Synthesis, Properties and Applications of Macrocyclic Azobenzenes

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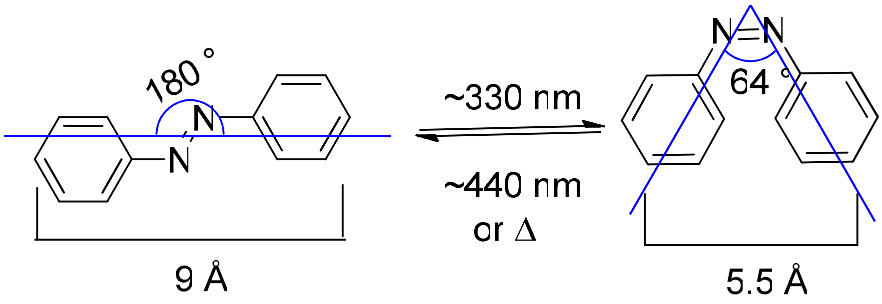
1. Introduction

1.1 General introduction

The major use of azobenzenes, since their first preparation in the mid 19th century[1] has been their application as dyes and pigments. Azobenzenes usually are absorbing light in the blue region and therefore the vast majority of azobenzenes exhibit a yellow, orange or red colour. Furthermore, their synthesis is usually cheap and convenient and a variety of substituents can be introduced to modify their colour or increase their adsorption on different materials. Owing to these circumstances, azobenzenes probably make up the most important class of colorants and today still contribute to more than half of the market for organic dyes and pigments.

1.2 Photochromism of azobenzenes

Besides their applicability as colorants, in 1937 another interesting property of azobenzenes, their photochemical $E \rightarrow Z$ isomerization was observed by S. Hartley.[2] This isomerization is reversible and normally does not involve side reactions. For this reason azobenzenes are today one of the most used structural motifs to incorporate into photochromic molecules.[3,4] The more stable isomer, for the vast majority of azobenzenes is the *trans*- or *E*-isomer, in which the two benzene units are pointing away from each other, spanning an angle of about 180°.[5] If an azobenzene is irradiated with ultraviolet light in the UV region at a wavelength of around 360 nm, a certain percentage of the molecule undergoes $E \rightarrow Z$ isomerization and is converted to the *cis*- or *Z*-isomer. During this process the geometry of the molecule is significantly changed. The two benzene moieties now approach each other and span an angle of around 64° which brings about a decrease in length by roughly 3.5 Å (Scheme 1). If the azobenzene motive is introduced into a functional molecule, its properties can thereby be altered reversibly by this significant change in shape. This property has been exploited for various applications.[6,7,8,9] Some of these are photoresponsive molecular sensors,[10,11] ion channels,[12] foldamers,[13] liquid crystals,[14,1516] or catalysts[17] just to name a few. Though the *Z*-isomer can in many cases be isolated by chromatographic methods, it is usually hard to obtain a pure sample of the species, since it undergoes thermal and photochemical back isomerization. The absorption spectrum of azobenzene shows three major transitions. Theoretically, all these transitions are suitable for isomerization in both directions. Yet, some important differences in the electronic structure of the two isomers make a directed isomerization possible.[18] The σ→π* transition appears for both isomers at around 220 nm but is normally not used for isomerization since its high energy induces unwanted side reactions.



Scheme 1: Reversible isomerization of azobenzene.

The π→π* transition occurs at around 330 nm for the *E*-isomer and at 290 nm for the *Z*-isomer. Therefore, when irradiation is done at 330 nm most of the light is absorbed by the *E*-isomer, which makes *E* → *Z* isomerization possible. At around 440 nm the n→π* transition takes place at almost the same wavelength for both isomers (Figure 1). However, for the *E*-isomer this excitation is formally symmetry forbidden. Therefore at this wavelength the *Z*-isomer absorbs to a higher degree and selective *Z* → *E* isomerization takes place. It is important to state that even though at certain wavelengths one isomer is more absorbing, the other one also always absorbs to a certain degree. Therefore, such isomerizations do not proceed quantitatively but rather an equilibrium is reached, where *E* → *Z* and *Z* → *E* isomerization take place at the same rate. This equilibrium is called the photostationary state (PSS).

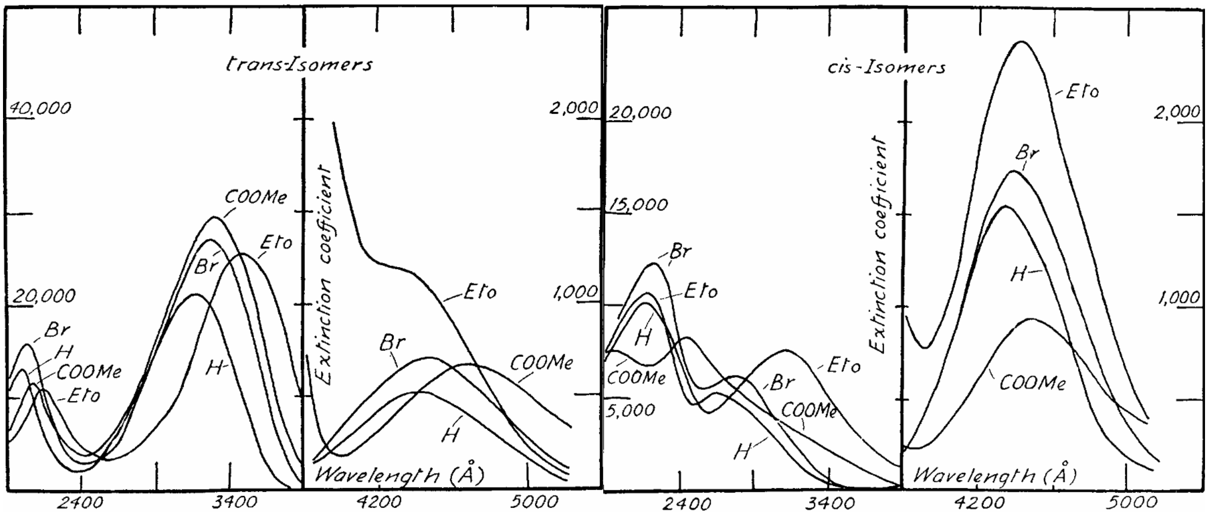
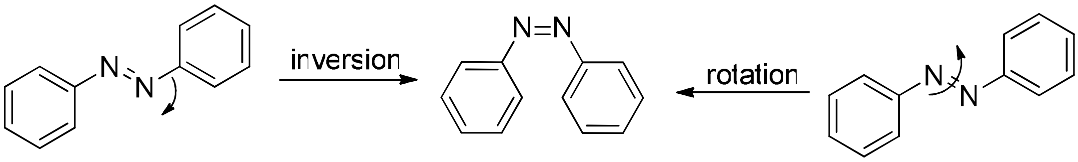


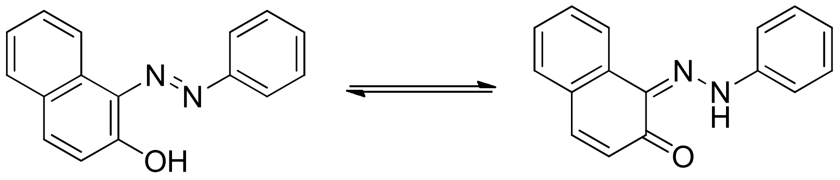
Figure 1: Absorption spectra of different *para* substituted azobenzenes. Left figure: *E*-isomers; Right figure: *Z*-isomers.[19]

The detailed mechanism of azobenzenes photochromism is in dispute since a long time.[20] There are two basic mechanisms which are discussed (Scheme 2). One mechanism is rotational, where the excited azobenzene can rotate around its weakened N=N double bond. [21,22,23] The second proposed mechanism happens by inversion at one nitrogen atom.[24,25,26,27,28] Since good evidence exists for either pathway, it is probable that both do occur.



Scheme 2: Two possible mechanisms of *E*→*Z* isomerization.

As it can be seen in Figure 1, the introduction of different side groups results in a change of the absorption spectrum and also has an effect on the photochromic properties. For industrial applications it is important to suppress photochromism, otherwise the colour of a dye would fade upon sunlight exposure. One major strategy is used to achive this goal by the introduction of hydroxy groups in the *ortho* position. Such azobenzenes undergo tautomery and do not isomerize (Scheme 3).[3]



1a **1b**

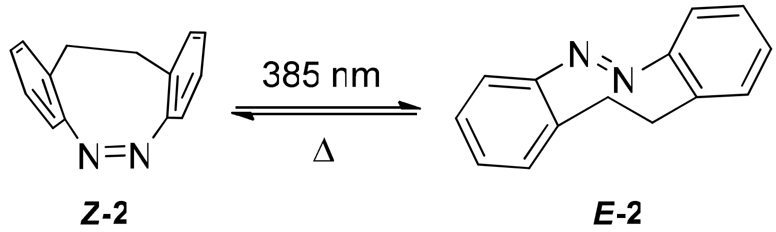
Scheme 3: Sudan I (**1**) as an example for tautomery in 2-hydroxyazobenzenes.

In contrast to the ease by which the *E*-isomer can be stabilized, this is not the case for the *Z*-isomer. As it was already mentioned, sterical reasons make the *Z*-isomer the less stable species and even though there are some substituents which have a stabilizing effect on it,[3] the thermal *E*→*Z* isomerization can usually only be slowed down to a small extent but can never be totally suppressed. This poses a problem as it limits the applicability of azobenzenes in certain areas, for example as optical storage devices. The only strategy which was employed so far to greatly enhance the lifetime of the *Z*-isomer or even make it thermally stable was to exploit the concept of macrocyclic strain found in azobenzenophanes.

1.3 Azobenzenophanes

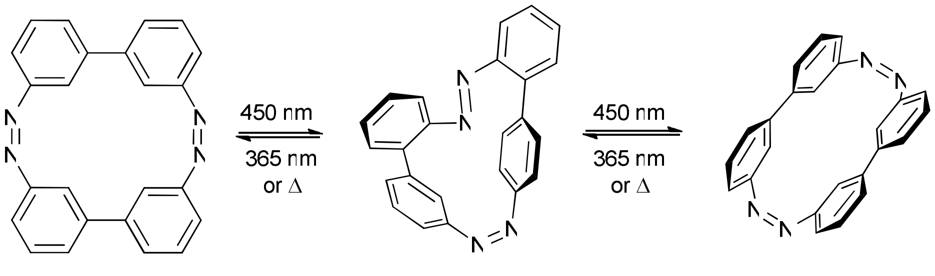
1.3.1 Macrocyclic strain and thermal stability

It has already been discussed, that the *Z*-isomer of azobenzene is less stable than the *E*-isomer. As the protons in the *ortho* position of the azobond experience steric hindrance, the two benzene rings twist out of planarity with a torsion angle of 8 °.[29] This decreases conjugation between the two phenyl rings and further destabilizes the isomer. As it was stated above, these steric factors can be overcome by introducing macrocyclic strain, as it is the case in azobenzenophanes. Rau and coworkers, one of the pioneers in the field of azobenzenophanes were the first to prepare a macrocyclic azobenzene, [2.2](4,4’)azobenzenophane (**6**), bridged by two thioethers at *para* position.[30,31,32] Since then, many other examples have been added to this substance class. In extreme cases the macrocyclic strain in the *E*-isomer can be so large that it even compensates the sterical demand of the *Z*-isomer, which then becomes the thermally most stable isomer. An impressive example of this strategy was published by Siewertsen and coworkers, who investigated the photochemical properties of azobenzenophane **2** bridged by an ethylene linker in the *ortho* position.[33] Due to the high distortion in the *E*-isomer, the *Z*-isomer is in this case the thermally more stable compound. Upon irradiation at 385 nm *Z* → *E* isomerization takes place. The *Z*-isomer can be recovered by heating the sample. The molecule shows a completely reversed behaviour to non-cyclic azobenzenes (Scheme 4).



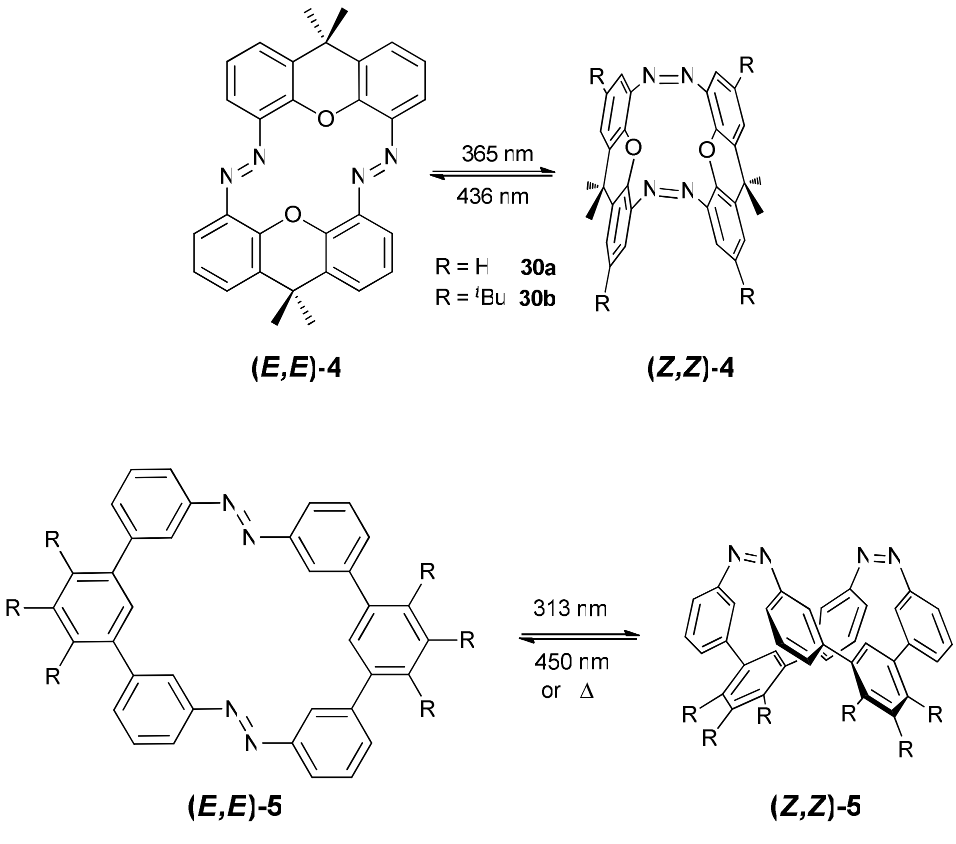
Scheme 4: Thermally stable *Z*-isomer by Siewertsen and coworkers.

There is a second example of a thermally stable *Z*-isomer, published by Tamaoki and coworkers.[34] They prepared molecule **3** in which two biphenyl units are connected by two azobenzene bonds in *meta* positions (Scheme 5). By the incorporation of two azobenzene bonds the compound now has three possible isomers [(*E,E*), (*E,Z*), (*Z,Z*)]. The (*E,E*)- and particularly the (*E,Z*)-isomer are highly strained and consequently the (*Z,Z*)-isomer is the most stable of the three isomers. However, in this example the molecule sacrifices much of its photochromic properties maybe because of the macrocyclic strain. Isomerization to the (*E,E*)-isomer only partially occurs after extended irradiation with a high intensity lamp.



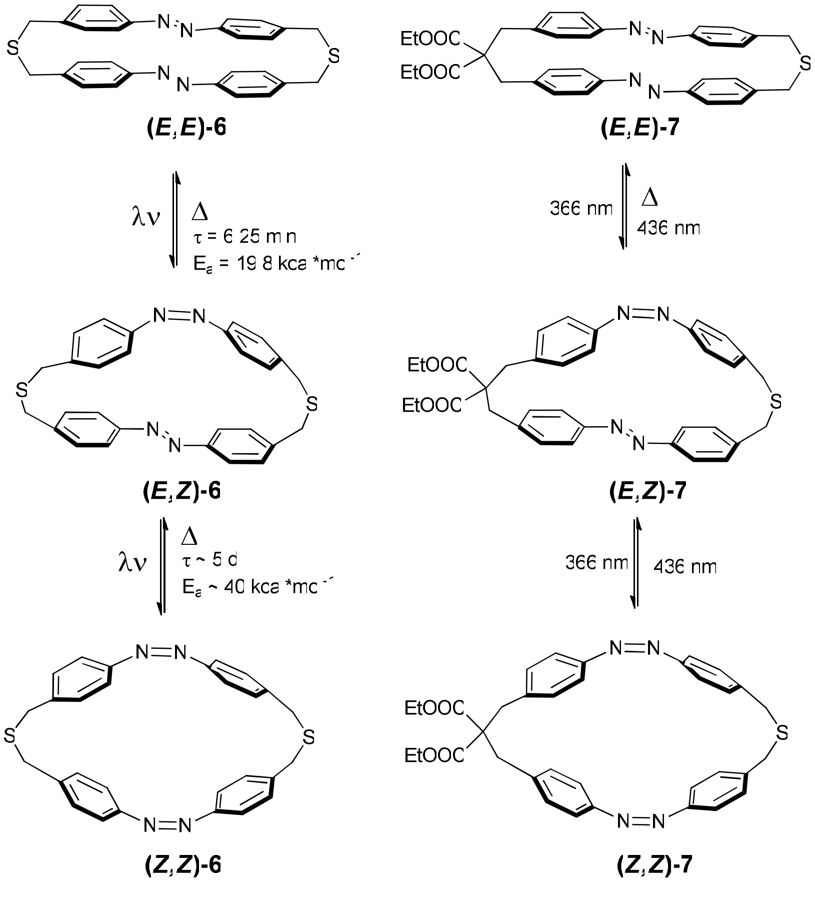
Scheme 5: Azobenzenophane with a stable (*Z,Z*)-isomer by Norikane et al.

To my knowledge the two discussed macrocycles are the only examples of thermally stable *Z*-isomers. However there are also some other instances of azobenzenophanes in which the *Z*-isomer exhibits a lifetime of more than one year. One of those cases was also published by Tamaoki and coworkers.[35,36] They were successful in preparing molecular hinge **4** where the (*E,E*)-isomer has a flat geometry whereas the (*Z,Z*)-isomer has a bent structure spanning an angle of 112° (Scheme 6). Due to the high distortion in the mixed (*E,Z*)-isomer, the bent (*Z,Z*)-isomer is exceptionally stable with a lifetime of 6.7 years. On the other hand, the lifetime of the unstable mixed isomer is only 2.73 minutes. However, the photoisomerization of this hinge, like in the previous example, can only be partially achieved. In the photostationary state after 366 nm irradiation only 32 % of the (*Z,Z*)-isomer are obtained. The structure of both isomers was confirmed by X-ray analysis, showing the structural features of a hinge. Major and coworkers prepared azobenzenophane **5** based on terphenyls which could also have the three dimensional structure of a hinge.[37] Yet, the structure was not confirmed with X-ray analysis. Furthermore, with a lifetime of several days the (*Z,Z*)-isomer lies in the range of other azobenzenophanes.



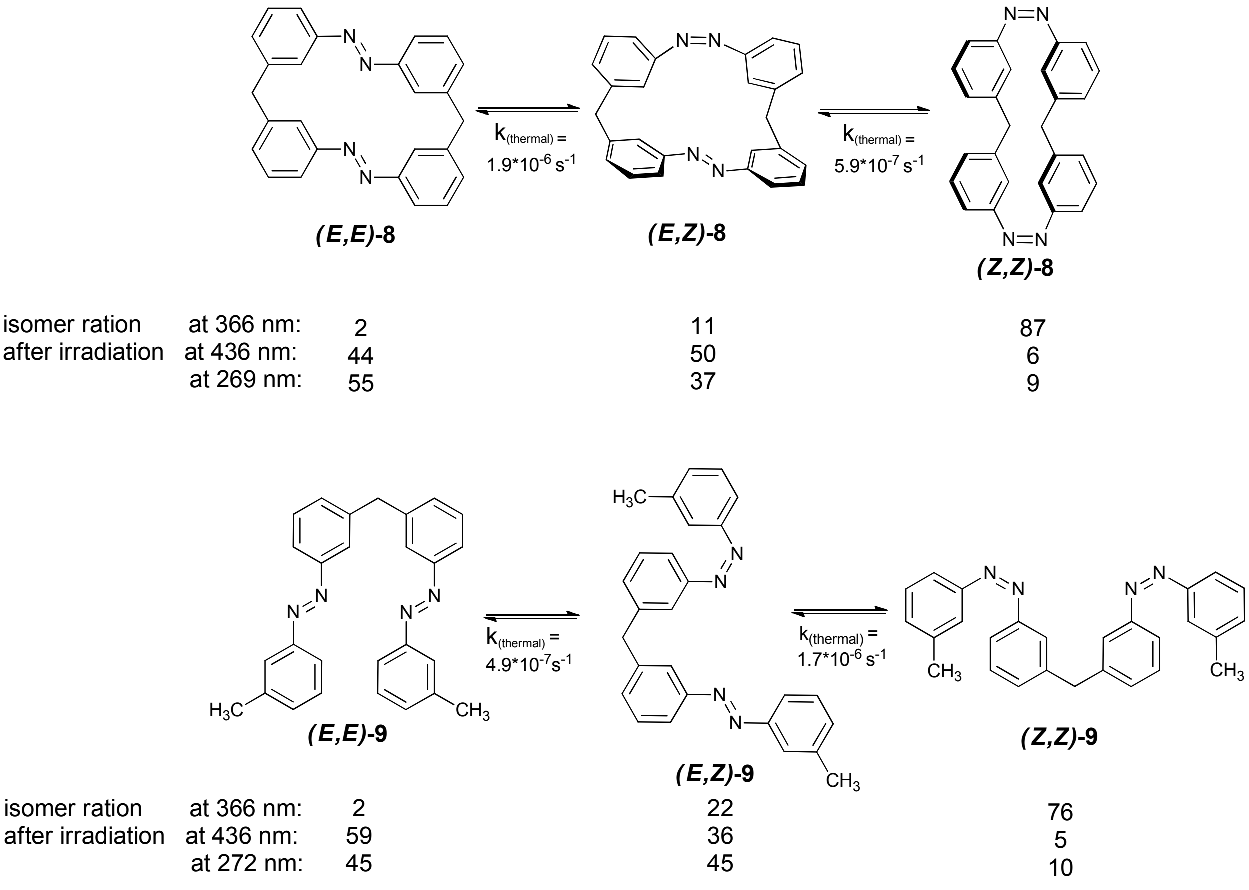
Scheme 6: Molecular hinges based on xanthene by Tamaoki and coworkers (top) and based on terphenyls by Major and coworkers (bottom).

Another remarkable example of a bistable azobenzenophane is a system of Rau and coworkers which shows how only small changes in the structure of azobenzenophanes can have a large effect on their stability and photochromism (Scheme 7). They prepared two [3.3](4,4')-azobenzenophanes with different tethers.[38] One macrocylce **6** was bridged by two thioether tethers, the other macrocycle **7** consisted of one malonic acid ester containing a C_3 linker and one thioether linker. Surprisingly, macrocycle **6** showed a usual lifetime for the (*Z,Z*)-isomer, whereas in the second example **7** the (*Z,Z*)-isomer had a very high lifetime of over 1 year. Furthermore it almost underwent complete photochemical *E* → *Z* conversion upon irradiation at 366 nm. The photochemical conversion from *Z* → *E* was also possible at 436 nm in contrast to the slow thermal isomerization. With almost complete photochemical conversion and high stability of both isomers this was the first system which could satisfy the requirements of an optical storage device.[39] Furthermore, the readout of the device would also be very beneficial since at 366 the *Z,Z*-isomer shows almost no absorption. Yet, the molecule decomposes upon irradiation of 313 nm with a photochemical side reaction taking place.



Scheme 7: Rau and coworkers' bistable azobenzenophane (right) and the structurally very similar derivative (left) with shorter lifetime (left).

A direct comparison between the stability of a macrocyclic azobenzene **8** and its linear analogue **9** was done by Tamaoki and coworkers (Scheme 8).[40] In their study, they found that not only the photostationary states are significantly different in the macrocyclic case, but also the thermal Z → E isomerization is diverging from the behaviour observed for the linear azobenzenes. While in the linear case the mixed (*E,Z*)-isomer is thermally more stable than the (*Z,Z*)-isomer, the macrocycle shows the opposite result with the (*Z,Z*)-isomer exhibiting a higher thermal stability.



		(*E,E*)-8	(*E,Z*)-8	(*Z,Z*)-8
isomer ration	at 366 nm:	2	11	87
after irradiation	at 436 nm:	44	50	6
	at 269 nm:	55	37	9

		(*E,E*)-9	(*E,Z*)-9	(*Z,Z*)-9
isomer ration	at 366 nm:	2	22	76
after irradiation	at 436 nm:	59	36	5
	at 272 nm:	45	45	10

Scheme 8: Comparison of photochromic properties: Linear vs. macrocyclic azobenzene.

1.3.2 Applications of azobenzenophane macrocycles.

One possible application of azobenzenophanes as optical storage devices was just briefly discussed regarding the example of Rau and coworkers bistable azobenzenophane **7**. Furthermore, azobenzenophanes combine the usual properties which are found in macrocyclic oligoaryl systems with photochemical (*E,Z*)-isomerization. This property enables the switching of macroscopic effects which stem from their unique intermolecular attractions, mainly π-π-stacking and van der Waals forces. Possible applications of such systems can be photoresponsible host-guest networks or photoswitchable discotic liquid crystals. The ability of azobenzenophanes to form intermolecular networks with guest molecules was shown by Shen et al., who mixed tetrameric [2.2](4,4')azobenzenophane **29** with 1,3,5-tris(10-carboxydecyloxy)-benzene (TCDB) in different ratios and investigated a variety of different network domains on a HOPG surface (Figure 2).[41] In their networks the macrocyclic azobenzene was incorporated into cavities of TCDB molecules. The interesting feature of their research was the formation of many distinct network domains with mixed isomers of the azobenzenophanes when solutions were irradiated before deposition.

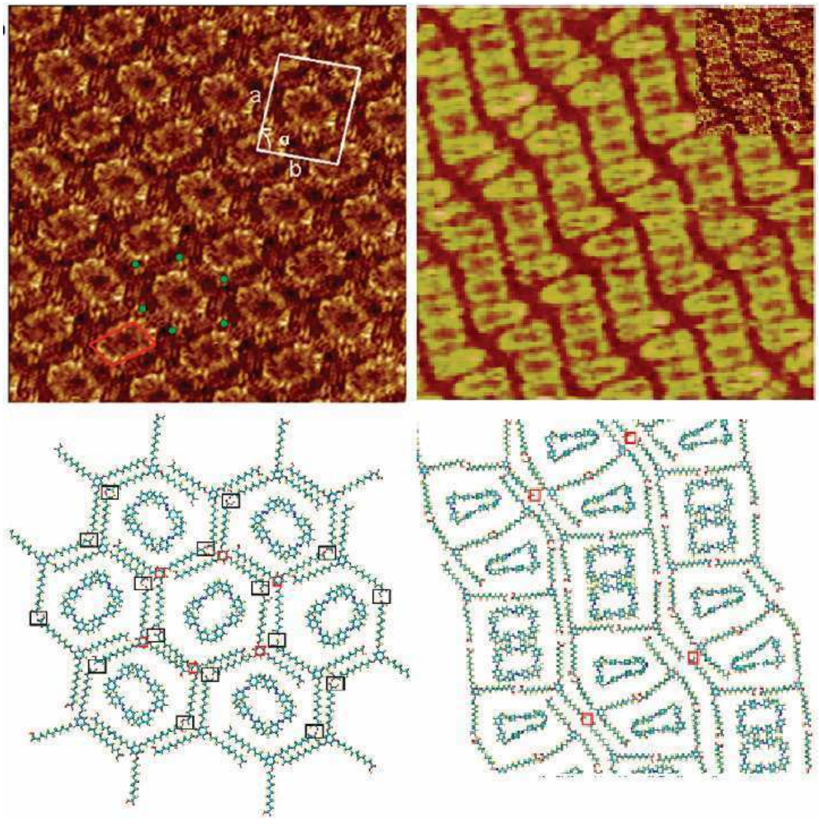


Figure 2: Azobenzenophane **29**/TCDB host-guest networks reported by Shen et al.

Photoresponsive liquid crystals are the second application of azobenzenophanes which should be referred to. Macrocyclic oligoaromatic compounds have the ability to form discotic liquid crystalline phases when long side chains are attached to their aryl moieties.[42,43,44] These phases are usually thermally unstable, since upon heating an isomeric melt is obtained. However, in an impressive example by Norikane and coworkers the liquid crystalline phase of azobenzenophanes **10** and **11** can not only be converted to an isotropic melt reversibly by heating, but also by UV-irradiation.[15] In their system this was not only possible for the liquid crystalline phase but they also observed an isothermal phase transition when solid crystals of their macrocycles were irradiated with UV-light (Figure 3). There are also other examples of photoresponsible liquid crystals based on macrocycles and linear azobenzenes.[45,46]

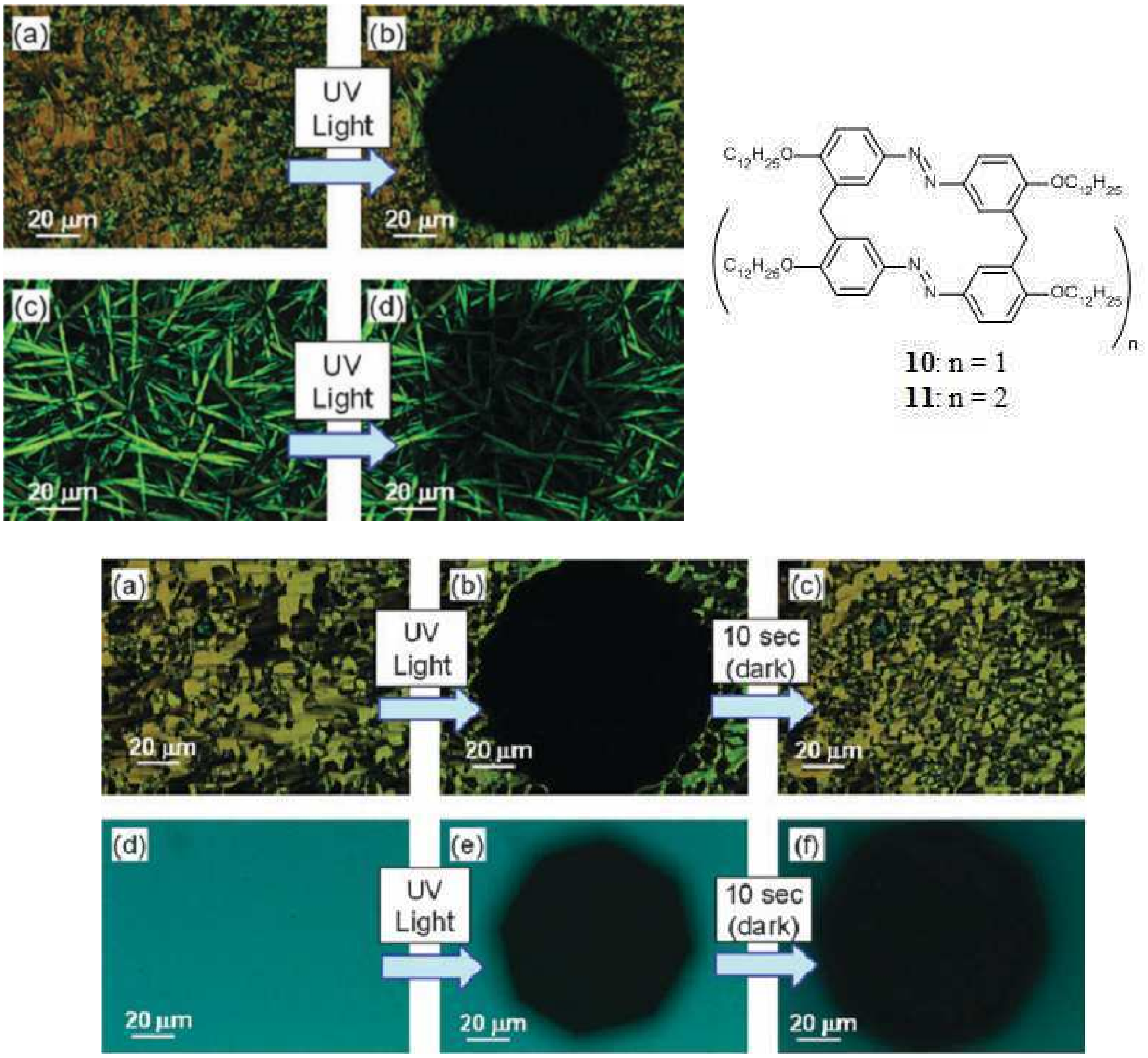
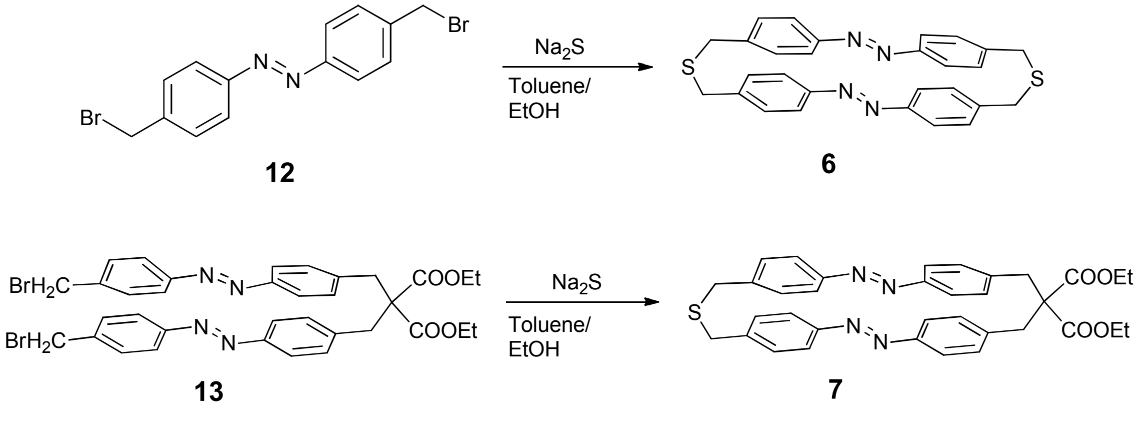
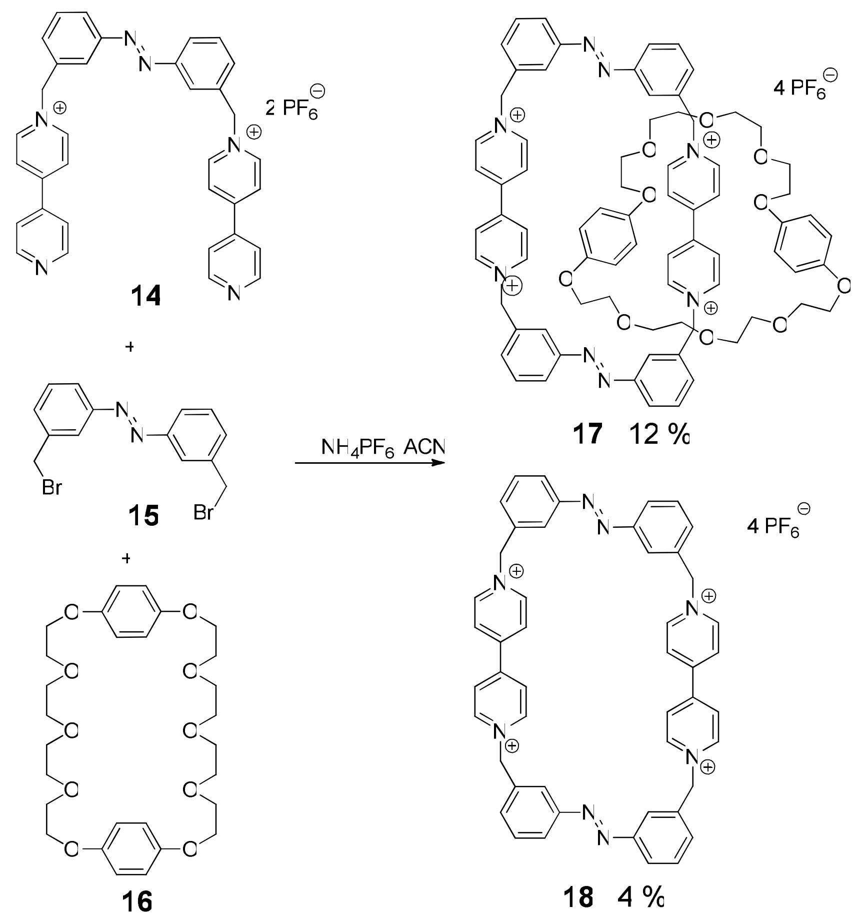


Figure 3: Photoswitchable liquid crystals and crystals by Norikane and coworkers. Upper picture: switching between crystalline and isotropic phase; lower picture: switching between liquid crystalline and isotropic phase.

1.3.3 Synthesis of azobenzenophanes.

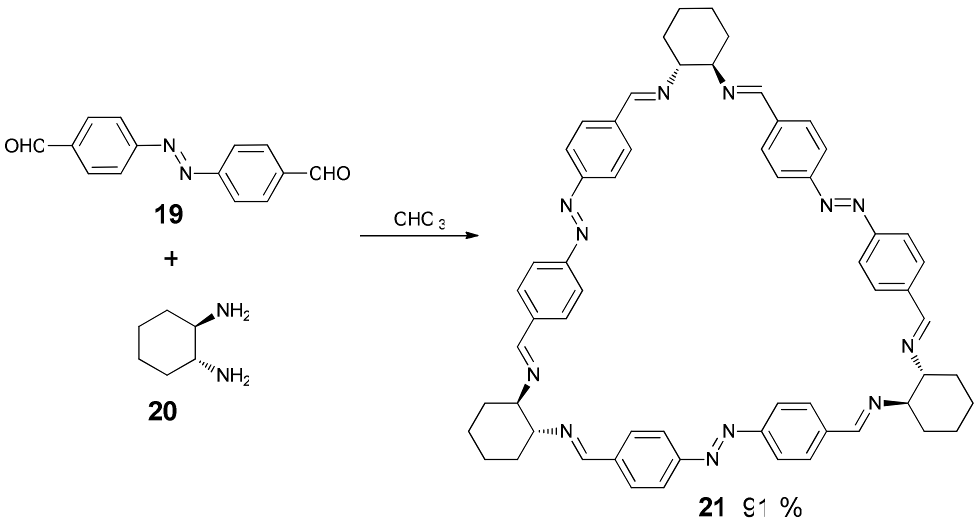
Almost all common methods to produce linear azobenzenes are also found in the synthesis of their macrocyclic analogues. Depending on the structure of the azobenzenophane, different strategies to afford macrocyclization in the last step are more applicable than others. Which methodology is the most promising depends largely on the nature of the tether which connects the azobenzene moieties. Yet, in almost all cases the synthesis of such macrocycles is a great challenge, since the intermolecular reaction path is always an unwanted side reaction. When the tether contains a heteroatom the azobenzene functionality can be prepared beforehand with subsequent connection of the tethers. Rau and coworkers adopted this strategy in their synthesis of thioether bridged azobenzenophane **6**.[29-31] They obtained cyclization yields of 40 % for the macrocyclization step by condensing the bisbenzylic bromide with sodium sulphide. Also, the nucleophilic substitution of benzylic bromides with nitrogen nuleophiles is feasible,[47] pyridines as an example in the synthesis of azobenzenophane catenane **17** (Scheme 8).[48,49]





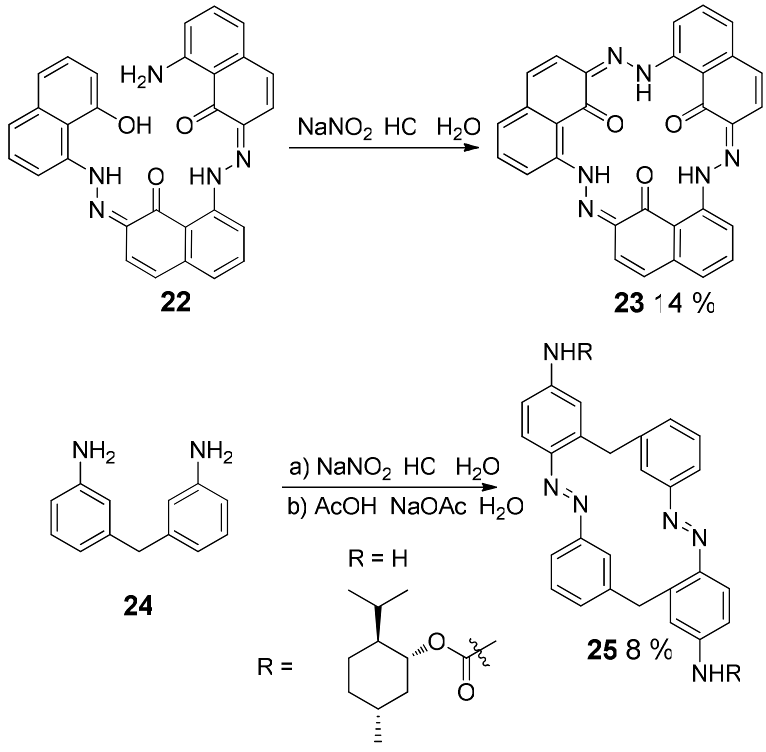
Scheme 8: Synthesis of azobenzenophanes by Williamson type substitution.

Besides the substitution of benzylic bromides with thiols or amines, a second very powerful method is the condensation of amines with benzaldehydes to produce imines. Tanaka and coworkers reacted azobenzene-4,4'-dicarbaldehyde **19** with enantiomerically pure 1,2-diaminocyclohexane **20** to obtain chiral azobenzenophane **21** in excellent yields (Scheme 9).[50] The good selectivity of the reaction is probably owed to the reversibility of imine formation.



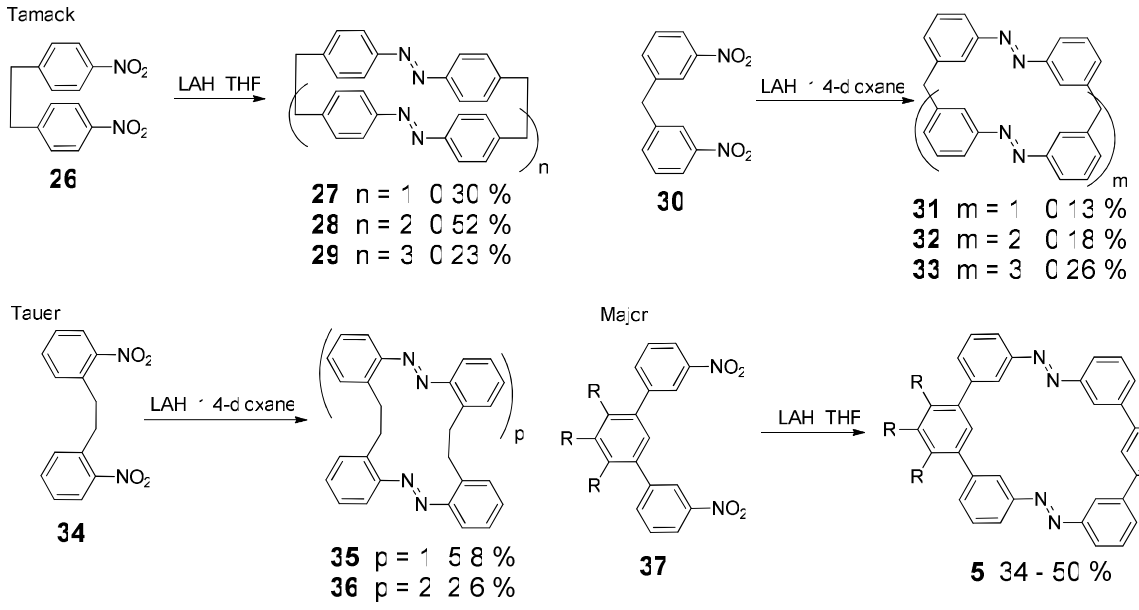
Scheme 9: Preparation of chiral macrocyclic azobenzenophane by oligocondensation.

In many literature known azobenzenophanes the tether does not contain any nucleophilic heteroatoms, which renders ring closure by a transformation of the side chain difficult. In those cases one or all azobonds have to be generated in the macrocyclization step. Electrophilic substitution of diazonium salts is one possibility to achieve this task. However, the requirement of electron donating groups for activation and direction limits the versatility of this transformation. If indeed the structure fits the requirements for the reaction to take place selectively, acceptable yields can be achieved. Yet, in most of the cases there are no directing groups installed and another method has to be used to connect the azobonds (Scheme 10).



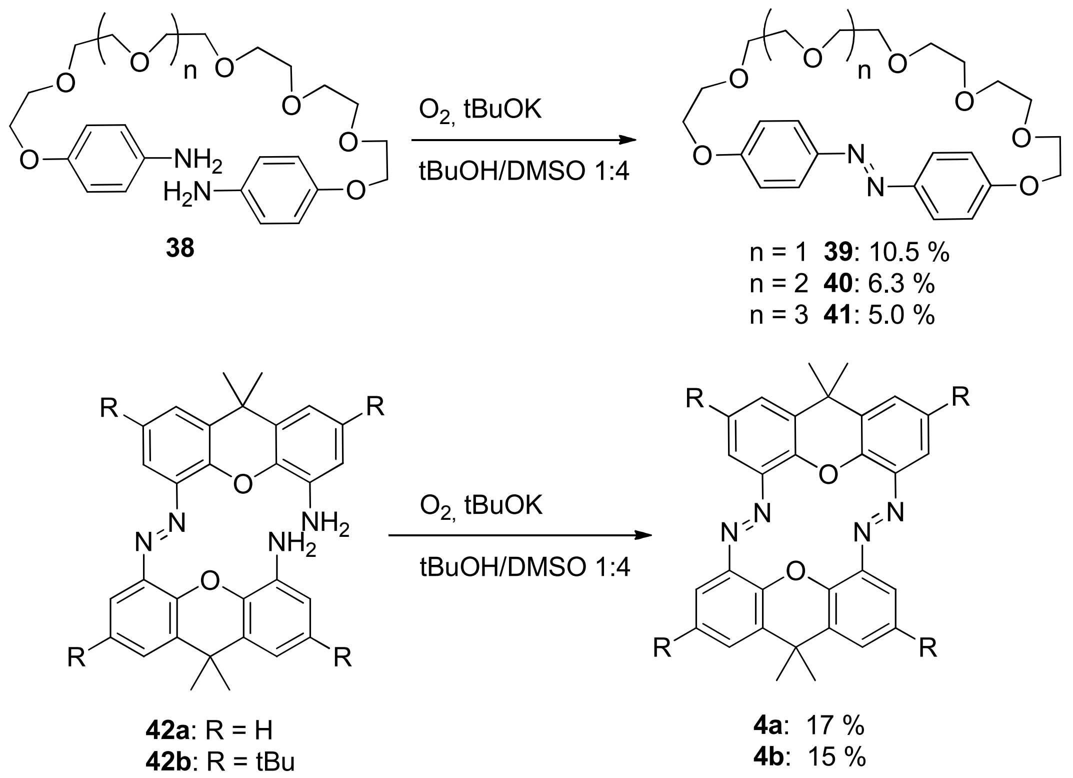
Scheme 10: Two syntheses of azobenzenophanes **23** and **25** by electrophilic aromatic substitution of diazonium salts.[14,15,51]

A second method to prepare azobonds is the reductive azocoupling of nitro groups. Several methods have been reported in literature for the reductive formation of azobonds, which include reduction with metals such as zinc dust or organic reducing agents like glucose.[52,53] The reduction can also be done electrochemically or by means of hydrogenation with heterogeneous transition metal catalysts.[54,55] Yet, all these methods have only been applied for the synthesis of linear azobenzenes so far. The method of choice for the preparation of macrocycles is the treatment of dinitro compounds with lithium aluminium hydride using high dilution conditions.[56] Many of the first azobenzenophanes were synthesized using this protocol. Even though the obtained yields are usually low, the reaction often produces several oligomers in one step which are all interesting for the exploration of their photochromic properties. Tamaoki and coworkers used this method to obtain [2.2](4,4')azobenzenophanes **27 - 29** with ethylene tethers in *para*-positions,[57,58,59,60] as well as [1.1](3,3')azobenzenophanes **31 - 33** with methylene tethers at *meta*-positions.[61,62,63] In both cases the dimeric, trimeric, as well as the tetrameric species were obtained. Tauer and coworkers completed the series by preparing the dimeric and trimeric derivative of the *ortho* substituted [2.2](2,2')azobenzenophane **35** and **36**.[64] The method was also used by Major and coworkers for their macrocycles **38**. In their case, the rigidity of the molecule is probably the cause of the much higher yields they obtained (Scheme 11).



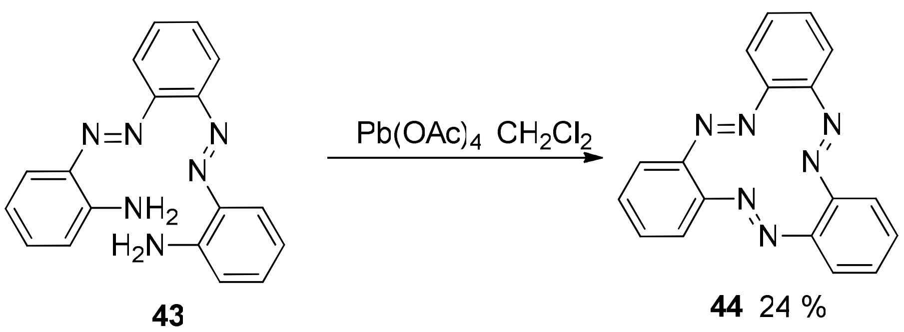
Scheme 11: Reductive azocoupling with lithium aluminium hydride for the preparation of various azobenzenophanes.

As a counterpart to the reductive strategy, the oxidative coupling of anilines is also an alternative to gain macrocyclic azobenzenes. In the case of linear azobenzenes, the most widely applied reagent to facilitate this transformation is activated manganese dioxide.[65] Other methods include treatment with sodium hypochlorite under basic conditions or the use of potassium hexacyanoferrate.[66,67] Another interesting protocol, especially because of environmental aspects, is the implementation of molecular oxygen as an oxidant. A protocol of Shinkai and Manabe uses oxygen with potassium *tert*-butoxide as a base in a mixed solvent of *tert*-butanol and DMSO to prepare photoresponsive crown ethers **40 - 42**, which change their complexation behaviour upon irradiation.[10,11] The same procedure was later also used by Tamaoki and coworkers for the synthesis of their molecular hinge **4** (Scheme 12).[35,36]



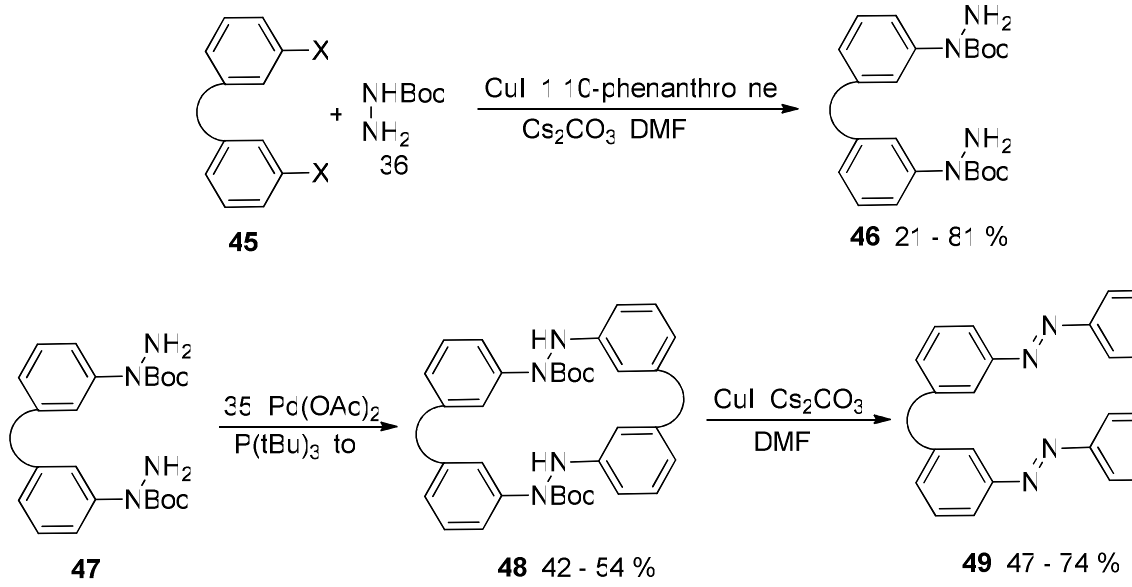
Scheme 12: Application of molecular oxygen in the synthesis of photoresponsive crown ethers and molecular hinges.

One reagent which also played a crucial role in this context is lead tetraacetate. This compound is usually used for the oxidative cleavage of 1,2-diols to aldehydes or ketones and there are only very few examples where this reagent was applied for the synthesis of linear azobenzenes. Yet, it was found by Dreiding and coworkers, that the oxidation of 2,2’’-bisazodiamine **43** with lead tetraacetate produced the macrocyclic azobenzene product **44** in good yields (Scheme 13).[68]



Scheme 13: Oxidative macrocyclization to cyclotrisazobenzene by Dreiding and coworkers.

A method which also has to be mentioned, since it applies the modern method of palladium catalyzed crosscoupling, was invented by Cho and coworkers (Scheme 14). It involves a three step transformation of dihalogenides **45** to azobenzenophanes **49**. In the first step a bis-Boc-hydrazine **46** is prepared using copper catalysis. This intermediate can then be coupled with a dihalogenide **45** under palladium catalysis. The obtained hydrazide **48** can then be oxidized with copper(I)iodide or NBS to the azobenzenophane **49**.[69,70]



Scheme 14: Protocol of Cho and coworkers for the palladium catalyzed synthesis of azobenzenophanes.

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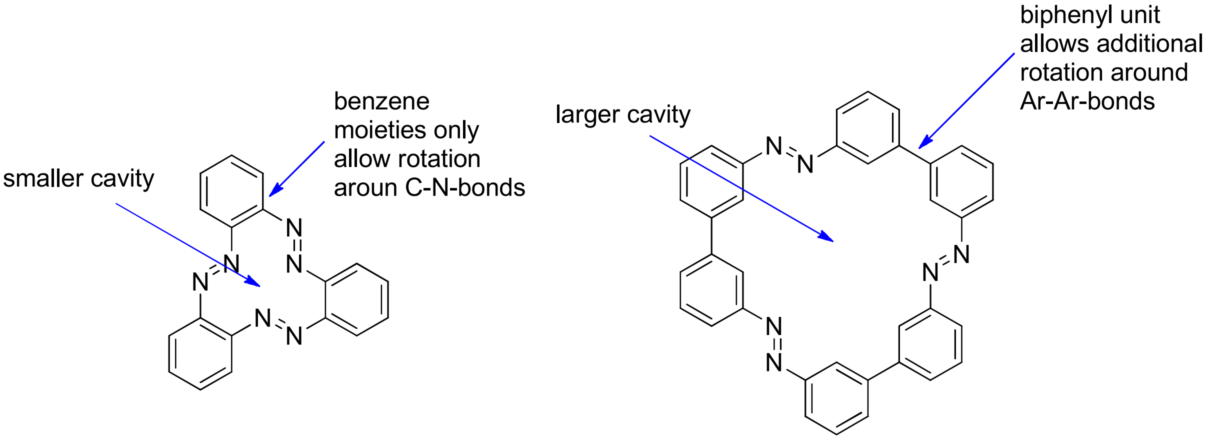
2. Aims of this Thesis

Macrocyclic azobenzenes show a drastically increased lifetime of the *Z*-isomer. Also, these macrocycles exhibit a large potential for applications in the field of material science. Yet, the problem of thermal stability has not been fully solved so far, since in the examples for which the *Z*-isomer is thermally stable, the *E*-isomer becomes unstable. Furthermore, minimal research has been done on macrocyclic oligoazobenzenes as multistate switches. The azobenzene functionalized crown ether by Shinkai and coworkers is the only working example of a molecular gripper based on azobenzene photochromism.

It was rationalized that a fully conjugated macrocycle with three azobenzene moieties should be most stable as its all-*E*-isomer with an almost flat structure and as the all-*Z*-isomer with a bowl shaped structure. The mixed isomers, however, should contain a larger ring strain. Two different systems were envisioned. Cyclotrisazobenzene (CTA), which was already prepared by Dreiding and coworkers for which no research on its photochromism was reported so far and cyclotrisazobiphenyl (CTB), which was not prepared so far and would differ from the smaller CTA by its larger cavity and lower rigidity.



Scheme 15: Cyclotrisazobenzene and cyclotrisazobiphenyl as the two azobenzenophanes in focus

Hence, the following points were set as goals to be achieved in the context of this work.

1. The development of an efficient and high yielding synthesis to azobenzene macrocycles which would allow the convenient introduction of various functionalities.

2. The conduction of a detailed isomerisation study for the macrocycles prepared and the investigation of multistate switches.

3. The study of the molecular interactions of the macrocycles with other molecules or with each other and their use in artificial light responsive supramolecular assemblies.

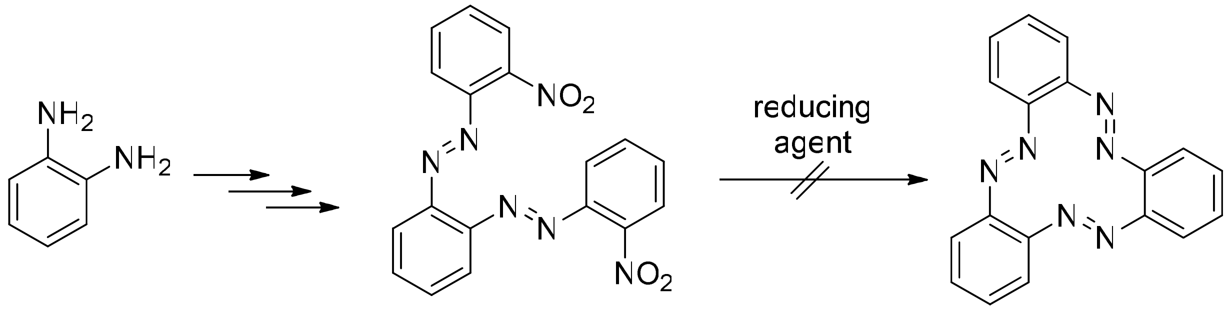
4. The application of such interactions in a molecular grippers which would selectively bind or release a guest molecule or ion after a photochemical stimulus is applied.

3. Results and Discussion

3.1 Cyclotrisazobenzenes

3.1.1 Synthesis of Cyclotrisazobenzenes

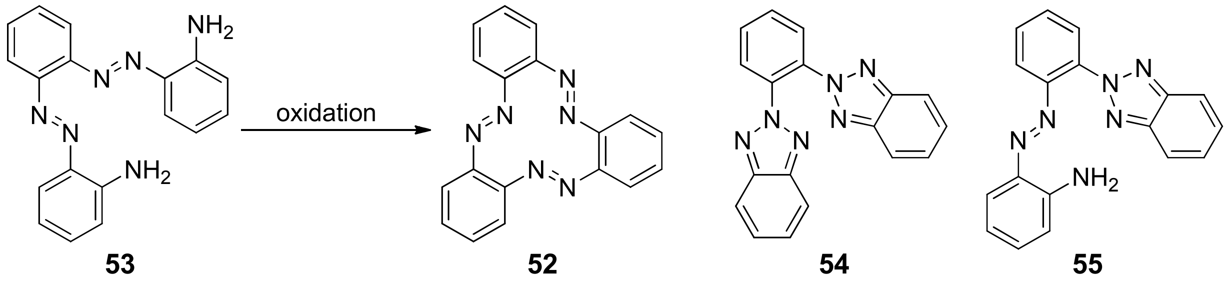
The first part of this work lines up with previous research which was done in my master thesis with the goal of preparing azobenzenophanes. An interesting, fully conjugated azobenzenophane which is the simplest modification containing three azobenzene moieties is the hexaazaanulene **52** or cyclotrisazobenzene (CTB) as it was named by Dreiding and coworkers. However, their previous synthesis of the compound yielded only 2.6 %.[1,2] Therefore, it was attempted to design an optimized synthesis of the macrocycle to be able to prepare CTB in higher yields for photoisomerization experiments as well as for binding studies with guest molecules. First, a strategy was investigated aiming at a reductive macrocyclization of dinitrobisazobenzene **51**. Even though the precursor could be prepared in good yields, the reductive cyclization was not successful with none of the tested reducing agents.



50 **51** **52**

Scheme 16: Previous unsuccessful strategy for preparation of CTB.

After these attempts it was decided to take a route similar to that of Dreiding and increase the yield of certain steps by further optimization. The first step of the synthesis was an oxidative coupling of *ortho*-phenylenediamine (**50**) with manganese dioxide, which yielded 2,2'-diaminoazobenzene (**53**) in 45 % yield. In a new synthesis this step was exchanged by a protocol which applied potassium dioxide in toluene.[3] Using this procedure, the yield of the step could be improved to 65 %. The next step would be a Mills reaction of **56** with one of the substituted nitrosobenzene derivatives **57 a-c**.[4] A solvent screening of the Mills reaction showed that the best results could be obtained by changing the solvent mixture from chloroform:AcOH (11:1) to four equivalents of AcOH in toluene at 60 °C. With these conditions yields of up to 68 % could be obtained. Deprotection of the mono acetylated diaminobisazobenzene **58** was done with KOH in aqueous methanol, like in the literature procedure, with almost quantitative yields.[2] The final step was an oxidative coupling of 2,2''-diaminobisazobenzene (**56**) with lead tetraacetate in DCM. In this key step of the reaction, Dreiding and coworkers obtained the desired macrocycle only as a side product in 24 % yield.[1] As their main product they obtained bisbenzotriazole **54** in 47 % yield. A similar result was obtained when the reaction was repeated with the same conditions. This pathway to benzotriazoles is well known in literature and had to be suppressed somehow to improve the yield of the reaction.[5] Different solvents were used in our screening. Surprisingly, when AcOH was used the bisbenzotriazole **54** was observed as the only product of the reaction. This observation was an indication that acidic medium was favouring the unwanted side reaction leading to benzotriazole formation. For this reason different bases were added to the reaction mixture to neutralize acetic acid, which is formed during the reaction. Indeed, the addition of base changed the result of the reaction. The highest ratio of macrocycle was obtained by the addition of NEt_3. With a base additive, formation of bisbenzotriazole could be suppressed completely with a CTB yield of up to 51 %. Monobenzotriazole **55** was still obtained as a side product but in lower yield.

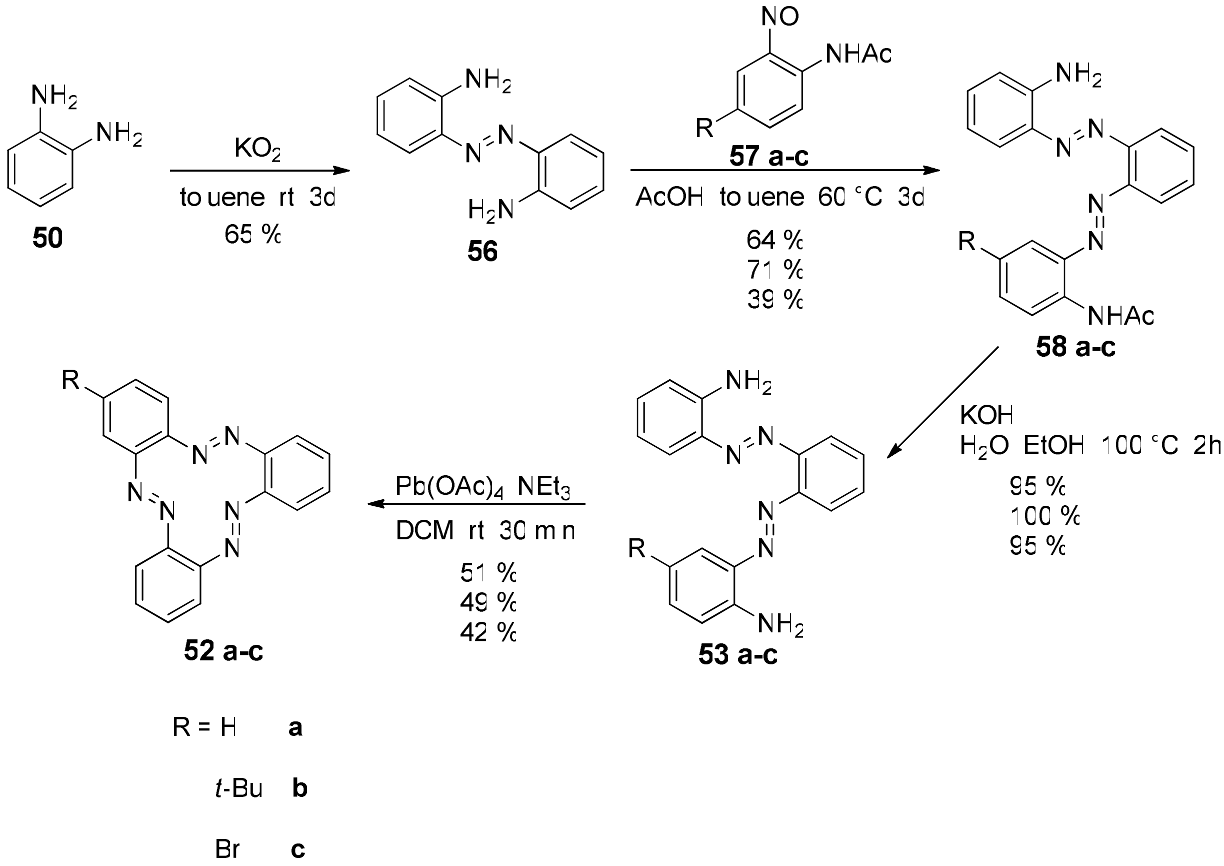


Scheme 17: Oxidation of 2,2''-daiminobisazobenzene to different products.

Table 1: Optimization of oxidative cyclization.

Oxidant/additive	Solvent	Ratio
$Pb(OAc)_4$	CH_2Cl_2	1:2:0
$Pb(OAc)_4$	Toluene	1:4:0
$Pb(OAc)_4$	AcOH	0:1:0
$Pb(OAc)_4$ / K_2CO_3	CH_2Cl_2	1 : 2.5 : 0
$Pb(OAc)_4$ / NEt_3	CH_2Cl_2	3.9 : 0 : 1
$Pb(OAc)_4$ / DBU	CH_2Cl_2	1 : 1.3 : 1.6
$PhI(OAc)_2$ / NEt_3	CH_2Cl_2	0:1:0

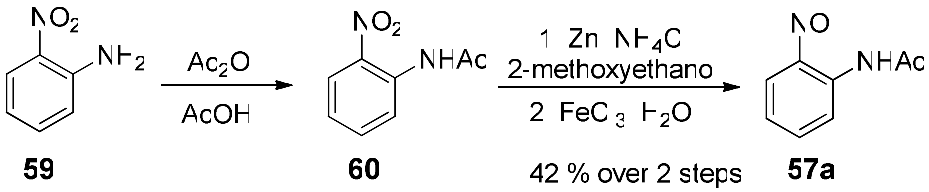
With the different optimizations and change of reagents the overall yield of the synthesis could be increased to 20 %, which was an almost 8-fold increase compared to the original strategy. Two new derivatives with a bromide **52c** and a *tert*-butyl group **52b** were also prepared with comparative results.



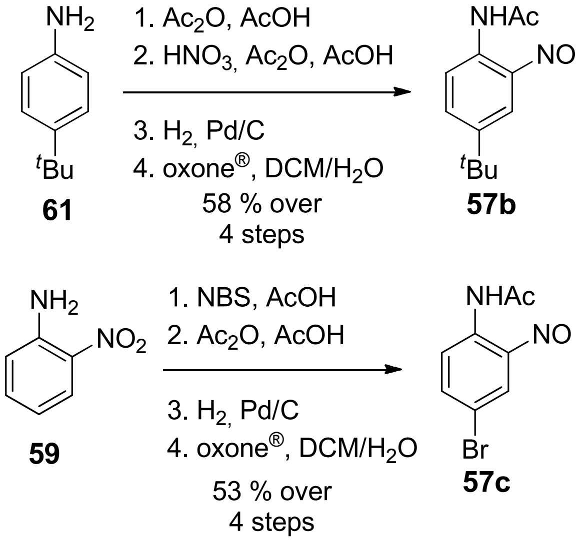
Scheme 18: Preparation of three different CTB derivatives.

The preparation of 2-acetaminonitrosobenzene (**57a**) was achieved, following known literature procedures.[6,7] 5-*tert*-butyl-2-acetaminonitrosobenzene (**57b**) was prepared out of 4-

tert-butylaniline (**61**) in four steps. First the aniline was protected by acetylation. Nitration with a nitric acid / acetic anhydride / acetic acid mixture[8] followed by hydrogenation of the nitro group installed an amine. Finally, the amine was oxidized to the nitroso compound with oxone®.[9] 5-bromo-2-acetaminonitrosobenzene (**57c**) was prepared out of 2-nitroaniline (**59**) by brominaion with NBS,[10] followed by acetylation of the amine, reduction of the nitro group and again oxidation with oxone®.



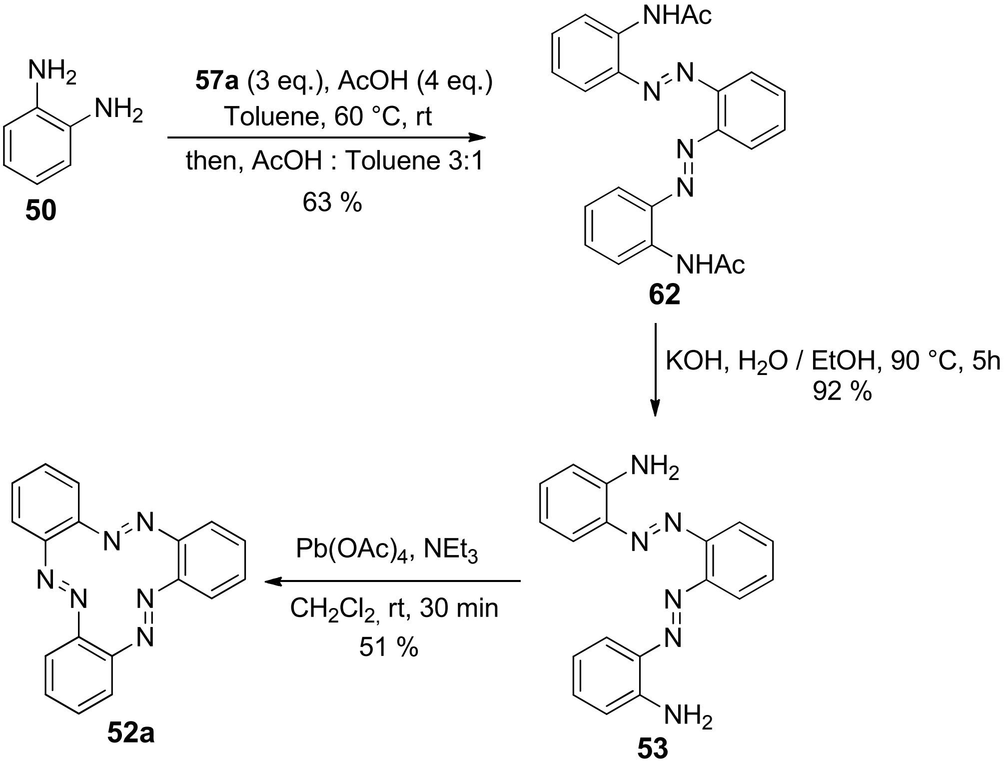
Scheme 19: Preparation of 2-acetaminonitrosobenzene.



Scheme 20: Preparation of the substituted nitroso derivatives

An interesting observation was made when *ortho*-phenylenediamine (**50**) was subjected to Mills conditions. The substrate was not reacting in pure acetic acid, but only in diluted medium. However, using the conditions with 4 eq. AcOH in toluene only afforded the monocoupled product, even after prolonged stirring at 60 °C for several days. In the literature, it was found that 2-aminoazobenzene reacted with nitrosobenzene to *ortho*-bisazobenzene, using classical Mills conditions in concentrated acetic acid.[11] For this reason the Mills reaction conditions of *ortho*-phenylenediamine with 2-acetaminonitrosobenzene were changed after one day by addition of acetic acid to get a solvent mixture of 3:1 AcOH/toluene.

The second coupling proceeded under these conditions and diacetaminobisazobenzene **62** could be obtained in 63 % yield. With this three step procedure the yield of the synthesis of unsubstituted CTA could be further improved to 30 %.



Scheme 21: Improved synthesis of CTA in three steps and 30 % by a twofold Mills reaction with changing solvent mixture.

3.1.2 Isomerization studies and solid state structures.

A solid state structure of the unfunctionalized compound had already been published by Dreiding and coworkers.[12] By slow evaporation from a TBME solution, needle shaped crystals of the *tert*-butyl derivative **52b** could be obtained which were suitable for X-ray structural analysis. As it can be clearly seen for the unsubstituted macrocycle **52a** two molecules are aligning over each other by replaced π-π-stacking interaction. The two macrocycles thereby adopt a slightly different conformation. In molecule **52b** those interactions are suppressed by the bulky *tert*-butyl group and therefore no sandwich like structure is observed. Surprisingly, the unit cell again can only be described by a set of two molecules with different geometry.

Isomerization studies of the macrocycle were first done with a xenon lamp at different wavelengths between 280 and 350 nm. However, no change in the absorption spectrum was observed. Consequently, it was followed that the compound does not switch or that the thermal *Z* → *E* isomerization is so fast that the *Z*-isomer cannot be detected using this method.

