3. Literature survey

This chapter focuses on the synthetic strategies used in the construction of shape persistent macrocycles and tries to draw a comprehensive picture of what has been done in this field specifically for the cases which contain heteroatoms in their backbones. It also describes the aggregation behaviour both in the solid and in solution, and, finally, a very short description of relevant Ru and Os complexes of bipyridines is given.

3.1. General aspects of synthetic strategies

A variety of reactions have been used to make the rigid back-bone of macrocycles. The most common reactions are palladium-catalyzed Sonogashira-Hagihara cross coupling between terminal alkynes and aryl halides, Suzuki cross coupling between aryl halides and aryl boronic ester or acids,[3] as well as Hay-Eglinton-Glaser coupling reaction between terminal alkynes.[11] In cycle synthesis the ring closure step is crucial. Synthetic strategies such as the use of high dilution,[12] and template effect,[13] as well as rigid groups effect,[14] have been investigated in order to facilitate this oftenly low yielding step. Strategies that have been used in macrocycles synthesis can be categorized into three major types: a) one-step oligomerization/cyclization; b) cyclization of two precursors; c) intramolecular ring-closure of one bisfunctionalized precursor (Figure 9).[1d]

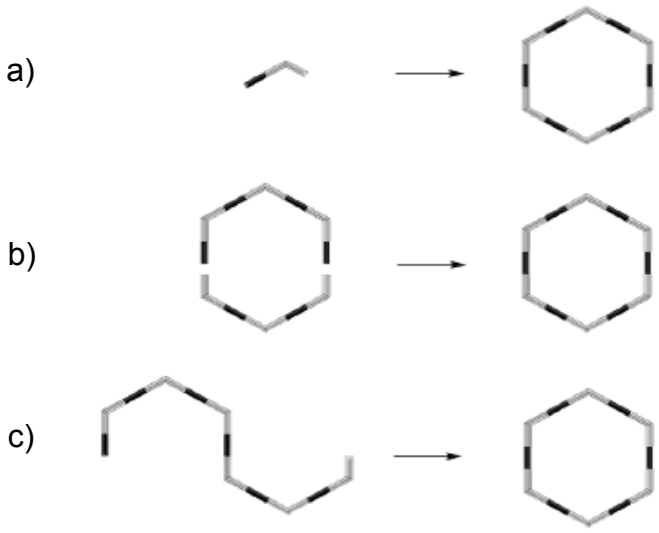
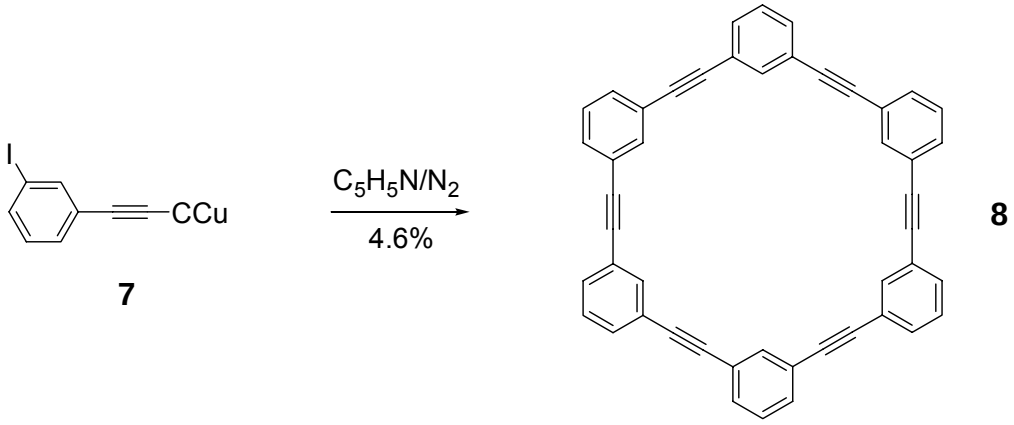


Figure 9. Schematic representation of cyclization strategies: a) one-step oligomerization/cyclization; b) cyclization of two precursors; c) intramolecular ring-closure of one bisfunctionalized precursor.

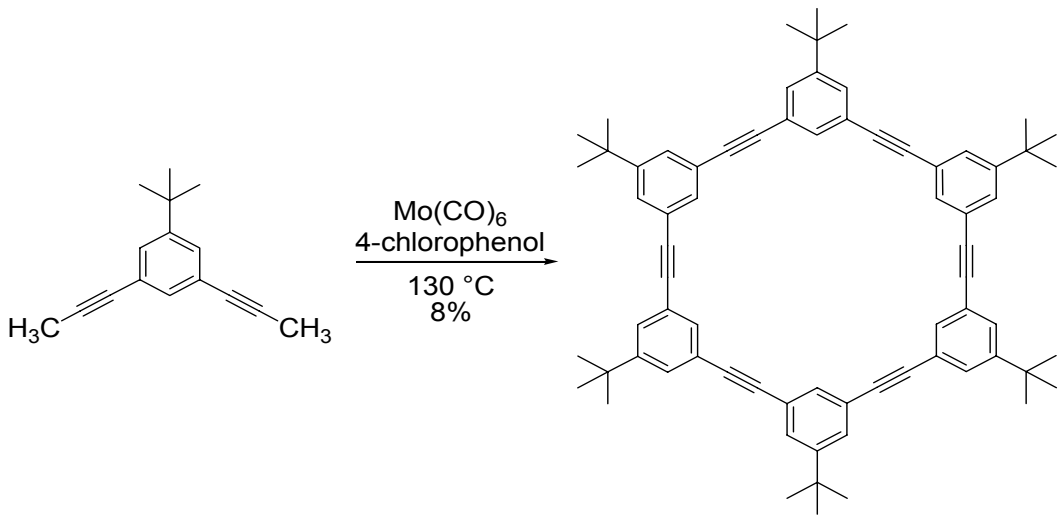
In the following concrete examples for these different approaches are given. In 1974 Staab prepared the hexakis(*m*-phenylene-ethynylene) macrocycle **8** using strategy (a) from m-iodophenyl acetylide **7** (Scheme 3). The cyclization proceeded in low yield because of severe competition by oligomerization/polymerization.[15] Nevertheless this work can be considered one of the foundations of nowadays cycle research.



7 **8**

Scheme 3. Staab's approach towards phenylacetylene macrocycle **8**.

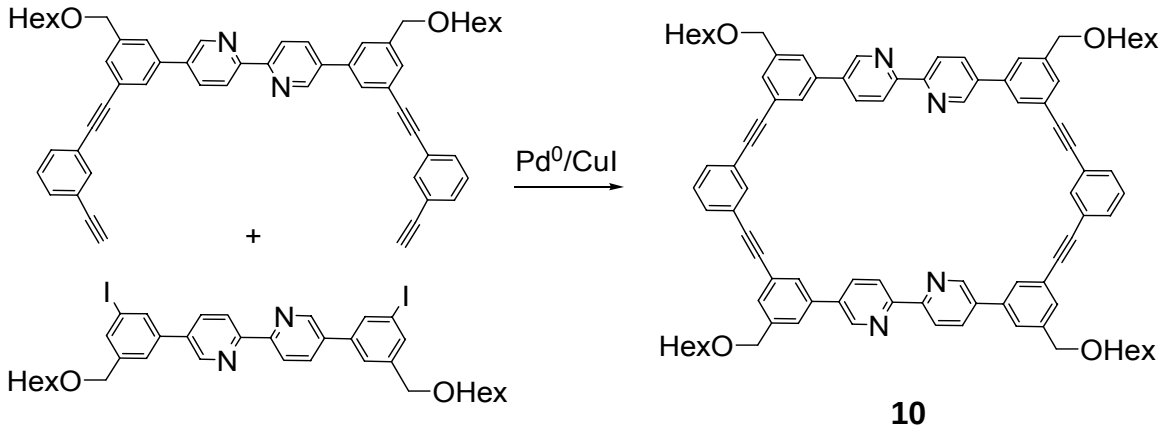
More recently, Bunz applied the same strategy but a different chemistry (alkyne metathesis) in preparing a similar macrocycle **9** (Scheme 4).[16] Also here the yield was disappointingly low. Already two examples show the main problem of strategy (a): oftenly the starting materials are easily accessible but the cycle yields are so low (4.6% and 8% in the case of Staab and Bunz, respectively) that purification of the desired compound from the oligomeric mixture becomes a problem.



9

Scheme 4. Bunz's strategies to phenylacetylene macrocycle **9**.

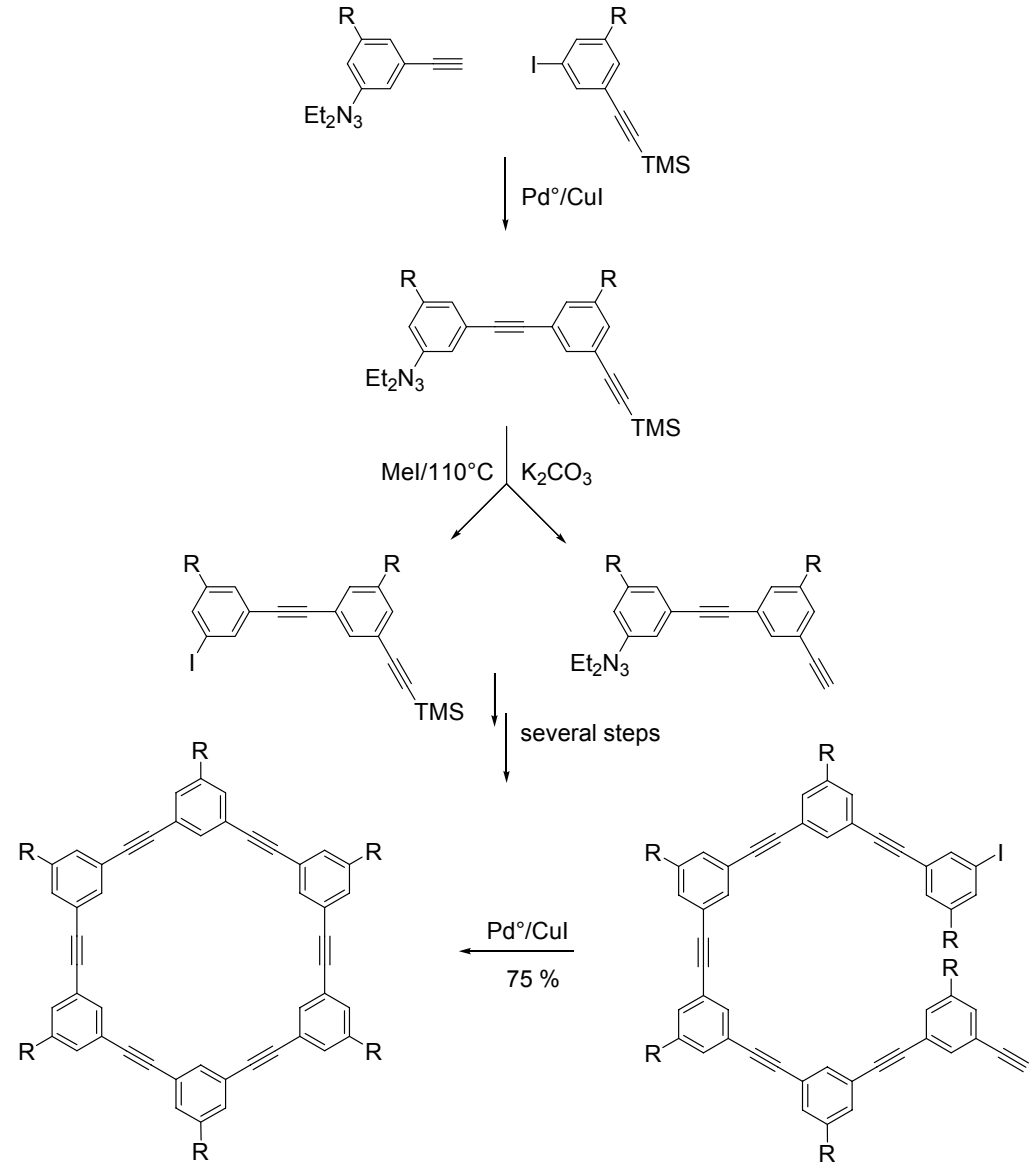
In approach (b) two ring precursors are reacted together in one pot using high dilution conditions. This method still gives relatively low cyclization yields (15-35%), but nevertheless is often used because a lower synthetic effort is required for the construction of ring precursors than in strategy (c). This approach was successfully applied in our group to the construction of bipyridine and terpyridine containing macrocycles. Scheme 5 shows a combination of two bipyridine ring precursors providing macrocycle **10**.[17]



10

Scheme 5. Synthesis of bipyridine macrocycle **10** from two different precursors.

