Self-assembly of Tetraurea Calix[4]arenes: Hydrogen Bonded Capsules with Supramolecular Chirality

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1. Introduction

1.1 Calixarenes

1.1.1 Definition, Synthesis and Conformations

In 1978 D. Gutsche introduced the name "calixarenes" to describe cyclic oligomers produced by condensation of p-substituted phenols with formaldehyde under alkaline conditions. In our days under this name different derivatives of [1_n]metacyclophanes (aromatic units connected via a -CHR-, -CH_2-, -S-, or -CH_2OCH_2- bridges) are presented. Started with the original *p-tert*-butylcalixarenes and calixresorcarenes derivatives like calixnaphthalene, calixpyrroles, calixfuranes, calixthiophenes, calixindoles, calixbenzofurans or thiacalixarenes are cited here just to illustrate the variety of compounds[1], each of them having specific features subject of research all over the world.

The number of aromatic units in one molecule is other factor of increasing diversity. Calixarenes having from 4 to 8 aromatic units are commonly used but derivatives like *p-tert*-butylcalix[9-20]arenes were also obtained.

In the very beginning the synthesis of calixarenes was not so easy. Clear reaction conditions were established for the synthesis of *p-tert*-butylcalix [4,6 and 8]arenes. They are reproducible and offer the compounds in relatively good yields and purity. The synthesis started with *p-tert*-butylphenol, HCHO and NaOH/KOH as base, followed by dissolution in an appropriate solvent (diphenyl ether or xylene) and reflux for several hours. These conditions work much less well for any other *p*-substituted phenol, but many specific conditions were found which cannot be summarized in here. No direct method could be found for the synthesis of calixarenes from 4-nitro-, 4-cyano- and 4-phenoxy-phenol, as well as from 4-hydroxybenzoic acid, and 4-hydroxyacetophenone. All these compounds have electronically deactivating groups in *para*-position to OH which disturb the course of reaction.

For a long time the chemists handling calixarenes could not understand why from simple alkylation reactions complicated mixture were obtained. Later was establish that calixarenes are flexible molecules and can adopt different conformations. Four main conformations were found and they are named *cone*, *partial cone*, *1,2-alternate* and *1,3-alternate* (figure 1). Using modern techniques to characterize chemical compounds, many examples were found possessing different conformations and symmetry in solution and/or

in solid state. In the *cone* conformations often two aryl ring are found almost parallel while the other two splays outward. This conformation was named "*pinched cone*" or "*flattened cone*" and we met it in our work.

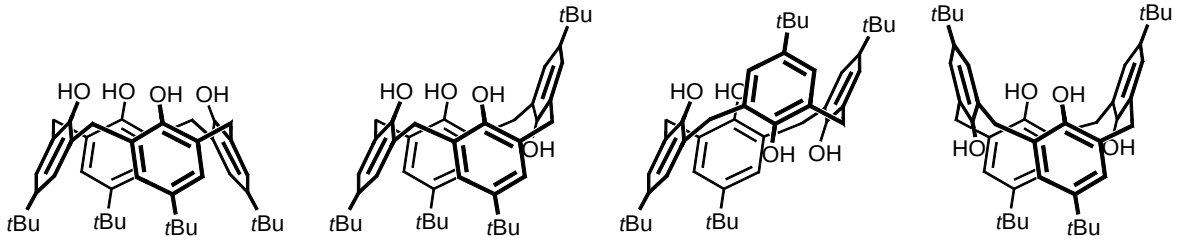


Figure 1: Representation of the four main conformations of *p-tert*-butylcalix[4]arene.

Two aspects should be mentioned:

- as long as in the molecule free OH, methoxy or ethoxy groups exist those phenolic units are able to pass the annulus and the conformation of the molecule is changed; propyl residues are large/long enough to prevent such an inversion and to "fix" a certain conformation.
- for a flexible compound the conformation in solution could be (totally) different from the one found in the solid state.[2]

Increasing the number of aromatic units has a direct influence in flexibility of the molecule. The conformational representation becomes more difficult and less precise.

1.1.2 Chemical modification of calix[4]arene

There are mainly two places to functionalize a calixarene: the phenolic OH groups (esterification, etherification) and the phenyl ring (most often the *para*-position). Conditions to get mono-, di- (1,2 and 1,3), tri- and tetraalkyl ether or, esters were found. Much research focused the elaboration of condition for the selective or exclusive formation of one isomer from all possible regioisomers and atropisomers.

A very interesting aspect in the chemistry of calixarene is the fact that selectivity introduced in the narrow rim can be transferred to wide rim as it is shown in the figure 2.[1]

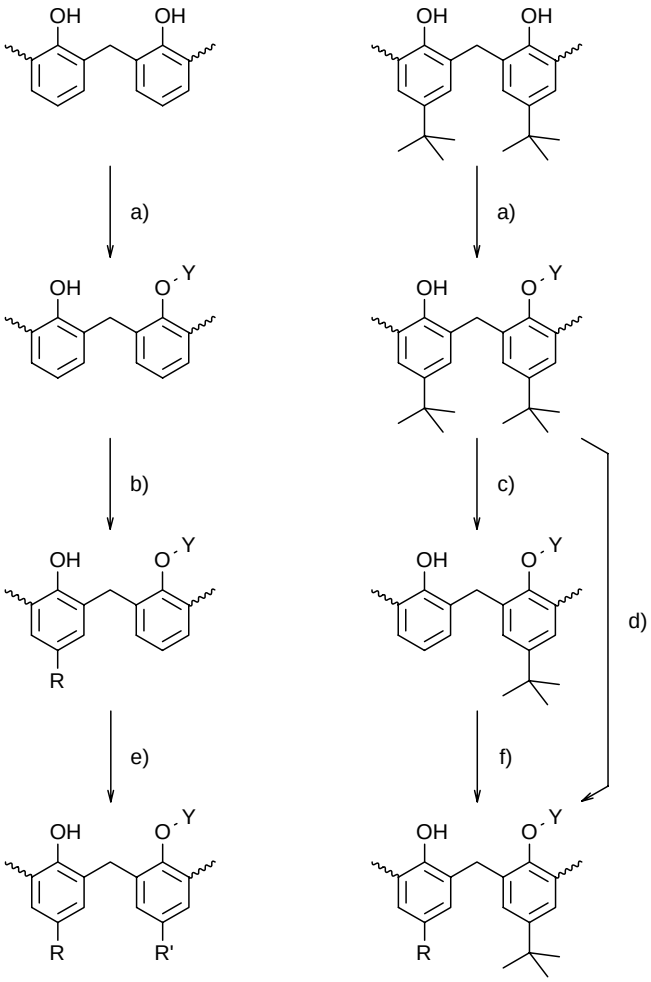


Figure 2: Selectivity transfer from the narrow to the wide rim, schematically presented for two units: **a)** selective introduction of ether residues; **b, f)** selective electrophilic substitution to the phenol units; **c)** selective debutylation, and **d)** selective *ipso*-substitution of phenol units; **e)** complete substitution phenylether units.

Reactions like sulfonation, nitration (to introduce four nitro group or selectively 1-3 groups), retro-Friedel-Crafts-alkylation (to remove the *t*-butyl moieties, all or selectively) are now well establish. The possibility to remove the *t*-butyl groups opens-up the options for further derivatisation. Subsequently, all the functions introduced at wide or at narrow rim can be further reacted.

We restrict this short presentation of the chemistry of calixarene to the calix[4]arene because it is the subject of this work and the whole variety of compounds and reactions which were done can not be summarized here. It should be mentioned that the reactions done with calix[4]arenes could be (or were already) underwent with other calixarenes.

1.2 Self-assembly with the help of hydrogen bonds

Understanding of processes that are taking place in biological systems (enzymes activity, DNA self-replication, membrane selectivity and many other) has attracted the attention of more and more teams biologists as well as chemists. The next goal is the design and synthesis of molecules that can imitate/mimic these natural processes. Following this direction, host-guest systems were developed and studied. A particular case exists when the guest is completely surrounded by the host which can be one huge molecule or a capsule formed by at least two molecules. These systems are governed by "reversible bonds" such as hydrogen bonds, charge transfer interactions, metal coordination, van der Waals or solvophobic forces. Most of these interactions are weak in comparison with covalent bonds and to achieve a certain stability of assemble a larger number of cooperative bonds are necessary. Cooperative bonds can be reached by preorganization of several binding groups on a suitable molecular skeleton.

In the following part, some examples of capsules obtained by self-assembly and held together by hydrogen bonds are presented.

1.2.1 Glycoluril derivatives

Glycoluril derivatives are used in construction of supramolecular assemblies.[3] The compounds of type **1** are forming a dimeric capsule (named tennis ball) held together by eight NH- - -O hydrogen bonds. The cavity is large enough to accommodate small molecules like methane, ethane, ethylene and noble gases while molecules with three carbon atoms are already too large to be encapsulated.[4] The monomer consists of two glycoluril moieties attached to a central aromatic unit. This structure brings the adequate spatial arrangement of the two glycoluril moieties and allows the formation of hydrogen bonds (figure 3).

Larger balls were obtained by changing the central units of the monomer. The capsule **2•2** is able to bind two molecules of benzene.[5] Monomers of threefold symmetry (**3**[6] and **4**[7], as example) were as well obtained and they are forming capsule in a similar manner.

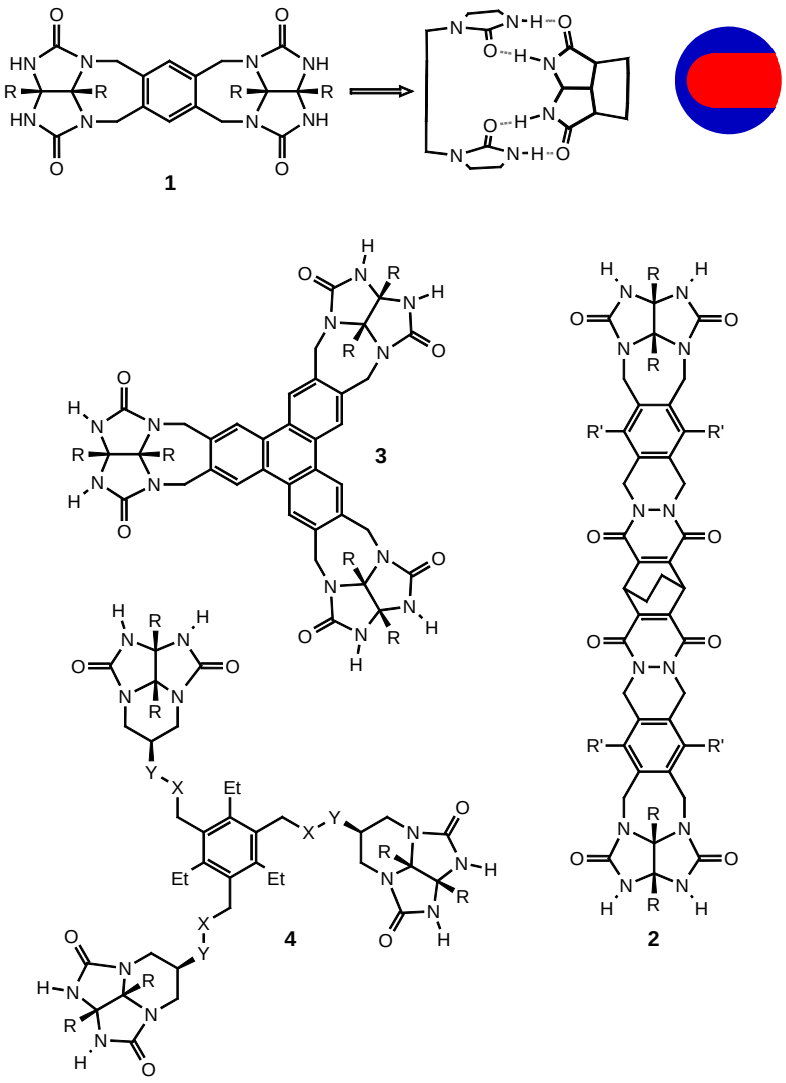


Figure 3: Compounds bearing glycoluril units form capsules with different size.

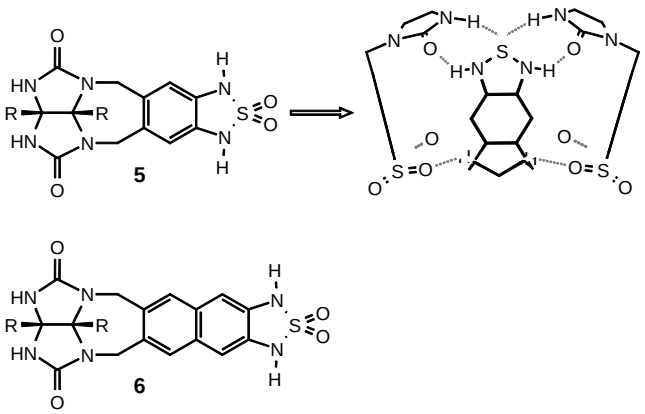


Figure 4: In the tetrameric capsules, the hydrogen bonds are formed between the glycoluril and sulfamides moieties. (For clarity in the figure, only the hydrogen bonds in the foreground are depicted and some atoms are omitted).

Glycoluril moieties are self-complementary hydrogen bonding patterns of cyclic sulfamides. If the two units are connected to the same core, they will form preferential heterodimeric hydrogen bonds and the result is a supramolecular system. The compounds shown in the figure 4 form tetrameric capsules.[8]

These were selected examples of capsules made by hydrogen bonds but the skeleton to which the binding sites are connected is not a calixarene. The following examples contain a calixarene platform.

1.2.2 Calix[4]arenes fixed in cone conformation

Calix[4]arenes fixed in cone conformation have a very advantageous shape for a chemist looking for molecules able to self-assemble to capsules. They have the right curvature being, in the same time, flexible.

2-Pyridone derivatives have the donor and the acceptor of hydrogen bonds sites and they dimerize. When one or two such groups were attached to the calixarene[9] (figure 5) it was found that **7a** gives a dimeric structure similar to the pyridone while **7b** forms oligomeric hydrogen bonded aggregates. These structures are just the first steps in the searching the self-assembly properties of derivatives of calixarene.

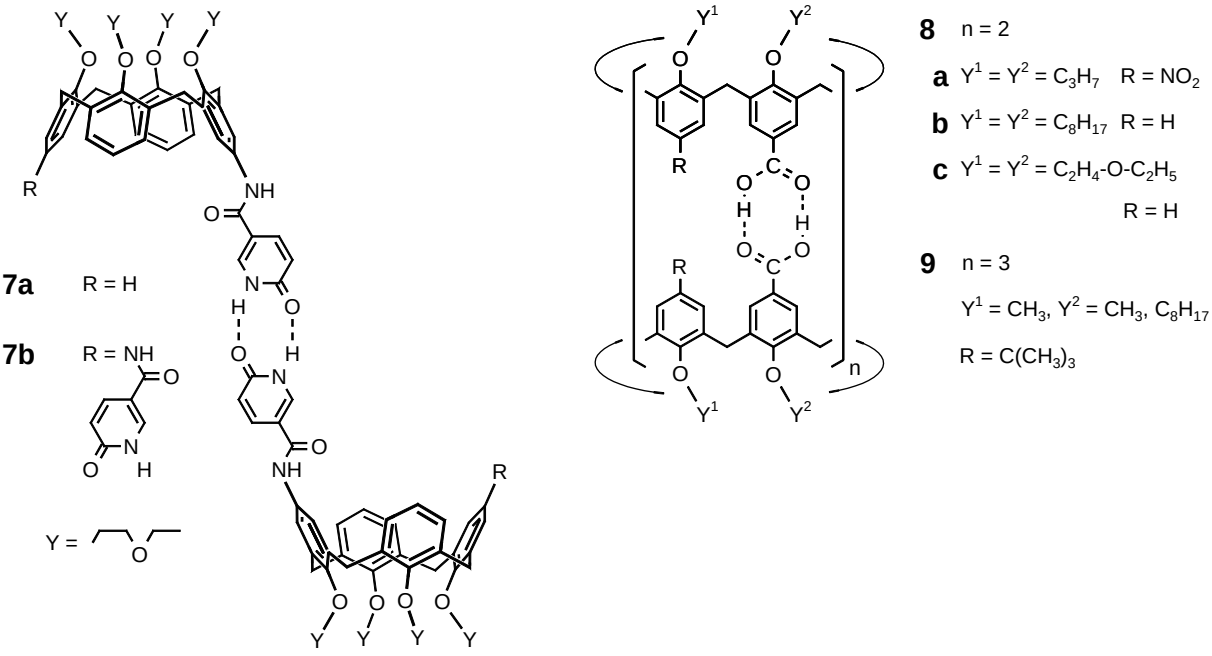


Figure 5: Hydrogen bond pattern in the assemblies of 2-pyridone **7** and carboxylic acid derivatives **8** and **9**.

The formation of well-defined hydrogen bonded dimers was observed in the case of the calix[4]arene dicarboxylic acid **8**.[10] In the crystalline state **8a** exists in a C_{2v}-symmetrical pinched cone conformation. The same conformation was found in the dimer and it makes the inner cavity too small for guest inclusion. The dimer is held together by four C=O···H-O hydrogen bonds.

In the case of calix[6]arenes **9** the existence of dimer in apolar solvents was proved by VPO and ^{1}H NMR.[11] The cavity thus formed is obviously large enough to include cations such as N-methylpyridinium and N-methyl-4-picolinium (but not N-methyl-2-picolinium) since significant upfield shifts were found for all signals upon addition of their iodides.

Tetrapyridyl derivative **10** solubilizes exactly one equivalent of the tetraacid **8d** in chloroform. The formation of dimers via four strong hydrogen bonds COOH---N is sustained just by VPO measurement while the ^{1}H NMR spectra do not show the expected shifts and no guest inclusion was reported.

Similarly, the tetraacid **8e** could be solubilized in $CDCl_3$ by the 4-pyridyl derivative **11a** and its 3-pyridyl analogue **11b** in a 1:1 ratio while no solubilization took place in the case of the 2-pyridyl derivative **11c**.[12] The formation of the suggested complexes **8e·11a** and **8e·11b** was additionally confirmed by VPO. Two signals observed for the aromatic protons of **8e** in aggregates with *all* pyridine derivatives (even with 4-picoline) indicate a pinched cone conformation.

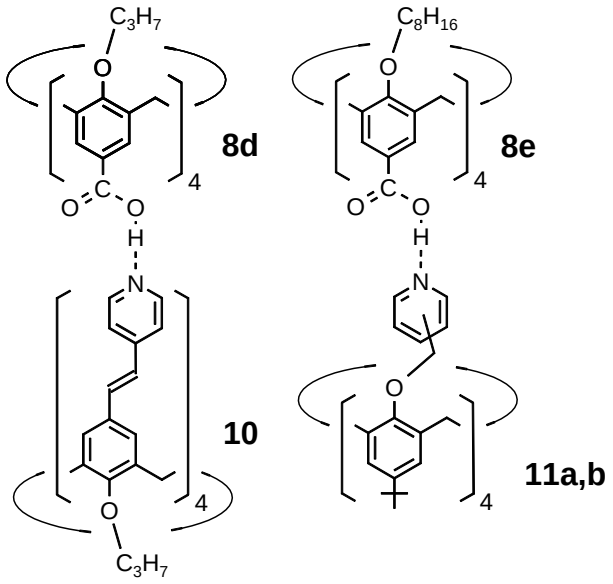


Figure 6: Dimers formed by COOH---N hydrogen bonds.

1.2.3 Rosettes

Melamine and barbiturates or cyanurates have complementary hydrogen bonding sites and have been used as structural motifs for self-assembly. This feature was successfully explored in the area of calixarene in the group of Reinhoudt.

Calixarenes diametrically substituted at the wide rim by two melamine units form a box-like assembly in the presence of two equivalents of barbiturates[13] or cyanurates[14]. The assembly is composed from three molecules of calixarene and 6 molecules of barbiturates or cyanurates and it is held together by a total of 36 hydrogen bonds. It is stable in apolar solvents (chloroform, toluene), but the stability strongly decreases by adding a polar solvent (DMSO, methanol).

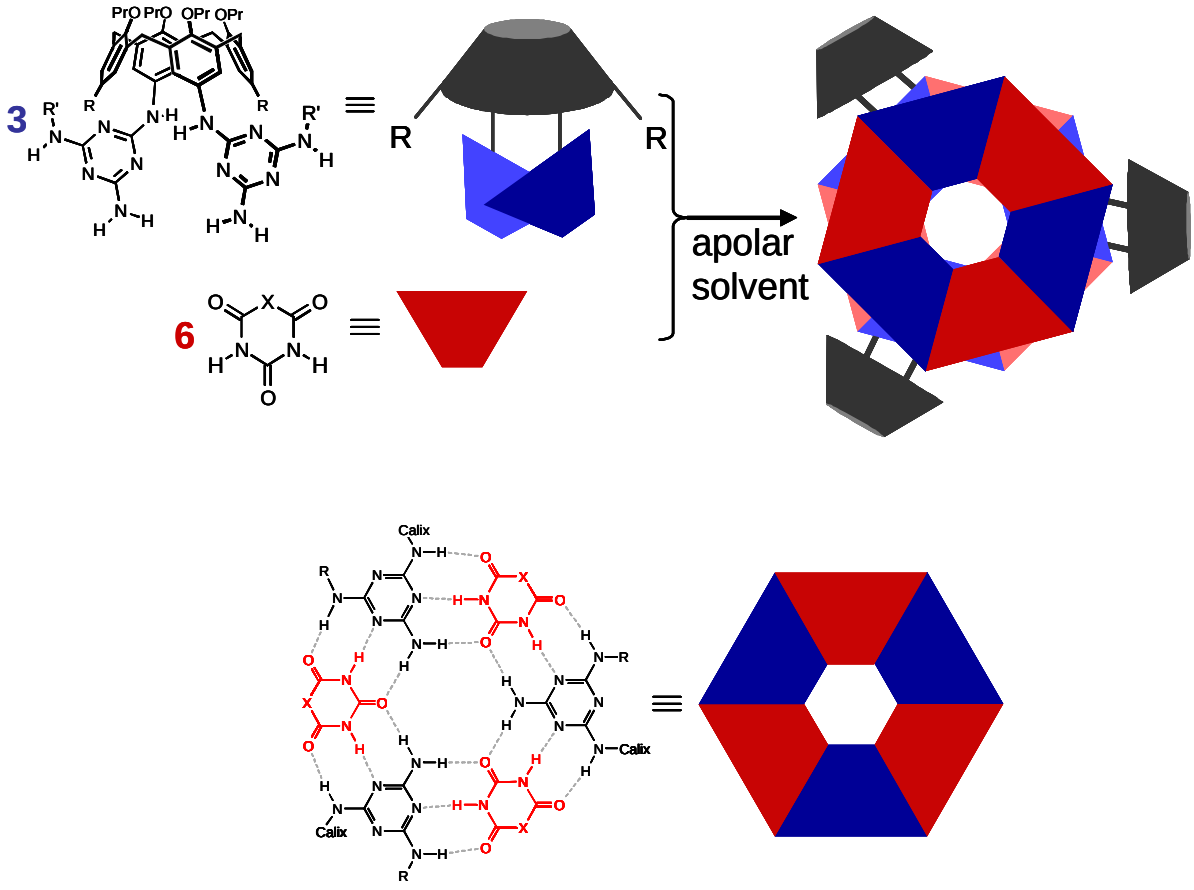


Figure 7: Schematic representation of the rosette formation (upper) and the hydrogen bond pattern between melamine and barbiturates/cyanurates forming one layer of the assembly.

The box consist of three molecules (one melamine units from each calixarene is on the top and the second on the bottom) and six barbiturates connected via 18 hydrogen bonds in a rosette shape (figure 7) while the three calixarene skeletons are forming the walls of the

box. The two rosettes are tightly stack on top of each other, so there is no space for a guest molecule.

In the calixarene, the two melamine units could have two orientations: staggered and eclipsed. Each isomer forms a rosette but the symmetry of the assembly is different (figure 8). All three calixarene belonging to one rosette must have the same orientation otherwise the whole assembly can not be formed.

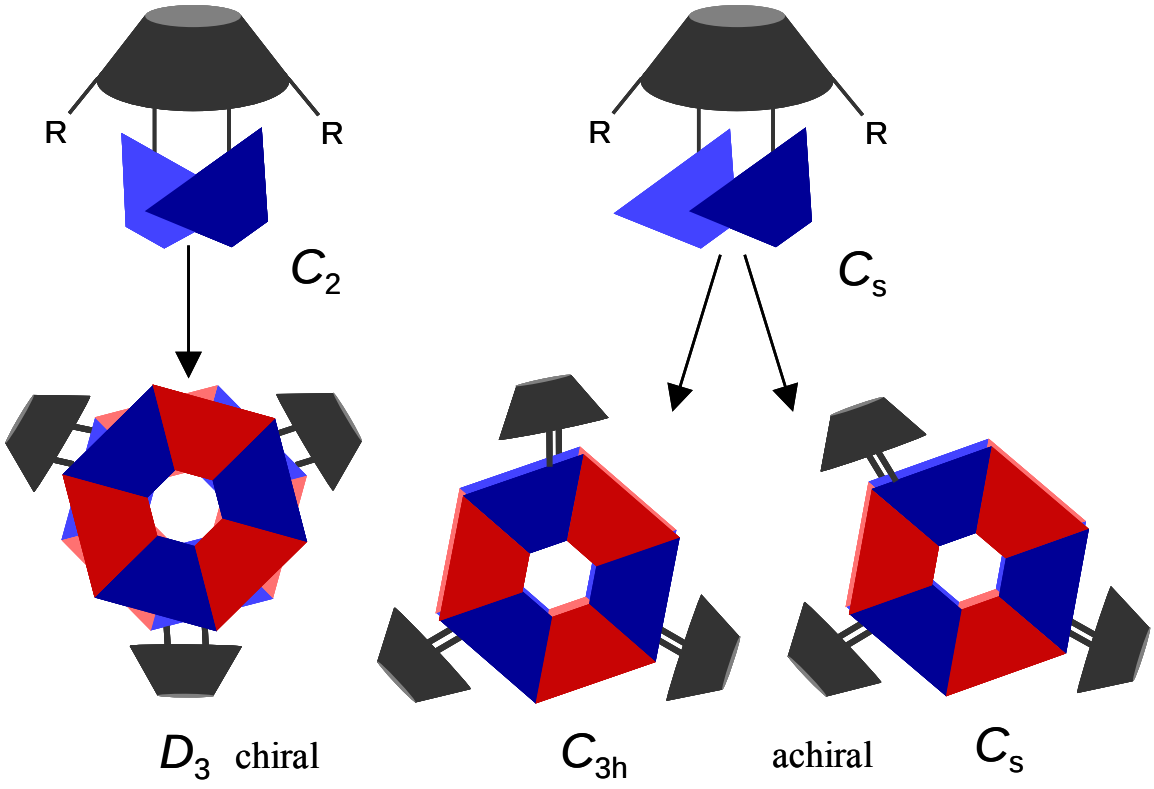
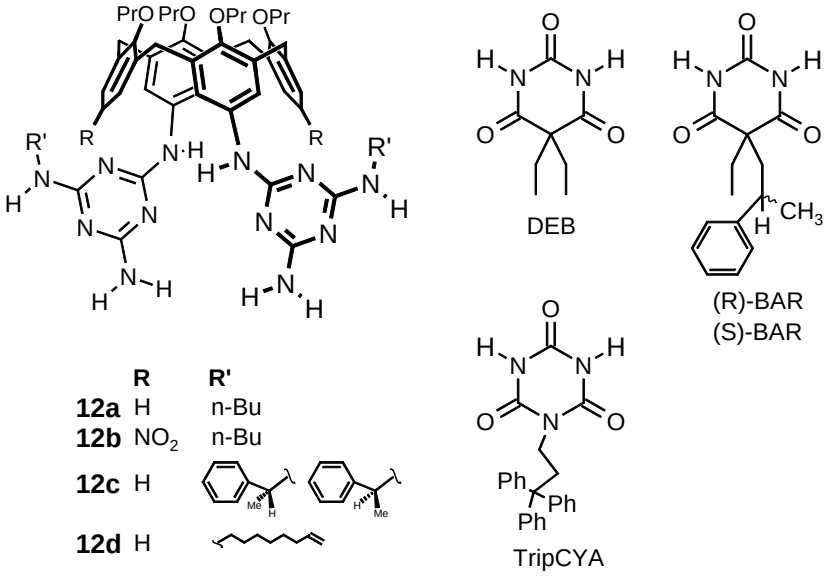


Figure 8: The two orientations of the melamine units in one calixarene and the three possible diastereomeric rosettes and their symmetry.

The mostly used tools in the analysis of the rosettes are ^{1}H NMR, CD spectroscopy, MALDI-TOF mass spectrometry (Ag^+ labeling) and X-ray spectroscopy. In the ^{1}H NMR spectra the most significant region is 13-16 ppm (free of other resonances) where imide NH signals appear after the hydrogen bonds are formed.



Our interest was focused on supramolecular chirality studied with these structures. When the melamine derivative **12b** is mixed with 5,5-diethylbarbiturate (**DEB**) in the ratio 1:2, in an apolar solvent, exclusively the staggered isomer (**12b**)$_3$•**DEB**$_6$ is formed as a racemic mixture of *M*- and *P*-enantiomers. The introduction of a chiral component results in asymmetric induction of supramolecular chirality in the assemblies.[15] The relative position of the chiral centers within the assemblies and the solvent are factors that influenced the degree of chiral induction. For the same complex, (**12a**)$_3$•[(*R*)**BAR**]$_6$ the chiral carbon which is two atoms remote from the barbituric acid ring leads to a mixture of *P*- and *M*-diastereomers with a diastereomeric excess of 17% in favor of *P* in $CDCl_3$, 85% in toluene-d_8 and >98% in benzene-d_6. [16,17] When the chiral substituents are directly connected either to the nitrogen atoms of the melamine units or to the cyanurate ring nitrogen atom, complete induction of chirality has been observed in all cases. For example, the melamine derivative (*R*,*R*)-**12c** gives in combination with a non chiral barbiturate the *M*-helical form (*de* > 95%) while (S,S) isomer forms the *P*-helical assembly.[18]

The chiral barbiturate within (*M*)-{(**12b**)$_3$•[(*R*)-BAR]$_6$} can be replaced by achiral cyanurates. The new assembly preserves the (*M*)-chirality introduced by the chiral barbiturate. When to solution containing the rosette with achiral cyanurate the chiral barbiturate was added no exchange was observed and no induction of chirality.

Heterodimeric[19] assemblies were obtained by mixing the solution in toluene-d_8 of (**12a**)$_3$•**DEB**$_6$ and (**12b**)$_3$•**DEB**$_6$. While at 0°C the exchange of the components is extremely slow and the heterodimer could not be observed, the equilibrium is reached with in seconds at 25°C. The composition (1:3:3:1) of the mixture was analyzed with the help of mass spectrometry and NMR techniques.

Ring closing metathesis (RMC) reaction using Grubb's catalyst was used as additional proof for the formation of C_{3h} and C_s isomers in the case of cyanurates. A melamine derivative carrying terminal double bonds **12d** was synthesized and its complex with **DEB** (exclusively the D_3 isomer is formed) underwent threefold metathesis reaction. The product (obtained in 96% yield)[20] was the macrocycle containing three calixarene units (Figure 9).

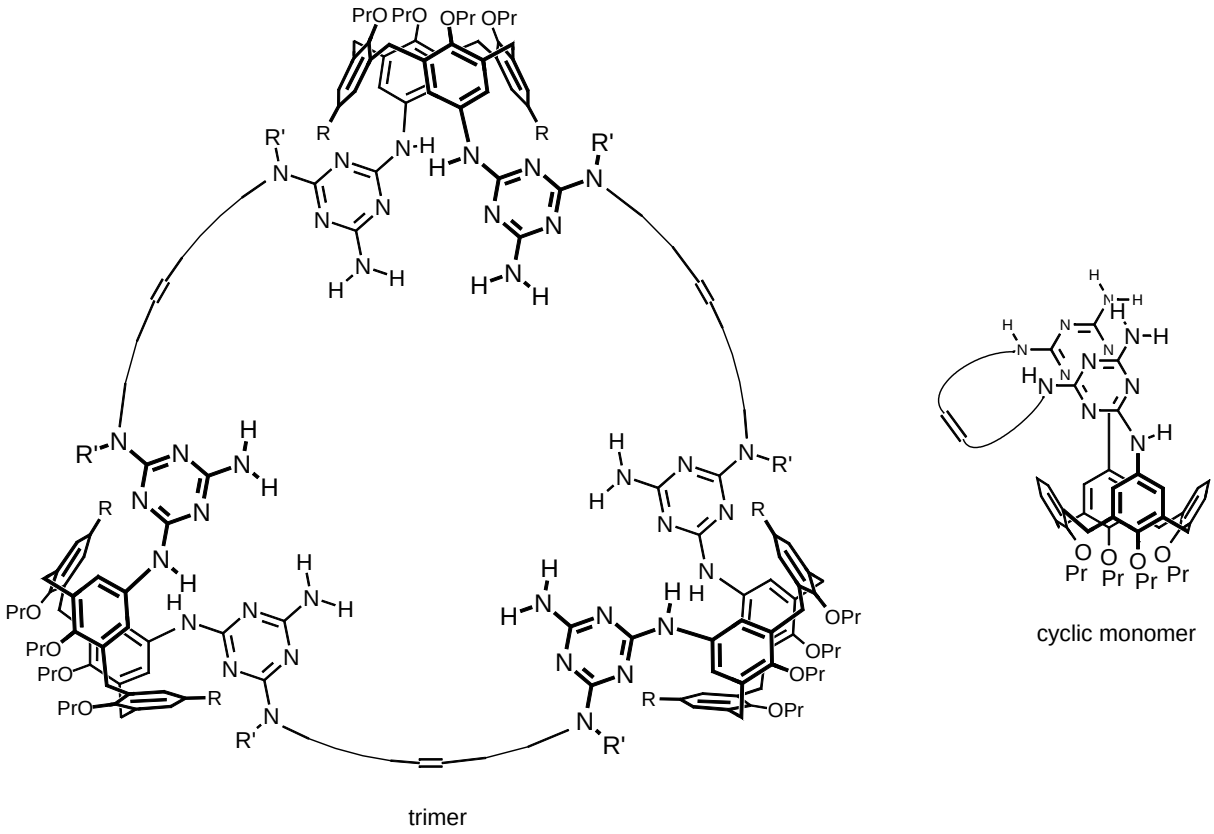


Figure 9: The trimer molecule obtained by threefold metathesis reaction of D_3 rosette and the cyclic monomer from C_{3h} rosette.

When the similar reaction was realized with (**12d**)$_3$•Trip**CYA**$_6$ the only product was the cyclic monomer. [14] In this way it was proved that the complex (**12d**)$_3$•Trip**CYA**$_6$ adopts the C_{3h} and not the D_3-arrangement.

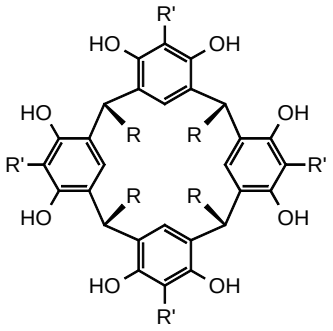
Larger assemblies double, tetra and hexarosettes obtained from double and triple calixarenes were obtained and characterized.[21]

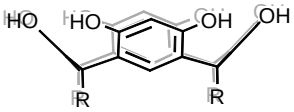
Urea groups are self-complementary when are forming hydrogen bonds. If four urea groups are attached to one calixarene and the product is dissolved in apolar solvents a

capsule stabilized by 16 hydrogen bonds is found. The next chapter offers a more detailed description of this type of dimers.

1.2.4 Capsules of resorcarene derivatives

Resorcarene derivatives are used as units in self-assembled capsules via hydrogen bonds. Like in the case of calixarenes, resorcarenes are the core to which specific functional groups are attached. These groups are responsible for the hydrogen bonds while the resorcarenes offer the right spatial arrangement of them. We present just few examples but the field is much larger.





13a R = Me; R' = H
13b R = $C_{11}H_{23}$; R' = H
13c R = *i*-propyl; R' = OH

McGillivray and Atwood[22] found that **13a** forms in the crystalline state a hexameric capsule with the internal volume of about 1375Å^3. 60 hydrogen bonds are formed with the help of eight molecules of water (figure 10). Guest molecules could not be identified from the X-ray experiment. A similar structure was indicated by ^{1}H NMR spectrum of **13b** in benzene but again no information about encapsulation could be reported.

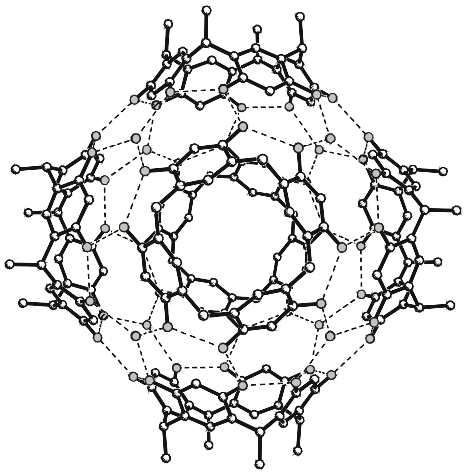


Figure 10: Crystal structure of (**13a**)$_6$•8H_2O

For **13c**[23] the octahedral assembly is formed via 72 hydrogen bonds and no water molecules are necessary. Ten acetonitrile molecules (solvent of crystallization) were found in the capsule, six of them occupy the cavity of each resorcarene molecule while the remaining four fill the rest of the cavity of the capsule. Evidence for the existence of the hexameric capsule in solution were found by NMR diffusion measurements [24] and NOE methods[25] .

When all pairs of adjacent oxygen atoms are connected via a methylene bridge the resorcarene is fixed in C_{4v} symmetry that is more suitable for self-assembly. The common name of this structure is cavitand (figure 11).[26]

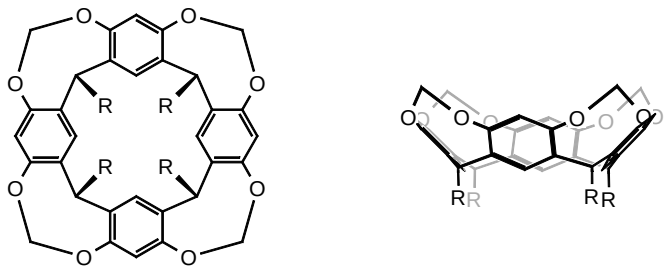


Figure 11: Planar and spatial arrangement of cavitands.

Tetrahydroxy cavitand **14** in form its of dianion (obtained with DBU = 1,8-diazabicyclo[5.4.0]undecen-7ene), in the presence of a suitable guest gives a capsule[27] held together by four strong charged hydrogen bonds O-H---O$^-$. Addition of acid destroys the capsule that means the pH could by used to control the process (figure 13).

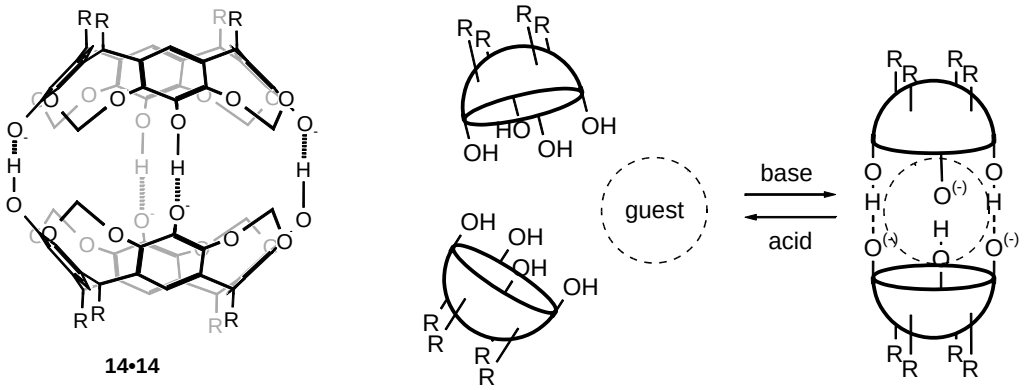


Figure 13: Schematic representation of the capsule formed by **14** (left, guest is omitted) and acid/base switched guest encapsulation and release (right).

The tetracarboxylic acid derivative **15** forms a capsule with the help of 2-aminopyrimidine (Figure 13).[28]

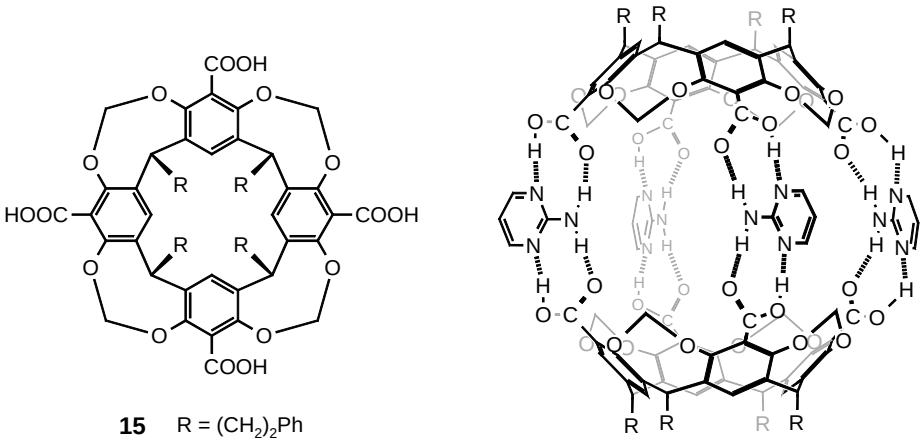


Figure 13: Schematic representation of the dimeric capsule of **15**.

Amide moieties in **16**[29] form hydrogen bonds with the groups of the opposite molecule (in solvent like toluene) leading to a capsule with an estimated volume of about 440 Å^3. The dimerisation is concentration and temperature dependent. Unexpectedly, one aliphatic chain (heptyl or octyl) of each monomer is self-included and occupies 57% of the cavity. This self-inclusion seems to be a condition for the dimerization. [30] The fact that **16a** and **16d** (figure 14) do not dimerize (because the length of the chain is too short or too long, respectively) confirmed this necessity.

Four glycoluril units were attached to the cavitand **14** and compound **17**[31] gives a dimer with a volume of the cavity of about 950 Å^3. The large interior volume allows for the "host within a host" supramolecular encapsulation of ionic cryptate complexes.

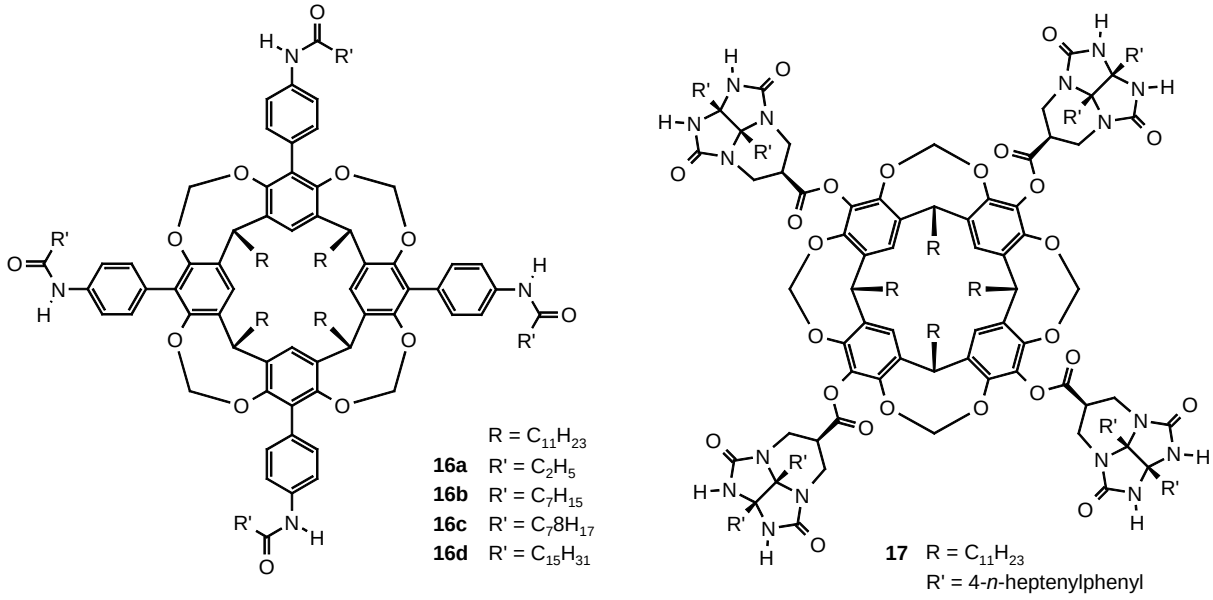


Figure 14: Cavitand derivatives that are forming capsules.

The cavitand **18** gives a large cylindrical capsule held together by eight bifurcated hydrogen bonds (figure 15).[32] The dimerization was unambiguously proved by ^{1}H NMR for various examples, showing signals for the host and upfield-shifted signals for the included guest(s).[33]

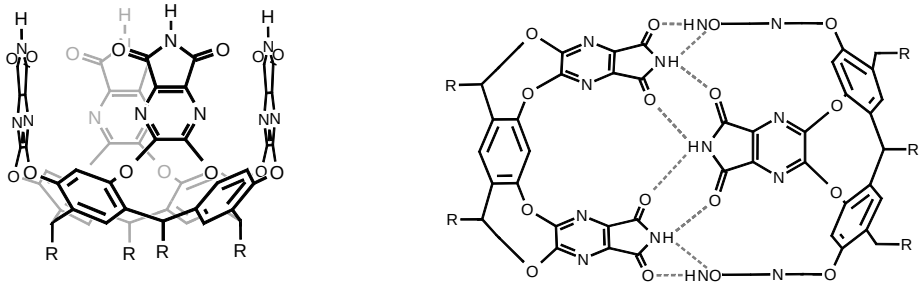


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Figure 15: The cavitands **18** and the hydrogen bonds pattern of the capsule.

The capsule can distinguish between E and Z isomers of stilbene with a selectivity of at least 50:1. For tertiary amides that prefer the E-isomer, the equilibrium is entirely shifted towards the Z-isomer upon complexation (figure 16). [34]

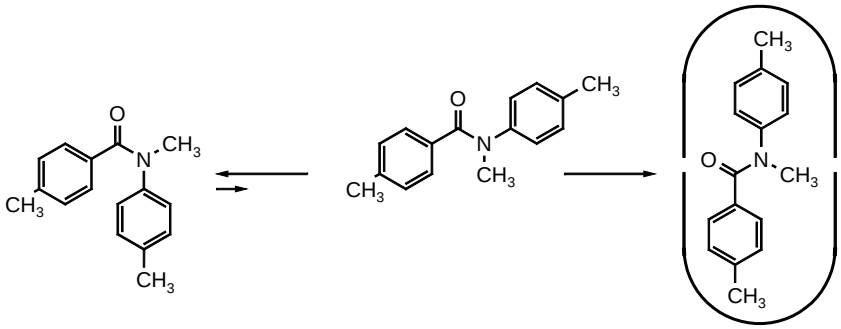


Figure 16: Shifting of the E/Z equilibrium by encapsulation.

For a series of 24 *N*-protected amino-acid esters[35] the ability to be included in the capsule of **18•18** was investigated. Other studies focused on inclusion of small molecules. Two molecules such as benzene, toluene, xylene, benzoic acid are encapsulated simultaneously. Three molecules of isopropyl chloride fit the cavity. Titration experiments with chloroform were done and the exchange of isopropyl chloride (one or two molecules) by chloroform was followed in ^{1}H NMR spectra.[36]

The examples presented here demonstrate that interest in self-assembly is at high level in chemical research, understanding of the laws governing them remains a challenging field of work for many scientists.

2. Tetraurea Derivatives of Calix[4]arene

Tetraurea derivatives are obtained from parent *p*-tert-butylcalix[4]arene in overall good yields by few steps: tetra-O-alkylation, *ipso*-nitration, reduction of nitro groups and reaction with an isocyanate or active urethane. In some cases it may be easier to activate the amino functions on the calixarene (to tetra-isocyanates or active urethanes) followed by the reaction with (excess) amine.

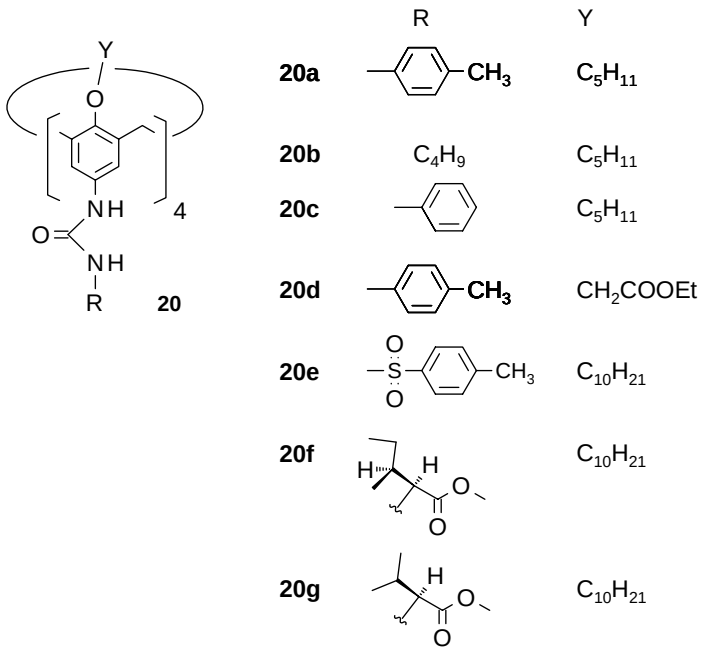


Figure 17: Selected examples of tetraureas.

2.1 Evidence of dimerization

The spectrum of tetratolylurea **20a** in DMSO-d_6 shows the expected signals and confirms the C_{4v}-symmetry (Figure 18a): two singlets for NH, two doublets with *ortho*-coupling for the aromatic hydrogens of the tolyl residues and one singlet for the corresponding methyl groups, one singlet for the aromatic hydrogens of the calixarene skeleton, and a pair of doublets with *geminal*-coupling for the methylene bridges. (These are the signals which we use for the characterization of a tetraurea.) Figure 1b shows the spectrum of **20a** in chloroform which has a different pattern. One NH signal is low-field shifted (typical for strong hydrogen bonds) while the signals which correspond to the skeleton of the calixarene appear as *meta*-coupled doublets. The spectrum recorded in benzene is very similar to the one measured in chloroform.

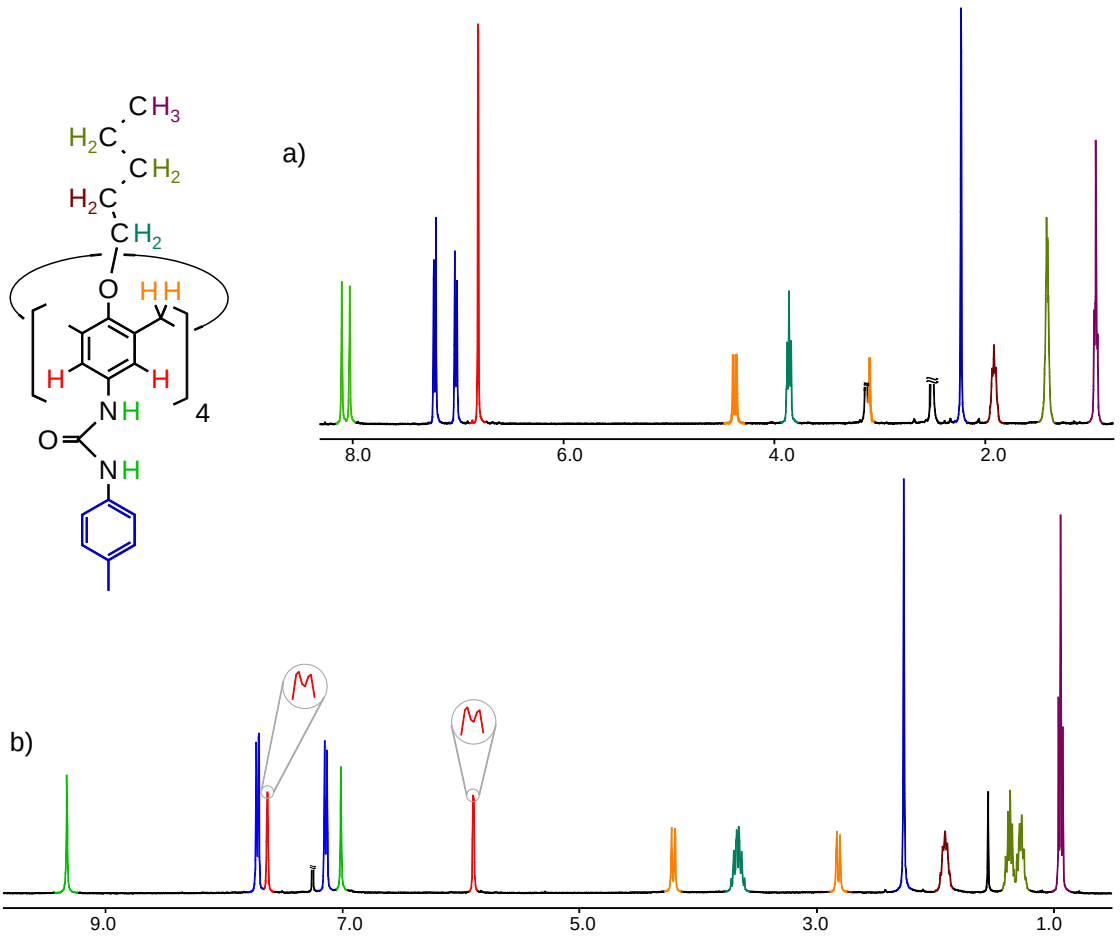


Figure 18: Spectra of **20a** in a) DMSO-d_6 and b) chloroform-d_1. All the signals are attributed as the colors indicate.

Rebek et al.[37] realized that in apolar solvents (like chloroform, benzene) the tetraurea calixarene forms dimeric capsules. The driving force of the dimerization process is the formation of 16 hydrogen bonds between the NH groups of one calixarene and CO functions of the other and vice versa. The two molecules of tetraurea are oriented "head-to-head" but turned by ~45° around their common axis relative to each other. This arrangement allows the formation of a hydrogen bonded belt of all urea functions. It was found by X-ray analysis[38], (figure 20) that the distances between NH and CO are distributed around two values. Those eight hydrogen bonds formed by the NH close to the residue R are shorter (and by consequence stronger) than the others formed by NH connected to the calixarene skeleton. This was observed first in the ^{1}H NMR spectrum by the shifts of the signals. In DMSO, there is practically no difference between the NH (probable forming hydrogen bonds with the solvent, 8 ppm)

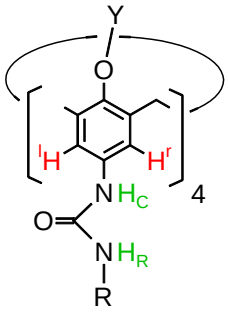


Figure 19

while in chloroform one set of signals appear around 9 ppm (stronger hydrogen bonds, Figure 19 H_R) and the second set around 7 ppm (H_C).

In principal, the urea functions can freely rotate around the single bonds. In the dimer, the rotation is slow enough on NMR time scale to observe an orientation of the C=O bonds and the hydrogen bonded belt has certain directionality (clockwise in one and counterclockwise in the other calixarene). This directionality makes the two protons of each phenolic unit different and therefore, they appear in the ^{1}H NMR spectra as one pair of *meta*-coupled doublets ($H^l \neq H^r$). Having this possibility in mind, the pattern of the spectrum in chloroform is perfectly explained by the formation of homodimer **20a•20a** which has S_8-symmetry.

Additional evidence was brought from the formation of heterodimers. The compounds **20b** and **20c** form homodimers when they are dissolved in apolar solvents. When an equimolar mixture was prepared in chloroform-d_1, the corresponding spectrum showed not only the peaks of both homodimers but also exactly an additional double set of signals for the heterodimer (Figure 21).

The dimerisation process takes place only in the presence of a suitable guest molecule. Quite often, the guest is the solvent itself. For non-deuterated guests two sets of signals are observed in the ^{1}H NMR spectra: the usual signal(s) of the free guest and up-field shifted signal(s) for the included guest.[37] In the X-ray structure of **20d** (presented in figure 20), the included guest is completely disordered because the cavity is too large to enforce a fixed position. The presence of the guest inside the capsule was additionally proved by ESI-MS when cationic guests (tetraalkyl ammonium ions) were used.[39]

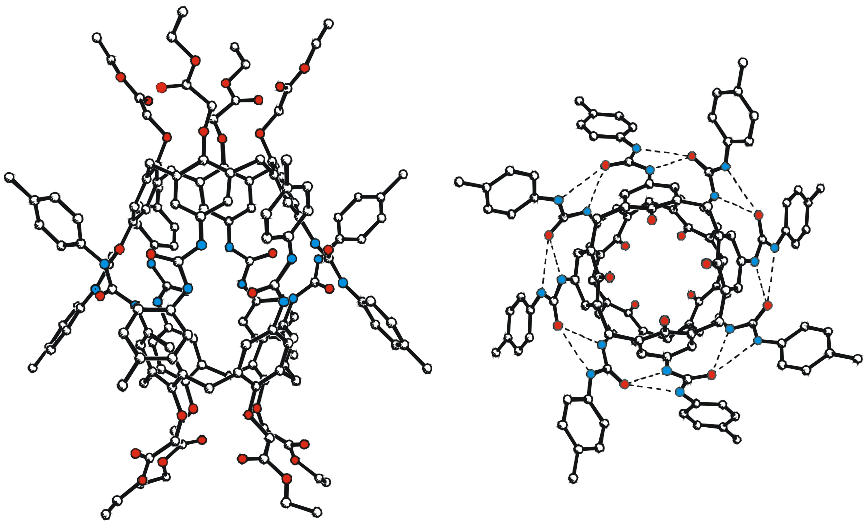


Figure 20: Single crystal X-ray structure of **20d** (R = $C_6H_4CH_3$, Y = CH_2COOEt). Disordered benzene molecules in the cavity, between the ester groups, and on other places in the crystal lattice are not shown.