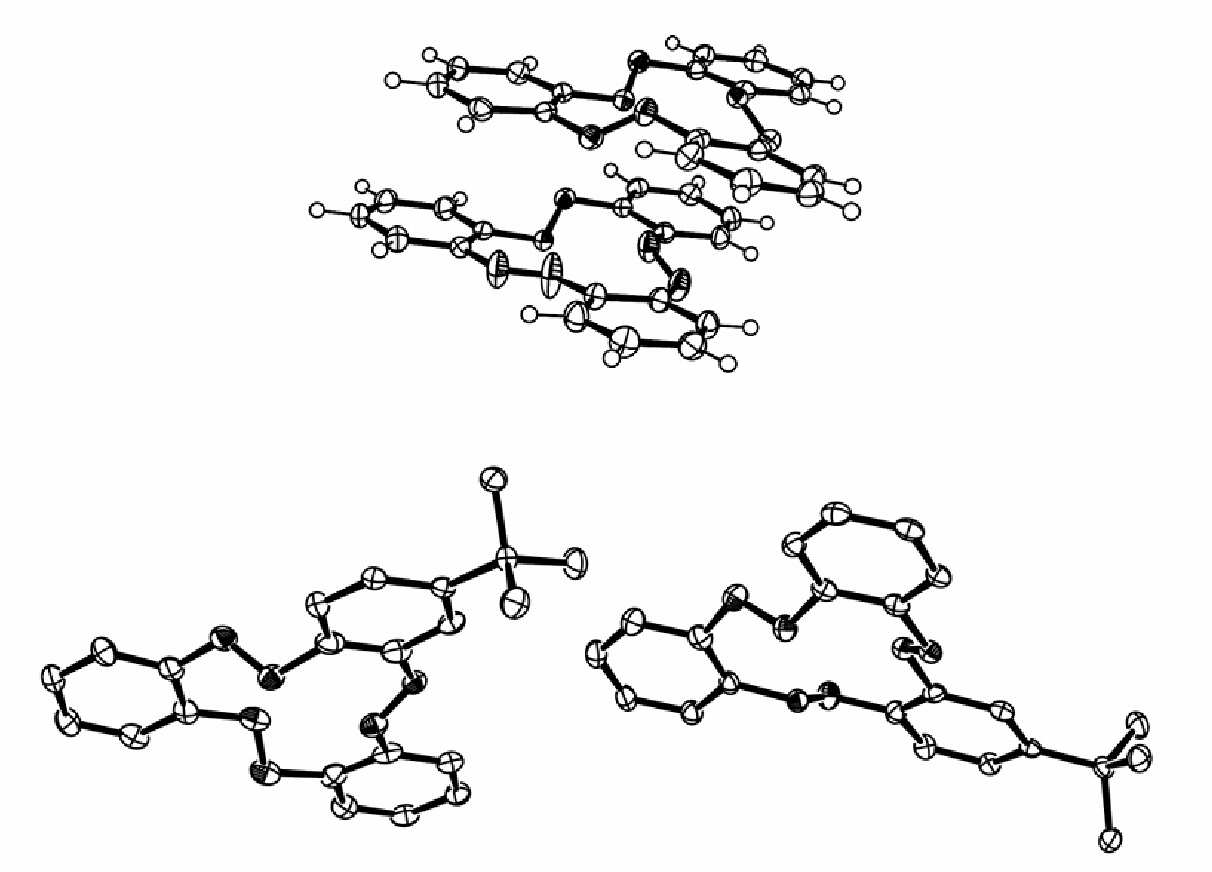


Figure 4: Solid state structures of CTB **52a** and *tert*-Bu-CTB **52b**.

To be sure that a fast back isomerization was not occurring, laser flash photolysis was done. However, the molecule still showed no photochromism. There are two possible reasons for this observation. Either the macrocyclic strain is so high in the *Z*-isomers that they cannot be accessed, or the *ortho* substitution pattern of the three azobonds influences the electronic structure of the molecule in a way that an isomerization is prohibited. It is already known that *para* substituted azobenzenes isomerize to a far lower degree than *meta* substituted.[13]

3.1.3 Binding studies with alkali metals and triphenylcarbenium cations.

The different synthesized CTA molecules all posses a cavity in the middle to where the unpaired electrons of three nitrogen atoms point. For the Schiff' base equivalent of CTA it is known that it forms complexes with different metal cations.[14] Albeit azobenzenes are weaker coordination sites because of the nitrogen atoms being less polarized, binding experiments with different alkali metals were conducted. Tamaoki and coworkers previously reported that alkali metal complexes of [1.1](3,3')-azobenzenophanes were observed by ESI-MS.[15] ESI-MS was therefore also chosen as an analytical method to investigate the possible occurrence of such binding interactions. Indeed, a certain degree of binding was observed for all cations which were used.

Table 2: Complexation of different alkali metal ions with CTB **52a**.

Entry	m/z	Complex	Relativ ESI-MS intensity
1	313	[**52a** + H^+]	1
2	319	[**52a** + Li^+]	3.2
3	335	[**52a** + Na^+]	9.6
4	351	[**52a** + K^+]	9.2
5	397	[**52a** + Rb^+]	16.1
6	631	[2 * **52a** + Li^+]	30.4
7	647	[2 * **52a** + Na^+]	15.7
8	663	[2 * **52a** + K^+]	3.2
9	708	[2 * **52a** + Rb^+]	3.2

After the alkali metal complexes could not be seen in solution, different small transition metal complexes (Cu^{2+}, Zn^{2+}) were also investigated without observing any complexation. Since the macrocycle did not seem to readily undergo interactions with metal cations in solution an organic alternative was tried. It was thought that the triphenylcarbenium ion would be a very suitable complexing agent. It does not only incorporate a positive charge, which would have an affinity to the nitrogen lone pairs, but also has three electron poor phenyl rings which could be able to undergo hydrophobic, or π-π-stacking interactions with the macrocycle. In a first experiment an excess of triphenylcarbenium tetrafluoroborate (TT) was added to a solution of CTA in acetonitrile and the colour of the solution immediately turned from brown to dark black, thus indicating some kind of reaction taking place. Consequently a more detailed titration study was conducted by increasing the amount of TT in solutions of constant concentration of CTA. The results which were observed showed a steadily increasing low field shift of the two CTA signals with increasing TT concentrations. This is in good accordance to the expectation, since a lowering of electron density should be observed when the phenyl rings of CTA would interact with the cationic triphenylcarbenium ion. Two plateaus were reached at ratios of about 1:1 TT:CTA and 2:1 TT:CTA. Therefore it was anticipated that there were two separate species appearing, namely a monomeric species and a "sandwich" complex of two TT molecules with one CTA in the middle. This would also be in good agreement with the results, obtained in the ESI-MS studies, where such dimeric complexes were also observed. A solution of CTA was also treated with ammonium tetrafluoroborate to see if the effect was caused by the anion. However no effect could be observed in this control experiment.

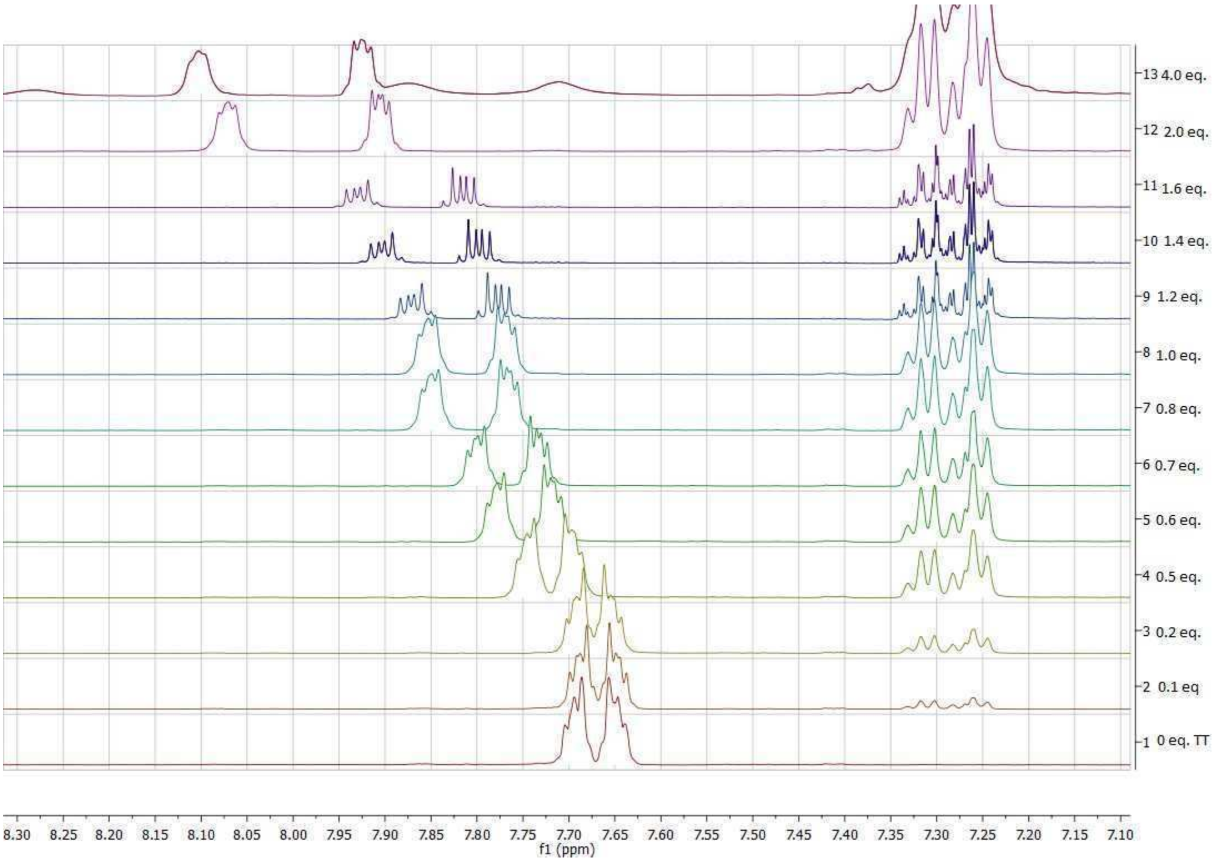
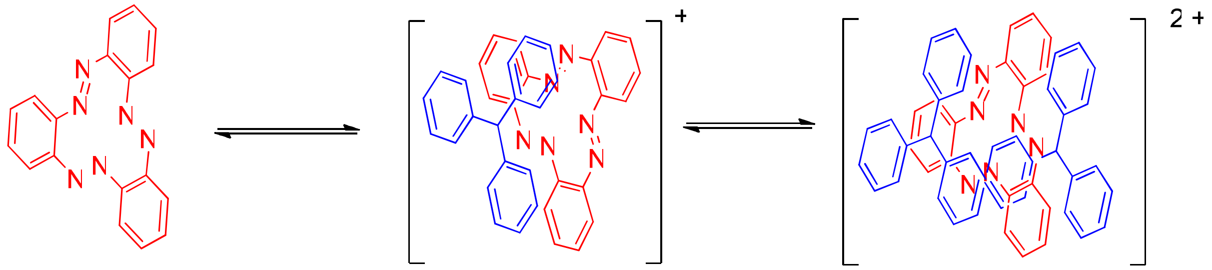


Figure 5: Titration of macrocycle **52a** with triphenylcarbenium tetrafluoroborate. Solutions in CD_3CN at constant concentration of CTA ($c = 1.5 * 10^{-2}$ M) with 0 eq. TT - 4.0 eq. TT.

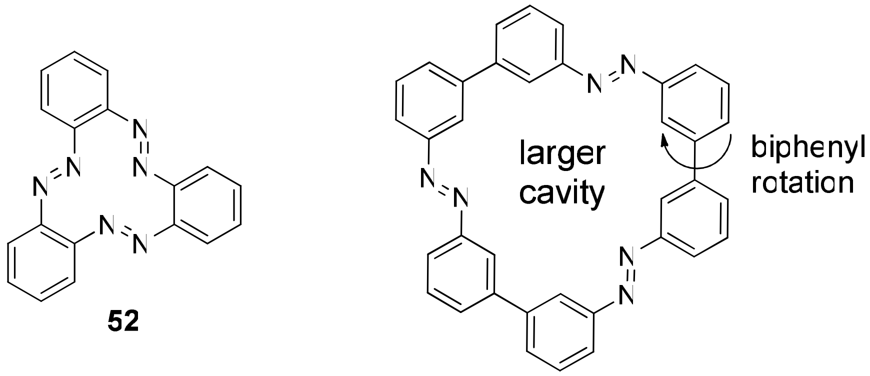
Different methods like simple evaporation, liquid diffusion and vapour diffusion have been tried to grow crystals, suitable for X-Ray analysis of the complexes. However, unfortunately no suitable crystals could be obtained to confirm the assumption.



Scheme 22: Estimated equilibrium of different complex species.

3.2 Cyclotrisazobiphenyls

Regarding the fact that CTA did not show any sign of photochromism, the molecule was lacking the main requirement for the investigation of switching properties. Therefore, any possible application of the system would not exhibit reversibility and certain effects could not be turned on and off photochemically. For this reason, the decision for a strategy change was made. Since it was anticipated that the large macrocyclic strain could be a possible reason for the lacking isomerisation, one idea was to prepare a larger azobenzenophane. However, it should still be fully conjugated. The system of choice was cyclotrisazobiphenyl **63** (CTB). It would resemble the smaller CTA **52a** in its shape, since it still has three azobenzene moieties. Yet, the use of biphenyl units instead of benzene rings would on the one hand enlarge the macrocycle and on the other hand lower the rigidity by the possibility of rotation around biphenyl units.

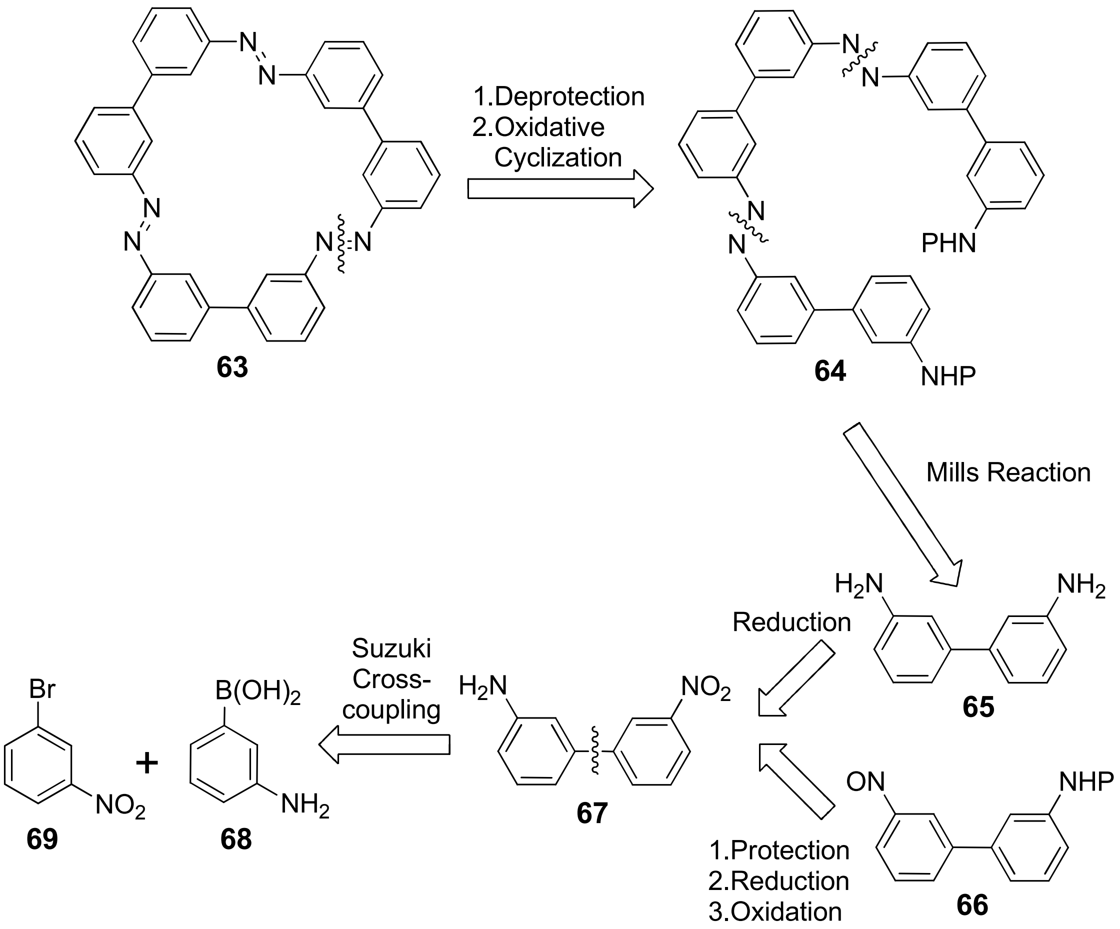


Scheme 23: comparison of cyclotrisazobenzene against cyclotrisazobiphenyl.

3.2.1 Unsubstituted Cyclotrisazobiphenyl

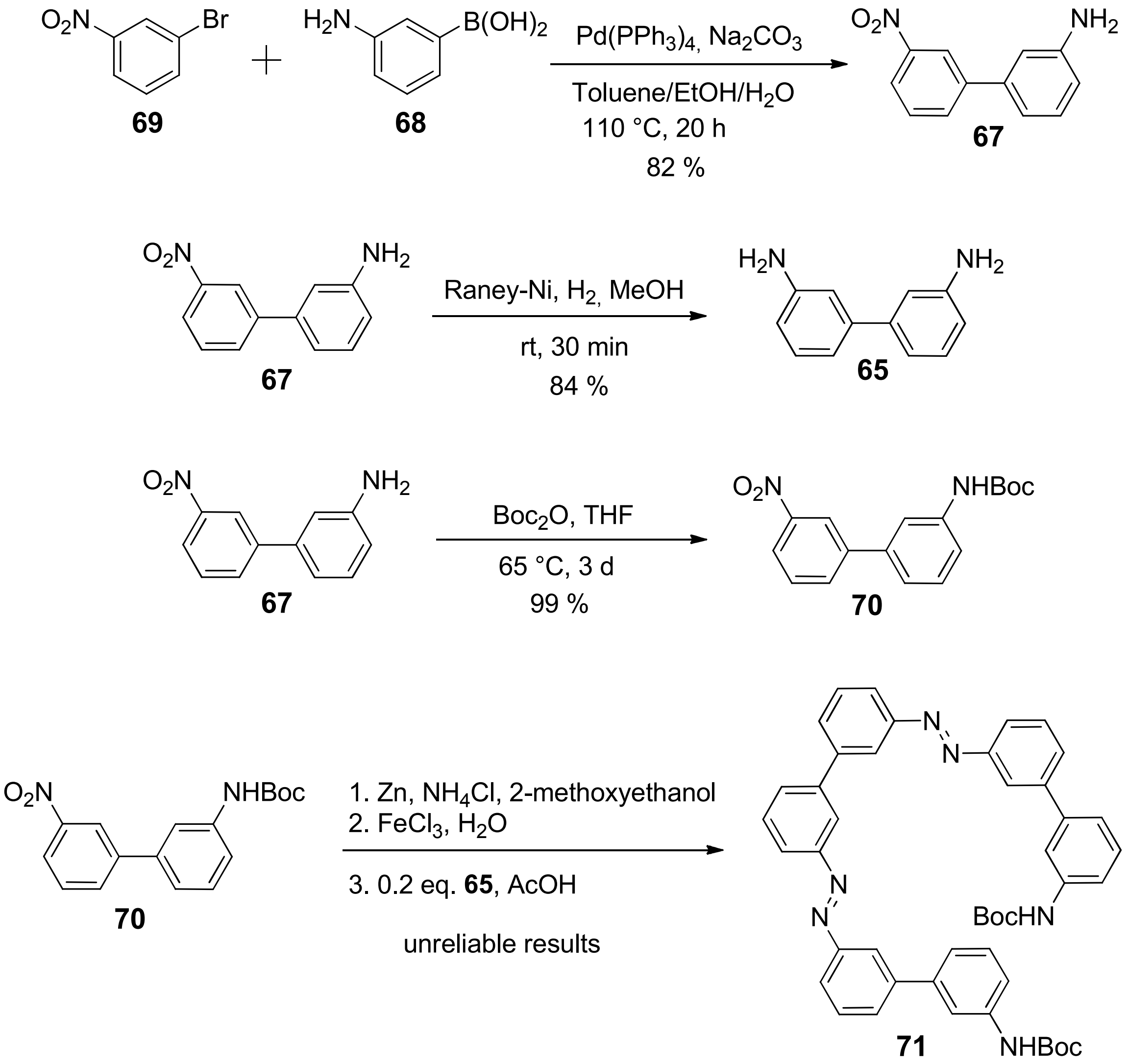
3.2.1.1 Rethrosynthetic analysis and synthesis

In our first rethrosynthetic approach towards the new macrocycle **63** the target molecule was about to be cyclised oxidatively from diamine precursor **64**, since a reductive method was not very promising in previous results for the synthesis of CTA. The next cut would be made at the two residual azobonds to gain two different functionalized biphenyls. One would be 3,3'-diaminobiphenyl (**65**), the second would be a 3-amino-3'-nitrosobiphenyl **66**, where the amino group should be protected. Both biphenyls could be prepared by 3-nitro-3'-aminobiphenyl (**67**) which is accessible by Suzuki-Miyaura crosscoupling of 3-aminophenylboronic acid (**68**) and 3-bromonitrobenzene (**69**). The synthesis of the molecule should be accomplishable in seven to eight steps, and for some of the chemistry it involves, experience had already been gained in the synthesis of CTA.



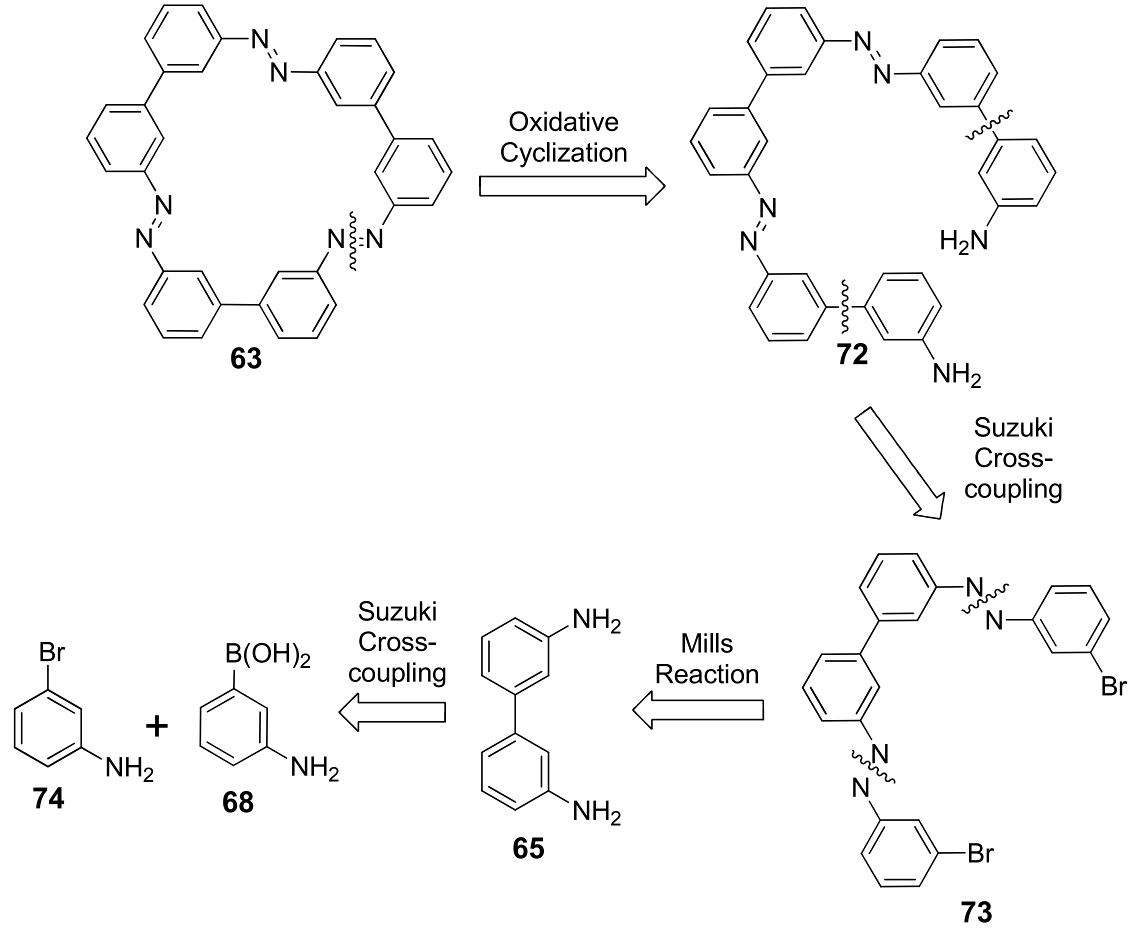
Scheme 24: First rethrosynthetic path to a CTB macrocycle **63**.

The first step in the synthesis was a straightforward Suzuki reaction of 3-bromonitrobenzene (**69**) and 3-aminophenylboronic acid (**68**), which worked in good yields (82 %) using $Pd(PPh_3)_4$ as a catalyst in a solvent mixture of toluene/ethanol and aqueous Na_2CO_3.[16] The obtained product 3-amino-3'nitrobiphenyl (**67**) was then used to prepare the next two intermediates in the total synthesis. Diamine **65** was prepared by hydrogenation with Raney-Ni in 84 % yield. To prepare nitroso compound **66** the amino group had to be protected. First the Boc-group was chosen for protection, since it could be installed in almost quantitative yield. For the transformation of the nitro group into the nitroso group, a protocol that was already used for the preparation of 2-acetaminonitrosobenzene was applied. Therefore, the Boc-protected derivative **70** was first reduced with zinc powder to the hydroxylamine which would then be reoxidized with ferric chloride to the corresponding nitroso benzene. Unfortunately, the nitroso product seemed to be unstable and decomposed during column chromatography or upon solvent removal. For this reason the following Mills coupling was done in the same step without isolation of the nitroso compound **66**. This method was not reproducible and varied in its results, probably because it was very prone to small changes in reaction conditions like reaction time and temperature.



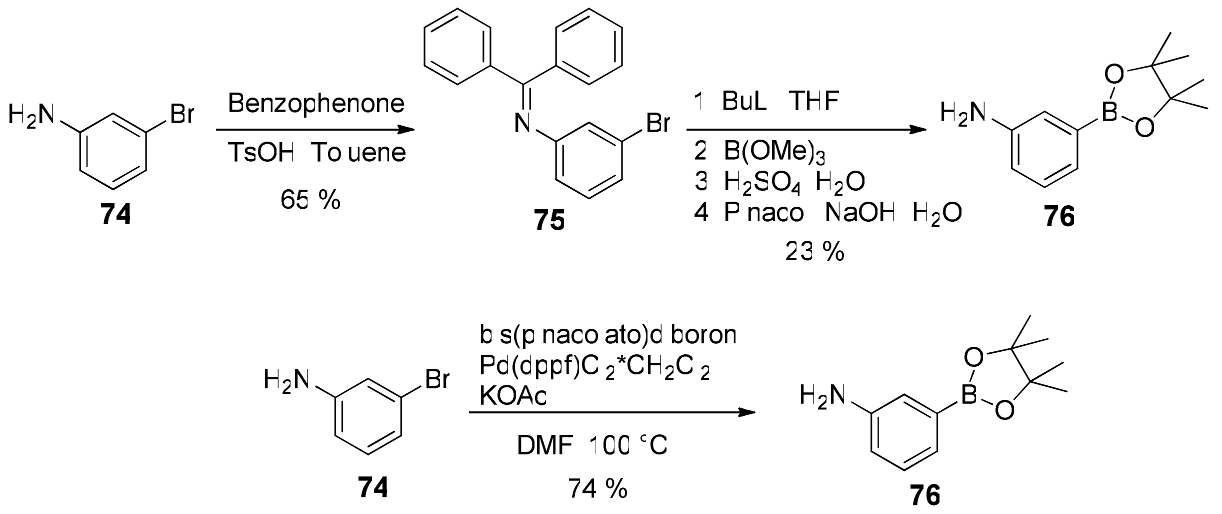
Scheme 25: Investigations done towards the synthesis of CTB applying the first synthetic strategy.

A second rethrosynthetic approach was developed. In the new strategy the first cut was again done on one of the azobonds. This bond would be formed by the oxidative coupling with Pb(OAc)$_4$. In the next step, two slices would be done at the biphenyl bonds at the end of the chain. A Suzuki-Miyaura cross-coupling reaction would be the choice for this transformation. The two azobonds are then cut in the next step which would leave 3,3'-diaminobiphenyl (**65**), which was already prepared for the last synthetic strategy, but could also be synthesized in a single step by Suzuki-Miyaura cross-coupling of 3-aminophenylboronic acid (**68**) and 3-bromoaniline (**74**). One big advantage of this approach would be that it only includes four steps. Furthermore, no protecting group chemistry has to be employed. One drawback would be that only a limited number of substitution patterns would be accessible, since in the second and third step two phenyl groups are introduced at a time.



Scheme 26: Second rethrosynthetic path to a CTB macrocycle **63**.

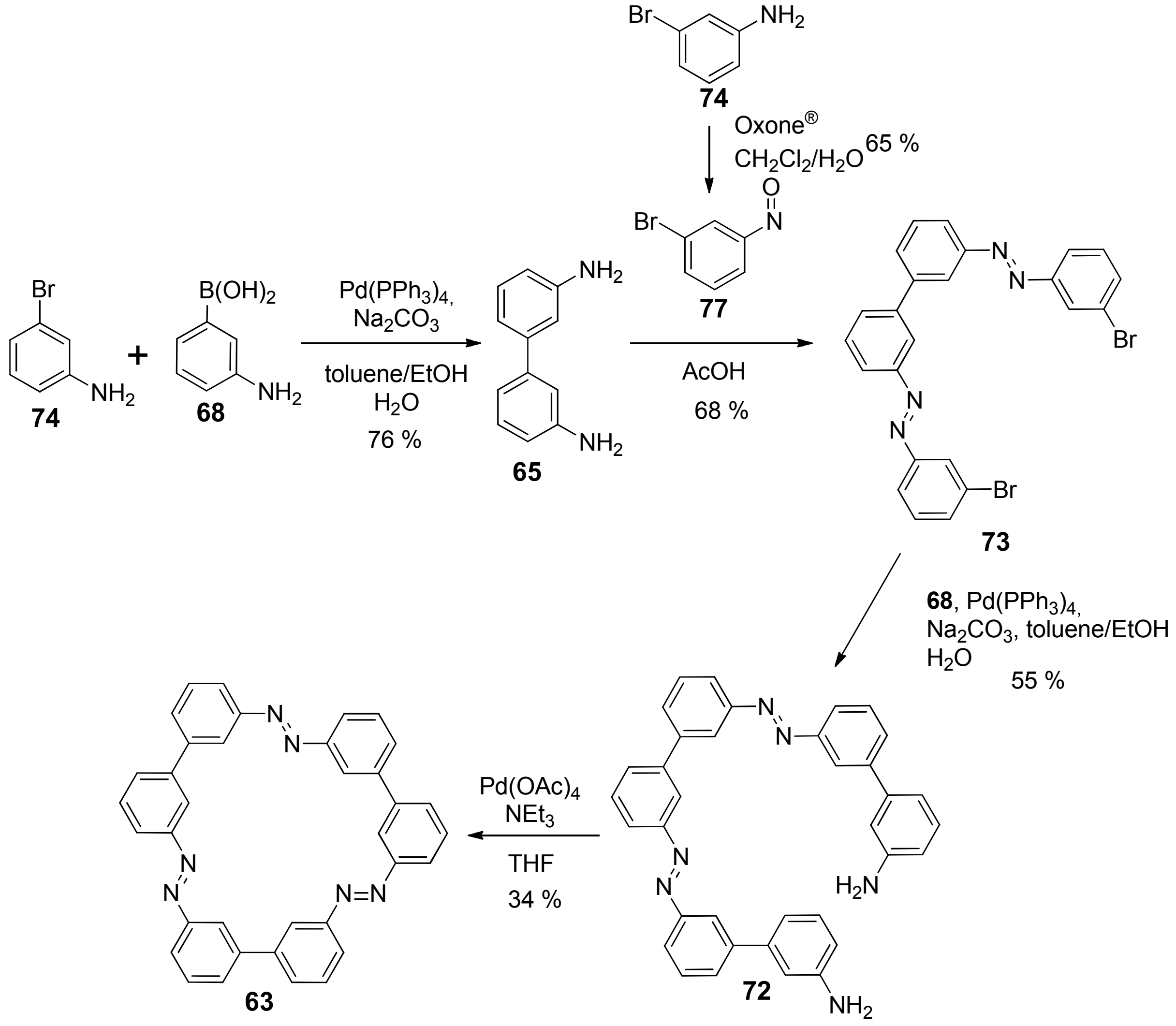
Because of the bad availability, long shipping times and expensive price of 3-aminophenylboronic acid (**74**) an analogue of it was prepared. This was done by protection of 3-bromoaniline as its benzophenoneimine **75**.[17] The protected amine was then converted to the lithiate, which was quenched with trimethoxyborane.[18] After acidic hydrolysis of the imine, the boronic acid was esterified with pinacol to alleviate purification.[19] In later experiments the boronic ester was prepared in one step via Miyaura borylation, probably the most powerful method to prepare boronic esters on a laboratory scale, since it tolerates most functional groups.[20]



Scheme 27: Preparation of pinacol-(3-aminophenyl)-boronate (**76**) in two different ways by transmetalation of the lithiate and palladium catalyzed Miyaura borylation.

The second approach towards the synthesis of CTB started with a Suzuki-Miyaura cross-coupling reaction of 3-bromoaniline (**74**) and 3-aminophenylboronic acid (**68**). The reaction proceeded in 76 % yield, using the same reaction conditions as in the previous approach. The diamine was then subjected to Mills reaction with 3-bromonitrosobenzene (**77**) to yield 68 % of the bisazodibromide **73**. The nitroso compound was prepared by oxone® oxidation of 3-bromoaniline (**74**) in 81 % yield. After the two azobonds had been installed successfully, the attached phenyl rings had to be converted to amino substituted biphenyls. This was done by using the same protocol as in the first reaction step, this time using three equivalents of boronic acid **68** to obtain diamine precursor **72** in 55 % yield. The following step was the intramolecular oxidative azobond formation with $Pb(OAc)_4$ as the key step of the sequence. Since the diamine was only slightly soluble in DCM the solvent was switched to THF. This did not change the reaction behaviour and the macrocycle **63** could be obtained in a moderate yield of 34 %. The overall yield of the synthesis was 10 %. However, major difficulties were encountered during the purification of macrocycle **63**. Since it precipitated out of solution and was also almost insoluble in every tested solvent, it first had to be obtained by simple filtration after complete conversion. Therefore, the product was still contaminated with lead salts which occurred as a side product of the reaction. A higher grade of purity could be obtained by addition of EDTA as a complexing agent for the lead ions and extraction with CS_2, which was the only solvent in which the product could be dissolved. A low concentrated ^{1}H-NMR could only be measured in a 1:1 mixture of $CDCl_3$:CS_2, which confirmed the right structure together with EI-MS which showed the expected mass of 540 g/mol. The low solubility of CTB probably stems from strong π-π-stacking interactions. It is known that CS_2

is a solvent which is capable of dissolving polyaromatic compounds.[21] However, carbon disulfide is an unpleasant solvent to work with, because of its carcinogenic properties and the foul stench.



Scheme 28: Preparation of CTB macrocycle **63** in an overall yield of 10 % in four steps.

3.2.1.2 Isomerization experiments

Since CS_2 is not a suitable solvent for absorption spectrometry it was fortunate that a small amount of the macrocycle could also be dissolved in benzene. This made it possible to do isomerisation experiments. The azobenzenophane showed the characteristic absorptions of the $\pi \rightarrow \pi^*$ transition at 320 nm and the $n \rightarrow \pi^*$ transition at 440 nm. Upon irradiation with a UV-lamp at 365 nm for different time intervals, several spectra were measured. The experiments show a steep decrease of the absorption at 320 nm accompanied by a slight increase of the band at 440 nm until a photostationary state is reached. Heating of the sample affects the return to the initial spectrum. These observations suggest that isomerisation of the different azobonds takes place.

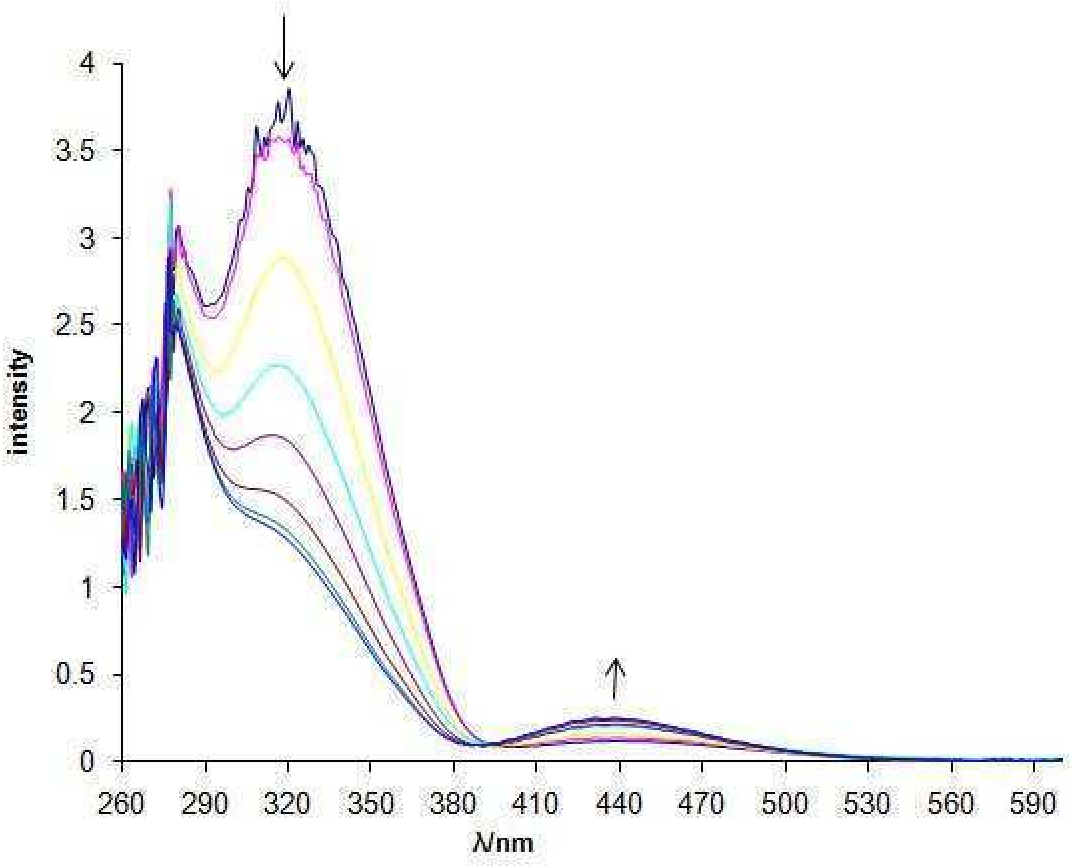
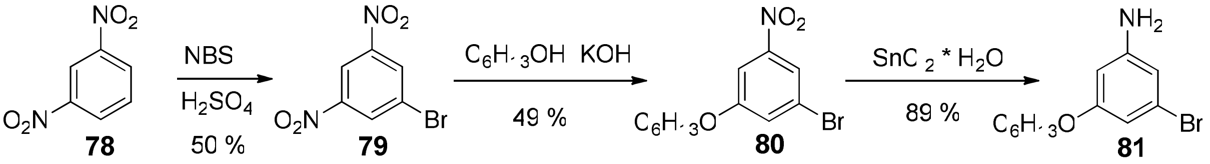


Figure 6: Absorption spectrum of CTB and photoisomerization at 365 nm irradiation (c = $2*10^{-5}$ mol*l^{-1}.

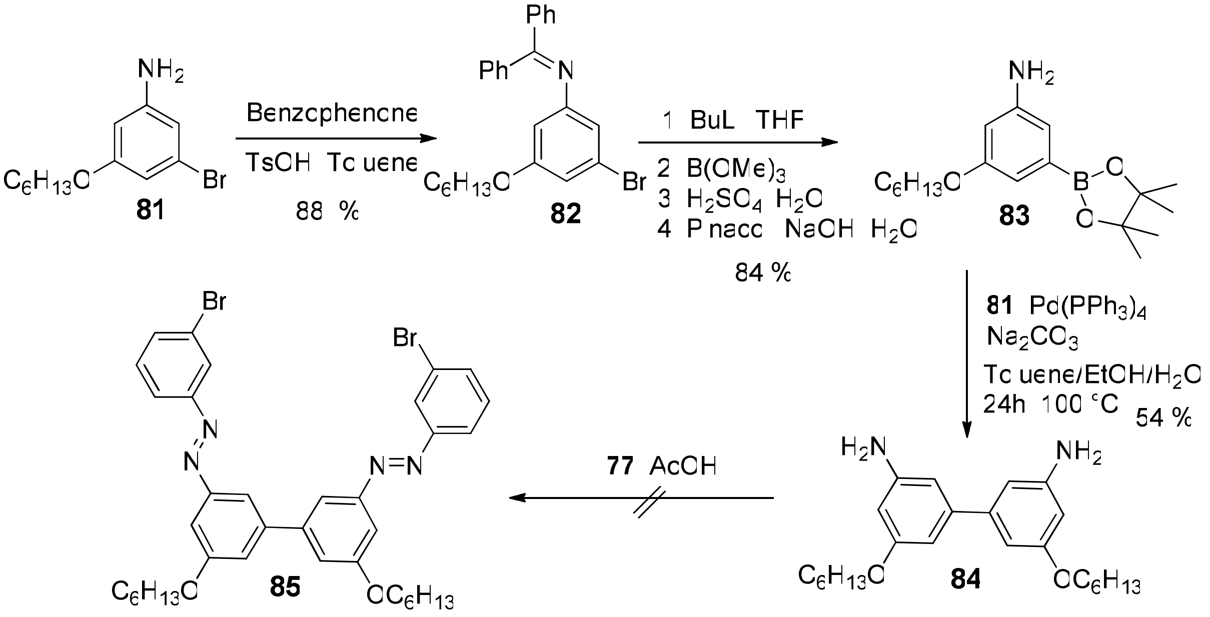
3.2.2 Approach towards hexyloxy substituted CTB

The low solubility of macrocycle **63** brought about new challenges. It made isomerisation experiments via ^{1}H-NMR spectroscopy impossible. However, these are needed for a more sophisticated observation of the photochromism, since observing all possible isomers is not possible by means of UV-VIS spectroscopy. Consequently, a more soluble derivative had to be accessed. The introduction of long alkyl chains is a commonly used strategy to enhance to solubility of molecules in apolar organic solvents. Therefore, a strategy to insert hexyloxy chains into a CTB macrocycle was envisaged. The synthetic path would be the same as for the unsubstituted molecule, only the bromoaniline and boronic ester building blocks had to be functionalized. For this purpose 3-bromo-5-(hexyloxy)aniline (**81**) was prepared in three steps from 1,3-dinitrobenzene (**78**) by bromination,[22] nucleophilic aromatic substitution of a nitro group[23] and reduction of the second nitro group with tin dichloride dihydrate.[24] The reaction sequence produced average to good yields of the fuctionalized 3-bromoaniline **81**.



Scheme 29: Preparation of 3-bromo-5-(hexyloxy)aniline (**81**).

The next step was the conversion of compound **81** to the corresponding boronic ester **83**. This was successfully done in the two step procedure, described before for the unsubstituted 3-bromoaniline (**74**). The yields were significantly higher for this substrate. The Suzuki crosscoupling of boronic ester **83** and bromide **81** was also successful, even though the yields were slightly worse than in the unsubstituted case. The following Mills reaction unfortunately failed in producing bisazocompound **85**. Maybe the mesomeric effect of the alkoxy substituent of biphenyl **84** has in some way a detrimental effect in Mills reactions.

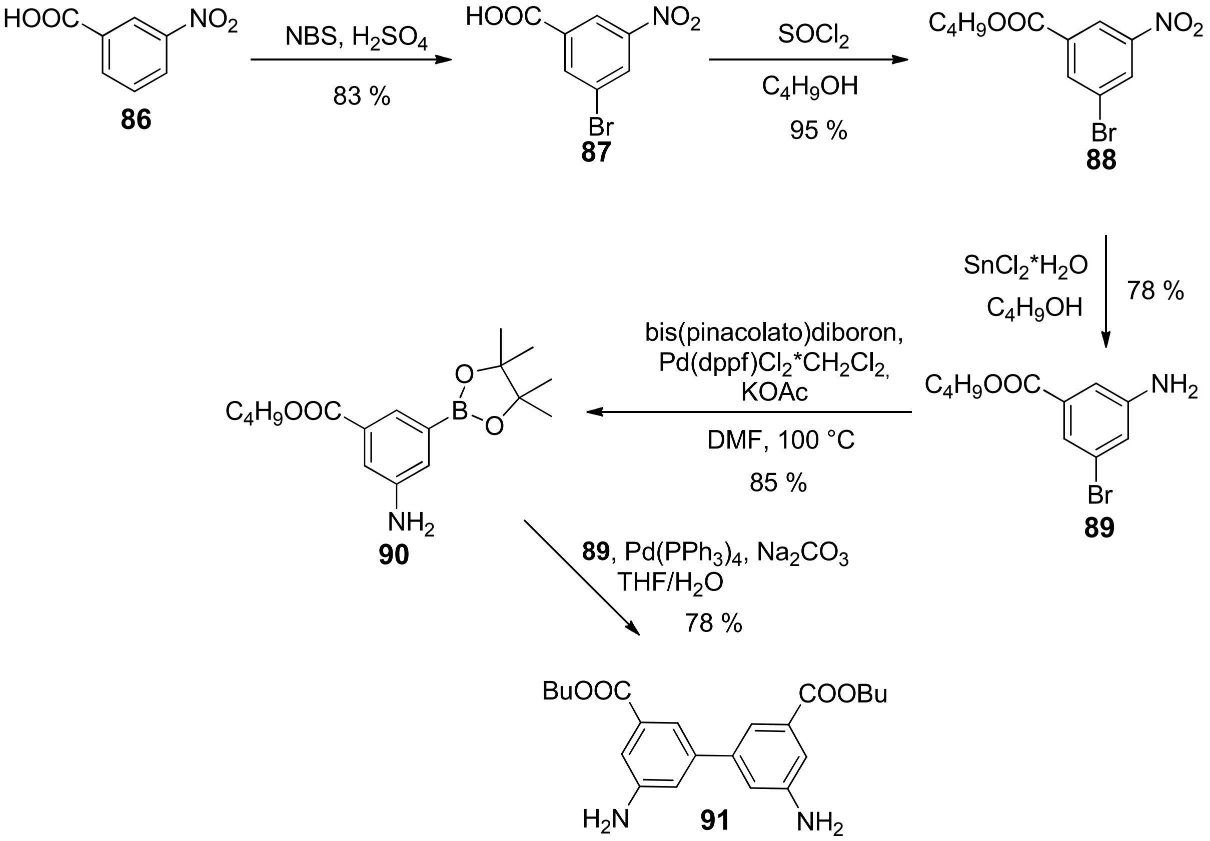


Scheme 30: Unsuccessful road towards hexyloxy substituted CTB due to failed Mills reaction.

3.2.3 Butylester substituted CTB

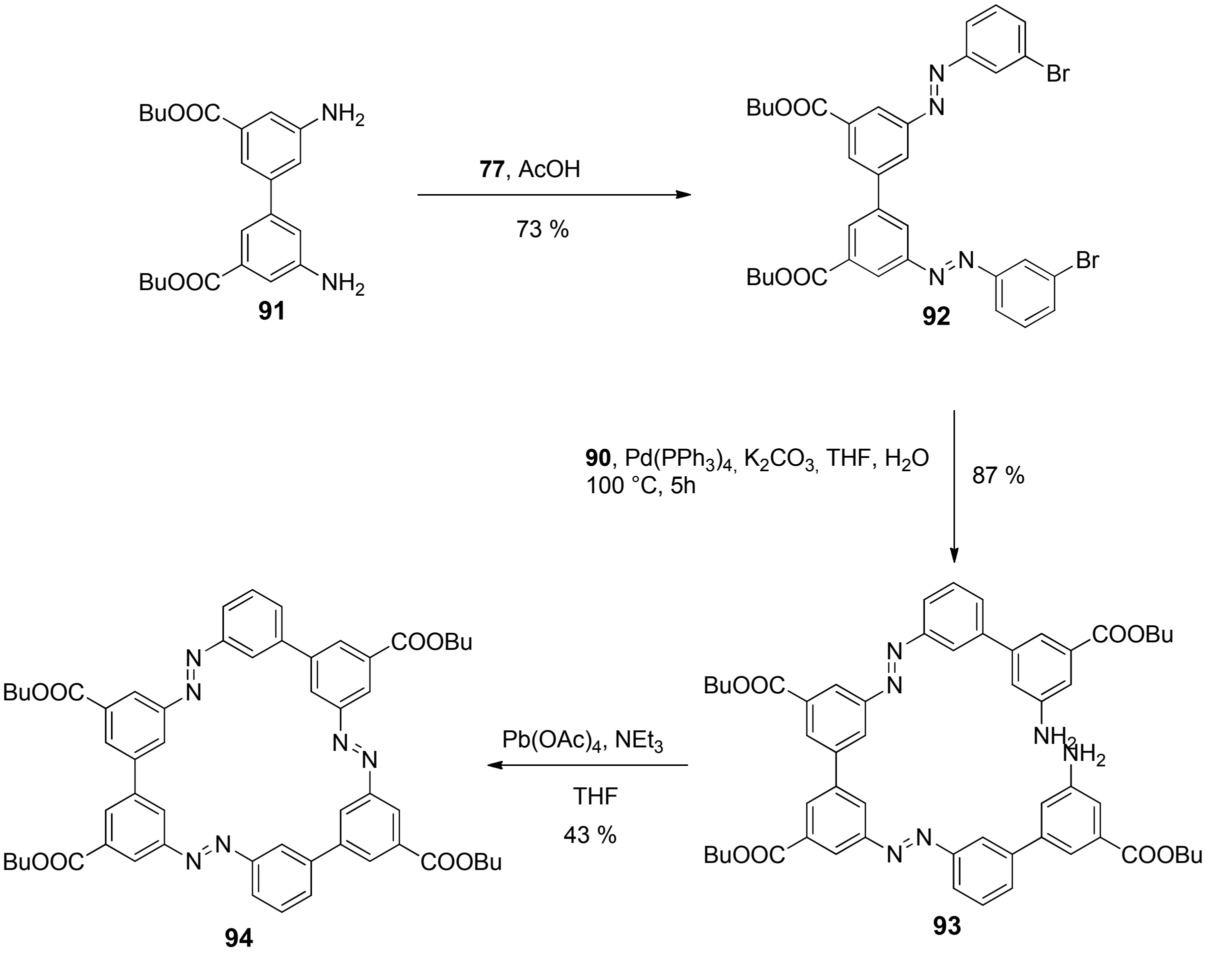
3.2.3.1 Synthesis

Since the alkoxy-group was not a suitable side group, an electron withdrawing ester group should be investigated next. The synthesis of butylester substituted 3-bromoaniline **89** was straightforward and worked in constantly good yields. Bromination of 3-nitrobenzoic acid was done, using the same protocol as for 1,3-dinitrobenzene and produced **87** in 83 % yield.[22] Esterification worked in excellent yields by treating **87** with thionyl chloride in refluxing butanol.[25] Then, the reduction of the nitro group was done, again with tin dichloride dihydrate.[24] The borylation of **89** was done by a Miyaura borylation in this case, since the other method turned out to be insufficient. The ester group is probably not stable to the harsh lithiation conditions with *n*-BuLi. After Suzuki-Miyaura crosscoupling of boronic ester **90** with bromide **89**, biphenyl **91** was obtained.



Scheme 31: Preparation of the building blocks for the synthesis of butylester substituted CTB and successful preparation of biphenyl **91**.

The next steps of the synthesis again included Mills coupling, Suzuki coupling and oxidative cyclization. Compared to the hexyloxy substituted biphenyl **84**, this time the Mills reaction with 3-bromonitrosobenzene (**77**) worked with a good yield of 73 %. It was initially envisioned to prepare a symmetrically substituted macrocycle and use butyl 3-nitroso-5-bromobenzoate as the nitroso derivative. Unfortunately we were not able to prepare this compound. The Suzuki conditions were altered this time, by using a solvent mixture of THF/H_2O and potassium carbonate as a base.[26] The previously used conditions did not lead to complete conversion in this case. The oxidative cyclization with lead tetraacetate worked well and the product was this time soluble in chloroform, DCM and toluene, which allowed purification by column chromatography. The yield was also better than for the unsubstituted derivative.



Scheme 32: Final three steps in the preparation of butylester substituted CTB **94**.

3.2.3.2 Isomerization studies and π-π-stacking interactions.

The fact that the new macrocycle **94** showed a good solubility in chloroform enabled a detailed investigation of the isomerization. To induce $E \rightarrow Z$ isomerization a ^{1}H-NMR sample was irradiated at 365 nm UV-light. The photoreaction was followed by measuring a spectrum after different time intervals. After the PSS was reached the sample was irradiated with visible light from a halogen floodlight to induce the reverse reaction. Upon irradiation at 365 nm the macrocycle isomerizes and a large number of new signals appear in the spectrum. After prolonged irradiation a set of major peaks can be distinguished. However, a certain assignment is not possible with these experiments, because of the complicated pattern. This result was not a surprise, since there are six different photoisomers which can be formed. Two of these isomers, the (*E,E,E*)-isomer and the (*Z,Z,Z*)-isomer, should have C_2 symmetry and show 10 aromatic signals. However, the other four mixed isomers are not symmetric and therefore should show up to 20 signals. Presuming that all possible isomers are observed this sums up to theoretically up to 100 signals, with some of them split into doublets or triplets. Besides the isomerization behaviour another interesting observation was made during the experiments. The peaks of the initial spectrum were slightly shifting to lower field upon irradiation at 365 nm and again shifted to higher field upon irradiation with visible light. Besides a photochemical explanation, this phenomenon could also be caused by a decrease in concentration, when the (*E,E,E*)-isomer is transformed to its isomeric species. Therefore, measurements of the macrocycle at different concentrations were done to further investigate this behaviour.

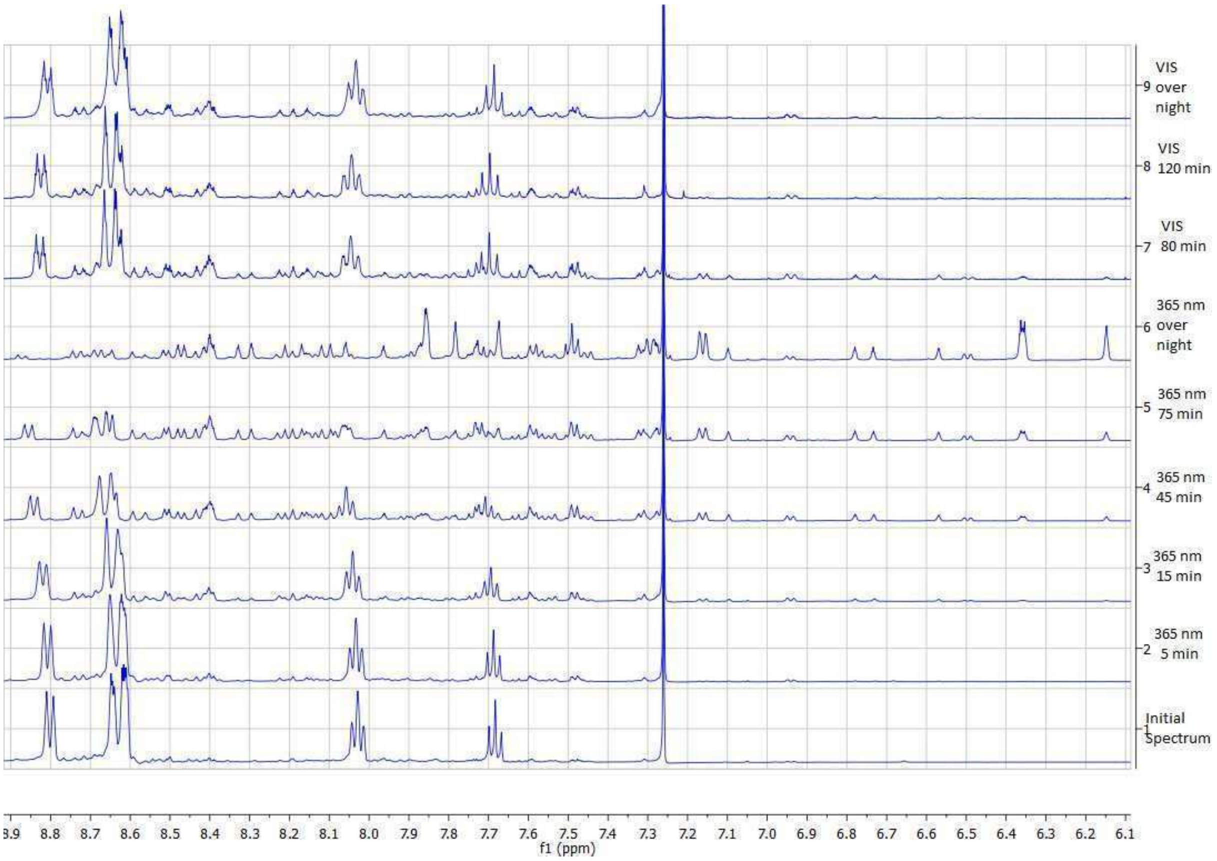


Figure 7: ^{1}H-NMR isomerization study of butylester substituted CTB **94**. First irradiated with 365 nm UV-light, then with visible light from a halogen floodlight (aromatic region).

The concentrations of the macrocycles which were measured changing the concentration from 2 mmol/l to 210 mmol/l. With increasing concentration all aromatic signals experienced a shift to higher field. The degree of this effect varied for the different signals and the strongest change in the δ value was 0.53 ppm for the signal shifting from 8.88 ppm to 8.35 ppm. Also the splitting of the signals changed, as it can be seen for the doublet at 8.88 ppm, which appears as a singulet at 8.35 ppm in the highest concentration. Also the multiplet at 8.72 – 8.62 ppm changes its shape.

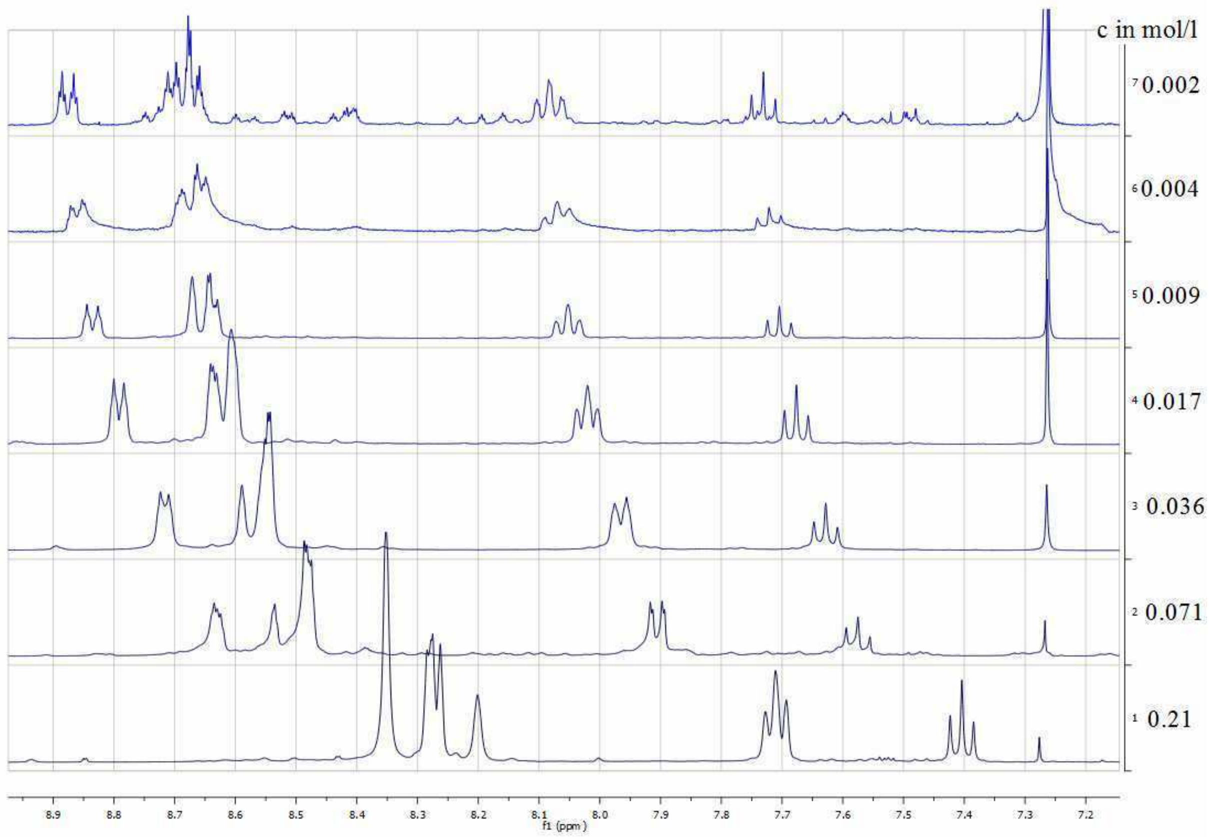


Figure 8: ^{1}H-NMR spectrum of butylester substituted CTB **94** at different concentrations in $CDCl_3$. A strong highfield shift as well as a change in the splitting of signals is observed with increasing concentration.

In literature the same behaviour can be found for macrocyclic phenylacetylenes.[27] The authors ascribe the effect to π-π-stacking interactions, whereas a dynamic equilibrium between a monomeric species and a dimeric or even more complex species is established. The dimeric species would have its signals at lower shifts because it is influenced by the π-orbitals of the second macrocycle. When the concentration is increased, the equilibrium is shifted to the dimeric species, which brings about a shift to higher fields. A clear indication that this behaviour is caused by stacking is that in benzene the chemical shifts do not depend on the concentration anymore. This should also be the case for the butylester substituted CTB macrocycle when measured in aromatic solvent. Yet, when two different concentrations are measured in benzene, the effect is even stronger than in $CDCl_3$. This result was the opposite of the expected observation, since an aromatic solvent should normally weaken the stacking of the macrocycles. It should also be emphasized that after isomerization the aromatic chemical shifts of the different *Z*-isomers were not influenced by alteration of the concentration. This property is therefore a reversible process.

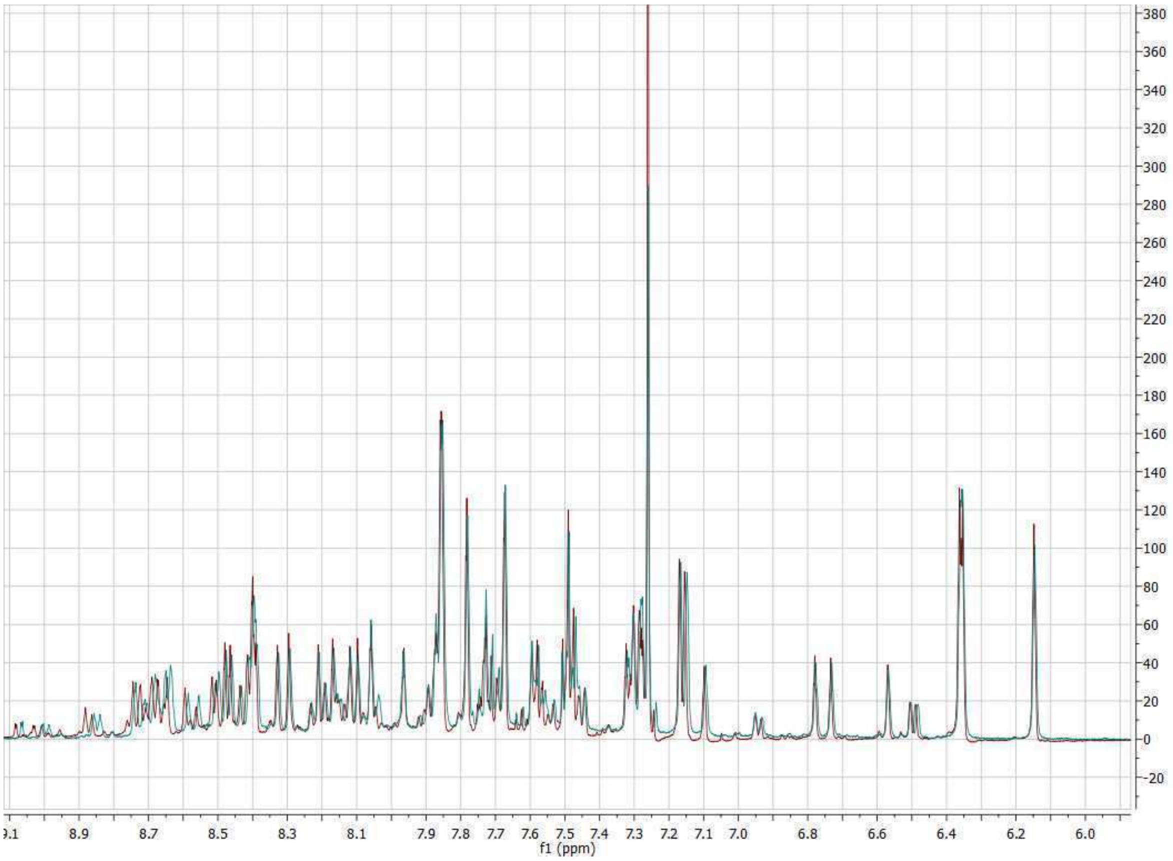


Figure 9: samples of **94** at different concentrations, after switching with 365 nm UV-light, do not show a concentration dependence of the chemical shifts.

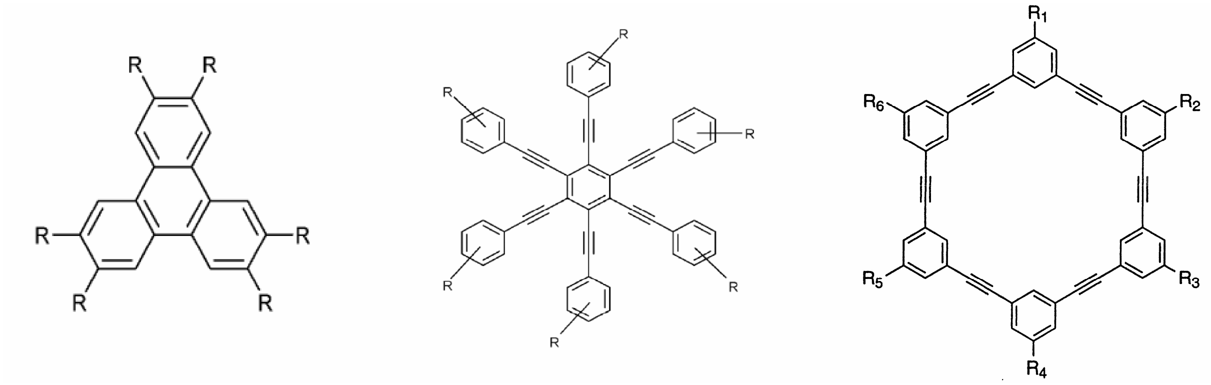
3.2.3.3 Liquid crystalline behaviour.

The vast majority of liquid crystalline compounds are made up of rod like structures.[28,29] Some of the examples are Schiff bases,[30] azobenzenes[31] or linear oligoaromatic compounds.[32] Such liquid crystalline compounds establish a mesophase in which the molecules are, though not in the solid phase, aligned in an ordered way to create anisotropy like in a crystal.

Two convenient ways of identifying such mesophases are polarized light microscopy and differential scanning calorimetry (DSC). Under polarized light birefringence can be observed, which only occurs if the molecules are arranged in an anisotropic fashion. In isotropic melts the molecules do not show any ordered alignment but rather engage in random directions. If a vector is drawn along a certain direction of the molecule, the net vector over all molecules combined is zero. Such phases are not visible under polarized light. However, when a substance is in an anisotropic phase the molecules adopt a specific alignment caused by specific intermolecular attractions in which the net vector has a certain direction. The two most common arrangements in rod shaped liquid crystals are the nematic and the smectic phase which themselves are divided into different subclasses. Anisotropic phases are birefringent and, therefore, can be investigated by polarized light microscopy. With this method it can even be concluded in which pattern the molecules arrange since every kind shows a typical texture under the microscope.

Differential scanning calorimetry is a powerful tool to observe phase transitions. Since the liquid crystalline phase is a mesophase between the solid and the liquid phase, substances with liquid crystalline behaviour show at least two or even more phase transitions between the solid and the liquid phase. In a DSC measurement a crystalline sample of a substance is heated in an isolated system and the difference in the amount of heat which is required to increase the temperature of the sample and a reference is measured. When a phase transition occurs, more energy is required to increase the temperature, since much of the heat is required for the transition. This increase in heat flux can be seen as a peak on a graph where heat flow is plotted against temperature. A cooling cycle is also measure which shows negative peaks when a phase transition occurs, as now heat is released upon phase transition.

The most important kind of liquid crystals for the application of liquid crystral displays show a twisted nematic phase. Besides some rod shaped molecules which adopt such mesophases, disc like molecules sometimes also show this behaviour. Tetraphenylenes as well as multiynes and macrocyclic phenylacetylenes are among the most important classes of disc like molecules showing liquid crystalline properties.[33] The mesophases which are observed are mostly nematic or columnar.



Scheme 33: Examples of discotic liquid crystals: Tetraphenylenes, hexakis(phenylethynyl)benzenes and phenyl acetylene macrocycles (PAMs).

Figure 10: Comparison between the arrangement of disc like molecules in a nematic phase (left) and a columnar phase (right).[34]

If the butylester substituted CTB forms a mesophase, it should be observable, using these methods. A solid sample of the macrocycle was melted on an object holder and allowed to cool down and solidify again. Then, it was slowly heated from room temperature to 220 °C. As it can be seen in Figure 11 the substance appears as dark spots at room temperature under a polarized light microscope. When heating to over 195 °C the dark areas become birefringent and change their colour to orange. The sample was heated up to 230 °C, when heating was stopped. However, no second phase transition to an isotropic melt could be observed. Also in the DSC spectrum, only one phase transition was observed. Probably the melting point of the compound is too high to be measured with the available equipment. In a melting point measurement the substance probably decomposed at 284 °C.

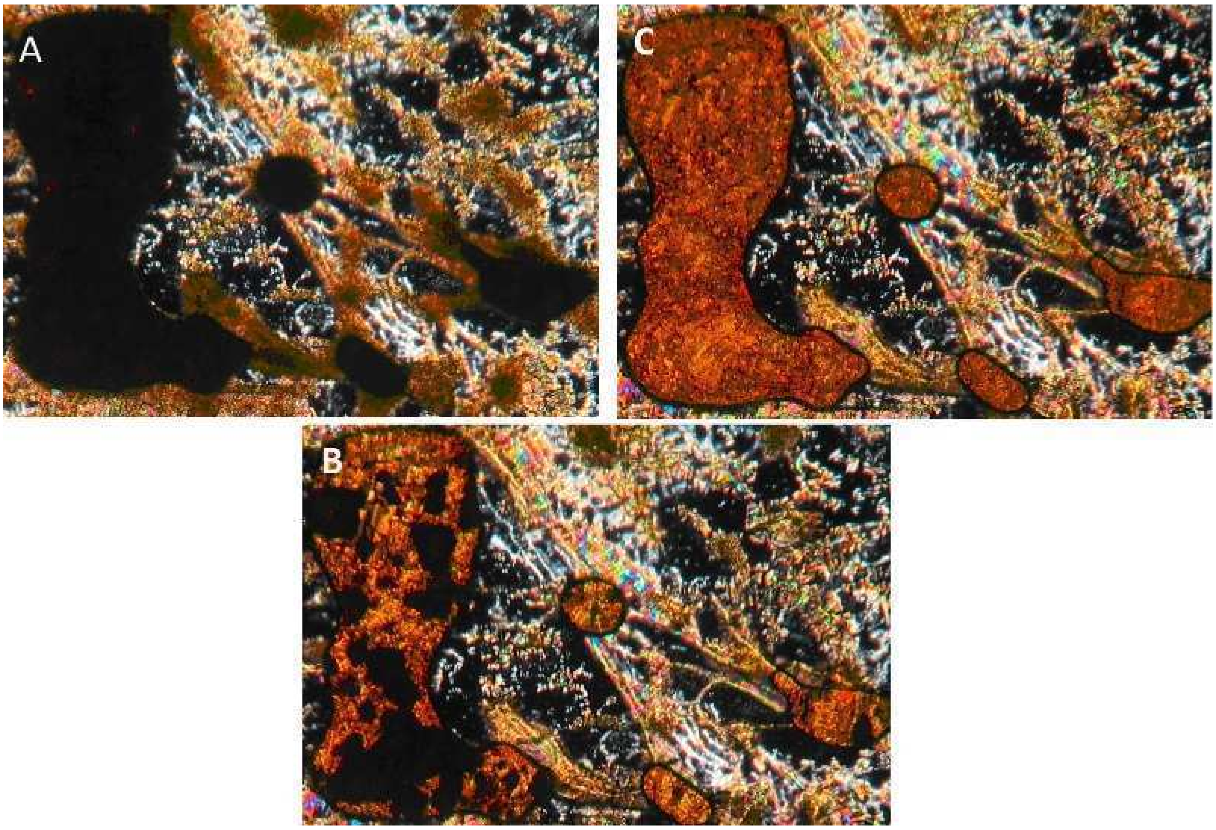
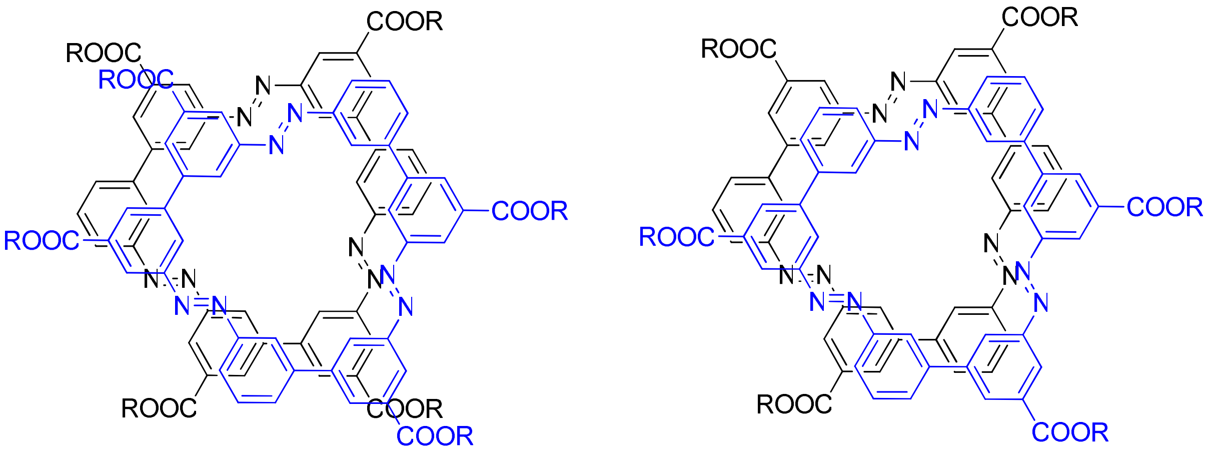


Figure 11: Pictures of butylester substituted CTB under a polarized light microscope. (A: at 23 °C solid phase. B: at 200 °C phase transition between solid phase and birefringent mesophase. C: at 210 °C orange birefringent mesophase.

