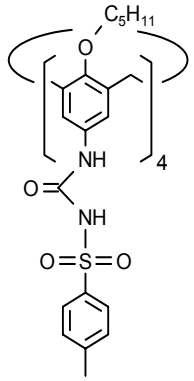


Figure 3. Characteristic parts of the ^{1}H NMR spectra of tetraurea **8** (Y = Alk) in DMSO-d_6 (a) and in $CDCl_3$ (b).

The formation of a heterodimer in addition to two homodimers in the mixture of two different tetraureas was an additional proof of the dimerization.[8] An exclusive heterodimerization was discovered in the case of tetraarylurea **8** (Y = alkyl) and tetratosylurea calix[4]arenes **9**[9] (Y = alkyl) mixed in apolar solvent in the ratio 1:1. The reason for this selectivity is not entirely clear until now. It can be partially explained by the increased acidity of the tosylurea **9**, which compensates own demands by the interaction with relatively basic arylurea groups.



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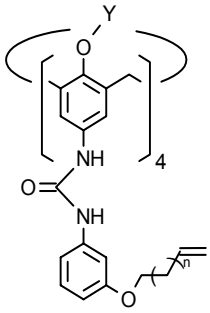
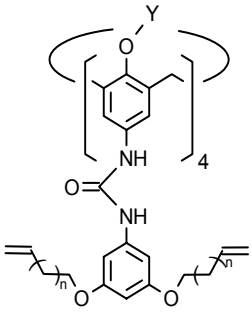
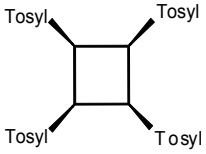
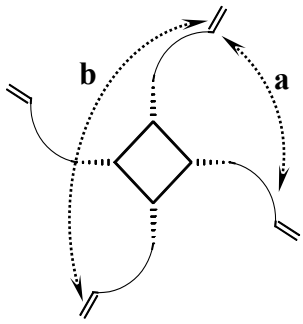


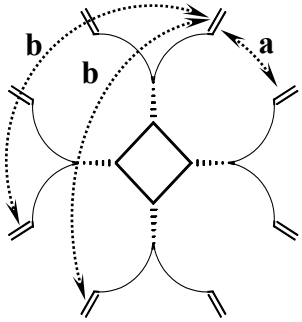
8b



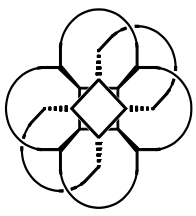
8c



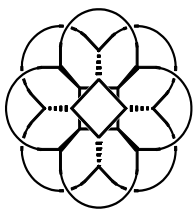




This selectivity has been used for the synthesis of a new class of multi-macrocycles **14a,b**.[10] The urea **9** works as a template, since it prevents transcavity **b**-connections allowing only the bridging of the adjacent phenolic units (**a**-connections). Therefore, the heterodimers of tetraurea calix[4]arenes **8b,c** (Y = alkyl) with the tosylurea **9** subjected to metathesis (Grubbs' catalyst) under high dilution conditions produce after hydrogenation bis- and tetra-"loop" tetraureas **10a** and **10b** in high yields (Scheme 1).



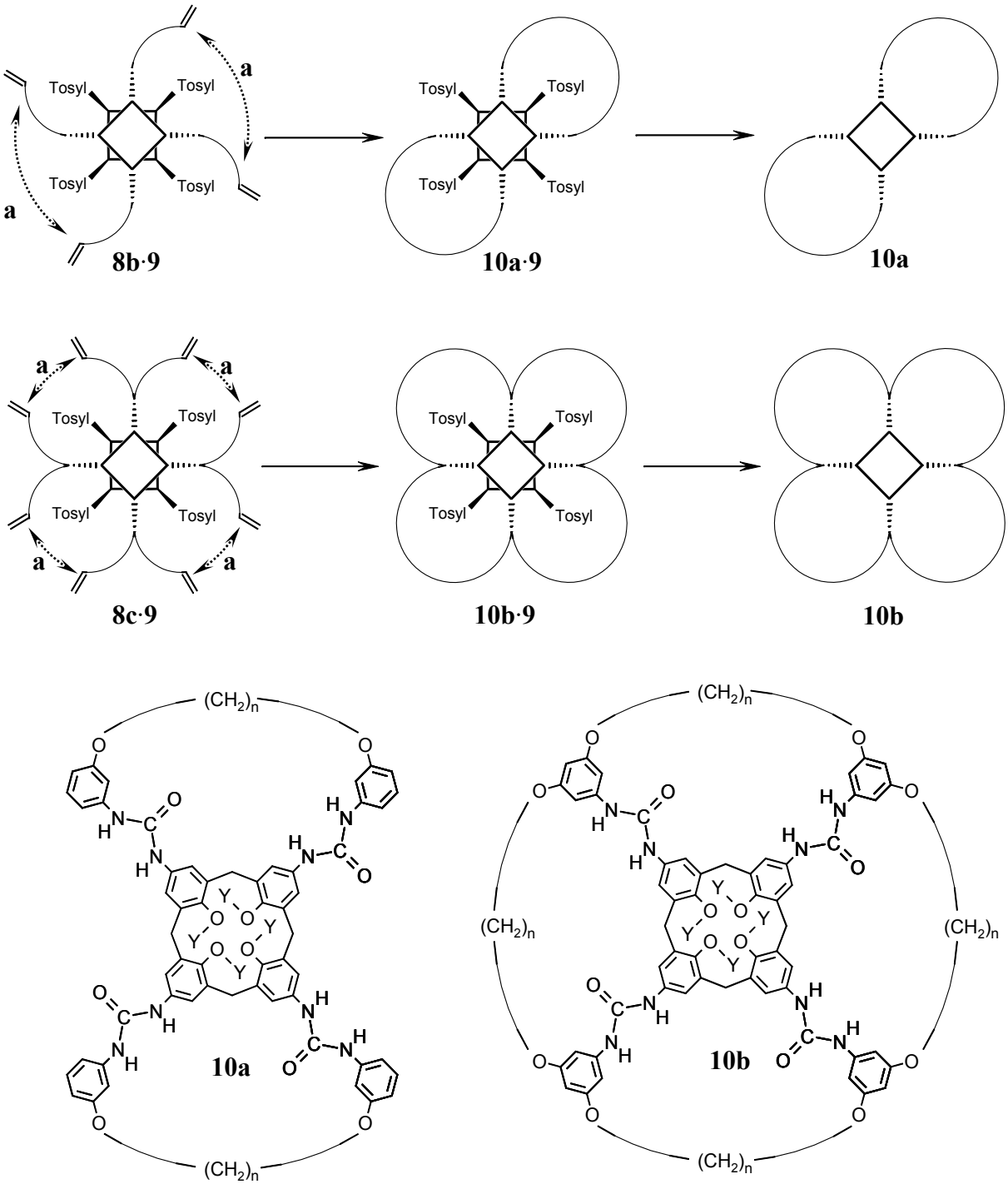
bis-[3]catenane



cyclic[8]catenane

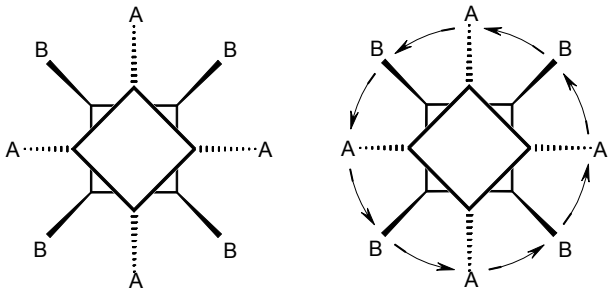
Since the bis- and tetraloop ureas **10a,b** cannot form homodimers (due to the repulsion of the loops), their heterodimerization with "open-chain" tetraureas **8** in apolar solvents becomes more

attractive than irregular aggregation. Such selectivity was applied for the synthesis of the *bis*-[3]catenanes and [8]catenanes via metathesis reaction from the heterodimers **10a·8b** and **10b·8c** respectively.



Scheme 1. Synthesis of bis- and tetraloop tetraureas **10a** and **10b**.

The heterodimer **8·9** (and also heterodimer **8·10b**) has C_{4v} symmetry and is chiral (C_4) only due to the directionality of the hydrogen bonded belt. This symmetry is reflected in the ^{1}H NMR spectrum of the heterodimer, where the following characteristic signals are found:



C_{4v} C_4

- 2 pairs of doublets for protons of the methylene bridges;
- 4 singlets for NH protons of the urea groups (2 of them are shifted downfield);
- 2 pairs of *m*-coupled doublets for protons of the aryl groups of calixarene skeleton.

The heterodimer formed by bis-loop tetraurea **10a** and open-chain tetraurea **8** has C_2 symmetry and the number of signals in ^{1}H NMR spectrum for the protons listed above is duplicated.

The tetraurea dimers are able to include some molecules or cations. Among neutral guest molecules dichloromethane, chloroform, 1,1,2,2-tetrachloroethane, benzene, toluene, halobenzenenes, bicyclic aliphatics[11] are known. ^{1}H NMR studies of the encapsulation of positively charged particles like tetraalkyl ammonium ions, tropylium[12] and cobaltocenium[13] in the tetraurea dimers has been described. The inclusion of tetraalkyl ammonium ions was also detected by electrospray ionization mass spectrometry.[14]

2.2 Potential complementary pair of tetraurea calix[4]arenes

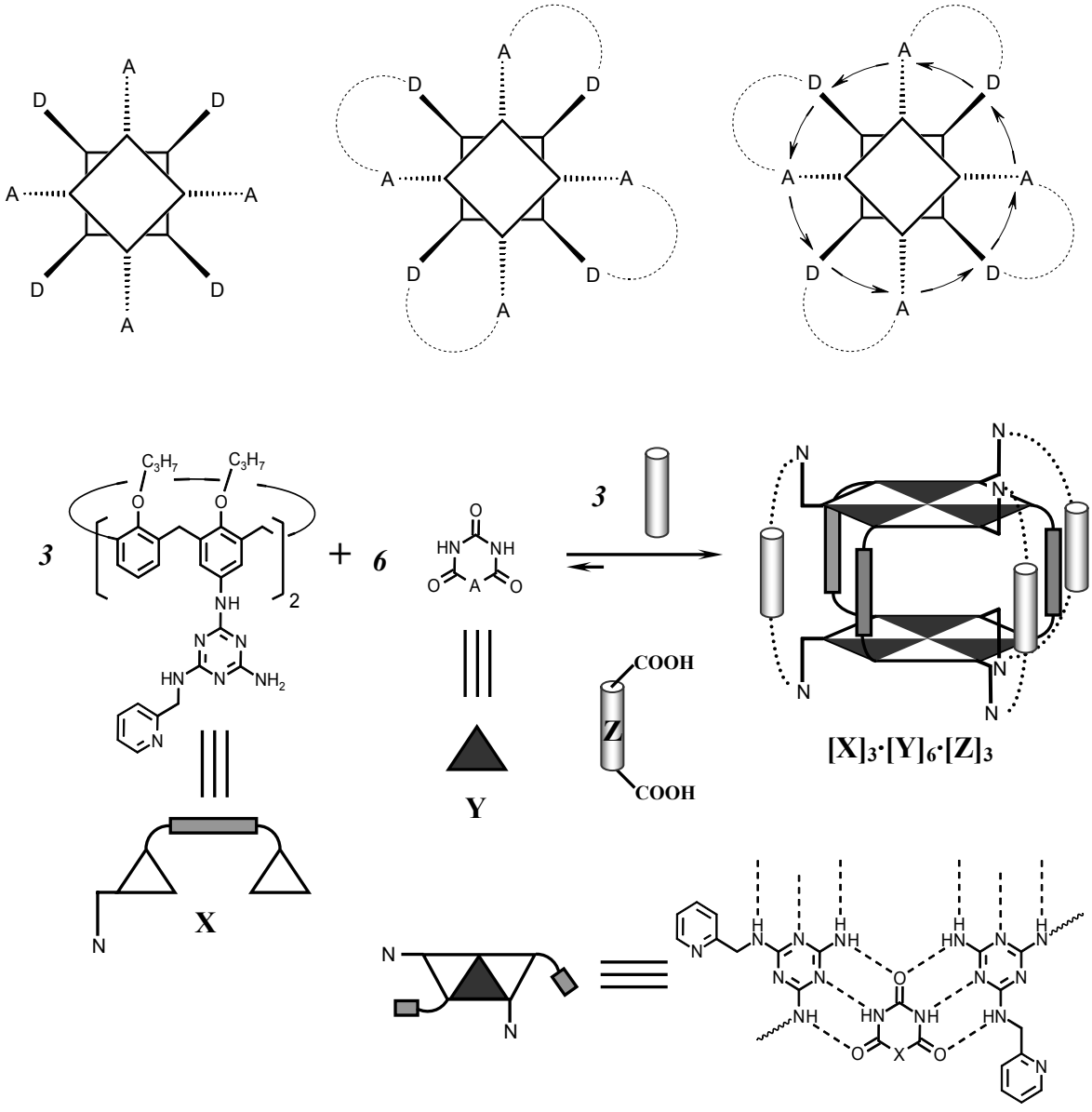
We planned to synthesize and study self-assembling properties of tetraurea calix[4]arenes having four donor "D" or acceptor groups "A" attached via a "spacer" or directly at the positions adjacent to the urea functions. The introduced D- and A-functions must be a complementary pair, for example carboxyl-pyridyl. Theoretically these functions should interact with each other in the heterodimer formed by the tetra-D- and tetra-A-tetraurea calix[4]arenes. Formation of four A-D hydrogen bonds additionally to the sixteen urea hydrogen bonds should provide a stabilization of the A-D-heterodimer.

Finally the tetra-D- and tetra-A-tetraureas could be used as potential building blocks for supramolecular structures constructed by programmed self-sorting via independent self-

organization motifs. The dendrimers formed by heterodimers of tetraurea-calix[4]arenes covalently connected via their narrow rims to the (tritolylurea triphenylmethane)$_2$-core are an example.[15]

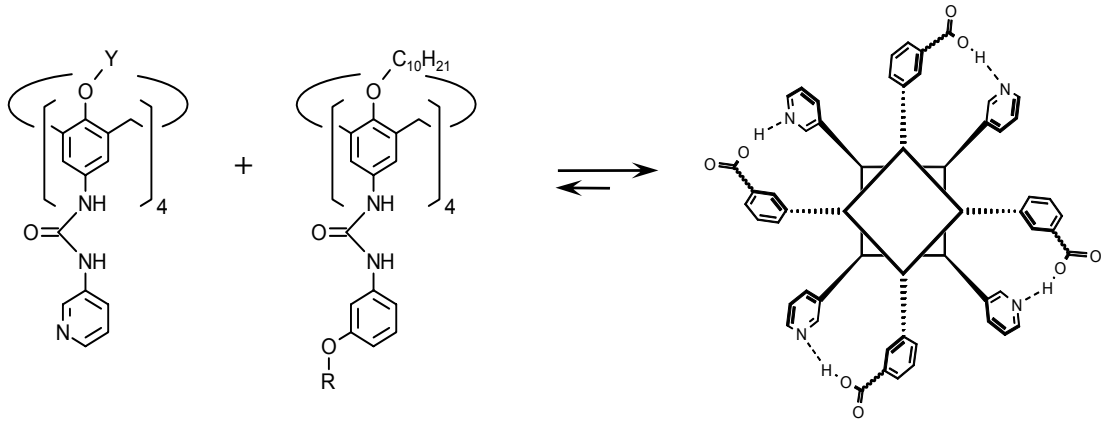
The idea of improving stability of assembly by increasing of the number of hydrogen bonds was already used by Reinhoudt group in their "double rosettes".[16] Three calix[4]arene-di-N-methylenepyridyl-melamine molecules **X** and six molecules barbituric/cyanuric acid derivatives **Y** (A = NBu or CEt_2)A were self-assembled in "double rosette". Different dicarboxylic acids **Z** were complexed by the readily formed assembly in the ratio 1 : 3.

Our idea is to attach pyridyl and carboxyl functions to the assembling molecules via covalent bonds. Will this increase or decrease the stability of tetraurea dimers?



Tetra-*m*-pyridyl- and tetra-*m*-carboxylalkoxyphenylureas calix[4]arenes **11** and **12** (Fig. 4) should be easily available by known procedures. They could serve as examples of tetra-D- and tetra-A-tetraureas and were tried for the preparation the heterodimers of A-D type.

In addition to the self-assembly studies the tetraureas **11** and **12** could be transformed by standard reactions (for example, a conversion of the tetraacids **12** to the corresponding tetraamides) to a series of new derivatives.



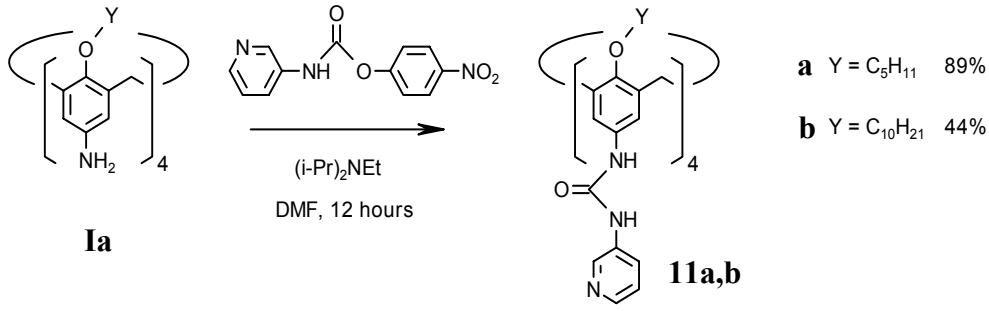
11 **12**

Y = Alk R = $(CH_2)_n$-COOH

Figure 4. The target derivatives tetraureas **11** and **12** and schematic representation of their heterodimer stabilized by additional hydrogen bonds between pyridyl and carboxyl groups.

2.3 Synthesis

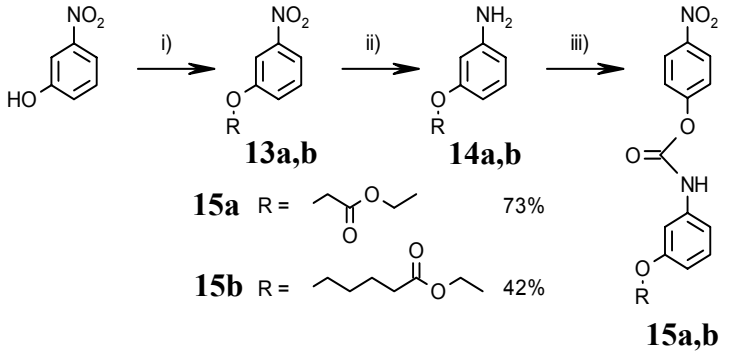
m-Pyridylurea calix[4]arenes **11a** and **11b** were prepared in 89% and 44% yield respectively by the acylation of the appropriate tetraamine **Ia** with *p*-nitrophenyl urethane of *m*-aminopyridine in the presence of an excess of Hünig base at room temperature in tetrahydrofurane or dimethylformamide (Scheme 2).



Ia **11a,b**

Scheme 2. Synthesis of the tetra-*m*-pyridylurea calix[4]arenes **11a,b**.

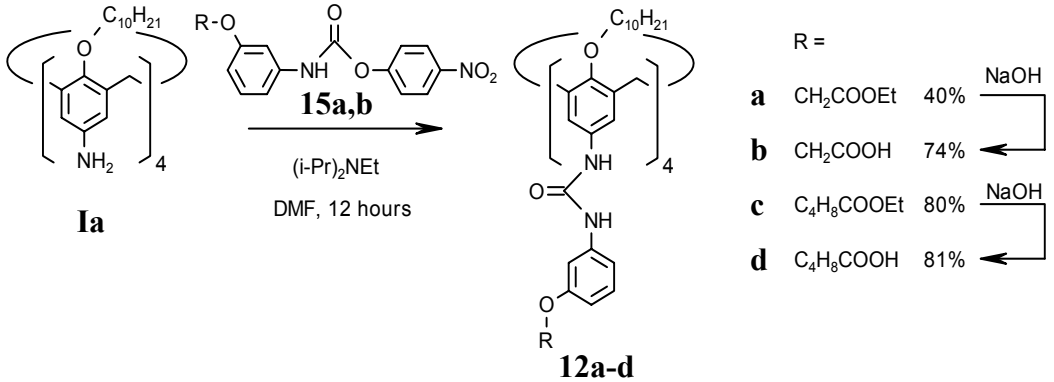
p-Nitrophenyl urethanes **15a,b** were synthesized for introduction of urea and carboxylic groups to the calixarene **Ia**. *m*-Nitrophenol was alkylated with appropriate alkyl bromides in the presence of potassium carbonate to form compounds **13a,b** which were hydrogenated with catalytic amount of Raney-Ni to produce anilines **14a,b**. Aacylation of the anilines with *p*-nitrophenyl chloroformate gave the urethanes in 73% (**15a**) and 42% (**15b**) yield (Scheme 3).



Scheme 3. Preparation of *p*-nitrophenyl urethanes. i) alkylbromide, potassium carbonate, acetonitrile, reflux; ii) H_2/Raney-Ni, ethanol; iii) *p*-nitrophenyl chloroformate, acetonitrile.

The tetraamine of calix[4]arene tetradecylether was converted into tetraureas **12a** and **12c** in yields 40% and 80% respectively, under similar conditions as compounds **11** (Scheme 4). Then the ester groups of the derivatives **12a** and **12c** were cleaved according standard procedures with sodium hydroxide in water/ethanol solution at room temperature yielding the appropriate tetraureas **12b** and **12d** (74% and 81%).

The structures of all new compounds **11-15** were confirmed by ^{1}H NMR and by FD or ESI mass spectroscopy.



Scheme 4. Synthesis of the tetraurea derivatives **12a-d**.

2.4 Self-organization

2.4.1 *m*-Pyridyl tetraurea calix[4]arenes

The *m*-pyridyl tetraurea calix[4]arenes **11a** and **11b** have in polar solvents as DMSO-d_6 a clear ^{1}H NMR spectrum (Fig. 5a). However in contrast to the other *p*-tetraurea calix[4]arenes they do not display the dimerization in apolar solvents like $CDCl_3$, C_6D_6 and 1,1,2,2-tetrachloroethane (TCE). Compound **11a** has low solubility in the apolar solvents used for dimerization except TCE. In TCE **11a** shows broad and complicated ^{1}H NMR spectrum attributed probably to the formation of some disordered aggregates (Fig. 5b). More lipophilic tetraurea **11b** (Y = $C_{10}H_{21}$) is soluble in these apolar solvents and shows the spectra similar to **11a**.

The signals of monomeric **11a** appeared in ^{1}H NMR spectrum after heating of its TCE solution over 75°C (Fig. 5c). Probably, the hydrogen bonded aggregates formed by **11a** at room temperature were dissociated to monomers at the higher temperature. Cooling back to room temperature reestablished the associates (identical to Fig. 5b). Remarkable, that in case of the tetraureas **8** heating of their TCE solutions up to 100°C does not lead to the dissociation of the dimers.[15]

We have tried to induce the dimerization of tetraureas **11a,b** by offering a positive charged guest (tetraethylammonium salts). But no inclusion of the guest and no dimers of those tetraureas were observed by the ^{1}H NMR spectra.

Then we decided to catch tetraureas **11a,b** by the formation of heterodimers with suitable "partners". Since tetratosylurea calix[4]arene **9** and tetraloop macrocycle **10b** are known to form exclusively heterodimers with the tetraarylurea calix[4]arenes in ratio 1 : 1, we have chosen them as "partners" for the heterodimerization. However, in case of tetratosylurea our *m*-pyridyl compounds seem to prefer the formation of irregular associates and neglect the suggested "partnership", and no significant changes were observed in the ^{1}H NMR spectra of **11a,b** in $CDCl_3$ in the presence of the compound **9**.

In the spectrum of the 1 : 1 mixture of tetraloop urea **10b** (n = 10, Y = CH_3) and **11b** in $CDCl_3$, the signals of the heterodimer **11b**·**10b** were observed together with the broad signals of the aggregates at room temperature. An increase of the temperature to 55°C led to the dissociation of the irregular aggregates: now predominantly the signals of the heterodimer **11b**·**10b** were detected by ^{1}H NMR (Fig. 6):

- 4 signals for NH protons of the tetraurea groups;
- 2 sets of *m*-coupled doublets for the aryl protons of calixarene skeletons.

Decrease of temperature leads back to associates. The results of ^{1}H NMR studies of compounds **11a,b** are summarized in Table 1 and represented schematically in Scheme 5.

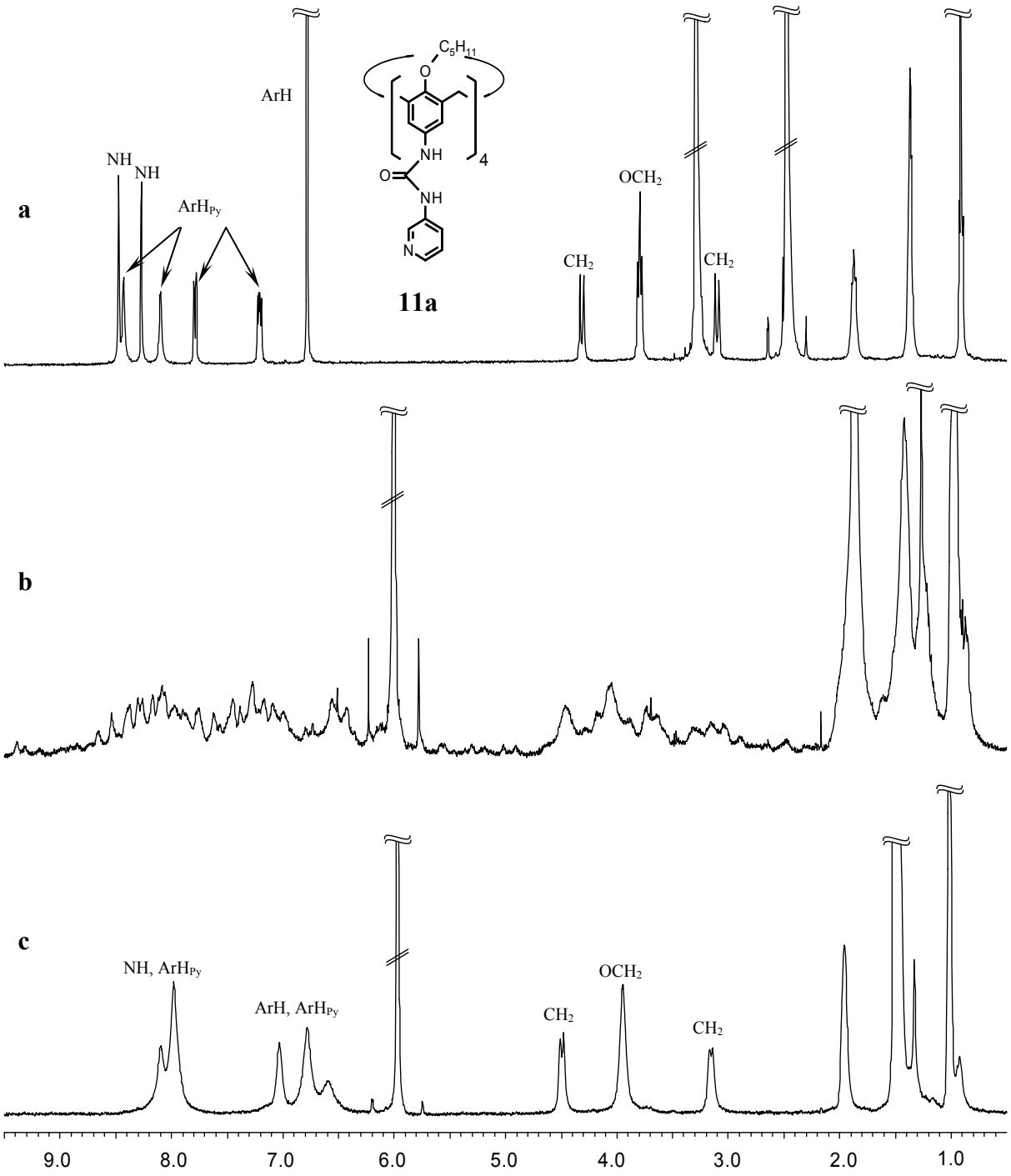


Figure 5. ^{1}H NMR spectra of **11a** in DMSO (a), in TCE (b) at room temperature and (c) at 75°C. Signals for the urea NH protons (NH), the pyridyl units (ArH$_{Py}$), the aromatic protons of calixarene skeleton (ArH) and for the doublets of the methylene bridges (CH$_2$) are indicated.

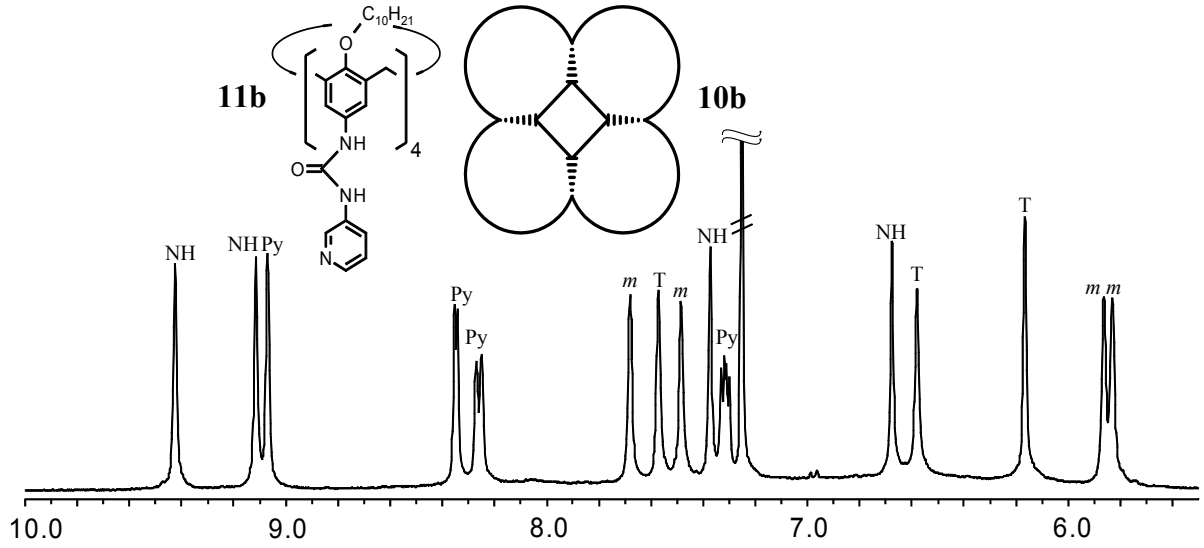
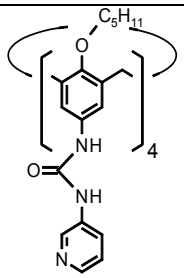
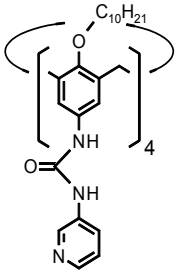
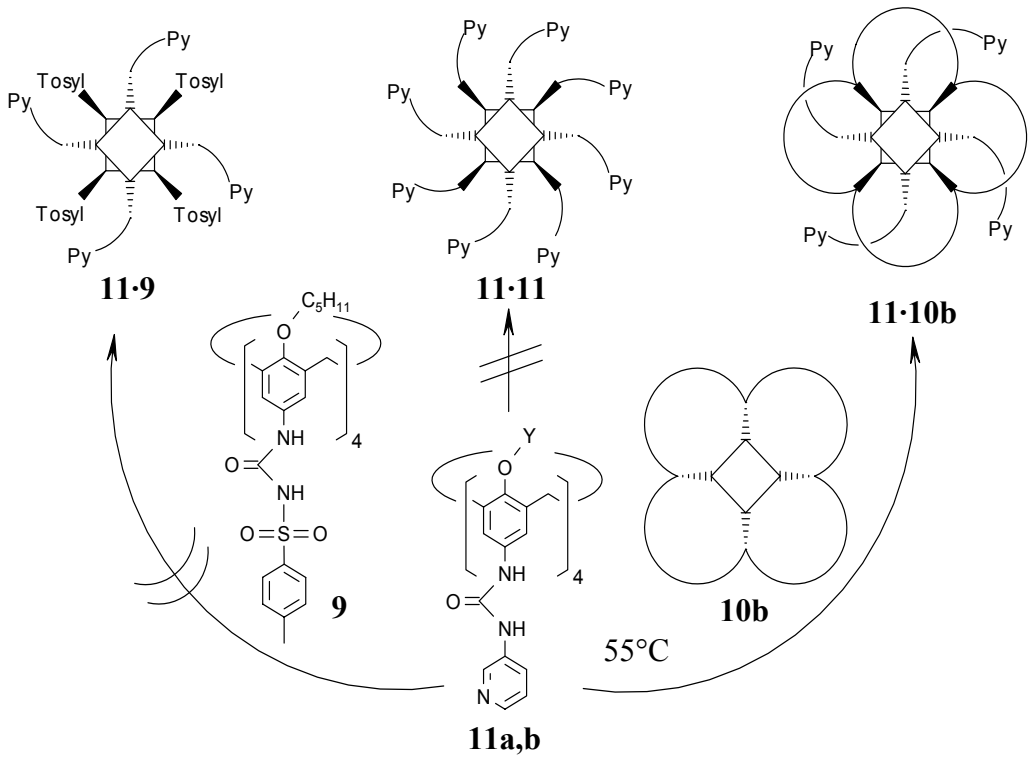


Figure 6. A part of ^{1}H NMR spectrum of the heterodimer **11b·10b** in $CDCl_3$ at 55°C. Signals for the urea NH protons (NH), of the pyridyl units (Py), the signals of **10b** aromatic protons (T) and of *m*-coupled doublets of the skeleton phenyl units (*m*) are indicated.

Table 1. Summary of the studies of tetraureas **11a,b** by ^{1}H NMR spectroscopy.

Component 1	Component 2	Solvent	Temperature	Observations ^{1}H NMR (400 MHz)
 **11a**	-	$CDCl_3$ CD_2Cl_2 C_6D_6	rt	insoluble
		TCE	rt	irregular associates
		TCE	>75°C	monomer
	9	TCE	rt	irregular associates
 **11b**	-	$CDCl_3$ C_6D_6	rt (also 75°C for C_6D_6)	irregular associates
	Et_4N^+ PF_6^-	$CDCl_3$	rt	aggregates and free ammonium cation
	9	$CDCl_3$	rt	irregular aggregates
	10b	$CDCl_3$	rt	heterodimer and aggregates
		$CDCl_3$	55°C	heterodimer
		$CDCl_3$	55°C → rt	heterodimer and aggregates



Scheme 5. Schematic representation of the expected self-assemblies of tetraureas **11a,b** in apolar solvents.

2.4.2 *m*-Carboxylalkoxyphenyl tetraurea calix[4]arenes

Tetraethylesters **12a,c** dimerize in $CDCl_3$, but their corresponding acids **12b,d** are not soluble in $CDCl_3$, C_6D_6, and TCE. The compound **12b** was heated to dissolve it in TCE. At temperatures above 100°C the compound was dissolved, but in the ^{1}H NMR spectrum only broad signals were observed which belong most probably to its monomer (Fig. 7a).

These tetraacids do not interact with tetratosylurea which was usually used to check the possibility of heterodimerization. Most probably the tetraacids form hydrogen bonds between themselves and/or with tetraurea groups similarly to *m*-pyridyltetraureas **11a,b**.

Judging from ^{1}H NMR spectrum (Fig. 7b) the tetraloop urea calix[4]arene **10b** (n = 10, Y = CH_3) forms heterodimer with the tetraacids **12b,d**:

- 4 signals for NH protons of the urea groups (2 of them are shifted downfield);
- 4 pairs of *m*-coupled doublets of aryl protons of calixarene skeleton.

Thus, the tetraacids **12b,d**, like *m*-pyridyltetraureas **11a,b**, do not form homodimers in apolar solvents; they do not dimerize in the presence of tetraammonium salts and do not form heterodimers with tetratosyl urea **9** (Table 2 and Scheme 6). But surprisingly these tetraacids form heterodimers with tetraloop calixarene **10b**.

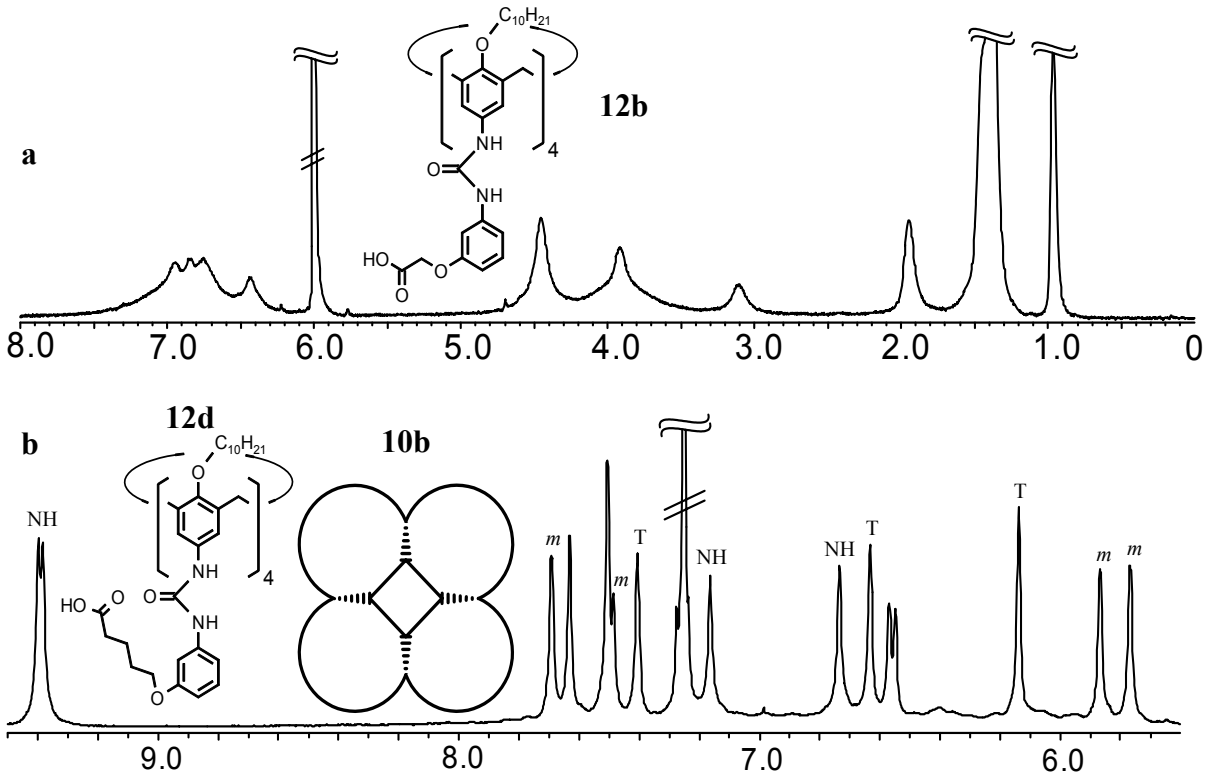
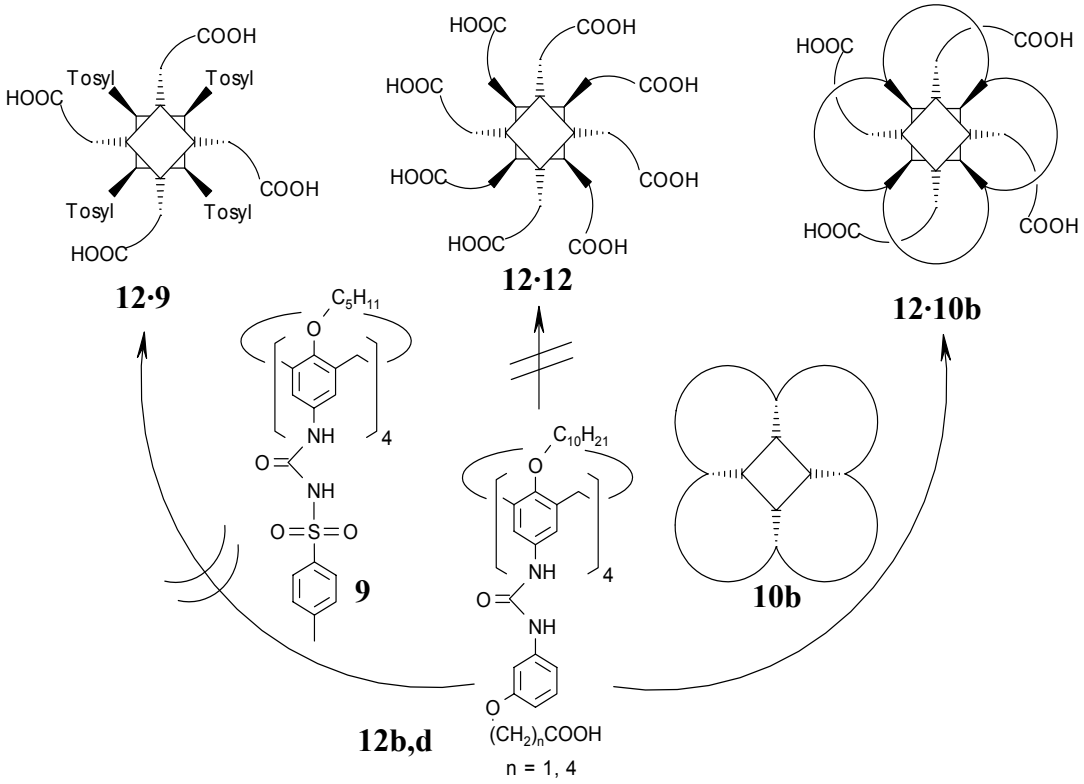
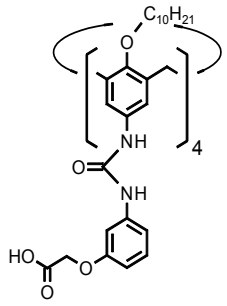
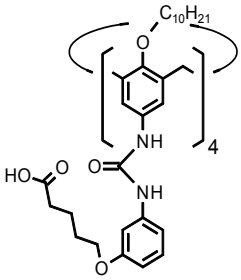


Figure 7. a) ^{1}H NMR spectrum of **12b** in TCE at 100°C. b) A part of ^{1}H NMR spectrum of the heterodimer **12d·10b** (n = 10, Y = CH_3) in $CDCl_3$. The signals of tetraloop-aromatic protons and of *m*-coupled doublets are indicated by "T" and "*m"* correspondingly.



Scheme 6. Schematic representation of the expected self-assemblies of tetraureas **12b,d** in apolar solvents.

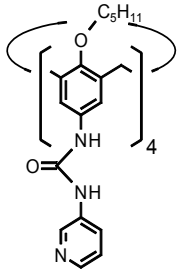
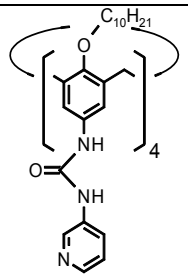
Table 2. Summary of the studies of tetraureas **12b,d** by ^{1}H NMR spectroscopy.

Component 1	Component 2	Solvent	Temperature	Observations ^{1}H NMR (400 MHz)
 **12b**	-	$CDCl_3$ C_6D_6 TCE	rt	insoluble
	-	TCE	100°C	monomer
	9 or **10b**	$CDCl_3$, TCE	rt	insoluble
	10b	TCE	75°C; 95°C	heterodimer and the traces of aggregates
 **12d**	-	$CDCl_3$ C_6D_6	rt	insoluble
	-	C_6D_6	75°C	monomer
	9 or Et_4N^+ PF_6^-	$CDCl_3$	rt	insoluble
	10b	$CDCl_3$	rt	heterodimer

2.4.3 Interaction of *m*-pyridyl with *m*-carboxylalkoxyphenyl tetraureas

Finally *m*-pyridyl tetraureas **11a,b** with tetraacids **12b,d** were mixed in different apolar solvents ($CDCl_3$, C_6D_6, and TCE) to check if they form heterodimers with each other. The mixture of **11a** and **12b** in ratio 1:1 was not soluble in any of the potential solvents. The more lipophilic pair of compounds **11b** and **12d** was dissolved in $CDCl_3$ at room temperature in ratio 1:1. It is remarkable that **12d** alone is not soluble in this solvent. Thus, such co-operative solubility is an evidence of interaction between compounds **11b** and **12d**. But the absence of the clear picture in the ^{1}H NMR spectrum is an indication rather for the formation of irregular aggregates than for a well-defined capsular assembly. Thus, *m*-pyridylureas **11a,b** and tetracids **12b,d** do not form the desired self-assembly (see the summary in Table 3).

Table 3. Summary of the studies of interaction between tetraureas **11a,b** and **12b,d** by ^{1}H NMR spectroscopy.

Component 1	Component 2	Solvent	Temperature	Observations ^{1}H NMR (400 MHz)
 **11a**	**12b** -CH_2COOH	$CDCl_3$ C_6D_6 TCE	rt; heating	insoluble
	12d -$(CH_2)_4COOH$	TCE	rt	insoluble
 **11b**	**12b** -CH_2COOH	$CDCl_3$	rt	insoluble
	12d -$(CH_2)_4COOH$	$CDCl_3$ C_6D_6	rt, heating	irregular associates

2.4.4 Synthesis of a *bis*-[3]catenane

The heterodimerization found for **12d** and tetraloop **10b** has been used for the synthesis of a novel *bis*-catenane **16**. Treatment of the heterodimer **10b·12** by 2 mole of DCC in benzene solution yielded the intramolecular dianhydride *bis*-catenane **16** exclusively (Fig. 8a). The ^{1}H NMR spectrum of the crude product (Fig. 9) entirely confirms the presence of the expected C_2-symmetrical *bis*-[3]catenane:

- 8 singlets for NH protons of urea functions (4 of them are shifted downfield, one is overlapped with the solvent peak);
- 8 doublets for the protons of methylene bridges (not shown in the spectrum);
- 4 sets of *m*-coupled doublets for the protons of aryl units of calixarene skeletons (proved also by COSY).

Acylation of the dianhydride **16** with 2 moles of a bulky amine should lead to *bis*-[2]rotaxanes **17a,b** (Fig. 8b).

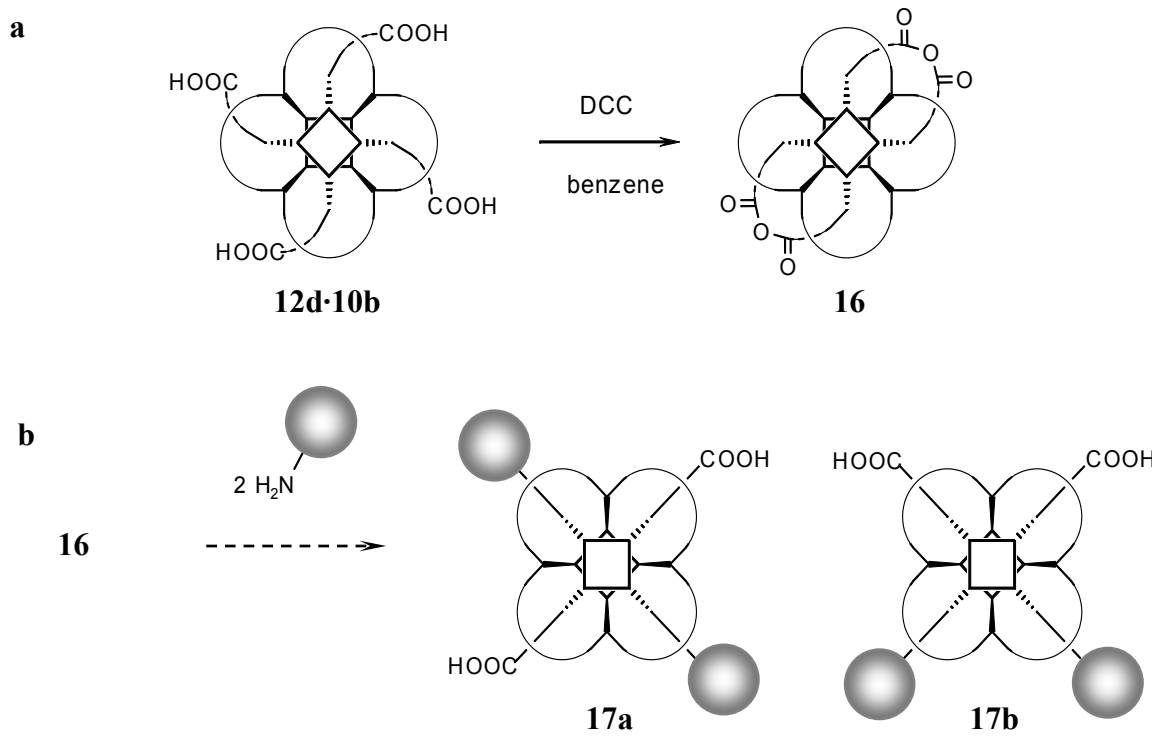


Figure 8. a) Synthesis of *bis*-catenane **16** from heterodimer **12d·10b**. An approach to *bis*-[2]rotaxanes **17a,b**.

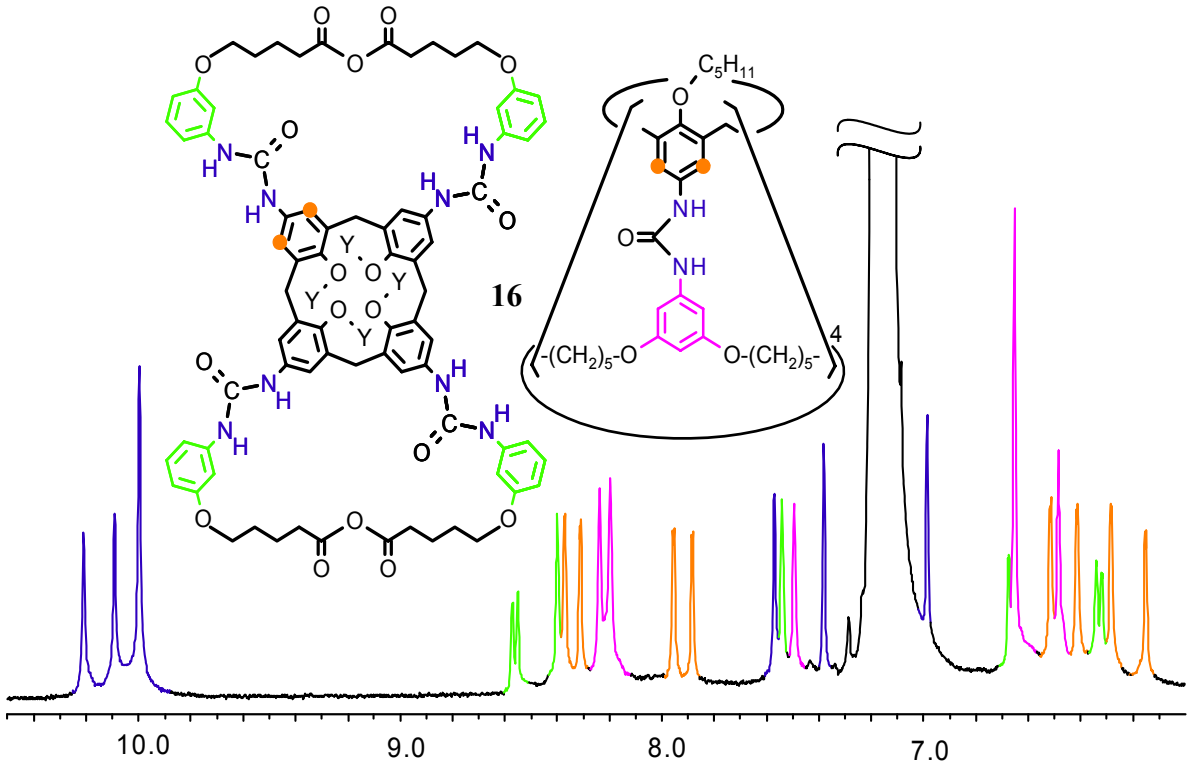


Figure 9. A part of ^{1}H NMR spectrum of the bis-[3]catenane **16** (Y = $C_{10}H_{21}$) in C_6D_6.

2.4.5 Conclusions and perspectives

In general, it could be concluded from the behavior of the tetraureas **11a,b** and **12b,d** that the hydrogen acceptor/donor groups, like carboxyl and pyridyl units, attached in positions adjacent to the urea groups disturb the dimerization of tetraurea calix[4]arenes.

A reason of such behavior of the tetraureas **11a,b** could be intramolecular or intermolecular interactions between pyridyl nitrogens (acceptor) and NH protons (hydrogen bond donor) of the urea groups (Fig. 10). Probably the pyridyl nitrogen destroys the belt of the hydrogen bonds which is necessary for the formation of tetraurea calix[4]arene dimers. For tetraureas **12b,d** beside the interactions mentioned for tetraureas **11a,b** also carboxyl-carboxyl interactions may lead to aggregation.

The heterodimerization of **11a,b** and **12b,d** with tetratosylurea **9** also does not take place. In case of **11a,b** this could be partially explained by an absence of the compensation of the acidity of **9** by "relative basicity" of tetraurea groups of **11a,b**,[9] since they are not so rich in electron density like those of **8**.

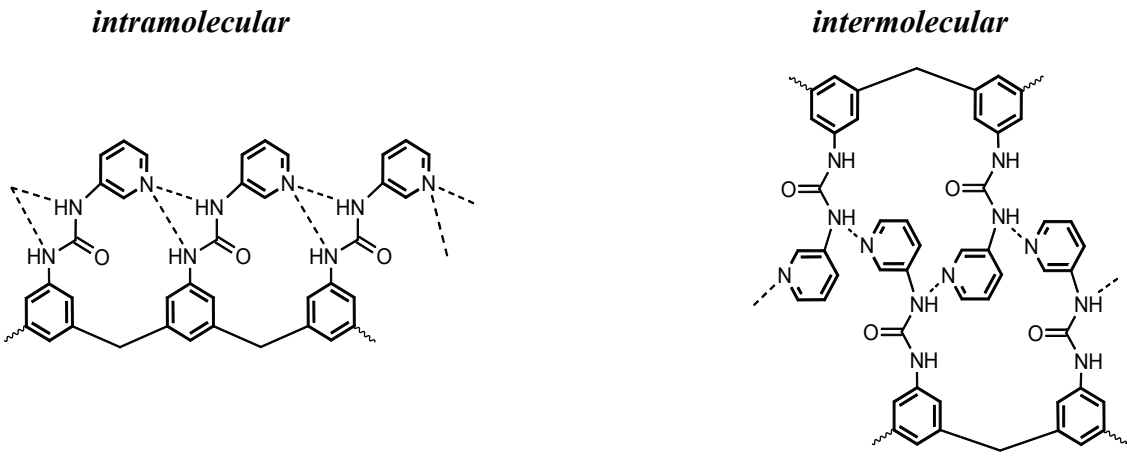


Figure 10. Schematic representation of interactions which could disturb homodimerization of *m*-pyridyl tetraureas **11a** and **11b**.

The heterodimerization of the tetraureas **11b** and **12d** with tetraloop **10b** is the case, in which self-assembly into polymeric structures is not profitable anymore. Since **10b** can not homodimerize, like tetratosylurea **9**, it combines with another tetraurea fitting in their loops.

The reaction of heterodimers **10b·12d** with amines in the presence of acylation reagents like DCC can be used as the alternative route for the preparation of the *bis-[3]catenanes* and *tetrakis-[2]rotaxanes* analogues of those described by Böhmer[10,17].

The introduction of diamines in **12d·10b** should lead to the formation of the appropriate *bis*-[3]catenanes **18** (Fig. 11). Acylation of **12d·10b** with 4 moles of bulky amine should produce *tetrakis*-[2]rotaxanes **19**.