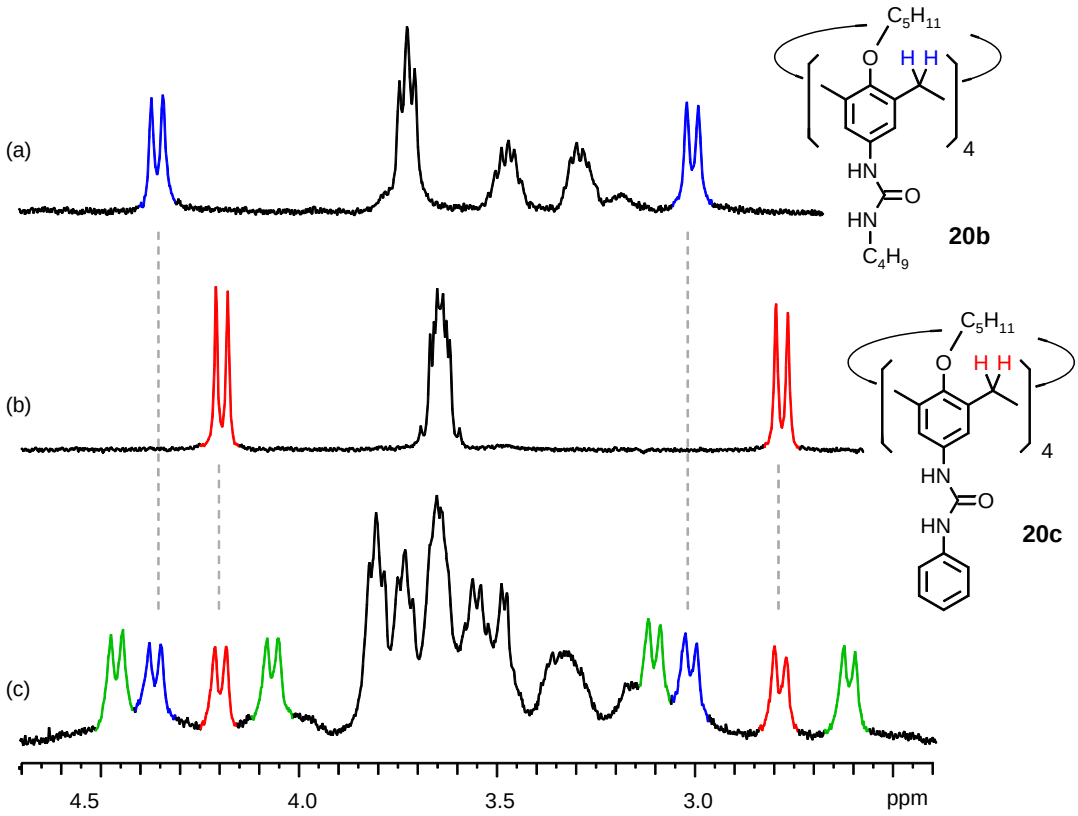


Figure 21: Sections of the ^{1}H NMR spectra in chloroform-d_1 of a) **20b**, b) **20c** and c) 1:1 mixture of **20b** and **20c**.

2.2 Symmetry and chirality in homo- and heterodimers of tetraurea

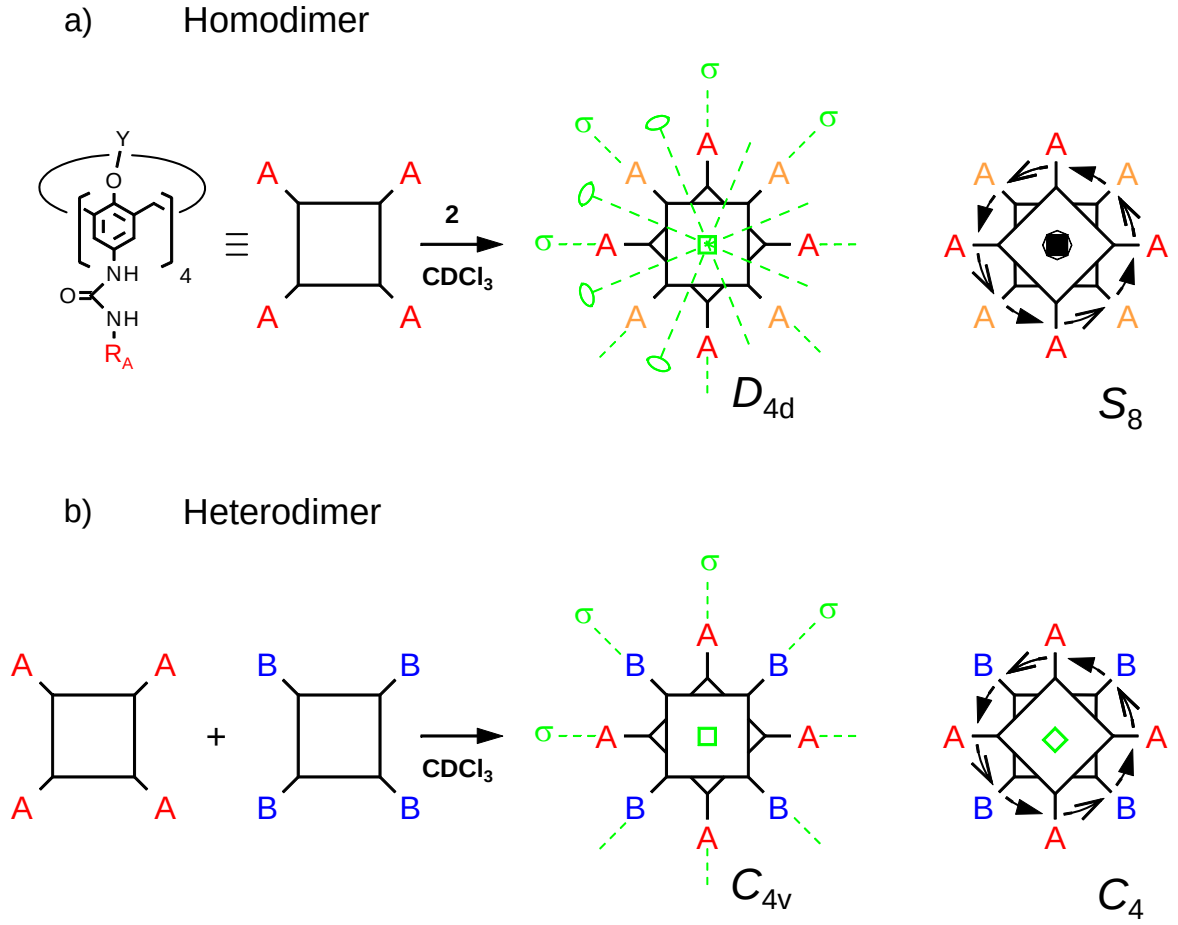


Figure 22: Schematic representation of the stereochemical properties of the homo- and heterodimers. The symmetry elements and symmetry class are indicated with and without directionality of the hydrogen bonds, which is symbolized by arrows.

A dimer formed by two molecules of the same tetraurea (homodimer) has one C_4 axis (perpendicular to the plane formed by the urea functions), four C_2 axes (perpendicular to the C_4 axis) and four symmetry planes (intersection in C_4 axis). This corresponds to the D_{4d}-symmetry. When the directionality of the hydrogen bonds is considered all C_2 axes and all symmetry planes disappear, and the overall S_8-symmetry remains (Figure 22a). The dimer is composed by two chiral units (each molecule of tetraurea has C_4-symmetry) but it is an achiral *meso* form.

For a dimer formed by two different tetraurea (heterodimer), there are one C_4 axis and four symmetry planes, which means C_{4v}-symmetry of the capsule (Figure 22b). The directionality reduces the symmetry to C_4 that means that the heterodimer is *chiral.* This chirality is due **only** to the directionality of the hydrogen bonded belt; the change of the directionality gives the other enantiomer (Figure 23).

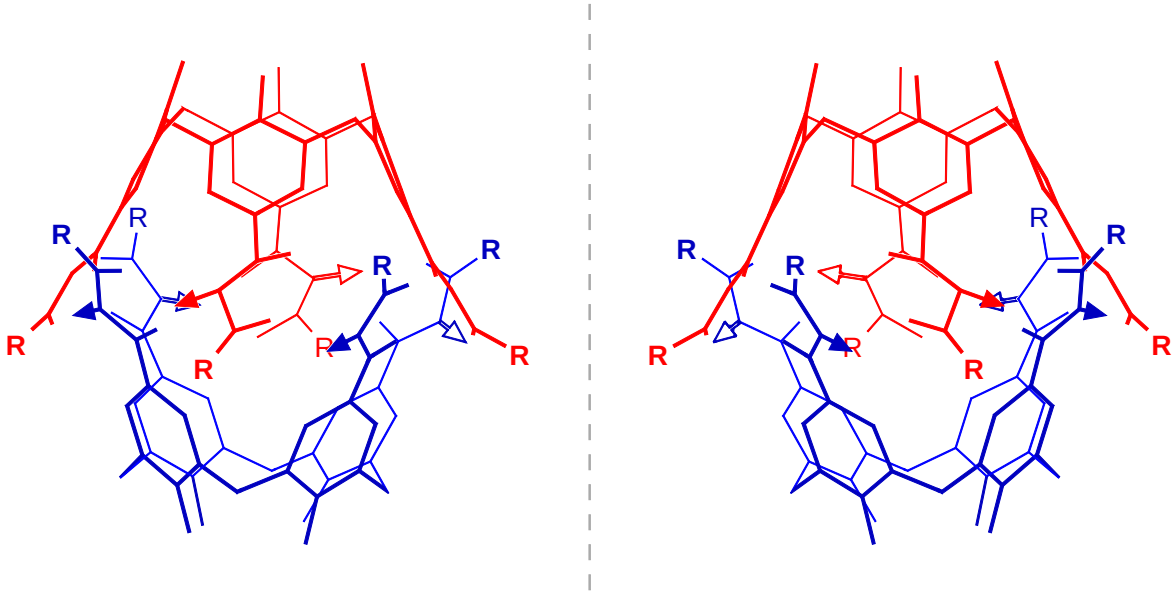


Figure 23: The two enantiomers formed by heterodimerization. The direction of the C=O bond is indicated by the arrow. When this direction reverses the other enantiomer is formed.

One of the early observations in heterodimerization studies was that aryl urea and alkyl urea are forming heterodimers in statistical ratio (see figure 21).[40] Short time after this report, the group of Rebek reported that aryl and sulfonylureas are forming exclusively the heterodimer.[41] This observation is well established although all the factors governing this selectivity are not completely understood.

A series of tetraureas having chiral amino acid residues attached to the urea were synthesized and their dimerization studied.[42] Two aspects should be followed in these experiments: the degree of heterodimerization over homodimerization and the degree of diastereoselectivity (the combination of a chiral tetraurea with a non-chiral tetraurea could provide two diastereomeric capsules). No heterodimerization could be observed between the amino acid tetraureas and tosylurea **20e**. 100% heterodimerization was reported for the mixture tolylurea (Y = $C_{10}H_{21}$) and **20f** and **20g** in benzene-d_6, while in chloroform only 90%. In almost all cases studied, only one diastereomeric heterodimer is formed; these heterodimers prefer one direction of the hydrogen bonds. This means that the chirality of the residue was transferred to the assembly. By CD-spectroscopy and molecular modeling, the directionality of the belt of the capsule of tolylurea and **20f** was determined. When the assembly is viewed from the tolylurea pole, the ureas rotate clockwise.

2.3 Guest encapsulation

The capsule of the homodimer has S_8-symmetry and it is achiral, but if a chiral guest is offered (only one enantiomer) the whole complex became chiral. The two halves are now diastereomeric and they show different signals in NMR spectra. If the guest is a racemic mixture, two diastereomeric capsules are formed.

In the case of a heterodimer, the assembly exists as a pair of enantiomers *r* and *l* (*r* and *l* refers to the directionality of the hydrogen bonds which may be to the right or to the left but it is fixed on the NMR-time scale). With a chiral guest (one enantiomer) the two capsules became diastereomers and the spectrum shows a doubling of the signals. When to a heterodimer a racemic mixture is added the following complexes can be formed: *r*-R, *r*-S, *l*-R and *l*-S. While the pairs *r*-R with *l*-S and *r*-S with *l*-R are in the relation of enantiomers the two pairs are diastereomers and gives different set of signals. Therefore, in the ^{1}H NMR spectra only two sets of signals are observed.

All these combination where checked and the spectra measured confirm entirely the predictions [41a,42] (even if some of the given explanations are not accurate).

2.4 Stereochemical analysis of homodimers of mixed tetraureas

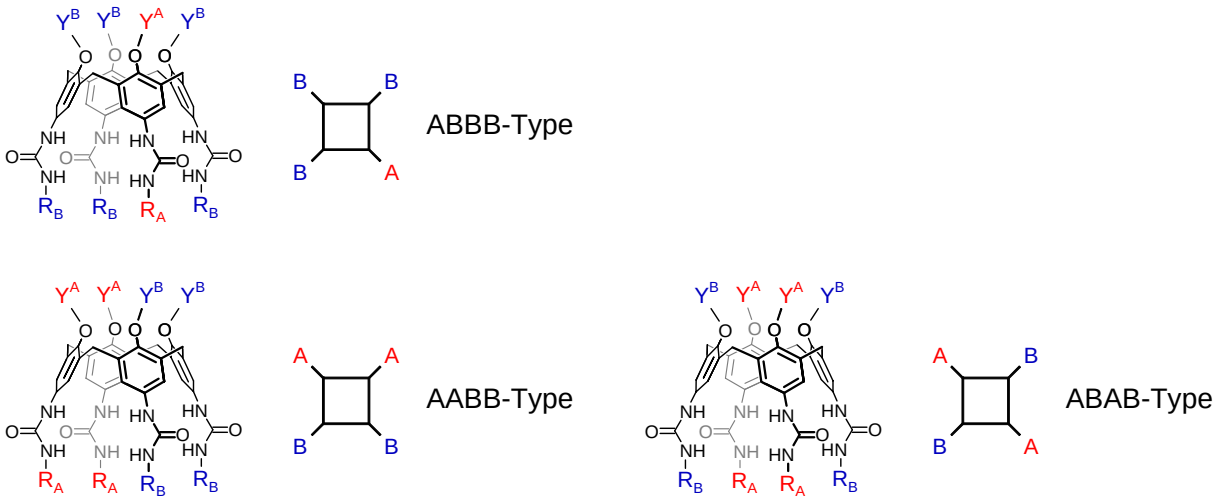


Figure 24: Schematic representation of the three types of mixed tetraureas.

In the previous discussion, the dimer was formed by derivatives in which all four urea functions where identical within one molecule. The next step in our analysis is the case where in one molecule there are two different phenolic units by different residues attached to the phenolic oxygens or to urea functions. So, theoretically there are three possibilities and they are showed in figure 24.

2.4.1 ABBB- and AABB-Types

Two regioisomeric homodimers are formed from the tetraureas of the ABBB- and AABB-types (Figure 25).

All have a C_2 axis that is lost when the directionality of the hydrogen bonds is considered. Each regioisomer has C_2-symmetry that means that they are chiral without directionality of the hydrogen bonded belt (Figure 26). The two halves consist of a pair of enantiomers, but the assembly cannot be a *meso* form because different phenolic units are present. For these types of dimers the chirality is due to the spatial arrangement of the two calixarenes that is why it is considered "**supramolecular chirality**". The directionality of the hydrogen bonds reduces the symmetry but does not create other enantiomer.

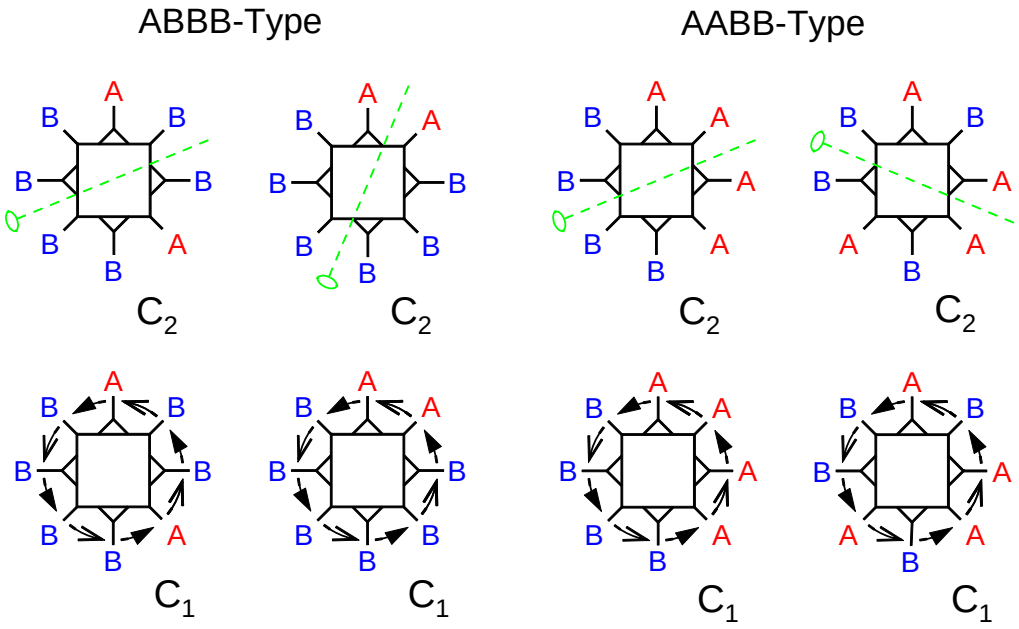


Figure 25: Schematic representation of the stereochemical properties of homodimers formed by tetraureas of the ABBB and AABB type. The symmetry elements and the symmetry class are indicated with and without directionality of the hydrogen bonds.

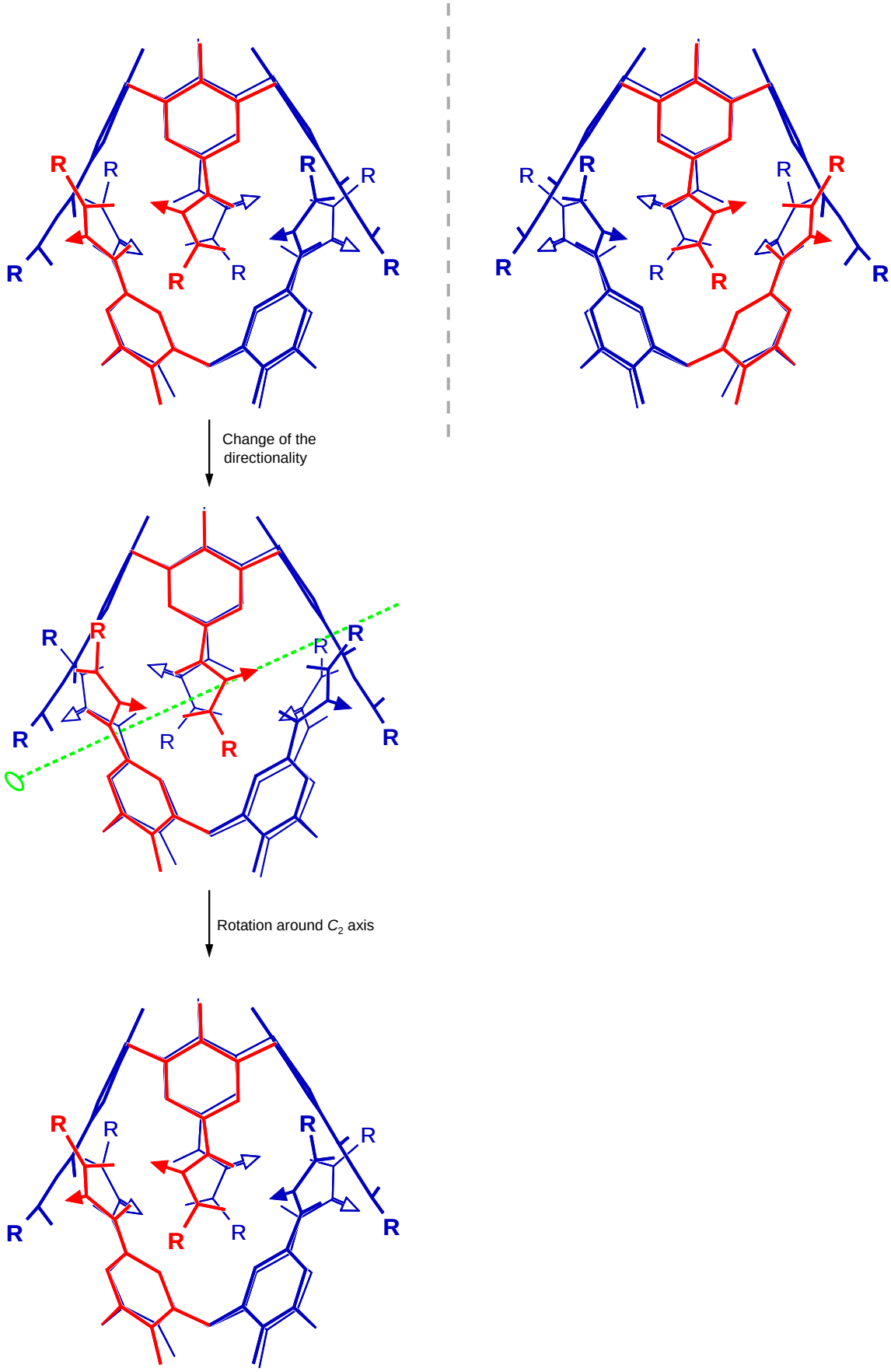


Figure 26: Graphical explanation of the chirality in homodimer of ABBB type. The phenolic unit drawn in red is the one having other residue than the rest of them.

Because of the directionality of the C=O groups the capsule has C_1-symmetry, so, each proton is expected to give its individual signal in the ^{1}H NMR spectra. Now, having two regioisomers one would expect two sets of signals, a situation which makes the spectra not easy to interpret.

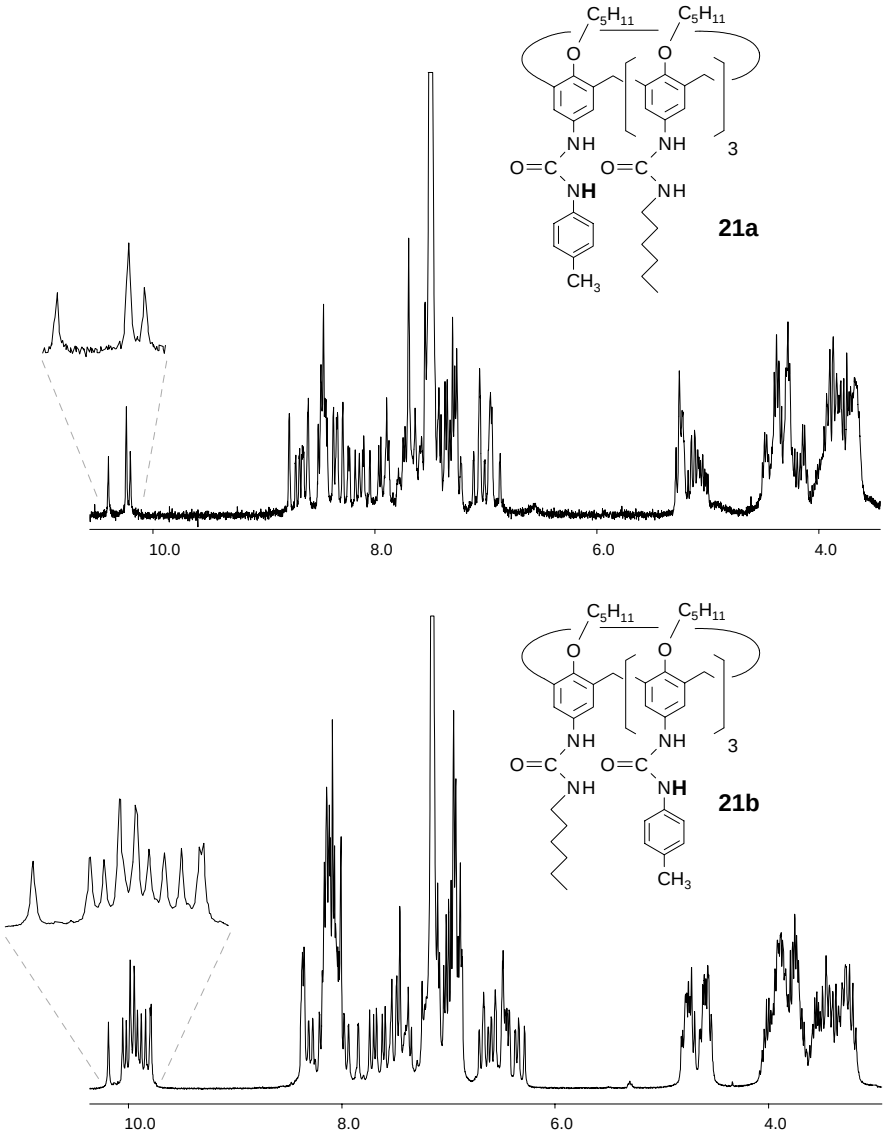


Figure 27: Section of the ^{1}H NMR spectra in benzene-d_6 of **21a** and **21b**. The signals which appear around 10 ppm correspond to the NH proton connected to tolyl groups. In one capsule there are two (**21a**) or six (**21b**) such protons, that means that in spectra four and 12 signals should be seen.

As examples, there are sections of tetraureas **21a**† and **21b**† (ABBB-type) in benzene (Figure 27). One can see that signals appear in the expected regions but most of them are overlapped, especially in the region of 6-8 ppm. There should appear signals of aromatic

† The compound was synthesized and spectra were measured by Dr. M. Saadioui.

substituent of urea, hydrogens of the skeleton of calixarene, NH_C and NH_R (when the residue R is aliphatic). An analysis of the structure of **21a** reveals that in each molecule there is one urea function substituted by tolyl residue (NH_R around 10 ppm in benzene). So, there are 2 signals for each regioisomer and overall 4 signals. For the compound **21b**, three tolyl residues mean 6 signals for each regioisomer and 12 in the spectrum. These observations are confirmed by the spectra in the figure 27 (some signals are overlapped but the integration of all signals is in agreement with the structure).

Compound **22a**† is of the AABB-type, and in the figure 28 is shown section of its spectrum in benzene. Having two tolyl groups in each tetraurea, one would expect 8 signals around 10 ppm for the two homodimers.

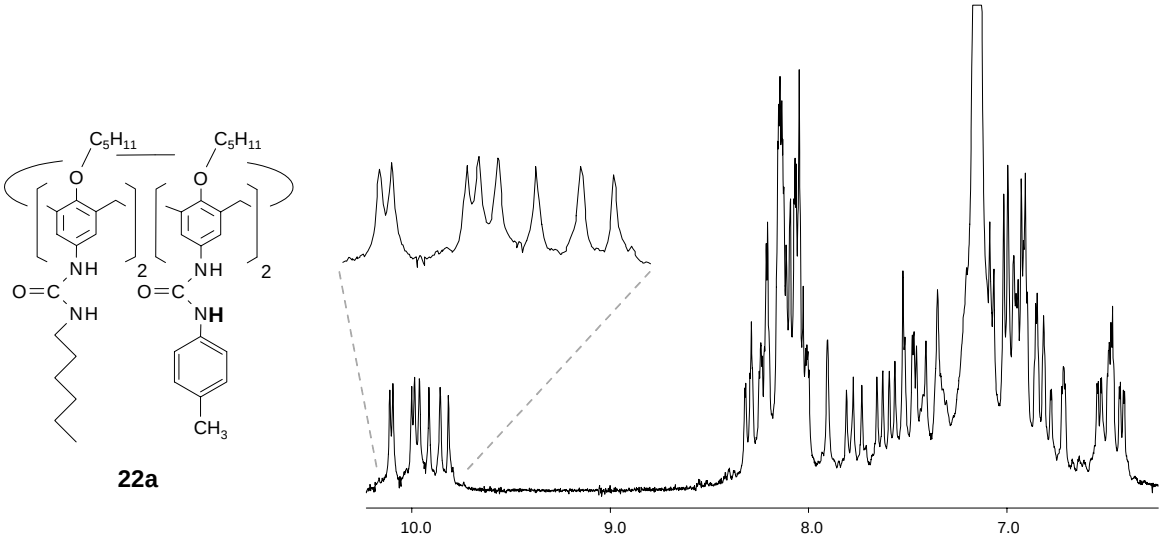


Figure 28: Low-field shifted region of the spectrum of **22a** in benzene-d_6 showing the expected eight signals for NH_{tolyl}.

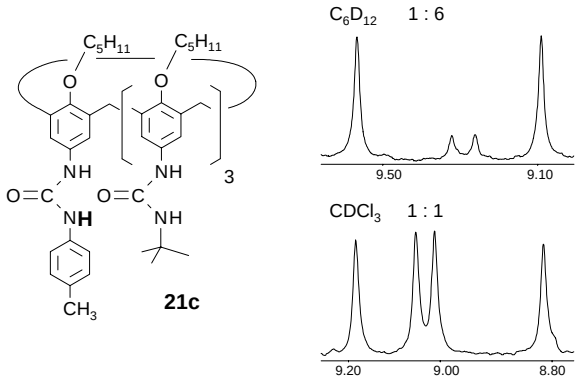


Figure 29: Influence of the solvent in the formation of regioisomers.

It was found that the ratio between the two regioisomers is influenced by the solvent and by the residue attached to the urea.[43] For example, the ratio between the two regioisomers of **21c**† formed in chloroform is 1:1, while it is ~1:6 in cyclohexane (Figure 29).

Replacement of the hexyl group by adamantyl changes the ratio from 1:1 to 1:2 for dimers formed in benzene (Figure 30). Up to now, there is not a reasonable explanation for this effect, but it remains very interesting in the field of supramolecular chemistry.

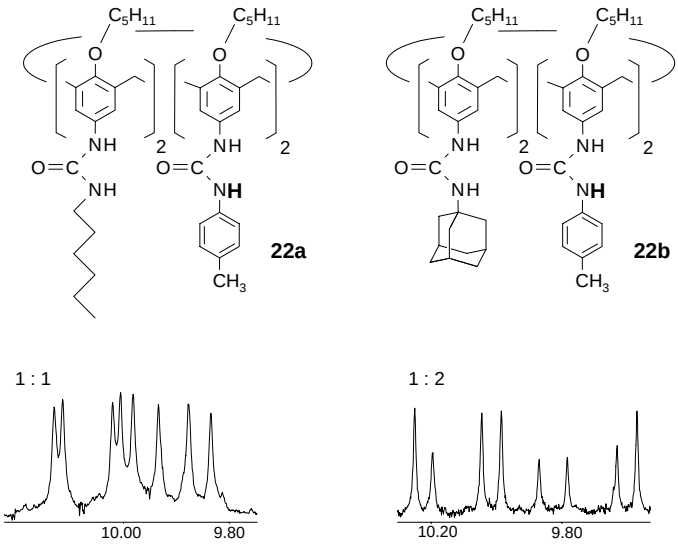


Figure 30: Influence of the residue in the formation of regioisomers. Only the most low-shifted protons of urea functions are shown.

2.4.2 ABAB-Type

Only one regioisomer can be formed in the case of an ABAB-type (Figure 31). Its chirality comes from the way how two achiral units are combined within the dimer. It is again supramolecular chirality. The fact that there is only one homodimer makes the situation much simpler to analyze.

In our group was synthesized and characterized a tetraurea derivative **23** having two different ether residues in an ABAB-arrangement (Y^1= Me, Y^2= C_5H_{11}, R = tolyl).[44]

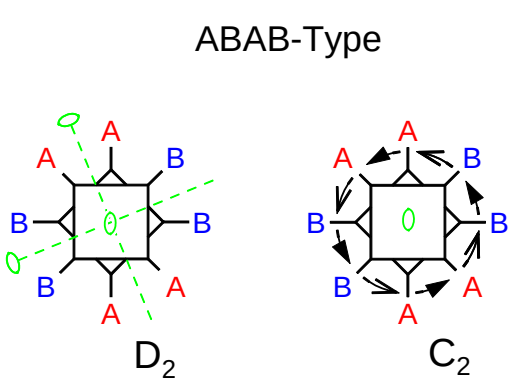


Figure 31: Schematic representation of the stereochemical properties of the homodimers of ABAB type. The symmetry elements and symmetry class are indicated with and without directionality of the hydrogen bonds.

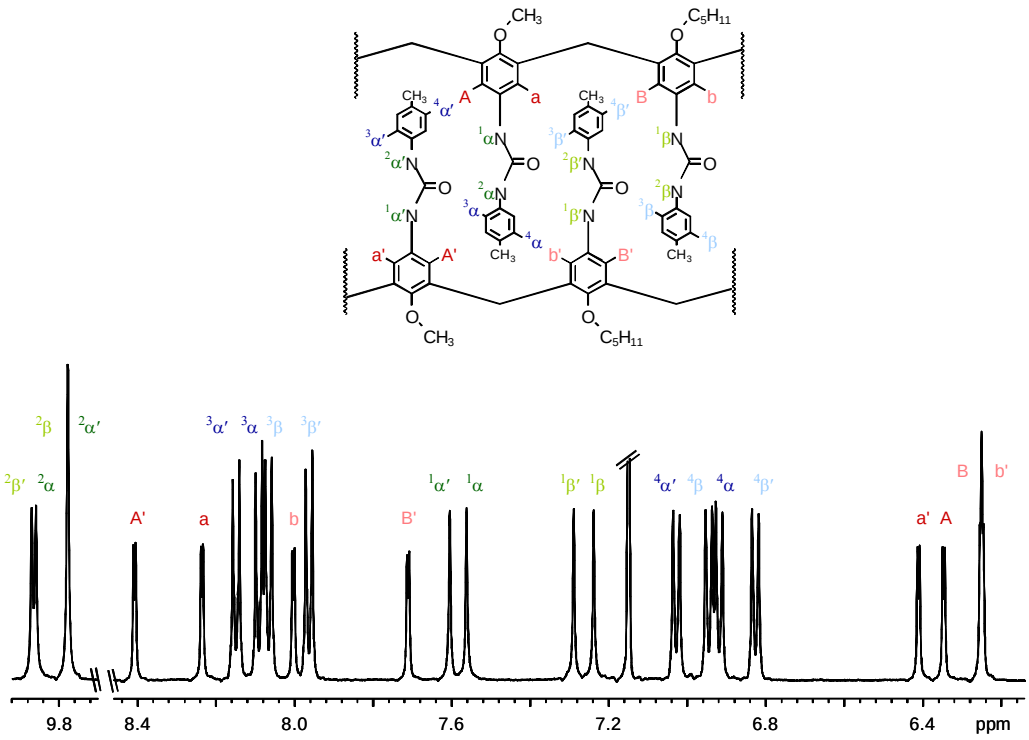


Figure 32: Aromatic section of the ^{1}H NMR spectrum (500 MHz) in benzene-d_6 of **23**. The schematic formula explains the peak assignment (based on NOEs/ROEs).

In the dimer, when the directionality of the hydrogen bond is considered, there is one C_2 axis of symmetry. Therefore, the chemically identical phenolic units in one tetraurea are equivalent but those from one half are different from others. In the spectra, one could expect eight *meta*-coupled doublets for the calixarene skeleton and four pairs of *geminal*-coupled doublets for the methylene bridges. All these were found in the spectrum of the compound **23** (Figure 32).

Up to now, we have several examples of tetraureas of ABBB- and AABB-types which form homodimers. All these dimers are chiral and they are obtained from achiral units. The chirality is due to the spatial arrangement of the two calixarenes, therefore, it is named "supramolecular chirality". Our attention was concentrated in these chiral dimers and we wanted to study them in detail. The optical resolution using HPLC with a chiral stationary phase is one step on the way to our studies.

In both cases (ABBB and AABB), two regioisomers are possible, each regioisomer exists as a pair of enantiomers. The isolation of pure enantiomers is complicated by the presence of four species in the mixture. To simplify the situation two directions could be envisaged.

By suitable substitution of the urea residues (e.g. bulky residues) one of the regioisomeric dimers might be favored. Ideal would be the formation of one dimer with 100% selectivity.

Strategies should be elaborated to synthesize tetraureas of the ABAB type which form only one pair of enantiomers. This is well known for different ether residues, but a much stronger enantiomeric discrimination is expected for ABAB tetraureas with different urea residues.

The dimerization of tetraureas occurs in apolar solvents (e.g. chloroform, benzene, cyclohexane). Small amounts of polar solvents (DMSO, alcohols, tetrahydrofurane) disrupt the hydrogen bonded belt and the dimer is destroyed. The tetraureas must be soluble in the solvent used for the separation, must form dimers in this solvent and must be kinetically stable enough to be separated. We have to synthesize compounds which fulfill all these conditions.

Tetraamino calixarenes are good starting material for the synthesis of tetraureas; they are easily obtained in gram quantities. One strategy to synthesizing tetraureas with different substituents at the urea functions is to find a protecting group for the amino functions in opposite position. Up to now, this problem was solved only for mono-, 1,2-di and tri- protected tetraamines; these derivatives have been used for the preparation of ABBB and AABB compounds.

In the chemistry of calixarene there are described several reactions in which just two opposite phenolic units are involved (di-alkylation, partial ipso-nitration, selective bromination). Our goal can be reached by finding the correct order in which such selective reaction should be done.

3. Syntheses

The efforts were oriented to elaborate a strategy to synthesize ABAB-tetraureas on a larger scale (grams) and with good reproducibility. In the same time, we are interested to study compounds of the AABB- and ABBB-type and find substituents which give regioselectivity in homo- and heterodimerization.

3.1 Partial protection

The starting point in this work was the analysis of the results[45] obtained by protection of one to three amino groups in a tetraamino derivative with Boc-anhydride (di-*tert*-butyl-dicarbonate). Here, reaction conditions to get mainly one product were found. Nevertheless, the crude product is always a mixture of at least two compounds. MonoBoc, 1,2-diBoc and triBoc derivatives were obtained, but 1,3-diBoc was never identified nor even detected in the products mixture.

1,2-diBoc derivative was used as starting materials in the synthesis of other tetraureas (see mono-loop derivatives). Thus, we improved the synthesis of 1,2-diBoc. By increasing the amount of Boc-anhydride (the ratio 1 mol tetraamine/ 2.2 mol Boc-anhydride) and prolonging the time of addition of Boc-anhydride solution (from 2-3 hours to 10-12 hours) the mixture contains just tri-Boc (22-25%) and the wanted 1,2-diBoc (60-68%, isolated yields).

3.2 Reaction with isocyanates

Since the protection methods do not offer an easy way to the wanted compounds (separation by column chromatography is always necessary), we decided to react tetraamine with an isocyanate (in different ratio) and then to separate the crude mixture.

We want to synthesize compounds having different residues attached to the urea NH. In the same time, we want to establish the influence of each residue. We have chosen the tolyl residue as the “reference substituent” because it gives typical signals in the NMR spectroscopy (one pair of doublets with *ortho*-coupling in the aromatic region and one singlet in around 2 ppm) which is an important tool in our work.

A solution of tolylisocyanate in dichloromethane was dropped (rate 20-25 mL/h) into a solution of tetraamino calixarene **35** (Y = n-pentyl) in dichloromethane (the ratio 1 mol tetraamine/ 2.2 mol isocyanate). The crude product was separated by column

chromatography and was shown by NMR measurements to be a mixture of tetra, tri- and 1,2-diurea. No 1,3-diurea was found in this mixture. When the solution of isocyanate was added with a lower rate (~5 mL/h) a new spot appeared on TLC analysis. The composition of the product was found after chromatographic separation (ethyl acetate/hexane from 1/4 to 5/1) and ^{1}H NMR measurements: tritolylurea-monoamine 17-20%, 1,2-ditolylurea-diamine 55-67%, 1,3-ditolylurea 5-7%. A similar result was found by using chloroform as solvent. No 1,3 derivative could be isolated with dimethylformamide as solvent.

Theoretically, in the reaction of tetraamino calixarene with an acylating reagent (taken in a ratio 1:2) the products mixture should contain the 1,2-derivative and 1,3-derivative in the ratio 2:1. The fact that we could not find the 1,3-diBoc and only a very small amount of 1,3-ditolylurea led to the idea that there are others factors involved in this selectivity. It was shown that for distal diurea- and bis-acetamido derivatives a *trans*-cavity hydrogen bond can be formed between the hydrogen of NH (urea or acetamido) and the opposite carbonyl oxygen atom. [46] The consequence of the hydrogen bond formation is that the molecule adopts a pinched-cone conformation (C_{2v} symmetry). Similar, for tetracarboxy-, tetraamido-, and tetrakis-(carboxymethyl)-tetraether-calixarenes[47] equilibrium between two pinched cone conformations was found by NMR spectroscopy. The barrier between the two possible pinched-cone conformations is determined by the strength of the hydrogen bond.

In our case, we suppose the formation of *trans*-cavity hydrogen bond between the hydrogen atom of urea and the amino function in distal position (Figure 33). The formation of such a hydrogen bond would decrease the reactivity of the amino group involved (by blocking its electron pair) and the pinched cone conformation would make the other two amino functions much more available for the reactant. All these observations are in good agreement with the high selectivity observed in the reactions of tetraamino calix[4]arene and Boc anhydride or isocyanates.

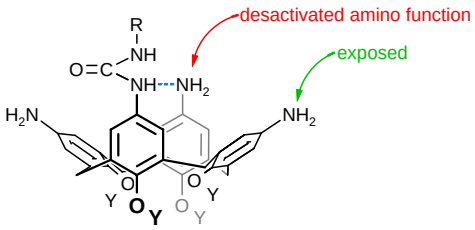
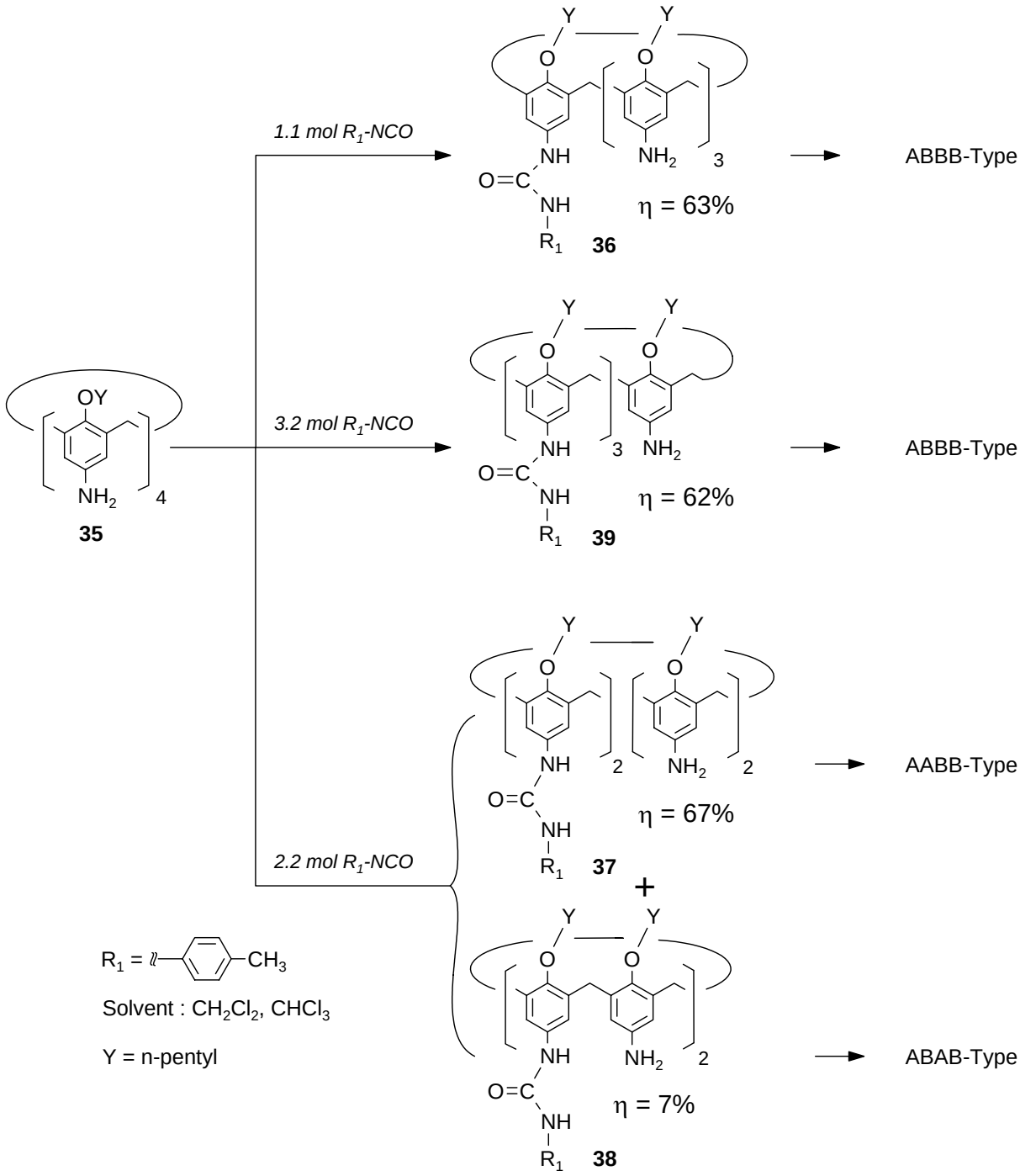


Figure 33: Formation of a hydrogen bond between the first urea group and the distal amine.

In spite of the fact that 1,3-diureas could not be obtained in sufficient quantity by the reaction with isocyanate, we have improved this method for all other substitution patterns of tetraureas.



Scheme 1: Reactions of tetraamine **35** with tolylisocyanate in different ratio

When the ratio between tetraamine **35** and tolylisocyanate was 1:1.1 the main product in the mixture was monotolylurea **36** (63% after chromatographic separation, eluent ethyl acetate/THF = 10/1, Scheme 1) and the reaction with a second isocyanate (hexylisocyanate or *tert*-butylisocyanate) leads to the compounds **21a,c** (see Table 1, pg. 42) with good

yields. Reacting tetraamine with tolylisocyanate in the ratio 1:3.2, the major product after separation (eluent ethyl acetate/hexane = 5/7) was tritolylurea **39** (62%). The remaining amino function of tritolylurea was activated by reaction with 4-nitrophenyl chloroformate followed by reaction with *tert*-butyltritylamine leading to **21d** (see Table 1, pg. 42).

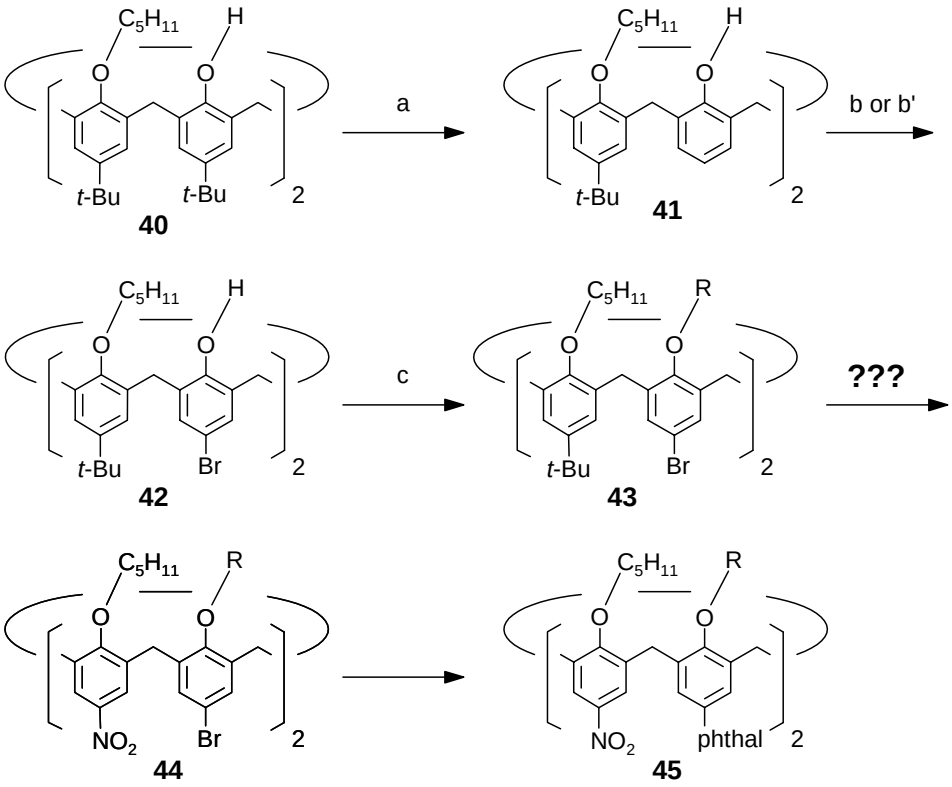
The compounds were characterized by NMR (DMSO-d_6, see chapter "Experimental") and the homodimers[43] obtained in different solvents were studied (see chapter "Results").

All the results obtained up to this point led to the idea that our goal to synthesize ABAB-type tetraureas in good yield can be achieved only by a multisteps synthesis.

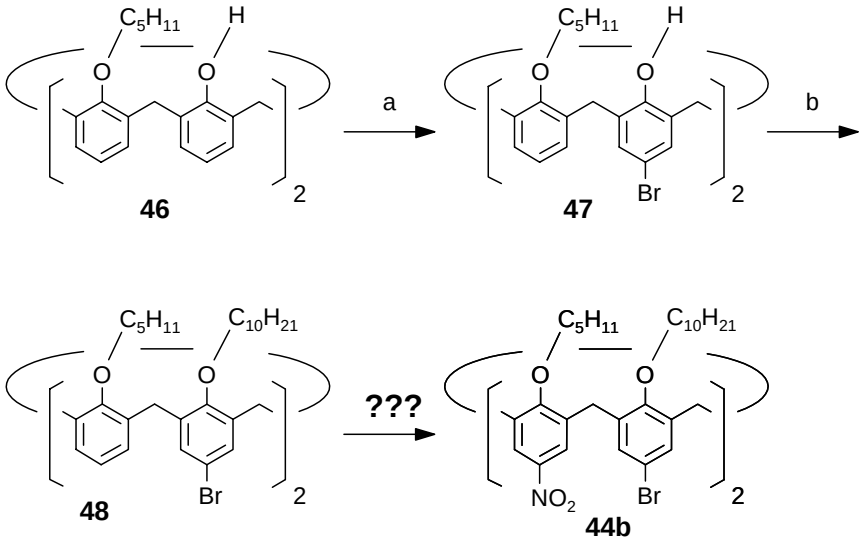
3.3 Multistep synthesis

Only one procedure describing a strategy to prepare a compound containing in distal positions two different functional groups which are precursors for amino functions was found[48]. It starts with the partial nitration of *p*-H-tetraether followed by iodination ($AgCF_3COO/I_2$ in $CHCl_3$). The two iodo atoms were transformed in to phthalimido moieties by reaction with phthalimide in the presence of Cu_2O (Gabriel reaction).

We have planned a procedure (Scheme 2) to synthesize the compound **44** which contain two bromine atoms in position 1 and 3 and phthalimido groups in 2 and 4. Simultaneously this pathway offers the possibility to introduce different substituents at the narrow rim. 1,3-dialkylated calixarene **40** was treated with $AlCl_3$ in toluene for partial de-*tert*-butylation following the procedure describe for dimethylether.[49] The precipitation and purification of the product brought some complication (higher solubility because of longer alkyl chain) and the compound **41** was obtained with a lower yield (25% compared with 78% described). Bromination was done with bromine in chloroform or NBS[50] in acetone leading to **42** in good yield. The alkylation of the two hydroxyl groups allows preparing a large variety of products. We have used pentyl- and decylbromide[51] and derivatives **43a** and **43b** were obtained. The step which interferes with our efforts was the *ipso*-nitration of di-bromo derivatives, conditions to the target compound **44** were not found. In all attempts the crude product consisted of a complicated mixture.



Scheme 2: The first plan to get the precursor for ABAB-type tetraureas; Conditions: a) $AlCl_3$, toluene; b) Br_2, chloroform, 0°C; b') NBS, acetone; c) alkyl halide, NaH, DMF; Conditions for the reaction step **43** to **44** were not found.

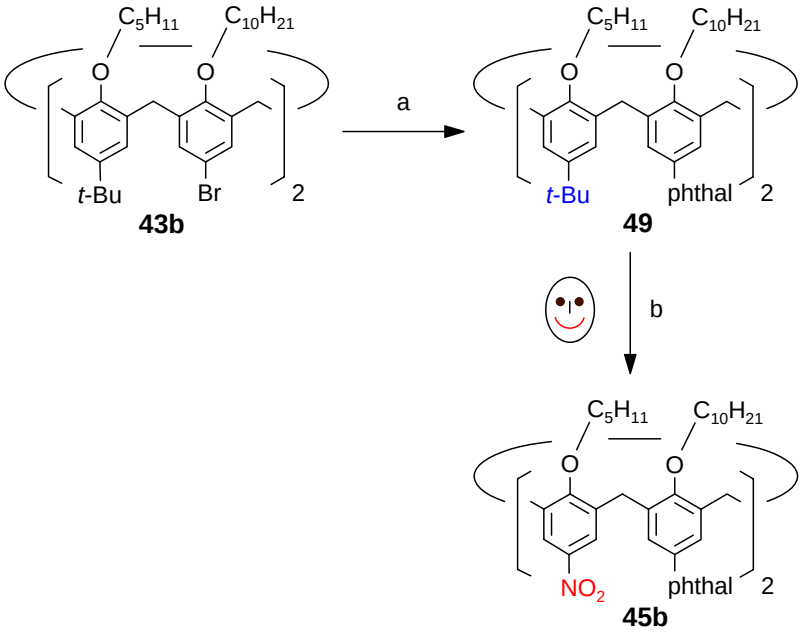


Scheme 3: The alternative route to **44**; Conditions: a) Br_2, chloroform, 0°C; b) decyl bromide, NaH, DMF; Conditions for the reaction step **48** to **44b** were not found.

An alternative route was chosen (Scheme 3). It replaces the *ipso*-nitration of the dibromo compound by nitration. Partial alkylation[51] of "naked" calixarene[52] leads to **46** which was then selectively brominated to **47**.[53] In the step of nitration **48** to **44b** similar difficulties were found.

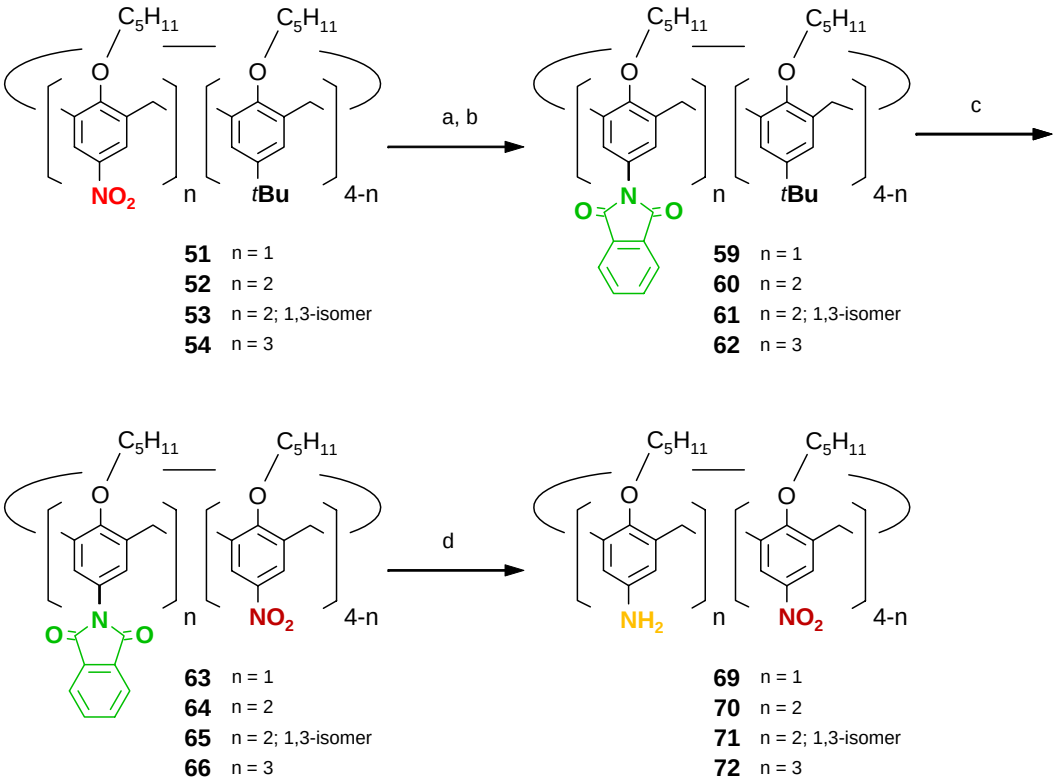
The solution for our synthetic difficulties was found when the *ipso*-nitration was carried out with compounds containing already the phthalimido moieties on the wide rim. Thus, the *ipso*-nitration of the compounds **49** with fuming nitric acid in dichloromethane gave **45a/b** in 86% yield (Scheme 4). The compound **49** was obtained by the reaction of dibromo derivative **43** with phthalimide. The mixture of **43**, phthalimide and Cu_2O (1:10:10) in collidine was refluxed for two days. After working up as described[48], the crude product (mixture of three compounds by TLC) was separated on column chromatography (chloroform/hexane = 2/1). The first eluted was unreacted material (5-15%), the second was mono-phthalimido derivative (~20%) and the last the wanted compound (36-50%). When the time of reaction was prolonged, the yield of the target compound decrease.