3.2.4 Trisubstituted CTBs as liquid crystals.

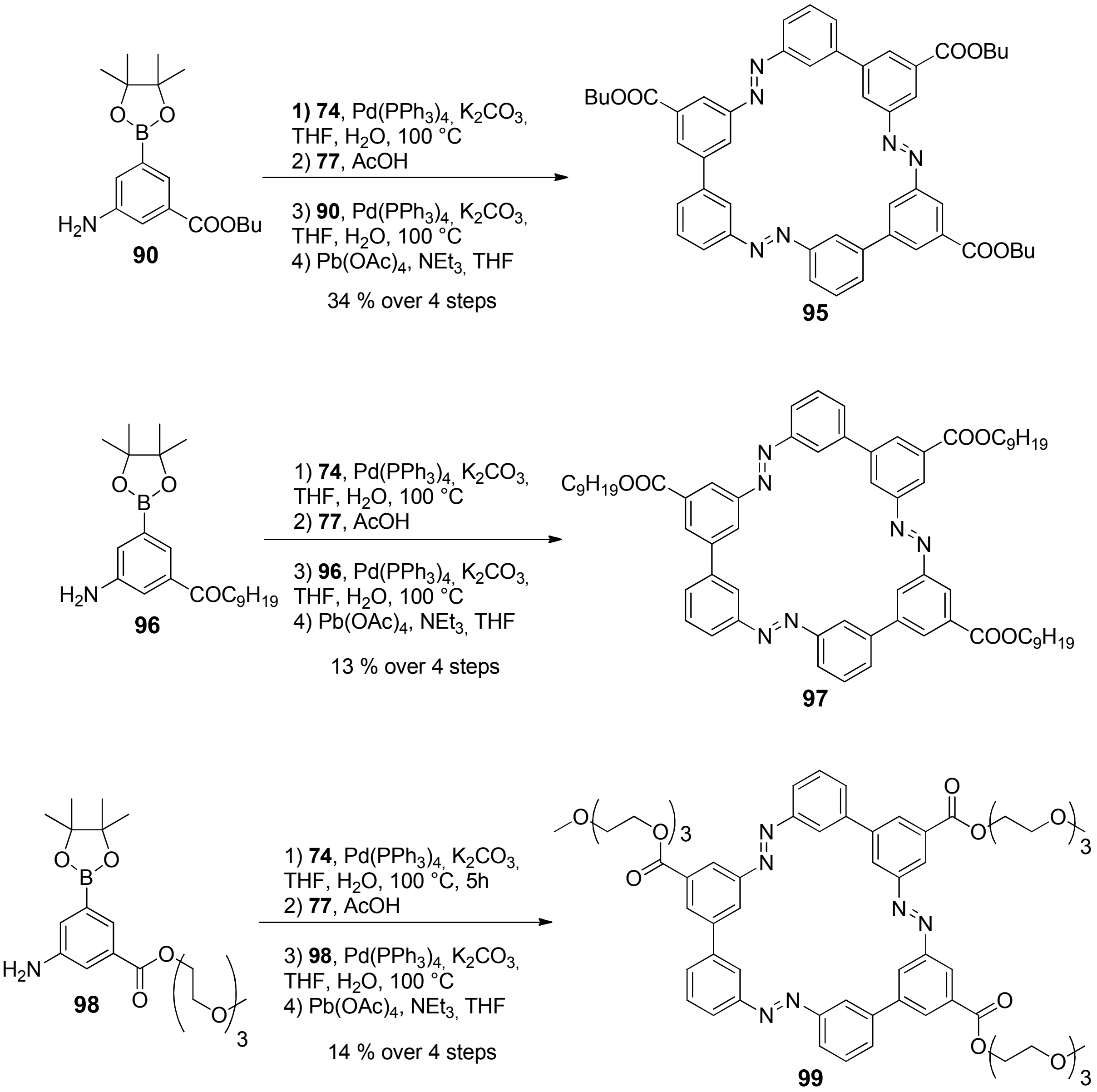
First experiments on the liquid crystalline behaviour of molecule **94** led to promising results and caused us to change the design of the molecule. One result of the modifications should be a lowering of the melting point and also an increase of the intermolecular interactions between the macrocycles. As it was still presumed that π-π-stacking was the driving force of aggregation a molecular structure was proposed with only three ester moieties. This way, the stacking should be enhanced since every butylester substituted benzene ring of macrocycle A could always place itself above an unsubstituted phenyl unit of macrocycle B. To accomplish a lowering of the melting point, the ester chains could be elongated with either a longer alkyl chain or an oligoethyleneglycol chain.



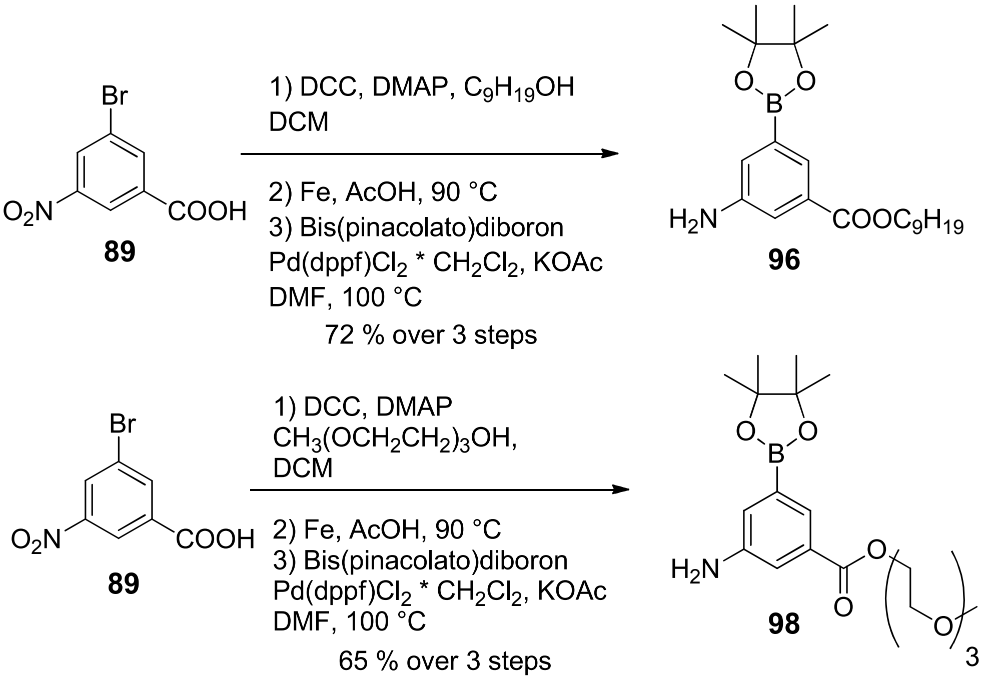
Scheme 34: Different assumed stacking modes of tetrasubstituted macrocycle (left) and trisubstituted macrocycle (right).

3.2.4.1 Synthesis of trisubstituted CTBs.

The preparation of the trisubstituted macrocycles was done in a similar way as for the tetrasubstituted macrocycle. The only difference in the case of butyl esters was that the first Suzuki-Miyaura cross-coupling reaction was done with 3-bromoaniline (**74**) instead of butyl 3-bromo-5-aminobenzoate (**89**). The synthesis of derivative **95** went smooth with slightly better yields than for the tetrasubstituted derivative **94** and in 18 % total yield from 3-nitrobenzoic acid (**86**). Two additional derivatives with longer chains were also prepared, one with a nonylester chain and one with a triethyleneglycol monomethylether chain. In the synthesis of the long chain derivatives the esterification was not done with thionyl chloride in the corresponding alcohol, but by using coupling conditions with DCC and DMAP.[35] The reduction was not done with tin dichloride dihydrate. Instead the milder Béchamp reduction was applied using iron powder in hot acetic acid.[36] The yield of the new building blocks was slightly higher than for the butyl ester substituted. The only problem was encountered in the purification of triethyleneglycol substituted CTB **99**. The combination of the flat hydrophobic core and the polar triethyleneglycol chains, made the purification by chromatography very difficult, since the product could not be eluted effectively even with very polar eluents. Therefore, after filtration over silica gel with 10 % methanol in ethyl acetate the compound was purified by preparative gel permeation chromatography with toluene as an eluent.



Scheme 35: Synthesis of different trisubstituted CTBs.



Scheme 36: Preparation of the boronic acid building blocks with a nonyl ester chain and a triethyleneglycol monomethylether chain.

3.2.4.2 Π-π-stacking and liquid crystalline behaviour

A concentrated and an unconcentrated sample of derivative **95** were compared to see how the removal of one ester unit expresses in the π-π-stacking behaviour of the macrocycles. A stacking effect can be clearly observed as the chemical shifts again move to higher field in the concentrated sample. However the shift of the peaks is not as strong as in the tetrasubstituted macrocycle. The two concentrations of the measured samples of **95** were 0.05 mol/l and 0.005 mol/l. The largest change in chemical shift was 0.15 ppm, whereas in the case for **94** the change was 0.2 ppm comparing the same concentration range. Probably the stacking efficiency is not primarily caused by the interaction of an electron deficient butyl substituted phenyl ring with a richer unsubstituted one, but the stacking interactions get stronger with the overall grade of substitution.

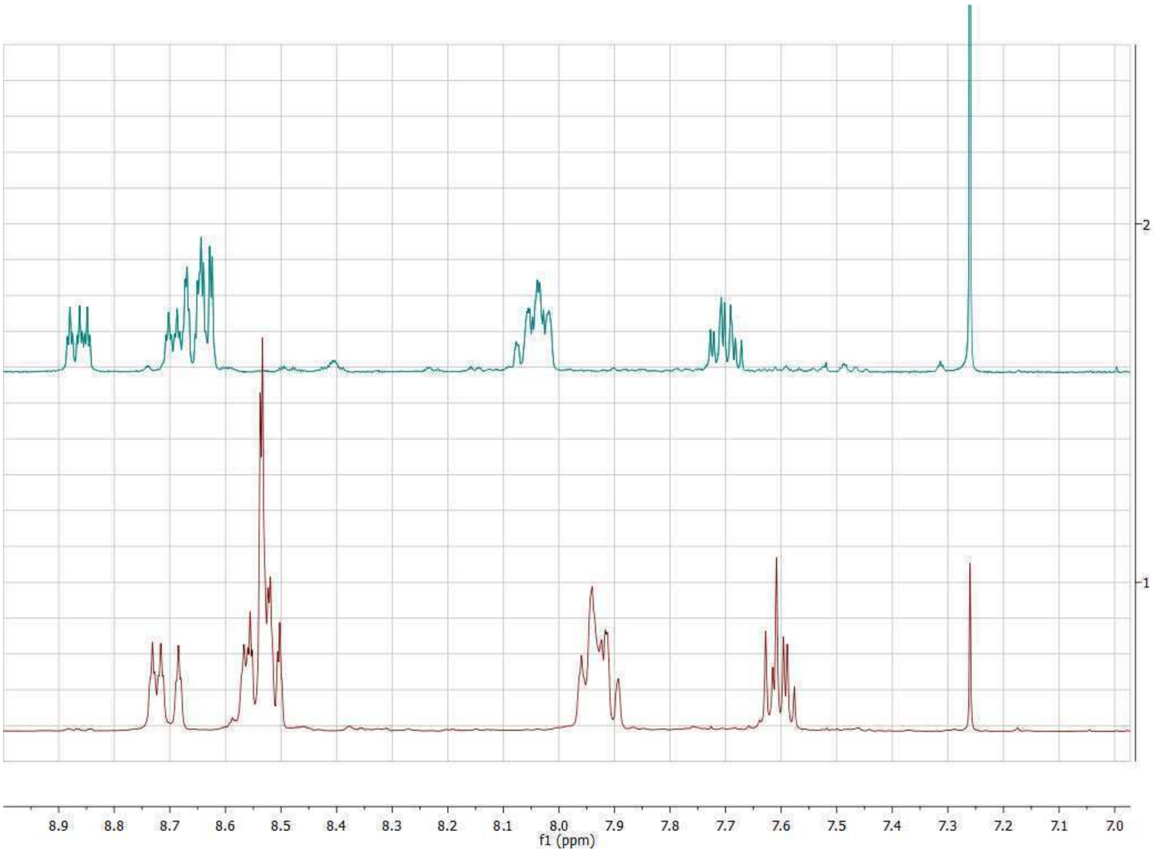


Figure 12: ^{1}H-NMR samples of macrocycle **95** at two different solutions 0.05 mol*l^{-1} (lower spectrum) and 0.005 mol*l^{-1} (upper spectrum), demonstrating the stacking effect.

One fortunate side effect of the decreased π-π-stacking of the new macrocycles was a lowering in the melting point. Whereas the tetrasubstituted CTB had a large melting range and decomposed before reaching an isotropic melt, trisubstituted derivative **95** was melting already at around 170 °C with a large melting range till 200 °C. The substance was also investigated on its liquid crystalline properties with polarized light microscopy. It turned out that the change from the solid phase to the liquid crystalline phase already occurred at around 180 °C. The pattern of the liquid crystals looked very similar to the last example with the distinction that a schlieren texture could be seen in the regions where there was only a very thin layer of material. Such a schlieren texture would be typical for a nematic phase in which the macrocycles have a rather replaced sense of stacking than in a highly ordered columnar phase. A sample of the macrocycle was irradiated with UV-light at 365 nm to induce *E* → *Z* isomerization. Since no stacking was observed in ^{1}H-NMR measurements of the *Z*-isomers of the macrocycle, it was assumed that a phase change from anisotropic to isotropic could be triggered photochemically. However, the liquid crystalline phase was not changed in its structure upon irradiation.

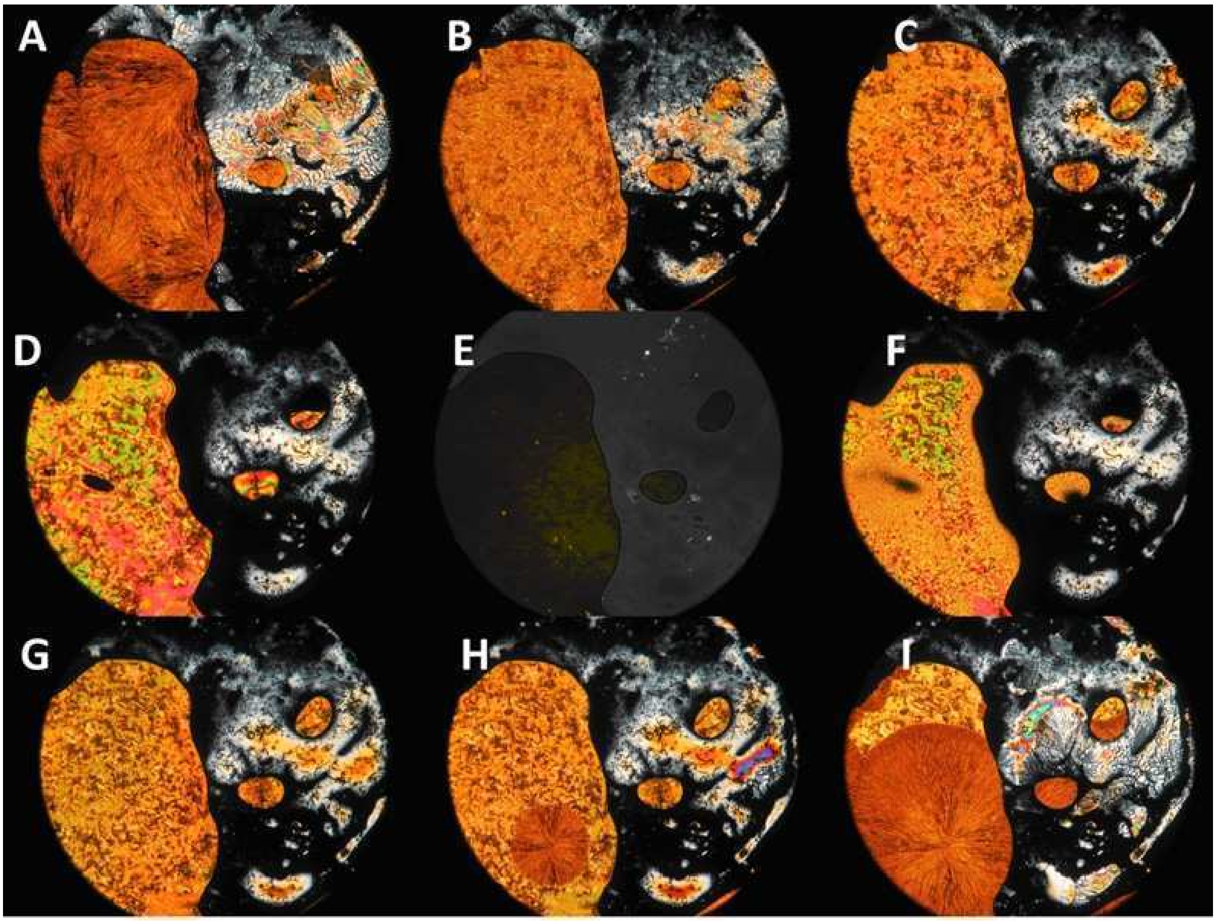


Figure 13: Complete heating and cooling cycle of macrocycle **95** under a polarized light microscope: Heating: A) solid phase. B) phase transition solid / LC. C) LC phase. D) phase transition LC / isotropic melt. E) isotropic melt. Cooling: F) phase transition isotropic melt / LC. G) LC phase. H) phase transition LC phase / solid I) almost solidified sample.

A second sample of macrocycle **95** was measured, which was prepared by evaporation of a DCM solution to generate a very thin substance layer. In this sample the texture of the LC phase could be seen much better. Because of the Schlieren texture which was observed under the microscope for this second sample, it is very probable that the liquid crystals are of the nematic discotic kind.

Like it was discussed before, DSC can be used to accurately measure phase transitions of liquid crystalline substances. In the DSC measurement of **94** only one phase transition could be seen, for the solid → LC transition. The DSC spectrum of compound **95** showed two peaks. One broad peak between 170 °C and 190 °C represents the phase transition from the solid phase to the liquid crystalline phase. In the cooling cycle the transition occurs between 127 °C and 143 °C. The peak which signifies the phase transition between the liquid crystalline phase and the liquid phase is very small and can only be seen when the measurement is carried out at a very slow rate. It appears at 195 °C upon heating and 193 °C upon cooling of the sample.

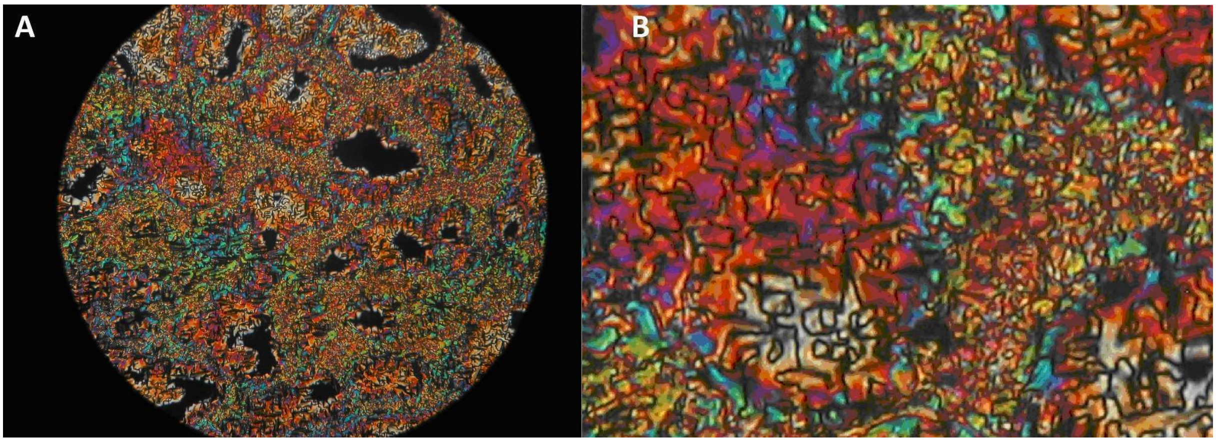


Figure 14: Polarized light microscopy of a thin layer of compound **95**. In the enlarged section B) a schlieren texture can be seen.

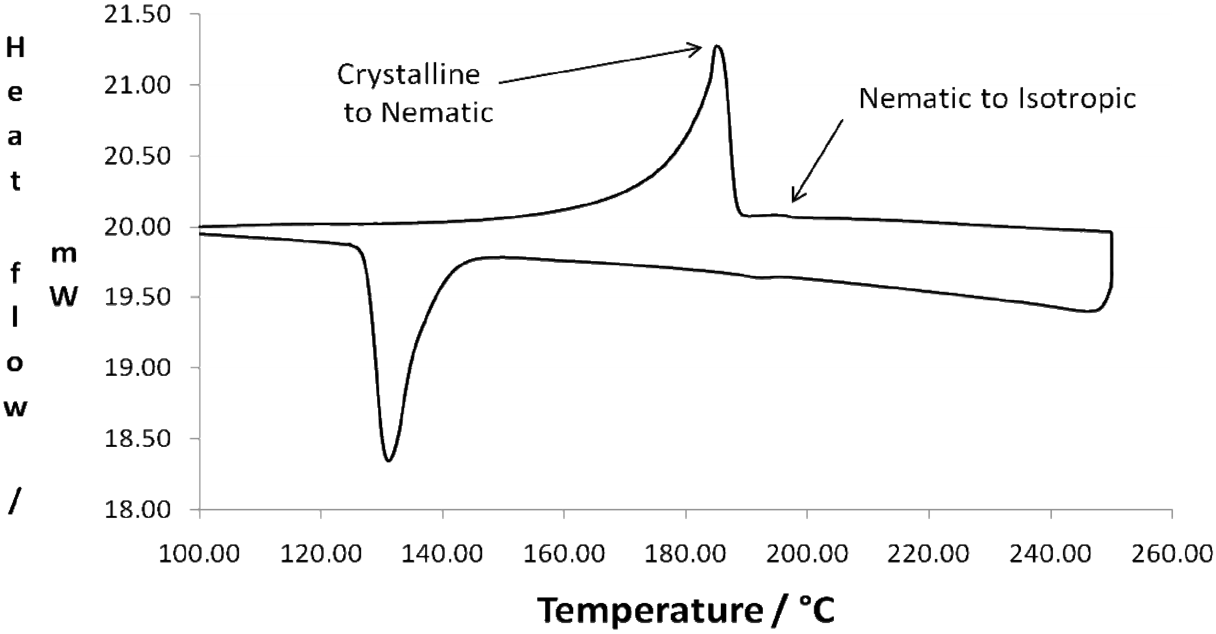


Figure 15: Differential scanning calorimetry (DSC) measurement of **95** showing two phase transitions.

Contrary to our prediction the stacking forces in the trisubstituted CTB derivative were weaker than in the tetrasubstituted macrocycle. However, a decrease in melting point was already achieved with the small butylester chains. The two macrocycles with longer chains showed an even lower melting point. Macrocycle **97** began melting at around 150 °C and **99** was not obtained as a crystalline substance but rather as an oil. An investigation of these two compounds with polarized light microscopy revealed that for macrocycle **97** no birefringence was observed and for derivative **99** with nonyl chains a direct phase transition from solid to isotropic melt could be seen. Maybe the stacking forces between the macrocycles decrease to such a degree that LCs are not forming again.

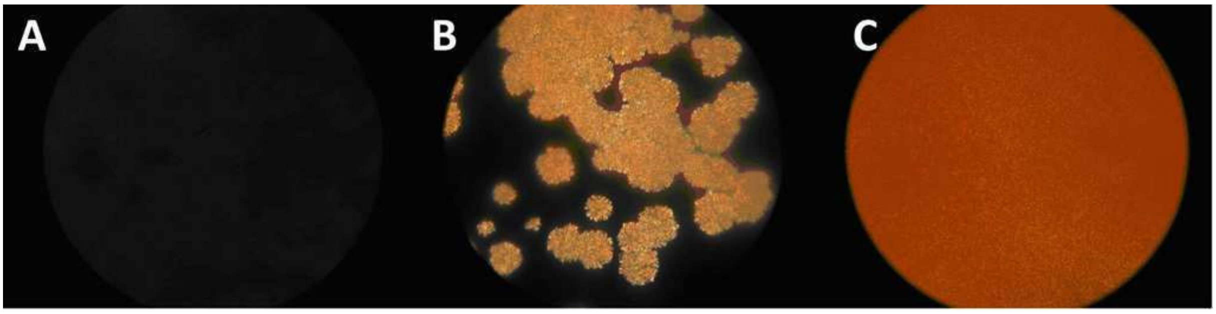


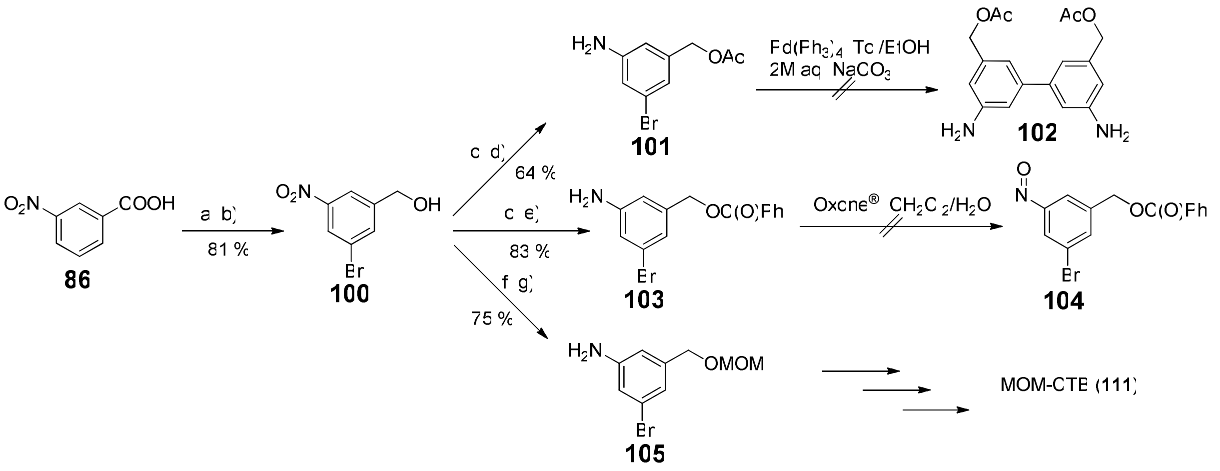
Figure 16: Pictures of compound **95** under polarized light show a straight transition from isotropic melt (A) to crystalline solid (C).

3.2.5 Hexasubstituted CTB macrocycles.

The tetra and trisubstituted macrocycles which were synthesized before already had beneficial properties which made it easier to work with them. Their good solubility in chloroalkanes and aromatic solvents made it possible to conduct NMRs in high concentration and get a more detailed picture of their isomerization behaviour. However, the very complicated NMR spectra after isomerization made a detailed investigation of the isomerization very inconvenient, since the different isomers could not be assigned. A macrocycle in which every phenyl ring would be substituted with the same moiety would have two major advantages compared to the macrocycles which were prepared so far. On the one hand it would have a higher symmetry (C_3), so there should only be four isomers [all-*E*, (*E,E,Z*), (*E,Z,Z*) and all-*Z*] and hence, the number of signals in the NMR would be lower. On the other hand, the 1,3,5-substitution pattern would have the advantage that only singulets should be seen in the aromatic region which would further simplify the interpretation of spectra.

3.2.5.1 Synthesis of hexabenzylic alcohol substituted CTB

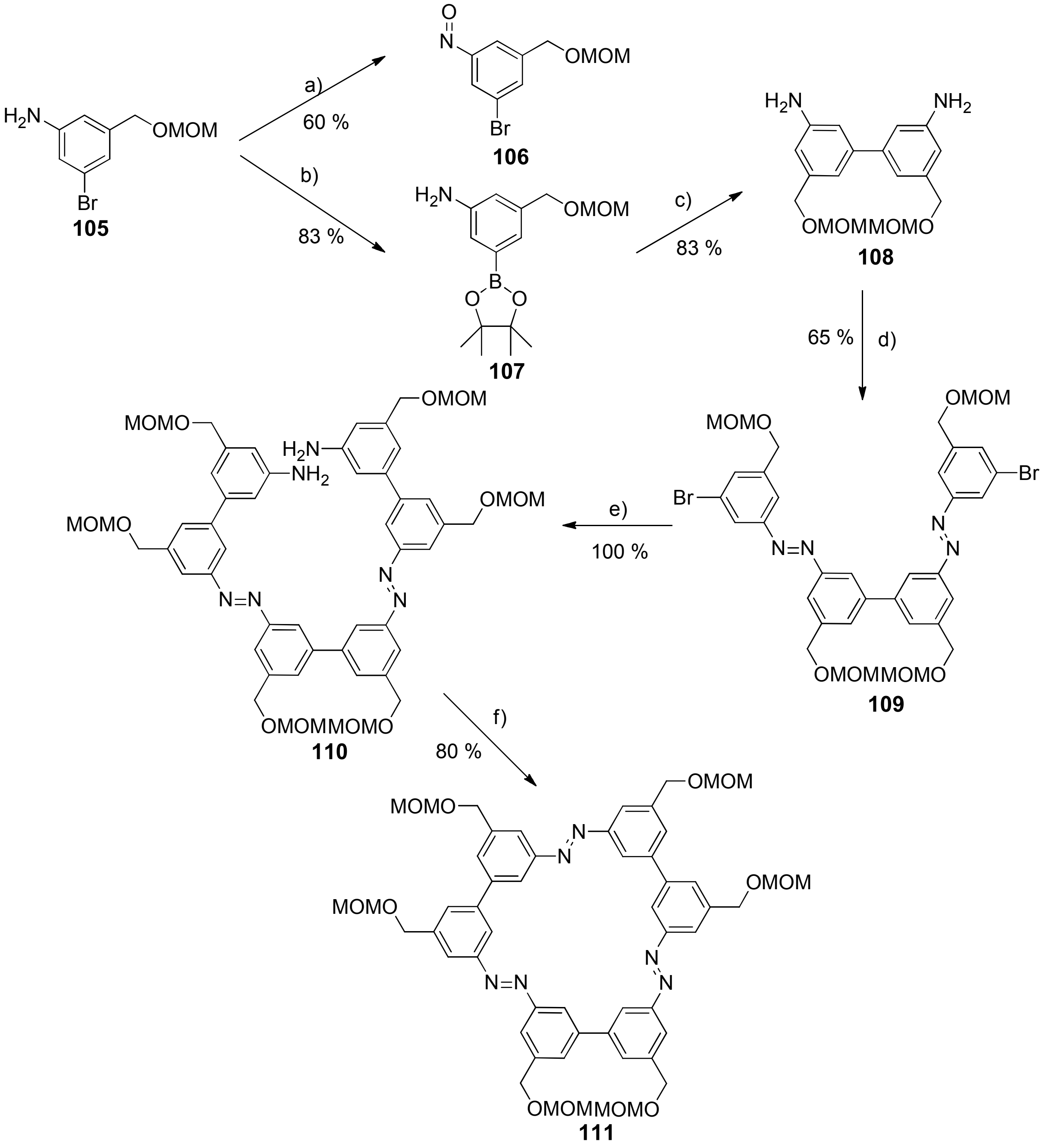
Yet, a fitting group still had to be found as in our previous synthetic approaches it was seen that an alkyloxygroup as the substituent posed a problem in the Mills reaction and was therefore not an option to create a fully substituted macrocycle (chapter 2.2.2). Also the ester was not a suitable group, because the oxidation to the nitroso benzene had failed (chapter 2.2.3.1). Therefore, a benzylic alcohol was chosen as an additional alternative, because the methylene group would only have a weak effect on the electronic properties of the aryl system with its inductive effect. Theoretically all steps along the synthesis should tolerate an alcohol group. However, to prevent the molecule from getting too polar, a protecting group strategy was thought to be more convenient, especially because purification should be much easier. One common protecting group for alcohols is the acetate group. To introduce it into the molecule 3-bromo-5-nitrobenzoic acid (**87**) first had to be reduced to the alcohol, which was done with borane dimethylsulfide complex in excellent yield (99 %).[37] The protection of the alcohol was done with acetic anhydride, catalyzed by 4-DMAP in moderate yield after reduction of the nitro group to the aniline.[38] After the preparation of the boronic acid, a Suzuki-Miyaura cross-coupling was done, but the symmetric biphenyl diamine **102** was not obtained, because a deprotection of the acetate group occurred, probably due to the basic conditions. To raise the stability towards base, the acetyl group was displaced by a benzoyl group. Indeed the Suzuki reaction worked this time but unfortunately no reaction occured when **103** was treated with oxone® to produce nitroso compound **104**. Consequently, this group was also not feasible for the total synthesis of a fully substituted macrocycle. Finally, the methoxymethyl group (MOM) turned out to be perfectly fitting for the task. The group could be introduced by reacting benzylic alcohol **100** with methyl chloro-methyl ether in good yield (90 %).[39]



Scheme 37: Different protecting group strategies for the synthesis of a fully substituted CTB macrocycle. a) NBS, H_2SO_4, 60°C, 20 h (83%); b) $BH_3{\cdot}SMe_2$, THF, 60°C, 3 h (99%); c) $SnCl_2{\cdot}2H_2O$, EtOH, 60°C, 1 h (99%); d) Ac_2O, DMAP, Et_3N, CH_2Cl_2 (64%); e) benzoic acid anhydride, DMAP, Et_3N, CH_2Cl_2 (83%); f) methyl chloro-methyl ether, $N(iPr)_2Et$, CH_2Cl_2, rt, 3 h (90%); g) Fe, AcOH, 100°C, 1 h (83%).

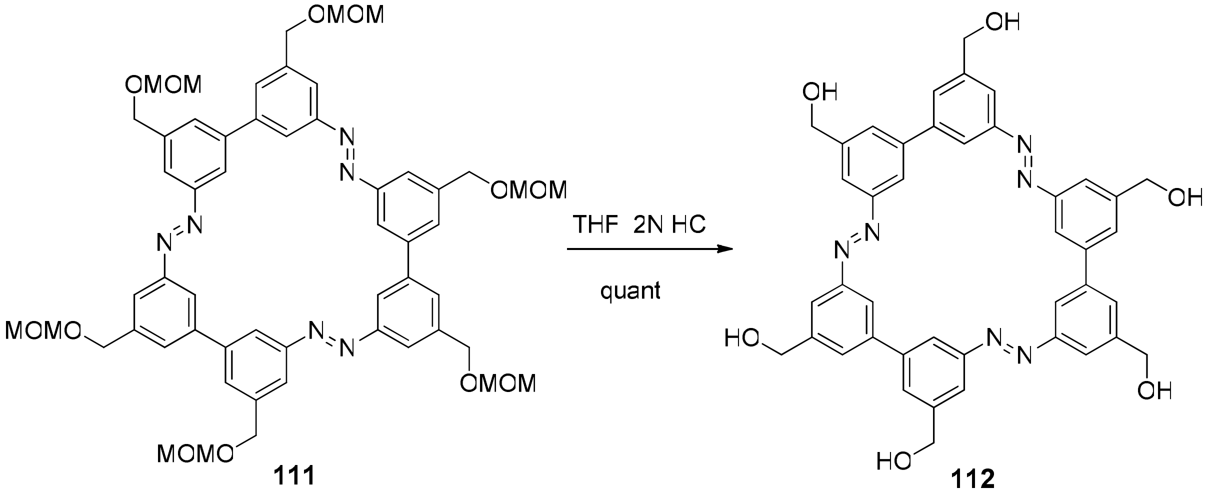
Since the group is cleaved with strong acid, the reduction of the nitro group could not be done with $SnCl_2$, since hydrochloric acid is formed during the reaction. Instead, a Béchamp reduction was done again this time to give aniline **105** in 83 % yield.

This intermediate was the core building block, from which all other substances for the total synthesis could be prepared. The Miyaura reaction of **105** produced boronic ester **107** in a good yield of 83 % and also Suzuki-Miyaura cross-coupling with the bromide proceeded in the same yield. The corresponding nitrosobenzene **106** could also be prepared (60 %). With all the needed building blocks in hand, the prerequisites for synthesizing macrocycle **111** were there. The Mills reaction worked in a satisfying yield of 65 %. The second Suzuki reaction proceeded in excellent yields, but the diamine precursor **110** could not be isolated in good purity. Yet, the minor impurities had no effect on the oxidative cyclization step, which gave much higher yields this time than for all the ester substituted macrocycles. The new macrocycle **111** (MOM-CTB) could be easily purified by column chromatography and its purity could be proven by elementary analysis. The compound was also soluble in most common organic solvents except in alcohols.



Scheme 38: Synthesis of hexasubstituted CTB **111** with MOM-protected benzylic alcohols. a) oxone®, DCM/H_2O; b) Bis(pinacolato)diboron, Pd(dppf)Cl_2 * CH_2Cl_2, KOAc, DMF, 100 °C; c) Pd(PPh_3)$_4$, K_2CO_3, THF/H_2O; d) **77**, AcOH; e) **107**, Pd(PPh_3)$_4$, K_2CO_3, THF/H_2O; f) Pb(OAc)$_4$, NEt_3, THF.

For the deprotection of the MOM-groups very harsh conditions were initially applied.[40,41] Treatment of the MOM protected macrocycle with 6 N HCl in THF as well as trifluoroacetic acid lead to degradation, probably due to protonation of the azobonds. However, when a 1:4 mixture of THF and 2 N HCl were applied a very slow deprotection of the macrocycle took place. After stirring at 45 °C temperature for 3 days the fully unprotected macrocycle precipitated out of solution.



Scheme 39: Deptrotection of MOM groups of molecule **111**.

3.2.5.2 Isomerization studies of MOM-CTB

The first isomerization experiments with macrocycle **111** were done using UV-VIS spectroscopy. The spectrum of the substance resembles the one of the unsubstituted derivative **63** and exhibits the typical pattern as it can be seen for azobenzenes. The n → π* transition lies at 330 nm as an intense, broad band and the n → π* transition has its maximum at 430 nm with only a very small intensity.

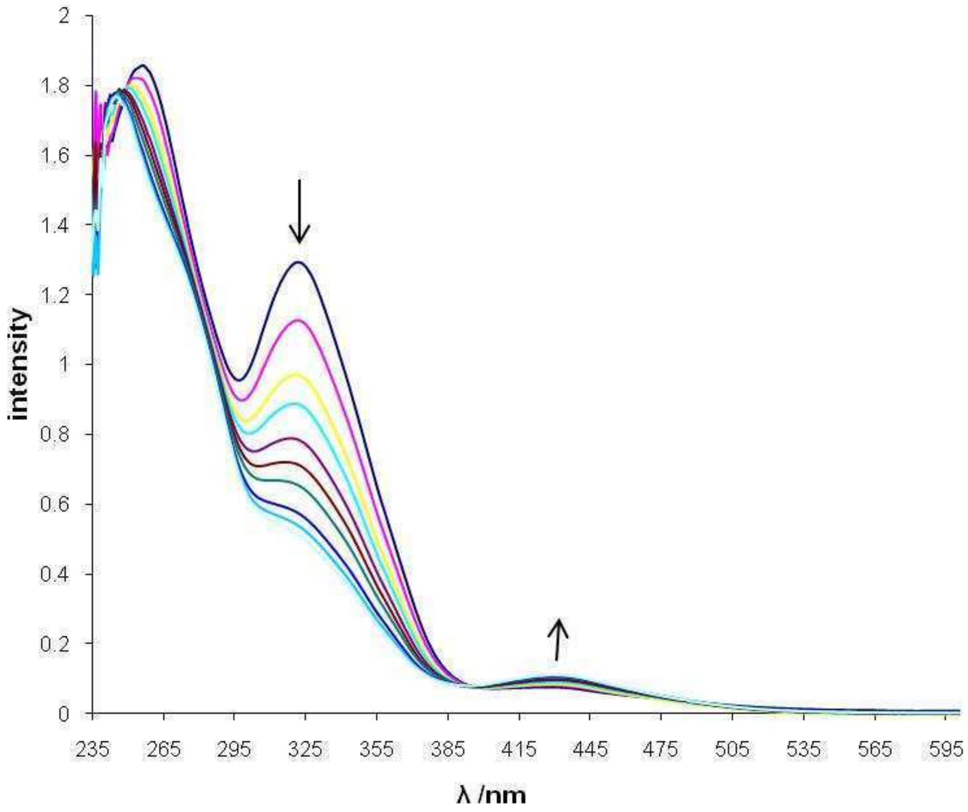


Figure 17: Absorption spectra of MOM-CTB **111** during isomerization at 365 nm irradiation. The π → π* transition lies at 330 nm and the n → π* transition occurs at 430 nm (c = 1*10^{-5} mol*l^{-1}).

Upon irradiation at 365 nm a steep decrease of the absorption at 330 nm is accompanied with a slight rise of the peak at 430 nm. The band at 260 nm also decreases and experiences a hypsochromic shift. When the sample is heated long enough the initial spectra is obtained.
Isomerization of the macrocycle was investigated in detail with ^{1}H-NMR spectroscopy. The initial compound shows three different singulets as it is expected, since all phenyls have the same substitution pattern. It should also be emphasized by now that the macrocycle does not show any concentration dependence on the chemical shifts of the aryl signals. Like in the previous NMR isomerization experiment, additional spectra were recorded after certain irradiation periods. By comparing the different spectra the different peaks could be assigned to four different isomers, as it can be seen in Figure 18. There are two isomers which show three signals. One of those is the all-*E* isomer which is the only species before irradiation. The predominant species after irradiation over night is the all-*Z* isomer.

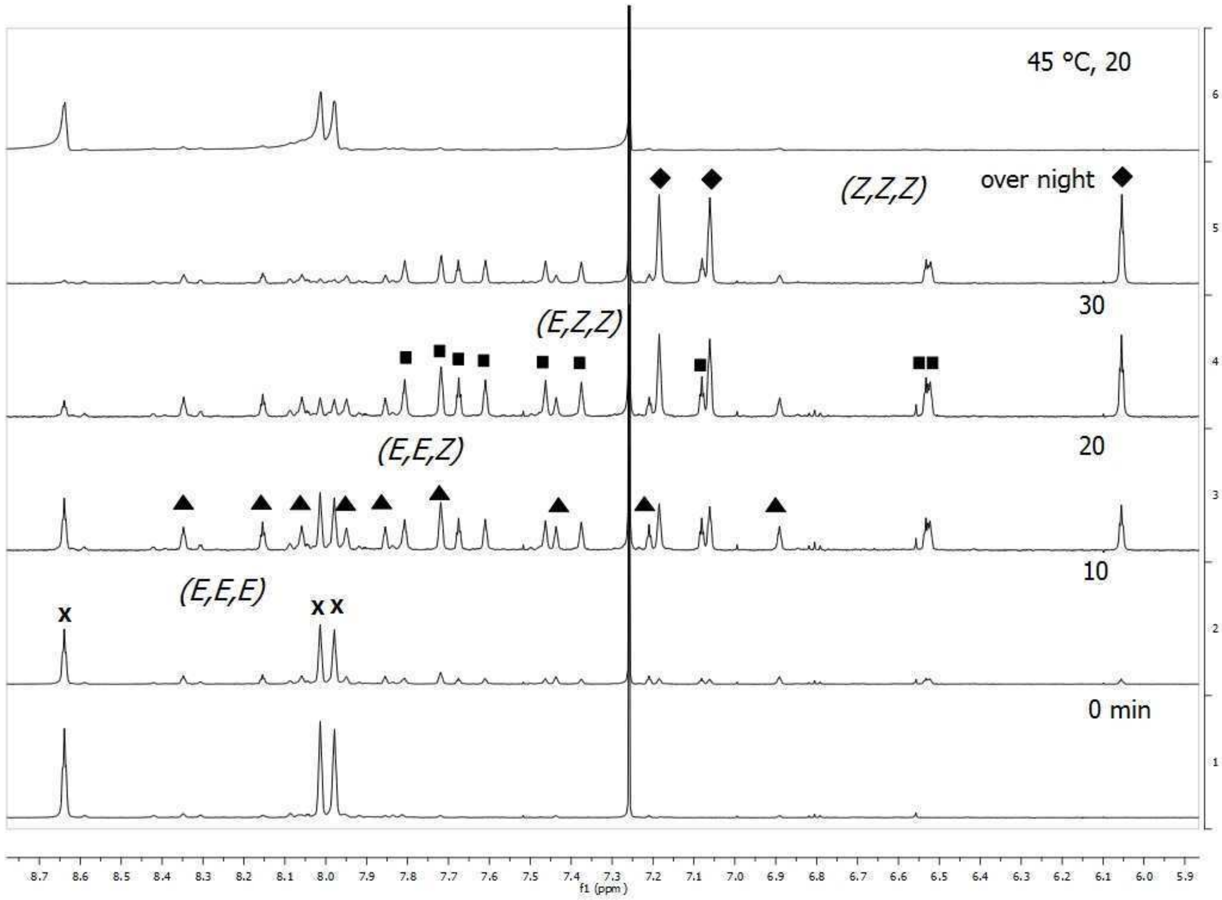


Figure 18: ^{1}H-NMR isomerization experiment of MOM-CTB **111**. Recording of different spectra after certain time periods of irradiation with 365 nm light.

Besides the two C_3 symmetric isomers, two other compounds were observed when the sample was measured after 20 and 30 minutes, before the PSS was reached. They both show nine signals, which would fit to a C_2 symmetry and, therefore, would correspond to the mixed isomers (*E,E,Z*) and (*E,Z,Z*). As it was expected, the macrocycle exists in four different isomeric forms, which can be easily assigned by NMR spectroscopy. After heating at 45 °C over night the initial spectrum is obtained.

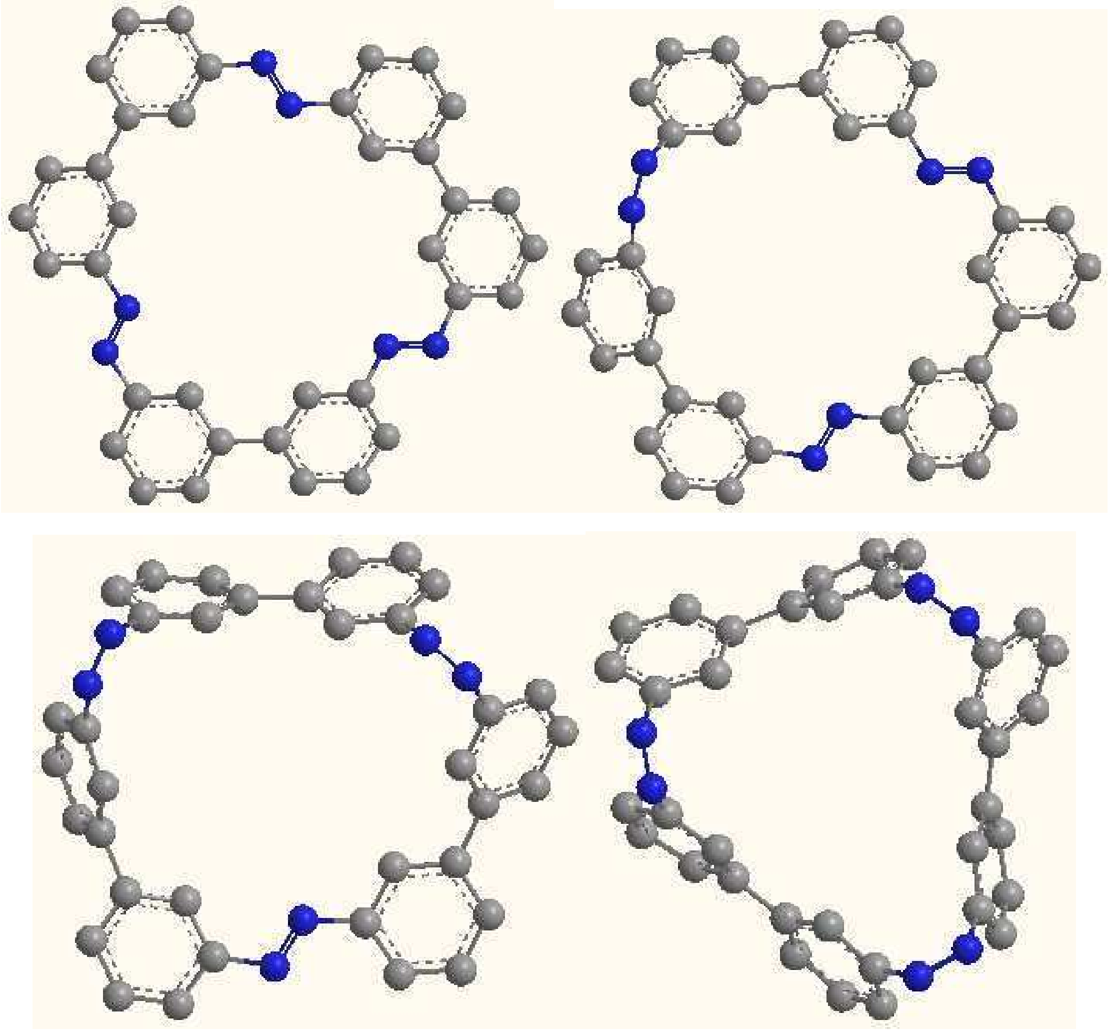


Figure 19: MM2-Calculations of different *E*/*Z*-Isomers of MOM-CTB macrocycle **111**.

The ratio of the different isomers at the photostationary state at 365 nm was measured in several solvents. The composition of the isomeric mixture seems to be very sensitive to solvent effects. In an apolar solvent like chloroform, the all-*Z*-isomer was making up for 48 % of all four isomers. When a more polar solvent like DMSO or acetonitrile was used as a solvent, this number went up almost ten percent. An even higher percentage of the all-*Z*-isomer was observed in aromatic solvents like benzene and toluene and the highest one in pyridine as a polar, aromatic solvent. This effect could have two possible explanations. The solvent could be enclosed by the all-*Z* isomer if it exists in a bowl shaped structure and stabilize it through host-guest interactions. Such interactions should be the largest for aromatic solvents. The effect that toluene as the more sterically hindered solvent has a lower percentage of the all-*Z*-derivative would substantiate this proposition. Another rather simple explanation would be that the absorption at 365 nm is slightly shifted when the solvent is changed and, therefore, different quantities of light are absorbed.

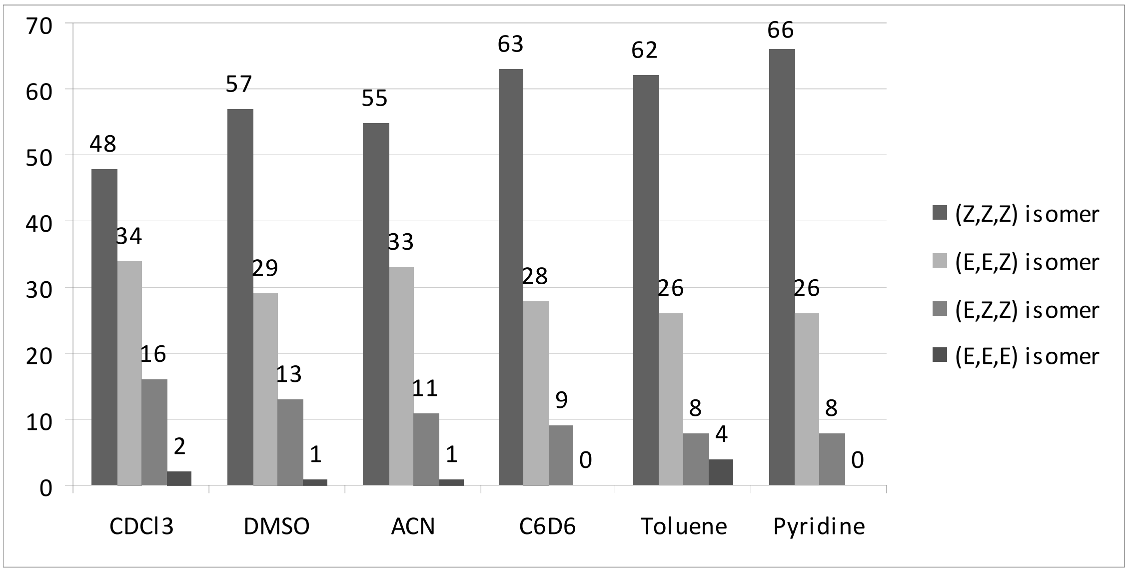


Figure 20: Ratios of isomers at the PSS in different solvents.

Additional samples of CTB **111** were irradiated at 365 nm overnight to reach the PSS. Then, another irradiation was done at different wavelength to see the influent of the light source on the ratio at different time intervals and at the PSS. The samples were irradiated with UV light of short and middle wavelength (254 nm and 302 nm) and with visible light from a halogen floodlight. For all samples several ratios were measured until the equilibrium was reached. Irradiation with 254 nm is targeted on the $\sigma \rightarrow \pi^*$ transition. It resulted in a strong increase of the all-*E* isomer, which was the dominant isomer in the photostationary state, followed by the (*E,E,Z*)-isomer. Interestingly, after irradiation with visible light the all-*E*-isomer was only the second most abundant isomer after the (*E,E,Z*)-isomer. If the irradiation was done at 302 nm the two mixed isomers were enriched, with the (*E,Z,Z*)-isomer being the dominant species. These results are interesting, since every isomer was once obtained as the major species. This could be done selectively just by the choice of the right wavelength. Even though, in every irradiated sample there is still a mixture of all different isomers, the fact that every one of them can be addressed as the major isomer is already a noteworthy effect.

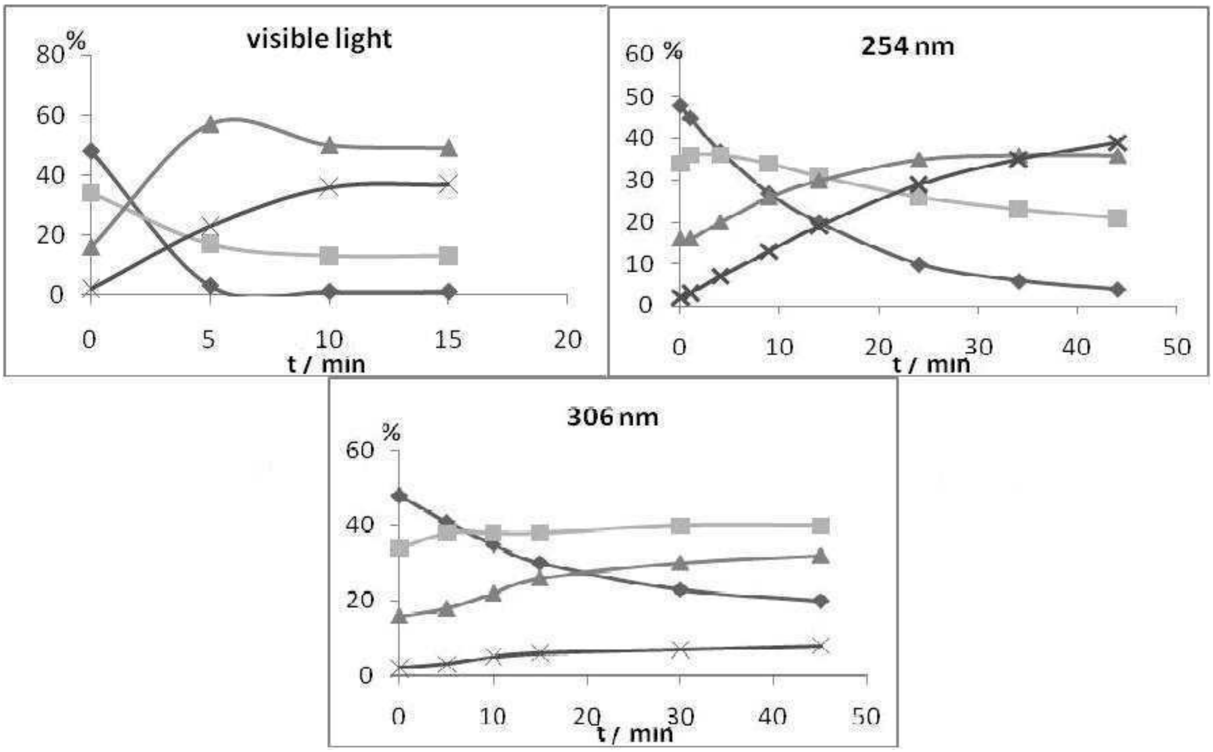


Figure 21: Isomerization of MOM-CTB **111** with different light sources after the PSS at 365 was reached.

It was already discussed in the introduction that azobenzenophanes often show lifetimes for the *Z*-isomers which largely deviate from their linear analogues. To see if this was also the case for MOM-CTB **111**, the thermal *Z* → *E* isomerization was investigated. After a sample of **111** in benzene had been irradiated at 365 nm over night it was stored in the dark and over a period of ten days several ^{1}H-NMR were measured to determine the change of the ratios of the different isomers. Under exclusion of light only the thermal *Z* → *E* isomerization takes place with a first order rate constant. Since it can be assumed that only one isomerization occurs at a time, three different reactions have to be considered.

The rate constant for the isomerisation reaction from all-*Z* to (*E,Z,Z*) was calculated out of these measurements to be $9.12 * 10^{-7}$ s^{-1} and the lifetime of the isomer to be 8.8 days at 27 °C in benzene. This value, when compared to that of linear azobenzene (τ = 3.5 d) suggests that there might be some effect of the macrocyclic strain which stabilizes the isomer. A lifetime of 4.8 days was measured in chloroform, which leads to the conclusion that the solvent also has a stabilizing effect on certain isomers which was already hypothesized out of the results for the PSS in different solvents.

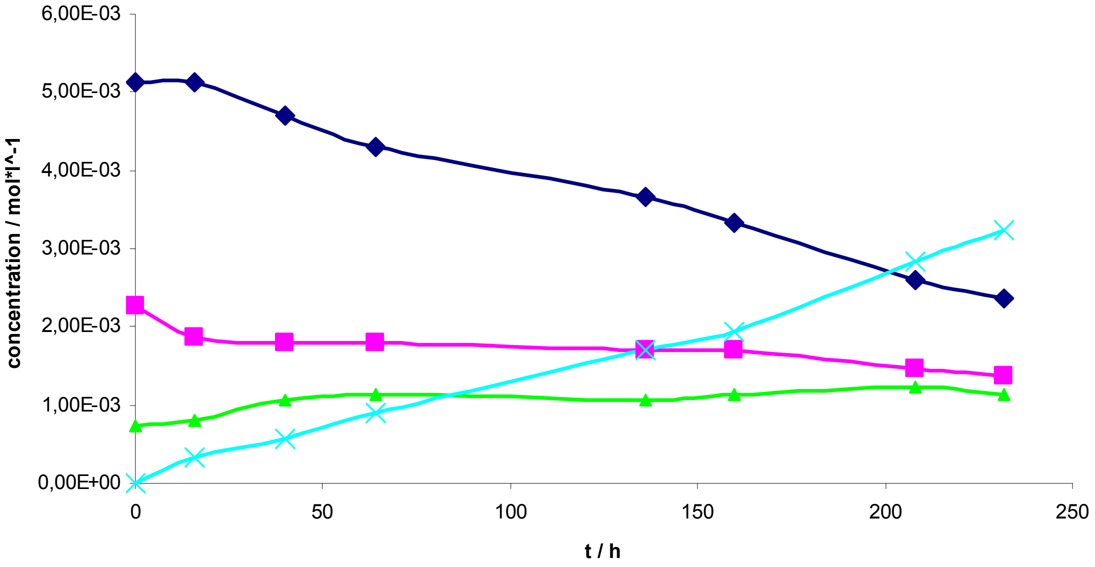
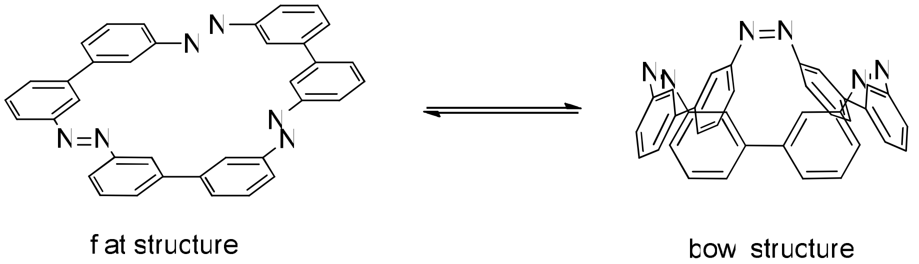


Figure 22: Kinetic measurements on the thermal *Z* → *E* isomerisation of MOM-CTB. Concentration of different isomers at certain times since end of irradiation at 365 nm (all-*Z*: blue line; (*E,Z,Z)*: pink line; (*E,E,Z)*: green line; all-*E*: turquois line).

3.2.5.3 Binding studies

One of the initial motivations of this research aimed at designing a molecular switch which would exhibit specific molecular recognition towards guest molecules of any sort. In the case of triscycloazobenzenes the binding to alkali metal ions could be detected by ESI-MS and the binding to triphenylcarbenium ions could be seen in ^{1}H-NMR studies (section 2.1). However, since these systems were unable to switch they were missing the essential requirement for a molecular gripper. It has already been shown that cyclotrisazobiphenyls are photochromic and an extensive study of their switching behaviour was done. As a next step the binding properties and ultimately the combined binding of guests and their release through photochemical switching had to be investigated. Like in the case for cyclotrisazobenzenes the larger macrocycles were also tested in ESI-MS experiments on their binding capacities for alkali metals. Yet, no metal complexes could be seen with those. An explanation could be the size of the cavity being to large for these ions. Consequently several aromatic molecules were tested. It was envisioned that again, coordination to the azobonds lone electron pairs as well as π-π-stacking interactions would be the main interactions which could be built to bind guest molecules. The shape change which was brought about by the switching should guarantee that binding only takes place with one particular isomer, either the all-*E* or the all-*Z* species. Due to the stacking which was observed for the all-*E* isomers it was assumed that a flat structure was the most probable conformation in this isomer. Since for the all-*Z* the same symmetry as for the all-*E* isomer was seen in the NMR, it was assumed that a C_3 symmetric bowl structure was a reasonable structure. However, no X-ray structural analysis was available to substantiate this hypothesis.



Scheme 40: Assumed structures of all-*E* and all-*Z* isomer and their geometric differences.

A variety of polyaromatic compounds and electron rich as well as electron poor aryls were tested on their suitability as guest molecules. No binding could be observed for any of these systems. The next guest ion was triphenylcarbenium tetrafluoroborate, which was already used as a guest for triscycloazobenzene. Indeed interactions could again be observed by a highfield shift of the aromatic protons of the macrocycle, but no isomerisation occurred upon irradiation of the mixture. A similar behaviour was observed for various ammonium ions. The protonated amines with aliphatic chains like tetrabutylammoniumchloride, cetyltrimethylammonium bromide or 1,3-(diammonium)propyl dichloride showed no shift of the aromatic protons of CTB at all or only a very small effect. On the other hand, aromatic ammonium ions had a strong effect on the shifting of the ^{1}H-NMR signals. The complexation was stronger for ions with two phenyl rings, like *N*-phenylbenzylammonium chloride, or 1,1-diphenylmethylammonium chloride and not so strong for anilinium hydrochloride which only possesses one aryl ring. This suggests that π-π-stacking or hydrophobic interactions played an important part. However, it is not clear why only aromatic ammonium ions were binding and not the other aromatic compounds. The ability to form strong hydrogen bonds with the MOM-groups of the macrocycle is one possible explanation for the selectivity. When samples with such aryl ammonium ions were irradiated, a large amount of undefined aromatic peaks was observed which could possibly point to the degradation of the macrocycle.

Table 3: Different guest molecules which were investigated for their binding abilities with MOM-CTB **111**.

Guest	MOM-CTB
Pyrene	No complexation, neither *Z* nor *E*
Biphenyl	No complexation, neither *Z* nor *E*
Trityl tetrafluoroborate	Complexation in *E* but no isomerization
1,3,5-Trimethoxybenzene	No complexation, neither *Z* nor *E*
1,3-Dinitrobenzene	No complexation, neither *Z* nor *E*
1,8-Diaminonaphthalene	No complexation, neither *Z* nor *E*
C60	No complexation, neither *Z* nor *E*
Anilinium hydrochloride	Almost no complexation in *E*, none in *Z*
TBAB	No complexation, neither *Z* nor *E*
Cetyltrimethylammonium chloride	No complexation, neither *Z* nor *E*
N-Phenylbenzylammonium chloride	Strong complexation in *E*, possible degradation in *Z*
1,1-diphenylmethylammonium chloride	Strong complexation in *E*, possible degradation in *Z*
p-phenylenediammonium triflate	Strong complexation in *E*, possible degradation in *Z*
Paraquat	No complexation, neither *Z* nor *E*
4,4'-bipyridinium chloride	Strong complexation in *E*, possible degradation in *Z*
2,2'bipyridyl	No complexation, neither *Z* nor *E*
1,3-(diammonium)propyl dichloride	very weak complexation in *E*, none in *Z*

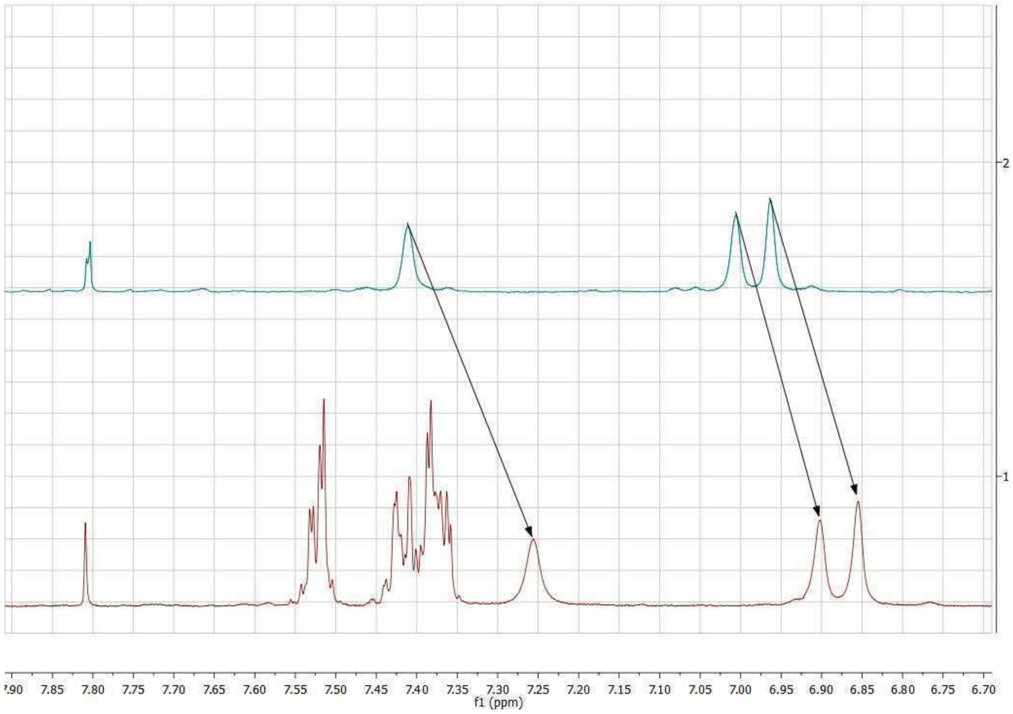


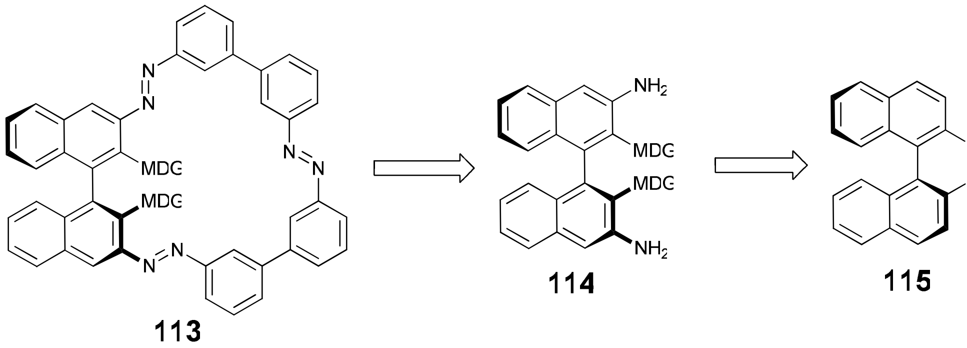
Figure 23: MOM-CTB **111** with benzylphenylammonium hydrochloride in MeOH:CDCl$_3$ 5:1.

3.2.6 Chiral Cyclotrisazobiphenyls

A particularly interesting application of azobenzenophanes is their potential use as molecular storage devices. It has already been demonstrated for the MOM-CTB macrocycle that by using different light sources all four isomers could be accessed as the major species. However, if UV-spectroscopy is used as the readout it cannot be differentiated between the specific isomers but only between the total number of *E* and *Z* azobonds. The insertion of chiral information would enable the measurement of chiroptical properties. Due to the incorporation of biphenyl moieties in our macrocycles, there would be the option of installing an axially chiral building block into the azobenzenophane core. In a macrocyclic molecule this should produce a system with helical chirality. The geometric differences of the photoisomers would probably induce a considerable change in the chiroptical properties of the molecule.

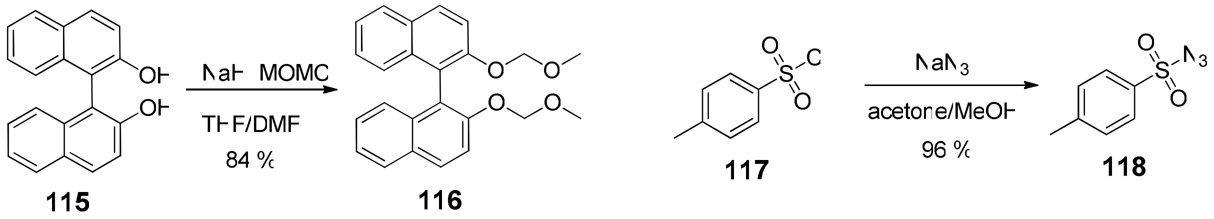
3.2.6.1 Synthetic approaches and synthesis of chiral CTB

One of the most common axially chiral structural motive which is used for various applications, mainly as ligands in asymmetric catalysis, is 1,1'-binaphthyl.[42] In these systems the rotation around the single bond which connects both naphthalenes is rotation restricted which makes them chiral. Most of the used systems containing 1,1'-binaphthyl moieties are substituted at 2 and 2' positions. However, to incorporate such a chiral building block into the macrocycle a 3,3'-substitution pattern would be needed. There are not many examples for the preparation of 3,3'-diamino substituted 1,1'-binaphthyls and therefore, an approach was followed in which 3,3'-diamino-1,1'-binaphthol **114** was to be prepared by using a metal directing group to introduce a diazide by *ortho*-lithiation which should be reduced to the diamine afterwards. If the diaminobinaphthol **114** could be prepared the rest of the synthesis should be straight forward like in the previous examples.



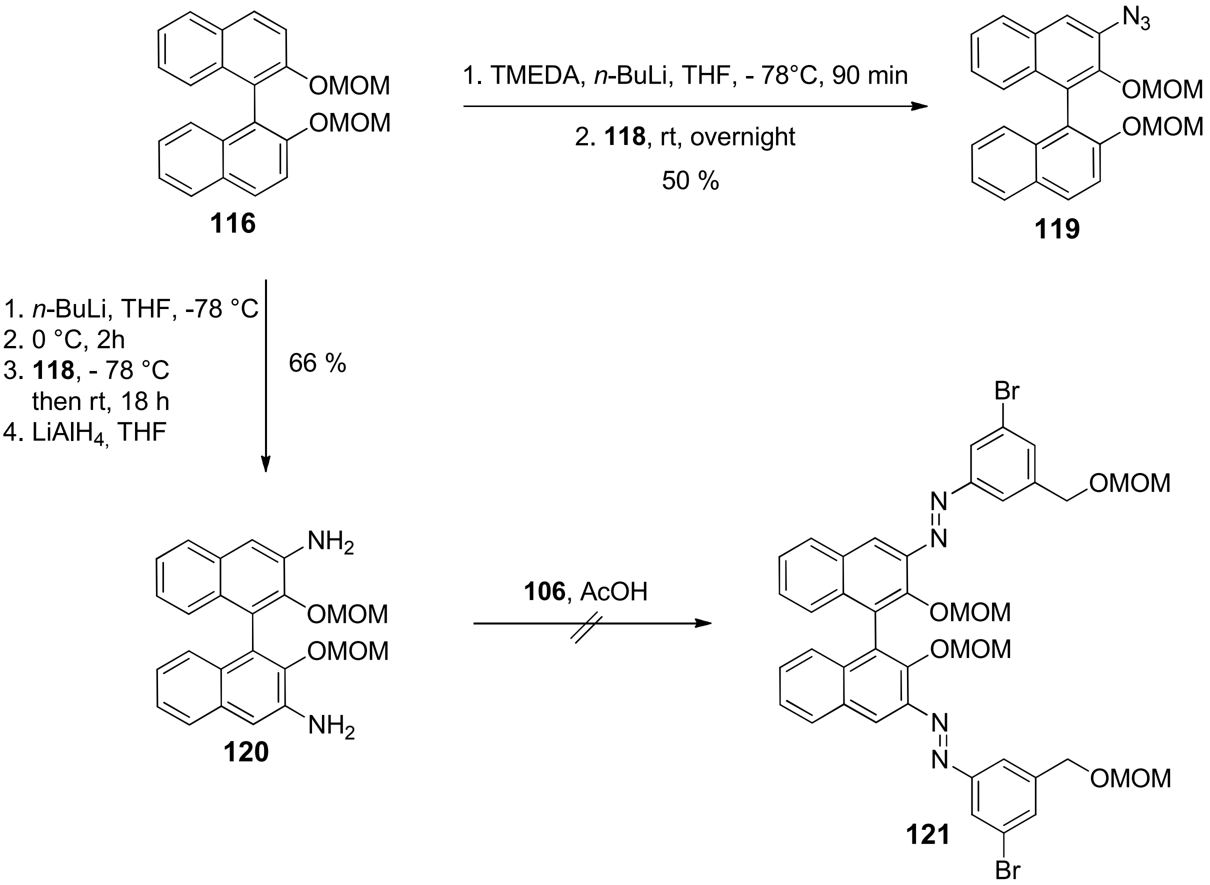
Scheme 41: Rethrosynthetic pathway to helically chiral CTB.