Strategy (c) was used for first time by Moore in the synthesis of self-evident cycle.[18] He prepared cycle **12** by an intramolecular reaction of a bifunctional oligomeric building block which was already the direct precursor for the cycle (Scheme 6). First an iodo-ethynyl precursor **11** was prepared by using a sequence of Sonogashira reactions between aryl-iodide and terminal acetylene, followed by deprotection/protection reactions. The trimethylsilyl group was easily removed under basic conditions, and the N,N-dialkyltriazine group replaced by iodo using methyl iodide. The cyclization was done using Sonogashira-Hagihara reaction and pseudo high dilution conditions to give macrocycle **12** in 75% isolated yield.

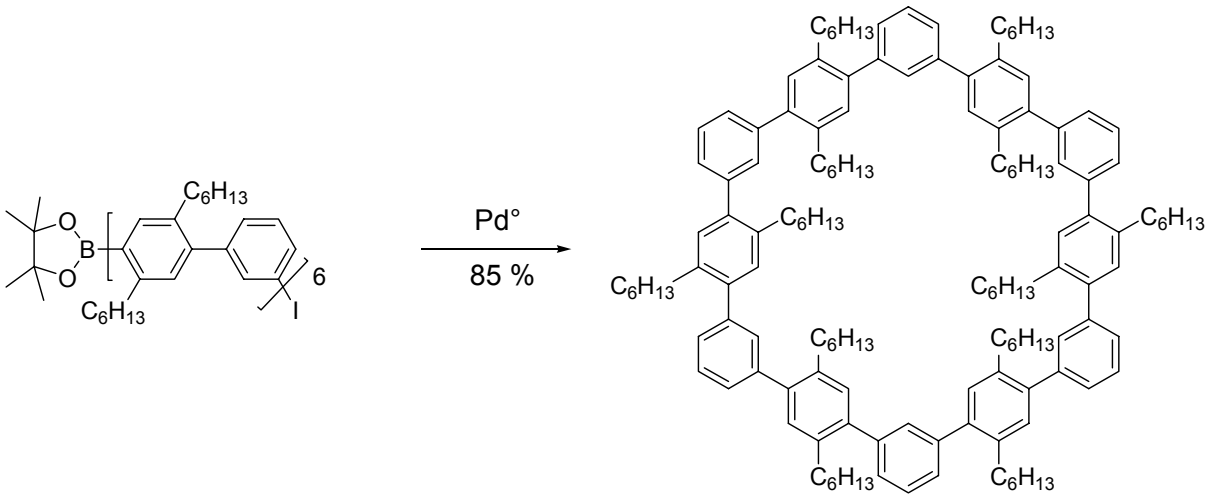


12a: R = H
12b: R = t-Bu

11a: R = H
11b: R = t-Bu

Scheme 6. Moore's repetitive synthesis to phenylacetylene macrocycles **12a** and **12b**.

The same strategy, but a different chemistry (Suzuki cross coupling) was used by Schlüter to construct macrocycle **2** and **13** (Chapter 1, p. 2, Scheme 1 and Scheme 7). Also here the yields were astonishingly high (68-85%) considering the size of the cycle.[4]



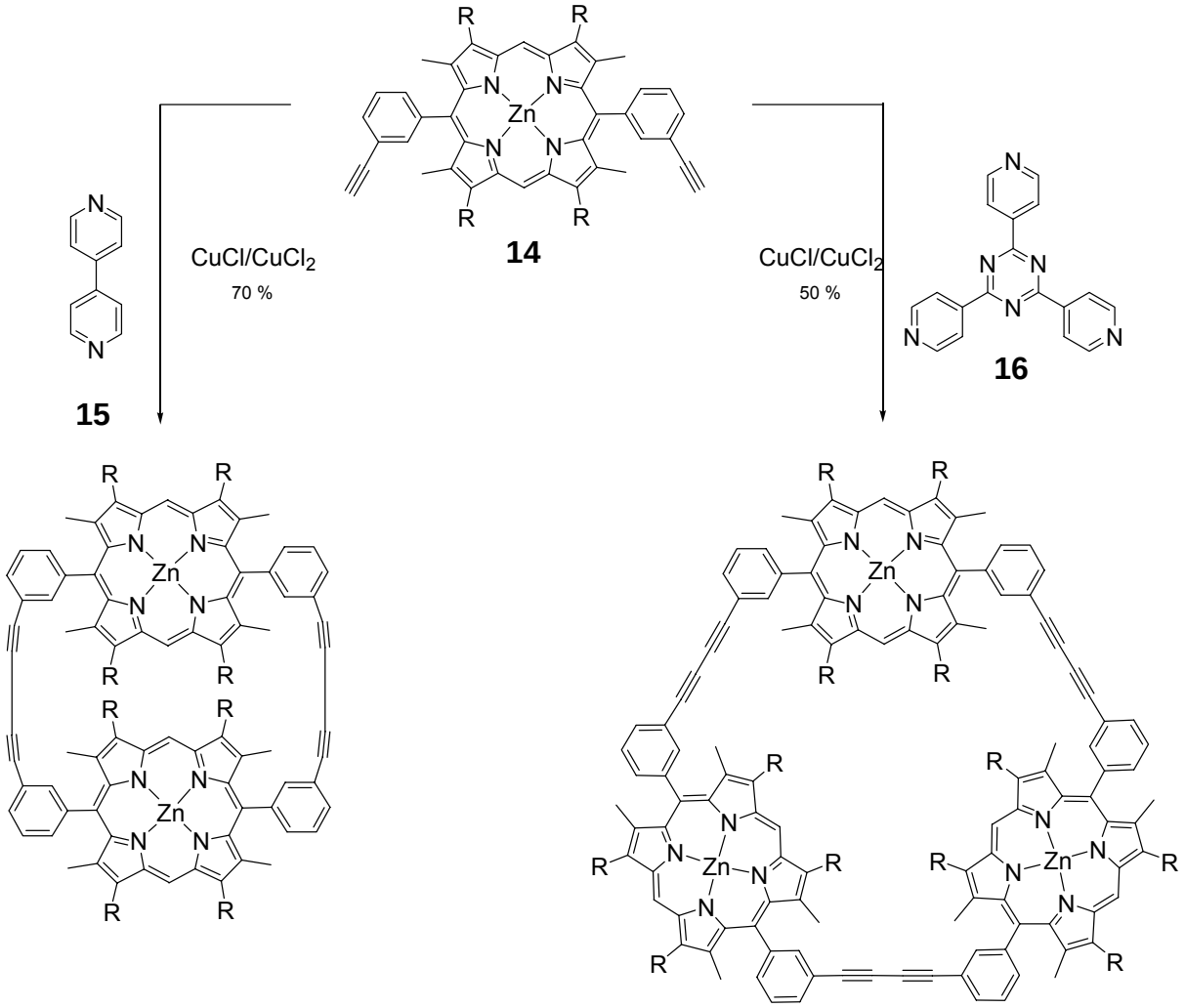
13

Scheme 7. Schlüter's synthesis to phenylenemacrocycle **13**.

An advantage of route (c) is that the stepwise synthesis allows for different functional groups to be introduced at defined positions of the ring precursor. The limitation of this method is to be seen in the time-consuming synthesis of the ring precursor and, thus, the final product, by a large number of repetitive protection, deprotection, and coupling steps.

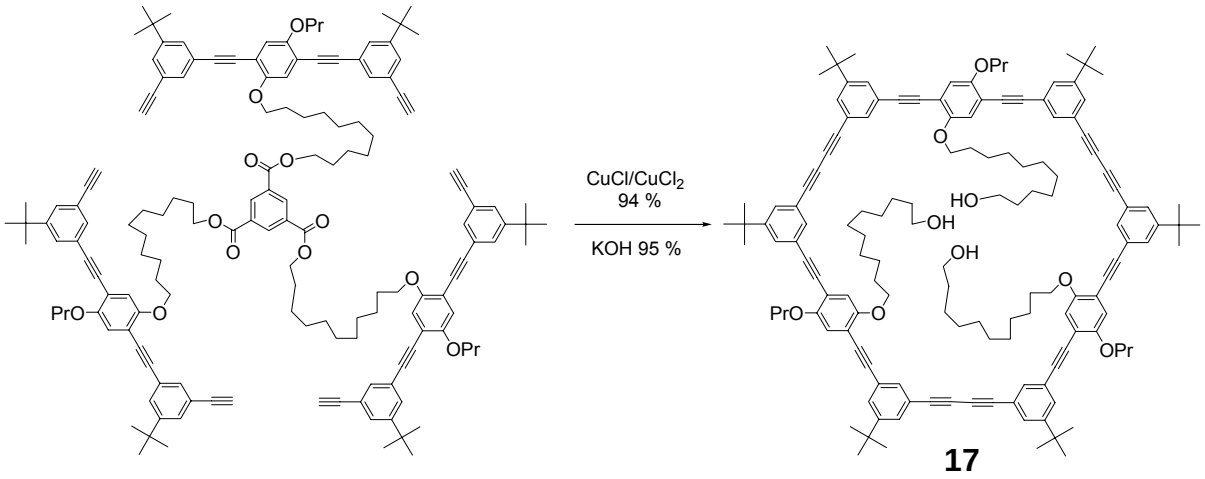
Although the template effects is known and applied in synthesis for quite some time ago, its use in macrocycles synthesis started relatively late. Templation promotes the formation of one component from a reaction that would otherwise result in a complex mixture. This is achieved by an appropriate preorganization of the individual building blocks prior to their connection.

In 1990 Sanders et. al. built porphyrin macrocycles from two or three identical precursors **14** using Glaser coupling conditions (Scheme 8).[19] The cyclization yield was greatly improved by using a template effect. When the 4,4'-bipyridyl **15**, or terpyridyl **16** were used as template, they obtained the cyclic dimer or trimer in 70 and 50% yield, respectively. This was attributed to a preorganization of the bisacetylenes around the template. Though clearly attractive, this method is restricted to metal-containing compounds and cannot be generally applied.



Scheme 8. Sander's cycle synthesis through templation of Zn porphyrins.

Höger et al. developed another interesting variant.[20] They used a covalent linkage of the macrocycle's precursor to the template, pseudo high-dilution, and Glaser coupling reaction conditions to obtain macrocycles **17** in impressive yields of 94% (Scheme 9). The high yields of these cyclizations were explained by a high local concentration of the terminal acetylenes at the template while their overall concentration in the solution is still low.



Scheme 9. Höger's template cyclization (The lasso method).

Solid-phase synthesis has also been used for the construction of macrocycles. Moore developed solid-phase methods to simplify purification of an oligomeric cycle precursor.[21] Toor applied this strategy to macrocycle formation by conducting the cyclization step on a polymer support. However, the desired cycle could not be isolated. The resin was not rigid enough to provide complete isolation of the end groups of ring precursors and interside reactions were observed.[22]

Whatever the nature of the starting material or the method used, the last step is almost invariably connection of the two ends of a ring precursor. This ring precursor can either be the starting material itself (like for route c) or results from the in situ assembly of bifunctional units (like in routes a and b). The fundamental problem in the synthesis of macrocycles is to favour the intramolecular reaction over the intermolecular one which gives linear polycondensation. Since the final ring closure step is first order, its rate is proportional to the precursor concentration. The intermolecular condensation reaction however, is second order and its rate is thus proportional to the square of the concentration. Consequently substrate concentrations favour polymerization and low concentrations cyclization. This is why high and pseudo-high dilution techniques play a crucial role in macrocycle synthesis.[23]