About 75% yield was reported[48] for the reaction of iodo derivatives to phthalimido compounds using a Gabriel type synthesis. Our best yield was about 50% after we have changed the reaction conditions. Comparing these two results, one could see the influence brought by the different halide atom on aromatic ring for this type of reaction. To replace the bromide atoms by phthalimido moieties is more difficult than a similar reaction on iodo derivatives.



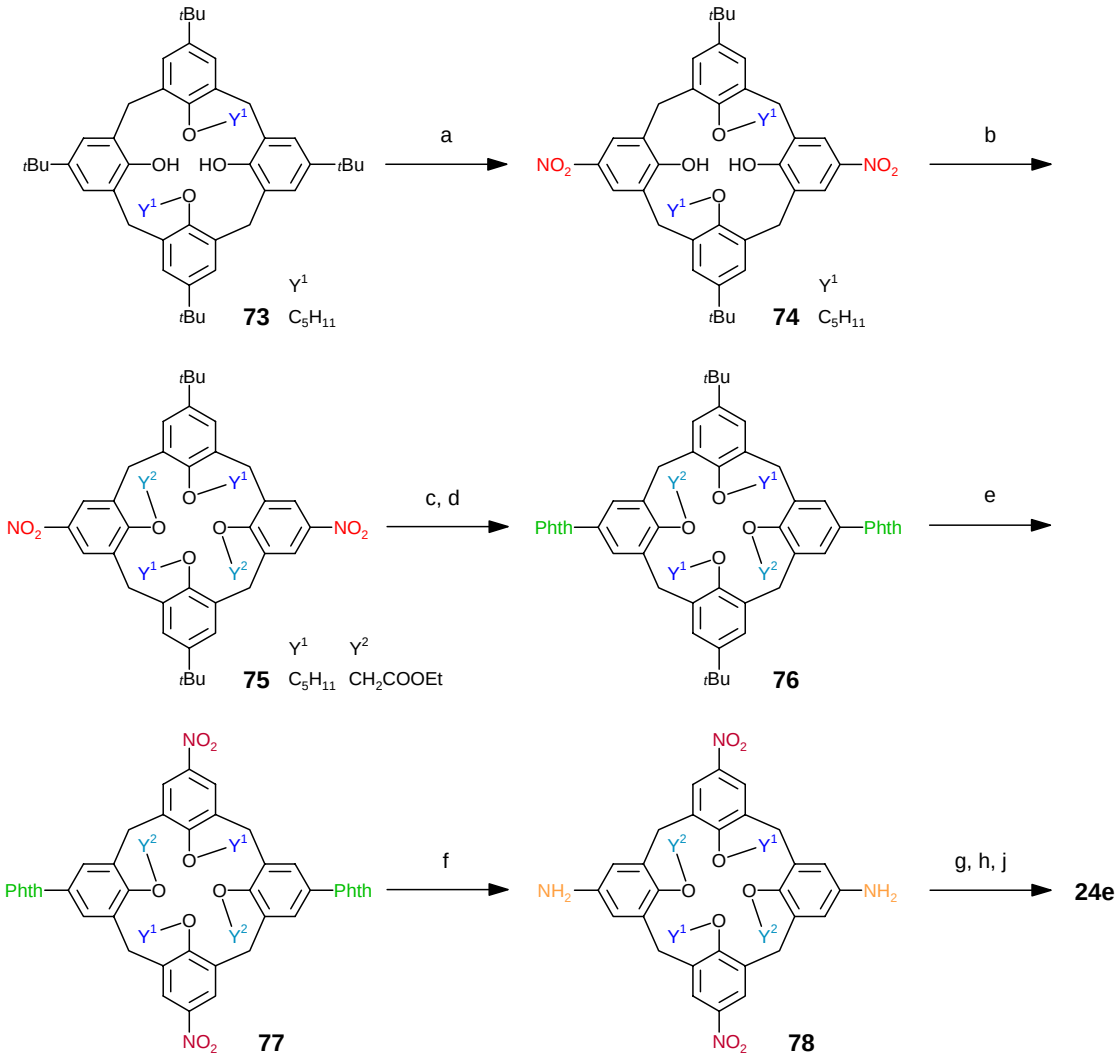
Scheme 4: Successful *ipso*-nitration on phthalimido derivative **49**; Conditions: a) phthalimide, Cu_2O, collidine, reflux, 2 days; b) HNO_3 100% fuming, dichloromethane.

The "surprisingly positive " result of the *ipso*-nitration of compound **49** had opened a new way in the synthesis of the target structure but it is, in the same time, a new method for the introduction of nitro groups in the presence of other(s) masked amino moiety(ies). So, we have changed our strategy in accordance with the new results. The phthalimido derivatives were obtained in an easier way as shown[54] (Scheme 5). The nitro groups in **51-54** are easily hydrogenated to amino groups with hydrogen in the presence of Raney-nickel. The amino derivatives are treated with phthalic anhydride (1.1 mol of phthalic anhydride to 1 mol amino group); triethylamine is necessary as catalyst. In most of the cases the phthalimides **59-62** can be crystallized from a dichloromethane methanol mixture without other procedures of purification. The *ipso*-nitration performed on these phthalimido derivatives leads to the desired compounds without any observable side reactions. Compounds **63-66** were obtained in yields from 55 to 90%. The sequence of steps is: a) tetra-O-alkylation; b) partial *ipso*-nitration; c) hydrogenation and protection with phthalic anhydride d) *ipso*-nitration of the remaining *tert*-butyl groups. The step which is limiting the overall yield is the partial *ipso*-nitration which works not selective at all. All the other reactions are very simple and especially the work up and purification of the products are much easier than the procedure described for Gabriel synthesis.



Scheme 5: The new way of synthesizing amino-nitro derivatives; Conditions: a) H_2, Ra-Ni, toluene, 2 hours; b) phthalic anhydride, triethylamine, toluene, reflux 12 hours; c) HNO_3 100% fuming, dichloromethane/acetic acid (19/1); d) hydrazine hydrate, ethanol/toluene (3/1), reflux.

On the other hand, the compounds **67** and **68** (they are regioisomers and contain two phthalimido moieties, one *tert*-butyl and one nitro group) were obtained from **60** and **61** by using a double amount of solvent in the nitration step. This feature should be interesting for a synthetic chemist.



Scheme 6: The pathway in the synthesis of the compound **24e**; Conditions: a) HNO_3 65%, dichloromethane/acetic acid (19/1), 5°C; b) ethyl bromoacetate, Na_2CO_3, acetonitrile, reflux 1 day; c) H_2, Ra-Ni, toluene, 2 hours; d) phthalic anhydride, triethylamine, toluene, reflux, 12 hours; e) HNO_3 100% fuming, dichloromethane/acetic acid (19/1); f) HCl, ethanol/toluene (3/1), reflux, one day; g) (*p*-decyloxy)-phenylisocyanate, chloroform, reflux, 12 hours; h) H_2, Ra-Ni, toluene, 2 hours; j) dodecylisocyanate, chloroform, reflux, 12 hours.

From the **63-66** two directions are possible. We have first cleaved the phthalimido groups with hydrazine hydrate (reflux in an ethanol/toluene = 3/1 mixture) and reacted the corresponding amino-nitro compounds **69-72** with an isocyanate. After the introduction of

the first urea, the nitro groups were hydrogenated to amino (in the presence of Raney-nickel) and reacted with the second isocyanate. In this way the tetraureas **24a-d** were obtained.

The second way: first hydrogenation of nitro groups followed by acylation reaction and second deprotection of phthalimido moieties it is also possible but it is not suitable in our case, because deprotection of phthalimido groups would affect the two urea functions.

To reach the final goal a tetraurea ABAB-type having the same pattern in the ether residues, we have developed some adjustments in our strategy (Scheme 6). Thus, instead of the partial *ipso*-nitration of the tetraether calixarene several steps are done: 1) di-alkylation; 2) *ipso*-nitration of the phenolic units; 3) alkylation of the p-nitrophenol units. The last steps must be done with more reactive halide like methyl iodide or ethyl bromoacetate. Following the strategy described above the compound **77** was obtained. For this compound cleavage of phthalimido group was done with hydrochloric acid in an ethanol/toluene mixture. No cleavage of the ester functions was observed and compound **24e** was obtained.

Table 1: Tetraureas synthesized by the methods described above

Type		R_A	R_B	Y_A	Y_B
ABBB	**21a**	tolyl	n-hexyl	n-pentyl	
	21b	hexyl	tolyl		
	21c	tolyl	*tert*-butyl		
	21d	*p*-*tert*-butyl-trityl	tolyl		
AABB	**22a**	tolyl	hexyl	n-pentyl	
	22b	tolyl	adamantyl		
ABAB	**24a**	tolyl	adamantyl	n-pentyl	
	24b	tolyl	*tert*-butyl		
	24c	tolyl	n-hexyl		
	24d	tolyl	-CH(CH3)Ph		
	24e	*p*-decyloxy-phenyl	dodecyl	-CH2COOEt	n-pentyl

We did not succeed to synthesize with good yields a tetraurea of ABAB-type by protection–deprotection of amino groups or direct reaction between tetraamine with an isocyanate. Nevertheless, we have synthesized in good yields (over 60% of purified product) monoBoc, 1,2-diBoc, triBoc and monotolylurea, 1,2-ditolylurea and tritolylurea

which lead to tetraurea of the AABB and ABBB-types. The synthesis of Schiff base is a way which should be checked as well.

We succeed to develop a multistep synthesis to ABAB-type, method which can be used for other compounds derived from amines. Mild reaction conditions and simple procedures of purification are used in all these steps. The yields are moderate to good. The method is flexible and allows introduction of very large number of substituents.

3.4 Synthesis of loop derivatives

A strategy to obtain tetraurea derivatives of AABB-type in which the two adjacent residues are connected via a bridge was another goal for this work. We named such compounds mono-loop when in the molecule only one bridge was introduced and di-loop when there are two loops (different or identical).

There are two pathways to build up a tetraurea with one or two loops:

- to connect two adjacent amino functions via a cyclisation reaction with a bi-functional derivative (di-isocyanate or di-urethane);
- intramolecular reaction between two adjacent functions which close a ring.

We found strategies for both ways and we explain them in this section.

Via cyclisation reaction a connection between two residues R can be obtained. There are two possibilities for ring closure as shown in figure 34. The connections named **a** should lead to the desired compound. The connection **b** leads to derivatives with one *trans*-cavity loop and isolated residues R and it is decreasing the overall yield. To avoid this second connection the four alkenyl moieties should be separated in space in a way that a *trans*-cavity approaching is not possible anymore.

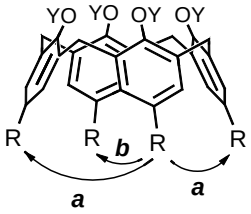
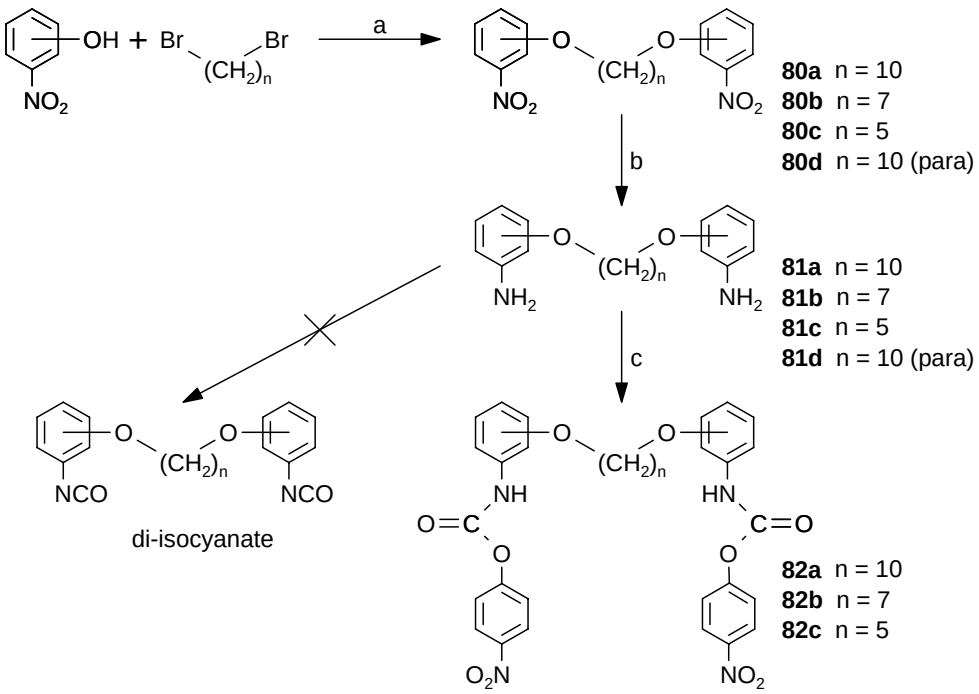


Figure 34: Two possible intramolecular connections **a** and **b** of residue R in a calixarene fixed in the *cone* conformation

3.4.1 Synthesis of mono-loop derivatives

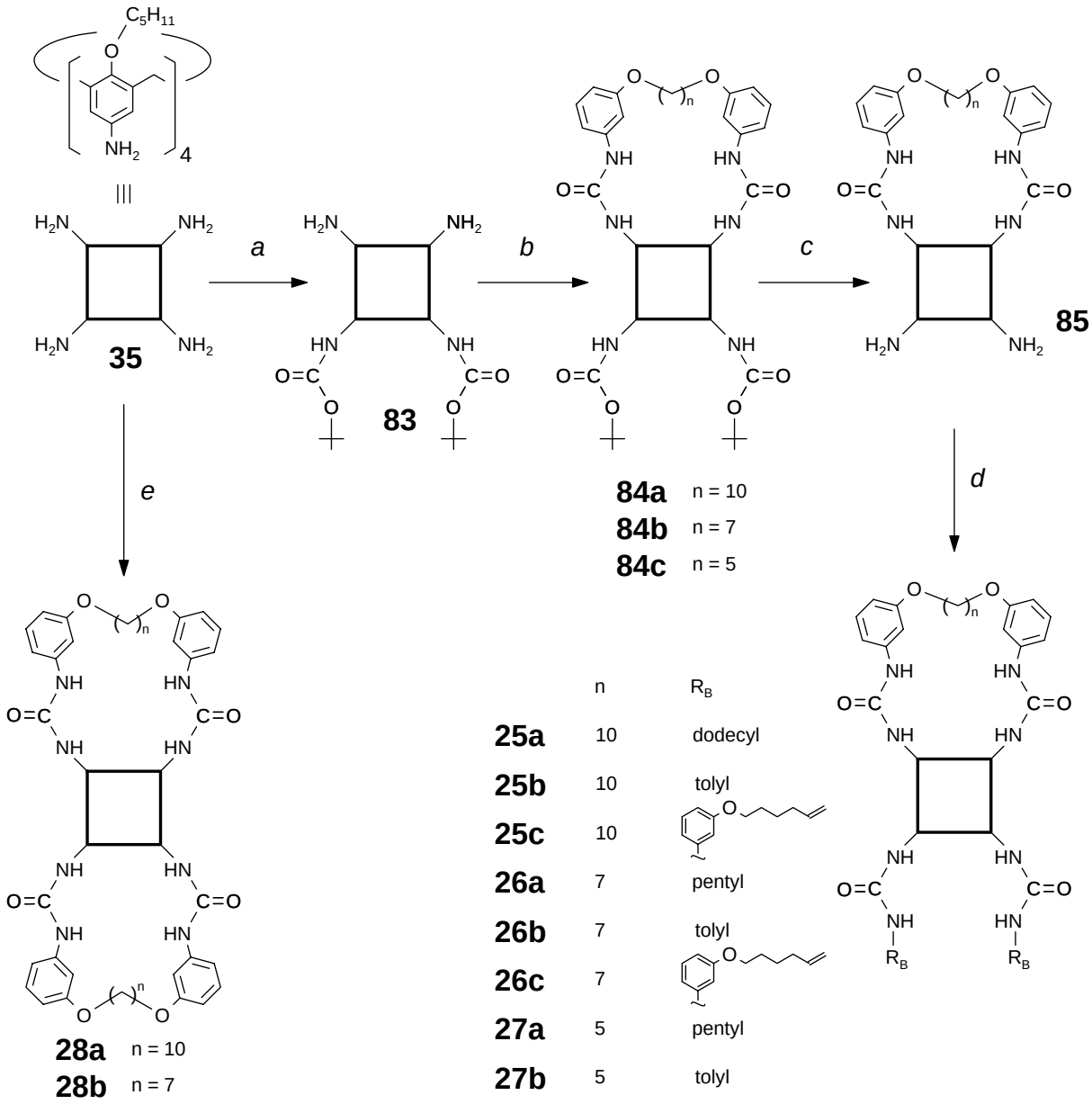
First, we obtain the bi-functional compounds and then, via an intermolecular cyclisation reaction with 1,2-diBoc derivative, they give diurea-diBoc compounds.

Protection of two adjacent amino functions in the molecule of tetraamine with Boc groups was the way to prevent undesired *trans*-cavity connection.



Scheme 7: Synthesis of di-urethane derivatives **82**; Conditions: a) acetonitrile, reflux 2 days; b) H_2, Ra-Ni, acetone, 2 hours; c) *p*-nitrophenyl chloroformate, 1,4-dioxane, reflux, 24 hours.

We tried to synthesize a di-isocyanate which has an aliphatic chain and an aromatic part as it is represented in the scheme 7. The *para*-nitrophenol reacts with 1,10-dibromodecane and the dinitro derivative **80d** was hydrogenated with hydrogen in the presence of Raney-nickel. The reaction of diamino **81d** with triphosgene [bis-(trichlormethyl)-carbonate] did not give the wanted product. The same reactions were done starting from *meta*-nitrophenol but the desired di-isocyanate could not be obtained. Most probable we could not found the proper conditions to conduct these reactions. On the other hand, isocyanates are not so easy to handle and store without taking special measures. Therefore, we changed the plan in the way to obtain di-urethanes 8 (Scheme 7). We start with *meta*-substituted phenyl rings because this appears appropriate from stereochemical/geometrical point of view. The compounds **81a**,**b,c** were synthesized starting from *meta*-nitrophenol. The next step in the synthesis is the N-acylation of diamino **81** with *p*-nitrophenyl chloroformate. After several attempts, 1,4-dioxane as solvent and reflux over 24 hours were found as best conditions and **82a,b,c** were obtained with yields of 80-95%. All these compounds are stable (can be easily handled) and easier to purify, a factor important especially for cyclisation reactions.



Scheme 8: Syntheses of mono-loop and di-loop derivatives; Conditions: a) see ref. [1]; b) DMF, slow addition of **82** (1.25 mol); c) TFA, $CHCl_3$, 2-3 hours; d) isocyanate or mono-urethane **88a** , $CHCl_3$, 12 hours; e) similar to b (2.5 mol **82**)

A solution of di-urethane **82** in DMF and a solution of 1,2-diBoc protected tetraamine **83** (see 3.1) and N,N-diisopropylethylamine (as catalyst) in DMF were slowly added in parallel into a flask containing DMF. The best results were obtained when the concentration of **83** was ~ 1 mM in the overall mixture and the solvent was DMF with a very low percent of water and amines (DMF for peptide synthesis). Compounds **84** (Scheme 8) were obtained after chromatographic purification (eluent ethyl acetate: hexane mixture) with yield ranging from 34% (n = 5) to 74% (n = 10). The yields are reduced to approximate half value when the DMF p.a. was used (due to the content of water and

amines). Deprotection with trifluoroacetic acid in chloroform and acylation with an isocyanate (tolylisocyanate, dodecylisocyanate or pentylisocyanate) or the active mono-urethane **88a** provide the wanted tetraureas **25** with one loop.

3.4.2 Synthesis of di-loop derivatives

Two strategies for the synthesis of di-loop derivatives were developed. One starts directly from the tetraamino calix[4]arene **35** and 2.5 mol of di-urethane **82** in DMF in the presence of N,N-diisopropylethylamine (in a similar procedure as described for mono-loop derivatives; Scheme 8). The yields of **28a,b** were lower (38-42%) in comparison to mono-loop (74%) but not too low taking into account that two cyclisation reactions occur in one molecule. In addition the undesired *trans*-cavity bridging could also take place as side reaction.

A di-loop derivative having two different loops can be obtained, in principle, from the diamine **85** and a second di-urethane **82**.

The second way was developed on the basis of metathesis reaction and selective heterodimerization.[55] Via metathesis reaction a connection between two chains with terminal double bonds can be obtained. In the heterodimer the two distal residue of one calixarene are kept apart by the other calixarene and in this way the wrong connection are not possible. (Figure 35)

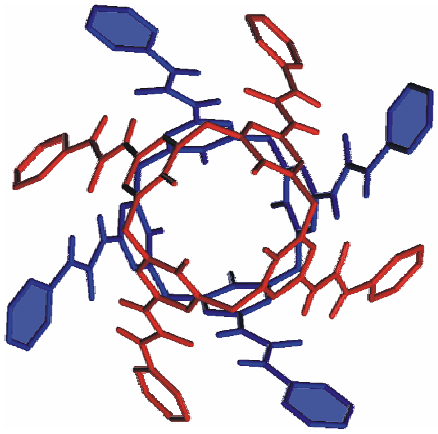
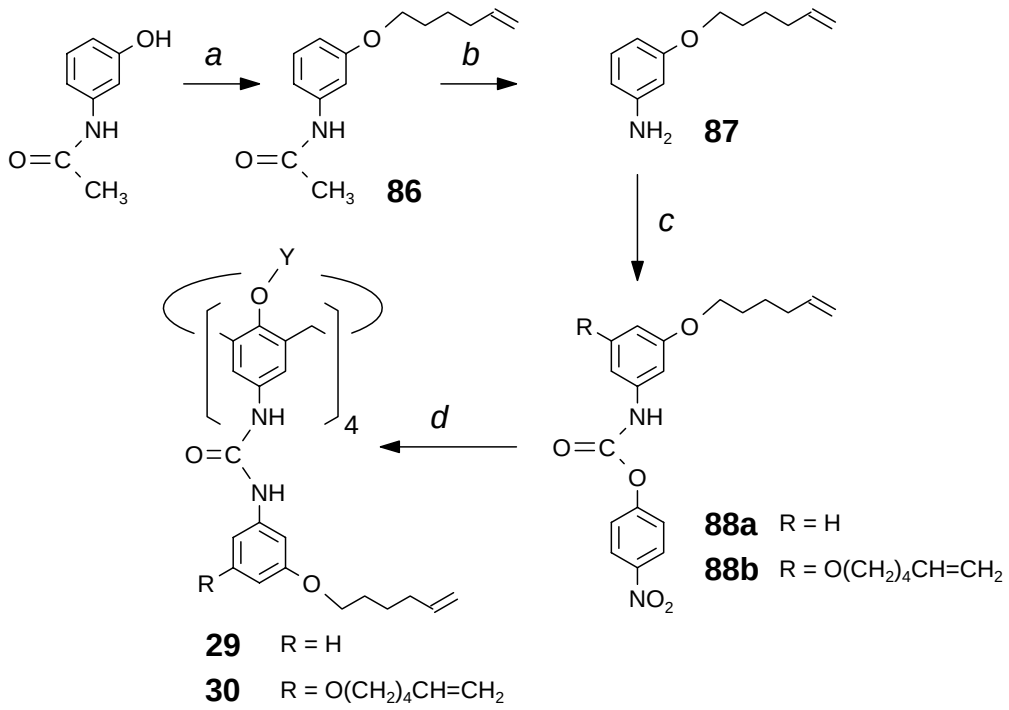


Figure 35: Schematic representation of a heterodimer (top-view), included guest and residues Y are omitted for clarity; the residues form distal positions are separated by the second calixarene.

It is known[56] that tetratosylureas form exclusively heterodimers with tetraarylureas. Thus, we have used tetratosylurea as heterodimerization partner for our synthesis within the heterodimer.

Tetraurea **29** was synthesized from tetraamine **35** and mono-urethane **88a**[57] as shown in scheme 9.



Scheme 9: Synthesis of tetraureas **29** and **30** having four and eight double bonds; Conditions: a) 6-Bromo-1-hexene, K_2CO_3, DMF, 70°C, 2-3 days; b) NaOH, ethanol/water 9/1, 4 hours; c) p-nitrophenyl chloroformate, chloroform/tetrahydrofuran 3/2, reflux, 12 hours; for the compound **88b** see ref. [12; 16] d) triethylamine, DMF, 12 hours.

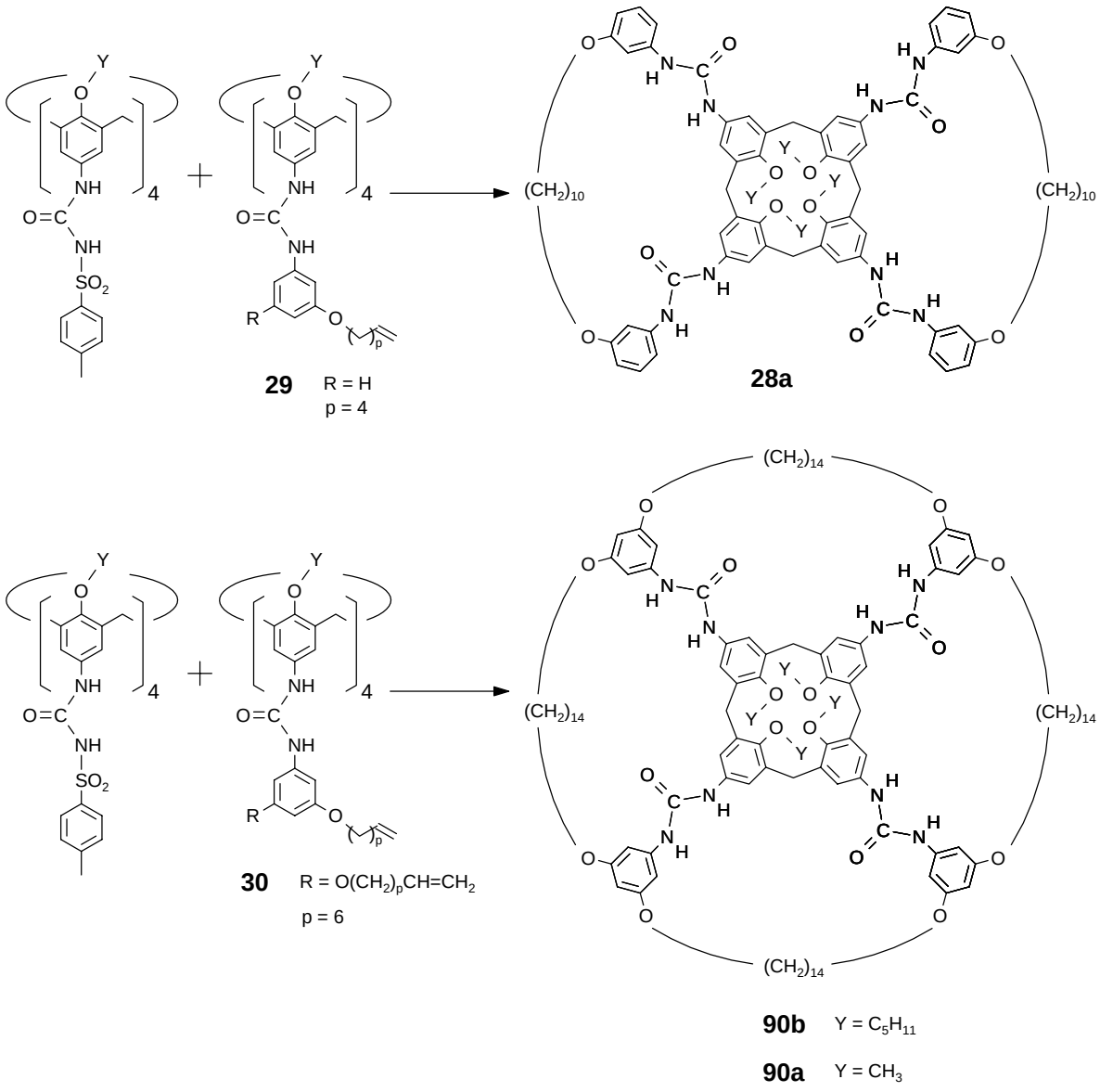
A mixture of **29** and tetratosylurea in a ratio 1:1.1, in benzene, was stirred over 2 days at 60°C, to become a clear solution. After checking by ^{1}H NMR the complete formation of the heterodimer, the solution is diluted with dichloromethane (kept over NaOH) till the concentration of heterodimer is ~ 0.3 mM and the calculated amount of catalyst is added. The whole mixture is stirred at room temperature under a slow stream of nitrogen for two days. After hydrogenation with platinum dioxide as catalyst and chromatographic purification the wanted compound **28a** was obtained in excellent yield 82% (Scheme 10).

In dichloromethane the heterodimer is formed faster (checked by NMR) but the yield of the final product was much lower ~25%.

In the ^{1}H NMR spectrum, signals of "impurities" (~5-10%) appear which could not be removed by any method. We later found that the bromide used in the synthesis of mono-urethane **88** contained as impurity 6-bromo-2-hexene. This means that in all our compounds we have chains with double bonds on the second carbon. They undergo metathesis reaction in the similar way but the product has other length of the loop. The

structure of the compounds is very similar and it was not possible to separate them by chromatographic methods. This problem did not appear with other alkenyl bromides.

In a similar way, from the heterodimer of **30** with tetratosylurea tetra-loop derivatives **90**‡ were obtained. [55;58]



Scheme 10: Template syntheses of di-loop and tetra-loop derivatives.

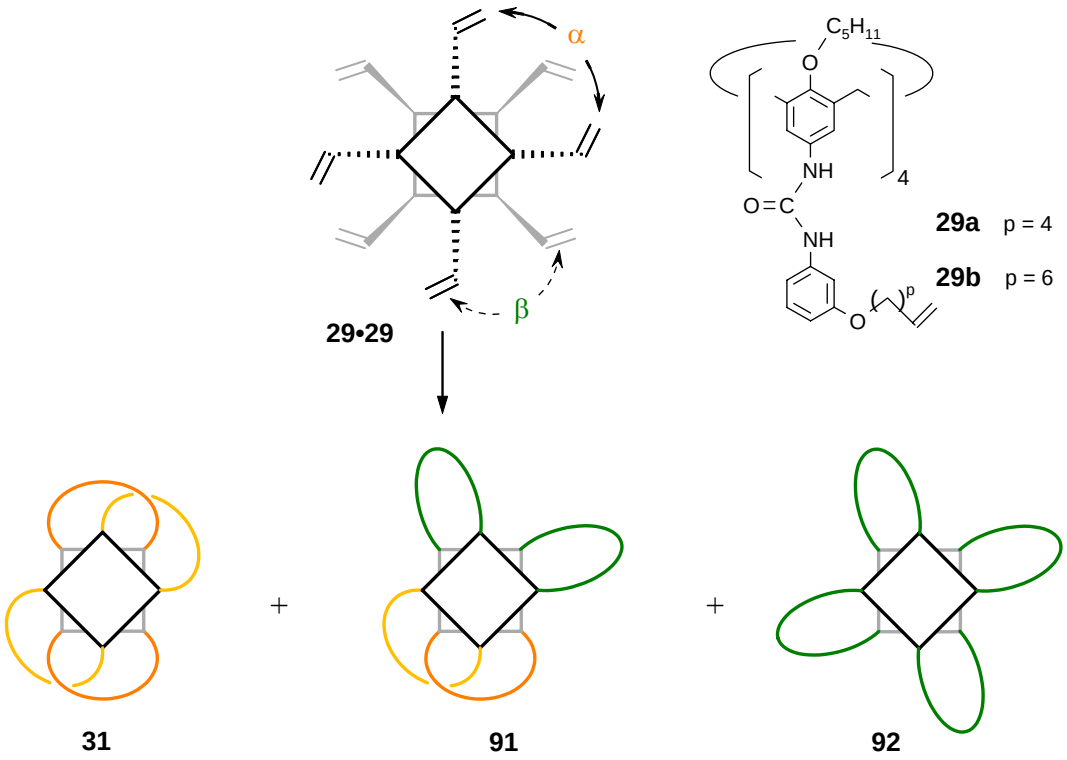
In the first synthesis (from tetraamine and di-urethane) the yield of the derivatives **28a** was 42%, while in the second (via metathesis) was 82%. A comparison between the two methods (not 100% correct since different reactions are taking place in the two methods) shows clearly the advantage of preorganization in the precursors. In the heterodimer the groups which undergo the metathesis are oriented in space in a favorable way and in the

‡ Tetra-loop compounds were synthesized by Dr. M. Vysotsky and Dr. L. Wang.

same time the wrong connections are suppressed. The intermolecular cyclisation can not avoid undesired side reactions.

3.5 Synthesis of bis-[2]catenanes

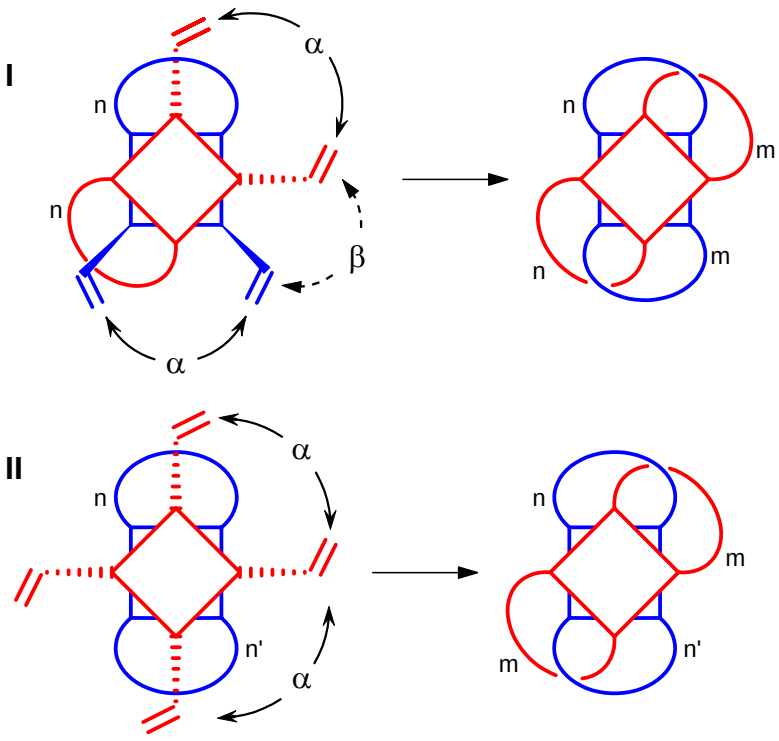
In our group a bis-[2]catenane[58] was synthesized via metathesis reaction starting from the homodimer of a tetraurea having ω-alkenyl chains **29b**. In the homodimer of this type, the 8 double bonds are distributed around the equatorial plane of the capsule, four are oriented towards one pole and the other four to the opposite, but nothing prevents the wrong connections (Scheme 11). When the two double bonds which undergo the metathesis reaction belong to the same calixarene we name it α-connection. In the case of β-connection the two double bonds are belonging to different calixarene within the same dimer. The derivative **31b** (n = 14) was isolated in 7 to 12% yield as a results of only α-connections. When p was shorter no bis-[2]catenanes could be isolated but only the other two products were formed, **91** as result of two α and two β-connections and **92** by β-connections only.



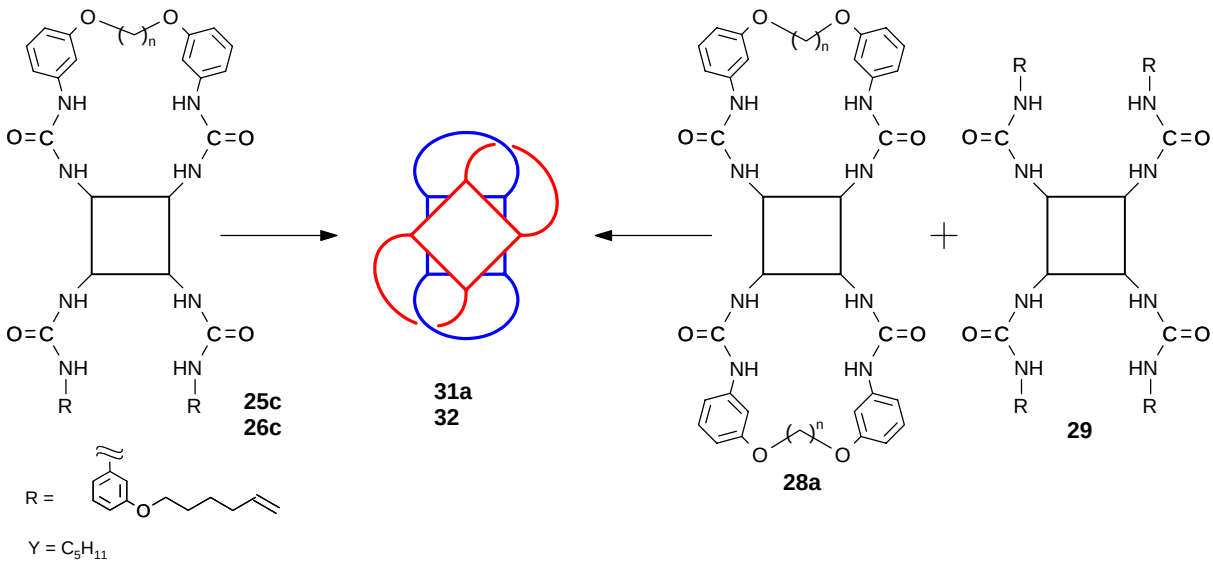
Scheme 11: Synthesis of bis-[2]catenanes, [2]catenane-doublebridged and tetrabridged derivatives in the statistical approach.

Having in mind the concept of preorganization which was successfully used in the synthesis of bis-loop compounds, we have analyzed how we could apply it to the synthesis of bis-[2]catenanes. Decreasing the number of new connections which should be made via metathesis and preventing the β-connections are the two directions to improve the synthesis. The first goal could be achieved by starting the synthesis from mono- or di-loop derivatives, while for the second the selective homo- and heterodimerization remains an adequate option.

The two strategies[58] found are presented in the scheme 12. One starts with a mono-loop derivatives with two alkenyl groups which forms a single homodimer (regioselective homodimerization, Scheme 12I) while the second is based on the exclusive formation of heterodimers from bis-loop compounds and open-chain tetraureas (Scheme 12II). In the homodimer (**I**) there is still one possibility of β-connection, while in the heterodimer (**II**) only α-connection are possible. So, if we could keep the reaction exclusively in the dimers we would expect 75% yield for the strategy **I** and 100% for **II**.



Scheme 12: The two strategies for the synthesis of bis-[2]catenanes: A) from homodimers of mono-loop derivatives; B) from heterodimer of bis-loop compound and tetraurea having alkenyl chains.



Scheme 13: The two bis-[2]catenanes obtained by the two methods.

The compounds needed for the first strategy must contain one loop and two alkenyl chains. Following the synthetic strategy described earlier for mono-loop derivatives **25c** (n = 10) and **26c** (n = 7) were synthesized and the complete formation of the homodimer in benzene and chloroform was checked by NMR.

The synthesis follows the procedure described above for the synthesis of bis-loop derivatives via metathesis reaction. Two catenanes were obtained **31a** (n = m = 10; yield 49%) and **32** (n =7; m = 10; yield 20%; Scheme 13).

Bis-loop derivative **28a** and open-chain tetraurea **29** were used in the second strategy. The exclusive formation of the heterodimer was proved by ^{1}H NMR measurement and the synthesis followed the procedure already described for bis-loop derivatives. The bis-[2]catenane **31a** was obtained in 65% yield.

In both cases the purification of the final compounds is complicated by side products which decrease the overall yield. We believe that the dichloromethane is not the best solvent for the metathesis reaction because it contains small amount of amylene for stabilization, a compound with a double bond which can influence the desired metathesis reaction. Some promising results were obtained when the formation of the dimer and the metathesis reaction was realized in benzene.

As was expected, the second procedure offers a better yield, since there is no possibility for incorrect connections but both are by far better than the statistical method. They are flexible and various catenanes can be obtained including regioisomeric compounds.[59]

4. Results

4.1 Homodimers of ABAB-type tetraureas

Compounds of the ABAB-type were synthesized as described (see Syntheses, Table 1, pg. 42). This chapter focused on their characterization.

A typical ^{1}H NMR spectrum (in DMSO-d_6) of the monomeric form of such tetraurea is shown for **24a** as an example in figure 35A. There are only four NH signals. Three of them (connected to aromatic rings) appear at ~8 ppm while the fourth (connected to the adamantyl residue) is found at 5.58 ppm. The hydrogens of the calixarene skeleton appeared as two sharp singlets (in red). The tolyl residues show two *ortho*-coupled doublets (typical AB system) and one singlet of the methyl groups (light blue). The methylene bridges appear as a pair of doublets with *geminal*-coupling. Two signals, namely one sharp singlet (12 protons) and a broad singlet (18 protons) were assigned to adamantyl groups (magenta). Thus, all signals observed confirm the expected C_{2v}-symmetry.

In accordance with the stereochemical analysis shown before, a tetraurea of ABAB-type forms only one regioisomer when it is dissolved in an appropriate apolar solvent (chloroform, benzene). The dimer should have C_2-symmetry (with the directionality of the hydrogen bonded belt) that makes the two calixarenes different within one dimer. Thus, one would expect two sets of signals for the phenolic units named A and two sets of signals for B for such a dimer. Therefore, the following set of signals is expected:

- 8 signals for NH
- 8 doublets with *meta*-coupling corresponding to the hydrogens of calixarene skeleton
- 4 pairs of doublets with *geminal*-coupling for the methylene bridges
- 2 sets of signals for each of the substituents A and B.

The compound **24a** was dissolved in benzene-d_6 (it takes few minutes at ~ 60°C) and the spectrum was measured (Figure 35B). Most of the signals are assigned with the help of two-dimensional ^{1}H NMR techniques (gs-COSY, gs-TOCSY, ROESY). Overall 8 *meta*-coupled doublets (^4J ~ 2 Hz) giving cross-peaks in gs-COSY (Figure 36) are ascribed to hydrogens of the calixarenes (marked from 1 to 8). The 8 singlets (no cross-peaks in gs-COSY) in the region from 10 to 6 ppm are attributed to the NH (a-h). The signals of NH connected to adamantyl which in DMSO-d_6 appear at 5.58, now are found at 7.81 and 7.57

ppm (signals d and e) while the two NH-Aryl signals appear at 10.12 and 9.59 ppm (a and b). The two pairs of doublets (α and δ; β and γ) correspond to the aromatic parts of tolyl residues. Four pairs of doublets (^2J ranging from 11 to 12 Hz) in the region 5 to 3 ppm are attributed to the methylene bridges. In the same area, other multiplets corresponding to alkyl residues -OCH_2- are observed. The signals which appear between 2.5 and 0.7 ppm are too difficult to interpret. With the help of gs-TOCSY spectrum the two signals at 2.06 and 1.93 ppm (light blue) can be attributed to the methyl groups of the tolyl residues.

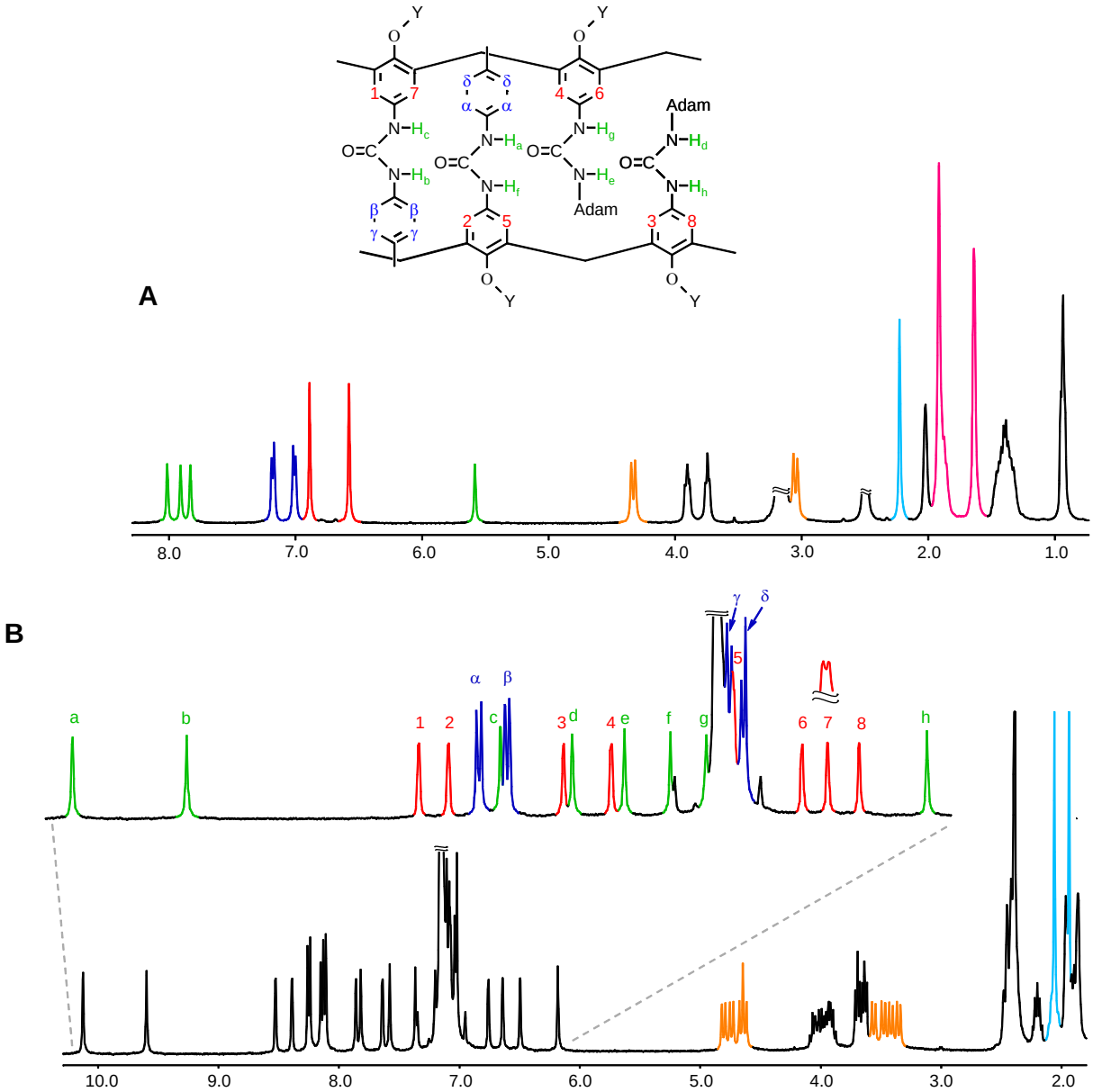


Figure 35: ^{1}H NMR (400 MHz) spectra of **24a** in DMSO-d_6 (A) and in benzene-d_6 (B). The signals of different functional groups are indicated with different colors: NH green; Ar_{calix}-H red; tolyl blue; adamantyl magenta; methylene bridges orange.

The signals corresponding to adamantyl groups can not be assigned in details because of their overlap with other signals. The whole spectrum is totally in agreement with the expected C_2-symmetry of the capsule.

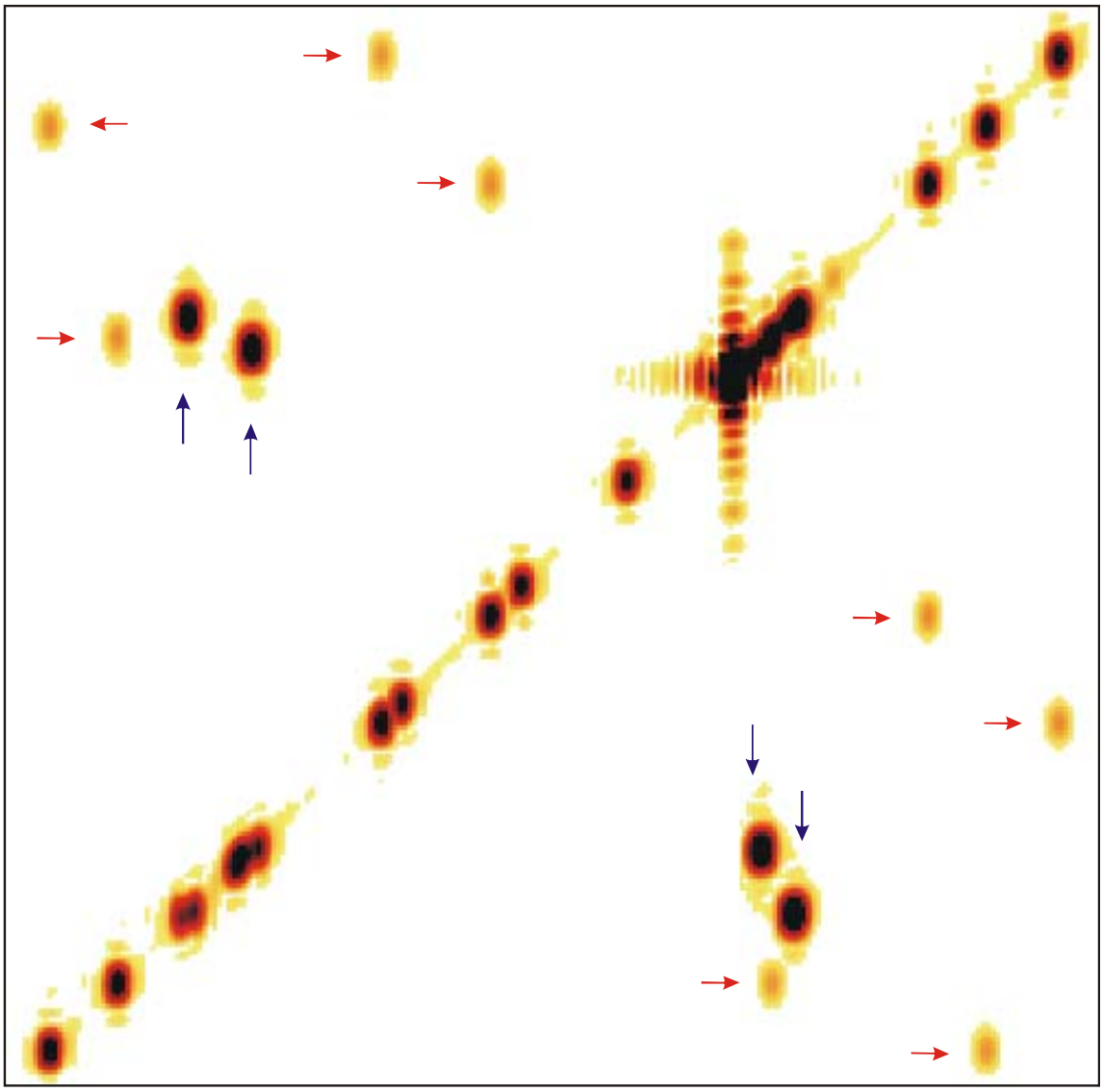


Figure 36: Section (8.6-6.1 ppm) of the gs-COSY spectrum of **24a** in benzene-d_6; red arrows indicate cross-peaks corresponding to the four pairs of *meta*-coupled doublets of the calixarene moieties, while the blue arrows correspond to tolyl residues.

The spectrum recorded in chloroform-d_1 shows the pattern, which again, corresponds to C_2-symmetry of the dimer. However, several signals (one doublet from tolyl, one doublet of the calixarene and one singlet of NH) overlap. Figure 37 shows one section of the ^{1}H NMR spectra (chloroform-d_1) of **24a** (A) and of its complex with tetraethyl ammonium tetrafluoroborat at 58°C. It is obvious that the capsule filled with the cation has the higher symmetry. There is only one pair of *ortho*-coupled doublets (in blue) of the tolyl

groups, two pairs of doublets of the methylene bridges, and only four NH signals. The protons of calixarene skeleton show just three signals in the ratio 1:2:1. The first and the third are coupled (in accordance with gs-COSY; integration indicate 4 protons) but the other four protons appear as a broad singlet.

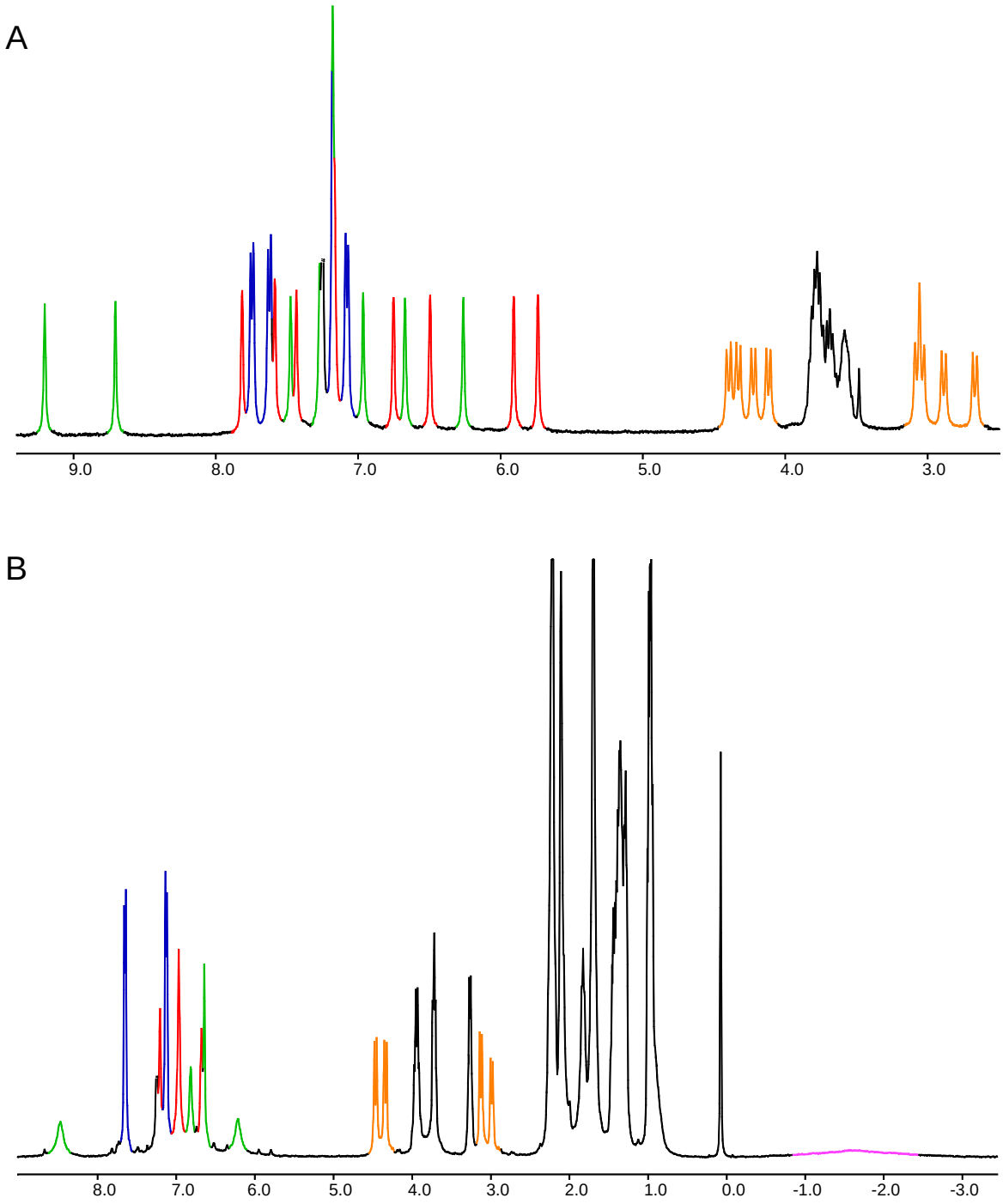


Figure 37: ^{1}H NMR spectra (400 MHz, chloroform-d_1) of **24a** at 25 °C (A) and of its tetraethyl ammonium complex **24a**•Et_4N^+•**24a** BF_4^- at 58°C (B). The signals of different functional groups are indicated with different colors: NH green; Ar_{calix}-H red; tolyl blue; methylene bridges orange; N-CH_2 magenta.

The very broad signal at -1.55 ppm (in pink) is attributed to the methyl groups of the included cation, which is high-field shifted since it experiences the shielding effect of the aromatic moieties of the calixarenes. The whole spectrum corresponds to D_2 symmetry.

This result confirms the reported results.[60] The arrangement of hydrogen bonds in the capsule filled with a cation consists of just 8 hydrogen bonds while cation-π interactions compensate the loose of hydrogen bonds and make the capsule stable. The directionality of the hydrogen bonded belt is changing fast on NMR time scale which leads to the observed overall D_2 symmetry.

Similar spectra were recorded for tetraureas **24b** and **24c**. A derivative containing two tolyl groups and two (R)-(+)-1-methylbenzyl residues attached to the urea functions **24d** was also synthesized and the formation of the dimer (homodimer or heterodimer with tolylurea or tosylurea) checked in benzene-d_6 and chloroform-d_1. However, ^{1}H NMR spectra could not be obtained due to the extremely low solubility of this compound in these two solvents.

Our next attempt was to study complexes of tetraurea ABAB-type with chiral guest molecules as N-methyl-N-ethyl-N-*n*-propyl-N-*i*-propylammonium iodide or tetrafluoro-borate, 1-bromo-2-methylbutane, pinen. Because of solubility problems these complexes could not be obtained.

The optical resolution of the compounds was attempted by chromatography, using chiral stationary phases. Up to now successful result was not obtained. Potential reasons for this failure could be the low solubility in the eluent appropriate for the separation (the solvent mixtures used for separation are hexane/ethanol, hexane/chloroform/ isopropanol) and/or low stability of the capsules in the presence of small amounts of polar solvents.