A strong metal directing group which can be readily introduced into binaphthol (**115**) is the MOM-group which was already used as a protecting group for benzylic alcohols. However, the procedure which was used in the former case proved to be insufficient for the less reactive phenol groups. Therefore, more harsh conditions using sodium hydride were used to fully deprotonate the phenol groups and facilitate substitution in a good yield of 84 %.[43] Tosyl azide (**118**), even though commercially available, was prepared out of tosyl chloride (**117**) by treating it with sodium azide in excellent yield.[44]



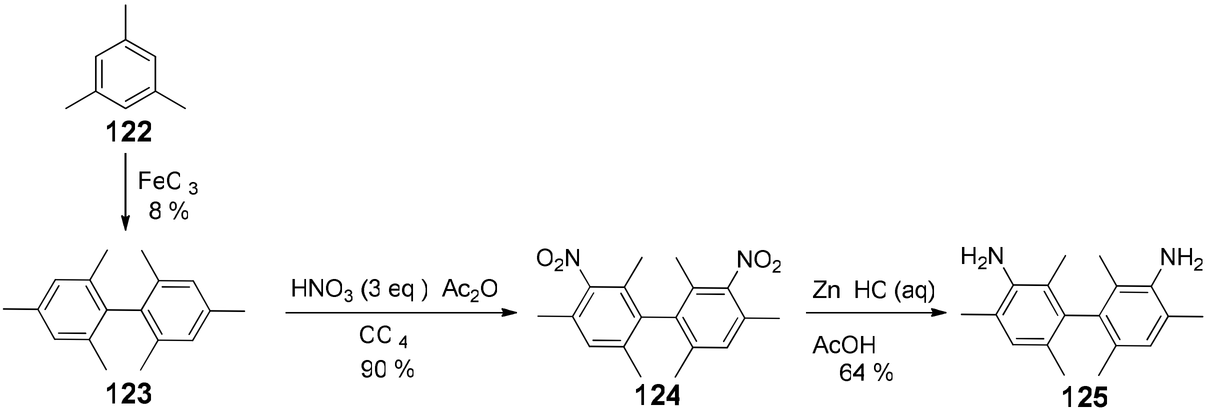
Scheme 42: MOM protection of binaphthol (**115**) and preparation of tosyl azide (**118**).

The *ortho* lithiation reaction turned out to be problematic. Since the double protected azide was the desired product, it was unfortunate that most reaction conditions which were tried only produced the mono functionalized azide. In these experiments the lithiation was done at -78 °C with tetramethylethylenediamine (TMEDA) as a chelating agent for the *n*-BuLi. These conditions were probably not strong enough to facilitate double lithiation. When TMEDA was not used and the mixture was warmed to 0 °C after addition of *n*-BuLi a change in colour from pink to dark purple occured. Before quenching with tosyl azide the mixture was again cooled to -78 °C. Following this procedure, the diazide was obtained as the main product of the reaction. However it turned out that the compound was unstable. For that reason it was directly reduced to the diamine with LAH in THF. This enhanced procedure produced 3,3'-diamino-2,2'-bis(methoxymethyl)-1,1'-binaphthyl (**120**) in a good yield of 66 %. The diamine was subjected to Mills reaction with nitroso derivative **106** in acetic acid. Unfortunately, no reaction took place. This result was already observed in the approached synthesis of the hexyloxy substituted CTB macrocycle (section 2.2.2). In general, phenol ether substituted anilines seem not to be suitable substrates for Mills couplings. In the case of diaminobinaphthyl **120** the effect of hydrogen bonds of the MOM oxygens to the amino groups probably further decreases nucleophilicity.



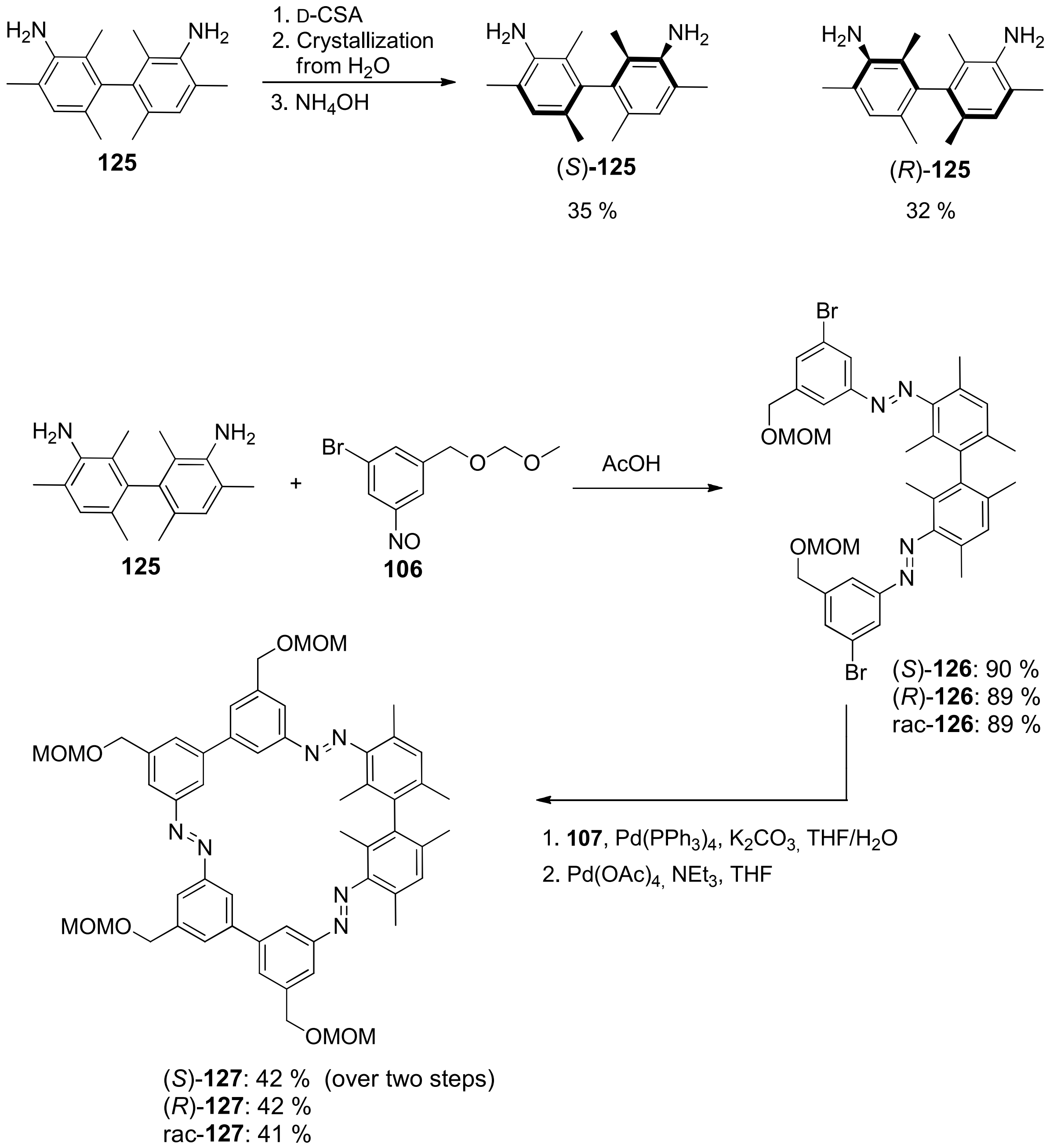
Scheme 43: Synthesis of mono- and diazidification of MOM protected binaphthol **119** and failed Mills coupling of diamine **120**.

Due to the failed Mills reaction of diamine **120** and the fact that there was no convenient alternative to prepare a resembling derivative without *ortho* ogygen substitution, it was necessary to look for an alternative solution. Another compound class exhibiting axial chirality are 2,2',6,6' tetrasubstituted biphenyls. In some cases when the substituents are large enough, these systems are also rotation restricted and therefore, they possibly exist in two enantiomeric forms. One of such systems which are easily accessible is bimesityl (**123**). Unsubstituted bimesityl can be prepared either by a Scholl reaction of mesitylene[45] or Ullmann coupling of 2,4,6-trimethyliodobenzene.[46] Despite the lower yield, a Scholl reaction was applied because of the cheap starting materials mesitylene (**122**) and ferric chloride. The reaction went in a far worse yield (8 %) than described in the literature procedure which was followed. However, it could be conducted on large scales providing enough material for further studies. The amino groups were inserted, following a known literature protocol.[46] The nitration conditions were slightly changed by preparing explosive acetyl nitrate from fuming nitric acid and acetic anhydride rather than using it neat. The nitration worked in a good yield of 90 %, but the reduction only went in 64 % using zinc powder in an HCl, AcOH mixture. Other reducing procedures did also not increase the yield.



Scheme 44: Preparation of 3,3’-diaminobimesityl.

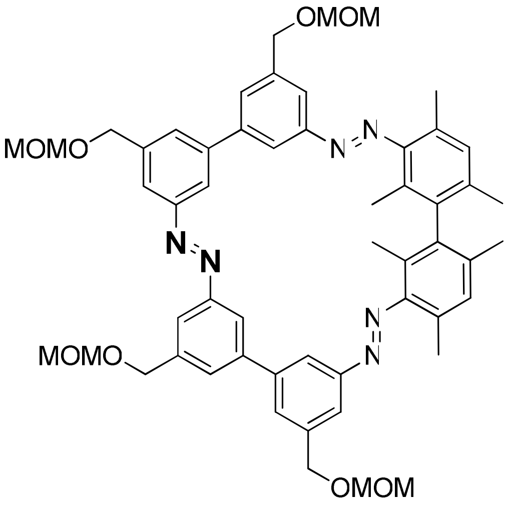
In the next step a chiral resolution of **125** had to done. A protocol of Moyer and Adams was applied, first converting the diamine to a diastereomeric salt with D-camphorsulfonic acid.[46] The two diastereomers could be separated by recrystallization from water. Because of the large solubility difference, two crystallizations were enough to get optical rotation values which only slightly deviated from literature. (+)-**125** ($[\alpha]^{20}_{D}$ = 42.1° [lit. 42.3°] was the enantiomer which showed a lower solubility in water and could be obtained as large crystals in slightly higher purity than (–)-**125** which was precipitated from the crystallization filtrate by basification with aqueous ammonia to obtain (–)-**125** ($[\alpha]^{20}_{D}$ = -41.5° [lit. -41.5°]). The crystals of (+)-**125** were redissolved in hot water and also basified with aqueous ammonia to precipitate diamine (+)-**125**. Bloch and coworkers determined the absolute configuration of the enantiomers and found that the stereoisomer with a positive rotation angle was the (*S*)-enantiomer and the one with the negative rotation angle was the (*R*)-enantiomer.[47] Both enantiomers as well as a racemic mixture of **125** were transformed in three steps to the corresponding macrocycle by the same strategy which was used in our previous syntheses. First a Mills coupling with MOM protected nitrosobenzene **106** was used to form the first two azobenzene bonds in 89 – 90 % yield. Then, Suzuki-Miyaura cross-coupling with MOM protected boronic ester **107** was done to create the biphenyls and yielded the diamine precursor. The oxidative macrocyclization with lead tetraacetate finally gave chiral macrocycle **127** in yields between 41 and 42 %. All steps of the synthesis worked with acceptable to good yields with convenient purification. The solubility of macrocycle **127** was very good in most solvents, probably due to introduction of the MOM groups. It should be mentioned that the rotation angles of the intermediates increased with their length and were the highest for macrocycle **127** with values of 2128 ° for (*S*)-**127** and – 2077 for (*R*)-**127**.



Scheme 45: Chiral resolution of 3,3'-diaminobimesityl (**125**) with D-CSA and total synthesis of chiral macrocycle **127**.

3.2.6.2 Photoisomerization experiments

Investigations on the photoisomerization of chiral macrocycle **127** were directly done by ^{1}H-NMR because a larger amount of information could be obtained. Unlike the fully substituted CTB **111** the chiral macrocycle **127** should show a larger number of isomers because the azobond between the biphenyls (bold letter) has a different chemical environment than the two azobonds adjacent to the bimesityl moiety. Theoretically there should be six possible *E*/*Z* isomers [(*E*,*E*,***E***), (*E*,*E*,***Z***), (*E*,*Z*,***E***), (*E*,*Z*,***Z***), (*Z*,*Z*,,***E***), (*Z*,*Z*,***Z***)] compared to only four in **111**. This made the assignment of the different isomers more complex. The aromatic signals were not suitable for this task. It was found that the methoxy signals of the MOM groups were the most convenient alternative to perform an easy assignment. All signals are singulets and there should not be more than four different signals per isomer. Furthermore, the fact that there are some symmetric isomers [(*E*,*E*,***E***), (*E*,*E*,***Z***), (*Z*,*Z*,***E***), (*Z*,*Z*,***Z***)] which should show only two signals and some unsymmetric isomers [(*E*,*Z*,***E***) and (*E*,*Z*,***Z***)] which should give four signals, could also allow further identification. After irradiation of **127** at a wavelength of 365 nm, 302 nm and with visible light, NMR measurements were done.



Scheme 46: Chiral macrocycle with highlighted azobond.

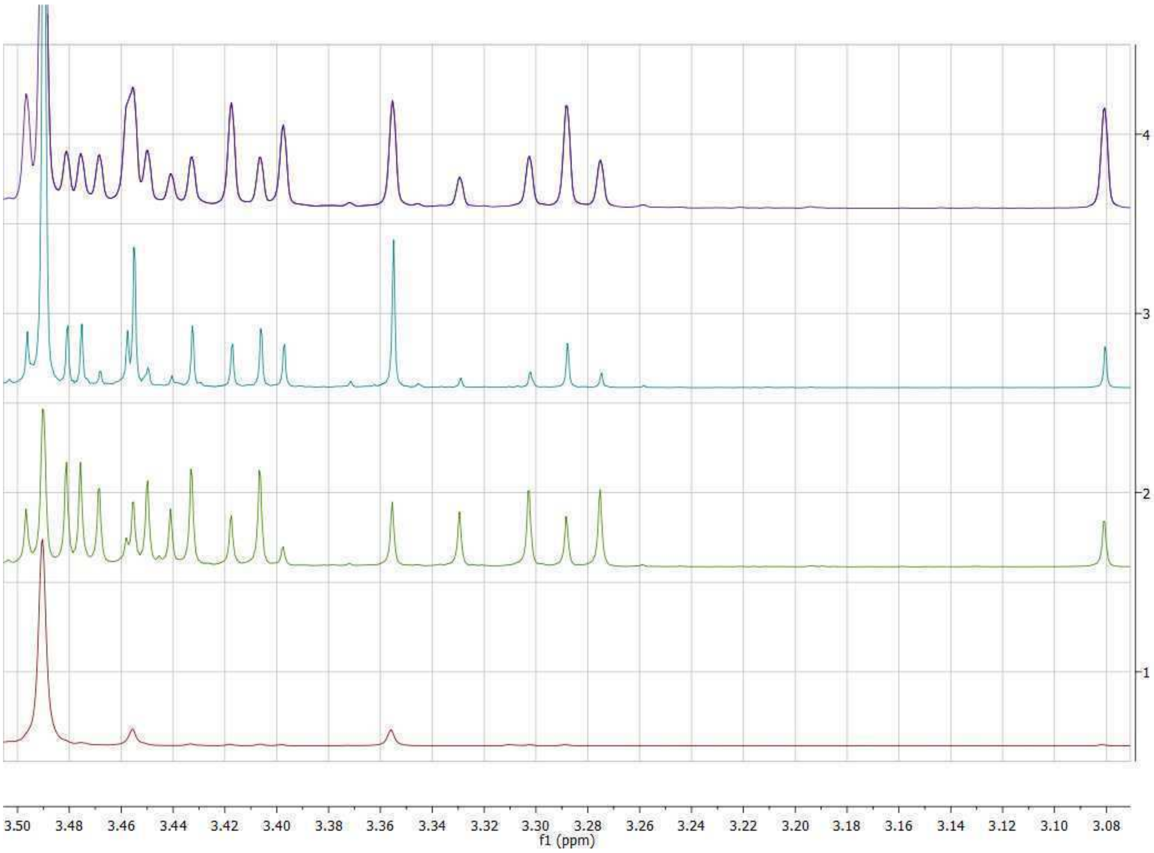


Figure 24: ^{1}H-NMR spectra of **127** before (red) and after irradiation (purple: 302 nm; blue: visible light; green: 365 nm.).

The region between 3.50 ppm and 3.08 ppm showed the methoxy groups of all different isomers. The all-*E* isomer at 3.49 ppm was the most abundant isomer before irradiation. Interestingly one mixed isomer was already present in the unirradiated sample. It should be mentioned that the spectrum of the unirradiated sample was obtained directly after macrocyclization. The ratios of this mixed isomer increased upon storing at sunlight. It could be assigned to the (*E,E,**Z***)-isomer since it only has two peaks and is therefore symmetric. The other isomers were assigned by comparing the integrals in the spectra. It was also assumed that the sample which was irradiated at 365 nm should have the highest proportion of *Z*-isomers whereas the sample irradiated with visible light should consist of mainly *E* isomers. Interestingly, it was found that there were not six but seven different isomers which could be assigned. All symmetric isomers could be assigned, but three instead of two unsymmetric isomers were seen. It is assumed that one of the isomers is a conformer of the (*Z,E,**E***)-isomer, since it is more abundant in the sample irradiated with visible light than the species with two *Z*-azobonds. However, it is possible that it could also be a conformer of the (*E,Z,**Z***)-isomer.

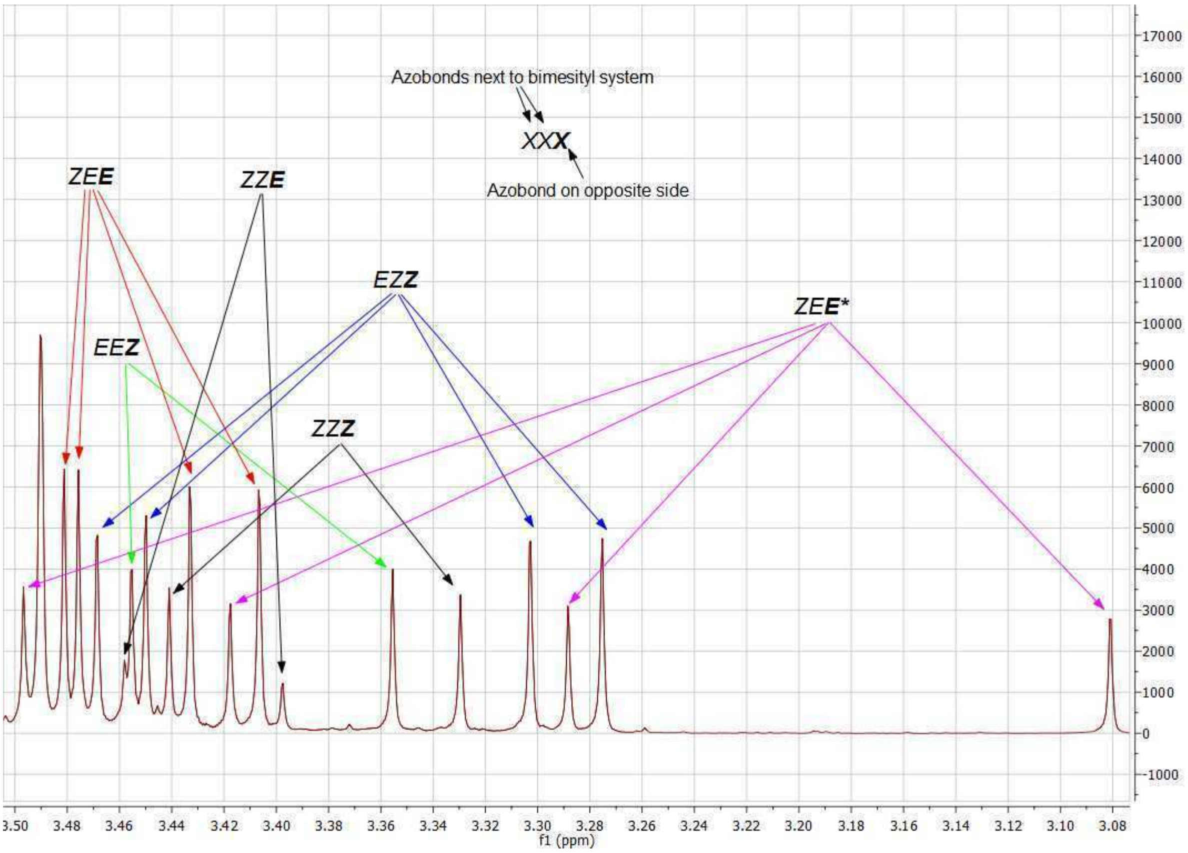


Figure 25: ^{1}H-NMR spectrum of **127** after irradiation at 365 nm with assignment of different *E*/*Z*-isomers.

Looking at the isomer ratios after irradiation at different wavelength, it is seen that the isomerization seems to be less complete than in the case for macrocycle **127**. Especially the all-*Z*-isomer is only obtained in small amounts. Even after irradiation at 365 nm it does not surpass the all-*E* isomer. Another surprising fact is that the symmetric (*Z*,*Z*,***E***)-isomer always seems to be lower in concentration than the unsymmetric (*E*,*Z*,***Z***)-isomer. This points to the conclusion that macrocycle **127** is probably more strained than the previous macrocycles because of the restricted rotation around the bimesityl bond.

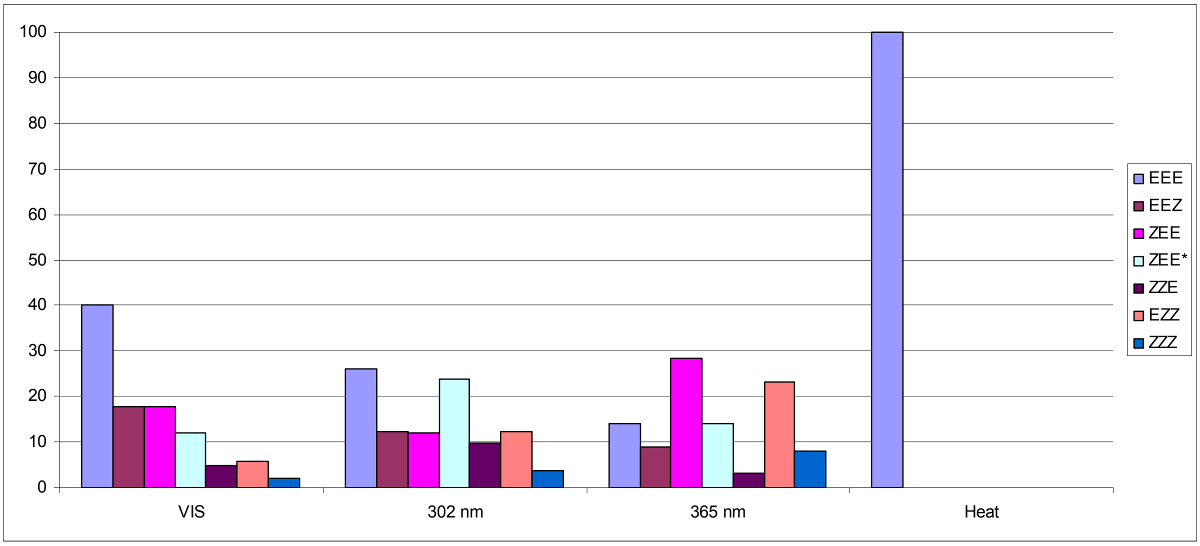


Figure 26: Isomer ratio of **127** at PSS after irradiation with different light sources and after heating.

3.2.6.3 UV-VIS spectroscopy and CD spectroscopy

Additionally to the isomerization studies by ^{1}H-NMR, absorption spectra were also measured while irradiating with 365 nm UV-light. The spectra of the chiral macrocycle **127** and MOM-CTB **111** resemble each other and show the same absorption maxima for the $\sigma \rightarrow \pi^*$ transition as well as the $\pi \rightarrow \pi^*$ transition. The band of the $n \rightarrow \pi^*$ transition is stronger in macrocycle **127**. When the sample is irradiated the spectrum shows the typical changes which signify isomerization. The peak at 326 nm decreases in intensity and the band at 444 nm increases. A hypsochromic shift is also observed for the $n \rightarrow \pi^*$ transition. A new phenomenon in this macrocycle is the occurrence of two peaks in the region below 280 nm. A decrease and hypsochromic shift of the $\sigma \rightarrow \pi^*$ transition was already observed for macrocycle **111** but in this case a second peak can be seen at 270 nm.

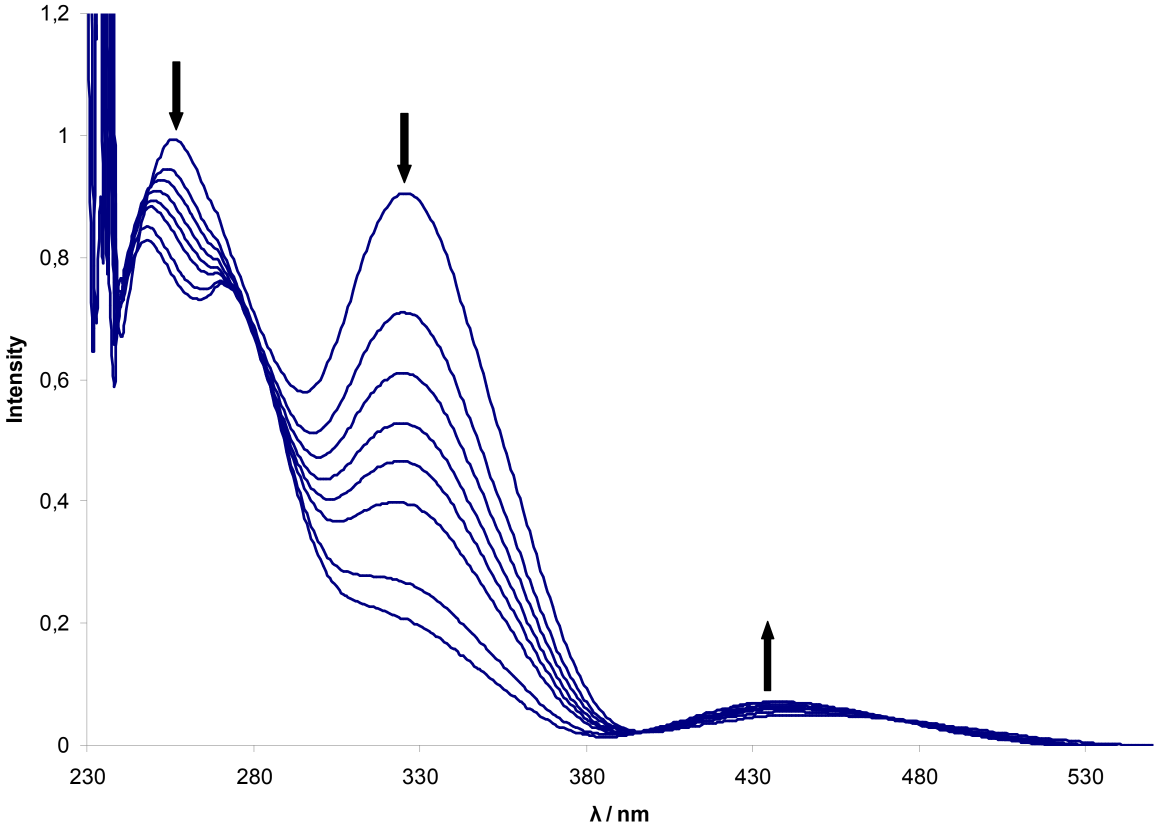


Figure 27: Absorption measurements of chiral macrocycle **127** and change upon irradiation with UV-light of 365 nm wavelength (c = $2*10^{-5}$ mol*l^{-1}).

The circular dichroism (CD) spectrum of both enantiomers of chiral CTB derivative **127** was measured in chloroform. To ensure that the pure all-*E* isomer was measured, the sample was heated at 45 °C over night. The spectra show the expected mirror image of the (*R*)-**127** and the (*S*)-enantiomer with no circular dichroism for the racemic mixture. There are four bands. For the (*S*)-enantiomer a large positive circular dichroism is observed at 460 nm. At 380 nm a minimum is seen until the second positive peak at 358 nm occurs. The values become negative below 345 nm and two additional bands with negative values can be observed at 323 nm and 246 nm. The CD sample of (*S*)-**127** was irradiated with light of different wavelength, like in the case for macrocycle **127**. The large band at 460 nm and the two smaller bands at 380 and 323 nm decrease in all cases. The lowest value is observed after irradiation at 365 nm. One noteworthy feature which is observed after irradiation is the splitting of the absorption at 246 nm into two distinguished peaks like it has already been seen in the UV-spectrum. The peak at lower wavelength is not as informative in this regard, since it does not change much during irradiation. However, the peak at around 275 nm reacts differently according to the irradiation wavelength.

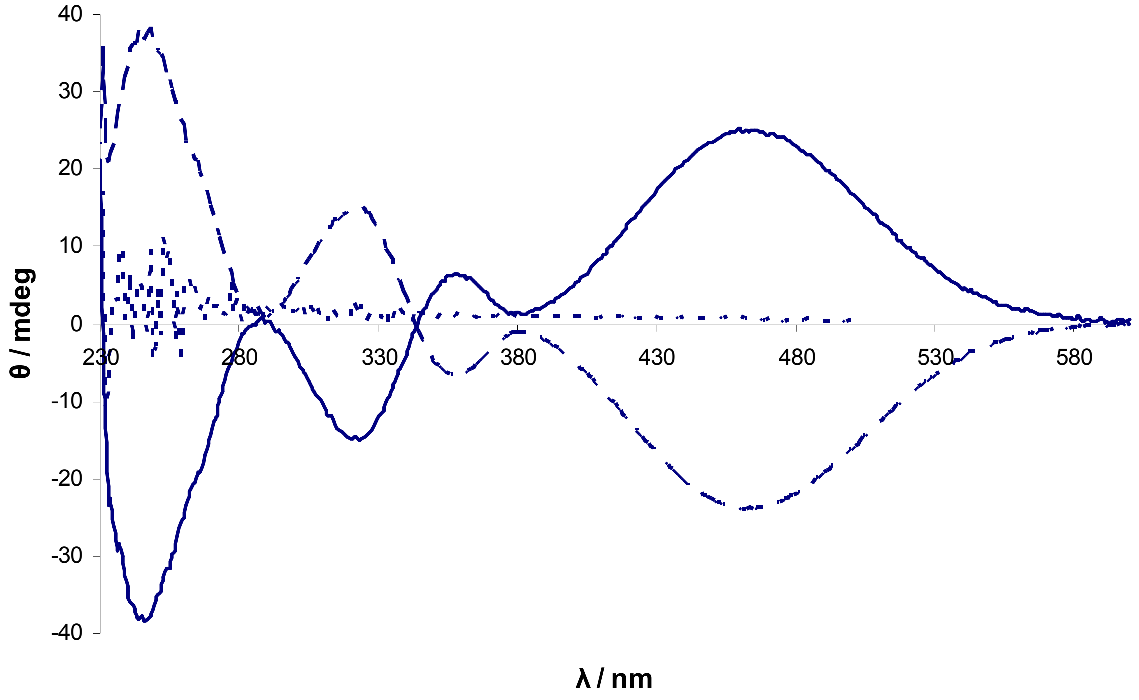


Figure 28: CD-spectra of both enantiomers of **127** and the racemic mixture. [(*S*)-**127**: straight line; (*R*)-**127**: dashed line; rac-**127**: dotted line] (c = 5.9*10^{-5} mol*l^{-1}).

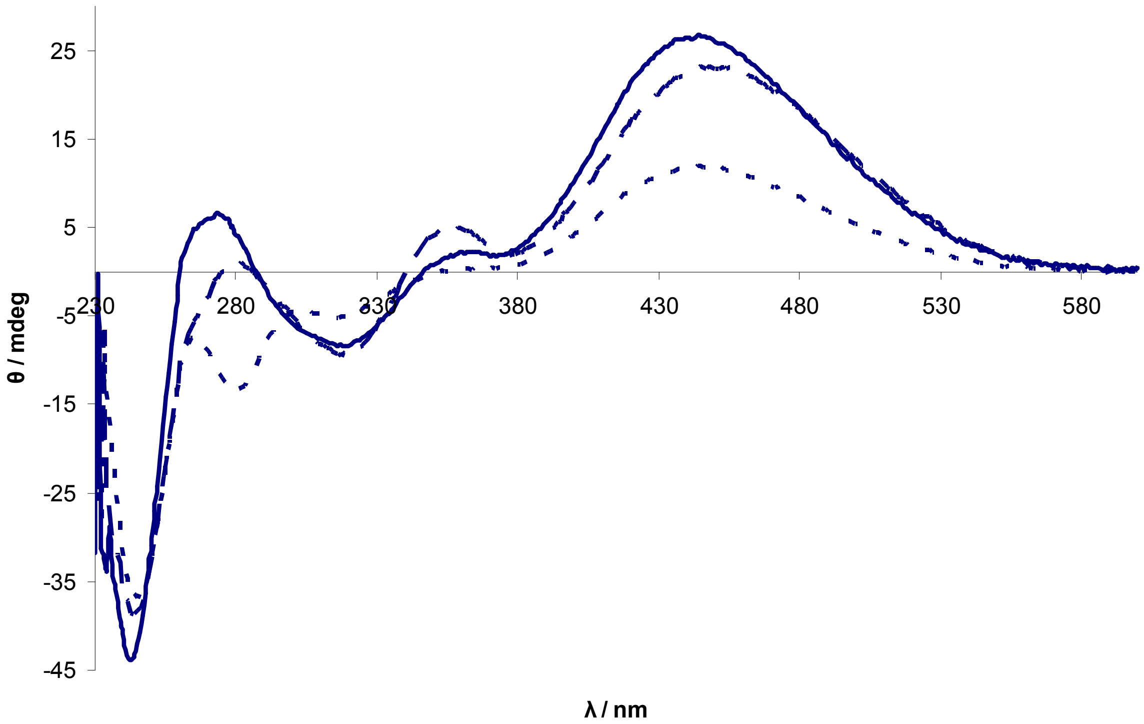


Figure 29: CD-spectra of (*S*)-**127** after irradiation with light of different wavelength. [302 nm: straight line; visible light: dashed line; 365 nm: dotted line] (c = 5.9*10^{-5} mol*l^{-1}).

The value at this specific wavelengths changes between positive, negative and zero. After irradiation at 365 nm the value at 275 nm is negative like in the non irradiated sample and has a value of around -12 mdeg. After irradiation at 302 nm it inverts to positive values of around 6 mdeg and irradiation with visible light affects an angle of almost 0 mdeg.

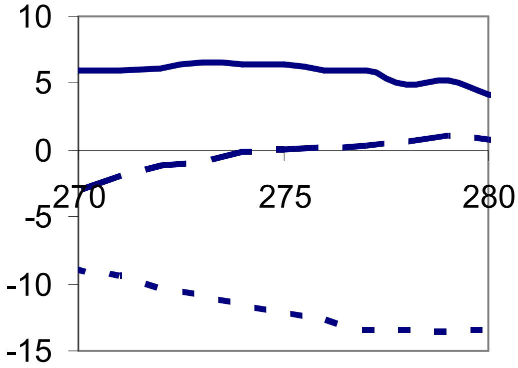


Figure 30: Zoom of the CD spectrum of different irradiated samples of (*S*)-**127** between 270 and 280 nm.

Eighteen switching cycles were performed, where the sample was irradiated at all three wavelengths randomly. After fifteen minutes the photostationary state was obtained and the switching was repeatable several times, obtaining the same results. This shows the reversibility of the switching between the three states.

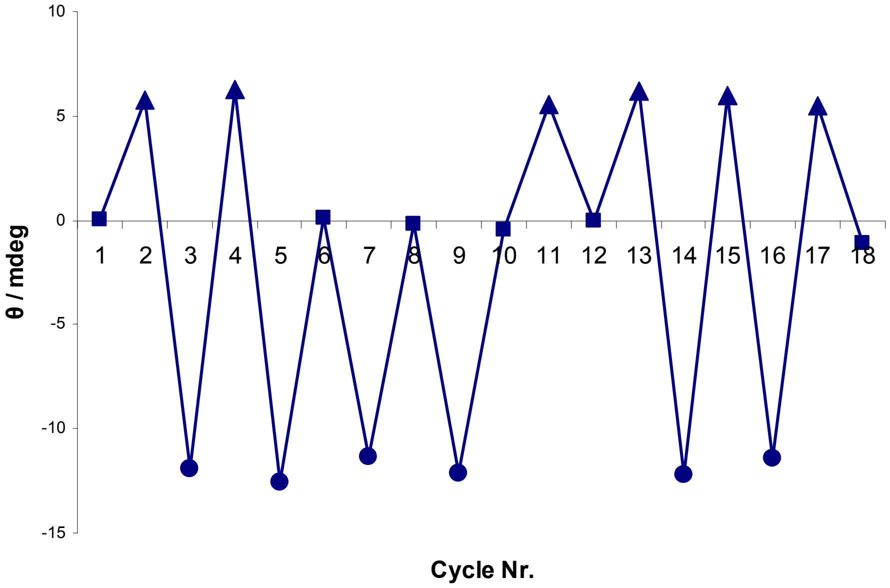


Figure 31: Different switching cycles of (*S*)-**127** with three light sources (302 nm ▲, 365 nm ● and vis ■).

This observation opens the possibility of a ternary switch with three possibilities +, - and 0. Although the photostationary states do always contain a mixture of many different isomers, the ratio of them differs enough that it results in a large change in circular dichroism takes place. In comparison to UV spectroscopy, where only a change in absorption is seen which can be different depending on the irradiation wavelength, in the case of circular dichroism, a change in sign or a diminishing to almost 0 mdeg can be observed. Such a ternary switch could be interesting for optical storage. Yet, it was already shown for previous examples that the CTB macrocycles do not show a notably higher lifetime than linear azobenzenes, and so the PSS probably did not have a good thermal stability.

To measure the thermal stability of the different irradiated samples, they were stored at 4 °C and a CD spectrum was measured after several days. For every sample a decrease of about 2 – 3 mdeg was observed after storing them in the dark for four days.

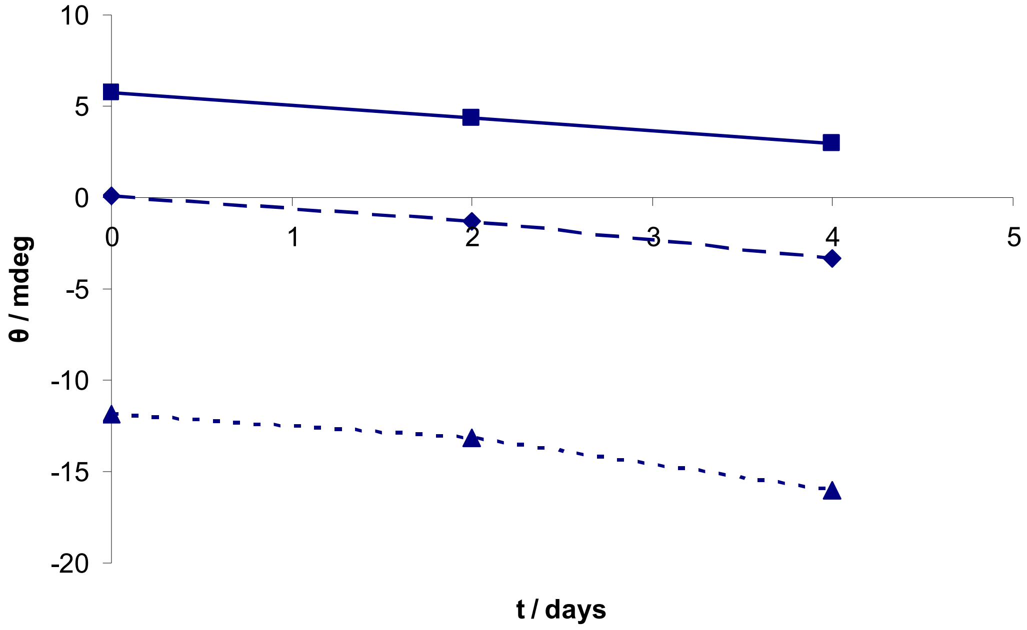


Figure 32: Effect of thermal $Z \rightarrow E$ isomerization on circular dichroism of the three irradiated samples.

3.2.7 Alkine funtionalized CTB macrocycles for click chemistry

The two mayor functionalities of the CTB macrocycles which were investigated so far were the stacking behaviour of the ester substituted derivatives as well as the geometrical change from a flat structure in the all-*E* isomer to a cone like structure in the all-*Z* isomer. One application of our macrocycles which was already investigated is their liquid crystalline behaviour, caused by stacking. The reversible stacking of CTBs could be used to reversibly build molecular networks, which would disintregrate upon irradiation.

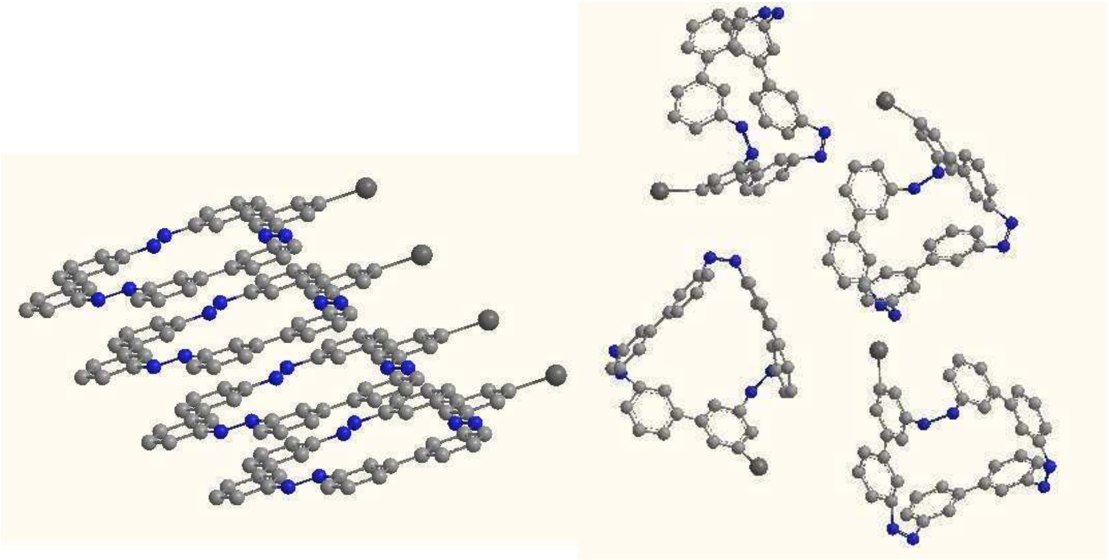
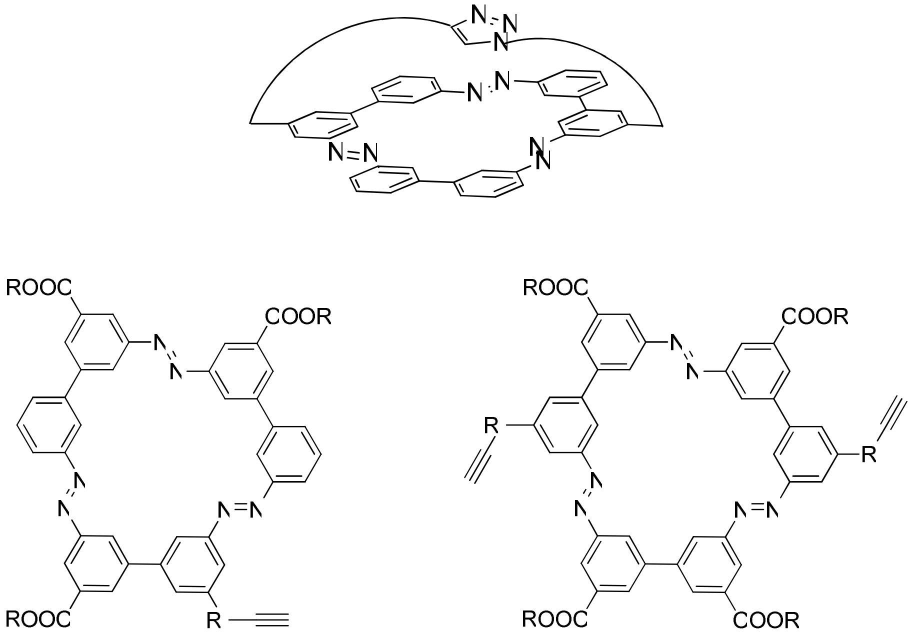


Figure 33: Comparison of stacked all-*E* macrocycle with side groups aligned through stacking interactions against non stacked all-*Z* macrocycle with randomly distributed side groups.

Switching of the macrocycles in their LC phase and a resulting phase transition to an isotropic phase has not been achieved. For other applications it was necessary to attach substituents to the macrocycle to gain a function. Therefore a CTB would have to be prepared with side groups that would enable the attachment of various molecules. Previous experiments in which the transesterification of the butyl ester substituted CTBs with Brønsted and Lewis acid catalysis was tried did all fail. This lead to the conclusion, that functionalization of the macrocycles needed an efficient transformation with a large driving force. Probably the most widely applied click reaction which is also applied in many biological transformation because of its convenience due to the high yield and selectivity is the Cu(I) catalyzed [2+3]-cycloaddition of alkines with azides to triazoles.[48] Due to its reliability, compatibility with many different reaction media and easy purification this process has gained much interest especially in the field of chemical biology.

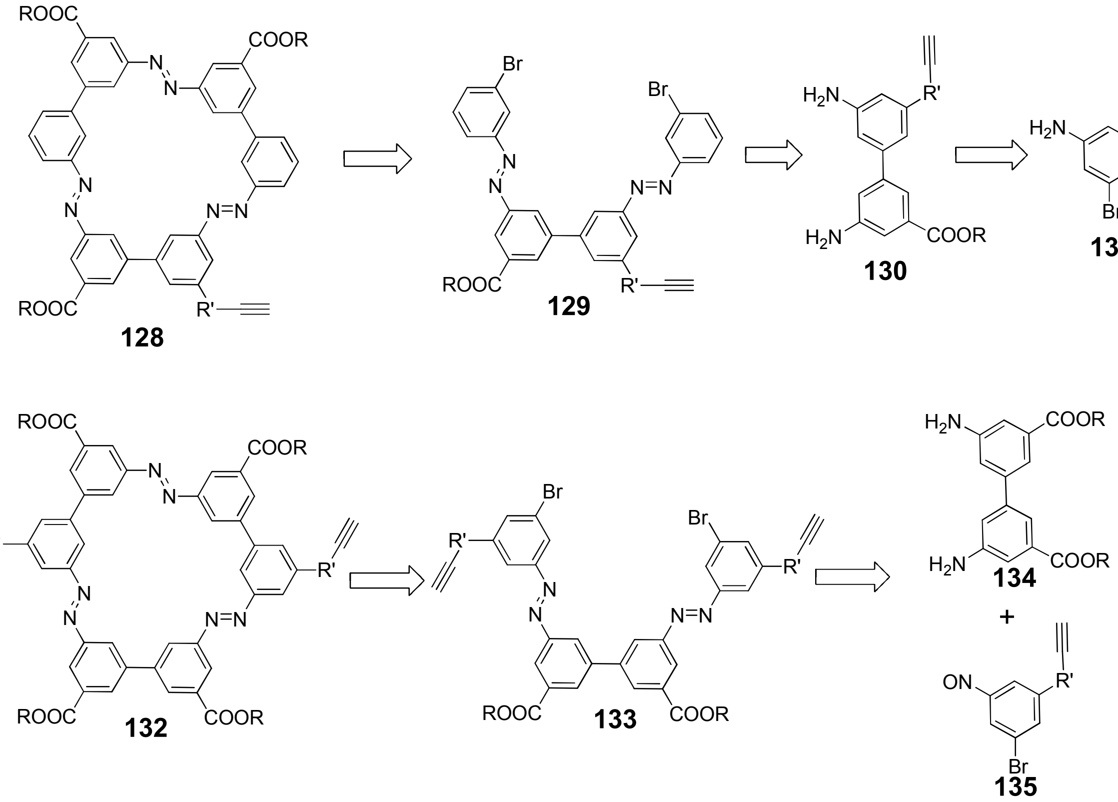
A second interesting objective which could be achieved by a click approach would be the synthesis of a molecular cage. The reversible complexation of host molecules has not lead to good results for the previously prepared macrocycles. The connection of two ends of CTB with a molecular tether could enhance the complexation behaviour of the macrocycles. For these reasons two macrocycles should be prepared, one substituted with one alkine chain and one with two alkine chains.



Scheme 47: Molecular CTB cage and monoalkine substituted and dialkine substituted CTB.

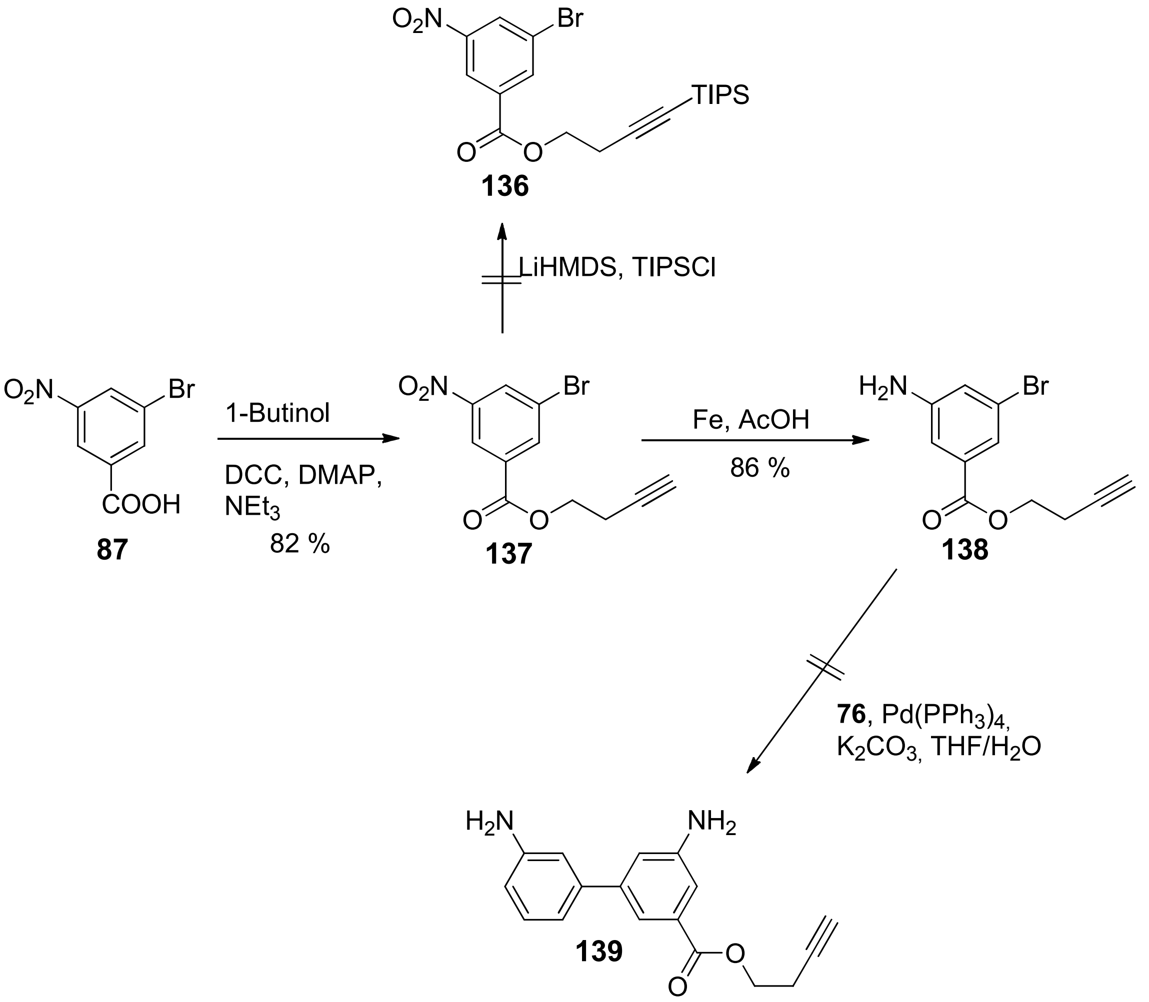
3.2.7.1 Synthesis of alkine functionalized CTB macrocycles

A rethrosynthetic approach for the two macrocycles was done, using the same synthetic transformations. However, the introduction of the alkine functionalized building block had to be performed at different stages. In the strategy for the mono functionalized CTB **128**, the building block would be introduced in the first Suzuki-Miyaura cross-coupling reaction, since in both following reactions two units are introduced at once. For the synthesis of the double functionalized CTB **132** the building block would have to be introduced at the stage of Mills coupling, which would be the only way to get the alkine groups on opposite sites of the macrocycle. Introduction in either one of the Suzuki-Miyaura cross-coupling reactions would place them in close vicinity. Therefore, the building block would have to be introduced as a nitroso compound, which could become a problem since the synthesis of nitroso compounds has been one of the most unreliable reactions so far concerning different substitution.



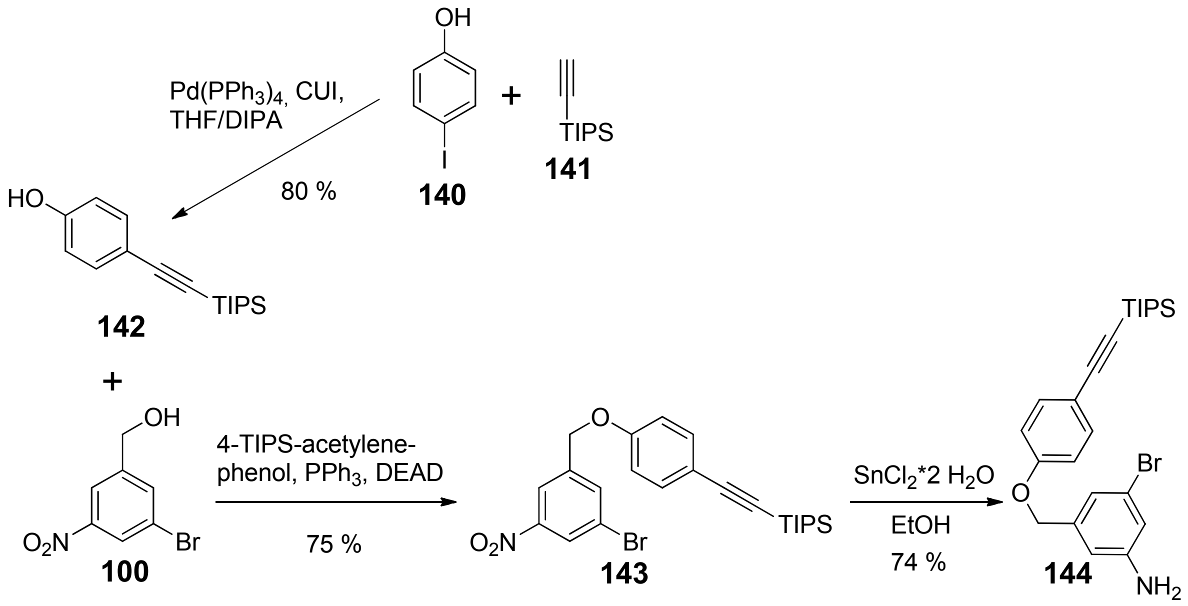
Scheme 48: Rethrosynthetic approach of mono- and difunctionalized alkine macrocycle.

The first approaches centered on the introduction of a terminal alkine building block by an ester coupling of 3-bromo-5-nitrobenzoic acid (**87**) with 3-butin-1-ol with DCC and DMAP catalysis. The reaction worked in a good yield of 82 %. After that, the nitro group was reduced with a Béchamp reaction to give the amine **138** in 86 % yield, which was subjected to Suzuki coupling. The Suzuki coupling however did not proceed as expected. Probably the triple bond is somehow interfering with the palladium catalyst leading to side reactions. A sterically hindered silyl group should be able to suppress the interference of the triple bond in Suzuki reactions. For that reason an experiment was conducted to protect compound **137** with a TIPS group, by deprotonation with LiHMDS followed by quenching with TIPSCl.[49] Unfortunately, the reaction did not yield the desired compound.



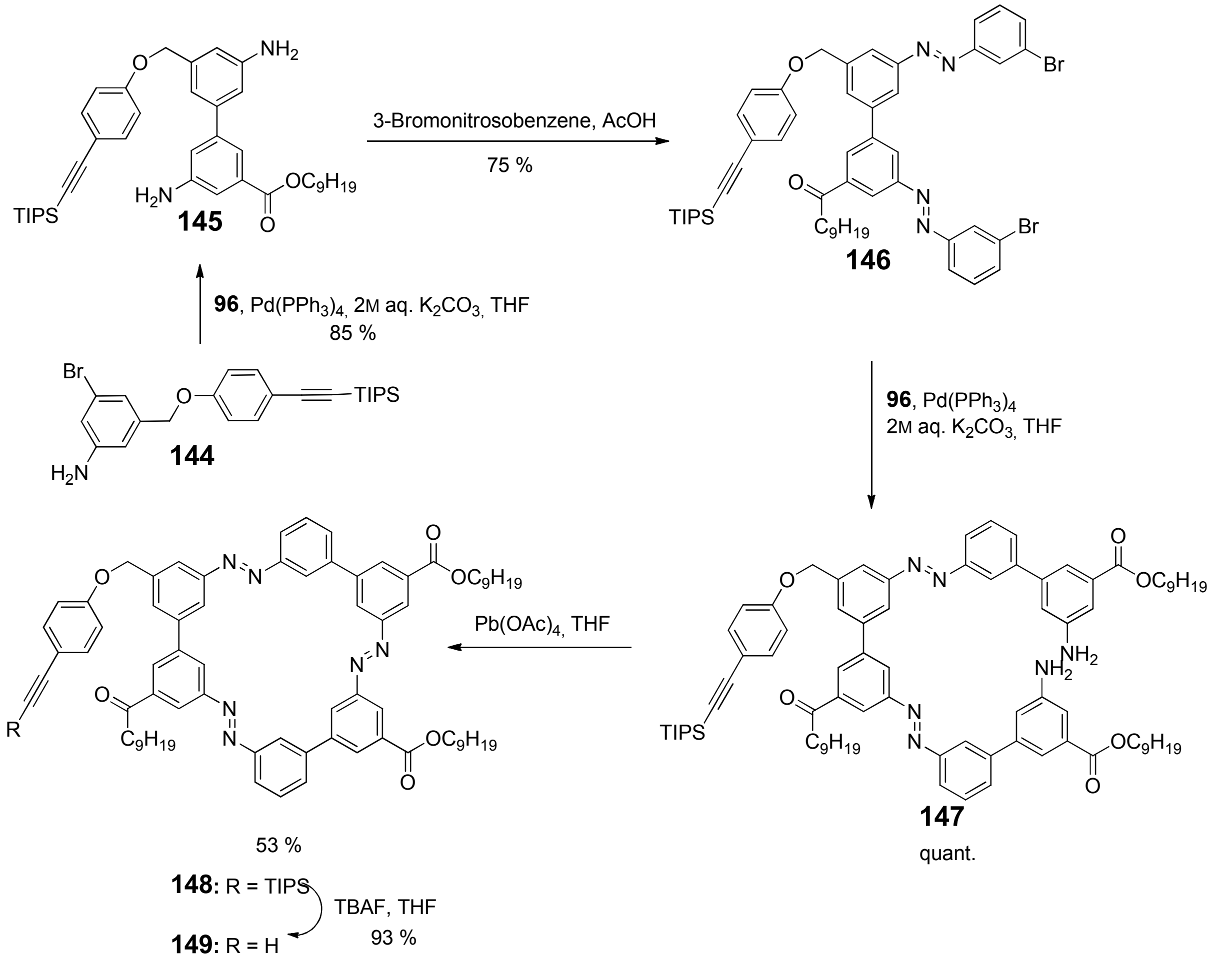
Scheme 49: First approaches towards the introduction of a triple bond substituted building block.

For the next approach the alkine was introduced into benzylic alcohol **100**. This transformation should be done by Mitsunobu reaction of the benzylic alcohol **100** with 4-TIPS-acetylene substituted phenol **142**,[50] which could be prepared by Sonogashira reaction of 4-iodophenol (**140**) with TIPS-acetylene (**141**).[51] This strategy had two main advantages. First, no protection had to be done, and secondly the building block probably had a higher chance to be converted to the corresponding nitrosobenzene than one with an ester group, which already gave problems in the oxidation to the nitroso compound. The Sonogashira reaction went well in 80 % yield, using $Pd(PPh_3)_4$ and CuI as the catalyst system in a THF/diisopropylamine solvent mixture. The obtained phenol **142** was then either coupled with 3-amino-5-bromobenzoic alcohol or with 3-nitro-5-bromobenzoic alcohol (**100**). The reaction with compound **100** went in better yields with 75 %. The amino group is probably interfering in the reaction as a competing nucleophile. After reduction of the nitro group to the amine with tin dichloride dihydrate, which went in a yield of 74 %, alkine building block **144** was obtained.



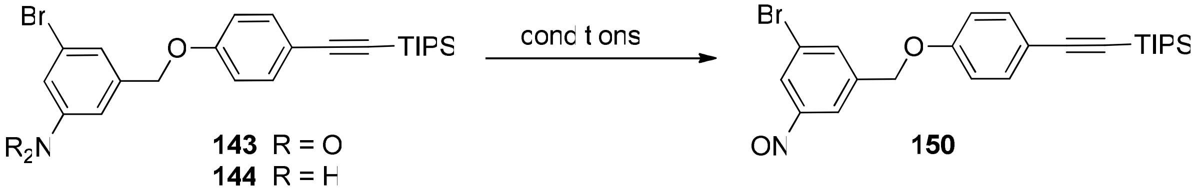
Scheme 50: Synthesis of alkine building block **144**.

The newly prepared building block **144** was then reacted with boronic ester **96** to yield biphenyl **145** now in a very good yield of 85 %. This showed that the triple bond was indeed the cause for side reactions which were now prevented by the introduction of the TIPS protecting group. Mills reaction with nitroso compound **77** yielded dibromide **146** in 75 % yield. The next Suzuki-Miyaura cross-coupling reaction gave diamine **147**, which could again not be obtained as a pure compound but was subjected to oxidative macrocyclization anyway. The obtained CTB was still protected at the alkine. Deprotection was done with TBAF in THF.[52] The reaction was very selective and the pure product could just be precipitated by quenching the reaction with saturated aqueous bicarbonate solution.



Scheme 51: Synthesis of mono alkine substituted CTB macrocycle **149**.

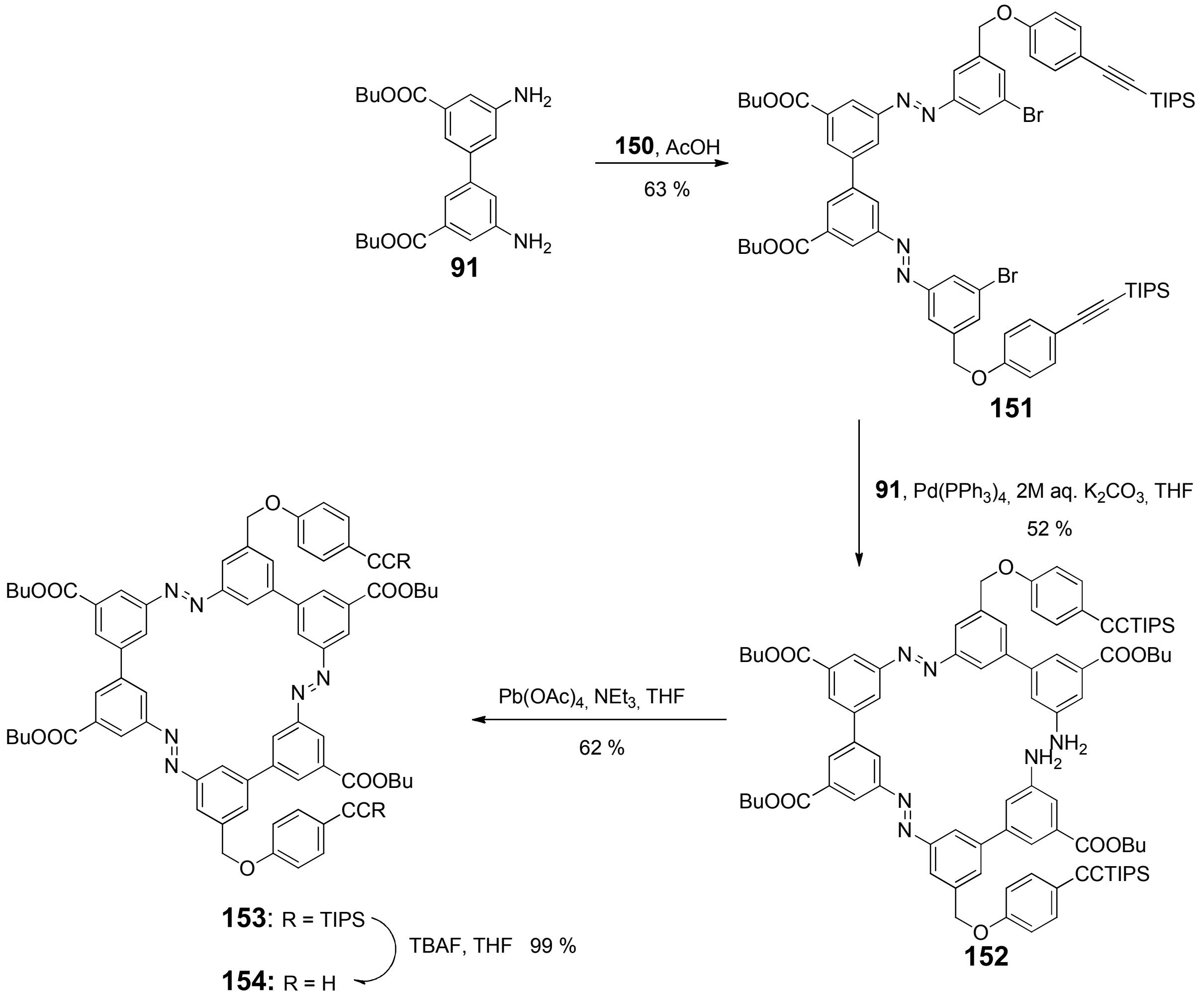
As it was already mentioned in the discussion of the rethrosynthetic approach, the nitrosoderivative of building block **144** had to be prepared for the synthesis of the difunctionalized CTB derivative. The most applied reaction in this thesis for the preparation of nitrosobenzenes was oxidation of aniline **144** by Oxone® in a biphasic system of DCM and water. Yet, an experiment on compound **144** did not show any transformation to the nitroso derivative even after prolonged reaction times. It was already seen that for too apolar substrates like aniline **144** this method was not very efficient, probably, because the transport between the two phases is too slow. However, there were two additional procedures which could be applied in the synthesis of nitrosobenzenes. One was the reduction of a nitrobenzene to a hydroxylamine with subsequent reoxidation to the nitrosobenzene with ferric chloride. This procedure was successfully used for 2-acetaminonitrosobenzene (**57a**). Unfortunately, the nitrosobenzene was not accessible by this method because treatment of nitrobenzene **143** with zinc only lead to overreduction to the amine. The last method which was available employed *m*CPBA to oxidize amine **144**.[53] When the reaction was done in DCM, it only led to a low yield of 8 %. When the solvent was changed to EtOAc the reaction proceeded much better in an acceptable yield of 47 %. The oxidation turned out to be the key step in this total synthesis. All following steps proceeded like expected in good yields and produced macrocycle **153** with two terminal alkines on opposite sites in an overall yield of 9 %.



Scheme 52: oxidation to nitroso benzene **150**.

Table 4: different conditions applied for the oxidation of **144**

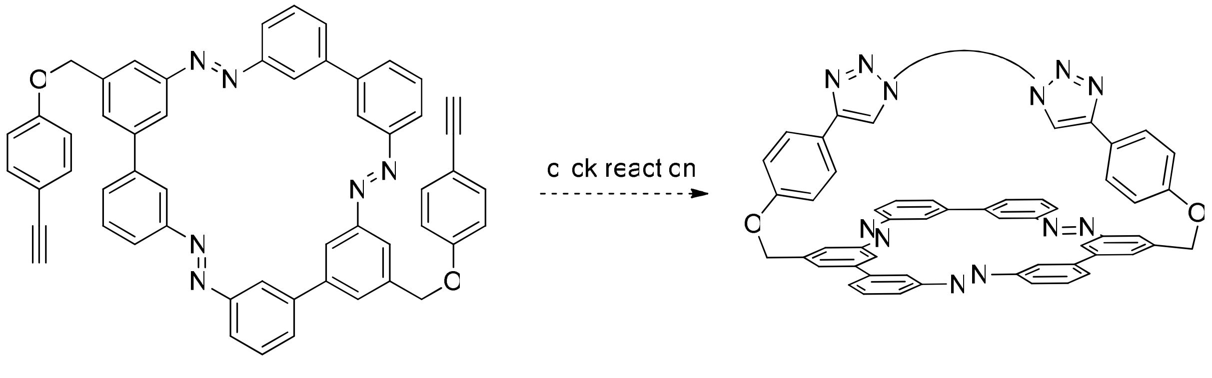
Entry	Conditions	Yield
A	Oxone®, DCM/H_2O	no reaction
B	1. Zn, 2-Methoxyethanol 2. $FeCl_3$, H_2O	overreduction to amine
C	*m*CPBA, DCM	8%
D	*m*CPBA, EtOAc	42%



Scheme 53: Synthesis of dialkine substituted CTB macrocycle **154**.

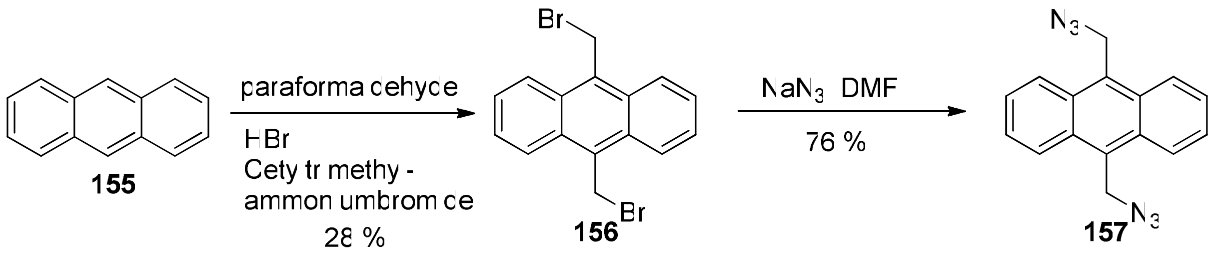
3.2.7.2 Approaches towards a molecular cage

With CTB derivative **153** in hand, experiments for the synthesis of a molecular cage were conducted. Yet, a suitable diazide as the tether still had to be found. Two factors were important for the design of the tether. First, the length of it should neither be too small nor to large, so the intramolecular reaction could take place. Second, the tether should be able to hold a molecule inside the cavity, either by a sterical blockade or by coordination to the guest.



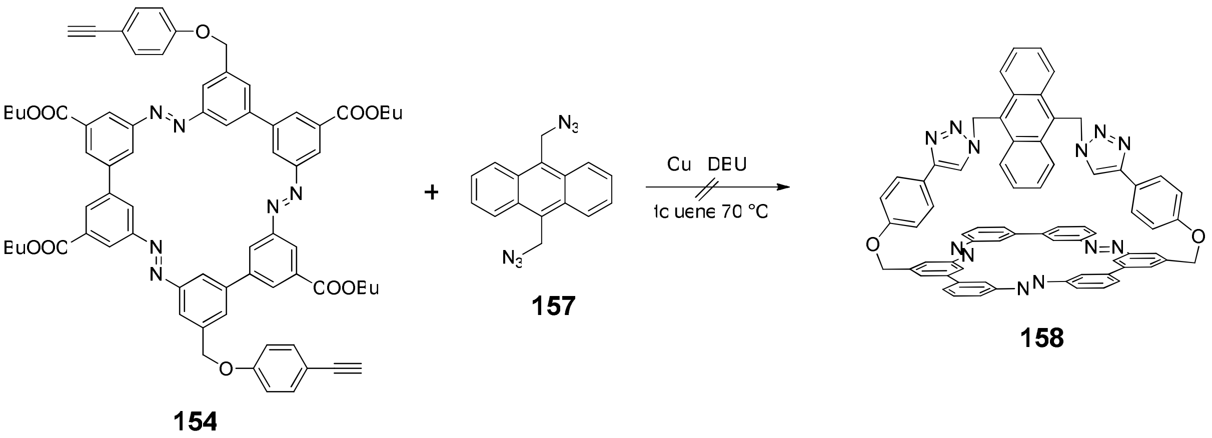
Scheme 54: Envisioned cycloaddition reaction to build up a molecular cage.

The first diazide which was considered was 9-10-(diazidomethyl)-anthracene (**157**). Even though the length of the molecule was quite short, the anthracene core would be able to block the sides of the cavity. Also, the synthesis of this diazide was straight forward in two steps from anthracene by first introducing a bromomethyl group. This was done in one pot by the treatment of anthracene with paraformaldehyde and hydrobromic acid.[54] Thereby, first a Friedel-Crafts-type reaction should take place where anthracene (**155**) attacks formaldehyde to produce a benzylic alcohol, which is then substituted by a bromide. The dibromide **156** can then be substituted with sodium azide in DMF to get the diazide **157**.[55] The first reaction with a yield of only 28 % did not give quite the results which were obtained in the applied literature procedure. However, the substitution reaction worked fine, and the diazide was obtained in 76 % yield.



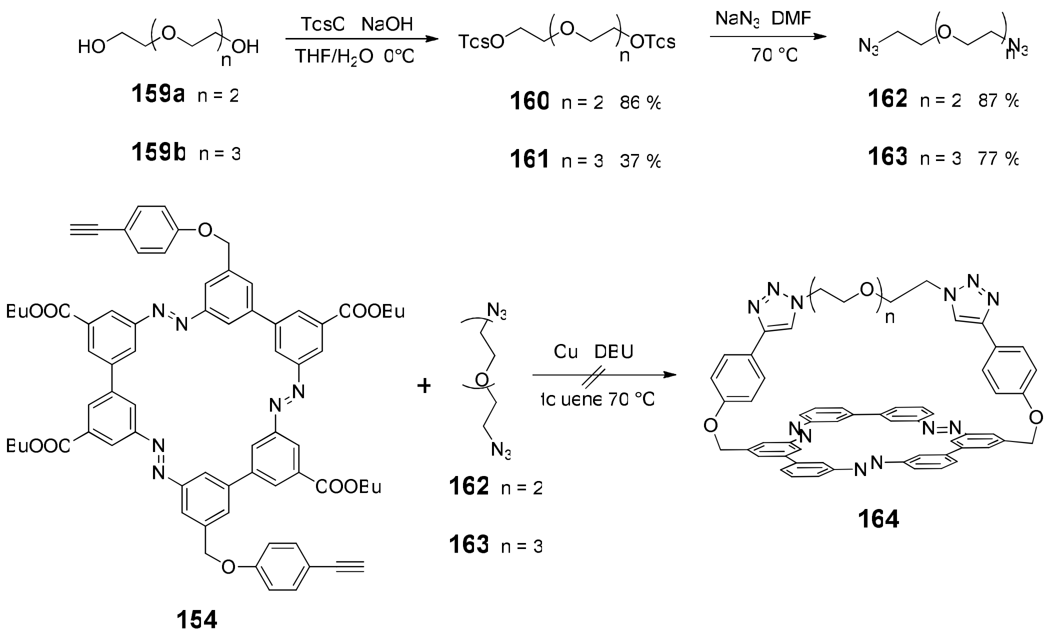
Scheme 55: Preparation of 9-10-(diazidomethyl)-anthracene (**157**) as the first envisaged tether for CTB **154**.