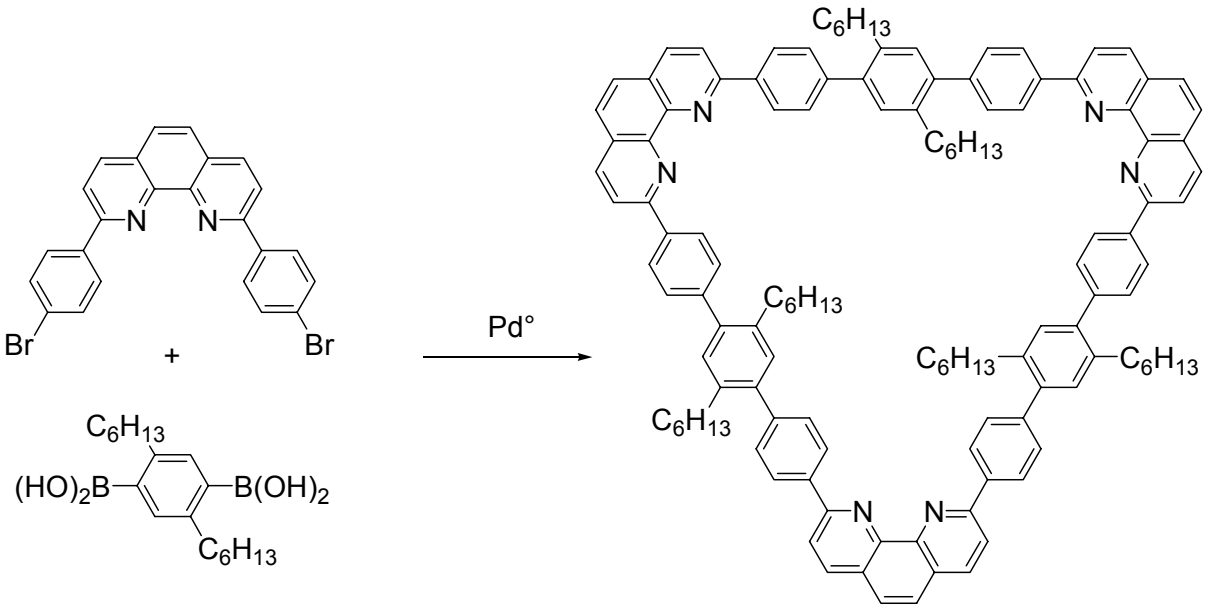
3.2. Relevant cases

The introduction of a heteroatom into macrocycle structures is of particular interest because of emerging potential biological, chemical, physical functions. Approximately half of the cycles reported till now are hydrocarbons, the other half contains heteroatom units such as pyridines, bipyridines, terpyridines, phenanthrolines, porphyrins, pyrroles, or thiophenes. The heteroatom of these macrocycles can have an *endo* or *exo*-cyclic orientation, or, in some cases, can rotate more or less freely between these two rotameric states. The introduction of heteroatoms into macrocycles makes their synthesis more difficult. Stepwise synthesis of one ring precursor leading to a sole cycle is time consuming and in some cases synthetically difficult to achieved, therefore is not feasible here. However, there are few cases where the cycles are closed from one precursor.[31] Normally, they are prepared from two half rings (Route b, Chapter 3.1., p. 10), when the macrocycle is formed in lower yields, but a less synthetic effort is invested in the synthesis of ring precursors. The precursors are reacted together under high or pseudo-high dilution conditions. Four cyclization reactions were most oftenly used: a) Suzuki-cross coupling, b) Sonogashira-Hagihara cross-coupling, c) oxidative alkynyl-alkynyl coupling, and d) acetylene coupling by “zirconocene coupling”.

In the following concrete examples are given:

a) By Suzuki cross coupling reaction:

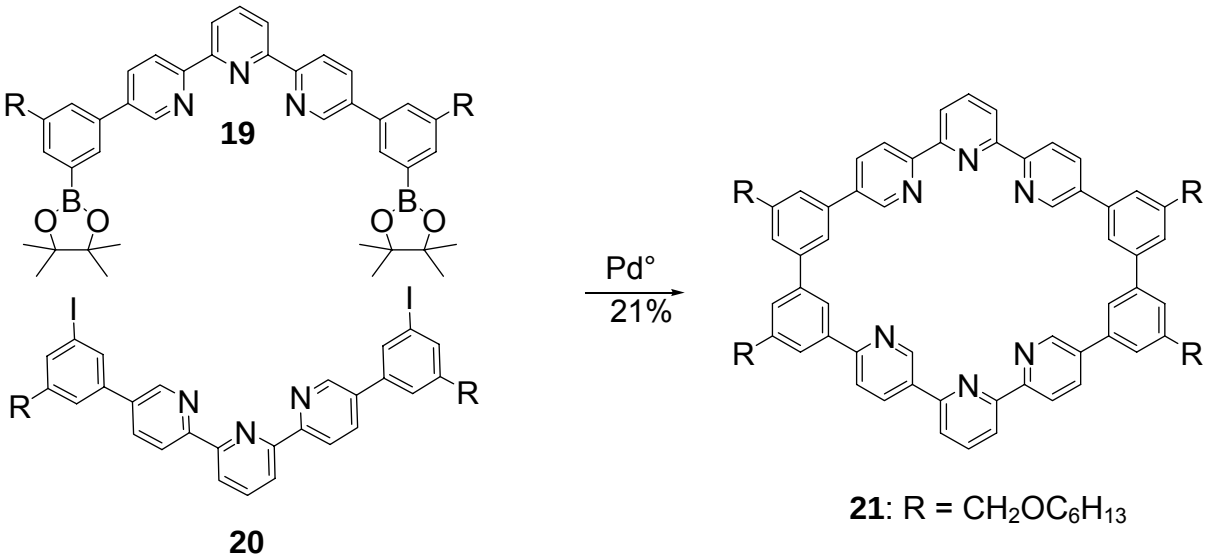
Rehahn obtained macrocycle **18** as a side product in a Suzuki polycondensation reaction (Scheme 10). It was shown that neither smaller oligomers were formed nor larger rings. This selectivity for the cyclization was explained by the fixed angles of the 2,9-substituted phenanthroline.[24]



18

Scheme 10. Synthesis of phenanthroline macrocycle **18** by Rehahn.

In our group, Lehmann prepared macrocycle **21** from the bisboronic acid ester **19** and its diiodo counterpart **20** in 20% yields on the130 mg scale (Scheme 11).[25] Attempts to make this cycle under Stille conditions with the corresponding stannyl-functionalized analogue of **19** were unsuccesfull.



19

20

21: R = $CH_2OC_6H_{13}$

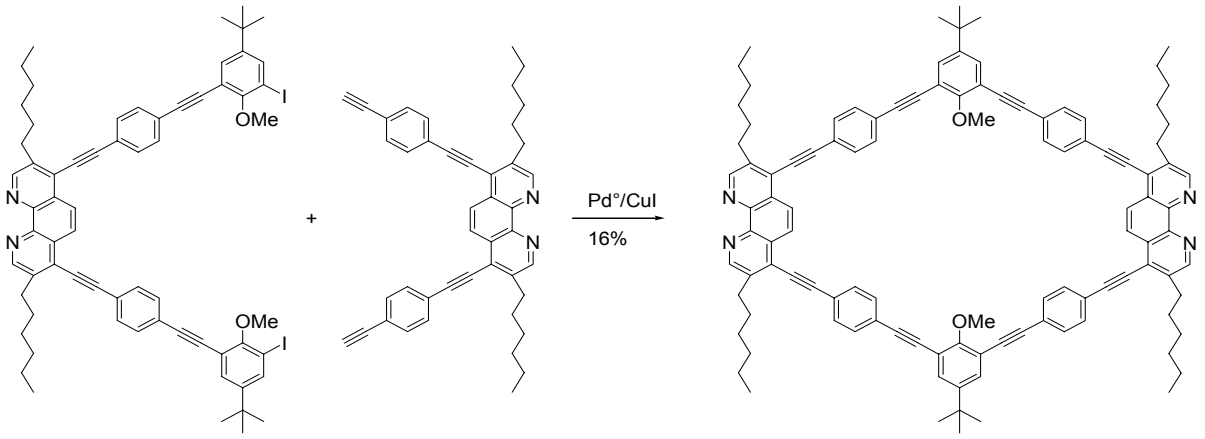
Scheme 11. Terpyridine macrocycle **21** by Lehmann.

Suzuki cross-coupling was not much used for ring closure reactions. This may be due to the difficulty of preparing one of the ring precursors, the bisboronic ester.

b) By Sonogashira-Hagihara reaction:

In contrast to the above, a large variety of heteromacrocycles were prepared using this reaction.[1c] Two different building blocks are required; one of which has two (typically) iodo functional groups and the other the terminal acetylenes.

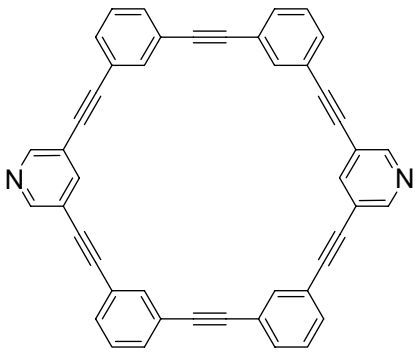
Schmittel obtained the rigid bisphenanthroline macrocycle **24** with exotopic phenanthroline sites, starting from precursor **22** and **23** in 16% yield (Scheme 12).[26] He uses the macrocycle for the construction of molecular boxes.



22 **23** **24**

Scheme 12. Macrocycle **24** with phenantroline units by Schmittel.

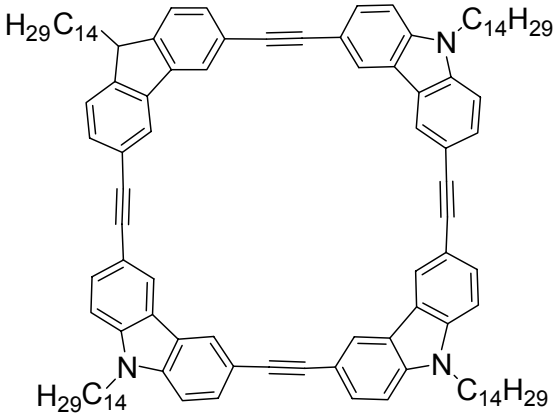
Lees synthesized a pyridine containing macrocycle **25** (Figure 10). The cyclization reaction was done from two precursors and gave macrocycle **25** in 54%. He also prepared the Re complex which shows strong emission at room temperature in solutions.[27]



25

Figure 10. Pyridine containing macrocycle **25** by Lees.

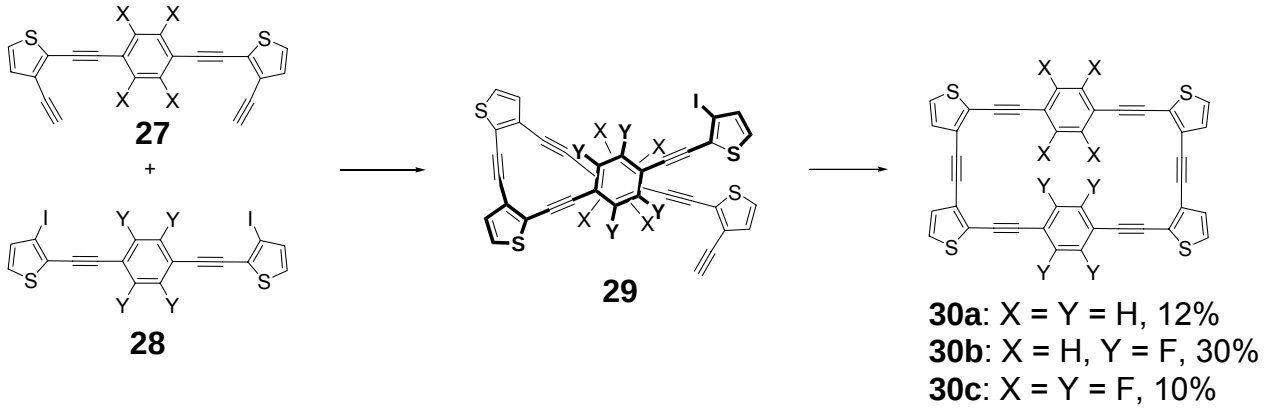
Maruyama prepared the carbazolylacetylene macrocycle **26** in 14% yield (Figure 11). From this reaction, the cyclic octamer was also isolated in 5.4% yield.[28]



26

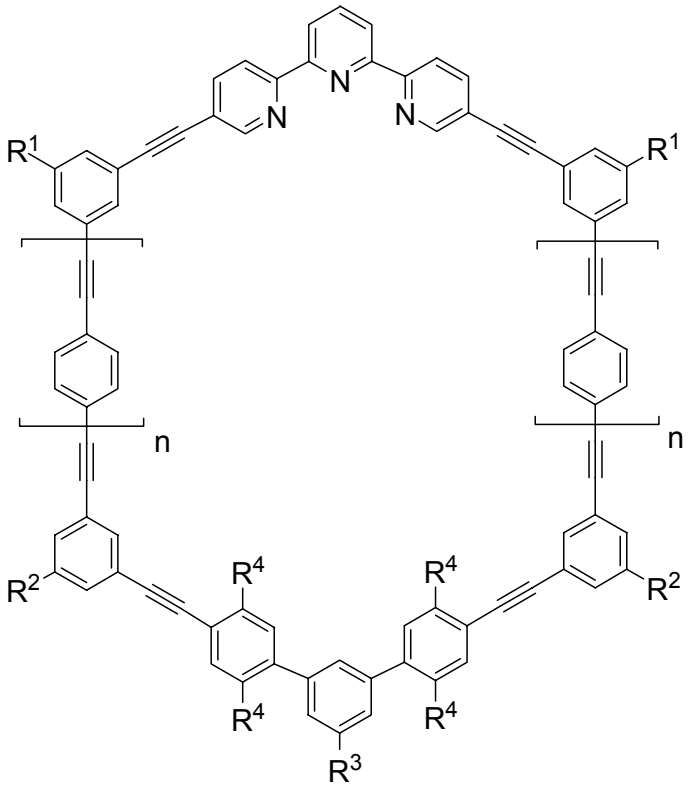
Figure 11. Macrocycle **26** by Maruyama.