The compound **24e** was designed especially to have a good solubility in apolar solvents. It poses long alkyl chains on the urea residues. Our goal concerning the solubility was achieved, this compound is soluble in cyclohexane good enough (~ 10 mg compound / 1 mL solvent at 60°C) to allows the measurement of NMR spectra in deuterated cyclohexane.

The formation of the complex of **24e** and N-methyl-N-ethyl-N-*n*-propyl-N-*i*-propylammonium tetrafluoroborate was checked in deuterated chloroform and deuterated dichloromethane. The sample measured in one hour after mixing in chloroform shows neither signals of the encapsulated ammonium cation nor definite dimer with chloroform as guest. After three days, while the sample was kept at 60°C, the spectrum was measured again. In the region -1.8 to -2.2 ppm weak signals appeared but the rest of the spectrum

remain broad. Measurements made later and with dichloromethane as solvent did not change the situation. An explanation for this result is that the ammonium cation having *n*-propyl and *i*-propyl is too large (or at the limit) and does not fit well into the cavity of the dimer. In the same time the presence of it in large excess disturbs the formation of the dimer with the solvent as guest.

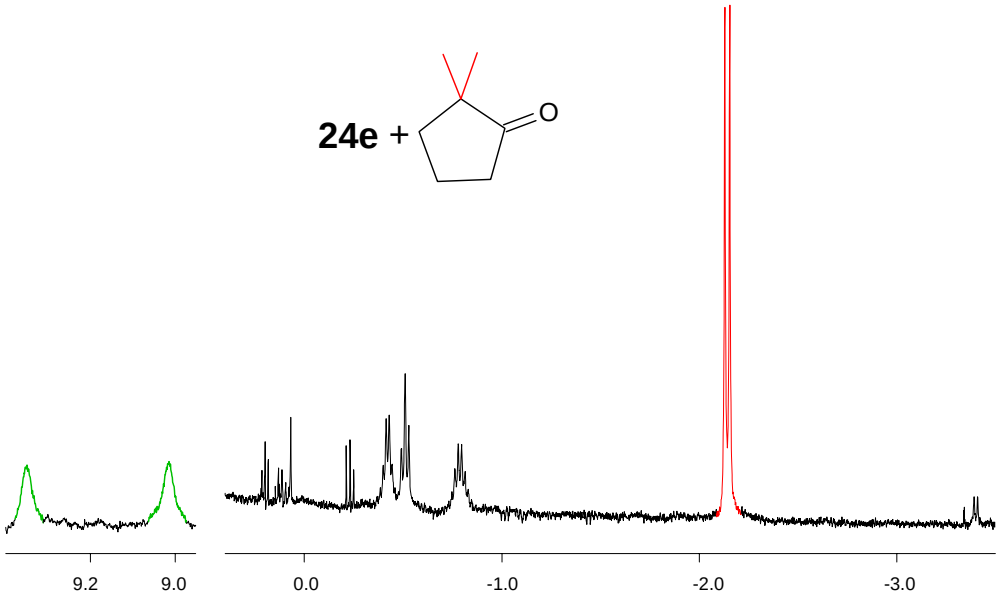


Figure 38: Sections of the spectrum (400 MHz, dichloromethane-d_2) of the mixture **24e** and 2,2-dimethylcyclopentanone. In green are drawn the most low-shifted NH-signals of tetraureas; in red the two methyl groups of the guest.

2,2-dimethylcyclopentanone and dimethylcyclohexane were the next molecules offered as guest. They are not chiral but have two methyl groups which are diastereotopic. In the chiral environment (the chiral capsule of ABAB-type) they should give different signals. We tried the formation of the capsule filled with 2,2-dimethylcyclopentanone (ratio 1:20) in three different solvents chloroform, dichloromethane and tetrachlorethane. Just for the sample prepared in dichloromethane we could see signals of the encapsulated guest molecule but this dimer is the minor component of the mixture. The largest amount of calixarene is present as a dimer with the solvent as guest. Two sections of the NMR spectrum in dichloromethane (Figure 38) show the complex of **24e** and 2,2-dimethylcyclopentanone. As expected, the two methyl groups appear as two doublets.

The capsule filled with dimethylcyclohexane could not be obtained in dichloromethane. Just the dimer with the solvent could be seen in the spectrum.

These results with neutral guest could be explain that the molecule are large and fit not so good or they are worse guests in comparison with the solvents.

4.2 Regioselective dimerization of ABBB-type tetraureas

In the previous chapter it was demonstrated that tetraureas of ABBB-type can form two regioisomeric capsules, with proximal or distal positions of groups A relative to each other. There are several examples where regioselectivity of the formation of such dimers was observed.

It was shown that tetraurea substituted with four trityl (triphenyl-methyl)[61] residues does not form homodimers in benzene and chloroform, but can form heterodimers with tetra-tritylphenylurea.

A derivative bearing three tolyl residues and one trityl group was synthesized (see chapter Syntheses). Figure 39 shows ^{1}H NMR spectra of this compound in DMSO-d_6 (60°C) and benzene-d_6. The spectrum in DMSO-d_6 (Figure 39A) shows five NH-signals (overall eight protons). The assignment of the signals in the region from 7.4 to 7.0 ppm was possible only with the help of gs-COSY (Figure 40). One AB-system was attributed to the aromatic protons of the trityl group (light blue); two other AB-systems in the ratio 1:2 are assigned to the tolyl residues (dark blue). This pattern corresponds to the expected C_s-symmetry of the compound where the symmetry plane goes through the trityl and the opposite tolyl residues, that makes the three tolyl groups not identical. The following signals were found for the calixarene skeleton (red): two singlets (overall four protons) and one singlet (four protons) at 60°C. The last signal is splitted into two close broad doublets at 25°C. The methylene bridges Ar-CH_2-Ar (not shown in figure 39) show two pairs of well resolved doublets. The methyl groups of the tolyl residues show two singlets at ~ 2.2 ppm (in the ratio 1:2; dark blue), while the *tert*-butyl-trityl groups show one singlet at 1.26 ppm (light blue). Thus whole spectrum corresponds to the tetraurea in its monomeric form with C_s-symmetry as it was expected for such a compound in DMSO.

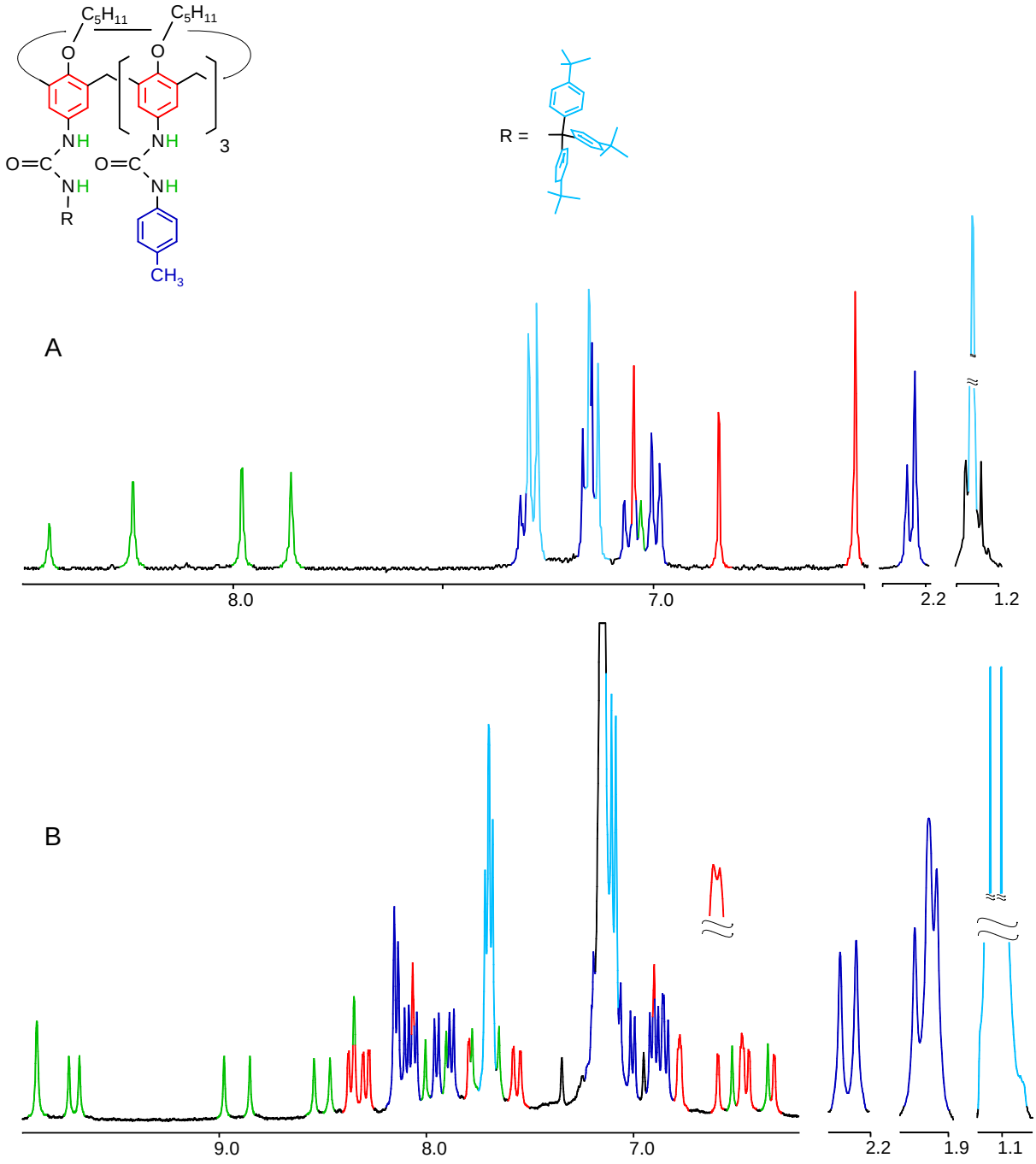


Figure 39: Section of ^{1}H NMR (400 MHz) spectra of **21d** in DMSO-d_6 at 60°C (A) and in benzene-d_6 25°C (B). The signals of different functional groups are indicated with different colours: NH green; Ar_{calix}-H red; tolyl dark blue; trityl light blue.

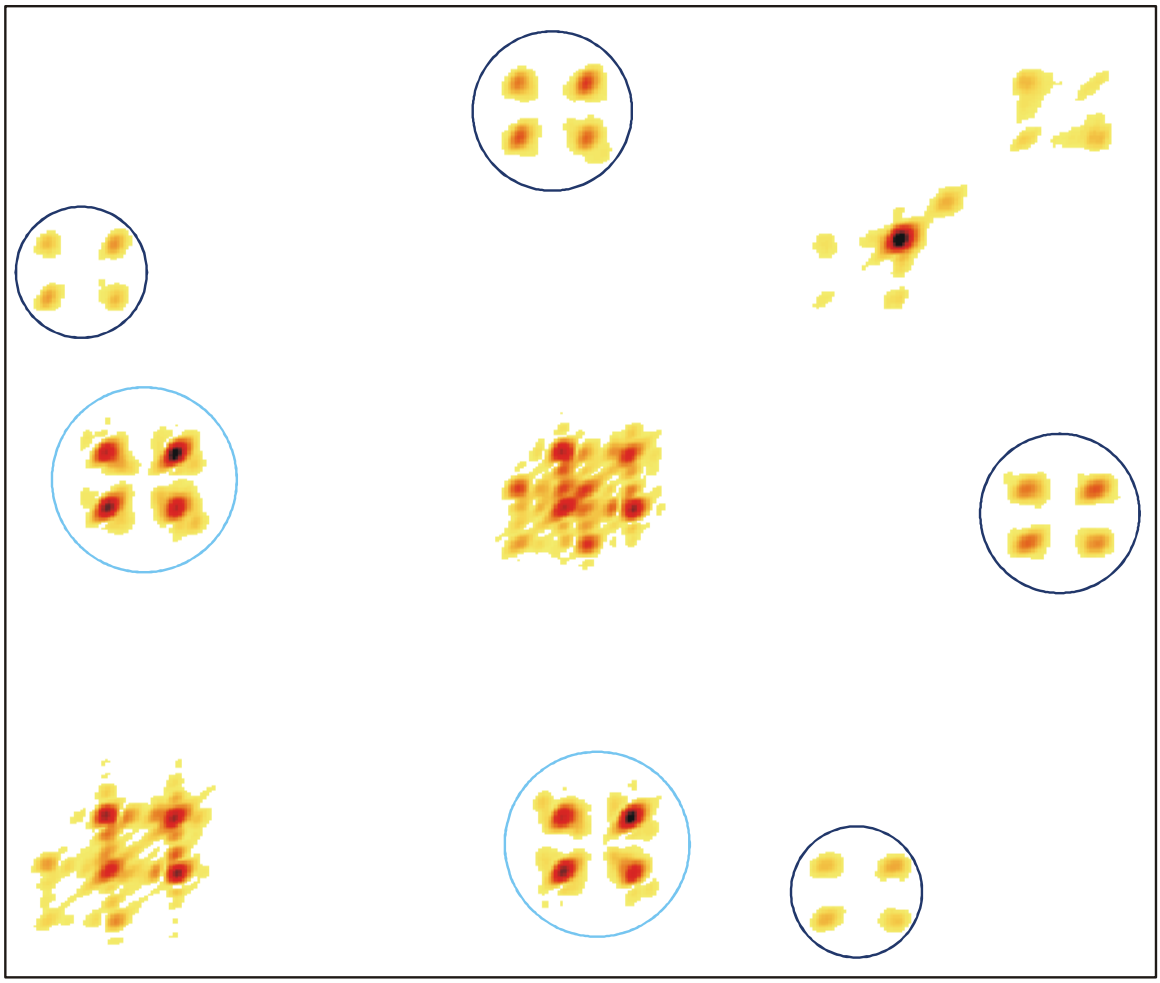


Figure 40: The section of gs-COSY spectrum of **21d** in DMSO-d6 (7.4-6.9 ppm) shows cross-peaks between protons of tolyl groups (dark blue circles), trityl (light blue).

In contrast to other ABBB ureas shown before, urea **21d** forms only one regioisomeric dimer, which is totally confirmed by ^{1}H NMR measurements (Figure 39B). For example, the NH groups close to the residues (NH_R) show just three signals in the ration 2:1:1 (four singlets with equal intensity are expected) while calixarene signals are clearly seen as only eight pairs of *meta*-coupled doublets. There are six pairs of doublets (dark blue) showing cross-peaks (dark blue arrows; Figure 41) for the tolyl groups and two pairs for the trityl (light blue and light blue arrows). In the region from 9 to 6 ppm other 11 signals (singlets, no cross-peak in two-dimensional spectrum) were attributed to NH groups. Therefore 15 NH protons are attributed without any doubts while the 16-th is supposed to lie under the first doublet of tolyl groups). A further confirmation is found in the region of 2.3-1.1 ppm of the proton NMR spectrum where six signals for the methyl groups (two of them not well resolved) of the tolyl residues and two for *tert*-butyl groups are found.

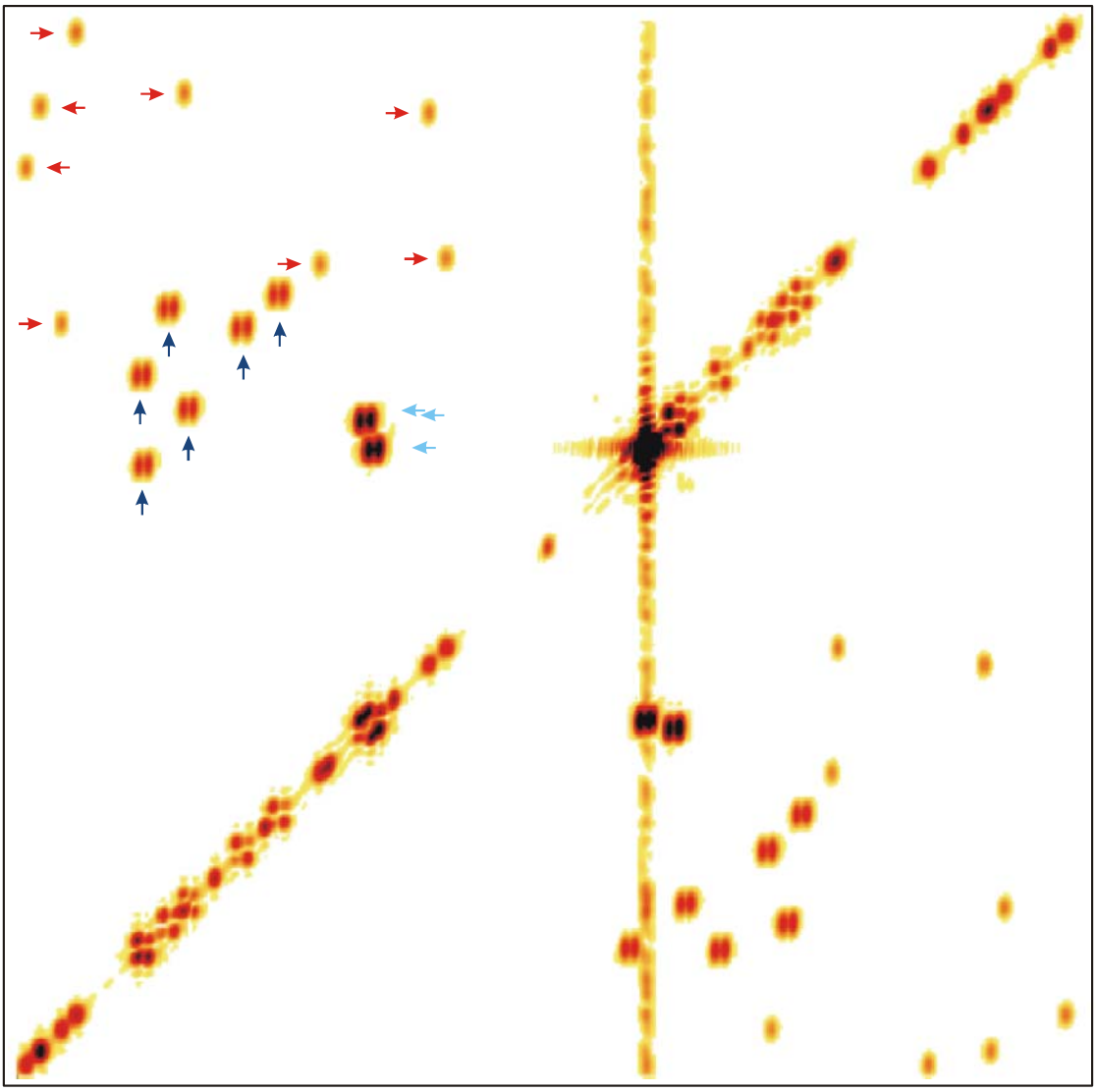


Figure 41: The section (8.4-6.2 ppm) of gs-COSY NMR of **21d** in benzene-d_6 proving the formation of only one regioisomer. Red arrows indicate the cross-peaks of the calixarenes signals, while dark blue arrows indicate the tolyl groups and light blue arrows the trityl groups.

The gs-TOCSY and NOESY spectra were measured to determine which regioisomer is formed. We could identify all the protons in the region 10-6 ppm. However, the conditions used for recording NOESY spectra (mixing time) were not optimal to observe sufficient intermolecular NOE contacts to prove the structure of the dimer.

4.3 Regioselective dimerization of AABB-type tetraureas

4.3.1 Mono-loop derivatives

A tetraurea of the AABB-type forms two regioisomers when it is dissolved in apolar solvents such as chloroform or benzene (see the previous chapter). It was also found that the equilibrium between the two isomers is influenced both by the substituents attached to the urea groups and by the solvent (guest). None of these tools led to the *exclusive* formation of only one regioisomer. A logical development of our research was the synthesis and characterization of compounds in which two residues attached to the adjacent urea groups, are covalently connected. In the figure 42 the formation of the two potential regioisomeric dimers of this type are represented. In the structure **I**, one residue **B** of each calixarene slips through the loop of the other calixarene because in this way the circular seam of the hydrogens bonds can be formed but the two loops are not coming in contact to each other (the angle between them is ~135°). During the formation of the structure **II** the two loops are coming towards each other (rotated with 45°). The urea functions are kept

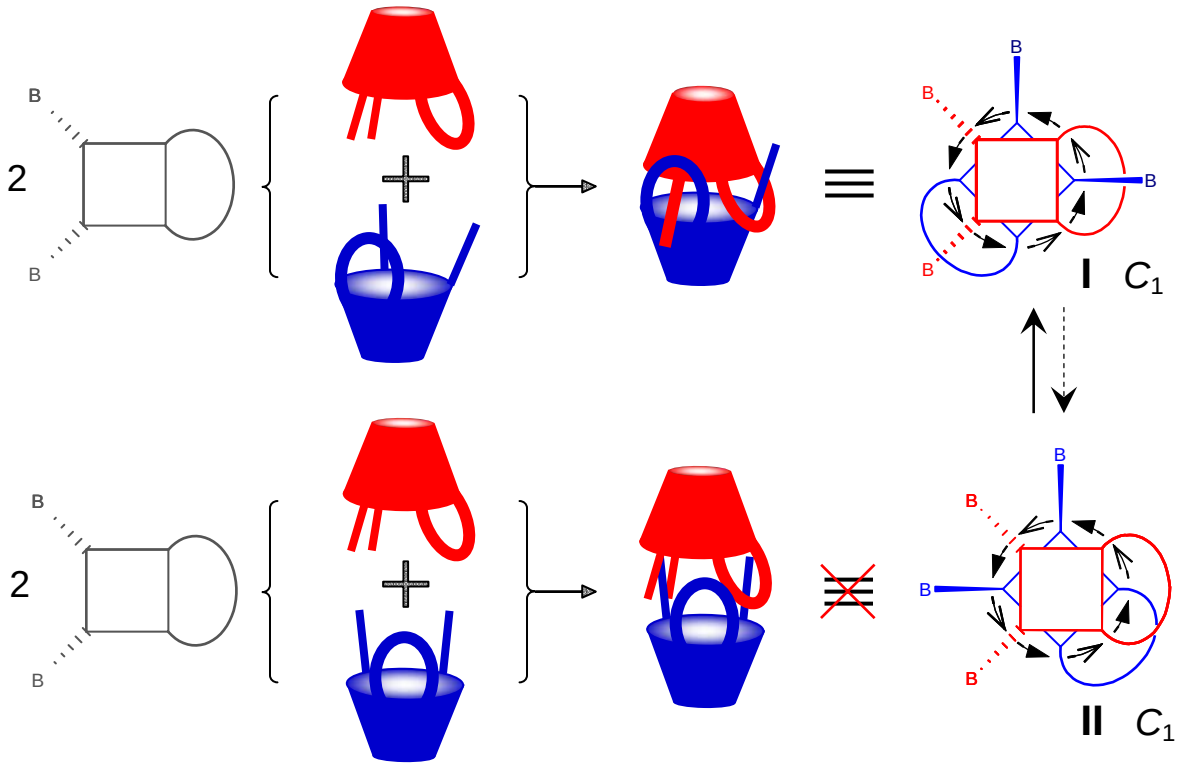
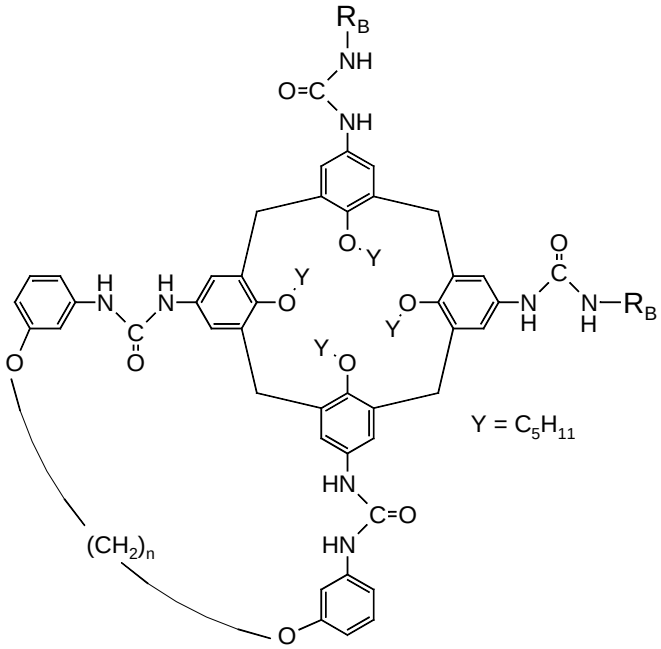


Figure 42: Schematic representation of the two possible regioisomers of the mono-loop derivative **I** and **II**. To obtain the structure **I**, B should slip through the loop. In the structure **II** overlapping of the loops should prevent an approach of the urea functions.

too far and the seam of hydrogen bonds can not be formed and the homodimer with the structure **II** is not formed.

We want to determine the following aspects:

- if the homodimer or heterodimers could be formed
- which structure has the homodimer (is our prediction correct?)
- the influence of the loop length
- the influence of the residue R_B.



Compound	n	R_B
25a	10	dodecyl
25b	10	tolyl
26a	7	pentyl
26b	7	tolyl
27a	5	pentyl
27b	5	tolyl

Scheme 14: Planar representation of the mono-loop derivatives and the series of synthesized compounds.

Six compounds of this type (**25a**, **25b**, **26a**, **26b**, **27a** and **27b**; Scheme 14) were synthesized (synthetic strategy is described in the chapter Syntheses) and are characterized in here. To prove their structure, ^{1}H NMR spectra were measured in DMSO-d_6 where these compounds exist in their monomeric form and display the pattern corresponding to C_s-symmetry. The symmetry plane (being the only symmetry element) intersects the loop and the two methylene bridges as is represented in figure 43. ^{1}H NMR spectrum of such derivative should show the following signals:

- four NH signals
- two pairs of *meta*-coupled doublets for calixarene
- four signals for the *meta*-disubtituted phenyl of the loop and corresponding signals for the aliphatic chain of the loop

- one set of signals corresponding to the other residues R_B.

In fact, only four NH signals were found in all spectra, from which one is a triplet when R_B is an aliphatic chain. There are four doublets with *meta*-coupling which are attributed to the calixarene skeleton. For the phenyl ring of the loop there are two triplets one with *ortho*-coupling (2) while the other is *meta*-coupled (1, not always visible as a triplet). The protons in *ortho* position to the oxygen (3) and to the nitrogen (3') atoms appear as doublets of doublets (*ortho* and *meta*-coupling). In all cases the signals of the methylene bridges are not well resolved. When R_B is an aliphatic group, the two protons of the methylene groups connected directly to the nitrogen atoms are diastereotopic and appear as multiplets close (or overlapped) to the equatorial protons of the methylene bridges. Two pairs of doublets with *ortho*-coupling are typical signals when R_B is tolyl. The corresponding signal of methyl groups of tolyl appears at 2.2 ppm as a sharp singlet. In the area of 2.1-0.7 ppm signals are found for aliphatic chain of the loop, for all alkyl chains from the narrow rim and in the cases of **25a**, **26a** and **27a** the rest of the R_B.

A common tendency for the series of these compounds is a better resolution of all signals (especially in the aromatic region) with shortening of the alkyl chain of the loop.

Figure 43 present the aromatic sections of the ^{1}H NMR spectra of **26b** (upper) and **26a** (lower) in DMSO-d_6, and shows all the expected signals and the difference induced by the residue R_B (see the forth signal of NH, green). The chemical shifts are collected in Table 2.

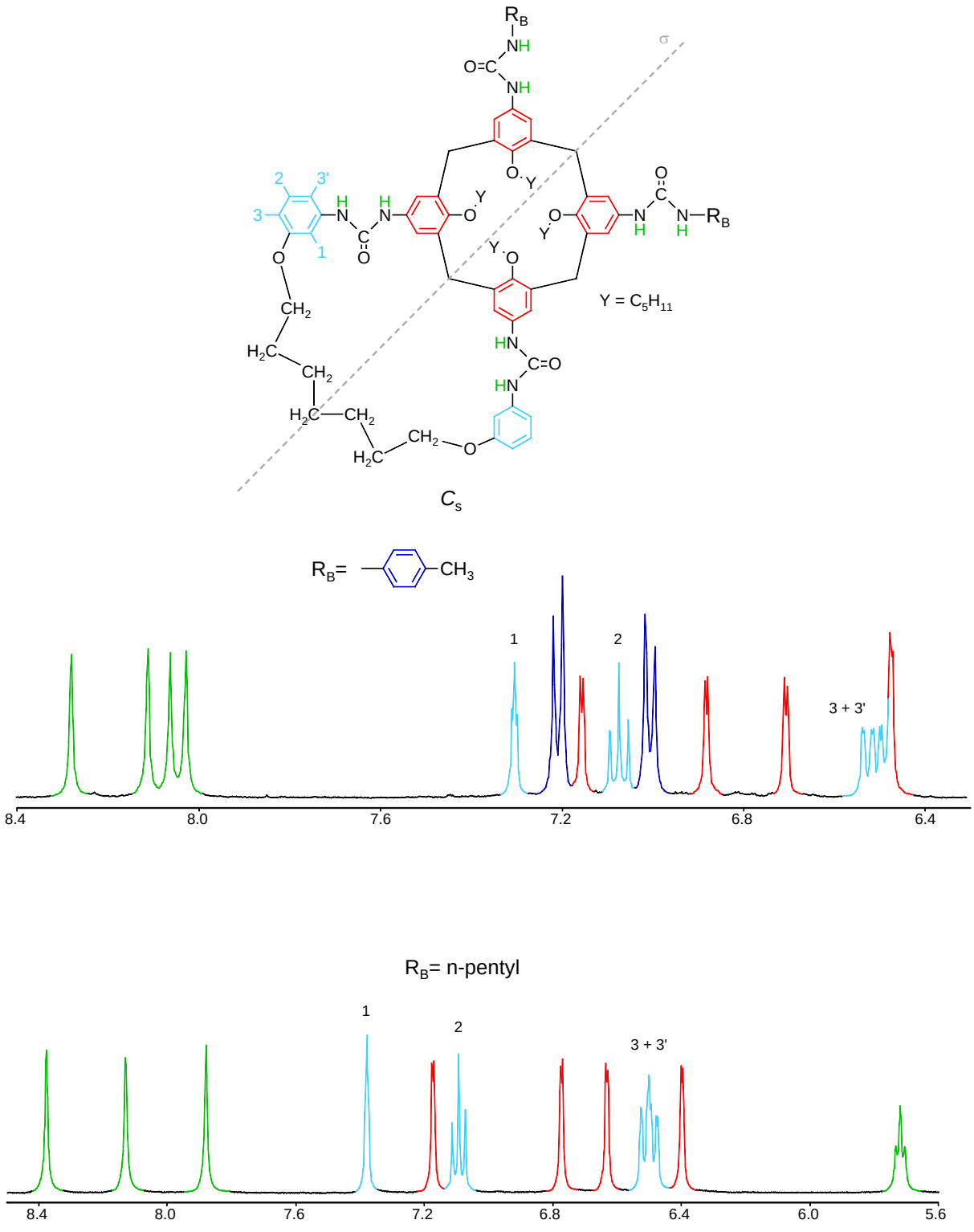


Figure 43: Sections of the ^{1}H NMR spectra of **26b** (up) and **26a** (down) in DMSO, 60°C; Different functional groups are marked by different colors: NH in green, calixarene skeleton in red, the phenyls of the loop in light blue and tolyl in dark blue.

Table 2: ^{1}H NMR spectra of mono-loop tetraureas in DMSO-d_6; chemical shifts (ppm) for selected signals. b = broad; s = singlet; m = multiplet

	25a	**26a**	**27a**	**25b**	**26b**	**27b**
NH	8.28	8.37	8.31	8.35	8.28	8.29
	8.01	8.12	8.04	8.22	8.11	8.10
	7.76	7.87	7.74	8.15	8.06	8.08
	5.66 t	5.71 t	5.67 t	8.15	8.02	8.01
Ar_{calix}-H	6.89	7.16	7.36	6.92 b	7.15	7.39
	6.74	6.76	6.83	6.83 b	6.88	6.94
	6.67	6.62	6.59	6.75 b	6.70	6.65
	6.64	6.39	6.28	6.66 b	6.47	6.30
Ar_{meta}-H	7.09	7.37	7.62	7.08	7.30	7.62
	7.07	7.09	7.09	7.03 s	7.07	7.08
	6.83 6.81	6.52-6.47 m	6.50 6.48	6.76 b	6.53 6.51	6.50 6.48
	6.49 6.47		6.37 6.35	6.47 b	6.50 6.47	6.30 6.28
R_B	3.04 m	3.04 m	3.1-3.05 m	7.21	7.20	7.20
				7.00	7.00	7.01

The dimer **I** of a mono-loop tetraurea should have C_1 symmetry (Figure 42) this means that each proton should give its own signal in the ^{1}H NMR spectra. Thus, the following signals are expected:

- overall 16 NH signals from which four for **25a** and eight for **25b** low-field shifted
- eight pairs of *meta*-coupled doublets for the calixarene moieties
- four sets of signals for the *meta*-disubstituted phenyl of the loop and corresponding signals for the aliphatic chain of the loop
- four sets of signals corresponding to the residues R_B.

The case that our prediction concerning the selectivity is not correct the spectra should be more complicated, showing a double set of signals.

^{1}H NMR spectra of **25a** and **25b** recorded in benzene-d_6 or chloroform-d_1 show signals in the expected area but they are not well resolved. Nevertheless, we could find important information in the region ~10 ppm. There are *eight* for **25b** in benzene (but not in chloroform) and *three* for **25a** (there are three signals in benzene and in chloroform in the

ratio 2:1:1 or 1:1:2 but the integration in both cases gives four protons) NH low-field shifted signals. By the number of signals we draw the conclusion that there is only one regioisomer formed. More information was found in gs-COSY spectra registered for **25a**. The 16 cross-peaks of calixarenes (8 on one side of the diagonal and 8 on the other) and eight corresponding to tolyl residues were found but the precise assignment in ^{1}H NMR spectrum of all this doublets was not possible. Figure 44 shows sections of the spectra of **25a** and **25b** in benzene.

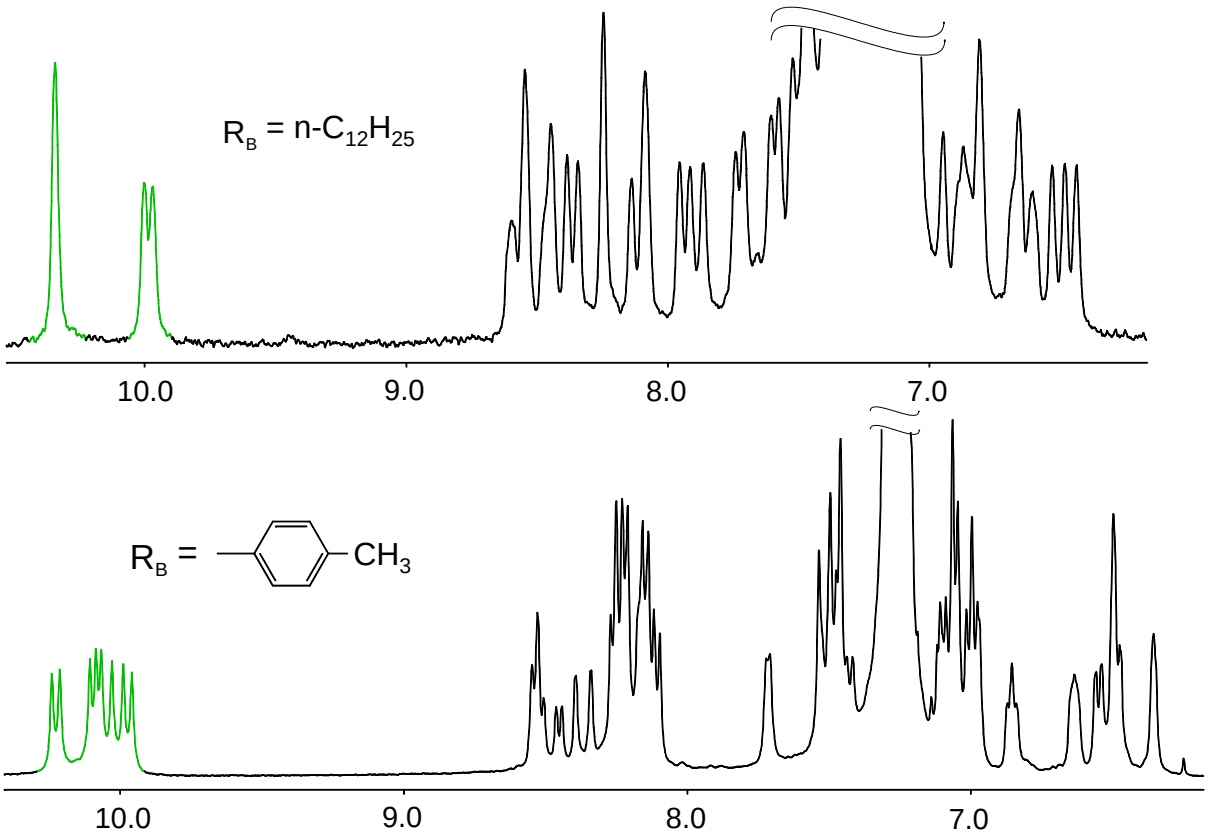


Figure 44: Section of the spectra of **25a** (upper) and **25b** (lower) in benzene-d_6. The green signals correspond to the NH. In the area from 8.7 to 6.2 ppm appear signals of the calixarenes, the aromatic part of the loops, tolyl (in the case of **25b**) and the solvent.

The complete interpretation of the spectra (in benzene-d_6 and in chloroform-d_1) was done for the mono-loop compounds with a shorter chain **26a** and **26b** (Figure 45). As expected for a dimer of **26a** having C_1-symmetry, there are four signals of NH around 10.0 ppm and 8 further singlets and three triplets (the fourth one is covered by the signal of benzene) were found in the region 8.1-6.5 ppm. All eight pairs of *meta*-coupled doublets of the calixarene (^{4}J ~ 2.3-2.6 Hz) were identified. For the aromatic part of the bridges four types of signals are found: four broad triplets with *meta*-coupling, four triplets with *ortho*-

coupling (partial overlapped by the signal of benzene), four doublets of doublets (not well resolved) and only three broad doublets of doublets while the fourth is covered by the signal of benzene.

A similar pattern is found for **26b** (Figure 45B). Additionally, signals of tolyl groups appear as AB-systems. The signals of NH (16, from which eight appear around 10 ppm) are all singlets. A section of gs-COSY spectrum of **26b** in benzene is shown in the figure 46 as an example.

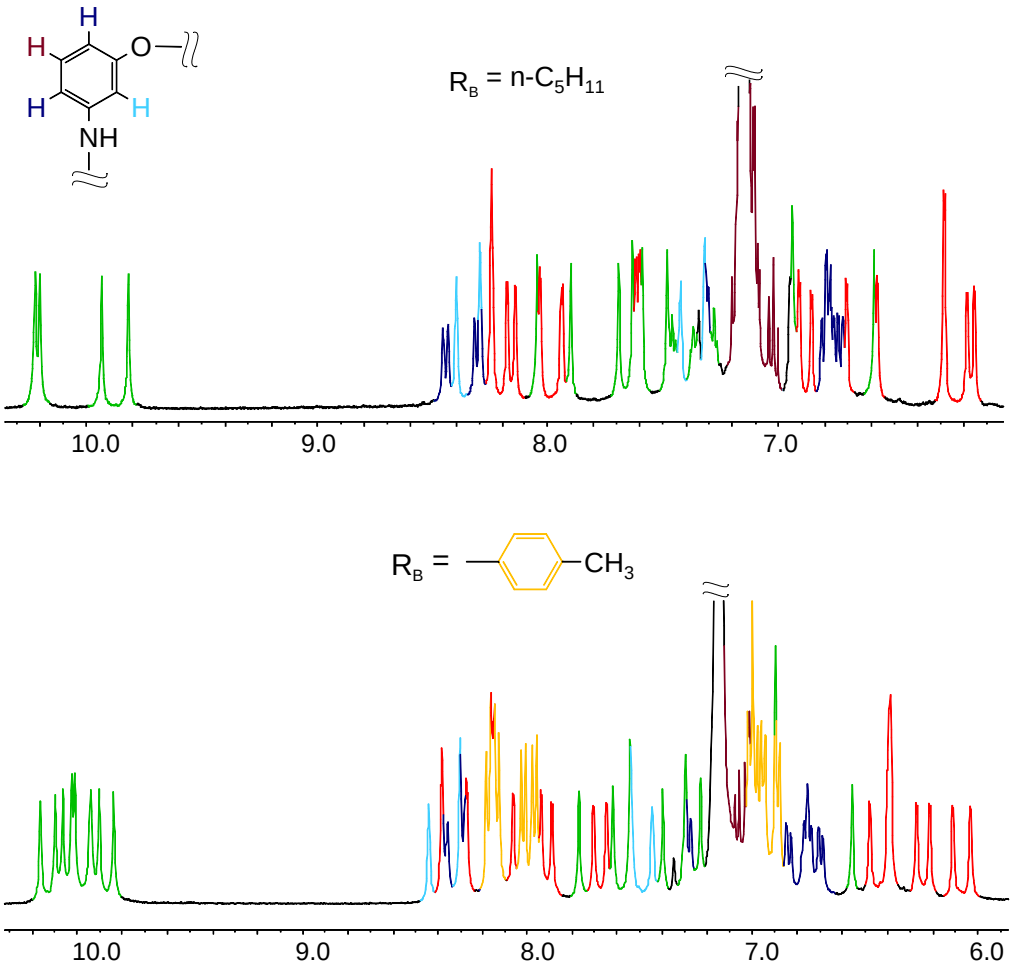


Figure 45: Sections of ^{1}H NMR spectra (400MHz, benzene-d_6) of **26a** (A) and **26b** (B). Different functional groups are indicated by different colors: NH green, calixarenes in red, aromatic part of the loops as indicated (light blue, dark blue and violet), tolyl in orange.

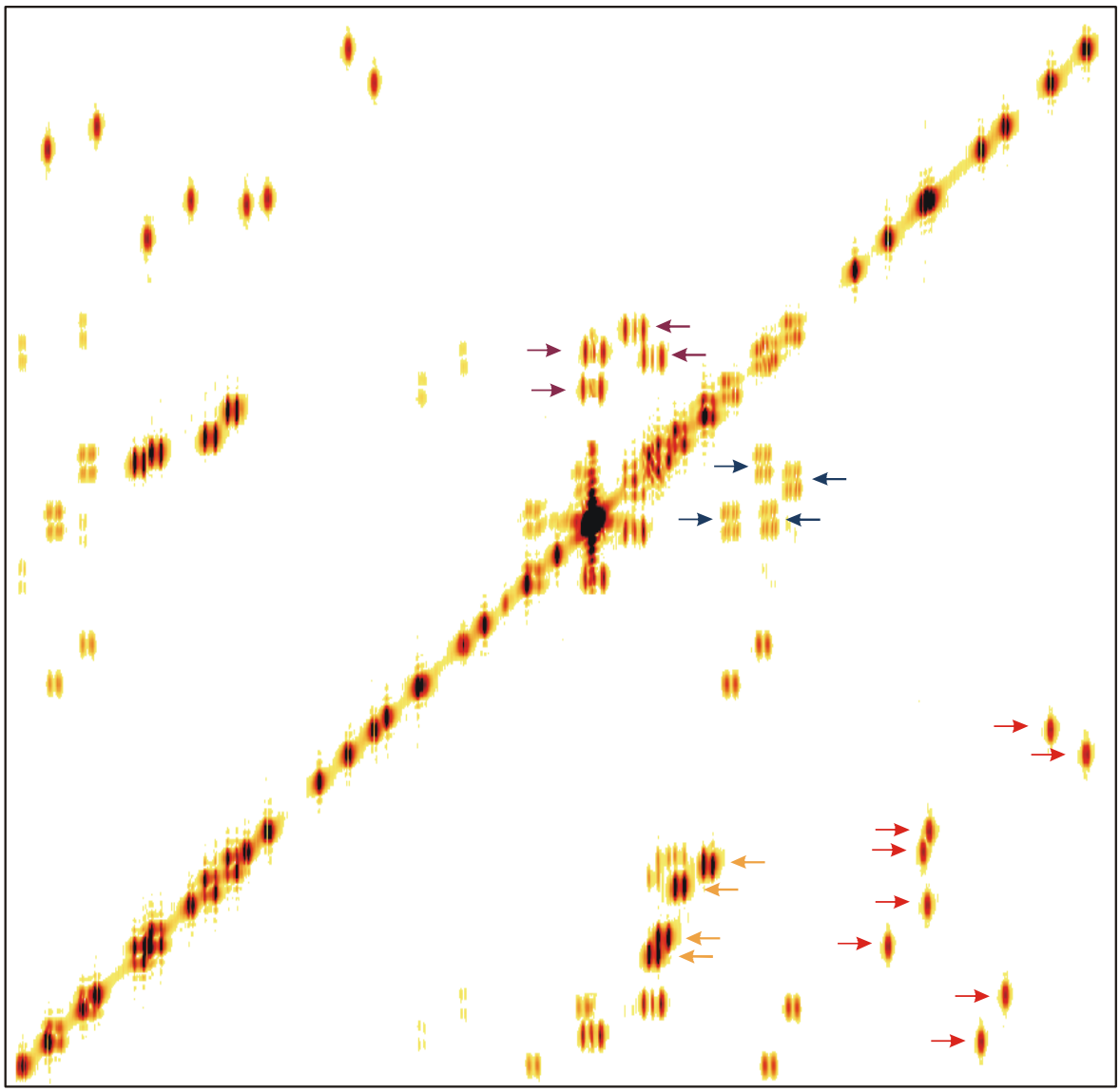


Figure 46: Section (8.5-6.0 ppm) of gs-COSY NMR of **26b** in benzene-d_6 proves the formation of a single dimer: there are 8 pairs of *meta*-coupled doublets (red arrows) belonging to the calixarene, four pairs of *ortho*-coupled doublets for tolyl groups (orange arrows), four triplets with *ortho*-coupling (violet arrows). Two of them are covered by the signal of the solvent in the ^{1}H NMR spectrum but they are identified through cross-peaks in gs-COSY. Four doublets of doublets are indicated with blue.

A different behavior was found for **27a** and **27b**. The solubility of the pure compounds in chloroform and benzene was much lower than that of previous mono-loop derivatives. Solutions of both compounds prepared in chloroform-d_1 remained turbid even after heating at 60°C for several days. Spectra measured for these samples are broad (Figure 47). There are few small signals (the intensities of them are much less than expected) indicating the formation of strong hydrogen bonds but the rest of the spectra do not allow any conclusion about capsule formation.

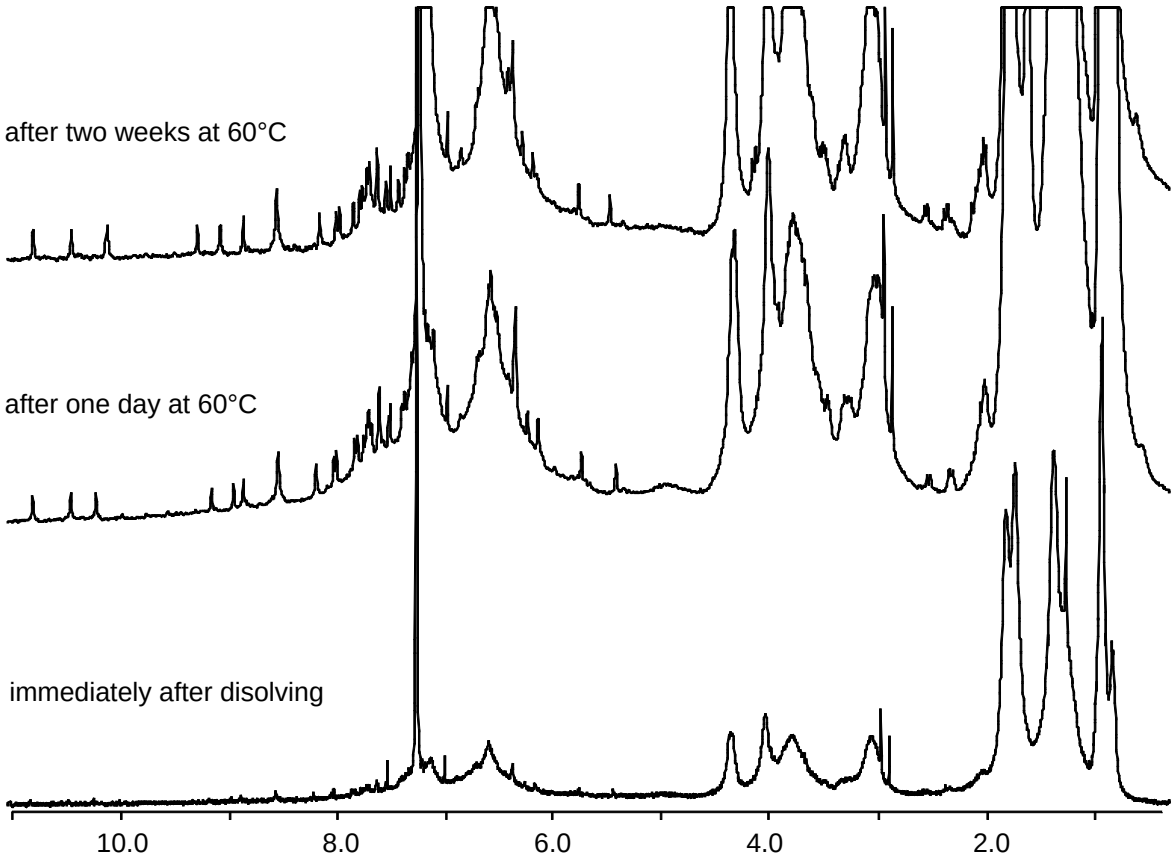


Figure 47: Spectra of **27b** in chloroform-d_1 showing broad signals.

When similar samples were prepared in benzene-d_6 and kept at 80°C for 4 days the mixture was still turbid. The spectra measured at room temperature for **27a** and **27b** are given in the figure 48. Analyzing the region around 10 ppm we observed the expected signals of NH: four in the case of **27a** (two overlapped) and eight for **27b**. All other parts of the spectra are not so well resolved because the parameters of measurement could not be adjusted properly (turbidity of the solution, low ratio signal noise). Nevertheless in the spectrum of **27b** at ~ 2.0 ppm there are four singlets which correspond to the methyl of the tolyl groups and they confirm that the dimer was formed after heating in spite of the low solubility.

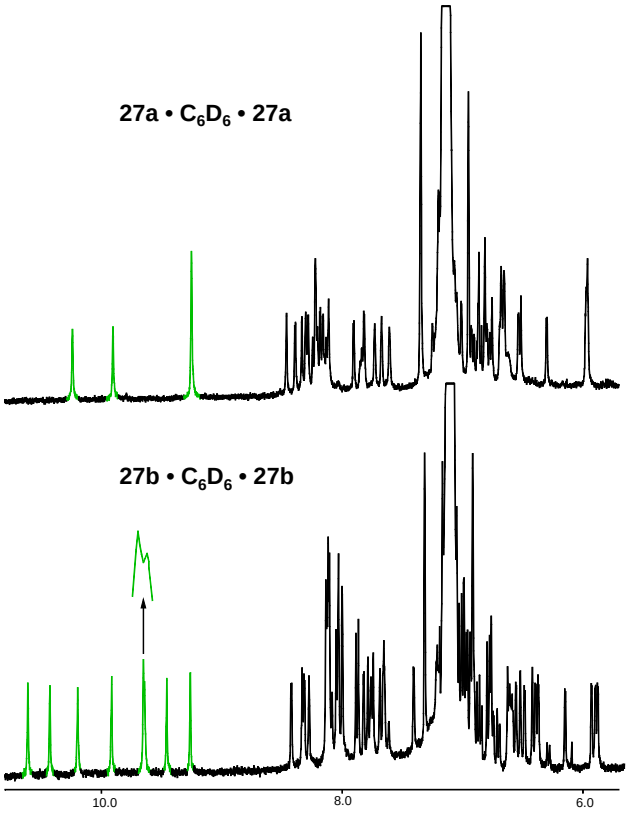


Figure 48: Sections of the spectra of **27a** (above) and **27b** (down) in benzene-d_6 measured at room temperature showing the two homodimers formed after prolonged heating.

With the results obtained for these mono-loop compounds with three different lengths of the bridge 10, 7 and 5 we could drawn some conclusions:

- mono-loop derivatives are forming only one homodimer of the expected structure **I**
- the chain length 10 allows the fast formation of dimer (immediately after dissolving) and it has some flexibility (some signals are broad)
- with a loop of 7 carbon atoms heating for several minutes is necessary and spectra of very good quality could be measured
- with 5 carbon atoms drastic conditions must be applied to overcome the kinetic problems. The loops are too small and they hinder the formation of the dimer
- We did not observe any different chemical property brought by the residue R_B.

Therefore, the chain length 7-10 carbon atoms are optimum for the synthesis of other loop derivatives which should be able to form dimers.

Additional evidence about the structure of the homodimer of mono-loop compounds is given by the syntheses of catenanes (explained in this chapter later and in the chapter Syntheses).

4.3.2 Di-loop derivatives

We have decided to complete the series by synthesizing compounds with two loops. The two synthetic routes are described in the chapter Syntheses. Such a compound has C_{2v}-symmetry in its monomeric form (in solvents like DMSO or THF) and this structure is supported by ^{1}H NMR spectra.

As expected and it is shown in figure 49, there are two singlets of the NH protons, two pairs of *meta*-coupled doublets for the protons of the calixarene aromatic moieties. The four signals of the phenyl ring of the loops are similar with the signals described for mono-loop derivatives. The first protons from the aliphatic part of the loops appear at ~ 3.9 ppm and they are overlapped by the signals of the pentyl chains of the narrow rim. The *equatorial* protons of the methylene bridges appear, as expected; as two doublets with *geminal*-coupling while the *axial* ones show just one doublet. This feature may be explained by the fact that the *equatorial* protons (because they are closer to the urea part of the molecule) feel the structural differences better than the *axial* protons which are facing the narrow rim. In the region of 2.0-1.0 ppm signals of the pentyl chains and the rest of the loop appear but they are not well resolved and partially covered by the signals of the solvent.

The compound with smaller loops **28b** (n=7) shows a similar spectrum in tetrahydrofurane-d_8 with the exception of some broad signals.

These compounds are sparingly soluble in apolar solvent such as benzene-d_6 or chloroform-d_1. The ^{1}H NMR spectra recorded shown broad featureless signals supporting our expectations that they will not homodimerize. To the mixture of **28b** in benzene-d_6 stoichiometric amount of tetratolylurea **20a** was added and after several hours the mixture became clear and ^{1}H NMR spectrum was recorded (Figure 50).

Urea functions will form hydrogen bonds with any other suitable groups from the environment (e. g. solvent, or other urea molecules). In chloroform, only urea functions from other calixarenes are available for hydrogen bonds, but the two loops do not allow the formation of well defined homodimers. Thus ill defined aggregates involving an indefinite number of molecules are possible. The spectrum in chloroform could be interpreted in this way.

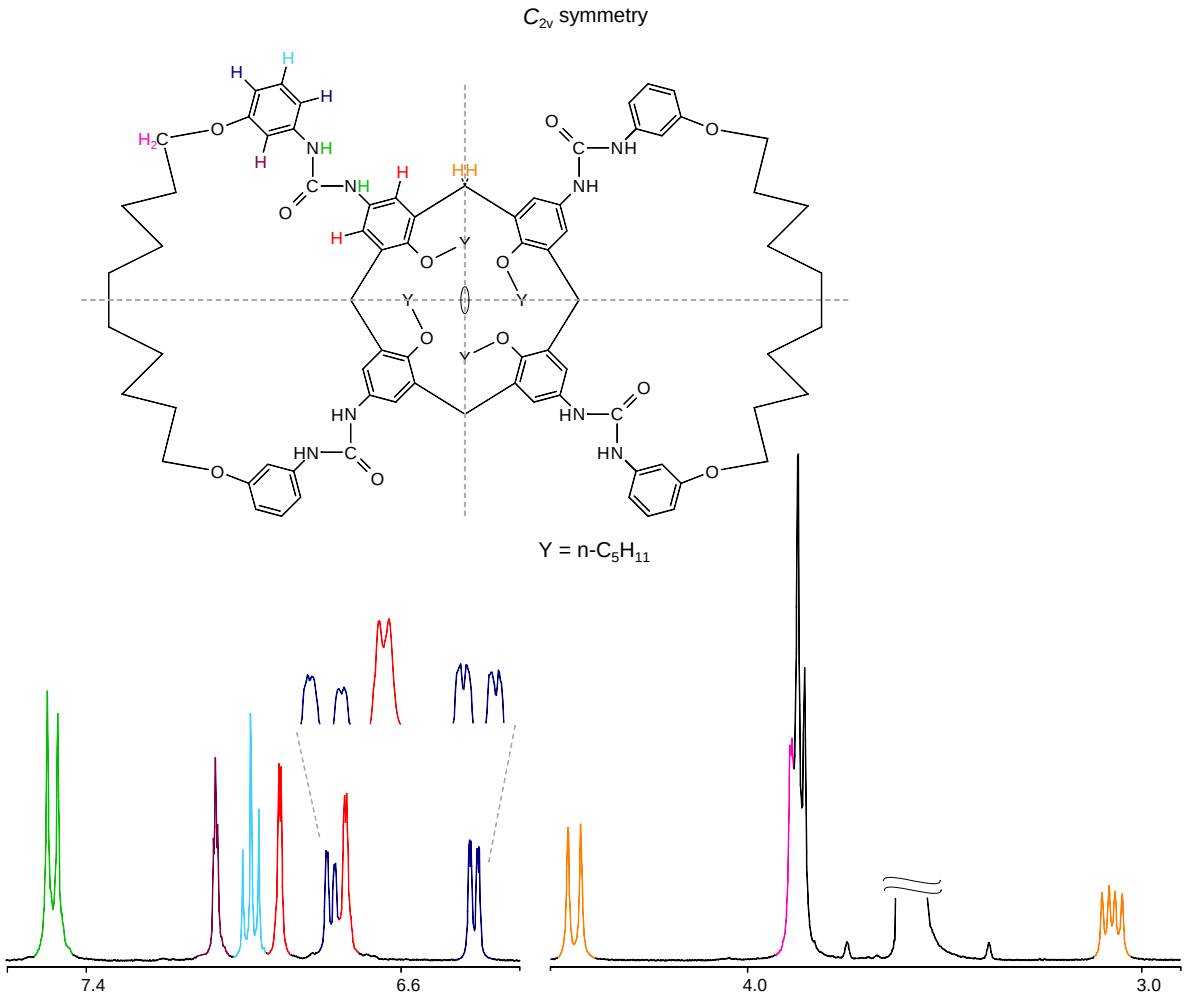


Figure 49: Sections of the ^{1}H NMR spectrum of **28a** (400 MHz, tetrahydrofurane-d_8, 25°C). Signals are indicated in different colors: NH (green); calixarene (red); phenyl ring of the loop (light blue, dark blue and mauve); methylene bridges (orange); first methylene groups –OCH_2– of the loop (pink).