To favour an intramolecular reaction the click reaction was carried out under high dilution conditions with concentrations of 0.5 – 2.5 mM. Also an experiment was done in which the macrocycle was irradiated before the addition of the other reagents to facilitate isomerization. This was done to see if the *Z*-isomers had a molecular geometry which would favour the intramolecular reaction. The click reaction was done in toluene with CuI as the catalyst and DBU as a base to stabilized the Cu(I). After stirring over night the reaction was monitored by TLC and complete conversion had been achieved. Unfortunately, only polimerized products were observed and also by MALDI-MS of the crude product no traces of the cage compound could be observed. A reason for these negative results could lie in the structure of the diazide. It is quite small compared to the large CTB macrocycle and it is also very rigid. This could be a reason why only the intermolecular reaction seemed to have taken place.



Scheme 56: Failed synthesis of cage compound **158**.

Two other tethers were investigated alternatively to 9-10-(diazidomethyl)-anthracene (**157**). The tethers should be more flexible as well as longer than the previous one. The tethers which fulfilled these criteria quite well were oligoethyleneglycols. The flexibility is even larger than for normal alkyl chains because of the oxygen atoms and the length can be chosen by the number of ethyleneglycol units. The trimer **162** as well as the tetramer **163** were chosen as possible tethers which could fit the task. The preparation of the diazides was straight forward by first preparing the ditosylate with tosyl chloride under basic conditions and subsequent nucleophilic substitution with sodium azide. The yields of the trimer **162** were good with the tosylation yielding 81 % and the diazide formation in 82 % yield.[56] The tetramer **163** gave lower yields with 37 % for the tosylation and 77 % for the substitution to the diazide.[57] The click reaction was carried out, using the same conditions than for anthracene tether **157** with high dilution. In one reaction the macrocycle was irradiated before addition of the other reagents. However, the only reaction which could again be observed was intermolecular polimerization and again no cage compound was observed.



Scheme 57: Preparation of oligoethyleneglycol diazide tethers and attempted click reactions with dialkine functionalized CTB **154**.

3.2.7.3 Click reactions with mono functionalized CTB.

The click reactions with the difunctionalized CTB macrocycle towards a cage compound have not been successful, but the starting material was consumed in all cases. This finding lead to the question if the desired [2+3]-cycloaddition really occurred. For that reason it was decided to look for a click reaction with the macrocycle with only one terminal alkine function. Again a suitable azide reagent for this transformation had to be chosen. It was envisaged to combine the π-π-stacking interactions of the ester substituted macrocycles with a second moiety with strong intermolecular attracting forces to prepare a system which could self assemble in complex systems. The strongest intermolecular force, which is also used by nature to build up complex assemblies, is hydrogen bonding. One of the most impressing biopolymers where hydrogen bonding is a crucial feature is DNA and RNA. In those systems complementary nucleobases can detect each other through multiple hydrogen bonding and recognize each other selectively. The strongest binding is established between guanine and cytosine with three hydrogen bonds. Consequently, it was decided to prepare azide functionalized derivatives of those two nucleobases and couple them to the macrocycle by means of a click reaction.

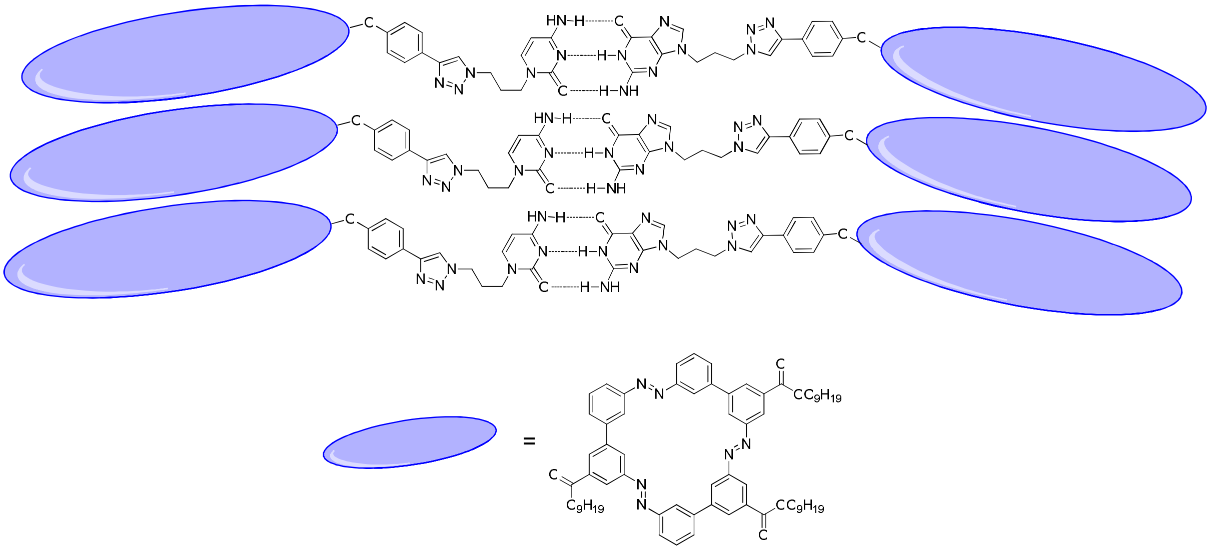
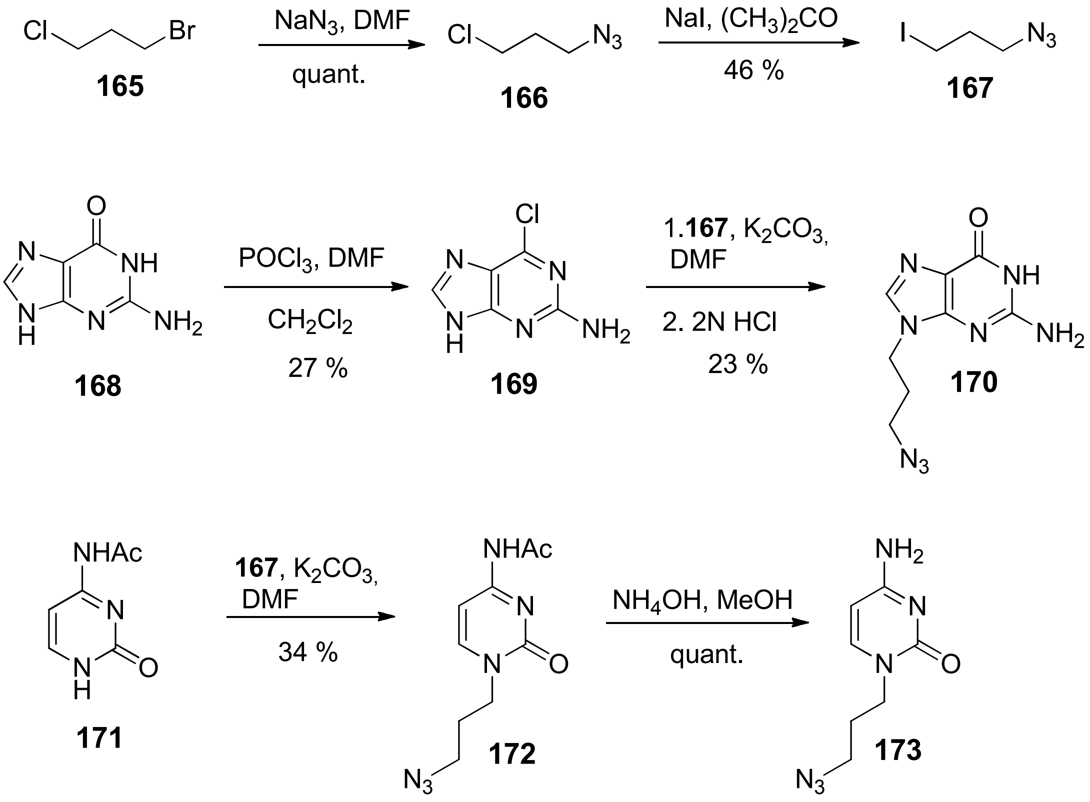


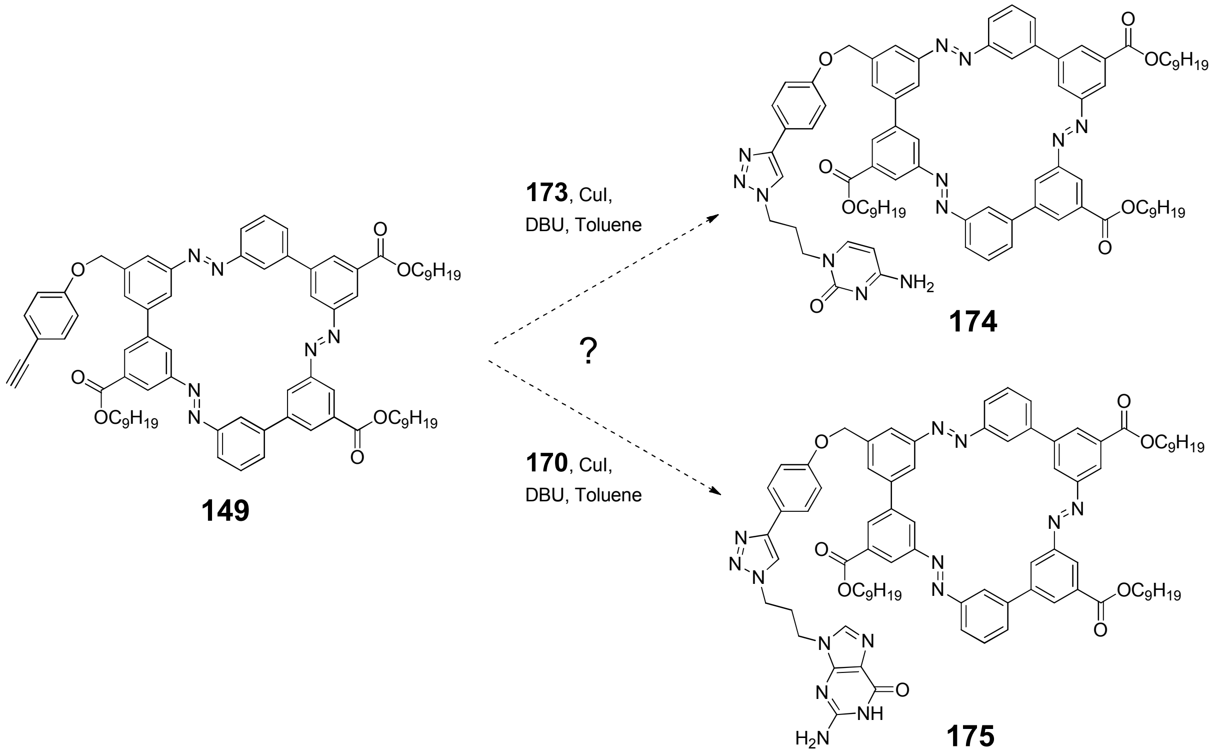
Figure 34: Envisaged mode of stacking in DNA. One "stack" could also contain different nucleobases.

After considering the synthetic feasibility and work which had already been done on azide functionalized nucleobases, it was chosen to attach an azidopropyl chain at the N1-position in each of the two nucleobases. At first, the azidopropyl unit to be incorporated into the nucleobases had to be synthesized. This task was done by converting 1-chloro-3-bromopropane (**165**) into 1-chloro-3-azidopropane (**166**) by reaction with one equivalent of sodium azide to selectively substitute the bromide, which is the better leaving group. Since the chloride was too unreactive towards nucleophilic substitution with a nucleobase, it had to be replaced by iodine to activate the C_3 unit towards nucleophilic substitution. This transformation was done by a Finkelstein reaction, exploiting the low solubility of sodium chloride in acetone as a driving force for the reaction.[58] The preparation of N1-(3-azidopropyl)-guanine (**170**) could be achieved in three steps. First, guanine (**168**) was treated with phosphoroxychloride to transform the carbonyl function into a chloride in an analogues way as a Vilsmeier-Haack-reaction.[59] The obtained 2-amino-6-chloropurine (**169**) was then reacted with molecule **167** in DMF to attach the azide functionality.[60] In the last step the chloride was again hydrolyzed to the amide to regain the guanine. Both steps only proceeded in low yields.



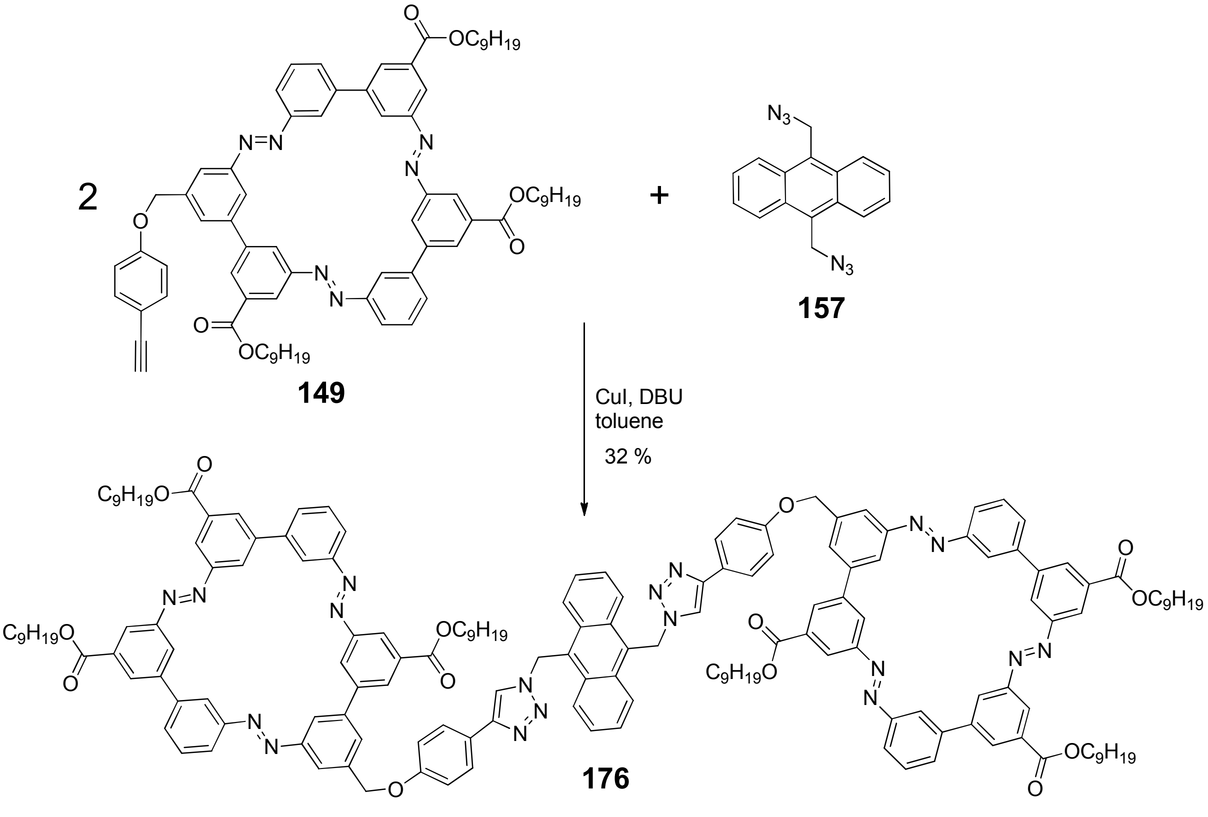
Scheme 58: Synthesis of the azido-nucleobases.

The synthesis of *N*-1-(3-Azidopropyl)-cytosine (**173**) was more straightforward and also literature known.[61] Commercially available N4-acetylcytosine (**171**) was reacted with compound (**167**) in DMF and in a second reaction the acetyl group was cleaved by treatment with aqueous ammonia to yield the target compound. Both functionalized nucleobases were subjected to click reactions with macrocycle **154**. In both cases an excess of the azido-nucleobases was used and a complete conversion of the macrocycle was achieved over night. Unfortunately, the products could not be purified, probably due to their amphiphilic structure with a hydrophobic core to which a very polar nucleobase is attached. In MALDI-MS measurements of both crude products the expected product masses could be observed. A clear peak at m/z = 1375 could be seen for the supposed cytosine macrocycle and a peak at m/z = 1415 for the guanosine macrocycle. However, the structure could not be confirmed by NMR spectroscopy. Both macrocycles showed such broadened signals that only in the cytosine case the characteristic peaks for the macrocycle part of the molecule could be seen but neither the cytosine functionality nor the triazole proton. In the guanine case the signals were broader which made an assignment even harder.



Scheme 59: Click reactions of macrocycle **154** with azido-nucleobases.

Despite the failed attempts to prepare a cage compound, another click reaction was done with 9-10-(diazidomethyl)-anthracene (**157**) and monofunctionalized macrocycle **149**. In this way two CTB macrocycles would be connected by an anthracene bridge. The reaction again proceeded with full conversion but this time the desired product was obtained and could be isolated in a purified yield of 32 %. The aromatic peaks of the dimeric macrocycle showed a significantly larger high field shift compared to the monomer. This could point to larger π-π-stacking in the dimer **176**.



Scheme 60: Preparation of dimeric macrocycle **176**.

Already before the workup of the reaction, it could be observed that the product formed a gel with the solvent. This behaviour to bind solvent molecules inside a gel was further explored with different solvents. The effect was only observed for aromatic solvents. At a concentration of 1.25 % (m/v) the formation of a gel could be observed for toluene and *ortho*-xylene. In other solvents like chloroform or methylene chloride this property was not observed. Also in THF no gelation took place. For the formation of the gel the molecule was first dissolved in the solvent and heated with a heat gun till all of the substance was dissolved. Afterwards, the solution was allowed to cool down to room temperature. The gel was stable for at least one day at room temperature. However, when the sample was irradiated with ultraviolet light at 365 nm the gel slowly liquefied and after three hours the solution had again obtained a liquid texture.

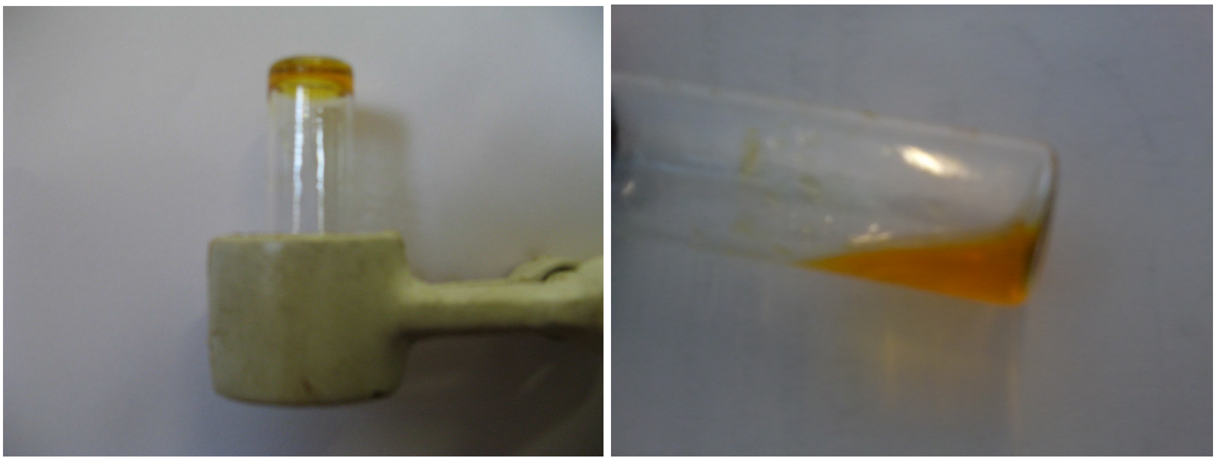


Figure 35: Solution of **176** in *o*-xylene [c = 1.25 % (m/v)]. Left: Gel before irradiation sticks at the top of a vial. Right: Solution after irradiation at 365 nm for 3 h. Gel disintegrates and solution flows again.

Several examples of switchable organogels already exist in literature.[62,63,64] To form a gel the molecules have to exhibit strong intermolecular interactions which can be based on different forces, mainly hydrogen bonding or Van-der-Waals interactions, to form networks. Furthermore, many solvent molecules have to be bound. In the case of molecule **176** there are 17000 molecules of *o*-xylene for one molecule of the dimacrocycle. It is hard to say which interactions are mainly responsible for the stacking behaviour. Since the compound has now a rather rod like structure and six long alkyl chains its Van-der-Waals interactions should be largely increased compared to monomer **149** which does not form gels. On the other hand, by π-π-stacking of two macrocycles instead of one these interactions are also increased and three dimensional networks could be formed. Most likely an interplay of multiple interactions is responsible for the gelation.

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4. Summary and Conclusion

An improved synthesis of cyclotrisazobenzene **52** was developed which provides the target molecule in up to 30 % yield in only three linear steps. Two additional derivatives of the azobenzenophane were prepared with a *tert*-butyl group **52b** and a bromide **52c**. The synthesis of a methoxy derivative was not successful because the oxidative cyclization did not lead to the macrocyclic product. Solid state structures of the *tert*-butyl derivative showed a different alignment of the molecules in the single crystal. Because of the bulky side groups the molecules do not align on top of each other but rather side by side. In isomerization studies using UV-VIS spectroscopy no photochromism could be observed. This finding was further confirmed in laser flash photolysis measurements. Complexes of cyclotrisazobenzene with triphenylcarbenium tetrafluoroborate were investigated by ^{1}H-NMR spectroscopy. However, no single crystals for X-ray crystallography could be obtained so far to further support this interaction.

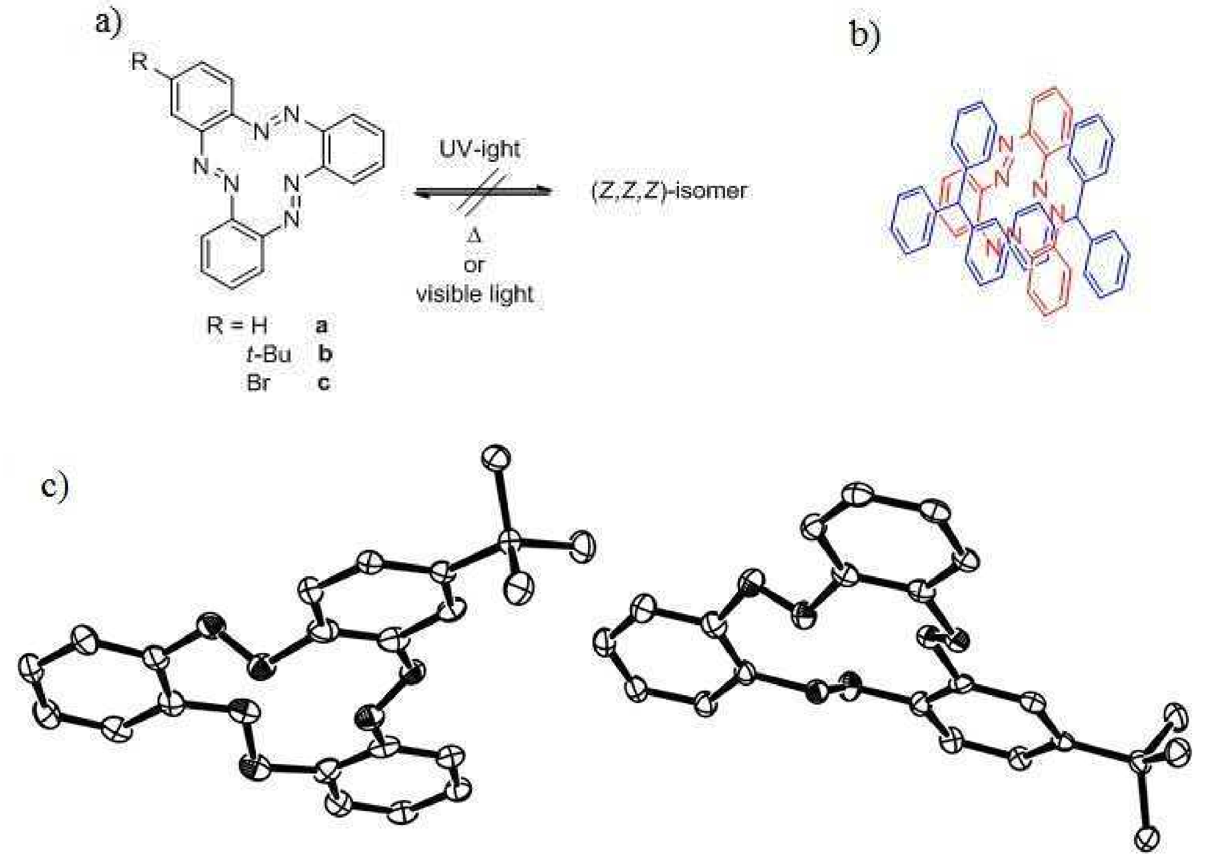


Figure 36: a) photochemical inertness, b) binding to triphenylcarbenium ions and c) solid structures of cyclotrisazobenzenes.

Cyclotrisazobiphenyls could be prepared by a Suzuki-Miyaura cross-coupling / Mills reaction approach, using a similar protocol as for **52** for the final oxidative cyclization key step with lead tetraacetate. Two derivatives of cyclotrisazobiphenyl **94** and **95** with butylester side groups were prepared. For these compounds π-π-stacking was observed in solution which was reversible upon irradiation. Both molecules showed liquid crystalline properties. A reversible switching of the liquid crystalline behaviour upon irradiation could not be achieved. Macrocycles with longer ester chains exhibited a lower melting point but did not show a liquid crystalline mesophase.

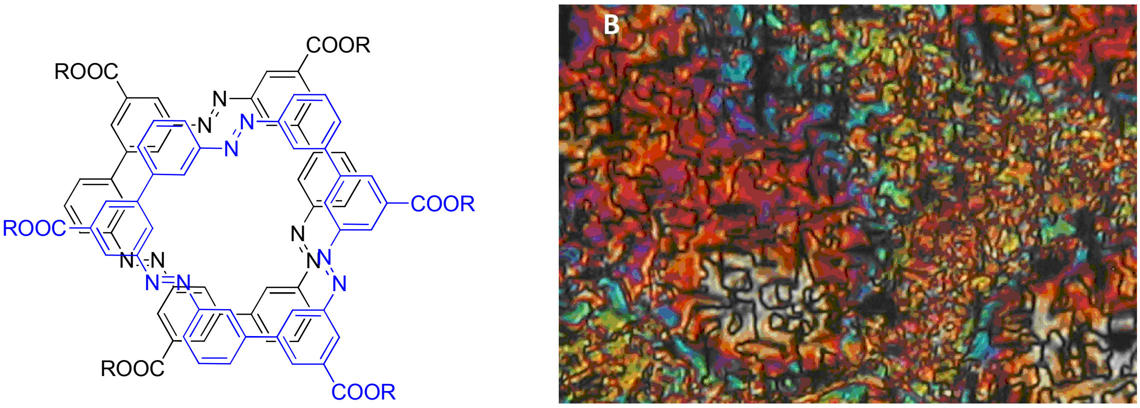
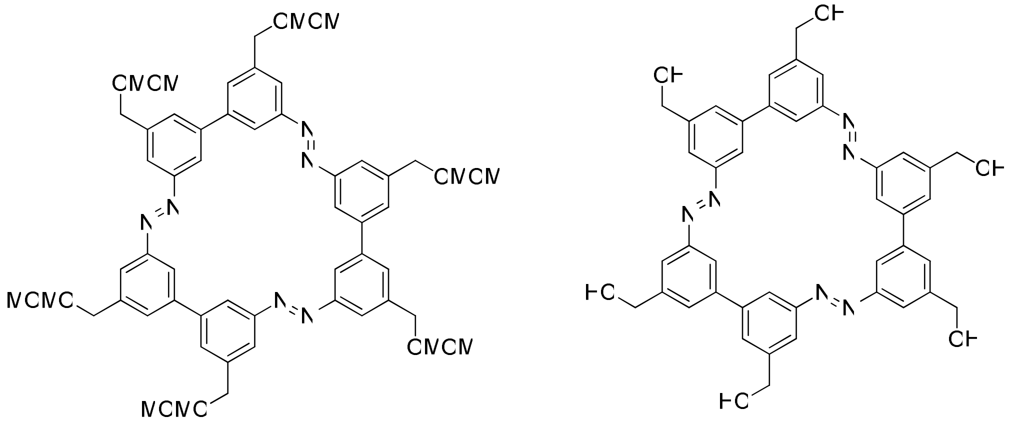


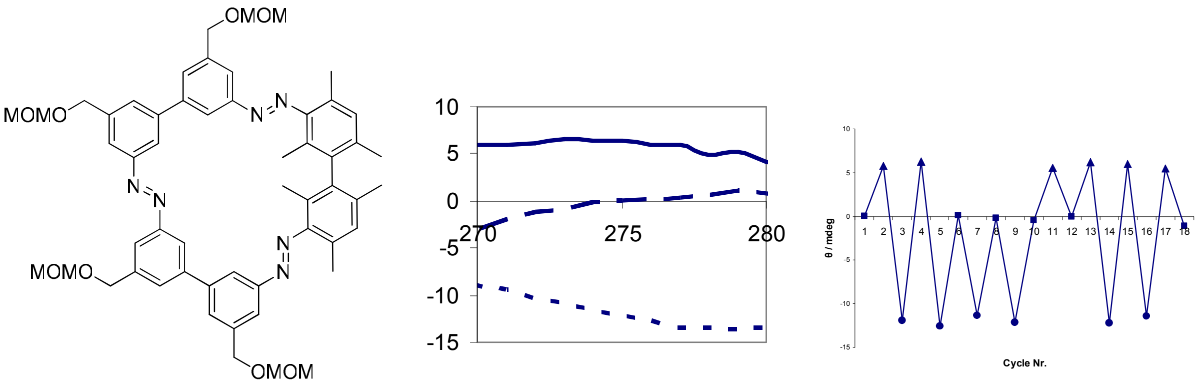
Figure 37: Ester substituted CTB macrocycle with liquid crystalline phase.

The low solubility of the macrocycle prevented further investigation. When substituents were attached to the macrocycle, its solubility could be improved dramatically and detailed isomerisation studies were conducted on a fully substituted derivative with MOM-protected benzylic alcohols. The four expected isomers were observed. In irradiation experiments at different wavelength each of the four isomers could be enriched as the predominant *E*/*Z*-isomer. The lifetime of the (*Z,Z,Z*)-isomer was higher compared to linear azobenzenes, but did not show an unusually high thermal stability as some macrocyclic azobenzenes. However, the stability was slightly higher than for liner azobenzenes. In aromatic solvents, especially benzene and pyridine, the (*Z,Z,Z*)-isomer was more abundant in the photostationary state at 365 nm than in chloroform, acetonitrile or DMSO. Calculations on the MOM-substituted macrocycle suggest that the envisaged bowl shaped conformation is adopted. Yet, no suitable host molecule for a reversible binding could be found.



Scheme 61: Hexasubstituted CTB macrocycle with and without MOM-protecting groups.

By the incorporation of a bimesityl moiety into the CTB macrocycle, a helically chiral macrocycle was synthesized. Isomerization experiments showed a significant change of the CD-spectrum of the chiral macrocycle, depending on the irradiation wavelength. At 275 nm a major change could be seen by a change in sign. Switching between three different photostationary states at different wavelengths could be done reversibly over several cycles.



Scheme 62: Chiral macrocycle showing photoresponsive circular dichroism.

For a convenient functionalization by means of a copper catalyzed [2+3] alkine azide cycloaddition reaction, two new CTB derivatives **149** and **154** were prepared. One macrocycle was derivatized with one alkine function to investigate the formation of macromolecular networks by attaching azide functionalized nucleobases. Even though the addition reaction of functionalized guanidine and cytosine were probably successful, the purification of the compounds was not achieved. Two CTB macrocycles were linked together by conducting a click reaction with 9,10-(diazidomethyl)-anthracene (**157**). The resulting bismacrocycle **176** formed organogels with aromatic solvents toluene and xylene. These gels disintegrated upon irradiation with UV-light. CTB macrocycle **154** which was functionalized with two alkine moieties was reacted with different diazide tethers to prepare a molecular cage. However, only polymerized product was obtained for tether **157** as well as triethylene glycol diazide (**162**) and tetraethylene glycol diazide (**163**).

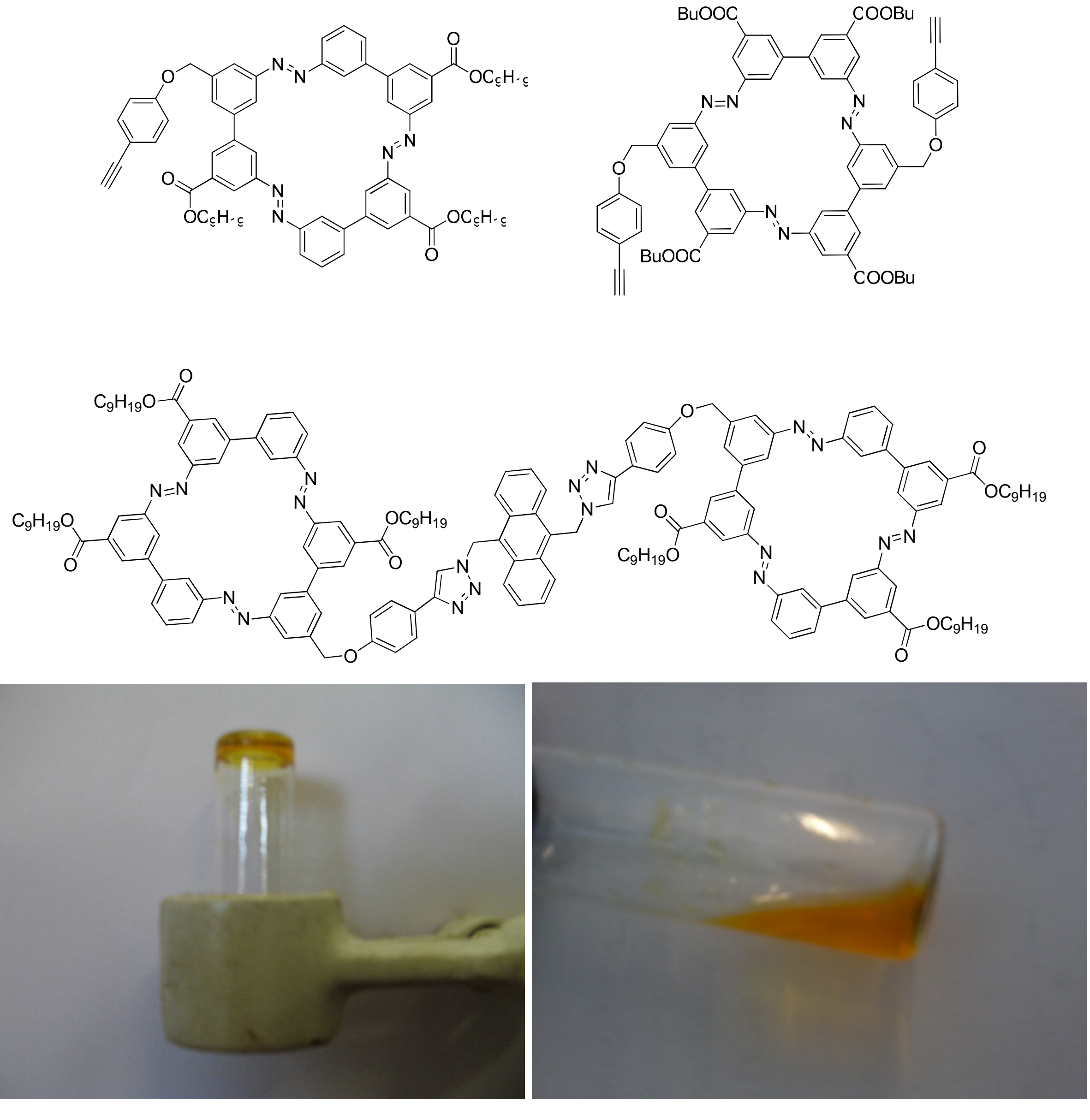


Figure 38: Alkine functionalized macrocycles and dimacrocycle as a switchable gel.

In summary, a new synthetic approach to azobenzene macrocycles was developed and their photochromic behaviour was investigated. It can also be stated that these compounds can undergo interactions like π-π-stacking or binding to triphenylcarbenium ions. Also macroscopic properties were observed for some of the macrocycles with the formation of liquid crystalline mesophases or a switchable organogel. The introduction of chiral information into the macrocycle allowed an easy readout of the switch by CD-spectroscopy and allowed a photochemical switching between three different states. Therefore, a major step towards a ternary molecular switch could be done. Even though, the different states are not thermally stable. The preparation of a molecular cage was not successful, but maybe the choice of another tether or another reaction, for example metathesis, could solve this problem.

5. Experimental Part

5.1 General Methods

Reagents and Solvents: All chemicals and solvents for reactions were purchased from one of the following commercial sources: Acros, Alfa Aesar, Fluka, Fluorochem, Sigma-Aldrich, Strem or VWR and used without further purification. Dry solvents were either bought in a crown cap flask over molecular sieve or taken from a Pure-Solv^{TM} drying system. THF was predried over $CaCl_2$ and destilled from potassium and benzophenone under nitrogen. For extraction and chromatography technical solvents were redistilled once with a rotatory evaporator prior to usage.

Reactions: All reactions were performed under ambient atmosphere if not stated otherwise. For air sensitive reactions, the solvent was purged by an argon stream and the reaction was done under an argon or nitrogen atmosphere. For moisture sensitive reactions the glass material was heated at 110 °C in a drying oven over night before usage.

Isomerizations: For photochemical isomerisations the azobenzenes four different lamps were used. A handheld 8 Watt 3UV lamp from UVP with switchable wavelengths of 254, 302 and 365 nm, a 150 W high-pressure mercury lamp, a Rayonet photoreactor with 300 nm and 350 nm lamps or a 140 W halogen floodlight were taken for the isomerisation. After irradiation analysis by UV-spectroscopy, CD-spectroscopy or ^{1}H-NMR spectroscopy were done immediately because of thermal back reaction.

Chromatography: For thin layer chromatography either silica gel 60 F_{254} glasses with a thickness of 0.25 mm from Merck or Polygram® Alox N/UV254 with a thickness of 0.2 mm from Macherey-Nagel were used. Furthermore, silica gel plates from Whatman (partisil, 250 µm * 20 cm * 20 cm, fluorescent model K6F) were used after cutting them to sizes of 25 * 100 mm for reaction control or 50 * 100 mm for column chromatography control with a glass cutter. Detection was done either by a UV-lamp at 254, 302 or 365 nm or by visualization with vanillin, $KMnO_4$, ninhydrin, iodine or *p*-anisaldehyde. For preparative thin layer chromatography silica gel plates from Analtech with a thickness of 2.0 mm were used. For column chromatography silica gel 60 (40 - 63 µm) from Fluka or neutral aluminium oxide from Merck or Fluka was used. Flash column chromatography was performed under nitrogen pressure. HPLC was done on an instrument consisting of a D-7000 interface, a L-7100 pump, an L-7200 autosampler, a L-7300 column oven, an L-7400 UV detector, a LiChrosphere® 100 RP-18 (5µm) column and a L-7622 solvent degasser. Gel permeation chromatography was conducted on a Shimadzu LC-8A instrument on a OligoPore 300 x 7.5 mm column with a particle size of 6 µm in toluene as an eluent.

^{1}H-NMR: For proton nuclear magnetic resonance a Bruker DPX-NMR (400 MHz), Bruker BZH-NMR (250 MHz) or Bruker Avance 500 (500 MHz) instrument was used to measure spectra. Two dimensional spectra and temperature measurements were conducted on the latter. Chemical shifts are reported in δ with the unit ppm relative to TMS if possible or otherwise residual solvent peaks. Coupling constants *J* are reported in Hz with the number of bonds over which the coupling occurs is written in superscript. NMR-solvents were bought from Cambridge Isotope Laboratories, Inc. or from ARMAR Ag. Multiplets are written as s for singulet, d for doublet, t for triplet, q for quartet, m for multiplet and bs for broad singulet.

^{1}C-NMR: For carbon nuclear magnetic resonance a Bruker DPX-NMR (100.6 MHz) or a Bruker Avance 500 (125.8 MHz) instrument was used. Chemical shifts are reported in δ with the unit ppm relative to residual solvent peaks.

UV/Vis-Spectroscopy: Absorption spectra throughout the ultraviolet and the visible part of the spectrum were recorded on an Agilent 8453 diode array spectrometer using Hellma quartz cuvettes with a length of 1 cm.

IR-Spectroscopy: Fourier-transform infrared spectra were done on a Shimadzu FTIR-8400S instrument. The neat compounds were measured through a Specac ATR attachment.

Optical rotation: Specific optical rotation was measured on a Perkin Elmer Polarimeter 341 in a 1 dm cuvette at 20 °C.

CD-Spectroscopy: Circular dichroism spectra were recorded using a Chirascan spectrometer with a spectral bandwith of 1 nm using Hellma quartz cuvettes with a length of 2 mm and are given as ellipticities θ in mdeg.

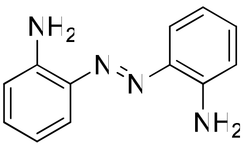
Mass Spectrometry: Electron ionization mass spectrometry (EI-MS) was measured by Dr. H. Nadig on a VG70-250 mass spectrometer. Fast atom bombardment mass spectrometry (FAB-MS) was also measured by Dr. H. Nadig on a MAR 312 mass spectrometer with 3-nitrobenzyl alcohol or glycine as a matrix and KCl as an additive if necessary. For matrix assisted laser desorption ionization - time of flight (MALDI-TOF) an Applied Bio Systems Voyager-De^{TM} instrument was used. The used matrices were 1,8-dihydroxy-10H-anthracen-9-on, 2,6-dihydroxyacetophenone or 2,4,6-trihydroxyacetophenone.

Melting Point: For the melting point measurements a Will Wetzlar or a Büchi 530 instrument were used.

Elementary Analysis: Elementary analyses were done in the Microanalytical Laboratory in the chemistry department of the university of basel by Mr. W. Kirsch on a Leco CHN-900 analyzer.

5.2 Synthesis of Compounds

2,2'-Diaminoazobenzene (56)



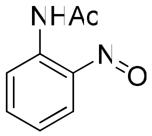
An oven dried three-neck flask was attached with a bubbler, and flushed with argon for 10 min. Then, *ortho*-phenylenediamine (**50**) (3.00 g, 27.8 mmol, 1.00 eq.) was added under argon and dissolved in dry toluene (150 ml). KO_2 chunks (6.00 g, 84.6 mmol, 3.04 eq.) were added, and the mixture was stirred at room temperature. After 2 d, another 3 g of KO_2 chunks were added and the reaction stirred for additional 2 d. Although the reaction mixture still showed traces of starting material, the remaining KO_2 was carefully quenched by slow addition of 200 ml of H2O, and stirring was continued for 30 minutes. The organic layer was separated, and the aqueous layer extracted with EtOAc (100 ml). The combined organic layers were washed with water (2 x 200 ml) and dried over MgSO4. After evaporation of the solvent under reduced pressure and purification by flash column chromatography (silica gel, hexanes:EtOAc 2:1) 1.9 g of 2,2'-diaminoazobenzene (**56**) was obtained as red crystals (65 %).

Mp: 136 – 138 °C (lit: 136).

^{1}H NMR: (400 MHz, CD_3OD, δ/ppm) 7.67 (d, $^3J_{HH}$ = 8.0 Hz, 2H), 7.16 (t, $^3J_{HH}$ = 7.3 Hz, 2H), 6.78 (t, $^3J_{HH}$ = 7.3 Hz, 2H), 6.76 (d, $^3J_{HH}$ = 8.0 Hz, 2H), 5.47 (bs, 4H).

The analytical data corresponded to the literature.[1]

2-Nitrosoacetanilide (57a)



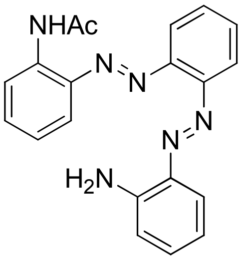
A solution of 2-Nitroaniline (**59**) (5.00 g, 35.5 mmol, 1.00 eq.) in 20 ml of acetic acid was treated with acetic anhydride (3.67 ml, 39.0 mmol, 1.10 eq.). The mixture was heated to 100 °C and stirred for 3 h. Then 100 ml of water was added and the precipitate was collected by filtration, washed with water and dissolved in 2-methoxyethanol (100 ml) and water (10 ml). Then ammonium chloride (2.25 g, 42.1 mmol, 1.19 eq.) and zinc dust (5.36 g, 82.0 mmol, 2.31 eq.) was added, and the mixture was stirred for 90 minutes, controlled by TLC to minimize overreduction. After this, the mixture was filtered into an ice cold solution of $FeCl_3$ (5.45 g, 33.6 mmol, 0.95 eq.) in H_2O (200 ml) and stirred at 0 °C for 1 h, when a green precipitate was observed. The Suspension was extracted with DCM (3 * 100 ml) and dried over $MgSO_4$. Recrystallization from hot ethanol yielded 2.5 g of **57a** as green crystals (42 %).

Mp: 107-109 °C (lit: 106-107)

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 10.79 (s, 1H, NH), 8.85 (d, $^3J_{HH}$ = 8.6 Hz, 1H, H_{aryl}), 7.71 (t, $^3J_{HH}$ = 7.9 Hz, 1H, H_{aryl}), 7.33 (s, 1H, H_{aryl}), 7.16 (t, $^3J_{HH}$ = 8.1 Hz, 1H, H_{aryl}), 2.35 [s, 3H, $NHC(O)CH_3$].

The analytical data corresponded to the literature.[2]

2-Amino-2''-acetanilidebisazobenzene (58a)



A solution of 2,2'-diaminoazobenzene (**56**) (1.20 g, 5.70 mmol, 1.00 eq.) in toluene was degassed with an argon stream for 15 minutes. Then, 2-nitrosoacetanilide (**57a**) (0.93 g, 5.70 mmol, 1.00 eq.) and acetic acid (2.60 ml) was added. The mixture was stirred under an argon atmosphere at 60 °C. After three days the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography (silica gel, hexane:EtOAc 2:1) yielding 1.38 g of red crystals (71 %).

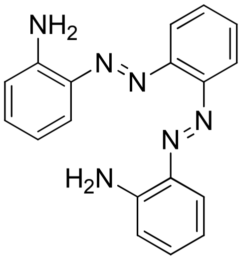
Mp: 168-170 °C (lit: 164-165 °C).

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 10.12 (s, 1H, NH), 8.68 (d, $^3J_{HH}$ = 7.8 Hz, 1H, H_{aryl}), 7.88 (d, $^3J_{HH}$ = 8.1 Hz, 1H, H_{aryl}), 7.85 (d, $^3J_{HH}$ = 8.1 Hz, 1H, H_{aryl}), 7.81 (d, $^3J_{HH}$ = 7.8 Hz, 1H, H_{aryl}), 7.72 (d, $^3J_{HH}$ = 7.8 Hz, 1H, H_{aryl}), 7.62 – 7.44 (m, 3H, H_{aryl}), 7.25 – 7.15 (m, 2H, H_{aryl}), 6.84 (dd, $^3J_{HH}$ = 8.2 Hz, $^3J_{HH}$ = 8.2 Hz, 1H, H_{aryl}), 6.74 (d, $^3J_{HH}$ = 8.2 Hz, 1H, H_{aryl}), 6.31 (bs, 2H, NH_2), 2.00 [s, 3H, $NHC(O)CH_3$].

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 169.5 (NH**C**(O)CH_3), 148.0 (C_{aryl}), 147.9 (C_{aryl}), 142.5 (C_{aryl}), 139.9 (C_{aryl}), 138.1 (C_{aryl}), 136.4 (C_{aryl}), 133.6 (C_{aryl}), 133.2 (C_{aryl}), 131.9 (C_{aryl}), 131.3 (C_{aryl}), 130.5 (C_{aryl}), 123.7 (C_{aryl}), 122.0 (C_{aryl}), 120.8 (C_{aryl}), 119.0 (C_{aryl}), 117.7 (C_{aryl}), 117.6 (C_{aryl}), 117.6 (C_{aryl}), 25.5 ($NHC(O)CH_3$).

The analytical data corresponded to the literature.[1]

2,2''-Diaminobisazobenzene (53a)



A solution of 2-amino,2''-acetanilidebisazobenzene (**58a**) (0.79 g, 2.2 mmole, 1.0 eq.) in ethanol (80 ml) was treated with a solution of KOH (7.1g, 0.13 mole, 58 eq.) in 46 ml of ethanol and 18 ml of water. The mixture was heated to 90 °C. After 1 h the mixture was poured onto 300 g of ice, extracted with CH_2Cl_2 (3 * 50 ml), dried over Na_2SO_4 and concentrated, to yield 660 mg of red oil, which crystallized in the fridge over night (95 %).

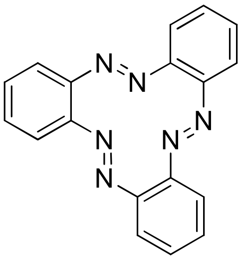
Mp: 94-96 (lit: 96-97).

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.89 (dd, $^3J_{HH}$ = 8.1 Hz, $^4J_{HH}$ = 1.5 Hz, 2H, H_{aryl}), 7.81 – 7.75 (m, 2H, H_{aryl}), 7.52 – 7.46 (m, 2H, H_{aryl}), 7.21 (ddd, $^3J_{HH}$ = 8.4 Hz, $^3J_{HH}$ = 7.1 Hz $^4J_{HH}$ = 1.6 Hz, 2H, H_{aryl}), 6.84 (ddd, $^3J_{HH}$ = 8.2 Hz, $^3J_{HH}$ = 7.1 Hz, $^4J_{HH}$ = 1.2 Hz, 2H, H_{aryl}), 6.72 (dd, $^3J_{HH}$ = 8.2 Hz, $^4J_{HH}$ = 1.1 Hz, 2H, H_{aryl}), 6.27 (bs, 4H, NH_2).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 148.3, 142.6, 138.3, 132.8, 130.8, 130.6, 117.6, 117.5, 117.0.

The analytical data corresponded to the literature.[1]

Cyclotrisazobenzene (52a)



Triethylamine (1.32 ml, 9.50 mmol, 10.0 eq.) was added to a solution of 2,2’’-diaminobisazobenzene (**53a**) (0.30 g, 0.95 mmol, 1.00 eq.) in CH_2Cl_2 (100 ml). Then, $Pb(OAc)_4$ (0.96 g, 2.20 mmol, 2.30 eq.) dissolved in 12 ml of CH_2Cl_2 was added dropwise. After complete addition, the mixture was stirred for 40 min. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (neutral alumina, Hexane/EtOAc 5:1) to yield 151 mg of golden brown crystals (51 %).

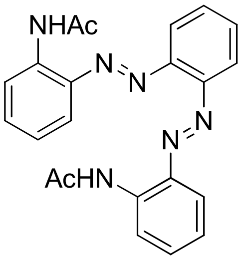
Mp: 180-182 (lit: 169-176)

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.72 – 7.66 (m, 6H, H_{aryl}), 7.59 – 7.53 (m, 6H, H_{aryl}).

^{13}C-NMR: (101 MHz, DMSO, δ/ppm): 146.6, 131.5, 122.7.

The analytical data corresponded to the literature.[3]

2,2’’-Diacetylaminobisazobenzene (62)



A solution of *ortho*-phenylenediamine (**50**) (200 mg, 1.85 mmol, 1.00 eq.) in toluene (36 ml) was degassed under an argon stream for 15 min. Then, 2-nitrosoacetanilde (**57a**) (911 mg, 5.55 mmol, 3.00 eq.) and acetic acid (215 µl, 3.76 mmol, 2.03 eq.) was added. The mixture was stirred at 60 °C for 18 h and more acetic acid (108 ml) was added. After stirring at 60 °C for 6 d the solvent was removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, Hexane/EtOAc 1:1) to yield 465 mg of a red solid (63 %).

Mp: 189-190 °C

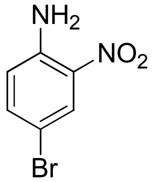
IR: (υ/cm^{-1}): 3304, 1658, 1591.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 10.03 (s, 2H, NH), 8.68 (d, $^3J_{HH}$ = 8.4 Hz, 2H, H_{aryl}), 7.85 (d, $^3J_{HH}$ = 8.1 Hz, 2H, H_{aryl}), 7.77 – 7.72 (m, 2H, H_{aryl}), 7.66 – 7.61 (m, 2H, H_{aryl}), 7.50 (t, $^3J_{HH}$ = 7.8 Hz, 2H, H_{aryl}), 7.17 (d, $^3J_{HH}$ = 7.8 Hz, 2H, H_{aryl}), 1.90 [s, 6H, $NHC(O)CH_3$].

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 169.2 ($NHC(O)CH_3$), 147.7 (C_{aryl}), 139.7 (C_{aryl}), 136.4 (C_{aryl}), 134.1 (C_{aryl}), 131.6 (C_{aryl}), 123.8 (C_{aryl}), 122.5 (C_{aryl}), 120.9 (C_{aryl}), 119.8 (C_{aryl}), 25.4 ($NHC(O)CH_3$).

Ms: (EI 70 eV): 401 (14) [M+1], 400 (55) [M^+], 211 (100).

2-Nitro-4-bromoaniline



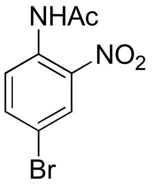
A solution of 2-Nitroaniline (**59**) (5.00 g, 35.4 mmol, 1.00 eq.) in 100 ml of glacial acetic acid was heated to 55 °C. Then, NBS (6.18g, 34.7 mmol, 0.98 eq.) was added in small portions over 1 hour. The mixture was stirred for additional two hours at 45 °C. Then, it was poured on 600 ml of ice water. An orange precipitate formed, which was collected and washed with water (50 ml). The solid was taken up in CH_2Cl_2, dried over Na_2SO_4 and the solvent was removed to yield 6.91 g of an orange solid. (90 %).

Mp: 110 – 112 °C (lit: 109 °C)

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.27 (s, 1H, H_{aryl}), 7.43 (d, $^3J_{HH}$ = 8.9, 1H, H_{aryl}), 6.72 (d, $^3J_{HH}$ = 8.9 Hz, 1H, H_{aryl}), 6.09 (bs, 2H, NH_2).

The analytical data corresponded to the literature.[4]

2-Acetamino-5-bromonitrobenzene



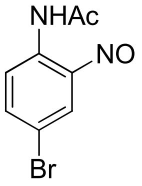
A solution of 2-Nitro-4-bromoaniline (6.00 g, 27.6 mmol, 1.00 eq.) in 45 ml of acetic acid, and acetic anhydride (2.85 ml, 30.4 mmol, 1.10 eq.) was heated to 100 °C and stirred for three hours. Then 100 ml of water was added and the precipitate was collected by filtration, washed with water and dissolved in CH_2Cl_2 (70 ml). The organic phase was separated, dried over $MgSO_4$ and after removal of the solvent 6.76 g of a yellow solid was obtained (94 %).

Mp: 102 – 105 °C (lit: 106-108 °C)

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 10.25 (s, 1H, NH), 8.71 (d, $^3J_{HH}$ = 9.1 Hz, 1H, H_{aryl}), 8.35 (s, 1H, H_{aryl}), 7.73 (d, $^3J_{HH}$ = 9.1 Hz, 1H, H_{aryl}), 2.29 (s, 3H, $NHC(O)CH_3$).

The analytical data corresponded to the literature.[5]

2-Acetamino-5-bromonitrosobenzene (57c)



Iron powder (4.20 g, 75.2 mmol, 3.25 eq.) was suspended in 15 ml H_2O and 0.4 ml of glacial acetic acid. Then, the mixture was heated to 70 °C, and the nitro compound (6.00 g, 23.3 mmol, 1.00 eq.) was added in small portions over 30 min. The temperature was raised to 80 °C and the mixture was stirred for an additional 10 min. Then, it was filtered over a celite® pad and the filter cake was washed with boiling ethanol (250 ml). The ethanol was removed under vacuum and 200 ml of water was added. The precipitate was collected by filtration. The solid was treated with 50 ml of ethanol and again filtered. Drying of the filtrate over $MgSO_4$ and removal of the solvent yielded 2.77 g of a pale brown solid, which was suspended in 60 ml of CH_2Cl_2. Oxone® (11.1 g, 18.0 ml, 0.78 eq.), dissolved in 300 ml of water, was added. The mixture was stirred for 2 h. The organic phase was separated, washed with 1M HCl, saturated aqueous $NaHCO_3$, and water (each 50 ml). After drying over $MgSO_4$ and removal of the solvent, the crude product was purified by flash column chromatography (silica gel, hexane:EtOAc 3:1) to yield 2.50 g of green crystals (63 %).

Mp: 137-139 °C

IR: (υ/cm^{-1}): 3322, 1674, 1581, 1418.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 10.66 (s, 1H, NH), 8.83 (d, $^3J_{HH}$ = 9.1, 1H, H_{aryl}), 7.79 (d, $^3J_{HH}$ = 9.1 Hz, 1H, H_{aryl}), 7.11 (s, 1H, H_{aryl}), 2.36 (s, 3H, $NHC(O)CH_3$).

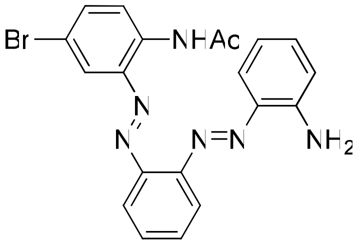
^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 169.6 (NH**C**(O)CH_3), 155.4 (C_{aryl}), 141.4 (C_{aryl}), 123.6 (C_{aryl}), 116.9 (C_{aryl}), 25.8 (NHC(O)**C**H_3).

Ms: (EI 70 eV): 244 (41), 242 (42) [M^+], 43 (100).

EA: calculated: C = 39.53, H = 2.90, N = 11.53

Found: C = 39.53, H = 2.78, N = 11.48

2-Amino-2''-acetamino-2''-bromobisazobenzene (58c)



To a solution of 2,2'-diaminoazobenzene (**56**) (1.00 g, 4.71 mmol, 1.00 eq.) and 2-acetamino-5-bromonitrosobenzene (**57c**) (1.26 g, 5.18 mmol, 1.10 eq.) in chloroform (27 ml), acetic acid (2.7 ml) was added. The mixture was stirred under reflux for two days. Then, it was diluted with 150 ml CH_2Cl_2, washed with water (2 x 200 ml), dried over Na_2SO_4, and concentrated. Flash column chromatography of the residue (silica gel, hexane:EtOAc 1:1) yielded 810 mg of the prduct (39 %).

Mp: 221-224 °C

IR: (υ/cm^{-1}): 3365, 1677, 1613, 1494, 758.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 9.70 (s, 1H, NH), 8.60 (d, $^3J_{HH}$ = 9.0 Hz, 1H, H_{aryl}), 7.95 (s, 1H, H_{aryl}), 7.88 (d, $^3J_{HH}$ = 8.1 Hz, 1H, H_{aryl}), 7.82 (d, $^3J_{HH}$ = 8.1 Hz, 1H, H_{aryl}), 7.72 (d, $^3J_{HH}$ = 7.9 Hz, 1H, H_{aryl}), 7.64 - 7.52 (m, 3H, H_{aryl}), 7.23 (t, $^3J_{HH}$ = 7.7 Hz, 1H, H_{aryl}), 6.84 (t, $^3J_{HH}$ = 7.6 Hz, 1H, H_{aryl}), 6.76 (d, $^3J_{HH}$ = 8.3 Hz, 1H, H_{aryl}), 2.01 (s, 3H, $NHC(O)CH_3$).

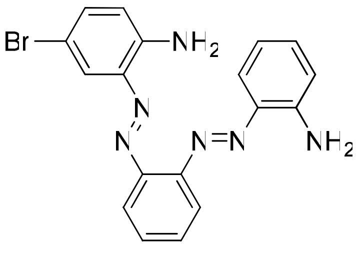
^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 168.8 (NH**C**OCH$_3$), 147.6 (C_{aryl}), 147.2 (C_{aryl}), 142.0 (C_{aryl}), 140.1 (C_{aryl}), 137.7 (C_{aryl}), 135.6 (C_{aryl}), 135.4 (C_{aryl}), 132.9 (C_{aryl}), 132.2 (C_{aryl}), 131.3 (C_{aryl}), 130.1 (C_{aryl}), 122.7 (C_{aryl}), 122.0 (C_{aryl}), 118.8 (C_{aryl}), 117.3 (C_{aryl}, 2C), 117.3 (C_{aryl}), 116.4 (C_{aryl}), 25.8 (NHCO**C**H$_3$).

Ms: (EI 70 eV): 438 (11), 436 (11) [M$^+$], 106 (100).

EA: calculated: C = 54.93, H = 3.92, N = 19.22.

Found: C = 54.95, H = 3.91, N = 19.20.

2,2''-Diamino-2''-bromobisazobenzene (53c)



A solution of 2-amino-2''-acetamino-2''-bromobisazobenzene (**58c**) (720 mg, 1.65 mmol, 1.00 eq.) in EtOH (40 ml) was prepared and treated with KOH (2.09 g, 37.2 mmol, 22.5 eq.), dissolved in 7 ml EtOH and 7 ml H_2O. The mixture was heated to 100 °C for 1 h, and then poured onto 130 g of crushed ice. Then, it was extracted with CH_2Cl_2 (3 x 100 ml), dried over Na_2SO_4. Evaporation of the solvent yielded 620 mg of the product (95 %).

Mp: 118-119 °C.

IR: (υ/cm^{-1}): 3438, 1602, 1482, 1393, 1159, 811.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.98 (s, 1H, H_{aryl}), 7.87 (d, $^3J_{HH}$ = 8.1 Hz, 1H, H_{aryl}), 7.82 - 7.73 (m, 2H, H_{aryl}), 7.56 – 7.45 (m, 2H, H_{aryl}), 7.28 (d, $^3J_{HH}$ = 8.7 Hz, 1H, H_{aryl}), 7.22 (t, $^3J_{HH}$ = 7.7 Hz, 1H, H_{aryl}), 6.84 (t, $^3J_{HH}$ = 8.7 Hz, 1H, H_{aryl}), 6.76 (d, $^3J_{HH}$ = 7.2 Hz, 1H, H_{aryl}), 6.65 (d, $^3J_{HH}$ = 8.7 Hz, 1H, H_{aryl}), 6.30 (d, 2H, NH_2), 6.08 (s, 2H, NH_2).

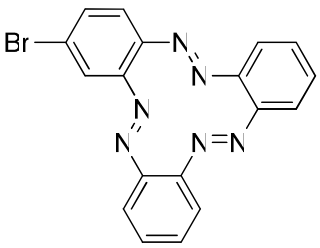
^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 148.2, 147.5, 142.2, 141.8, 138.4, 137.9, 134.7, 132.5, 131.1, 130.4, 130.3, 130.2, 118.6, 117.3, 117.2, 116.7, 116.4, 108.8.

Ms: (EI 70 eV): 396 (31), 394 (33) [M$^+$], 106 (100).

EA: calculated: C = 54.70, H = 3.82, N = 21.26.

Found: C = 54.58, H = 3.80, N = 21.05.

3-bromocyclotrisazobenzene (52c)



Triethyl amine (1.75 ml, 12.6 mmol, 10.0 eq.) was added to a stirring solution of 2,2’’-diamino-2’’-bromobisazobenzene (**53c**) (500 mg, 1.26 mmol, 1.00 eq.) in 150 ml of CH_2Cl_2. Then, lead tetraacetate (1.27 g, 2.87 mmol, 2.28 eq.), dissolved in 10 ml CH_2Cl_2 was added dropwise. After stirring for 30 min, the solvent was removed under reduced pressure. The residue was purified by flash column chromatography (neutral alox, Hexan:EtOAc 10:1) to yield 208 mg of the product (42 %).

Mp: 140-142 °C.

IR: (υ/cm^{-1}): 3054, 1757, 1373, 1203, 1009, 690.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.79 (d, $^4J_{HH}$ = 2.0 Hz, 1H, H_{aryl}), 7.74 – 7.52 (m, 10H, H_{aryl}).

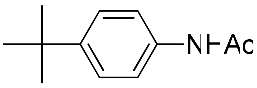
^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 148.6, 147.9, 142.6, 142.2, 138.8, 135.1, 132.9, 131.5, 130.8, 130.7, 130.6, 119.0, 117.7, 117.6, 117.1, 116.8, 110.0, 109.2.

Ms: (EI 70 eV): 392 (100), 390 (86) [M^+].

EA: calculated: C = 55.26, H = 2.83, N = 21.48.

Found: C = 55.34, H = 2.87, N = 21.25.

4-*tert*-Butylacetanilide



To a solution of 4-*tert*-Butylaniline (**61**) (5.00 g, 33.5 mmol, 1.00 eq.) in 30 ml of acetic acid, acetic anhydride (3.46 ml, 36.9 mmol, 1.10 eq.) was added. The mixture was heated to 100 °C and stirred for 3 h. Then, 70 ml of water was added and a white precipitate was collected by filtration and washed with water. After drying under high vacuum, 5.54 g of colourless crystals were obtained (87 %).

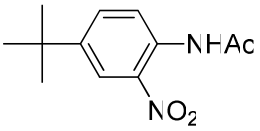
MP: 171-174 °C (lit: 170-171).

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.43 – 7.30 (m, 5H, NH, H_{aryl}), 2.16 (s, 3H, $NHC(O)CH_3$), 1.30 [s, 9H, $C(CH_3)_3$].

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 168.9 ($NHC(O)CH_3$), 147.8 (C_{aryl}), 135.6 (C_{aryl}), 126.2 (C_{aryl}), 120.3 (C_{aryl}), 34.8 [$C(CH_3)_3$], 31.8 [$C(CH_3)_3$], 24.9 ($NHC(O)CH_3$).

The analytical data corresponded to the literature.[6]

2-Nitro-4-*tert*-butylacetanilide



A mixture of acetic acid (14.4 ml) and acetic anhydride (11.8) ml were introduced into a three neck flask, attached with a dropping funnel and a thermometer. The mixture was cooled in an ice/salt bath to – 5 °C. Then, fuming nitric acid (3.53 ml, 78.5 mmol, 2.50 eq.) was added dropwise, keeping the temperature below 0 °C. After complete addition, 4-*tert*-butylacetanilide (6.00 g, 31.4 mmol, 1.00 eq.) was added in portions, that the temperature was kept below 5 °C. The mixture was stirred, until TLC showed complete conversion (around 15 minutes). After quenching by the addition of ice, the precipitated product was dissolved in 150 ml CH_2Cl_2, washed with 2M aqueous NaOH (2 x 100 ml) and water (3 x 100 ml). Drying over $MgSO_4$ and removal of the solvent under reduced pressure yielded a yellow solid, which was recrystallized in hot hexane (6.40 g, 86 %).

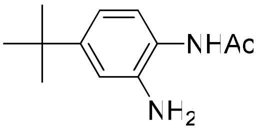
Mp: 107-109 (lit: 107-109)

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 10.20 (s, 1H, NH), 8.64 (d, $^3J_{HH}$ = 8.9 Hz, 1H, H_{aryl}), 8.18 (s, 1H, H_{aryl}), 7.68 (d, $^3J_{HH}$ = 8.9 Hz, 1H, H_{aryl}), 2.23 [s, 3H, NHC(O)**C**H$_3$], 1.34 [s, 9H, C(CH$_3$)$_3$].

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 169.4 (NHC(O)CH$_3$), 147.4 (C_{aryl}), 136.6 (C_{aryl}), 133.9 (C_{aryl}), 132.7 (C_{aryl}), 122.5 (C_{aryl}), 122.4 (C_{aryl}), 35.0 (C(CH$_3$)$_3$), 31.4 [C(CH$_3$)$_3$], 26.0 (NHC(O)CH$_3$).

The analytical data corresponded to the literature.[7]

2-Amino-4-*tert*-butylacetanilide (18)



A solution of 2-Nitro-4-*tert*-butylacetanilide (5.00 g, 21.2 mmol, 1.00 eq.) in 100 ml of methanol was prepared and palladium on activated charcoal (370 mg) was added. The mixture was stirred under a hydrogen atmosphere over night. Then, it was filtered over a celite® pad and the solvent was removed under reduced pressure, to obtain 4.21 g of a pale brown solid (96 %).

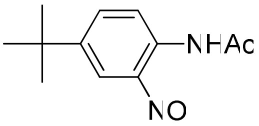
Mp: 150-154 (lit: 148.5-149.5)

^{1}H-NMR: (400 MHz, DMSO, δ/ppm): 9.03 (s, 1H, NH), 7.02 (d, $^3J_{HH}$ = 8.3 Hz, 1H, H_{aryl}), 6.74 (d, $^4J_{HH}$ = 2.2 Hz, 1H, H_{aryl}), 6.56 (dd, $^3J_{HH}$ = 8.3 Hz, $^4J_{HH}$ = 2.2 Hz, 1H, H_{aryl}), 4.74 (bs, 2H, NH_2), 2.01 [s, 3H, $NHC(O)CH_3$], 1.22 [s, 9H, $C(CH_3)_3$].

^{13}C-NMR: (101 MHz, DMSO, δ/ppm): 169.0 [NH**C**(O)CH_3], 149.0 (C_{aryl}), 142.3 (C_{aryl}), 125.8 (C_{aryl}), 122.0 (C_{aryl}), 114.1 (C_{aryl}), 113.7 (C_{aryl}), 34.8 [$C(CH_3)_3$], 32.1 [$C(CH_3)_3$], 24.1 [$NHC(O)CH_3$].

The analytical data corresponded to the literature.[8]

2-Nitroso-4-*tert*-butylacetanilide (57b)



A solution of 2-Amino-4-*tert*-butylacetanilide (3.00 g, 14.5 mmol, 1.00 eq.) in CH_2Cl_2 (65 ml) was treated with Oxone® (13.4 g, 21.8 mmol, 1.50 eq.), dissolved in water (260 ml). The mixture was stirred for 30 min. Then, the organic layer was separated and the aequous layer was extracted with 100 ml of CH_2Cl_2. The combined organic layers were washed with 1M aq. HCl, sat. aq. $NaHCO_3$ and water (100 ml each). Drying over $MgSO_4$ and removal of the solvent left a black residue, which was purified through flash column chromatography (silica gel, hexane:EtOAc 5:1). A green oil was obtained, which crystallized while standing at room temperature for several hours yielding 2.57 g of green crystals (81 %).

Mp: 88-89 °C

IR: (υ/cm^{-1}): 3238, 2955, 1664, 1591, 1475.

^{1}H-NMR: (400 MHz, CHCl$_3$, δ/ppm): 10.69 (s, 1H, NH), 8.74 (d, $^3J_{HH}$ = 8.9 Hz, 1H, H$_{aryl}$), 7.78 (d, $^3J_{HH}$ = 8.9 Hz, 1H, H$_{aryl}$), 7.35 (bs, 1H, H$_{aryl}$), 2.33 [s, 3H, NHC(O)CH$_3$], 1.33 [s, 9H, C(CH$_3$)$_3$].

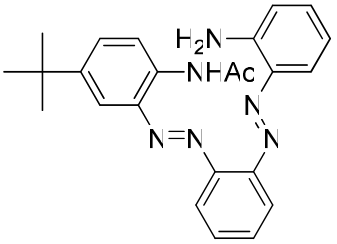
^{13}C-NMR: (101 MHz, CDCl$_3$, δ/ppm): 169.9 (C(O)NHCH$_3$), 156.4 (C$_{aryl}$), 146.5 (C$_{aryl}$), 137.3 (C$_{aryl}$), 121.2 (C$_{aryl}$), 110.0 (C$_{aryl}$), 34.8 [C(CH$_3$)$_3$] 31.4 [C(CH$_3$)$_3$], 25.8 [NHC(O)CH$_3$].

Ms: (EI 70 eV): 221, (7) [M+1], 220 (51) [M$^+$], 163 (100).

EA: calculated: C = 65.43, H = 7.32, N = 12.72

found: C = 65.55, H = 7.18, N = 12.68

2-Amino-2’’-acetamino-4’’-*tert*-butylbisazobenzene (58b)



A solution of 2,2’-diaminoazobenzene (**56**) (1.00 g, 4.71 mmol, 1.00 eq.) was dissolved in toluene and degassed with an argon stream for 15 min. Then, 2-nitroso-4-*tert*-butylacetanilide (**57b**) (1.14 g, 5.18 mmol, 1.10 eq.) and 2.6 ml of acetic acid was added. The mixture was stirred under an argon atmosphere at 60 °C. After three days the solvent was evaporated under reduced pressure, and the residue was purified by flash column chromatography (silica gel, hexane:EtOAc 2:1) yielding 1.38 g of red crystals (71 %).

Mp: >270 °C

IR: (υ/cm^{-1}): 2918, 1757, 1373, 1203, 1009.

^{1}H-NMR: (400 MHz, CHCl$_3$, δ/ppm): 10.18 (s, 1H, NH), 8.59 (d, $^3J_{HH}$ = 8.8 Hz, 1H, H$_{aryl}$), 7.91 (s, 1H, H$_{aryl}$), 7.88 (d, $^3J_{HH}$ = 8.1 Hz, 1H, H$_{aryl}$), 7.80 (d, $^3J_{HH}$ = 7.3 Hz, 1H, H$_{aryl}$), 7.73 (d, $^3J_{HH}$ = 7.5 Hz, 1H, H$_{aryl}$), 7.61 – 7.51 (m, 3H, H$_{aryl}$), 7.22 (dd, $^3J_{HH}$ = 8.4 Hz, $^3J_{HH}$ = 8.4 Hz, 1H, H$_{aryl}$), 6.83 (dd, $^3J_{HH}$ = 8.0 Hz, $^3J_{HH}$

= 8.0 Hz, 1H, H$_{aryl}$), 6.73 (d, $^3J_{HH}$ = 8.3 Hz, 1H, H$_{aryl}$), 6.24 (bs, 2H, NH$_2$), 1.97 [s, 3H, NHC(O)CH$_3$], 1.37 [s, 9H, C(CH$_3$)$_3$].

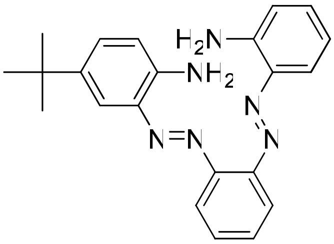
^{13}C-NMR: (101 MHz, CDCl$_3$, δ/ppm): 169.5 (NH**C**(O)CH$_3$), 148.0 (C$_{aryl}$), 148.0 (C$_{aryl}$), 146.8 (C$_{aryl}$), 142.5 (C$_{aryl}$), 139.6 (C$_{aryl}$), 138.1 (C$_{aryl}$), 133.6 (C$_{aryl}$), 133.2 (C$_{aryl}$), 131.8 (C$_{aryl}$), 131.1 (C$_{aryl}$), 130.9 (C$_{aryl}$), 130.6 (C$_{aryl}$), 120.7 (C$_{aryl}$), 119.7 (C$_{aryl}$), 118.9 (C$_{aryl}$), 117.8 (C$_{aryl}$), 117.7 (C$_{aryl}$), 117.6 (C$_{aryl}$), 35.0 (**C**(CH$_3$)$_3$), 31.7 (C(**C**H$_3$)$_3$), 25.5 (NHC(O)**C**H$_3$).