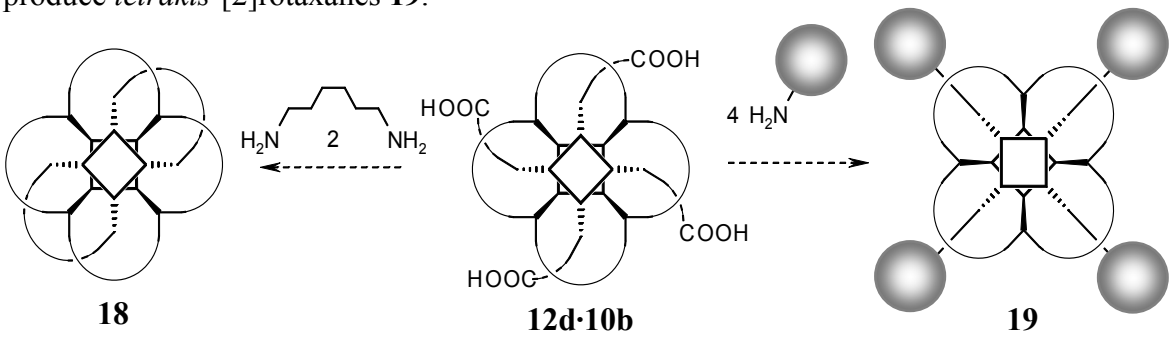
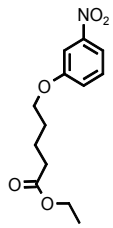


Figure 11. A schematic representation of the pathways from heterodimer **12d·10b** to *bis*-[3]catenanes **18** and *tetrakis*-[2]rotaxanes **19**.

2.5 Experimental

Materials.

Solvents and all other chemicals were purchased from Acros, Aldrich, Lancaster and used without further purification. ^{1}H NMR spectra were recorded on a Bruker DRX400 Avance instrument (at 400 MHz). FD and ESI mass spectra were measured on a Finnigan MAT 8230 spectrometer and a Micromass Q-TOF Ultima3 instrument respectively. Melting points are uncorrected. *m*-Pyridinyl carbamic acid *p*-nitrophenyl ester, *m*-ethoxycarbonylmethoxy nitrobenzene, *m*-ethoxycarbonylmethoxy aniline and *p*-tetraamino calix[4]arene tetraethers were prepared as described.[18, 19] Tetraloop-tetraurea calix[4]arenes **10b** (n = 10, Y = CH_3 or C_5H_{11}) was prepared as described.[10]

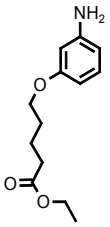


m-Ethoxycarbonylbutyloxy nitrobenzene **13b** :

A suspension of *m*-nitrophenol (3.000 g, 21.566 mmol), potassium carbonate (3.28 g, 23.72 mmol) and ethyl 5-bromovalerate (4.96 g, 23.72 mmol) in acetonitrile (60 ml) was refluxed for 24 hours. Then the solvent was evaporated in vacuum, the residue was dissolved in Et_2O/water, organic layer was washed with water, separated and dried ($MgSO_4$). Et_2O was removed under reduced pressure and the oily residue was dried until crystallization to give the product as yellowish powder. Yield: 5.44 g (94%).

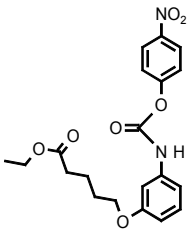
m.p. 39-40°C; MS (FD): m/z 267.2 (M^+); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.79 (dd, Ar-*H*, 1 H, $^3J_{HH}$ 8.1 Hz, $^4J_{HH}$ 1.1 Hz), 7.69 (t, Ar-*H*, 1 H, $^3J_{HH}$ 2.2 Hz), 7.40 (t, Ar-*H*, 1 H, $^3J_{HH}$ 8.3 Hz),

7.19 (dd, Ar-*H*, 1 H, $^3J_{HH}$ 8.3 Hz, $^4J_{HH}$ 2.4 Hz), 4.12 (q, -O-C*H*$_2$-CH$_3$, 2 H, $^3J_{HH}$ 7.2 Hz), 4.03 (t, -O-C*H*$_2$-, 2 H, $^3J_{HH}$ 5.7 Hz), 2.38 (br. t, -C*H*$_2$-C(O)-, 2 H, $^3J_{HH}$ 6.8 Hz), 1.91-1.77 (m, 4 H, -C*H*$_2$-), 1.25 (t, -O-CH$_2$-C*H*$_3$, 3 H, $^3J_{HH}$ 7.2 Hz).



m-Ethoxycarbonylbutyloxy aniline **14b** :

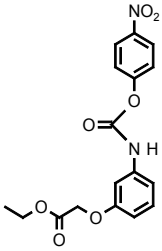
A solution of *m*-ethoxycarbonylbutyloxy nitrobenzene **13b** (2.42 g, 9.04 mmol) in ethanol (105 ml) was vigorously stirred in hydrogen atmosphere at rt in the presence of catalytic amount of Raney-Ni for 8 hours (a degree of conversion was controlled by TLC). Then the catalyst was filtered off and the solvent was removed in vacuum to give the appropriate aniline as yellowish oil which was used for the next step without further purification. Yield: 1.89 g (88%).



m-Ethoxycarbonylbutyloxyphenyl carbamic acid p-nitrophenyl ester **15b** :

p-nitrophenyl chloroformate (2.58 g, 9.95 mmol) was added to a stirred solution of *m*-ethoxycarbonylbutyloxy aniline **14b** (1.89 g, 7.96 mmol) in acetonitrile (30 ml) at rt. Then the reaction mixture was refluxed for 5 hours. After the solvent was evaporated *in vacuo* and the residue was triturated with Et_2O. A solid was filtered off, washed with Et_2O and dried to give product as a light yellow powder. Yield: 1.35 g (42%).

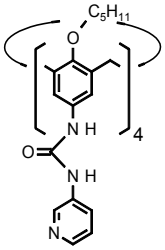
m.p. 89°C; MS (FD): m/z 402.2 (M^+); ^{1}H NMR (DMSO-d$_6$): δ 10.44 (s, N-*H*, 1 H), 8.31 (d, Ar-*H*, 2 H, $^3J_{HH}$ 9.2 Hz), 7.54 (d, Ar-*H*, 2 H, $^3J_{HH}$ 9.2 Hz), 7.23 (t, Ar-*H*, 1 H, $^3J_{HH}$ 8.3 Hz), 7.15 (s, Ar-*H*, 1 H), 7.06 (d, Ar-*H*, 1 H, $^3J_{HH}$ 8.1 Hz), 6.65 (dd, Ar-*H*, 1 H, $^3J_{HH}$ 8.3 Hz, $^4J_{HH}$ 2.0 Hz), 4.04 (q, -O-C*H*$_2$-CH$_3$, 2 H, $^3J_{HH}$ 7.1 Hz), 3.94 (t, -O-C*H*$_2$-, 2 H, $^3J_{HH}$ 5.7 Hz), 2.35 (t, -C(O)-C*H*$_2$-, 2 H, $^3J_{HH}$ 6.8 Hz), 1.79-1.59 (m, -C*H*$_2$-, 4 H), 1.17 (t, -C*H*$_3$, 3 H, $^3J_{HH}$ 7.0 Hz).



m-Ethoxycarbonylmethoxyphenyl carbamic acid p-nitrophenyl ester **15a** :

Prepared as described above for **14b** from *m*-ethoxycarbonylmethoxy aniline (4.21 g, 21.57 mmol), *p*-nitrophenyl chloroformate (6.61 g, 25.46 mmol), acetonitrile (60 ml), 12 hours reflux. Yield: 5.90 g (73%).

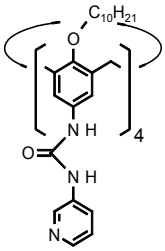
m.p. 127°C; MS (FD): m/z 360.3 (M^+); ^{1}H NMR (DMSO-d$_6$): δ 10.47 (s, N-*H*, 1 H), 8.31 (d, Ar-*H*, 2 H, $^3J_{HH}$ 9.2 Hz), 7.54 (d, Ar-*H*, 2 H, $^3J_{HH}$ 8.8 Hz), 7.25 (t, Ar-*H*, 1 H, $^3J_{HH}$ 8.4 Hz), 7.18-7.07 (m, Ar-*H*, 2 H), 6.65 (d, Ar-*H*, 1 H, $^3J_{HH}$ 8.1 Hz), 4.74 (s, -O-C*H*$_2$-C(O)-, 2 H), 4.16 (q, -O-C*H*$_2$-CH$_3$, 2 H, $^3J_{HH}$ 7.1 Hz), 1.20 (t, -C*H*$_3$, 3 H, $^3J_{HH}$ 7.1 Hz).



Calix[4]arene **11a**:

A solution of tetraamine tetrapenthylether **Ia** (0.055 g, 0.072 mmol) and di-*iso*-propylethylamine (0.674 g, 0.5 ml, 5.467 mmol) in THF (4 ml) were added to a solution of *m*-pyridinyl carbamic acid *p*-nitrophenyl ester (0.112 g, 0.432 mmol) in THF (2 ml) and stirred for 12 h at rt under nitrogen. Methanol (2 ml) was added to the reaction mixture and the solvent was evaporated *in vacuo*. The residue was reprecipitated from Et_2O/methanol/water to give pure urea **11a** as white powder. Yield: 0.080 g (89%).

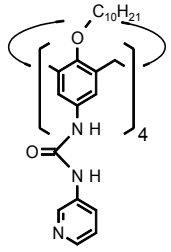
m.p. > 225°C (decomp.); MS (ESI): m/z 1267.8 ($M+Na^+$); ^{1}H NMR (DMSO-d_6): δ 8.50 (s, N-*H*, 4 H), 8.46 (s, Ar-*H*, 4 H), 8.30 (s, N-*H*, 4 H), 8.12 (d, Ar-*H*, 4 H, $^3J_{HH}$ 2.9 Hz), 7.81 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.4 Hz), 7.23 (dd, Ar-*H*, 4 H, $^3J_{HH}$ 8.1 Hz, $^4J_{HH}$ 4.8 Hz), 6.81 (s, Ar-*H*, 8 H), 4.34 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 12.8 Hz), 3.82 (t, -O-C*H*$_2$-, 8 H, $^3J_{HH}$ 7.1 Hz), 3.13 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 13.2 Hz), 1.90 (m, 8 H, -O-CH$_2$-C*H*$_2$-), 1.45-1.32 (m, 16 H, -C*H*$_2$-), 0.93 (t, -C*H*$_3$, 12 H, $^3J_{HH}$ 7.0 Hz).

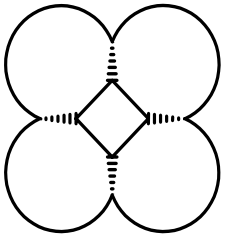


Calix[4]arene **11b**:

Prepared as described above for **11a** from tetraamine tetradecylether **Ia** (0.070 g, 0.0670 mmol), di-*iso*-propylethylamine (0.5 ml, 0.674 g, 5.467 mmol), *m*-pyridinyl carbamic acid *p*-nitrophenyl ester (0.120 g, 0.463 mmol), THF (5 ml); reprecipitation from methanol/water the precipitate was washed with Et_2O, dried and reprecipitated again from Et_2O/methanol/water to give the product as yellowish powder. Yield: 0.045 g (44%).

m.p. >190°C (decomp.); MS (ESI): m/z 1527.3 ($M+H^+$), 1549.3 ($M+Na^+$); ^{1}H NMR (DMSO-d_6): δ 8.52 (s, N-*H*, 4 H), 8.46 (d, Ar-*H*, 4 H, $^4J_{HH}$ 2.2 Hz), 8.30 (s, N-*H*, 4 H), 8.13 (dd, Ar-*H*, 4 H, $^3J_{HH}$ 4.6 Hz, $^4J_{HH}$ 1.1 Hz), 7.82 (d, Ar-*H*, 4 H, $^3J_{HH}$ 9.2 Hz), 7.24 (dd, Ar-*H*, 4 H, $^3J_{HH}$ 8.2 Hz, $^4J_{HH}$ 4.6 Hz), 6.80 (s, Ar-*H*, 8 H), 4.32 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 12.8 Hz), 3.80 (br.t, -O-C*H*$_2$-, 8 H, $^3J_{HH}$ 7.0 Hz), 3.11 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 13.2 Hz), 1.89 (m, -O-CH$_2$-C*H*$_2$-, 8 H), 1.51-1.12 (m, 56 H, -C*H*$_2$-), 0.85 (br.t, -C*H*$_3$, 12 H, $^3J_{HH}$ 6.8 Hz).

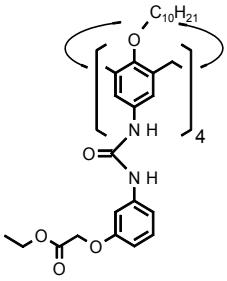




Heterodimer ***11b*** *:* ***10b*** *(n = 10, Y = CH$_3$):*

^{1}H NMR ($CDCl_3$, 55°C): δ 9.42 (s, N-*H*, 4 H), 9.11 (s, N-*H*, 4 H), 9.07 (d, Ar-*H*, 4 H, $^4J_{HH}$ 2.2 Hz), 8.35 (d, Ar-*H*, 4 H, $^4J_{HH}$ 4.0 Hz), 8.26 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.1 Hz), 7.68 (s, Ar-*H*, 4 H, $^4J_{HH}$ 1.8 Hz), 7.57 (s, Ar-*H*, 4 H), 7.48

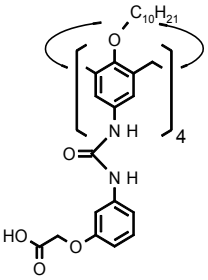
(s, Ar-*H*, 4 H, $^4J_{HH}$ 1.8 Hz), 7.37 (s, N-*H*, 4 H), 7.31 (dd, Ar-*H*, 4 H, $^3J_{HH}$ 8.1 Hz, $^4J_{HH}$ 4.8 Hz), 6.68 (s, N-*H*, 4 H), 6.58 (s, Ar-*H*, 4 H), 6.17 (s, Ar-*H*, 4 H), 5.86 (s, Ar-*H*, 4 H), 5.83 (s, Ar-*H*, 4 H), 4.18 (d, Ar-CH_2-Ar, 8 H, $^2J_{HH}$ 11.7 Hz), 4.01 (br.t, -O-CH_2-, 8 H), 3.85 (br.t, -O-CH_2-, 8 H), 3.75 (s, -CH_3, 12 H), 3.72-3.55 (m, -O-CH_2-, 8 H), 2.87 (d, Ar-CH_2-Ar, 4 H, $^2J_{HH}$ 12.1 Hz), 2.73 (d, Ar-CH_2-Ar, 4 H, $^2J_{HH}$ 11.7 Hz), 2.00-0.95 (m, -CH_2-, 128 H), 0.90 (t, -CH_3, 12 H, $^3J_{HH}$ 6.8 Hz).



Calix[4]arene **12a**:

Prepared as described above for **11a** from tetraamine tetradecylether **Ia** (0.113 g, 0.108 mmol), di-*iso*-propylethylamine (0.063 g, 0.487 mmol), *m*-ethoxycarbonylmethoxyphenyl carbamic acid *p*-nitrophenyl ester (0.182 g, 0.487 mmol), THF (5 ml); reprecipitation from ethylacetate/methanol. Yield: 0.057 g (27%).

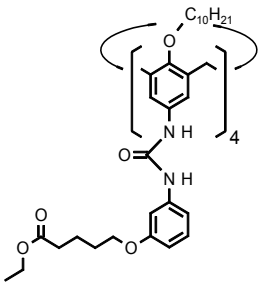
m.p. > 200°C (decomp.); MS (ESI): m/z 1953.2 (M+Na^+); ^{1}H NMR (DMSO-d_6): δ 8.36 (s, N-*H*, 4 H), 8.18 (s, N-*H*, 4 H), 7.17-7.03 (m, Ar-*H*, 8 H), 6.87-6.74 (m, Ar-*H*, 12 H), 6.44 (dd, Ar-*H*, 4 H, $^3J_{HH}$ 8.4 Hz, $^4J_{HH}$ 2.0 Hz), 4.65 (s, -O-CH_2-C(O)-, 8 H), 4.29 (d, Ar-CH_2-Ar, 4 H, $^2J_{HH}$ 12.5 Hz), 4.11 (q, -O-CH_2-CH$_3$, 8 H, $^3J_{HH}$ 7.1 Hz), 3.77 (broad t, -O-CH_2-, 8 H, $^3J_{HH}$ 5.5 Hz), 3.07 (d, Ar-CH_2-Ar, 4 H, $^2J_{HH}$ 12.5 Hz), 1.87 (m, 8 H, -O-CH$_2$-CH_2-), 1.46-1.20 (m, 56 H, -CH_2-), 1.17 (t, -O-CH$_2$-CH_3, 12 H, $^3J_{HH}$ 7.0 Hz), 0.83 (t, -CH_3, 12 H, $^3J_{HH}$ 6.8 Hz).



Calix[4]arene **12b**:

A suspension of compound **12a** (0.057 g, 0.0295 mmol) and NaOH (0.150 g, 3.750 mmol) in EtOH (12 ml) and water (12 ml) was stirred at rt for 24 hours. The solvents were evaporated in vacuum and 5% hydrochloric acid water solution was added to the residue. A precipitate was filtered off, washed with water and dried to give **12b** as a brown powder. Yield: 0.040 g (74%).

m.p. >170°C (decomp.); MS (ESI): 1841.4 (M+Na^+), 932.2 (M+2Na^+); ^{1}H NMR (DMSO-d_6): δ 8.41 (s, N-*H*, 4 H), 8.21 (s, N-*H*, 4 H), 7.10 (t, Ar-*H*, 4 H, $^3J_{HH}$ 8.2 Hz), 7.05 (s, Ar-*H*, 4 H), 6.83 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.1 Hz), 6.78 (s, Ar-*H*, 8 H), 6.45 (dd, Ar-*H*, 4 H, $^3J_{HH}$ 8.2 Hz, $^4J_{HH}$ 2.0 Hz), 4.58 (s, -O-CH_2-C(O)-, 8 H), 4.32 (d, Ar-CH_2-Ar, 4 H, $^2J_{HH}$ 12.5 Hz), 3.80 (br. t, -O-CH_2-, 8 H), 3.10 (d, Ar-CH_2-Ar, 4 H, $^2J_{HH}$ 12.5 Hz), 1.90 (m, 8 H, -O-CH$_2$-CH_2-), 1.49-1.15 (m, 56 H, -CH_2-), 0.85 (t, -CH_3, 12 H, $^3J_{HH}$ 6.6 Hz).

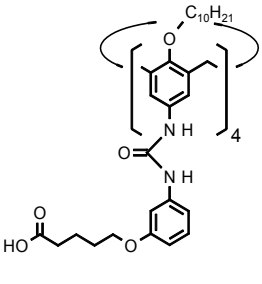


Calix[4]arene **12c**:

Prepared as described above for **11a** from tetraamine tetradecylether **Ia** (0.105 g, 0.100 mmol), di-*iso*-propylethylamine (0.052 g, 0.402 mmol), *p*-nitrophenyl ester **15b** (0.176 g, 0.437 mmol), THF (5 ml); reprecipitation from ethanol/water. Yield: 0.169 g (80%).

m.p. >155°C (decomp.); MS (ESI): 2121.3 ($M+Na^+$), 1072.2 ($M+2Na^+$); ^{1}H NMR (DMSO-d_6): δ 8.30 (s, N-*H*, 4 H), 8.15 (s, N-*H*, 4 H), 7.13-7.01 (m, Ar-*H*, 8 H), 6.86-6.70 (m, Ar-*H*, 12 H), 6.47 (d, Ar-*H*, 4 H, $^3J_{HH}$ 7.7 Hz), 4.32 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 11.7 Hz), 4.03 (q, -O-C*H*$_2$-CH$_3$, 8 H, $^3J_{HH}$ 7.1 Hz), 3.95-3.68 (m, -O-C*H*$_2$-, 16 H), 3.09 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 11.4 Hz), 2.32 (br. t, -C*H*$_2$-C(O)-, 8 H), 1.89 (m, 8 H, -O-CH$_2$-C*H*$_2$-), 1.66 (m, 16 H, -C*H*$_2$-), 1.49-1.20 (m, 56 H, -C*H*$_2$-), 1.15 (t, -O-CH$_2$-C*H*$_3$, 12 H, $^3J_{HH}$ 7.0 Hz), 0.85 (br. t, -C*H*$_3$, 12 H).

(12c)$_2$: ^{1}H NMR ($CDCl_3$): δ 9.40 (s, N-*H*, 8 H), 7.64 (s, Ar-*H*, 8 H), 7.58 (s, Ar-*H*, 8 H), 7.38-7.15 (m under solvent peak, Ar-*H*, 8 H), 6.92 (s, N-*H*, 8 H), 6.54 (d, Ar-*H*, 8 H, $^3J_{HH}$ 7.7 Hz), 5.85 (s, Ar-*H*, 4 H), 4.20 (d, Ar-C*H*$_2$-Ar, 8 H, $^2J_{HH}$ 11.4 Hz), 4.08 (q, -O-C*H*$_2$-, 16 H, $^3J_{HH}$ 7.0 Hz), 3.97-3.78 (m, -O-C*H*$_2$-, 16 H), 3.65 (t, -O-C*H*$_2$-, 16 H, $^3J_{HH}$ 7.3 Hz), 2.82 (d, Ar-C*H*$_2$-Ar, 8 H, $^2J_{HH}$ 11.7 Hz), 2.25 (t, -C(O)-C*H*$_2$-, 16 H, $^3J_{HH}$ 6.8 Hz), 2.00-1.85 (m, -C*H*$_2$-, 16 H), 1.78-1.60 (m, -C*H*$_2$-, 32 H), 1.42-1.13 (m, -C*H*$_2$-, 112 H, overlapped with t, -C*H*$_3$, 24 H, $^3J_{HH}$ 7.1 Hz), 0.88 (t, -C*H*$_3$, 24 H, $^3J_{HH}$ 6.4 Hz).

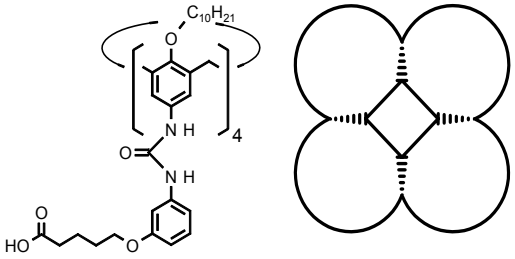


Calix[4]arene **12d**:

A suspension of compound **12c** (0.17 g, 0.08 mmol) and NaOH (0.15 g, 3.75 mmol) in THF (20 ml), EtOH (15 ml) and water (10 ml) was stirred at rt for 48 hours. The solvents were evaporated in vacuum and 5% hydrochloric acid water solution was added to the residue. A precipitate was filtered off, washed with water and dried to give **12d** as a brown powder. Yield: 0.13 g (81%).

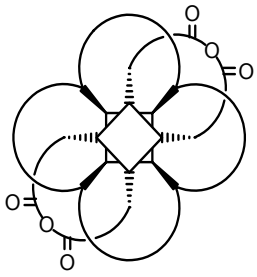
m.p. >150°C (decomp.); MS (ESI): 2009.6 ($M+Na^+$), 1016.3 ($M+2Na^+$); ^{1}H NMR (DMSO-d_6): δ 12.00 (s, -C(O)O-*H*, 4 H), 8.30 (s, N-*H*, 4 H), 8.17 (s, N-*H*, 4 H), 7.13-7.01 (m, Ar-*H*, 8 H), 6.86-6.70 (m, Ar-*H*, 12 H), 6.48 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.1 Hz), 4.32 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 12.1 Hz), 3.87 (br. t, -O-C*H*$_2$-, 8 H, $^3J_{HH}$ 6.1 Hz), 3.80 (br. t, -O-C*H*$_2$-, 8 H), 3.10 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 12.5 Hz), 2.26 (t, -C*H*$_2$-C(O)-, 8 H, $^3J_{HH}$ 7.0 Hz), 1.90 (m, 8 H, -O-CH$_2$-

C*H*$_2$-), 1.75-1.55 (m, 16 H, -C*H*$_2$-), 1.49-1.12 (m, 56 H, -C*H*$_2$-), 0.85 (t, -C*H*$_3$, 12 H, $^3J_{HH}$ 6.8 Hz).



Heterodimer ***12d*** *:* ***10b*** *(n = 10, Y = CH$_3$):*

^{1}H NMR ($CDCl_3$): δ 9.40 (s, N-*H*, 4 H), 9.38 (s, N-*H*, 4 H), 7.69 (d, Ar-*H*, 4 H, $^4J_{HH}$ 2.2 Hz), 7.63 (s, Ar-*H*, 4 H), 7.51 (s, Ar-*H*, 4 H), 7.49 (s, Ar-*H*, 4 H), 7.40 (s, Ar-*H*, 4 H), 7.29-7.21 (m under solvent peak, Ar-*H*, 4 H), 7.17 (s, N-*H*, 4 H), 6.73 (s, N-*H*, 4 H), 6.63 (s, Ar-*H*, 4 H), 6.56 (dd, Ar-*H*, 4 H, $^3J_{HH}$ 8.3 Hz, $^4J_{HH}$ 1.7 Hz), 6.14 (s, Ar-*H*, 4 H), 5.87 (d, Ar-*H*, 4 H, $^4J_{HH}$ 2.2 Hz), 5.77 (d, Ar-*H*, 4 H, $^4J_{HH}$ 2.2 Hz), 4.18-4.06 (m, Ar-C*H*$_2$-Ar, 8 H), 4.05-3.90 (m, -O-C*H*$_2$-, 16 H), 3.86 (br.t, -O-C*H*$_2$-, 8 H, $^3J_{HH}$ 5.9 Hz), 3.73 (s, -C*H*$_3$, 12 H), 3.69-3.53 (m, -O-C*H*$_2$-, 8 H), 2.85 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 12.1 Hz), 2.69 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 11.7 Hz), 2.33 (t, -C(O)-C*H*$_2$-, 8 H, $^3J_{HH}$ 6.4 Hz), 2.00-1.60 (m, -C*H*$_2$-, 40 H), 1.56-0.94 (m, -C*H*$_2$-, 104 H), 0.88 (t, -C*H*$_3$, 12 H, $^3J_{HH}$ 6.6 Hz).



Bis-catenane ***16****:*

The tetraurea **12d** (0.020 g, 0.0101 mmol) and tetraloop **10b** (n = 10, Y = C_5H_{11}) (0.0194 g, 0.0101 mmol) were dissolved together in benzene (30 ml) to form heterodimer **12d·10b**. The mixture was stirred for 20 min at rt. Then the solution of DCC (0.0042 g, 0.0202 mmol) in benzene (10 ml) was added to the heterodimer solution. The reaction mixture was stirred for 2 hours and then left in the fridge for 12 hours to form precipitate (di-*c*-hexylurea). The solid was filtered off, washed with benzene. The solvent from the mother liquid was removed in vacuum. The residual solid is the target bis-catenane **16**. Yield: 0.038 g (99%).

^{1}H NMR (C_6D_6): δ 10.17 (s, N-*H*, 2 H), 10.06 (s, N-*H*, 2 H), 9.96 (s, N-*H*, 4 H), 8.52 (dd, Ar-*H*, 2 H, $^3J_{HH}$ 8.3 Hz, $^4J_{HH}$ 1.3 Hz), 8.36 (s, Ar-*H*, 2 H), 8.34 (d, Ar-*H*, 2 H, $^4J_{HH}$ 2.6 Hz), 8.28 (d, Ar-*H*, 2 H, $^4J_{HH}$ 2.2 Hz), 8.20 (s, Ar-*H*, 2 H), 8.16 (s, Ar-*H*, 2 H), 7.92 (d, Ar-*H*, 2 H, $^4J_{HH}$ 2.2 Hz), 7.85 (d, Ar-*H*, 2 H, $^4J_{HH}$ 2.2 Hz), 7.53 (s, N-*H*, 2 H), 7.50 (s, Ar-*H*, 2 H), 7.46 (s, Ar-*H*, 2 H), 7.35 (s, N-*H*, 2 H), 7.30-7.00 (m under solvent peak, N-*H*, Ar-*H*, 10 H), 6.95 (s, N-*H*, 2 H), 6.67-6.58 (dd and s: 6.62 overlapped, Ar-*H*, 4 H, $^4J_{HH}$ 1.5 Hz), 6.48 (d, Ar-*H*, 2 H, $^4J_{HH}$ 2.2 Hz), 6.45 (s, Ar-*H*, 2 H), 6.38 (d, Ar-*H*, 2 H, $^4J_{HH}$ 2.2 Hz), 6.29 (dd, Ar-*H*, 2 H, $^3J_{HH}$ 8.4 Hz, $^4J_{HH}$ 1.8 Hz), 6.25 (d, Ar-*H*, 2 H, $^4J_{HH}$ 2.2 Hz), 6.16 (d, Ar-*H*, 2 H, $^4J_{HH}$ 2.6 Hz), 4.59 (d, Ar-C*H*$_2$-Ar, 2 H, $^2J_{HH}$ 11.4 Hz), 4.57 (d, Ar-C*H*$_2$-Ar, 2 H, $^2J_{HH}$ 11.4 Hz), 4.47 (d, Ar-C*H*$_2$-Ar, 2 H, $^2J_{HH}$ 11.7 Hz), 4.39 (d, Ar-C*H*$_2$-Ar, 2 H, $^2J_{HH}$ 11.4 Hz), 4.20-3.45 (m, -O-C*H*$_2$-,

48 H), 3.40 (d, Ar-CH_2-Ar, 2 H, $^2J_{HH}$ 12.1 Hz), 3.36 (d, Ar-CH_2-Ar, 2 H, $^2J_{HH}$ 11.7 Hz), 3.11 (d, Ar-CH_2-Ar, 2 H, $^2J_{HH}$ 12.5 Hz), 3.05 (d, Ar-CH_2-Ar, 2 H, $^2J_{HH}$ 11.7 Hz), 2.41 (t, -C(O)-CH_2-, 4 H, $^3J_{HH}$ 6.8 Hz), 2.33-0.80 (m, -CH_2-, 192 H).

2.6 Literature and comments

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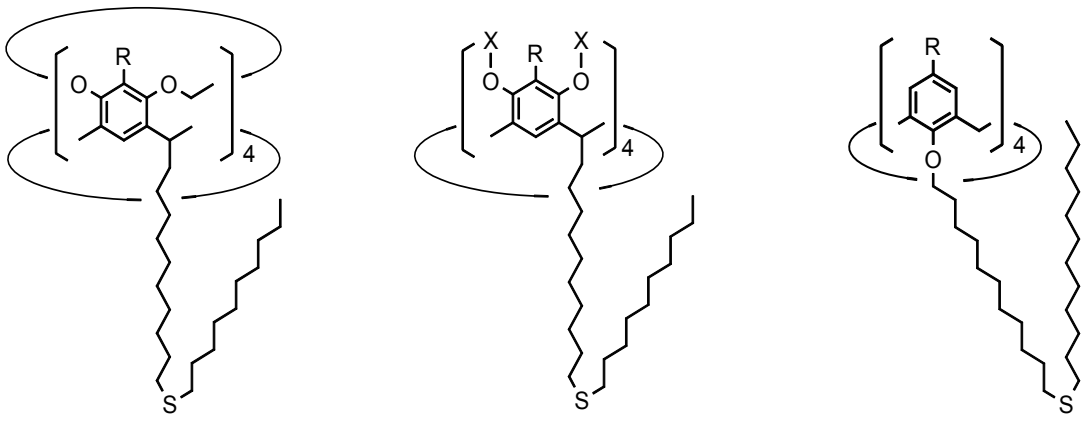
Chapter 3

Tetraurea-calix[4]arene capsules self-assembled in monolayers on gold

3.1 Introduction

Thin ordered organic films ranging from a few nanometers (a single monolayer) to several hundred nanometers have been proposed as a perspective material to replace the components in electronic and optical devices.[1]

Self-assembled monolayers (SAMs) are ordered molecular assemblies spontaneously formed by the adsorption of an active surfactant on a solid surface. Due to their dense and stable structure, SAMs have potential applications in corrosion prevention, wear protection, and more. Especially the self-assembly of organosulfur adsorbates on gold has attracted considerable attention. The high specifity of the sulfur-gold interaction allows the introduction of various functional groups which do not interfere in the adsorption process.



20 **21** **22**

R = H, Me R = H, Me, OAc, OMe; X = H, Alk, Ac R = H, *t*-Bu

Figure 1. The first calixarene molecules used for the preparation and characterization of self-assembled monolayers on gold: resorc[4]arenes **20**, **21** and calix[4]arenes **22**.

The number of reported surface active organosulfur compounds that form monolayers on gold has increased in recent years. These include di-*n*-alkyl sulfide,[2] di-*n*-alkyl disulfides,[3] thiophenols, mercaptopyridines,[4] mercaptoanilines,[5] thiophenes,[6] cysteines,[7] xanthates,[8] thiocarbaminates,[9] thiocarbamates,[10] thioureas[11] and mercaptoimidazoles.[12] However, the best studied, and probably best understood SAM is that of alkanethiolates on Au(111) surfaces.

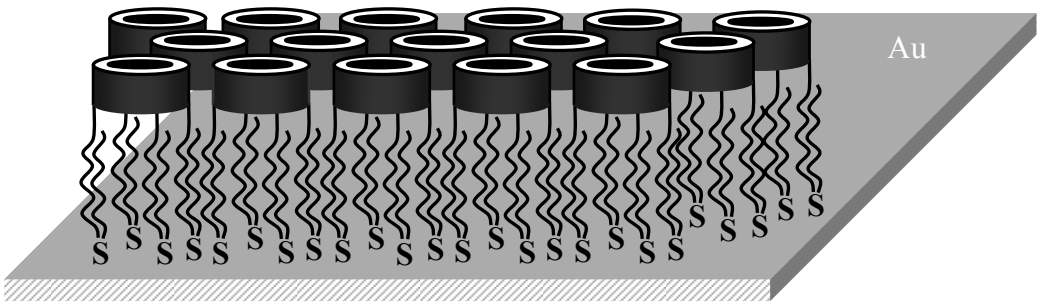
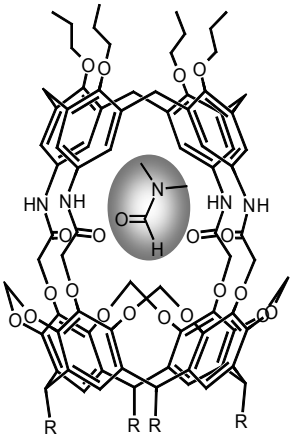


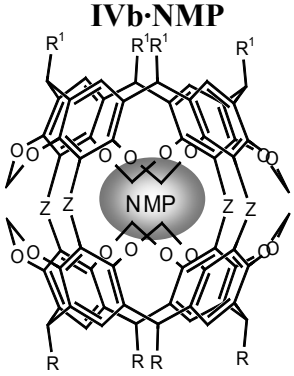
Figure 2. Schematic representation of the stable well-organized monolayers formed from resorc[4]arenes **20** and **21** on gold surface.

Among calixarenes, cavitands **20** and resorc[4]arenes **21** (Fig. 1) with four dialkyl sulfide chains attached at the methine linkages were the first molecules used for the preparation and characterization of self-assembled monolayers on gold.[13] It was found that the resorc[4]arenes form disordered layers at room temperature (due to the fast adsorption of dialkylsulfide groups) which reorganize into the stable well-organized monolayers at higher temperature (60°C) (thermodynamically controlled resorption and packing of the dialkylsulfide chains). In these monolayers the resorc[4]arene headgroups point to the outer interface and have a densely packed alkyl chain layer below (Fig. 2).

IVa·DMF



IVb·NMP



Similar monolayers were also obtained from *p-tert*-butyl- and de-*tert*-butylated calix[4]arenes **22**,[14] carceplex **IVa·DMF** (R = $(CH_2)_{10}$-S-$(CH_2)_9$-CH_3)[15] and hemi-carceplex **IVb·NMP** (Z = O-$(CH_2)_5$-O, R^1 = C_5H_{11}, R = $(CH_2)_{10}$-S-$(CH_2)_9$-CH_3).[16]

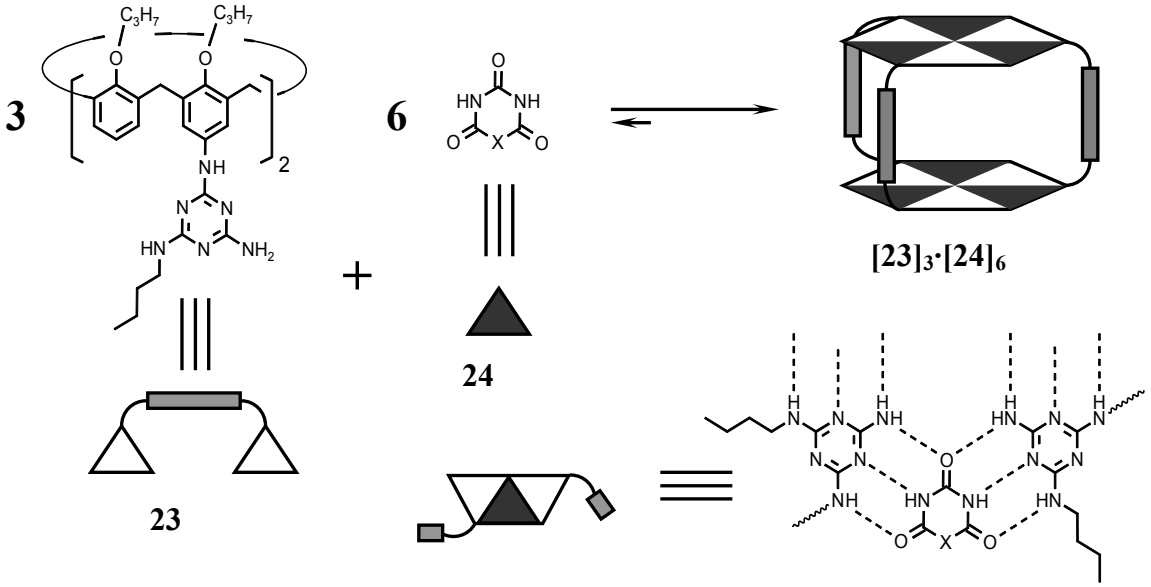


Figure 3. Schematic representation of self-assembly into "double rosette" of calix[4]arene dimelamines **23** and barbituric/cyanuric acid derivatives **24** (X = $C(CH_2CH_3)_2$; $NCH_2C(O)NH(CH_2)_6S(CH_2)_5CH_3$).

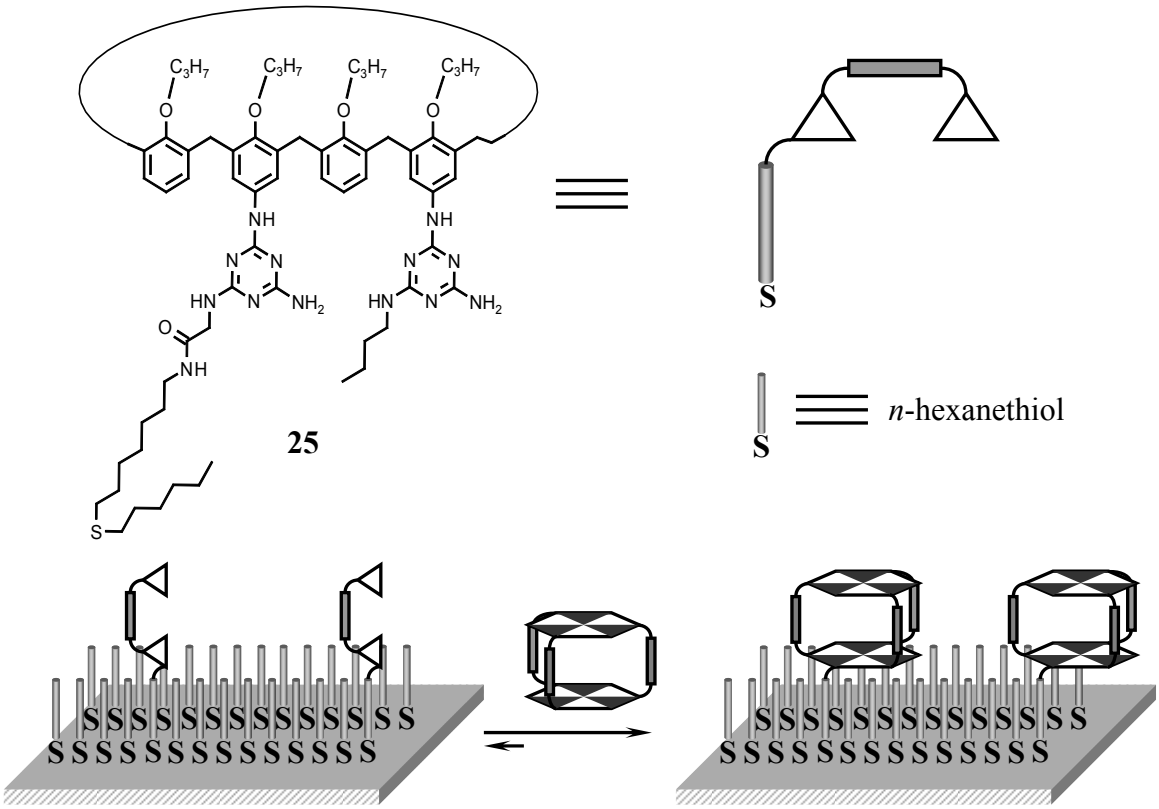


Figure 4. Schematic representation of the growth of assemblies $[\mathbf{23}]_2 \cdot \mathbf{25} \cdot [\mathbf{24}]_6$.

The first example of synthetic hydrogen-bonded assemblies adsorbed on gold was reported by Reinhoudt *et al.*[17] The self-assembly motif is based on calix[4]arene dimelamines **23** and barbituric/cyanuric acid derivatives which in apolar solvents spontaneously form stable hydrogen bonded assemblies $[\mathbf{23}]_3\cdot[\mathbf{24}]_6$ (so-called "double rosette"), where 9 molecules are held together by 36 hydrogen bonds (see Fig. 3).[18]

The growth of individual nanometer-sized hydrogen bonded assemblies $[\mathbf{23}]_2\cdot\mathbf{25}\cdot[\mathbf{24}]_6$ on gold monolayers was achieved through an exchange reaction between single isolated calix[4]arene dimelamine **25** pre-adsorbed on *n*-hexanethiol monolayers and double rosette assembly $[\mathbf{23}]_3\cdot[\mathbf{24}]_6$ in solution (Fig. 4). The growth process was monitored by tapping mode atomic force microscopy (TM-AFM).

However the inclusion of charged particles or neutral molecules in the double rosette monolayers was not reported. Also no guest inclusion was observed in the capsules consisting of two oppositely charged calix[4]arenes (tetraguanidinium and tetrasulfonate)[19] anchored on *β*-cyclodextrin SAM on gold.

3.2 Tetraurea calix[4]arene capsules attached to gold and their potential application

The tetraurea calix[4]arene dimers which include some neutral molecules or cations can be potentially used for the preparation of the stable hosting monolayers on the gold surface.

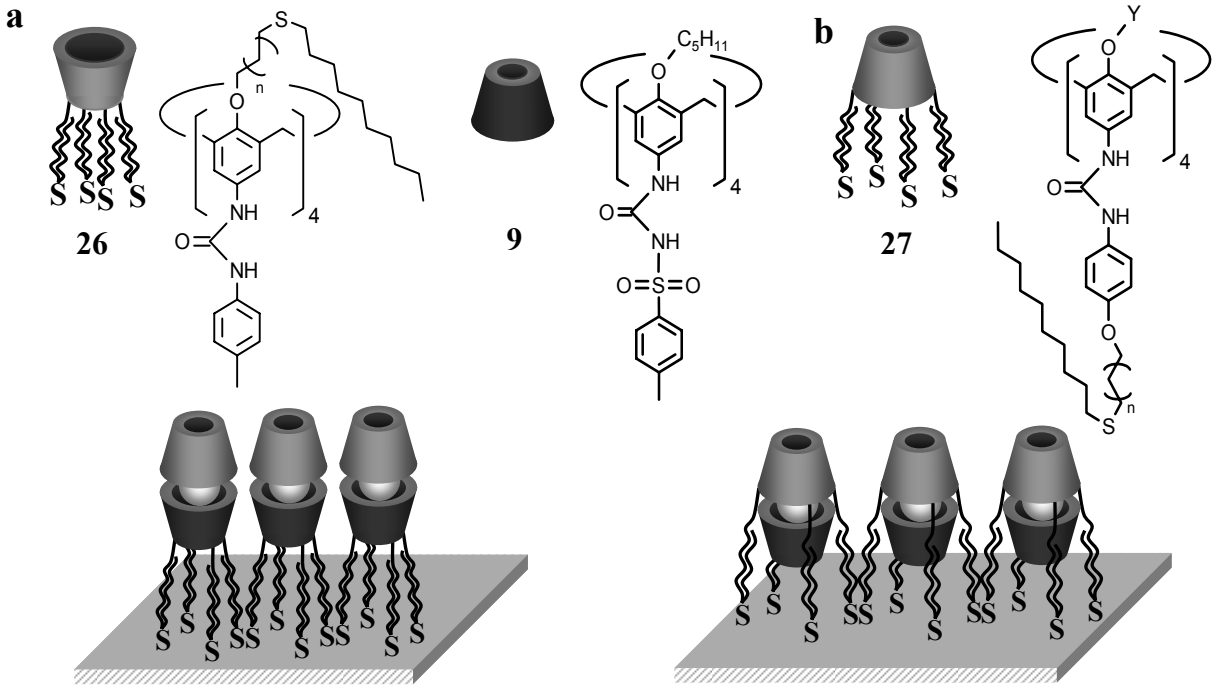


Figure 5. The target derivatives and schematic representation of their SAMs on gold.

To achieve the "vertical" alignment of the capsules only one tetraurea counterpart should contain sulfide groups at their narrow rim (Fig. 5a) or wide rim (Fig. 5b). Tetratosylurea **9** or multi-macrocycles **10a**,**b** (Fig. 6) which prefer the formation of heterodimers can be the second counterpart.

The attachment of the capsule to the gold surface via the wide rim of the upper tetraurea (**27**) should produce more stable monolayers. In this case the lower counterpart has less mobility (tetratosylurea **9**) or is "trapped" by the upper calixarene (macrocycles **10a,b**). Obviously the SAMs formed by the dimers **27·10b** might be stable also under hydrogen-bond breaking conditions. Thus, the inclusion properties of such SAMs could be studied under various conditions.

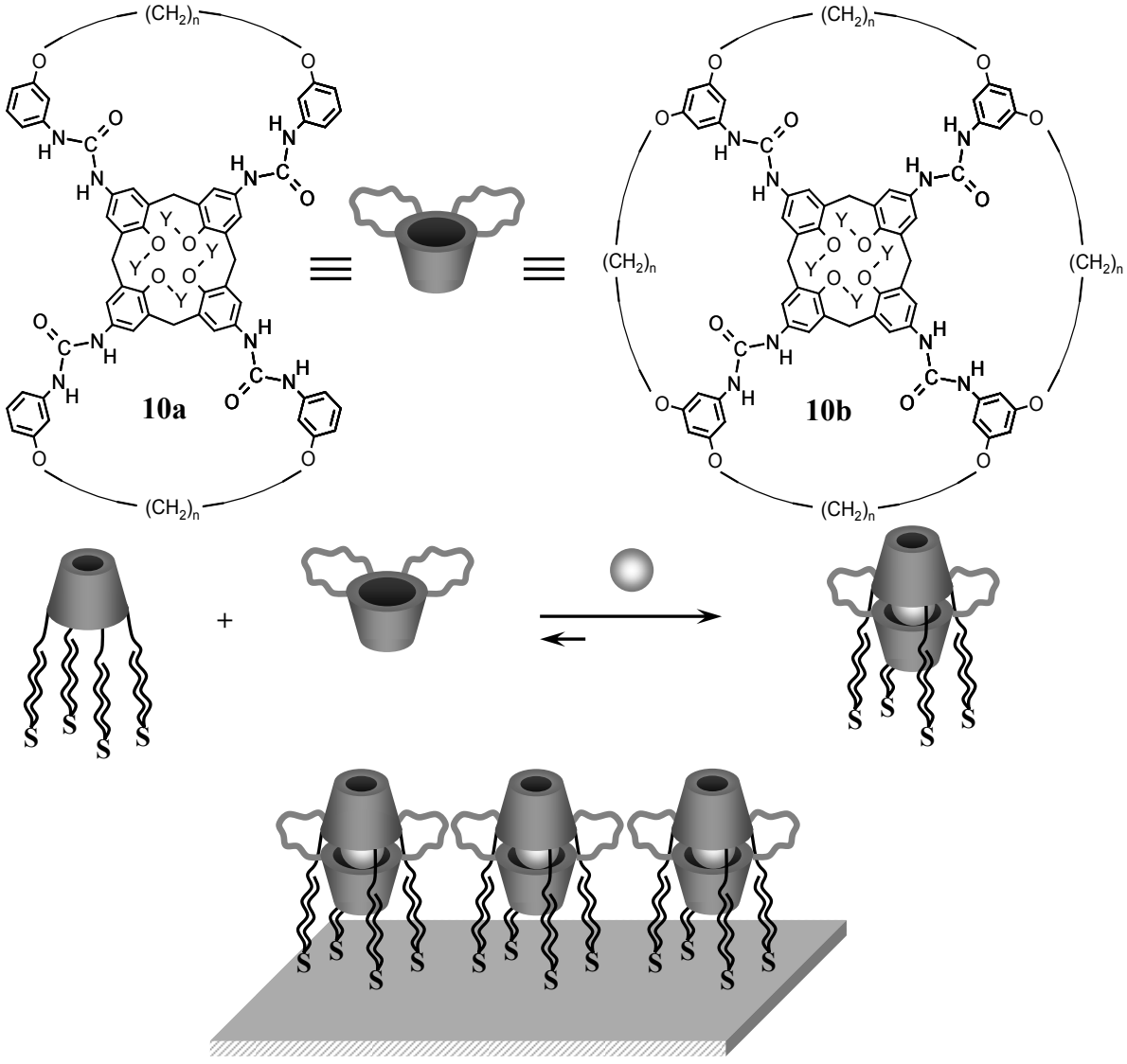


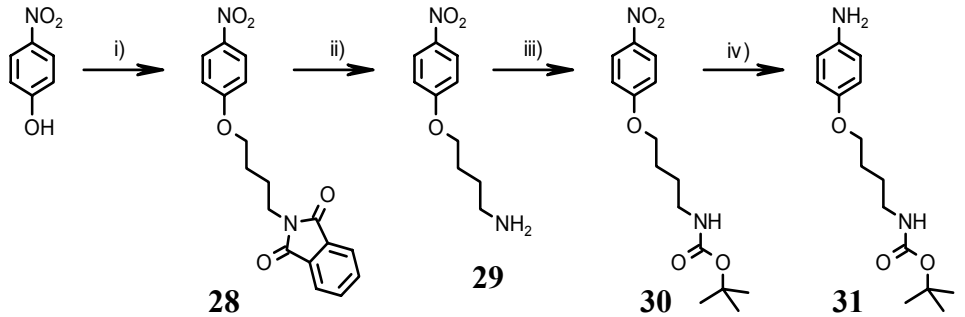
Figure 6. Schematic representation of the heterodimers **27·10a** (**27·10b**) and their SAMs on gold.

The cobaltocenium cation was found as an attractive guest for the tetraurea capsule.[20] In spite of its relatively large dimensions (75-80% of inner volume of the tetraurea calix[4]arene dimer) cobaltocenium shows a high tendency for encapsulation. This is not the case for cobaltocene which has approximately the same size (since cobaltocene is paramagnetic the ^{1}H NMR studies were provided with its analogue – ferrocene). The inclusion of cobaltocenium in the dimers is explained by cation-π interactions between the charged guest and the aryl units of the calixarene. The strength of these interactions overcomes even the steric demands (the ideal packing coefficient was considered to be about 55%).[21] Cobaltocene analogously to ferrocene should not fit in such capsules. Therefore, the reduction of cobaltocenium included in the simple dimeric tetraurea dimer should lead to the exchange of the cobaltocene against more suitable guest, for example a solvent molecule. In the SAMs formed by the dimers **27·10b** exchange of cobaltocene (ferrocene) could be hindered due to the trapping of the lower tetraurea counterpart. Such systems could find an application in the field of materials with electrochemically controlled properties.

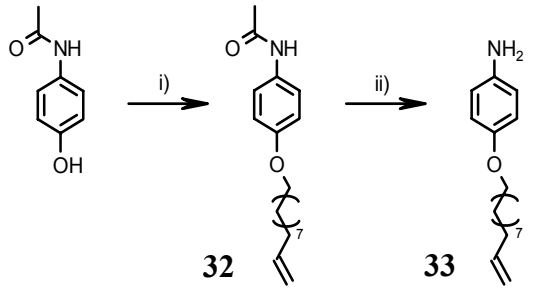
3.3 Synthesis

The tetraurea calix[4]arenes bearing sulfide functions at the wide rim could be synthesized via acylation of the starting tetraamine **Ia** by appropriately functionalized isocyanates/urethanes or via conversion of the tetraamine **Ia** to tetra-*p*-nitrophenylurethane followed by reaction with corresponding anilines. The sulfide functions could be introduced in the last step by simple procedures such as the addition of alkylthiol to double bond[22] or deprotection of the amino group followed by acylation with *α*-lipoic acid.

The amino groups which are used for attachment of *α*-lipoic acid could be phthalimide- or Boc-protected. The *p*-(*N*-butyloxyphthalimide)nitrobenzene **28** (Scheme 1) was synthesized by alkylation of the *p*-nitrophenol with *N*-4-(bromobutyl) phthalimide in the presence of potassium carbonate in 84% yield. The nitrobenzene **28** was reduced to the appropriate aniline which was reacted with tetra-*p*-nitrophenyl urethane **34** producing the corresponding tetraurea. However, the urea groups do not survive at the conditions of the phthalimide cleavage (hydrazine, ethanol, reflux). Therefore, only the Boc-protection could be used. For this purpose the compound **28** was converted to the aniline **31** via cleavage of the phthalimide functions by hydrazine-hydrate (80% yield) followed by Boc-protection of the formed amine **29** with Boc-anhydride (84% yield) and hydrogenation of the nitro derivative **30** in the presence of catalytic amount of Raney/Ni (85% yield).



Scheme 1. Synthesis of aniline **31**. i) *N*-4-(bromobutyl) phthalimide, K_2CO_3, acetonitrile, reflux; ii) hydrazine-hydrate, ethanol, reflux; iii) Boc_2O, THF, rt; iv) Raney/Ni, toluene, rt.



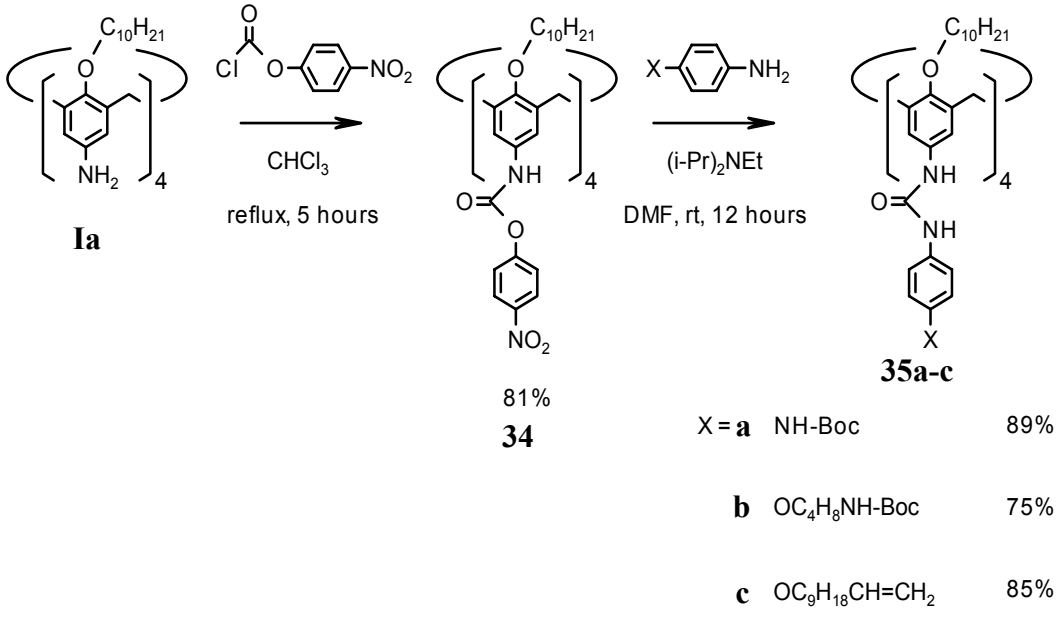
Scheme 2. Synthesis of aniline **33**. i) 11-Bromo-1-undecene, K_2CO_3, acetonitrile, reflux; ii) NaOH, ethanol/water, reflux.