By adding the stoichiometrical amount of tetratolylurea the situation is changed. Now, each molecule of the di-loop compound has a counterpart suitable for the formation of a well defined dimer with the circular array of 16 hydrogen bonds. This fact is observed by two aspects: first, the compound is solubilized in benzene, and the second, the ^{1}H NMR spectrum shows nice resolved peaks, characteristic for a heterodimer as in figure 48 which shows the spectrum of the heterodimer of **28b** and tetratolylurea **20a** in benzene.

This kind of heterodimer should possess C_2-symmetry, with the C_2 symmetry axis perpendicular to the plane of the hydrogen bonds. As an indication of this associate, 8 low-field shifted signals of NH, four pairs of *meta*-coupled doublets for the calixarene, two AB-systems for tolyl residues, and two sets of four signals (*meta* substituted phenyl ring) corresponding to the loops, should appear. The signals of the methylene bridges are very

well resolved in this case. The small signals in black belong to small amount of homodimer of tetratolylurea (which obviously was present in slightly excess).

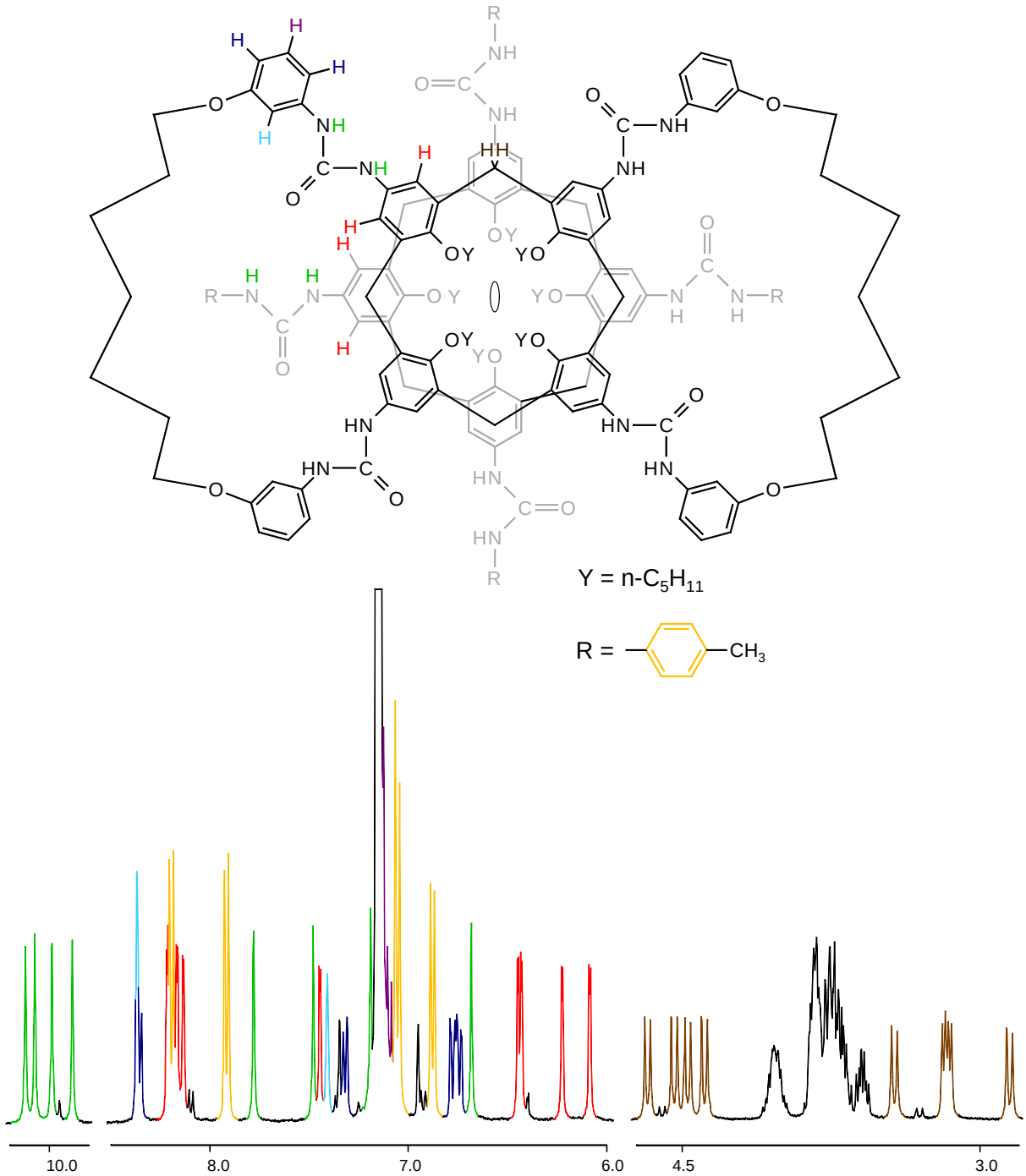
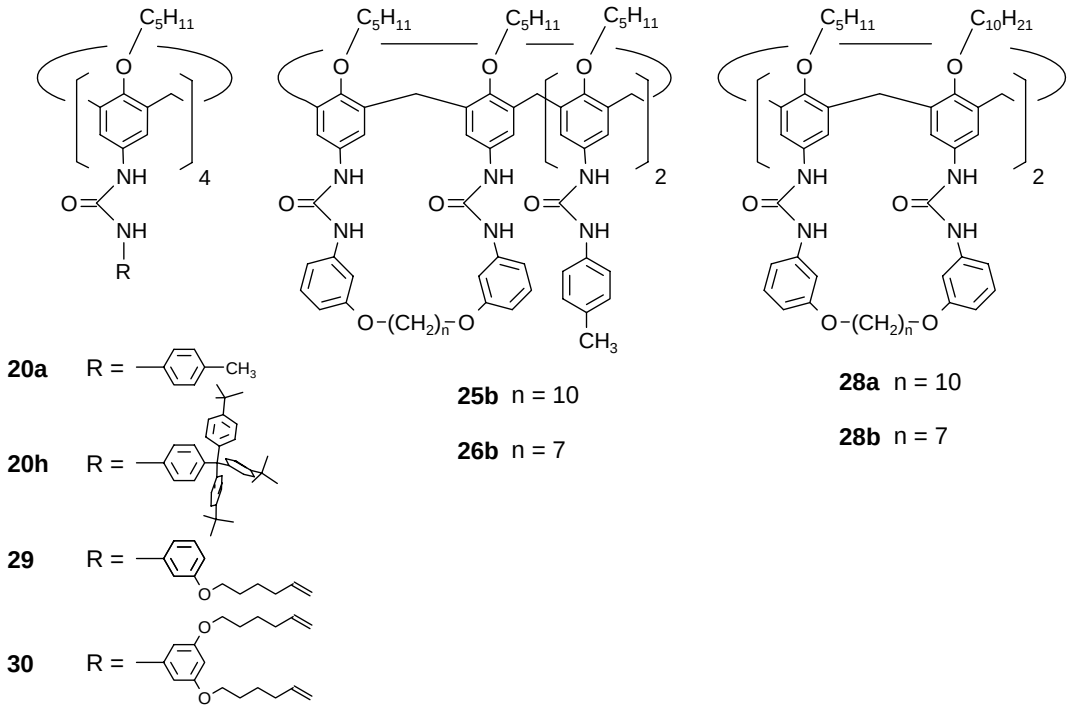


Figure 50: Sections of the ^{1}H NMR spectrum of the heterodimer **28b•20a** in benzene-d_6. The functional groups are distinguished by different colors as indicated.

4.4 Heterodimerization experiments

4.4.1 Programmed self-assembly



Scheme 15: The three classes of compounds used in the heterodimerization experiments

The compounds which we have synthesized could be divided in three classes: open-chain tetraureas, mono-loops and di-loops (Scheme 15).

The open-chain and mono-loop compounds can homodimerize and heterodimerize while the di-loop derivatives can just heterodimerize.

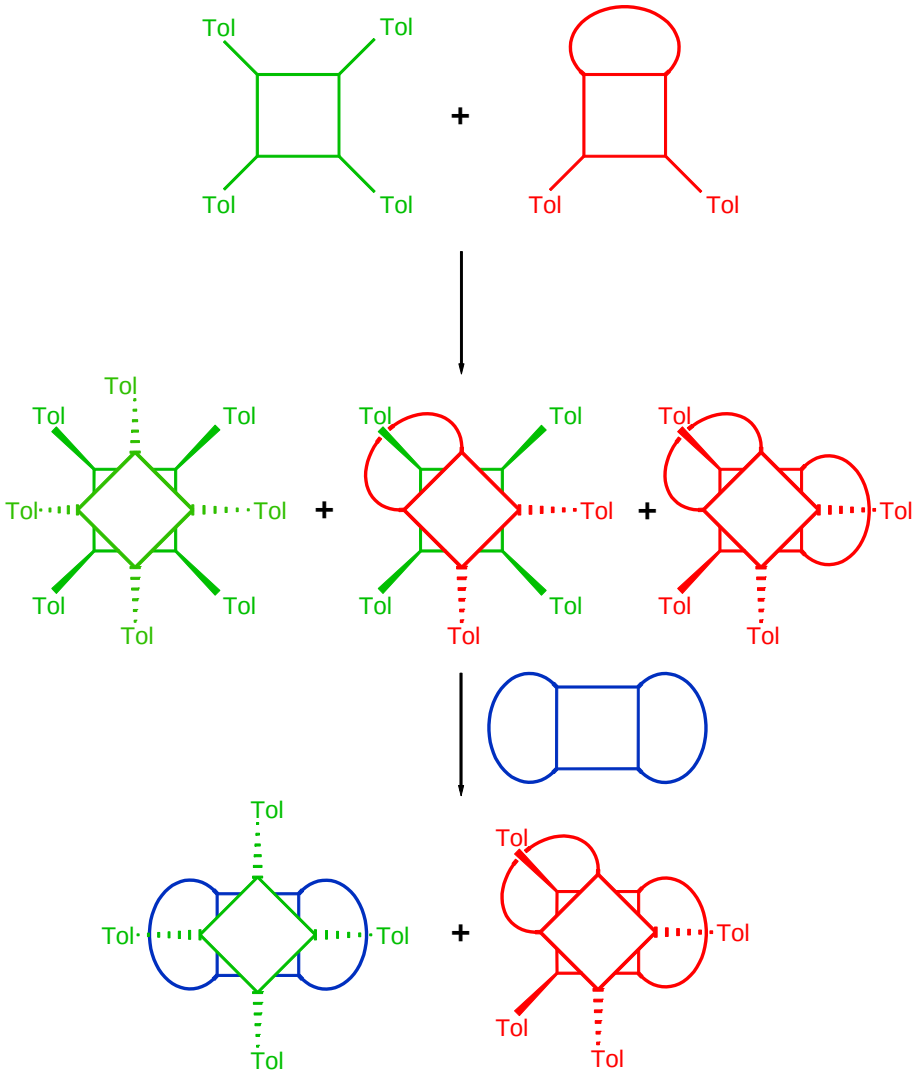
We already know that mono-loop derivatives (R = tolyl) are able to homodimerize.Thus, heterodimers between mono-loop and **20a** are expected to be formed. In deed, figure 51 shows the spectrum of the mixture **25b** and **20a** in benzene-d_6. As expected, the equilibrium mixture contains both homodimers and the heterodimer although the ratio between them is difficult to estimate because most of the signals are partially overlapped and an accurate integration was not possible. We get this conclusion after analyzing in details the section from 10.2-9.8 ppm of the ^{1}H NMR spectra of the mixture and of the pure compounds. The homodimer **20a•20a** has S_8 symmetry and shows one signal (Figure 51A), while **25b•25b** has C_1 symmetry and eight signals in that area (Figure 51B). The heterodimer has, as well, C_1 symmetry and further eight signals are expected. In the figure 51C the signals which belong to the two homodimers are marked in different

colors (red and green). Analyzing the intensity of the signals we drawn the conclusion that the signals marked in orange correspond to the heterodimer.

Now, the question is how we could shift the equilibrium in a way to simplify its composition?

The answer to our question is a di-loop derivative. Therefore, to the equilibrium mixture of **25b** and **20a** a stoichiometrical amount of **28a** was added. **28a** can just heterodimerize so, it is supposed that will form heterodimer with **20a** (**20a** being the only component from that mixture able to heterodimerize with a di-loop compound). This means that the **20a•20a** and the **25b•20a** will be consumed in the formation of the heterodimer **28a•20a**, while **25b** will homodimerize. From the initial mixture, by adding the third compound, we would get a mixture of one heterodimer **28a•20a** and one homodimer **25b•25b**.

Scheme 16 gives a graphical explanation of the experiment described above.



Scheme 16: Graphical explanation of the equilibrium experiment

Figure 51D shows the spectrum measured for the mixture after adding of **28a** (the mixture became clear solution again after ~ 12 hours at 50°C). For a complete image we have measured the spectrum of the heterodimer **28a•20a** in benzene and it is presented in figure 51E. The symmetry class of heterodimer **28a•20a** is C_2, what means that the section around 10 ppm should show four signals of NH urea protons. In practice, we observed just three signals but the integration of them shows that the highest one corresponds to two protons.

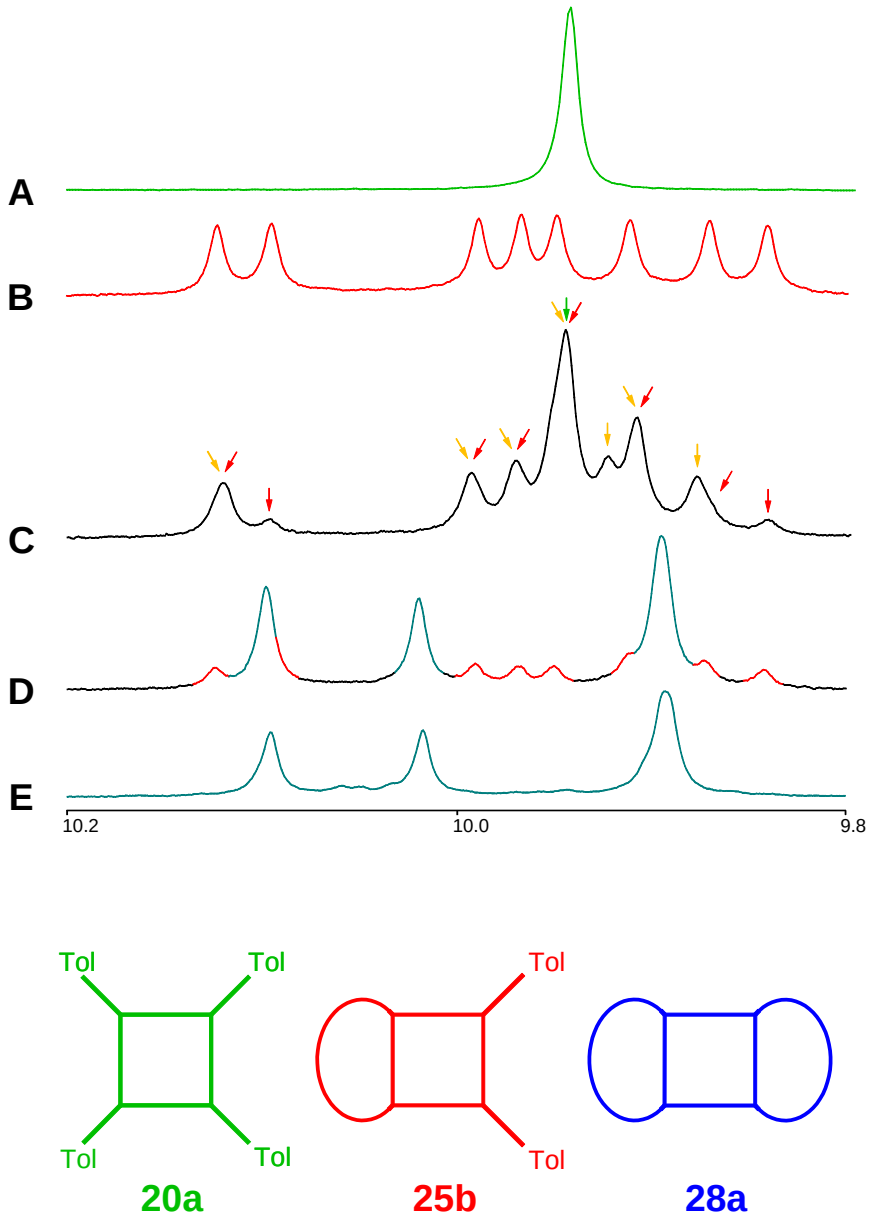


Figure 51: Sections from 10.2 to 9.8 ppm of ^{1}H NMR spectra in benzene-d_6 of A) homodimer **20a•20a**; B) homodimer **25b•25b** ; C) mixture of **25b** and **20a** consisting in two homodimers **20a•20a** and **25b•25b** marked with red and green arrows, respectively and one heterodimer **25b•20a** marked by orange arrows; D) the mixture after addition of **28a**, reduced to one homodimer **25b•25b** and one heterodimer **28a•20a**; E) heterodimer **28a•20a**.

Now, by comparing E + B with D in the figure 51 we have seen that the signals in D are in exactly the same position as in "isolated" dimers. The different intensity of the signals comes from the fact that the two species have different concentrations and different symmetries. The final mixture has the ratio among the three components 1:1:1. **28a** with **20a** form heterodimer while **25b** gives homodimer so the concentration of the homodimer is half to the concentration of heterodimer. On the other side the number of signals is different in homodimer to heterodimer as was already explained in the discussion about symmetry. The intensity of the peaks in the spectrum (figure 51D) fits well with the relative concentration of the dimers in the solution and with their symmetry.

Therefore, the results obtained in our experiment totally confirm our predictions/ expectations. Starting with a complex mixture of three dimers obtained from two tetraureas, by adding the third compound, the mixture became "simpler" containing only two dimers.

4.4.2 Size selectivity

We have studied the influence of the size and shape of the residue R in open-chain tetraureas in the heterodimerization with di-loop derivatives. The heterodimer **28b•20a** was already presented and discussed in details while figure 51E contains a section of the spectrum of the heterodimer **28a•20a**, so, the tolyl group has a shape and/or size which allows to slip through the loops, as was expected by the homodimers of mono-loop derivatives.

In the other experiment we have demonstrated that the mono-loop compound **25b** forms heterodimer with **20a** even if the heterodimer is not the only dimer formed. As a confirmation, in the figure 52A we present a section of the spectrum of the mixture **26b** and **20a**. The heterodimer is formed (not exclusively) even if the loop is shorted.

The spectrum measured for the mixture **28a** and **20h** in chloroform is shown in the figure 52B. It is obviously that the heterodimer is not formed. The sharp signals belong to the homodimer **20h•20h** while the broad ones represent the aggregate of **28a**. This means that the residue tritylphenyl is too large and can not slip through the loop of **28a**. Because the compound **28a** has the largest loop in this series we did not check the heterodimers of **20h** with other loop derivatives.

The residue R in compound **29** contains an 1,3-disubstituted phenyl ring, while a 1,3,5-trisubstituted ring is present in **30**. We supposed that our loop derivatives will feel this difference.

A 1:1 mixture of **28a** and **29** in benzene was kept at 60°C for 2-3 hours after which a clear solution was formed. The spectrum in benzene-d_6 (Figure 53A) proves the formation of the heterodimer.

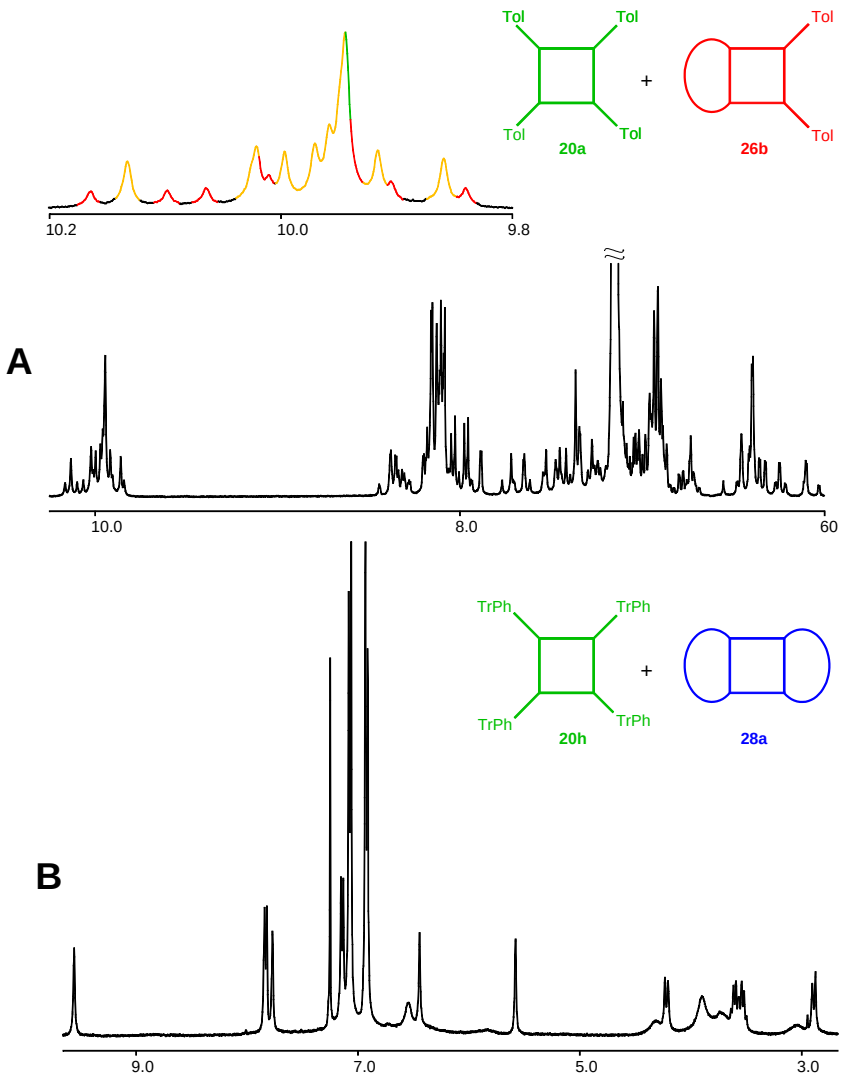


Figure 52: A) Section of the spectrum of a 1:1 mixture of **26b** and **20a** in benzene-d_6 at room temperature. The signal in green indicates the homodimer **20a•20a**, red signals are assigned for the homodimer **26b•26b** and orange signals for the heterodimer **26b•20a**. B) Spectrum in chloroform-d_1 of the mixture of **28a** and **20h** showing clear signals for the homodimer **20h•20h** and broad signals for **28a**.

When **28a** and **30** were mixed (in ratio 1:1) in benzene-d_6 a turbid solution was formed. This mixture was kept at 60°C for 8 days, and for a sample the ^{1}H NMR spectrum was measured (Figure 53C). One can see that the heterodimer **28a•30** is formed but the homodimer **30•30** still exists in the solution.

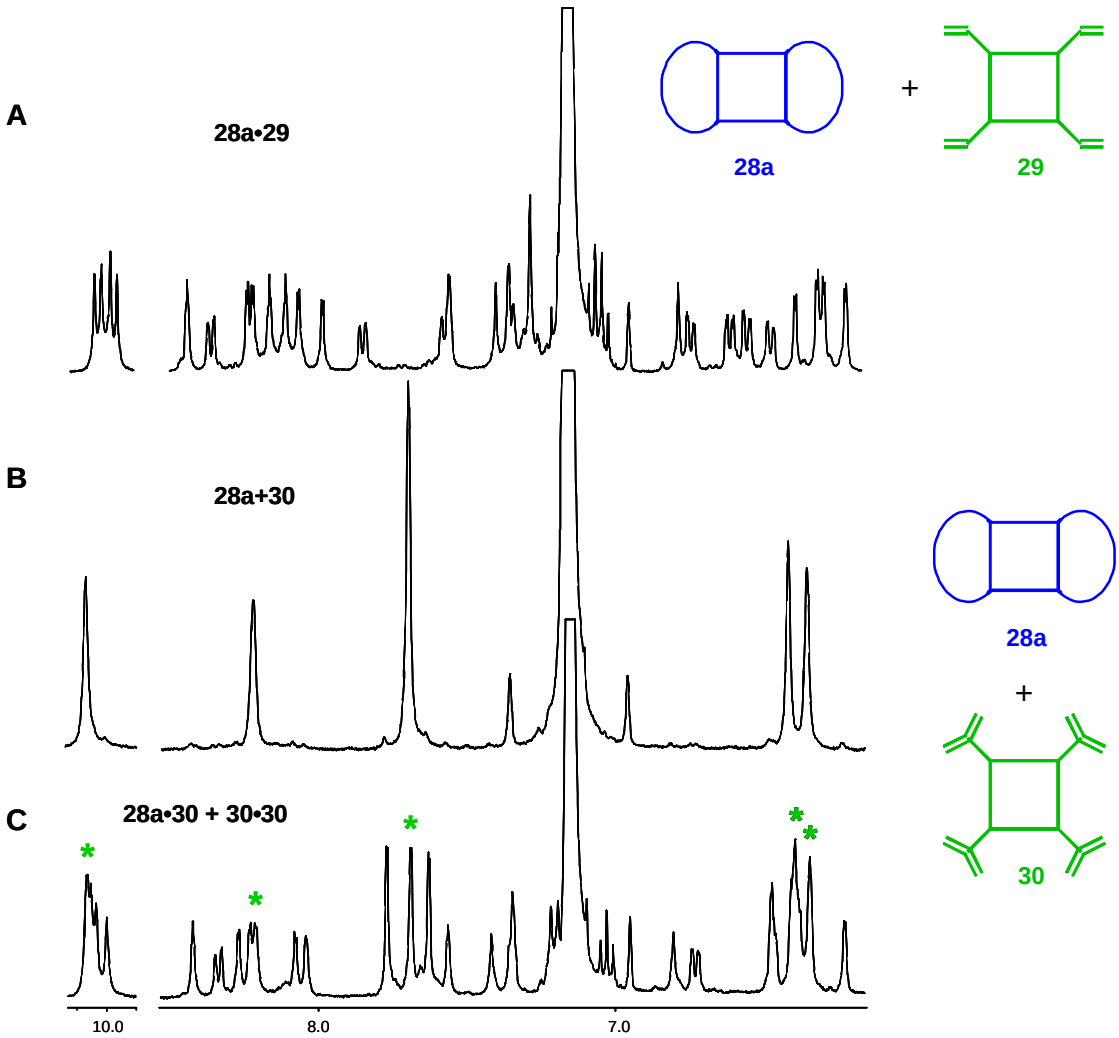


Figure 53: Spectra in benzene-d_6 of A) heterodimer **28a•29** obtained after heating the 1:1 mixture for one day at 60°C; B) the mixture of **28a** and **30** after one day at 60°C showing the homodimer **30•30**; C) the mixture after 8 days at 60°C. Signals marked with asterisk belong to the homodimer **30•30** while the others to the heterodimer **28a•30**.

We have tried to obtain similar heterodimers from the bis-loop compounds with shorter loops **28b**. The heterodimer **28b•29** was obtained when the mixture was kept in benzene-d_6 at 80°C for one day, while **28b•30** could not be seen in the spectrum even after the samples was kept two weeks at 80°C. This facts lead to the conclusion that the loop with seven carbon atoms can differentiate between the residue with one arm or two arms in *meta*-position of the phenolic ring.

From these experiments we could drawn some conclusions:

- a di-loop derivative is able to shift the equilibrium of other dimers
- the ability of di-loop compounds to form only heterodimer prevents undesired homodimerization

- the size and shape of the residues in open-chain tetraureas or mono-loop compounds has a decisive role in the formation of dimers.
- the length of the loop can be chosen in a way to favor one dimer over the other

These features can be used in construction of larger assemblies based on tetraureas.

In this work we present just the way how we synthesized catenanes in very good to excellent yields. The strategies are based on the features described above.

4.5 Catenanes

We developed two strategies for the synthesis of bis-[2]catenanes. They are described in the chapter Syntheses. Here we present the spectral data of the precursors and of the final products.

The formation of the heterodimer **28a•29** was already discussed and its C_2 symmetry is proved by the number of the NH signals. The rest of the signals are not so well separated. There are two multiplets attributed to the four double bonds at 5.7 (=CH-) and 4.9 ($=CH_2$) ppm. The product obtained after metathesis reaction, hydrogenation and column purification has, as well, C_2 symmetry proved by the ^{1}H NMR spectrum (Figure 54). There are four NH singlets low-field shifted (~9.5 ppm in chloroform-d_1 and ~10 ppm in benzene-d_6) and four further singlets partially overlapped with signals of the *meta*-substituted phenyl ring of the loops. Four well resolved pairs of *meta*-couplet doublets (^4J = 2.3-2.5 Hz) appear for the aromatic protons of the calixarene. Four sets of signals corresponding to the aromatic part of the loops were found and they are marked in the figure 54. In the region 3.4-3.0 ppm (spectrum in benzene-d_6, not shown in the figure 54) four doublets with geminal coupling (^2J = 11.5-11.8 Hz) are attributed to the equatorial protons of the methylene bridges while the corresponding axial protons are not so well resolved.

The same compound should be obtained from the homodimer **25c•25c**. The dimerisation abilities of mono-loop compounds were discussed earlier. The main difference in **25c** is the *meta*-substituted phenyl ring of the R_B residue. The ^{1}H NMR in benzene-d_6 demonstrates that it gives a similar homodimer like **25b** in the same conditions (the homodimer **25c•25c** is not shown because a much better spectrum was obtained for **26c** and shown in the figure 56).

The bis-[2]catenanes obtained by the two methods were compared by physical (melting point) and chemical (spectra) methods and they are identical.

Bis-[2]catenanes **31** are "permanently" chiral and cannot racemize when the hydrogen bonds between the urea functions are broken. In hydrogen bond breaking solvents the symmetry become D_2 but the structure remains chiral. Consequently their enantiomers can be separated by chromatography on chiral stationary phases. For **31** this is illustrated in figure 55.

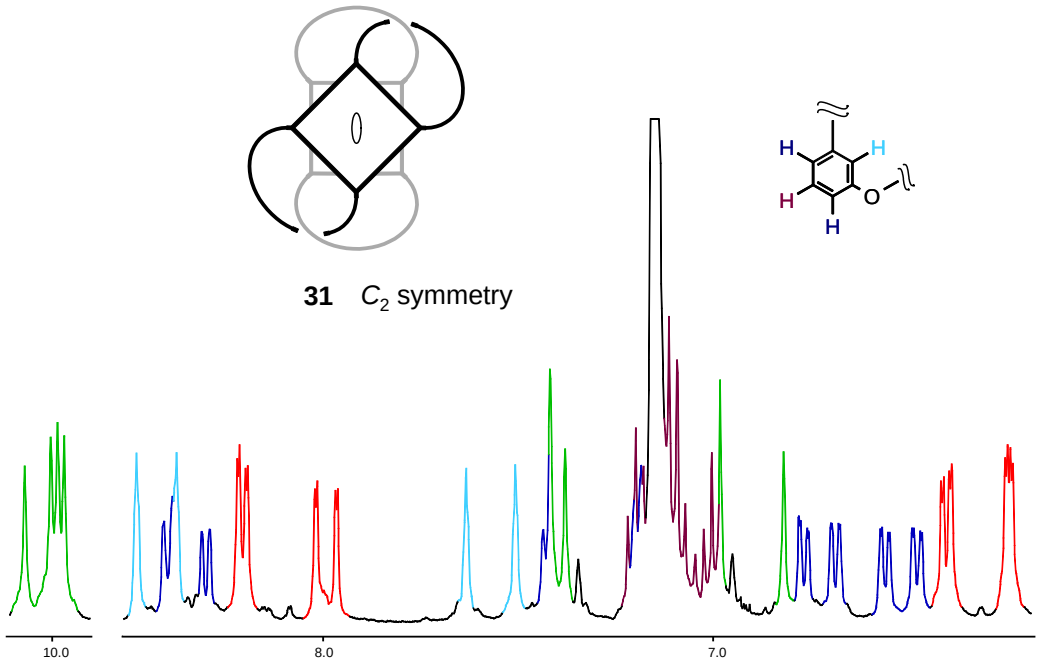


Figure 54: Aromatic region of the spectrum in benzene-d_6 of bis-[2]catenane **31**. The signals are drawn in different colors: green NH, red calixarene skeleton, and the signals of the aromatic part of the loops as indicated.

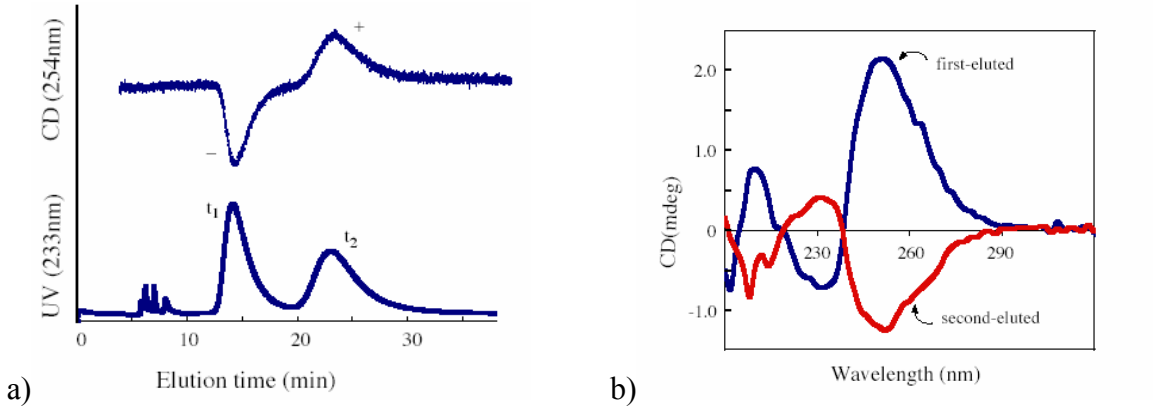


Figure 55**:** a) Chromatographic separation of **31** column: Chiralcel OD, eluent: hexane/ethanol (90/10, v/v), flow rate: 0.5 mL/min; b) CD-spectra of both fractions, proving that they consist of enantiomers, solvent: hexane/ethanol (90/10, v/v), cell length: 25 mm.

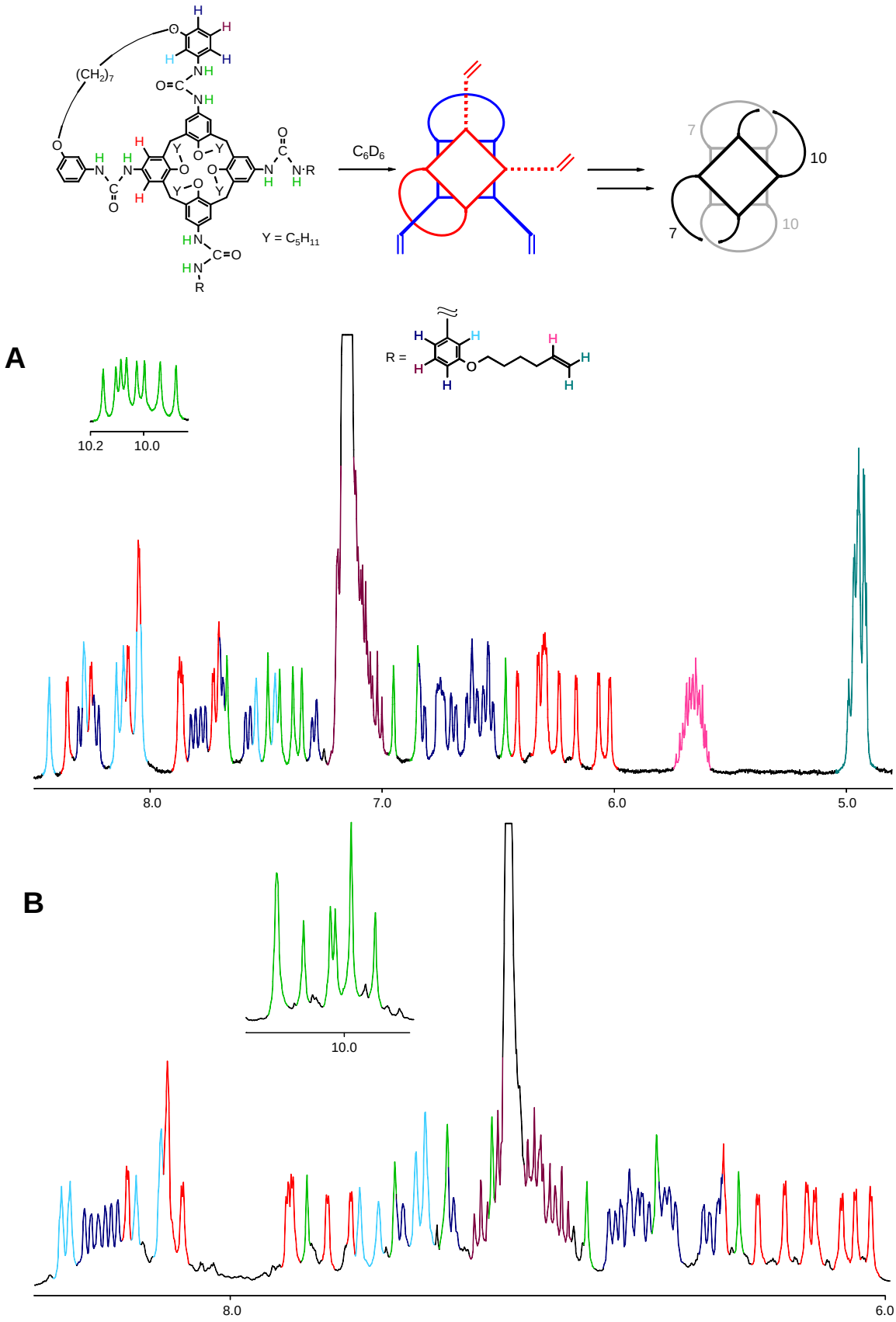


Figure 56: Spectra in benzene-d6 of the homodimer **26c•26c** (A) which is the precursor of the bis-[2]catenane **32** (B).

From the homodimer **26c•26c** was obtained other bis-[2]catenane. The behavior of **26c** is similar to **26b** and the homodimer is formed in benzene-d_6 (Figure 56A). The bis-[2]catenane **32** has two different lengths of the loops, and they are arranged in such a way that the whole molecule has C_1 symmetry. This is confirmed by the NMR spectra (Figure 56B). In the spectrum of the catenane **32** there are small signals of impurities which could not be completely separated from the crude product after metathesis and hydrogenation. In the mass spectrum of this compound (ESI-MS) we found the peaks for M^+= 3077.8, $M+Na^+$ = 3102.8 and $M+Na^+$+$CHCl_3$ = 3222.7. Additionally two peaks could not be explained and they are with 218 and 217, respectively, higher mass than the corresponding peaks $M+Na^+$ and $M+Na^+$+$CHCl_3$. We supposed that it is a second compound produced during the metathesis having a similar structure that is why we have difficulties to separate them.

We are now concentrated on improving the reaction and purification conditions to get catenanes as pure compounds with good yields.

5. Summary

We have elaborated a multistep strategy to synthesize ABAB-type tetraureas. There are overall nine steps but they involve very simple chemistry. The sequence starts with a 1,3-dialkylation and this is the step in which a difference between distal phenolic units is introduced. The selective *ipso*-nitration in the next step is based on the difference in reactivity between free phenolic units and alkylated ones. Alkylation of the nitrophenol units must be done with more active halides (e.g. methyl iodide, allyl bromide, ethyl bromoacetate). Hydrogenation to amino derivatives and reaction with phthalic anhydride leads to phthalimide compounds which were *ipso*-nitrated with good yields and without observable side reactions. After this step we have a compound with two distal phthlimido units and two nitro groups. Four additional steps (phthalimide deprotection, acylation, hydrogenation and the second acylation) give the desired ABAB tetraureas.

We have synthesized tetraureas with the ABAB pattern only in the urea rim as well as compounds where it occurs in the urea and ether rim at the same time. For all these compounds the formation of dimers with the expected symmetry has been proved by NMR-spectroscopy. Samples of this type were sent to Japan (Prof. Okamoto group) were optical resolution of the compounds was attempted by chromatography, using chiral stationary phases. Up to now, satisfactory conditions for the separation could not be found.

If the sequence starts with selective mono- or 1,2-dialkylation the final compounds would have the ABBB or AABB pattern, respectively.

The direct reaction of tetraamino calixarene with tolylisocyanate appears not to be an appropriate method to synthesize 1,3-ditolylurea calixarenes but can be used to get tetraureas of ABBB- and AABB-types in two steps with yields of about 60%.

Based on the information obtained from the heterodimerization of trityl- and tolyltetraureas (four identical residues in each calixarene) we have chosen these residues to induce regioselectivity in the dimerization of ABBB compounds. In fact a monotrityl-tritolyl compound gives only one set of ^{1}H NMR signals corresponding to one capsule when it is dissolved in benzene or chloroform. This definitely proves that only one regioisomer is formed. Although the NOESY spectra have too low resolution to establish which regioisomer is formed, it seems likely, that the two bulky groups are not adjacent.

A complete regioselective dimerization was obtained with mono-loop derivatives in which two adjacent urea residues are covalently connected. As predicted/expected the loop prevents the formation of one regioisomer, and only the dimer in which the open-chain

residue slips through the loop is formed. To synthesize mono-loop tetraureas 1,2-diBoc protected tetraamino calixarene was acylated with activated di-urethanes under high dilution conditions. The active urethanes were synthesized in three steps from the corresponding α,ω-dibromides and *meta*-nitrophenol. For longer alkyl chain the yield of this step is quite good (74%) but is significantly lower for shorter chain. This tendency can be explained by an increasing sterical tension in the molecule with the smaller ring. Cleavage of the protecting groups and formation of the other two urea functions was possible with yields of about 90-95%.

Di-loop compounds were synthesized by two different ways. In the reaction of tetraamine and di-urethanes the yield is about 30-40%. For loops of 7-10 carbon atoms this method is still reasonable. In the case of even shorter loops the method gives low yields and the reaction mixture is difficult to separate.

The second method to obtain di-loop derivatives is based on the metathesis reaction within a suitable heterodimer. For this strategy, tetraurea derivatives with residues which have terminal double bonds were prepared. The exclusive formation of the heterodimer with tetratosylurea as template is the key point in this strategy. Metathesis followed by hydrogenation give exceptionally good yields (> 80%) of the loop compounds.

All the NMR data for di-loop compounds confirm that the loops prevent the interaction of the urea residues which are connected and thus, as expected, the di-loop derivatives do not form homodimers. The heterodimer between di-loop compounds and tetratolylurea (open-chain tetraureas) was the only species observed for a 1:1 mixture in benzene or chloroform.

We have learned more about the selectivity of the mono-loop and di-loop derivatives by realizing two experiments. A 1:1 mixture of an open-chain and mono-loop tetraurea consists of two homodimers and one heterodimer. After addition of a di-loop derivative, the final mixture contained only two species, the homodimer of the mono-loop derivative and the heterodimer from open-chain tetraurea and di-loop compound. In a second experiment, compounds with residues different by size or by shape were mixed and we checked how fast the heterodimer is formed. The conclusion was that the loop derivatives can differentiate size and shape of the open-chain substituents. Based on these with these three classes of tetraureas larger self-assembled structure can be built up selectively in the future.

The rational synthesis of bis-[2]catenanes was a consequence of the selective formation of one regioisomer of mono-loop derivatives and the exclusive formation of heterodimers

by di-loop derivatives. The formation of interlocking-ring in the synthesis of bis-[2]catenanes is an additional evidence that one open-chain residue slips through the loop in mono- or di-loop derivatives. Exceptionally good yields in the synthesis of bis-[2]catenanes are due to the high preorganization in the dimer which undergoes the metathesis. This preorganization decreases the number of the wrong connections and favors the new connections to be formed. Although the procedure for working up the reaction mixture should be still improved, these results are promising.

A C_2-symmetrical bis-[2]catenane was successfully resolved by column chromatography using a chiral stationary phase. Thus it should be possible to separate a larger amount to obtain pure enantiomers for further studies.

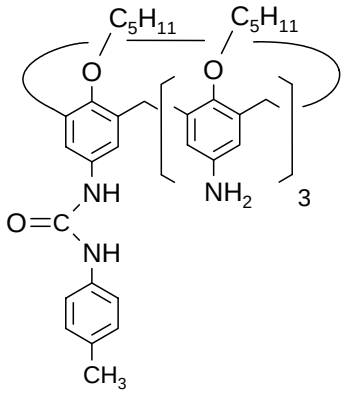
6. Experimental Part

DMF (peptide synthesis grade) was purchased from ACROS. Dichloromethane (p.a. grade) was kept over sodium hydroxide for one day before it was used in the metathesis reactions. The Grubbs' catalyst[62] (bis(tricyclohexylphosphine)benzylidine ruthenium (IV) dichloride) was purchased from Strem. Deuterated solvents were bought from Deutero GmbH. All metathesis reactions were carried out under nitrogen. Column chromatography was performed with silica gel (Merck, 0.040-0.063 mm). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DRX400 Avance Instrument (at 400 and 100 MHz, respectively). Chemical shifts were referenced to the residual signal of a deuterated solvent. Mass spectra were obtained on a Finnigan MAT 8230 spectrometer. Melting points were not corrected.

Reaction of tetraamine with tolylisocyanate

Compounds **35**[51] was obtained as described in the literature.

***5-Monotolylurea-11,17,23-triamine-25,26,27,28-tetrapentyloxycalix[4]arene* 36**

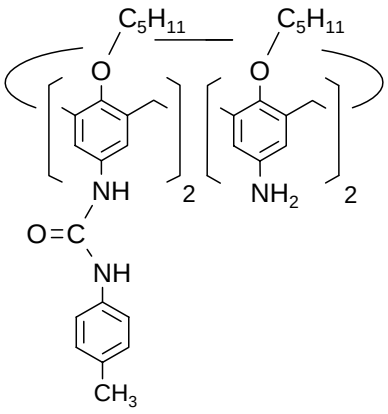


To a solution of aminocalixarene **35** (0.765 g; 1 mmol) in CH_2Cl_2 (100 mL) was added (dropwise during one day) a solution of tolylisocyanate (0.146 g; 1.1 mmol) in CH_2Cl_2 (100 mL). The reaction mixture was stirred under nitrogen, for additionally 12 hours for completion, followed by treatment with methanol (10 ml). After the chromatographic separation (ethylacetate with 10% THF) the desired compound was obtained.

yield = 0.6 g (63%); m.p. > 250 °C (decomposition without melting);

^{1}H-NMR (DMSO-d_6, 400 MHz, rt): δ (ppm) = 8.16 (s, 1H, NH), 8.09 (s, 1H, NH), 7.22 and 7.01 (2d, 4H, ^{3}J = 7.9 Hz, Ar_{tolyl}-H), 6.59 (s, 2H, Ar_{calix}-H), 6.01 (d, 4H, ^{4}J = 3.5 Hz, Ar_{calix}-H), 5.84 (s, 2H, Ar_{calix}-H), 4.35 (brs, 6H, NH_2), 4.21 (d, 2H, ^{2}J = 12.6 Hz, Ar-CH_2-Ar*ax*), 4.13 (d, 2H, ^{2}J = 12.6 Hz, Ar-CH_2-Ar*ax*), 3.69 (m, 6H, OCH_2-), 3.60 (t, 2H, ^{3}J = 6.7 Hz, OCH_2-), 2.90 (d, 2H, ^{2}J = 12.6 Hz, Ar-CH_2-Ar*eq*), 2.76 (d, 2H, ^{2}J = 12.6 Hz, Ar-CH_2-Ar*eq*), 2.19 (s, 3H, -CH_3), 1.84-1.82 (m, 8H, -CH_2-), 1.34-1.23 (m, 16H, -$(CH_2)_2$-), 0.9 (brt, 12H, -CH_3).

***5,11-Diamino-17,23-ditolylurea-25,26,27,28-tetrapentyloxycalix[4]arene* 37**

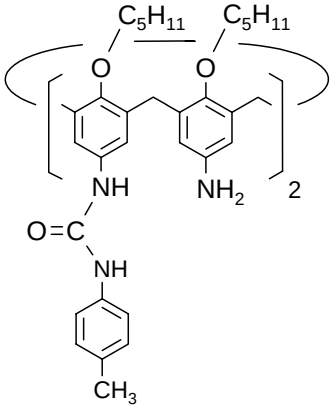


To a solution of aminocalixarene (1.0 g; 1.3 mmol) in $CHCl_3$ (50 mL) was added (dropwise during 5 hours) a solution of tolylisocyanate (0.38 g; 2.87 mmol) in $CHCl_3$ (50 mL). The reaction mixture was stirred under nitrogen, for additionally 12 hours for completion, followed by treatment with methanol (10 ml). By chromatographic separation three fraction were obtained: tritolylurea (0.26 g, 17%, eluent ethylacetate/hexane 1/1), 1,3-ditolylurea (0.1 g, 7%, eluent ethylacetate/hexane 10/1), 1,2-ditolylurea (0.74 g , 67%, eluent ethylacetate).

m.p. > 210 °C (decomposition without melting);

^{1}H NMR (DMSO-d_6, 400 MHz, 60°C): δ (ppm) = 8.08 (s, 2H, NH), 8.02 (s, 2H, NH), 7.25 and 7.03 (2d, 8H, ^3J = 8.2 Hz, Ar_{tolyl}-H), 6.75 (d, 2H, ^4J=2.4 Hz, Ar_{calix}-H), 6.70 (d, 2H, ^4J=2.4 Hz, Ar_{calix}-H), 5.97 (s, 4H, Ar_{calix}-H), 4.35 (d, 1H, ^2J = 12.5 Hz, Ar-CH_2-Ar*ax*), 4.27 (d, 2H, ^2J = 12.7 Hz, Ar-CH_2-Ar*ax*), 4.19 (d, 1H, ^2J = 12.7 Hz, Ar-CH_2-Ar*ax*), 4.10 (brs, 4H, NH), 3.81 (m, 4H, OCH_2-), 3.72 (m, 4H, OCH_2-), 3.08 (d, 1H, ^2J = 12.5 Hz, Ar-CH_2-Ar*eq*), 2.93 (d, 2H, ^2J = 12.7 Hz, Ar-CH_2-Ar*eq*), 2.82 (d, 1H, ^2J = 12.7 Hz, Ar-CH_2-Ar*eq*), 2.23 (s, 6H, -CH_3), 1.86 (m, 8H, -CH_2-), 1.42-1.2 (m, 16H, -$(CH_2)_2$-), 0.87 (t, 12H, ^3J = 6.6 Hz, -CH_3).

***1,3-Ditolylurea-2,4-diamine* 38**

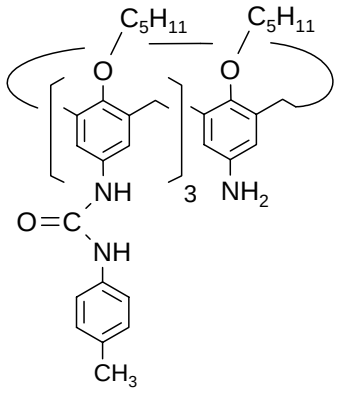


yield = 7%; m.p. > 250 °C (decomposition without melting); ^{1}H-NMR (DMSO-d_6, 400 MHz, 25°C): δ (ppm) = 8.24 (s, 4H, NH), 8.08 (s, 4H, NH), 7.21 (d, 4H, ^3J = 8.3 Hz, Ar_{tolyl}-H), 7.02 (t, 4H, ^3J = 8.3 Hz, Ar_{tolyl}-H), 6.70 (s, 4H, Ar_{calix}-H), 6.05 (s, 4H, Ar_{calix}-H), 4.25 (d, 4H, ^2J = 12.4 Hz, Ar-CH_2-Ar*ax*), 3.76-3.71 (m, 8H, OCH_2-), 3.50-3.40 (brs, NH_2 + H_2O), 2.94 (d, 4H, ^2J = 12.7 Hz, Ar-CH_2-Ar*eq*), 2.22 (s, 6H, -CH_3), 1.90-1.86 (m, 8H, -CH_2-), 1.42-1.35 (m, 16H, -CH_2-), 0.92 (t, 12H, ^3J = 6.7 Hz, -CH_3);

^{13}C-NMR (DMSO-d_6, 100 MHz, 25°C): δ (ppm) = 152.69, 151.24, 147.91, 137.54, 134.77, 134.49, 133.26, 130.35, 129.24, 118.38, 118.11, 114.66, 74.96, 74.81, 30.89,29.64, 29.47, 28.21, 28.18, 22.58, 22.52, 20.49,14.22, 14.14;

MS (FD), m/z 1031.5 (M calc $C_{64}H_{82}N_6O_6$: 1031.4).

5-Monoamino-11,17,23-tritolylurea-25,26,27,28-tetrapentyloxycalix[4]arene **39**



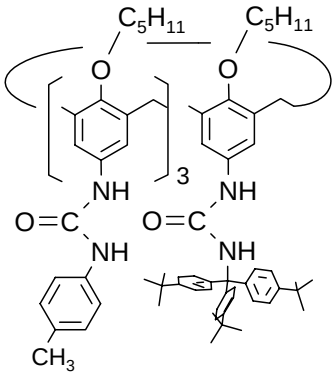
To a solution of aminocalixarene (1.13 g; 1.5 mmol) in CH_2Cl_2 (100 mL) was added (dropwise during one day) a solution of tolylisocyanate (0.64 g; 4.8 mmol) in CH_2Cl_2 (100 mL). The reaction mixture was stirred under nitrogen, for additionally 12 hours for completion, followed by treatment with methanol (10 ml). After the chromatographic separation (ethylacetate/hexane 5/7) the desired compound was obtained; additionally 0.5 g (28%) of tetratolylurea was eluted before the desired compound.

yield = 1.08 g (62%); m.p. > 250 °C (decomposition without melting);

^{1}H-NMR (DMSO-d6, 400 MHz, 60°C): δ (ppm) = 8.11 (s, 2H, NH), 8.09 (s, 1H, NH), 8.05 (s, 1H, NH), 7.99 (s, 2H, NH), 7.26 and 7.03 (2d, 4H, ^3J = 8.3 Hz, Ar_{tolyl}-H), 7.23 and 7.02 (2d, 8H, ^3J = 8.4 Hz, Ar_{tolyl}-H), 6.79 (d, 2H, ^4J = 2.4 Hz, Ar_{calix}-H), 6.78 (s, 2H, Ar_{calix}-H), 6.75 (d, 2H, ^4J = 2.4 Hz, Ar_{calix}-H), 6.01 (s, 2H, Ar_{calix}-H), 4.4-4.2 (brs, 2H, NH_2), 4.37 (d, 2H, ^2J = 12.7 Hz, Ar-CH_2-Ar*ax*), 4.30 (d, 2H, ^2J = 12.7 Hz, Ar-CH_2-Ar*ax*), 3.88-3.75 (m, 8H, OCH_2-), 3.07 (d, 2H, ^2J = 12.7 Hz, Ar-CH_2-Ar*eq*), 2.97 (d, 2H, ^2J = 12.9 Hz, Ar-CH_2-Ar*eq*), 2.23 (s, 9H, -CH_3), 1.91-1.87 (m, 8H, -CH_2-),1.40-1.39 (m, 16H, -CH_2-), 0.94 (brt, 12H, -CH_3);

^{13}C-NMR (DMSO-d_6, 100 MHz, 60°C): δ (ppm) = 150.28, 150.21, 149.07, 148.88, 145.30, 139.68, 135.01, 134.98, 132.28, 132.13, 131.96, 131.91, 131.79, 130.97, 130.90, 127.96, 127.90, 126.60, 126.57, 116.72, 116.28, 116.05, 115.99, 115.91, 115.83, 112.01, 72.28, 72.22, 72.18, 28.44, 28.42, 26.92, 26.88, 26.86, 25.63, 25.57, 19.83, 19.79, 17.83, 11.42, 11.40;

Mono-tert-butyltritylurea-tritolylurea-25,26,27,28-tetrapentyloxycalix[4]arene **21d**



39 (0.35 g; 0.3 mmol) and 4-nitrophenyl chloroformate (0.09 g; 0.45 mmol) were dissolved in a mixture THF/CH_2Cl_2 = 1/1 (20 mL) and refluxed for 12 hours. The solvents were evaporated under reduce pressure and the yellowish solid was used in the next reaction.