Marsella synthesized the thiophene containing macrocycles **30a**-**30c** using the precursors **27** and **28** (Scheme 13).[29] The electrostatic interactions between Ar_H-Ar_F were used as a template-directed synthesis in solution. The macrocyclization involved a linear intermediate **29** which the authors believe to play a decisive role in macrocycle formation by acting both substrate and template. As expected, the macrocycle **30** (X = H, Y = F), where the template can form, is obtained in highest yield (30% versus 12% and 10% for **30b**, **30a** and **30c**, respectively). The quantity of the precursors with which the cyclization experiments were done and also the quantity of isolated macrocycles are not mentioned. Also it was not reported how reproducible these yields are.

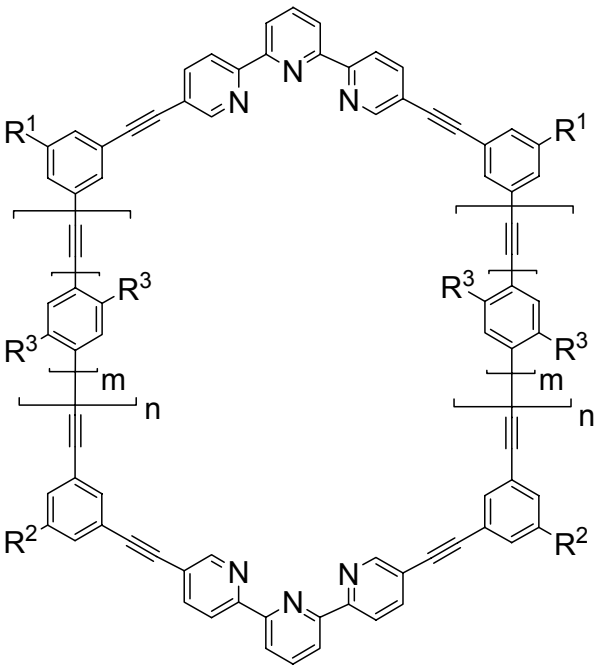


Scheme 13. Thiophene derived macrocycles by Marsella.

Grave prepared the macrocycles **31a**-**31c** and **32a**-**32d** containing one and two terpyridine units.[30] They varied in size and substituent pattern (Figure 12). He investigated the solubility of these macrocycles in chloroform and concluded that it depends on the number and nature of the side chains, number of terpyridine units, and the ring size. He also studied the packing behavior in single crystals.



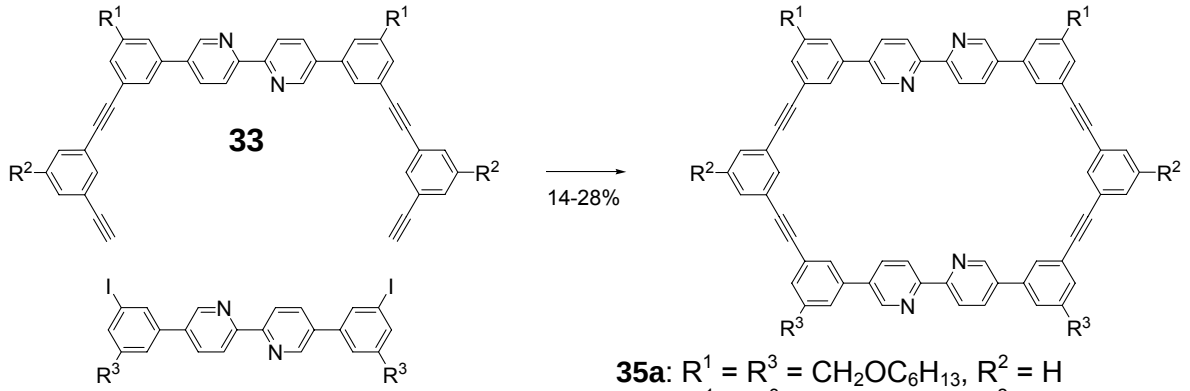
31a: n = 0, $R^1 = R^2 = R^3 = OC_6H_{13}$, $R^4 = H$
31b: n = 0, $R^1 = R^2 = OC_6H_{13}$, $R^3 = H$, $R^4 = C_6H_{13}$
31c: n = 0, $R^1 = R^2 = CH_2OC_6H_{13}$, $R^3 = OC_6H_{13}$, $R^4 = H$
31d: n = 0, $R^1 = CH_2OC_6H_{13}$, $R^2 = CH_2OTHP$, $R^3 = OC_6H_{13}$, $R^4 = H$
31e: n = 1, $R^1 = R^2 = CH_2OC_6H_{13}$, $R^3 = OC_6H_{13}$, $R^4 = H$



32a: n = m = 0, $R^1 = R^2 = CH_2OC_6H_{13}$
32b: n = m = 1, $R^1 = R^2 = CH_2OC_6H_{13}$, $R^3 = H$
32c: n = m = 1, $R^1 = CH_2OC_6H_{13}$, $R^2 = CH_2OTHP$, $R^3 = H$
32d: n = m = 1, $R^1 = R^2 = CH_2OC_6H_{13}$, $R^3 = C_6H_{13}$

Figure 12. Terpyridine containing macrocycles by Grave.

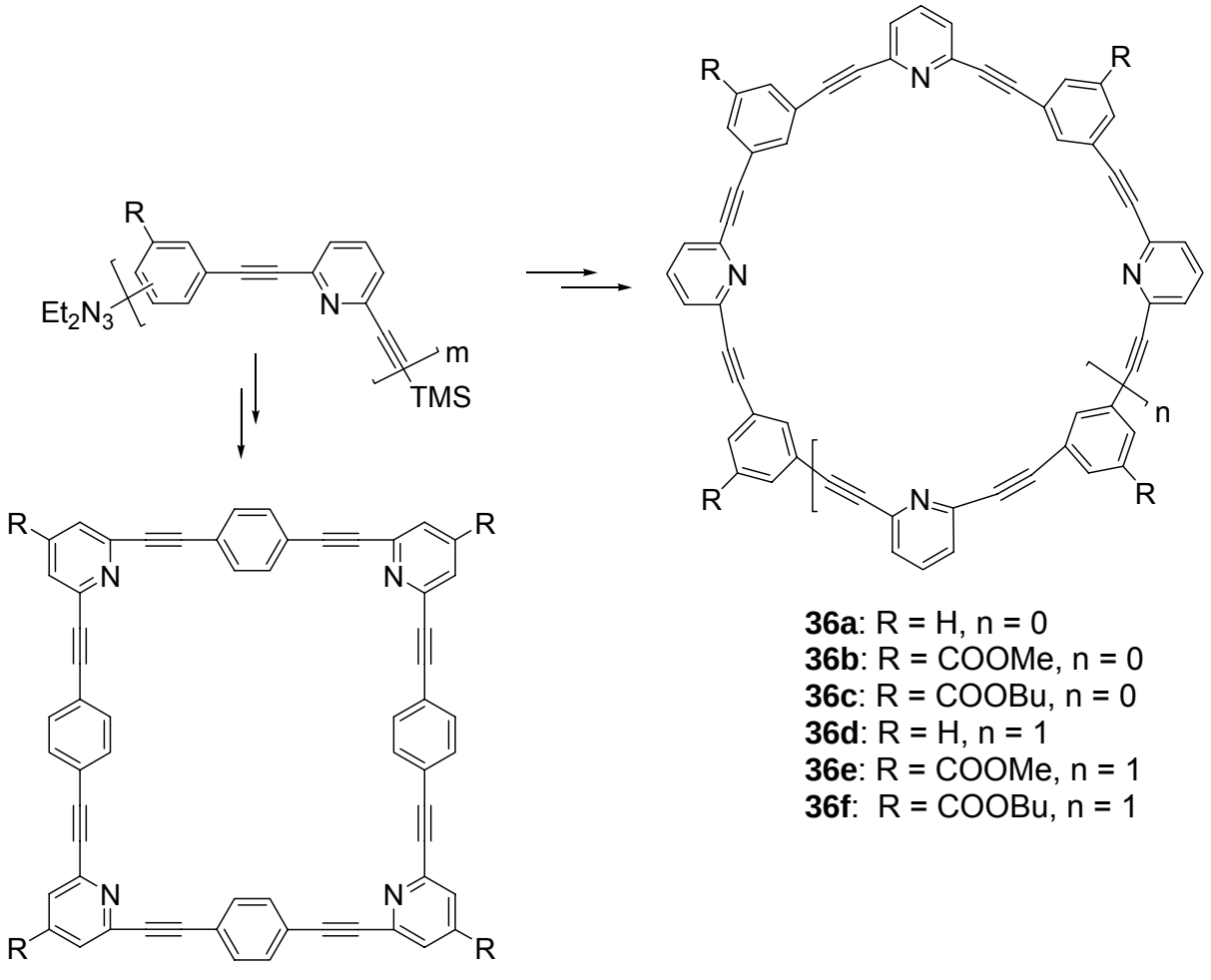
A set of phenylacetylene macrocycles **35** containing two bipyridine units in opposite sides were obtained by Henze from two different precursors **33** and **34** (Scheme 14).[17] He also studied the complexation of such macrocycle with Ru.[17b]



35a: $R^1 = R^3 = CH_2OC_6H_{13}$, $R^2 = H$
35b: $R^1 = R^3 = CH_2OMOM$, $R^2 = CH_2OC_6H_{13}$
35c: $R^1 = R^3 = CH_2OTHP$, $R^2 = CH_2OC_6H_{13}$
35d: $R^1 = CH_2OTHP$, $R^2 = R^3 = CH_2OC_6H_{13}$

Scheme 14. Bipyridine containing macrocycles by Henze.

The shape-persistent azamacrocycles **36a**-**f** and **37** prepared by Yoshiba contain alternately arranged pyridine and benzene rings in a *meta* or *para*-bonding fashion (Scheme 15).[31] They differ in ring sizes and were prepared by an effective method in which the Sonogashira reaction is repeatedly used as coupling reaction. Macrocycles **36a**-**c** give a specific recognition for Sn (V) ion, and macrocycle **37e** can include two molecules of [Cu(hfac)$_2$] (hfac = 1,1,1,5,5,5-hexafluoro-2,4-pentanedione). Unfortunately, the authors did not mention the amounts and the yields in which the macrocycles were obtained.

