Journal of Inclusion Phenomena and Macrocyclic Chemistry **33:** 427–457, 1999.

Review Article

Very Large Cyclic Compounds

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(Received: 27 April 1998)

Abstract. Very large ring systems, containing more than 50 ring members, are becoming increasingly important in different topics in natural sciences. These so-called 'gigantocycles' differ from smaller macrocycles in physical properties, special structural features and chemical behaviour. This article is meant to be the first summary of such ring systems and a synopsis of the most remarkable examples with their fascinating nano-scaled structures and ingenious synthesis. To restrict the scope of the article, only isolated and completely characterized, monodisperse compounds are presented. Furthermore, attention is mainly directed at organic gigantocycles. Some 'ultracycles' with more than 100 ring members, mainly occurring in polymer chemistry and nature, will also be described.

Key words: supramolecular chemistry, nanostructures, macrocycles, large rings, cyclopolymers

1. Introduction

Cyclic compounds, especially macrocycles, have played an important role in chemistry for a long time. In the last decade interest in macrocycles and macroheterocycles has tremendously increased as the number of symposia about this topic shows [1]. The fascinating structural symmetries and new stereochemical aspects of these compounds may be responsible for this development. Another reason is that they build a new class of host systems and can be used as concave building blocks in supramolecular chemistry [2] and nanochemistry. Examples such as large crown ethers, calixarenes and porphyrins as well as siderophores, cyclic peptides [3] and macrolide antibiotics [4] illustrate the significance.

In recent years compounds with very high numbers of ring members have attracted increasing attention. They have been emphasized from common ring systems and have been named gigantocycles [5] or ultralarge rings [6]. These classes of cyclic compounds with ring sizes ranging up to several hundred ring atoms are developing quickly. This fact can be explained by the improvement of cyclization methods and the analysis optimisation for molecules with high molecular weights. Particularly improved mass spectrometry (FAB, MALDI-TOF, ES)

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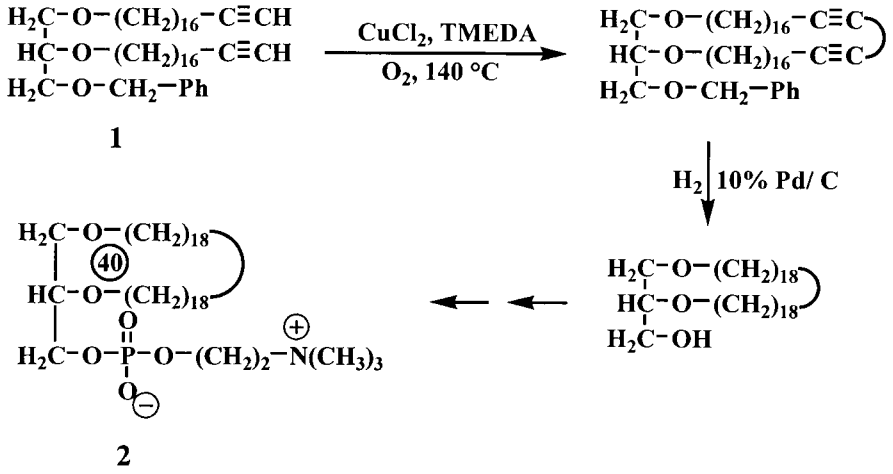


1 **2**

Scheme 1.

and NMR-spectroscopy methods are responsible for the current progress in gigantocycle research. Nowadays the synthesis of catenanes, rotaxanes, knots and other mechanically intertwined and interlocked structures, formerly extremely difficult, is possible on a preparative scale [7–9]. Thus, large and very large rings are indispensable and needed in greater variation. The theoretical treatment of high-numbered rings including polymeric cycles has also advanced. For these reasons it seems to be overdue to present a first survey without any claim for completeness. At first, we would like to explain what is meant by gigantocycles and ultracycles, afterwards we demonstrate some characteristic examples from aliphatic, aromatic, heteroaromatic and polymeric chemistry. We will confine ourselves to structurally perfect, monodisperse cycles which have been characterized in a pure form.

2. History

The expression ‘gigantocycle’ was introduced by Menger *et al*. in 1992 [5]. They synthesized huge circular lipids with the aim of investigating the chemical behaviour of membrane lipids of the thermophilic *archae bacteria*. By ring closure reactions the independent flexibility of the lipophilic hydrocarbon chains had been limited. Thus, a change of membrane permeability and thermophilic properties was expected. The intention was to get further information about the thermophilicity of such *bacteria*. The decisive step in this synthesis was a Glaser oxidation of the terminal alkyne functionalities in **1** (Scheme 1). Reduction and two further steps led to the 40-membered gigantocyclic phospholipid **2**.