A solution of the tritolylurea-monourethane (0.13 g; 0.1 mmol) and p-*tert*-butyl-tritylamine (0.085 g; 0.2 mmol) and few drops of triethylamine in chloroform (4 mL) was refluxed for 12 hours. The chloroform solution was diluted to 50 mL and washed with K_2CO_3 solution (until the aqueous layer was colorless) and with water. The organic layer was dried over $MgSO_4$ and the solution was concentrated at reduced pressure to 10 mL. The pure product was obtained after precipitation with methanol.

yield = 86%; m.p. > 250 °C (decomposition without melting);

^{1}H-NMR (DMSO-d6, 400 MHz, 60°C): δ (ppm) = 8.43 (s, 1H, NH), 8.24 (s, 2H, NH), 7.98 (s, 2H, NH), 7.86 (s, 2H, NH), 7.32-7.28 (m, 8H, Ar_{tolyl}-H+ Ar_{trityl}-H), 7.17-7.13 (m, 10H, Ar_{tolyl}-H+ Ar_{trityl}-H), 7.07-7.05 (m, 4H, Ar_{tolyl}-H+Ar_{calix}-H), 7.03 (s, 1H, NH), 6.99 (d, 4H, ^3J = 8.3 Hz, Ar_{tolyl}-H), 6.84 (s, 2H, Ar_{calix}-H), 6.52 (s, 4H, Ar_{calix}-H), 4.35 (d, 2H, ^2J = 12.9 Hz, Ar-CH_2-Ar*ax*), 4.31 (d, 2H, ^2J = 12.9 Hz, Ar-CH_2-Ar*ax*), 3.96-3.89 (m, 4H, OCH_2-), 3.72 (t, 4H, ^3J = 6.9 Hz, OCH_2-), 3.09 (d, 2H, ^2J = 12.9 Hz, Ar-CH_2-Ar*eq*), 3.03 (d, 2H, ^2J = 12.7 Hz, Ar-CH_2-Ar*eq*), 2.24 (s, 3H, -CH_3), 2.22 (s, 6H, -CH_3), 1.94-1.82 (m, 8H, -CH_2-), 1.51-1.29 (m, 16H, -CH_2-), 1.26 (s, 27H, -*t*Bu), 0.95-0.90 (m, 12H, -CH_3);

^{13}C-NMR (THF-d_8, 100 MHz, 25°C): δ (ppm) = 150.76, 152.22, 152.17, 152.15, 151.68, 151.09, 148.57, 143.45, 137.94, 137.82, 135.83, 134.81, 134.09, 133.84, 133.77, 133.69, 130.10, 128.69, 128.57, 123.94, 118.44, 118.25, 117.88, 117.83, 74.92, 74.83, 74.70, 68.72, 33.92, 31.12, 31.09, 30.69, 30.01, 29.70, 29.56, 28.59, 28.30, 22.82, 22.80, 22.66, 19.74, 19.72, 13.66, 13.64, 13.49, 0.32;

MS (FD), m/z 1641.0 (M+Na calc $C_{104}H_{128}N_8O_8Na$: 1641.2).

General procedure for the reaction of amino derivative with isocyanates

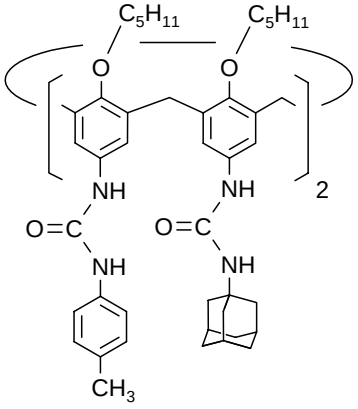
A solution of the amino derivative and the isocyanate (adamantylisocyanate, *tert*-butylisocyante, hexylisocyanate, dodecylisocyanate, (R)-(+)-1-phenyl-ethylisocyanate; in

the ratio 1 mol amino group/1.1 mol isocyanate) in chloroform was stirred for 12 hours at room temperature. The crude compound is precipitated with methanol from the reaction mixture and the pure compound was obtained after one or two recrystallizations from chloroform/methanol mixture (yield 80-90%).

1,3-Ditolylurea-2,4-diadamantylurea **24a**

yield = 87%; m.p. > 210 °C (decomp);

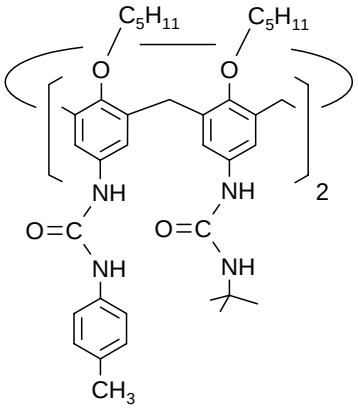
^{1}H-NMR (DMSO-d_6, 400 MHz, 60°C): δ (ppm) = 8.01 (s, 2H, NH), 7.90, (s, 2H, NH), 7.82 (s, 2H, NH), 7.17 (d, 4H, ^{3}J = 7.8 Hz, Ar_{tolyl}-H), 7.00 (t, 4H, ^{3}J = 8.1 Hz, Ar_{tolyl}-H), 6.88 (s, 4H, Ar_{calix}-H), 6.57 (s, 4H, Ar_{calix}-H), 5.58 (s, 2H, NH), 4.33 (d, 4H, ^{2}J = 12.7 Hz, Ar-CH_2-Ar *ax*), 3.90 (t, 4H, ^{3}J = 7.5 Hz, OCH_2-), 3.74 (t, 4H, ^{3}J = 6.6 Hz, OCH_2-), 3.05 (d, 4H, ^{2}J = 12.9 Hz, Ar-CH_2-Ar *eq*), 2.22 (s, 6H, -CH_3), 2.02 (m, 8H, -CH_2-), 1.91-1.85 (m, 18H, -CH_2-+ -CH-), 1.63 (m, 12H, -CH_2-), 1.45-1.32 (m, 16H, -CH_2-), 0.93 (m, 12H, -CH_3);



^{13}C-NMR (DMSO-d_6, 100 MHz, 60°C): δ (ppm) = 153.80, 152.14, 150.44, 137.02, 134.55, 134.20, 133.24, 132.90, 129.88, 128.58, 117.90, 117.78, 117.61, 74.57, 74.10, 49.42, 41.63, 35.80, 30.46, 29.11, 28.74, 28.67, 27.71, 27.51, 21.89, 21.81, 19.88, 13.54, 13.41;

MS (FD), m/z 1407.94 (M+Na calc $C_{86}H_{112}N_8O_8Na$: 1407.84).

1,3-Ditolylurea-2,4-ditert-butylurea **24b**

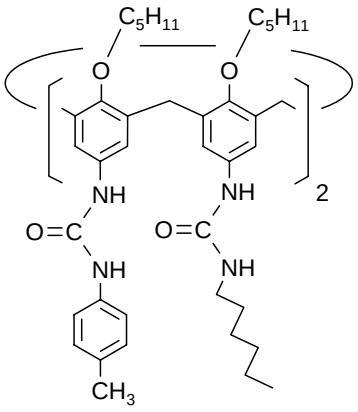


yield = 80%; mp > 230 °C (decomp);

^{1}H-NMR (DMSO-d_6, 400 MHz, 60°C): δ (ppm) = 7.99 (s, 2H, NH), 7.86, (s, 2H, NH), 7.82 (s, 2H, NH), 7.16 (d, 4H, ^{3}J = 8.3 Hz, Ar_{tolyl}-H), 7.00 (t, 4H, ^{3}J = 8.1 Hz, Ar_{tolyl}-H), 6.92 (s, 4H, Ar_{calix}-H), 6.54 (s, 4H, Ar_{calix}-H), 5.69 (s, 2H, NH), 4.33 (d, 4H, ^{2}J = 12.7 Hz, Ar-CH_2-Ar *ax*), 3.92 (t, 4H, ^{3}J = 7.8 Hz, OCH_2-), 3.73 (t, 4H, ^{3}J = 7.0 Hz, OCH_2-), 3.06 (d, 4H, ^{2}J = 12.7 Hz, Ar-CH_2-Ar *eq*), 2.22 (s, 6H, -CH_3), 1.91-1.85 (m, 8H, -CH_2-), 1.47-1.31 (m, 16H, -CH_2-), 1.27 (s, 18H, ^{t}Bu), 0.94 (t, 6H, ^{3}J = 7.1 Hz, -CH_3), 0.93 (t, 6H, ^{3}J = 7.0 Hz, -CH_3);

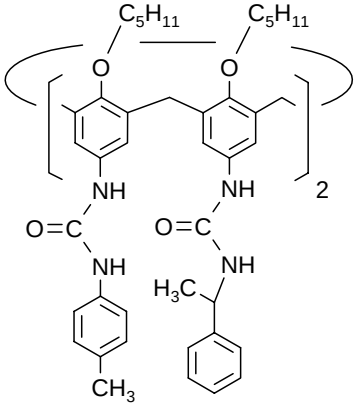
^{13}C-NMR (DMSO-d_6, 100 MHz, 60°C): δ (ppm) = 154.22, 152.11, 150.54, 150.38, 137.00, 134.69, 134.17, 133.09, 132.88, 129,84, 128.55, 117.87, 117.74, 74.57, 74.02, 48.90, 30.43, 29.12, 28.84, 28.67, 27.71, 27.47, 21.86, 21.77, 19.86, 13.52, 13.37;
MS (FD), m/z 1251.70 (M+Na calc $C_{74}H_{100}N_8O_8Na$: 1252.64).

1,3-Ditolylurea-2,4-dihexylurea **24c**



yield = 87%; mp > 200 °C (melting with decomp);
^{1}H-NMR (DMSO-d_6, 400 MHz, 25°C): δ (ppm) = 8.15 (s, 2H, NH), 8.04, (s, 2H, NH), 7.99 (s, 2H, NH), 7.19 (d, 4H, ^3J = 8.4 Hz, Ar_{tolyl}-H), 7.02 (t, 4H, ^3J = 8.4 Hz, Ar_{tolyl}-H), 6.84 (s, 4H, Ar_{calix}-H), 6.65 (s, 4H, Ar_{calix}-H), 5.83 (t, 2H, ^3J = 5.5 Hz, NH), 4.30 (d, 4H, ^2J = 12.6 Hz, Ar-CH_2-Ar *ax*), 3.84 (t, 4H, ^3J = 7.6 Hz, OCH_2-), 3.74 (t, 4H, ^3J = 7.1 Hz, OCH_2-), 3.05 (d, 4H, ^2J = 12.6 Hz, Ar-CH_2-Ar *eq*), 3.00 (m, 4H, NCH_2-), 2.22 (s, 6H, -CH_3), 1.90 (m, 8H, -CH_2-), 1.44-1.24 (m, 32H, -CH_2-), 0.93 (t, 12H, ^3J = 6.8 Hz, -CH_3), 0.85 (t, 6H, ^3J = 6.6 Hz, -CH_3);
^{13}C-NMR (DMSO-d_6, 100 MHz, 60°C): δ (ppm) = 155.09, 152.31, 150.65, 150.56, 137.19, 134.50, 134.27, 133.79, 133.17, 130.07, 128.91, 117.94, 117.85, 74.83, 74.57, 38.91, 30.93, 30.58, 29.71, 29.39, 29.16, 27.95, 27.79, 25.97, 22.27, 22.22, 22.00, 20.21, 13.94, 13.85, 13.81;
MS (FD), m/z 1307.89 (M+Na calc $C_{78}H_{108}N_8O_8Na$: 1307.81).

1,3-Ditolylurea-2,4-dimethylbenzyllurea **24d**



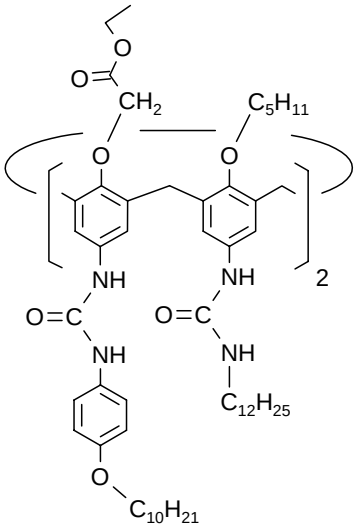
yield = 90%; mp > 280 °C (decomposition without melting);
^{1}H-NMR (DMSO-d_6, 400 MHz, 25°C): δ (ppm) = 8.09 (s, 2H, NH), 8.07, (s, 2H, NH), 7.97 (s, 2H, NH), 7.30-7.29 (m, 8H, Ar_{phenyl}-H), 7.22 (m, 2H, Ar_{phenyl}-H), 7.16 (d, 4H, ^3J = 8.5 Hz, Ar_{tolyl}-H), 7.02 (t, 4H, ^3J = 8.3 Hz, Ar_{tolyl}-H), 6.92 (d, 2H, ^4J = 2.2 Hz Ar_{calix}-H), 6.89 (d, 2H, ^4J = 2.2 Hz Ar_{calix}-H), 6.57 (d, 2H, ^4J = 2.2 Hz Ar_{calix}-H), 6.54 (d, 2H, ^4J = 2.2 Hz Ar_{calix}-H), 6.40 (d, 2H, ^3J = 7.9 Hz, NH), 4.81-4.74 (m, 2H, NCH-), 4.28 (d, 4H, ^2J = 12.5 Hz, Ar-CH_2-Ar *ax*), 3.85 (t, 4H, ^3J = 7.7 Hz, OCH_2-), 3.69 (t, 4H, ^3J = 6.8 Hz, OCH_2-), 3.03 (d, 4H, ^2J = 12.5 Hz, Ar-CH_2-Ar *eq*), 2.23 (s, 6H, -CH_3),

1.94-1.82 (m, 8H, -CH_2-), 1.47-1.29 (m, 22H, -CH_2-+-CH_3), 0.92 (t, 6H, ^3J = 7.0 Hz, -CH_3), 0.91 (t, 6H, ^3J = 7.1 Hz, -CH_3);

^{13}C-NMR (DMSO-d_6, 100 MHz, 60°C): δ (ppm) = 154.82, 152.80, 151.32, 151.03, 145.91, 137.72, 135.40, 135.37, 134.64, 133.98, 133.66, 130.58, 129.43, 128.69, 126.97, 126.14, 118.37, 118.33, 118.27, 75.42, 74.99, 48.91, 31.06, 29.97, 29.58, 28.51, 28.24, 23.70, 22.78, 22.71, 20.73, 14.47, 14.33;

MS (FD), m/z 1325.78 (M^+ calc $C_{82}H_{100}N_8O_8$: 1325.74).

***1,3-Di-(p-decyloxyphenyl)-urea-2,4-didodecylurea* 24e**



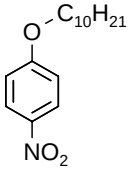
yield = 96%; mp > 250 °C (decomposition without melting);

^{1}H-NMR (DMSO-d_6, 400 MHz, 60°C): δ (ppm) = 8.09 (s, 2H, NH), 8.08 (s, 2H, NH), 7.69 (s, 2H, NH), 7.25 (d, 4H, ^3J = 8.9 Hz, Ar_{tolyl}-H), 6.89 (s, 4H, Ar_{calix}-H), 6.80 (t, 4H, ^3J = 8.9 Hz, Ar_{tolyl}-H), 6.62 (s, 4H, Ar_{calix}-H), 5.62 (t, 2H, ^3J = 5.4 Hz, NH), 4.68 (s, 4H, OCH_2CO), 4.52 (d, 4H, ^2J = 13.2 Hz, Ar-CH_2-Ar *ax*), 4.14 (q, 4H, ^3J = 7.1 Hz, CH_2CH_3), 3.90 (t, 4H, ^3J = 6.4 Hz, OCH_2-), 3.79 (t, 4H, ^3J = 7.2 Hz, OCH_2-), 3.07 (d, 4H, ^2J = 13.2 Hz, Ar-CH_2-Ar *eq*), 3.79 (m, 4H, NCH_2-), 1.85 (q, 4H, ^3J = 7.1 Hz, -CH_2-), 1.68 (q, 4H, ^3J = 7.1 Hz, -CH_2-), 1.39-1.20 (m, 82H, -CH_2-), 0.92 (t, 6H, ^3J = 6.8 Hz, -CH_3), 0.86 (m, 12H, -CH_3);

^{13}C-NMR (DMSO-d_6, 100 MHz, 60°C): δ (ppm) = 169.75, 155.66, 154.36, 153.14, 151.08, 150.88, 135.09, 134.71, 134.60, 134.02, 133.37, 120.41, 118.85, 118.75, 115.21, 75.29, 71.19, 68.36, 60.32, 49.00, 31.63, 30.21, 29.46, 29.39, 29.34, 29.33, 29.27, 29.20, 29.16, 29.12, 29.01, 28.98, 28.34, 26.82, 25.90, 22.51, 22.38, 14.34, 14.16, 14.15;

MS (FD), m/z 1792.9 (M+Na calc $C_{106}H_{160}N_8O_{14}Na$: 1793.5).

Nitro-derivative



A slurry of 4-nitrophenol (3 g; 21.5 mmol), decylbromide (5 mL; 24 mmol) and potassium carbonate (3.3 g; 24 mmol) in acetonitrile (40 mL) was refluxed for one day (TLC control, eluent ethylacetate/hexane 1/2). The solvent was evaporated under reduced pressure and the crude product taken up in

dichloromethane (250 mL). The organic layer was washed with water until the aqueous phase remained colorless (2-4 x 100 mL), dried over $MgSO_4$ and concentrated. Precipitation with hexane gave the wanted compounds as a white to yellowish powder.

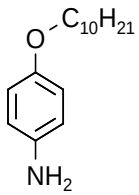
yield = 92%; m.p.= 40°C;

^{1}H NMR ($CHCl_3$-d_1, 200MHz, 25°C); δ (ppm) = 8.17 and 6.92 (two d AB-system, 4H, ^3J = 9.3 Hz, Ar-H), 4.03 (t, 2H, ^3J = 6.6 Hz, OCH_2-), 1.80 (q, 2H, ^3J = 7.0 Hz, -CH_2-), 1.44-1.26 (m, 14H, -CH_2-), 0.87 (t, 3H, ^3J = 6.6 Hz, -CH_3),

^{13}C-NMR ($CHCl_3$-d_1, 100 MHz, rt): δ (ppm) = 164.23, 141.25, 125.85, 114.34, 68.86, 31.84, 29.48, 29.26, 28.93, 25.86, 22.63, 14.06;

MS (FD): m/z 280.1 (M calc $C_{16}H_{25}NO_3$: 279.3).

Aniline



The nitro-derivative (5.0 mmol) was dissolved in acetone (125 mL) and hydrogenated (1 atm.) in the presence of Raney-nickel until the hydrogen uptake was completed (~3h). The catalyst was filtered off, washed with acetone (2 x 25 mL), the solvent was evaporated. The viscous residue became solid in few days.

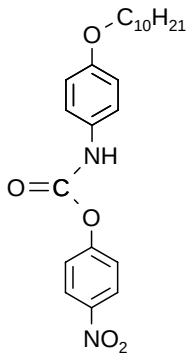
yield = 96%; amorphous solid ;

^{1}H NMR ($CHCl_3$-d_1, 400MHz, 25°C); δ (ppm) = 6.73 and 6.61 (two d AB-system, 4H, ^3J = 8.6 Hz, Ar-H), 3.87 (t, 2H, ^3J = 6.6 Hz, OCH_2-), 1.72 (q, 2H, ^3J = 7.3 Hz, -CH_2-), 1.44-1.28 (m, 14H, -CH_2-), 0.89 (t, 3H, ^3J = 6.9 Hz, -CH_3),

^{13}C-NMR ($CHCl_3$-d_1, 100 MHz, 25°C): δ (ppm) = 152.49, 139.90, 116.44, 115.89, 68.93, 31.85, 29.54, 29.51, 29.46, 29.38, 29.24, 26.05, 22.60, 13.96;

MS (FD): m/z 200.3 (M calc $C_{16}H_{27}NO$: 249.4).

Urethane



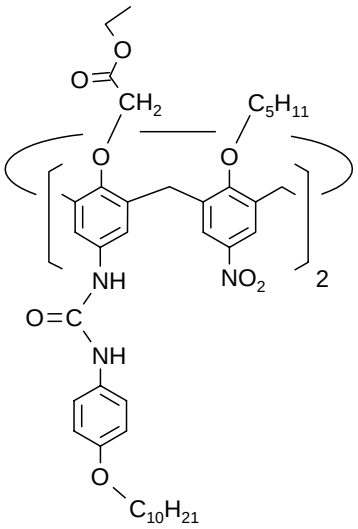
The aniline (2.27 g; 9.1 mmol) was dissolved in dioxane (50 mL), 4-nitrophenyl chloroformate (2.2 g; 10.9 mmol) was added and the mixture was refluxed under nitrogen for 24 hours (a clear solution was obtained in ~3 h). The solvent was evaporated to dryness and the residue was triturated with acetonitrile. The desired products, a white powder, was filtered off, washed with acetonitrile (2 x 15 mL) and dried.

yield = 70%; m.p. = 134-136 (decomp.);

^{1}H NMR ($CHCl_3$-d_1, 400 MHz, 25°C); δ (ppm) = 8.26 and 6.87 (two d AB-system, 4H, ^3J = 9.1 Hz, Ar-H), 7.37 and 7.32 (two d AB-system, 4H, ^3J = 9.0 Hz, Ar-H), 3.92 (t, 2H, ^3J = 6.6 Hz, OCH_2-), 1.76 (q, 2H, ^3J = 7.0 Hz, -CH_2-), 1.44 (m, 2H, -CH_2-), 1.30-1.24 (m, 12H, -CH_2-), 0.87 (t, 3H, ^3J = 6.7 Hz, -CH_3),

^{13}C-NMR ($CHCl_3$-d_1, 100 MHz, rt): δ (ppm) = 156.31, 155.53, 150.44, 144.95, 129.32, 125.17, 122.05, 121.03, 115.06, 68.35, 31.87, 29.55, 29.53, 29.37, 29.29, 29.23, 26.00, 22.66, 14.09;

Dinitro-didodecylurea

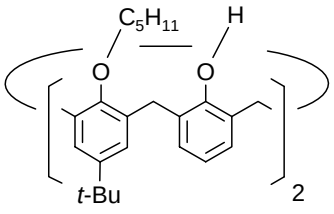


A solution of diamino-dinitro derivative **78**, urethane (see above; in the ration 1:2.1) and few drops of triethylamine in THF was refluxed for 12 hours. Then, the solvent was evaporated, the residue was dissolved in dichloromethane, and washed with K_2CO_3 solution (until the aqueous layer was colorless) and with water. The organic layer was dried over $MgSO_4$ and the solution was concentrated at reduced pressure to 4-5 mL. The pure product was obtained after precipitation with methanol. yield = 87%, yellow crystals;

^{1}H-NMR (DMSO-d_6, 400 MHz, 25°C): δ (ppm) = 8.56 (s, 2H, NH), 8.45 (s, 2H, NH), 7.36-7.24 (m, 8H, Ar_{tolyl}-H+ Ar_{calix}-H), 6.92 (s, 4H, Ar_{calix}-H), 6.85 (d, 4H, ^3J = 8.9 Hz, Ar_{tolyl}-H), 4.68-4.65 (m, 8H, OCH_2CO+ Ar-CH_2-Ar *ax*), 4.11 (q, 4H, ^3J = 7.0 Hz, $C\underline{H}_2CH_3$), 3.90 (t, 4H, ^3J = 6.1 Hz, OCH_2-), 3.79 (brt, 4H, OCH_2-), 3.31-3.29 (m, 4H, ^2J = 13.2 Hz, Ar-CH_2-Ar *eq*+H_2O), 1.82 (q, 4H, ^3J = 7.1 Hz, -CH_2-), 1.68 (q, 4H, ^3J = 7.1 Hz, -CH_2-), 1.49-1.20 (m, 42H, -CH_2-), 0.92 (t, 12H, ^3J = 7.1 Hz, -CH_3), 0.84 (m, 6H, -CH_3);

Multistep synthesis

5,17-Di-tert-butyl-26,28-dihydroxy-25,27-dipentoxycalix[4]arene[63] **41**

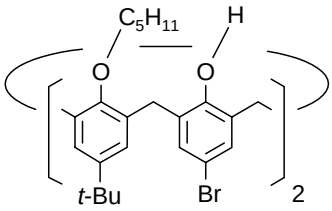


The pure compound was obtained after several recrystallisations from acetone. Yield 25%, white crystals; m.p.= 126°C;

^{1}H NMR ($CHCl_3$-d_1, 200MHz, 25°C); δ = 7.99 (s, 2H, OH),

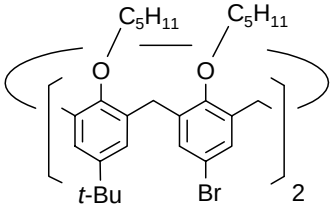
7.02 (d, 4H, ^3J = 7.3 Hz, Ar-H), 6.47 (s, 4H, Ar-H), 6.61 (t, 2H, ^3J = 7.3 Hz, Ar-H), 4.29 (d, 4H, ^2J =12.7 Hz, Ar-CH_2-Ar*ax*), 3.96 (t, 4H, ^3J = 6.8 Hz, OCH_2-), 3.32 (d, 4H, ^2J = 12.7 Hz, Ar-CH_2-Ar*eq*), 2.04 (q, 4H, ^3J = 6.8 Hz, -CH_2-), 1.6-1.4 (m, 8H, -CH_2-), 1.1-0.9 (m, 24 H, CH_3+ ^{t}Bu).

5,17-Di-tert-butyl-11,23-dibromo-25,27-dihydroxy-26,28-dipento-xycalix[4]arene[63] **42**



^{1}H NMR ($CHCl_3$-d_1, 200MHz, 25°C) δ (ppm) = 8.36 (s, 2H, OH), 7.12 (s, 4H, Ar-H), 6.91 (s, 4H, Ar-H), 4.24 (d, 4H, ^2J =13.8 Hz, Ar-CH_2-Ar*ax*), 3.94 (t, 4H, ^3J = 6.8 Hz, OCH_2-), 3.28 (d, 4H, ^2J = 13.8 Hz, Ar-CH_2-Ar*eq*), 2.05 (q, 4H, ^3J = 6.8 Hz, -CH_2-), 1.6-1.4 (m, 8H, -CH_2-), 1.1 (s, 18 H, ^{t}Bu), 0.98 (t, 6H, ^3J = 7.3 Hz, -CH_3).

5,17-Di-tert-butyl-11,23-dibromo-25,26,27,28-tetrapentoxycalix-[4]arene[51] **43a**

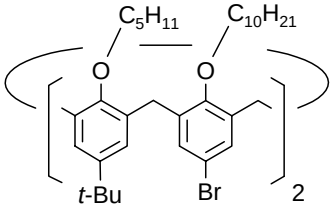


yield = 84.4%; m.p. = 157-158°C;

^{1}H NMR ($CHCl_3$-d_1, 200MHz, 25°C) δ (ppm) = 7.04 (s, 4H, Ar-H), 6.29 (s, 4H, Ar-H), 4.37 (d, 4H, ^2J = 13.2 Hz, Ar-CH_2-Ar*ax*), 3.66 (t, 4H, ^3J = 8.5 Hz, OCH_2-), 3.66 (t, 4H, ^3J = 6.6 Hz, OCH_2-), 3.07 (d, 4H, ^2J = 13.2 Hz, Ar-CH_2-Ar*eq*), 1.95-1.90 (m, 4H, -CH_2-), 1.88-1.82 (m, 4H, -CH_2-), 1.48-1.19 (m, 16H, -CH_2-), 1.34 (s, 18H, ^{t}Bu), 0.93 (t, 6H, ^3J = 6.8 Hz, -CH_3), 0.91 (t, 6H, ^3J = 6.8 Hz, -CH_3);

MS (FD), m/z 975.7 (M calc $C_{56}H_{78}Br_2O_4$: 975.05) .

5,17-Di-tert-butyl-11,23-dibromo-25,27-didecyloxy-26,28-dipentoxycalix-[4]arene[52] **43b**



yield = 90%; amorphous solid;

^{1}H NMR ($CHCl_3$-d_1, 400MHz, 25°C) δ = 7.04 (s, 4H, Ar-H), 6.31 (s, 4H, Ar-H), 4.37 (d, 4H, ^2J = 13.2 Hz, Ar-CH_2-Ar*ax*), 3.98 (m, 4H, OCH_2-), 3.66 (t, 4H, ^3J = 6.6 Hz, OCH_2-), 3.07 (d, 4H, ^2J = 13.2 Hz, Ar-CH_2-Ar*eq*), 1.95-1.90 (m, 4H, -CH_2-), 1.88-1.82 (m, 4H, -CH_2-), 1.55-1.48 (m, 4H, -CH_2-), 1.38-1.19 (m, 52H, -CH_2-+ ^{t}Bu), 0.93 (t, 6H, ^3J = 7.2 Hz, -CH_3), 0.87 (t, 6H, ^3J = 6.8 Hz, -CH_3);

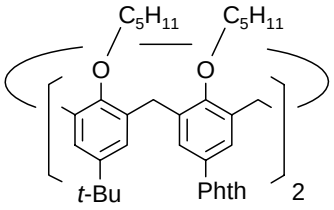
^{13}C-NMR ($CHCl_3$-d_1, 100 MHz, 25°C): δ (ppm) = 154.98, 154.41, 145.06, 135.64, 135.11, 130.16, 125.82, 114.98, 75.52, 74.98, 34.12, 31.89, 31.63, 31.16, 30.41, 29.74, 29.71, 29.34, 28.13, 26.55, 22.97, 22.68, 14.33, 14.09;

MS (FD), m/z 1116.1 (M calc $C_{66}H_{98}Br_2O_4$: 1115.32) .

General procedure for the substitution of bromide with phthalimide

A mixture of dibromo derivative **43**, phthalimide and Cu_2O (in ratio 1:9:9) in collidine (50ml/mmol **43**) was refluxed for 2 days under nitrogen. The solvent was evaporated under reduce pressure and the solid was taken in dichloromethane, washed two times with 5% H_2SO_4, one time with 2N NaOH, with water, dried over $MgSO_4$ and concentrated under reduce pressure. The crude product was purified by column chromatography (eluent $CHCl_3$/hexane = 1/1) and three fractions were separated: 25-28% starting material, 15-20% monophthalimido-monobromo and 40-50% the desired **49** derivatives.

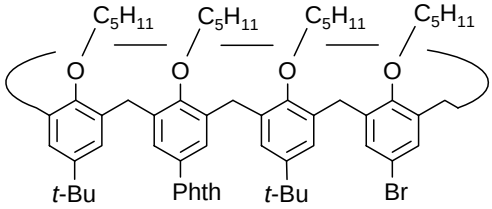
***5,17-Di-tert-butyl-11,23-diphthalimido* 49a**



This compound is identical with **61**.

^{1}H-NMR ($CHCl_3$-d_1, 200MHz, rt): δ (ppm) = 7.39-7.33 (m, 8H, Ar_{phth}-H), 6.98 (s, 4H, Ar-H), 6.50 (s, 4H, Ar-H), 4.47 and 3.18 (2d, 8H, ^2J = 12.7 Hz, Ar-CH_2-Ar *ax* + *eq*), 4.00 (t, 4H, ^3J = 8.0 Hz, OCH_2-), 3.80 (t, 4H, ^3J = 6.83 Hz, OCH_2-), 2.00-193 (m, 8H, -CH_2-), 1.48-1.33 (m, 16H, -CH_2-), 1.22 (s, 18H, ^{t}Bu), 0.96 (t, 6H, ^3J = 7.08 Hz, -CH_3), 0.95 (t, 6H, ^3J = 7.07 Hz, -CH_3).

5,17-Di-tert-butyl-11-monobromo-23-monophthalimido



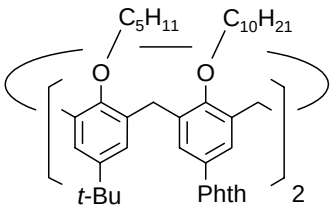
This product is the second product isolated in the reaction between **43a** and phthalimide.

^{1}H NMR ($CHCl_3$-d_1, 400MHz, 25°C) δ = 7.80 (m, 2H, Ar_{phth}-H), 7.66 (m, 2H, Ar_{phth}-H), 7.00 (d, 2H, ^4J = 2.2 Hz, ArH), 6.94 (d, 2H, ^4J = 2.2 Hz, ArH), 6.72 (s, 2H, ArH), 6.53(s, 4H, ArH), 4.50 (d, 4H, ^2J = 12.9 Hz, Ar-CH_2-Ar*ax*), 4.41 (d, 4H, ^2J = 12.9 Hz, Ar-CH_2-Ar*ax*), 3.97 (t, 4H, ^3J = 8.2 Hz, OCH_2-), 3.85 (t, 2H, ^3J = 7.04 Hz,, OCH_2-), 3.77 (t, 2H, ^3J = 7.04 Hz,, OCH_2-), 3.22 (d, 2H, ^2J = 13.2 Hz, Ar-CH_2-Ar*eq*), 3.10 (d, 2H, ^2J = 13.2 Hz, Ar-CH_2-Ar*eq*), 2.01 - 1.88 (m, 8H, -CH_2-), 1.54-1.37 (m, 12H, -CH_2-), 1.34-1.27 (m, 4H, -CH_2-), 1.27 (s, 18H, ^{t}Bu), 1.00-0.94 (m, 12H, -CH_3);

^{13}C-NMR ($CHCl_3$-d_1, 100 MHz, 25°C): δ (ppm) = 166.44, 154.82, 154.59, 154.50, 144.88, 136.26, 134.52, 134.42, 133.95, 133.57, 132.01, 130.44, 126.26, 125.89, 125.43, 124.28, 123.13, 114.57, 75.30, 75.17, 33.99, 31.53, 31.30, 31.10, 30.06, 29.94, 29.82, 28.56, 28.51, 28.20, 22.87, 22.76, 22.73, 14.24, 14.13, 14.09;

MS (FD), m/z 1043.0 (M calc $C_{64}H_{82}BrNO_6$: 1041.27).

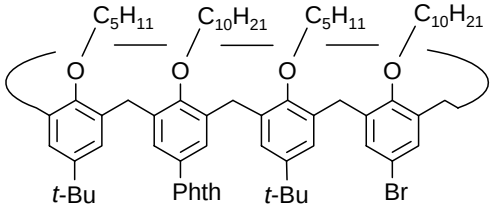
***5,17-Di-tert-butyl-11,23-diphthalimido* 49b**



^{1}H NMR ($CHCl_3$-d_1, 200MHz, 25°C) δ (ppm) = 7.65-7.57 (m, 8H, Ar_{phth}-H), 6.86 (s, 4H, ArH), 6.57 (s, 6H, ArH), 4.48 (d, 4H, ^2J = 13.2 Hz, Ar-CH_2-Ar*ax*), 3.95-3.82 (m, 8H, OCH_2-), 3.19 (d, 4H, ^2J = 13.2 Hz, Ar-CH_2-Ar*eq*), 2.04 - 1.82 (m, 8H, -CH_2-), 1.54-1.21 (m, 36H, -CH_2-), 0.98-0.84 (m, 12H, -CH_3);

MS (FD), m/z 1135.9 (M^+ calc $C_{74}H_{90}N_2O_8$: 1135.48) .

5,17-Di-tert-butyl-11-monobromo-23-monophthalimido



This product is the second product isolated in the reaction between **43b** and phthalimide.

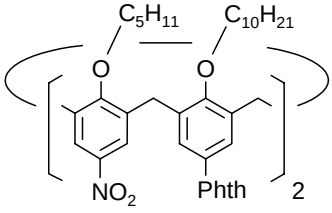
yield = 14%, m.p.= 112-113°C;

^{1}H NMR ($CHCl_3$-d_1, 400MHz, 25°C) δ = 7.90 (m, 2H, Ar_{phth}-H), 7.75 (m, 2H, Ar_{phth}-H), 7.02 (s, 2H, ArH), 6.99(s, 2H, ArH), 6.46 (d, 2H, ^3J = 4.6 Hz, ArH), 6.38 (t, 2H, ^3J = 4.6 Hz, ArH), 4.47 (d, 2H, ^2J = 13.5 Hz, Ar-CH_2-Ar*ax*), 4.39 (d, 2H, ^2J = 13.4 Hz, Ar-CH_2-Ar*ax*), 3.99 (t, 2H, ^3J = 7.8 Hz, OCH_2-), 3.94 (t, 2H, ^3J = 7.8 Hz,, OCH_2-), 3.78 (t, 4H, ^3J = 7.0 Hz,, OCH_2-),3.19 (d, 2H, ^2J = 13.4 Hz, Ar-CH_2-Ar*eq*), 3.09 (d, 2H, ^2J = 13.2 Hz, Ar-CH_2-Ar*eq*), 1.93-1.84 (m, 8H, -CH_2-), 1.42-1.39 (m, 4H, -CH_2-), 1.34-1.20 (m, 32H, -CH_2-), 0.94 (t, 6H, ^3J = 6.8 Hz, -CH_3), 0.88 (t, 6H, ^3J = 6.8 Hz, -CH_3);

^{13}C-NMR ($CHCl_3$-d_1, 100 MHz, 25°C): δ (ppm) = 167.35, 156.61, 156.39, 155.74, 138.14, 136.39, 134.06, 133.67, 133.22, 131.88, 131.01, 128.12, 127.82, 125.93, 125.35, 123.44, 122.44, 114.29, 75.31, 75.25, 75.20, 31.91, 31.01, 30.82, 30.22, 30.07, 30.02, 29.94, 29.91, 29.68, 29.65, 29.35, 28.51, 26.09, 22.74, 22.66, 14.13, 14.07;

MS (FD), m/z 1071.0 (M^+ calc $C_{66}H_{86}BrNO_6$: 1069.33) .

***Nitro-phthalimido* 45b**



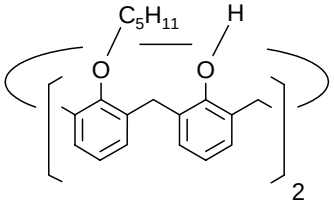
The procedure is described later in this section.

yield = 86%; yellow crystals, m.p.= 177-178°C;

^{1}H NMR (C_6H_6-d_6, 400MHz, 25°C) δ =. 8.12 (s, 4H, Ar-H), 6.77 (m, 4H, Ar_{phth}-H), 6.65 (s, 4H, Ar-H), 6.44 (m, 4H, Ar_{phth}-H), 4.37 (d, 4H, ^2J = 13.5 Hz, Ar-CH_2-Ar*ax*), 4.15 (t, 4H, ^3J =

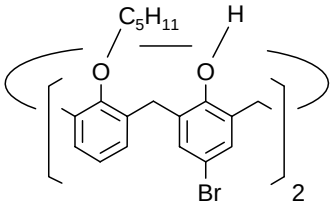
7.9 Hz, OCH_2-), 3.58 (t, 4H, ^3J = 6.4 Hz,, OCH_2-), 3.02 (d, 4H, ^2J = 13.5 Hz, Ar-CH_2-Ar*eq*), 1.96 (q, 4H, ^3J = 7.9 Hz, -CH_2-), 1.80 (q, 4H, ^3J = 7.9 Hz, -CH_2-), 1.49-1.25 (m, 36H, -CH_2-), 1.01 (t, 6H, ^3J = 7.0 Hz, -CH_3), 0.92 (t, 6H, ^3J = 7.04 Hz, -CH_3);
MS (FD), m/z 1225.8 (M^+ calc $C_{74}H_{88}N_4O_{12}$: 1225.48) .

25,27-Dipentoxy-26,28-dihydroxycalix[4]arene[64] **46**



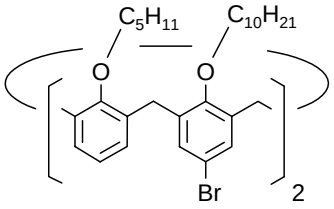
m.p. = 168-171°C;
^{1}H NMR ($CHCl_3$-d_1, 200MHz, 25 °C) δ(ppm) = 8.23 (s, 2H, OH), 7.05 (d, 4H, ^3J = 7.3 Hz, Ar-H), 6.91 (d, 4H, ^3J = 7.3 Hz, Ar-H), 6.76-6.69 (m, 2H, Ar-H), 6.63 (t, 2H, ^3J = 7.3 Hz, Ar-H), 4.31 (d, 4H, ^2J =13.2 Hz, Ar-CH_2-Ar*ax*), 3.99 (t, 4H, ^3J = 6.6 Hz, OCH_2-), 3.37 (d, 4H, ^2J = 13.2 Hz, Ar-CH_2-Ar*eq*), 2.07 (q, 4H, ^3J = 6.5 Hz, -CH_2-), 1.68 (m, 4H, -CH_2-), 1.5 (m, 4H, -CH_2 -), 0.99 (t, 6H, ^3J = 7.3 Hz, -CH_3).

5,17-Dibromo-26,28-dihydroxy-25,27-dipentoxycalix[4]arene[65] ***47***



yield = 88%; m.p.= 274-276°C;
^{1}H NMR ($CHCl_3$-d_1, 200MHz, 25 °C) δ (ppm) = 8.29 (s, 2H, OH), 7.15 (s, 4H, Ar-H), 6.91 (m, 4H, Ar-H), 6.78 (m, 2H, Ar-H), 4.24 (d, 4H, ^2J =13.2 Hz, Ar-CH_2-Ar*ax*), 3.95 (t, 4H, ^3J = 6.8 Hz, OCH_2-), 3.31 (d, 4H, ^2J = 13.2 Hz, Ar-CH_2-Ar*eq*), 2.04 (q, 4H, ^3J = 6.8 Hz, -CH_2-), 1.72-1.56 (m, 4H, -CH_2-), 1.52-1.38 (m, 4H, -CH_2 -), 0.98 (t, 6H, ^3J = 7.1 Hz, -CH_3).

5,17-Dibromo-26,28-didecyloxy-25,27-dipentoxycalix[4]arene[66] **48**



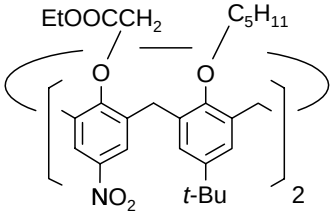
yield = 79%; oil;
^{1}H NMR ($CHCl_3$-d_1, 400MHz, 25 °C) δ (ppm) = 6.78 (s, 4H, Ar-H), 6.60 (m, 6H, Ar-H), 4.38 (d, 4H, ^2J =13.4 Hz, Ar-CH_2-Ar*ax*), 3.84 (t, 4H, ^3J = 7.0 Hz, OCH_2-), 3.10 (d, 4H, ^2J = 13.2 Hz, Ar-CH_2-Ar*eq*), 1.89-1.86 (m, 8H, -CH_2-), 1.37-1.27 (m, 36H, -CH_2 -), 0.93 (t, 6H, ^3J = 7.0 Hz, -CH_3), 0.88 (t, 6H, ^3J = 6.7 Hz, -CH_3);
^{13}C-NMR ($CHCl_3$-d_1, 100 MHz, 25°C): δ (ppm) = 156.30, 155.78, 137.32, 134.28, 130.75, 128.34, 122.44, 114.64, 75.35, 75.22, 31.91, 30.86, 30.19, 29.86, 29.68, 29.36, 28.37, 26.24, 22.81, 22.68, 14.19, 14.09;
MS (FD), m/z 1004.1 (M^+ calc $C_{58}H_{82}Br_2O_4$: 1002.42).

The strategy via ipso-nitration of phthalimido derivatives

The derivatives **51-54, 55-58,**[66] **73** and **74** [67] were obtained in accordance with literature.

General procedure for alkylation of nitro derivative 74

A slurry of **74**, Na_2CO_3 and alkylating reagent (3 mmol salt / 3 mmol ethyl bromoacetate / 1 mmol **74**) in acetonitrile was refluxed two days. The solvent was evaporated to dryness under reduced pressure and the crude product was taken in dichloromethane, washed with water (2x200 mL), dried over $MgSO_4$ and precipitated from a dichloromethane/methanol mixture. Yield of crystalline compound was 82-92%.



75

yield = 82%; m.p.= 146-147°C;

^{1}H-NMR ($CHCl_3$-d_1, 400 MHz, rt): δ (ppm) = 7.32 (s, 4H, Ar-H), 6.92 (s, 4H, Ar-H), 4.69 (s, 4H, OCH_2CO), 4.57 (d, 4H, ^2J = 13.4 Hz, Ar-CH_2-Ar*ax*), 4.22 (q, 4H, ^3J = 7.2 Hz, OCH_2-), 3.93 (t, 4H, ^3J = 7.8 Hz, OCH_2-), 3.27 (d, 4H, ^2J = 13.7 Hz, Ar-CH_2-Ar*eq*), 1.88 (m, 4H, -CH_2-), 1.37-1.34 (m, 8H, -CH_2-), 1.29 (t, 6H, ^3J = 7.2 Hz, $CH_2C\underline{H}_3$), 1.19 (s, 18H, ^{t}Bu), 0.92 (t, 6H, ^3J = 7.1 Hz, -CH_3),

^{13}C-NMR ($CHCl_3$-d_1, 100 MHz, rt): δ (ppm) = 168.67, 160.05, 154.12, 145.99, 142.91, 135.81, 133.33, 126.06, 123.24, 75.47, 71.01, 61.02, 34.05, 31.69, 31.41, 29.64, 28.11, 22.73, 14.17, 14.10;

MS (FD) m/z 938.8 (M^+ calc $C_{54}H_{70}N_2O_{12}$: 938.49).

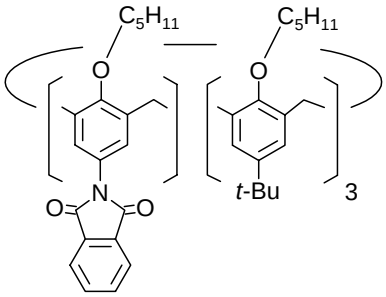
If potassium carbonate was used the product was obtained in the partial cone conformation. Yield after two crystallizations from CH_2Cl_2-MeOH was 36%;

m.p.= 172-173°C;

^{1}H-NMR ($CHCl_3$-d_1, 200 MHz, rt): δ (ppm) = 8.24 (s, 2H, Ar-H), 7.99 (s, 2H, Ar-H), 7.05 and 6.51 (2brd, 4H, Ar-H), 4.37 (s, 2H, OCH_2CO), 4.13 (s, 2H, OCH_2CO), 4.25-3.25 (m, 16H, Ar-CH_2-Ar + OCH_2-), 1.82 (m, 4H, -CH_2-), 1.42-1.39 (m, 8H, -CH_2-), 1.29 (t, 6H, ^3J=7.1 Hz, $CH_2C\underline{H}_3$), 1.19 (t, 6H, ^3J=7.1 Hz, $CH_2C\underline{H}_3$), 1.02 (s, 2H, ^{t}Bu), 0.95 (brs, 6H, -CH_3);

General procedure for the reaction of amino derivatives 55-58 with phthalic anhydride

A toluene solution of **55-58** and **75'** (di-amine obtained from 75) obtained after the reduction was treated with phthalic anhydride (1.1-1.2 mmol of phthalic anhydride per 1 mmol of amino group) and a few drops of triethylamine as catalyst. The reaction mixture was refluxed for 1-2 days when became clear orange solution. The solvent was evaporated in vacuo and the residue first was passed through a short silica column and then recrystallised from dichloromethane / methanol or acetonitrile. Yield 70-85%.



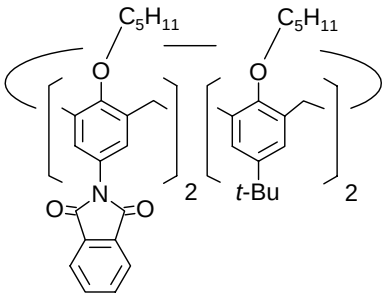
59

yield = 72%; m.p.: 161-162°C;

^{1}H-NMR ($CHCl_3$-d_1, 400 MHz, rt): δ (ppm) = 7.73 (m, 2H, Ar_{phth}-H), 7.72 (m, 2H, Ar_{phth}-H), 7.03 (s, 2H, Ar-H), 6.77 (s, 2H, Ar-H), 6.73 s, 4H, (Ar-H), 4.46 (d, 2H, ^2J = 13.4 Hz, Ar-CH_2-Ar*ax*), 4.42 (d, 2H, ^2J = 12.9 Hz, Ar-CH_2-Ar*ax*), 3.96 (t, 2H, ^3J = 7.6 Hz, OCH_2-), 3.90 (t, 2H, ^3J = 7.5 Hz, OCH_2-), 3.82 (m, 4H, OCH_2-), 3.17 (d, 2H, ^2J = 12.6 Hz, Ar-CH_2-Ar*eq*), 3.12 (d, 2H, ^2J = 12.9 Hz, Ar-CH_2-Ar*eq*), 2.03 (m, 4H, -CH_2-), 1.96 (m, 4H, -CH_2-), 1.39 (m, 16H, -CH_2-), 1.05 (s, 18H, ^{t}Bu), 1.02 (s, 9H, ^{t}Bu), 0.96 (m, 12H, -CH_3);

^{13}C-NMR ($CHCl_3$-d_1, 100 MHz, rt): δ (ppm) = 166.99, 155.64, 153.91, 153.56, 144.41, 144.27, 135.82, 134.16, 133.85, 133.48, 132.59, 131.90, 125.72, 125.20, 125.09, 124.84, 123.28, 75.50, 75.28, 75.20, 33.77, 33.67, 31.38, 31.20, 31.11, 30.06, 30.01, 29.81, 28.39, 28.30, 22.88, 22.86, 22.80, 14.24, 14.14;

MS (FD) m/z 1017.9 (M^+ calc $C_{68}H_{91}NO_6$: 1017.68).



60

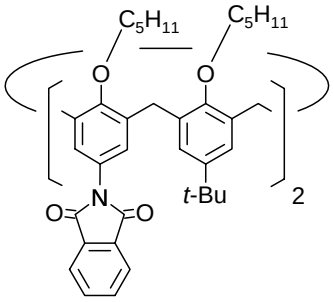
yield = 82%; m.p.: 293-294°C;

^{1}H-NMR ($CHCl_3$-d_1, 400MHz, rt): δ (ppm) = 7.72 (m, 4H, Ar_{phth}-H), 7.68 (m, 4H, Ar_{phth}-H), 7.06 (d, 2H, ^4J = 1.9 Hz, Ar-H), 6.93 (d, 2H, ^4J = 1.9 Hz, Ar-H), 6.77 (brd, 2H, Ar-H), 6.74 (brd, 2H, Ar-H), 4.52 (d, 1H, ^2J = 13.0 Hz, Ar-CH_2-Ar*ax*), 4.47 (d, 2H, ^2J = 12.7 Hz, Ar-CH_2-Ar*ax*), 4.46 (d, 1H, ^2J = 12.7 Hz, Ar-CH_2-Ar*ax*), 3.96-3.88 (m, 8H, OCH_2-), 3.26 (d, 1H, ^2J = 12.7 Hz, Ar-CH_2-Ar*eq*), 3.18 (d, 2H, ^2J

= 13.4 Hz, Ar-CH_2-Ar*eq*), 3.14 (d, 1H, ^2J = 14.3 Hz, Ar-CH_2-Ar*eq*), 1.99 (m, 8H, -CH_2-), 1.43-1.39 (m, 16H, -CH_2-), 1.01 (s, 18H, ^{t}Bu), 0.96 (t, 12H, ^3J = 6.2 Hz, -CH_3);

^{13}C-NMR ($CHCl_3$-d_1, 100 MHz, rt): δ (ppm) = 166.87, 155.37, 153.70, 144.73, 135.36, 134.62, 133.81, 133.65, 133.06, 131.85, 125.87, 125.49, 125.46, 125.33, 124.83, 123.23, 75.50, 75.32, 33.72, 31.21, 31.06, 30.96, 30.07, 29.88, 28.41, 28.32, 22.84, 22.81, 14.19, 14.17;

MS (FD) m/z 1106.7 (M^+ calc $C_{72}H_{86}N_2O_8$: 1106.6).



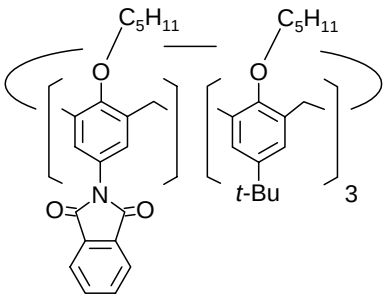
61

yield = 82%; m.p.: 240-241°C;

^{1}H-NMR ($CHCl_3$-d_1, 400MHz, rt): δ (ppm) = 7.35 (m, 4H, Ar_{phth}-H), 7.32 (m, 4H, Ar_{phth}-H), 6.99 (s, 4H, Ar-H), 6.51 (s, 4H, Ar-H), 4.48 (d, 4H, ^2J = 13 Hz, Ar-CH_2-Ar*ax*), 4.01 (t, 4H, ^3J = 8.1 Hz, OCH_2-), 3.81 (t, 4H, ^3J = 6.8 Hz, OCH_2-), 3.18 (d, 4H, ^2J = 13.0 Hz, Ar-CH_2-Ar*eq*), 2.01 (q, 4H, ^3J = 7.8 Hz, -CH_2-), 1.94 (q, 4H, ^3J = 7.5 Hz, -CH_2 -), 1.54-1.50 (m, 4H, -CH_2-), 1.45-1.39 (m, 8H, -CH_2-), 1.32-1.28 (m, 4H, -CH_2-), 1.23 (s, 18H, ^{t}Bu), 0.98 (t, 6H, ^3J = 7.1 Hz, -CH_3), 0.96 (t, 6H, ^3J = 7.2 Hz, -CH_3);

^{13}C-NMR ($CHCl_3$-d_1, 100 MHz, rt): δ (ppm) = 166.33, 154.73, 154.66, 144.84, 134.55, 134.06, 133.13, 131.69, 125.74, 125.56, 125.45, 122.54, 75.35, 75.18, 33.99, 31.53, 31.25, 30.12, 29.86, 28.60, 28.24, 22.93, 22.76, 14.29, 14.12;

MS (FD) m/z 1108.0 (M^+ calc $C_{72}H_{86}N_2O_8$: 1106.6).

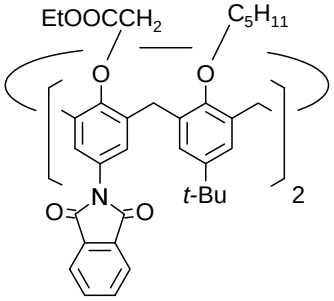


62

yield = 87%; m.p.: 290-291°C (decomp);

^{1}H-NMR (CH_2Cl_2-d_2, 400 MHz, rt): δ (ppm) = 7.84 (m, 2H, Ar_{phth}-H), 7.75 (m, 2H, Ar_{phth}-H), 7.35 (m, 4H, Ar_{phth}-H), 7.26 (m, 4H, Ar_{phth}-H), 7.20 (s, 2H, Ar-H), 7.06 (s, 2H, Ar-H), 6.51 (d, 2H, ^4J = 2.4 Hz, Ar-H), 6.50 (d, 2H, ^4J = 2.4 Hz, Ar-H), 4.57 d, 2H, ^2J = 13.4 Hz, (Ar-CH_2-Ar*ax*), 4.52 d, 2H, ^2J = 13 Hz, (Ar-CH_2-Ar*ax*), 4.18 t, 2H, ^2J = 8.3 Hz, (OCH_2-), 4.07 (t, 2H, ^3J = 8.2 Hz, OCH_2-), 3.86-3.80 (m, 4H, OCH_2-), 3.29 (d, 2H, ^2J = 13.4 Hz, Ar-CH_2-Ar*eq*), 3.22 (d, 2H, ^2J = 13.2 Hz, Ar-CH_2-Ar*eq*), 2.07-2.01 (m, 4H, -CH_2-), 2.00-1.92 (m, 4H, -CH_2-), 1.58-1.53 (m, 4H, -CH_2-), 1.48-1.40 (m, 8H, -CH_2-), 1.37-1.31 (m, 4H, -CH_2-), 1.23 (s, 9H, ^{t}Bu), 0.98 (t, 6H, ^3J = 7.2 Hz, -CH_3), 0.97 (t, 6H, ^3J = 7.2 Hz, -CH_3),

^{13}C-NMR (CD_2Cl_2-d_2, 100 MHz, rt): δ (ppm) = 167.60, 166.74, 157.17, 155.30, 155.12, 145.40, 136.86, 135.28, 134.45, 134.33, 133.76, 133.61, 132.35, 131.95, 126.68, 126.48, 126.37, 126.18, 126.07, 125.77, 123.59, 122.85, 76.06, 75.78, 75.73, 34.27, 31.60, 31.56, 30.58, 30.34, 30.09, 29.07, 28.65, 28.60, 23.35, 23.14, 14.48, 14.28, 1.13;
MS (FD), m/z 1195.5 (M^+ calc $C_{76}H_{81}N_3O_{10}$: 1195.59).