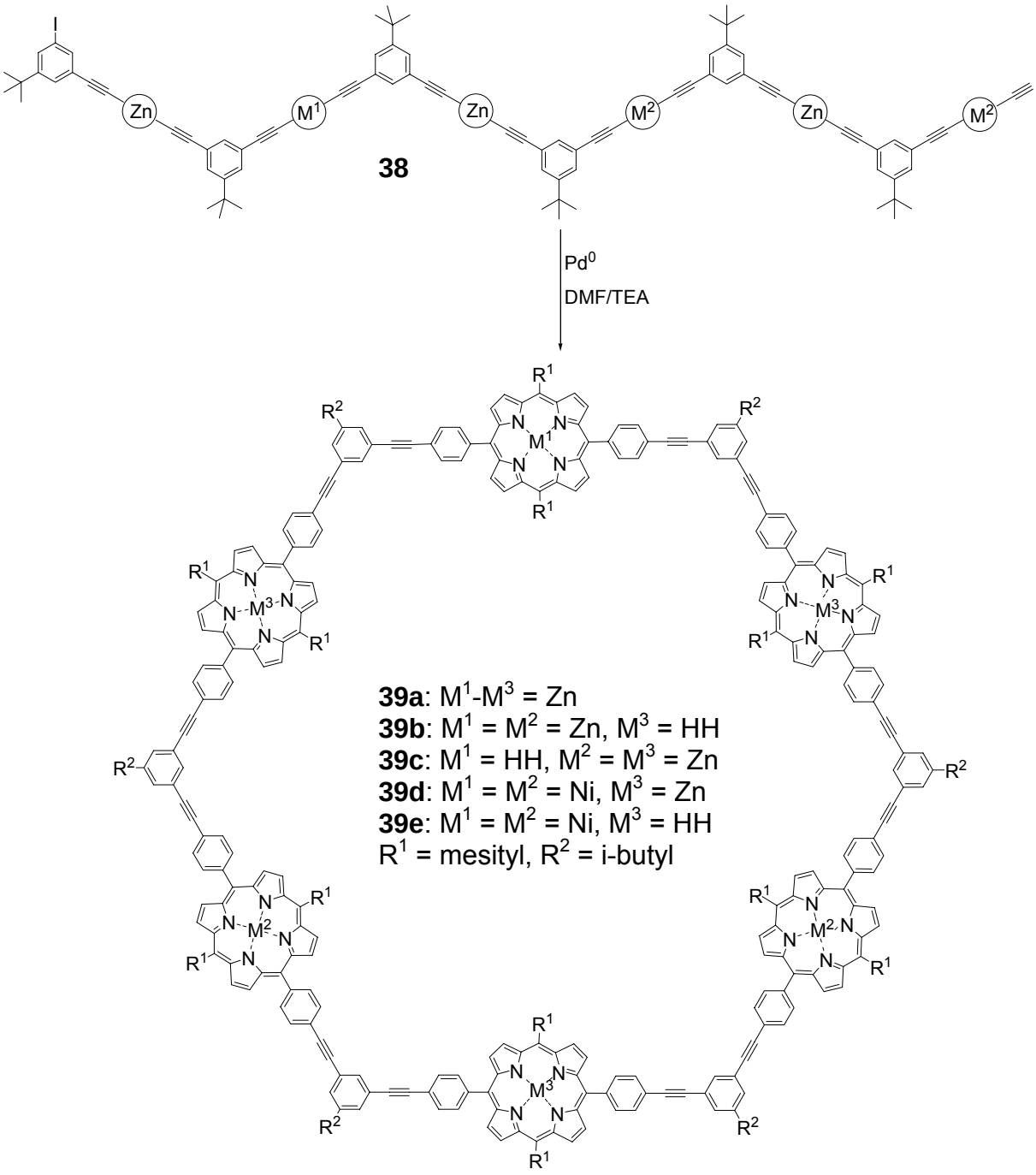


36a: R = H, n = 0
36b: R = COOMe, n = 0
36c: R = COOBu, n = 0
36d: R = H, n = 1
36e: R = COOMe, n = 1
36f: R = COOBu, n = 1

37a: R = H
37b: R = COOMe

Scheme 15. Macrocycles with pyridine moieties by Yoshida.

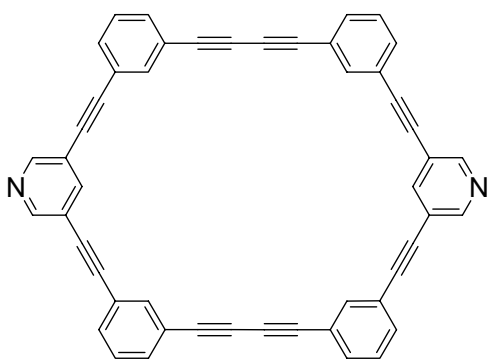
Gossauer reported the synthesis of the large macrocyclic porphyrin hexamers **39** (Scheme 16) with a diameter of 4.6 nm, the largest rigid macrocycles, which have been synthesised so far.[32] A multi-step synthesis led to the precursors **38** which was then subjected to cyclization according to strategy (c).



Scheme 16. Porphyrin containing macrocycles by Gossauer.

c) By oxidative acetylene-acetylene coupling

Cycles **40** and **41** with exotopic pyridine sites (Figure 13) were prepared by Lees and Tykwinski, respectively, by an oxidative acetylene coupling of two identical precursors.[33]



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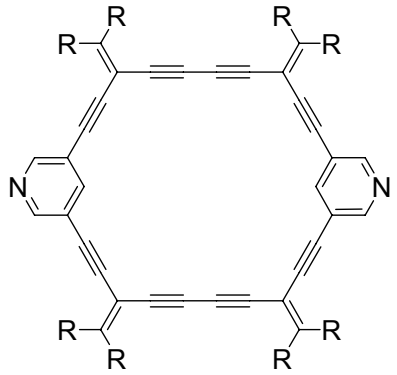
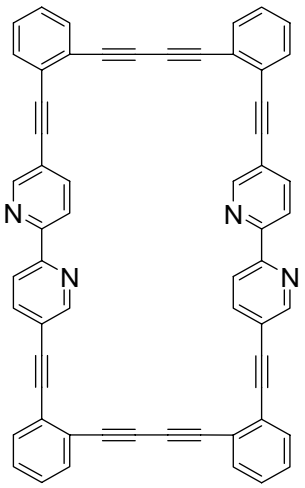


41a: R = Me
41b: R = Ph
41c: R = adamantanyliden

Figure 13. Other macrocycles with exotopic ligand sites by Lees and Tykwinski.

Baxter reported the synthesis of conjugated phenylethynyl macrocycles of the tetrabenzodehydroannulene-type, which have incorporated bipyridine (**42** and **43**), pyridine (**44**), or pyridine and thiophene units (**45**) (Figure 14).[34] Detailed ion-binding studies revealed that **42**-**44** function as fluorescence ion sensors. **42** was found to be a selective chromogenic sensor for Zn^{2+} ions, **43** functions as fluorescence sensor for Cu^{2+} ions, **44** gave a specific interaction with Hg^{2+} and $PdCl_2$, and **45** functions as sensor for Ag^{+}.



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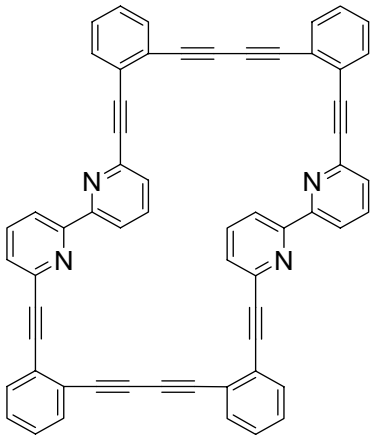

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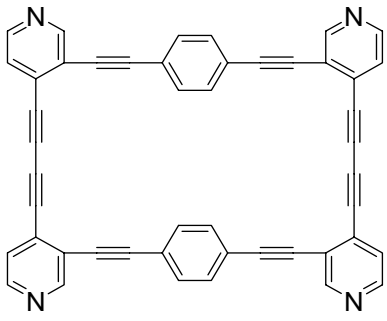

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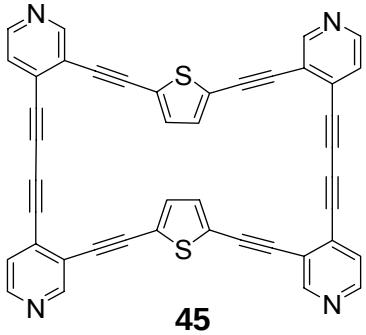
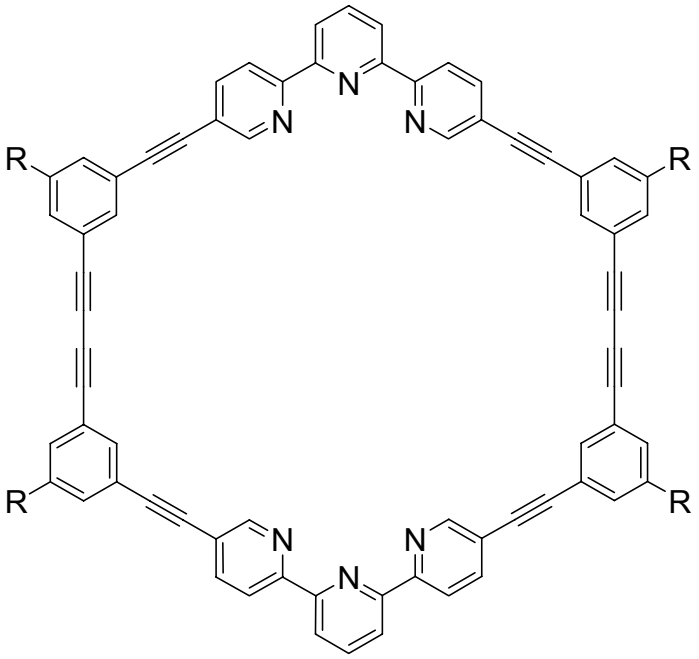


45

Figure 14. Macrocycles with ligand sites by Baxter.

Two terpyridine containing macrocycles **46a**[30] and **46b**[35] were prepared using a Glaser type reaction in yields of 8% and 39%, respectively (Figure 15).

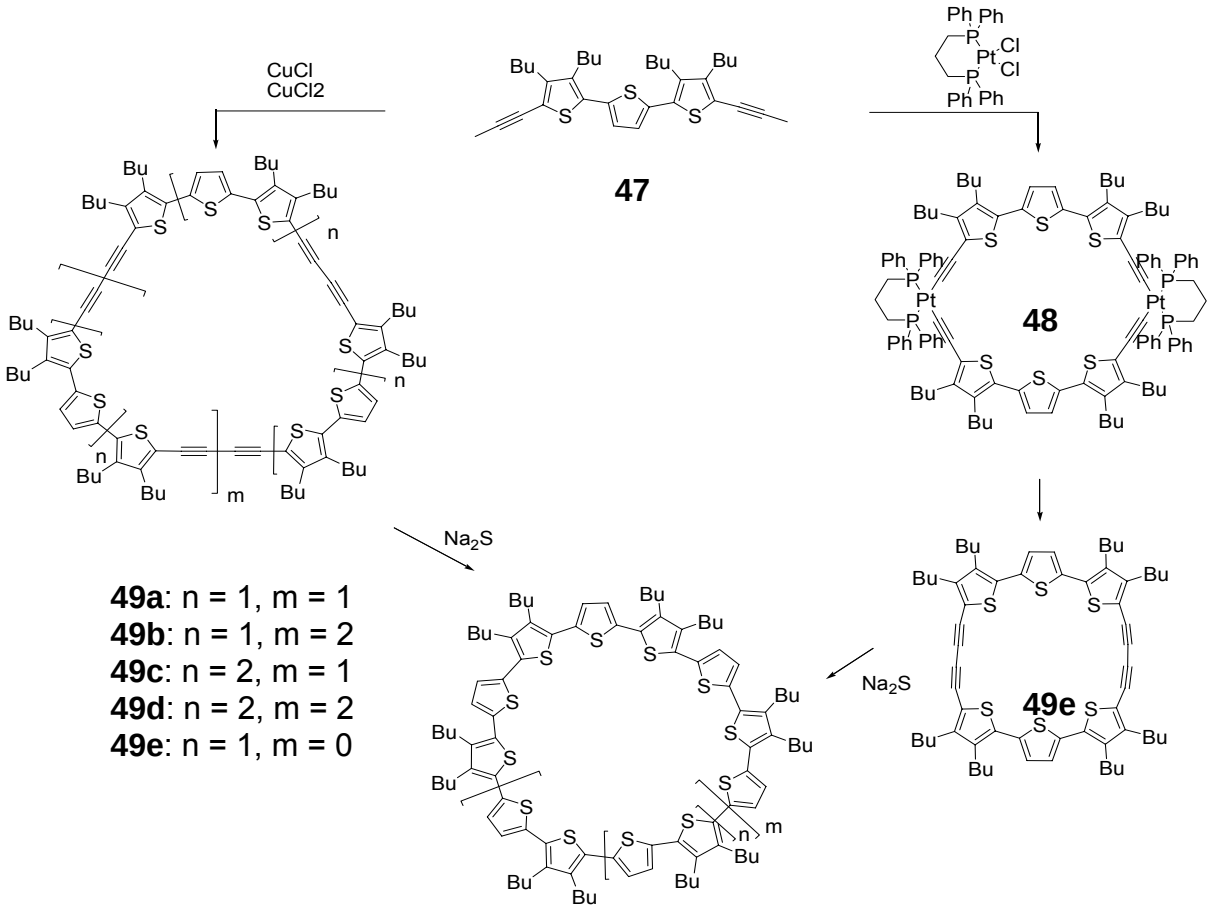


46a: R = $CH_2OC_6H_{13}$

46b: R = ≡—TIPS

Figure 15. Terpyridine macrocycles obtained from an oxidative acetylene coupling by Grave (**46a**) and by Baxter (**46b**).