The aniline **32** was synthesized starting from *p*-acetamidophenol (Scheme 2) which was alkylated with 11-bromo-1-undecene by reflux in acetonitrile with potassium carbonate as base yielding 89% of **32**. Then acetyl group was hydrolyzed with sodium hydroxide in refluxing ethanol/water yielding the target aniline **33** (93%).

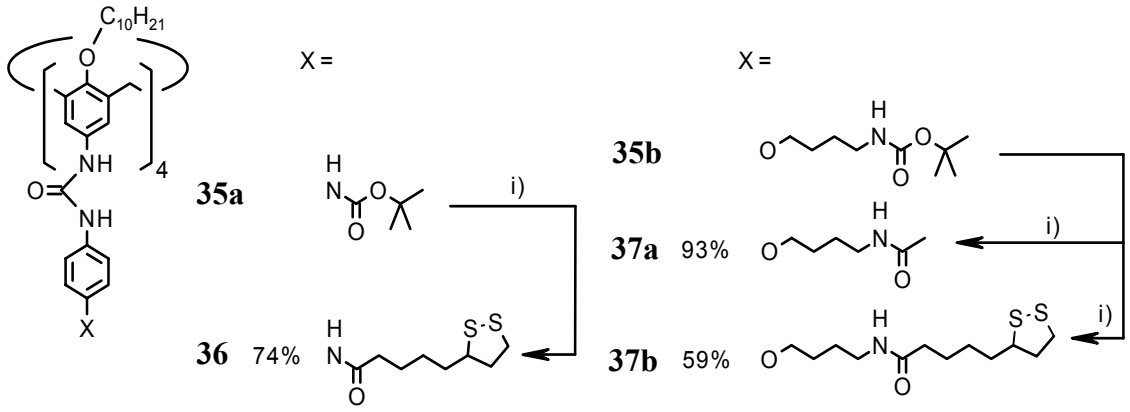
Tetra-*p*-nitrophenyl urethane **34** was prepared to activate the tetraamine of calix[4]arene tetradecylether **Ia** for further transformation into its tetraurea derivatives. The amine was refluxed with *p*-nitrophenyl chloroformate in chloroform and urethane **34** was isolated in 81% yield (Scheme 3).

The urethane **34** was reacted with *N*-Boc-*p*-phenylenediamine in DMF in the presence of Hünig base to produce tetraurea **35a** in 89% yield. Tetraureas **35b** and **35c** were synthesized in similar way in 75% and 85% yield respectively.

The tetraureas **36** and **37a,b** (Scheme 4) were synthesized in 74%, 93% and 59% overall yields respectively.



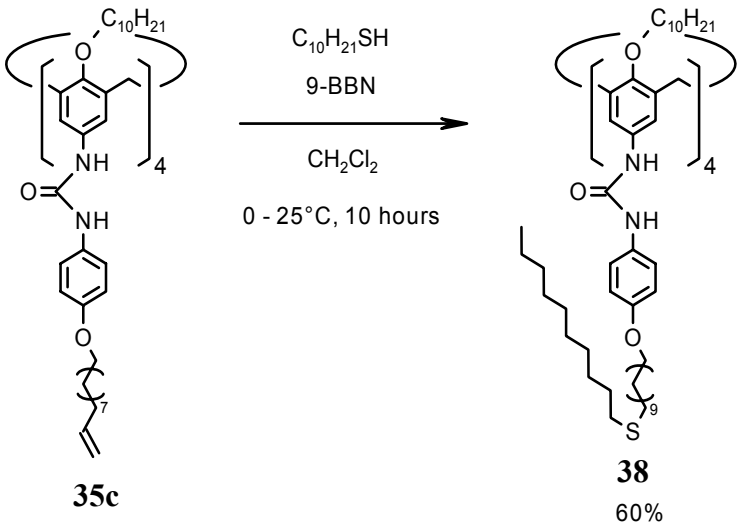
Scheme 3. Synthesis of tetraurea calix[4]arenes **35a-c**.



Scheme 4. Synthesis of tetraurea calix[4]arene **36** and **37a,b**. i) CF_3COOH, CH_2Cl_2, rt; followed by *i*-Pr_2EtN, $(AcO)_2O$ (a) or α-lipoic anhydride (b), THF, rt.

The synthetic procedure involved deprotection of amino groups with trifluoroacetic acid in dichloromethane at room temperature followed by neutralization of the salt by Hünig base and further acylation with acetic anhydride or anhydride of α-lipoic acid (prepared from α-lipoic acid and DCC in benzene as published[23]). The compounds **36** and **37b** seem to be sensitive to the light and temperature due to the instability of the disulfide rings.

The tetraurea **38** bearing dialkylsulfide groups was synthesized in 60% yield under mild conditions by radical addition of the *n*-decylthiol to the alkenyl residues of the tetraurea **35c** in the presence of 9-borabicyclo[3.3.1]nonane (9-BBN) (Scheme 5).



Scheme 5. Synthesis of tetraurea calix[4]arene **38**.

The synthesized compounds were characterized by FD or ESI mass spectrometry. ^{1}H NMR spectra of tetraurea calix[4]arenes **CS35a-c**, **36**, **37a,b** and **38** were described for their monomeric form (in DMSO-d_6) and as well as for their self-assemblies.

3.4 Self-organization

3.4.1 Conditions for the formation of the tetraurea dimer-cobaltocenium complex

To prepare SAMs from tetraurea calix[4]arene dimers, the self-assembly and complexation properties of the compounds **36**, **37a,b** and **38** in solution must be thoroughly studied prior to their deposition to the gold surface.

Dimers of tetratolylurea calix[4]arene **8a** with cobaltocenium as guest were formed in 60 hours in DCE.[20] But DCE (as well as TCE) cannot be used for the further studies by physical methods, such as SPR. Therefore, we were looking for conditions for the quantitative formation of the dimer-cobaltocenium complexes in solvents suitable for the preparation of stable SAMs on the gold surface and for their further studies. Tetratolylurea calix[4]arene **8a** was chosen as the model compound.

The compound **8a** and cobaltocenium hexafluorophosphate were mixed in $CDCl_3$ in the ratio 1 : 1. Two downfield shifted signals of the NH protons were observed in the ^{1}H NMR spectrum after 5 min (Fig. 7a). Obviously, one of them belongs to the dimer filled with cobaltocenium (40%) and another belongs to the dimer filled with $CDCl_3$ (60%). The equilibrium was achieved with 86% of the homodimer with cobaltocenium and 14% of the

homodimer with $CDCl_3$ approximately in 20 hours after mixing (Fig. 7b). Similar equilibrium was found for heterodimers **8a·9** mixed with cobaltocenium salt in $CDCl_3$. Obviously, chloroform necessarily present in excess is too "good" as guest for the dimers (forms too stable homodimers) and competes with cobaltocenium.

Since benzene is even more preferred guest than chloroform, it is also not appropriate solvent for the preparation of SAMs on gold.

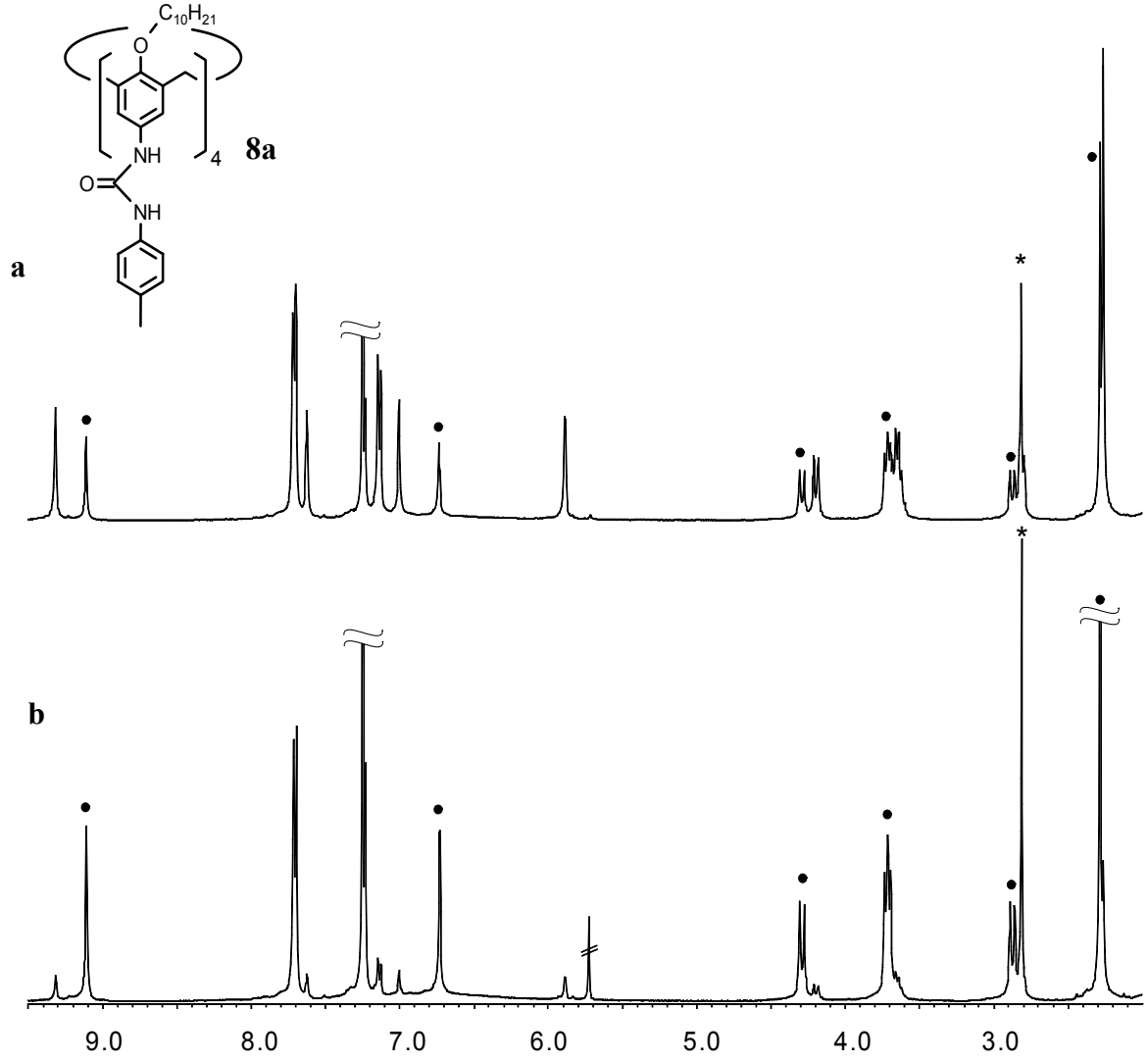


Figure 7. The parts of ^1H NMR spectra of tetraurea **8a** in $CDCl_3$ at rt (a) 5 min after mixing and (b) 60 hours after mixing. The signals of the homodimer including cobaltocenium are marked with black points; the signals of included cobaltocenium are marked by asterisk.

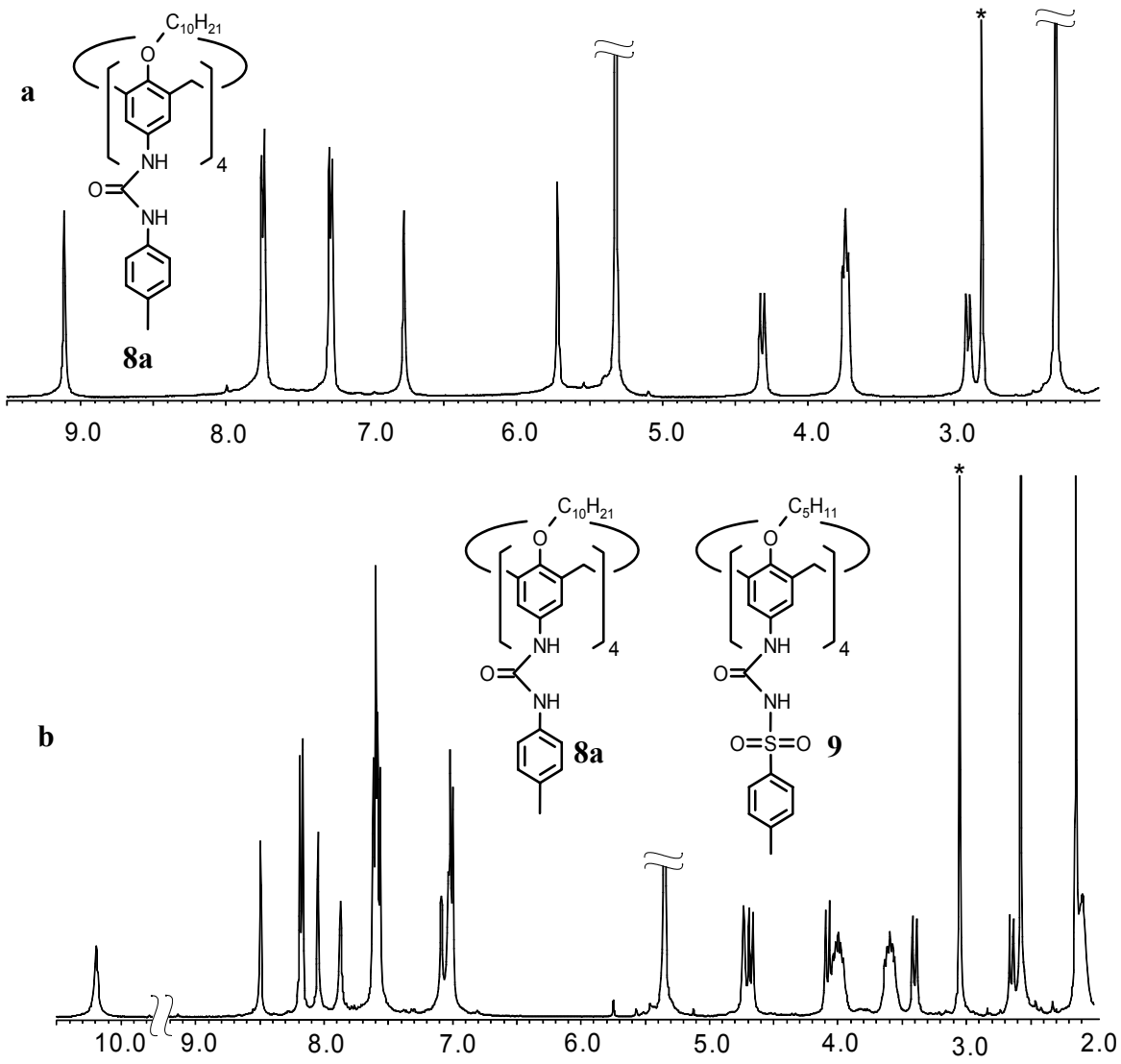


Figure 8. The parts of ^{1}H NMR spectra in CD_2Cl_2 at rt (a) of the homodimer of tetraurea **CS22** and (b) of the heterodimer **8a·9** (Y = C_5H_{11}). The signals of included cobaltocenium are marked by asterisk.

Dichloromethane is a less favourable guest in comparison to the solvents mentioned before. The quantitative formation of (**8a**)$_2$ containing cobaltocenium was observed in the spectrum immediately after mixing in CD_2Cl_2 (Fig. 8a). The same is also true for the heterodimers **8a·9** in the presence of stoichiometrical amount of cobaltocenium·PF_6^- in CD_2Cl_2 (Fig. 8b). Therefore, dichloromethane is the solvent meeting all the requirements.

3.4.2 Tetraureas functionalized for attachment of sulfide groups

The precursor tetraureas **35a-c** were checked by ^{1}H NMR in $CDCl_3$ or TCE (Table 1). The compounds **35b** and **35c** form the dimeric structures in $CDCl_3$ as usual arylureas:

- signals of 8 NH protons of the urea groups are shifted downfield;

- two pairs of *m*-coupled doublets for the protons of calixarene skeleton.

The compound **35a** is insoluble in $CDCl_3$. In TCE solution it shows a complicated spectrum consisting of the homodimer signals overlapped with the signals of further assemblies which are difficult to interpret (Fig. 9). From the dimer **$(35a)_2$** only following signals were observed clearly:

- singlet for NH protons shifted downfield (9.22 ppm);
- two (pseudo)doublets (at 7.65 ppm and 7.28 ppm) for the protons of aryl units adjacent to the urea groups;
- the splitted signals of aryl protons of calixarene skeleton (at 7.55 and 5.82 ppm);
- two doublets of the methylene bridges (at 4.18 ppm and 2.82 ppm).

Obviously, other assemblies were formed from compound **35a** due to the participation of amide groups in the hydrogen bonding.

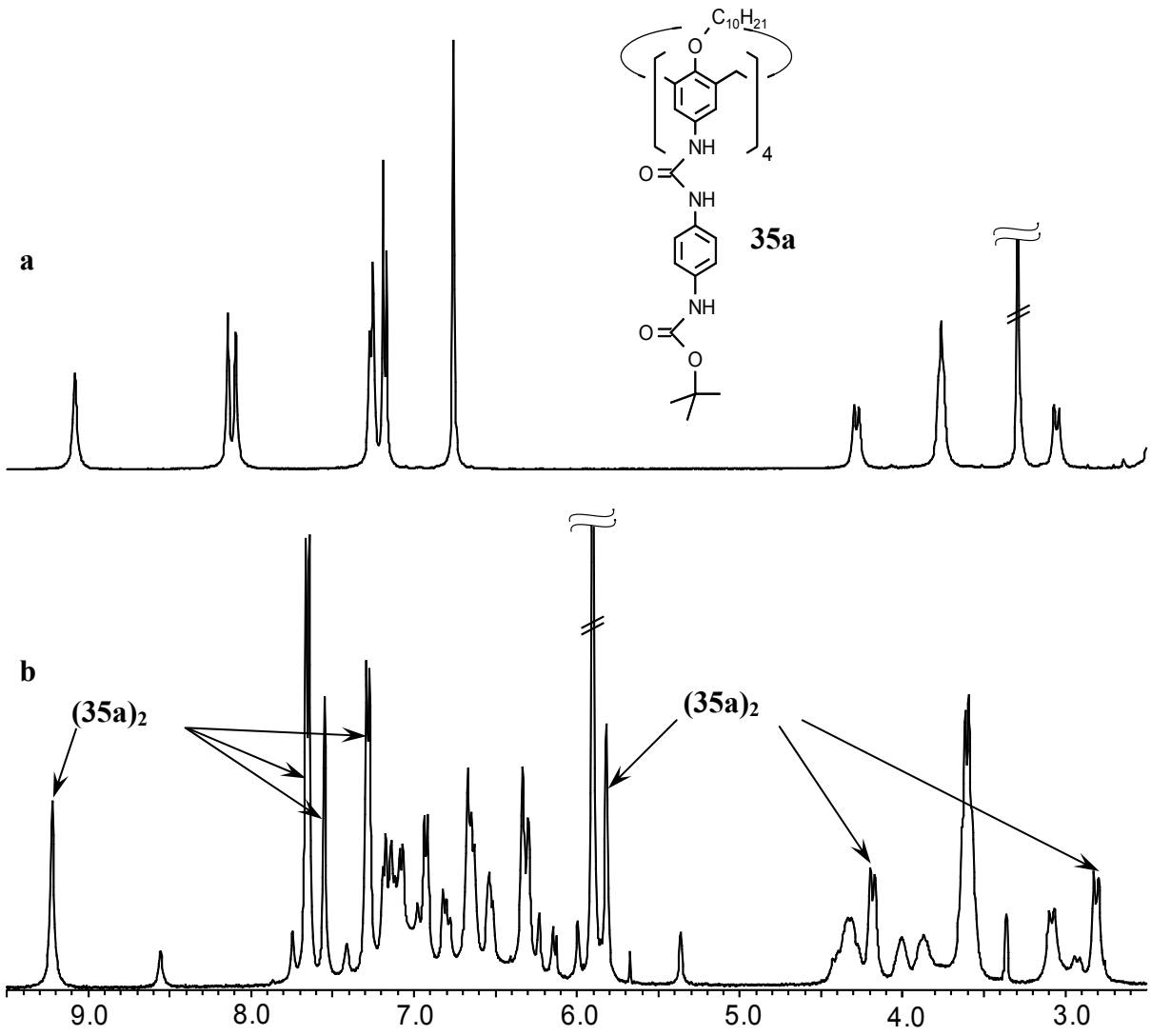


Figure 9. A part of the ^{1}H NMR spectrum of **35a**: (a) in DMSO-d_6, (b) in TCE-d_2.

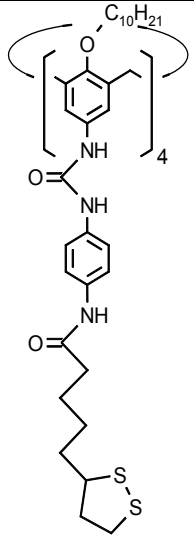
Table 1. The self-assembly properties of tetraureas **35a-c**.

Component 1	Component 2	Solvent	Temperature	Observations ^{1}H NMR (400 MHz)
35a	-	$CDCl_3$	rt	insoluble
	-	TCE	rt	homodimer and aggregates
35b	-	$CDCl_3$	rt	homodimer
35c	-	$CDCl_3$	rt	homodimer

3.4.3 Tetraureas with α-lipoic acid attached to *p*-positions of phenylurea units via amide function

Similarly to its precursor (tetraurea **35a**) the tetraurea **36** is insoluble in the apolar solvents most frequently used for dimerization ($CDCl_3$, CD_2Cl_2, C_6D_6). It does not dimerize in the presence of cations and does not form heterodimers with tosylurea **9** or tetraloop **10b** at room temperature. However, it shows the formation of **36**·**10b** heterodimer in TCE at 75°C in the ^{1}H NMR spectrum. The signals of the heterodimer are present in solution together with broad signals which belong either to aggregates formed by an excess of one of the compounds or to aggregates formed from heterodimers (due to further interactions between amide groups).

Table 2. The self-assembly properties of tetraurea **36**.

Component 1	Component 2	Solvent	Temperature	Observations ^{1}H NMR (400 MHz)
 **36**	-	CD_2Cl_2 $CDCl_3$ C_6D_6	rt	insoluble
	-	TCE	rt	aggregates
	-	TCE	75°C	aggregates/monomer
	9	$CDCl_3$	rt	insoluble
	$Et_4N^+PF_6^-$	$CDCl_3$	rt	insoluble
	10b	$CDCl_3$ TCE	rt	insoluble
		TCE	75°C	heterodimer predominantly

3.4.4 Tetraureas with acetyl and α-lipoyl residues attached to *p*-positions of phenylurea units via aminobutoxy groups

The compounds **37a,b** form irregular aggregates in CD_2Cl_2, $CDCl_3$ and C_6D_6. This irregular association could be caused by the interference of the amide functions in hydrogen bonding like in case of tetraurea **36**. After staying at room temperature at day light for 48-72 hours **37b** precipitates from the solutions in CD_2Cl_2, $CDCl_3$ and C_6D_6. This precipitates look like a polymeric film and are insoluble in the most organic solvents. In the same conditions tetraurea **37a** forms a gel from $CDCl_3$ solution.

37a,b

R =

a

b

However, tetraureas **37a,b** dimerize partially in TCE or in the presence of a cationic guest (cobaltocenium, tetraethylammonium) in other solvents. The equilibrium between disordered associates and the dimer "D" of **37b** exists in TCE solution at room temperature (Fig. 10a). The increase of temperature to 75 and 100°C leads to the growth of the signals which could be interpreted as the signals of tetraurea monomer "M" (Fig. 10c). The same was observed for **37a**.

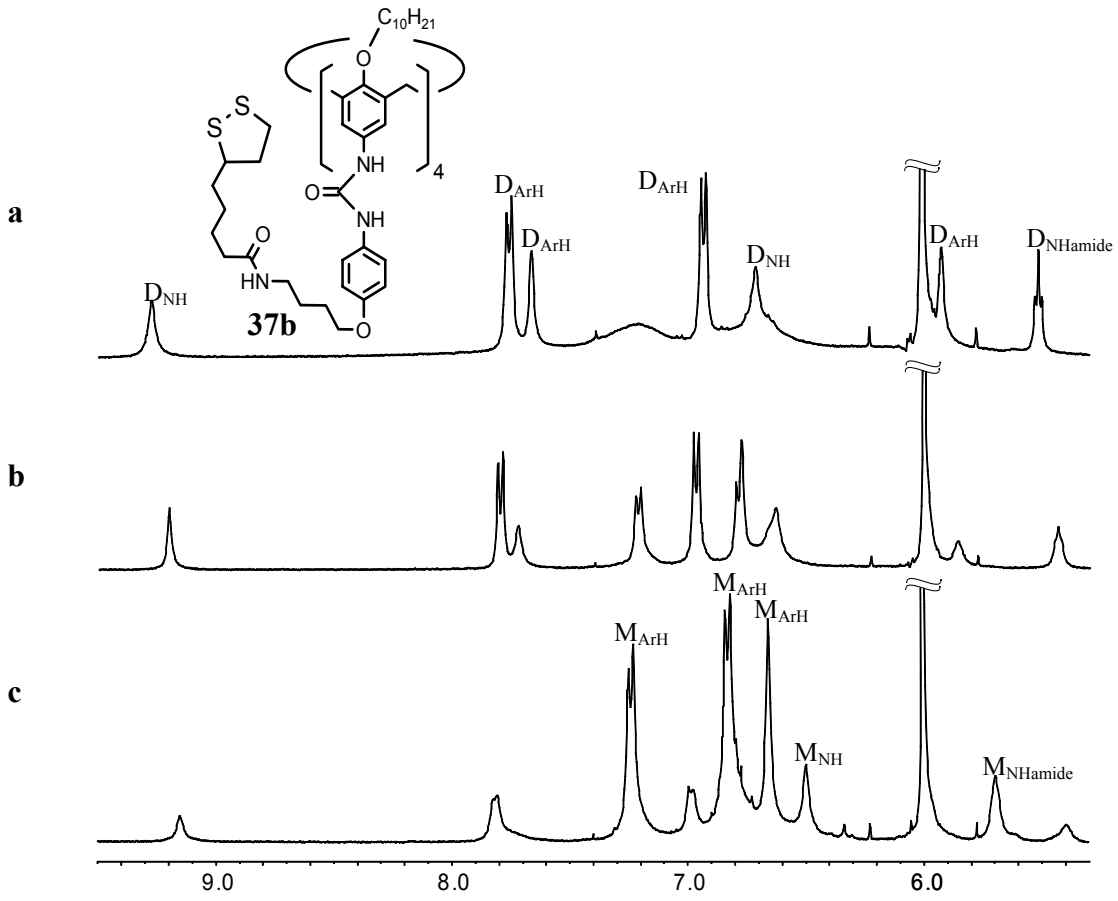
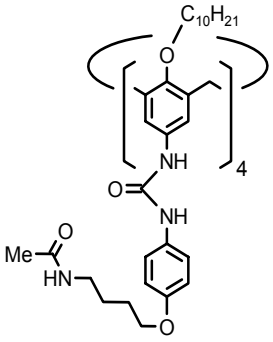
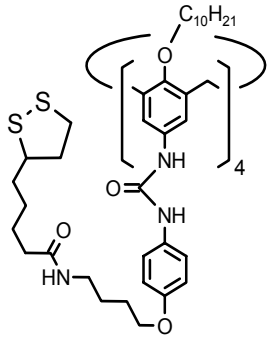


Figure 10. ^{1}H NMR spectra of **37b** in TCE at 25°C (a), 75°C (b) and 100°C (c).

In TCE **37b** and tetratosylurea **9** (Y = C_5H_{11}) form predominantly the heterodimer **37b·9** (Fig. 11). Remarkably, the heterodimer **37b·9** was not observed in dichloromethane-d_2 in ^{1}H NMR spectrum. In chloroform the signals of the heterodimer **37b·9** are present in the spectrum together with broad signals of other assemblies. The heterodimer of **37b·10b** in $CDCl_3$ solution exists also not exclusively (Table 3).

Table 3. The self-assembly properties of tetraurea **37a,b**.

Component 1	Component 2	Solvent	Temperature	Observations ^{1}H NMR (400 MHz)
 **37a**	-	$CDCl_3$	rt	irregular aggregates
	-	C_6D_6	rt, 75°C	insoluble
	-	TCE	rt	insoluble
	-	TCE	75°C	homodimer and monomer
 **37b**	-	$CDCl_3$ C_6D_6 CD_2Cl_2	rt	irregular aggregates
	-	TCE	rt	homodimer/aggregates
	-	TCE	75°C	homodimer (33%) and monomer (67%)
	-	TCE	100°C	homodimer (13%) and monomer (87%)
	Cobaltocenium PF_6^-	CD_2Cl_2	rt	homodimer-complex/ irregular aggregates
	10b	$CDCl_3$, C_6D_6	rt	heterodimer/irregular aggregates
	9	$CDCl_3$	rt	heterodimer/irregular aggregates
		CD_2Cl_2	rt	irregular aggregates
		TCE	rt	heterodimer

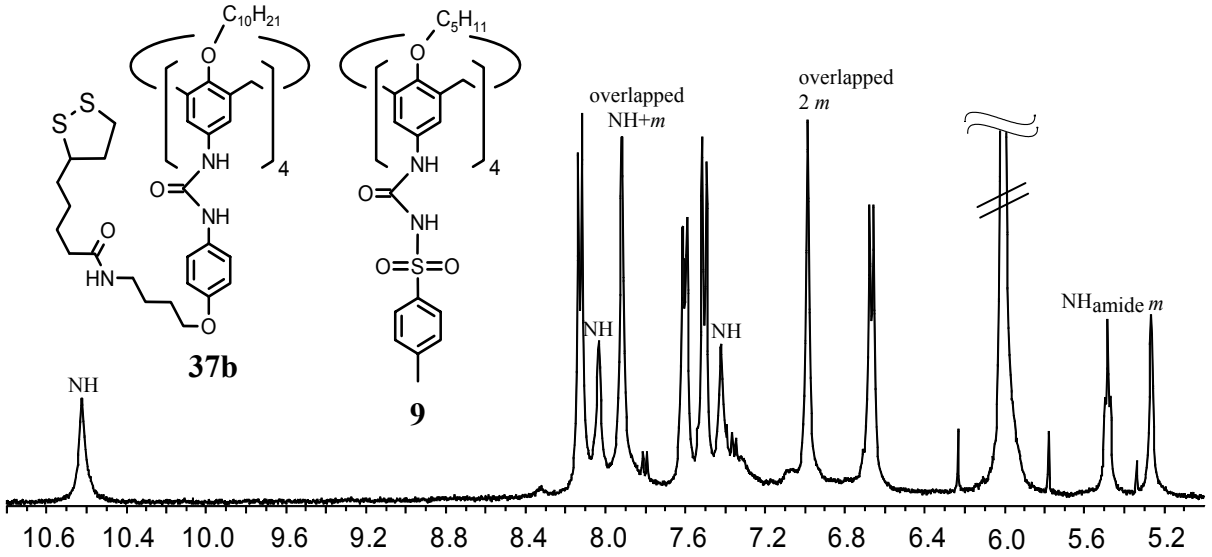
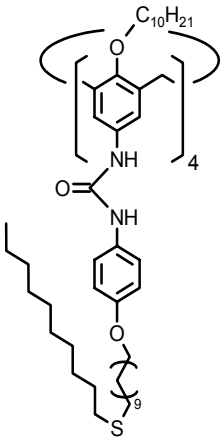


Figure 11. A part of ^{1}H NMR spectrum of heterodimer **37b**·**9** (Y = C_5H_{11}) in TCE. The urea and amide NH protons and *m*-coupled doublets of the skeleton phenyl units are indicated.

Table 4. The self-assembly properties of tetraurea **38**.

Component 1	Component 2	Solvent	Temperature	Observations ^{1}H NMR (400 MHz)
 **38**	-	$CDCl_3$ C_6D_6	rt	homodimer
	9	$CDCl_3$, C_6D_6	rt	heterodimer
	$Et_4N^+PF_6^-$	CD_2Cl_2	rt	homodimer-complex
	Cobaltocenium PF_6^-	CD_2Cl_2	rt	homodimer-complex
	10b	C_6D_6	rt	heterodimer
	10b + Cobaltocenium PF_6^-	CD_2Cl_2	rt	heterodimer-complex
	9 + Cobaltocenium PF_6^-	CD_2Cl_2	rt	heterodimer-complex

3.4.5 Tetraureas with dialkylsulfide chains attached to *p*-positions of phenylurea units via ether links

The tetraurea **38** forms homodimers and heterodimers with tetratosylurea **9** and tetraloop **10b** in $CDCl_3$ and C_6D_6 at room temperature. Similarly to tetraurea **8a** the dimers (**38**)$_2$ include rapidly the tetraammonium or cobaltocenium cations in CD_2Cl_2. The sets of *m*-coupled doublets for the aryl protons of each calixarene were deduced from their COSY

spectra. Also the heterodimers **38·9** and **38·10b** easily include the cobaltocenium guest. Its signal appears as singlet at 3.05 ppm for **38·9** and in the interval 2.86-2.73 ppm for **38·10b**. The integral intensities of the protons of included cobaltocenium are in 1 : 1 ratio with corresponding heterodimer which is an evidence of the quantitative formation of cobaltocenium complexes. The summary of self-assembly properties of **38** is outlined in Table 4.

3.4.6 Summary

The derivatives of calixarenes **35a-c** could be divided in three groups according to the increase of complexity of their structure and their self-assembling properties.

- Tetraurea **38** with long dialkylsulfide chains.

It behaves similarly to "classical" tetraurea calix[4]arenes, like **8a** and **35c**, and forms all possible kinds of dimers, heterodimers and their complexes with cobaltocenium and Et_4N^+ cations.

- Tetraurea **36** having α-lipoic acid attached to *p*-positions of the phenolic units adjacent to the urea bond via amide functions.

It forms neither homodimers, nor heterodimers with tetratosylurea **9** or in the presence of cation (cobaltocenium or Et_4N^+) in the solvents used for dimerization. Obviously the amide groups interfere in the dimerization process and therefore irregular aggregates are formed. However, the compound **35a** (the precursor of tetraurea **36**) which has amide functions in the same positions forms nevertheless dimers in TCE (in addition to other assemblies). Probably in this case the Boc-groups of **35a** could partially "shield" amide functions and prevent their interaction with urea groups.

At higher temperature (75°C) tetraurea **36** dissolves in TCE together with tetraloop **10b** showing in ^{1}H NMR spectrum the signals of the heterodimer **36·10b** predominantly.

- Tetraureas **37a,b** having acetyl (**a**) and α-lipoyl (**b**) residues attached to *p*-positions of the phenolic units adjacent to the urea bond via butoxyamino groups.

In contrast to the tetraurea **35b** having amide groups in the same positions compounds **37a,b** do not form dimers in chloroform. Most probably, like in the case of the tetraurea **35a** the bulky Boc-residues block intermolecular interaction of the amide groups and prevent irregular aggregation.

Tetraurea **37b** forms irregular aggregates in addition to dimers either in the presence of cations (cobaltocenium) or the tetraureas **9** or **10b**. The compound **36** which has the same α-lipoylamide residues forms dimers in the presence of **10b** in TCE only at higher temperatures.

Obviously the amide influence on dimerization of those tetraureas weakens with the distance increase between the amide and the urea functions.

The following general conclusions can be drawn from the study of tetraureas **35a-c**, **36**, **37a,b** and **38**:

- Attachment of amide groups to the phenolic units adjacent to the urea groups of tetraurea calix[4]arenes can lead to the formation of irregular aggregates in apolar solvents. It is difficult to determine, if these irregular associates are formed by the monomers or the dimers.
- Among the synthesized compounds finally only tetraurea **38** was found to fulfil the conditions for the preparation of SAMs on gold.

The compound **38** is currently under investigation with SPR and CV in the research group of Prof. Dr. S. Mittler.[24] The SPR experiments have shown the formation of stable SAMs from heterodimers **38·9** on gold surface. The first results of CV measurements are presented in Fig. 12.

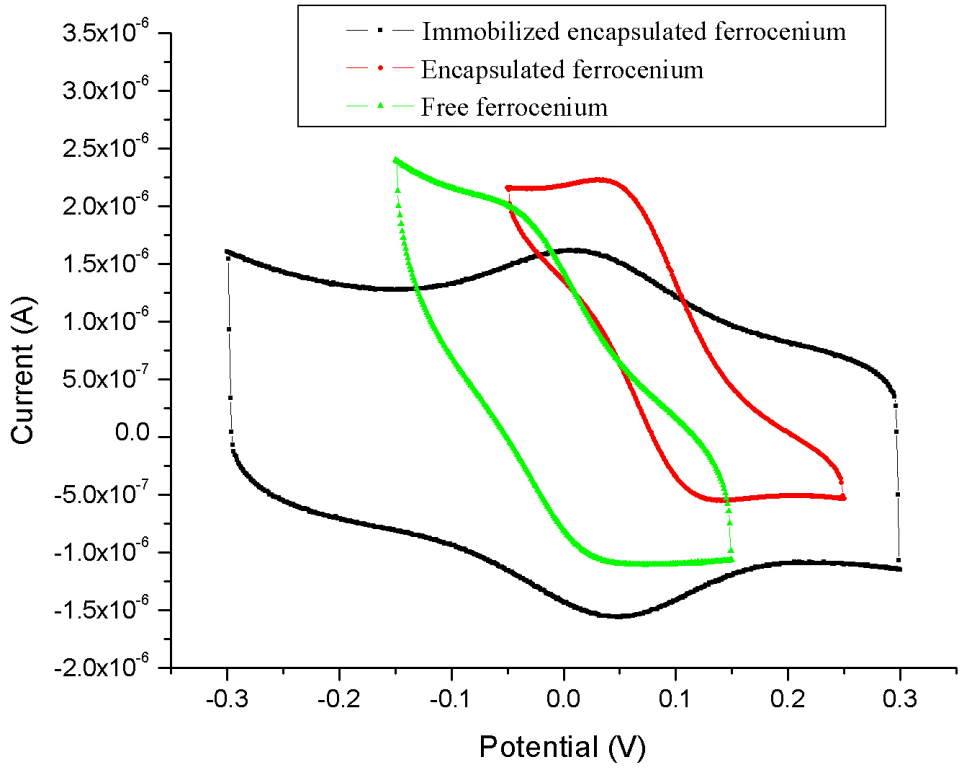


Figure 12. The electrochemical response of immobilized encapsulated ferrocenium, encapsulated ferrocenium and free ferrocenium.[25] "Free ferrocenium" means a solution of ferrocenium and the electrolyte ($Bu_4N^+PF_6^-$) in dichloromethane. "Encapsulated ferrocenium" is a solution of tetraurea **38·9**-ferrocenium complex and of electrolyte in dichloromethane. "Immobilized encapsulated ferrocenium" is a solution of tetraurea **38·9**-ferrocenium complex self-assembled on gold electrode.

The voltammograms for free ferrocenium and for **38·9**-ferrocenium complex show the oxidation/reduction peaks in both cases. From them we can conclude that:

- the complexed ferrocenium still keeps its electrochemical activity as well as the free ferrocenium;
- for the **38·9**-ferrocenium complex the redox peaks moved to a higher value than for free ferrocenium.

SAMs of **38·9**-ferrocenium complex on gold show reversible cyclic voltammetric peaks around 0.02V versus quasi-silver reference electrode. The redox reaction potential for ferrocenium in SAMs is more negative than for the free **38·9**-ferrocenium complex.

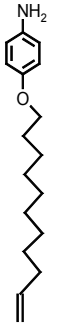
3.5 Experimental

p-Tetraamino calix[4]arene tetradecylether **Ia** was prepared according to published procedures.[26]

4-(10'-Undecenyloxy)-acetamide **32**:

A suspension of 4-acetamidophenol (3.00 g, 19.846 mmol) and potassium carbonate (5.49 g, 39.693 mmol) in acetonitrile (150 ml) was refluxed for 1 hour. Then 11-bromo-1-undecene (6.02 g, 25.815 mmol) was added and the mixture refluxed for a further 48 hours. After removal of the solvent *in vacuo*, the mixture was partitioned between $CHCl_3$ and H_2O. The organic layer was washed 2 times with sodium carbonate water solution, dried ($MgSO_4$) and the solvent was removed *in vacuo*. The residue was purified by recrystallisation from acetonitrile/methanol. Yield: 5.35 g (89%).

m.p. 89.5°C; MS (FD): m/z 303.2 (M^+);^{1}H NMR ($CDCl_3$): δ 7.35 (d, Ar-*H*, 2 H, $^3J_{HH}$ 8.1 Hz), 7.02 (s, -N-*H*-, 1 H), 6.83 (d, Ar-*H*, 2 H, $^3J_{HH}$ 8.1 Hz), 5.88-5.73 (m, -C*H*=CH_2, 1 H), 5.04-4.86 (m, -CH=CH_2, 2 H), 3.91 (t, -O-CH_2-, 2 H, $^3J_{HH}$ 6.2 Hz), 2.14 (s, -CH_3, 3 H), 2.08-1.96 (m, -O-CH_2-CH_2-, 2 H), 1.82-1.67 (m, -CH_2-, 2 H), 1.49-1.17 (m, -(CH_2)$_6$-, 12 H).

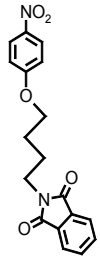


4-(10'-Undecenyloxy)-aniline **33**:

A mixture of O-alkylated acetamide (5.35 g, 17.644 mmol) and sodium hydroxide (24.70 g, 617.538 mmol) was refluxed in EtOH-H_2O solution (EtOH : H_2O = 100 ml : 10 ml) for 12 hours. Then the solvent was evaporated. The residue was partitioned between ether and H_2O. The organic layer was washed 2 times with sodium carbonate water solution, dried over $MgSO_4$ and the solvent was removed under reduced

pressure. The residue (a brown solid) was analytically pure product and used in further reactions without additional purification. Yield: 4.30 g (93%).

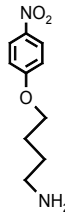
m.p. 37-38°C; MS (FD): m/z 261.2 (M^+); ^{1}H NMR ($CDCl_3$): δ 6.74 (d, Ar-H, 2 H, $^3J_{HH}$ 8.8 Hz), 6.62 (d, Ar-H, 2 H, $^3J_{HH}$ 8.8 Hz), 5.96-5.68 (m, -C*H*=CH_2, 1 H), 5.12-4.85 (m, -CH=C*H*$_2$, 2 H), 3.86 (t, -O-C*H*$_2$-, 2 H, $^3J_{HH}$ 6.6 Hz), 3.39 (br. s, -N*H*$_2$, 2 H), 2.18-1.92 (m, -O-CH_2-C*H*$_2$-, 2 H), 1.87-1.56 (m, -C*H*$_2$-, 2 H), 1.54-1.15 (m, -(C*H*$_2$)$_6$-, 12 H).



p-N-Phthalimidobutyloxy nitrobenzene **28**:

A suspension of *p*-nitrophenol (2.02 g, 14.52 mmol), potassium carbonate (2.21 g, 15.97 mmol) and brombutylphthalimide (4.51 g, 15.97 mmol) in acetonitrile (80 ml) was refluxed for 24 hours. Then potassium carbonate was filtered from the hot reaction mixture off, washed with hot acetonitrile. The solvent was evaporated from the filtrate and the oily residue was recrystallized from acetonitrile (50 ml) to give the product as white needles. Yield: 4.15 g (84%).

m.p. 120°C; MS (FD): m/z 340.3 (M^+); ^{1}H NMR ($CDCl_3$): δ 8.16 (d, Ar-*H*, 2 H, $^3J_{HH}$ 8.8 Hz), 7.89-7.78 (m, Ar-*H*, 2 H), 7.77-7.65 (m, Ar-*H*, 2 H), 6.91 (d, Ar-*H*, 2 H, $^3J_{HH}$ 8.8 Hz), 4.08 (br.t, -O-C*H*$_2$-, 2 H), 3.77 (br.t, -O-C*H*$_2$-, 2 H), 1.97-1.78 (m, 4 H, -C*H*$_2$-).

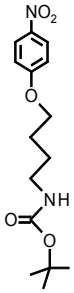


p-Aminobutyloxy nitrobenzene **29**:

Slurry of *p*-phthalimidobutyloxy nitrobenzene (1.00 g, 2.92 mmol), hydrazine-hydrate (7.2 ml, 146.91 mmol) in ethanol (50 ml) was refluxed for 4 hours. Then the solvent was removed under reduced pressure, the product was extracted from the residue by dichloromethane, washed with sodium hydroxide water solution and with water, separated and dried ($MgSO_4$). Dichloromethane was removed under reduced pressure to give an appropriate amine as a yellow solid which was used for the next step without further purification. Yield: 0.50 g (80%).

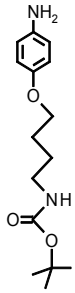
m.p. 40°C; MS (FD): m/z 210.1 (M^+); ^{1}H NMR ($CDCl_3$): δ 8.18 (d, Ar-*H*, 2 H, $^3J_{HH}$ 9.2 Hz), 6.93 (d, Ar-*H*, 2 H, $^3J_{HH}$ 9.2 Hz), 4.06 (t, -O-C*H*$_2$-, 2 H, $^3J_{HH}$ 6.2 Hz), 2.80 (t, -C*H*$_2$-NH_2, 2 H, $^3J_{HH}$ 6.8 Hz), 1.93-1.57 (m, -C*H*$_2$-, N-*H*$_2$, 6 H).

p-tert-Butyloxycarbonylamidobutyloxy nitrobenzene **30**:



The solution of p-aminobutyloxy nitrobenzene (1.50 g, 7.13 mmol) and Boc-anhydride (1.56 g, 7.13 mmol) in THF (80 ml) was stirred at rt for 24 h. Then the solvent was evaporated from the reaction mixture to give an oily residue, which solidified after drying at vacuum (oil pump). The solid was triturated with hexane, filtered off and dried to give the *N*-Boc-protected product as yellowish powder. Yield: 1.87 g (84%).

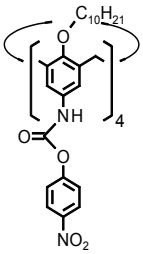
m.p. 58-60°C; MS (FD): m/z 310.1 (M^+); ^{1}H NMR ($CDCl_3$): δ 8.18 (d, Ar-*H*, 2 H, $^3J_{HH}$ 9.2 Hz), 6.93 (d, Ar-*H*, 2 H, $^3J_{HH}$ 9.2 Hz), 4.57 (br.s, -N*H*-, 1 H), 4.06 (t, -O-CH_2-, 2 H, $^3J_{HH}$ 6.2 Hz), 3.25-3.13 (m, -CH_2-NH-, 2 H), 1.90-1.80 (m, -CH_2-, 2 H), 1.72-1.62 (m, -CH_2-, 2 H), 1.43 (s, -CH_3, 9 H).



p-tert-Butyloxycarbonylamidobutyloxy aniline **31**:

A solution of *p-tert*-butyloxycarbonylamidobutyloxy nitrobenzene (1.80 g, 5.80 mmol) in toluene (50 ml) was vigorously stirred in hydrogen atmosphere at rt in the presence of catalytic amount of Raney-Ni for 6-8 hours (a degree of conversion was controlled by TLC). Then the catalyst was filtered off and the solvent was removed in vacuum to give pure aniline as yellowish solid. Yield: 1.38 g (85%).

m.p. 46-47°C; MS (FD): m/z 280.1 (M^+); ^{1}H NMR ($CDCl_3$): δ 6.72 (d, Ar-*H*, 2 H, $^3J_{HH}$ 8.7 Hz), 6.62 (d, Ar-*H*, 2 H, $^3J_{HH}$ 8.5 Hz), 4.62 (br.s, N-*H*, 1 H), 3.88 (t, -O-CH_2-, 2 H, $^3J_{HH}$ 6.1 Hz), 3.40 (br.s, N-H_2, 2 H), 3.25-3.07 (m, -CH_2-, 2 H), 1.86-1.54 (m, -CH_2-, 4 H), 1.43 (s, -CH_3, 9 H).

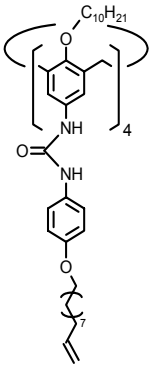


Calix[4]arene **34**:

A solution of tetraamine **Ia** (2.00 g, 1.91 mmol) in THF (15 ml) was added to the stirred solution of 4-nitrophenylchloroformate (2.55 g, 12.63 mmol) in $CHCl_3$ (22 ml). Then the reaction mixture was refluxed for 12 hours. After the solvent was evaporated in *vacuo*, the residue was triturated with ethylacetate and stored in a refrigerator for 4-8 hours. The solid was filtered off, washed with ethylacetate and dried to give pure product as light-yellow powder. Yield: 2.65 g (81%).

m.p. 181°C; MS (FD): m/z 1706.0 (M^+); ^{1}H NMR (DMSO-d_6): δ 9.93 (s, N-*H*, 4 H), 8.18 (d, Ar-*H*, 8 H, $^3J_{HH}$ 7.0 Hz), 7.35 (d, Ar-*H*, 8 H, $^3J_{HH}$ 6.6 Hz), 6.90 (s, Ar-*H*, 8 H), 4.33 (d, Ar-CH_2-Ar, 4 H, $^2J_{HH}$ 10.6 Hz), 3.78 (br.s, -O-CH_2-, 8 H), 3.08 (d, Ar-CH_2-Ar, 4 H, $^2J_{HH}$ 10.3

Hz), 1.87 (br.s, -O-CH_2-CH_2-, 8 H), 1.54-1.03 (m, -CH_2-, 56 H), 0.84 (t, -CH_3, 12 H, $^3J_{HH}$ 6.8 Hz).

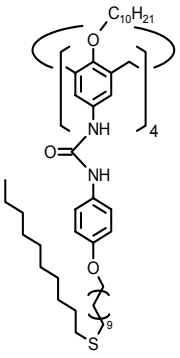


Calix[4]arene **35c**:

To a stirred solution of active urethane **34** (0.72 g, 0.42 mmol) in DMF (15 ml) in one portion aniline **33** (0.50 g, 1.90 mmol) and diisopropylethylamine (0.27 g, 2.11 mmol) in DMF (20 ml) were added and then the mixture was stirred at room temperature for 24 hours. Then the reaction mixture was partitioned between $CHCl_3$ and H_2O. The organic layer was washed 2 times with sodium carbonate water solution, 2 times with H_2O, dried over $MgSO_4$ and the solvent was removed in vacuum. The oily residue was treated with acetonitrile to give solid colourless product, which was filtered off and washed several times with acetonitrile to give analytically pure product as white powder. Yield: 0.63 g (68%).

m.p. : 155°C (decomp.); MS (ESI): m/z 2217.7 ($M+Na^+$); ^{1}H NMR (DMSO-d_6, 80°C): δ 7.89 (s, N-*H*, 4 H), 7.84 (s, N-*H*, 4 H), 7.21 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.7 Hz), 6.80 (s, Ar-*H*, 8 H), 6.77 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.7 Hz), 5.87-5.73 (m, C*H*=CH_2, 4 H), 5.04-4.87 (m, CH=CH_2, 8 H), 4.38 (d, Ar-CH_2-Ar, 4 H, $^2J_{HH}$ 12.6 Hz), 3.97-3.81 (m, -O-CH_2-, 16 H), 3.09 (Ar-CH_2-Ar, 4 H, $^2J_{HH}$ 12.9 Hz), 2.07-1.97 (m, -O-CH_2-CH_2-, 8 H), 1.96-1.83 (m, -O-CH_2-CH_2-, 8 H), 1.74-1.62 (m, -CH_2-, 8 H), 1.49-1.19 (m, -CH_2-, 104 H), 0.88 (br.t, -CH_3, 12 H).

(35c)$_2$ *:* ^{1}H NMR ($CDCl_3$): δ 9.22 (s, N-*H*, 8 H), 7.71 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.8 Hz), 7.60 (d, Ar-*H*, 8 H, $^2J_{HH}$ 2.4 Hz), 7.02 (s, N-*H*, 8 H), 6.87 (d, Ar-*H*, 16 H, $^3J_{HH}$ 8.8 Hz), 5.94 (d, Ar-*H*, 8 H, $^2J_{HH}$ 2.4 Hz), 5.86-5.74 (m, C*H*=CH_2, 8 H), 5.02-4.88 (m, CH=CH_2, 16 H), 4.20 (d, Ar-CH_2-Ar, 8 H, $^2J_{HH}$ 11.2 Hz), 3.94-3.82 (m, -O-CH_2-, 16 H), 3.64 (br.t, -O-CH_2-, 16 H, $^3J_{HH}$ 8.1 Hz), 2.81 (d, Ar-CH_2-Ar, 8 H, $^2J_{HH}$ 11.7 Hz), 2.07-1.99 (m, -CH_2-, 16 H), 1.98-1.87 (m, -CH_2-, 16 H), 1.78-1.67 (m, -CH_2-, 16 H), 1.48-1.19 (m, -CH_2-, 208 H), 0.88 (t, -CH_3, 24 H, $^3J_{HH}$ 6.8 Hz).



Calix[4]arene **38**:

A solution of tetra-*p*-undecenyloxyphenylurea calixarene **35c** (0.31 g, 0.14 mmol), 1-decanethiol (0.30 g, 1.70 mmol) in THF (10 ml) was degassed with nitrogen and cooled to 0-5°C. Then 0.5 M solution of 9-BBN in THF (0.2 ml, 0.1 mmol) was added to the reaction mixture and it was stirred for 24 h during these time it was allowed to warm to rt. The solvent was evaporated and the residue was triturated with acetonitrile. The solid was filtered off and dried to give pure sulfide product as white powder. Yield: 0.25 g (60%).

m.p. 104°C (decomp.); MS (ESI): m/z 2915.4 ($M+Na^+$), 1469.2 ($M+2Na^+$); ^{1}H NMR ($DMSO\text{-}d_6/CDCl_3$): δ 8.02 (s, N-*H*, 8 H), 7.18 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.8 Hz), 6.76 (s, Ar-*H*, 8 H), 6.71 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.8 Hz), 4.33 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 12.7 Hz), 4.00-3.59 (m, -O-C*H*$_2$-, 16 H), 3.04 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 11.7 Hz), 2.41 (t, -S-C*H*$_2$-, 16 H), 1.90 (m, 8 H, -O-CH$_2$-C*H*$_2$-), 1.77-0.99 (m, -C*H*$_2$-, 192 H), 0.96-0.70 (m, -C*H*$_3$, 24 H).

***(38)*$_2$:** ^{1}H NMR ($CDCl_3$): δ 9.22 (s, N-*H*, 8 H), 7.71 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.2 Hz), 7.60 (s, Ar-*H*, 8 H), 7.02 (s, N-*H*, 8 H), 6.87 (d, Ar-*H*, 16 H, $^3J_{HH}$ 8.2 Hz), 5.94 (s, Ar-*H*, 8 H), 4.21 (d, Ar-C*H*$_2$-Ar, 8 H, $^2J_{HH}$ 11.0 Hz), 3.99-3.79 (m, -O-C*H*$_2$-, 16 H), 3.64 (br.t, -O-C*H*$_2$-, 16 H), 2.81 (d, Ar-C*H*$_2$-Ar, 8 H, $^2J_{HH}$ 11.0 Hz), 2.48 (t, -S-C*H*$_2$-, 32 H, $^3J_{HH}$ 7.0 Hz), 2.03-1.84 (m, -C*H*$_2$-, 16 H), 1.81-1.65 (m, -C*H*$_2$-, 16 H), 1.65-1.02 (m, -C*H*$_2$-, 368 H), 1.00-0.75 (m, -C*H*$_3$, 48 H).