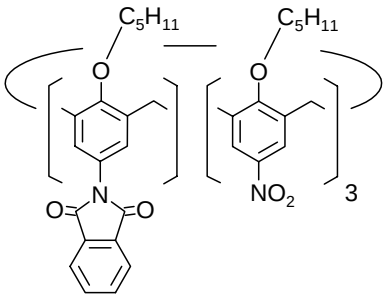


76

yield = 92%; m.p.: 290°C (decomp);
^{1}H-NMR ($CHCl_3$-d_1, 400 MHz, rt): δ (ppm) = 7.51 (m, 8H, Ar_{phth}-H), 6.85 (s, 4H, Ar-H), 6.74 (s, 4H, Ar-H), 4.73 (s, 4H, OCH_2CO), 4.65 (d, 4H, ^2J = 13.2 Hz, Ar-CH_2-Ar*ax*), 4.23 (q, 4H, ^3J = 7.2 Hz, OCH_2-), 3.96 (t, 4H, ^3J = 7.6 Hz, OCH_2-), 3.24 (d, 4H, ^2J = 13.2 Hz, Ar-CH_2-Ar*eq*), 1.95 (q, 4H, ^3J = 7.5 Hz, -CH_2-), 1.41-1.34 (m, 8H, -CH_2-), 1.30 (t, 6H, ^3J = 7.3 Hz, $CH_2C\underline{H}_3$), 1.12 (s, 18H, ^{t}Bu), 0.94 (t, 6H, ^3J = 7 Hz, -CH_3);
^{13}C-NMR ($CHCl_3$-d_1, 100 MHz, rt): δ (ppm) =169.66, 166.60, 154.40, 154.18, 144.99, 134.81, 133.48, 133.28, 131.74, 126.15, 126.04, 125.61, 122.89, 75.43, 71.07, 60.57, 33.90, 31.64, 31.42, 29.74, 28.30, 22.79, 14.21, 14.17;
MS (FD) m/z 1140.9 (M^+ calc $C_{70}H_{78}N_2O_{12}$: 1138.55).

General procedure for complete *ipso*-nitration of phthalimido compounds

A phthalimide derivative **59-62** and **76** was dissolved in a mixture of dichloromethane and glacial acetic acid (19:1; 50 ml solvent / 1 mmol), and fuming nitric acid (Merck, 100% extra pure; 5-6 mmol acid / 1 mmol tert-butyl group) was added in one portion while stirring. The reaction mixture become violet and in few minutes yellow. The course of reaction could be followed by TLC and if it was not complete, additional amount of nitric acid had to be added. The reaction mixture was washed with water till neutral pH and then concentrated in vacuo. The crude product was precipitated with methanol and, in general, it was pure enough for the next reaction. If the phthalimide derivatives **60** or **61** were dissolved in a double amount of solvent the main products were mono-*ipso*-nitrated **67** or **68**, respectively.



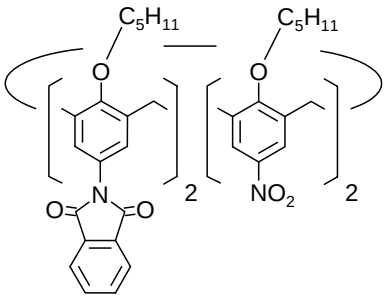
63

yield = 55%; m.p.: 272°C;

^{1}H-NMR ($CHCl_3$-d_1, 400 MHz, rt): δ (ppm) = 7.88 (s, 4H, Ar-H), 7.83 (m, 2H, Ar_{phth}-H), 7.72 (m, 2H, Ar_{phth}-H), 7.39 (s, 2H, Ar-H), 6.49 (s, 2H, Ar-H), 4.52 (d, 2H, ^2J = 13.4 Hz, Ar-CH_2-Ar*ax*), 4.51 (d, 2H, ^2J = 13.7 Hz, Ar-CH_2-Ar*ax*), 4.22-4.09 (m, 4H, OCH_2-), 3.85-3.83 (m, 4H, OCH_2-), 3.37 (d, 4H, ^2J = 13.7 Hz, Ar-CH_2-Ar*eq*), 1.94-189 (m, 4H, -CH_2-), 1.48-1.32 (m, 16H, -CH_2-), 0.98-0.93 (m, 12H, -CH_3);

^{13}C-NMR ($CHCl_3$-d_1, 100 MHz, rt): δ (ppm) = 166.55, 162.40, 160.68, 154.90, 143.64, 142.74, 136.82, 135.67, 134.07, 133.92, 133.19, 131.48, 126.51, 126.26, 124.64, 124.03, 123.60, 77.15, 76.31, 76.10, 76.02, 75.83, 31.09, 30.01, 29.90, 29.71, 28.39, 28.21, 27.96, 22.68, 22.65, 22.57, 14.09, 14.01, 13.94;

MS (FD) m/z 984.5 (M^+ calc $C_{56}H_{64}N_4O_{12}$: 984.45).



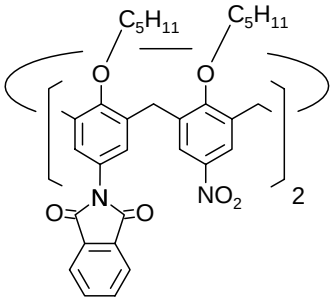
64

yield = 78%; m.p.: 197-199°C;

^{1}H-NMR ($CHCl_3$-d_1, 400 MHz, rt): δ (ppm) = 7.83 (m, 4H, Ar_{phth}-H), 7.69 (m, 4H, Ar_{phth}-H), 7.68 (brd, 2H, Ar-H), 7.63 (brd, 2H, Ar-H), 6.88 (d, 2H, ^4J = 2.4 Hz, Ar-H), 6.79 (d, 2H, ^4J = 2.4 Hz, Ar-H), 4.53 (d, 4H, ^2J = 13.6 Hz, Ar-CH_2-Ar*ax*), 4.06-3.92 (m, 8H, OCH_2-), 3.35 (d, 1H, ^2J = 13.6 Hz, Ar-CH_2-Ar*eq*), 3.33 (d, 2H, ^2J = 13.2 Hz, Ar-CH_2-Ar*eq*), 3.31 (d, 2H, ^2J = 13.2 Hz, Ar-CH_2-Ar*eq*), 1.94-1.91 (m, 8H, -CH_2-), 1.44-1.39 (m, 16H, -CH_2-), 0.98-0.93 (m, 12H, -CH_3);

^{13}C-NMR ($CHCl_3$-d_1, 100 MHz, rt): δ (ppm) = 166.81, 161.64, 155.46, 143.27, 135.86, 135.13, 134.59, 134.00, 133.77, 131.73, 126.61, 126.33, 125.94, 124.60, 123.90, 123.53, 75.94, 75.73, 31.15, 31.08, 29.93, 29.84, 28.31, 28.18, 22.77, 22.69, 14.15, 14.07;

MS (FD) m/z 1084.5 (M^+ calc $C_{64}H_{68}N_2O_{12}$: 1084.48).



65

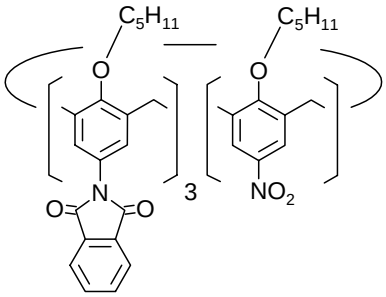
yield = 92%; m.p.: 262-264°C;

^{1}H-NMR ($CHCl_3$-d_1, 400 MHz, rt): δ (ppm) = 7.95 (s, 4H, Ar-H), 7.39 (m, 4H, Ar_{phth}-H), 7.29 (m, 4H, Ar_{phth}-H), 6.52 (s, 4H, Ar-H), 4.52 (d, 4H, ^2J = 13.6 Hz, Ar-CH_2-Ar*ax*), 4.22 (t, 4H, ^3J

= 8.1 Hz, OCH_2-), 3.80 (t, 4H, ^3J = 6.9 Hz, OCH_2-), 3.37 (d, 4H, ^2J = 13.6 Hz, Ar-CH_2-Ar*eq*), 1.97 (q, 4H, ^3J = 7.8 Hz, -CH_2-), 1.91 (q, 4H, ^3J = 7.8 Hz, -CH_2-), 1.50-1.20 (m, 16H, -CH_2-), 0.97 (t, 6H, ^3J = 7.0 Hz, -CH_3), 0.96 (t, 6H, ^3J = 7.0 Hz, -CH_3);

^{13}C NMR ($CHCl_3$-d_1, 100 MHz, rt): δ = 166.31, 163.04, 154.51, 142.47, 136.87, 133.47, 132.43, 131.39, 126.27, 126.13, 124.37, 122.92, 75.95, 75.75, 31.12, 30.11, 29.79, 28.51, 28.03, 22.78, 22.69, 14.19, 14.05;

MS (FD) m/z 1084.5 (M^+ calc $C_{64}H_{68}N_2O_{12}$: 1084.48).



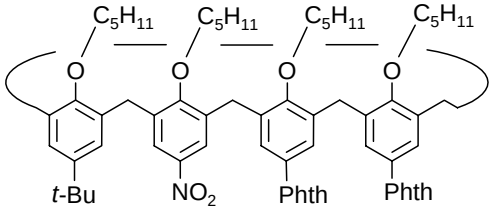
66

yield = 86%; m.p.: over 200°C (decomp);

^{1}H-NMR ($CHCl_3$-d_1, 400 MHz, rt): δ (ppm) = 7.84 (s, 2H, Ar-H), 7.82 (m, 2H, Ar_{phth}-H), 7.68 (m, 2H, Ar_{phth}-H), 7.39 (m, 4H, Ar_{phth}-H), 7.35 (m, 4H, Ar_{phth}-H), 7.04 (s, 2H, Ar-H), 6.79 (d, 2H, ^4J = 1.9 Hz, Ar-H), 6.64 (d, 2H, ^4J = 1.9 Hz, Ar-H), 4.54 (d, 2H, ^2J = 13.2 Hz, Ar-CH_2-Ar*ax*), 4.53 (d, 2H, ^2J = 13.2 Hz, Ar-CH_2-Ar*ax*), 4.15 (brt, 2H, ^3J = 7.8 Hz, OCH_2-), 4.06 (t, 2H, ^3J = 7.9 Hz, OCH_2-), 3.89-3.84 (m, 4H, OCH_2-), 3.34 (d, 2H, ^2J = 13.7 Hz, Ar-CH_2-Ar*eq*), 3.30 (d, 2H, ^2J = 13.7 Hz, Ar-CH_2-Ar*eq*), 2.01-1.92 (m, 8H, -CH_2-), 1.49-1.33 (m, 16H, -CH_2-), 0.99-0.94 (m, 12H, -CH_3);

^{13}C-NMR ($CHCl_3$-d_1, 100 MHz, rt): δ (ppm) = 166.93, 166.43, 162.59, 156.08, 154.89, 142.72, 136.31, 135.51, 134.12, 133.86, 133.37, 132.65, 131.90, 131.57, 126.49, 126.26, 126.03, 125.95, 125.78, 124.26, 123.34, 122.86, 75.66, 75.49, 31.15, 31.09, 30.02, 29.84, 29.79, 28.44, 28.21, 28.11, 22.83, 22.74, 22.72, 14.22, 14.14, 14.08, 0.97;

MS (FD), m/z 1184.1 (M^+ calc $C_{72}H_{72}N_4O_{12}$: 1184.5).



67

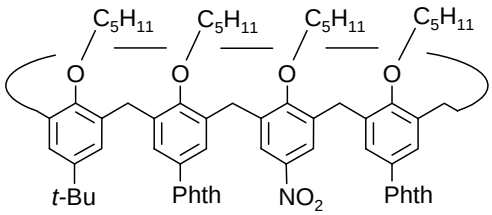
yield = 86%; m.p.: 211-213°C;

^{1}H-NMR (CD_2Cl_2-d_2, 400 MHz, rt): δ (ppm) = 7.88 (m, 2H, Ar_{phth}-H), 7.77 (m, 2H, Ar_{phth}-H), 7.74 (m, 2H, Ar_{phth}-H), 7.68 (m, 2H, Ar_{phth}-H), 7.28 (d, 1H, ^4J = 2.7 Hz, Ar-H), 7.26 (brs, 1H, Ar-H), 7.25 (brs, 1H, Ar-H), 7.20 (d, 1H, ^4J = 2.4 Hz, Ar-H), 7.07 (d, 1H, ^4J = 2.4 Hz, Ar-H), 7.05 (d, 1H, ^4J = 2.4 Hz, Ar-H), 6.47 (d, 1H, ^4J = 2.4 Hz, Ar-H), 6.44 (d, 1H, ^4J = 2.4 Hz, Ar-H), 4.56 (d, 2H, ^2J = 13.4 Hz, Ar-CH_2-Ar*ax*), 4.51 (d, 1H, ^2J = 13.2 Hz, Ar-CH_2-Ar*ax*), 4.50 (d, 1H, ^2J = 13.2 Hz, Ar-CH_2-Ar*ax*), 4.18-4.01 (m, 4H, OCH_2-), 3.87-3.82 (m, 4H, OCH_2-), 3.30 (d, 1H, ^2J = 13.4 Hz,

Ar-CH_2-Ar*eq*), 3.29 (d, 1H, ^2J = 13.4 Hz, Ar-CH_2-Ar*eq*), 3.24 (d, 1H, ^2J = 13.4 Hz, Ar-CH_2-Ar*eq*), 3.23 (d, 1H, ^2J = 13.2 Hz, Ar-CH_2-Ar*eq*), 2.03-1.91 (m, 8H, -CH_2-), 1.55-1.50 (m, 4H, -CH_2-), 1.47-1.40 (m, 8H, -CH_2-), 1.34-1.30 (m, 4H, -CH_2-), 1.23 (s, 9H, ^{t}Bu), 0.99-0.95 (m, 12H, -CH_3);

^{13}C-NMR (CD_2Cl_2-d_2, 100 MHz, rt): δ (ppm) = 155.01, 145.84, 143.88, 136.91, 135.87, 135.66, 135.44, 134.94, 134.82, 134.58, 134.33, 134.17, 134.06, 132.23, 132.16, 127.03, 126.92, 126.55, 126.47, 126.41, 126.17, 125.99, 125.58, 124.16, 123.71, 123.46, 76.37, 76.14, 75.86, 75.73, 34.31, 31.55, 31.48, 31.41, 30.54, 30.43, 30.25, 30.11, 29.03, 28.85, 28.60, 28.53, 23.32, 23.30, 23.13, 23.06, 14.44, 14.28, 14.21;

MS (FD) m/z 1095.6 (M^+ calc $C_{68}H_{77}N_3O_{10}$: 1095.55).



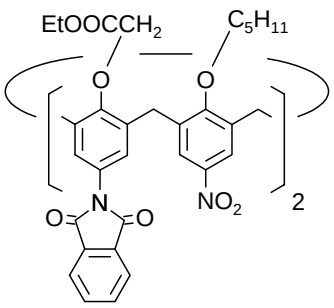
68

yield = 70%; m.p.: 305–307°C;

^{1}H-NMR (CD_2Cl_2-d_2, 400 MHz, rt): δ (ppm) = 7.69 (m, 4H, Ar_{phth}-H), 7.59 (m, 4H, Ar_{phth}-H), 7.61 (s, 2H, Ar-H), 6.97 (brs, 2H, Ar-H), 6.91 (brs, 2H, Ar-H), 6.52 (s, 2H, Ar-H), 4.52 (d, 2H, ^2J = 13.3 Hz, Ar-CH_2-Ar*ax*), 4.47 (d, 2H, ^2J = 13.0 Hz, Ar-CH_2-Ar*ax*), 4.04 (m, 2H, OCH_2-), 3.95 (m, 4H, OCH_2-), 3.85 (t, 2H, ^3J = 7.2 Hz, OCH_2-), 3.28 (d, 2H, ^2J = 13.3 Hz, Ar-CH_2-Ar*eq*), 3.22 (d, 2H, ^2J = 13.0 Hz, Ar-CH_2-Ar*eq*), 2.20-1.80 (m, 8H, -CH_2-), 1.50-1.20 (m, 16H, -CH_2-), 1.00-0.90 (m, 12H, -CH_3);

^{13}C NMR ($CHCl_3$-d_1, 100 MHz): δ (ppm) = 166.91, 161.84, 155.79, 153.54, 146.22, 145.51, 142.59, 136.22, 135.57, 134.05, 133.79, 132.66, 131.75, 127.07, 125.79, 125.40, 123.81, 123.23, 76.00, 75.45, 33.63, 31.14, 31.06, 30.14, 29.91, 28.48, 28.27, 22.84, 22.68, 14.23, 14.15, 14.07;

MS (FD) m/z 1095.4 (M^+ calc $C_{68}H_{77}N_3O_{10}$: 1095.55).



77

yield = 79%; m.p.= 290°C (decomp);

^{1}H-NMR ($CHCl_3$-d_1, 400 MHz, rt): δ (ppm) = 7.80 (s, 4H, Ar-H), 7.45 (m, 4H, Ar_{phth}-H), 7.42 (m, 4H, Ar_{phth}-H), 6.71 (s, 4H, Ar-H), 4.70 (d, 4H, ^2J = 13.8 Hz, Ar-CH_2-Ar*ax*), 4.54 (s, 4H, OCH_2CO), 4.27-4.20 (m, 8H, $OCH_2C\underline{H}_3$ + OCH_2-), 3.38 (d, 4H, ^2J = 13.8 Hz, Ar-CH_2-Ar*eq*), 1.93 (q, 4H, ^3J = 7.3 Hz, -CH_2-), 1.42-1.36 (m, 8H, -CH_2-), 1.31 (t, 6H, ^3J = 7.2 Hz, CH_2CH_3), 0.94 (t, 6H, ^3J = 6.9 Hz, -CH_3);

^{13}C-NMR ($CHCl_3$-d_1, 100 MHz, rt): δ (ppm) = 168.79, 166.39, 162.67, 154.10, 142.57, 136.23, 133.70, 133.05, 131.40, 127.04, 126.52, 124.19, 123.1176.09, 71.54, 60.91, 31.33, 29.63, 28.06, 22.63, 14.21, 14.09;
MS (FD) m/z 1117.7 (M^+ calc $C_{62}H_{60}N_4O_{16}$: 1117.19).

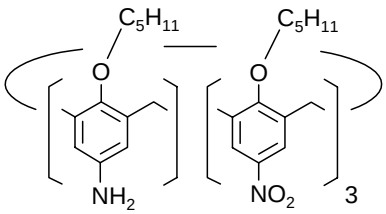
General procedure for cleavage of phthalimides protection

Method A (with hydrazine hydrate):

A phthalimido-nitro derivative **63-66** was dissolved in a warm mixture of ethanol and toluene (3:1). When a clear solution was formed, the calculated amount of hydrazine (minimum 10 mmol of hydrazine per 1 mmol phthalimido group) was added and the reaction mixture was refluxed for two hours. After cooling to the room temperature, hydrochloric acid (37 %) was added (2-3 ml) and a white precipitate appeared. This mixture was diluted with toluene and washed with water till neutral pH. The water layer was extracted with toluene again and the combined organic layer was dried over $MgSO_4$ and evaporated to dryness. The product was crystallized from dichloromethane / methanol mixture to give yellow crystals. Yield 85-97%.

Method B (with hydrochloric acid):

A phthalimido-nitro compound **77** was dissolved in a warm ethanol toluene mixture (3:1, 5-10 ml solvent per 0.1 mmol compound). To the clear warm solution was added concentrated hydrochloric acid (50 mmol / phthalimido group) and refluxed for 1-2 days. The work up was done in a way similar to the method A.



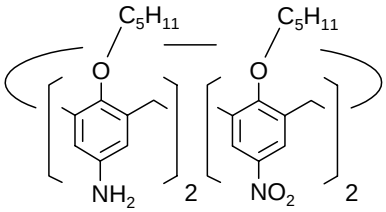
69 (Method A)

yield = 85%; m.p.: 175-176°C;

^{1}H-NMR ($CHCl_3$-d_1, 400 MHz, rt): δ (ppm) = 7.89 (s, 4H, Ar-H), 7.21 (s, 2H, Ar-H), 5.53 (s, 2H, Ar-H), 4.51 (d, 2H, ^2J = 13.9 Hz, Ar-CH_2-Ar*ax*), 4.37 (d, 2H, ^2J = 13.7 Hz, Ar-CH_2-Ar*ax*), 4.16-4.11 (m, 4H, OCH_2-), 4.04-4.00 (m, 4H, OCH_2-), 3.86 (t, 2H, ^3J = 6.8 Hz, OCH_2-), 3.66 (t, 2H, ^3J = 6.7 Hz, OCH_2-), 3.35 (d, 2H, ^2J = 13.9 Hz, Ar-CH_2-Ar*eq*), 3.18 (d, 2H, ^2J = 13.9 Hz, Ar-CH_2-Ar*eq*), 2.92 (brs, 2H, NH_2), 1.87-1.78 (m, 8H, -CH_2-), 1.47-1.24 (m, 16H, -CH_2-), 0.96-0.90 (m, 12H, -CH_3);

^{13}C-NMR ($CHCl_3$-d_1, 100 MHz, rt): δ (ppm) = 163.03, 161.23, 148.29, 142.59, 142.46, 141.73, 137.80, 136.00, 134.78, 133.03, 124.84, 123.75, 123.50, 114.42, 76.07, 75.84, 75.60, 31.13, 29.97, 29.93, 29.84, 28.56, 28.32, 27.92, 22.71, 22.60, 14.10, 14.07, 14.01, 1.01;

MS (FD) m/z 854.4 (M^+ calc $C_{48}H_{62}N_4O_{10}$: 854.8).



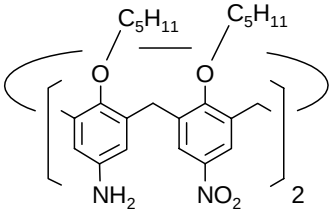
70 (Method A)

yield = 90%; m.p.: 197-199°C;

^{1}H-NMR ($CHCl_3$-d_1, 400 MHz, rt): δ (ppm) = 7.60 (d, 2H, ^4J = 2.2 Hz, Ar-H), 7.52 (brd, 2H, Ar-H), 5.97 (brd, 2H, Ar-H), 5.89 (brd, 2H, Ar-H), 4.51 (d, 1H, ^2J = 14.0 Hz, Ar-CH_2-Ar*ax*), 4.38 (d, 2H, ^2J = 13.8 Hz, Ar-CH_2-Ar*ax*), 4.24 (d, 1H, ^2J = 13.4 Hz, Ar-CH_2-Ar*ax*), 4.05-3.99 (m, 2H, OCH_2-), 3.93-3.87 (m, 2H, OCH_2-), 3.08-3.67 (m, 4H, OCH_2-), 3.31 (d, 1H, ^2J = 14 Hz, Ar-CH_2-Ar*eq*), 3.12 (d, 2H, ^2J = 13.8 Hz, Ar-CH_2-Ar*eq*), 3.25-3.05 (brs, 4H, NH_2), 2.91 (d, 1H, ^2J = 13.4 Hz, Ar-CH_2-Ar*eq*), 1.85-1.78 (m, 8H, -CH_2 -), 1.38-1.33 (m, 16H, -CH_2 -), 0.94-0.90 (m, 12H, -CH_3);

^{13}C-NMR ($CHCl_3$-d_1, 100 MHz, rt): δ (ppm) = 162.40, 149.24, 142.28, 141.17, 137.13, 136.01, 135.25, 133.88, 124.34, 123.22, 115.58, 114.48, 75.65, 75.25, 31.23, 31.14, 31.04, 29.91, 29.79, 28.36, 28.15, 22.77, 22.66, 14.14, 14.06;

MS (FD) m/z 824.8 (M^+ calc $C_{48}H_{64}N_4O_8$: 825.07).



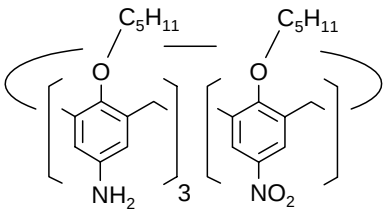
71 (Method A)

yield = 95%; mp ≤ 200°C decomp;

^{1}H-NMR ($CHCl_3$-d_1, 400 MHz, rt): δ (ppm) = 7.50 (s, 4H, Ar-H), 6.03 (s, 4H, Ar-H), 4.38 (d, 4H, ^2J = 13.6 Hz, Ar-CH_2-Ar*ax*), 3.93 (t, 4H, ^3J = 7.3 Hz, OCH_2-), 3.78 (t, 4H, ^3J = 7.6 Hz, OCH_2-), 3.25 (brs, 4H, NH_2), 3.11 (d, 4H, ^2J = 13.6 Hz, $ArCH_2$Ar*eq*), 1.83 (q, 8H, ^3J = 7.2 Hz, -CH_2-), 1.45-1.30 (m, 16H, -CH_2-), 0.93 (t, 12H, ^3J = 6.7 Hz, -CH_3);

^{13}C-NMR ($CHCl_3$-d_1, 100 MHz, rt): δ (ppm) = 162.25, 149.25, 142.40, 141.45, 136.42, 134.56, 123.39, 115.98, 75.65, 75.35, 31.16, 29.92, 29.72, 28.32, 28.21, 22.78, 22.67, 14.14, 14.07;

MS (FD) m/z 824.7 (M^+ calc $C_{48}H_{64}N_4O_8$: 825.07).



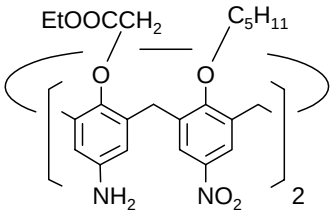
72 (Method A)

yield = 90%; mp >200°C (decomp);

^{1}H-NMR ($CHCl_3$-d_1, 400 MHz, rt): δ (ppm) = 7.39 (s, 2H, Ar-H), 6.26 (brd, 2H, Ar-H), 6.22 (brd, 2H, Ar-H), 5.79 (s, 2H, Ar-H), 4.38 (d, 2H, ^2J = 13.6 Hz, Ar-CH_2-Ar*ax*), 4.24 (d, 2H, ^2J = 13.3 Hz, Ar-CH_2-Ar*ax*), 3.88-3.83 (m, 4H, OCH_2-), 3.78-3.72 (m, 2H, OCH_2-), 3.65 (t, 2H, ^3J = 7.0 Hz, OCH_2-), 3.36 (brs, 6H, NH_2), 3.07 (d, 2H, ^2J = 13.6 Hz, Ar-CH_2-Ar*eq*), 2.90 (d, 2H, ^2J = 13.6 Hz, Ar-CH_2-Ar*eq*), 1.83-1.80 (m, 8H, -CH_2-), 1.38-1.35 (m, 16H, -CH_2-), 0.94-0.89 (m, 12H, -CH_3);

^{13}C-NMR ($CHCl_3$-d_1, 100 MHz, rt): δ (ppm) = 150.59, 143.14, 142.22, 140.47, 139.31, 137.00, 136.23, 135.06, 134.80, 123.39, 117.15, 116.02, 114.81, 75.43, 75.09, 75.05, 31.17, 31.05, 29.94, 29.65, 28.49, 28.25, 22.81, 22.74, 22.62, 14.17, 14.10, 14.03;

MS (FD), m/z 796.5 (M^+ calc $C_{48}H_{66}N_4O_6$: 795.08).



78 (Method B)

yield = 90%; mp ≥200°C decomp.;

^{1}H-NMR ($CHCl_3$-d_1, 400 MHz, rt): δ (ppm) = 7.24 (s, 4H, Ar-H), 6.32 (s, 4H, Ar-H), 4.67 (d, 4H, ^2J = 13.7 Hz, Ar-CH_2-Ar*ax*), 4.56 (s, 4H, OCH_2CO), 4.16 (q, 4H, ^3J = 7.2 Hz, $OC\underline{H}_2CH_3$), 3.86 (t, 4H, ^3J = 7.1 Hz, OCH_2-), 3.37 (s, 4H, NH_2), 3.12 (d, 4H, ^2J = 13.9 Hz, Ar-CH_2-Ar*eq*), 1.83 (q, 4H, ^3J = 7.1 Hz, -CH_2-), 1.43-1.34 (m, 8H, -CH_2 -), 1.25 (t, 6H, ^3J = 7.1 Hz, $CH_2C\underline{H}_3$), 0.91 (t, 6H, ^3J = 7 Hz, -CH_3);

^{13}C-NMR ($CHCl_3$-d_1, 100 MHz, rt): δ (ppm) = 169.86, 161.31, 148.83, 142.62, 142.12, 135.46, 135.34, 123.01, 116.22, 75.83, 70.83, 60.38, 31.30, 29.66, 28.19, 22.56, 14.15, 13.98;

MS (FD) m/z 858.0 (M^+ calc $C_{46}H_{56}N_4O_{12}$: 856.98).

Loop-Compounds

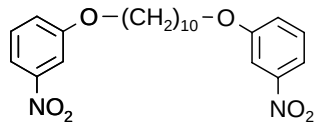
***Di-urethanes* 82**

a) Dinitro derivatives **80**:

A slurry of 3-nitrophenol (11 mmol), α,ω-dibromo-alkane (5 mmol) and potassium carbonate (11 mmol) in acetonitrile (50 mL) was refluxed for two days (TLC control , eluent ethyl acetate/hexane 1/2). The solvent was evaporated under reduced pressure and

the crude product taken up in dichloromethane (250 mL). The organic layer was washed with water until the aqueous phase remained colorless (2-4 x 100 mL), dried over $MgSO_4$ and concentrated. Precipitation with methanol gave the wanted compounds as a white to yellowish powder.

***Dinitro* 80a**



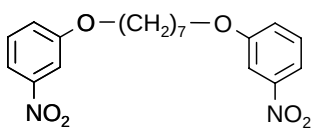
yield = 84%; m.p. = 80-81 °C;

^{1}H NMR ($CHCl_3$-d_1, 400 MHz): δ = 7.79 and 7.77 (ddd, ^3J = 8.1 Hz, ^4J = 2.2 Hz, ^4J = 0.9 Hz, 2H, Ar-H), 7.70 (t, ^4J = 2.3 Hz, 2H, Ar-H), 7.39 (t, ^3J = 8.2 Hz, 2H, Ar-H), 7.20 and 7.18 (ddd, ^3J = 8.4 Hz, ^4J = 2.5 Hz, ^4J = 0.9 Hz, 2H, Ar-H), 4.01 (t, ^3J = 6.6 Hz, 4H, OCH_2-), 1.80 (q, ^3J = 6.5 Hz, 4H, -CH_2-), 1.48-1.43 (m, 4H, -CH_2-), 1.37-1.32 (m, 8H, -CH_2-);

^{13}C NMR ($CHCl_3$-d_1): δ = 159.66, 149.21, 129.82, 121.66, 115.50, 108.65, 68.70, 29.41, 29.26, 28.97, 25.91;

MS (FD): m/z 416.3 (M calc $C_{22}H_{28}N_2O_6$: 416.48).

***Dinitro* 80b**



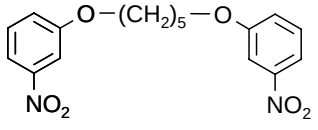
yield = 88%; m.p. = 79°C;

^{1}H-NMR ($CHCl_3$-d_1, 400 MHz, rt): δ (ppm) = 7.80 and 7.78 (ddd, 2H, ^3J = 8.1 Hz, ^4J = 1.9 Hz, ^4J = 0.8 Hz, Ar-H), 7.70 (t, 2H, ^4J = 2.3 Hz, Ar-H), 7.40 (t, 2H, ^3J = 8.2 Hz, Ar-H), 7.21 and 7.19 (ddd, 2H, ^3J = 8.3 Hz, ^4J = 2.44 Hz, ^4J = 0.8 Hz, Ar-H), 4.06 (t, 4H, ^3J = 6.3 Hz, OCH_2-), 1.94-1.87 (m, 4H, -CH_2-), 1.73-1.67 (m, 2H, -CH_2-).

^{13}C-NMR ($CHCl_3$-d_1, 100 MHz, rt): δ (ppm) = 159.63, 149.20, 129.85, 121.66, 115.57, 108.63, 68.58, 28.99, 28.91, 25.88.

MS (FD): m/z 374.2 (M calc $C_{19}H_{22}N_2O_6$: 374.4).

***Dinitro* 80c**



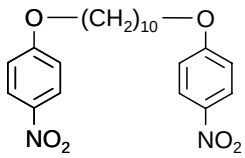
yield = 92%; mp = 96-97°C;

^{1}H-NMR ($CHCl_3$-d_1, 400 MHz, rt): δ (ppm) = 7.80 and 7.78 (ddd, 2H, ^3J = 8.1 Hz, ^4J = 2.2 Hz, ^4J = 0.8 Hz, Ar-H), 7.70 (t, 2H, ^4J = 2.3 Hz, Ar-H), 7.40 (t, 2H, ^3J = 8.2 Hz, Ar-H), 7.21 and 7.19 (ddd, 2H, ^3J = 8.3 Hz, ^4J = 2.6 Hz, ^4J = 0.9 Hz, Ar-H), 4.03 (t, 4H, ^3J = 6.4 Hz, OCH_2-), 1.87-1.80 (q, 4H, ^3J = 6.6 Hz, -CH_2-), 1.54-1.44 (m, 6H, -CH_2-).

^{13}C-NMR ($CHCl_3$-d_1, 100 MHz, rt): δ (ppm) = 159.51, 149.19, 129.89, 121.62, 115.65, 108.64, 68.36, 28.70, 22.63;

MS (FD): m/z 346.1 (M calc $C_{17}H_{18}N_2O_6$: 346.3).

Dinitro **80d**



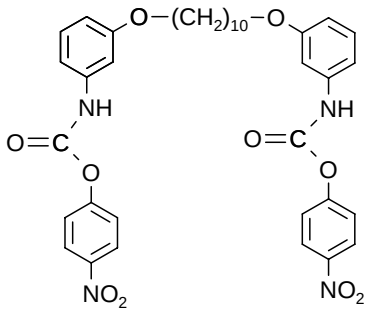
yield = 94%; m.p. = 82-83 °C;

^{1}H NMR ($CHCl_3$-d_1, 200 MHz): δ = 8.18 and 6.92 (two d AB-system, ^3J = 9.3 Hz, 4H, Ar-H), 4.03 (t, ^3J = 6.3 Hz, 4H, OCH_2-), 1.81 (q, ^3J = 6.3 Hz, 4H, -CH_2 -), 1.44-1.33 (m, 12H, -CH_2 -).

b) Di-urethanes **82**

The di-nitro derivative 80 (5.0 mmol) was dissolved in acetone (125 mL) and hydrogenated (1 atm.) in the presence of Raney-nickel until the hydrogen uptake was completed (~3h). The catalyst was filtered off, washed with acetone (2 x 25 mL), the solvent was evaporated and the product was used in the next step without analysis. The white solid residue was dissolved in dioxane (150 mL), 4-nitrophenyl chloroformate (11.15 mmol) was added and the mixture was refluxed under nitrogen for 24 hours (a clear solution was obtained in ~3 h). The solvent was evaporated to dryness and the residue was triturated with chloroform. The desired products, a white powder, was filtered off, washed with chloroform (2 x 15 mL) and dried.

Di-urethane **82a**



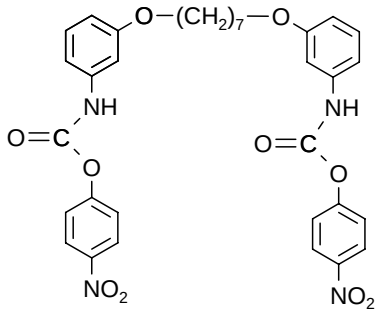
yield = 94%; m.p. = 177-178°C (decomp);

^{1}H NMR (DMSO-d_6, 400 MHz, rt): δ = 10.41 (s, 2H, NH), 8.30 and 7.53 (2d, ^3J = 8.9 Hz, 8H, Ar-H), 7.21 (t, ^3J = 8.1 Hz, 2H, Ar_{meta}-H), 7.15 (s, 2H, Ar_{meta}-H), 7.06 and 7.04 (dd, ^3J = 8.1 Hz, 2H, Ar_{meta}-H), 6.65 and 6.63 (2brd, ^3J = 7.7 Hz, 2H, Ar_{meta}-H), 3.91 (t, ^3J = 6.24 Hz, 4H, OCH_2-), 1.68 (q, ^3J = 6.6 Hz, 4H, -CH_2 -), 1.38 (m, 4H, -CH_2 -), 1.28 (m, 8H, -CH_2 -);

^{13}C NMR (DMSO-d_6, 100 MHz, rt): δ = 159.01, 155.49, 150.36, 144.49, 139.19, 129.66, 125.12, 122.81, 110.74, 109.14, 104.97, 67.26, 66.25, 28.82, 28.63, 28.51, 25.38;

MS (FD): [M^+] was not detected due to decomposition.

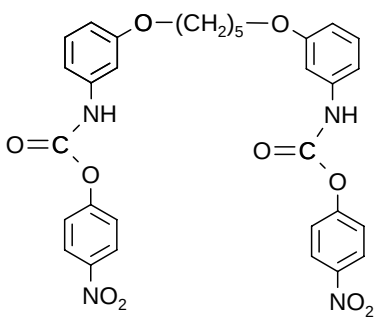
***Di-urethane* 82b**



yield = 81%; m.p. = 173-174°C with decomp.,
^{1}H-NMR (DMSO-d_6, 400 MHz, rt): δ (ppm) = 10.42 (s, 2H, NH), 8.30 and 7.53 (2d, 8H, ^{3}J = 8.9 Hz, Ar-H), 7.21 (t, 2H, ^{3}J = 8.2 Hz, Ar_{meta}-H), 7.16 (s, 2H, Ar_{meta}-H), 7.07 and 7.05 (2s, 2H, ^{3}J = 7.8 Hz, Ar_{meta}-H), 6.65 and 6.63 (dd, 2H, ^{3}J = 8.3 Hz, ^{4}J = 2.2 Hz, Ar_{meta}-H), 3.92 (t, 4H, ^{3}J = 6.48 Hz, OCH_2-), 1.70 (q, 4H, ^{3}J = 6.6 Hz, -CH_2 -), 1.46-1.38 (m, 6H, -CH_2 -).

^{13}C-NMR (DMSO-d_6, 100 MHz, rt): δ (ppm) = 159.02, 155.41, 150.37, 144.48, 139.21, 129.65, 125.13, 122.80, 110.76, 109.14, 105.00, 67.26, 28.49, 28.42, 25.37;
MS (FD): [M^+] was not detected due to decomposition.

***Di-urethane* 82c**

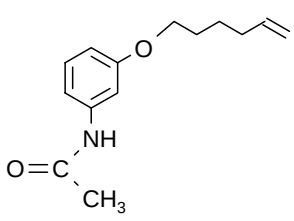


yield = 77.6%; m.p. = 174-177°C;
^{1}H-NMR (DMSO-d_6, 400 MHz, rt): δ (ppm) = 10.42 (s, 2H, NH), 8.30 and 7.53 (2d, 8H, ^{3}J = 9.1 Hz, Ar-H), 7.22 (t, 2H, ^{3}J = 8.04 Hz, Ar_{meta}-H), 7.17 (s, 2H, Ar_{meta}-H), 7.08 and 7.06 (d, 2H, ^{3}J = 8.04 Hz, Ar_{meta}-H), 6.66 and 6.64 (dd, 2H, ^{3}J = 8.04 Hz, ^{4}J = 2.02 Hz, Ar_{meta}-H), 3.95 (t, 4H, ^{3}J = 6.32 Hz, OCH_2-), 1.77 (q, 4H, ^{3}J = 6.92 Hz, -CH_2 -), 1.56-1.53 (m, 2H, -CH_2 -);

^{13}C-NMR (DMSO-d_6, 100 MHz, rt): δ (ppm) = 159.01, 155.41, 150.36, 144.48, 139.21, 129.66, 125.11, 122.79, 110.80, 109.14, 105.03, 67.24, 28.30, 22.14;
MS (FD): [M^+] was not detected due to decomposition.

Mono-urethane **88a**

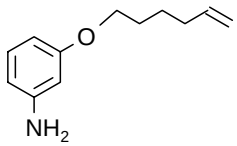
***3-Hexenyloxy-acetanilide* 86**



A mixture of 3-hydroxyacetanilide (1.634 g, 10.8 mmol), ω-bromohexene-1 (2.041 g, 11.9 mmol) and K_2CO_3 (1.641 g, 11.9 mmol) in 20 mL of DMF was stirred at 70 °C during 6 hours. After cooling, the reaction mixture was poured into 150 mL of water and extracted with chloroform (4 x 20 mL). The organic layer was washed with water (2 x 20 mL), dried over $MgSO_4$ and evaporated at reduced

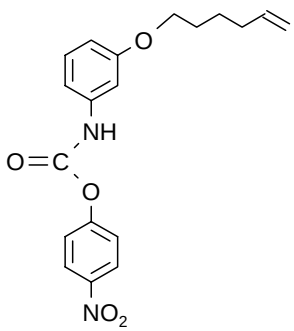
pressure. After recrystallisation from hexane (15 mL) a white crystalline powder was obtained 2.04 g (65 %). m.p.: 69 °C. found, %: C 71.10, H 8.03, N 5.90, calc. for $C_{12}H_{17}NO$, %: 72.07, H 8.21, N 6.00. ^{1}H NMR ($CHCl_3$-d_1): δ = 7.30 (brs, 1H, NH), 7.25 (s, 1H, Ar-H), 7.17 (t, ^3J = 7.6 Hz, 1H, Ar-H), 6.92 (d, ^3J = 7.6 Hz, 1H, Ar-H), 6.63 (d, ^3J = 8.2 Hz, 1H, Ar-H), 5.82 (m, 1H, -CH=CH_2), 5.02 (dd, ^2J = 17.0 Hz, ^3J = 1.2 Hz, 1H, -CH=CH_2), 4.96 (dd, ^2J = 10.0 Hz, ^3J = 1.0 Hz, 1H, -CH=CH_2), 3.94 (t, ^3J = 6.5 Hz, 2H, OCH_2-), 2.15 (s, 3H, $COCH_3$), 2.10 (q, ^3J = 7 Hz, 2H, CH_2CH=CH_2), 1.77 (q, ^3J = 7.3 Hz, 2H, -CH_2-), 1.54 (q, ^3J = 7.3 Hz, 2H, -CH_2-); ^{13}C NMR ($CHCl_3$-d_1): δ = 159.66, 139.04, 138.51, 129.58, 129.45, 114.70, 111.72, 110.62, 106.17, 67.77, 33.39, 28.64, 25.28, 24.68; FD MS: m/z 233.4 [M^+].

***3-Hexenyloxy-aniline* 87**



A solution of 86 (0.27 g, 1.16 mmol) and NaOH (1.62 g, 40.5 mmol) in a mixture of ethanol (20 mL) and water (2 mL) was refluxed for 6 hours. After cooling, the mixture was evaporated under reduced pressure, 200 mL water was added and the mixture was extracted with dichloromethane (4 x 20 mL). The organic layer was washed with water (2 x 30 mL), dried over $MgSO_4$ and evaporated, giving 0.21 g (95%) of a yellow oil. found, %: C 75.10, H 9.02, N 7.12, calc. for $C_{12}H_{17}NO$, %: 75.35, H 8.91, N 7.32. ^{1}H NMR ($CHCl_3$-d_1): δ = 7.07 (t, ^3J = 8.2 Hz, 1H, Ar-H), 6.35 (dd, ^3J = 8.2 Hz, ^4J = 1.8 Hz, 1H, Ar-H), 6.29 (dd, ^3J = 8.2 Hz, ^4J = 1.8 Hz, 1H, Ar-H), 6.25 (t, ^3J = 1.8 Hz, 1H, Ar-H), 5.86 (m, 1H, -CH=CH_2), 5.07 (dd, ^2J = 17.0 Hz, ^3J = 1.8 Hz, 1H, -CH=CH_2), 4.96 (d, ^3J = 10.6 Hz, 1H, CH=CH_2), 3.94 (t, ^3J = 6.5 Hz, 2H, OCH_2-), 3.63 (brs, 2H, NH_2), 2.15 (q, ^3J = 7 Hz, 2H, CH_2CH=CH_2), 1.81 (q, ^3J = 8.2 Hz, 2H, -CH_2-), 1.59 (q, ^3J = 7.6 Hz, 2H, -CH_2-); ^{13}C NMR ($CHCl_3$-d_1): δ = 160.09, 147.68, 138.44, 129.87, 114.55, 107.60, 104.36, 101.46, 67.35, 33.29, 28.60, 25.19; FD MS: 191.6 [M^+].

***Mono-urethane* 88a**

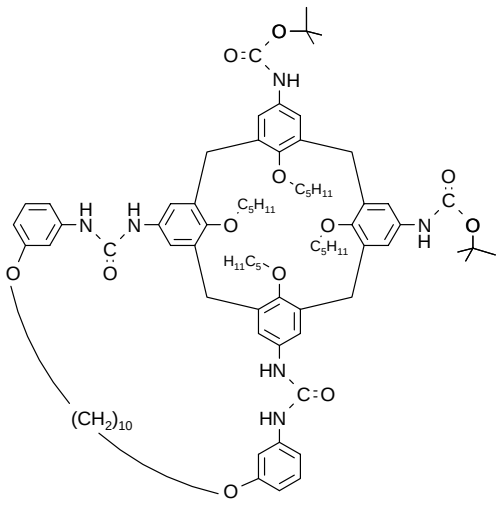


A solution of 87 (1.9 g, 10 mmol) and 4-nitrophenyl chloroformate (2.0 g, 10 mmol) in a mixture of chloroform (45 mL) and tetrahydrofuran (30 mL) was refluxed for 12 hours. The solvents were evaporated and the residue was dissolved in chloroform and precipitated with diethylether, yielding 2.7 g (77%) of a white compound; m.p. = 102-103 °C;

^{1}H NMR ($CHCl_3$-d_1): δ (ppm) = 8.27 and 7.38 (2d, ^3J = 9.1 Hz, 4H, Ar-H), 7.22 (t, ^3J = 8.2 Hz, 1H, Ar_{meta}-H), 7.13 (s, 1H, Ar_{meta}-H), 6.92 (brs, 1H, NH), 6.91 and 6.89 (dd, ^3J = 8.1 Hz, ^4J = 1.9 Hz, 1H, Ar_{meta}-H), 6.69 and 6.67 (dd, ^3J = 8.2 Hz, ^4J = 2.3 Hz, 2H, Ar_{meta}-H), 5.86-5.76 (m, 1H, -CH=CH_2), 5.04-4.95 (m, 2H, -CH=CH_2), 3.96 (t, ^3J = 6.4 Hz, 2H, OCH_2-),2.14-2.09 (m, 2H, -CH_2-), 1.82-1.76 (m, 2H, -CH_2 -), 1.60-1.52 (m, 2H, -CH_2-);
^{13}C NMR ($CHCl_3$-d_1): δ (ppm) = 159.92, 155.31, 150.02, 145.08, 138.45, 137.76, 129.95, 125.20, 122.13, 114.75, 110.91, 110.79, 105.28, 67.86, 33.37, 28.61, 25.26;
FD MS: [M^+] was not detected due to decomposition.

The compounds **84**

A solution of di-urethane **82** (0.73 mmol) in DMF (50 mL) and a solution of **83** (0.56 mmol, and 3-5 drops of triethylamine) in DMF (50 mL) were added under stirring during 12 hours to a 1 L round bottom flask filled with DMF (550 mL). The yellow reaction mixture was stirred for further 24 hours at room temperature. Then, the solvent was evaporated, the residue was dissolved in dichloromethane (250 mL), and washed with K_2CO_3 solution (3-5 x 200 mL) until the aqueous layer was colorless) and with water (1 x 200 mL). The organic layer was dried over $MgSO_4$ and the solution was concentrated at reduced pressure to 4-5 mL. The pure product was obtained after column chromatography (eluent ethyl acetate/hexane 1/4) as a white powder.



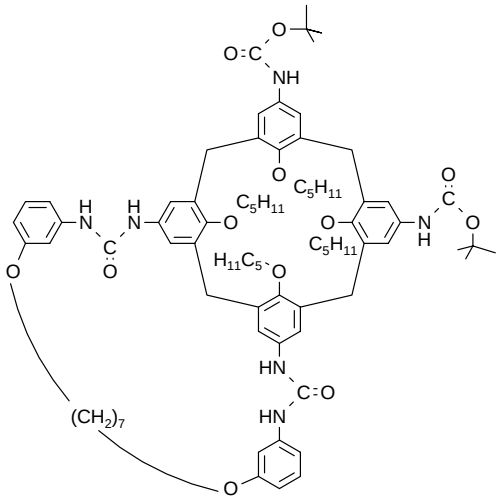
84a

yield = 74%; m.p.= 270°C (decomp);
^{1}H NMR (DMSO-d_6, 400 MHz, 60°C) δ = 8.51 (s, 2H, NH), 8.21 (s, 2H, NH), 8.02 (s, 2H, NH), 7.10 (t, ^3J = 8.1 Hz, 2H, Ar_{meta}-H), 7.08 (t, ^4J = 2.2 Hz, 2H, Ar_{meta}-H), 6.87 (d, ^4J = 2.4 Hz, 2H, Ar_{calix}-H), 6.82 and 6.80 (dd, ^3J = 8.2 Hz, ^4J = 1.72 Hz, 2H, Ar_{meta}-H), 6.80 (brs, 4H, Ar_{calix}-H), 6.62 (brd, 2H, Ar_{calix}-H), 6.49 and 6.47 (dd, ^3J = 8.1 Hz, ^4J = 2.2 Hz, 2H, Ar_{meta}-H), 4.36 (d, ^2J = 12.72 Hz, 4H, Ar-CH_2-Ar*ax*), 4.34 (d, ^2J = 12.96 Hz, 4H, Ar-CH_2-Ar*ax*), 4.33 (d, ^2J = 12.72 Hz, 4H, Ar-CH_2-Ar*ax*), 3.93 (t, ^3J = 6.2 Hz, 4H, OCH_2-), 3.86-3.80 (m, 8H, OCH_2-), 3.10 (d, ^2J = 13.72 Hz, 4H, Ar-CH_2-Ar*eq*), 3.06 (d, ^2J = 13.44 Hz, 4H, Ar-CH_2-Ar*eq*), 3.03 (d, ^2J = 14.2

Hz, 4H, Ar-CH_2-Ar*eq*), 1.91-1.85 (m, 8H, -CH_2-), 1.68 (q, ^3J = 6.5 Hz, 4H, -CH_2-), 1.41-1.35 (m, 34H, ^{t}Bu + -CH_2-), 1.29 (m, 12H, -CH_2-), 0.94 (brt, 12H, -CH_3);

^{13}C NMR (DMSO-d_6, 60°C) δ = 158.80, 152.56, 151.97, 151.05, 150.92, 140.71, 134.03, 133.91, 133.77, 133.72, 132.84, 132.77, 128.89, 118.67, 118.56, 118.48, 118.23, 110.08, 107.28, 104.54, 78.01, 74.26, 66.93, 30.52, 30.40, 28.86, 28.84, 28.09, 27.97, 27.86, 27.79, 27.54, 27.53, 24.89, 21.77, 13.39;

MS (FD), m/z 1373.9 (M calc $C_{82}H_{112}N_6O_{12}$: 1373.82).



84b

yield = 60%; m.p. = 270°C (decomp);

^{1}H-NMR (DMSO-d_6, 400 MHz, 60°C): δ (ppm) = 8.46 (s, 2H, NH), 8.19 (s, 2H, NH), 8.03 (s, 2H, NH), 7.36 (t, 2H, ^4J = 2.06 Hz, Ar_{meta}-H), 7.13 (d, 2H, ^4J = 2.32 Hz, Ar_{calix}-H), 7.36 (t, 2H, ^3J = 8.08 Hz, Ar_{meta}-H), 6.79 (brs, 4H, Ar_{calix}-H), 6.57 and 6.55 (dd, 2H, ^3J = 7.92 Hz and ^4J = 1.2 Hz, Ar_{meta}-H), 6.50 and 6.48 (dd, 2H, ^3J = 7.92 Hz and ^4J = 2.2 Hz, Ar_{meta}-H), 6.39 (d, 2H, ^4J = 2.08 Hz, Ar_{calix}-H), 4.38-4.32 (m, 4H, Ar-CH_2-Ar *ax*), 3.95 (brt, 4H, OCH_2-), 3.86-3.81 (m, 8H, OCH_2-), 3.08-3.02 (m, 4H, Ar-CH_2-Ar *eq*), 1.90-1.85 (m, 8H, -CH_2-), 1.69 (m, 4H, -CH_2-), 1.44-1.38 (m, 40H, ^{t}Bu + -CH_2-), 0.93 (t, 12H, ^2J = 6.6 Hz, -CH_3).

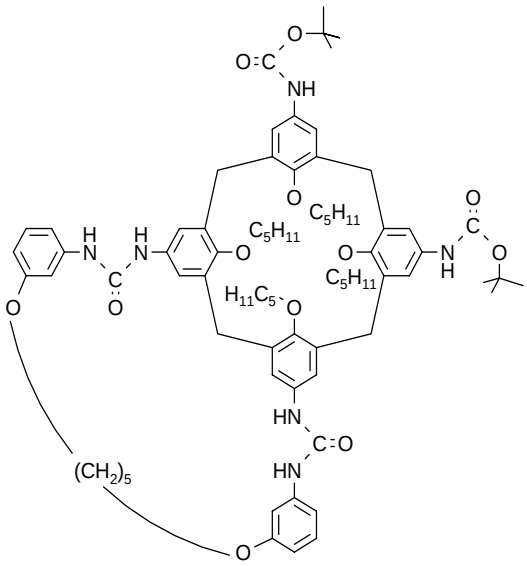
^{13}C-NMR (DMSO-d_6, 100 MHz, 60°C): δ (ppm).= 158.75, 152.56, 151.94, 151.10, 150.88, 140.67, 134.10, 133.85, 133.78, 133.72, 132.87, 132.75, 128.79, 118.69, 118.55, 118.43, 117.87, 110.07, 107.02, 104.92, 78.02, 74.27, 74.23, 66.67, 30.76, 30.53, 30.27, 28.85, 28.83, 28.02, 27.80, 27.64, 27.54, 27.52, 25.06, 21.76, 13.38.

MS (FD), m/z 1332.1 (M calc $C_{79}H_{106}N_6O_{12}$: 1331.76).

84c

yield = 47%; m.p. = 250°C decomp;

^{1}H-NMR (DMSO-d_6, 400 MHz, 60°C): δ (ppm) = 8.75 (s, 2H, NH), 8.33 (s, 2H, NH), 8.19 (s, 2H, NH), 7.66 (t, 2H, ^4J = 2.06 Hz, Ar_{meta}-H), 7.41 (d, 2H, ^4J = 1.2 Hz, Ar_{calix}-H), 7.10 (t, 2H, ^3J = 8.06 Hz, Ar_{meta}-H), 6.84 (brs, 2H, Ar_{calix}-H), 6.81 (brs, 2H, Ar_{calix}-H), 6.49 and 6.47 (dd, 2H, ^3J = 8.2 Hz and ^4J = 2.34 Hz, Ar_{meta}-H), 6.33 and 6.31 (dd, 2H, ^3J = 7.92 Hz and ^4J = 1.48 Hz, Ar_{meta}-H), 6.23 (d, 2H, ^4J = 1.76 Hz, Ar_{calix}-H), 4.35-4.29 (m, 4H, Ar-



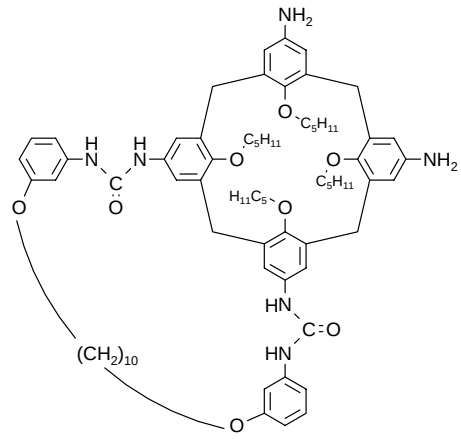
CH_2-Ar *ax*), 3.99 (m, 2H, OCH_2-), 3.86-3.76 (m, 10H, OCH_2-), 3.09-3.00 (m, 4H, Ar-CH_2-Ar *eq*), 1.92-1.85 (m, 8H, -CH_2-), 1.75-1.71 (m, 4H, -CH_2-), 1.40-1.34 (m, 36H, ^{t}Bu + -CH_2-), 0.92 (t, 12H, ^2J = 6.74 Hz, -CH_3).

^{13}C-NMR (DMSO-d_6, 100 MHz, 60°C): δ (ppm).= 158.98, 152.59, 151.91, 151.08, 150.84, 140.68, 134.10, 133.85, 133.78, 133.75, 132.96, 132.87, 128.83, 118.60, 118.50, 117.72, 109.90, 105.61, 105.46, 78.05, 74.39, 74.34, 66.66, 31.06, 30.64, 30.23, 28.91, 28.88, 28.13, 27.85, 27.58, 27.57, 22.45, 21.84, 21.82, 13.46, 13.45.

MS (FD), m/z 1304.1 (M calc $C_{77}H_{102}N_6O_{12}$: 1303.7).

Di-amines **85**

Trifluoracetic acid (15 mL) was added to a solution of **84** (0.23 mmol) in chloroform (15 mL). The reaction mixture was stirred under nitrogen for four hours, diluted with toluene (20 mL) and evaporated. The residue was dissolved in dichloromethane, washed with water until neutrality and dried over $MgSO_4$. The crude product was used in the next reaction without analysis. For one example, the pure product was obtained after precipitation with hexane as a white powder.