There are not many shape persistent macrocycles which contain sulphur in the back-bone and also have a useable interior. Basically this is restricted to work done by Bäuerle et al. They prepared a set of fully conjugated cyclo[n]thiophenes **50** (n = 8, 12, 16, 18) (Scheme 17) and showed that macrocyclization yields can be increased from 9-12%[36] to 90%[37] when precursor **47** is not used directly but first converted to metalla-macrocycle **48** followed by a C-C bound formation through elimination of the transition metal units with an oxidant. Reaction of macrocycles **49a-d** with sodium sulphide converted the butadiyne units into thiophenes giving cyclo[n]thiophenes **50** in 7-27% yields.



Scheme 17. Thiophene containing macrocycles by Bäuerle.

Tobe et al. prepared butadiyne-bridged pyridinophanes by one intramolecular reaction of a single precursor under Eglinton-Glaser conditions to give **51** and **52** in 50% and 29% yield, respectively (Figure 16). Cycles **51** and **52** did not show concentration dependence of chemical shift in the ^{1}H NMR spectra in $CDCl_3$, indicating that they do not tend to self-associate.[28]

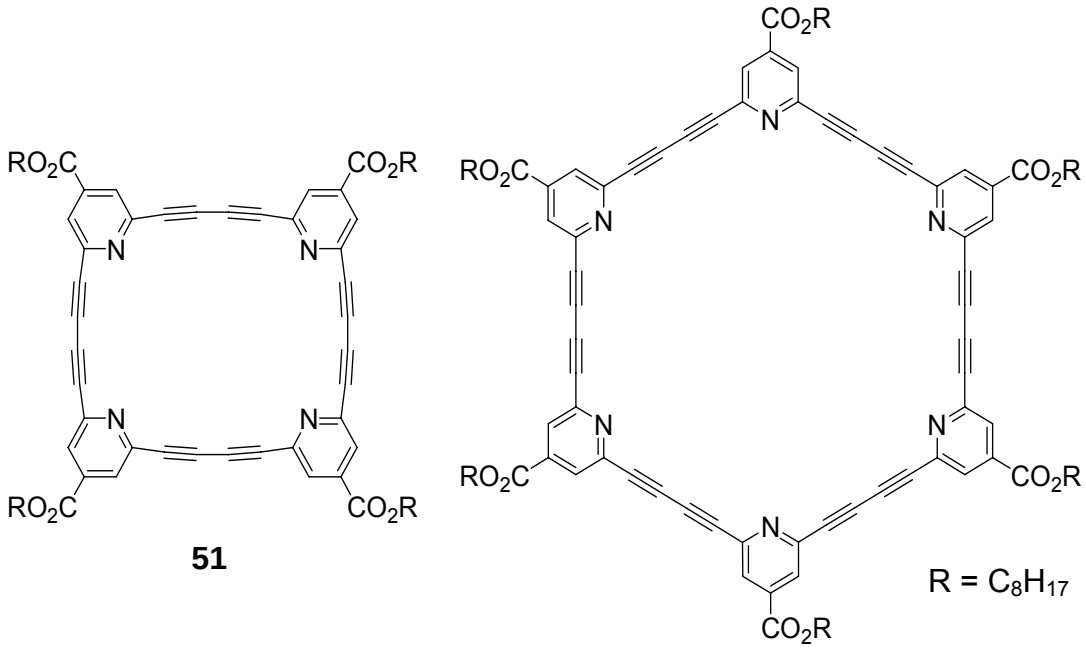
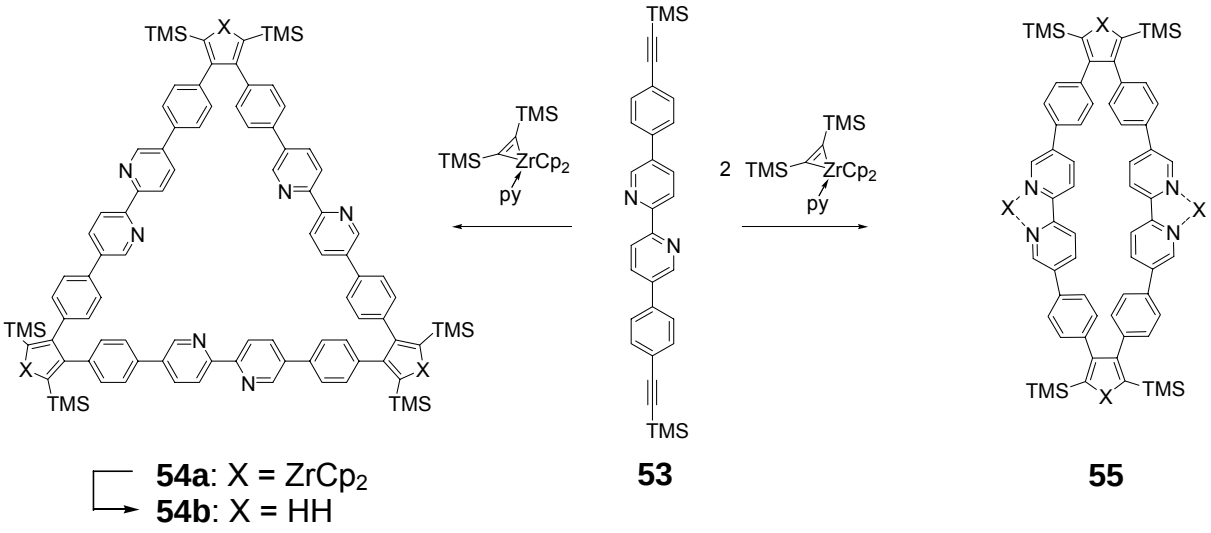


Figure 16. Tobe's macrocycles **51** and **52**.

d) By acetylene zirconocene coupling

Zirconocene coupling of silyl-terminated bis-alkynes has been shown to be a high-yielding route for the assembly of C-C bonded macrocyclic compounds.[39] Tilley used zirconocene-coupling reactions of different 2,2'-bipyridines derivatives and obtained a set of macrocycles in very high yields which differ in shapes, sizes, and number of bipyridines (Scheme 18 and Figure 17).[39] These high yields were explained by the reversibility of the zirconocene coupling in presence of donor solvents, such that the reaction is thermodynamically controlled. A representative example is given in Scheme 18. The diyne **53** was reacted with 1 equiv. of $ZrCp_2$ to give macrocycle **54**. When a higher ratio of $ZrCp_2$ was used, the pipyridine units formed complexes with Zr and the dimeric macrocycle **55** was obtained. The cycles can be demetalated under acid conditions.



Scheme 18. Tilley's macrocycle using zirconocene coupling.

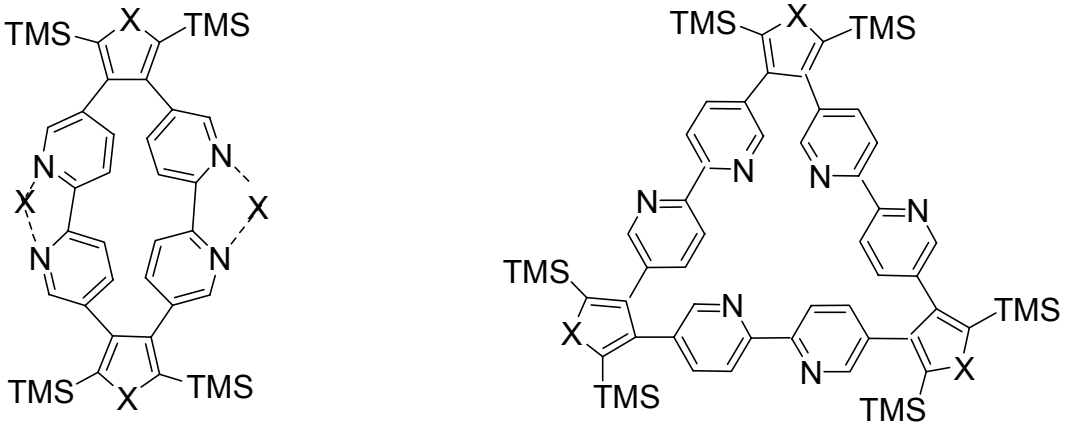


Figure 17. Bipyridine containing mcrocycles by Tilley.

A few conclusions can be drawn from this literature analysis. The field is clearly dominated by Sonogashira (30 cycles) and Glaser-type coupling reactions (16 cycles) (See Table 1), whereas the other two Suzuki and "zirconocene coupling" reactions were seldomly used (2 and 4 cycles, respectively). Despite the numerous representatives prepared the synthetic access to most of them is still tedious and complicated. This is reflected by the low yields and the small quantities of isolated cycles (Table 1). Taking in account the cyclization step, the macrocycles can be divided in three yield categories: < 25% (27 cycles), 25-50% (8 cycles) and > 50% (7 cycles). For six cycles the cyclization yields were not mention. Most of the cycles were closed from two (34 cycles) or more (3 cycles) precursors, but few examples

where ring closure reaction was done with one precursor are also known (14 cycles) (Table 1). By far the best cyclization yields (85-95%) and the biggest amounts of cycles were obtained by a zirconocene coupling of acetylenes. Gram quantities of cycles were prepared by this method. However this cyclization reaction provides macrocycles with triangular geometry and does not easily allow for attaching different functional groups on the macrocycle.

Tabele 1. Synthesis of heteromacrocycles shown in Chapter 3.2.

Compound	Coupling method	No. of precursors	Yield %	Isolated cycle in mg
18	A	6	-	-
21	A	2	20.5	132
24	B	2	16	-
25	B	2	54	220
26	B	2	14	209
30a	B	2	12	-
30b	B	2	30	-
30c	B	2	10	-
31a	B	2	21	25
31b	C	2	17	42
31c	B	2	9	132
31d	B	2	5	38
31e	B	2	18	216
32a	B	2	27	40
32b	B	2	11	181
32c	B	2	19	46
32d	B	2	11	45
35a	B	2	28	383
35b	B	2	25	250
35c	B	2	14	160
35d	B	2	20	162
36a-e	B	1	-	-
37a,b	B	1	-	-
39a-e	B	1	8-30	0.4-1.8 mg

Table 1. (*continued*)

Compound	Coupling method	No. of precursors	Yield %	Isolated cycle in mg
40	C	2	32	90
41a	C	2	39	152
41b	C	2	-	-
41c	C	2	51	29
42	C	2	34	45
43	C	2	13	21
44	C	2	71	130
45	C	2	46	92
46a	C	2	8	28
46b	C	2	39	77
49a-d	C	2	9-12	-
51	C	1	-	-
52	C	1	-	-
54	D	3	91	1970
55	D	2	95	895
56	D	2	96	806
57	D	3	92	3490

The coupling methods were A: Suzuki, B: Sonogashira, C: oxidative alkyne homocoupling, and D: zirconocene coupling.

3.3. Aggregation of mesogenic compounds with specific emphasis on cylindrical stacks

Inspired by the remarkable properties of tubular structures in biology, the design of molecules able to self organise into tubular structures has been a fascinating and difficult to reach goal. Much effort was invested in understanding the driving forces for the molecules to self organise. Weak interactions like hydrogen bonding, donor-acceptor interactions, Van der Waals forces, and π-π staking recognition motifs play an important role in molecular packing in crystals. [40]. For example DeSantis recognised that peptides comprising of an even number of alternating D- and L-amino acids are able to form hollow cylindrical ensembles through backbone-backbone hydrogen bonding NH···O=C (Figure 18).[41] Since then a large variety of nanotubes have been designed based on cyclic peptides of alternating D,L-α-amino acids, β-amino acids, alternating α,β-amino acids, alternating α,γ-amino acids, δ-amino acids and oligoureas. .[42]

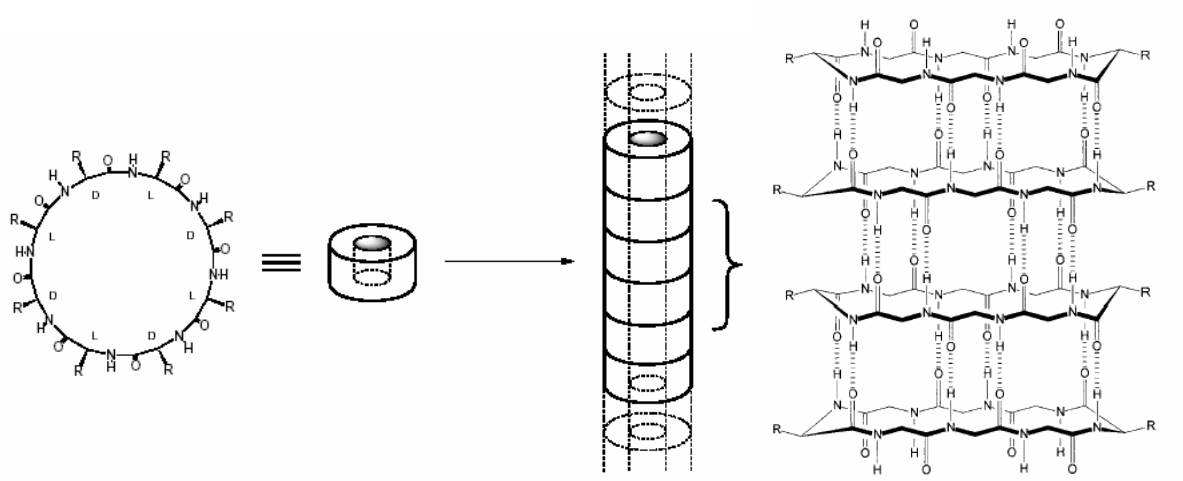


Figure 18. Nanotube assembly from cyclic D,L-peptides.