Ms: (EI 70 eV): 415 (8) [M+1], 414 (32) [M$^+$], 267 (100).

EA: calculated: C = 69.54, H = 6.32, N = 20.28

found: C = 69.42, H = 6.29, N = 20.31

2,2’’-Diamino-4’’-*tert*-butylbisazobenzene (53b)



To a solution of 2-amino-2’’-acetamino-4’’-*t*-butylbisazobenzene (**58b**) (1.23 g, 2.97 mmol, 1.00 eq.) in 75 ml of ethanol was added potassium hydroxide (3.77 g, 67.2 mmol, 22.7 eq.), dissolved in a mixture of 50 ml ethanol and 20 ml water. The reaction was stirred at 100 °C for 2 h. Then, the mixture was allowed to cool to room temperature and diluted with water. After extraction with CH$_2$Cl$_2$, washing four times with water and drying over Na$_2$SO$_4$, the solvent was removed under reduced pressure, yielding 1.13 g of a red solid (100 %).

Mp: 103-105 °C

IR: (υ/cm^{-1}): 3456, 2957, 1614, 1385, 1157, 1139.

^{1}H-NMR: (400 MHz, CDCl$_3$, δ/ppm): 7.91 (d, $^4J_{HH}$ = 8.8 Hz, 1H, H$_{aryl}$), 7.89 (d, $^3J_{HH}$ = 8.1 Hz, 1H, H$_{aryl}$), 7.80 – 7.76 (m, 2H, H$_{aryl}$), 7.51 – 7.46 (m, 2H, H$_{aryl}$), 7.29 (dd, $^3J_{HH}$ = 8.6 Hz, $^4J_{HH}$ = 2.4 Hz, 1H, H$_{aryl}$), 7.24 – 7.18 (m, 1H, H$_{aryl}$), 6.86 –

6.81 (m, 1H, H_{aryl}), 6.73 (d, $^3J_{HH}$ = 8.5 Hz, 1H, H_{aryl}), 6.71 (d, $^3J_{HH}$ = 8.6 Hz, 1H, H_{aryl}), 5.95 (bs, 4H, NH_2), 1.34 [s, 9H, $C(CH_3)_3$].

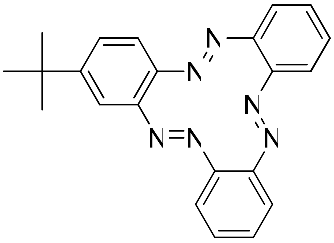
^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 148.5 (C_{aryl}), 148.2 (C_{aryl}), 142.4 (C_{aryl}), 140.6 (C_{aryl}), 140.1 (C_{aryl}), 138.2 (C_{aryl}), 137.9 (C_{aryl}), 132.7 (C_{aryl}), 131.8 (C_{aryl}), 130.8 (C_{aryl}), 130.7 (C_{aryl}), 130.6 (C_{aryl}), 127.1 (C_{aryl}), 124.7 (C_{aryl}), 117.6 (C_{aryl}), 117.5 (C_{aryl}), 117.3 (C_{aryl}), 117.1 (C_{aryl}), 34.4 ($\mathbf{C}(CH_3)_3$), 31.8 ($C(\mathbf{C}H_3)_3$).

Ms: (EI 70 eV): 372 (96) [M^+], 162 (100).

EA: calculated: C = 70.94, H = 6.49, N = 22.56

found: C = 70.85, H = 6.55, N = 22.70

3-*tert*-Butylcyclotrisazobenzene (52b)



Triethylamine (0.75 ml, 5.37 mmol, 10.0 eq.) was added to a solution of 2,2''-diamino-4''-*tert*-butylbisazobenzene (**53b**) (200 mg, 0.54 mmol, 1.00 eq.) in CH_2Cl_2 (65 ml). Then, $Pb(OAc)_4$ (541 mg, 1.22 mmol, 2.26 mmol) dissolved in 7 ml of CH_2Cl_2 was added dropwise. After complete addition the mixture was stirred for 30 min. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (alumina, TBME/Hexane 1:7). A red-brown oil was obtained, which crystallized after a few days to give 97 mg of brown crystals (49 %).

Mp: 128-132 °C

IR: (υ/cm^{-1}): 2952, 1456, 1360, 825, 758.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.73 – 7.52 (m, 11H, H_{aryl}), 1.43 (s, 9H, $C(C\mathbf{H}_3)_3$).

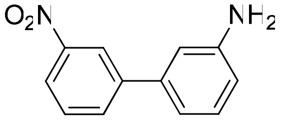
^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 154.4 (C_{aryl}, 1C), 147.0 (C_{aryl}, 1C) , 146.9 (C_{aryl}, 1C), 146.8 (C_{aryl}, 1C), 146.7 (C_{aryl}, 1C), 146.7 (C_{aryl}, 1C), 144.4 (C_{aryl}, 1C), 130.5 (C_{aryl}, 1C), 130.4 (C_{aryl}, 1C), 130.4 (C_{aryl}, 1C), 130.4 (C_{aryl}, 1C), 127.6 (C_{aryl}, 1C), 122.8 (C_{aryl}, 1C), 122.7 (C_{aryl}, 1C), 122.0 (C_{aryl}, 1C), 121.8 (C_{aryl}, 1C), 121.8 (C_{aryl}, 1C), 119.7 (C_{aryl}, 1C), 37.6 ($\mathbf{C}(CH_3)_3$, 1C), 31.7 ($C(\mathbf{C}H_3)_3$, 3C).

Ms: (EI 70 eV): 368 (12) [M^+], 353 (100).

EA: calculated: C = 71.72, H = 5.47, N = 22.81

found: C = 71.55, H = 5.61, N = 22.49

3-nitro-3'-aminobiphenyl (67)



A 3-necked falsk was attached with a reflux condenser, and flushed with argon for ten minutes. Then, 3-aminophenylboronic acid (**68**) (2.41 g, 17.6 mmol, 1.21 eq.), 3-bromonitrobenzene (**69**) (2.95 g, 14.6 mmol, 1.00 eq.) and tetrakis(triphenylphosphine)palladium (511 mg, 0.44 mmol, 3 mol%) was added. The substrates were dissolved in 300 ml toluene and 20 ml ethanol. After that, 10 ml of a 5M aq. Na_2CO_3 solution was added. The mixture was degassed by bubbling argon through it for 30 minutes, and stirred at 120 °C for 16 hours under an argon atmosphere. The mixture was then allowed to cool down and diluted with 300 ml EtOAc and 100 ml H_2O. The organic layer was washed with brine (100 ml) and dried over $MgSO_4$. After removal of the solvent, the residual brown oil was purified by column chromatography (silica gel, hexane:EtOAc 3:2) to yield 2.57 g of a yellow oil (82 %).

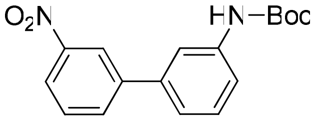
Mp: 128-132 °C

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.40 (t, $^4J_{HH}$ = 2.0 Hz, 1H, H_{aryl}), 8.16 (d, $^3J_{HH}$ = 8.2 Hz, 1H, H_{aryl}), 7.86 (d, $^3J_{HH}$ = 8.2 Hz, 1H, H_{aryl}), 7.56 (t, $^3J_{HH}$ = 8.0 Hz, 1H, H$_{aryl}$), 7.26 (t, $^3J_{HH}$ = 8.0 Hz, 1H, H$_{aryl}$), 6.98 (d, $^3J_{HH}$ = 8.0 Hz, 1H, H$_{aryl}$), 6.91 (s, $^4J_{HH}$ = 2.0 Hz, 1H, H$_{aryl}$), 6.74 (d, $^3J_{HH}$ = 8.0 Hz, 1H, H$_{aryl}$), 3.84 (bs, NH_2).

^{13}C-NMR: (101 MHz, $CDCl_3$), δ/ppm): 149.0 (C-8, 2C), 147.6 (C$_{aryl}$), 143.5 (C$_{aryl}$), 140.2 (C$_{aryl}$), 133.4 (C$_{aryl}$), 130.5 (C$_{aryl}$), 130.0 (C$_{aryl}$), 122.4 (C$_{aryl}$), 122.3 (C$_{aryl}$) 117.8 (C$_{aryl}$), 115.6 (C$_{aryl}$), 114.0 (C$_{aryl}$).

The analytical data corresponded to the literature.[9]

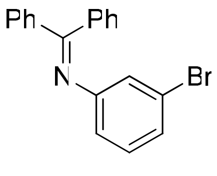
3-N-Boc-3'-nitrobiphenyl 70



3-Nitro-3'-aminobiphenyl (**67**) (1.17 g, 5.44 mmol, 1.00 eq.) was dissolved in THF (200 ml) and Boc-anhydride (3.56 g, 16.3 mmol, 3.00 eq.) was added. The mixture was stirred at 65 °c for three days. Then, the solvent was removed under reduced pressure and the residue was dissolved in DCM, washed with sat. aq. NH_4Cl, sat aq. $NaHCO_3$, brine and water (each 50 ml), dried over $MgSO_4$ and concentrated. Flash column chromatographie of the residue (silica gel, Hexane: EtOAc 4:1) yielded 1.69 g of a yellow oil which solidified in the freezer (99 %).

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.43 (t, $^4J_{HH}$ = 2.0 Hz, 1H, H$_{aryl}$), 8.19 (d, $^3J_{HH}$ = 8.2 Hz, 1H, H$_{aryl}$), 7.92 (d, $^3J_{HH}$ = 8.0 Hz, 1H, H$_{aryl}$), 7.76 (s, 1H, H$_{aryl}$), 7.59 (d, $^3J_{HH}$ = 8.0 Hz, 1H, H$_{aryl}$), 7.40 (t, $^3J_{HH}$ = 8.0 Hz, 1H, H$_{aryl}$), 7.34 – 7.30 (m, 1H, H$_{aryl}$), 7.29 – 7.26 (m, 1H, H$_{aryl}$), 6.61 (bs, 1H, $NHCOO(CH_3)_3$), 1.54 (s, 9H, $NHCOO(CH_3)_3$).

benzhydryliden-(3-bromo-phenyl)-amine (75)

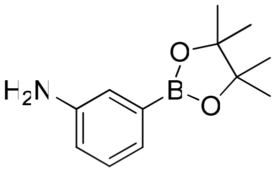


A mixture of 3-bromoaniline (**74**) (5.00 g, 28.5 mmol, 1.00 eq.), pTsOH monohydrate (260 mg, 1.37 mmol, 4.80 mol%) and benzophenone (4.93 g, 27.1 mmol, 0.95 eq.) was dissolved in toluene (30 ml). The mixture was stirred at 120 °C for 20 hours, while the water was removed with a water separator. Then, the solvent was removed at reduced pressure and after the addition of methanol (10 ml) the mixture was cooled to -30 °C in a freezer. After a few hours yellow crystals precipitated (4.08 g). These were collected, washed with methanol and dried. Another, less clean fraction was obtained by concentrating the filtrate and freezing it again (2.16 g) to give a total yield of 65 %.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.75 (d, $^3J_{HH}$ = 7.1 Hz, 2H), 7.49 (t, $^3J_{HH}$ = 7.4 Hz, 1H), 7.41 (t, $^3J_{HH}$ = 7.4 Hz, 2H), 7.33 – 7.26 (m, 3H), 7.12 (d, $^3J_{HH}$ = 7.9 Hz, 2H), 7.05 (d, $^3J_{HH}$ = 8.7 Hz, 1H), 6.99 (t, $^3J_{HH}$ = 7.9 Hz, 1H), 6.93 (s, 1H), 6.62 (d, $^3J_{HH}$ = 7.9 Hz, 1H).

The analytical data corresponded to the literature.[10]

3-aminophenylboronic acid pinacol ester 76



benzhydryliden-(3-bromo-phenyl)-amine (**75**) (5.00 g, 14.9 mmol, 1.00 eq.) was dissolved in dry THF (42 ml) in an oven dried three-necked-flask which was kept under an argon atmosphere. Then, the mixture was cooled down to -78 °C with a dry ice/acetone cooling bath, and 2.5M n-Butyllithium in hexane (6.56 ml, 16.4 mmol, 1.10 eq.) was slowly added during 20 min.. The mixture was stirred for 1 h., after which the temperature was further decreased to -86 °C with a 2-butanone/liquid N_2 cooling bath. Trimethyl borate (2.03 ml, 17.8 mmol, 1.20 eq.) was now added dropwise and the mixture was again stirred for 1 h. and then left to warm up to -10 °C. After that, the mixture was poured onto 35 ml of 6.5 % aq. sulfuric acid, which was covered with a layer of 13 ml of toluene. The mixture was stirred for one hour, after which the aqueous layer was separated and treated with 50 ml of fresh toluene. After addition of pinacol (2.11 g, 17.8 mmol, 1.20 eq.) and 14.0 g of a 10 % aqueous NaOH solution, the mixture was stirred at room temperature over night. The organic layer was separated and the aqueous layer was extracted with toluene (20 ml). After drying of the combined organic layers over $MgSO_4$ and removal of the solvent, the brown oil was purified with flash column chromatography (silica gel, hexane:EtOAc 3:1). 755 mg of a colourloss solid was obtained (23 %).

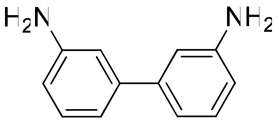
MP: 87 - 90 °C

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): δ = 7.14 (d, $^3J_{HH}$ = 8.4 Hz, 1H), 7.15 (s, 1H), 6.76 (t, J = 7.3 Hz, 1H), 6.68 (d, J = 8.3 Hz, 1H), 3.64 (bs, s, 2H), 1.23 (s, 12H).

^{13}C NMR: (101 MHz, $CDCl_3$, δ/ppm): 146.2 (C_{aryl}), 129.1 (C_{aryl}), 124.8 (C_{aryl}), 118.4 (C_{aryl}), 115.0 (C_{aryl}), 83.5 (C_{aryl}), 24.7 (C_{aryl}).

The analytical data corresponded to the literature.[11]

3,3'-Diaminobiphenyl (65)



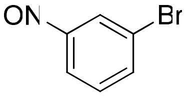
A 3-necked falsk was attached with a reflux condenser, and flushed with argon for ten minutes. Then, 3-bromoaniline (**74**) (0.949 ml, 8.55 mmol, 1.00 eq.), 3-aminophenylboronic acid (**68**) (1.75 g, 12.8 mmol, 1.50 eq.), and $Pd(PPh_3)_4$ (299 mg, 256 μmmol, 3 mol%) were added and dissolved in a mixture of 260 ml of toluene, 15 ml of ethanol and 8 ml of 2M Na_2CO_3. The mixture was degassed with an argon stream, heated at 100 °C for 16 hours and afterwards allowed to cool down to room temperature. Then, the mixture was diluted with 300 ml EtOAc and 100 ml H_2O. The organic layer was washed with brine (100 ml) and dried over $MgSO_4$. After removal of the solvent, the residual brown oil was purified by flash column chromatography (silica gel, Hexane:EtOAc 1:1) to yielded 1.19 g of **12** as a pale yellow oil which crystallized upon standing at room temperature (76 %).

MP: 93 °C

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.21(t, $^3J_{HH}$ = 7.8 Hz, 2H, H_{aryl}), 6.97 (d, $^3J_{HH}$ = 7.7 Hz, 2H, H_{aryl}), 6.88 (s, 2H, H_{aryl}), 7.67 (d, $^3J_{HH}$ = 7.9 Hz, 2H, H_{aryl}), 3.72 (bs, 4H, NH_2).

The analytical data corresponded to the literature.[12]

3-Bromonitrosobenzene (77)

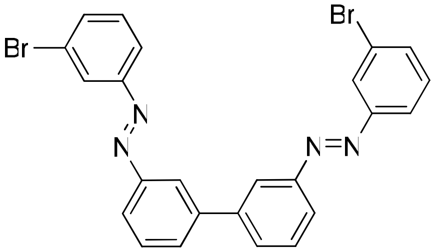


A solution of 3-bromoaniline (**74**) (1.50 g, 8.55 mmol, 1.00 eq.) in 40 ml of DCM and treated with a solution of Oxone® (10.5 g, 17.1 mmol, 2.00 eq.) in 160 ml H_2O. After vigorous stirring for five hours at room temperature, the organic layer was separated and washed with sat. aq. NH_4Cl, sat. aq. $NaHCO_3$, and brine. The combined organic phases were dried over $MgSO_4$, the solvent was removed under reduced pressure and 1.29 g of a brown solid was obtained, which consisted of a 4:1 mixture of 3-bromo-nitrosobenzene (1.08 g, 65 %) and 3-bromonitrobenzene. The mixture was used for Mills reactions without further purification.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.11 (d, $^3J_{HH}$ = 7.9 Hz, 1H, H_{aryl}), 7.84 (d, $^3J_{HH}$ = 7.9 Hz, 1H, H_{aryl}), 7.77 (s, 1H, H_{aryl}), 7.67 (d, $^3J_{HH}$ = 7.9 Hz, 2H, H_{aryl}), 7.57 (t, 1H, H_{aryl}).

The analytical data corresponded to the literature.[13]

Bisazodibromide 73

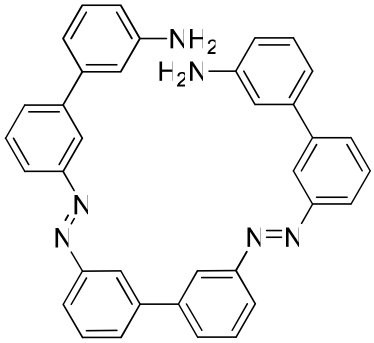


To a solution of 3,3'-diaminobiphenyl (**65**) ((646 mg, 3.50 mmol, 1.00 eq.) in acetic acid (50 ml) 3-bromonitrosobenzene (**77**) (1.63 g, 8.76 mmol, 2.50 eq.) was added. The suspension was stirred over night and a precipitate formed, which was collected by filtration and taken up in DCM. After drying over $MgSO_4$ and removal of the solvent, the residue was purified by flash column chromatography (silica gel, hexane:DCM 1:1) yielding 1.24 g of dibromide **10** as an orange solid (68 %).

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.25 (s, 2H), 8.10 (s, 2H), 7.94 (t, $^3J_{HH}$ = 8.7 Hz, 4H), 7.83 (d, $^3J_{HH}$ = 7.7 Hz, 2H), 7.64 (t, $^3J_{HH}$ = 7.9 Hz, 2H), 7.62 (d, $^3J_{HH}$ = 7.7 Hz, 2H), 7.43 (t, $^3J_{HH}$ = 7.9 Hz, 2H).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 153.9 (C_{aryl}), 153.2 (C_{aryl}), 141.8 (C_{aryl}), 134.2 (C_{aryl}), 130.9 (C_{aryl}), 130.5 (C_{aryl}), 130.2 (C_{aryl}), 125.1 (C_{aryl}), 123.6 (C_{aryl}), 123.5 (C_{aryl}), 122.8 (C_{aryl}), 122.2 (C_{aryl}).

Bisazodiamine 72



A three necked flask was charged with bisazodibromide **73** (937 mg, 2.11 mmol, 1.00 eq.), 3-phenylboronic acid (**68**) (867 mg, 6.33 mmol, 3.00 eq.), $Pd(PPh_3)_4$ (148 mg, 127 µmmol, 6 mol%) and a solvent mixture of 65 ml of toluene, 5 ml of ethanol and 2.5 ml of aq. 2M Na_2CO_3. The mixture was degassed with an argon stream for 20 min before it was heated at 100°C under an argon atmosphere for 20 h. Then the mixture was cooled down and diluted with 300 ml EtOAc and 100 ml H_2O. The organic phase was washed with brine (100 ml) and dried over $MgSO_4$. After removal of the solvent, the residual brown oil was purified by column chromatography (silica gel, hexane:EtOAc 1:1) yielded 636 mg of **72** as an orange solid (55 %).

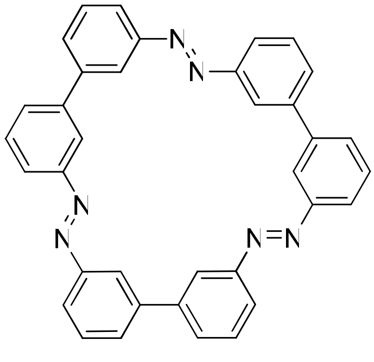
MP: 167 – 170 °C

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.30 (s, 2H), 8.19 (s, 2H), 7.98 (d, $^3J_{HH}$ = 7.9 Hz, 4H), 7.93 (d, $^3J_{HH}$ = 7.9 Hz, 2H), 7.83 (d, $^3J_{HH}$ = 7.6 Hz, 2H), 7.71 (d, $^3J_{HH}$ = 7.6 Hz, 2H), 7.65 (t, $^3J_{HH}$ = 7.8 Hz, 2H), 7.58 (t, $^3J_{HH}$ = 7.8 Hz, 2H), 7.27 (t, $^3J_{HH}$ = 7.8 Hz, 2H), 7.10 (d, $^3J_{HH}$ = 7.6 Hz, 2H), 7.02 (s, 2H), 6.72 (d, $^3J_{HH}$ = 7.7 Hz, 2H).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 153.6 (C_{aryl}), 153.4 (C_{aryl}), 147.3 (C_{aryl}), 142.8 (C_{aryl}), 142.0 (C_{aryl}), 141.8 (C_{aryl}), 130.2 (C_{aryl}), 130.14 (C_{aryl}), 130.09 (C_{aryl}), 130.07 (C_{aryl}), 129.8 (C_{aryl}), 122.5 (C_{aryl}), 122.2 (C_{aryl}), 122.13 (C_{aryl}), 122.06 (C_{aryl}), 118.1 (C_{aryl}), 114.9 (C_{aryl}), 114.3 (C_{aryl}).

MS: (EI, 70 ev): *m/z* (%) = 544 (61) [M^+], 168 (100).

Cyclotrisazobenzene (63)



A solution of 3,3''-diaminobisazobiphenyl **72** (432 mg, 739 mmol, 1.00 eq.) was dissolved in dry THF (90 ml) and freshly crystallized $Pb(OAc)_4$ (809 mg, 1.82 mmol, 2.30 eq.) dissolved in dry THF (12 ml) was added dropwise. After stirring over night, 1.16 g EDTA and 80 ml of water and 80 ml of CH_2Cl_2 were added. Then, the mixture was stirred for half an hour after which it was extracted with CS_2, dried over Na_2SO_4, and the solvent removed at reduced pressure. The residual solid was washed with CH_2Cl_2 and acetone to obtain 120 mg of an orange powder (34 %).

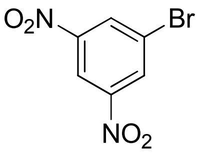
MP: > 245 °C

IR: (υ/cm^{-1}): 3032, 2338, 1736, 1597, 1474, 1157, 1080, 918, 895, 795, 694.

^{1}H-NMR: (400 MHz, $CS_2/CDCl_3$ 1:1, δ/ppm): 8.68 (s, 6H), 8.00 (d, $^3J_{HH}$ = 7.9 Hz, 6H), 7.93 (d, $^3J_{HH}$ = 7.4 Hz, 6H), 7.65 (d, $^3J_{HH}$ = 7.8 Hz, 6H).

MS: (EI, 70 ev): *m/z* (%) = 540 (52) [M^+], 481 (100).

5-Bromo-1,3-dinitrobenzene (79)



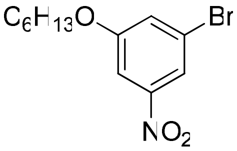
To 60 ml of conc. H_2SO_4 was added 1,3-dinitrobenzene (**78**) (20.0 g, 119 mmol, 1.00 eq.) and the mixture was heated to 60 °C. Then, NBS (26.8 g, 143 mmol, 1.20 eq.) was added in three portions every 20 minutes. Then, the reaction was stirred over night, when the conversion was not complete. Another 13 g of NBS was added and after stirring for additional 6 hours, there was still some starting material left. The reaction was poured onto 300 ml of crushed ice, the precipitate was collected and washed with water. Recrystallization with methanol yielded 14.7 g of colourless needles (50 %).

MP: 78 – 79 °C.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.97 (s, 1H), 8.68 (s, 2H).

The analytical data corresponded to literature.[14]

5-Bromo-3-(hexyloxy)-5-nitrobenzene (80)

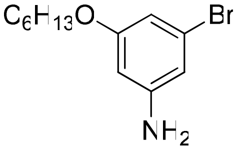


Potassium hydroxide (7.07 g, 113 mmol, 2.00 eq.) and hexanol (14.1 ml, 113 mmol, 2.00) were dissolved in DMF (30 ml) and heated to 75 °C. Then, a solution of 3-bromo-1,5-dinitrobenzene (**79**) (14.0 g, 56.7 mmol, 1.00 eq.) in DMF (30 ml) was added and the mixture was stirred over night at 75 °C. The mixture was allowed to cool down and poured into water (300 ml) and acidified with 1M aq. HCl. After extraction with DCM (4x) and washing with conc. aq. $NaHCO_3$, and brine, the organic layers were dried over $MgSO_4$, concentrated and purified by flash column chromatography (silica gel, hexane:DCM 3:1) to yield 8.30 g of a yellow oil (49 %).

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.90 (s, 1H, H_{aryl}), 7.63 (s, 1H, H_{aryl}), 7.32 (s, 1H, H_{aryl}), 3.99 (t, $^3J_{HH}$ = 6.5 Hz, 2H, OCH_2), 1.82 – 1.75 (m, 2H, CH_2), 1.50 – 1.39 (m, 2H, CH_2), 1.38 – 1.26 (m, 4H, CH_2), 0.88 (t, $^3J_{HH}$ = 7.0 Hz, 3H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$), δ/ppm): 160.6 (C_{aryl}), 149.9 (C_{aryl}), 124.7 (C_{aryl}), 123.3 (C_{aryl}), 119.1 (C_{aryl}), 108.6 (C_{aryl}), 69.6 (OCH_2), 31.9 (CH_2), 29.2 (CH_2), 26.0 (CH_2), 23.0 (CH_2), 14.4 (CH_3).

5-Bromo-3-hexyloxyaniline (81)

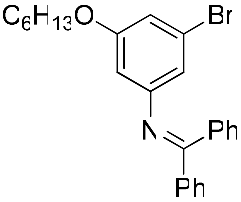


1-Bromo-3-(hexyloxy)-5-nitrobenzene (**80**) (8.19 g, 27.1 mmol, 1.00 eq.) was dissolved in ethanol (140 ml) and stanneous chloride dehydrate (30.6 g, 136 mmol, 5.00 eq.) was added. The mixture was stirred at 80 °C over night and then allowed to warm to room temperature. After neutralization with 10 % aq. NaOH and extraction with DCM (3 x), the organic layers were dried over $MgSO_4$. Removal of the solvent under reduced pressure yielded 6.55 g of a pale yellow oil, which crystallized in the fridge to give a colourless solid (89 %).

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 6.46 (s, 1H, H_{aryl}), 6.42 (s, 1H, H_{aryl}), 6.13 (s, 1H, H_{aryl}), 3.85 (t, $^3J_{HH}$ = 6.5 Hz, 2H, OCH_2), 3.66 (bs, NH_2), 1.77 – 1.65 (m, 2H, CH_2), 1.46 – 1.26 (m, 6H, CH_2), 0.89 (t, $^3J_{HH}$ = 7.0 Hz, 3H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$), δ/ppm): 161.2 (C_{aryl}), 149.0 (C_{aryl}), 123.6 (C_{aryl}), 111.1 (C_{aryl}), 108.4 (C_{aryl}), 100.8 (C_{aryl}), 68.5 (OCH_2), 32.0 (CH_2), 29.5 (CH_2), 26.1 (CH_2), 23.0 (CH_2), 14.4 (CH_3).

Benzhydryliden-(3-hexyloxy-5-bromo-phenyl)-amine (82)



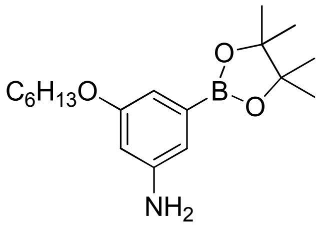
A solution of 3-hexyloxy-5-bromoaniline (**81**) (2.89 g, 10.6 mmol, 1.00 eq.), benzophenone (1.83 g, 10.1 mmol, 0.950 eq.), and p-TSOH (101 mg, 530 µmol, 5 mol%) in toluene was stirred at 120 °C for 48 h. Then, the mixture was cooled down to room temperature and basified with 0.5 M NaOH. The organic layer was separated and the aqueous layer was extracted with DCM. After drying over $MgSO_4$ and removal of the solvent, the residue was purified by column chromatography (silica: hexane/EtOAc 15:1), to yield a yellow oil, which crystallized upon standing in the freezer for a short time. (88 %).

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.74 (d, $^3J_{HH}$ = 7.1 Hz, 2H, H_{aryl}), 7.49 (t, $^3J_{HH}$ = 7.3 Hz, 1H, H_{aryl}), 7.41 (t, $^3J_{HH}$ = 7.4 Hz, 2H, H_{aryl}), 7.35 – 7.27 (m, 3H, H_{aryl}), 7.17 –

7.11 (m, 2H, H_{aryl}), 6.64 (s, 1H, H_{aryl}), 6.48 (s, 1H, H_{aryl}), 6.21 (s, 1H, H_{aryl}), 3.77 (t, $^3J_{HH}$ = 6.6 Hz, 2H, OCH_2), 1.70 – 1.63 (m, 2H, CH_2), 1.43 – 1.25 (m, 6H, CH_2), 0.94 – 0.87 (m, 3H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$), δ/ppm): 169.5 (N=**C**Ph_2), 160.3 (C_{aryl}), 153.7 (C_{aryl}), 139.6 (C_{aryl}), 136.1 (C_{aryl}), 131.4 (C_{aryl}), 129.8 (C_{aryl}, 2C), 129.7 (C_{aryl}, 2C), 129.3 (C_{aryl}), 128.7 (C_{aryl}, 2C), 128.5 (C_{aryl}, 2C), 122.4 (C_{aryl}), 116.7 (C_{aryl}), 113.5 (C_{aryl}), 106.5 (C_{aryl}), 68.6 (OCH_2), 31.9 (CH_2), 29.4 (CH_2), 26.0 (CH_2), 23.0 (CH_2), 14.5 (CH_3).

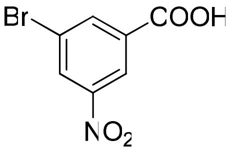
3-Hexyloxy-5-aminophenylboronic acid pinacol ester 83



A three necked flask was flushed with argon and charged with Benzhydryliden-(3-hexyloxy-5-bromo-phenyl)-amine **82** (3.13 g, 7.18 mmol, 1.00 eq.). After 20 ml of dry THF had been added, the mixture was cooled to -78 °C. Then, a solution of 2.5M n-Butyllithium (3.20 ml, 8.00 mmol, 1.11 eq.) in hexane was added dropwise. The mixture was stirred for one hour, followed by the slow addition of trimethyl borate (980 ml, 8.62 mmol, 1.20 eq.), keeping the temperature at -78 °C. After the mixture was stirred for one hour, the mixture was allowed to warm to room temperature and stirred over night. The mixture was poured onto 5 ml of 10% aq. H_2SO_4 and stirred for one hour. Then, 20 ml of 10 % aq. NaOH was added, and the mixture was stirred for half an hour, followed by the addition of 20 ml of sat. aq. NH_4Cl to slightly acidify the mixture. After extraction with DCM (3x) the organic layers were treated with pinacol (1.02 g, 8.62 mmol, 1.20 eq.) and stirred for six hours. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (silica gel: hexane/EtOAc 3:1) to yield 1.92 g of a pale brown oil 84 %.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 6.75 – 6.72 (m, 2H, H_{aryl}), 6.35 (s, 1H, H_{aryl}), 3.94 (t, $^3J_{HH}$ = 6.6 Hz, 2H, OCH_2), 3.62 (bs, 2H, CH_2), 1.77 – 1.69 (m, 2H, CH_2), 1.48 – 1.39 (m, 2H, CH_2), 1.37 – 1.28 (m, 17H, CH_2, CH_3).

3-Nitro-5-bromobenzoic acid (87)



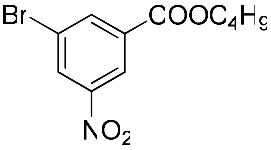
A flask was charged with 3-nitrobenzoic acid (**86**) (30.4 g, 180 mmol, 1.00 eq.) and 82 ml of conc. sulphuric acid was added. The solution was heated to 60 °C. Then, NBS (38.8 g, 216 mmol, 1.20 eq.) was added in three portions over 3 h, keeping the temperature between 60 and 70 °C. After complete addition the mixture was stirred over night at 60 °C and poured onto crushed ice (300 g), filtered and washed with water and hexane. The solid was then dissolved in EtOAc (200 ml) and dried over sodium sulphate. Then solution was concentrated till a precipitate was observed. Then, hexane was slowly added to crystallize the product out of solution to obtain 36.9 g of a white solid (83 %).

MP: 160 – 163 °C

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 10.26 (bs, 1H, COOH), 8.88 (s, 1H, H_{aryl}), 8.64 (s, 1H, H_{aryl}), 8.57 (s, 1H, H_{aryl}).

The analytical data corresponded to the literature.[14]

3-Nitro-5-bromobutylbenzoate (88)



A solution of 3-nitro-5-bromobenzoic acid (**87**) (8.11 g, 33.0 mmol, 1.00 eq.) in butanol (60 ml) was cooled to 0 °C. Then, thionyl chloride (3.61 ml, 49.5 mmol, 1.50 eq.) was slowly added dropwise during 10 minutes. After that, the mixture was stirred at 100 °C for three hours and the allowed to cool to room temperature and 50 ml of water was added. Extraction with ethyl acetate (2x) was followed by washing with sat. aq. $NaHCO_3$ and drying over $MgSO_4$. The solvent was removed under reduced pressure and the residue was dried under high vacuum to obtain 9.50 g of a yellow oil (95 %).

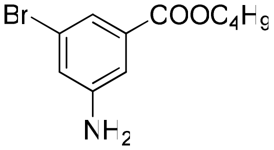
IR: (υ/cm^{-1}): 2932, 2870, 1720, 1535, 1342, 1265, 1150, 941, 733.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.79 (s, 1H, H_{aryl}), 8.56 (s, 1H, H_{aryl}), 8.49 (s, 1H, H_{aryl}), 4.42 (t, $^3J_{HH}$ = 6.7 Hz, 2H, OCH_2), 1.87 – 1.76 (m, 2H, CH_2), 1.58 – 1.43 (m, 2H, CH_2), 1.02 (t, $^3J_{HH}$ = 7.3 Hz, 3H, CH_3).

^{13}C-NMR: (400 MHz, $CDCl_3$, δ/ppm): 163.3 (C=O), 148.8 (C_{aryl}), 138.2 (C_{aryl}), 133.7 (C_{aryl}), 130.3 (C_{aryl}), 123.12 (C_{aryl}), 123.05 (C_{aryl}), 66.3 (OCH_2), 30.6 (CH_2), 19.2 (CH_2), 13.7 (CH_2).

MS: (EI, 70 ev): *m/z* (%) = 301 (2.7) [M^+], 303 (2.6) [M^++1], 56 (100).

3-Amino-5-bromobutylbenzoate (89)



A flask was charged with 3-nitro-5-bromobutylbenzoate (**88**) (9.03 g, 29.9 mmol, 1.00 eq.), $SnCl_2*2H_2O$ (32.7 g, 145 mmol, 5.00 eq.) and ethanol (60 ml) was added. The mixture was stirred at 60 °C for 3 h and then poured onto 300 mg of ice. The mixture was basified with 2M Na_2CO_3 and extracted with ethyl acetate (3*50 ml). Drying over Na_2SO_4, removal of the solvent and drying under high vacuum, gave 6.36 g of a white solid (78 %).

MP: 67 – 72 °C

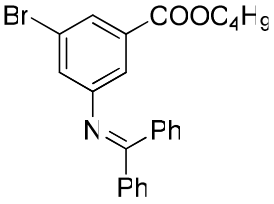
IR: (υ/cm^{-1}): 3379, 2870, 1704, 1620, 1566, 1304, 1242, 987, 849, 764, 733.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.51 (s, 1H, H_{aryl}), 7.25 (s, 1H, H_{aryl}), 6.98 (s, 1H, H_{aryl}), 4.29 (t, $^3J_{HH}$ = 6.4 Hz, 2H, OCH_2), 3.85 (bs, 2H, NH_2), 1.76 – 1.69 (m, 2H, CH_2), 1.50 – 1-41 (m, 2H, CH_2), 0.97 (t, $^3J_{HH}$ = 7.4 Hz, 3H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 166.0 (C=O), 148.1 (C_{aryl}), 133.4 (C_{aryl}), 123.3 (C_{aryl}), 122.6 (C_{aryl}), 122.0 (C_{aryl}), 114.9 (C_{aryl}), 65.6 (OCH_2), 31.1 (CH_2), 19.6 (CH_2), 14.1 (CH_3).

MS: (EI, 70 ev): *m/z* (%) = 271 (71) [M^+], 273 (70) [M^++1], 215 (100).

butyl 3-bromo-5-(diphenylmethyleneamino)benzoate

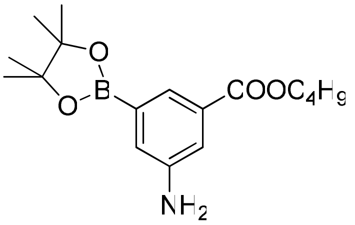


A solution of butyl 3-amino-5-bromobenzoate (3.00 g, 11.0 mmol, 1.00 eq.), benzophenone (1.97 g, 10.8 mmol, 0.980 eq.), and p-TSOH (105 mg, 550 μmol, 5 mol%) in toluene (10 ml) was stirred at 120 °C for 48 h. Then, the mixture was cooled down to room temperature and basified with 0.5 M NaOH. The organic layer was separated and the aqueous layer was extracted with DCM. After drying over $MgSO_4$ and removal of the solvent, the residue was purified by column chromatography (silica: hexane/EtOAc 10:1), to yield a yellow oil, which still contained traces of benzophenone, which were removed by distillation. The yellow residue crystallized upon standing (3.13 g, 65 %).

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.78 – 7.70 (m, 3H, H_{aryl}), 7.50 (t, $^3J_{HH}$ = 7.3 Hz, 1H, H_{aryl}), 7.42 (t, $^3J_{HH}$ = 7.4 Hz, 2H, H_{aryl}), 7.35 – 7.26 (m, 4H, H_{aryl}), 7.14 – 7.08 (m, 2H, H_{aryl}), 7.04 (s, 1H, H_{aryl}), 4.25 (t, $^3J_{HH}$ = 6.7 Hz, 2H, OCH_2), 1.72 – 1.65 (m, 2H, CH_2), 1.46 – 1.37 (m, 2H, CH_2), 0.96 (t, $^3J_{HH}$ = 7.4 Hz, 3H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 170.5 (N=CPh_2), 165.6 (C=O) 153.0 (C_{aryl}), 139.3 (C_{aryl}), 135.7 (C_{aryl}), 132.7 (C_{aryl}), 131.7 (C_{aryl}), 129.9 (C_{aryl}, 2C), 129.7 (C_{aryl}, 2C), 129.5 (C_{aryl}), 128.7 (C_{aryl}, 2C), 128.6 (C_{aryl}, 2C), 128.5 (C_{aryl}), 127.4 (C_{aryl}), 122.5 (C_{aryl}), 121.4 (C_{aryl}), 65.5 (OCH_2), 31.1 (CH_2), 19.6 (CH_2), 14.2 (CH_3).

butyl 3-amino-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate 90



A three necked flask was charged with 3-amino-5-bromobutylbenzoate (**89**) (4.00 g, 14.7 mmol, 1.00 eq.), bis(pinacolato)diboron (4.11 g, 16.2 mmol, 1.10 eq.), Pd(dppf)Cl_2*CH_2Cl_2 (960 mg, 8 mol%) and potassium acetate (4.33 g, 44.1 mmol, 3.00 eq.). The flask was flushed with argon for 5 minutes and dry DMF (80) was added with a syringe. After degassing the mixture with an argon stream for 20 minutes, the mixture was stirred at 100 °C for 1 h. Then, the reaction mixture was cooled down, diluted with ether (200 ml) and washed with brine and water. Drying over $MgSO_4$, removal of the solvent and flash column chromatography over a short column (silica gel, hexane:EtOAc 2:1) yielded 3.99 g of a pale green oil which solidified upon standing in the fridge for one week (85 %).

MP: 79 – 81 °C

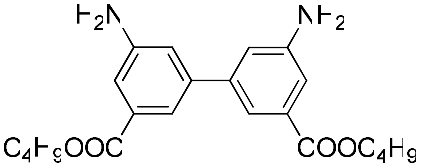
IR: (υ/cm^{-1}): 3472, 3371, 2970, 2932, 1697, 1381, 1242, 1119, 964, 702.

^{1}H-NMR: (400 MHz, $CDCl_3$ 1:1, δ/ppm): 7.83 (s, 1H, H_{aryl}), 7.43 – 7.41 (m, 1H, H_{aryl}), 7.29 – 7.26 (m, 1H, H_{aryl}), 4.28 (t, $^3J_{HH}$ = 6.8 Hz, 2H, OCH_2), 3.77 (bs, 2H, NH_2), 1.77 – 1.67 (m, 2H, CH_2), 1.49 – 1.39 (m, 2H, CH_2), 1.32 (s, 12H, CH_3), 0.95 (t, $^3J_{HH}$ = 7.4 Hz, 3H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 167.3 (C=O), 146.4 (C_{aryl}), 131.4 (C_{aryl}), 126.2 (C_{aryl}), 125.8 (C_{aryl}), 111.8 (C_{aryl}), 84.4 (OCH_2 2C), 65.1 (OCH_2), 31.2 (CH_2), 25.3 ($CH_{3,}$ 4C) 19.6 (CH_2), 14.2 (CH_3).

MS: (EI, 70 ev): *m/z* (%) = 319 (100) [M^+].

Dibutyl 5,5'-bis((E)-(3-bromophenyl)diazenyl)biphenyl-3,3'-dicarboxylate 91



A flask was charged with butyl 3-amino-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate **90** (1.41 g, 4.40 mmol, 1.20 eq.), butyl 3-amino-5-bromobenzoate **89** (1.00 g, 3.67 mmol, 1.00 eq.) and $Pd(PPh_3)_4$ (129 mg, 3 mol%) and flushed with argon for 5 minutes. Then, toluene (110 ml), 1-butanol (8 ml) and 2 M Na_2CO_3 (5 ml) was added. The mixture was degassed with an argon stream for 20 minutes, heated to 100 °C and stirred at this temperature for 38 hours. After mixture had cooled town to room temperature, EtOAc (200 ml) was added and the mixture was washed with brine and water. The organic layer was dried over $MgSO_4$, the solvent was removed under reduced pressure and the residue was purified via flash column chromatography to yield 78 % of a colourless solid (silica gel, hexane:EtOAc 1:1, 1% NEt_3).

MP: 89 – 93 °C

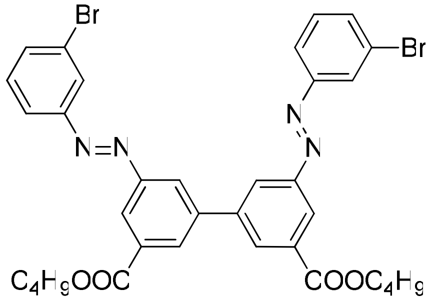
IR: (υ/cm^{-1}): 3364, 2955, 2854, 1697, 1589, 1312, 1242, 1119, 856, 764, 679.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.63 (s, 2H, H_{aryl}), 7.34 (s, 2H, H_{aryl}), 7.05 (s, 2H, H_{aryl}), 4.32 (t, $^3J_{HH}$ = 6.7 Hz, 4H, OCH_2), 3.87 (bs, 4H, NH_2), 1.79 – 1.72 (m, 4H, CH_2), 1.52 – 1.43 (m, 4H, CH_2), 0.98 (t, $^3J_{HH}$ = 7.4 Hz, 6H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 167.1 (C=O), 147.2 (C_{aryl}), 142.3 (C_{aryl}), 132.4 (C_{aryl}), 119.0 (C_{aryl}), 118.3 (C_{aryl}), 115.4 (C_{aryl}), 65.3 (OCH_2), 31.2 (CH_2), 19.7 (CH_2), 14.2 (CH_3).

MS: (EI, 70 ev): *m/z* (%) = 384 (100) [M^+].

Dibutyl 5,5'-bis((E)-(3-bromophenyl)diazenyl)biphenyl-3,3'-dicarboxylate 92



A solution of dibutyl 5,5'-diaminobiphenyl-3,3'-dicarboxylate **91** (100 mg, 260 µmol, 1.00 eq.) was treated with 3-bromonitrosobenzene (**77**) (145 mg, 780 µmol, 3.00 eq.). The mixture was stirred at room temperature over night and the solvent was removed under reduced pressure. Purification by flash column chromatography (silica gel, hexane:DCM 1:1) yielded 136 mg of an orange solid (73 %).

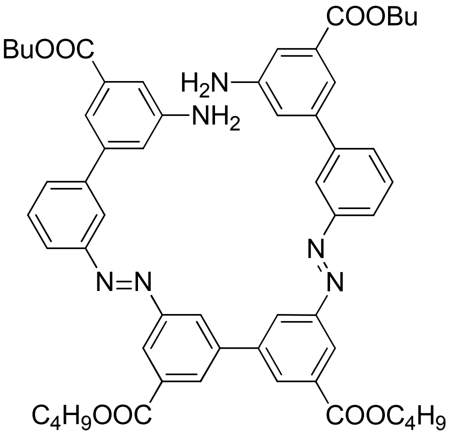
IR: (υ/cm^{-1}): 2932, 2870, 1720, 1574, 1535, 1458, 1334, 1227, 887, 764, 687.

^{1}H-NMR: (400 MHz, CDCl$_3$, δ/ppm): 8.61 (s, 2H, H$_{aryl}$), 8.52 (s, 2H, H$_{aryl}$), 8.43 (s, 2H, H$_{aryl}$), 8.14 (s, 2H, H$_{aryl}$), 7.97 (d, $^3J_{HH}$ = 9.4 Hz, 2H, H$_{aryl}$), 7.65 (d, $^3J_{HH}$ = 9.4 Hz, 2H, H$_{aryl}$),7.45 (t, $^3J_{HH}$ = 9.4 Hz, 2H, H$_{aryl}$), 4.44 (t, $^3J_{HH}$ = 6.7 Hz, 4H, OCH$_2$), 1.88 – 1.80 (m, 4H, CH$_2$), 1.58 – 1.49 (m, 4H, CH$_2$), 1.02 (t, $^3J_{HH}$ = 7.4 Hz, 6H, CH$_3$).

^{13}C-NMR: (101 MHz, CDCl$_3$, δ/ppm): 166.2 (C=O), 153.7 (C$_{aryl}$), 153.3 (C$_{aryl}$), 141.2 (C$_{aryl}$), 134.7 (C$_{aryl}$), 133.0 (C$_{aryl}$), 131.1 (C$_{aryl}$), 131.0 (C$_{aryl}$), 125.6 (C$_{aryl}$), 125.3 (C$_{aryl}$), 124.5 (C$_{aryl}$), 123.7 (C$_{aryl}$), 123.7 (C$_{aryl}$), 66.0 (OCH$_2$), 31.2 (CH$_2$), 19.7 (CH$_2$), 14.2 (CH$_3$).

MS: (MALDI-TOF): *m/z* (%) = 718.3 [M$^+$] (43); 719.3(100).

Bisazodiamine 93



A flask was charged with dibutyl 5,5'-bis((E)-(3-bromophenyl)diazenyl)biphenyl-3,3'-dicarboxylate **92** (818 mg, 1.14 mmol, 1.00 eq.), butyl 3-bromo-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate **90** (798 mg, 2.50 mmol, 2.20 eq.) and Pd(PPh$_3$)$_4$ (80.0 mg, 6 mol%) and degassed by an argon stream for 5 min. Then, THF (75 ml) and 25 ml of a 2M K_2CO_3 solution was added and the mixture was degassed for 20 minutes. After stirring for 5 h at 85 °C, the mixture was allowed to cool to room temperature and the organic layer was collected and washed with brine. The mixture was dried over $MgSO_4$, the solvent was removed and the residue was purified by column chromatography (silica gel, hexane:EtOAc 1:1) to yield an orange oil (1.05 g, 98 %).

MP: 88 – 92 °C.

IR: (υ/cm^{-1}): 3371, 2955, 2870, 1705, 1597, 1450, 1342, 1227, 1165, 864.

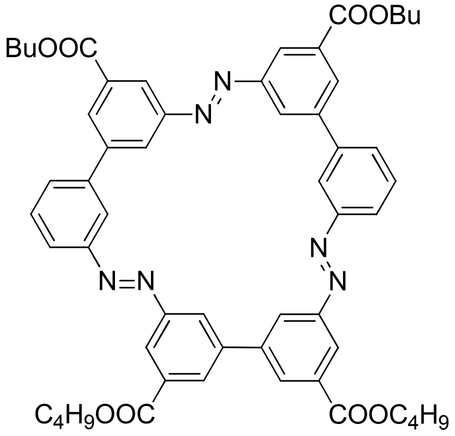
^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.63 (s, 2H, H$_{aryl}$), 8.52 (s, 2H, H$_{aryl}$), 8.47 (s, 2H, H$_{aryl}$), 8.22 (s, 2H, H$_{aryl}$), 7.99 (d, $^3J_{HH}$ = 7.8 Hz, 2H, H$_{aryl}$), 7.77 – 7.72 (m, 4H, H$_{aryl}$), 7.61 (t, $^3J_{HH}$ = 7.8 Hz, 2H, H$_{aryl}$), 7.38 (s, 2H, H$_{aryl}$), 7.18 (s, 2H, H$_{aryl}$), 4.45 (t, $^3J_{HH}$ = 6.7 Hz, 4H, OCH$_2$), 4.34 (t, $^3J_{HH}$ = 6.7 Hz, 4H, OCH$_2$), 3.93 (bs, 4H, NH$_2$), 1.89 – 1.72 (m, 8H, CH$_2$), 1.57 – 1.43 (m, 8H, CH$_2$), 1.05 - 0.95 (m, 12H, CH$_3$).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 166.7 (C=O), 165.93 (C=O), 153.2, (C$_{aryl}$), 152.8 (C$_{aryl}$), 147.1 (C$_{aryl}$), 141.7 (C$_{aryl}$), 141.6 (C$_{aryl}$), 140.9 (C$_{aryl}$), 132.5 (C$_{aryl}$), 132.2 (C$_{aryl}$), 130.3 (C$_{aryl}$), 130.2 (C$_{aryl}$), 129.6 (C$_{aryl}$), 125.2 (C$_{aryl}$), 123.8

(C_{aryl}), 122.4 (C_{aryl}), 121.8 (C_{aryl}), 118.6 (C_{aryl}), 117.8 (C_{aryl}), 115.2 (C_{aryl}), 65.5 (OCH_2), 65.0 (OCH_2), 30.8 (CH_2), 19.3 (CH_2), 13.8 (CH_3).

MS: (MALDI-TOF): *m/z* (%) = 944.6 [M^+] (100).

Macrocycle 94



Dibutyl 5,5'-bis((E)-(3'-amino-5'-(butoxycarbonyl)biphenyl-3-yl)diazenyl)biphenyl-3,3'-dicarboxylate **93** (973 mg, 1.03 mmol, 1.00 eq.) was dissolved in THF (120 ml) and triethylamine (1.43 ml, 10.3 mmol, 10.0 eq.) was added. Then, lead tetraacetate (3.15 g, 7.11 mmol, 6.9 eq.), dissolved in THF (100 ml) was added dropwise over two minutes, while stirring. After stirring for 3 h, EDTA (3.01 g, 10.3 mmol, 10.0 eq.), DCM (50 ml) and water (50 ml) was added and the mixture was rapidly stirred for an additional hour. The organic layer was collected and the aqueous layer was extracted with DCM (50 ml). After washing with brine and drying over $MgSO_4$, the solvent was removed and the residue was purified by flash column chromatography (silica gel, hexane:EtOAc 2:1) to yield an orange solid (463 mg, 48 %).

MP: > 245 °C

IR: (υ/cm^{-1}): 2932, 2870, 1720, 1597, 1458, 1335, 1227, 1150, 1065, 887, 764.

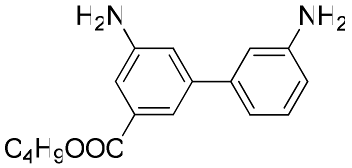
^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.86 (d, $^3J_{HH}$ = 9.6 Hz, 4H, H_{aryl}), 7.72 – 7.63 (m, 10H, H_{aryl}), 8.10 – 8.04 (m, 4H, H_{aryl}), 7.72 (t, $^3J_{HH}$ = 7.8 Hz, 2H, H_{aryl}), 4.50 –

4.43 (m, 8H, OCH_2), 1.91 – 1.83 (m, 8H, CH_2), 1.62 – 1.52 (m, 8H, CH_2), 1.05 (t, $^3J_{HH}$ = 7.5 Hz, 12H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$ δ/ppm): 165.91 (C=O), 165.86 (C=O), 152.9 (C_{aryl}), 152.81 (C_{aryl}), 152.79 (C_{aryl}), 139.9 (C_{aryl}), 139.2 (C_{aryl}), 138.8 (C_{aryl}), 132.6 (C_{aryl}), 132.5 (C_{aryl}), 130.0 (C_{aryl}), 129.4 (C_{aryl}), 129.3 (C_{aryl}), 129.0 (C_{aryl}), 125.5 (C_{aryl}), 125.3 (C_{aryl}), 123.4 (C_{aryl}), 123.0 (C_{aryl}), 122.7 (C_{aryl}), 121.8 (C_{aryl}), 65.53 (OCH_2), 65.51 (OCH_2), 30.86 (CH_2), 30.84 (CH_2), 19.36 (CH_2), 19.34 (CH_2), 13.9 (CH_3).

MS: (MALDI-TOF): *m/z* (%) = 940.3 [M^+] (75).

Butyl 3',5-diamino-[1,1'-biphenyl]-3-carboxylate



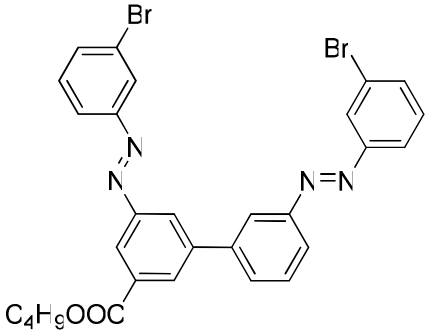
A flask was charged with butyl 3-amino-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate **90** (501 mg, 1.57 mmol, 1.00 eq.), 3-bromoaniline (**74**) (331 mg, 1.88 mmol, 1.20 eq.) and $Pd(PPh_3)_4$ (55 mg, 3 mol%) and flushed with argon for 5 minutes. Then, THF (100 ml) and 2 M aq. K_2CO_3 (25 ml) was added. The mixture was degassed with an argon stream for 20 minutes, heated to 60 °C and stirred at this temperature for 20 hours. After the mixture had cooled town to room temperature, the organic phase was seperated and washed with brine. The organic layer was dried over $MgSO_4$, the solvent was removed under reduced pressure and the residue was purified via flash column chromatography (neutral alox, hexane:EtOAc 1:1) to obtain 350 mg of a colourless oil (76 %).

IR: (υ/cm^{-1}): 3364, 2932, 2870, 1697, 1227, 1103, 864, 686.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.63 (s, 1H, H_{aryl}), 7.32 (s, 1H, H_{aryl}), 7.21 (t, $^3J_{HH}$ = 7.8 Hz, 1H, H_{aryl}), 7.04 (s, 1H, H_{aryl}), 6.97 (d, $^3J_{HH}$ = 7.8 Hz, 1H, H_{aryl}), 6.89 (s, 1H, H_{aryl}), 6.69 (d, $^3J_{HH}$ = 7.9 Hz, 1H, H_{aryl}), 4.32 (t, $^3J_{HH}$ = 6.6 Hz, 2H, OCH_2), 3.83 (bs, 2H, NH_2), 3.75 (bs, 2H, NH_2), 1.80 – 1.71 (m, 2H, CH_2), 1.53 – 1.42 (m, 2H, CH_2), 0.98 (t, $^3J_{HH}$ = 7.4 Hz, 3H, CH_2).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 167.3 (C=O), 147.14 (C_{aryl}), 147.09 (C_{aryl}), 143.2 (C_{aryl}), 142.1 (C_{aryl}), 132.3 (C_{aryl}), 130.1 (C_{aryl}), 119.2 (C_{aryl}), 118.3 (C_{aryl}), 118.0 (C_{aryl}), 115.1 (C_{aryl}), 114.8 (C_{aryl}), 114.3 (C_{aryl}), 65.3 (OCH_2), 31.2 (CH_2), 19.7 (CH_2), 14.2 (CH_3).

Butylester bisazodibromide

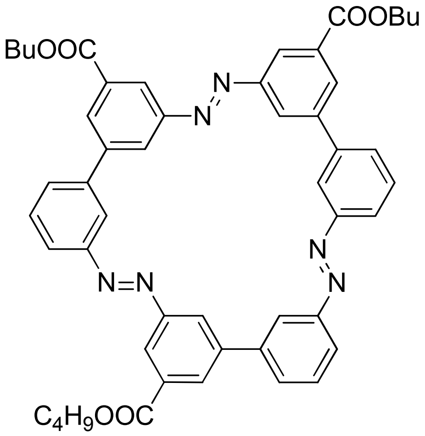


Butyl 3',5-diamino-[1,1'-biphenyl]-3-carboxylate (330 mg, 1.16 mmol, 1.00 eq.) was dissolved in 20 ml of acetic acid and 3-bromonitrosobenzene (**77**) (647, 3.48, 1.00 eq.) was added. The suspension was stirred at room temperature for two days. After removal of the solvent at reduced pressure, the residue was purified by flash column chromatography (silica gel: Hexane:DCM 1:1) to yield 576 mg of an orange solid (79 %).

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.58 (s, 1H, H_{aryl}), 8.50 (s, 1H, H_{aryl}), 8.41 (s, 1H, H_{aryl}), 8.27 (s, 1H, H_{aryl}), 8.13 (s, 1H, H_{aryl}), 8.11 (s, 1H, H_{aryl}), 8.00 – 7.91 (m, 3H, H_{aryl}), 7.85 (d, $^3J_{HH}$ = 7.9 Hz, 1H, H_{aryl}), 7.70 – 7.60 (m, 3H, H_{aryl}), 7.47 – 7.40 (m, 2H, H_{aryl}), 4.43 (t, $^3J_{HH}$ = 6.8 Hz, 2H, OCH_2), 1.88 – 1.78 (m, 2H, CH_2), 1.58 – 1.49 (m, 2H, CH_2), 1.02 (t, $^3J_{HH}$ = 7.4 Hz, 3H, CH_2).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 166.1 (C=O), 153.7 (C_{aryl}), 153.5 (C_{aryl}), 153.1 (C_{aryl}), 153.0 (C_{aryl}), 141.9 (C_{aryl}), 140.7 (C_{aryl}), 134.4 (C_{aryl}), 134.1 (C_{aryl}), 132.7 (C_{aryl}), 130.9 (C_{aryl}), 130.8 (C_{aryl}), 130.7 (C_{aryl}), 130.3 (C_{aryl}), 130.1 (C_{aryl}), 125.3 (C_{aryl}), 125.0 (C_{aryl}), 124.9 (C_{aryl}), 123.9 (C_{aryl}), 123.50 (C_{aryl}), 123,46 (C_{aryl}), 123.4 (C_{aryl}), 123.3 (C_{aryl}), 123.0 (C_{aryl}), 122.1 (C_{aryl}), 65.7 (OCH_2), 31.0 (CH_2), 19.5 (CH_2), 14.3 (CH_3).

Macrocycle 95



A flask was charged with butyl 3-amino-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2 yl)benzoate **90** (749 mg, 2.35 mmol, 2.70 eq.), butylester bisazodibromide (539 mg, 869 mmol, 1.00 eq.) and $Pd(PPh_3)_4$ (61 mg, 6 mol%) and flushed with argon for 5 minutes. Then, THF (60ml) and 2 M aq. K_2CO_3 (15 ml) was added. The mixture was degassed with an argon stream for 20 minutes, heated to 60 °C and stirred at this temperature for 17 hours. After the mixture had cooled town to room temperature, the organic phase was seperated and washed with brine. The organic layer was dried over $MgSO_4$, the solvent was removed under reduced pressure and the residue was purified via flash column chromatography (neutral alox, hexane:EtOAc 1:1) to obtain 780 mg of an orange oil which still contained impurities and was used directly like this in the next step (quant). To a solution of the obtained diamine (200 mg, 237 µmol, 1.00 eq.) in THF (100 ml) and triethylamine (329 µl, 2.37 mmol, 10.0 eq.), a suspension of $Pb(OAc)_4$ (725 mg, 1.64 mmol, 6.90 eq.) in THF (150 mll) was added dropwise over 20 min. After stirring for additional three hours, EDTA (693 mg) was added and 20 ml of water and DCM was added. After stirring for 5 minutes, The organic layer was separated and the aqueous layer was extracted with DCM (4*20 ml). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The dark residue was purified by column chromatography (neutral alox, toluene:EtOAc 20:1) to yield 112 mg of an orange solid (56 %).

MP: 185 – 190 °C

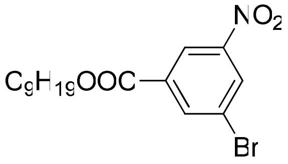
IR: (υ/cm^{-1}): 2932, 2870, 1713, 1597, 1227, 1150, 1072, 887, 764.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.73 (s, 1H, H_{aryl}), 8.71 (s, 1H, H_{aryl}), 8.68 (s, 1H, H_{aryl}), 8.58 – 8.48 (m, 9H, H_{aryl}), 7.98 – 7.87 (m, 6H, H_{aryl}), 7.64 – 7.56 (m, 3H, H_{aryl}),, 4.48 – 4.41 (m, 6H, OCH_2), 1.91 – 1.82 (m, 6H, CH_2), 1.62 – 1.52 (m, 6H, CH_2), 1.10 – 1.02 (m, 9H, CH_2).

^{13}C-NMR: (101 MHz, $CDCl_3$ δ/ppm): 166.1 (C=O), 166.04 (C=O), 166.01 (C=O), 153.03 (C_{aryl}), 152.98 (C_{aryl}, 2C), 152.92 (C_{aryl}), 152.90 (C_{aryl}), 152.86 (C_{aryl}), 140.1 (C_{aryl}), 139.95 (C_{aryl}), 139.94 (C_{aryl}), 138.84 (C_{aryl}), 138.83 (C_{aryl}), 138.71 (C_{aryl}), 132.53 (C_{aryl}), 132.49 (C_{aryl}), 132.43 (C_{aryl}), 130.06 (C_{aryl}), 130.01 (C_{aryl}), 129.97 (C_{aryl}), 129.5 (C_{aryl}, 2C), 129.2 (C_{aryl}), 129.0 (C_{aryl}), 128.8 (C_{aryl}), 128.7 (C_{aryl}), 126.2 (C_{aryl}), 125.0 (C_{aryl}), 124.8 (C_{aryl}), 123.70 (C_{aryl}), 123.65 (C_{aryl}), 123.26 (C_{aryl}), 122.56 (C_{aryl}), 122.53 (C_{aryl}), 122.3 (C_{aryl}), 122.13 (C_{aryl}), 122.07 (C_{aryl}), 121.1 (C_{aryl}), 65.59 (OCH_2), 65.54 (OCH_2), 31.0 (CH_2), 19.5 (CH_2), 19.34 (CH_2), 14.0 (CH_3).

MS: (MALDI-TOF): *m/z* (%) = 840.5 [M$^+$] (100).

nonyl 3-bromo-5-nitrobenzoate



To a solution of 3-nitro-5-bromocarboxylic acid **(89)** (6.50 g, 26.4 mmol, 1.00 eq.) in CH_2Cl_2 (100 ml), DMAP (1.61 mg, 13.2 mmol, 0.50 eq.) and 1-nonanol (13.8 ml, 79.2 mmol, 3.00 eq.) was added. The mixture was cooled to 0 °C and DCC (11.4 g, 79.2 mmol, 1.10 eq.) was added in small portions. Then, the mixture was allowed to warm to rt and stirred for 3 h. The precipitate was removed by filtration and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane:EtOAc 15:1) to yield 8.93 g of a pale yellow oil (91 %).

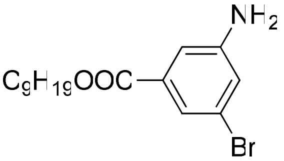
IR: (υ/cm^{-1}): 2924, 2854, 2114, 1728, 1535, 1342, 1265, 1150, 733.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.77 (s, 1H, H_{aryl}), 8.54 (s, 1H, H_{aryl}), 8.47 (s, 1H, H_{aryl}), 4.38 (t, $^3J_{HH}$ = 6.8 Hz, 2H, OCH_2), 1.83 – 1.76 (m, 2H, CH_2), 1.48 – 1.20 (m, 12H, CH_2), 0.88 (t, $^3J_{HH}$ = 7.8 Hz, 3H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$ δ/ppm): 163.7 (C=O), 149.2 (C_{aryl}), 138.6 (C_{aryl}), 134.0 (C_{aryl}), 130.7 (C_{aryl}), 123.5 (C_{aryl}), 123.4 (C_{aryl}), 67.0 (OCH_2), 32.2 (CH_2), 29.8 (CH_2), 29.62 (CH_2), 29.61 (CH_2), 29.0 (CH_2), 26.3 (CH_2), 23.1 (CH_2), 14.5 (CH_3).

MS: (EI, 70 ev): *m/z* (%) = 371 (1.2) [M^+], 373 (1.2) [M^++2], 69 (100).

nonyl 3-bromo-5-aminobenzoate



A solution of nonyl 3-bromo-5-nitrobenzoate (8.15 g, 21.9 mmol, 1.00 eq.) in acetic acid (40 ml) was heated to 80°C. Then, iron powder (6.60 g, 118 mmol, 5.40 eq.) was added slowly during 90 min to keep the temperature below 90°C. After complete addition, the reaction was stirred for additional 30 min, when it was diluted with water (130 ml). After extraction with *tert*BuOMe (2*100 ml), washing of the combined organic phases with water (70 ml) and drying over $MgSO_4$, the solvent was evaporated under reduced pressure to yield 7.49 g of compound **13** as a yellow oil as the product (quant).

IR: (υ/cm^{-1}): 3379, 2924, 2854, 1713, 1574, 1450, 1304, 1234, 1188, 849, 725.

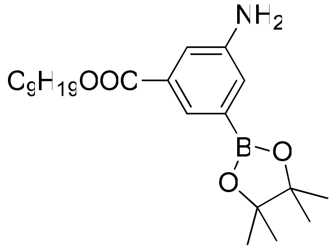
^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.51 (s, 1H, H_{aryl}), 7.25 (s, 1H, H_{aryl}), 6.98 (s, 1H, H_{aryl}), 4.27 (t, $^3J_{HH}$ = 6.7 Hz, 2H, OCH_2), 3.84 (bs, 2H, NH_2), 1.77 – 1.70 (m, 2H, CH_2), 1.45 – 1.21 (m, 12H, CH_2), 0.88 (t, $^3J_{HH}$ = 7.8 Hz, 3H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$ δ/ppm): 166.0 (C=O), 148.1 (C_{aryl}), 133.4 (C_{aryl}), 123.3 (C_{aryl}), 122.6 (C_{aryl}), 122.0 (C_{aryl}), 115.0 (C_{aryl}), 65.9 (OCH_2), 32.3 (CH_2), 29.9

(CH$_2$), 29.67 (CH$_2$), 29.64 (CH$_2$), 29.1 (CH$_2$), 26.4 (CH$_2$), 23.1 (CH$_2$), 14.5 (CH$_3$).

MS: (EI, 70 ev): *m/z* (%) = 341 (59) [M$^+$], 343 (58) [M$^+$+2], 215 (100).

Boronic ester 96



A three necked flask was charged with nonyl 3-bromo-5-aminobenzoate (3.00 g, 8.76 mmol, 1.00 eq.), Pd(dppf)Cl$_2$*CH$_2$Cl$_2$ (572 mg, 701 µmol, 8 mol%), bis(pinacolato)diboron (2.45 g, 9.64 mmol, 1.10 eq.) and potassium acetate (3.00 g, 26.3 mmol, 3.00 eq.). The flask was flushed with argon for 5 minutes and dry DMF (65 ml) was added with a syringe. After degassing the mixture with an argon stream for 20 minutes, the mixture was stirred at 100 °C for 1 h. After the reaction mixture was cooled down, it was diluted with ether (250 ml) and washed with brine and water. Drying over MgSO$_4$, removal of the solvent and flash column chromatography over a short column (silica gel, hexane:EtOAc 4:1) yielded 2.70 g a pale green oil (79 %).

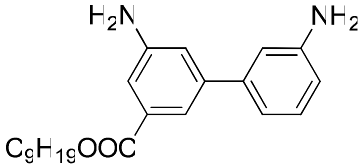
IR: (υ/cm^{-1}): 3379, 2924, 2847, 1697, 1366, 1242, 1142, 702.

^{1}H-NMR: (400 MHz, CDCl$_3$, δ/ppm): 7.85 (s, 1H, H$_{aryl}$), 7.43 (s, 1H, H$_{aryl}$), 6.29 (s, 1H, H$_{aryl}$), 4.28 (t, $^3J_{HH}$ = 6.8 Hz, 2H, OCH$_2$), 1.78 – 1.71 (m, 2H, CH$_2$), 1.46 – 1.22 (m, 24H, CH$_2$, CH$_3$), 0.89 – 0.86 (m, 3H, CH$_3$).

^{13}C-NMR: (101 MHz, CDCl$_3$ δ/ppm): 167.3 (C=O), 146.3 (C$_{aryl}$), 131.5 (C$_{aryl}$), 126.3 (C$_{aryl}$), 125.7 (C$_{aryl}$), 118.8 (C$_{aryl}$), 110.0 (C$_{aryl}$), 84.4 (OC), 65.5 (OCH$_2$), 32.6 (CH$_2$), 29.9 (CH$_2$), 29.7 (CH$_2$), 29.6 (CH$_2$), 29.2 (CH$_2$), 26.4 (CH$_2$), 25.3 (CH$_3$), 23.1 (CH$_2$), 14.5 (CH$_3$).

MS: (EI, 70 ev): *m/z* (%) = 389 (100) [M$^+$].

nonyl 3',5-diamino-[1,1'-biphenyl]-3-carboxylate



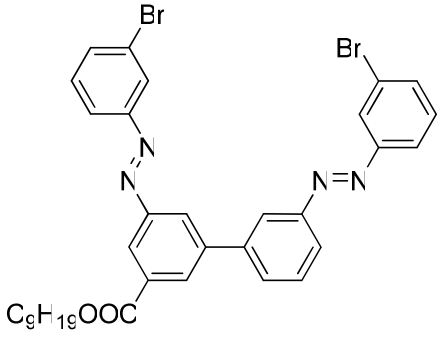
A flask was charged with nonyl 3-amino-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate **96** (1.00 g, 2.57 mmol, 1.00 eq.), 3-bromoaniline (**74**) (286 µl, 2.57 mmol, 1.00 eq.) and $Pd(PPh_3)_4$ (90 mg, 3 mol%) and flushed with argon for 5 minutes. Then, THF (130 ml) and 2 M aq. K_2CO_3 (35 ml) was added. The mixture was degassed with an argon stream for 20 minutes, heated to 60 °C and stirred at this temperature for 18 hours. After the mixture had cooled town to room temperature, the organic phase was seperated and washed with brine. The organic layer was dried over $MgSO_4$, the solvent was removed under reduced pressure and the residue was purified via flash column chromatography (neutral alox, hexane:EtOAc 1:1) to yield 640 mg of a pale yellow oil (70 %).

IR: (υ/cm^{-1}): 3363, 2924, 2854, 1697, 1597, 1350, 1227, 1103, 864.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.63 (s, 1H, H_{aryl}), 7.32 (s, 1H, H_{aryl}), 7.21 (t, $^3J_{HH}$ = 7.8 Hz, 1H, H_{aryl}), 7.03 (s, 1H, H_{aryl}), 6.97 (d, $^3J_{HH}$ = 6.9 Hz, 1H, H_{aryl}), 6.89 (s, 1H, H_{aryl}), 6.68 (d, $^3J_{HH}$ = 6.7 Hz, 1H, H_{aryl}), 4.30 (t, $^3J_{HH}$ = 6.7 Hz, 2H, OCH_2), 3.84 (bs, 2H, NH_2), 3.75 (bs, 2H, NH_2), 1.79 – 1.72 (m, 2H, CH_2), 1.48 – 1.20 (m, 12H, CH_2), 0.88 (t, $^3J_{HH}$ = 6.8 Hz, 3H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$ δ/ppm): 167.2 (C=O), 147.12 (C_{aryl}), 147,08 (C_{aryl}), 143.1 (C_{aryl}), 142.1 (C_{aryl}), 132.3 (C_{aryl}), 130.1 (C_{aryl}), 119.2 (C_{aryl}), 118.3 (C_{aryl}), 118.0 (C_{aryl}), 115.1 (C_{aryl}), 114.8 (C_{aryl}), 114.2 (C_{aryl}), 65.6 (OCH_2), 32.3 (CH_2), 29.9 (CH_2), 29.71 (CH_2), 29.66 (CH_2), 29.2 (CH_2), 26.5 (CH_2), 23.1 (CH_2), 14.5 (CH_3).

Nonylester bisazodibromide



Butyl 1-(3'-aminophenyl)3-aminobenzoate (521 mg, 1.47 mmol, 1.00 eq.) was dissolved in 25 ml of acetic acid and 3-bromonitrosobenzene (**77**) (820, 4.41, 1.00 eq.) was added. The suspension was stirred at room temperature for 20 hours. After removal of the solvent at reduced pressure, the residue was purified by column chromatography (silica gel: Hexane:DCM 1:1) to yield 796 mg of a red oil (78 %).