Heterodimer ***38*****:*****9****:*

^{1}H NMR (C_6D_6): δ 11.10 (s, N-*H*, 4 H), 8.66 (s, N-*H*, 4 H), 8.56 (s, Ar-*H*, 4 H), 8.53 (s, N-*H*, 4 H), 8.19 (d, Ar-*H*, 8 H, $^3J_{HH}$ 7.8 Hz), 7.96 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.8 Hz), 7.85 (s, N-*H*, 4 H), 7.77 (s, Ar-*H*, 4 H), 7.51 (s, Ar-*H*, 4 H), 6.78 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.3 Hz), 6.68 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.8 Hz), 5.55 (s, Ar-*H*, 4 H), 4.92 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 11.2 Hz), 4.28 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 11.2 Hz), 4.07 (t, -O-C*H*$_2$-, 8 H, $^3J_{HH}$ 7.6 Hz), 3.96 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 11.7 Hz), 3.57 (t, -O-C*H*$_2$-, 8 H, $^3J_{HH}$ 7.8 Hz), 3.53-3.43 (m, -O-C*H*$_2$-, 4 H), 3.43-3.32 (m, -O-C*H*$_2$-, 4 H), 3.01 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 11.7 Hz), 2.50-2.39 (m, -S-C*H*$_2$-, 16 H), 2.38-2.25 (m, -C*H*$_2$-, 8 H), 2.02-1.90 (m, -C*H*$_2$-, 8 H), 1.85 (s, -C*H*$_3$, 12 H), 1.69-1.09 (m, -C*H*$_2$-, 208 H), 1.03-0.95 (m, -C*H*$_3$, 24 H), 0.92 (t, -C*H*$_3$, 12 H, $^3J_{HH}$ 7.1 Hz).

Heterodimer ***38*****:*****10b****:*

^{1}H NMR (C_6D_6): δ 10.08 (s, N-*H*, 4 H), 9.75 (s, N-*H*, 4 H), 8.22 (s, Ar-*H*, 4 H), 8.17 (s, Ar-*H*, 4 H), 8.08 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.8 Hz), 7.97 (s, Ar-*H*, 4 H), 7.49 (s, N-*H*, 4 H), 7.27 (s, Ar-*H*, 4 H), 7.01 (s, N-*H*, 4 H), 6.84 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.3 Hz), 6.54 (s, Ar-*H*, 4 H), 6.36 (s, Ar-*H*, 4 H), 6.31 (s, Ar-*H*, 4 H), 4.45 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 11.7 Hz), 4.32 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 11.7 Hz), 4.15-3.40 (m, -O-C*H*$_2$-, -O-C*H*$_3$, 44 H), 3.33-3.08 (m, Ar-C*H*$_2$-Ar, 8 H), 2.43 (m, -S-C*H*$_2$-, 16 H), 2.15-1.94 (m, -C*H*$_2$-, 8 H), 1.80-1.04 (m, -C*H*$_2$-, 256 H), 1.03-0.82 (m, -C*H*$_3$, 24 H).

Complex of ***(38)$_2$*** *and cobaltocenium :*

^{1}H NMR (CD_2Cl_2): δ 9.03 (s, N-*H*, 8 H), 7.75 (d and s overlapped, Ar-*H*, 24 H, $^3J_{HH}$ 8.4 Hz), 6.99 (d, Ar-*H*, 16 H, $^3J_{HH}$ 8.8 Hz), 6.74 (s, N-*H*, 8 H), 5.64 (br.s, Ar-*H*, 8 H), 4.34 (d, Ar-C*H*$_2$-Ar, 8 H, $^2J_{HH}$ 11.7 Hz), 3.98-3.82 (m, -O-C*H*$_2$-, 16 H), 3.74 (t, -O-C*H*$_2$-, 16 H, $^3J_{HH}$ 7.1 Hz), 2.93 (d, Ar-C*H*$_2$-Ar, 8 H, $^2J_{HH}$ 11.7 Hz), 2.82 (s, included cobaltocenium, 10 H), 2.48 (t, -S-C*H*$_2$-, 32 H, $^3J_{HH}$ 7.1 Hz), 2.00-1.86 (m, -C*H*$_2$-, 16 H), 1.78-1.66 (m, -C*H*$_2$-, 16 H), 1.62-1.48 (m under water peak, -C*H*$_2$-, 16 H), 1.48-1.14 (m, -C*H*$_2$-, 352 H), 0.98-0.82 (m, -C*H*$_3$, 48 H).

Complex of ***(38)$_2$*** *and tetraethylammonium :*

^{1}H NMR (CD_2Cl_2): δ 8.95 (s, N-*H*, 8 H), 7.79 (d and s overlapped, Ar-*H*, 24 H, $^3J_{HH}$ 9.3 Hz), 7.00 (d, Ar-*H*, 16 H, $^3J_{HH}$ 8.8 Hz), 6.36 (s, N-*H*, 8 H), 5.61 (br.s, Ar-*H*, 8 H), 4.33 (d, Ar-C*H*$_2$-Ar, 8 H, $^2J_{HH}$ 11.7 Hz), 3.90 (m, -O-C*H*$_2$-, 16 H, $^3J_{HH}$ 6.1 Hz), 3.76 (t, -O-C*H*$_2$-, 16 H, $^3J_{HH}$ 8.1 Hz), 2.97 (d, Ar-C*H*$_2$-Ar, 8 H, $^2J_{HH}$ 12.2 Hz), 2.47 (t, -S-C*H*$_2$-, 32 H, $^3J_{HH}$ 7.3 Hz), 2.03-1.86 (m, -C*H*$_2$-, 16 H), 1.78-1.64 (m, -C*H*$_2$-, 16 H), 1.62-1.48 (m under water peak, -C*H*$_2$-, 16 H), 1.48-1.17 (m, -C*H*$_2$-, 352 H), 1.14 (br.s, included Et_4N^+, N-C*H*$_2$-, 4 H), 0.98-0.82 (m, -C*H*$_3$, 48 H), 0.50 (br.s, included Et_4N^+, N-C*H*$_2$-, 4 H), -0.15 (br.s, included Et_4N^+, N-C*H*$_3$, 6 H), -3.29 (br.s, included Et_4N^+, N-C*H*$_3$, 6 H).

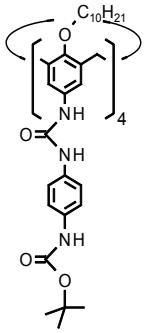
Complex of heterodimer ***38*****:*****9*** *and cobaltocenium :*

^{1}H NMR (CD_2Cl_2): δ 11.16 (s, N-*H*, 4 H), 8.40 (s, N-*H*, 4 H), 8.14 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.3 Hz), 7.93 (s, N-*H*, 4 H), 7.84 (br.s, Ar-*H*, 4 H), 7.59 (d, Ar-*H*, 8 H, $^3J_{HH}$ 9.3 Hz), 7.53 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.3 Hz), 7.50 (s, N-*H*, 4 H), 7.11 (br.s, Ar-*H*, 4 H), 7.00 (br.s, Ar-*H*, 4 H), 6.69 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.8 Hz), 4.86 (br.s, Ar-*H*, 4 H), 4.64 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 11.7 Hz), 4.09 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 11.7 Hz), 4.04-3.87 (m, -O-C*H*$_2$-, 8 H), 3.80-3.65 (m, -O-C*H*$_2$-, 8 H), 3.56 (t, -O-C*H*$_2$-, 8 H, $^3J_{HH}$ 7.8 Hz), 3.37 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 12.2 Hz), 3.05 (s, included cobaltocenium, 10 H), 2.69 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 11.7 Hz), 2.53 (s, -C*H*$_3$, 12 H), 2.52-2.44 (t 2.49 and t 2.48 overlapped, -S-C*H*$_2$-, 16 H, $^3J_{HH}$ 7.3 Hz and $^3J_{HH}$ 7.3 Hz), 2.14-2.00 (m, -C*H*$_2$-, 8 H), 2.85-1.72 (m, -C*H*$_2$-, 8 H), 1.66-1.49 (m, -C*H*$_2$-, 8 H), 1.48-1.16 (m, -C*H*$_2$-, 200 H), 1.00-0.78 (m, -C*H*$_3$, 36 H).

Complex of heterodimer ***38*****:*****10b*** *and cobaltocenium:*

^{1}H NMR (CD_2Cl_2): δ 9.14 (s, N-*H*, 4 H), 9.01 (s, N-*H*, 4 H), 7.81 (s, Ar-*H*, 4 H), 7.79 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.8 Hz), 7.67 (s, Ar-*H*, 4 H), 7.44 (s, Ar-*H*, 4 H), 7.06 (s, N-*H*, 4 H), 7.03 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.8 Hz), 6.71 (s, Ar-*H*, 4 H), 6.52 (s, N-*H*, 4 H), 6.19 (s, Ar-*H*, 4 H), 5.68 (s, Ar-*H*, 4 H), 5.43 (s, Ar-*H*, 4 H), 4.25 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 11.7 Hz), 4.27 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 11.7 Hz), 4.09-3.61 (m, -O-C*H*$_2$-, -O-C*H*$_3$, 44 H), 2.98 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$

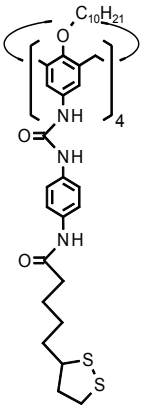
12.1 Hz), 2.86-2.73 (d and s of included cobaltocenium overlapped, Ar-CH_2-Ar, 14 H), 2.48 (m, -S-CH_2-, 16 H, $^3J_{HH}$ 6.6 Hz), 1.99-1.65 (m, -CH_2-, 32 H), 1.62-0.98 (m, -CH_2-, 232 H), 0.97-0.80 (m, -CH_3, 24 H).



Calix[4]arene **35a**:

Prepared as described above for **35c** from active urethane **34** (0.132 g, 0.0774 mmol), di-*iso*-propylethylamine (0.050 g, 0.387 mmol), *N*-Boc-1,4-phenylene diamine (0.081 g, 0.387 mmol), DMF (5 ml); reprecipitation from THF/methanol. Yield: 0.137 g (89%).

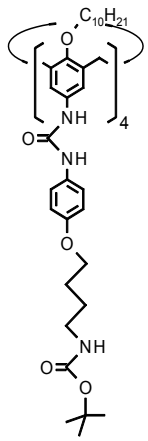
m.p. >195°C (decomp.); MS (ESI): m/z 2005.3 (M+Na^+), 1014.2 (M+2Na^+); ^{1}H NMR (DMSO-d_6): δ 9.11 (s, N-*H*, 4 H), 8.17 (s, N-*H*, 4 H), 8.12 (s, N-*H*, 4 H), 7.29 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.4 Hz), 7.21 (d, Ar-*H*, 8 H, $^3J_{HH}$ 9.2 Hz), 6.78 (s, Ar-*H*, 8 H), 4.31 (d, Ar-CH_2-Ar, 4 H, $^2J_{HH}$ 12.1 Hz), 3.80 (broad t, -O-CH_2-, 8 H), 3.08 (d, Ar-CH_2-Ar, 4 H, $^2J_{HH}$ 12.5 Hz), 1.90 (m, 8 H, -O-CH_2-CH_2-), 1.45 (s, 36 H, -CH_3), 1.42-1.15 (m, 56 H, -CH_2-), 0.85 (br.t, -CH_3, 12 H).



Calix[4]arene **36b**:

A solution of calixarene **35a** (0.137 g, 0.0691 mmol) in dichloromethane (10 ml) and trifluoroacetic acid (4 ml) was stirred at rt for 2 h. Then the solvent was evaporated and the residue was triturated with Et_2O. A solid was filtered off, washed with Et_2O and dried to give an appropriate tetraammonium salt which was dissolved in THF (10 ml), treated with an excess of Et_3N (0.5 ml) and with *α*-lipoic acid anhydride which was prepared from *α*-lipoic acid (0.071 g, 0.345 mmol) and DCC (0.036 g, 0.173 mmol) in benzene (5 ml) as described.[23] The reaction mixture was stirred at rt for 2 h. Then the solvent was removed in vacuum, the residue was triturated with methanol and a solid was filtered off, dried to give pure product as yellowish powder. Yield: 0.120 g (74%).

m.p. >190°C (decomp.); MS (ESI): m/z 2358.3 (M+Na^+), 1190.7 (M+2Na^+); ^{1}H NMR (DMSO-d_6): δ 9.07 (s, N-*H*, 4 H), 8.23 (s, N-*H*, 4 H), 8.14 (s, N-*H*, 4 H), 7.43 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.8 Hz), 7.25 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.4 Hz), 6.79 (s, Ar-*H*, 8 H), 4.31 (d, Ar-CH_2-Ar, 4 H, $^2J_{HH}$ 11.0 Hz), 3.90 (m, -O-CH_2-, 8 H), 3.90 (m, -S-C*H*-, 4 H), 3.23-2.97 (m, -S-CH_2-, Ar-CH_2-Ar, 12 H), 2.50-2.35 (m, -CH_2-, 8 H), 2.26 (br.t, -CH_2-C(O)-, 8 H), 2.02-1.80 (m, -CH_2-, 8 H), 1.78-1.48 (m, -CH_2-, 16 H), 1.49-1.14 (m, -CH_2-, 64 H), 0.85 (br.t, -CH_3, 12 H).

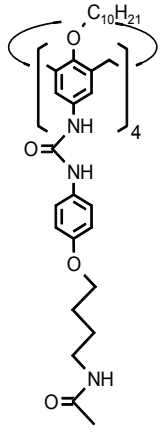


Calix[4]arene **35b**:

Prepared as described above for **35c** from active urethane **34** (0.195 g, 0.114 mmol), di-*iso*-propylethylamine (0.070 g, 0.510 mmol), aniline **31** (0.130 g, 0.464 mmol), DMF (10 ml); reprecipitation from THF/acetonitrile. Yield: 0.195 g (75%).

m.p. >165°C (decomp.); MS (ESI): m/z 2293.6 ($M+Na^+$), 1158.3 ($M+2Na^+$); ^{1}H NMR (DMSO-d_6): δ 8.11 (s, N-*H*, 4 H), 8.09 (s, N-*H*, 4 H), 7.21 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.9 Hz), 6.88-6.69 (m, Ar-*H*, N-*H*, 20 H), 4.31 (d, Ar-CH_2-Ar, 4 H, $^2J_{HH}$ 11.9 Hz), 3.87 (t, -O-CH_2-, 8 H, $^3J_{HH}$ 6.3 Hz), 3.79 (br.t, -O-CH_2-, 8 H), 3.07 (d, Ar-CH_2-Ar, 4 H, $^2J_{HH}$ 12.3 Hz), 3.02-2.87 (m, -NH-CH_2-, 8 H), 1.90 (m, -O-CH$_2$-CH_2-, 8 H), 1.70-1.58 (m, -CH_2-, 8 H), 1.56-1.16 (m and s (1.36) overlapped, -CH_2-, -CH_3, 100 H), 0.85 (br.t, -CH_3, 12 H, $^3J_{HH}$ 6.3 Hz).

(35b)$_2$: ^{1}H NMR ($CDCl_3$): δ 9.20 (s, N-*H*, 8 H), 7.70 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.9 Hz), 7.60 (s, Ar-*H*, 8 H), 7.03 (s, N-*H*, 8 H), 6.87 (d, Ar-*H*, 16 H, $^3J_{HH}$ 8.9 Hz), 5.96 (s, Ar-*H*, 8 H), 4.59 (br.s, N-*H*, 8 H), 4.22 (d, Ar-CH_2-Ar, 8 H, $^2J_{HH}$ 11.6 Hz), 3.97-3.85 (m, -O-CH_2-, 16 H), 3.65 (t, -O-CH_2-, 16 H, $^3J_{HH}$ 7.8 Hz), 3.24-3.06 (m, -NH-CH_2-16 H), 2.82 (d, Ar-CH_2-Ar, 8 H, $^2J_{HH}$ 11.9 Hz), 2.02-1.87 (m, -CH_2-, 16 H), 1.84-1.71 (m, -CH_2-, 16 H), 1.69-1.53 (m, -CH_2-, 16 H), 1.43 (s, -CH_3, 72 H), 1.38-1.19 (m, -CH_2-, 112 H), 0.88 (t, -CH_3, 24 H, $^3J_{HH}$ 6.8 Hz).

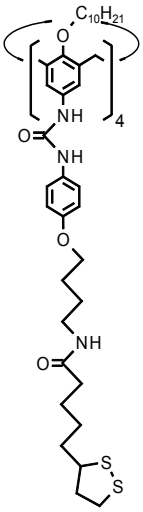


Calix[4]arene **37a**:

A solution of calixarene **35b** (0.100 g, 0.0440 mmol) in dichloromethane (10 ml) and trifluoroacetic acid (1 ml) was stirred at rt for 2 h. Then the solvent was evaporated and the residue was dissolved in THF (15 ml), treated with an excess of di-*iso*-propylethylamine (0.114 g, 0.880 mmol) and with acetic anhydride (0.045 g, 0.440 mmol). The reaction mixture was stirred 12 h at rt and then the solvent was removed in vacuum. The oily residue was triturated with acetonitrile; the solid was filtered off and dried to give pure product as white powder. Yield: 0.083 g (93%).

m.p. >150°C (decomp.); MS (ESI): m/z 2061.4 ($M+Na^+$), 1042.2 ($M+2Na^+$); ^{1}H NMR (DMSO-d_6): δ 8.13 (s, N-*H*, 4 H), 8.11 (s, N-*H*, 4 H), 7.82 (br.t, N-*H*, 4 H, $^3J_{HH}$ 5.1 Hz), 7.22 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.8 Hz), 6.86-6.71 (m, Ar-*H*, 16 H), 4.31 (d, Ar-CH_2-Ar, 4 H, $^3J_{HH}$ 12.2 Hz), 3.88 (t, -O-CH_2-, 8 H, $^3J_{HH}$ 6.4 Hz), 3.79 (br.t, -O-CH_2-, 8 H), 3.14-3.00 (m, -NH-CH_2-, Ar-CH_2-Ar, 12 H), 1.98-1.84 (m, -CH_2-, 8 H), 1.78 (s, -CH_3, 12 H), 1.72-1.60 (m, -CH_2-, 8

H), 1.57-1.46 (m, -CH_2-, 8 H), 1.46-1.17 (m, -CH_2-, 52 H), 0.86 (br.t, -CH_3, 12 H, $^3J_{HH}$ 6.6 Hz).



Calix[4]arene **37b**:

Prepared as described above for **36b** from calixarene **35b** (0.195 g, 0.0859 mmol), *α*-lipoic acid (0.100 g, 0.504 mmol) and DCC (0.050 g, 0.252 mmol) in benzene (5 ml) and THF (8 ml). The oily product was triturated with acetonitrile; a solid was filtered off and dried to give pure product as white powder. Yield: 0.156 g (59%).

m.p. >145°C (decomp.); MS (MALDI-TOF): m/z 2623.4 (M^+); ^{1}H NMR (DMSO-d_6): δ 8.12 (s, N-*H*, 4 H), 8.09 (s, N-*H*, 4 H), 7.78 (br.t, N-*H*, 4 H), 7.22 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.2 Hz), 6.94-6.63 (m, Ar-*H*, 16 H), 4.43-4.17 (br.d, Ar-CH_2-Ar, 4 H), 3.97-3.66 (m, -O-CH_2-, 16 H), 3.58 (m, -S-C*H*-, 4 H), 3.20-2.89 (m, -S-CH_2-, Ar-CH_2-Ar, 12 H), 2.50-2.28 (m, -CH_2-, 8 H), 2.04 (br.t, -CH_2-C(O)-, 8 H), 1.96-1.74 (m, -CH_2-, 8 H), 1.73-1.05 (m, -CH_2-, 80 H), 0.85 (br.t, -CH_3, 12 H).

*Heterodimer **37b**:tosylurea **9**:*

^{1}H NMR (TCE): δ 10.62 (s, N-*H*, 4 H), 8.12 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.0 Hz), 8.02 (s, N-*H*, 4 H), 7.91 (s, N-*H*, Ar-*H*, 8 H), 7.59 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.3 Hz), 6.50 (d, Ar-*H*, 8 H, $^3J_{HH}$ 8.4 Hz), 7.41 (s, N-*H*, 4 H), 6.98 (s, Ar-*H*, 8 H), 6.66 (d, Ar-*H*, 8 H, $^3J_{HH}$ 9.1 Hz), 7.48 (t, N-*H*, 4 H, $^3J_{HH}$ 5.6 Hz), 5.26 (s, Ar-*H*, 4 H), 4.54 (d, Ar-CH_2-Ar, 4 H, $^2J_{HH}$ 11.5 Hz), 4.09 (d, Ar-CH_2-Ar, 4 H, $^2J_{HH}$ 11.1 Hz), 4.01-3.65 (m, -O-CH_2-, 16 H), 3.65-3.48 (m, -O-CH_2-, -S-C**H*-, 8 H + 2 H), 3.38 (d, Ar-CH_2-Ar, 4 H, $^2J_{HH}$ 11.1 Hz), 3.32-3.08 (m, -NH-CH_2-,-S-CH_2-,-S-C**H*-, 18 H), 2.71 (d, Ar-CH_2-Ar, 4 H, $^2J_{HH}$ 12.5 Hz), 2.59-2.32 (m overlapped with s: 2.52, -CH_3, -CH_2-, 12 H + 8 H), 2.22-2.02 (m, -CH_2-, 16 H), 2.00-1.10 (m, -CH_2-, 120 H), 1.00-0.78 (m, -CH_3, 24 H).

3.6 Literature and comments

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[25] Immobilized encapsulated ferrocenium: Au, Pt, and Ag electrodes, scan rate = 0.5 V/s; electrolyte 0.06M $TBA^+PF_6^-$; encapsulated ferrocenium: Pt, Pt, and Ag electrodes, scan rate = 0.02 V/s; electrolyte 0.15M $TBA^+PF_6^-$; free ferrocenium: Pt, Pt, and Ag electrodes, scan rate = 0.02 V/s; electrolyte 0.15M $TBA^+PF_6^-$.

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Chapter 4

Self-assembled polymers based on *bis*-tetraurea calix[4]arenes connected via the wide rim

4.1 *Bis*-calix[4]arenes singly-bridged via the wide rim

Selective modification of calix[4]arenes[1] allowed the construction of multi-calixarenes. In Fig. 1 selected examples of double calix[4]arenes **39-42** singly-bridged via the wide rim are presented.

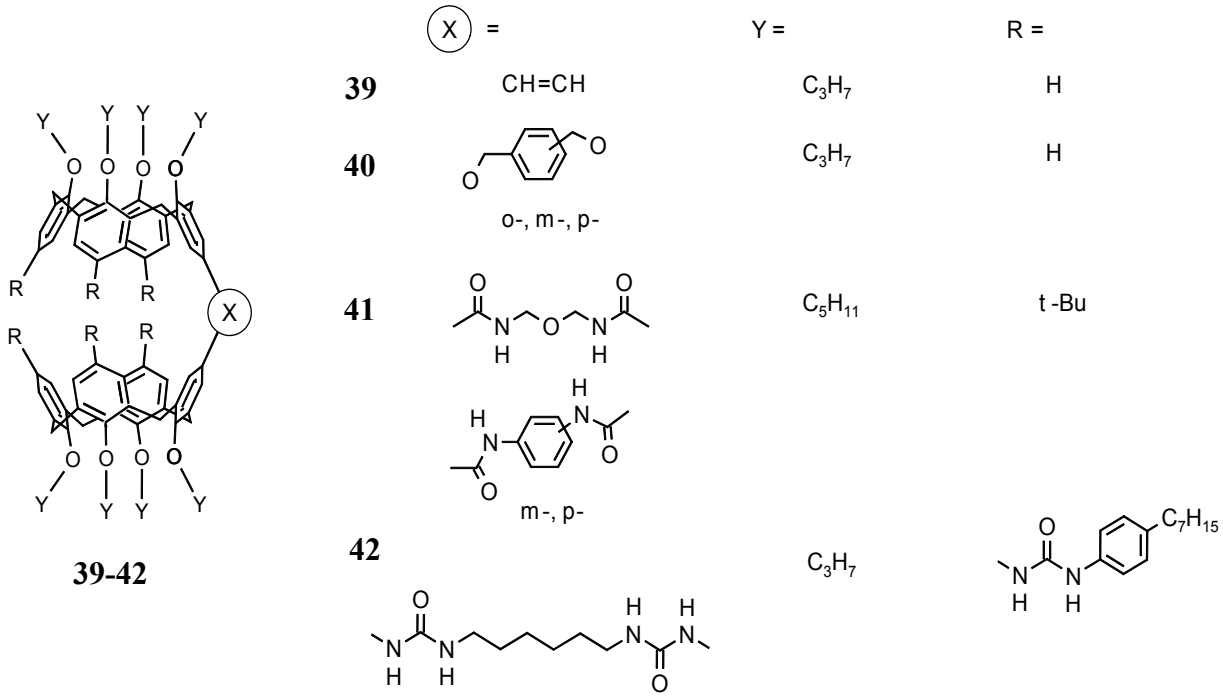


Figure 1. Examples for double calix[4]arenes **39-42** singly-bridged via the wide rim.

Calix[4]arenes mono-functionalized at their wide rim with amino-, formyl-, hydroxyl- or halogen-groups are most frequently used for the synthesis of these *bis*-calixarenes. Monoformyl calix[4]arene tetraether can be converted into the appropriate dimer **39** via reductive coupling in 35% yield.[2] Similar double calixarenes were achieved via a Stille cross-coupling of the monobromo calix[4]arene tripropylether with (E)-1,2-

bis(tributylstannyl)ethylene.[3] *Bis*-calixarenes **40** with aromatic spacers were prepared in moderate yields by alkylation of monohydroxy calix[4]arene tetrapropylether with *o*-, *m*- and *p*-*bis*-(bromomethyl)benzenes in DMF using NaH as a base.[4]

A single amino function at the wide rim can be easily introduced by controlled *ipso*-nitration of *p*-*tert*-butylcalix[4]arene tetraethers or by selective nitration of triethers and subsequent reduction. Various double calixarenes **41** (a couple of examples are shown in Fig. 1) were obtained by acylation of the monoamino calix[4]arene with diacid chlorides.[5]

Only one example of *bis*-tetraureacalix[4]arene linked via the urea functions (**42**) is known.[6] The synthesis started with the *p*-trinitrocalix[4]arene tetraether (by partial nitration) which was iodinated in the fourth *para*-position. Than iodine was substituted by phthalimide and hydrazinolysis of the latter gave an amino group. Two monoamino derivatives were bridged with 1,6-diisocyanatohexane producing the corresponding double calixarene in 33% yield. After reduction of the nitro groups followed by reaction with (*n*-heptyl)phenyl-isocyanate *bis*-tetraureacalixarene **42** was isolated in 48% yield. Nowadays, the synthesis of a compound like **42** could be done much easier by partial *N*-Boc-protection/deprotection of tetraamino calix[4]arene tetraether[7] (see in Chapter 4.3).

The ^{1}H NMR spectrum of **42** in $CDCl_3$ shows downfield shifts of the signals for NH protons of the urea functions which are characteristic for the dimerization (details see in Chapter 2.1). There are three possibilities for self-organization of this double calixarene (Fig. 2):

- *intra*-molecular dimerization,
- *inter*-molecular dimerization,
- polymerization.

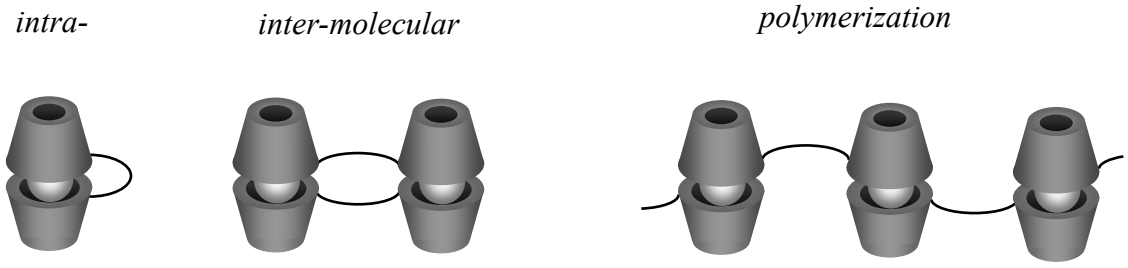


Figure 2. Possible kinds of self-assembly of **42**.

On the basis of ^{1}H NMR and ESI MS studies[8] of **42** it was concluded that the intramolecular dimer (Fig. 2a) is predominantly formed.

Bis-calixarene **42** self-assembles also with tetratosylurea calix[4]arene **9** in a way where each tetraurea calixarene counterpart of **42** forms a heterodimer with tetratosylurea (*bis*-heterodimer). When tetratolylurea calix[4]arene was mixed with **42** two structures were found: the homodimer of tetratolylurea and the intramolecular dimer of **42**, but no heterodimer.

The formation of linear polymeric structures by tetraurea dimerization, so-called "polycaps", was observed only from the double calix[4]arenes bridged via the narrow rim[9] (discussed in Chapter 5.1).

4.2 *Bis*-tetraurea calix[4]arenes preorganized for intermolecular interactions

We planned to synthesize *bis*-calixarenes linked via their urea functions which prefer an intermolecular interaction. Their self-assembly in apolar solvents must lead then to polymers (Fig. 3). The introduction of a rigid spacer between the calix[4]arene counterparts will prevent the undesired ways of self-organization. Since benzidine, di-(4,4'-amino) phenylacetylene and azodianiline are commercially available or could be easily prepared,[10] their diisocyanates or active diurethanes could be used for the synthesis of **43** (Fig. 4).

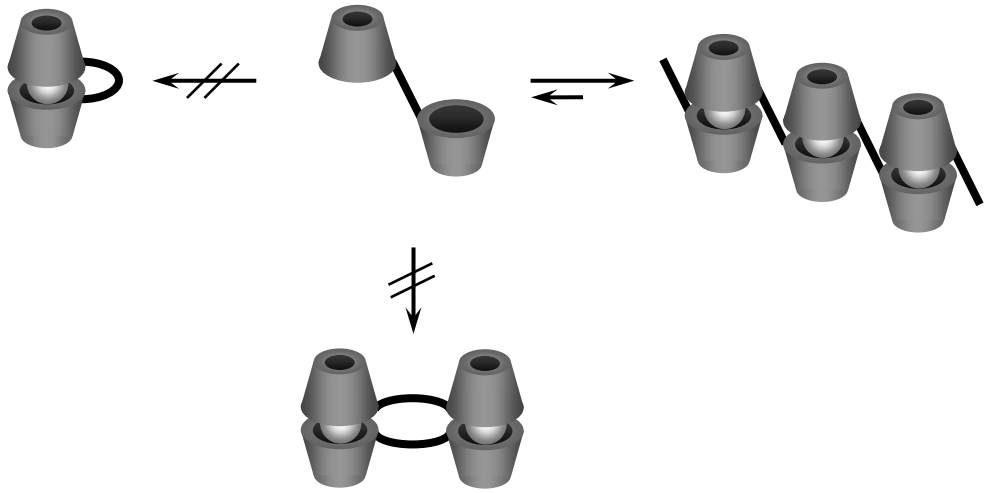


Figure 3. Schematical representation the expected self-organization of the target *bis*-calixarenes in apolar solvents.

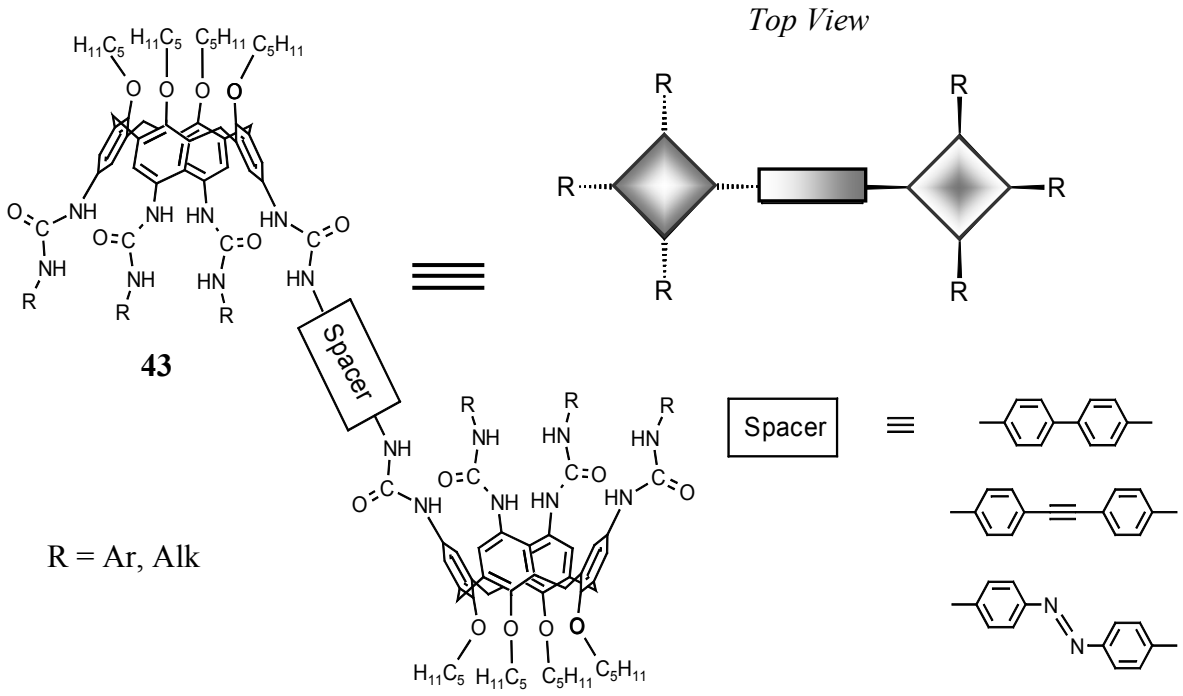


Figure 4. Schematical representation of the target *bis*-calix[4]arenes **43**.

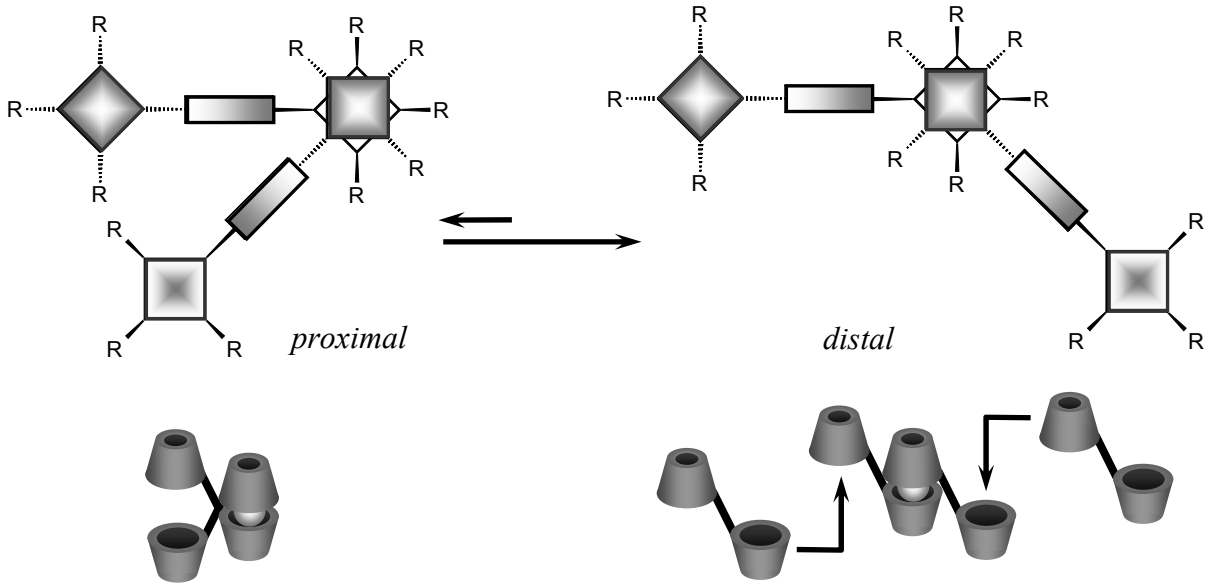
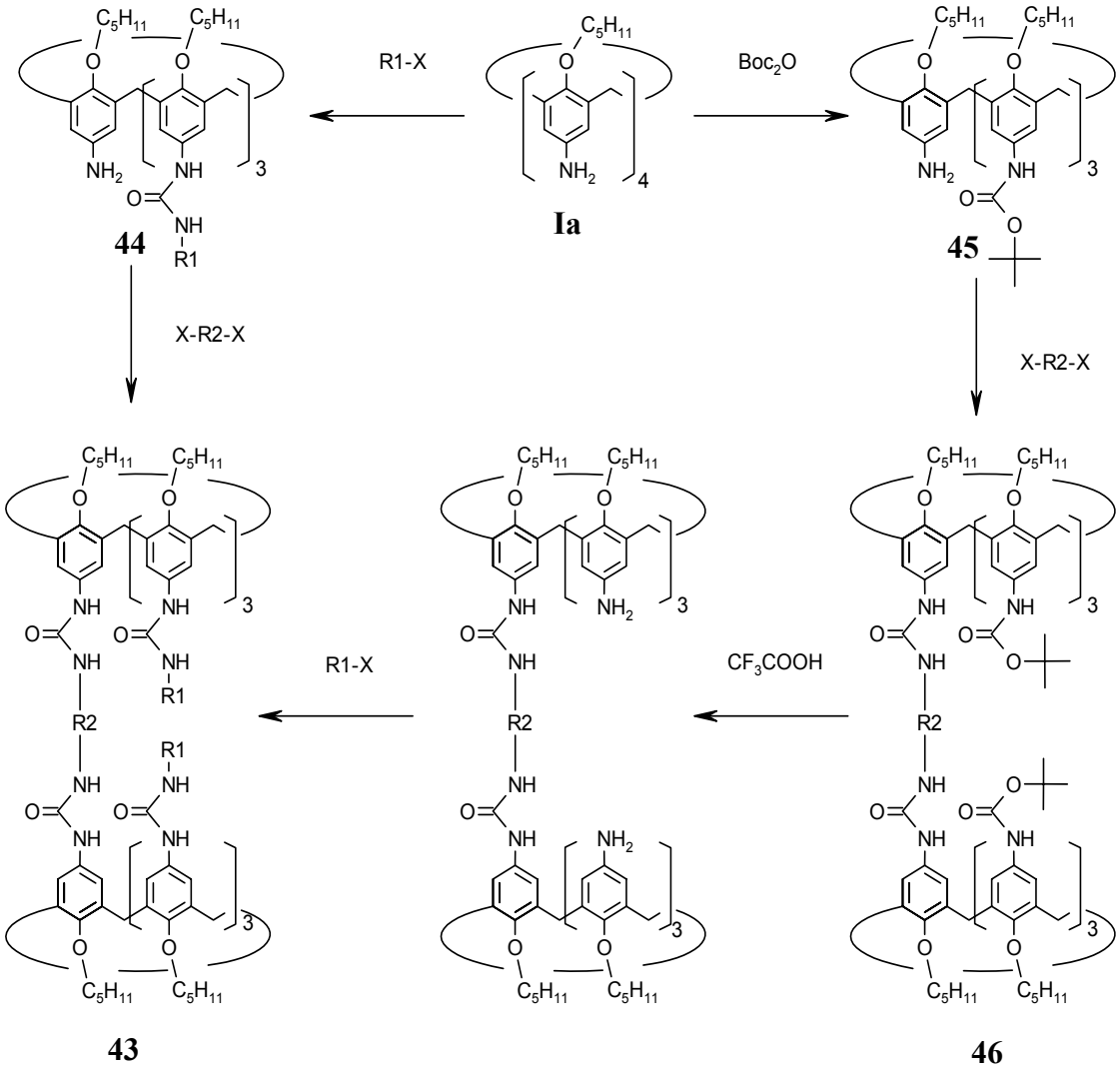


Figure 5. Possible arrangements of the *bis*-calixarene **43** molecules in the dimer.

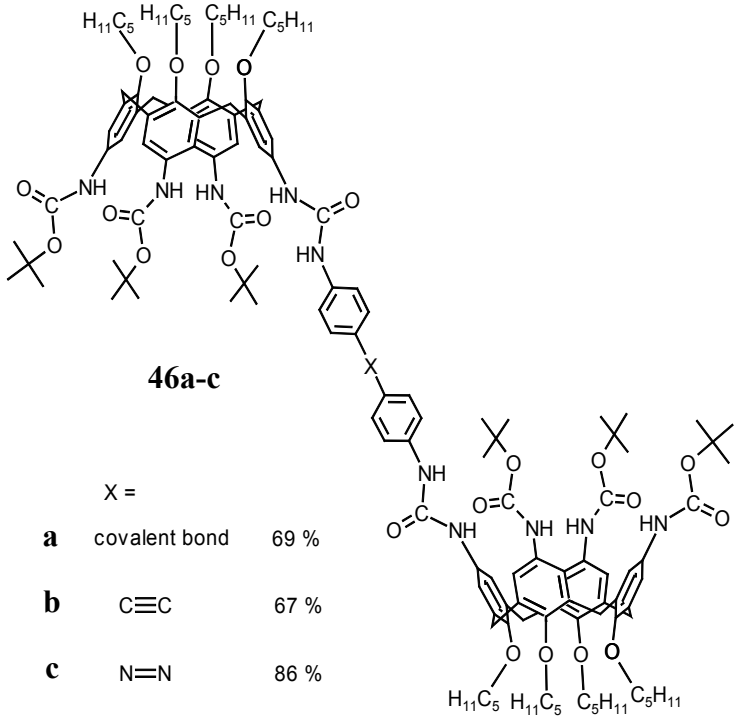
There are two possible arrangements of the *bis*-calixarene **43** molecules in the dimer: distal and proximal (Fig. 5). The angle of 45° (proximal) leads to reduced space between the *bis*-calixarene molecules within the dimer which makes the dimerization with the next molecule difficult. Obviously, the molecules of **43** should change their arrangement into one which is more suitable for further dimerization. This tendency should lead to the preference of the distal arrangement and to the angle of 135° between two *bis*-calixarene molecules.



Scheme 1. Two pathways to *bis*-calixarenes **43**. X = NCO or *p*-nitrophenyl urethane; R1 – variable residue; R2 – variable spacer.

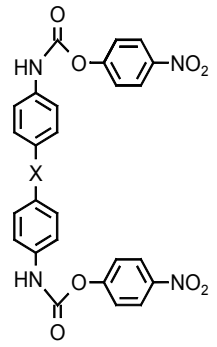
4.3 Synthesis

Bis-calix[4]arenes **43** can be prepared from tetraamino calix[4]arene tetraether **Ia** by stepwise mono- and tri-N-acylation with isocyanates or active urethanes. It can be performed in two ways (Scheme 1). One of the ways is statistical mono- or tri-N-protection with *tert*-butyloxycarbonyl (Boc) anhydride.[7] Since tri-Boc acylated product **45** can be prepared in higher yield (55%), than mono-Boc (36%), it is rational to base the synthesis on the tri-Boc derivative. **45** can be acylated with bifunctional reagent X-R2-X (X = NCO or *p*-nitrophenyl urethane) yielding *bis*-calixarene **46**. Boc-deprotection and acylation with R1-X should lead to **43**. A similar strategy has been used for the synthesis of tritolylurea monoacetamide calix[4]arene.[11] Another strategy uses directly a partial acylation of tetraamine **Ia** with R1-X followed by acylation with X-R2-X. The advantage of this procedure is the absence of protection-deprotection steps. Finally, both strategies were attempted.



46a-c

X =		
a	covalent bond	69 %
b	C≡C	67 %
c	N=N	86 %



47a-c

X =		
a	covalent bond	85 %
b	C≡C	70 %
c	N=N	84 %

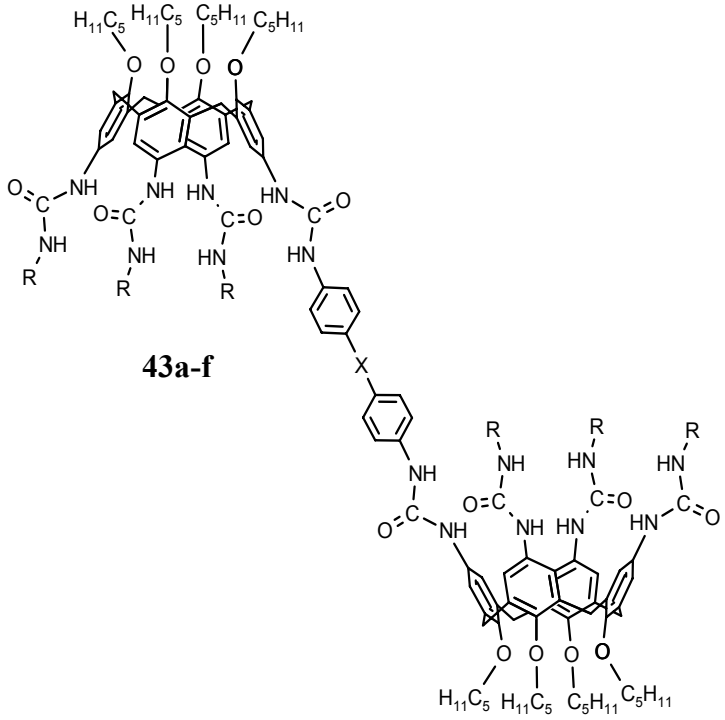
According the first strategy *bis*-calixarenes **46a-c** were synthesized in good yields (67-86%) by reaction of **45** with diurethanes **47a-c** in the presence of Hünig base. The hexa-*N*-Boc derivatives **46a-c** were easily purified by simple recrystallization in methanol.

Bis-*p*-nitrophenyl urethanes **47a-c** were prepared in 70-85% yield by acylation of appropriate dianilines with an excess of *p*-nitrophenyl chloroformate.

Deprotection of hexa-*N*-Boc *bis*-calixarenes **46a-c** by trifluoroacetic acid in dichloromethane followed by deprotonation with *i*-Pr_2EtN and reaction with appropriate

isocyanate or *p*-nitrophenyl urethane produced the target *bis*-calixarenes **43a-f** in 69-87% yield.

Simultaneously with the Boc-protection/deprotection strategy the direct acylation of tetraamine **Ia** with tolylisocyanate has been tried. A reaction of 3 mole of tetramine **Ia** with 3.1 mole of tolylisocyanate leads to the reaction mixture in which tetratolylurea and target tritolylurea calix[4]arene **44** are predominantly present. The compound **44** was extracted from the mixture by dichloromethane : methanol (1 : 4) in 51% yield.



43a-f

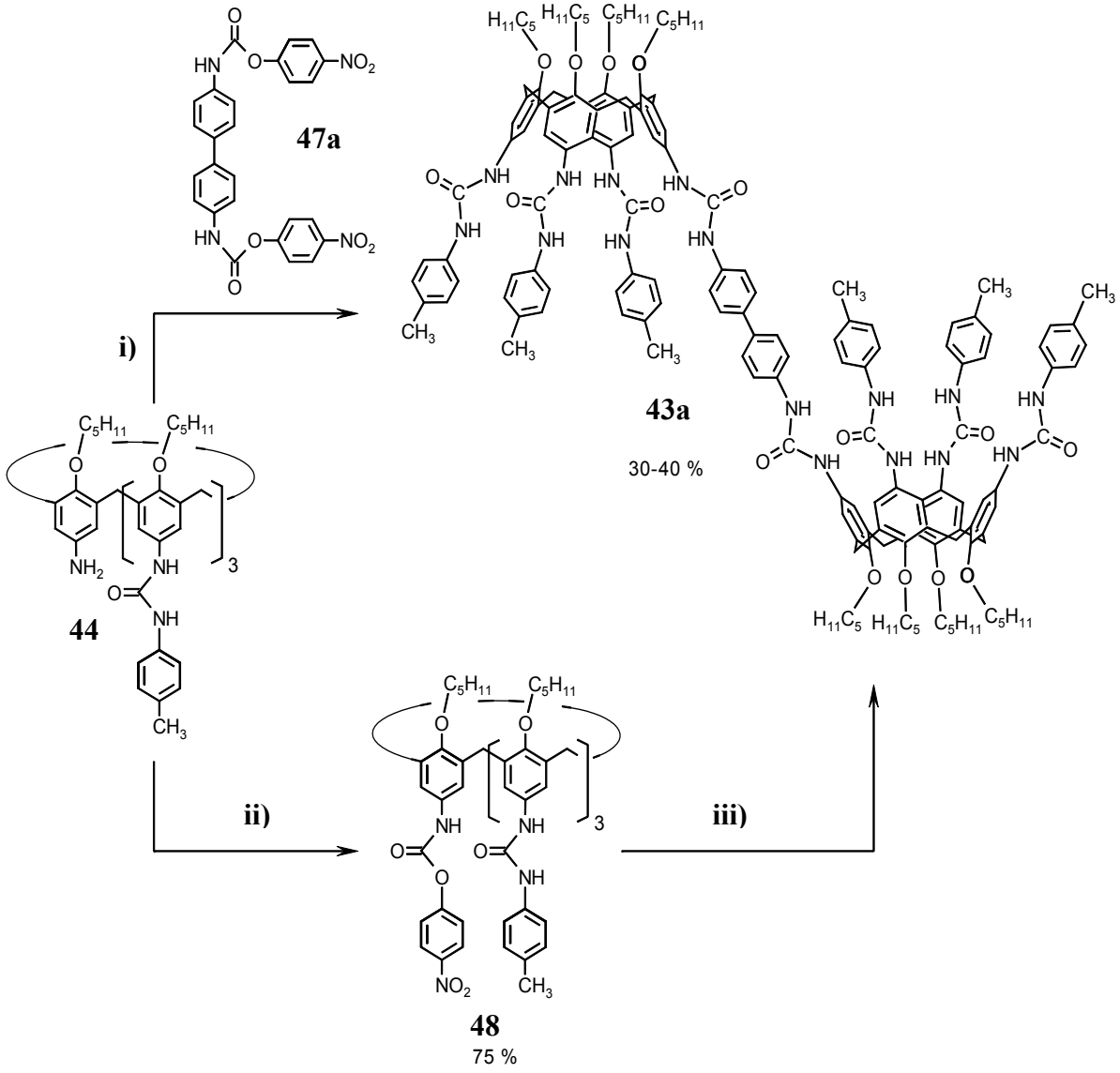
	X =	R =	
a	covalent bond	Tolyl	81 %
b	covalent bond	p-Ph-$OC_{10}H_{21}$	69 %
c	covalent bond	n-Hexyl	79 %
d	C≡C	Tolyl	80 %
e	N=N	Tolyl	87 %
f	N=N	p-Ph-$OC_{10}H_{21}$	87 %

Acylation of monoamine **44** with diurethane **46a** in THF in the presence of Hünig base (di-*iso*-propylethylamine) resulted in *bis*-calix[4]arene **43a** in 40% yield (Scheme 2). The synthetic pathway via monourethane **48** (prepared by reflux of **44** with an excess of *p*-nitrochloroformate in chloroform in 75% yield) leads to **43a** in 30-40% yield. Such low yields were caused by difficulties during the purification of **43a**.

Unfortunately, *bis*-calixarene **43a** has only a low solubility in apolar solvents. This solubility is in the sensitivity range of ^{1}H NMR spectroscopy but not sufficient for light scattering measurements, in which more concentrated solutions are required. Thus, it is necessary to introduce additional lipophilic residues into the *bis*-calixarene. For this purpose the protection/deprotection route is more convenient.

In summary, the tri-Boc-protection/deprotection strategy was found more effective for the preparation of *bis*-calixarenes of type **43** than the direct tri-functionalization. Due to easy

purification of hexa-*N*-Boc *bis*-calixarenes **46a-c** the purity of the target *bis*-calixarenes **43a-f** and their overall yield were considerably higher.



Scheme 2. Alternative synthesis of **43a.** i) *i*-Pr_2NEt, THF, rt, 24 h; ii) *p*-nitrophenyl chloroformate, chloroform, reflux, 4 h; iii) benzidine, *i*-Pr_2NEt, DMF, 24 h.

4.4 Studies of self-assembled *bis*-tetraurea calixarenes by ^{1}H NMR spectroscopy and by atomic force microscopy (AFM)

Bis-calixarene **43a** (R = tolyl) shows a sharp ^{1}H NMR spectrum in DMSO-d_6 (Fig. 6a) reflecting D_{2h}-symmetry:

- 3 singlets at 6.84, 6.82 and 6.80 ppm for 16 protons of the aryl groups of calixarene skeleton;

- 2 doublets at 7.46 and 7.39 ppm for 8 protons of the aryl rings of the diphenyl spacer;
- 6 singlets at 8.33, 8.15, 8.14, 8.09 and 8.06 ppm for 16 protons of the urea groups;
- 2 doublets at 7.22 and 7.01 ppm for 8 protons of the phenyl rings adjacent to urea groups.

In apolar solvents the signals for the NH protons of the urea groups in the spectrum are downfield-shifted (Fig. 6b). The signals for protons of the phenolic units of calixarene skeleton are divided into 2 broad singlets and one of them appears at 6 ppm in chloroform-d_1. These are clear indications for the dimerization of tetraurea counterparts. The width of the signals in the ^{1}H NMR spectrum in apolar solvents is explained by the formation of polymer-like structures. These are common features of all *bis*-calixarenes **43** with one exception – the compound **43c** (R = C_6H_{13}) (see Table 1), which is not soluble in apolar solvents.

An additional proof for the dimerization is the formation of *bis*-heterodimer between *bis*-calixarene **43a** and two molecules of tetratosylurea calix[4]arene (Fig. 6c). The downfield shift of the signals for NH protons of tetratosylurea **9** (10.4 - 10.8 ppm) and the sharpness of the signals in ^{1}H NMR spectrum in $CDCl_3$ reveals the formation of *bis*-heterodimer **43a**·(tosylurea)$_2$. Similar spectra were recorded also for compound **43b** (R = Ph-$OC_{10}H_{21}$) and **43e** (R = tolyl).

Analogously to single tetraurea dimers, polymers formed from *bis*-calixarenes **43** are able to include molecules or cations. The inclusion of molecules was proved by exchange of chloroform against *p*-difluorobenzene which is known as “better guest” for tetraurea dimers than chloroform. F-Ph-F (5% from the volume of chloroform) was added to the solution of **43b** (R = Ph-$OC_{10}H_{21}$) in chloroform-d_1. In 25 min the positions of the signals in ^{1}H NMR spectrum for urea NH protons, for aromatic protons of calixarene skeleton and for the protons of methylene bridges were shifted due to the guest exchange (Fig. 7). The signal of *p*-difluorobenzene included in the dimeric capsules appeared at 2.78 ppm.

The inclusion of tetraethylammonium cation in the dimeric capsules of f **43b** (R = Ph-$OC_{10}H_{21}$) is evident from its ^{1}H NMR spectrum in $CDCl_3$. The signals for protons of the methyl groups of the cation included are splitted and shifted to -0.14 and -3.29 ppm. Simultaneously the signals of **43b** (R = Ph-$OC_{10}H_{21}$) in the presence of this cation became significantly wider. Unfortunately, precise integration of the signals in the spectrum is not possible because of their overlap.