Another approach into this matter was explored by Stoddart and co-workers. They prepared cyclic (1→4)-α linked oligomers of L-rhamnopyranose-(1→4)α-D-mannopyranose. The X-ray crystallographic analysis revealed that they stack in the solid state and form hollow tubular structures with an interior diameter of 1 nm. The solid state structure show no intramolecular [OH···O] hydrogen bonding between adjacent monosaccharide units, but they connect adjacent columns.[43]

Numerous examples in which halogen atoms bound to other fragments, or in which chalcogen species of type R-X-R', have intermolecular X···X distances

significantly shorter (0.1-0.4 Å) than the sum of their Van der Waals radii are known in literature. Thus, close chalcogen-chalcogen contacts play an important role in formation of two- and three-dimensional networks in the solid state. These interactions could be rationalised in terms of electrophilic-nucleophilic interactions of for example different sulphur centres. The occupied 3p orbital on one unit interacts with the empty σ* orbital of either the RS or RS' bonds (Figure 19). Gleiter et al. prepared a variety of cyclic compounds containing sulphur. They were able to shown that one driving force for tubular structure formation are Van der Waals forces between the sulphur centers.[44]

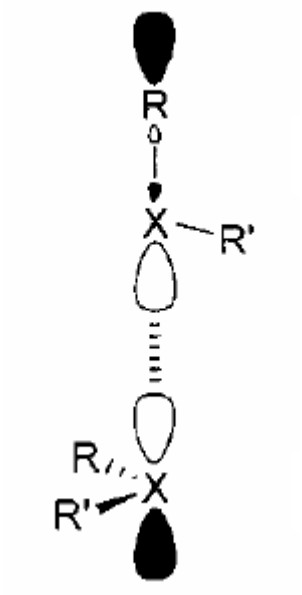
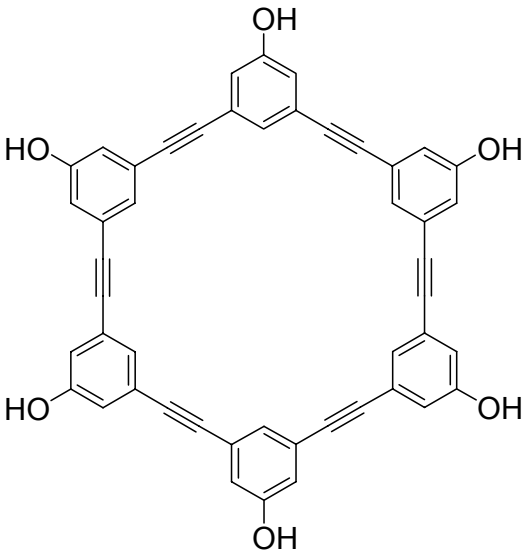


Figure 19. Directional bonding of two chalcogen centers in R-X-R' units by interaction of an occupied p orbital with an unoccupied σ* orbital.

3.3.1. Solid state structures in shape persistent macrocycles

Shape persistent macrocycles have a high tendency to self-organise into supramolecular architectures through π-π interactions. They normally form two-dimensional layered structures stacked in a ···ABCABC··· sequence[1c] which form channels, but not strictly cylindrical array in which one cycle is positioned directly on top of the other. These channels are not empty but rather filled with the substituent groups with which the macrocycles are decorated and with solvent molecules. This feature has also been observed for the packing of terpyridine and bipyridine containing macrocycles prepared in our group.[17], [30] This packing behavior can be explained by an attractive interaction between the positively charged σ-frame and the

negatively charged π-system. Other directive forces like hydrogen bonds can be used to generate channel structures in crystals. These forces were successfully exploited by Moore. He prepared macrocycle **58** decorated with 6 exo-cyclic hydroxyl groups. In crystals, the macrocycles are connected to each other by hydrogen bounds and form layer structures, where the layers are aligned so that extended channels with diameters of ~9 Å are formed (Figure 20).[45]



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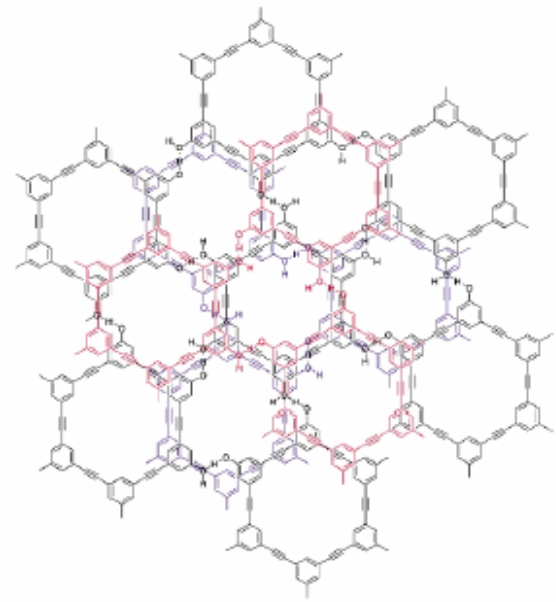
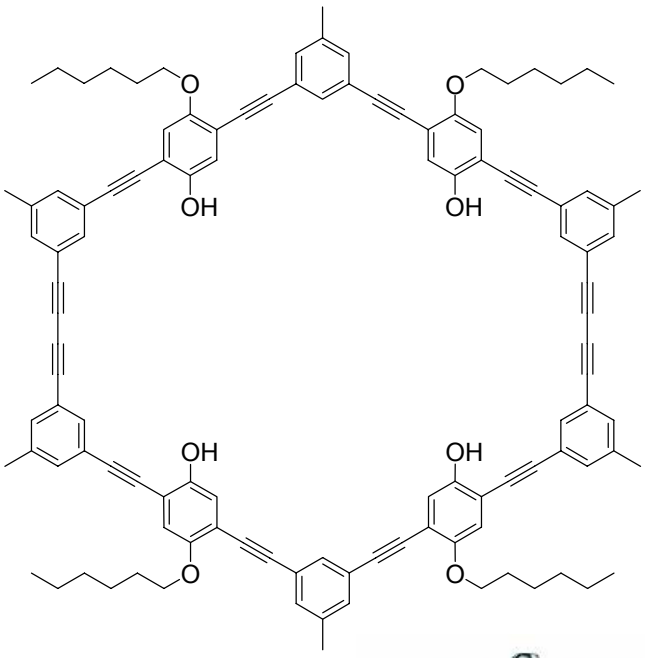


Figure 20. Schematic packing of three layers of **58** in the crystalline lattice.

Recently Höger observed that the nature of the solvent influences the packing of the macrocycle **59** in its single crystals (Figure 21).[46] Crystallization of **59** from pyridine gave rise to channel structures where two phenolic and two hexyloxy groups point inside of channel with a pore size of ~4-5 Å, whereas the crystallization from THF, where all hexyloxy groups point outside of the macrocycle, leads to formation of supramolecular tubes with large channels having pore sizes of 8 × 12 Å. Such pore sizes are larger than those found in cyclodextrines.



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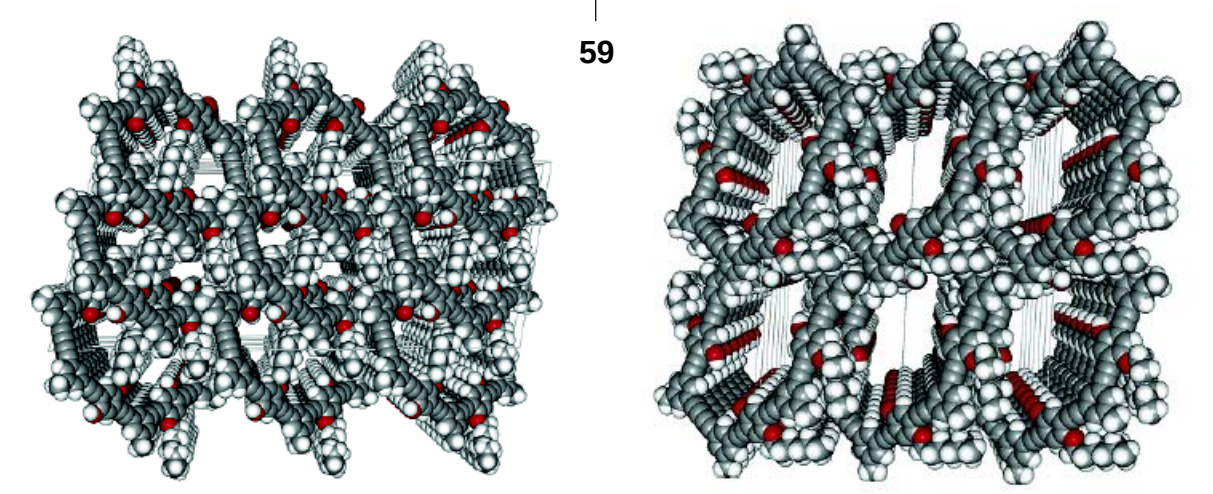


Figure 21. Höger macrocycle **59** with two different aggregation patterns depending on the recrystalization solvent: left from pyridine and right from THF (solvent molecules were removed in both cases).

3.3.2. Aggregation of shape persistent macrocycles in solution

The aggregation of shape-persistent macrocycles through π-π interactions in solution has attracted much attention since 1992 when Moore and co-workers found that chemical shifts in ^{1}H NMR spectra of phenylacetylene macrocycles **12a** and **12b** in chloroform are dependent on the concentration.[47] It was observed that self association abilities of macrocycles strongly depend on a number of factors.[1c],[1d] Thus, the backbone and side chain structures influence the tendency of macrocycles to aggregate. It was found that electron-poor aromatic systems, such as benzoic ester groups, linked to the backbone favour aggregation, while in the case of

electron-rich aromatic systems, like phenyl ethers and benzyl ethers, no aggregation was observed.

It is sensitive to the geometry of the ring size. Thus, cyclic hexamers having a planar framework exhibit a strong tendency to self-associate compared with its cyclic analogues pentamer and heptamer having a non-planar geometry.

Steric hindrance helps to keep the cycles apart from one another rendering the packing energetically less favorable. Thus bulky groups and endo-cyclic chains disturb aggregation.

It is also very sensitive to solvents, which one would, of course, expect anyway. The association of macrocycles in solution can be investigated quantitatively on the basis of the concentration dependence of the chemical shift and the molar osmotic coefficient Φ determined by vapour pressure osmomerty (VPO). The chemical shifts of the aromatic protons show remarkable concentration dependence when aggregation occurs. The observed upfield shift indicates that the aggregates adopt a structure in which the macrocyclic frameworks stack in a face to face manner. For a more exhaustive description of the aggregation of shape persistent macrocycles in solution reader is referred to the pertinent literature.[1c], [1d]

3.4. Ru and Os complexes of bipyridines

Ru and Os complexes by and large became intense research targets during the last decades. The main reason for this is their facile accessibility, low cost, and rich photophysics. Several research groups have shown that the complexes not only fluoresce with sometimes high quantum yield but can also be used for energy and electron transfer studies. This latter aspect can be seen in light of the intense activity in the direction of artificial photosynthesis and the search for model systems. Bipyridines are oftenly used ligands in these complexes. In some cases even bridging bipyridines (Figure 22) were used to obtained di-, and oligometallic assemblies.

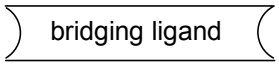


Figure 22. Cartoon representation of bridging ligand between metal centers.