85a

yield = 96%;. m.p. >200°C (decomp);

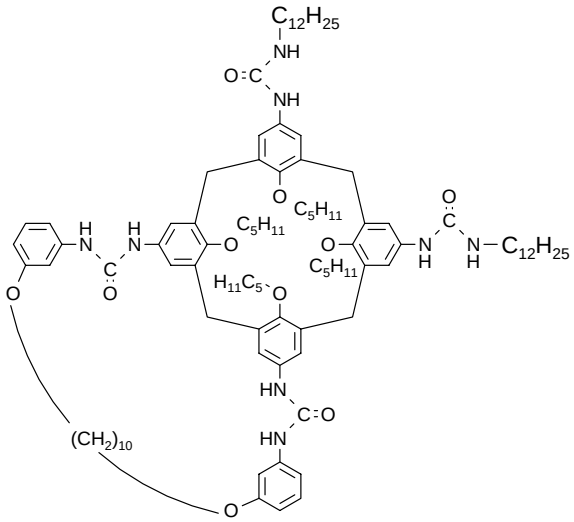
^{1}H NMR (DMSO-d_6, 400 MHz, rt) δ (ppm) = 8.35 (s, 2H, NH), 8.18 (s, 2H, NH), 7.10 (m, 4H, Ar_{meta}-H), 6.83 (s, 2H, Ar_{calix}-H), 6.78 (d, ^3J = 8.1 Hz, 2H, Ar_{meta}-H), 6.62 (s, 2H, Ar_{calix}-H), 6.47 (d, ^3J = 8.8 Hz, 2H, Ar_{meta}-H), 5.97 (s, 4H, Ar_{calix}-H), 4.35 (brs, 4H, NH_2), 4.33 (d, ^2J = 12.8 Hz, 1H, Ar-CH_2-Ar*ax*), 4.24 (d, ^2J = 12.8 Hz, 2H, Ar-CH_2-Ar*ax*), 4.17 (d, ^2J = 12.5 Hz, 1H, Ar-CH_2-Ar*ax*), 3.90 (t, ^3J = 5.8 Hz, 4H, OCH_2-), 3.80 (t, ^3J = 6.98 Hz, 4H, OCH_2-), 3.78 (m, 4H, OCH_2-), 3.08 (d, ^2J = 12.8 Hz, 1H, Ar-CH_2-Ar*eq*), 2.95 (d, ^2J = 12.8 Hz, 2H, Ar-CH_2-Ar*eq*), 2.81 (d, ^2J = 12.5

Hz, 1H, Ar-CH_2-Ar*eq*), 1.90-1.85 (m, 8H, -CH_2-), 1.66 (brq, 4H, -CH_2-), 1.36 (m, 16H, -CH_2-), 1.28 (m, 12H, -CH_2-), 0.95 (brt, 12H, -CH_3).

Tetraureas **25**, **26**, **27**

A solution of **85** (0.2 mmol), isocyanate (tolylisocyanate, pentylisocyanate, dodecyl-isocyanate) or **88** (0.42 mmol and few drops of triethylamine) in chloroform (10 mL when isocyanate is used) or in DMF (10 mL for mono-urethane), was stirred for 12 hours at room temperature. For the reactions done with isocyanates the crude compound is precipitated with methanol from the reaction mixture and the pure compound was obtained after one recrystallization from chloroform/methanol mixture (yield 80-90%).

Similar work up as described for **84** was done for **25c**, **26c** was used and gave (90-96%) of a white powder.



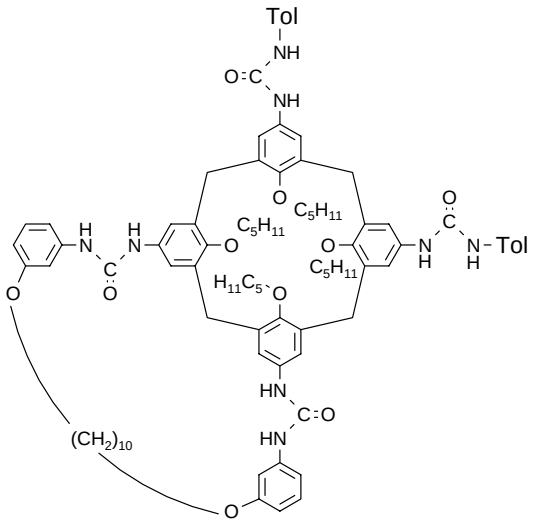
25a

mp > 250 °C (decomposition without melting);

^{1}H-NMR (DMSO-d_6, 400 MHz, rt): δ (ppm) = 8.28 (s, 2H, N**H**), 8.01 (s, 2H, N**H**), 7.76 (s, 2H, N**H**), 7.09 (t, 2H, ^3J = 8.2 Hz, Ar_{meta}-**H**), 7.07 (brt, 2H, Ar_{meta}-**H**), 6.90 (d, 2H, ^4J = 2.3 Hz, Ar_{calix}-**H**), 6.83 and 6.81 (dd, 2H, ^3J = 7.8 Hz, ^4J = 1.3 Hz, Ar_{meta}-**H**), 6.74 (d, 2H, ^4J = 2.3 Hz, Ar_{calix}-**H**), 6.67 (d, 2H, ^4J = 2.3 Hz, Ar_{calix}-**H**), 6.65 (d, 2H, ^4J = 2.3 Hz, Ar_{calix}-**H**), 6.49 and 6.47 (dd, 2H, ^3J = 8.2 Hz, ^4J = 2.0 Hz, Ar_{meta}-**H**), 5.66 (t, 2H, ^3J = 5.6 Hz, N**H**), 4.35-4.30 (m, 4H, Ar-C**H**$_2$-Ar *ax*), 3.93 (t, 4H, ^3J = 6.2 Hz, OC**H**$_2$-), 3.85-3.79 (m, 8H, OC**H**$_2$-), 3.07-2.96 (m, 6H, Ar-C**H**$_2$-Ar *eq* + NC**H**$_2$-), 1.89 (m, 8H, -C**H**$_2$-), 1.68 (q, 4H, ^3J = 6.6 Hz, -C**H**$_2$-), 1.40-1.22 (m, 68H, -C**H**$_2$-), 0.93 (t, 12H, ^3J = 6.6 Hz, -C**H**$_3$), 0.85 (t, 6H, ^3J = 6.9 Hz, -C**H**$_3$).

^{13}C-NMR (DMSO-d_6, 100 MHz, 60°C): δ (ppm) = 158.83, 154.91, 152.00, 150.91, 150.33, 140.74, 134.09, 134.05, 133.89, 133.87, 133.72, 132.90, 128.91, 118.16, 118.00, 117.92, 117.74, 110.06, 107.22, 104.51, 74.32, 66.92, 30.86, 29.41, 28.92, 28.60, 28.57, 28.35, 28.24, 28.13, 28.00, 27.90, 27.60, 26.01, 24.93, 21.84, 21.62, 13.47, 13.42;

MS (FD), m/z 1619.1 ($M+Na^+$ calc $C_{98}H_{146}N_8O_{10}Na$: 1619.3).

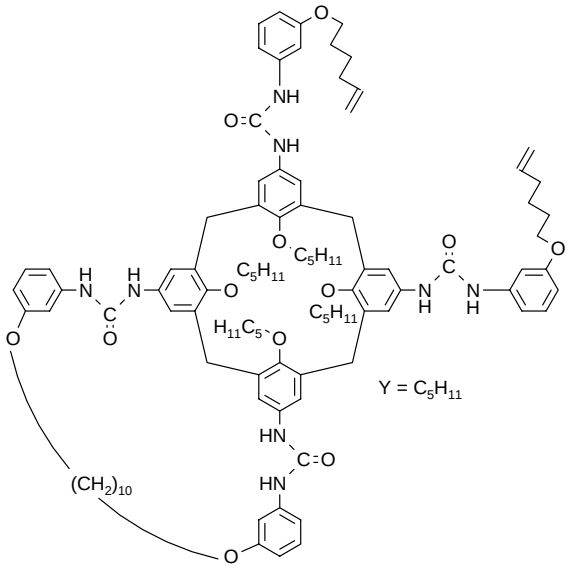


25b

mp > 250 °C (decomposition without melting);

^{1}H-NMR (DMSO-d_6, 400 MHz, rt): δ (ppm) = 8.35 (s, 2H, NH), 8.22 (s, 2H, NH), 8.15 (s, 4H, NH), 7.21 (d, 4H, ^{3}J = 8.1 Hz, Ar_{tolyl}-H), 7.08 (t, 2H, ^{3}J = 8.4 Hz, Ar_{meta}-H), 7.03 (s, 2H, Ar_{meta}-H), 7.00 (d, 4H, ^{3}J = 8.4 Hz, Ar_{tolyl}-H), 6.92 (s, 2H, Ar_{calix}-H), 6.83 (s, 2H, Ar_{calix} -H), 6.76 (m, 4H, Ar_{meta}-H + Ar_{calix}-H), 6.66 (s, 2H, Ar_{calix} -H), 6.47 (d, 2H, ^{3}J = 6.9 Hz, Ar_{meta}-H), 4.33 (d, 4H, ^{2}J = 12.4 Hz, Ar-CH_2-Ar *ax*), 3.88 (t, 4H, ^{3}J = 6.24 Hz, OCH_2-), 3.81 (brt, 8H, OCH_2-), 3.11 (d, 4H, ^{2}J = 12.44 Hz, Ar-CH_2-Ar *eq*), 2.2 (s, 6H, -CH_3), 1.90 (m, 8H, -CH_2-), 1.64 (q, 4H, ^{3}J = 6.6 Hz, -CH_2-), 1.38 (m, 16H, -CH_2-), 1.23 (m, 12H, -CH_2-), 0.93 (brt, 12H, -CH_3).

^{13}C-NMR (DMSO-d_6, 100 MHz, 60°C): δ (ppm) = 152.20, 152.01, 150.89, 140.69, 136.98, 134.06, 134.03, 133.96, 133.14, 133.01, 129.93, 128.93, 128.59, 118.12, 117.84, 110.12, 107.32, 104.49, 74.35, 66.91, 28.93, 28.10, 27.97, 27.85, 27.59, 24.90, 21.83, 19.85, 13.45; MS (FD), m/z 1462.8 ($M+Na^+$ calc $C_{88}H_{110}N_8O_{10}Na$: 1462.9).



25c

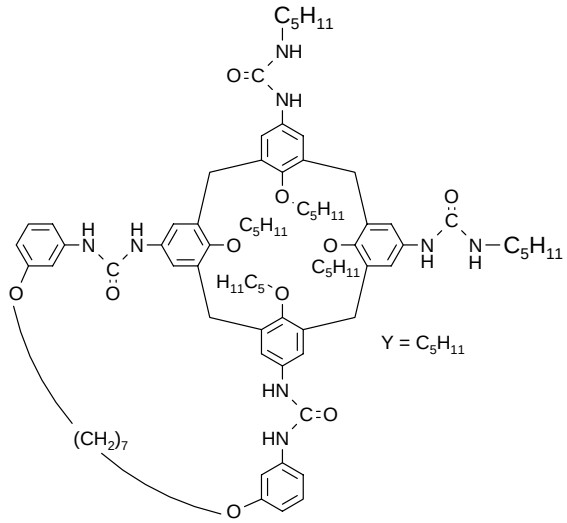
m.p. > 190 °C (decomposition without melting);

^{1}H-NMR (DMSO-d_6, 400 MHz, 60°C): δ (ppm) = 8.25 (s, 2H, NH), 8.22 (s, 2H, NH), 8.06 (s, 2H, NH), 8.02 (s, 2H, NH), 7.09-7.05 (m, 6H, Ar_{meta}-H), 7.01 (t, 2H, ^{4}J = 2.04 Hz, Ar_{meta}-H), 6.91 (d, 2H, ^{4}J = 2.36 Hz, Ar_{calix}-H), 6.83 (d, 2H, ^{4}J = 2.72 Hz, Ar_{calix}-H), 6.80-6.77 (m, 6H, Ar_{meta}-H), 6.76 (d, 2H, ^{4}J = 2.4 Hz, Ar_{calix}-H), 6.68 (d, 2H, ^{4}J = 2.4 Hz, Ar_{calix}-H), 6.48 (brs, 2H, Ar_{meta}-H), 6.46 (brs, 2H, Ar_{meta}-H), 5.84-5.77 (m, 2H, =C-H), 5.03-4.94 (m, 4H, =C-H_2), 4.37 (d, 4H, ^{2}J = 12.56 Hz, Ar-CH_2-Ar *ax*), 3.88 (m, 16H, -OCH_2), 3.20 (m, Ar-CH_2-Ar *eq*+H_2O), 2.07 (m, 4H, -CH_2-),1.90 (q, 8H, ^{3}J = 7.14 Hz, -

CH_2-), 1.71-1.64 (m, 8H, -CH_2-), 1.52-1.47 (m, 4H, -CH_2-), 1.41-1.39 (m, 16H, -CH_2-), 1.28-1.25 (m, 12H, -CH_2-),0.94 (t, 12H, ^3J = 6.98 Hz, -CH_3);

^{13}C-NMR (DMSO-d_6, 100 MHz, 25°C): δ (ppm) = 158.97, 152.29, 152.27, 151.12, 140,96, 140.93, 138.45, 134.40, 134.36, 133.28, 133.26, 129,30, 118.27, 118.20, 118.16, 114.83, 110.16, 110.09, 107.28, 104.35, 104.15, 74.74, 74.72, 66.94, 48.52, 32.77, 30.49, 29.31, 28.39, 28.17, 28.14, 28.10, 27.90, 25.16, 24.67, 22.27, 13.92;

MS (FD), m/z 1629.87 (M+Na^+ calc $C_{98}H_{126}N_8O_{12}Na$: 1629.9).



26a

m.p. > 250 °C (decomposition without melting);

^{1}H-NMR (DMSO-d_6, 400 MHz, 25°C): δ (ppm) = 8.37 (s, 2H, NH), 8.12 (s, 2H, NH), 7.87 (s, 2H, NH), 7.37 (t, 2H, ^4J = 1.9 Hz, Ar_{meta}-H), 7.17 (d, 2H, ^4J = 2.4 Hz, Ar_{calix}-H), 7.09 (t, 2H, ^3J = 8.1 Hz, Ar_{meta}-H), 6.77 (d, 2H, ^4J = 2.4 Hz, Ar_{calix}-H), 6.63 (d, 2H, ^4J = 2.2 Hz, Ar_{calix}-H), 6.52-6.47 (m, 4H, Ar_{meta}-H), 6.39 (d, 2H, ^4J = 2.2 Hz, Ar_{calix}-H), 5.71 (t, 2H, ^3J = 5.5 Hz, NH), 4.34-4.27 (m, 4H, Ar-CH_2-Ar *ax*), 3.96-3.91 (m, 4H, OCH_2-), 3.83-3.75 (m, 8H, OCH_2-), 3.10-3.97 (m, 4H, Ar-CH_2-Ar *eq*), 2.97-2.95 (m, 4H, NCH_2), 1.90-1.86 (m, 8H, -CH_2-), 1.73-1.61 (m, 4H, -CH_2-), 1.45-1.29 (m, 26H, -CH_2-), 1.26-1.16 (m, 8H, -CH_2-), 0.92 (t, 12H, ^3J = 6.7 Hz, -CH_3), 0.82 (t, 6H, ^3J = 6.9 Hz, -CH_3);

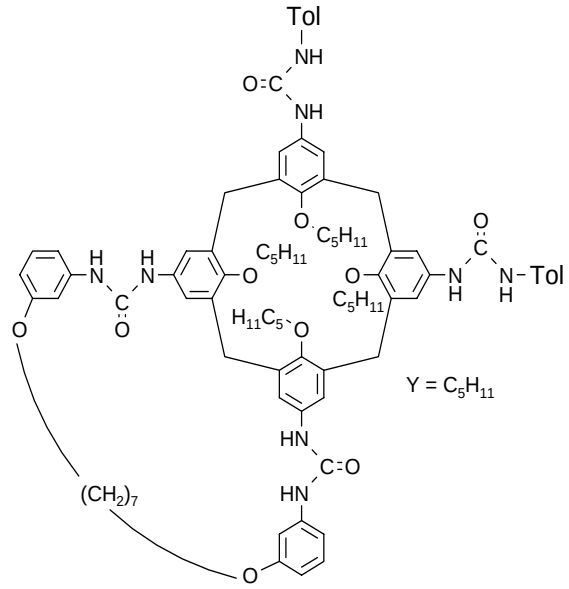
^{13}C-NMR (DMSO-d_6, 100 MHz, rt): δ (ppm) = 158.96, 155.08, 152.18, 151.05, 150.47, 140.88, 134.37, 134.15, 133.96, 133.15, 129.22, 118.18, 117.98, 117.86, 117.76, 110.08, 106.77, 104.83, 74.69, 74.66, 66.59, 38.89, 31.02, 30.75, 30.30, 29.37, 29.28, 29.24, 28.50, 28.22, 27.88, 25.38, 22.24, 21.74;

MS (FD), m/z 1357.85 (M^+ calc $C_{81}H_{112}N_8O_{10}$: 1357.84).

26b

m.p. > 250 °C (decomposition without melting);

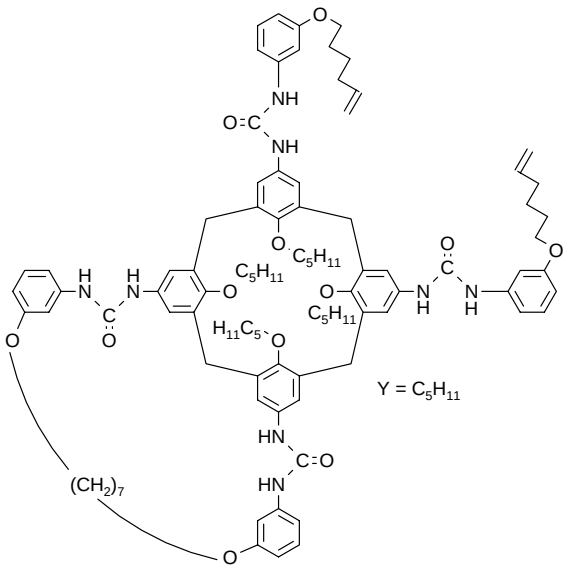
^{1}H-NMR (DMSO-d_6, 400 MHz, 60°C): δ (ppm) = 8.28 (s, 2H, NH), 8.11 (s, 2H, NH), 8.06 (s, 2H, NH), 8.02 (s, 2H, NH), 7.30 (t, 2H, ^4J = 2.2 Hz, Ar_{meta}-H), 7.20 (d, 4H, ^3J = 8.5 Hz, Ar_{tolyl}-H), 7.15 (d, 2H, ^4J = 2.6 Hz, Ar_{calix}-H), 7.07 (t, 2H, ^3J = 8.2 Hz, Ar_{meta}-H), 7.00 (d,



4H, ^3J = 8.52 Hz, Ar_{tolyl}-H), 6.88 (d, 2H, ^4J = 2.64 Hz, Ar_{calix}-H), 6.70 (d, 2H, ^4J = 2.64 Hz, Ar_{calix}-H), 6.53 and 6.51 (dd, 2H, ^4J = 1.3 Hz, ^3J = 8.1 Hz, Ar_{meta}-H), 6.50 and 6.47 (dd, 2H, ^4J = 2.1 Hz, ^3J = 9 Hz, Ar_{meta}-H), 6.47 (d, 2H, ^4J = 2.6 Hz, Ar_{calix}-H), 4.36 (d, 4H, ^2J = 12.92 Hz, Ar-CH_2-Ar *ax*), 3.96 (m, 4H, OCH_2-), 3.87 (m, 8H, OCH_2-), 3.11 (d, 4H, ^2J = 12.92 Hz, Ar-CH_2-Ar *eq*), 2.21 (s, 6H, -CH_3), 1.90 (m, 8H, -CH_2-), 1.68 (m, 4H, -CH_2-), 1.41-1.40 (m, 22H, -CH_2-), 0.93 (t, 12H, ^3J = 6.9 Hz, -CH_3).

^{13}C-NMR (DMSO-d_6, 100 MHz, rt): δ (ppm).= 158.93, 152.41, 152.27, 151.08, 151.02, 140.87, 137.17, 134.42, 134.34, 134.25, 133.38, 133.29, 130.16, 129.24, 128.96, 118.32, 118.24, 118.08, 117.94, 117.83, 110.22, 106.92, 104.80, 74.77, 74.71, 66.64, 31.00, 30.71, 30.31, 29.33, 29.28, 28.21, 28.01, 27.90, 25.38, 22.26, 20.22, 13.91.

MS (FD), m/z 1398.8 (M^+ calc $C_{85}H_{104}N_8O_{10}$: 1398.8).



26c

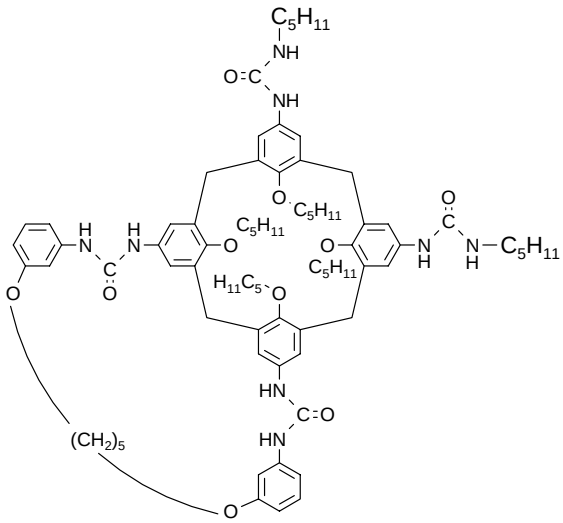
m.p. > 190 °C (decomposition without melting);

^{1}H-NMR (THF-d_8, 400 MHz, 25°C): δ (ppm) = 7.51 (s, 2H, N**H**), 7.48 (s, 2H, N**H**), 7.48 (s, 2H, N**H**), 7.39 (s, 2H, N**H**), 7.21 (t, 2H, ^4J = 2.1 Hz, Ar_{meta}-**H**), 7.17 (t, 2H, ^4J = 2.2 Hz, Ar_{meta}-**H**), 7.01 (d, 2H, ^4J = 2.6 Hz, Ar_{calix}-**H**), 6.96 (t, 2H, ^3J = 8.1 Hz, Ar_{meta}-**H**), 6.95 (t, 2H, ^3J = 8.1 Hz, Ar_{meta}-**H**), 6.85 (d, 2H, ^4J = 2.6 Hz, Ar_{calix}-**H**), 6.76 (d, 2H, ^4J = 1.8 Hz, Ar_{calix}-**H**), 6.66 and 6.64 (brdd, 2H, ^3J = 7.9 Hz, Ar_{meta}-**H**), 6.64 (brd, 2H, Ar_{calix}-**H**), 6.61 and 6.59 (brdd, 2H, ^3J = 7.0 Hz, Ar_{meta}-**H**), 6.43 and 6.41 (dd, 2H, ^3J = 8.2 Hz, ^4J = 1.8 Hz, Ar_{meta}-**H**), 6.41 and 6.39 (dd, 2H, ^3J = 8.2 Hz, ^4J = 1.8 Hz, Ar_{meta}-**H**), 5.83-5.76 (m, 2H, =C-**H**), 5.01-4.89 (m, 4H, =C-**H**$_2$), 4.44 (d, 4H, ^2J = 12.6 Hz, Ar-C**H**$_2$-Ar *ax*), 3.95-3.85 (m, 16H, OC**H**$_2$-),3.08 (m, 4H, Ar-C**H**$_2$-Ar *eq*), 2.09 (m, 4H, -C**H**$_2$-),1.94 (q, 8H, ^3J = 7.0

Hz, -C**H**$_2$-), 1.57-1.51 (m, 8H, -C**H**$_2$-), 1.51-1.43 (m, 16H, -C**H**$_2$-), 0.96 (t, 12H, ^3J = 7.0 Hz, -C**H**$_3$);

^{13}C-NMR (THF-d$_8$,, 100 MHz, rt): δ (ppm) = 160.69, 160.56, 153.14, 153.11, 152.66, 142.45, 142.40, 139.48, 135.89, 135.84, 134.97, 134.94, 129.84, 129.75, 119.33, 119.23, 119.10, 118.94, 114.91, 111.27, 110.96, 108.22, 108.13, 106.07, 105.28, 75.92, 68.10, 67.98, 34.41, 30.90, 29.80, 29.51, 26.37, 25.84, 23.79, 14.62;

MS (FD), m/z 1588.8 (M+Na$^+$ calc $C_{95}H_{120}N_8O_{12}Na$: 1589.0).



27a

m.p. > 190 °C (decomposition);

^{1}H-NMR (DMSO-d$_6$, 400 MHz, 60°C): δ (ppm) = 8.31 (s, 2H, NH), 8.04 (s, 2H, NH), 7.74 (s, 2H, NH), 7.62 (t, 2H, *J* = 2.2 Hz, Ar-H), 7.37 (d, 2H, J = 2.64 Hz, Ar-H), 7.09 (t, 2H, J = 8.08 Hz, Ar-H), 6.83 (d, 2H, J = 2.64 Hz, Ar-H), 6.59 (d, 2H, J = 2.64 Hz, Ar-H), 6.50 and 6.48 (dd, 2H, J = 8.06 Hz, J = 2.2 Hz, Ar-H), 6.37 and 6.35 (dd, 2H, J = 7.76 Hz, J = 1.6 Hz, Ar-H), 6.28 (d, 2H, J = 2.64 Hz, Ar-H), 5.67 (t, 2H, J = 5.56 Hz, NH), 4.38-4.30 (m, 4H, Ar-CH$_2$-Ar ax), 4.02-3.93 (m, 2H, OCH$_2$), 3.93-3.90 (m, 2H, OCH$_2$), 3.87-3.79 (m, 8H, OCH$_2$), 3.10-3.05 (m, 4H, Ar-CH$_2$-Ar eq), 3.02-2.96 (m, 4H, NCH$_2$), 1.90-1.86 (m, 8H, -CH$_2$-),1.76-1.70 (m, 4H, -CH$_2$-), 1.56-1.50 (m, 2H, -CH$_2$-), 1.40-1.31 (m, 20H, -CH$_2$-),1.29-1.23 (m, 8H, -CH$_2$-),0.93 (t, 12H, J = 7.04 Hz, -CH$_3$), 0.83 (t, 6H, J = 6.9 Hz, -CH$_3$).

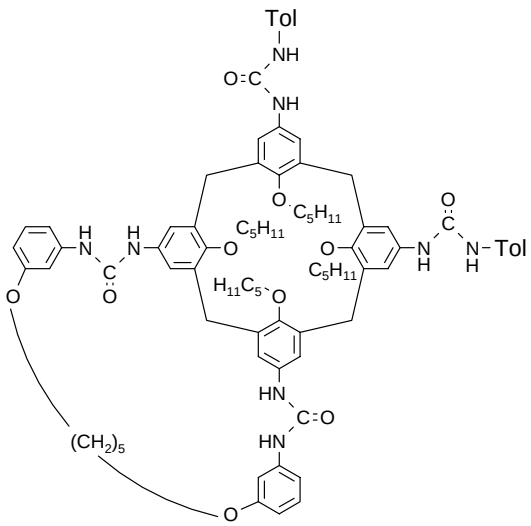
^{13}C-NMR (DMSO-d$_6$, 100 MHz, rt): δ (ppm) = 159.25, 155.16, 152.22, 151.14, 150.52, 140.90, 134.45, 134.38, 134.21, 134.18, 133.98, 133.16, 129.99, 118.52, 118.06, 117.98, 117.73, 109.98, 105.43, 105.20, 74.79, 66.71, 48.57, 31.36, 30.90, 30.26, 29.43, 29.35, 29.32, 28.54, 28.41, 27.95, 22.31, 21.81, 13.96, 13.89;

MS (FD), m/z 1351.54 (M+Na$^+$ calc $C_{79}H_{108}N_8O_{10}Na$: 1351.80).

27b

m.p. > 200 °C (decomposition without melting);

^{1}H-NMR (DMSO-d$_6$, 400 MHz, 60°C): δ (ppm) = 8.29 (s, 2H, NH), 8.10 (s, 2H, NH), 8.08 (s, 2H, NH), 8.01 (s, 2H, NH), 7.62 (t, 2H, ^4J = 2.2 Hz, Ar$_{meta}$-H), 7.39 (d, 2H, ^4J = 2.6 Hz,



Ar_{calix}-H), 7.20 (d, 4H, ^3J = 8.2 Hz, Ar_{tolyl}-H), 7.08 (t, 2H, ^3J = 8.0 Hz, Ar_{meta}-H), 7.01 (d, 4H, ^3J = 8.5 Hz, Ar_{tolyl}-H), 6.94 (d, 2H, ^4J = 2.6 Hz, Ar_{calix}-H), 6.65 (d, 2H, ^4J = 2.3 Hz, Ar_{calix}-H), 6.50 and 6.48 (dd, 2H, ^4J = 2.0 Hz, ^3J = 8.5 Hz, Ar_{meta}-H), 6.30 (d, 2H, ^4J = 2.3 Hz, Ar_{calix}-H), 6.30 and 6.28 (dd, 2H, ^4J = 2.0 Hz, ^3J = 8.0 Hz, Ar_{meta}-H), 4.37 (d, 2H, ^2J = 12.3 Hz, Ar-CH_2-Ar *ax*), 4.36 (d, 2H, ^2J = 12.9 Hz, Ar-CH_2-Ar *ax*), 4.03-4.00 (m, 2H, OCH_2-),3.94-3.80 (m, 10H, OCH_2-),3.11 (m, Ar-CH_2-Ar *eq* + H_2O), 2.21 (s, 6H, -CH_3), 1.91 (q, 8H, ^3J = 6.9 Hz, -CH_2-), 1.74 (m, 4H, -CH_2-), 1.6-1.5 (m, 2H, -CH_2-), 1.41-1.39 (m, 16H, -CH_2-), 0.96-0.92 (m, 12H, -CH_3).

^{13}C-NMR (DMSO-d_6, 100 MHz, 60°C): δ (ppm) = 159.16, 152.36, 152.17, 151.06, 150.96, 140.83, 137.13, 134.32, 134.18, 133.37, 133.21, 130.16, 129.20, 128.93, 118.46, 118.29, 117.94, 117.85, 109.96, 105.31, 105.18, 74.77, 74.73, 66.65, 31.31, 30.79, 30.12, 29.31, 29.26, 28.35, 27.87, 22.71, 22.24, 20.20, 13.90.

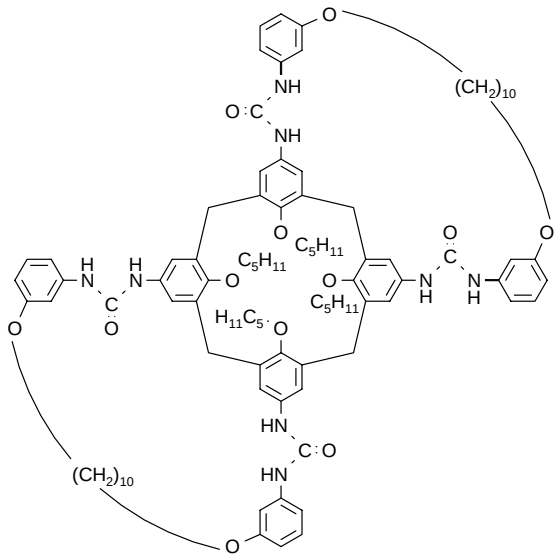
MS (FD), m/z 1391.7 ($M+Na^+$ calc $C_{83}H_{100}N_8O_{10}$: 1391.7).

Di-loop derivatives **28**

a) from tetraamine and di-urethane: A solution of di-urethane **82** (1.25 mmol) in DMF (50 mL) and a solution of tetraamine **35** (0.50 mmol) and triethylamine (3-5 drops) in DMF (50 mL) were added under stirring during 12 hours to a 1 L round bottom flask filled with DMF (400 mL) and the yellow reaction mixture was stirred for additional three days. Then, the solvent was evaporated and the residue was dissolved in chloroform (400 mL, the solubility of the product is very low), washed with K_2CO_3 solution (3-5 x 200 mL, until the aqueous layer was colorless) and with water (1 x 200 mL). The organic layer was dried over $MgSO_4$ and concentrated at reduced pressure to 4-5 mL. The product was isolated by column chromatography (eluent tetrahydrofuran/hexane 1/2) and recrystallized from tetrahydrofuran / methanol, yielding a white powder.

b) via metathesis reaction: A mixture of **29** (0.33 g, 0.2 mmol) and tetratosylurea (0.37 g, 0.24 mmol) in benzene (50 mL) was stirred at 60°C for one day when became a transparent solution. After 800 mL dichloromethane and 41 mg of Grubb's catalyst were added the

mixture was stirred at room temperature, under nitrogen for two days. 1 mL triethylamine was added and after one hour the solvent was evaporated under reduce pressure; the solid was taken in THF and hydrogenated in the presence of PtO_2. The crude product was purified on column chromatography (eluent THF/hexane = 1/2) giving 0.2 g (82%) of white powder.



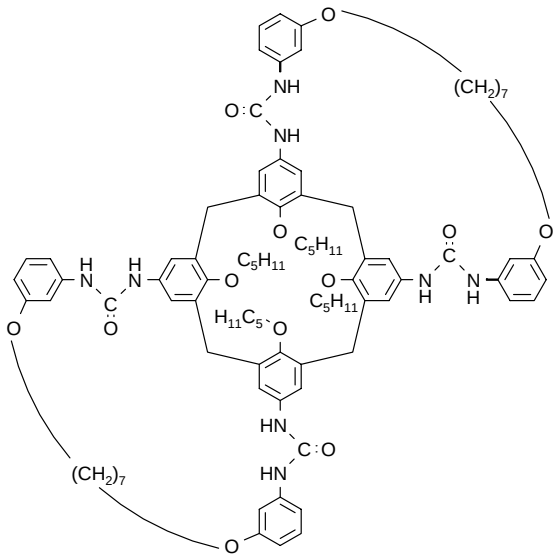
***di-loop* 28a**

yield = 38%; m.p. > 250 °C (decomp);

^{1}H NMR (THF-d_8, 400 MHz, rt): δ = 7.49 (s, 4H, NH), 7.47 (s, 4H, NH), 7.07 (d, ^4J = 2.0 Hz, 4H, Ar_{meta}-H), 6.98 (t, ^3J = 8.2 Hz, 4H, Ar_{meta}-H), 6.90 (d, ^4J = 2.6 Hz, 4H, Ar_{calix}-H), 6.79 and 6.76 (dd, ^3J = 8.1 Hz; ^4J = 1.4 Hz, 4H, Ar_{meta}-H), 6.74 (d, ^4J = 2.4 Hz, 4H, Ar_{calix}-H), 6.42 and 6.40 (dd, ^3J = 8.1 Hz; ^4J = 1.6 Hz, 4H, Ar_{meta}-H), 4.44 (d, ^2J = 12.9 Hz, 4H, Ar-CH_2-Ar*ax*), 3.89-3.85 (m, 16H, OCH_2-), 3.08 (d, ^2J = 13.2 Hz, 2H, Ar-CH_2- Ar*eq*), 3.06 (d, ^2J = 13.2 Hz, 2H, Ar-CH_2-Ar*eq*), 1.96 (m, 8H, -CH_2-), 1.77 (m, 8H, -CH_2-), 1.49-1.43 (m, 24H, -CH_2-),1.30 (m, 16H, -CH_2-), 0.96 (t, ^3J = 7.0 Hz, 12H, -CH_3);

^{13}C NMR (THF-d_8, 100 MHz, rt): δ = 160.67, 153.03, 152.63, 142.46, 135.87, 135.81, 134.97, 129.81, 119.27, 119.00, 111.08, 108.16, 105.54, 75.92, 75.92, 67.97, 32.21, 32.09, 30.90, 30.02, 29.71, 29.64, 29.51, 26.69, 23.77, 14.60;

MS (FD), m/z 1582.8 (M calc $C_{96}H_{124}N_8O_{12}$: 1582.1).



***di-loop* 28b**

yield = 42%; m.p. > 250 °C (decomp);

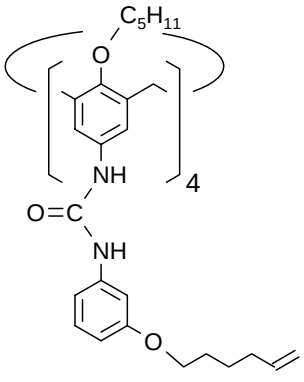
^{1}H NMR (THF-d_8, 400 MHz, rt): δ = 7.47 (s, 4H, NH), 7.44 (s, 4H, NH), 7.32 (brt, 4H, Ar_{meta}-H), 7.05 (d, ^4J = 2.4 Hz, 4H, Ar_{calix}-H), 6.91 (t, ^3J = 8.0 Hz, 4H, Ar_{meta}-H), 6.57 (brd, 4H, Ar_{calix}-H), 6.45 and 6.43 (brdd, ^3J = 7.8 Hz; 4H, Ar_{meta}-H), 6.42 and 6.40 (dd, ^3J = 8.2 Hz; ^4J = 2.0 Hz, 4H, Ar_{meta}-H), 4.43 (d, ^2J = 12.9 Hz, 4H, Ar-CH_2-Ar*ax*), 3.99-3.83 (m,

16H, OCH_2-), 3.08 (d, ^2J = 12.9 Hz, 2H, Ar-CH_2-Ar*eq*), 3.04 (d, ^2J = 13.3 Hz, 2H, Ar-CH_2-Ar*eq*), 1.93 (m, 8H, -CH_2-), 1.49-1.39 (m, 26H, -CH_2-), 0.96 (t, ^3J = 6.9 Hz, 12H, -CH_3);

^{13}C NMR (THF-d_8, 100 MHz, rt): δ = 159.53, 151.86, 151.55, 141.35, 134.85, 134.78, 133.99, 128.77, 118.02, 117.60, 110.20, 106.74, 105.08, 74.84, 67.02, 31.32, 30.92, 29.85, 29.69, 28.78, 28.48, 25.58, 22.75, 13.58;

MS (FD), m/z 1496.7 (M calc $C_{90}H_{112}N_8O_{12}$: 1497.9).

***Tetraurea* 29**



A solution of **35** (0.5 g, 0.65 mmol), **88a** (1 g, 2.8 mmol) and triethylamine (few drops) in DMF (30 mL) was stirred for two days at room temperature. Similar work up described for 3, gave 0.93 g (88%) of a white powder; m.p. = 210 - 213 °C;

^{1}H NMR (DMSO-d_6, 400 MHz, 25°C): δ (ppm) = 8.31 (s, 4H, NH), 8.16 (s, 4H, NH), 7.10-7.05 (m, 8H, Ar_{meta}-H), 6.79 (s, 8H, Ar_{calix}-H), 6.76 (d, ^3J = 8.2 Hz, 4H, Ar_{meta}-H), 6.47 (d, ^3J = 7.0 Hz, 4H, Ar_{meta}-H), 5.77 (m, 4H, -CH=CH_2), 5.02 (d, ^2J = 17.2 Hz, 4H, -CH=CH_2), 4.94 (d, ^3J = 9.9 Hz, 4H, -CH=CH_2), 4.33 (d, ^2J = 12.7 Hz, 4H, Ar-CH_2-Ar*ax*), 3.87 (t, ^3J = 6.4 Hz, 8H, OCH_2-), 3.81 (t, ^3J = 6.4 Hz, 8H, OCH_2-), 3.11 (d, ^2J = 12.7 Hz, 4H, Ar-CH_2-Ar*eq*), 2.06 (q, ^3J = 6.8 Hz, 8H, -CH_2CH=CH_2), 1.90 (m, 8H, -CH_2-), 1.67 (q, ^3J = 7.6 Hz, 8H, -CH_2-), 1.47 (q, ^3J = 7.7 Hz, 8H, -CH_2-), 1.40 (br m, 16H, CH_2CH_3), 0.94 (br t, 12H, CH_3);

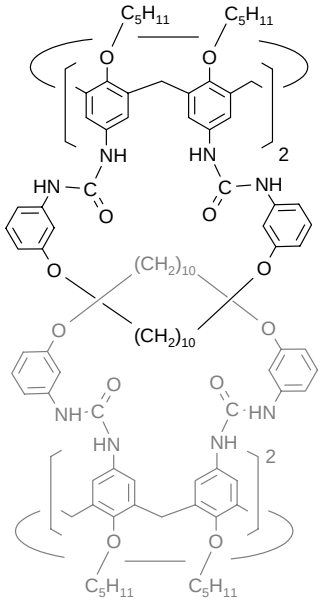
^{1}H NMR ($CHCl_3$-d_1, 400 MHz, 25°C): δ (ppm) = 9.43 (s, 8H, NH), 7.66 and 5.85 (two AB d, ^4J = 1.8 Hz, 16H, Ar_{calix}-H), 7.56 (br t, 8H, Ar_{meta}-H), 7.35 (d, ^3J = 7.9 Hz 8H, Ar_{meta}-H), 7.23 (t, ^3J = 8.1 Hz, 8H, Ar_{meta}-H), 6.90 (s, 8H, NH), 6.54 (dd, ^3J = 8.1 Hz, ^4J = 1.6 Hz, 8H, Ar_{meta}-H), 5.73 (m, 8H, -CH=CH_2), 4.94 (dd, ^3J = 18.3 Hz, ^4J = 1.4 Hz, 8H, -CH=CH_2), 4.88 (d, ^3J = 10.8 Hz, 8H, -CH=CH_2), 4.21 (d, ^2J = 11.8 Hz, 16H, Ar-CH_2-Ar*ax*), 3.90–3.75 (m, 16H, OCH_2-), 3.70–3.60 (m, 16H, OCH_2-), 2.83 (d, ^2J = 11.8 Hz, 16H, Ar-CH_2-Ar*eq*), 1.99 (q, ^3J = 7.1 Hz, 16H, -CH_2CH=CH_2), 1.92 (q, ^3J = 6.7 Hz, 16H, -CH_2-), 1.68 (q, ^3J = 8.0 Hz, 16H, -CH_2-), 1.35 (m, 32H, -CH_2-), 1.27 (q, ^3J = 7.2 Hz, 16H, -CH_2-), 0.94 (t, ^3J = 7.3 Hz, 24H, -CH_3);

^{13}C NMR (DMSO-d_6): δ = 158.94, 152.26, 151.07, 140.95, 138.42, 134.34, 133.25, 129.25, 118.14, 114.81, 110.11, 107.25, 104.15, 74.71, 66.90, 32.75, 30.54, 29.30, 28.08, 27.89, 24.66, 22.25, 13.91; FD MS: 1634.1 [M^+ + 1].

***Bis-[2]catenanes* 31**

a) From homodimer: A solution of 5 (0.2 g, 0.12 mmol) in benzene (50 mL) was stirred at room temperature for three hours. The formation of the homodimer was checked by a ^{1}H NMR measurement. The solution was diluted with dichloromethane (1 L) and a solution of Grubbs' catalyst (10 mg, 12.4 μmol) in dichloromethane (25 mL) was added. The reaction mixture was stirred for two days, two drops of DMSO were added, and the stirring was continued for 12 hours. The solution was concentrated to ~400 mL and washed with water (2 x 400 mL), dried over $MgSO_4$, and evaporated. The residue was disolved in THF (20 mL) and hydrogen (1 atm.) added in the presence of PtO_2 (50 mg). A white compound was obtained after chromatographic separation (eluent chloroform/ ethyl acetate 95/5) and crystallization from chloroform/methanol mixture (0.4 g, 49%).

b) From a heterodimer: A solution of 6 (0.2 g, 0.12 mmol) and 7a (0.2 g, 0.12 mmol) in benzene (10 mL) was prepared by stirring at 40 °C for two days. The complete formation of the heterodimer was checked and confirmed and by ^{1}H NMR. The metathesis reaction, hydrogenation and the chromatographic purification was carried out as described above. A white precipitate was obtained 0.26 g (65%);



m.p. > 200 °C (decomposition);

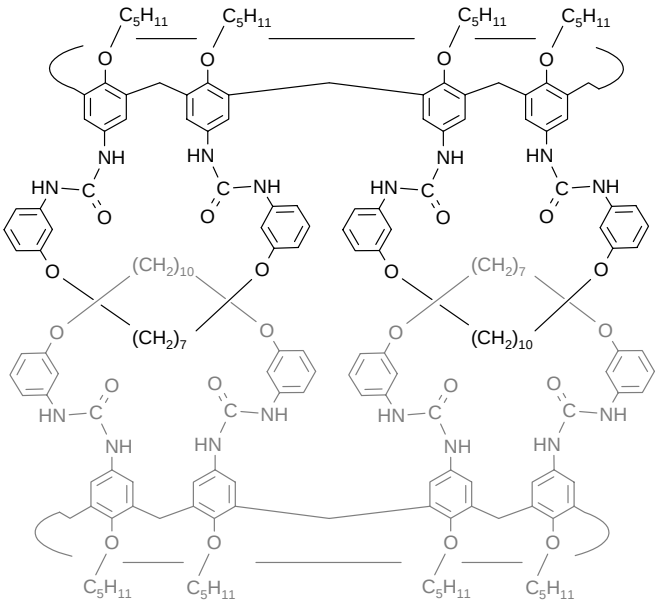
^{1}H NMR (C_6H_6-d_6, 400 MHz, 25°C): δ = 10.07 (s, 2H, NH), 10.00 (s, 2H, NH), 9.98 (s, 2H, NH), 9.96 (s, 2H, NH), 8.47 (brt, 2H, Ar_{meta}-H), 8.40 and 8.38 (dd, ^3J = 8.8 Hz; ^4J = 0.9 Hz, 2H, Ar_{meta}-H), 8.37 (brt, 2H, Ar_{meta}-H), 8.31 and 8.29 (dd, ^3J = 8.2 Hz; ^4J = 0.9 Hz, 2H, Ar_{meta}-H), 8.21 and 6.39 (two AB d, ^4J = 2.5 Hz, 4H, Ar_{calix}-H), 8.19 and 6.40 (two AB d, ^4J = 2.5 Hz, 4H, Ar_{calix}-H), 8.01 and 6.23 (two AB d, ^4J = 2.5 Hz, 4H, Ar_{calix}-H), 7.96 and 6.24 (two AB d, ^4J = 2.5 Hz, 4H, Ar_{calix}-H), 7.63 (brt, 2H, Ar_{meta}-H), 7.50 (brt, 2H, Ar_{meta}-H), 7.43 and 7.42 (dd, ^3J = 8.8 Hz; ^4J = 0.9 Hz, 2H, Ar_{meta}-H), 7.41 (s, 2H, NH), 7.37 (s, 2H, NH), 7.21-7.19 (m, 4H, Ar_{calix}-H), 7.11 (t, ^4J = 8.2 Hz, 2H, Ar_{meta}-H), 7.09 (t, ^4J = 8.2 Hz, 2H, Ar_{meta}-H), 7.00 (t, ^4J = 8.2 Hz, 2H, Ar_{meta}-H), 6.98 (s, 2H, NH), 6.81 (s, 2H, NH), 6.77 and 7.75 (dd, ^3J = 8.2 Hz, ^4J = 1.8 Hz, 2H, Ar_{meta}-H), 6.69 and 6.67 (dd, ^3J = 8.2 Hz, ^4J = 1.4 Hz, 2H, Ar_{meta}-H), 6.56 and 6.54 (dd, ^3J = 8.2 Hz, ^4J = 1.8 Hz, 2H, Ar_{meta}-H), 6.48 and 6.46 (dd, ^3J = 8.2 Hz; ^4J = 1.8 Hz, 2H, Ar_{meta}-H), 4.54 (d, ^2J = 12.0 Hz, 2H, Ar-CH_2-Ar*ax*), 4.51 (d, ^2J = 11.7 Hz, 2H, Ar-CH_2-Ar*ax*), 4.47 (d, ^2J = 10.8 Hz, 2H, Ar-CH_2-Ar*ax*), 4.44 (d, ^2J = 11.4 Hz, 4H, Ar-CH_2-Ar*ax*), 4.15 - 3.50 (m, 32H; OCH_2-), 3.35 (d, ^2J

= 12.0 Hz, 2H, Ar-CH_2-Ar*eq*), 3.22 (d, ^2J = 11.7 Hz, 2H, Ar-CH_2-Ar*eq*), 3.21 (d, ^2J = 11.4 Hz, 2H, Ar-CH_2-Ar*eq*), 3.08 (d, ^2J = 11.8 Hz, 2H, Ar-CH_2-Ar*eq*), 2.15-1.90 (m, 16H, -CH_2-), 1.72 - 1.58 (m, 8H, -CH_2-), 1.50 - 1.10 (m, 88H, -CH_2-), 1.00 - 0.93 (m, 24H, -CH_3);

^{13}C NMR ($CHCl_3$-d_1, 100 MHz, 25°C): δ (ppm) = 160.08, 159.96, 159.89, 154.52, 154.24, 154.18, 153.93, 151.45, 151.41, 151.23, 151.18, 140.69, 140.61, 135.52, 135.33, 135.27, 134.99, 134.78, 134.52, 134.24, 133.24, 133.11, 133.01, 132.86, 131.09, 131.00, 130.21, 117.88, 117.82, 117.43, 116.69, 116.63, 116.33, 116.26, 110.81, 110.76, 110.70, 110.52, 110.18, 109.34, 109.27, 104.18, 104.15, 103.60, 103.41, 75.93, 75.74, 75.48, 75.31, 68.73, 68.66, 67.89, 67.74, 30.68, 30.61, 30.44, 30.31, 29.91, 29.72, 29.69, 29.23, 29.03, 28.92, 28.72, 28.65, 28.63, 28.53, 28.36, 28.29, 28.16, 28.09, 25.99, 25.87, 25.54, 25.41, 22.87, 22.84, 22.76, 22.74, 14.23, 14.20, 14.13, 14.10; MALDI-TOF MS: m/z: 3187.7 [M + Na^+].

***Bis-[2]catenane* 32**

This compound was obtained from the homodimer of **26c**.



m.p. > 250 °C (decomposition without melting);

^{1}H NMR (C_6H_6-d_6, 400 MHz, 25 °C) = 10.20 (s, 2H, N**H**), 10.12 (s, 1H, N**H**), 10.04 (s, 1H; N**H**), 10.02 (s, 1H; N**H**), 9.97 (s, 2H; N**H**), 9.90 (s, 1H; N**H**), 8.51 (brt, 1H, Ar_{meta}-**H**), 8.49 (brt, 1H, Ar_{meta}-**H**), 8.44 and 8.42 (brdd, 1H, ^3J = 8.3 Hz, Ar_{meta}-**H**), 8.40 and 8.38 (brdd, 1H, ^3J = 8.8 Hz, Ar_{meta}-**H**), 8.36 and 8.34 (brdd, 1H, ^3J = 7.9 Hz, Ar_{meta}-**H**), 8.31 (d, 1H, ^4J = 2.2 Hz, Ar_{calix}-**H**), 8.28 (brt, 1H, Ar_{meta}-**H**), 8.21 (brt, 1H, Ar_{meta}-**H**), 8.19 (m, 3H, Ar_{calix}-**H**+ Ar_{meta}-**H**), 8.14 (d, 1H, ^4J = 2.2 Hz, Ar_{calix}-**H**), 7.82 (d, 1H, ^4J = 2.5 Hz, Ar_{calix}-**H**), 7.81 (d, 1H, ^4J = 2.2 Hz, Ar_{calix}-**H**), 7.76 (s, 1H, N**H**), 7.70 (d, 1H, ^4J = 2.2 Hz, Ar_{calix}-**H**), 7.63 (d, 1H, ^4J = 2.2 Hz, Ar_{calix}-**H**), 7.60 (brt, 1H, Ar_{meta}-**H**), 7.54 (brt, 1H, Ar_{meta}-**H**), 7.49-7.47 (m, 2H, N**H**+ Ar_{meta}-**H**), 7.43 (brt, 1H, Ar_{meta}-**H**), 7.40 (brt, 1H, Ar_{meta}-**H**), 7.33-7.31 (m, 2H, N**H**+ Ar_{meta}-**H**), 7.23 (t, 1H, ^4J = 8.1 Hz, Ar_{meta}-**H**), 7.20 (s, 1H, N**H**), 7.18 (t, 1H, ^4J = 7.8 Hz, Ar_{meta}-**H**), 7.16 (t, benzene + Ar_{meta}-**H**), 7.15 (t, benzene + Ar_{meta}-

H), 7.14 (t, benzene + Ar_{meta}-**H**), 7.07 (t, 1H, ^4J = 7.8 Hz, Ar_{meta}-**H**), 7.02 (t, 1H, ^4J = 7.8 Hz, Ar_{meta}-**H**), 6.98 (t, 1H, ^4J = 8.3 Hz, Ar_{meta}-**H**), 6.91 (s, 1H, N**H**), 6.84 and 6.82 (dd, 1H, ^3J = 7.9 Hz, ^4J = 1.8 Hz, Ar_{meta}-**H**), 6.77 and 6.75 (dd, 1H, ^3J = 8.3 Hz, ^4J = 2.2 Hz, Ar_{meta}-**H**), 6.74 and 6.72 (dd, 1H, ^3J = 8.6 Hz; ^4J = 1.9 Hz, Ar_{meta}-**H**), 6.69 (s, 1H, N**H**), 6.69 and 6.67 (brdd, 1H, ^3J = 8.5 Hz, Ar_{meta}-**H**), 6.66 and 6.64 (brdd, 1H, ^3J = 7.6 Hz, Ar_{meta}-**H**), 6.55 and 6.53 (dd, 1H, ^3J = 8.3 Hz, ^4J = 1.9 Hz, Ar_{meta}-**H**), 6.51 and 6.49 (dd, 1H, ^3J = 7.9 Hz, ^4J = 1.9 Hz, Ar_{meta}-**H**), 6.49 (brd, 1H, Ar_{calix}-**H**), 6.44 (s, 1H, N**H**), 6.38 (d, 1H, ^4J = 2.2 Hz, Ar_{calix}-**H**), 6.30 (d, 1H, ^4J = 2.2 Hz, Ar_{calix}-**H**), 6.23 (d, 1H, ^4J = 2.5 Hz, Ar_{calix}-**H**), 6.21 (d, 1H, ^4J = 2.5 Hz, Ar_{calix}-**H**), 6.13 (d, 1H, ^4J = 2.5 Hz, Ar_{calix}-**H**), 6.09 (d, 1H, ^4J = 2.2 Hz, Ar_{calix}-**H**), 6.04 (d, 1H, ^4J = 2.2 Hz, Ar_{calix}-**H**), 4.53 (d, 1H, ^4J = 11.7 Hz, Ar-C**H**$_2$-Ar *ax*), 4.52 (d, 1H, ^4J = 11.7 Hz, Ar-C**H**$_2$-Ar *ax*), 4.51 (d, 1H, ^4J = 11.4 Hz, Ar-C**H**$_2$-Ar *ax*), 4.48 (d, 1H, ^4J = 12.7 Hz, Ar-C**H**$_2$-Ar *ax*), 4.46 (d, 1H, ^4J = 11.4 Hz, Ar-C**H**$_2$-Ar *ax*), 4.44 (d, 1H, ^4J = 11.7 Hz, Ar-C**H**$_2$-Ar *ax*), 4.39 (d, 1H, ^4J = 11.1 Hz, Ar-C**H**$_2$-Ar *ax*), 4.36 (d, 1H, ^4J = 11.1 Hz, Ar-C**H**$_2$-Ar *ax*), 4.18 - 3.43 (m, 32H, -OC**H**$_2$), 3.38 (d, 1H, ^4J = 12.0 Hz, Ar-C**H**$_2$-Ar *eq*), 3.24 (d, 1H, ^4J = 12.0 Hz, Ar-C**H**$_2$-Ar *eq*), 3.20 (d, 1H, ^4J = 12.4 Hz, Ar-C**H**$_2$-Ar *eq*), 3.16 (d, 1H, ^4J = 12.4 Hz, Ar-C**H**$_2$-Ar *eq*), 3.13 (d, 1H, ^4J = 12.4 Hz, Ar-C**H**$_2$-Ar *eq*), 3.03 (d, 1H, ^4J = 11.4 Hz, Ar-C**H**$_2$-Ar *eq*), 2.97 (d, 1H, ^4J = 11.7 Hz, Ar-C**H**$_2$-Ar *eq*), 2.81 (d, 1H, ^4J = 11.7 Hz, Ar-C**H**$_2$-Ar *eq*), 2.23-2.09 (m, 8H, -C**H**$_2$-), 1.95 - 1.65 (m, 16H, -C**H**$_2$-), 1.50 - 1.11 (m, 64H, -CH_2-), 1.01 - 0.93 (m, 24H, -CH_3);

^{13}C-NMR (C_6H_6-d_6, 100 MHz, 25°C): δ (ppm) = 161.52, 161.25, 161.09, 161.07, 160.97, 160.67, 160.60, 160.19, 155.55, 155.37, 155.05, 154.94, 154.76, 154.72, 154.51, 154.42, 154.40, 154.28, 154.24, 152.12, 151.99, 151.94, 151.88151.86, 142.24, 142.00, 141.73, 141.66, 141.58, 141.07, 140.91, 137.01, 136.96, 136.32, 136.26, 136.20, 136.10, 135.49, 135.16, 134.68, 134.61, 134.57, 134.46, 134.03, 133.63, 133.33, 133.19, 132.81, 131.90, 131.85, 131.78, 131.68, 130.63, 130.48, 130.26, 119.87, 119.53, 119.30, 119.22, 118.82, 118.65, 118.56, 118.46, 118.31, 118.26, 117.90, 117.30, 117.20, 116.97, 116.85, 113.63, 113.57, 112.58, 112.16, 112.14, 111.57, 110.97, 110.89, 110.67, 110.43, 110.28, 110.24, 109.54, 109.37, 108.32, 106.39, 106.17, 103.86, 103.69, 103.51, 103.10, 102.79, 102.14, 76.52, 76.50, 76.21, 76.18, 75.77, 75.60, 75.40, 75.35, 69.36, 69.10, 69.08, 68.88, 68.31, 68.06, 67.63, 67.14, 31.45, 31.32, 31.17, 31.05, 31.01, 30.90, 30.50, 30.42, 30.36, 30.31, 30.35, 30.02, 29.99, 29.25, 29.19, 29.15, 29.13, 29.10, 29.02, 28.98, 28.95, 28.80, 28.77, 28.76, 28.57, 28.53, 28.51, 26.35, 26.31, 26.08, 25.66, 25.45, 23.39, 23.36, 23.33, 23.24, 23.20, 23.17, 23.12, 14.56, 14.54, 14.49, 14.36, 14.34, 14.30, 14.27;

MS (FD), m/z 3102.79 (M+Na^+ calc $C_{186}H_{236}N_{16}O_{24}Na$: 3100.76).

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