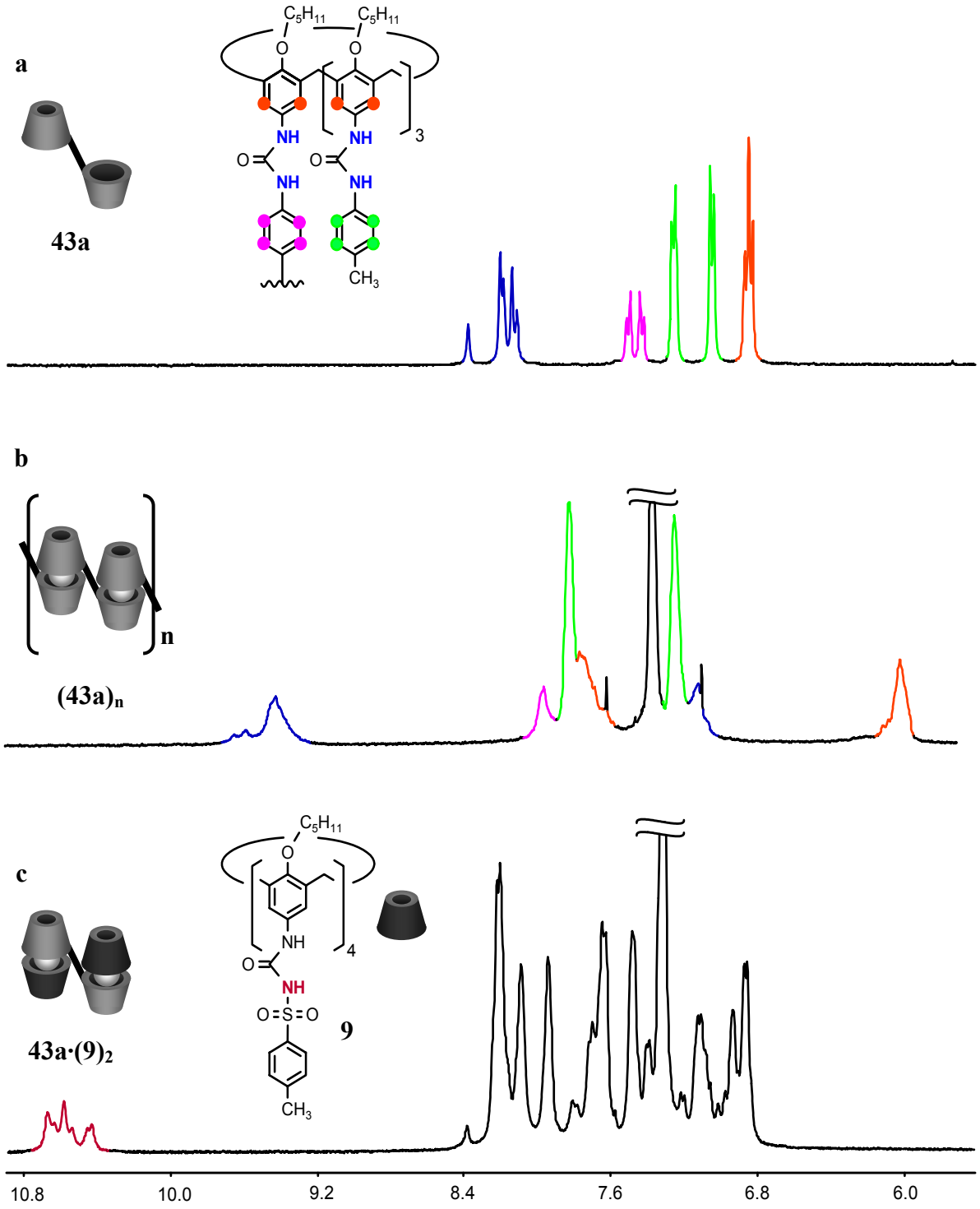
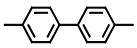
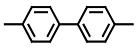
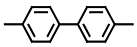
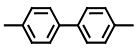
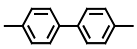
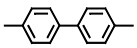
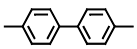
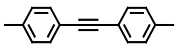
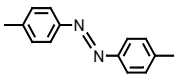
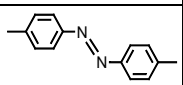
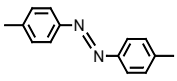
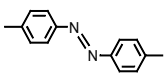


Figure 6. ^{1}H NMR spectra of *bis*-calixarene **43a** (R = tolyl). a) **43a** in DMSO-d_6, 50°C; b) **43a** in $CDCl_3$, rt; c) **43a** and tetratosylurea calix[4]arene **9** in ratio 1 : 2 correspondingly, $CDCl_3$, rt (*bis*-heterodimer **43a·(9)$_2$**).

Table 1. The self-assembling properties of *bis*-tetraureacalix[4]arenes **43a-f** monitored by ^{1}H NMR spectroscopy.

Component 1		**Component 2**	**Solvent**	**Temperature**	**Observations** ^{1}**H NMR (400 MHz)**
number (R)	spacer				
43a (R = tolyl)		-	$CDCl_3$	rt	polymerization
43a (R = tolyl)		-	C_6D_6	75°C	polymerization
43a (R = tolyl)		**9**	$CDCl_3$	rt	*bis*-heterodimer
43b (R = Ph-$OC_{10}H_{21}$)		-	$CDCl_3$ C_6D_6	rt	polymerization
43b (R = Ph-$OC_{10}H_{21}$)		**9**	$CDCl_3$	rt	*bis*-heterodimer
43c (R = C_6H_{13})		-	$CDCl_3$ TCE, C_6D_6	rt, 55°C	insoluble
43c (R = C_6H_{13})		-	TCE	75°C	insoluble
43d (R = tolyl)		-	$CDCl_3$	rt	polymerization
43e (R = tolyl)		-	$CDCl_3$	rt, 55°C	polymerization
43e (R = tolyl)		**9**	$CDCl_3$	rt	*bis*-heterodimer
43e (R = tolyl)		-	TCE	75°C	polymerization
43f (R = Ph-$OC_{10}H_{21}$)		-	$CDCl_3$	rt	polymerization

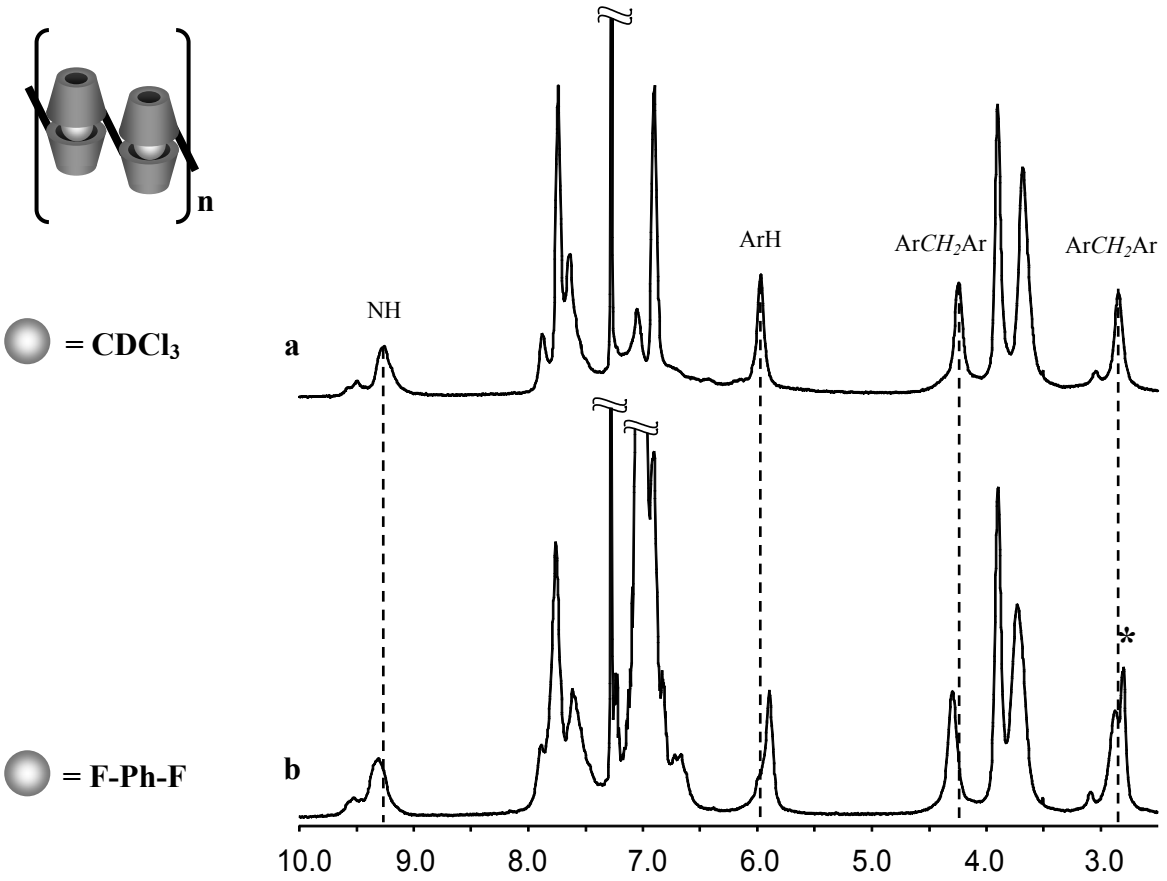


Figure 7. ^{1}H NMR spectra of *bis*-calixarene **43b** (R = Ph-$OC_{10}H_{21}$) a) in chloroform-d_1; b) in chloroform-d_1 + 5% of *p*-difluorobenzene. The signal for included *p*-difluorobenzene is marked by asterisk.

The polymers formed by **43** dissociate to monomers in the presence of polar solvents. For example, a complete dissociation of assemblies of **43b** (R = Ph-$OC_{10}H_{21}$) in chloroform solution takes places when 25% of dimethylsulfoxide was added in the solution.

According to the AFM measurements[12] the *bis*-calixarene **43b** (R = Ph-$OC_{10}H_{21}$) self-assembles into fibers with width about 15.5 nm and height of 1.8 nm from the chloroform solution (Fig. 8). The sample of the same concentration but with 5% *p*-difluorobenzene produces the fibers with width of 7.8 nm and height of 2.4 nm.

Obviously, the fibers do not correspond to single polymer chains formed by molecules turned alternatively in 135° in respect to each other (Fig. 9). Dimensions of this polymeric structure were estimated on the base of the dimensions of the tetraurea calix[4]arene dimers (2.2 x 1.6 nm).[13] Thus, a diameter of such "stretched" polymer might be about 4 nm.

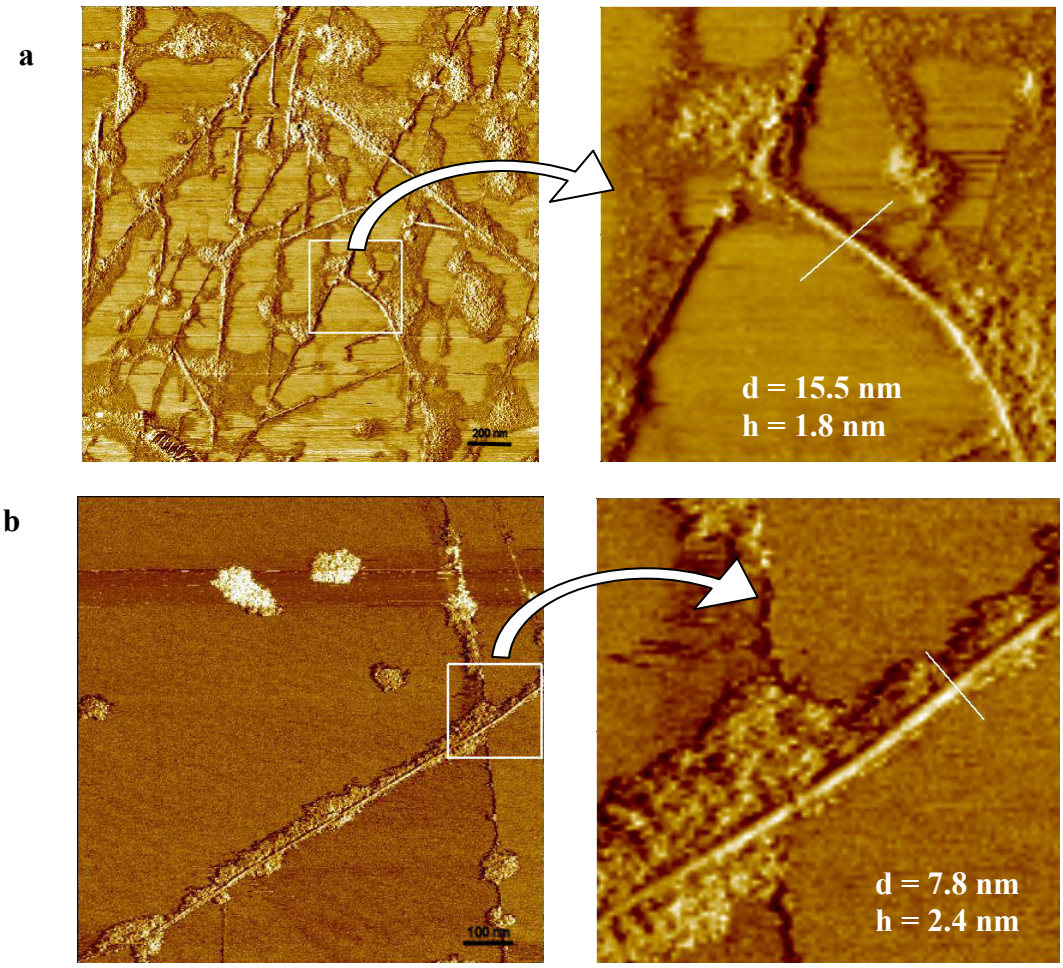


Figure 8. SFM phase images[14] of the *bis*-calixarene **43b** (R = Ph-$OC_{10}H_{21}$) on HOPG prepared by spin-coating of solutions C = 0.01 mg/ml a) in chloroform; b) in chloroform + 5% of *p*-difluorobenzene.

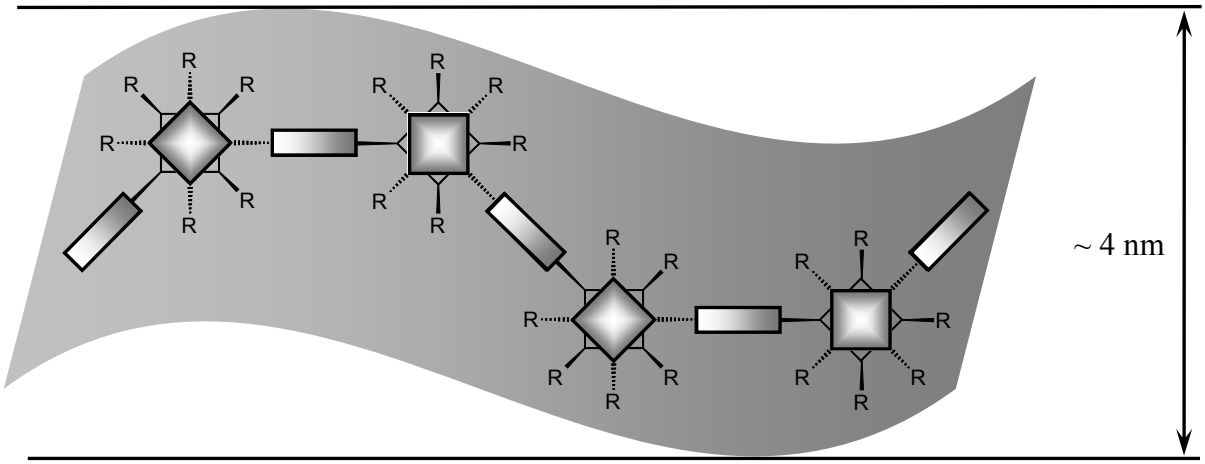


Figure 9. Schematic representation of "stretched" polymer structures based on the self-assembled *bis*-calixarenes **43**.

The molecules in the polymer turned in the same direction could form a helical structure (Fig. 10). A diameter of this helix might be about 8 nm, which is more in agreement with the dimensions of fibers. Possibly, the fiber consists of one or several polymeric chains in the helical conformation (for example, double or triple helix).

The folding of the polymers in helix can be stimulated by interactions between the turns of helix. The introduction of appropriate functional groups at the narrow rim of calix[4]arenes could also provide an additional stabilization of the helical conformation by the formation of intermolecular hydrogen bonds or by π-π-interactions. Change of the length of the spacers connecting *bis*-calixarenes **43** as well as guest inclusion may also have an influence on the conformation of the assemblies formed.

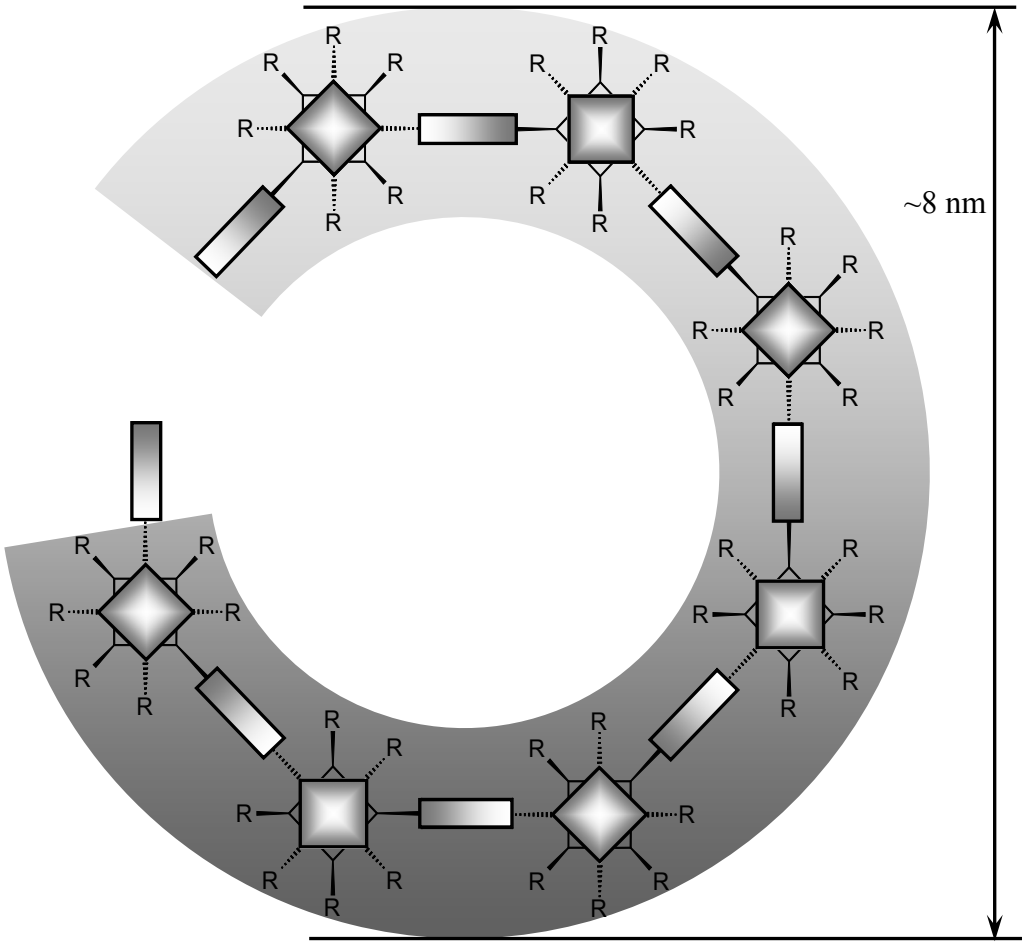
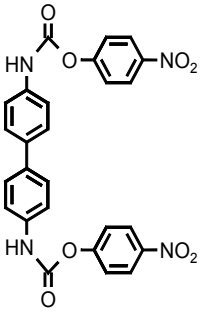


Figure 10. Schematic representation of helical structures based on the self-assembled *bis*-calixarenes **43**.

4.5 Experimental

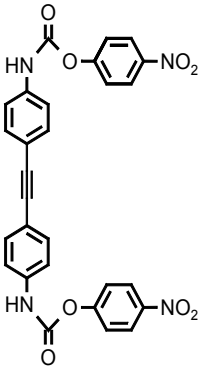
p-Tetraamino calix[4]arene tetrapentylether **Ia** and tri-*N*-Boc monoamine **45** were prepared according to published procedures.[7, 15]



*Di-p-nitrophenylurethane of benzidine **47a**:*

4-Nitrophenyl chloroformate (1.64 g, 8.14 mmol) was added to a solution of benzidine (0.50 g, 2.71 mmol) in THF (15 ml). Then the reaction mixture was refluxed for 2 hours. The solid was filtered off, washed with ethylacetate and dried to give the product as a gray powder. Yield: 1.19 g (85%).

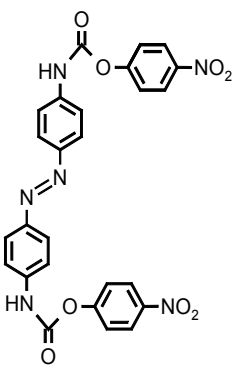
m.p. >270°C (decomp.); MS (FD): m/z 514.0 (M^+); ^{1}H NMR (DMSO-d_6): δ 10.57 (s, N-*H*, 2 H), 8.29 (d, Ar-*H*, 4 H, $^3J_{HH}$ 9.2 Hz), 7.72-7.50 (m, Ar-*H*, 12 H).



*Di-p-nitrophenylurethane of 4, 4'-aminodiphenylacetylene **47b**:*

4-Nitrophenyl chloroformate (0.21 g, 1.03 mmol) was added to a solution of 4,4'-aminodiphenylacetylene (0.10 g, 0.49 mmol) in THF (25 ml). Then the reaction mixture was refluxed for 4 hours. The solvent was removed under reduced pressure and to the residue acetonitrile (25 ml) was added. The solid was filtered off, washed with acetonitrile and dried to give product as a beige powder. Yield: 0.19 g (70%).

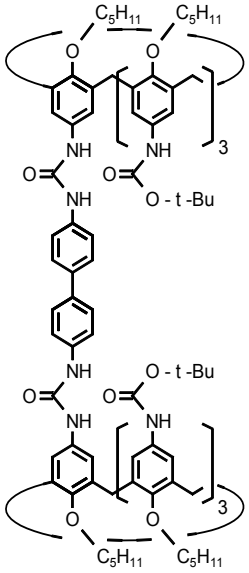
m.p. >240°C (decomp.); MS (FD): m/z 538.3 (M^+); ^{1}H NMR (DMSO-d_6, 35°C): δ 10.75 (s, N-*H*, 2 H), 8.31 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.8 Hz), 7.59 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.8 Hz), 7.56 (d, Ar-*H*, 4 H, $^3J_{HH}$ 9.2 Hz), 7.52 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.8 Hz).



*Di-p-nitrophenylurethane of 4, 4'-azodianiline **47c**:*

4-Nitrophenyl chloroformate (1.04 g, 5.13 mmol) was added to a solution of 4,4'-azodianiline (0.50 g, 2.36 mmol) in THF (30 ml). Then the reaction mixture was refluxed for 4 hours. The solvent was removed under reduced pressure and to the residue acetonitrile (50 ml) was added. The solid was filtered off, washed with acetonitrile and dried to give product as an orange powder. Yield: 1.08 g (84%).

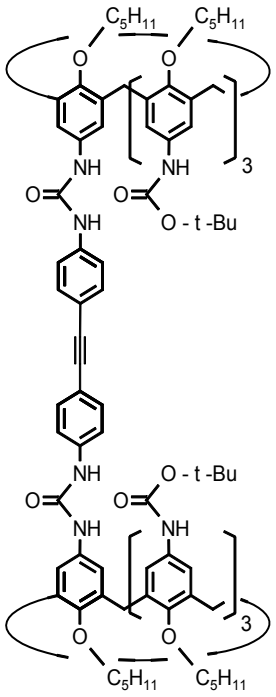
m.p. >220°C (decomp.); MS (FD): m/z 542.3 (M^+), 581.3 ($M+K^+$); ^{1}H NMR (DMSO-d_6): δ 10.83 (s, N-*H*, 2 H), 8.33 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.9 Hz), 7.89 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.5 Hz), 7.74 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.9 Hz), 7.58 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.9 Hz).



Bis-calix[4]arene ***46a****:*

Di-*p*-nitrophenylurethane **47a** (0.076 g, 0.148 mmol) and a solution of di-*iso*-propylethylamine (0.040 g, 0.310 mmol) in THF (5 ml) were added to a solution tri-*N*-Boc monoamine **45** (0.30 g, 0.28 mmol) in THF (5 ml) and the reaction mixture was stirred at rt for 24 hours. Then the solvent was removed in vacuum. The oily residue was triturated with methanol. The solid was filtered off, washed with methanol to give analytically pure double calixarene as white powder. Yield: 0.23 g (69%).

m.p. >260°C (decomp.); MS (ESI): m/z 2551.9 ($M+Na^+$) 1287.5 ($M+2Na^+$); ^{1}H NMR (DMSO-d_6): δ 8.90 (s, N-*H*, 4 H), 8.60 (s, N-*H*, 2 H), 8.27 (s, N-*H*, 2 H), 8.08 (s, N-*H*, 2 H), 7.49 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.8 Hz), 7.40 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.3 Hz), 6.96 (s, Ar-*H*, 8 H), 6.72-6.49 (m, Ar-*H*, 8 H), 4.40-4.22 (2 d overlapped, Ar-CH_2-Ar, 8 H, $^2J_{HH}$ 12.2 Hz), 3.87 (t, -O-CH_2-, 8 H, $^3J_{HH}$ 7.6 Hz), 3.78-3.64 (m, -O-CH_2-, 8 H), 3.12-2.94 (2 d overlapped, Ar-CH_2-Ar, 8 H, $^2J_{HH}$ 13.2 Hz), 1.98-1.78 (m, -O-CH$_2$-CH_2-, 16 H), 1.50-1.26 (m and 2 s: 1.43, 1.34 overlapped, -CH_2-, -CH_3, 86 H), 0.97-0.87 (m, -CH_3, 24 H).

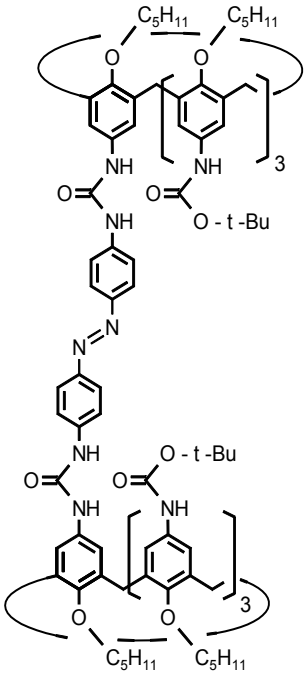


Bis-calix[4]arene ***46b****:*

Tri-*N*-Boc monoamine **45** (0.30 g, 0.28 mmol) and a solution of diisopropylethylamine (0.06 g, 0.48 mmol) in THF (4 ml) were added to a solution of di-*p*-nitrophenylurethane **47b** (0.08 g, 0.15 mmol) in THF (2.5 ml) and the reaction mixture was stirred at rt for 24 hours. Then acetonitrile (20 ml) was added to the reaction mixture. The precipitate was filtered off, washed with acetonitrile to give analytically pure double calixarene as white powder. Yield: 0.23 g (67%).

m.p. >270°C (decomp.); MS (ESI): m/z 2413.7 ($M+Na^+$), 1218.4 ($M+2Na^+$); ^{1}H NMR (DMSO-d_6): δ 8.88 (s, N-*H*, 4 H), 8.68 (s, N-*H*, 2 H), 8.60 (s, N-*H*, 2 H), 8.30 (s, N-*H*, 2 H), 7.40 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.8 Hz), 7.37 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.8 Hz), 7.07-6.80 (m, Ar-*H*, 8 H),

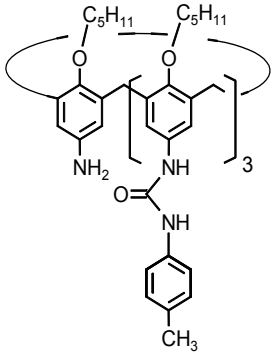
6.76-6.47 (m, Ar-*H*, 8 H), 4.42-4.20 (m, Ar-C*H*$_2$-Ar, 8 H), 3.85 (br.t, -O-C*H*$_2$-, 8 H), 3.79-3.59 (m, -O-C*H*$_2$-, 8 H), 3.12-2.91 (m, Ar-C*H*$_2$-Ar, 8 H), 2.00-1.76 (m, -O-CH$_2$-C*H*$_2$-, 16 H), 1.56-1.18 (m, -C*H*$_2$-, -C*H*$_3$, 86 H), 0.92 (t, -C*H*$_3$, 24 H, $^3J_{HH}$ 6.6 Hz).



Bis-calix[4]arene ***46c****:*

Tri-*N*-Boc monoamine **45** (0.32 g, 0.30 mmol) and a solution of diisopropylethylamine (0.062 g, 0.479 mmol) in THF (5 ml) were added to a suspension of di-*p*-nitrophenylurethane **47c** (0.09 g, 0.16 mmol) in THF (5 ml) and the reaction mixture was stirred at rt for 24 hours. Then acetonitrile (30 ml) was added to the reaction mixture. The precipitate was filtered off, washed with acetonitrile to give analytically pure double calixarene as white powder. Yield: 0.31 g (86%).

m.p. >290°C (decomp.); MS (ESI): m/z 2417.4 (M+Na$^+$), 1220.2 (M+2Na$^+$); ^{1}H NMR (DMSO-d$_6$, 75°C): δ 8.55 (s, N-*H*, 4 H), 8.44 (s, N-*H*, 2 H), 8.18 (s, N-*H*, 2 H), 8.01 (s, N-*H*, 2 H), 7.75 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.8 Hz), 7.55 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.8 Hz), 7.00-6.89 (m, Ar-*H*, 8 H), 6.64-6.55 (m, Ar-*H*, 8 H), 4.42-4.29 (m, Ar-C*H*$_2$-Ar, 8 H), 3.91 (t, -O-C*H*$_2$-, 8 H, $^3J_{HH}$ 7.6 Hz), 3.84-3.72 (m, -O-C*H*$_2$-, 8 H), 3.12-2.97 (m under water peak, Ar-C*H*$_2$-Ar, 8 H), 1.95-1.80 (m, -O-CH$_2$-C*H*$_2$-, 16 H), 1.52-1.28 (m, -C*H*$_2$-, -C*H*$_3$, 86 H), 1.00-0.87 (m, -C*H*$_3$, 24 H).

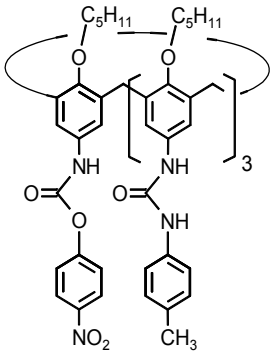


Calix[4]arene ***44:***

A solution of tolylisocyanate (0.54 g, 4.05 mmol) in dichloromethane (100 ml) was added dropwise to a vigorously stirred solution of tetraamino calix[4]arene (1.00 g, 1.31 mmol) in dichloromethane (100 ml). After 24 h of stirring at rt, the solvent from the reaction mixture was evaporated in vacuum. Then the residue was dissolved in dichloromethane and tetraurea product was precipitated by methanol. The solid was filtered off to give tetraurea product as a white powder. The methanol from the mother liquid was removed in vacuum. The residue was reprecipitated from dichloromethane/hexane to give the product **44** as a white powder. Yield: triurea **44** 0.78 g (51%); tetraurea product 0.52 g (30%).

44: m.p.: >250°C (decomp.); ^{1}H NMR (DMSO-d$_6$): δ 8.34-8.06 (m, N-*H*, 6 H), 7.32-7.14 (m, Ar-*H*, 6 H), 7.10-6.94 (m, Ar-*H*, 6 H), 6.87-6.67 (m, Ar-*H*, 6 H), 6.03 (s, Ar-*H*, 2 H),

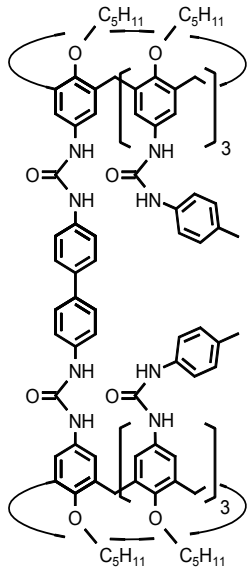
5.16-4.42 (br.s, N-*H*$_2$, 2 H), 4.33 (d, Ar-C*H*$_2$-Ar, 2 H, $^2J_{HH}$ 12.5 Hz), 4.25 (d, Ar-C*H*$_2$-Ar, 2 H, $^2J_{HH}$ 12.5 Hz), 3.90-3.63 (m, -O-C*H*$_2$-, 8 H), 3.09 (d, Ar-C*H*$_2$-Ar, 2 H, $^2J_{HH}$ 12.8 Hz), 2.97 (d, Ar-C*H*$_2$-Ar, 2 H, $^2J_{HH}$ 12.8 Hz), 2.22 (s, -C*H*$_3$, 9 H), 1.98-1.76 (m, -O-CH$_2$-C*H*$_2$-, 8 H), 1.49-1.25 (m, -C*H*$_2$-, 16 H), 0.93 (br.t, -C*H*$_3$, 12 H).



Calix[4]arene ***48:***

Monoamine **44** (2.00 g, 1.91 mmol) was added to a stirred solution of 4-nitrophenylchloroformate (2.55 g, 12.63 mmol) in $CHCl_3$ (22 ml). Then the reaction mixture was refluxed for 4 hours. Then the solvent was evaporated in vacuum, the residue was triturated with acetonitrile and stored in a refrigerator for 4-8 hours. The solid was filtered off, washed with acetonitrile and dried to give pure product as light-yellow powder. Yield: 2.65 g (75%).

m.p. >200°C; ^{1}H NMR (DMSO-d$_6$): δ 9.95 (s, N-*H*, 1 H), 8.25 (s, N-*H*, 3 H), 7.21 (d, Ar-*H*, 2 H, $^3J_{HH}$ 8.8 Hz), 8.15 (s, N-*H*, 3 H), 7.37 (d, Ar-*H*, 2 H, $^3J_{HH}$ 8.8 Hz), 7.30-7.18 (m, Ar-*H*, 6 H), 7.16-6.97 (m, Ar-*H*, 6 H), 6.94 (s, Ar-*H*, 2 H), 6.81 (s, Ar-*H*, 4 H), 6.75 (s, Ar-*H*, 2 H), 4.35 (d, Ar-C*H*$_2$-Ar, 2 H, $^2J_{HH}$ 12.3 Hz), 4.33 (d, Ar-C*H*$_2$-Ar, 2 H, $^2J_{HH}$ 12.6 Hz), 3.82-3.67 (m, -O-C*H*$_2$-, 8 H), 3.11 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 12.9 Hz), 2.21 and 2.20 (2s, -C*H*$_3$, 9 H), 2.00-1.84 (m, -O-CH$_2$-C*H*$_2$-, 8 H), 1.49-1.30 (m, -C*H*$_2$-, 16 H), 0.93 (t, -C*H*$_3$, 12 H, $^3J_{HH}$ 6.8 Hz).



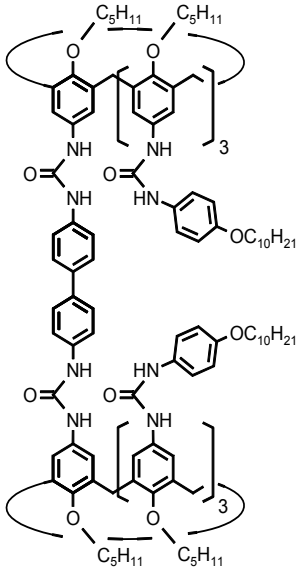
Bis-calix[4]arene ***43a****:*

Procedure A: A solution of hexa-*N*-Boc-protected *bis*-calix[4]arene **46a** (0.097 g, 0.0410 mmol) in dichloromethane (10 ml) and trifluoroacetic acid (6 ml) was stirred at rt for 2 h. Then the solvent was evaporated and the residue was triturated with Et_2O. A white solid was filtered off, washed with Et_2O and dried to give an appropriate tetraammonium salt which was dissolved in THF (5 ml) and treated with diisopropylethylamine (0.034 g, 0.265 mmol). After 15 min a white precipitate appeared which was dissolved slowly again when a solution of *p*-tolylisocyanate (0.049 g, 0.367 mmol) in THF (5 ml) was added. The reaction mixture was stirred at rt for 10 h under nitrogen.

Then a half of the solvent was removed in vacuum, and methanol (15 ml) was added to the residue to precipitate the product. The solid was filtered off, washed with methanol and dried to give the product as a light-beige powder. Yield: 0.085 g (81%).

Procedure B: Benzidine (0.008 g, 0.0435 mmol) and di-*iso*-propylethylamine (0.017 g, 0.131 mmol) were added to a solution of the monourethane **47a** (0.116 g, 0.0870 mmol) in DMF (5 ml). The reaction mixture was stirred at 50°C for 72 h under nitrogen. Then it was poured into the cooled water (15 ml), a precipitate was filtered off, washed with water and methanol. A reprecipitation from THF/methanol gave the desired product as a beige powder. Yield: 0.060 g (40%).

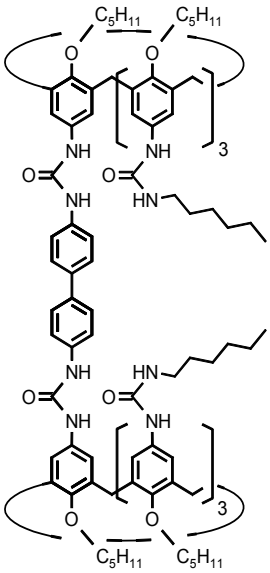
m.p.: >255°C (decomp.); MS (MALDI-TOF): m/z 2565.7 (M^+); ^{1}H NMR (DMSO-d_6, 50°C): δ 8.33 (s, N-*H*, 2 H), 8.21-8.01 (s: 8.15, s: 8.14, s: 8.09 and s: 8.06 overlapped, N-*H*, 14 H), 7.46 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.3 Hz), 7.39 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.8 Hz), 7.22 (d, Ar-*H*, 12 H, $^3J_{HH}$ 8.3 Hz), 7.01 (d, Ar-*H*, 12 H, $^3J_{HH}$ 7.8 Hz), 6.90-6.73 (s: 6.84, s: 6.82 and s: 6.80 overlapped, Ar-*H*, 16 H), 4.36 (d, Ar-CH_2-Ar, 8 H, $^2J_{HH}$ 12.7 Hz), 3.85 (m, -O-CH_2-, 16 H), 3.11 (d, Ar-CH_2-Ar, 8 H, $^2J_{HH}$ 11.2 Hz), 2.21 (s, -CH_3, 18 H), 1.92 (m, -O-CH$_2$-CH_2-, 16 H), 1.41 (m, -CH_2-, 32 H), 0.95 (br.t, -CH_3, 24 H).



Bis-calix[4]arene ***43b:***

Prepared according to the *procedure A* from hexa-*N*-Boc-protected *bis*-calix[4]arene **46a** (0.080 g, 0.0338 mmol), *p*-nitrophenyl urethane of *p*-decyloxyaniline (0.140 g, 0.338 mmol), diisopropylethylamine (0.063 g, 0.487 mmol) in THF (10 ml); reprecipitation from THF/methanol. Yield: 0.080 g (69%).

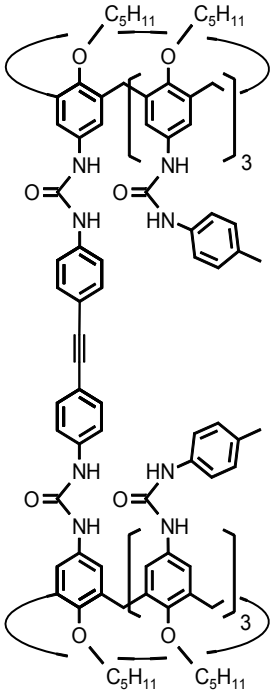
m.p.: >210°C (decomp.); MS (ESI): 3440.4 (M+Na^+); 1732.3 (M+2Na^+); ^{1}H NMR (DMSO-d_6, 65°C): δ 8.28 (s, N-*H*, 2 H), 8.07 (s, N-*H*, 2 H), 8.04-7.89 (s: 8.00 and s: 7.97 overlapped, N-*H*, 12 H), 7.46 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.5 Hz), 7.39 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.2 Hz), 7.22 (d, Ar-*H*, 12 H, $^3J_{HH}$ 8.5 Hz), 6.90-6.68 (m, Ar-*H*, 28 H), 4.37 (d, Ar-CH_2-Ar, 8 H, $^2J_{HH}$ 12.0 Hz), 4.98-3.75 (m, -O-CH_2-, 28 H), 3.20 (d under water peak, Ar-CH_2-Ar, 8 H), 1.92 (m, -O-CH$_2$-CH_2-, 16 H), 1.66 (m, -O-CH$_2$-CH_2-, 12 H), 1.50-1.14 (m, -CH_2-, 116 H), 0.95 (br.t, -CH_3, 24 H), 0.85 (br.t, -CH_3, 18 H).



Bis-calix[4]arene ***43c:***

Prepared according to the *procedure A* from hexa-*N*-Boc-protected *bis*-calix[4]arene **46a** (0.100 g, 0.042 mmol), diisopropylethylamine (0.063 g, 0.487 mmol) and *n*-hexylisocyanate (0.054 g, 0.422 mmol) in THF (20 ml); reprecipitation from THF/methanol. Yield: 0.085 g (79%).

m.p.: >230°C (decomp.); MS (ESI): 2551.9 ($M+Na^+$); 1287.5 ($M+2Na^+$); ^{1}H NMR (DMSO-d_6): δ 8.40 (s, N-*H*, 2 H), 8.11 (s, N-*H*, 2 H), 7.97 (s, N-*H*, 4 H), 7.82 (s, N-*H*, 2 H), 7.48 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.4 Hz), 7.42 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.4 Hz), 6.82 (s, Ar-*H*, 4 H), 6.79 (s, Ar-*H*, 4 H), 6.70 (s, Ar-*H*, 4 H), 6.61 (s, Ar-*H*, 4 H), 5.82 (br.t, N-*H*, 4 H, $^3J_{HH}$ 4.8 Hz), 5.69 (br.t, N-*H*, 2 H, $^3J_{HH}$ 5.3 Hz), 4.44 (m, Ar-CH_2-Ar, 8 H), 3.98-3.61 (m, -O-CH_2-,-NH-CH_2-, 28 H), 3.17-2.86 (m, Ar-CH_2-Ar, -NH-CH_2-CH_2-, 12 H), 2.05-1.70 (m, -O-CH_2-CH_2-, 16 H), 1.60-1.05 (m, -CH_2-, 68 H), 1.01-0.73 (m, -CH_3, 42 H).

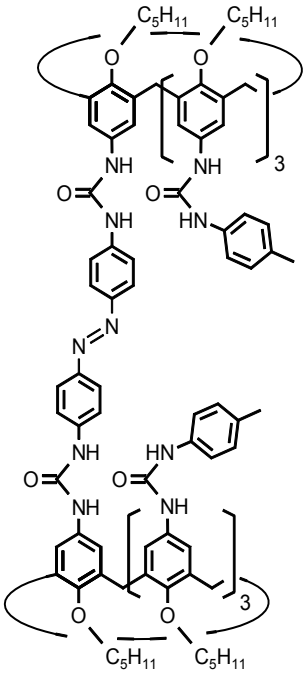


Bis-calix[4]arene ***43d****:*

A solution of hexa-*N*-Boc-protected *bis*-calix[4]arene **46b** (0.100 g, 0.0418 mmol) in dichloromethane (10 ml) and trifluoroacetic acid (2.5 ml) was stirred at rt for 2 h. Then the solvent was evaporated and the residue was triturated with Et_2O. A white solid was filtered off, washed with Et_2O and dried to give an appropriate tetraammonium salt which was dissolved in THF (5 ml) and treated with diisopropylethylamine (0.108 g, 0.836 mmol). After 15 min a white precipitate appeared which was dissolved slowly again when a solution of *p*-tolylisocyanate (0.056 g, 0.418 mmol) in THF (5 ml) was added. The reaction mixture was stirred at rt for 12 h under nitrogen. Then a half of the solvent was removed in vacuum, and acetonitrile (15 ml) was added to the residue to precipitate the product. The solid was filtered off, washed with acetonitrile and dried to give the product as a light-beige powder. Yield: 0.072 g (66%).

m.p.: >250°C (decomp.); ^{1}H NMR (DMSO-d_6, 50°C): δ 8.54 (s, N-*H*, 2 H), 8.28-8.02 (m, N-*H*, 14 H), 7.36 (s, Ar-*H*, 4 H), 7.28-7.12 (m, Ar-*H*, 16 H), 7.07-6.93 (m, Ar-*H*, 12 H), 6.88-6.68 (m, Ar-*H*, 20 H), 4.33 (d, Ar-CH_2-Ar, 8 H, $^2J_{HH}$ 11.7 Hz), 3.97-3.67 (m, -O-CH_2-, 16 H),

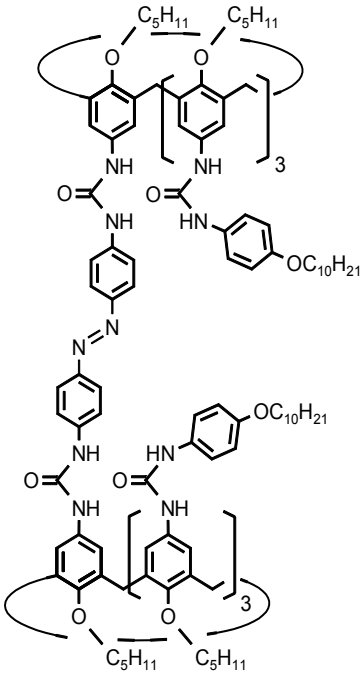
3.10 (d, Ar-C*H*$_2$-Ar, 8 H, $^2J_{HH}$ 11.4 Hz), 2.29-2.07 (m, -C*H*$_3$, 18 H), 2.01-1.76 (m, -O-CH$_2$-C*H*$_2$-, 16 H), 1.50-1.28 (m, -C*H*$_2$-, 32 H), 0.94 (br.t, -C*H*$_3$, 24 H).



Bis-calix[4]arene ***43e***:

A solution of hexa-*N*-Boc-protected *bis*-calix[4]arene **46c** (0.100 g, 0.0417 mmol) in dichloromethane (10 ml) and trifluoroacetic acid (1 ml) was stirred at rt for 2 h. Then the solvent was evaporated and the residue was dissolved in THF (10 ml) and treated with diisopropylethylamine (0.108 g, 0.834 mmol). After 15 min a yellow precipitate appeared which was dissolved slowly again when a solution of *p*-tolylisocyanate (0.049 g, 0.367 mmol) in THF (7 ml) was added. The reaction mixture was stirred at rt for 12 h under nitrogen. Then methanol (15 ml) was added to the reaction mixture and the solvent was removed under reduced pressure. The residue was triturated with acetonitrile (20 ml). The solid was filtered off, washed with acetonitrile and dried to give pure product as yellow powder. Yield: 0.095 g (87%).

m.p.: >290°C (decomp.); MS (ESI): m/z 2615.5 (M+Na$^+$), 1319.8 (M+2Na$^+$); ^{1}H NMR (DMSO-d$_6$, 75°C): δ 8.54 (s, N-*H*, 2 H), 8.17-7.97 (s: 8.12, s: 8.08, s: 8.05 and s: 8.02 overlapped, N-*H*, 12 H), 7.94 (s, N-*H*, 2 H), 7.73 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.3 Hz), 7.51 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.8 Hz), 7.28-7.15 (m, Ar-*H*, 12 H), 7.06-6.95 (m, Ar-*H*, 12 H), 6.91-6.73 (s: 6.87, s: 6.85, s: 6.80 and s: 6.77 overlapped, Ar-*H*, 16 H), 4.40 (d, Ar-C*H*$_2$-Ar, 8 H, $^2J_{HH}$ 12.2 Hz), 3.96-3.79 (m, -O-C*H*$_2$-, 16 H), 3.19-3.08 (m, Ar-C*H*$_2$-Ar, 8 H), 2.22 (s, -C*H*$_3$, 18 H), 1.92 (br.s, -O-CH$_2$-C*H*$_2$-, 16 H), 1.42 (br.s, -C*H*$_2$-, 32 H), 0.95 (br.s, -C*H*$_3$, 24 H).



Bis-calix[4]arene ***43f***:

Prepared as described for **43e** from hexa-*N*-Boc-protected *bis*-calix[4]arene **46c** (0.050 g, 0.0209 mmol), diisopropylethylamine (0.108 g, 0.834 mmol) and *p*-nitrophenyl urethane of *p*-decyloxyaniline (0.087 g, 0.209 mmol) in THF (10 ml); reprecipitation from THF/acetonitrile gave pure product as yellow powder. Yield: 0.063 g (87%).

m.p.: > 200°C (decomp.); MS (ESI): m/z 1746.4 ($M+2Na^+$); ^{1}H NMR (DMSO-d_6, 75°C): δ 8.55 (s, N-*H*, 2 H), 8.11 (s, N-*H*, 2 H), 8.04-7.84 (s: 7.99, s: 7.96 and s: 7.90 overlapped, N-*H*, 12 H), 7.73 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.7 Hz), 7.51 (d, Ar-*H*, 4 H, $^3J_{HH}$ 9.1 Hz), 7.29-7.10 (m, Ar-*H*, 12 H), 6.94-6.63 (m, Ar-*H*, 28 H), 4.40 (d, Ar-CH_2-Ar, 4 H, $^2J_{HH}$ 12.8 Hz), 4.38 (d, Ar-CH_2-Ar, 4 H, $^2J_{HH}$ 12.8 Hz), 4.00-3.73 (m, -O-CH_2-, 28 H), 3.19-3.08 (m, Ar-CH_2-Ar, 8 H), 2.00-1.83 (m, -O-CH$_2$-CH_2-, 16 H), 1.73-1.59 (m, -O-CH$_2$-CH_2-, 12 H), 1.52-1.14 (m, -CH_2-, 118 H), 0.95 (t, -CH_3, 24 H, $^3J_{HH}$ 6.4 Hz), 0.85 (t, -CH_3, 18 H, $^3J_{HH}$ 6.8 Hz).

4.6 Literature and comments

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Chapter 5

Narrow rim-bridged tetraurea calix[4]arenes as potential building blocks for self-assembled polymers with defined structure

5.1 Linear polymers prepared by self-assembly of *bis*-tetraurea calix[4]arenes

Bis-tetraurea calix[4]arenes **49-52** (Fig. 1) singly bridged via the narrow rim self-organize in apolar solvents into polymers by intermolecular dimerization of their tetraurea counterparts (Fig. 2aI,2bI).[1] Such polymers must include molecules (solvent) or cations of suitable size and shape in their "dimeric" capsules (similarly to tetraurea calix[4]arene dimers, see in Chapter 2.1). The polymerization of *bis*-tetraurea calix[4]arenes was proved by characteristic downfield-shifts of the signals for urea NH-protons in ^{1}H NMR spectrum. An additional evidence of the intermolecular dimerization of these *bis*-calixarenes is the formation of *bis*-heterodimers between compounds **49** (or **50**) and two molecules of tetratosylurea calix[4]arene (Fig. 2aII) or between compound **52** and two molecules of tetraarylurea (Fig. 2bII). The existence of these *bis*-heterodimers has been proved by ^{1}H NMR spectroscopy, gel permeation chromatography and by ESI mass-spectroscopy.[2]

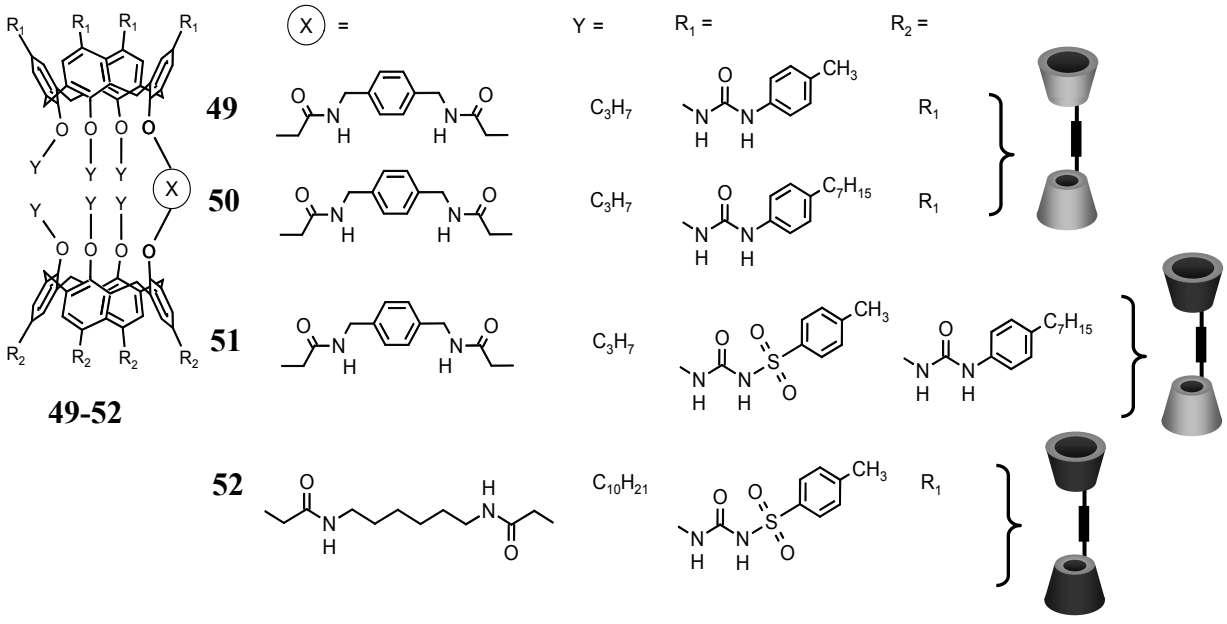


Figure 1. Examples for *bis*-tetraurea calix[4]arenes **49-52** singly-bridged via the narrow rim.

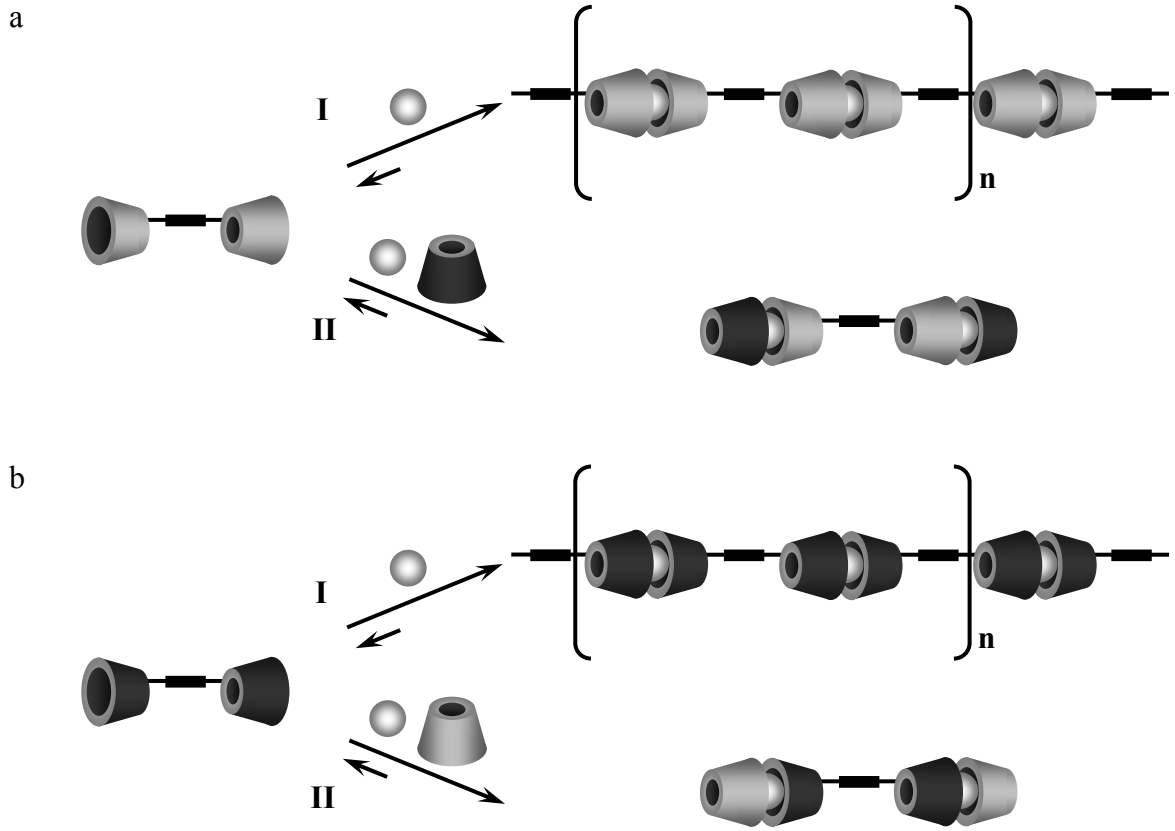


Figure 2. Schematic representation of self-assembled structures formed by *bis*-calixarenes **49,50** and **52** in apolar solvents. I) *bis*-calixarene itself; II) *bis*-calixarene in the presence of 2 moles of single tetratosyl-(for **49** and **50**) or tetratolylureas (for **52**). The ball represents a guest molecule.