This whole area has produced such an enormous bouquet of novel complexes that it cannot be reasonably reviewed within the context of the present work. The interested reader is rather referred to the pertinent review articles which address both synthetic as well as physico-chemical and photophysical aspects.[48]

Since energy and electron transfer processes of Ru-Os binuclear complexes plays some role in this thesis at least one case should be mentioned where related studies have been undertaken. Balzani investigated the influence the bridging ligand length on the rate of electron and energy transfer.[49] For this purpose, the mixed Ru/Os complexes **60a**-**c** were prepared, whereby the metal centres are connected by a bridging ligand whose oligophenylene spacer is made of a progressively increasing number of rigid phenylene groups (Figure 23). It was found that the energy transfer does not depend on temperature, but strongly so on the spacer length, whereby it decreased with increasing length. The rate of energy-transfer proceses from Ru to Os in acetonitrile solution at 293 K were found to be: $k_{en} = 6.7\times10^{8}$ s^{-1} for n = 3, $k_{en} = 1.0\times10^{7}$ s^{-1} for n = 5, and $k_{en} = 1.3\times10^{6}$ s^{-1} for n = 7.

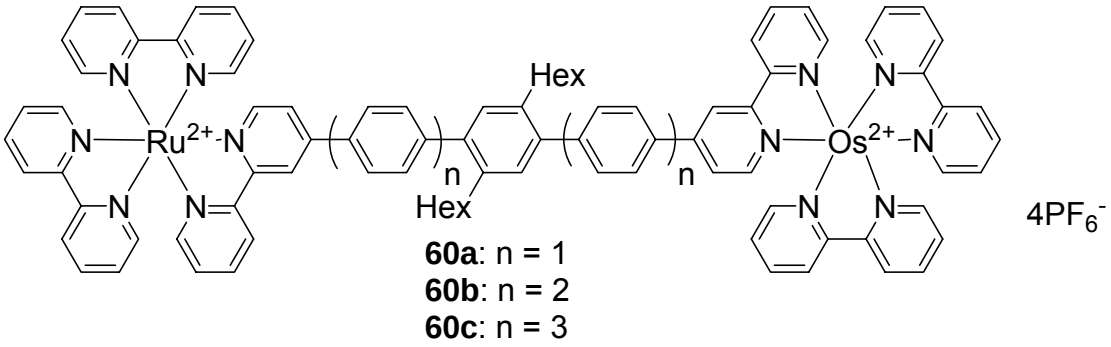


Figure 23. Mixed Ru/Os complexes by Balzani containing bridging ligand with different length.

Monometallic complexes of a given ligand, e.g. a bpy derivative, are normally prepared by reacting the Ru or Os source, $RuCl_3$ and $OsCl_3$ with parent bpy in the presence of $Na_2S_2O_4$ which reduces the metal III salt to metal II. The resulting Ru or Os bpy halides are then reacted with the ligand of choice. If this ligand happens to carry two bpy units itself, which can be individually addressed, then the option arises to either prepare homodimetallic or heterodimetallic complexes. The former are easily accessible by just refluxing the ligand with more than two equivalents of the above mentioned Ru or Os bpy halides (Figure 24a). A concrete example with relevance to the present work is shown in Figure 25. This ligand in the present case was, of course, a shape-persistent cycle. According to figure 24a, Henze prepared the dinuclear-Ru complex **61** from macrocycle **10** using a small excess of $[Ru(bpy)_2Cl_2]$ in a mixture of ethylene glycol/dioxane (Figure 25).[17b]

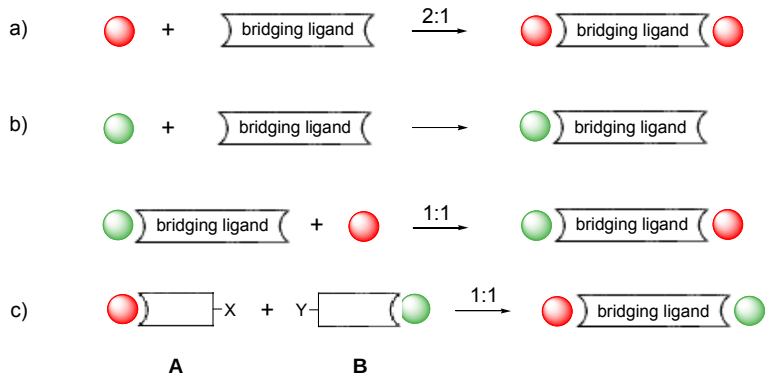


Figure 24. Synthetic ways to a) homodinuclear complexes, b) heterodinuclear complexes, and c) the convergent approach to heterodinuclear complexes formed from the existing mononuclear complexes through a reaction between two functional groups X and Y.

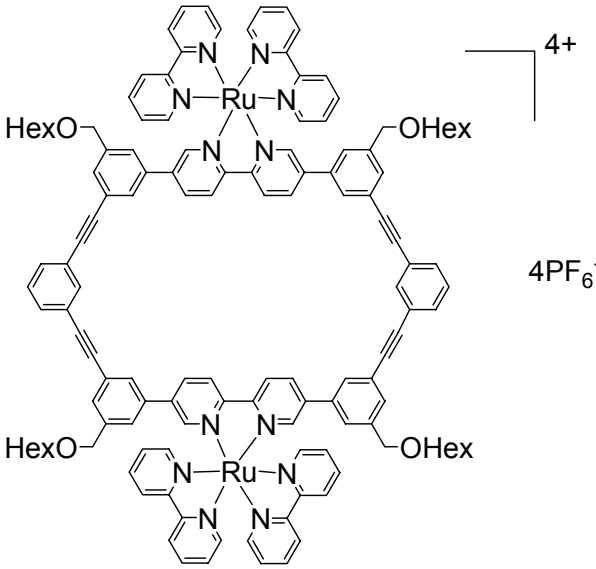
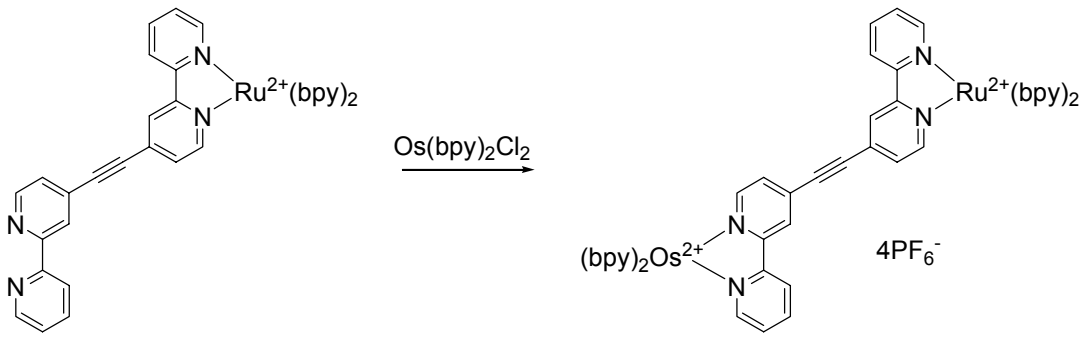


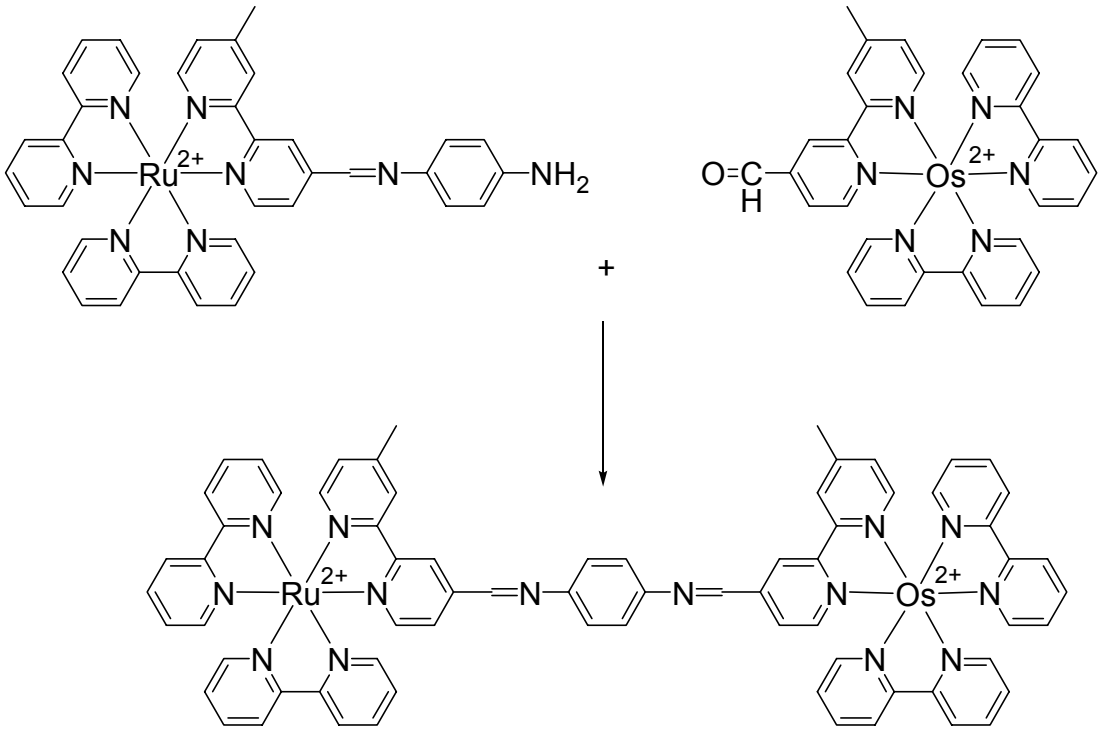
Figure 25. Ru complex **61** prepared by Henze.

A bit more complex is the synthesis of dinuclear heterometallic complexes which can be done by using two approaches (Figure 24b,c). The first approach involves two steps. An excess of bridging ligand is reacted with one equivalent of Os bpy dihalide followed by the isolation of the mononuclear complex formed. In the next step the Ru fragment is added by reacting the mononuclear Os complex with Ru bpy dihalide to furnish the dinuclear heterometallic species. There is one important advantage in this approach which should be noted. With Os, in contrast to Ru, much less of dinuclear homometallic complex is formed in its first step. It is not yet understood why this is so, specifically in light of the fact that the two bpy units in a given macrocycle are so far apart from another that they should not feel each other. Also there is evidence in the literature where exactly the opposite order of metal addition led to success (Scheme 19).[50]



Scheme 19. A mixed Ru/Os complex prepared by Ziessel.

In the second approach, individually prepared mononuclear complexes **A** and **B** are coupled together by a reaction between the two functional groups X and Y to form a rigidly linked compound (Figure 24c). This method was successfully applied by Keene, Paul, and others.[51] A representative example is given in scheme 20.



Scheme 20. Convergent approach to heterodinuclear complexe formed from the existing mononuclear complexes through a reaction between two functional groups by Paul.

Bipyridines induce stereoisomerism at six-coordinated centers due to their bidentate nature. Complexes like $[M(bpy)_3]^{n+}$ exist in two enantiomeric forms. If the two coordinating nitrogens are not equivalent, like in some substituted bpy, two geometrical isomers, *fac* and *mer* are possible. When a symmetrical bridging ligand with two bpy units is used the situation is even more complex. There are meso (ΔΛ) and rac (ΛΛ/ΔΔ) diastereoisomeric forms (Figure 26).[52] The differences arising from the presence of isomeric species are negligible in the electrochemical and spectroscopic properties. Thus it is not normally necessary to isolate stereoisomers but the overall purity of the isomer mixture plays an important role. Photophysical properties tend to strongly depend on trace impurities which can serve as electron sinks, excitation quenchers and alike.

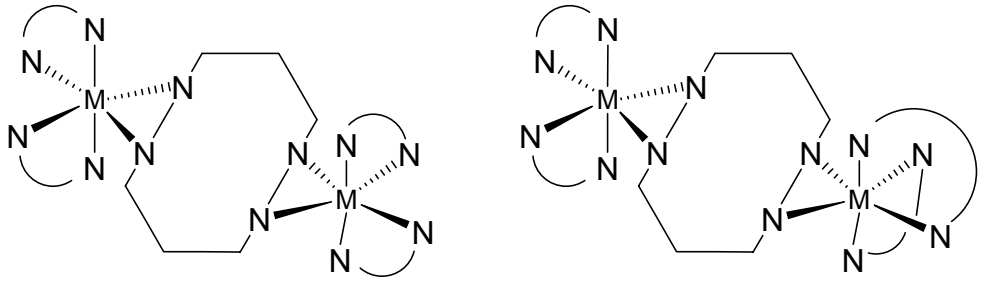


Figure 26. Cartoon representation of two stereoisomeric forms of the dinuclear ligand-bridged species in which the axis of the two “bites” are linear: Λ,Δ (left), Λ,Λ (right).