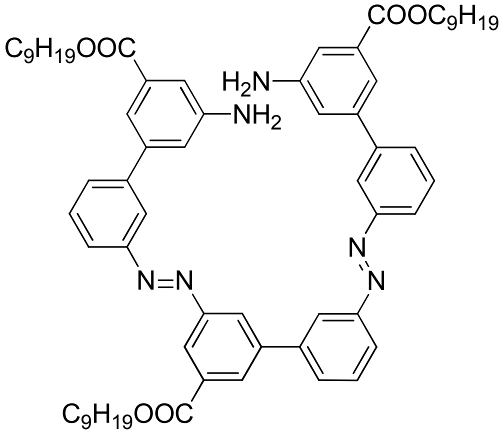
IR: (υ/cm^{-1}): 2916, 2854, 1720, 1574, 1458, 1242, 1196, 887, 764, 687.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.57 (s, 1H, H_{aryl}), 8.48 (s, 1H, H_{aryl}), 8.39 (s, 1H, H_{aryl}), 8.26 (s, 1H, H_{aryl}), 8.11 (d, $^3J_{HH}$ = 7.0 Hz, 2H, H_{aryl}), 7.98 – 7.91 (m, 3H, H_{aryl}), 7.84 (d, $^3J_{HH}$ = 7.8 Hz, 1H, H_{aryl}), 7.68 – 7.59 (m, 3H, H_{aryl}), 7.46 – 7.39 (m, 2H, H_{aryl}), 4.41 (t, $^3J_{HH}$ = 6.8 Hz, 2H, OCH_2), 1.88 – 1.81 (m, 2H, CH_2), 1.54 – 1.21 (m, 12H, CH_2), 0.87 (t, $^3J_{HH}$ = 6.3 Hz, 3H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$ δ/ppm): 166.3 (C=O), 153.8 (C_{aryl}), 153.7 (C_{aryl}), 153.24 (C_{aryl}), 153.18 (C_{aryl}), 142.0 (C_{aryl}), 140.8 (C_{aryl}), 134.6 (C_{aryl}), 134.3 (C_{aryl}), 132.8 (C_{aryl}), 131.1 (C_{aryl}), 130.93 (C_{aryl}), 130.89 (C_{aryl}), 130.5 (C_{aryl}), 130.3 (C_{aryl}), 125.5 (C_{aryl}), 125.2 (C_{aryl}), 125.1 (C_{aryl}), 124.0 (C_{aryl}), 123.7 (C_{aryl}), 123.64 (C_{aryl}), 123.59 (C_{aryl}), 123.51 (C_{aryl}), 123.1 (C_{aryl}), 122.3 (C_{aryl}), 66.2 (OCH_2), 32.3 (CH_2), 29.9 (CH_2), 29.72 (CH_2), 29.67 (CH_2), 29.2 (CH_2), 26.5 (CH_2), 23.1 (CH_2), 14.5 (CH_3).

MS: (MALDI-TOF): *m/z* (%) = 688 [M^+] (57), 689 [M^+ + 1] (100).

Nonylester bisazodiamine



A flask was charged with nonyl 3-amino-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate **96** (959 mg, 2.46 µmol, 2.50 eq.), nonylester bisazodibromide (680 mg, 985 µmol, 1.00 eq.) and $Pd(PPh_3)_4$ (68 mg, 6 mol%) and flushed with argon for 5 minutes. Then, THF (50 ml) and 2 M aq. K_2CO_3 (13 ml) was added. The mixture was degassed with an argon stream for 20 minutes, heated to 60 °C and stirred at this temperature for 19 hours. After the mixture had cooled town to room temperature, the organic phase was seperated and washed with brine. The organic layer was dried over $MgSO_4$, the solvent was removed under reduced pressure and the residue was purified via flash column chromatography (neutral alox, hexane:EtOAc 1:1) to obtain 748 mg of an orange oil which still contained impurities and was used like this in the next step (72 %).

IR: (υ/cm^{-1}): 3371, 2924, 2854, 1705, 1597, 1458, 1234, 1103, 771, 694.

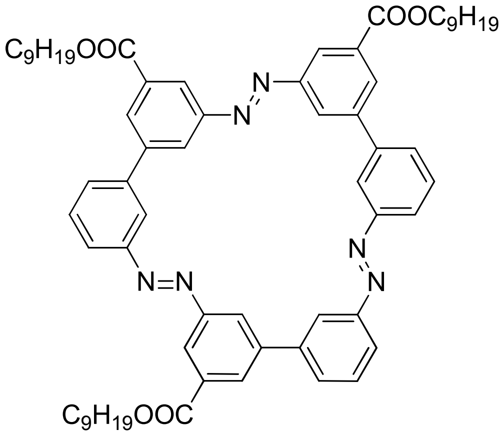
^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.60 (s, 1H, H_{aryl}), 8.50 (s, 1H, H_{aryl}), 8.45 (s, 1H, H_{aryl}), 8.32 (s, 1H, H_{aryl}), 8.21 (s, 1H, H_{aryl}), 8.19 (s, 1H, H_{aryl}), 8.00 – 7.94 (m 3H, H_{aryl}), 7.85 (d, $^3J_{HH}$ = 8.0 Hz, 2H, H_{aryl}), 7.79 – 7.70 (m, 4H, H_{aryl}), 7.66 (t, $^3J_{HH}$ = 7.8 Hz, 1H, H_{aryl}), 7.59 (t, $^3J_{HH}$ = 7.8 Hz, 1H, H_{aryl}), 7.38 (s, 2H, H_{aryl}), 7.17 (s, 2H, H_{aryl}), 4.42 (t, $^3J_{HH}$ = 6.8 Hz, 2H, OCH_2), 4.32 (t, $^3J_{HH}$ = 6.7 Hz, 4H, OCH_2), 3.94 (bs, 4H, NH_2), 1.89 – 1.72 (m, 6H, CH_2), 1.51 – 1.18 (m, 36H, CH_2), 0.86 (t, $^3J_{HH}$ = 6.7 Hz, 9H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$ δ/ppm): 167.1 (C=O), 166.4 (C=O), 153.53 (C_{aryl}), 153.48 (C_{aryl}), 153.4 (C_{aryl}), 153.2 (C_{aryl}), 147.4 (2C, C_{aryl}), 142.05 (C_{aryl}), 142.02 (C_{aryl}), 142.00 (C_{aryl}), 141.9 (2C, C_{aryl}), 140.9 (C_{aryl}), 132.7 (C_{aryl}), 132.58

(C_{aryl}), 132.55 (C_{aryl}), 130.7 (C_{aryl}), 130.5 (C_{aryl}), 130.2 (2C, C_{aryl}), 130.1 (C_{aryl}), 130.0 (C_{aryl}), 129.9 (C_{aryl}), 125.6 (C_{aryl}), 123.8 (C_{aryl}), 122.8 (C_{aryl}), 122.7 (C_{aryl}), 122.5 (C_{aryl}), 122.3 (C_{aryl}), 122.2 (C_{aryl}), 122.1 (C_{aryl}), 119.1 (2C, C_{aryl}), 118.2 (2C, C_{aryl}), 115.6 (2C, C_{aryl}), 66.1 (OCH_2), 65.7 (OCH_2), 32.3 (CH_2), 29.9 (CH_2), 29.72 (CH_2), 29.66 (CH_2), 29.2 (CH_2), 26.5 (CH_2), 23.1 (CH_2), 14.5 (CH_3).

MS: (MALDI-TOF): *m/z* (%) = 1055.8 [M^+] (57), 1052.7 (100).

Macrocycle 97



To a solution of nonylester bisazodiamine (570 mg, 540 µmol, 1.00 eq.) in THF (200 ml) and triethylamine (751 µl, 5.40 mmol, 10.0 eq.), a suspension of $Pb(OAc)_4$ (1.65 g, 3.73 mmol, 6.90 eq.) in THF (300 ml) was added dropwise over 20 min. After stirring for additional three hours, EDTA (1580 mg) was added and 30 ml of water and DCM was added. After stirring for 5 minutes, The organic layer was separated and the aqueous layer was extracted with DCM (2*50 ml). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The dark residue was purified by column chromatography (silica gel, toluene) to yield 180 mg of an orange solid (32 %).

MP: 148 – 153 °C

IR: (υ/cm^{-1}): 2924, 2854, 1720, 1450, 1312, 1242, 1142, 887, 764, 687.

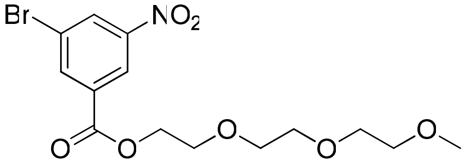
^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.86 (s, 1H, H_{aryl}), 8.84 (s, 1H, H_{aryl}), 8.83 (s, 1H, H_{aryl}), 8.70 – 8.59 (m, 9H, H_{aryl}), 8.07 – 7.98 (m, 6H, H_{aryl}), 7.72 – 7.65 (m, 3H,

H_{aryl}), 4.47 – 4.41 (m, 6H, OCH_2), 1.93 – 1.82 (m, 6H, CH_2), 1.57 – 1.22 (m, 36H, CH_2), 0.92 – 0.85 (m, 9H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$ δ/ppm): 165.93 (C=O), 165.90 (C=O), 165.86 (C=O), 152.90 (C_{aryl}), 152.86 (C_{aryl}, 2C), 152.84 (C_{aryl}), 152.80 (C_{aryl}), 152.78 (C_{aryl}), 152.74 (C_{aryl}), 139.9 (C_{aryl}), 139.8 (2C, C_{aryl}), 138.7 (2C, C_{aryl}), 138.6 (C_{aryl}), 132.42 (C_{aryl}), 132.38 (C_{aryl}), 132.32 (C_{aryl}), 129.91 (C_{aryl}), 129.87 (C_{aryl}), 129.82 (C_{aryl}), 129.3 (2C, C_{aryl}), 129.1 (C_{aryl}), 128.9 (C_{aryl}), 128.61 (C_{aryl}), 128.57 (C_{aryl}), 126.0 (C_{aryl}), 124.9 (C_{aryl}), 124.6 (C_{aryl}), 123.5 (2C, C_{aryl}), 123.1 (C_{aryl}), 122.5 (C_{aryl}), 122.4 (C_{aryl}), 122.1 (C_{aryl}), 122.04 (C_{aryl}), 121.99 (C_{aryl}), 120.9 (C_{aryl}), 65.8 (OCH_2), 65.7 (OCH_2), 31.9 (CH_2), 29.6 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 28.8 (CH_2), 26.1 (CH_2), 22.7 (CH_2), 14.1 (CH_3).

MS: (MALDI-TOF): *m/z* (%) = 1051.6 [M^+], 1049.6 (100).

2-(2-(2-Methoxyethoxy)ethoxy)ethyl 3-bromo-5-nitrobenzoate

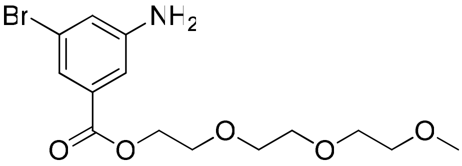


To a solution of 3-nitro-5-bromocarboxylic acid **89** (6.50 g, 26.4 mmol, 1.00 eq.) in CH_2Cl_2 (100 ml), DMAP (1.61 mg, 13.2 mmol, 0.50 eq.) and triethyleneglycol monomethylether (12.4 ml, 79.2 mmol, 3.00 eq.) was added. The mixture was cooled to 0 °C and DCC (11.4 g, 79.2 mmol, 1.10 eq.) was added in small portions. Then, the mixture was allowed to warm to rt and stirred for 3 h. The precipitate was removed by filtration and the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, hexane:EtOAc 5:1) to yield 8.72 g of a pale yellow oil (84 %).

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.78 (s, 1H, H_{aryl}), 8.54 (s, 1H, H_{aryl}), 8.48 (s, 1H, H_{aryl}), 4.54 – 4.53 (m, 2H, OCH_2), 3.86 – 3.83 (m, 2H, CH_2), 3.73 – 3.61 (m, 6H, CH_2), 3.56 – 3.50 (m, 2H, CH_2), 3.55 (s, 3H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$ δ/ppm): 163.7 (C=O), 149.1 (C_{aryl}), 138.7 (C_{aryl}), 133.7 (C_{aryl}), 130.9 (C_{aryl}), 123.7 (C_{aryl}), 123.4 (C_{aryl}), 72.3 (OCH_2), 71.07 (OCH_2), 71.04 (OCH_2), 71.01 (OCH_2), 69.7 (OCH_2), 65.7 (OCH_2), 59.4 (OCH_3).

2-(2-(2-Methoxyethoxy)ethoxy)ethyl 3-amino-5-bromobenzoate



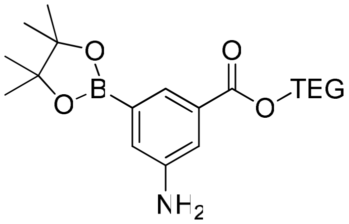
A solution of 2-(2-(2-Methoxyethoxy)ethoxy)ethyl 3-bromo-5-nitrobenzoate (7.77 g, 19.8 mmol, 1.00 eq.) in acetic acid (40 ml) was heated to 80°C. Then, iron powder (5.97 g, 107 mmol, 5.40 eq.) was added slowly during 90 min to keep the temperature below 90°C. After complete addition, the reaction was stirred for additional 30 min, when it was diluted with water (130 ml). After extraction with *tert*BuOMe (2*100 ml), washing of the combined organic phases with water (70 ml) and drying over $MgSO_4$, the solvent was evaporated under reduced pressure to yield 7.49 g of compound **13** as a yellow oil as the product (quant).

IR: (υ/cm^{-1}): 3356, 2878, 2815, 1713, 1450, 1304, 1227, 1095, 849, 764.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.51 (s, 1H, H_{aryl}), 7.25 (s, 1H, H_{aryl}), 6.97 (s, 1H, H_{aryl}), 4.61 – 4.41 (m, 2H, OCH_2), 3.86 (bs, 2H, NH_2), 3.82 – 3.77 (m, 2H, CH_2), 3.71 – 3.62 (m, 6H, CH_2), 3.56 – 3.50 (m, 2H, CH_2), 3.56 (s, 3H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$ δ/ppm): 165.9 (C=O), 148.2 (C_{aryl}), 132.9 (C_{aryl}), 123.2 (C_{aryl}), 122.6 (C_{aryl}), 122.0 (C_{aryl}), 115.1 (C_{aryl}), 72.3 (OCH_2), 71.10 (OCH_2), 71.00 (OCH_2), 70.99 (OCH_2), 69.5 (OCH_2), 64.7 (OCH_2), 59.4 (OCH_3).

Boronic ester 98



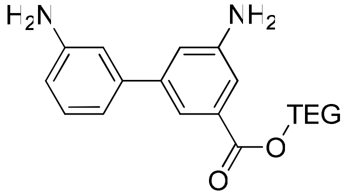
A three necked flask was charged with 2-(2-(2-Methoxyethoxy)ethoxy)ethyl 3-amino-5-bromobenzoate (3.00 g, 8.28 mmol, 1.00 eq.), Pd(dppf)Cl_2*CH_2Cl_2 (541 mg, 662 µmol, 8 mol%), bis(pinacolato)diboron (2.31 g, 9.11 mmol, 1.10 eq.) and potassium acetate (2.84 g, 24.8 mmol, 3.00 eq.). The flask was flushed with argon for 5 minutes and dry DMF (65 ml) was added with a syringe. After degassing the mixture with an argon stream for 20 minutes, the mixture was stirred at 100 °C for 1 h. After the reaction mixture was cooled down, it was diluted with ether (250 ml) and washed with brine and water. Drying over $MgSO_4$, removal of the solvent and flash column chromatography over a short column (silica gel, hexane:EtOAc 1:2) yielded 2.72 g of a pale green oil (80 %).

IR: (υ/cm^{-1}): 3364, 2878, 1713, 1373, 1265, 1227, 1142, 1103, 964, 702.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.85 (s, 1H, H_{aryl}), 7.43 (s, 1H, H_{aryl}), 7.28 (s, 1H, H_{aryl}), 4.45 – 4.43 (m, 2H, OCH_2), 3.82 (bs, 2H, NH_2), 3.82 – 3.79 (m, 2H, CH_2), 3.71 – 3.62 (m, 6H, CH_2), 3.55 – 3.49 (m, 2H, CH_2), 3.55 (s, 3H, CH_3), 1.33 (s, 12H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$ δ/ppm): 167.2 (C=O), 146.3 (C_{aryl}), 131.0 (C_{aryl}), 126.5 (C_{aryl}), 125.9 (C_{aryl}), 118.9 (C_{aryl}), 110.2 (C_{aryl}), 84.4 (C), 72.3 (OCH_2), 71.08 (OCH_2), 71.02 (OCH_2), 70.97 (OCH_2), 69.6 (CH_2), 64.4 (CH_2), 59.4 (CH_3), 25.3 (CH_3).

Triethyleneglycolester 3,3'-diaminobiphenyl



A flask was charged with boronic ester **98** (1.00 g, 2.44 mmol, 1.00 eq.), 3-bromoaniline (**74**) (271 µl, 2.44 mmol, 1.00 eq.) and $Pd(PPh_3)_4$ (85 mg, 3 mol%) and flushed with argon for 5 minutes. Then, THF (130 ml) and 2 M aq. K_2CO_3 (35 ml) was added. The mixture was degassed with an argon stream for 20 minutes, heated to 60 °C and stirred at this temperature for 20 hours. After the mixture had cooled town to room temperature, the organic phase was seperated and washed with brine. The organic layer was dried over $MgSO_4$, the solvent was removed under reduced pressure and the residue was purified via flash column chromatography (neutral alox, hexane:EtOAc 1:5) to yield 470 mg of a pale yellow oil (51 %).

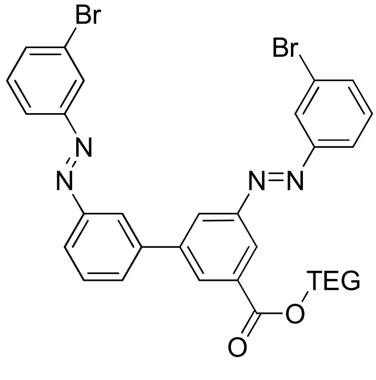
IR: (υ/cm^{-1}): 3356, 2870, 1705, 1597, 1458, 1350, 1227, 1095, 864, 687.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.63 (s, 1H, H_{aryl}), 7.33 (s, 1H, H_{aryl}), 7.20 (t, $^3J_{HH}$ = 7.8 Hz, 1H, H_{aryl}), 7.03 (s, 1H, H_{aryl}), 6.95 (d, $^3J_{HH}$ = 8.2 Hz, 1H, H_{aryl}), 6.88 (s, 1H, H_{aryl}), 6.67 (d, $^3J_{HH}$ = 6.9 Hz, 1H, H_{aryl}), 4.50 – 4.44 (m, 2H, OCH_2), 3.86 (bs, 2H, NH_2), 3.85 – 3.80 (m, 2H, CH_2), 3.78 (bs, 2H, NH_2), 3.74 – 3.62 (m, 6H, CH_2), 3.54 – 3.49 (m, 2H, CH_2), 3.55 (s, 3H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$ δ/ppm): 167.1 (C=O), 147.2 (2C, C_{aryl}), 143.1 (C_{aryl}), 142.0 (C_{aryl}), 131.8 (C_{aryl}), 130.5 (C_{aryl}), 119.2 (C_{aryl}), 118.4 (C_{aryl}), 117.9 (C_{aryl}), 115.2 (C_{aryl}), 114.8 (C_{aryl}), 114.2 (C_{aryl}), 72.3 (OCH_2), 71.13 (OCH_2), 71.02 (OCH_2), 71.00 (OCH_2), 69.7 (CH_2), 64.5 (CH_2), 59.4 (CH_3).

MS: (FAB) *m/z* (%) = 375.2 (85) [M + H$^+$], 211 (100).

Triethyleneglycolester bisazodibromide



Triethyleneglycolester 3,3'-diaminobiphenyl (378 mg, 1.01 mmol, 1.00 eq.) was dissolved in 20 ml of acetic acid and 3-bromonitrosobenzene (564, 3.03 mmol, 3.00 eq.) was added. The suspension was stirred at room temperature for 21 hours. After removal of the solvent at reduced pressure, the residue was purified by column chromatography (silica gel: hexane:EtOAc 4:1) to yield 580 mg of a red oil (81 %).

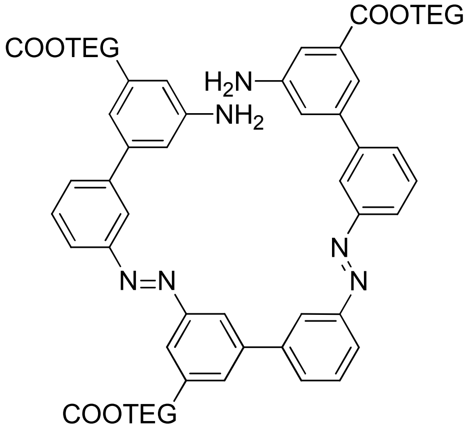
IR: (υ/cm^{-1}): 2870, 2824, 1720, 1573, 1458, 1242, 1196, 1103, 887, 764, 687.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.59 (s, 1H, H_{aryl}), 8.50 (s, 1H, H_{aryl}), 8.40 (s, 1H, H_{aryl}), 8.26 (s, 1H, H_{aryl}), 8.11 (d, $^3J_{HH}$ = 6.1 Hz, 2H, H_{aryl}), 7.98 – 7.91 (m, 3H, H_{aryl}), 7.85 (d, $^3J_{HH}$ = 7.7 Hz, 1H, H_{aryl}), 7.69 – 7.59 (m, 3H, H_{aryl}), 7.46 – 7.39 (m, 2H, H_{aryl}), 4.61 – 4.56 (m, 2H, OCH_2), 3.94 – 3.88 (m, 2H, OCH_2), 3.77 – 3.73 (m, 2H, OCH_2), 3.71 – 3.67 (m, 2H, OCH_2), 3.66 – 3.63 (m, 2H, OCH_2), 3.53 – 3.48 (m, 2H, OCH_2), 3.33 (s, 3H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$ δ/ppm): 166.2 (C=O), 153.8 (C_{aryl}), 153.7 (C_{aryl}), 153.24 (C_{aryl}), 153.18 (C_{aryl}), 142.0 (C_{aryl}), 140.8 (C_{aryl}), 134.6 (C_{aryl}), 134.3 (C_{aryl}), 132.4 (C_{aryl}), 131.2 (C_{aryl}), 131.0 (C_{aryl}), 130.9 (C_{aryl}), 130.5 (C_{aryl}), 130.3 (C_{aryl}), 125.8 (C_{aryl}), 125.2 (C_{aryl}), 125.1 (C_{aryl}), 124.1 (C_{aryl}), 123.7 (C_{aryl}), 123.63 (C_{aryl}), 123.58 (C_{aryl}), 123.51 (C_{aryl}), 123.2 (C_{aryl}), 122.3 (C_{aryl}), 72.3 (OCH_2), 71.14 (OCH_2), 71.08 (OCH_2), 71.02 (OCH_2), 69.6 (CH_2), 65.0 (CH_2), 59.4 (CH_3).

MS: (FAB) *m/z* (%) = 711.1 (98) [M + H^+], 59 (100).

Triethyleneglycolester bisazodiamine



A flask was charged with boronic ester **98** (711 mg, 1.74 mmol, 2.50 eq.), triethyleneglycolester bisazodibromide (494 mg, 695 µmol, 1.00 eq.) and $Pd(PPh_3)_4$ (48 mg, 6 mol%) and flushed with argon for 5 minutes. Then, THF (35 ml) and 2 M aq. K_2CO_3 (9 ml) was added. The mixture was degassed with an argon stream for 20 minutes, heated to 60 °C and stirred at this temperature for 19 hours. After the mixture had cooled town to room temperature, the organic phase was separated and washed with brine. The organic layer was dried over $MgSO_4$, the solvent was removed under reduced pressure and the residue was purified via flash column chromatography (neutral alox, hexane:EtOAc 1:1) to obtain 716 mg of an orange oil which still contained impurities and was used like this in the next step (92 %).

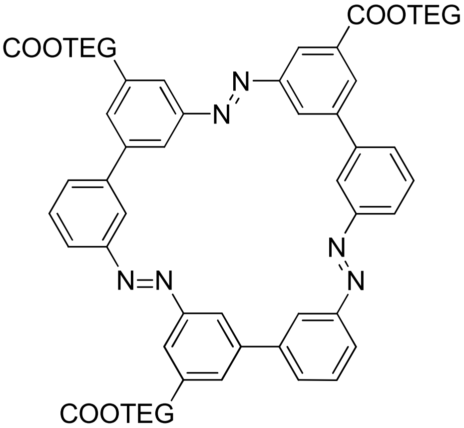
IR: (υ/cm^{-1}): 2870, 2824, 1713, 1597, 1450, 1227, 1095, 1026, 764, 694.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.60 (s, 1H, H_{aryl}), 8.49 (s, 1H, H_{aryl}), 8.45 (s, 1H, H_{aryl}), 8.30 (s, 1H, H_{aryl}), 8.18 (s, 1H, H_{aryl}), 8.17 (s, 1H, H_{aryl}), 8.01 – 7.91 (m 3H, H_{aryl}), 7.84 (d, $^3J_{HH}$ = 8.0 Hz, 1H, H_{aryl}), 7.77 – 7.49 (m, 5H, H_{aryl}), 7.49 – 7.42 (m, 2H, H_{aryl}), 7.38 (s, 2H, H_{aryl}), 7.16 (s, 2H, H_{aryl}), 4.59 – 4.56 (m, 2H, OCH_2), 4.48 – 4.46 (m, 4H, OCH_2), 4.00 (bs, 4H, NH_2), 3.93 – 3.89 (m, 2H, OCH_2), 3.84 – 3.82 (m, 4H, OCH_2), 3.75 – 3.59 (m, 16H, OCH_2), 3.50 – 3.47 (m, 2H, OCH_2), 3.32 (s, 6H, CH_3), 3.30 (s, 3H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$ δ/ppm): 167.0 (C=O), 166.3 (C=O), 153.52 (C_{aryl}), 153.45 (C_{aryl}), 153.3 (C_{aryl}), 153.2 (C_{aryl}), 147.6 (C_{aryl}), 142.1 (C_{aryl}), 141.99 (C_{aryl}), 141.96 (C_{aryl}), 141.91 (C_{aryl}), 141.89 (C_{aryl}), 140.81 (C_{aryl}), 132.52 (C_{aryl}), 132.42 (C_{aryl}), 132.34 (C_{aryl}), 132.31 (C_{aryl}), 132.12 (C_{aryl}), 132.09 (C_{aryl}), 130.79 (C_{aryl}), 130.5 (C_{aryl}), 130.22 (C_{aryl}), 130.16 (C_{aryl}), 130.0 (C_{aryl}), 129.9 (C_{aryl}), 129.0 (C_{aryl}), 128.8 (C_{aryl}), 125.8 (C_{aryl}), 123.9 (C_{aryl}), 122.9 (C_{aryl}), 122.8 (C_{aryl}), 122.6 (C_{aryl}), 122.3 (C_{aryl}), 122.1 (C_{aryl}), 122.1 (C_{aryl}), 119.1 (C_{aryl}), 118.3 (C_{aryl}), 115.7 (C_{aryl}),), 72.3 (OCH_2), 71.14 (OCH_2), 71.11 (OCH_2), 71.04 (OCH_2), 71.02 (OCH_2), 70.98 (OCH_2), 69.62 (OCH_2), 69.58 (OCH_2), 65.0 (OCH_2), 64.6 (OCH_2), 59.4 (OCH_3).

MS: (FAB) *m/z* (%) = 1115.5 (23) [M^+], 279 (100).

Macrocycle 99



To a solution of triethyleneglycolester bisazodiamine (571 mg, 512 µmol, 1.00 eq.) in THF (200 ml) and triethylamine (712 µl, 5.12 mmol, 10.0 eq.), a suspension of $Pb(OAc)_4$ (1.57 g, 3.53 mmol, 6.90 eq.) in THF (300 ml) was added dropwise over 20 min. After stirring for additional three hours, EDTA (1400 mg) was added and 30 ml of water and DCM was added. After stirring for 5 minutes, the organic layer was separated and the aqueous layer was extracted with DCM (2*50 ml). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The dark residue was first subjected to column chromatography (silica gel, EtOAc:MeOH 1:10) and then purified by preparative GPC to yield 210 mg of an orange solid (37 %).

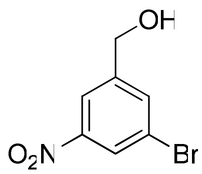
IR: (υ/cm^{-1}): 2870, 1713, 1450, 1312, 1234, 1095, 1026, 686.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.91 – 8.86 (m, 3H, H_{aryl}), 8.72 – 8.63 (m, 9H, H_{aryl}), 8.09 – 8.01 (m, 6H, H_{aryl}), 7.74 – 7.67 (m, 3H, H_{aryl}), 4.64 – 4.58 (m, 6H, OC**H**$_2$), 3.97 – 3.91 (m, 6H, OCH_2), 3.80 – 3.65 (m, 18H, OCH_2), 3.56 – 3.51 (m, 6H, OCH_2), 3.37 – 3.30 (m, 9H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$ δ/ppm): 165.82 (C=O), 165.76 (C=O), 165.73 (C=O), 152.85 (C_{aryl}), 152.81 (C_{aryl}), 152.79 (C_{aryl}), 152.74 (C_{aryl}), 152.72 (C_{aryl}), 152.68 (C_{aryl}), 140.0 (C_{aryl}), 139.8 (2C, C_{aryl}), 138.6 (2C, C_{aryl}), 138.5 (C_{aryl}), 132.01 (C_{aryl}), 131.97 (C_{aryl}), 131.89 (C_{aryl}), 129.95 (C_{aryl}), 129.88 (C_{aryl}), 129.85 (C_{aryl}), 129.5 (2C, C_{aryl}), 129.2 (C_{aryl}), 129.0 (C_{aryl}), 128.65 (C_{aryl}), 128.63 (C_{aryl}), 126.0 (C_{aryl}), 125.1 (C_{aryl}), 124.9 (C_{aryl}), 123.6 (C_{aryl}), 123.5 (C_{aryl}), 123.0 (C_{aryl}), 122.7 (C_{aryl}), 122.2 (2C, C_{aryl}), 122.1 (C_{aryl}), 121.9 (C_{aryl}), 121.0 (C_{aryl}), 71.92 (OCH_2), 71.88 (OCH_2), 70.75 (OCH_2), 70.73 (OCH_2), 70.69 (OCH_2), 70.61 (OCH_2), 69.2 (OCH_2), 64.6 (OCH_2), 59.0 (OCH_3).

MS: (MALDI-TOF): *m/z* (%) = 1111.5 (9) [M^+], 59 (100).

3-Nitro-5-bromobenzoic alcohol (100)



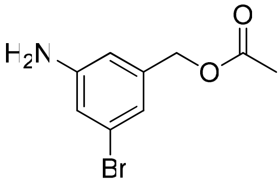
An oven-dried three-necked flask was put under an argon atmosphere and charged with 3-nitro-5-bromobenzoic acid (**89**) (30.0 g, 122 mmol, 1.00 eq.) and 85 ml of dry THF. The solution was cooled to -15 °C and a 2M BH_3*SMe_2 complex in THF (62.0 ml, 124 mmol, 1.02 eq.) was added dropwise so that the temperature stayed below -10 °C. After complete addition, the mixture was stirred for one hour at -15 °C, and then for 5 h at 60 °C. The solvent were removed under reduced pressure and the residue was slowly poured onto 200 ml of sat. aq. $NaHCO_3$. The mixture was extracted with EtOAc (3 * 100 ml), washed with water and brine, dried over $MgSO_4$ and concentrated under reduced pressure. The white solid was dried under high vacuum to afford 17.1 g (99 %) of (**14**) as a white solid.

MP: 88 °C;

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.28 (s, 1H), 8.17 (s, 1H), 7.86 (s, 1H), 4.82 (s, 2H, CH_2), 2.05 (bs, 1H, OH).

The analytical data corresponded to the literature.[15]

3-amino-5-bromobenzyl acetate (101)



A solution of 3-amino-5-btromobenzyl acetate (1.55g, 7.66 mmol, 1.00 eq.) in CH_2Cl_2 (30 ml) was treated with triethylamine (3.19 ml, 23.0 mmol 3.00 eq.) and DMAP (93.6 mg, 766 mmol, 0.1 eq.). Then, acetic anhydride (791 ml, 8.43 mmol, 1.00 eq.) was added dropwise. After stirring for 90 min, the solvent was evaporated and the yellow residue was subjected to flash column chromatography (silica gel, hexane/EtOAc 1:1) to obtain 1.19 g of a colourless oil (64 %).

IR: (υ/cm^{-1}): 3217, 2986, 2885, 1728, 1543, 1373, 1227, 1011, 818, 648.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 6.86 (s, 1H, H_{aryl}), 6.77 (s, 1H, H_{aryl}), 6.56 (s, 1H, H_{aryl}), 4.96 (s, 2H, CH_2) 3.76 (bs, 2H, NH_2), 2.10 (s, 2H, CH_3).

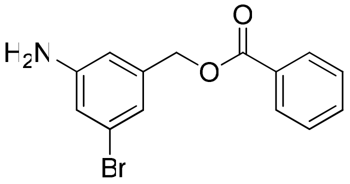
^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 171.2 (C=O), 148.3 (C_{aryl}), 139.3 (C_{aryl}), 123.5 (C_{aryl}), 121.2 (C_{aryl}), 117.9 (C_{aryl}), 113.6 (C_{aryl}), 65.8 (CH_2), 21.3 (CH_3).

MS: (ESI): m/z (%) = 268 [M+2+Na$^+$], 266 [M+Na$^+$].

EA: calculated: C = 44.29, H = 4.13, N = 5.74

found: C = 44.10, H = 4.18, N = 5.79

3-amino-5-bromobenzyl benzoate (103)



A solution of 3-amino-5-btromobenzylic alcohol (889 mg, 4.40 mmol, 1.00 eq.) in CH_2Cl_2 (17 ml) was treated with triethylamine (3.19 ml, 23.0 mmol 3.00 eq.) and DMAP (93.6 mg, 766 mmol, 0.1 eq.). Then, benzoic anhydride (791 ml, 8.43 mmol, 1.00 eq.) was added dropwise. After stirring for 90 minutes the solvent was evaporated and the yellow residue was subjected to flash column chromatography (silica gel, hexane/EtOAc 2:1) to obtain 1.12 g of **103** as a white solid (83 %).

MP: 78 – 79 °C.

IR: (υ/cm^{-1}): 3426, 3325, 3209, 1697, 1574, 1281, 1173, 825.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.10 – 8.05 (m, 2H, H_{aryl}), 7.57 (t, $^3J_{HH}$ = 7.4 Hz, 1H, H_{aryl}), 7.45 (t, $^3J_{HH}$ = 7.7 Hz, 1H, H_{aryl}), 6.95 (s, 1H, H_{aryl}), 6.79 (s, 1H, H_{aryl}), 6.65 (s, 1H, H_{aryl}), 5.22 (s, 2H, CH_2), 3.77 (bs, 2H, NH_2).

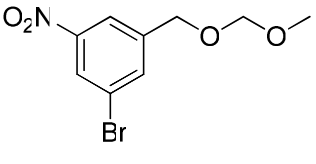
^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 176.7 (C=O), 148.3 (C_{aryl}), 139.4 (C_{aryl}), 133.6 (C_{aryl}), 130.3 (C_{aryl}), 130.2 (2C, C_{aryl}), 128.8 (2C, C_{aryl}), 123.6 (C_{aryl}), 121.2 (C_{aryl}), 117.9 (C_{aryl}), 113.6 (C_{aryl}), 66.2 (CH_2).

MS: (ESI): m/z (%) = 330 [M+2+Na$^+$], 328 [M+Na$^+$].

EA: calculated: C = 54.92, H = 3.95, N = 4.58

Found: C = 54.77, H = 3.90, N = 4.66

1-Bromo-3-[(methoxymethoxy)methyl]-5-nitrobenzene



A solution of 3-bromo-5-nitrobenzylic alcohol (**100**) (9.17 g, 39.5 mmol, 1.00 eq.) in CH_2Cl_2 (115 ml) was first treated with di*iso*propylethylamine (20.6 ml, 119 mmol, 3.00 eq.) and then with chloromethyl methyl ether (9.00 ml, 119 mmol, 3.00 eq.). After stirring for 3 h at room temperature, a nitrogen stream was bubbled through the reaction mixture for 15 minutes. Then, the reaction was quenched by the addition of aq. sat. NH_4Cl (50 ml). The organic phase was separated and the aqueous phase was extracted with DCM (100 ml). The combined organic phases were washed with brine, dried over $MgSO_4$ and the solvent was removed under reduced pressure. Flash column chromatography (silica gel, Hexane:EtOAc 5:1) of the residue yielded 9.82 g of the product as a pale orange oil (90 %).

IR: (υ/cm^{-1}): 2947, 2885, 1528, 1342, 1211, 1150, 1111, 1042, 733.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.29 (s, 1H, H_{aryl}), 8.17 (s, 1H, $H_{aryl,}$), 7.84 (s, 1H, H_{aryl}), 4.75 (s, 2H, CH_2) 4.67 (s, 2H, CH_2), 3.42 (s, 3H, CH_3).

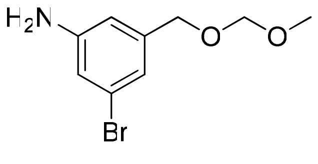
^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 149.2 (C_{aryl}), 142.6 (C_{aryl}), 136.5 (C_{aryl}), 126.1 (C_{aryl}), 123.2 (C_{aryl}), 121.2 (C_{aryl}), 96.6 (CH_2), 67.7 (CH_2), 56.1 (CH_3).

MS: (FAB) *m/z* (%) = 274 (M^+, 4), 276 (M^++2, 5), 45 (100).

EA: calculated: C = 39.15, H = 3.65, N = 5.07;

Found: C = 39.27, H = 3.78, N = 5.13

1-Bromo-3-[(methoxymethoxy)methyl]-5-aminobenzene (105)



A solution of 1-bromo-3-[(methoxymethoxy)methyl]-5-nitrobenzene (9.50 g, 34.4 mmol, 1.00 eq.) in acetic acid (70 ml) was heated to 80°C. Then, iron powder (10.5 g, 186 mmol, 5.40 eq.) was added slowly during 90 min to keep the temperature below 90°C. After complete addition, the reaction was stirred for additional 30 min, when it was diluted with water (200 ml). After extraction with TBME (2*150 ml), washing of the combined organic phases with water (100 ml) and drying over $MgSO_4$, the solvent was evaporated under reduced pressure.

Flash column chromatography (silica gel, hexane:EtOAc 1:1) of the residue yielded 7.03 g of compound **105** as a yellow oil (83 %).

IR: (υ/cm^{-1}): 3364, 2932, 2885, 1574, 1450, 1304, 1103, 1042, 987, 818.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 6.87 (s, 1H, H_{aryl}), 6.75 (s, 1H, H_{aryl}), 6.58 (s, 1H, H_{aryl}), 4.68 (s, 2H, CH_2) 4.46 (s, 2H, CH_2), 3.73 (bs, 2H, NH_2) 3.40 (s, 3H, CH_3).

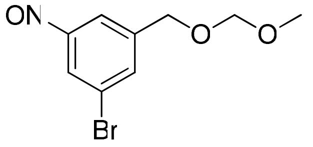
^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 148.2 (C_{aryl}), 141.4 (C_{aryl}), 123.4 (C_{aryl}), 120.9 (C_{aryl}), 117.4 (C_{aryl}), 113.2 (C_{aryl}), 96.1 (CH_2), 68.7 (CH_2), 55.8 (CH_3).

MS: (EI, 70 ev) *m/z* (%) = 245 (M^+, 22), 247 (M^++2, 21), 185 (100).

EA: calculated: C = 43.92, H = 4.91, N = 5.69

Found: C = 43.80, H = 5.03, N = 5.67

1-bromo-3-[(methoxymethoxy)methyl]-5-nitrosobenzene (106)



1-bromo-3-[(methoxymethoxy)methyl]-5-aminobenzene (**105**) (2.53 g, 10.3 mmol, 1.00 eq.) in DCM (50 ml) was treated with oxone® (12.7 g, 20.6 mmol, 2.00 eq.), dissolved in water (200 ml). The mixture was stirred at room temperature for 3 h. Afterwards, the organic layer was separated and washed with sat aq. NH_4Cl (100 ml), sat aq. $NaHCO_3$ (100 ml) and water (100 ml). After drying over $MgSO_4$ and removal of the solvent, a dark green oil was obtained, which was purified by column chromatography (silica gel, hexane:EtOAc 5:1) to yield 1.61 g of **106** as a green oil, which crystallized in the freezer to a brown solid (60 %).

IR: (υ/cm^{-1}): 3364, 2931, 2885, 1597, 1265, 1142, 1041, 964, 710.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.04 (s, 1H, H_{aryl}), 7.87 (s, 1H, H_{aryl}), 7.74 (s, 1H, H_{aryl}), 4.78 (s, 2H, CH_2) 4.74 (s, 2H, CH_2), 3.44 (s, 3H, CH_3)

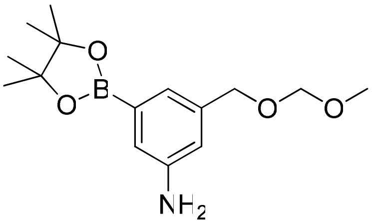
^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 165.4 (C_{aryl}), 142.6 (C_{aryl}), 136.7 (C_{aryl}), 124.2 (C_{aryl}), 121.6 (C_{aryl}), 120.7 (C_{aryl}), 96.6 (CH_2), 67.9 (CH_2), 56.1 (CH_3);

MS: (EI, 70 ev): *m/z* (%) = 259 (12) [M^+], 45 (100).

EA: calculated: C = 41.56, H = 3.88, N = 5.39

Found: C = 41.65, H = 4.07, N = 5.41.

Boronic ester 107



A three necked flask was charged with 1-bromo-3-[(methoxymethoxy)methyl]-5-aminobenzene (**106**) (3.00 g, 12.2 mmol, 1.00 eq), $Pd(dppf)Cl_2*CH_2Cl_2$ (797 mg, 0.98 mmol, 8 mol%), bis(pinacolato)diboron (3.41 g, 13.4 mmol, 1.1 eq.) and potassium acetate (4.18 g, 36.6 mmol, 3.00 eq.). The flask was flushed with argon for five minutes and dry DMF (90 ml) was added with a syringe. After degassing the mixture with an argon stream for 20 min, the mixture was stirred at 100°C for 1 h. After the reaction mixture had cooled down, it was diluted with ether (150 ml) and washed with brine (50 ml) and water (50 ml). Drying over $MgSO_4$, removal of the solvent and flash column chromatography over a short column (silica gel, hexane:EtOAc 1:1) yielded 2.95 g of **107** as a pale brown oil (83 %).

IR: (υ/cm^{-1}): 2978, 2932, 1597, 1366, 1265, 1142, 1103, 1041, 964, 710.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.18 (s, 1H, H_{aryl}), 7.07 (s, 1H, H_{aryl}), 6.82 (s, 1H, H_{aryl}), 4.69 (s, 2H, CH_2) 4.52 (s, 2H, CH_2), 3.66 (bs, 2H, NH_2), 3.41 (s, 3H, CH_3), 1.33 (s, 12H, CH_3).

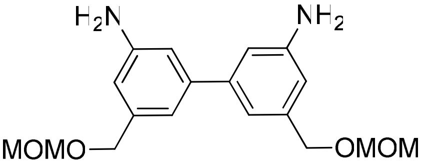
^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 146.1 (C_{aryl}), 138.4 (C_{aryl}), 124.4 (C_{aryl}), 120.6 (C_{aryl}), 117.4.6 (C_{aryl}), 95.7 (CH_2), 83.7 [$C(CH_3)_2$] 69.1 (CH_2), 55.3 (CH_3), 24.9 [$C(CH_3)_2$].

MS: (FAB) m/z (%) = 293 (66) [M^+], 45 (100).

EA: calculated: C = 61.45, H = 8.25, N = 4.78

Found: C = 61.03, H = 8.66, N = 4.58.

Diamine 108



A three-necked flask was charged with boronic ester **107** (1.34 g, 4.55 mmol, 1.10 eq.), 1-bromo-3-[(methoxymethoxy)methyl]-5-aminobenzene (**105**) (1.02 g, 4.14 mmol, 1.00 eq.) and $Pd(PPh_3)_4$ (145 mg, 0.12 mmol, 3 mol%) and flushed with argon. Then, THF (200 ml) and sat. aq. 2M K_2CO_3 (50 ml) was added and the mixture was degassed with an argon stream for 20 min. The mixture was stirred at 80°C over night. Then, the reaction was allowed to cool down and the organic layer was separated and washed with water and brine (100 ml). After drying over $MgSO_4$ and removal of the solvent under reduced pressure the residue was purified by column chromatography (silica gel, EtOAc:Hexane 3:1 to 5:1) to yield (**108**) as a yellow oil which still contained residual EtOAc even after extensive drying under high vacuum (1.15 g, 83 %).

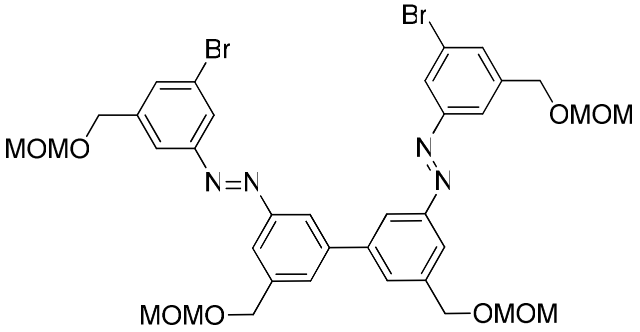
IR: (υ/cm^{-1}): 3356, 2932, 2885, 1597, 1458, 1381, 1095, 1034, 995, 910, 841.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 6.94 (s, 2H, H_{aryl}), 6.80 (s, 2H, H_{aryl}), 6.67 (s, 2H, H_{aryl}), 4.72 (s, 4H, CH_2) 4.55 (s, 4H, CH_2), 3.74 (bs, 4H, NH_2) 3.42 (s, 6H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 147.2 (C_{aryl}), 143.0 (C_{aryl}), 139.8 (C_{aryl}), 117.6 (C_{aryl}), 113.9 (C_{aryl}), 113.7 (C_{aryl}), 96.0 (CH_2), 69.5 (CH_2), 55.8 (CH_3).

MS: (EI, 70 ev) *m/z* (%) = 332 (44) [M^+], 272 (100).

Bisazodibromide 109



A solution of 5,5'-bis[(methoxymethoxy)methyl]biphenyl-3,3'-diamine (**108**) (967 mg, 2.91 mmol, 1.00 eq.) and 1-bromo-3-[(methoxymethoxy)methyl]-5-nitrosobenzene (**77**) (1.59 g, 6.11 mmol, 2.10 eq.) in acetic acid (70 ml) was stirred for 19 h at rt. Then, the solvent was removed under reduced pressure and the black residue was purified by flash column chromatography (silica gel, hexane:EtOAc 3:1 to 3:2) to yield 1.54 g of **109** as a red oil which crystallized upon standing at room temperature (65 %).

MP: 86 °C

IR: (υ/cm^{-1}): 2893, 2824, 1574, 1435, 1373, 1150, 1103, 1057, 1003, 910, 864.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.19 (s, 2H, H_{aryl}), 8.03 (s, 2H, H_{aryl}), 7.96 (s, 2H, H_{aryl}), 7.92 (s, 2H, H_{aryl}), 7.84 (s, 2H, H_{aryl}), 7.65 (s, 2H, H_{aryl}), 4.81 (s, 4H, CH_2), 4.79 (s, 4H, CH_2), 4.77 (s, 4H, CH_2), 4.69 (s, 4H, CH_2), 3.48 (s, 6H, CH_3) 3.45 (s, 6H, CH_3).

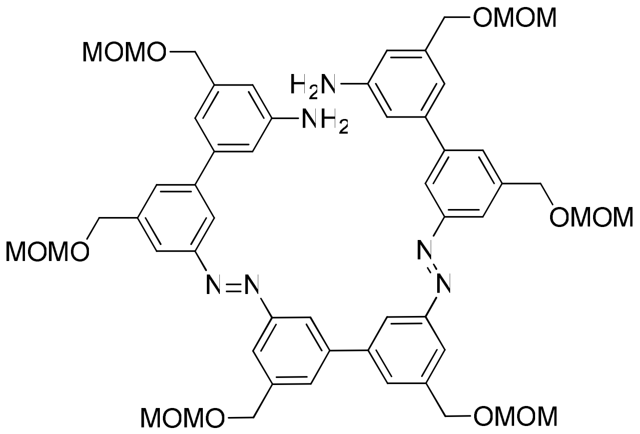
^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 153.8 (C_{aryl}), 153.4 (C_{aryl}), 141.8 (C_{aryl}), 141.7 (C_{aryl}), 140.5 (C_{aryl}), 133.1 (C_{aryl}), 129.7 (C_{aryl}), 124.5 (C_{aryl}), 123.6 (C_{aryl}), 122.3 (C_{aryl}), 122.0 (C_{aryl}), 121.6 (C_{aryl}), 96.41 (CH_2), 96.39 (CH_2), 69.1 (CH_2), 68.4 (CH_2), 56.0 (CH_3).

MS: (FAB, NBA): *m/z* (%) = 817 (18) [$M + H^+$], 45 (100).

EA: calculated: C = 52.95, H = 4.94, N = 6.86;

Found: C = 52.98, H = 5.03, N = 6.83.

Bisazodiamine 110



A three-necked flask was charged with boronic ester **107** (1.19 g, 4.07 mmol, 2.20 eq.), bisazodibromide **109** (1.51 g, 1.85 mmol, 1.00 eq.) and $Pd(PPh_3)_4$ (130 mg, 0.11 mmol, 6 mol%) and flushed with argon. Then, THF (90 ml) and sat. aq. 2M K_2CO_3 (23 ml) was added and the mixture was degassed with an argon stream for 20 min. The mixture was stirred at 80°C over night. The reaction mixture was allowed to cool down and the organic layer was separated and washed with water and brine (50 ml). After drying over $MgSO_4$ and removal of the solvent under reduced pressure the residue was purified by column chromatography (silica gel, DCM:MeOH 100:3) to yield 1.61 g of a red oil still containing impurities, which did not influence the next step (quant.)

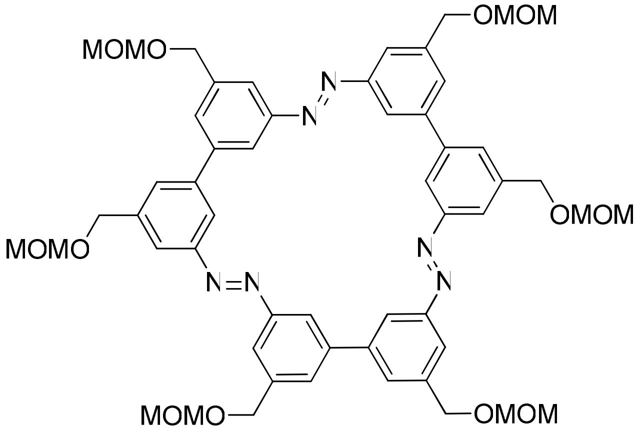
IR: (υ/cm^{-1}): 3356, 2932, 2885, 1605, 1381, 1103, 1041, 910, 849, 694.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.24 (s, 2H, H_{aryl}), 8.12 (s, 2H, H_{aryl}), 7.98 (s, 2H, H_{aryl}), 7.94 (s, 2H, H_{aryl}), 7.84 (s, 2H, H_{aryl}), 7.72 (s, 2H, H_{aryl}), 7.08 (s, 2H, H_{aryl}), 6.95 (s, 2H, H_{aryl}), 6.73 (s, 2H, H_{aryl}), 4.82 (s, 4H, CH_2), 4.80 (s, 4H, CH_2), 4.79 (s, 4H, CH_2), 4.76 (s, 4H, CH_2), 4.74 (s, 4H, CH_2), 4.60 (s, 4H, CH_2), 3.81 (s, 4H, NH_2), 3.48 (s, 6H, CH_3), 3.46 (s, 6H, CH_3), 3.44 (s, 6H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 153.7 (C_{aryl}), 153.5 (C_{aryl}), 147.5 (C_{aryl}), 142.9 (C_{aryl}), 142.0 (C_{aryl}), 140.3 (C_{aryl}), 140.2 (C_{aryl}), 140.0 (C_{aryl}), 132.5 (C_{aryl}), 129.42 (C_{aryl}), 129.35 (C_{aryl}), 122.0 (C_{aryl}), 121.8 (C_{aryl}), 121.4 (C_{aryl}), 121.1 (C_{aryl}), 117.5 (C_{aryl}), 114.3 (C_{aryl}), 113.7 (C_{aryl}), 96.4 (CH_2), 96.3 (CH_2), 96.1 (CH_2), 69.5 (CH_2), 69.2 (4C, CH_2), 56.0 (CH_3), 55.9 (CH_3) 55.8 (CH_3).

MS: (FAB): *m/z* (%) = 989 (9) [M + H^+], 45 (100).

Macrocycle 111



To a solution of bisazodiamine **110** (1.57 g, 1.59 mmol, 1.00 eq.) in THF (150 ml) and triethylamine (2.21 ml, 15.9 mmol, 10.0 eq.) a suspension of $Pb(OAc)_4$ (4.86 g, 11 mmol, 6.90 eq.) in THF (250 ml) was added dropwise over 20 min. After stirring for additional 3 h, EDTA (4.65 g, 15.9 mmol, 10.0 eq.) and 100 ml of water and CH_2Cl_2 was added. After stirring for 20 minutes, the organic layer was separated and the aqueous layer was extracted with DCM (4*50 ml). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The dark residue was purified by column chromatography (neutral alox, hexane:toluene:EtOAc 1:1:2) to yield 1.26 g of an orange red solid (80 %).

MP: 162 – 165 °C

IR: (υ/cm^{-1}): 2932, 2877, 1589, 1435, 1373, 1211, 1103, 1041, 910, 864, 694.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.64 (s, 6H $H_{aryl,}$), 8.01 (s, 6H, H_{aryl}), 7.98 (s, 6H, H_{aryl}), 4.83 (s, 12H, CH_2), 4.82 (s, 12H, CH_2), 3.49 (s, 18H, CH_3).

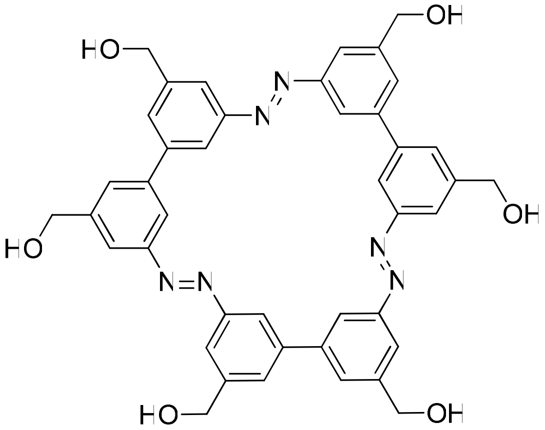
^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 153.6 (C_{aryl}), 140.4 (C_{aryl}), 140.3 (C_{aryl}), 128.2 (C_{aryl}), 121.8 (C_{aryl}), 121.7 (C_{aryl}), 96.4 (CH_2), 69.3 (CH_2), 56.0 (CH_3).

MS: (FAB) *m/z* (%) = 985 (7) [$M + H^+$], 45 (100).

EA: calculated: C = 52.95, H = 4.94, N = 6.86

Found: C = 52.98, H = 5.03, N = 6.83

Macrocylce 112



Macrocycle **111** (120 mg, 122 µmol, 1.00 eq.) was dissolved in THF (8 ml) and 2M aq. HCl (2 ml) was added. The mixture was stirred at 45 °C for 6d. Then, water (20 ml) was added and the precipitate was collected by filtration and dried under high vacuum to yield a yellow solid (70 mg, 80 %).

MP: > 245 °C

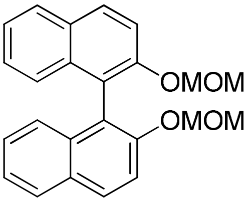
IR: (υ/cm^{-1}): 3032, 2862, 1605, 1435, 1227, 1142, 1049, 856, 694.

^{1}H-NMR: (400 MHz, DMSO, δ/ppm): 8.65 (s, 1H, H_{aryl}), 8.13 (s, 1H, H_{aryl}), 7.99 (s, 1H, H_{aryl}), 5.54 (bs, 1H, OH), 4.77 (s, 2H, CH_2).

^{13}C-NMR: (101 MHz, $CDCl_3$): δ = 152.6 (C_{aryl}), 145.2 (C_{aryl}), 138.8 (C_{aryl}), 126.5 (C_{aryl}), 119.7 (C_{aryl}), 119.4 (C_{aryl}), 62.6 (CH_2).

MS: (MALDI-TOF): *m/z* (%) = 720.8 (65) [M^+], 721.7 (100).

2,2′-Bis(methoxymethyl)-1,1′-binaphthyl (116)



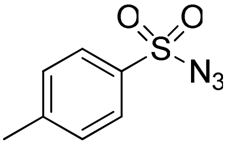
A flask was charged with dry DMF (14 ml), dry THF (28 ml) and sodium hydride 60 % on mineral oil (642 mg, 16.1 mmol, 2.30 eq.). The suspension was cooled to 0 °C and a solution of binol (**115**) (2.00 g, 6.98 mmol, 1.00 eq.) in THF (10 ml) was added dropwise. The mixture was stirred for one hour at room temperature, after which chloromethyl methyl ether (1.86 ml, 22.0 mmol, 3.15 eq.) was added. After stirring for 1 h, the mixture was quenched with water and extracted with EtOAc three times. The combined organic phases were washed with brine and dried over $MgSO_4$. After removal of the solvent at reduced pressure, the residue was recrystallized in MeOH to yield 2.20 g of colourless needles (84 %).

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.95 (d, $^3J_{HH}$ = 9.0 Hz, 2H, H_{aryl}), 7.87 (d, $^3J_{HH}$ = 8.2 Hz, 2H, H_{aryl}), 7.58 (d, $^3J_{HH}$ = 9.0 Hz, 2H, H_{aryl}), 7.35 (t, $^3J_{HH}$ = 7.4 Hz, 2H, H_{aryl}), 7.22 (t, $^3J_{HH}$ = 7.6 Hz, 2H, H_{aryl}), 7.16 (d, $^3J_{HH}$ = 8.4 Hz, 2H, H_{aryl}), 5.08 (d, $^3J_{HH}$ = 6.8 Hz, 2H, CH_2), 4.98 (d, $^3J_{HH}$ = 6.8 Hz, 2H, CH_2), 3.14 (s, 6H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 153.1 (C_{aryl}), 134.4 (C_{aryl}), 130.3 (C_{aryl}), 129.8 (C_{aryl}), 128.3 (C_{aryl}), 126.7 (C_{aryl}), 126.0 (C_{aryl}), 124.5 (C_{aryl}), 121.7 (C_{aryl}), 117.7 (C_{aryl}), 95.6 (CH_2), 56.2 (CH_3).

The analytical data corresponded to the literature.[16]

Tosyl azide (118)

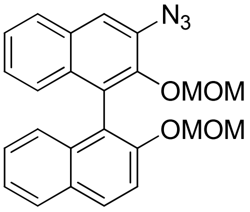


A solution of *p*-toluenesulfonyl chloride (**117**) (10.0 g, 52.5 mmol, 1.00 eq.) in acetone (45 ml) was added to a suspension of sodium azide (3.79 g, 57.5 mmol, 1.10 eq.) in ethanol (15 ml) at rt. This mixture was stirred for 3 h. The solvent was then removed under reduced pressure. The residue was dissolved in a mixture of CH_2Cl_2 (100 ml) and water (100 ml). The organic phase was dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure to yield 9.93 g of a colourless oil (96 %).

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.84 (d, $^3J_{HH}$ = 8.4 Hz, 2H, H_{aryl}), 7.40 (d, $^3J_{HH}$ = 8.0 Hz, 2H, H_{aryl}), 2.48 (s, 3H, CH_3).

The analytical data corresponded to the literature.[17]

3-Azido-2,2′-bis(methoxymethyl)-1,1′-binaphthyl (119)



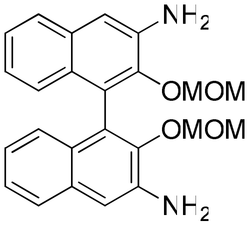
An oven dried three necked flask was charged with 2,2′-Bis(methoxymethyl)-1,1′-binaphthyl (**116**) (200 mg, 534 µmol, 1.00 eq.) and TMEDA (167 µl, 1.11 mmol, 2.07 eq.) and flushed with an argon stream for 15 minutes. Then, dry THF (2 ml) was added and the mixture was cooled to -78 °C. After the addition of 2.5 M BuLi (460 µl, 1.15 mmol, 2.15 eq.) in hexane, the mixture was stirred for 90 minutes at - 78 °C. Then, tosyl azide (263 mg, 1.33 mmol, 2.50 eq.) was added and the mixture was stirred for 16 h at room temperature. The reaction was quenched by the addition of 0.5 ml of water, and the mixture was extracted with DCM (3*5 ml). After drying of the organic phase with $MgSO_4$ and removal of the solvent under reduced pressure, the residue was purified by column chromatography (silica gel, hexane:TBME 5:1) to yield 110 mg of a pale brown gel (50 %).

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.96 (d, $^3J_{HH}$ = 9.0 Hz, 1H, H_{aryl}), 7.86 (d, $^3J_{HH}$ = 8.1 Hz, 1H, H_{aryl}), 7.82 (d, $^3J_{HH}$ = 8.2 Hz, 1H, H_{aryl}), 7.68 (s, 1H, H_{aryl}), 7.59 (d,

$^3J_{HH}$ = 9.1 Hz, 1H, H_{aryl}), 7.41 (t, $^3J_{HH}$ = 7.3 Hz, 1H, H_{aryl}), 7.36 (t, $^3J_{HH}$ = 7.5 Hz, 1H, H_{aryl}), 7.27 (t, $^3J_{HH}$ = 7.6 Hz, 1H, H_{aryl}) 7.22 – 7.13 (m, 3H, H_{aryl}), 5.14 (d, $^3J_{HH}$ = 7.0 Hz, 1H, CH_2), 5.04 (d, $^3J_{HH}$ = 7.0 Hz, 1H, CH_2), 4.78 (d, $^3J_{HH}$ = 5.7 Hz, 1H, CH_2), 4.71 (d, $^3J_{HH}$ = 5.7 Hz, 1H, CH_2), 3.20 (s, 3H, CH_3), 2.73 (s, 3H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 153.3 (C_{aryl}), 146.0 (C_{aryl}), 134.3 (C_{aryl}), 133.6 (C_{aryl}), 131.8 (C_{aryl}), 131.4 (C_{aryl}), 130.4 (C_{aryl}), 130.0 (C_{aryl}), 128.3 (C_{aryl}), 128.2 (C_{aryl}), 127.2 (C_{aryl}), 127.1 (C_{aryl}), 126.5 (C_{aryl}), 126.3 (C_{aryl}), 126.1 (C_{aryl}), 125.9 (C_{aryl}), 124.6 (C_{aryl}), 120.2 (C_{aryl}), 117.7 (C_{aryl}), 116.8 (C_{aryl}), 99.3 (CH_2), 95.3 (CH_2), 56.9 (CH_3), 56.4 (CH_3).

Diaminobinaphthol 120

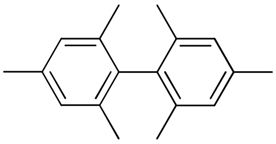


A solution of MOM protected binaphthol **116** (700 mg, 1.87 mmol, 1.00 eq.) in 10 ml of dry THF was cooled down to -78 °C under an argon atmosphere. Then, 1.6 M n-BuLi in hexanes (2.81 ml, 4.49 mmol, 2.4 eq.) was added dropwise. The mixture was allowed to warm up to 0 °C by placing an ice bath under the flask. After stirring for 2h the temperature was decreased to -78 °C again, and p-tosylsulfonic acid azide (**118**) (1.11 g, 5.61 mmol, 3.00 eq.) was added dropwise. The mixture was stirred for one hour at room temperature, after which TLC showed complete conversion of the starting material. The mixture was quenched by the addition of 2 ml of water and extracted trice with DCM. The combined organic phases were dreid over $MgSO_4$ and the solvent was reduced under reduced pressure. The residue was again taken up into 20 ml of dry THF and cooled to 0 °C. Then, $LiAlH_4$ (284 mg, 7.48 mmol, 4.00 eq.) was added slowly to the solution. A decoloration of the mixture was observed, and after one hour of stirring at 0 °C water (10 ml) was added very carefully to quench residual $LiAlH_4$. After extraction with DCM (3*20 ml), washing with water, drying over $MgSO_4$ and removal of the solvent at reduced pressure, the residue was purified by flash column chromatography (silica gel, hexane:EtOAc 1:1) to yield 500 mg (66 %) of **120** as a pale red oil.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.64 (d, $^3J_{HH}$ = 8.2 Hz, 2H, H_{aryl}), 7.30 (t, $^3J_{HH}$ = 6.8 Hz, 2H, H_{aryl}), 7.20 (s, 2H, H_{aryl}), 7.09 (d, $^3J_{HH}$ = 8.4 Hz, 2H, H_{aryl}), 7.05 – 7.00 (m, 2H, H_{aryl}), 4.62 (d, $^3J_{HH}$ = 5.8 Hz, 2H, CH_2), 4.58 (d, $^3J_{HH}$ = 5.8 Hz, 2H, CH_2), 4.27 (bs, 4H, NH_2), 3.05 (s, 6H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$), δ/ppm): 145.2 (C_{aryl}), 140.2 (C_{aryl}), 132.5 (C_{aryl}), 128.4 (C_{aryl}), 126.1 (C_{aryl}), 125.8 (C_{aryl}), 123.3 (C_{aryl}), 110.5 (C_{aryl}), 99.4 (CH_2), 57.5 (CH_3).

Bimesityl (123)



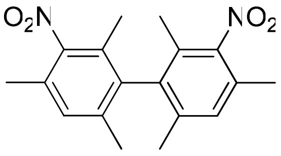
Mesitylene (**122**) (25.0 ml, 180 mmol, 1.00 eq.), was cooled to 0 °C under a nitrogen atmosphere. Then, $FeCl_3$ (14.6 g, 90 mmol, 0.50 eq.) was added. The mixture was removed from the ice bath and stirred heavily till the start of the reaction was monitored by the development of HCl. Then, the suspension was again cooled and stirred for 2.5h. After the addition of ice (50 g), the mixture was extracted with DCM (3*100 ml), washed with water and dried over $MgSO_4$. The solvent, residual starting material and 2-chloromesitylene was destilled out of the reaction mixture and the solid residue was recrystallized from EtOH to yield 1.72 g (8 %) of pale brown crystals.

MP: 99 – 101 °C

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 6.94 (s, 4H, H_{aryl}), 2.34 (s, 6H, CH_3), 1.87 (s, 12H, CH_3).

The analytical data corresponded to the literature.[18]

3,3’-Dinitrobimesityl (124)



Fuming nitric acid (0.96 ml, 21.3 mmol, 3.00 eq.) was slowly dropped to acetic anhydride (5ml) which was cooled to -15 °C, so that the temperature stayed under -5 °C. After complete addition, the mixture was added slowly to a solution of bimesityl (**123**) (1.70 g, 7.11 mmol, 1.00 eq.) in carbon tetrachloride (5 ml). The mixture was stirred over night at room temperature and then cautiously quenched with water. The organic layer was collected and the aqueous layer was extracted with DCM (10 ml). The combined organic phases were washed with sat. aq. $NaHCO_3$ and brine. After drying over $MgSO_4$ and removal of the solvent under reduced pressure, 2.10 g of a white solid was obtained, which still contained traces of mononitrated product (90 %).

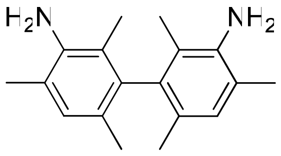
MP: 160 – 163 °C

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.10 (s, 1H, H_{aryl}), 2.33 (s, 3H, CH_3), 1.91 (s, 3H, CH_3), 1.85 (s, 3H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 151.5 (C_{aryl}), 138.7 (C_{aryl}), 137.6 (C_{aryl}), 131.0 (C_{aryl}), 129.1 (C_{aryl}), 127.7 (C_{aryl}), 20.34 (CH_3), 17.7 (CH_3) 15.1 (CH_3).

The analytical data corresponded to the literature.[19]

3,3’-Diaminobimesityl (125)



To a solution of 3,3’-Dinitrodimesitylene (**124**) (5.19 g, 16.5 mmol, 1.00 eq.) in glacial acetic acid (57 ml), water (13 ml) and conc. HCl (3 ml) was added zinc dust (19.2, 294 mmol, 17.8 eq.) in small portions so that the temperature rised to 80 °C to 90 °C. After complete addition, TLC control showed complete conversion and water (100 ml) was added. The mixture was filtered over celite, and the filtrate was basified with aqueous ammonia. The mixture was extracted with ethyl acetate (3*50 ml). The combined organic phases were washed with water, dried over $MgSO_4$ and purified by flash column chromatography (silica gel, hexane:EtOAc 2:1) to yield 2.84 g of the product as a white solid (64 %).

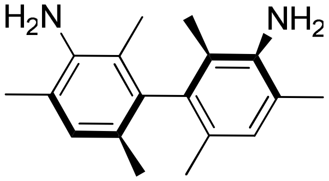
MP: 204 – 209 °C

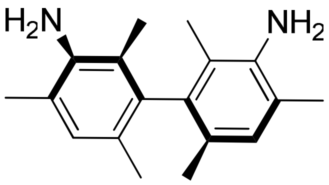
^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 6.86 (s, 1H, H_{aryl}), 3.50 (bs, 2H, NH_2), 2.22 (s, 3H, CH_3), 1.77 (s, 3H, CH_3), 1.75 (s, 3H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 140.8 (C_{aryl}), 139.4 (C_{aryl}), 129.5 (C_{aryl}), 125.8 (C_{aryl}), 120.6 (C_{aryl}), 120.4 (C_{aryl}), 19.8 (CH_3), 18.1 (CH_3) 14.2 (CH_3).

The analytical data corresponded to the literature.[19]

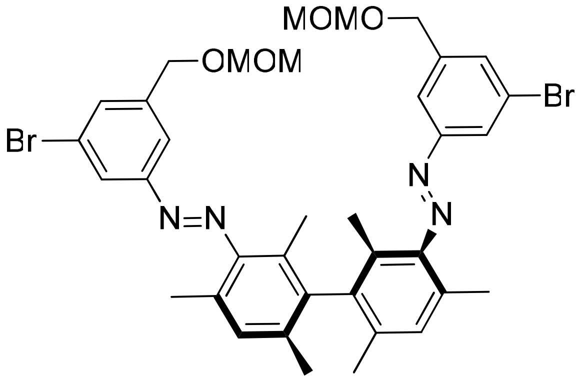
Chiral resolution of 3,3'-diaminodimesitylene





A solution of (+)-10-camphorsulfonic acid (4.74 g, 20.4 mmol, 2.10 eq.) in water (97 ml) was heated to 100 °C and 3,3'-diaminodimesitylene (**125**) (2.61 g, 9.72 mmol, 1.00 eq.) was added. The solution turned pink and was stirred at 100 °C. When complete solution was achieved, the mixture was allowed to cool down to rt and was then put into the fridge at 4 °C. After three days large pink crystals separated, which were collected by filtration (3.48 g, 98 %). This solid was recrystallized with boiling water. After three days the precipitated crystals were again collected (710 mg, 20 %). A small crystal was dissolved in hot water, which was basified with ammonia to precipitate the amine. The chemical rotation was 42.1 °. Additional 543 mg (15 %) precipitated after three weeks. The mother liquor of the first crystallization was concentrated to 5 - 10 ml and allowed to stand at rt for one day. Then it was filtered and the filtrate was basified to precipitate the second stereoisomer of the diamine (421 mg, 32 %). The chemical rotation of the second isomer was -41.6 °.

Bisazodibromide (*S*)-126



A flask was charged with (*S*)-3,3'-diaminobimesityl (*S*)-**125** ((373 mg, 1.39 mmol, 1.00 eq.) and 1-bromo-3-((methoxymethoxy)methyl)-5-nitrosobenzene (855 mg, 3.48 mmol, 2.50 eq.). Then, glacial acetic acid (40 ml) was added and the mixture was stirred under an argon atmosphere for 16 h. Afterwards, the solvent was removed at reduced pressure and the residue was purified by column chromatography (silica gel, hexane:EtOAc 5:1) to yield 924 mg of a red oil (90 %). The (*R*)-species and the racemic mixture were obtained in comparable yields by the same procedure, both in 89 % yield.

IR: (υ/cm^{-1}): 2921, 1565, 1437, 1373, 1149, 1043, 861.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.93 (s, 1H, H_{aryl}), 7.83 (s, 1H, H_{aryl}), 7.63 (s, 1H, H_{aryl}), 6.86 (s, 1H, H_{aryl}), 4.76 (s, 2H, CH_2), 4.68 (s, 2H, CH_2), 3.44 (s, 3H, CH_3), 2.38 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 1.96 (s, 3H, CH_3).

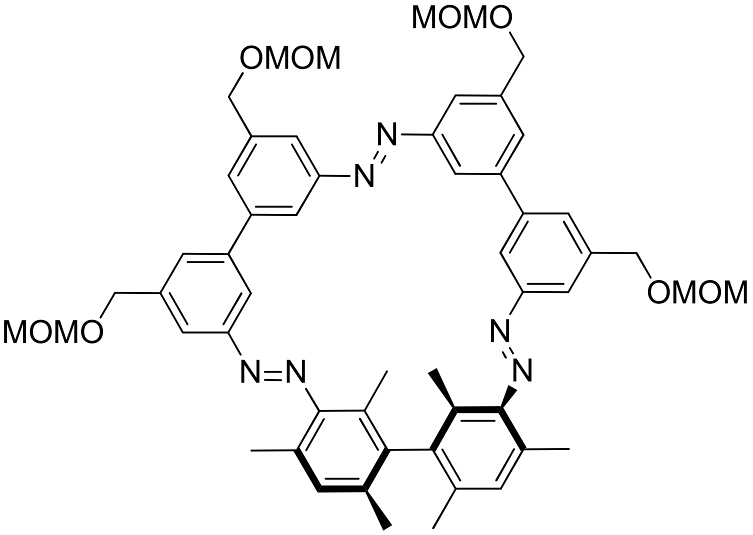
^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 154.2 (C_{aryl}), 150.0 (C_{aryl}), 141.6 (C_{aryl}), 138.9 (C_{aryl}), 137.5 (C_{aryl}), 132.7 (C_{aryl}), 131.7 (C_{aryl}), 131.5 (C_{aryl}) 128.6 (C_{aryl}), 124.0 (C_{aryl}), 123.6 (C_{aryl}), 121.9 (C_{aryl}), 96.4 (CH_2), 68.5 (CH_2), 56.0 (CH_3), 20.6 (CH_3), 20.0 (CH_3) 15.7 (CH_3).