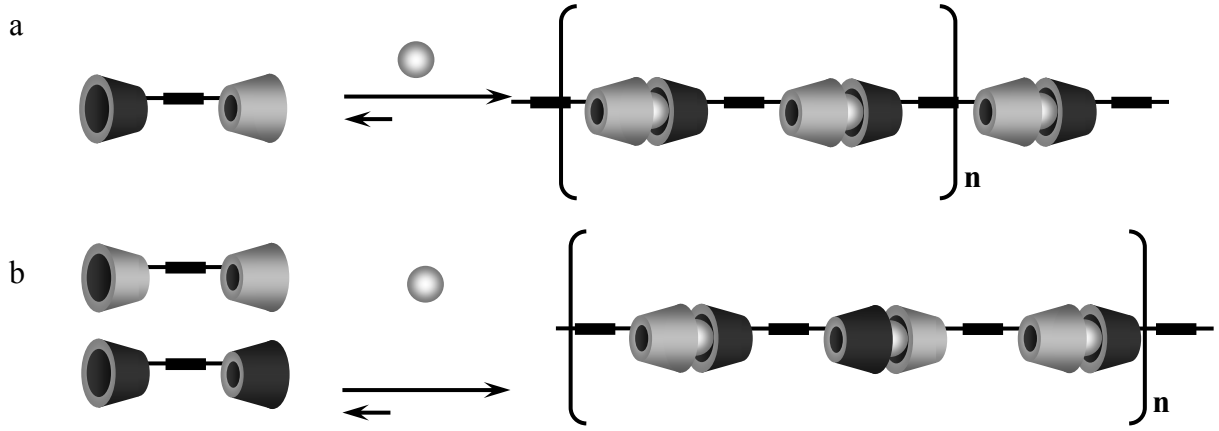
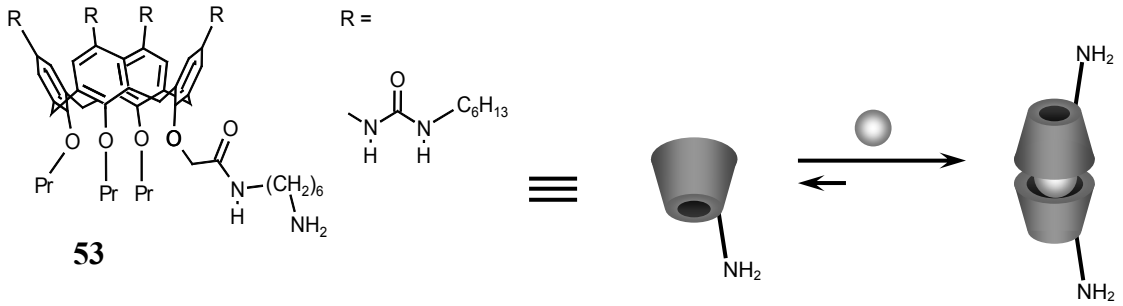
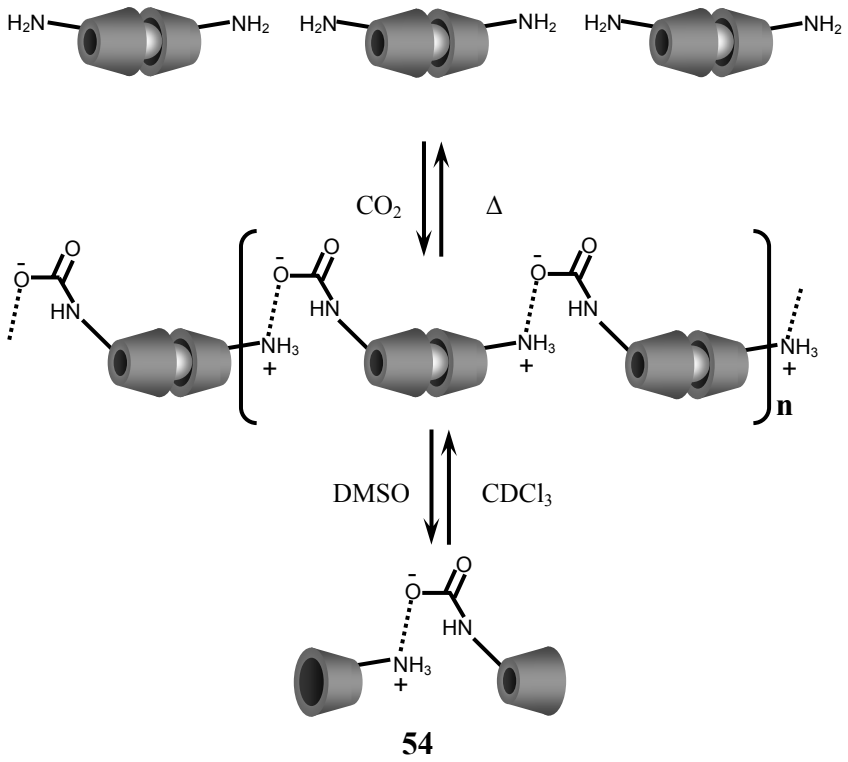


Figure 3. Schematic representation of self-assembled structures formed by *bis*-calixarenes **51** and **52** in apolar solvents.



53

Figure 4. Schematic representation of tetraurea calix[4]arene **53** and its dimer.



54

Figure 5. Schematic representation of the synthesis of polymers and *bis*-calixarene **54** from tetraurea calix[4]arene **53**.

The polymers consisting of heterodimers were prepared by self-organization of *bis*-calixarene **51** having both tetraaryl- and tetratosylurea counterparts (Fig. 3a) and by self-assembly of *bis*-tetraarylurea calixarenes **49** or **50** with *bis*-tetratosylurea calixarene **52** (Fig. 3b).[3]

In the presence of polar solvents like methanol or dimethylsulfoxide hydrogen bonds are broken and the polymeric assemblies dissociate. Polymers based on self-assembling capsules

were also built from single tetraurea calix[4]arene **53** bearing an amino group at the narrow rim (Fig. 4).

Since tetraurea **53** forms dimers in apolar solvents, the connection of their amino residues with bifunctional reagent should lead to appropriate polymers. Thus, the dimers of **53** in benzene were reacted with CO_2 resulting in polymers which precipitated from the solution[4] (Fig. 5). The ^{1}H NMR spectrum of the precipitate in DMSO-d_6 shows the presence of carbamate salt **54** which is formed after dissociation of the polymers. In chloroform the polymer-precipitate dissolves displaying in the spectrum a set of downfield-shifted signals for NH protons of the urea groups.

5.2 Towards self-assembled cyclic oligomers

Our idea is to construct and synthesize *bis*-tetraurea calix[4]arenes which could self-assemble into cyclic oligomers. For this purpose two tetraurea calix[4]arenes must be connected with a spacer via the narrow rim under a certain angle. The angle induced by the spacer should lead to the formation of cyclic trimer (60°), tetramer (90°) or hexamer (120°) (Fig. 6).

The rigidity of the connection between the tetraurea calixarene counterparts is necessary to prevent intramolecular dimerization of the *bis*-tetraurea calixarenes.

Calix[4]arene **55** (X = NH_2) is an example for derivatives which could be easily synthesized by standard procedures and used for the preparation of target *bis*-calixarenes (Fig. 7). Looking for available compounds which could be used as “a bridge” at the narrow rim of calix[4]arene **55** we have found 3-nitroisophthalic acid and derivatives of 3,6-dihydroxy-1,8-naphthalic anhydride[5]. These compounds could be converted into more reactive derivatives (acid chlorides or esters) and reacted with calix[4]arene **55** (X = NH_2). Sonogashira cross-coupling between iodine and triple bond can be used then to attach the bridge units at various spacers (Fig. 8).

Derivatives of *o*-dibromo- or *o*-diiodobenzene and of 2,9-difunctionalized-[1,10]phenanthrolene are the most easily available spacers to introduce a 60° angle into *bis*-calixarenes. As 120° angle directing spacers 2,7-difunctionalized naphthalene or *m*-dibromo- or diiodobenzene (or their derivatives) could be used.

Of course, a geometrical shape of the *bis*-calixarene molecules could play not the main role in their self-assembly. Also the formation of polymers instead of cyclic oligomers is possible. However, the geometrical preorganization should increase the probability for the existence of cyclic structures. Anyway, both kinds of the possible associates will be interesting objects for studies by surface force microscopy and light scattering.

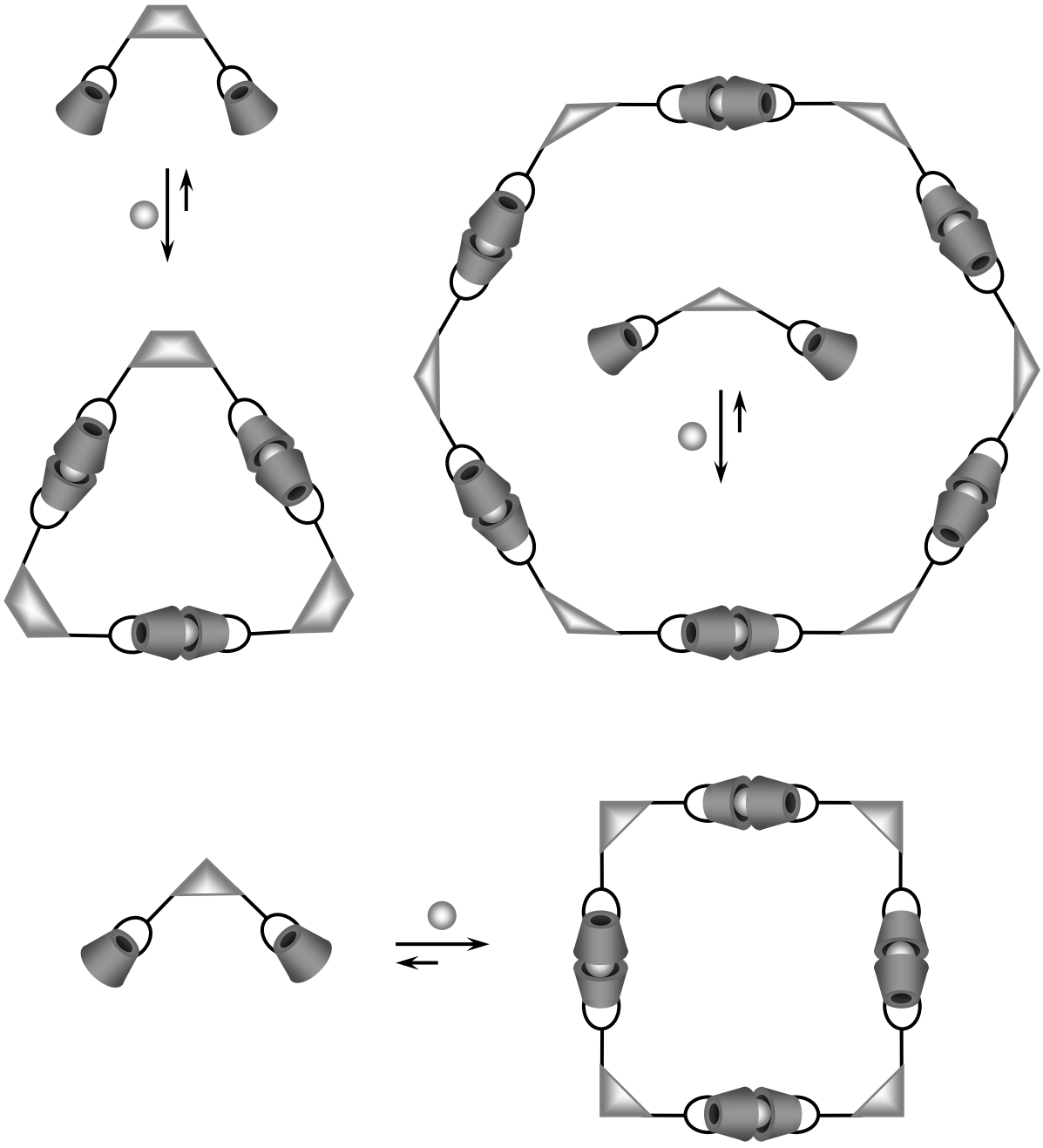


Figure 6. Schematic representation the target self-organization of the *bis*-calixarenes in apolar solvents.

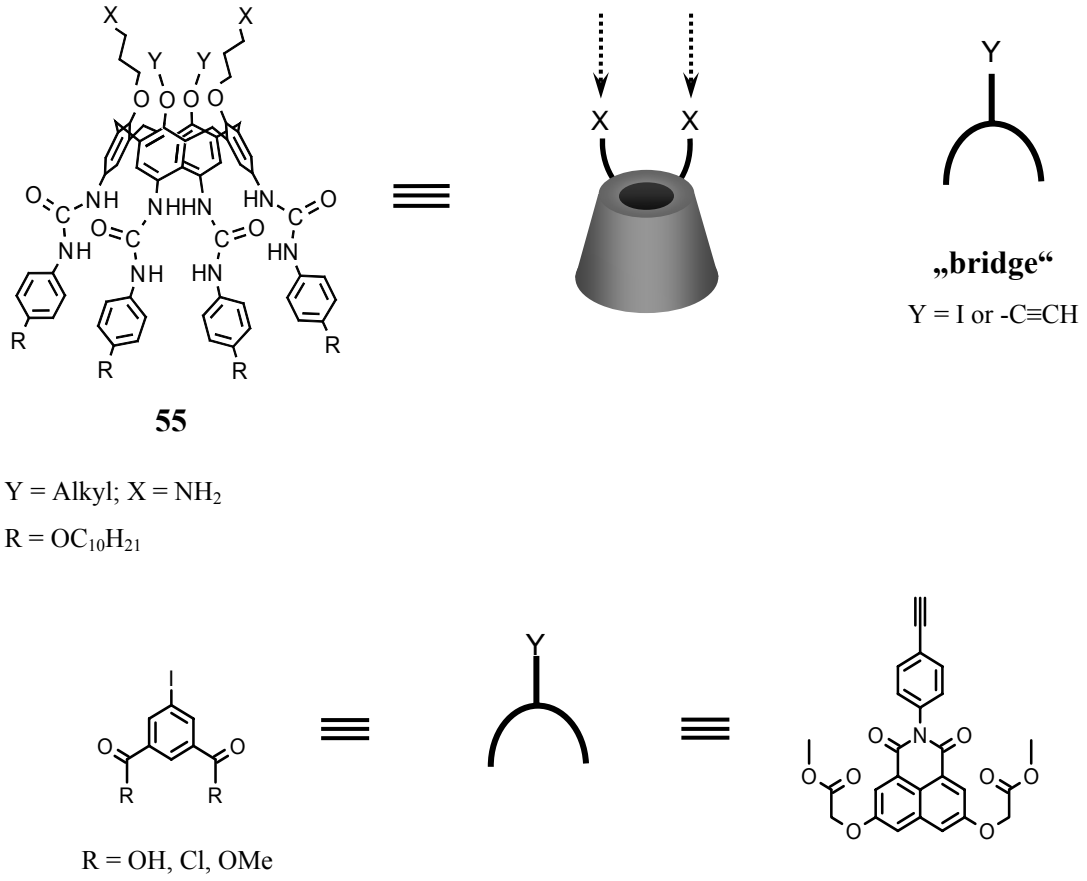


Figure 7. Synthetic blocks for the construction of target *bis*-calixarenes.

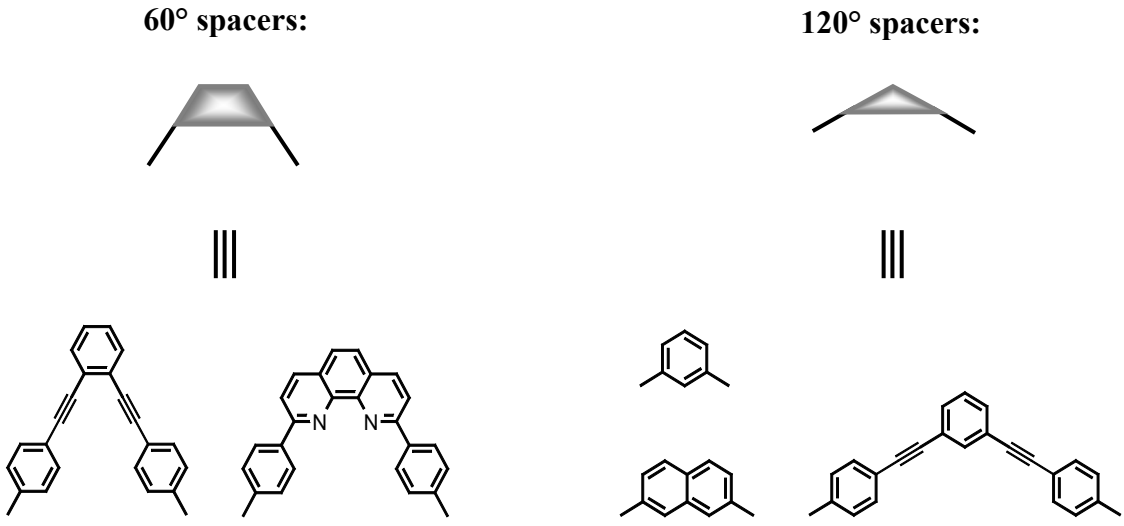


Figure 8. Rigid units which could be applied as angle directors in target *bis*-calixarenes.

5.3 Synthesis of narrow rim-bridged tetraurea calix[4]arenes

Starting from calixarene **56** there are two synthetic pathways to the calixarene **BC13** which can be transformed into **BC20** (Scheme 1). The intramolecular bridge may be introduced before or after the urea functions. Both strategies have their pro and cons and were applied for the synthesis of **BC13**.

Diphthalimidopropyl calixarene **56** was synthesized by stepwise O-alkylation of tetra-*tert*-butyl calix[4]arene as described.[6] Diamine **57** obtained by hydrazinolysis of **56** (75% yield) was acylated under high dilution conditions by 3-iodoisophthalic acid dichloride yielding the desired product **58** (14%) by columnar chromatography on silica gel (dichloromethane / methanol, 30/1, *v*/*v*).

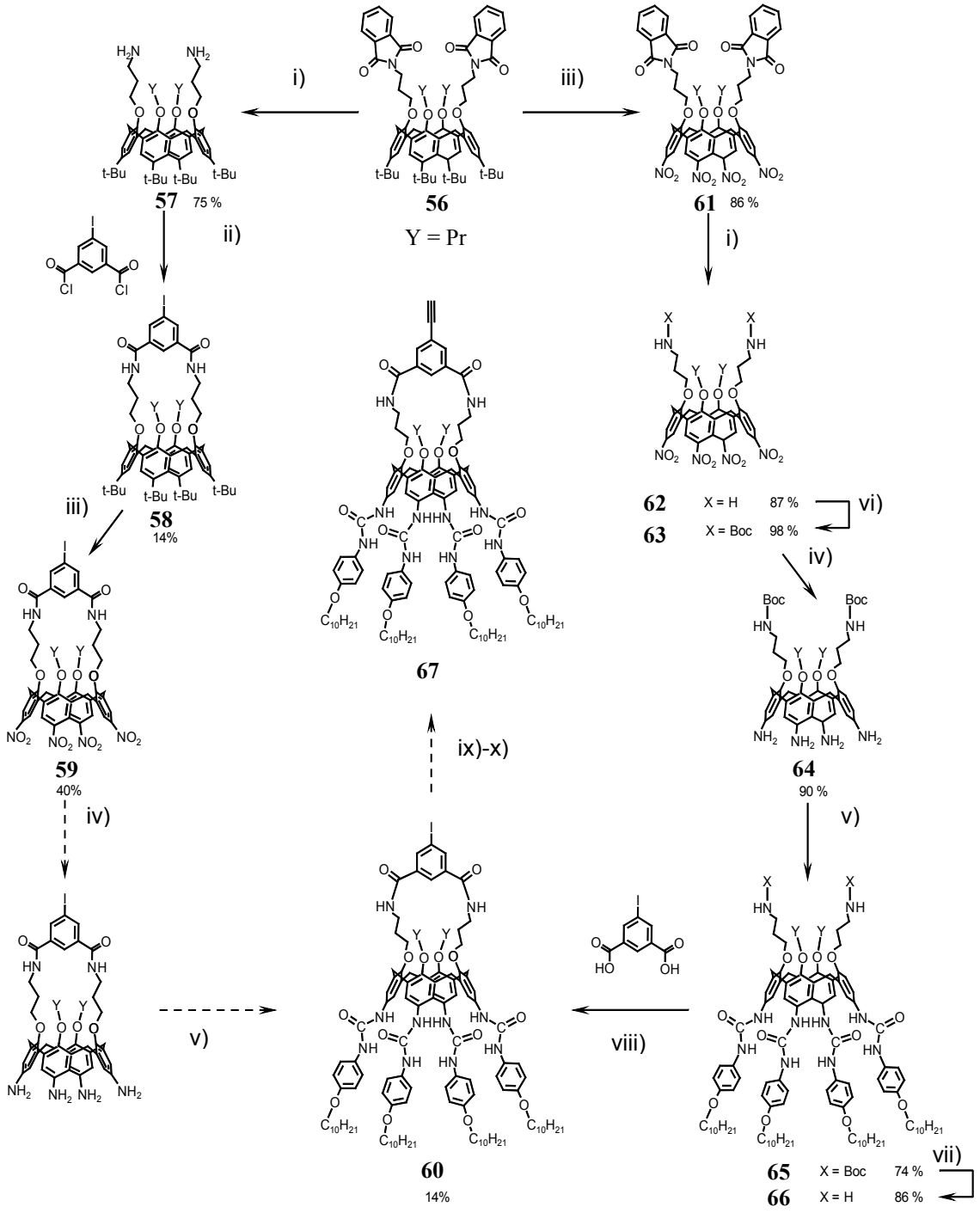
ipso-Nitration of the compound **58** under standard conditions (100% HNO_3, HOAc/dichloromethane, rt) gave hardly soluble compound **59** containing approximately 20% of side products (as concluded from its ^{1}H NMR spectrum). The low yield in the bridging step and the purification difficulties of the tetranitro derivative **59** forced us to try the other strategy.

The di-*N*-phthalimidopropyl calixarene **56** was *ipso*-nitrated as published[6] and the phthalimido groups were cleaved from compound **61** by reflux with hydrazine/ethanol to produce diamine **62** in 87% yield.

The acylation of the diamine **62** by 3-iodoisophthalic acid dichloride has been tried but the cyclic diamide could not be isolated from the reaction mixture.

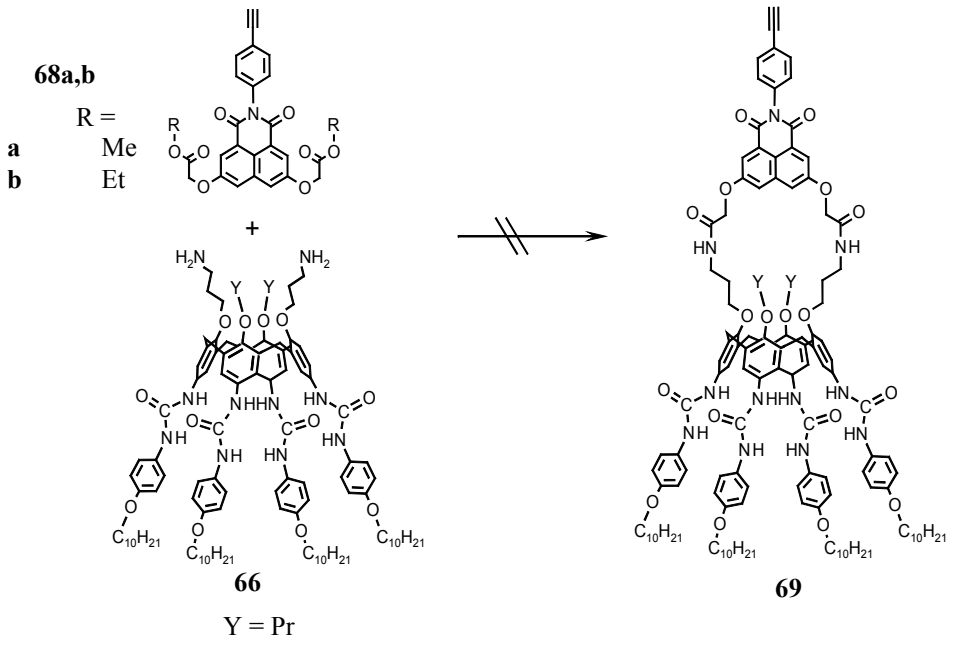
Since urea groups could be destroyed under the phthalimide-cleavage conditions, the phthalimides were cleaved before introduction of the urea groups producing diamine **62**. The amino groups of compound **62** were *N*-Boc-protected (84% yield). The resulting tetranitro **63** was hydrogenated in toluene using Raney-Ni as catalyst (90%) and the tetraamine **64** was acylated by *p*-nitrophenyl urethane of *p*-*n*-decyloxyaniline (74%).

The Boc-groups were cleaved from tetraurea **65** by trifluoroacetic acid (86%) and the diamino tetraurea **66** was acylated by 3-iodoisophthalic acid in the presence of PyBOP in DMF to produce after purification by column chromatography (THF/hexane, 3/4, *v*/*v*) **60** in 14% yield.



Scheme 1. Planned and realized pathways to synthesize **67**. i) $NH_2NH_2 \cdot H_2O$, EtOH, reflux; ii) *i*-Pr_2EtN, CH_2Cl_2; iii) HNO_3/HOAc, CH_2Cl_2; iv) H_2, Raney-Ni, toluene or THF; v) *p*-nitrophenyl urethane of *p*-*n*-decyloxyaniline, *i*-Pr_2EtN, THF; vi) Boc_2O, THF; vii) CF_3COOH, CH_2Cl_2; viii) *i*-Pr_2EtN, PyBOP, DMF; xi) HC≡C-TMS, $Pd(PPh_3)_4$, *i*-Pr_2NH, benzene, 80°C; x) KF, MeOH.

3,6-Dimethoxy- and 3,6-diethoxycarbonylmethoxy-1,8-naphthalic anhydrides (their preparation is described in Chapter 5) were reacted with commercially available *p*-ethynylaniline to produce appropriate imides **68** in 50% yield. Acylation of diamine **66** by imides **68a,b** bearing two ester functions was tried in methanol/toluene at room temperature, in refluxing tetrahydrofurane/methanol solution and in pyridine at 80°C (Scheme 2). Unfortunately all these attempts failed. Probably these diester-imides **68a,b** or diamine **66** have lower reactivity than it is necessary for their conversion to diamide derivative **69**. Only starting material was observed in the reaction mixture by thin layer chromatography and by ^{1}H NMR spectroscopy.



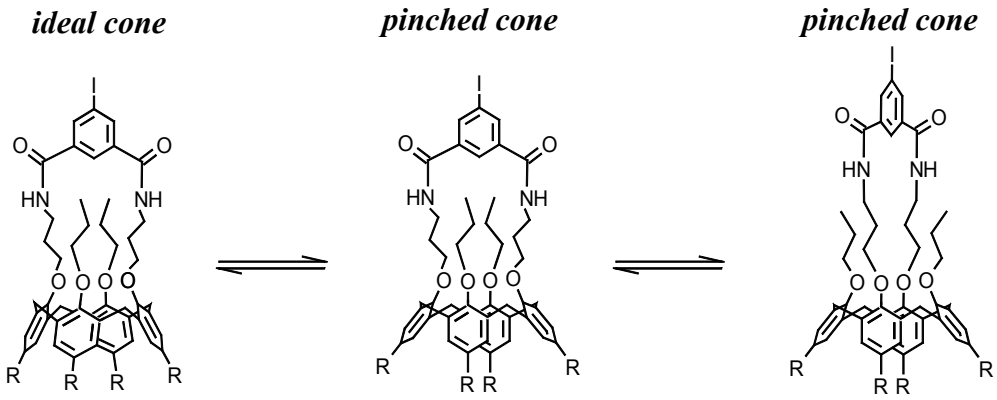
Scheme 2. Attempted acylation of diamine **66** by imides **68a,b**.

5.4 Self-organization of narrow rim-bridged tetraurea

In polar solvents like DMSO tetraurea **60** displays a ^{1}H NMR spectrum corresponding to a C_{2v} symmetrical molecule (Fig. 10a):

- 2 singlets at 6.43 and 7.24 ppm for protons of the aryl groups of the calixarene skeleton;
- 2 pairs of doublets at 6.73, 6.84, 7.10 and 7.34 ppm for protons of the aryl groups adjacent to the urea functions;

- 4 singlets at 7.82, 8.17, 8.34 and 8.43 ppm in ratio 1 : 1 : 1 : 1 for protons of the urea groups;
- 2 triplets at 3.90 and 3.83 ppm for -OCH_2-protons of the decyloxy groups attached to the phenyl rings adjacent to urea groups.



The splitting of the signals for -OCH_2- protons of decyloxy groups together with the large difference in shifts of the signals for the aromatic protons (for singlets of calixarene skeleton $\Delta\delta$ = 0.81 ppm) and for protons of the urea groups suggests a *pinched cone* conformation of the molecule. It is a typical conformation of tetraethers of calix[4]arene, which exist in solution as equilibrium between two pinched cone conformations.

The pinched cone conformation was also observed for **58** in the solid state (see below). Obviously, the introduction of too short or long rigid bridge in the narrow rim of calixarene may fix the molecule in one of the pinched cones. However, usual tetraurea tetraethers adopt an ideal cone conformation in their dimers. Thus, the bridging could potentially hinder the dimerization of tetraurea calix[4]arenes.

Nevertheless, in apolar solvents the bridged **60** forms capsule-like dimers similarly to normal "open chain" tetraureas. This calix[4]arene can be classified as a tetraurea of the ABAB-type.[7] The dimer formed by two calixarenes **60** has D_2 symmetry and is chiral only due to the different arrangement of calixarenes (Fig. 9). Such type of chirality is known as *supramolecular chirality*. In this case the directionality of the hydrogen bonded belt does not create additional stereoisomers but reduce the symmetry of the capsule (C_2).

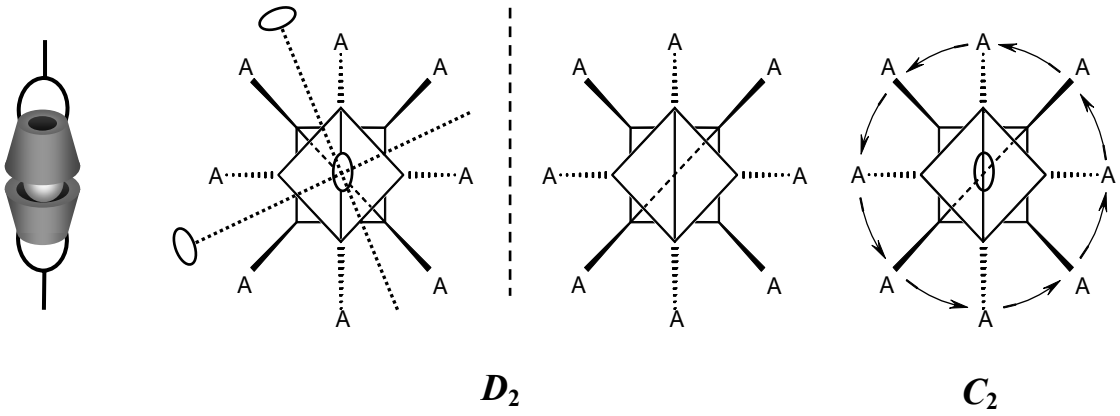


Figure 9. Schematic representation of the symmetry properties of the homodimer of calixarene **60**. The symmetry class is indicated with and without directionality of the hydrogen bonded belt (symbolized by arrows); 0 represent C_2 axes.

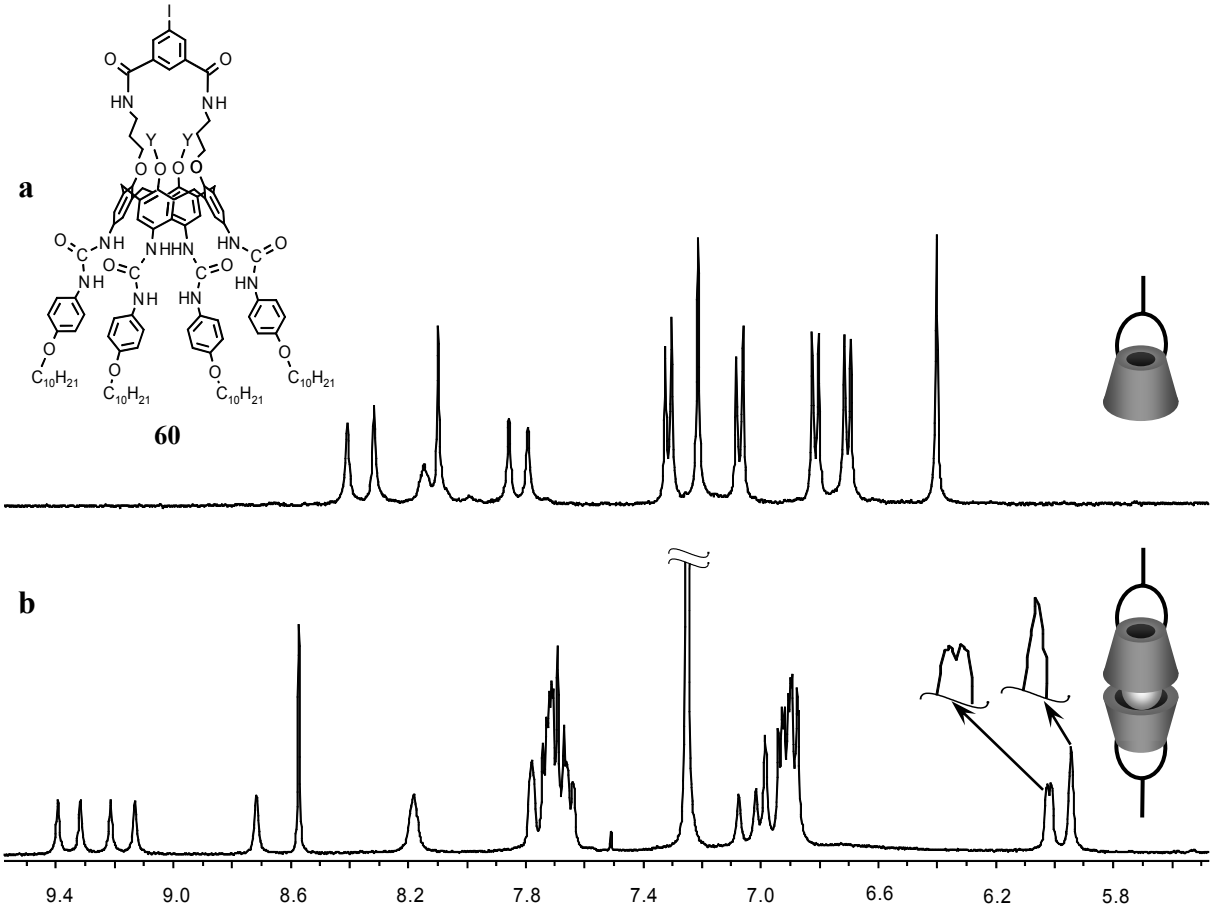


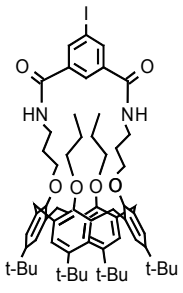
Figure 10. The parts of ^{1}H NMR spectra of calixarene **60**. a) in DMSO-d_6, rt; b) in $CDCl_3$, rt.

In ^{1}H NMR-spectrum C_2 symmetry of the assembly is reflected in additional splitting of the signals (Fig. 10b):

- 4 singlets in ratio 1 : 1 : 1 : 1 for downfield shifted protons of the urea groups (9.39, 9.31, 9.21 and 9.13 ppm);
- 4 pairs of *m*-coupled doublets for protons of the aryl groups of calixarene skeleton, from them 4 doublets shifted upfield (6.03, 6.01 and 2 signals overlapped at 5.94 ppm) and 4 doublets shifted downfield (2 signals overlapped at 8.18 ppm and 2 signals overlapped at 7.78 ppm).

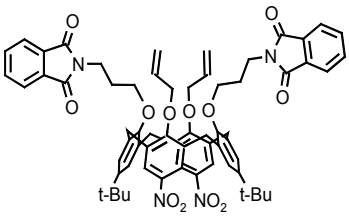
In summary, the calixarene **60** is able to form dimers in apolar solvents and could be used for the construction of the target *bis*-calixarenes. Unfortunately the low yield in the "bridging" (14%) limits the application of **60** considerably.

5.5 Single crystal X-ray analysis of narrow rim bridged calixarene



58

The structure of **58** was proved also by X-ray analysis[8] (Fig. 11a). Single crystals were obtained by slow evaporation of a solution in dichloromethane/ ethylacetate/methanol. A water molecule in the crystal is fixed by hydrogen bonds which are formed with two hydrogens of amide functions and the oxygen of propoxy group. The distances between the atoms are O(1W)-N(124) = 3.062 Å, O(1W)-N(324) = 3.063 Å and O(1W)-O(42) = 2.911 Å. In the same time a methanol molecule forms bifurcated hydrogen bonds to the amide oxygen O(1M)-O(125) = 2.676 Å and to the water molecule O(1M)-O(2W) = 2.698 Å fixed in the adjacent molecule of calix[4]arene **58**. Thus, the calixarene molecules are connected with each other via chains of hydrogen bonds formed with water and methanol molecules (Fig. 11b).



70

Calixarene **58** adopts a *pinched cone* conformation in the solid state and its molecule has non-crystallographic C_{2v} symmetry. A similar conformation was found by X-ray for compound **70**[9], which has at the narrow rim the chains of the three-carbons-length between the A,C-phenolic oxygens and the nitrogens like **58** and allyl groups (also three carbons) attached to other two phenolic oxygens.

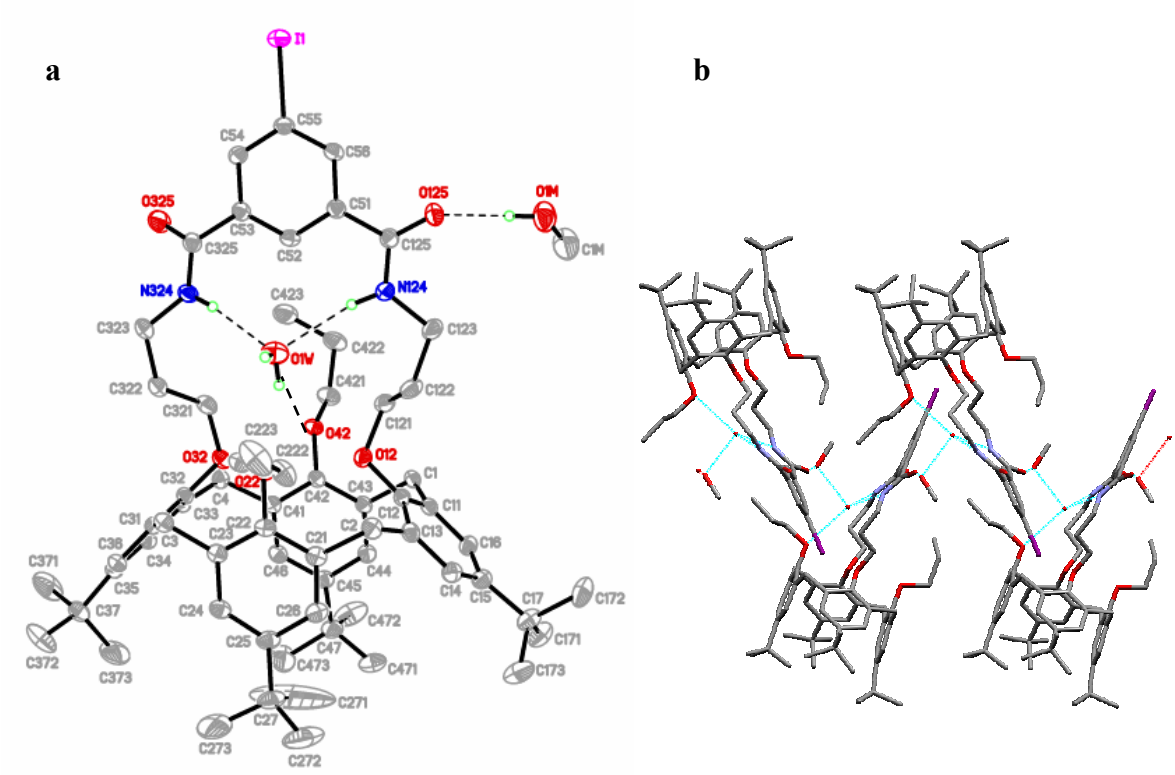


Figure 11. The X-ray structure of the calix[4]arene **58**·H_2O·MeOH including a numbering scheme (a) and packing of molecules (b); red points represent oxygen of water molecules.

A general description of the conformation of calixarenes is possible, using the torsion angles around the σ-bonds connecting the methylene bridges and the aromatic units (Table 2). The conformation of a given calix[4]arene is characterised by a typical sequence of the signs of these torsion angles. Like all compounds in a *cone* conformation, for compound **58** these sequences were found: (+,-)(+,-)(+,-)(+,-).[10]

The inclinations of the single phenolic units with respect to a reference plane (the best plane through the four methylene carbon atoms (C1 – C4)) may be used for additional characterization of the calix[4]arene conformation. These δ-values[11] are also included in Table 2. Values larger then 90° mean that the phenolic unit is bent outwards.

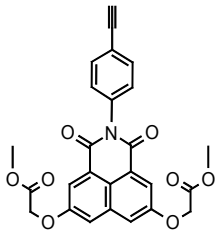
Two phenolic units of compound **58** as well as the bridge phenyl (C51-C56) are almost parallel to each other and perpendicular to the best plane (91.8°, 98.1° and 89.6° correspondingly). The other two phenolic rings are bent outwards in 133.8° and 135.1°. In case of the compound **70** two nitrophenyl units are bent inwards and the other two phenyl rings pointed outwards.

Table 2. Comparison of crystallographic data of **58** with calix[4]arene **70**: **I)** Torsion angles (°) around the Ar-CH_2-bonds; **II)** Distances within the reference plane; **III)** Inclination δ (°) of the aromatic units with respect to the reference plane.

I. Torsion angles	**58**	**70**
C42-C41-C4-C33	-111.9	133.2
C41-C4-C33-C32	74.4	-71.1
C32-C31-C3-C23	-73.1	61.3
C31-C3-C23-C22	116.2	-113.6
C22-C21-C2-C13	-118.9	136.6
C21-C2-C13-C12	76.9	-78.4
C12-C11-C1-C43	-75.8	66.8
C11-C1-C43-C42	111.5	-115.4
II. Reference planes C1 – C4		
Distance C1 − C2 (Å)	5.045	4.962
Distance C2 − C3 (Å)	5.124	5.122
Distance C3 − C4 (Å)	5.066	4.988
Distance C1 − C4 (Å)	5.097	5.117
Distance C1 − C3 (Å)	7.267	7.471
Distance C2 − C4 (Å)	7.108	6.729
III. Inclination of the aromatic units (δ)		
C11 − C16	133.8	134.4
C21 − C26	91.8	78.9
C31 − C36	135.1	142.4
C41 − C46	98.1	79.8
C51 − C56	89.6	-

5.6 Experimental

Tetra-*tert*-butyl- and -nitrocalix[4]arene 1,3-dipropyl-2,4-diphthalimidopropylethers **56** and **61** were prepared as described.[6]

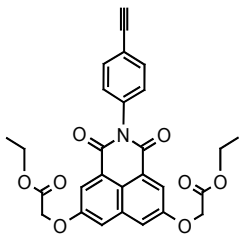


N-p-ethynylphenyl-3,6-dimethoxycarbonylmethoxy-1,8-naphthalimide ***68a****:*

The *p*-ethynylaniline (0.17 g, 1.47 mmol) and 3,6-dimethoxycarbonylmethoxy 1,8-naphthalic anhydride (0.50 g, 1.34 mmol) were refluxed in dry pyridine (5 mL) for 24 h. After cooling to rt the reaction mixture was poured into cold acetic acid/water solution (20 : 50 mL). The precipitate was filtered off, washed with water (2 x 20 mL) and methanol (2 x 20 mL). The solid was reprecipitated from THF/methanol to give the product as a beige powder.

Yield: 0.33 g (51%).

m.p. 232-233°C; MS (FD): m/z 473.4 (M^+); ^{1}H NMR ($CDCl_3$): δ 8.16 (d, Ar-*H*, 2 H, $^4J_{HH}$ 2.6 Hz), 7.65 (d, Ar-*H*, 2 H, $^3J_{HH}$ 8.5 Hz), 7.44 (d, Ar-*H*, 2 H, $^4J_{HH}$ 2.2 Hz), 7.25 (d, Ar-*H*, 2 H, $^3J_{HH}$ 8.1 Hz), 4.84 (s, -O-C*H*$_2$-COOCH$_3$, 4 H), 3.83 (s, -C*H*$_3$, 6 H), 3.13 (s, -C≡C*H*, 1 H).



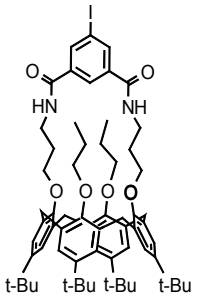
N-p-ethynylphenyl-3,6-diethoxycarbonylmethoxy-1,8-naphthalimide ***68b****:*

Prepared as described above for **BC21a** from *p*-ethynylaniline (0.13 g, 1.09 mmol) and 3,6-diethoxycarbonylmethoxy 1,8-naphthalic anhydride (0.40 g, 0.99 mmol) and pyridine (5 mL), reflux, 24 h. The solid was reprecipitated from THF/methanol to give the product as a beige powder.

Yield: 0.25 g (50%).

m.p. 227-228°C; MS (FD): m/z 501.2 (M^+); ^{1}H NMR ($CDCl_3$): δ 8.16 (d, Ar-*H*, 2 H, $^4J_{HH}$ 2.0 Hz), 7.65 (d, Ar-*H*, 2 H, $^3J_{HH}$ 8.2 Hz), 7.44 (d, Ar-*H*, 2 H, $^4J_{HH}$ 2.0 Hz), 7.25 (d under solvent peak, Ar-*H*, 2 H), 4.84 (s, -O-C*H*$_2$-COOCH$_3$, 4 H), 4.30 (q, -C*H*$_2$-, 4 H, $^3J_{HH}$ 7.0 Hz), 3.12 (s, -C≡C*H*, 1 H), 1.31 (t, -C*H*$_3$, 6 H, $^3J_{HH}$ 7.0 Hz).

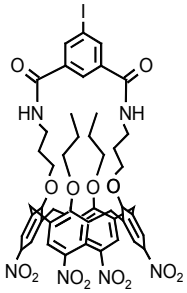
Calix[4]arene ***58****:*



5-Iodoisophthalic acid (0.178 g, 0.608 mmol) and oxalyl chloride (0.435 g, 3.424 mmol) were mixed in toluene (10 ml). Then 1 drop of DMF was added to the reaction mixture and the mixture was stirred for 4 h at 60°C. The reaction mixture was cooled to the room temperature, the liquid was decanted and the solvent was evaporated in vacuum to give the corresponding acid chloride. A solution of the acide chloride in dichloromethane (200 ml) and a solution of calixarene diamine (0.515 g, 0.608 mmol) and diisopropylethylamine (0.236 g, 1.824 mmol) in dichloromethane (200 ml) were simultaneously dropped in the stirring dichloromethane (150 ml). The reaction mixture was stirred for 24 h. Then the solvent was evaporated and the residue was passed through the column (silica, THF/CH_2Cl_2, 1/30) to produce the product as a white powder. Yield: 0.093 g (14%).

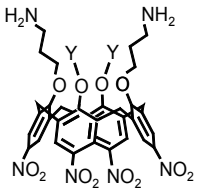
m.p. >290°C (decomp.); MS (FD): m/z 1103.7 (M^+); ^{1}H NMR ($CDCl_3$): δ 8.53 (s, Ar-*H*, 2 H), 8.50 (s, Ar-*H*, 1 H), 7.58 (s, N-*H*, 2 H), 7.13 (s, Ar-*H*, 4 H), 6.58 (s, Ar-*H*, 4 H), 4.38 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 12.3 Hz), 4.33 (br.t, -O-C*H*$_2$-, 4 H, $^3J_{HH}$ 7.3 Hz), 3.68 (t, -O-C*H*$_2$-, 4 H, $^3J_{HH}$ 7.5 Hz), 3.57-3.49 (m, -NH-C*H*$_2$-, 4 H), 3.18 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 12.3 Hz), 2.25-2.13 (m, -NH-CH$_2$-C*H*$_2$-, 4 H), 1.89-1.79 (m, -O-CH$_2$-C*H*$_2$-, 4 H), 1.32 (s, -C*H*$_3$, 18 H), 0.88 (t, -C*H*$_3$, 6 H, $^3J_{HH}$ 7.3 Hz), 0.83 (s, -C*H*$_3$, 18 H).

Calix[4]arene ***59****:*



Glacial acetic acid (1 ml) and fuming nitric acid (1,6 ml) were added to a solution of the bridged calixarene (0.132 g, 0.120 mmol) in dichloromethane (25 ml). The reaction mixture was stirred 2 h, and then water was added. From the reaction mixture a precipitate was formed. The water layer was decanted. The suspension in dichloromethane was washed additionally with water (3 x 100 ml). The solvent was evaporated from the suspension. The residue was dried by toluene distillation. Recrystallization of the residue in dichloromethane gave the product as yellowish powder. Yield: 0.050 g (39%).

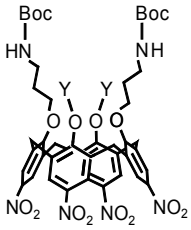
m.p. >240°C (decomp.); ^{1}H NMR (DMSO-d$_6$): δ 8.45 (s, Ar-*H*, 4 H), 8.21 (s, N-*H*, 2 H, $^3J_{HH}$ 5.3 Hz), 8.12 (s, Ar-*H*, 2 H), 8.07 (s, Ar-*H*, 1 H), 6.89 (s, Ar-*H*, 4 H), 4.55-4.42 (m, -O-C*H*$_2$-, 4 H), 4.35 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 13.6 Hz), 3.76-3.59 (m, -O-C*H*$_2$-, Ar-C*H*$_2$-Ar, 8 H), 3.43-3.33 (m, -NH-C*H*$_2$-, 4 H), 1.87-1.73 (m, -NH-CH$_2$-C*H*$_2$-, 4 H), 1.67-1.54 (m, -O-CH$_2$-C*H*$_2$-, 4 H), 0.74 (t, -C*H*$_3$, 6 H, $^3J_{HH}$ 7.3 Hz).



Calix[4]arene ***62*** *: ethanol 1:1.*

Hydrazine hydrate (60 ml) was added to a stirred suspension of tetranitrocalix[4]arene 1,3-dipropyl-2,4-diphthalimidopropylether **61** (7.472 g, 7.029 mmol) in ethanol (240 ml). A reaction mixture was refluxed for 2 hours. Then it was cooled to room temperature and left for 2 hours in fridge. The precipitate was filtered off, washed with ethanol (2 x 50 ml) and dried (in high vacuum) to give product as yellow powder. Yield: 4.853 g (86 %).

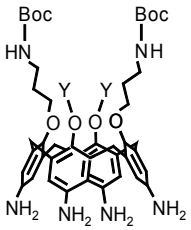
m.p. >165°C (decomp.); MS (ESI): m/z 803.4 (M^+); ^{1}H NMR (DMSO-d_6): δ 7.79 (s, Ar-*H*, 4 H), 7.51 (s, Ar-*H*, 4 H), 4.39 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 13.7 Hz), 4.04 (t, -O-C*H*$_2$-, 4 H, $^3J_{HH}$ 6.8 Hz), 3.99 (t, -O-C*H*$_2$-, 4 H, $^3J_{HH}$ 7.3 Hz), 3.69 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 13.7 Hz), 3.54-2.92 (q: 3.44 and br.s overlapped, -O-C*H*$_2$-CH$_3$, N-*H*$_2$, 10 H, $^3J_{HH}$ 7.0 Hz), 2.71 (t, NH$_2$-C*H*$_2$-, 4 H, $^3J_{HH}$ 6.6 Hz), 1.98-1.78 (m, -NH-CH$_2$-C*H*$_2$-, -O-CH$_2$-C*H*$_2$-, 8 H), 1.05 (t, -C*H*$_3$, 3 H, $^3J_{HH}$ 7.1 Hz), 0.96 (t, -C*H*$_3$, 6 H, $^3J_{HH}$ 7.3 Hz).



Calix[4]arene ***63****:*

Boc anhydride (1.071 g, 4.908 mmol) was added to a solution of tetranitrocalix[4]arene 1,3-dipropyl-2,4-diaminopropylether·ethanol (1.894 g, 2.231 mmol) in THF (30 ml) and the reaction mixture was stirred at rt for 12 h. Then the solvent was evaporated and the oily residue was reprecipitated from dichloromethane/hexane to give pure product as white powder. Yield: 2.193 g (98%).

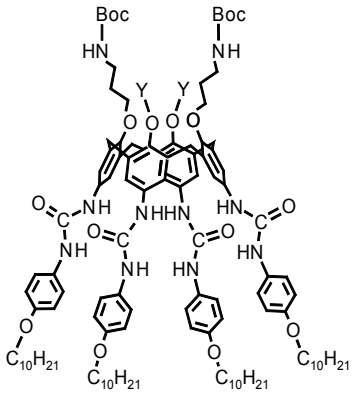
m.p. > 125°C (decomp.); MS (FD): m/z 1002.6 (M^+); ^{1}H NMR (DMSO-d_6): δ 7.78 (s, Ar-*H*, 4 H), 7.50 (s, Ar-*H*, 4 H), 6.92 (br.t, N-*H*, 2 H), 4.37 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 13.7 Hz), 4.00 (t, -O-C*H*$_2$-, 4 H, $^3J_{HH}$ 7.6 Hz), 3.95 (t, -O-C*H*$_2$-, 4 H, $^3J_{HH}$ 6.6 Hz), 3.68 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 14.2 Hz), 3.18-3.05 (m, NH-C*H*$_2$-, 4 H), 2.04-1.92 (m, -NH-CH$_2$-C*H*$_2$-, 4 H), 1.92-1.79 (m, -O-CH$_2$-C*H*$_2$-, 4 H), 1.37 (s, -C*H*$_3$, 18 H), 0.94 (t, -C*H*$_3$, 6 H, $^3J_{HH}$ 7.3 Hz).



Calix[4]arene ***64****:*

A solution of tetranitro calix[4]arene (1.860 g, 1.854 mmol) in toluene (100 ml) was vigorously stirred in hydrogen atmosphere at rt in the presence of catalytic amount of Raney-Ni for 5-6 hours (a degree of conversion was controlled by TLC). Then the catalyst was filtered off and the solvent was removed in vacuum. The oily residue was reprecipitated from chloroform/hexane to give appropriate tetraamino product as white powder. Yield: 1.49 g (90%).

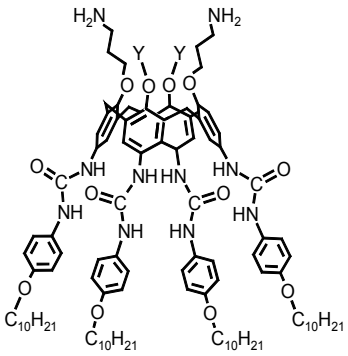
m.p. >125°C (decomp.); MS (FD): m/z 882.7 (M^+); ^{1}H NMR (DMSO-d_6): δ 6.78 (br.t, N-*H*, 2 H), 5.97 (s, Ar-*H*, 4 H), 5.92 (s, Ar-*H*, 4 H), 4.34-4.03 (s and d: 4.16 overlapped, N-H_2, Ar-CH_2-Ar, 12 H, $^2J_{HH}$ 12.2 Hz), 3.80-3.53 (m, -O-CH_2-, 8 H), 3.13-2.96 (m, NH-CH_2-, 4 H), 2.77 (d, Ar-CH_2-Ar, 4 H, $^2J_{HH}$ 12.7 Hz), 2.12-1.70 (m, -NH-CH$_2$-CH_2-, -O-CH$_2$-CH_2-, 8 H), 1.38 (s, -CH_3, 18 H), 0.89 (t, -CH_3, 6 H, $^3J_{HH}$ 7.3 Hz); (CDCl$_3$): δ 6.22 (s, Ar-*H*, 4 H), 5.87 (s, Ar-*H*, 4 H), 5.00 (br.s, N-*H*, 2 H), 4.24 (d, Ar-CH_2-Ar, 4 H, $^2J_{HH}$ 13.3 Hz), 3.84 (t, -O-CH_2-, 4 H), 3.63 (br.t, -O-CH_2-, 4 H), 3.28-3.10 (m, NH-CH_2-, 4 H), 2.77 (br.s and d: 2.91, N-H_2, Ar-CH_2-Ar, $^2J_{HH}$ 14.0 Hz, 12 H), 2.06 (br.s, -NH-CH$_2$-CH_2-, 4 H), 1.90-1.69 (m, -O-CH$_2$-CH_2-, 4 H), 1.44 (s, -CH_3, 18 H), 0.95 (t, -CH_3, 6 H, $^3J_{HH}$ 7.3 Hz).



Calix[4]arene ***65****:*

The solution of tetraamino calix[4]arene (0.515 g, 0.580 mmol) and diisopropylethylamine (0.315 g, 2.438 mmol) in THF (10 ml) was added to the solution of *p*-decyloxyphenylamido p-nitrophenyl carbamic acid ester (1.016 g, 2.438 mmol) in THF (10 ml). Then the reaction mixture was stirred at rt for 12 h and acetonitrile (60 ml) was added to the reaction mixture which was stirred for further 12 h. During this time a solid has precipitated from the reaction mixture. The solid was filtered off and washed thoroughly with acetonitrile to give the product as a beige powder. Yield: 0.856 g (74%).

m.p. >170°C (decomp.); MS (ESI): m/z 2007.4 (M+Na^+); ^{1}H NMR (DMSO-d_6): δ 8.26-7.95 (m, N-*H*, 8 H), 7.31-7.12 (m, Ar-*H*, 8 H), 6.95-6.64 (br.t: 6.88, s: 6.83 and m overlapped, N-*H*, Ar-*H*, 18 H), 4.32 (d, Ar-CH_2-Ar, 4 H, $^2J_{HH}$ 12.2 Hz), 3.99-3.65 (br.t: 3.87 and m overlapped, -O-CH_2-, 16 H), 3.18-2.97 (m, -NH-CH_2-, Ar-CH_2-Ar, 8 H), 2.05 (m, -NH-CH$_2$-CH_2-, 4 H), 1.98-1.82 (m, -CH_2-, 4 H), 1.74-1.57 (m, -O-CH$_2$-CH_2-, 8 H), 1.49-1.13 (s: 1.39 and m, -CH_3, -CH_2-, 74 H), 0.95 (t, -CH_3, 6 H, $^3J_{HH}$ 7.3 Hz), 0.85 (br.t, -CH_3, 12 H).

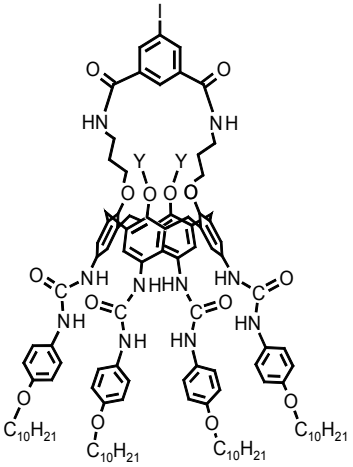


Calix[4]arene ***66****:*

Trifluoroacetic acid (3 ml) was added to the solution of tetraurea calix[4]arene di-*N*-Boc-aminopropylether (0.303 g, 0.153 mmol) in dichloromethane (10 ml) and the reaction mixture was stirred at rt for 2 h. Then the solvent was removed in vacuum and the salt was dissolved in dichloromethane and washed by sodium hydrocarbonate solution. The diamine was extracted by

dichloromethane, the solution was dried ($MgSO_4$) and finally the solvent was removed under reduced pressure to give oily residue. The residue was triturated with methanol; the solid was filtered off and washed thoroughly with methanol to give the product as a beige powder. Yield: 0.236 g (86%).

m.p. >205°C (decomp.); MS (ESI): m/z 1985.2 ($M+H^+$); ^{1}H NMR (DMSO-d_6): δ 8.30 (s, N-*H*, 2 H), 8.23 (s, N-*H*, 4 H), 8.13 (s, N-*H*, 2 H), 7.23 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.5 Hz), 7.19 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.5 Hz), 6.90-6.63 (m, Ar-*H*, 16 H), 4.31 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 12.3 Hz), 3.99-3.72 (m, -O-C*H*$_2$-, 16 H), 3.08 (d, Ar-C*H*$_2$-Ar, 4 H, $^2J_{HH}$ 12.6 Hz), 2.82 (br.t, NH_2-C*H*$_2$-, 4 H), 2.03 (m, -NH-CH_2-C*H*$_2$-, 4 H), 1.98-1.82 (m, -C*H*$_2$-, 4 H), 1.74-1.57 (m, -O-CH_2-C*H*$_2$-, 8 H), 1.46-1.13 (m, -C*H*$_2$-, 56 H), 0.95 (t, -C*H*$_3$, 6 H, $^3J_{HH}$ 7.2 Hz), 0.84 (br.t, -C*H*$_3$, 12 H).



Calix[4]arene ***60****:*

Trifluoroacetic acid (4 ml) was added to the solution of tetraurea calix[4]arene di-*N*-Boc-aminopropylether (0.170 g, 0.0856 mmol) in dichloromethane (10 ml) and the reaction mixture was stirred at rt for 2 h. Then the solvent was removed in vacuum and the salt was dissolved in THF (10 ml). An excess of Et_3N (1 ml) was added to convert the salt into the appropriate amine. Then the solvent was evaporated until dryness. The residual amine was dissolved in DMF (100 ml). The 5-iodoisophthalic acid (0.025 g, 0.0856 mmol) was mixed with PyBOP (0.089 g, 0.171 mmol) in DMF (100 ml) and the mixture was stirred for 20 min under nitrogen. Then the solution of the amine in DMF and the solution of isophthalic acid and PyBOP were simultaneously added dropwise into the stirring DMF (50 ml). The reaction mixture was stirred under nitrogen for further 24 h. Then DMF was removed under reduced pressure and water (100 ml) was added to the residue to precipitate the products. The precipitate was filtered off, washed with water and methanol. The target product was isolated by column chromatography (silica, THF/He, 3/4) as white powder. Yield:0.025 g (14%).

m.p. >220°C (decomp.); MS (ESI): m/z 2063.2 ($M+Na^+$), 1043.1 ($M+2Na^+$); ^{1}H NMR (DMSO-d_6): δ 8.43 (s, N-*H*, 2 H), 8.43 (s, N-*H*, 2 H), 8.34 (s, N-*H*, 2 H), 8.17 (br.t, N-*H*, 2 H), 8.12 (s, Ar-*H*, 3 H), 7.88 (s, N-*H*, 2 H), 7.82 (s, N-*H*, 2 H), 7.34 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.9 Hz), 7.24 (s, Ar-*H*, 4 H), 7.10 (d, Ar-*H*, 4 H, $^3J_{HH}$ 9.2 Hz), 6.84 (d, Ar-*H*, 4 H, $^3J_{HH}$ 9.2 Hz), 6.73 (d, Ar-*H*, 4 H, $^3J_{HH}$ 8.9 Hz), 6.43 (s, Ar-*H*, 4 H), 4.47-4.22 (m and d: 4.34 overlapped, -O-C*H*$_2$-, Ar-C*H*$_2$-Ar, 8 H, $^2J_{HH}$ 12.6 Hz), 3.90 (t, -O-C*H*$_2$-, 4 H, $^3J_{HH}$ 6.3 Hz), 3.83 (t, -O-C*H*$_2$-

, 4 H, $^{3}J_{HH}$ 6.5 Hz), 3.54 (t, -O-CH_2-, 4 H, $^{3}J_{HH}$ 7.3 Hz), 3.46-3.35 (m, -NH-CH_2-, 4 H), 3.08 (d, Ar-CH_2-Ar, 4 H, $^{2}J_{HH}$ 11.9 Hz), 2.02-1.88 (m, -NH-CH_2-CH_2-, 4 H), 1.74-1.53 (m, -O-CH_2-CH_2-, 12 H), 1.46-1.12 (m, -CH_2-, 56 H), 0.92-0.77 (m, -CH_3, 12 H), 0.67 (t, -CH_3, 6 H, $^{3}J_{HH}$ 7.5 Hz).

5.6 Literature and comments

[1] R. K. Castellano, D. M. Rudkevich, J. Rebek, Jr. *Proc. Natl. Acad. Sci. USA* **1997**, *94*, 7132-7137.

[2] C. A. Schalley, R. K. Castellano, M. S. Brody, D. M. Rudkevich, G. Siuzdak, J. Rebek, Jr. *J. Am. Chem. Soc.* **1999**, *121*, 4568-4579.

[3] R. K. Castellano, J. Rebek, Jr. *J. Am. Chem. Soc.* **1998**, *120*, 3657-3663.

[4] H. Xu, E. M. Hampe, D. M. Rudkevich *Chem. Commun.* **2003**, 2828-2829.

[5] 3,6-Dialkoxy-1,8-naphthalic anhydrides were prepared mainly for the functionalization of tetraamino calix[8]arene (Chapter 6).

[6] V. Böhmer, J.-F. Dozol, C. Grüttner, K. Liger, S. E. Matthews, S. Rudershausen, M. Saadioui, P. Wang *Org. Biomol. Chem*. **2004**, *2*, 2327–2334.

[7] A. Pop, M. O. Vysotsky, M. Saadioui, V. Böhmer *Chem. Comm.* **2003**, 1124-1125.

[8] Crystallographic measurement was performed by Dr. M. Bolte (Institut für Organische Chemie, Johann Wolfgang Von Goethe Universität, Frankfurt/Main) at 173 K using a STOE-IPDS-II diffractometer with graphite monochromated MoKα radiation. Empirical formula is $C_{65}H_{89}IN_2O_8$; M = 1153.28; crystal size 0.35 x 0.27 x 0.25 mm;[3] orthorhombic crystal system; space group P 212121; unit cell dimensions a = 11.2099(5) Å, b = 15.8759(6) Å, c = 35.5340(15) Å, α = β = γ = 90°; V = 6323.9(5) Å^3; Z = 4. Structure was solved by direct methods (G. M. Sheldrick *Acta Cryst.* **1990**, *A46*, 467-473), structure refinement by full-matrix least-squares with SHELXL (G. M. Sheldrick, Universität Göttingen, Germany, 1997). 35791 reflections collected, 11121 independent, Rint = 0.0489, R_1 = 0.0387, wR_2 = 0.1059 for I>2σ(I). Largest diff. peak and hole were 0.929 and -0.740 e/Å^3.

[9] C. Danila, M. Bolte, V. Böhmer *Org. Biomol. Chem.* **2004**, *3*, 172-184.

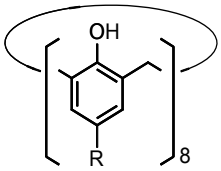
[10] Since starting point and direction are in principle arbitrary, the sequence (+,-)(+,-)(-,-)(+,+) is identical to (-,+)(+,+)(-,-)(-,+), listed in Table 2.

[11] M. Perrin, D. Oehler in *"Calixarenes, A Versatile Class of Macrocyclic Compounds"* (Eds. J. Vicens, V. Böhmer), Kluwer Academic Publishers, 1991.

Chapter 6

Functionalized calix[8]arenes as building blocks for columnar structures.

6.1 Most frequently found conformations of calix[8]arene



I

Calix[8]arenes are conformationally more flexible than calix[4]arenes. A variety of conformations has been observed in the solid state by X-ray crystallography for basic calix[8]arenes **I** and their derivatives.[1] Most stable of them found is the so-called "pleated loop conformation" stabilized by a cyclic array of intramolecular hydrogen bonds formed between hydroxy groups of the phenolic units (Fig. 1). The internal diameter of the cavity deduced from X-ray[2] is about 0.7-0.8 nm.

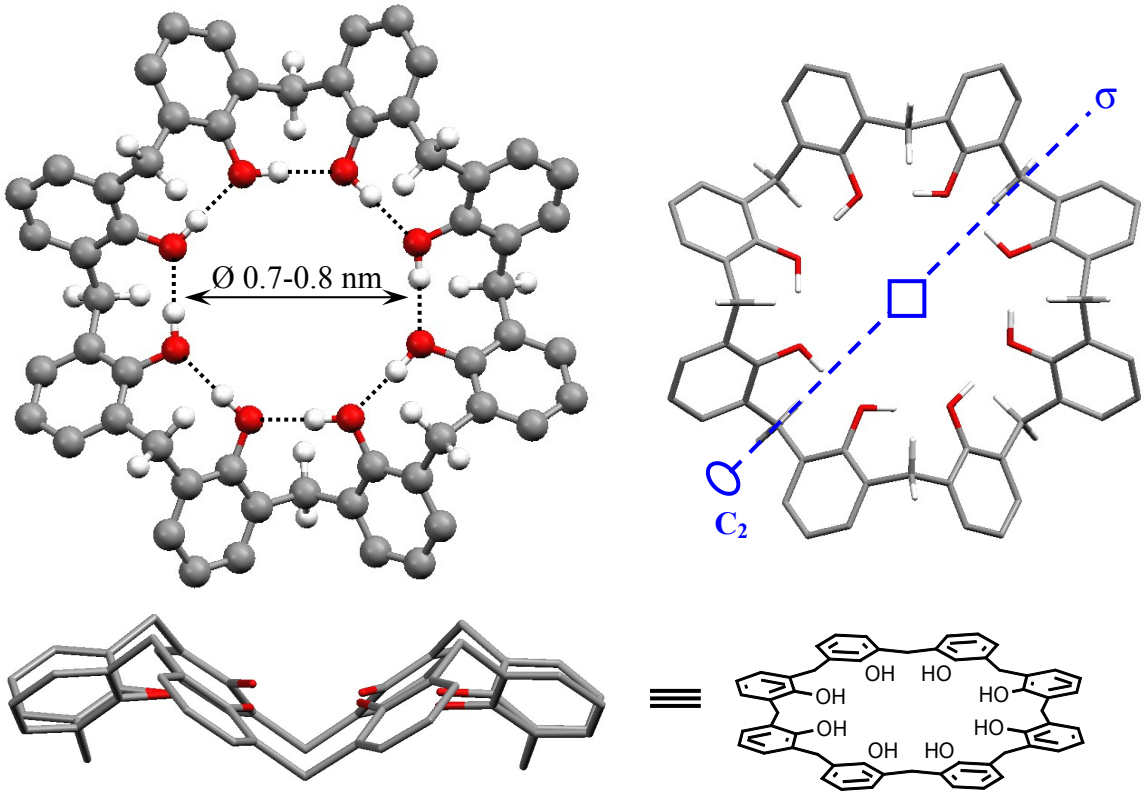
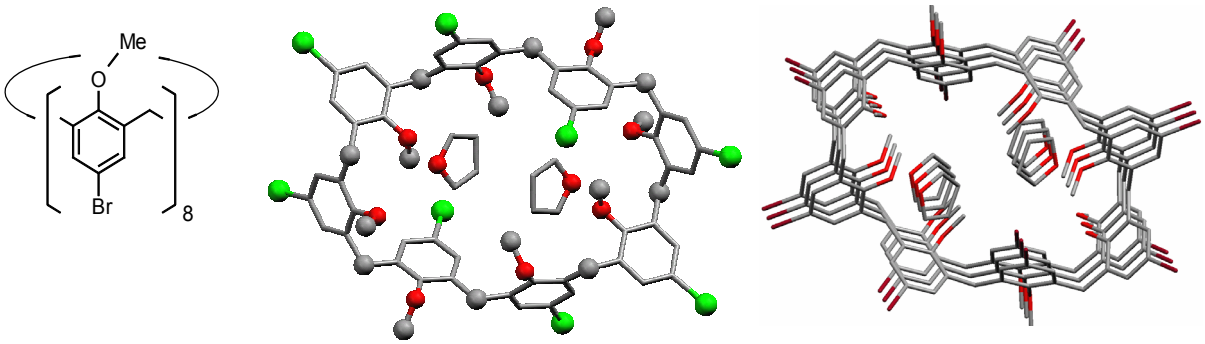


Figure 1. A representation of the idealized "pleated loop" conformation of calix[8]arene.

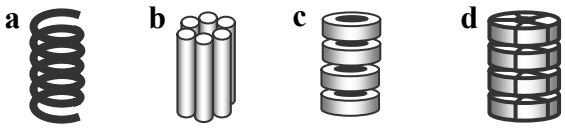
A similar conformation for calixarene **I** (R = *t*-Bu) was found at low temperature in solution. The protons of the methylene bridges of the calix[8]arene at this temperature are seen as a pair of doublets in ^{1}H NMR spectrum. This can be explained only by a time averaged D_{4d}-symmetrical conformation (known as a "pleated loop"). At higher temperatures doublets of the methylene bridges collapse to one singlet due fast exchange of the molecular conformations. The signal of the hydroxy groups of that calixarene is shifted downfield, which is a sign of strong hydrogen bonding.



For calix[8]arene ethers a centrosymmetric oval-shaped conformation is usually observed in the solid state. The X-ray structure of *p*-bromocalix[8]arene octamethyl ether is an example.[3] The only distinction of this structure from the others is that the calixarene molecules are stacked there in columns. Two "rods" formed by stacked tetrahydrofurane molecules are included in the calixarene columns.

6.2 Calix[8]arenes preorganized for self-assembly in columnar structures

There are four main strategies[4] for the preparation of tubular materials by self-assembly of organic molecules:



a) coilation of helical molecules,

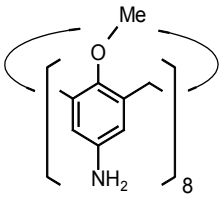
b) assembly of rod-like molecules,

c) stacking of macrocycles,

d) assembly of sector or wedge-shaped molecules into discs which stack to form cylinders.

Potentially calix[8]arenes may also be arranged by stacking (c) to tubular assemblies. Specific interactions, like hydrogen-bonding or π-π-stacking, between the stacked molecules could keep molecules together. This can be achieved by introduction of appropriate substituents in *p*-position of the phenolic units of calix[8]arenes (Fig. 2). The connections

between the calixarene skeleton and the residues (R) should be rigid but freely rotating. This is necessary for the adjustment the optimum distances between the functional groups for their intermolecular interactions.



71

The *p*-octaamine **71** can be a starting material for the preparation of various compounds. Calixarenes functionalized at their *p*-positions by urea and amido groups could be used to build up assemblies by hydrogen bonding. The introduction of naphthalic units in the calixarenes via the imide-connection should help them to form the desired structures by π-π-stacking. *O*-Alkoxy groups at the narrow rim of calixarene are necessary for the synthesis of the amine **71** and its derivatives. However, an ideal case is the presence of the hydroxy groups at the narrow rim of the fuctionalized calix[8]arenes which should fix the molecule in the pleated loop conformation by circular hydrogen bonding. Thus, the methylether groups could be used for the protection of hydroxyls and in the last step could be cleaved by BBr_3 at low temperature.

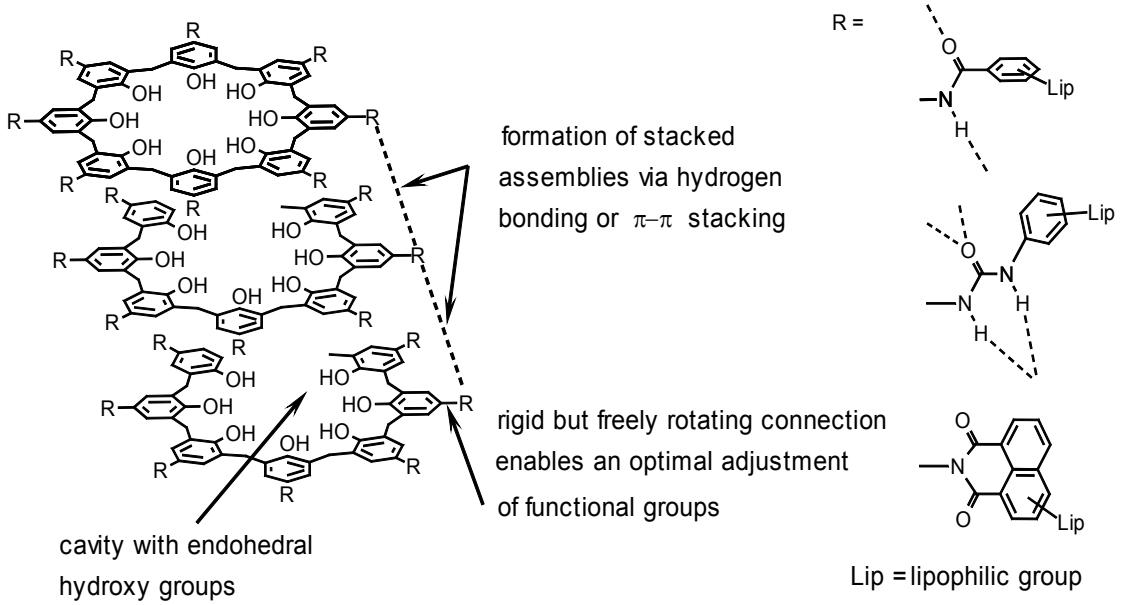


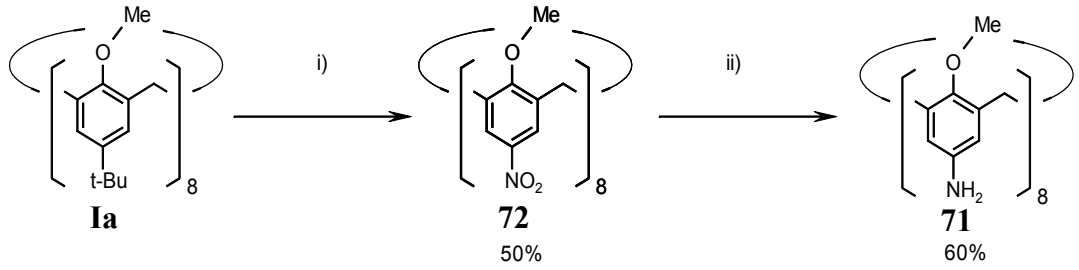
Figure 2. Schematic presentation of the expected tubular self-assembly composed of suitably functionalized calix[8]arenes.

Of course, the pleated loop conformation of calixarene is an ideal case and it does not mean that only octahydroxy calixarenes could be used for self-organization. Still the derivatives with small methyl groups could adopt more or less flattened conformations and

include even guest molecules.[3] The necessary solubility of the calixarene derivatives in apolar solvents can be achieved by the attachment of long alkyl chains (Lip) to the subunits.

6.3 Synthesis of octaamino calix[8]arene and its derivatives

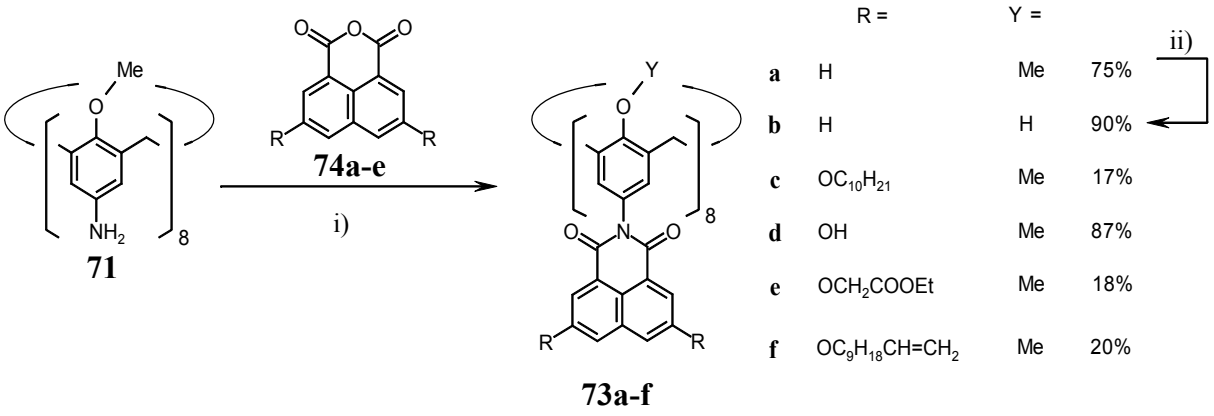
The introduction of amido-, urea- and imido groups to the wide rim of calix[8]arene requires octaamino calix[8]arene octamethylether (Scheme 1). *p-tert*-Butyl calix[8]arene was transformed into its octamethylether **Ia** by alkylation with methyliodide in THF/DMF in the presence of NaH as base according to the procedure described by Gutsche *et al* (96%).[5] The derivative **Ia** was converted into the octanitro derivative **72** (50-55%) by *ipso*-nitration in the mixture of AcOH/HNO_3/chloroform at 0°C. The reduction of **72** by reflux with hydrazine hydrate in the presence of a catalytic amount of Pd/C in THF/ethanol gave octaamine **71** in 60% yield.[6]



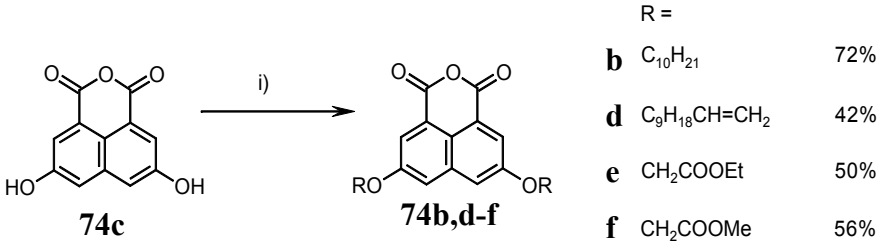
Scheme 1. Synthesis of octaamine **71**. i) HNO_3/AcOH, $CHCl_3$, 0°C, 4 hours; ii) $NH_2NH_2{\cdot}H_2O$, Pd/C, THF/EtOH, reflux, 24 hours.

The amino calixarene **71** was converted into octaimides **73a,c-f** (Scheme 2) by reaction with the corresponding 1,8-naphthyl anhydrides **74a-d** (25% excess) in pyridine (110-125°C, 72 hours) with $Zn(OAc)_2$ as catalyst (or $(i\text{-Pr})_2$EtN in case of **73e**). 3,6-Di-O-alkylated-1,8-naphthyl anhydrides **74b,d-f** were prepared in 42-72% yields from 3,6-dihydroxy-1,8-naphthalic anhydride **74c** by alkylation with alkylbromides/iodides with NaH as base in DMF at room temperature (Scheme 3).

The imide **73b** was easily obtained in 90% yield from imide **73a** by cleavage of the methoxy groups with BBr_3 (CH_2Cl_2, -70°C to rt). Since the imide **73a** is poorly soluble in most solvents, its ^{1}H NMR spectrum was recorded only in DMSO-d_6 at high temperature (75°C) to prove its purity. The spectrum of **73b** was recorded in the same conditions and it confirms the absence of the methoxy groups.



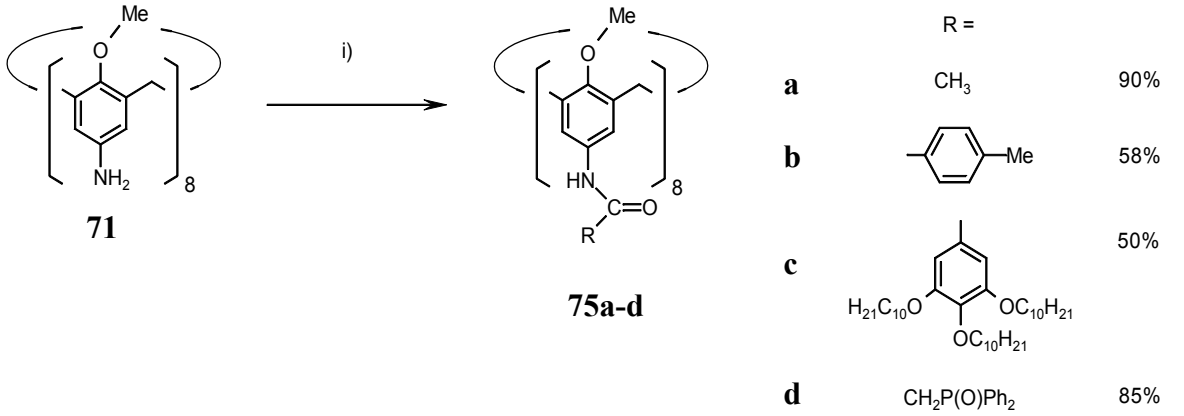
Scheme 2. Synthesis of octaimides **73a-f**. i) $Zn(OAc)_2$ or $(i\text{-Pr})_2NEt$ (in case of **73e**), pyridine, reflux, 72 hours. ii) BBr_3, CH_2Cl_2, -70°C to rt.



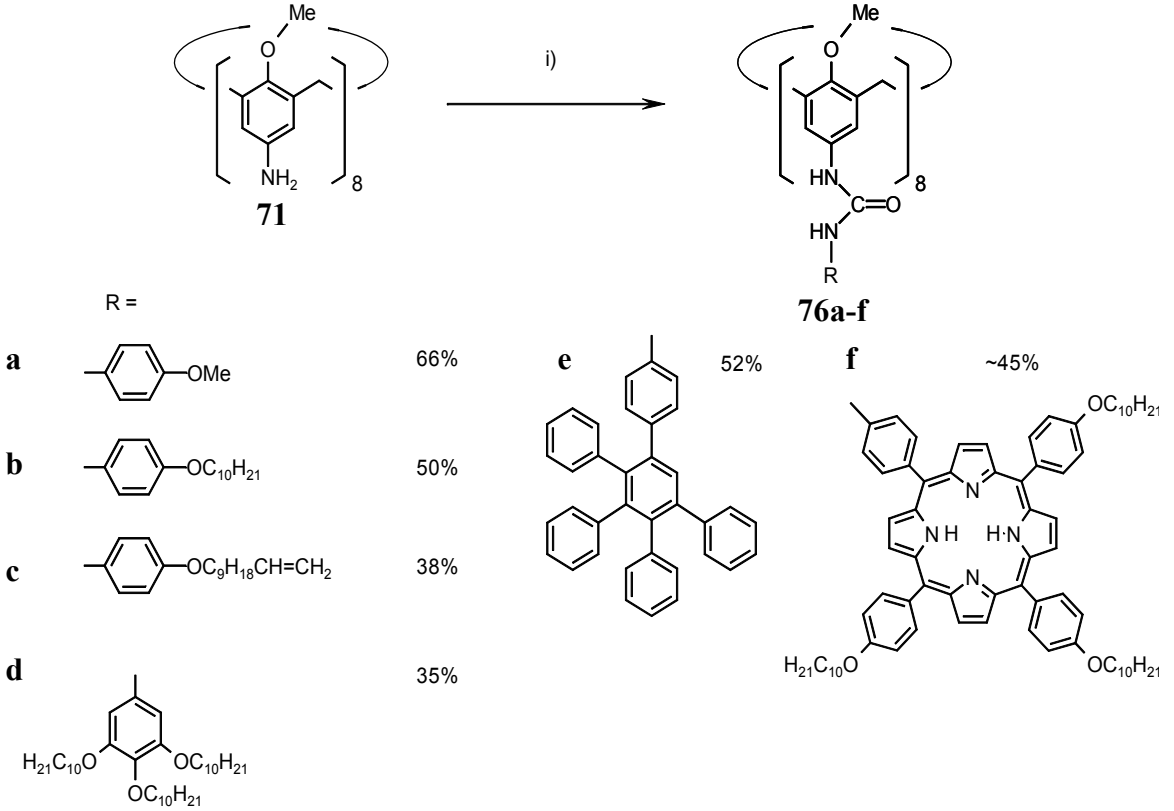
Scheme 3. Synthesis of anhydrides **74b,d-f**. i) Alk-I (b) or Alk-Br (c,d,f), NaH, DMF, room temperature, 12 hours.

The yield of the octaimide depends remarkably on the size of the substituents in 3,6-positions of the naphthyl units. It is lower for imides **73c** (17%) and **73f** (20%), disubstituted by R = $OC_{10}H_{21}$, $OC_9H_{18}CH{=}CH_2$ than for compounds **73a** (75%) and **73d** (87%) with smaller substituents (R = H, OH). Most probably with an increasing degree of acylation the approach of the acylating reagent to the unreacted amino groups is sterically more and more hindered.

Acylation of the octaamino calix[8]arene with appropriate anhydrides, acid chlorides or active esters in the presence of $(i\text{-Pr})_2EtN$ at room temperature (12 hours) leads to amides **75a-d** in 51-90% (Scheme 4). The gallic acid chloride *tris*-decylether (used for the preparation of **75c**) was synthesized by reflux of the corresponding gallic acid with an excess of oxalyl chloride in toluene and used for further acylation without additional purification. The amide **75c** shows a clear ^1H NMR spectrum in THF-d_8, but the significant broadening of signals in $CDCl_3$ at room temperature indicates the formation of aggregates via hydrogen bonding between the amide units.



Scheme 4. Synthesis of octaamides **75a-d**. i) $(RCO)_2O$ (a), RCOCl (b,c), $RC(O)OPhNO_2$ (d), (*i*-$Pr)_2NEt$, THF, room temperature, 12 hours.



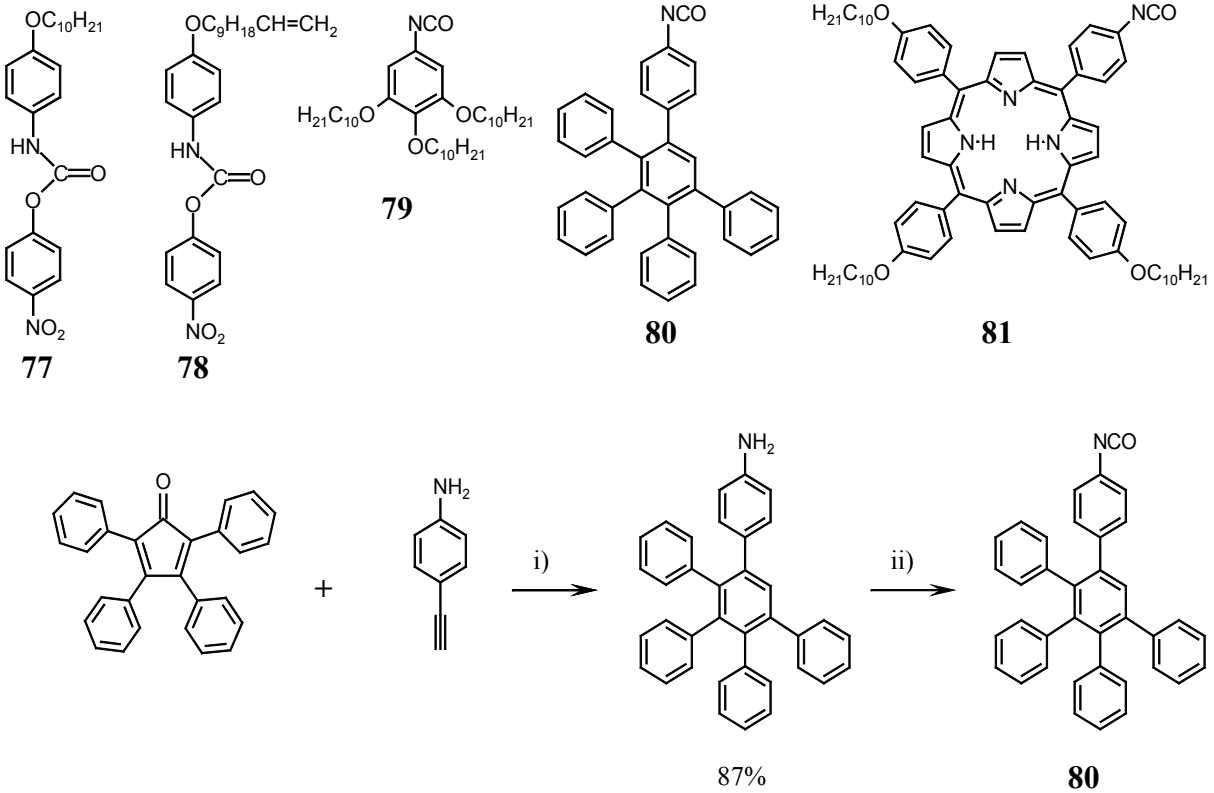
Scheme 5. Synthesis of octaureas **76a-f**. For **76a,d-f**: i) RNCO, THF, room temperature, 12 hours; for **76b** and **76c**: i) **77** or **78** respectively, *i*-Pr_2EtN, THF, room temperature, 12 hours.

The octaureas **76a-f** were prepared in 35-66% yield by reaction of octaamine **71** with an appropriate isocyanate or *p*-nitrophenylurethane at room temperature (Scheme 5). Very broad signals the octaureas in the ^1H NMR spectra in $CDCl_3$, CD_2Cl_2 and THF-d_8 at room temperature suggest again that an association of the molecules takes place in solution due to hydrogen bonding ($CDCl_3$, CD_2Cl_2) or π-π-stacking of aryl units (THF). Clear ^1H NMR spectra were observed only in DMSO-d_6. In the case of compounds **76a**, **76d** and **76e** higher

temperature (120-130°C) was required to dissolve the compounds for the measurements and/or to obtain a better resolution of the signals.

The active urethanes **77** and **78** were synthesized from appropriate anilines (the preparation of *p*-undecenyloxy aniline was described in Chapter 3) by acylation with *p*-nitrophenyl chloroformate. The isocyanate **79** was prepared from the corresponding acid via modified Curtius rearrangement (in the presence of diphenylphosphorylazide and Hünig base).

The isocyanate **80** was synthesized from the corresponding aniline (a product of condensation of *p*-ethynylaniline with tetraphenylcyclopentadienone)[7] by reaction with triphosgene (Scheme 6). Similarly to **80** the isocyanate **81** was prepared from porphyrine-monoamine. The freshly prepared isocyanates **79**-**81** were used for further reactions without isolation.



Scheme 6. Synthesis of isocyanate **80**. i) Ph_2O, reflux, 12 hours; ii) triphosgene, *i*-Pr_2EtN, CH_2Cl_2, room temperature.

The structure of most compounds was confirmed by ^1H NMR spectra and by FD or ESI mass-spectroscopy. The structure of compound **72** was also proved by single crystal X-ray analysis (see in Chapter 6.5). However, the structure and purity of the compound **76f** was

difficult to confirm by standard methods. The ^{1}H NMR spectra of **76f** recorded in different solvents give only broad signals. This could be explained by incomplete conversion. However, the broadening of the signals could be also caused by many different conformations which **76f** can assume or by the formation of intermolecular aggregates via hydrogen bonding or via stacking of porphyrine units. Only one conclusion could be made from the spectra: there are only porphyrine containing calixarene products. In MALDI-TOFF spectrum the peak of the octaurea **76f** m/z 10056 (M^+) was found. The other peaks in the spectrum could belong either to incompletely converted calixarenes or to decomposition products of the octasubstituted **76f** which were also found in case of the tetraporphyrineurea calix[4]arene analogues.[8]

6.4 Self-organization of calix[8]arene derivatives on graphite surface[9]

Scanning force microscopy experiments were performed by J. Zhang and A. Janshoff; (Institut für Physikalische Chemie, Fachbereich Chemie und Pharmazie, Johannes Gutenberg-Universität, Mainz).[10]

The octaimide **73c**, octaamide **75c**, octaureas **76b,d** and **76f** were selected from the synthesized compounds due to their good solubility. They were deposited on graphite and investigated by scanning force microscopy (SFM).

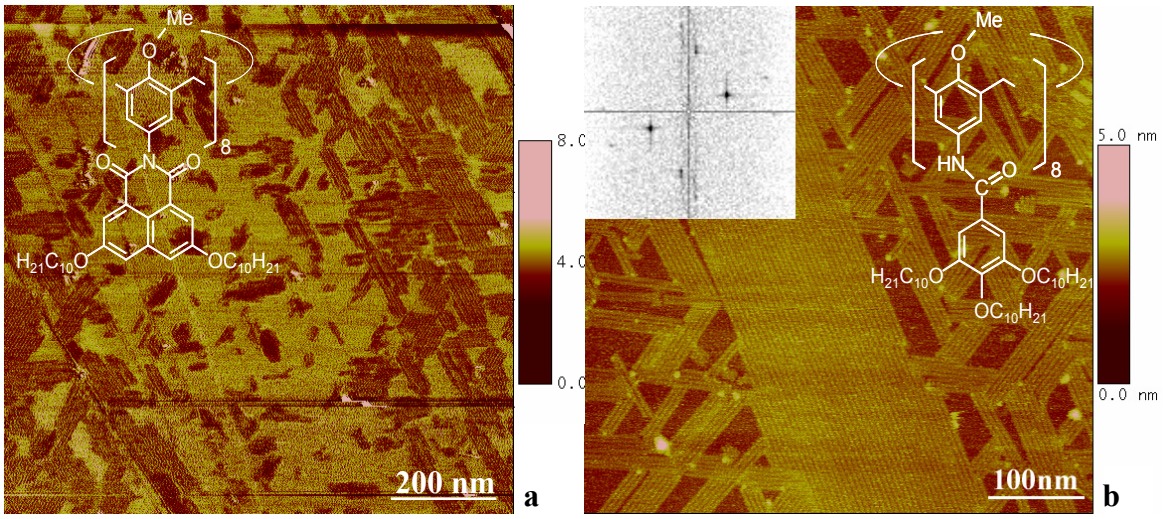


Figure 3. SFM micrographs of calix[8]arene derivatives spin-coated on HOPG from solution: a) **73c**, CH_2Cl_2 (10^{-4} mg ml^{-1}). b) **75c**, CH_2Cl_2 (10^{-4} mg ml^{-1}). The 2D power spectrum of the region with densely packed nanorods given in the inset indicates the lateral diameter of nanorods.

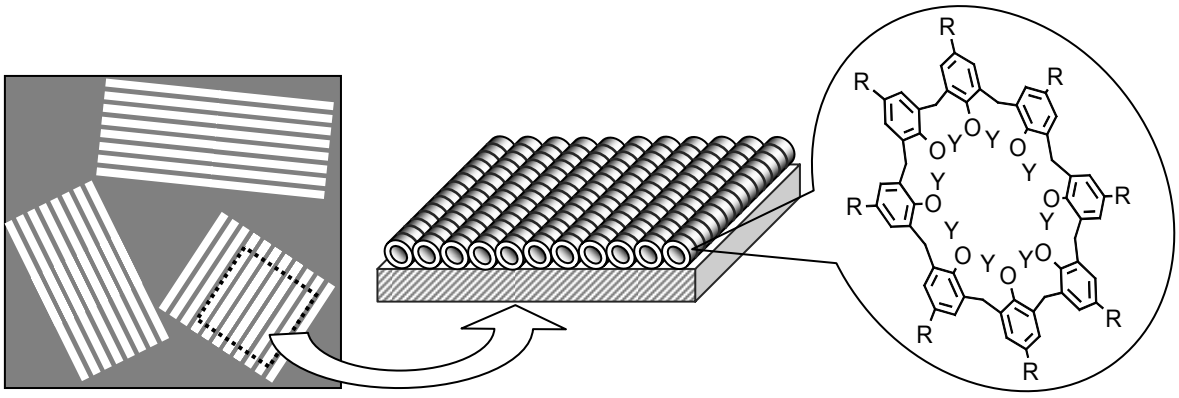


Figure 4. Schematic representation of parallel aligned individual nanorods composed of stacked calix[8]arenes attached to the graphite surface edge-on.

Often single molecules of calix[8]arene adsorbed flatly on the surface can be found by SFM or STM, like it has been done in a recent publication of Bai *et al.*[11] Figure 3 shows SFM images of the calix[8]arene derivatives **73c** and **75c** deposited on a highly oriented pyrolytic graphite (HOPG).[12] On both images the formation of domains of parallel-aligned rod-like structures orientated parallel (0°) or at an angle of 60° or 120° with respect to each other was observed. A mean spacing between the individual rods is 5.2 ± 0.5 nm. The average width of the domains is about 50 nm, while the length of them varies between 50-500 nm up to 1.5 µm in rare cases. The height of these structures is about 1 nm. These dimensions are in agreement with columnar assemblies consisting of stacked single calix[8]arenes (Fig. 4). These objects composed of individual calix[8]arenes may be named “nanotubes” or “nanorods”.

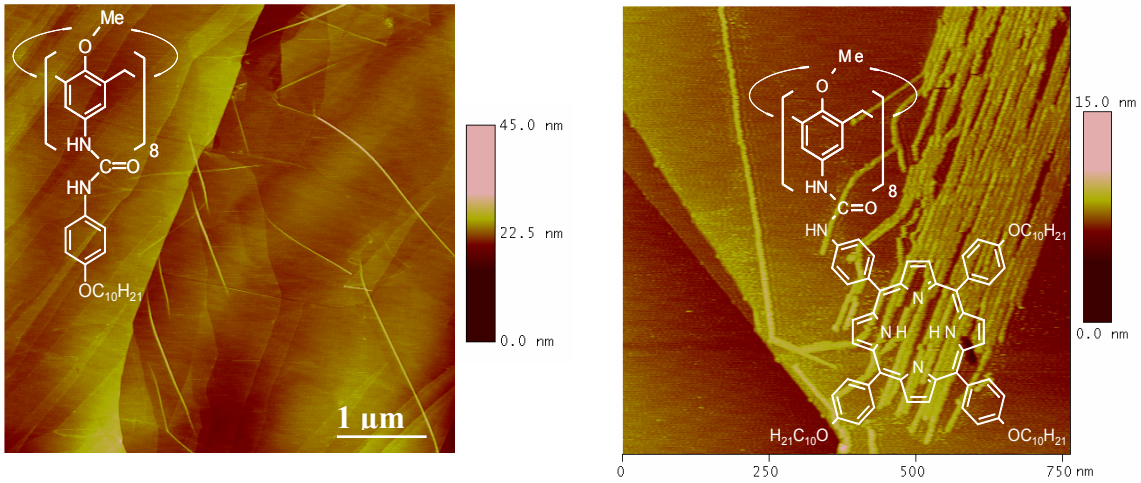


Figure 5. SFM micrographs of calix[8]arenes spin-coated on HOPG from solution (10^{-3} mg ml^{-1}) a) **76b** in CH_2Cl_2 and b) **76f** in THF.

The orientation could be attributed to the influence of the underlying graphite with its hexagonal structure. [13]

Spin-coating of solutions of calix[8]arene derivatives **76b** and **76d** results in different superstructures on HOPG. Single long "nanofibers", which are not aligned with respect to the graphite lattice, were found. The length of these nanofibers ranges from several hundred nanometers to several micrometers, while their height elevates up to 7 nm in the center (see an example on Fig. 5). Possibly, they are composed of bundles of individual nanotubes (Fig. 6). This could explain also that the width and height of the fibers decrease from the middle to both ends. Higher concentration of these compounds usually results in the deposition of amorphous material.

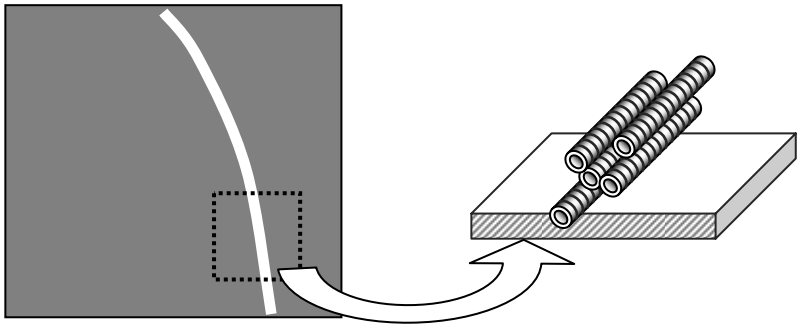


Figure 6. Schematic representation of micrometer long bundles of nanorods.

Obviously nanofibers are predominately formed due to the stronger intermolecular interactions (for example, between urea groups) than the interaction with the surface (HOPG). As a consequence, the assembly is not driven by the hexagonal structure of the substrate. The condensation of single nanotubes (perhaps already formed in solution) into nanofibers occurred during evaporation of solvent. However, it remains difficult to find a safe relationship between molecular structure and the assembly formed.

The octaporphyrineurea **76f** according to the preliminary results forms both types of assembly. This compound organizes into nanofibers from the solution with concentration 10^{-3} mg·ml^{-1}. The lateral diameter of the fibers is approximately 10-15 nm and their height is 1.5-2.0 nm. These dimensions could be corresponding to the single nanotube formed by these huge molecules. The parallel aligned nanorods were observed at the SFM images prepared from solution with concentration 10^{-4} mg·ml^{-1}. These objects were found to be 5-6 nm of lateral diameter and height 1.0-1.5 nm. The formation of this assembly is difficult to explain.

6.5 Single crystal X-ray analysis of octanitro calix[8]arene octamethylether[6]

Single crystals of **72** suitable for an X-ray analysis were obtained by slow crystallisation from THF.

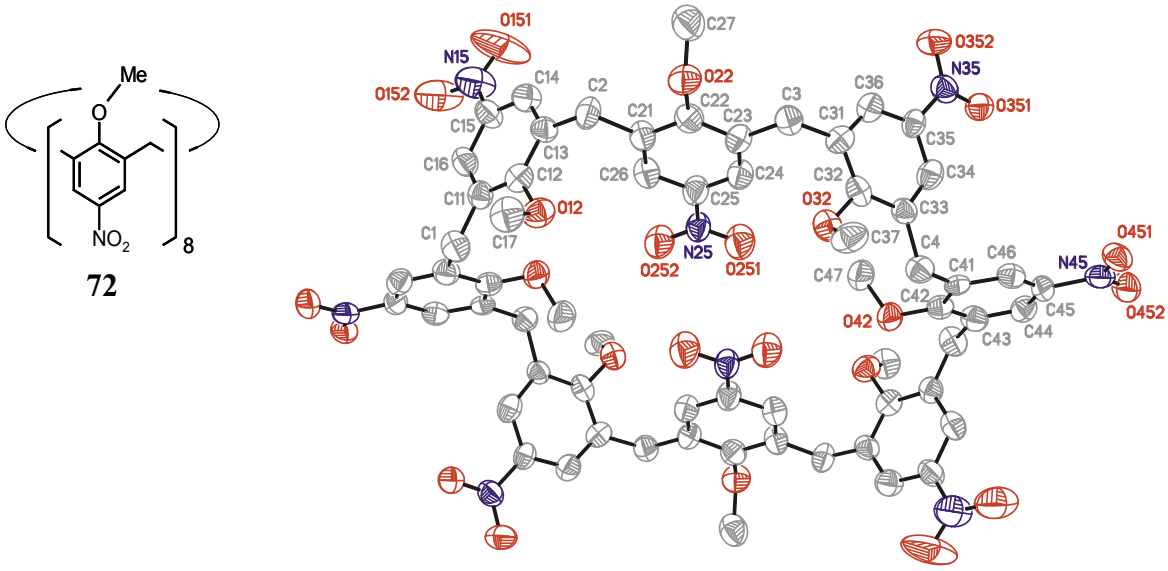


Figure 9. Molecular structure of **72** including the numbering scheme (hydrogen atoms omitted for clarity).

Table 1. Comparison of the torsion angles around the Ar-CH_2-bonds (°) of **72** with the *p*-bromo analogue.[3]

	72	*p*-Br-calix[8]arene octa-methylether
C42-C41-C4-713	-95.5	-83.3
C41-C4-713-712	163.5	134.6
712-711-71-C23	-77.9	-73.1
711-71-C23-C22	-172.0	146.0
C22-C21-C2-C13	172.8	-175.2
C21-C2-C13-C12	80.4	110.3
C12-C11-C1-C43^{i} *)	-141.0	-164.3
C11-C1-C43^{i}-C42^{i} *)	63.5	86.2

*) Symmetry operator to generate equivalent atoms: (i) 1-x, 1-y, 1-z

As found for other octa-methylethers of calix[8]arenes the molecule assumes a centrosymmetric conformation (Fig. 9).[14] Two nitroanisole units fill the cavity nearly completely by their nitro groups. Comparison of the torsion angles around the Ar-CH_2-Ar bonds with those found for the octabromo analogue[3] also crystallized from THF reveals differences ranging from 4.8 to 42° with a mean difference of 22.0°. The strong distortion of the macrocycle is also evident by the distances between opposite *p*-C-atoms which range between 6.0 and 17.4 Å (9.4 to 16.9 Å for the bromo analogue).

In the crystal lattice (Fig. 10) the **72** molecules are arranged to stacks and sheets with π-π-contacts between opposite nitroanisole units. Four of the six included THF molecules lie above and below the macrocycle within a stack while the remaining two fill gaps between molecular stacks.

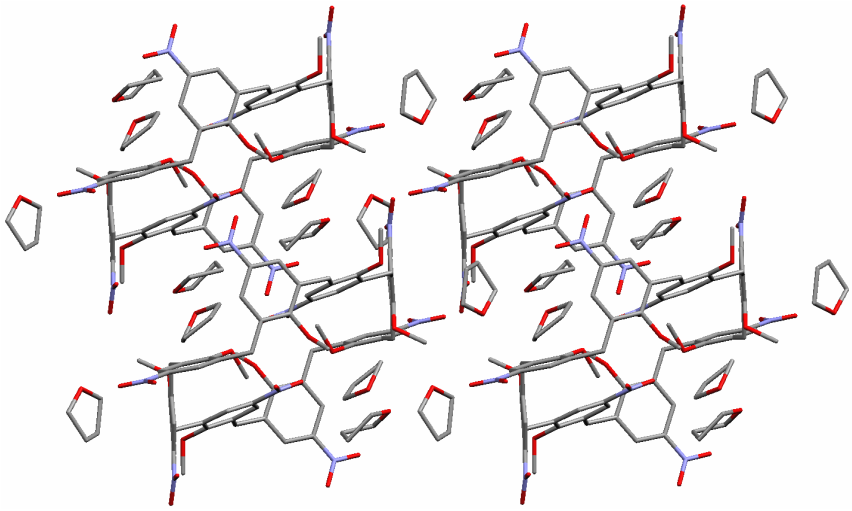
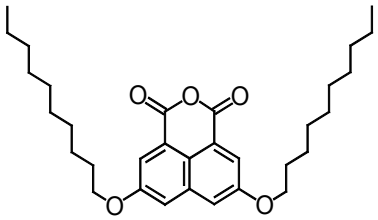


Figure 10. Packing of molecules of compound **72**.