MS: (EI, 70 eV): m/z (%) = 754.0 (28) $[M+4]^+$, 753.1 (21) $[M+3]^+$, 752.1 (53) $[M+2]^+$, 751.0 (13) $[M+1]^+$, 750.0 (26) $[M]^+$, 236.1 (100).

EA: calculated: C = 57.46, H = 5.36, N = 7.45

Found: C = 57.79, H = 5.26, N = 7.32.

Macrocycle (*S*)-127



A flask was charged with *(S)*-bisazodibromide (*S*)-**126** (828 mg, 1.10 mmol, 1.00 eq.), 3-((methoxymethoxy)methyl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (**107**) (774 mg, 2.64 mmol, 2.40 eq.), tetrakistriphenylphosphin palladium(0) (76 mg, 6 mol%). The Flask was put under an argon atmosphere and THF (50 ml) and 2M aq. K_2CO_3 (12.5 ml) was added. The mixture was degassed by an argon stream for 15 minutes and then stirred at 80 °C for 18 hours. Then, the mixture was allowed to cool down to rt, the organic phase was collected and the aqueous phase was extracted with a small amount of THF. The combined organic phases were washed with brine, dried over $MgSO_4$, concentrated under reduced pressure and the residue purified by flash column chromatography (silica gel, hexane:EtOAc 1:5). The resulting orange bisazodiamin (870 mg) was dissolved in THF (40 ml) and triethylamine (1.31 ml, 9.40 mmol, 10.0 eq.) was added. Then, lead tetraacetate (2.88 g, 6.49 mmol, 6.90 eq.) dissolved in the same amount of THF was slowly added while stirring. After complete addition, the mixture was stirred at rt over night and EDTA (2.75 g, 9.40 mmol, 10.0 eq.), DCM (50 ml) and water (100 ml) was added. The organic layer was separated and the aqueous layer was extracted with DCM (50 ml). After drying of the combined organic phases over $MgSO_4$ and removal of the solvent at reduced pressure, the residue was purified by column chromatography (silica gel, toluene:EtOAc 2:1) to yield 430 mg (42% over both steps) of a red oil which solidified upon drying under high vacuum. The (R)-species (42 %) and the racemic mixture (41 %) were obtained in comparable yields.

$[\alpha]^{20}_{D}$: (CHCl$_3$): 2128 ° [(*S*)-**127**]; 2077 ° [(*R*)-**127**].

MP: 99 – 102 °C.

IR: (υ/cm^{-1}): 2945, 2885, 1605, 1436, 1373, 1210, 1148, 1101, 1041, 916, 861.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.48 (s, 1H, H_{aryl}), 8.421 (s, 1H, H_{aryl}), 8.010 (s, 1H, H_{aryl}), 7.98 (s, 1H, H_{aryl}), 7.96 (s, 1H, H_{aryl}), 7.91 (s, 1H, H_{aryl}), 7.08 (s, 1H, H_{aryl}), 4.83 – 4.80 (m, 8H, CH_2), 3.50 (s, 3H, CH_3), 2.44 (s, 3H, CH_3), 2.12 (s, 3H, CH_3), 1.87 (s, 3H, CH_3).

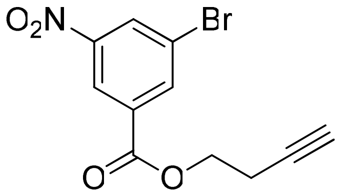
^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 153.7 (C_{aryl}), 153.5 (C_{aryl}), 152.2 (C_{aryl}), 140.4 (C_{aryl}), 140.23 (C_{aryl}), 140.19 (C_{aryl}), 140.15 (C_{aryl}), 139.2 (C_{aryl}), 136.1 (C_{aryl}), 130.7 (C_{aryl}), 130.2 (C_{aryl}), 129.1 (C_{aryl}), 128.0 (C_{aryl}), 127.6 (C_{aryl}), 124.9 (C_{aryl}), 121.7 (C_{aryl}), 121.6 (C_{aryl}), 117.8 (C_{aryl}), 96.4 (CH_2), 96.3 (CH_2), 69.4 (CH_2), 69.2 (CH_2), 55.9 (CH_3), 20.3 (CH_3), 18.7 (CH_3) 16.8 (CH_3).

MS: (FAB): m/z (%) = 921.4 (33) $[M+1]^+$, 45.0 (100).

EA: calculated: C = 70.42, H = 6.57, N = 9.12

Found: C = 70.40, H = 5.59, N = 8.96.

but-3-ynyl 3-bromo-5-nitrobenzoate (137)



A solution of 3-bromo-5-nitrobenzoic acid (**87**) (5.00 g, 20.3 mmol, 1.00 eq.), 4-DMAP (1.24 g, 10.2 mmol, 0.50 eq.) and 3-butyn-1-ol (4.75 ml, 60.9 mmol, 3.00 eq.) in CH_2Cl_2 (100 ml) was cooled to 0 °C. Then DCC (4.61 g, 22.3 mmol, 1.10 eq.) was added slowly. After stirring for one hour, a white solid crushed out of the solution. The mixture was stirred for another hour till TLC showed complete conversion. After filtering over celite, the filtrate was dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by column chromatography (silica gel, hexane:EtOAc 5:1) to yield 4.93 g of a colourless oil (82 %).

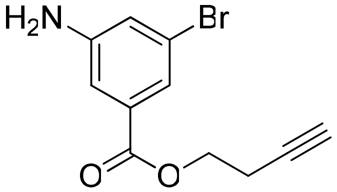
IR: (υ/cm^{-1}): 3286, 3094, 1728, 1520, 1350, 1265, 1157, 910, 733, 671, 633.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.79 (s,1H, H_{aryl}), 8.55 (s,1H, H_{aryl}), 8.49 (s,1H, H_{aryl}), 4.49 (t, $^3J_{HH}$ = 6.7 Hz, 2H, CH_2), 2.71 (dt, $^3J_{HH}$ = 6.7 Hz, $^4J_{HH}$ = 2.7 Hz 2H, CH_2), 2.05 (t, $^4J_{HH}$ = 2.7 Hz, 1H, CH).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 163.4 (C=O), 149.2 (C_{aryl}), 138.7 (C_{aryl}), 131.0 (C_{aryl}), 123.7 (C_{aryl}), 123.5 (C_{aryl}), 79.8 (C), 70.9 (CH) 64.2 (OCH_2), 19.4 (CH_2).

MS: (EI, 70 eV): m/z (%) = 297 (3) [M^+], 299 (3) [M^++ 2], 228 (100) [M^+ - C_4H_5O], 230 (98) [M^+ + 2 - C_4H_5O].

but-3-ynyl 3-bromo-5-aminobenzoate (138)

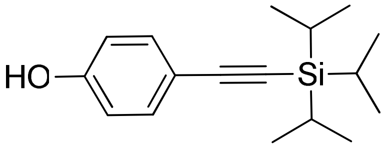


A solution of but-3-ynyl 3-bromo-5-nitrobenzoate (**137**) (4.71 g, 15.8 mmol, 1.00 eq.) in acetic acid (50 ml) was heated to 80 °C. Then Iron powder (4.81 g, 85.3 mmol, 5.40 eq.) was added slowly during 60 minutes to keep the temperature below 90 °C. After complete addition the reaction was stirred for additional thirty minutes, when it was diluted with water (150 ml). After extraction with TBME (3*80 ml), washing of the combined organic phases with water and drying over $MgSO_4$, the solvent was evaporated under reduced pressure to yield 3.64 g (86 %) of a pale yellow oil, which crystallized upon standing at rt.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.79 (s,1H, H_{aryl}), 8.55 (s,1H, H_{aryl}), 8.49 (s,1H, H_{aryl}), 4.49 (t, $^3J_{HH}$ = 6.7 Hz, 2H, CH_2), 4.02 (bs, 2H, NH_2), 2.71 (dt, $^3J_{HH}$ = 6.7 Hz, $^4J_{HH}$ = 2.7 Hz 2H, CH_2), 2.05 (t, $^4J_{HH}$ = 2.7 Hz, 1H, CH).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 163.4 (C=O), 149.2 (C_{aryl}), 138.7 (C_{aryl}), 131.0 (C_{aryl}), 123.7 (C_{aryl}), 123.5 (C_{aryl}), 79.8 (C), 70.9 (CH) 64.2 (OCH_2), 19.4 (CH_2).

4-((triisopropylsilyl)ethynyl)phenol (142)



A flask was charged with 4-iodophenol (**140**) (2.00 g, 9.00 mmol, 1.00 eq.), triisopropylsilylacetylene (**141**) (2.06 ml, 9.00 mmol, 1.00 eq.), $Pd(PPh_3)_4$ (520 mg, 5 mol%) and copper(I) iodide (171 mg, 10 mol%). The flask was flushed with argon and dry THF (60 ml) and diisopropylamine (20 ml) was added. The mixture was degassed by an argon stream for 15 minutes and then stirred at 70 °C for 2 h. After the solution had cooled down, it was washed with sat. aq. NH_4Cl (2*100 ml) and brine (100 ml). After drying over $MgSO_4$ and removal of the solvent, the residue was purified by flash column chromatography (silica gel, cyclohexane:EtOAc 3:2) to yield 1.98 g of a brown solid (80 %).

MP: 85 – 88 °C

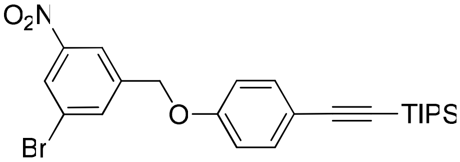
IR: (υ/cm^{-1}): 3302, 2939, 2862, 2152, 1589, 1504, 1219, 1165, 995, 879, 833, 787.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.37 (d, $^3J_{HH}$ = 8.6 Hz, 2H, H_{aryl}), 6.75 (d, $^3J_{HH}$ = 8.6 Hz, 2H, H_{aryl}), 4.87 (bs, 1H, OH), 1.12 (s, 21H, $CH(CH_3)_2$).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 155.6 (C_{aryl}), 133.7 (C_{aryl}, 2C), 116.1 (C_{aryl}), 115.3 (C_{aryl}, 2C), 106.9 ($C_{C\equiv C}$), 88.7 ($C_{C\equiv C}$), 18.7 (CH_3), 11.4 (CH).

MS: (EI, 70 eV): m/z (%) = 274 (15) [M^+], 231 (100) [M^+ - C_3H_7].

((4-((3-bromo-5-nitrobenzyl)oxy)phenyl)ethynyl)triisopropylsilane (143)



Triphenylphosphine (1.93 g, 7.36 mmol, 1.00 eq.) was dissolved in 40 ml of dry THF and cooled to 0 °C. To this solution diethyl azo diformate (1.19 ml, 7.36 mmol, 1.00 eq.) was added dropwise. This mixture was stirred for 30 minutes at 0 °C and a solution of 3-bromo-5-aminobenzylic alcohol (**100**) (1.71 g, 7.36 mmol, 1.00 eq.) and 4-((triisopropylsilyl)ethynyl)phenol (**142**) (2.02 g, 7.36 mmol, 1.00 eq.) in THF (30 ml) was added. The mixture was stirred for 1 h at 0°C and 16 h at rt. The solvent was removed under reduced pressure and the residue was subjected to flash column chromatography (silica gel, hexane:EtOAc 15:1) to yield 2.70 g of a pale yellow solid (75 %).

MP: 101 – 104 °C

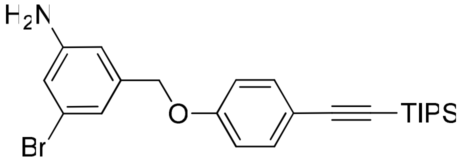
IR: (υ/cm^{-1}): 2939, 2862, 2152, 1605, 1528, 1504, 1211, 879, 795, 656.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.33 (s, 1H, H_{aryl}), 8.24 (s, 1H, H_{aryl}), 7.91 (s, 1H, H_{aryl}), 7.44 (d, $^3J_{HH}$ = 8.8 Hz, 2H, H_{aryl}), 6.89 (d, $^3J_{HH}$ = 8.8 Hz, 2H, H_{aryl}), 5.13 (s, 2H, CH_2), 1.12 (s, 21H, $CH(CH_3)_2$).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 157.7 (C_{aryl}), 140.7 (C_{aryl}), 135.8 (C_{aryl}), 133.7 (C_{aryl}, 2C), 126.2 (C_{aryl}), 123.1 (C_{aryl}), 120.7 (C_{aryl}), 117.1 (C_{aryl}) 114.6 (C_{aryl}, 2C), 106.6 ($C_{C\equiv C}$), 100.0 (C_{aryl}), 89.5 ($C_{C\equiv C}$), 68.0 (CH_2), 18.7 (CH_3), 11.4 (CH).

MS: (EI, 70 eV): m/z (%) = 444 (95) [$M^+ – C_3H_7$], 446 (100) [$M^+ - C_3H_7 + 2]^+$.

3-bromo-5-((4-((triisopropylsilyl)ethynyl)phenoxy)methyl)aniline (144)



A flask was charged with ((4-((3-bromo-5-nitrobenzyl)oxy)phenyl)ethynyl)triisopropylsilane (**143**) (1.89 g, 3.87 mmol, 1.00 eq.), $SnCl_2 * 2H_2O$ (4.36 g, 19.3 mmol, 5.00 eq.) and ethanol (20 ml) was added. The mixture was stirred at 60 °C for 2 h and then poured onto 300 mg of ice. The mixture was basified with saturated sodium bicabonat solution and extracted with ethyl acetate (3*40 ml). Drying over Na_2SO_4, removal of the solvent and purification with flash column (silica gel, hexane:EtOAc 3:1) afforded 1.31 g of a yellow oil which solidified upon standing at room temperature (74 %).

MP: 71 – 72 °C

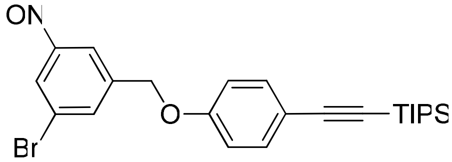
IR: (υ/cm^{-1}): 3379, 2939, 2862, 2152, 1574, 1504, 1234, 825, 671.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.40 (d, $^3J_{HH}$ = 8.8 Hz, 2H, H_{aryl}), 6.91 (s, 1H, H_{aryl}), 6.85 (d, $^3J_{HH}$ = 8.8 Hz, 2H, H_{aryl}), 6.76 (s, 1H, H_{aryl}), 6.62 (s, 1H, H_{aryl}), 4.93 (s, 1H, CH_2), 3.74 (bs, 2H, NH_2), 1.12 (s, 21H, $CH(CH_3)_2$).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 158.5 (C_{aryl}), 148.0 (C_{aryl}), 139.8 (C_{aryl}), 133.6 (C_{aryl}, 2C), 123.2 (C_{aryl}), 120.0 (C_{aryl}), 117.3 (C_{aryl}), 114.7 (C_{aryl}, 2C), 112.2 (C_{aryl}), 107.0 ($C_{C\equiv C}$), 88.9 ($C_{C\equiv C}$), 69.2 (CH_2), 18.7 (CH_3), 11.4 (CH).

MS: (EI, 70 eV): m/z (%) = 457 (21) [M^+], 459 (22) [$M^+ + 2$], 416 (100).

((4-((3-bromo-5-nitrosobenzyl)oxy)phenyl)ethynyl)triisopropylsilane (150)



To a solution of compound **144** (1.33 g, 2.90 mmol, 1.00 eq) in EtOAc (40 mL), mCPBA (1.20 g, 6.95 mmol, 2.40 eq) was added. The reaction mixture was stirred at room temperature for 1 h and the solvent was removed under reduced pressure. A light-green oil was obtained, which was purified by column chromatography on silica gel (hexane/DCM 6:1) to yield **7** as an orange oil, which crystallized in the freezer to form a orange-red solid (0.57 g, 42%).

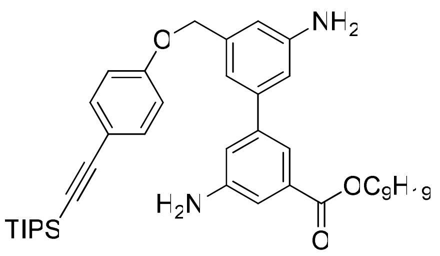
IR: (υ/cm^{-1}): 2939, 2862, 2152, 1605, 1504, 1234, 1173, 995, 879, 671.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.11 (s, 1H, H_{aryl}), 7.94 (s, 1H, H_{aryl}), 7.78 (s, 1H, H_{aryl}), 7.45 (d, $^3J_{HH}$=8.8 Hz, 2H, H_{aryl}), 6.92 (d, $^3J_{HH}$=8.8 Hz, 2H, H_{aryl}), 5.20 (s, 2H, CH_2), 1.12 (s, 21H, CH, $CH(CH_3)_2$).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 164.8 (C_{aryl}), 157.9 (C_{aryl}), 140.8 (C_{aryl}), 135.9 (C_{aryl}), 133.7 (C_{aryl}, 2C), 124.1 (C_{aryl}), 121.6 (C_{aryl}), 120.0 (C_{aryl}), 116.9, 114.7 (C_{aryl}, 2C), 106.7 ($C_{C\equiv C}$), 89.4 ($C_{C\equiv C}$), 68.2 (CH_2), 18.7 (CH_3), 11.4 (CH).

MS: (EI, 70 eV): m/z (%) = 428 (95) [$M^+ - C_3H_7$], 430 (100) [$M^+ - C_3H_7 + 2]^+$.

Diamine 145



A solution of 3-bromo-5-((4-(triisopropylsilyl)phenoxy)methyl)aniline (**144**) (980 mg, 2.25 mmol, 1.10 eq.) and nonyl 3-amino-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (**96**) (798 mg, 2.05 mmol, 1.00 eq.) in THF (100 ml) and 2M aq. K_2CO_3 (25 ml) was degassed by an argon stream for 15 minutes, and $Pd(PPh_3)_4$ (71.1 mg, 3 mol %) was added. The mixture was stirred under an argon atmosphere for 3 hours at 65 °C and then allowed to cool down to rt. The organic layer was separated, washed with brine (50 ml), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, hexane:EtOAc 1:2) to yield 1.11 g of a pale yellow oil (85 %).

IR: (υ/cm^{-1}): 3371, 2924, 2862, 2152, 1705, 1597, 1504, 1227, 995, 771, 671.

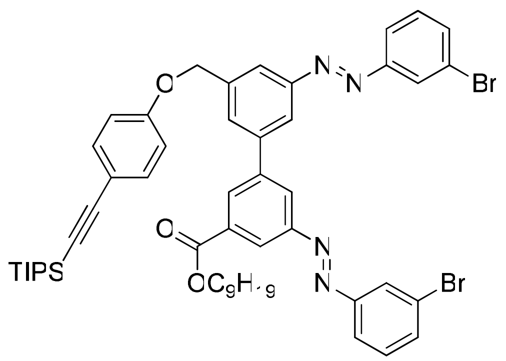
^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.62 (s, 1H, H_{aryl}), 7.41 (d, $^3J_{HH}$ = 8.7 Hz, 2H, H_{aryl}), 7.33 (s, 1H, H_{aryl}), 7.03 (s, 1H, H_{aryl}), 6.99 (s, 1H, H_{aryl}), 6.90 (d, $^3J_{HH}$ =

8.7 Hz, 2H, H$_{aryl}$), 6.84 (s, 1H, H$_{aryl}$), 6.74 (s, 1H, H$_{aryl}$), 5.02 (s, 2H, CH$_2$), 4.30 (t, $^3J_{HH}$ = 6.7 Hz, 2H, CH$_2$), 3.79 (bs, 4H, NH$_2$), 1.82 – 1.70 (m, 2H, CH$_2$), 1.49 – 1.20 (m, 12H, CH$_2$), 1.12 (s, 21H, CH(CH$_3$)$_2$), 0.87 (t, $^3J_{HH}$ = 6.9 Hz, 3H, CH$_3$).

^{13}C-NMR: (101 MHz, CDCl$_3$, δ/ppm): 166.8 (C=O), 158.8 (C$_{aryl}$), 147.0 (C$_{aryl}$), 146.7 (C$_{aryl}$), 142.4 (C$_{aryl}$), 142.1 (C$_{aryl}$), 138.4 (C$_{aryl}$), 133.5 (C$_{aryl}$, 2C), 131.9 (C$_{aryl}$), 118.8 (C$_{aryl}$), 117.9 (C$_{aryl}$), 116.5 (C$_{aryl}$), 116.1 (C$_{aryl}$), 114.9 (C$_{aryl}$), 114.8 (C$_{aryl}$, 2C), 113.6 (C$_{aryl}$), 113.2 (C$_{aryl}$), 107.1 (C$_{C≡C}$), 88.8 (C$_{C≡C}$), 70.0 (CH$_2$), 65.2 (CH$_2$), 31.9 (CH$_2$), 29.5 (CH$_2$), 29.3 (CH$_2$), 28.8 (CH$_2$), 26.0 (CH$_2$), 24.9 (CH$_2$), 22.7 (CH$_2$), 18.7 (CH$_3$), 14.1 (CH$_3$), 11.4 (CH).

MS: (EI, 70 eV): m/z (%) = 640 (29) [M$^+$], 597 (48) [M$^+$ - C$_3$H$_7$], 471 (100).

Dibromide 146



Diamine **145** (784 mg, 1.27 mmol, 1.00 eq.) was dissolved in acetic acid (30 ml) and 3-bromonitrosobenzene (**77**) ((945 mg, 5.08 mmol, 4.00 eq.) was added. The mixture was stirred for 3d at rt. The solvent was removed at reduced pressure and the black residue was purified by flash column chromatography (silica gel, hexane:DCM 2:1) to yield 905 mg of an orange oil (75 %).

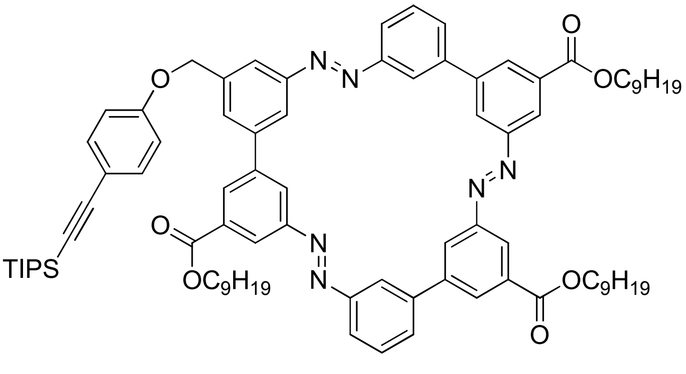
^{1}H-NMR: (400 MHz, CDCl$_3$, δ/ppm): 8.58 (s, 1H, H$_{aryl}$), 8.49 (s, 1H, H$_{aryl}$), 8.40 (s, 1H, H$_{aryl}$), 8.23 (s, 1H, H$_{aryl}$), 8.12 (d, $^3J_{HH}$ = 6.7 Hz, 2H, H$_{aryl}$), 8.04 (s, 1H, H$_{aryl}$), 7.94 (t, $^3J_{HH}$ = 8.1 Hz, 2H, H$_{aryl}$), 7.90 (s, 1H, H$_{aryl}$), 7.63 (t, $^3J_{HH}$ = 7.0 Hz, 2H, H$_{aryl}$), 7.48 – 7.40 (m, 4H, H$_{aryl}$), 6.97 (d, $^3J_{HH}$ = 8.9 Hz 2H, H$_{aryl}$), 5.25 (s, 2H,

CH_2), 4.42 (t, $^3J_{HH}$ = 6.8 Hz, 2H, CH_2), 1.89 – 1.80 (m, 2H, CH_2), 1.53 – 1.21 (m, 12H, CH_2), 1.12 (s, 21H, $CH(CH_3)_2$), 0.93 – 0.82 (m, 3H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 165.9 (C=O), 158.5 (C_{aryl}), 153.4 (C_{aryl}), 153.3 (C_{aryl}), 153.1 (C_{aryl}), 152.8 (C_{aryl}), 141.3 (C_{aryl}), 140.9 (C_{aryl}), 138.9 (C_{aryl}), 134.2 (C_{aryl}), 134.0 (C_{aryl}), 133.7 (C_{aryl}, 2C), 132.5 (C_{aryl}), 130.7 (C_{aryl}), 130.6 (C_{aryl}), 130.5 (C_{aryl}), 128.8 (C_{aryl}), 125.3 (C_{aryl}), 124.8 (C_{aryl}), 123.7 (C_{aryl}), 123.31 (C_{aryl}), 123.26 (C_{aryl}), 123.24 (C_{aryl}), 123.20 (C_{aryl}), 121.8 (C_{aryl}), 121.4 (C_{aryl}), 116.5 (C_{aryl}), 114.8 (C_{aryl}, 2C), 106.9 ($C_{C\equiv C}$), 89.0 ($C_{C\equiv C}$), 69.4 (CH_2), 65.8 (CH_2), 31.9 (CH_2), 31.6 (CH_2), 29.5 (CH_2), 29.3 (CH_2), 28.8 (CH_2), 26.0 (CH_2), 22.7 (CH_2), 18.7 (CH_3), 14.1 (CH_3), 11.4 (CH).

MS: (MALDI-TOF): *m/z* (%) = 976.1 [M^+] (58), 977.1 [M^++1] (100), 978.1 [M^++2] (92).

Macrocycle 148



A solution of dibromide **146** (809 mg, 849 μmol, 1.00 eq.) and nonyl 3-amino-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (**96**) (826 mg, 2.12 mmol, 2.50 eq.) in THF (50 ml) and 2M aq. K_2CO_3 (12 ml) was degassed by an argon stream for 15 minutes, and $Pd(PPh_3)_4$ (58.9 mg, 3 mol %) was added. The mixture was stirred under an argon atmosphere for 18 hours at 65 °C and then allowed to cool down to rt. The organic layer was separated, washed with brine (20 ml), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica gel, hexane:EtOAc 2:3) to yield 1.18 g of **147** as a pale yellow oil which was used directly in the next step in spite of impurities (106 %). ^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.62 (s, 1H, H_{aryl}), 8.51 (s, 1H, H_{aryl}), 8.47 (s, 1H, H_{aryl}), 8.29 (s, 1H, H_{aryl}), 8.22 (s, 1H, H_{aryl}), 8.21 (s, 1H, H_{aryl}), 8.08 (s, 1H,

H_{aryl}), 7.98 (t, $^{3}J_{HH}$ = 8.1 Hz, 2H, H_{aryl}), 7.92 (s, 1H, H_{aryl}), 7.79 – 7.72 (m, 4H, H_{aryl}), 7.61 (td, $^{3}J_{HH}$ = 7.8 Hz, $^{4}J_{HH}$ = 3.0 Hz, 2H, H_{aryl}), 7.45 (d, $^{3}J_{HH}$ = 8.8 Hz, 2H, H_{aryl}), 7.38 (s, 2H, H_{aryl}), 7.18 (s, 2H, H_{aryl}), 6.98 (d, $^{3}J_{HH}$ = 8.9 Hz, 2H, H_{aryl}), 5.27 (s, 2H, CH_2), 4.42 (t, $^{3}J_{HH}$ = 6.8 Hz, 2H, CH_2), 4.32 (t, $^{3}J_{HH}$ = 6.4 Hz, 4H, CH_2), 4.21 (bs, 4H, NH_2), 1.90 – 1.72 (m, 6H, CH_2), 1.53 – 1.18 (m, 36H, CH_2), 1.12 (s, 21H, $CH(CH_3)_2$), 0.90 – 0.81 (m, 9H, CH_3). To a solution of the diamine (1.11 g, 826 µmol, 1.00 eq.) in THF (80 ml) and triethylamine (1.15 ml, 8.26 mmol, 10.0 eq.), a suspension of $Pb(OAc)_4$ (2.53 g, 5.70 mmol, 6.90 eq.) in THF (140 ml) was added dropwise over 20 min. After stirring for additional three hours, EDTA (2.41 g, 8.26 mmol, 10.0 eq.) was added and 70 ml of water and DCM was added. After stirring for 5 minutes, The organic layer was separated and the aqueous layer was extracted with DCM (2*15 ml). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The dark residue was purified by column chromatography (silica gel, toluene) to yield 588 mg of an orange solid (53 %).

MP: 146 – 148 °C

IR: (υ/cm^{-1}): 2924, 2854, 2152, 1713, 1450, 1242, 887, 764, 687.

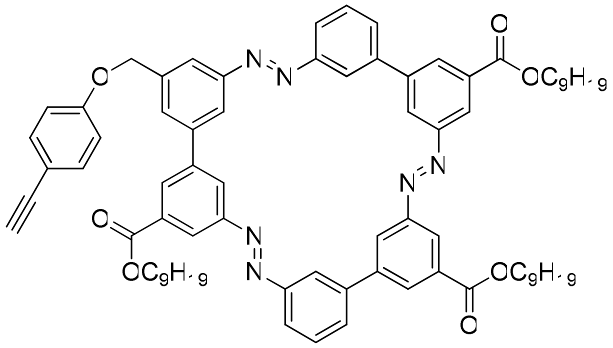
^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm, c ~ 50 mg/ml): 8.77 – 8.72 (m, 3H, H_{aryl}), 8.61 – 8.58 (m, 2H, H_{aryl}), 8.58 – 8.53 (m, 7H, H_{aryl}), 8.01 – 7.93 (m, 6H, H_{aryl}), 7.63 (t, $^{3}J_{HH}$ = 7.8 Hz, 2H, H_{aryl}), 7.48 (d, $^{3}J_{HH}$ = 8.8 Hz, 2H, H_{aryl}), 7.00 (d, $^{3}J_{HH}$ = 8.8 Hz, 2H, H_{aryl}), 5.22 (s, 2H, CH_2), 4.43 (t, $^{3}J_{HH}$ = 6.7 Hz, 6H, CH_2), 1.92 – 1.82 (m, 6H, CH_2), 1.56 – 1.24 (m, 36H, CH_2), 1.13 (s, 21H, $CH(CH_3)_2$), 0.91 – 0.85 (m, 9H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm, c ~ 50 mg/ml): 165.94 (C=O, 2C), 165.91 (COO, 1C) 158.5 (C_{aryl}), 153.1 (C_{aryl}), 152.91 (C_{aryl}), 152.92 (C_{aryl}), 152.84 (C_{aryl}), 152.82 (C_{aryl}), 152.80 (C_{aryl}), 140.0 (C_{aryl}), 139.9 (C_{aryl}), 139.6 (C_{aryl}), 139.2 (C_{aryl}), 138.84 (C_{aryl}), 138.80 (C_{aryl}), 138.7 (C_{aryl}), 133.7 (C_{aryl}, 2C), 132.5 (C_{aryl}), 132.4 (C_{aryl}, 2C), 130.0 (C_{aryl}, 2C), 129.42 (C_{aryl}), 129.40 (C_{aryl}), 129.2 (C_{aryl}), 129.0 (C_{aryl}), 128.8 (C_{aryl}), 127.3 (C_{aryl}), 126.1 (C_{aryl}), 124.9 (C_{aryl}), 124.8 (C_{aryl}), 123.7 (C_{aryl}), 123.6 (C_{aryl}), 123.3 (C_{aryl}), 122.6 (C_{aryl}), 122.4 (C_{aryl}), 121.97 (C_{aryl}), 121.95 (C_{aryl}), 121.0 (C_{aryl}), 120.7 (C_{aryl}), 116.5 (C_{aryl}), 114.8 (C_{aryl}, 2C), 107.0 ($C_{C\equiv C}$), 89.0 ($C_{C\equiv C}$), 69.5 (CH_2), 65.8 (CH_2), 31.9

(CH_2), 29.6 (CH_2), 29.4 (CH_2), 29.3 (CH_2), 28.8 (CH_2), 26.1 (CH_2), 22.7 (CH_2), 18.7 (CH_3), 14.1 (CH_3), 11.4 (CH).

MS: (MALDI-TOF): *m/z* (%) = 1337.7 [M^+] (68), 1339.7 (100).

Macrocycle 149



Macrocycle **148** (100 mg, 89.8 µmol, 1.00 eq.) was dissolved in THF (5 ml) and cooled to 0 °C. Then, a 1M solution of TBAF in THF (216 µl, 216 µmol, 2.40 eq.) was added dropwise, and the mixture was stirred for 19 hours at rt. The reaction was quenched by the addition of 25 ml of sat. aq. $NaHCO_3$. The orange precipitate was collected by filtration and washed with water and hexane. After drying under high vacuum, 71 mg of an orange solid was obtained (99 %).

MP: 183 – 185 °C

IR: (υ/cm^{-1}): 2924, 2854, 1713, 1605, 1450, 1242, 1204, 887, 687.

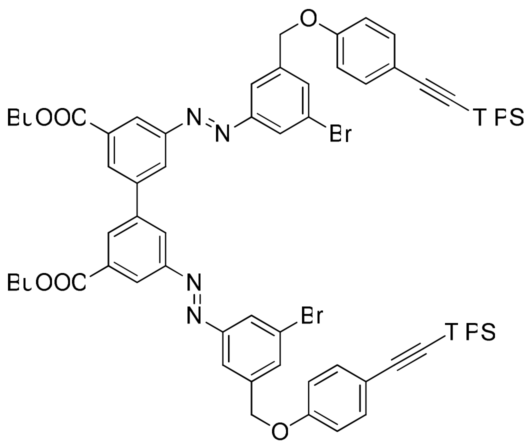
^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm, c ~ 4 mg/ml): 8.75 – 8.68 (m, 6H, H_{aryl}), 8.09 – 7.94 (m, 12H, H_{aryl}), 7.71 – 7.64 (m, 4H, H_{aryl}), 7.51 – 7.46 (m, 4H, H_{aryl}), 7.04 – 7.00 (m, 4H, H_{aryl}), 5.29 (s, 4H, CH_2), 3.02 (s, 1H, CH).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm, c ~ 50 mg/ml): 165.92 (C=O, 2C), 165.89 (C=O, 1C), 158.9 (C_{aryl}), 153.1 (C_{aryl}), 152.91 (C_{aryl}), 152.88 (C_{aryl}), 152.82 (C_{aryl}), 152.80 (C_{aryl}), 152.78 (C_{aryl}), 140.0 (C_{aryl}), 139.9 (C_{aryl}), 139.6 (C_{aryl}), 139.2 (C_{aryl}), 138.79 (C_{aryl}), 138.72 (C_{aryl}), 138.69 (C_{aryl}), 133.8 (C_{aryl}, 2C), 132.5 (C_{aryl}), 132.4 (C_{aryl}, 2C), 130.0 (C_{aryl}, 2C), 129.41 (C_{aryl}), 129.39 (C_{aryl}), 129.1

($\mathrm{C_{aryl}}$), 129.0 ($\mathrm{C_{aryl}}$), 128.8 ($\mathrm{C_{aryl}}$), 127.3 ($\mathrm{C_{aryl}}$), 126.1 ($\mathrm{C_{aryl}}$), 124.9 ($\mathrm{C_{aryl}}$), 124.8 ($\mathrm{C_{aryl}}$), 123.8 ($\mathrm{C_{aryl}}$), 123.6 ($\mathrm{C_{aryl}}$), 123.2 ($\mathrm{C_{aryl}}$), 122.6 ($\mathrm{C_{aryl}}$), 122.4 ($\mathrm{C_{aryl}}$), 122.0 ($\mathrm{C_{aryl}}$), 121.94 ($\mathrm{C_{aryl}}$), 121.0 ($\mathrm{C_{aryl}}$), 120.7 ($\mathrm{C_{aryl}}$), 114.88 ($\mathrm{C_{aryl}}$, 2C), 114.86 ($\mathrm{C_{aryl}}$), 100.0 ($\mathrm{C_{C\equiv C}}$), 83.5 ($\mathrm{C_{C\equiv C}}$), 76.1 ($\mathrm{CH_2}$), 69.5 ($\mathrm{CH_2}$), 65.81 ($\mathrm{CH_2}$), 65.79 ($\mathrm{CH_2}$), 31.9 ($\mathrm{CH_2}$), 29.6 ($\mathrm{CH_2}$), 29.4 ($\mathrm{CH_2}$), 29.3 ($\mathrm{CH_2}$), 28.8 ($\mathrm{CH_2}$), 26.1 ($\mathrm{CH_2}$), 22.7 ($\mathrm{CH_2}$), 14.1 ($\mathrm{CH_3}$).

MS: (MALDI-TOF): *m/z* (%) = 1180.7 [$\mathrm{M^+}$] (83), 1179.7 (100).

Bisazodibromide 151



A solution of compound **91** (211 mg, 0.55 mmol, 1.00 equiv) and compound **150** (570 g, 1.21 mmol, 2.20 eq) in acetic acid (15 mL) was stirred for 19 h at room temperature. The solvent was removed under reduced pressure and the red residue was purified by flash column chromatography on silica gel (hexane/DCM 4:1) to yield **151** as a red oil, which crystallized upon standing at room temperature (450 mg, 63%).

MP: 149 – 152 °C

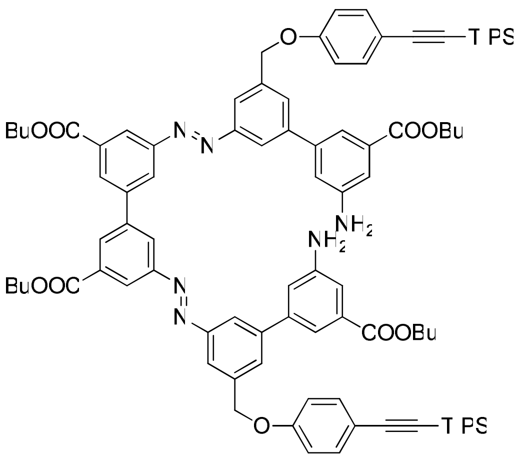
IR: (υ/$\mathrm{cm^{-1}}$): 2939, 2862, 2152, 1720, 1504, 1458, 1234, 1173, 995, 879, 663.

^{1}H-NMR: (400 MHz, $\mathrm{CDCl_3}$, δ/ppm): 8.62 (t, $^3J_{\mathrm{HH}}$=1.6, 1H, $\mathrm{H_{aryl}}$), 8.53 (t, $^3J_{\mathrm{HH}}$=1.6, 1H, $\mathrm{H_{aryl}}$), 8.44 (t, $^3J_{\mathrm{HH}}$=1.6 Hz, 1H, $\mathrm{H_{aryl}}$), 8.10 (t, $^3J_{\mathrm{HH}}$=1.6, 1H, $\mathrm{H_{aryl}}$), 8.03 (t, $^3J_{\mathrm{HH}}$=1.6, 1H, $\mathrm{H_{aryl}}$), 7.74 (t, $^3J_{\mathrm{HH}}$=1.6, 1H, $\mathrm{H_{aryl}}$), 7.44 (d, $^3J_{\mathrm{HH}}$=8.8 Hz, 2H, $\mathrm{H_{aryl}}$), 6.93 (d, $^3J_{\mathrm{HH}}$=8.8 Hz, 2H, $\mathrm{H_{aryl}}$), 5.17 (s, 2H, $\mathrm{CH_2}$), 4.46 (t, $^3J_{\mathrm{HH}}$=6.5 Hz, 2H, CH_2), 1.85 (quintet, $^3J_{HH}$=6.5 Hz, 2H, CH_2), 1.56 (s, 6H, CH_3), 1.12 (s, 21H, $CH(CH_3)_2$).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 165.7 (C=O), 158.2 (C_{aryl}), 153.3 (C_{aryl}), 152.8 (C_{aryl}), 140.7 (C_{aryl}), 140.0 (C_{aryl}), 133.7 (C_{aryl}, 2C), 132.67 (C_{aryl}), 132.65 (C_{aryl}), 130.8 (C_{aryl}), 125.2 (C_{aryl}), 124.6 (C_{aryl}), 124.1 (C_{aryl}), 123.5 (C_{aryl}), 121.8 (C_{aryl}), 116.6 (C_{aryl}), 114.7 (C_{aryl}, 2C), 106.8 ($C_{C\equiv C}$), 89.0 ($C_{C\equiv C}$), 68.7 (CH_2), 65.6 (CH_2), 30.8 (CH_2), 19.3 (CH_2), 18.7 (CH_3), 13.8 (CH), 11.4 (CH_3).

MS: (MALDI-TOF): *m/z* (%) = 1292.5 [M^+] (100), 1293.4 (72).

Bisazodiamine 152



A three-necked flask was charged with boronic ester **91** (217 mg, 0.68 mmol, 2.20 eq), bisazodibromide **151** (400 mg, 0.31 mmol, 1.00 eq), THF (20 ml) and aqueous K_2CO_3 (2 M, 23 mL). The solution was flushed with argon for 20 min. [$Pd(PPh_3)_4$] (34 mg, 0.10 mmol, 9.5 mol%) was added to the reaction mixture, which was degassed with an argon stream for 20 min and stirred at 80°C over the weekend. The reaction mixture was allowed to cool down and the organic layer was separated and washed with brine (5 mL). After drying over $MgSO_4$ and removal of the solvent under reduced pressure, the residue was purified by column chromatography on silica gel (hexane/EtOAc 5:2) to yield **7** as a red oil (250 mg, 53%).

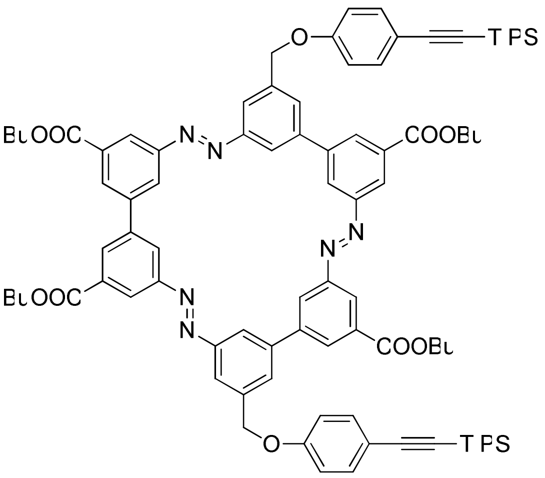
IR: (υ/cm^{-1}): 3371, 2939, 2862, 2152 1713, 1605, 1458, 1227, 1173, 764, 671.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.65 (s, 1H, H_{aryl}), 8.54 (s, 1H, H_{aryl}), 8.49 (s, 1H, H_{aryl}), 8.20 (s, 1H, H_{aryl}), 8.07 (s, 1H, H_{aryl}), 7.78 (s, 1H, H_{aryl}), 7.75 (s, 1H, H_{aryl}), 7.44 (d, $^3J_{HH}$=8.8 Hz, 2H, H_{aryl}), 7.39(s, 1H, H_{aryl}), 7.18 (s, 1H, H_{aryl}), 6.96 (d, $^3J_{HH}$=8.8 Hz, 2H, H_{aryl}), 5.25 (s, 2H, CH_2), 4.45 (t, $^3J_{HH}$=6.5 Hz, 2H, CH_2), 4.34 (t, $^3J_{HH}$=6.5 Hz, 2H, CH_2), 3.93 (s, 2H, CH_2), 1.90-1.70 (m, 4H, CH_2), 1.58-1.43 (s, 12H, CH_3), 1.11 (s, 21H, $CH(CH_3)_2$).

^{13}C-NMR: (101 MHz, $CDCl_3$), δ/ppm): 166.7 (COO), 165.9 (COO), 158.5 (C_{aryl}), 153.1 (C_{aryl}), 153.0 (C_{aryl}), 147.0 (C_{aryl}), 142.1 (C_{aryl}), 141.3 (C_{aryl}), 140.9 (C_{aryl}), 138.6 (C_{aryl}), 133.6 (C_{aryl}, 2C), 132.6 (C_{aryl}), 132.2 (C_{aryl}), 130.5 (C_{aryl}), 128.9 (C_{aryl}), 125.3 (C_{aryl}), 123.9 (C_{aryl}), 121.7 (C_{aryl}), 121.0 (C_{aryl}), 118.7 (C_{aryl}), 117.9 (C_{aryl}), 116.4 (C_{aryl}), 115.3 (C_{aryl}), 114.8 (C_{aryl}, 2C), 106.9 ($C_{C\equiv C}$), 89.0 ($C_{C\equiv C}$), 75.1 (CH_2), 69.5 (CH_2), 65.6 (CH_2), 65.0 (CH_2), 30.8 (CH_2), 24.9 (CH_2), 19.3 (CH_2), 18.7 (CH_3), 13.8 (CH_3), 11.4 (CH_3).

MS: (MALDI-TOF): *m/z* (%) = 1516.6 [M^+] (61), 1517.5 [M^++1] (89), 1518.5 (100).

Macrocycle 153



A suspension of $Pb(OAc)_4$ (0.50 g, 1.14 mmol, 6.90 equiv) in THF (25 mL) was added dropwise to a solution of bisazodiamine **152** (243 mg, 0.16 mmol, 1.00 equiv) in THF (15 mL) and triethylamine (0.22 mL, 1.59 mmol, 10.0 equiv) over 20 min. After stirring for an additional 3 h, ethylenediaminetetraacetatic acid (0.47 g, 1.59 mmol, 10.0 equiv) and water/CH_2Cl_2 (1:1, 20 mL) was added. After the mixture had been stirred for 20 min, the organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (4 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by column chromatography (toluene) to yield **153** as an orange-red oil (150 mg, 62%).

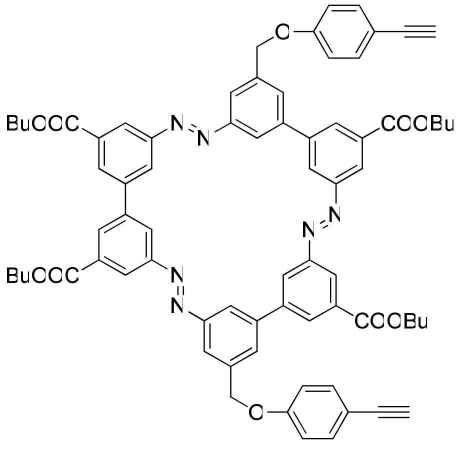
IR: (υ/cm^{-1}): 2939, 2862, 2152, 1720, 1605, 1504, 1458, 1242, 879, 794, 733, 671.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.83-8.78 (s, 2H, H_{aryl}), 8.68-8.60 (s, 5H, H_{aryl}), 8.12 (s, 1H, H_{aryl}) 8.08 (s, 1H, H_{aryl}), 7.48 (d, $^3J_{HH}$=8.8 Hz, 2H, H_{aryl}), 7.02 (d, $^3J_{HH}$=8.8 Hz, 2H, H_{aryl}), 5.28 (s, 2H, CH_2), 4.46 (t, $^3J_{HH}$=6.5 Hz, 4H, H_{aryl}), 1.92-1.80 (m, 4H, CH_2), 1.63-1.50 (s, 12H, CH_3), 1.13 (s, 21H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$), δ/ppm): 166.6 (C=O), 165.5 (C=O), 158.5 (C_{aryl}), 152.7 (C_{aryl}), 152.5 (C_{aryl}), 152.4 (C_{aryl}), 139.0 (C_{aryl}), 138.8 (C_{aryl}), 138.6 (C_{aryl}), 138.5 (C_{aryl}), 133.7 (C_{aryl}, 2C), 132.4 (C_{aryl}), 132.2 (C_{aryl}), 129.00 (C_{aryl}), 128.98 (C_{aryl}), 127.0 (C_{aryl}), 125.0 (C_{aryl}), 124.7 (C_{aryl}), 123.4 (C_{aryl}), 123.1 (C_{aryl}), 121.1 (C_{aryl}), 120.8, (C_{aryl}), 116.5 (C_{aryl}), 114.7 (C_{aryl}, 2C), 107.0 ($C_{C\equiv C}$), 89.0 ($C_{C\equiv C}$), 69.2 (CH_2), 65.5 (CH_2), 30.8 (CH_2), 19.4 (CH_2), 18.7 (CH_3), 13.9 (CH_3), 11.4 (CH_3).

MS: (MALDI-TOF): *m/z* (%) = 1512.4 [M$^+$] (71), 1513.4 [M$^+$+1] (100).

Macrocycle 154



Macrocycle **153** (100 mg, 89.8 µmol, 1.00 eq.) was dissolved in THF (5 ml) and cooled to 0 °C. Then, a 1M solution of TBAF in THF (216 µl, 216 µmol, 2.40 eq.) was added dropwise, and the mixture was stirred for 19 hours at rt. The reaction was quenched by the addition of 25 ml of sat. aq. $NaHCO_3$. The orange precipitate was collected by filtration and washed with water and hexane. After drying under high vacuum, 71 mg of an orange solid was obtained (99 %).

MP: > 245 °C

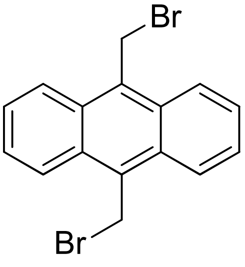
IR: (υ/cm^{-1}): 3255, 2932, 2870, 1720, 1605, 1234, 1373, 1165.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.73 (s, 2H, H_{aryl}), 8.72 (s, 2H, H_{aryl}), 8.60 (s, 2H, H_{aryl}), 8.57-8.54 (m, 3H, H_{aryl}), 8.53 (s, 2H, H_{aryl}) 8.03 (s, 2H, H_{aryl}), 8.01 (s, 2H, H_{aryl}), 7.50 (d, $^3J_{HH}$=8.8 Hz, 2H, H_{aryl}), 7.03 (d, $^3J_{HH}$=8.8 Hz, 2H, H_{aryl}), 5.24 (s, 2H, CH_2), 4.45 (t, $^3J_{HH}$=6.8 Hz, 4H, H_{aryl}), 3.03 (s, 1H, CCH), 1.92-1.80 (m, 4H, CH_2), 1.64-1.51 (s, 4H, CH_2), 1.06 (t, $^3J_{HH}$=7.4 Hz, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$), δ/ppm): 165.8 (C=O), 165.8 (C=O), 158.8 (C_{aryl}), 153.0 (C_{aryl}), 152.8 (C_{aryl}), 152.7 (C_{aryl}), 139.5 (C_{aryl}), 139.04 (C_{aryl}), 139.01 (C_{aryl}), 138.9 (C_{aryl}), 133.8 (C_{aryl}, 2C), 132.6 (C_{aryl}), 132.5 (C_{aryl}), 129.37 (C_{aryl}), 129.34 (C_{aryl}), 127.5 (C_{aryl}), 125.5 (C_{aryl}), 125.2 (C_{aryl}), 123.5 (C_{aryl}), 123.2 (C_{aryl}), 121.4 (2C, C_{aryl}), 114.9 (C_{aryl}), 114.9 (C_{aryl}, 2C), 83.5 ($C_{C\equiv C}$), 76.1 (CH_2), 69.4 (CH_2), 65.6 (CH_2), 30.8 (CH_2), 19.3 (CH_2), 13.9 (CH_3).

MS: (MALDI-TOF): *m/z* (%) = 1200.6 [M$^+$] (83), 1199.6 (100).

9,10-(Dibromomethyl)anthracene (156)



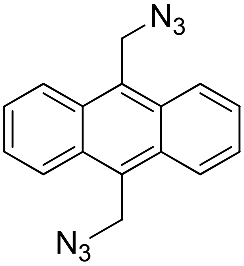
A suspension of anthracene (**155**) (2.00 g, 11.2 mmol, 1.00 eq.), paraformaldehyde (708 mg, 22.4 mmol, 2.00 eq.) and hexadecyltrimethylammonium bromide (45.0 mg, 1 mol%) in acetic acid (2.8 ml) was stirred at room temperature, while hydrobromic acid (47 %, 7 ml) was added dropwise over 1 h. After complete addition, the reaction was stirred at 80 °C for 5 h. Then, it was allowed to cool down. The precipitate was collected by filtration and washed with water. After drying of the crude product, it was recrystallized from hot toluene to yield 1.10 g of an orange solid (28 %).

MP: > 190 °C (decomposition)

^{1}H-NMR: (400 MHz, $(CD_3)_2O$, δ/ppm): 8.55 – 8.52 (m, 4H, H_{aryl}), 7.76 – 7.74 (m, 4H, H_{aryl}), 5.77 (s, 4H, CH_2).

The analytical data corresponded to the literature.[20]

9,10-(Dibromomethyl)anthracene (157)



A solution of 9,10-(Dibromomethyl)anthracene (**156**) (502 mg, 1.38 mmol, 1.00 eq.) in DMF was treated with sodium azide (906 mg, 13.8 mmol, 10.0 eq.) and stirred at 70 °C for three days. Then, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography (silica gel, hexane:EtOAc 15:1) to yield 304 mg of yellow crystals (76 %).

MP: > 150 °C (decomposition)

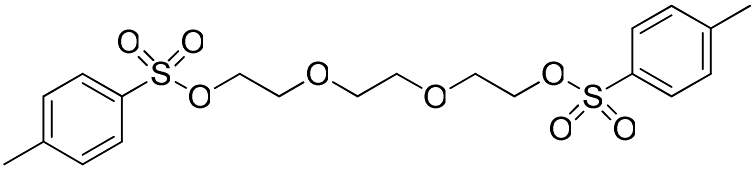
IR: (υ/cm^{-1}): 2923, 2060, 1443, 1234, 864, 810, 748, 694, 617.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 8.40 – 8.35 (m, 4H, H_{aryl}), 7.67 – 7.62 (m, 4H, H_{aryl}), 5.36 (s, 4H, CH_2).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 130.4 (C_{aryl}), 128.2 (C_{aryl}), 126.7 (C_{aryl}), 124.5 (C_{aryl}, 2C), 46.5 (C_{aryl}).

MS: (EI, 70 eV): m/z (%) = 288 (64) [M^+], 218 (100).

Triethyleneglycol ditosylate (160)



A solution of triethylene glycol (**159a**) (4.47 ml, 33.3 mmol, 1.00 eq.) in THF (10 ml) was treated with a solution of sodium hydroxide (3.80 g, 95.0 mmol, 2.85 eq.) in H_2O (12 ml). The mixture was cooled to 0 °C and a solution of *p*-toluenesulfonyl chloride (12.1 g, 63.5 mmol, 1.90 eq.) in THF (12 ml) was added slowly while stirring to keep the temperature under 10 °C. After complete addition the mixture was stirred for four hours at this temperature and the precipitate collected by filtration and washed with Et_2O to yield 12.4 g of a colourless solid (81 %).

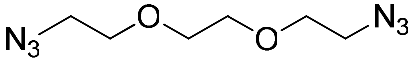
MP: 79 – 81 °C

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.79 (d, $^3J_{HH}$=8.2 Hz, 2H, H_{aryl}), 7.35 (d, $^3J_{HH}$=8.2 Hz, 2H, H_{aryl}), 4.14 (t, $^3J_{HH}$=4.8 Hz, 2H, CH_2), 3.66 (t, $^3J_{HH}$=4.8 Hz, 2H, CH_2), 3.52 (s, 2H, CH_2), 2.44 (s, 3H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 144.9 (C_{aryl}), 133.0 (C_{aryl}), 129.9 (2C, C_{aryl}), 127.9 (2C, C_{aryl}), 70.67 (CH_2), 69.2 (CH_2), 68.7 (CH_2), 21.6 (CH_3).

The analytical data corresponded to the literature.[21]

Triethyleneglycol diazide (162)



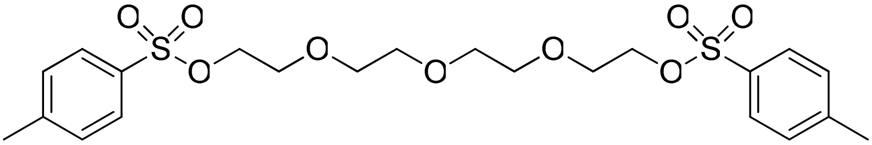
A solution of triethyleneglycol ditosylate (**160**) (1.00 g, 2.18 mmol, 1.00 eq.) in DMF (40 ml) was treated with sodium azide (573 mg, 8.72 mmol, 4.00 eq.) and stirred at 40 °C for 2 days. Then, water (100 ml) was added and the mixture was extracted with TBME (3 * 50 ml). After drying of the ether phases over $MgSO_4$ and removal of the solvent, the residue was purified by column chromatography (silica gel, hexane:EtOAc 5:1 to 2:1) to obtain 356 mg of a colourless oil (82 %).

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 3.72 – 3.66 (m, 2H, CH_2), 3.39 (t, $^3J_{HH}$=5.2 Hz, 1H, CH_2).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 70.7 (CH_2), 70.1 (CH_2), 50.7 (CH_2).

The analytical data corresponded to the literature.[21]

Tetraethyleneglycol ditosylate (161)



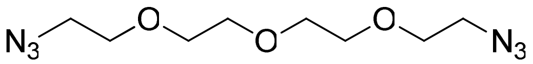
The product was prepared using the same procedure than for triethyleneglycol ditosylate. Tetraethylene glycol (**159b**) (1.79 ml, 10.3 mmol, 1.00 eq.) was treated with NaOH (1.17 g, 29.3 mmol, 2.84 eq.) and toluensulfonyl chloride (5.89 g, 30.9 mmol, 3.00 eq.). Since the product did not precipitate, the mixture was extracted with TBME (3 * 30 ml), dried over $MgSO_4$, concentrated and purified by flash column chromatography (silica gel, hexane:EtOAc 2:1) to yield 1.92 g of a colourless oil (37 %).

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.79 (d, $^3J_{HH}$=8.2 Hz, 2H, H_{aryl}), 7.34 (d, $^3J_{HH}$=8.2 Hz, 2H, H_{aryl}), 4.15 (t, $^3J_{HH}$=4.9 Hz, 2H, CH_2), 3.68 (t, $^3J_{HH}$=4.9 Hz, 2H, CH_2), 3.56 (s, 4H, CH_2), 2.44 (s, 3H, CH_3).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 144.8 (C_{aryl}), 133.0 (C_{aryl}), 129.8 (2C, C_{aryl}), 128.0 (2C, C_{aryl}), 70.7 (CH_2), 70.5 (CH_2), 69.3 (CH_2), 68.7 (CH_2), 21.6 (CH_3).

The analytical data corresponded to the literature.[22]

Triethyleneglycol diazide (163)



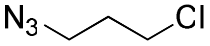
A solution of tetraethyleneglycol ditosylate (**161**) (1.87 g, 3.73 mmol, 1.00 eq.) in DMF (60 ml) was treated with sodium azide (980 mg, 14.9 mmol, 4.00 eq.) and stirred at 40 °C for 2 days. Then, water (100 ml) was added and the mixture was extracted with TBME (3 * 50 ml). After drying of the ether phases over $MgSO_4$ and removal of the solvent, the residue was purified by column chromatography (silica gel, hexane:EtOAc 2:1) to obtain 700 mg of a colourless oil (77 %).

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 3.71 – 3.65 (m, 3H, CH_2), 3.39 (t, $^{3}J_{HH}$=5.2 Hz, 1H, CH_2).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 70.70 (CH_2), 70.69 (CH_2), 70.0 (CH_2), 50.7 (CH_2).

The analytical data corresponded to the literature.[22]

1-Azido-3-chloropropane (166)



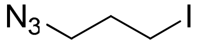
A solution of 1-bromo-3-chloropropane (**165**) (630 µl, 6.35 mmol, 1.00 eq.) in DMF (20 ml) was treated with sodium azide (417 µg, 6.35 mmol, 1.00 eq.) and stirred at rt for 2 h. Then, the mixture was partitioned between Et2O (40 ml) and water (50 ml). The organic phase was washed with water (3 * 50 ml), dried over MgSO4 and the solvent was evaporated at reduced pressure (800 mbar, 40 °C) to yield a colourless oil (803 mg, quant.).

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 3.61 (t, $^3J_{HH}$ = 6.2 Hz, 2H, CH_2), 3.48 (t, $^3J_{HH}$ = 6.4 Hz, 2H, CH_2), 1.99 (p, $^3J_{HH}$ = 6.3 Hz, 2H, CH_2).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 48.3 (CH_2), 41.6 (CH_2), 36.5 (CH_2).

The analytical data corresponded to the literature.[23]

1-Azido-3-iodopropane (167)



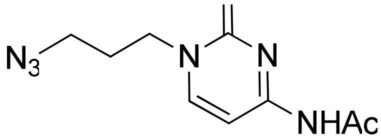
A solution of 1-azido-3-chloropropane (**166**) (803 mg, 6.72 mmol, 1.00 eq.) in acetone (40 ml) was treated with sodium iodide (2.02 g, 13.4 mmol, 2.00 eq.) and stirred at 60 °C for 18 hours. After the solution had cooled down, the mixture was partitioned between EtOAc (100 ml) and water (100 ml). The organic layer was seperated and the aqueous phase was extracted with EtOAc twice (30 ml). Then, the combined organic phases were dried over $MgSO_4$, concentrated under reduced pressure and the residue was purified by flash column chromatography (silica gel, hexane:EtOAc 4:1) to yield 650 mg of a colourless oil (46 %).

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 3.43 (t, $^3J_{HH}$ = 6.4 Hz, 2H, CH_2), 3.25 (t, $^3J_{HH}$ = 6.6 Hz, 2H, CH_2), 2.04 (p, $^3J_{HH}$ = 6.5 Hz, 2H, CH_2).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 49.2 (CH_2), 30.1 (CH_2), 0.0 (CH_2).

The analytical data corresponded to the literature.[23]

N-1-(3-Azidopropyl)-N4-acetylcytosine (172)



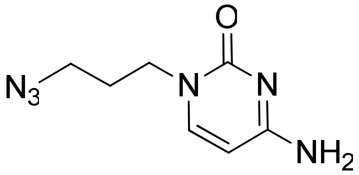
N-4-Acetylcytosine (**171**) (100 mg, 653 µmol, 1.00 eq.) and 1-azido-3-iodopropane (**167**) (207 mg, 980 µmol, 1.50 eq.) was dissolved in DMF (5 ml) and stirred at rt for 16 hours.

Then, the solvent was removed at reduced pressure and the residual oil was subjected to column chromatography (silica gel, DCM:MeOH 20:1 to 10:1) to yield an oil, which was dried under high vacuum to get 53 mg of a colourless solid (34 %).

^{1}H-NMR: (400 MHz, DMSO, δ/ppm): 10.80 (s, 1H, NH), 8.06 (d, $^3J_{HH}$ = 7.2 Hz, 1H, CH), 7.14 (d, $^3J_{HH}$ = 7.2 Hz, 1H, CH), 3.85 (t, $^3J_{HH}$ = 7.0 Hz, 2H, CH_2), 3.39 (t, $^3J_{HH}$ = 6.6 Hz, 2H, CH_2), 2.09 (s, 3H, CH_3), 1.93 - 1.86 (m, 2H, CH_2).

The analytical data corresponded to the literature.[24]

N-1-(3-Azidopropyl)-cytosine (173)

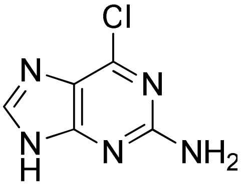


A flask was charged with N-1-(3-azidopropyl)-N4-acetylcytosine (**172**) (45 mg, 190 µmol, 1.00 eq.) was charged with 5 ml of a 1:19 mixture of 27 % aq. NH_4OH and MeOH and stirred at rt for 3 h. After removal of the solvent at reduced pressure, the residue was dried under high vacuum to yield 37 mg of a white solid (100 %).

^{1}H-NMR: (400 MHz, DMSO, δ/ppm): 7.50 (d, $^3J_{HH}$ = 7.2 Hz, 1H, CH), 5.76 (d, $^3J_{HH}$ = 7.2 Hz, 1H, CH), 3.67 (t, $^3J_{HH}$ = 6.9 Hz, 2H, CH_2), 3.27 (t, $^3J_{HH}$ = 6.6 Hz, 2H, CH_2), 1.82 - 1.75 (m, 2H, CH_2).

The analytical data corresponded to the literature.[24]

2-Amino-6-chloropurine (169)



DMF (6.13 ml, 79.2 mmol, 6.00 eq.) and phosphorous oxychloride (3.73 ml, 39.6 mmol, 3.00 eq.) was added to 1,2-dichloroethane (22 ml) and stirred at rt. Then, guanine (**168**) (2.00 g, 13.2 mmol, 1.00 eq.) was added, followed by stirring at 80 °C for 16 hours. The reaction mixture was cooled to 0 °C and water (52 ml) was added. Then, 7.72 g of sodium carbonate was slowly added and the mixture was stirred for additional 30 min. The aqueous layer was seperated and 1.1 g of NaOH was added gradually. The white precipitate was collected, washed with water and dissolved in 26 ml of 12 % aq. AcOH. After stirring at 70 °C for 3 h, the precipitate was collected by filtration, washed with water and dissolved in 50 ml of 10 % aq. NaOH. The mixture was stirred for additional 2 h and neutralized with conc. aq. HCl. The greenish precipitate was collected, washed with water and dried under high vacuum to yield 607 mg (27 %) of the product.

MP: > 245 °C

IR: (υ/cm^{-1}): 3302, 3132, 2785, 1620, 1558, 1366, 1250, 903, 825.

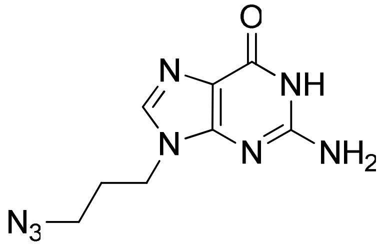
^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 12.93 (bs, 1H, NH), 8.07 (s, 1H, CH), 6.75 (bs, 2H, NH_2).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 159.1 (C_{purine}), 153.9 (C_{purine}), 151.5 (C_{purine}), 142.3 (C_{purine}), 125.4 (C_{purine}), 48.2 (CH_2), 40.1 (CH_2), 28.9 (CH_2).

MS: (ESI): m/z (%) = 170 [M+H^{+}].

The analytical data corresponded to the literature.[25]

N-1-(3-azidopropyl)-guanine (170)



A solution of 2-amino-6-chloropurine (**169**) (100 mg, 590 µmol, 1.00 eq.) and 1-azido-3-iodopropane (**167**) (187 mg, 885 µmol, 1.50 eq.) in DMF (5 ml) was stirred at rt for 16 hours. Then, the solvent was removed at reduced pressure and the residual oil was subjected to column chromatography (silica gel, DCM:MeOH 50:1 to 20:1) to yield an oil, which was dried under high vacuum to get 65 mg colourless crystals (44 %) which were directly used for the next step. ^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 7.76 (s, 1H, CH), 5.15 (bs, 2H, NH_2), 4.20 (t, $^3J_{HH}$ = 6.7 Hz, 2H, CH_2), 3.36 (t, $^3J_{HH}$ = 6.3 Hz, 2H, CH_2), 2.14 - 2.07 (m, 2H, CH_2). A flask was charged with N-1-(3-azidopropyl)-2-amino-6-chloropurine (54.0 mg, 214 µmol, 1.00 eq.) and 2 N aq. HCl. The suspension was stirred at 70 °C for three hours whereas a solution was obtained. Then, the solution was allowed to cool down and neutralized with 27 % aq. NH_4OH. The white precipitate was collected by filtration, washed with water and dried under high vacuum to yield 26 mg of a colourless solid (52 %).

MP: > 220 °C (decomposition

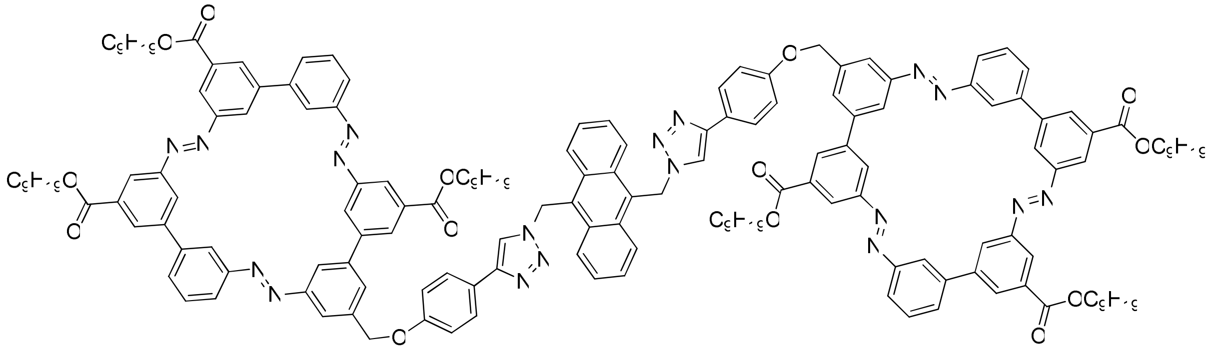
IR: (υ/cm^{-1}): 3205, 2098, 1720, 1628, 1389, 1072, 910, 864, 679, 602.

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm): 10.52 (bs, 1H, NH), 7.69 (bs, 1H, CH), 6.42 (bs, 2H, NH_2), 4.01 (bs, 2H, CH_2), 3.33 (bs, 2H, CH_2), 1.99 (bs, 2H, CH_2).

^{13}C-NMR: (101 MHz, $CDCl_3$, δ/ppm): 156.8 (C_{purine}), 153.5 (C_{purine}), 151.1 (C_{purine}), 137.3 (C_{purine}), 116.6 (C_{purine}), 48.0 (CH_2), 40.2 (CH_2), 28.6 (CH_2).

MS: (ESI): m/z (%) = 235 [M+H$^+$].

Bismacrocycle 176



A flask was charged with macrocycle **149** (50.0 mg, 42.3 µmol, 2.00 eq.), 9,10-(diazidomethyl)anthracene (**157**) (6.10 mg, 21.1 µmol, 1.00 eq.), DBU (16.1 µl, 106 µmol, 5.00 eq.) and toluene (20 ml). The solution was degassed by an argon stream for 15 min and CuI (1.2 mg, 30 mol%) was added under argon backflow. After stirring at 70 °C for 20 hours, the mixture was allowed to coold down. Then, it was washed with 1M aq. HCl (2 * 20 ml) and water (20 ml). The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was dissolved in a small amount of THF and precipitated in cold hexane (150 ml). After standing in the fridge for 5 h, the precipitate was collected by filtration to yield 18 mg of orange flakes (32 %). Another 40 mg (72 %) fraction of lesser purity could be obtained as an orange gel by removing the solvent from the filtrate and drying it under high pressure.

MP: > 245 °C

^{1}H-NMR: (400 MHz, $CDCl_3$, δ/ppm, c ~ 8 mg/ml): 8.74 – 8.66 (m, 6H, H_{aryl}), 8.59 – 8.47 (m, 18H, H_{aryl}), 7.99 – 7.85 (m, 12H, H_{aryl}), 7.73 - 766 (m, 4H, H_{aryl}), 7.65 – 7.52 (m, 8H, H_{aryl}), 7.20 (s, 2H, $H_{triazene}$), 7.00 (d, $^3J_{HH}$ = 8.5 Hz, 4H, H_{aryl}), 6.63 (d, 4H, CH_2), 5.17 (s, 4H, CH_2), 4.48 – 4.32 (m, 12H, CH_2), 1.93 – 1.77 (m, 12H, CH_2), 1.66 – 1.19 (m, 72H, CH_2), 0.93 – 0.81 (m, 18H, CH_3).

MS: (MALDI-TOF): *m/z* (%) = 2650.1 [M^+] (100).

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6. Appendix

6.1 Abbreviations

Å	angstrom	Alox	aluminium oxide
BOC	*tert*-butyloxycarbonyl	BuLi	butyllithium
CD	circular dichroism	CSA	camphersulfonic acid
CTA	cyclotrisazobenzene	CTB	cyclotrisazobiphenyl
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene		
DCC	dicyclohexylcarbodiimide	DCE	dichloroethane
DCM	dichloromethane	DEAD	diethyl azodicarboxylate
DMF	N,N-dimethylformamide	DMAP	4-dimethylaminopyridine
DMSO	dimethylsulfoxide		
DSC	differential scanning calorimetry		
EA	elemental analysis		
EI	electron impact	ESI	electron spray ionisation
Et_3N	triethylamine	EtOAc	ethyl acetate
EtOH	ethanol	eq.	equivalents
eV	electron volts	FAB	fast electron bombardment
FT	fourier transform	GPC	gel permeation chromatography
Hex	hexane		
HPLC	high performance liquid chromatography		
IR	infrared	LAH	lithium aluminium hydride
LiHMDS	lithiumhexamethyldisilazane	*m*	*meta*
MALDI	matrix assisted laser desorption ionisation		
mdeg	millidegree	MOM	methoxymethyl
MP	melting point	m/z	mass to charge ratio
NBS	N-bromosuccinimide	NMR	nuclear magnetic resonance
o	*ortho*	*p*	*para*
PG	protecting group	Ph	phenyl
ppm	parts per million	PSS	photostationary state
TBAB	tetrabutylammonium bromide		
TES	triethyleneglycol	THF	tetrahydrofurane
TsOH	toluenesulfonic acid	rt	room temperature

TBAF	tetrabutylammonium fluoride	TBME	*tert*-butylmethyl ether
TFA	trifluoroacetic acid	TIPS	triisopropylsilyl
trityl	triphenylcarbenium	TLC	thin layer chromatography
TMEDA	tetramethylethylenediamine	UV	ultraviolet
VIS	visible		

6.2 Curriculum Vitae

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2011	R. Reuter, H. A. Wegner, *A Chiral Cyclotrisazobiphenyl Macrocycle as a Ternary Chiroptical Switch*, submitted. R. Reuter, H. A. Wegner, *Oligoazobenzenophanes – Synthesis, photochemistry and properties*, *Chem. Commun.,* accepted.

2010 R. Reuter, H. A. Wegner, *Synthesis and Isomerization Studies of Cyclotrisazobiphenyl*, *Chem. Eur. J.*, 2011, **17**, 2987.

R. Reuter, N. Hostettler, M. Neuburger, H. A. Wegner, *Oligoazobenzenes – Switching in a new Dimension*, *Chimia*, 2010, **64**, No. 3, 180.

2009 Raphael Reuter, Nik Hostettler, Markus Neuburger, Hermann A. Wegner, *Synthesis and Property Studies of Cyclotrisazobenzenes, Eur. J. Org. Chem.,* **2009**, *32*, 5647-5652.

Posters:

2010 *Reversible π-π-stacking in Cyclotrisazobenzenes* at the BASF Summer School in ludwigshafen, Germany and at the 2010 Fall meeting of the Swiss Chemical Society in Zurich, Switzerland.

Switching in 3D – Cyclotrisazobenzenes at the F-pi-9 conference on Functional pi-Electron Systems in Atlanta, Georgia (USA).

2009 *Oligoazobenzenes – Switching in a new Dimension* at the 2009 Fall meeting of the Swiss Chemical Society, Lausanne, Switzerland.

2008 *Cyclotrisazobenzene – Switching in 3D* at the CUSO Summer School in Villars-Sur-Olons.

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2009 Best Poster Prize at the Fall Meeting of the Swiss Chemical Society September 4, 2009

Memberships:

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