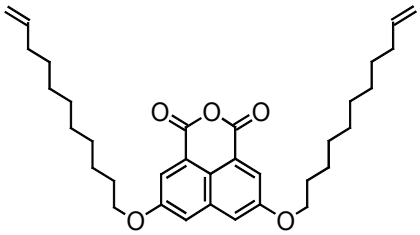
6.6 Experimental



3,6-Didecyloxy-1,8-naphthalic anhydride **74a**:

NaH (0.062 g, 2.564 mmol) was added to a solution of 3,6-dihydroxy-1,8-naphthalic anhydride (0.281 g, 1.221 mmol) in DMF (40 ml) at rt under nitrogen. The dark-red reaction mixture was stirred for 20 min before decyl iodide (0.91 ml, 3.662 mmol) was added. After 12 h at rt a beige precipitate had formed. Then glacial acetic acid (20 mL) followed by cold water (100 ml) were poured carefully to the stirred mixture. The solid was filtered off, washed with water and methanol. Recrystallization from acetone gave the desired anhydride as white powder. Yield: 0.623 g (72%).

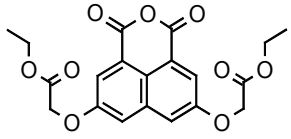
m.p. 162°C; MS (FD): m/z 510.8 (M^+); ^{1}H NMR ($CDCl_3$): δ 8.05 (d, Ar-*H*, 2 H, $^4J_{HH}$ 2.2 Hz), 7.44 (d, Ar-*H*, 2 H, $^4J_{HH}$ 2.2 Hz), 4.12 (t, -O-C*H*$_2$-, 4 H, $^3J_{HH}$ 6.6 Hz), 1.92-1.80 (m, -O-CH$_2$-C*H*$_2$-, 4 H), 1.57-1.44 (m, -O-(CH$_2$)$_2$-C*H*$_2$-, 4 H), 1.43-1.18 (m, -(C*H*$_2$)$_6$-CH$_3$, 24 H), 0.87 (t, -C*H*$_3$, 6 H, $^3J_{HH}$ 7.1 Hz).



3,6-Didecenyloxy-1,8-naphthalic anhydride **74b**:

Prepared as described above from 3,6-dihydroxy-1,8-naphthalic anhydride (1.207 g, 5.244 mmol), NaH (0.264 g, 11.012 mmol), dodecene bromide (2.9 ml, 13.109 mmol), DMF (40 ml); recrystallization from acetone. Yield: 1.188 g (42%).

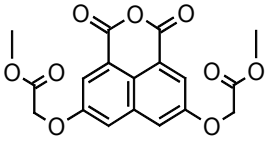
m.p. 142°C; MS (FD): m/z 534.74 ($M+H^+$); ^{1}H NMR ($CDCl_3$): δ 8.04 (d, Ar-*H*, 2 H, $^4J_{HH}$ 1.8 Hz), 7.43 (d, Ar-*H*, 2 H, $^4J_{HH}$ 2.2 Hz), 5.90-5.70 (m, -C*H*=CH$_2$, 2 H), 5.05-4.85 (m, -CH=C*H*$_2$, 4 H), 4.11 (t, -O-C*H*$_2$-, 4 H, $^3J_{HH}$ 6.4 Hz), 2.13-1.95 (m, -C*H*$_2$-CH=CH$_2$, 4 H), 1.95-1.76 (m, -OCH$_2$-C*H*$_2$-, 4 H), 1.61-1.15 (m, -(C*H*$_2$)$_6$-, 24 H).



3,6-Diethoxycarbonylmethoxy-1,8-naphthalic anhydride **74c***:*

Prepared as described above from 3,6-dihydroxy-1,8-naphthalic anhydride (3.260 g, 14.163 mmol), NaH (0.714 g, 29.742 mmol), ethyl bromacetate (3.5 ml, 29.742 mmol), DMF (60 ml); recrystallization from ethyl acetate. Yield: 2.848 g (50%).

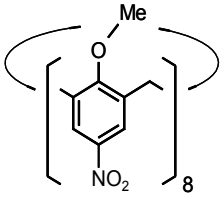
m.p. 187°C; MS (FD): m/z 402.5 (M^+); ^{1}H NMR ($CDCl_3$): δ 8.12 (d, Ar-*H*, 2 H, $^4J_{HH}$ 1.8 Hz), 7.46 (d, Ar-*H*, 2 H, $^4J_{HH}$ 1.8 Hz), 4.81 (s, -O-C*H*$_2$-COOEt, 4 H), 4.30 (q, -O-C*H*$_2$-CH$_3$, 4 H, $^3J_{HH}$ 7.0 Hz), 1.31 (t, -C*H*$_3$, 6 H, $^3J_{HH}$ 7.0 Hz).



3,6-Dimethoxycarbonylmethoxy-1,8-naphthalic anhydride **74d***:*

Prepared as described above from 3,6-dihydroxy-1,8-naphthalic anhydride (2.557 g, 11.111 mmol), NaH (0.560 g, 23.333 mmol), methyl bromacetate (3.570 g, 23.333 mmol), DMF (60 ml); recrystallization from chloroform. Yield: 2.350 g (56%).

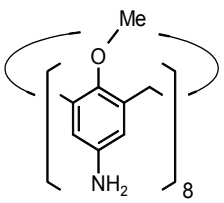
m.p. 199-200°C; MS (FD): m/z 374.3 (M^+); ^{1}H NMR (DMSO): δ 7.92 (d, Ar-*H*, 2 H, $^4J_{HH}$ 2.2 Hz), 7.83 (d, Ar-*H*, 2 H, $^4J_{HH}$ 1.8 Hz), 5.08 (s, -O-CH_2-COOCH_3, 4 H), 3.74 (s, -CH_3, 6 H).



Octanitro-calix[8]arene **72:**

A stirred solution of compound **Ia** (3 g, 2.128 mmol) in chloroform (80 ml) was cooled to 5°C in ice bath. Then glacial acetic acid (8 ml) and fuming nitric acid (10 ml) were added to the solution (the colour of the mixture has changed immediately from light yellow into dark-violet). The reaction mixture was stirred for 4 hours allowing warming to room temperature. Then water (100 ml) was poured into the reaction mixture. The organic layer was separated and washed with water (4 x 100 ml). After chloroform was removed under reduced pressure methanol (100 ml) was added to the residue. A yellow solid was filtered off, washed with methanol and dried. The crude product was refluxed in dichloromethane (100 ml) for 10 min. After cooling to room temperature the suspension was left in the fridge for 8-10 hours. The light yellow solid was filtered off and washed with dichloromethane to give after drying pure product **72.** Yield: 1.428 g (50%).

m.p. >240°C (decomp.); MS (FD): 1323.3 ($M+H^+$); ^{1}H NMR (DMSO-d_6, 300 MHz): 7.80 (s, Ar-*H*, 16 H), 4.19 (s, Ar-CH_2-Ar, 16 H), 3.66 (s, -O-CH_3, 24 H).



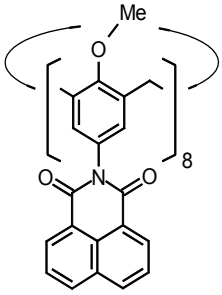
Octaamino-calix[8]arene **71:**

A suspension of octanitro calix[8]arene **72** (0.390 g, 0.295 mmol) and hydrazine-hydrate (15 ml) in THF/EtOH (25 ml / 35 ml) was refluxed for 24 hours in the presence of Pd/C (finally, a colour of the solution must change from yellowish to uncoloured and a gray precipitate of product-catalyst must be formed). Then the solid was filtered off and washed twice with MeOH/HCl (80 ml / 4 ml) to remove the product from the catalyst. A 2/3 of the solvent was removed under reduced pressure and water (80 ml) added to the residue. Then NaOH was pill by pill added to the stirred solution until a precipitate has been formed. The precipitate was extracted by ethylacetate (100 ml); the organic phase was washed twice by water. Then ethylacetate was

removed under reduced pressure and the residue was reprecipitated in ethylacetate/methanol. The solid was filtered off and washed with methanol to give **71** as a beige powder**.** Yield: 0.192 g (60%).

m.p. >370°C (decomp.); MS(FD): 1083.1 ($M+H^+$); ^{1}H NMR (DMSO-d_6, 400 MHz): 6.07 (s, Ar-*H*, 16 H), 4.56 (s, -NH_2, 16 H), 3.69 (s, Ar-CH_2-Ar, 16 H), 3.44 (s, -O-CH_3, 24 H).

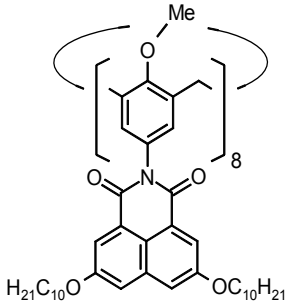
General procedure for the preparation of octaimido-calix[8]arenes **73a, 73c-73f**: The octaamino calix[8]arene octamethylether **71** (0.050 g, 0.0462 mmol) and the respective 1,8-naphthalic anhydride (0.462 mmol) were refluxed in dry pyridine (2 mL) in the presence of $Zn(OAc)_2$ (0.085 g, 0.462 mmol) for 48-72 h. After cooling to rt the reaction mixture was poured into cold 10% HCl solution (15-20 mL). A brown precipitate was filtered off, washed with water (2 x 20 mL) and methanol (2 x 20 mL).



Calix[8]arene **73a**:

Octaamine **71** (0.20 g, 0.093 mmol), 1,8-naphtalic anhydride (0.37 g, 0.93 mmol), $Zn(OAc)_2$ (0.37 g, 0.93 mmol). The precipitate was suspending in CH_3CN/THF, filtered and dried to give **73a** as brown powder. Yield: 0.47 g (75%).

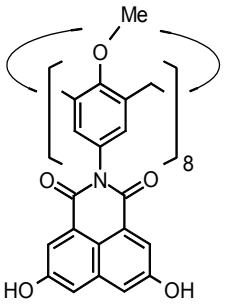
m.p. >420°C (decomp.); MS(FD): 2526.3 ($M+H^+$); ^{1}H NMR (DMSO-d_6, 400 MHz, 70°C): 8.22 (d, Ar-*H*, 16 H, $^3J_{HH}$ 8.3 Hz), 8.07 (d, Ar-*H*, 16 H, $^3J_{HH}$ 6.8 Hz), 7.64 (m, Ar-*H*, 16 H), 7.02 (s, Ar-*H*, 16 H), 4.11 (s, Ar-CH_2-Ar, 16 H), 3.64 (s, -O-CH_3, 24 H).



Calix[8]arene **73c**:

Octaamine **71** (0.050 g, 0.0462 mmol), 3,6-didecyloxy-1,8-naphthalic anhydride (0.24 g, 0.46 mmol), $Zn(OAc)_2$ (0.085 g, 0.462 mmol). The precipitate was dissolved in dichloromethane (2-3 mL) and passed through a column (THF/hexane, 1:5, followed by THF) to collect compound **73c**. The solvent was removed under reduced pressure and the residue was triturated with acetone (10 mL), filtered and washed with acetone (10 mL) to give imide **73c** as a light-orange powder. Yield: 0.040 g (17%).

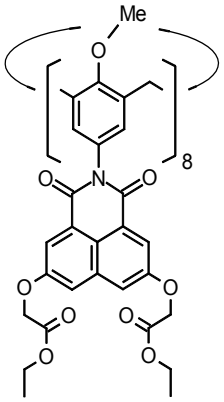
m.p. 228°C; MS (ESI): m/z 5047.72 ($M+Na^+$), 2534.24 ($M+2Na^+$). ^{1}H NMR (THF-d_8): δ 7.72 (s, Ar-*H*, 16 H), 7.28 (s, Ar-*H*, 16 H), 7.06 (s, Ar-*H*, 16 H), 4.10 (s, Ar-CH_2-Ar, 16 H), 4.00 (m, -O-CH_2-, 32 H), 3.53 (s, -O-CH_3, 24 H), 1.79 (m, -O-CH_2-CH_2-, 32 H), 1.47 (m, -O-$(CH_2)_2$-CH_2-, 32 H), 1.28 (m, -$(CH_2)_6$-CH_3, 192 H), 0.86 (m, -CH_3, 48 H).



Calix[8]arene **73d**:

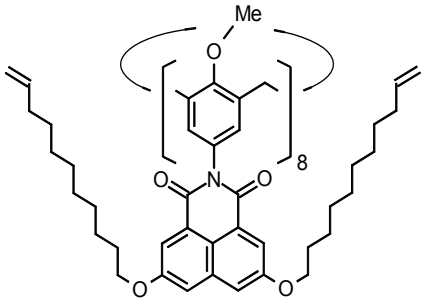
Octaamine **71** (0.050 g, 0.0462 mmol), 3,6-dihydroxy-1,8-naphthalic anhydride (0.106 g, 0.462 mmol), $Zn(OAc)_2$ (0.085 g, 0.462 mmol). The precipitate was refluxed in acetonitrile (20 mL) or in methanol (20 mL), cooled to rt and filtered off to give compound **73d**. Yield: 0.112 g (87%).

m.p. > 370°C (decomp.); MS (ESI): m/z 1411.92 ($M+2Na^+$). ^{1}H NMR (DMSO-d_6): δ 10.24 (s, Ar-O*H*, 16 H), 7.66 (s, Ar-*H*, 16 H), 7.40 (s, Ar-*H*, 16 H), 6.99 (s, Ar-*H*, 16 H), 4.08 (s, Ar-CH_2-Ar, 16 H), 3.46 (s, -O-CH_3, 24 H).



Calix[8]arene **73e**:

Octaamine **71** (0.050 g, 0.0462 mmol), 3,6-diethoxycarbonylmethoxy-1,8-naphthalic anhydride (0.186 g, 0.462 mmol), (*i*-Pr)$_2$NEt (0.060 g, 0.462 mmol) has been used instead of $Zn(OAc)_2$ to avoid side reactions. The precipitate was dissolved in dichloromethane (2-3 mL) and passed through a column (THF/hexane/dichloromethane (2:1:1), followed by THF) to collect compound **73e**. Trituration with hexane (3 x 10 mL) finally gave imide **73e** as a light-orange powder. Yield: 0.034 g (18%). m.p. > 155°C (decomp.); MS (ESI): m/z 4179.21 ($M+Na^+$), 2100.72 ($M+2Na^+$). ^{1}H NMR ($CDCl_3$): δ 7.92 (s, Ar-*H*, 16 H), 7.29 (s, Ar-*H*, 16 H), 6.99 (s, Ar-*H*, 16 H), 4.72 (s, -O-CH_2-COOEt, 32 H), 4.23 (q, -O-CH_2-CH$_3$, $^3J_{HH}$ 7.0 Hz, 32 H), 4.13 (s, Ar-CH_2-Ar, 16 H), 3.57 (s, -O-CH_3, 24 H), 1.25 (t, -O-CH$_2$-CH_3, $^3J_{HH}$ 7.0 Hz, 48 H).

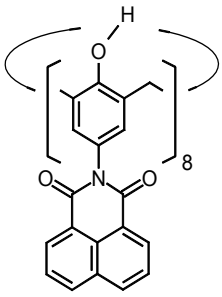


Calix[8]arene **73f:**

Octaamine **71** (0.023 g, 0.0213 mmol), 3,6-diundecenyloxy-1,8-naphthalic anhydride (0.222 g, 0.415 mmol), $Zn(OAc)_2$ (0.113 g, 0.613 mmol). The precipitate was dissolved in dichloromethane (2-3 mL) and passed through a column (THF/hexane, 1:5, followed by THF) to collect compound **73f**. The solvent was removed under reduced pressure and the residue was triturated with acetone (10 mL), filtered and washed with acetone (10 mL) to give imide **73f** as a light-orange powder. Yield: 0.022 g (20%).

m.p. >120°C (decomp.); ^{1}H NMR (THF-d_8): δ 7.73 (s, Ar-*H*, 16 H), 7.28 (s, Ar-*H*, 16 H), 7.06 (s, Ar-*H*, 16 H), 5.86-5.64 (m, -C*H*=CH$_2$, 16 H), 5.06-4.77 (m, -CH=CH_2, 32 H), 4.10 (br.s, Ar-CH_2-Ar, 16 H), 4.00 (m, -O-CH_2-, 32 H), 3.53 (s, -O-CH_3, 24 H), 2.14-1.91 (m, -

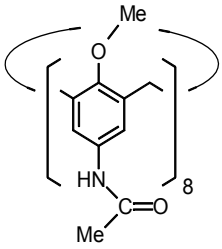
C*H*$_2$-CH=CH$_2$, 16 H), 1.90-1.64 (m overlapped with solvent peak, -O-CH$_2$-C*H*$_2$-, 32 H), 1.60-1.06 (m, -(C*H*$_2$)$_6$-CH$_3$, 192 H).



Calix[8]arene **73b**:

The compound **73b** was obtained by cleavage of methyl groups from octamethoxy compound **73a** (0.36 g, 0.14 mmol) in 7 ml of dichloromethane by an addition of BBr_3 (1 M in dichloromethane, 3 ml, 3 mmol) at -78°C under nitrogen. After for 4 h of stirring the resulting mixture was allowed to warm slowly to r.t. and then was stirred at rt over 12 h. Water was added to hydrolyze the excess of BBr_3 and the solution was stirred for further 20 min. Then it was neutralized with aqueous concentrated ammonia (10 ml). The precipitate was filtered off and washed with methanol and CH_3CN to give pure product **73b**. Yield: 0.31 g (90%).

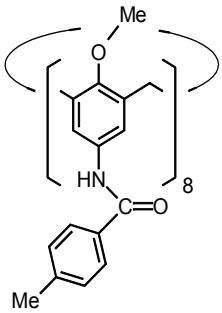
m.p. >350°C (decomp.); MS (ESI): m/z 2499.7 (M+2MeOH+Na$^+$), 1260.83 (M+2MeOH+2Na$^+$). ^{1}H NMR (DMSO-d$_6$, 400 MHz, 70°C): 8.11-8.60 (overlapped, Ar-*H*, 32 H), 7.78 (t, Ar-*H*, 16 H, $^3J_{HH}$ 7.6 Hz), 6.99 (s, Ar-*H*, 16 H), 4.06 (s, Ar-C*H*$_2$-Ar, 16 H).



Calix[8]arene **75a**:

Octaamine **71** (0.073 g, 0.0675 mmol), acetic anhydride (2 mL), and 2-3 drops of Et_3N were refluxed in THF (5 mL) for 5 min (to dissolve the octa-amine) and stirred for 14 h at rt. Then THF was removed under reduced pressure and the residue was poured into cold water (25 mL) to form an orange-brown solid. The precipitate was filtered off, washed with water (2 x 20 mL) and methanol (2 x 10 mL) and recrystallized from THF (5 mL)/methanol (10 mL) to give **75a** as a light-orange powder. Yield: 0.086 g (90%).

m.p. > 240°C (decomp.); MS (FD): m/z 1414.4 (M$^+$). ^{1}H NMR (DMSO-d$_6$): δ 9.68 (s, -N*H*-, 8 H), 7.13 (s, Ar-*H*, 16 H), 3.85 (s, Ar-C*H*$_2$-Ar, 16 H), 3.39 (s, -O-C*H*$_3$, 24 H), 1.90 (s, -CO-C*H*$_3$, 24 H).

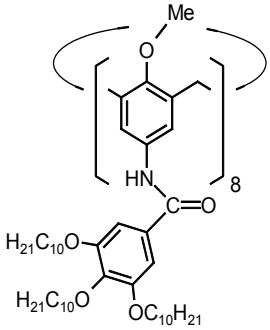


Calix[8]arene **75b**:

A solution of *p*-toluoyl chloride (0.033 g, 0.213 mmol) in THF (3 mL) was added to a suspension of the octaamine **71** (0.023 g, 0.0213 mmol) and Et_3N (0.1 mL, 0.712 mmol) in THF (2 mL). The reaction mixture was stirred for 24 h at rt. Then the THF was removed under reduced pressure and to the residue was triturated with methanol (10 mL). A thin brown powder was filtered off, and washed with water (5 mL) and methanol (2 x 15 mL).

Reprecipitation from THF (2 mL)/hexane (10 mL) gave **75b** as a thin beige powder. Yield: 0.022 g (51%).

m.p. > 235°C (decomp.); MS (FD): m/z 2028.9 ($M+H^+$). ^{1}H NMR (DMSO-d_6): δ 9.98 (s, -N*H*-, 8 H), 7.73 (d, Ar-*H*, 16 H, $^3J_{HH}$ 7.7 Hz), 7.39 (s, Ar-*H*, 16 H), 7.18 (d, Ar-*H*, 16 H, $^3J_{HH}$ 8.1 Hz), 3.91 (s, Ar-CH_2-Ar, 16 H), 3.45 (s, -O-CH_3, 24 H), 2.31 (s, -CH_3, 24 H).

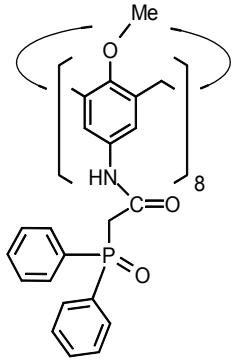


Calix[8]arene **75c**:

To a solution of acid chloride of gallic acid tris-decylether (0.028 g, 0.462 mmol) in 3 ml of THF a suspension of amino compound **71** (0.050 g, 0.0462 mmol) in 3 ml of THF was added and the resulting mixture was stirred for 24 h in presence of an excess of (*i*-Pr)$_2$NEt at rt. After 3 ml of methanol was added to the reaction mixture. Then the solvent was removed under reduced pressure to dryness and the residue was recrystallized from ethyl acetate. The precipitate (gallic acid methylester) was filtered off, washed with ethyl acetate. The mother liquid was concentrated in vacuum, diluted with ethanol and left for 3-4 h in the fridge. A formed white solid was filtered off to give **75c**. Yield: 50% (0.130 g).

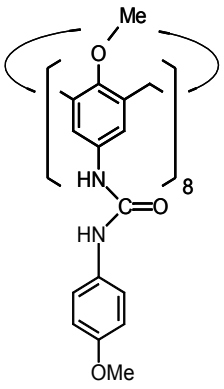
m.p. 204°C; ^{1}H NMR (THF-d_8, 400 MHz): 9.13 (s, -N*H*-, 8 H), 7.36 (s, Ar-*H*, 16 H), 7.10 (s, Ar-*H*, 16 H), 3.90 (m, Ar-CH_2-Ar, -O-CH_2-, 64 H), 3.47 (s, -O-CH_3, 24 H), 1.72 (m under THF, -O-CH$_2$-CH_2-, 48 H), 1.44 (m, -O-CH$_2$-CH$_2$-CH_2-, 48 H), 1.28 (m, -(CH_2)$_6$-CH$_3$, 288 H), 0.88 (br.t, -CH_3, 72 H).

Calix[8]arene **75d:**



A *p*-nitrophenyl (diphenylphosphoryl)acetate (0.071 g, 0.185 mmol) (prepared as described)[15] and 4 drops of triethylamine were added to a suspension of the calix[8]arene **71** (0.020 g, 0.0185 mmol) in CH_2Cl_2 (2 mL). The reaction mixture was stirred under nitrogen for 24 h at rt, then the solvent was removed under reduced pressure and methanol (5 mL) was added to the residue to form a solid that was filtered off, and washed with methanol (2 x 5 mL). Recrystalization from acetone gave the pure product **75d** as a light-orange powder. Yield: 0.056 g (85%).

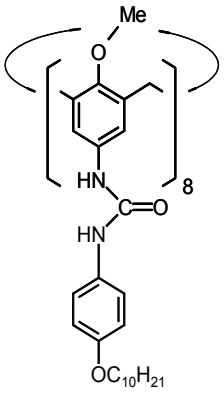
m.p. > 220°C (decomp.); MS (ESI): m/z 1532.55 ($M+2Na^+$). ^{1}H NMR (DMSO-d_6): δ 9.88 (s, -N*H*-, 8 H), 7.75 (d, Ar-*H*, 16 H, $^3J_{HH}$ 7.7 Hz), 7.72 (d, Ar-*H*, 16 H, $^3J_{HH}$ 7.0 Hz), 7.56-7.30 (m, Ar-*H*, 48 H), 7.02 (s, Ar-*H*, 16 H), 3.76 (s, Ar-CH_2-Ar, 16 H), 3.62 (d, -NH-CH_2-P(O)-, 16 H, $^2J_{PH}$ 13.6 Hz), 3.23 (s, -O-CH_3, 24 H).



Calix[8]arene **76a**:

A solution of *p*-methoxyphenyl isocyanate (0.083 g, 0.555 mmol) in THF (3 mL) was added to a suspension of the calix[8]arene **71** (0.050 g, 0.0462 mmol) in THF (2 mL). The reaction mixture was stirred under nitrogen for 24 h at rt, the THF was removed under reduced pressure and methanol (5 mL) was added to the residue to form a brown thin solid that was filtered off, and washed with methanol (2 x 10 mL). The light-brown powder was refluxed in THF (5 mL)/methanol (10 mL) for 5 min, cooled to rt and filtered off. This operation was repeated twice to give the pure product **76a** as a thin light-brown powder. Yield: 0.069 g (66%).

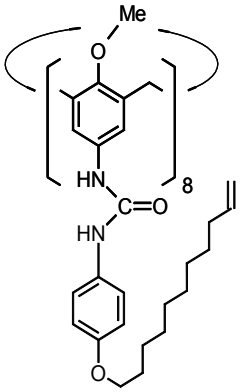
m.p. > 500°C (decomp.); MS (ESI): m/z 2297.28 ($M+Na^+$), 1160.12 ($M+2Na^+$). ^{1}H NMR (DMSO-d_6, 130°C): δ 8.03 (s, -N*H*-, 8 H), 7.91 (s, -N*H*-, 8 H), 7.23 (d, Ar-*H*, 16 H, $^3J_{HH}$ 5.4 Hz), 7.08 (s, Ar-*H*, 16 H), 6.78 (d, Ar-*H*, 16 H, $^3J_{HH}$ 5.9 Hz), 3.91 (s, Ar-CH_2-Ar, 16 H), 3.71 (s, -O-CH_3, 24 H), 3.45 (s, -O-CH_3, 24 H).



Calix[8]arene **76b**:

An excess of Et_3N (0.10 mL, 0.712 mmol) was added to a suspension of calix[8]arene **71** (0.020 g, 0.0185 mmol) and *p*-nitrophenylurethane of *p*-decyloxyaniline (0.12 g, 0.30 mmol) in THF (5 mL)/CH_2Cl_2 (1 mL). The reaction mixture was refluxed for 5 min and left in an ultrasonic bath at rt for 1.5 h. After the reaction was complete, indicated by the formation of a clear solution, methanol (20 mL) was added and the mixture was refluxed for 5 min to form after cooling to rt a yellowish precipitate which was filtered off, and washed with methanol (3 x 10 mL) to give pure **76b** as a beige powder. Yield: 0.031 g (50%).

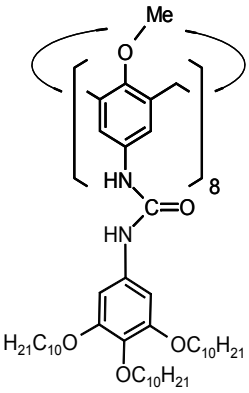
m.p. > 220°C (decomp.); MS (ESI): m/z 3307.67 ($M+Na^+$), 1665.20 ($M+2Na^+$). ^{1}H NMR (DMSO-d_6): δ 8.34 (s, -N*H*-, 8 H), 8.17 (s, -N*H*-, 8 H), 7.09 (d, Ar-*H*, 16 H, $^3J_{HH}$ 6.8 Hz), 6.93 (s, Ar-*H*, 16 H), 6.63 (d, Ar-*H*, 16 H, $^3J_{HH}$ 6.2 Hz), 3.83 (br.s, Ar-CH_2-Ar, -O-CH_2-, 32 H), 3.40 (s, -O-CH_3, 24 H), 1.64 (br.s, -O-CH_2-CH_2-, 16 H), 1.35 (br.s, -O-$(CH_2)_2$-CH_2-, 16 H), 1.23 (br.s, -$(CH_2)_7$-CH_3, 112 H), 0.84 (br.s, -CH_3, 24 H).



Calix[8]arene **76c**:

An excess of Et_3N (0.10 mL, 0.712 mmol) was added to a suspension of calix[8]arene **71** (0.024 g, 0.0222 mmol) and *p*-nitrophenylurethane of *p*-dodecenyloxyaniline (0.18 g, 0.43 mmol) in THF (5 mL). The reaction mixture was refluxed for 5 min and left in an ultrasonic bath at rt for 2 h. After the reaction was complete the solvent was removed in vacuum and to the residue ethanol (30 mL) was added. A solid was filtered off and then refluxed for 5 min in ethanol. Insoluble part was filtered off from hot solution, triturated with methanol to give pure **76c** as a beige powder. Yield: 0.029 g (38%).

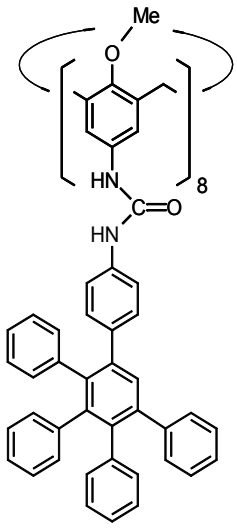
m.p. > 190°C (decomp.); ^{1}H NMR (DMSO-d_6): δ 8.34 (s, -N*H*-, 8 H), 8.17 (s, -N*H*-, 8 H), 7.21 (d, Ar-*H*, 16 H, $^3J_{HH}$ 6.8 Hz), 7.04 (s, Ar-*H*, 16 H), 6.74 (d, Ar-*H*, 16 H, $^3J_{HH}$ 6.2 Hz), 5.85-5.68 (m, -C*H*=CH_2, 8 H), 5.06-4.84 (m, -CH=CH_2, 16 H), 3.83 (br.s, Ar-CH_2-Ar, -O-CH_2-, 32 H), 3.39 (s, -O-CH_3, 24 H), 2.07-1.89 (m, -CH_2-CH=CH_2, 16 H), 1.73-1.52 (m, -O-CH_2-CH_2-, 16 H), 1.48-1.05 (m, -(CH_2)$_6$-, 96 H).



Calix[8]arene **76d**:

To a suspension of the amino compound **71** (0.050 g, 0.0462 mmol) in 2 ml of dry THF a solution of isocyanate (prepared from gallic acid *tris*-decylether (0.410 g, 0.694 mmol) according to procedure described by Ninomiya, K.; Shioiri, T.; Yamada, S. *Tetrahedron* **1974**, *30*, 2151-2157) in 3 ml of THF was added. The reaction was stirred for 24 h at rt. Then 3 ml of methanol was added into the solution. After the solvent was removed in vacuum the oily residue was suspended in *n*-hexane and left for 5 h in the fridge. The formed solid (urethane of gallic acid) was filtered off and washed with hexane. The solvent from mother liquid was evaporated under reduced pressure to dryness and the residue was reprecipitated from THF/MeOH to give product **76d**. Yield: 34% (0.093 g).

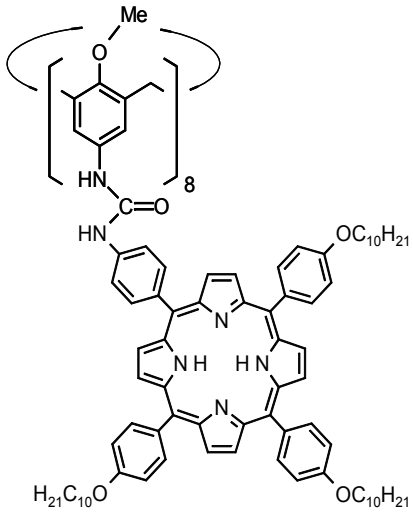
m.p. >210°C (decomp.); ^{1}H NMR (DMSO-d_6, 400 MHz, 130°C): 7.97 (s, -N*H*-, 8 H), 7.92 (s, -N*H*-, 8 H), 7.07 (s, Ar-*H*, 16 H), 6.66 (s, Ar-*H*, 16 H), 3.89 (m, Ar-CH_2-Ar, -O-CH_2-, 64 H), 3.45 (s, -O-CH_3, 24 H), 1.66 (m, -O-CH_2-CH_2-, 48 H), 1.42 (m, -O-CH_2-CH_2-CH_2-, 48 H), 1.29 (m, -(CH_2)$_6$-CH_3, 288 H), 0.86 (m, -CH_3, 72 H).



Calix[8]arene **76e**:

A suspension of the calix[8]arene **71** (0.020 g, 0.0185 mmol) in THF (5 mL) was added under nitrogen to a stirred solution of 4-(2',3',4',5'-tetraphenyl)biphenyl isocyanate, prepared from the corresponding amine (0.088 g, 0.185 mmol), triphosgene (0.019g, 0.0647 mmol) and (*i*-Pr)$_2$NEt (0.010 g, 0.0740 mmol) in toluene (100 mL). The reaction mixture was stirred for 48 h at rt under nitrogen, the solvent was removed under reduced pressure and methanol (10 mL) was added to form a brown solid which was filtered off and washed with methanol (2 x 10 mL). The powder was dissolved in THF (1 mL) and reprecipitated by hexane (20 mL) to give **76e** as a light-brown powder. Yield: 0.049 g (52%).

m.p. > 450°C (decomp.); MS (ESI): m/z 2562.35 ($M+2Na^+$). ^{1}H NMR (DMSO-d_6, 120°C): δ 8.10 (s, -N*H*-, 8 H), 8.07 (s, -N*H*-, 8 H), 7.39 (s, Ar-*H*, 8 H), 6.66-7.28 (m, Ar-*H*, 26 H), 3.88 (s, Ar-CH_2-Ar, 16 H), 3.40 (s, -O-CH_3, 24 H).



Calix[8]arene **76f**:

A suspension of the calix[8]arene **71** (0.010 g, 9.41 μmol) in DMF (2 mL) was added under nitrogen to a stirred solution of porphyrine isocyanate, prepared from the corresponding amine (0.124 g, 0.113 mmol), triphosgene (0.011 g, 0.038 mmol) and (*i*-Pr)$_2$NEt (0.024 g, 0.188 mmol) in dichloromethane (105 mL). The reaction mixture was stirred for 48 h at rt under nitrogen. Then the solvent was removed under reduced pressure and methanol (10 mL) was added to the residue. A dark-violate solid was filtered off and washed with methanol (2 x 10 mL). The powder was dissolved in dichloromethane (5 mL) and the solution was passed through the column (silica, THF/hexane, 1 : 2, followed by THF/hexane, 1 : 1, v/v). The product **76f** was collected in the last fractions; the solvent was removed in vacuum. The residue was reprecipitated from dichloromethane by slow addition of hexane to give **76f** as a dark-violet powder. Yield: 0.042 g (45%).

MS (MALDI-TOF): m/z 10056.1 (M^+).

6.6 Literature and comments

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[3] M. Bolte, V. Brusko, V. Böhmer *Acta Cryst.* **2003**, *E59*, o1691-o1693.

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[8] M. Vysotsky, unpublished results.

[9] J. Zhang, G. Podoprygorina, V. Brusko, V. Böhmer, A. Janshoff *Chem. Mater.* **2005**, *17*, 2290-2297.

[10] Submonolayers of calix[8]arene derivatives were prepared by spin casting. A drop (ca. 10µl) of solution was deposited on a freshly cleaved HOPG (highly oriented pyrolytic graphite, purchased from Plano GmbH, Wetzlar, Germany) surface and the sample was spun at 1000 rpm for 30 s. Calix[8]arene derivatives were dissolved in dichloromethane, tetrahydrofuran or chloroform resulting at a concentration between 10^{-3}~10^{-6} mg ml^{-1}.
Samples were imaged at room temperature with a commercial SFM (Nanoscope IIIa, Digital Instruments, Santa Barbara, California) employing TappingMode™ using rectangular silicon cantilevers (Nanosensors, 125µm long, 30µm wide, 4µm thick) with an integrated tip, a nominal spring constant of 42 N m^{-1}, and a resonance frequency of 330 kHz. To control and enhance the range of the attractive interaction regime the instrument was equipped with a special active feedback circuit, called Q-control (Nanoanalytics, Germany). The quality factor Q of this oscillating system is increased by one order of magnitude. As a consequence, the sensitivity and lateral resolution are enhanced, allowing us to prevent the onset of intermittent repulsive contact and thereby to operate the SFM constantly in the attractive interaction regime.

[11] G. B. Pan, J. M. Liu, H. M. Zhang, L. J. Wan, Q. Y. Zheng, C. L. Bai *Angew. Chem. Int. Ed.* **2003**, *42*, 2747.

[12] Employment of non-contact mode using enhanced Q-values makes rendering the imaging procedure less destructive and increases the lateral resolution by roughly 30%. B. Anczykowski, J. P. Cleveland, D. Krüger, V. Elings, H. Fuchs *Appl. Phys. A* **1998**, *66*, S885.

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[14] Crystallographic measurement was performed by Dr. M. Bolte at 100 K using a STOE-IPDS-II diffractometer with graphite monochromated MoKα radiation. Structure was solved by direct methods, structure refinement by full-matrix least-squares with SHELXL. 30103 reflections, 8038 independent, Rint = 0.096, R_1 = 0.1047, wR_2 = 0.2583 for I>2σ(I). Largest diff. peak and hole were 0.480 and -0.368 e/$Å^3$.
The crystal was non-merohedrally twinned (twin matrix: -1 0 0 / -0.70 1 -0.86 / 0 0 -1). The ratio of the two twin components refined to 0.434(3)/0.566(3). Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC No 224043.

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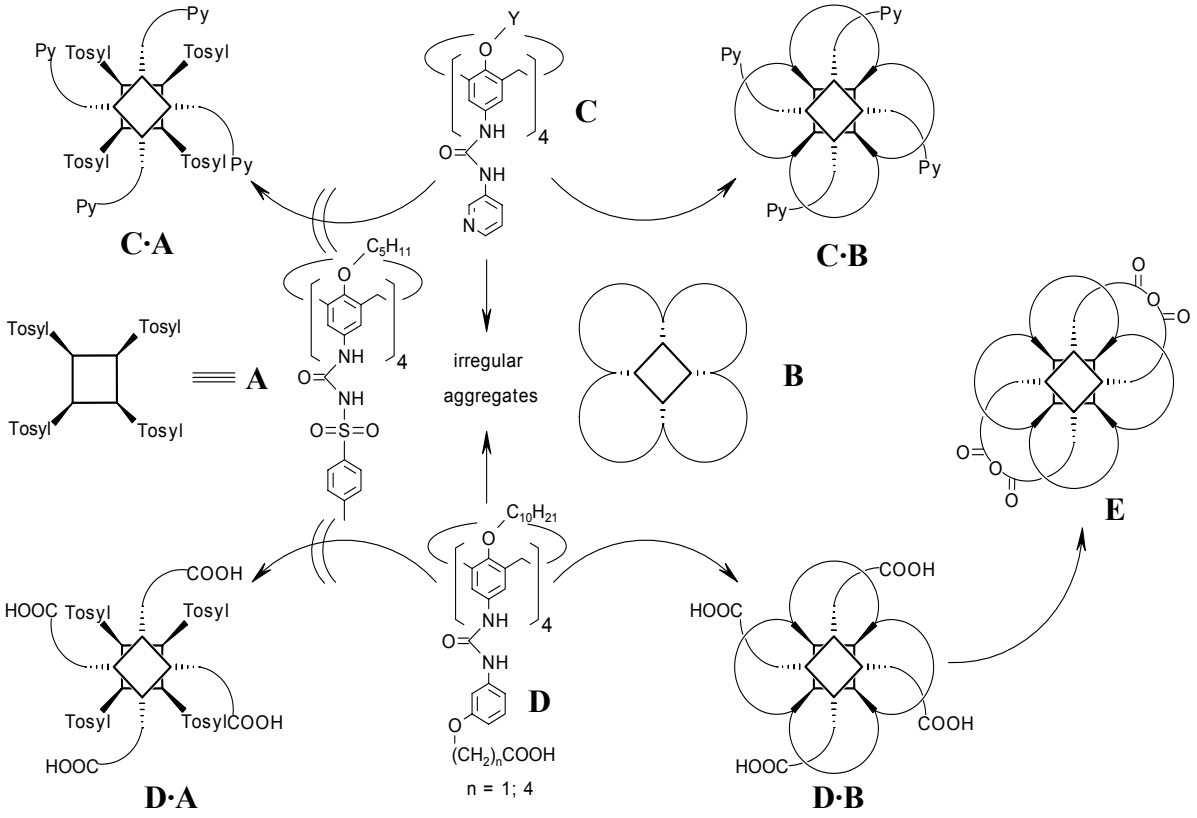
Summary

Specifically functionalized tetraurea calix[4]arenes and various calix[8]arene derivatives were synthesized and their self-assembly was studied. According to the desired features of the derivatives the presentation is divided in the following sections:

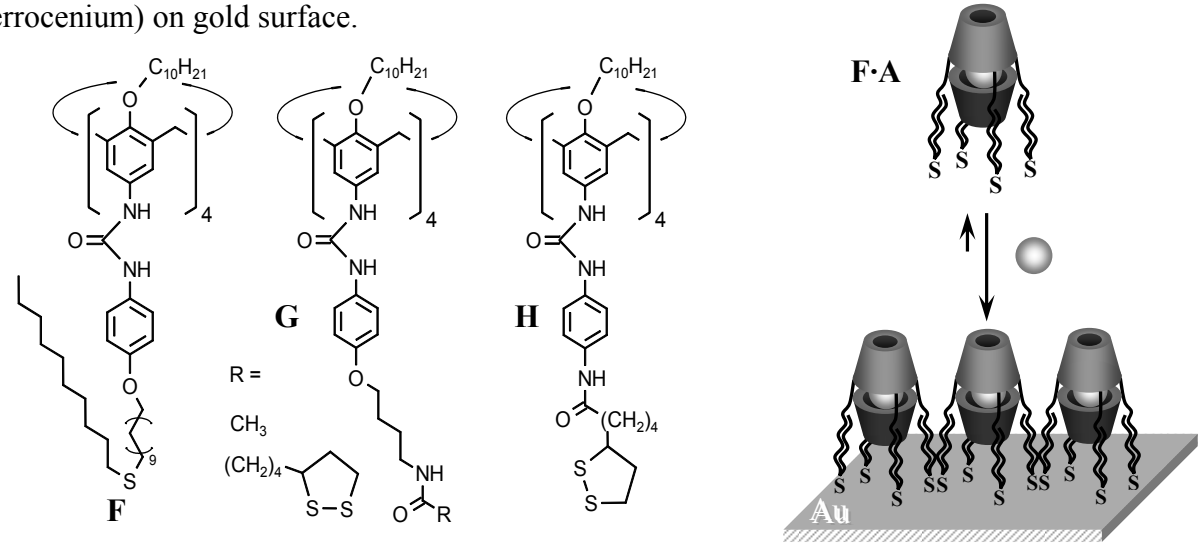
1. Calix[4]arenes functionalized with four urea groups at the wide rim (further "tetraureas") form dimers in apolar solvents. In the dimers two calixarene counterparts are held together by a seam of hydrogen bonds between the urea groups. A solution of two different tetraaryl- or tetraalkylurea calix[4]arenes in the ratio 1 : 1 contains usually two homodimers and a heterodimer. However, there are tetraureas which prefer the formation of heterodimers exclusively. This is tetratosylurea **A** which can homodimerize but in combination with tetraarylureas produces only heterodimers. Another example is the tetraurea **B** (or "tetraloop") which has four bridges connecting adjacent phenyl rings and therefore cannot form homodimers.



Tetraureas **C** and **D** were prepared from calix[4]arene tetraamines by acylation with active urethanes of *m*-pyridyl- or *m*-carboxylalkoxyphenylanilines. Their heterodimer **C·D** was expected to be stabilized by additional hydrogen bonds formed between carboxyl and pyridyl

groups. Self-assembly of these tetraureas was studied by ^{1}HMR spectroscopy in different solvents. Individually or in the mixture these tetraureas form irregular aggregates. In a 1 : 1 mixture with tetratosyl urea **A** such aggregates were also observed in the spectra. Probably the hydrogen bond donor or acceptors, like carboxyl or pyridyl, adjacent to the urea groups participate in hydrogen bonding in a way which disturbs the formation of dimers. However, the pyridyl and carboxyl containing tetraureas form heterodimers with tetraloop tetraurea **B**. The dimerization of urea **D** (n = 4) with tetraloop urea **B** was used for the synthesis of a *bis*-[3]catenane **E** via anhydride formation.

2. Tetraurea calix[4]arenes (**F**, **G** and **H**) with alkylsulfide functions attached at the wide rim via ether or amide links were synthesized to study electrochemical properties of self-assembled monolayers (SAMs) formed by tetraurea dimers containing cobaltocenium (ferrocenium) on gold surface.



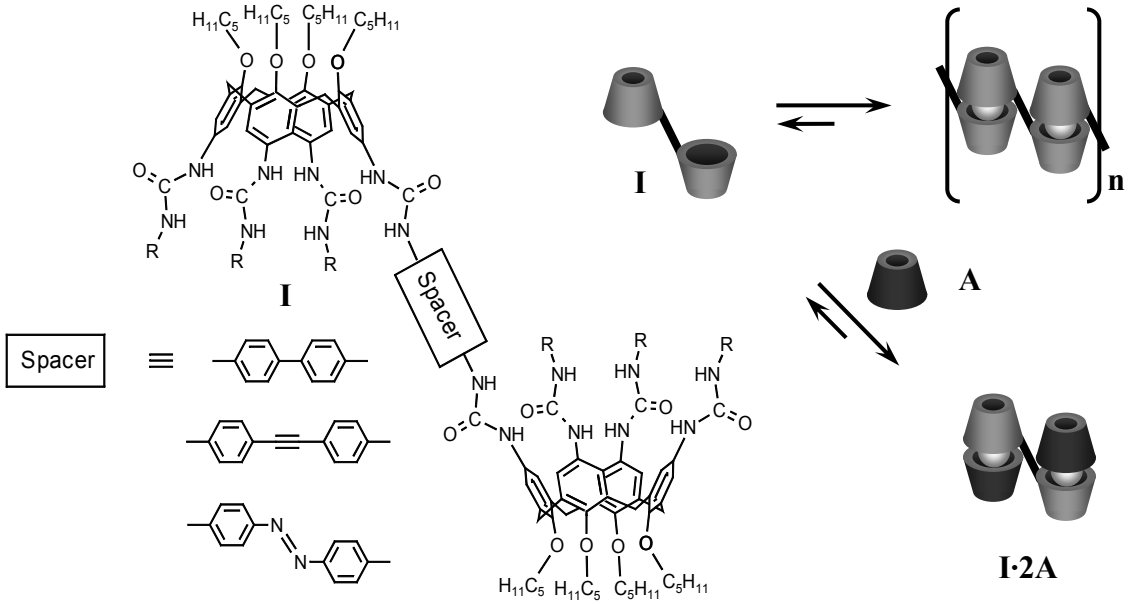
Since ferrocenium is paramagnetic the ^{1}H NMR studies were performed only with its analogue – cobaltocenium. The (hetero)dimerization of these tetraureas was studied by ^{1}HMR spectroscopy in different solvents to find the optimum conditions for the complexation of cobaltocenium in the dimers.

In apolar solvents the tetraurea calix[4]arenes **G** and **H** form irregular aggregates in addition to the desired dimers. Heating of their TCE solutions leads to dissociation of dimers and aggregates to monomers which was not observed for tetraarylurea calix[4]arenes studied before. The formation of irregular aggregates can be attributed to hydrogen bonding of the amide groups.

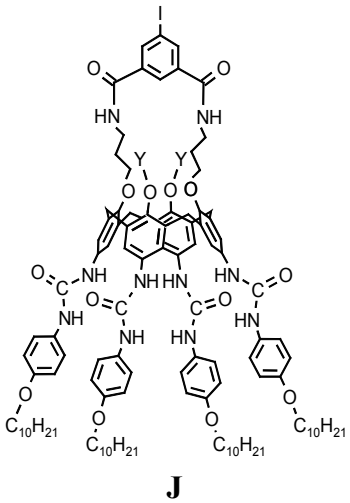
The calixarene **F** readily forms (hetero)dimers with cobaltocenium as guest in dichloromethane. Its heterodimers with tetratosylurea **A** and their SAMs on gold were investigated by surface plasmon resonance (SPR) and cyclic voltammetry (Prof. Dr. S.

Mittler, S. Xu, Canada). The SPR experiments show the formation of stable SAMs from the tetraurea dimers on the gold surface. Reduction/oxidation peaks of the ferrocenium encapsulated in the dimers in solution and in SAMs on a gold electrode are shifted to higher values in the voltammograms in comparison to free ferrocenium.

3. *Bis*-tetraureacalix[4]arenes **I** singly-linked via one of the urea functions by rigid spacers were synthesized starting from tetraamino calix[4]arene tetraether. Their self-assembly to polymers and to *bis*-heterodimers **I·2A** in apolar solvents was proved by the ^{1}H NMR spectra. Polymers formed by *bis*-calixarenes **I** include quantitatively tetraethylammonium or *p*-difluorobenzene similarly to single tetraureas.



AFM studies revealed fibers formed by self-assembly of *bis*-calixarenes **I** on HOPG (in collaboration with M. Janke, Prof. A. Janshoff, Mainz). The dimensions of the fibers (width of 7.8-15.5 nm, height of 1.8-2.4 nm) do not correspond to single "linear" polymer (diameter of ~ 4 nm). The fibers could consist of several polymer chains either in "stretched" or in a helical conformation.



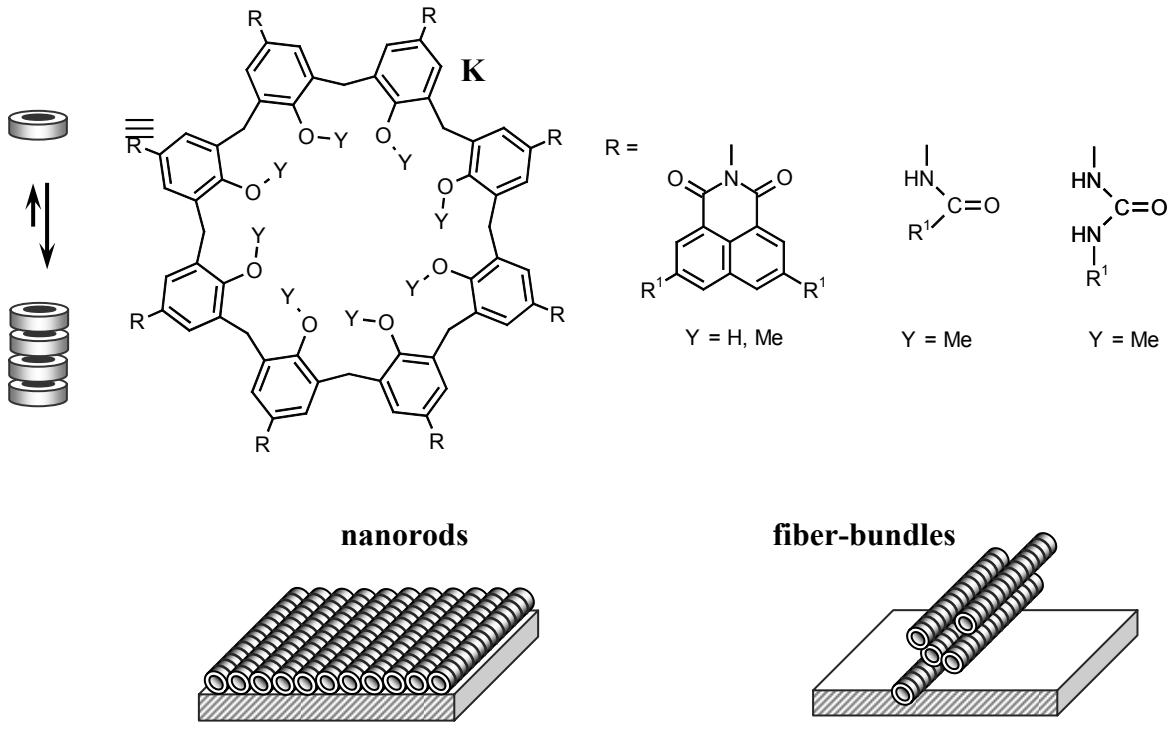
J

4. Tetraurea calix[4]arene **J** bridged in 1,3-positions at the narrow rim by 5-iodoisophthalic acid has been synthesized as building block for *bis*-calixarenes singly-linked via their narrow rims, where the symmetrically bridged blocks **J** are connected under 60 or 120° angle using appropriate spacers. Such *bis*-

tetraurea calix[4]arenes might assemble to cyclic oligomers or to polymers via intermolecular dimerization. Iodine in the bridge should be used for attachment of the tetraurea **J** to appropriately functionalized spacers by Sonogashira coupling.

The compound **J** is the first example of a 1,3-narrow rim-bridged tetraurea calix[4]arene. Bridging of tetraurea at the narrow rim could fix the molecule in a conformation which is unfavourable for the dimerization. However, the ^{1}H NMR spectra proved the dimerization of the bridged tetraurea **J** in apolar solvents. Therefore, the selected bridge is appropriate for the preparation of the target *bis*-calixarenes.

5. Calix[8]arenes appropriately substituted in *p*-positions of the phenolic rings should self-organize by stacking in columnar assemblies. Specific interactions like hydrogen-bonding or π-π-stacking between the stacked molecules should keep the molecules together. For this purpose the *p*-octaamine calix[8]arene octamethylether was synthesized and used for the preparation of various derivatives **K**. Calix[8]arenes functionalized by urea or amido groups at their *p*-positions were expected to build up columnar assemblies by hydrogen bonding (in apolar solvents they form aggregates). The naphthalic octaimides should form the desired structures by π-π-stacking.



The calix[8]arene derivatives **K** spin-coated on HOPG were studied by scanning force microscopy (in collaboration with Prof. A. Janshoff, Mainz) and two types of self-assembled 1D nanostructures were detected: parallel aligned nanorods and fiber-bundles.

Abbreviations

The following abbreviations were used in this work:

A	acceptor
AFM	atomic force microscopy
9-BBN	9-borabicyclo[3.3.1]nonane
Boc	*tert*-butyloxy carbonyl
COSY	correlation spectroscopy
CV	cyclic voltammetry
D	donor
DCC	*N,N'*-dicyclohexylcarbodiimide
DCE	1,2-dichloroethane
DMF	*N,N'*-dimethylformamide
DMSO	dimethyl sulfoxide
ESI	electrospray ionisation
FD	field desorption
HOPG	highly oriented pyrolytic graphite
MALDI-TOF	Matrix Assisted Laser Desorption Ionization - Time of Flight
NBS	*N*-bromosuccinimide
NMP	*N*-methyl-2-pyrrolidone
Nu	nucleophile
PyBOP	benzotriazol-1-yl-*N*-oxy-tris(pyrrolidino)phosphonium hexafluorophosphate
rt	room temperature
SAM	self-assembled monolayer
SFM	scanning force microscopy

SPR	surface plasmon resonance
STM	scanning tunneling microscopy
TCE	1,1,2,2-tetrachloroethane
THF	tetrahydrofurane
VPO	vapour-pressure osmometry

Author's list of publications

"Supramolecular Structures Formed by Calix[8]arene Derivatives"

G. Podoprygorina, J. Zhang, V. Brusko, M. Bolte, A. Janshoff, V. Böhmer

Org. Lett. **2003**, *5*, 5071-5074.

"Functionalized Calix[8]arenes, Synthesis and Self-assembly on Graphite"

J. Zhang, G. Podoprygorina, V. Brusko, V. Böhmer, A. Janshoff

Chem. Mater. **2005**, *17*, 2290-2297.

"Tetraurea calix[4]arenes with Sulfur Functions. Synthesis, Dimerization to Capsules and Self-Assembly on Gold"

S. Xu, G. Podoprygorina, V. Böhmer, Z. Ding, D. Rooney, C. Rangan, S. Mittler

in preparation

The Thesis were also partly presented in following conferences:

7th International Conference on Calixarenes

August 13-16 2003, Vancouver, BC Canada

8th International Conference on Calixarenes

July 25-29 2005, Prague, Czech Republic

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