3. Definitions

In literature cyclic compounds are classified as follows: Molecules with 3–4 ring atoms are called ‘small rings’. 5 to 7-membered molecules are named ‘normal rings’ because they are generally low in energy and have a smaller ring strain. Species with 8–12 ring members are called ‘medium rings’. They reveal some peculiarities, such as transannular strain. Cyclic systems with more than 12 ring atoms are defined as ‘larger rings’ or ‘macrocycles’ [10].

The majority of publications on macrocycles refer to compounds with less than 20 ring members [11, 12], larger ring systems have been described as gigantocycles [5] or huge rings. Based on that definition, the calix[6]arene **3**, *all*-homocalix[5]arene **4a** and the analogous -pyridine compound **4b** [13], the poly(ethoxycarbonyl)[3_4]metacyclophane **5** [14] and cyclic peptide **6** [15] could in principle be called gigantocycles (Scheme 2). These cycles, however, do not strongly differ from ring systems with less than 20 ring atoms with respect to their synthesis or energy. So it does not seem to be justified to combine these species in a new class of cyclic compounds.

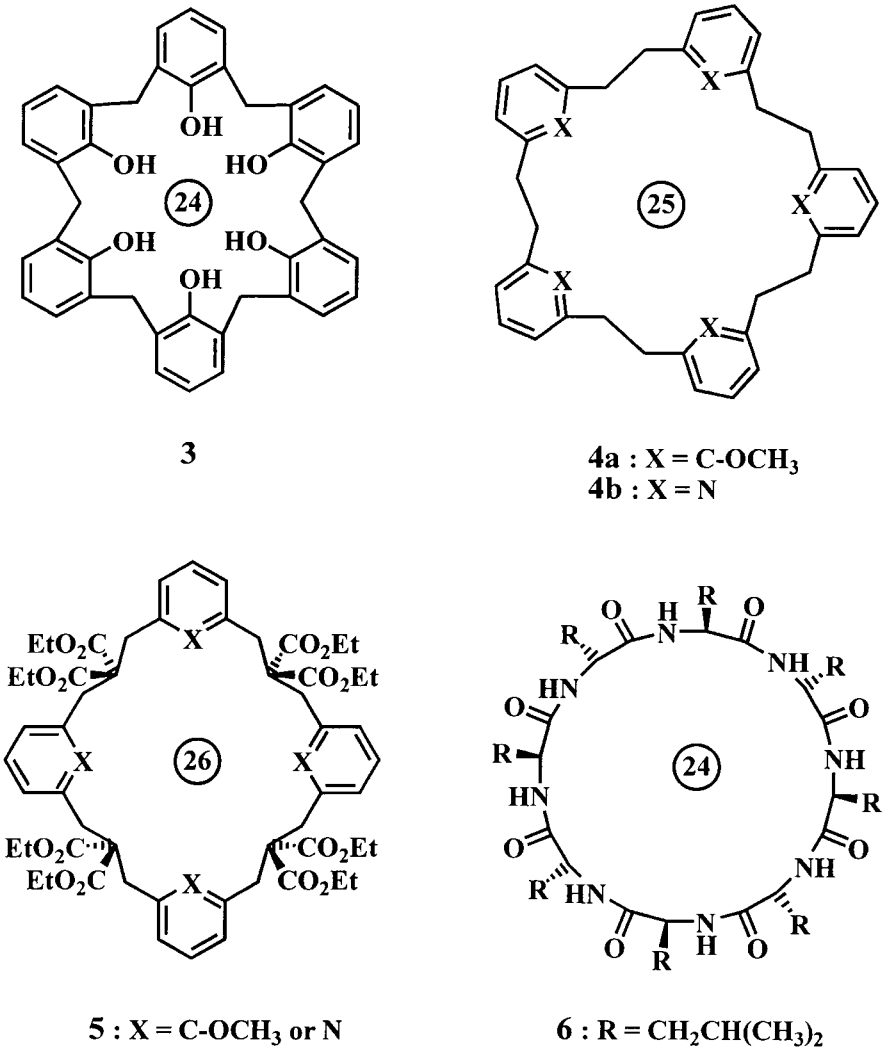
To us the definition of a new class of macrocycles as gigantocycles is justified only in the case of the less known, hitherto scarcely accessible cyclic molecules with 50 to 100 ring members. Larger rings with 100 and more ring atoms, in an isolated form, have rarely been described until now. They already represent the transition from medium heavy molecules (oligomers) to polymers. Thus, the question of monodispersity/structural perfection is getting more important. For this macrocyclic class Rothe *et al*. introduced the expression ‘ultralarge rings’ [6]. We here use the expression ‘ultracycles’ for these species. The numbers 50 and 100 are arbitrarily chosen and are not meant to be a sharp dividing line, but to serve the heuristic principle.

4. Aliphatic Ring Systems

The majority of aliphatic gigantocycles consist of long hydrocarbon chains which are linked by lacton, lactam or ether bridges. These compounds often play an important role in natural processes (e.g. macrolides or amphiphiles) or in host-guest chemistry (e.g. crown ethers). High-membered cycloalkanes and cyclic oligoacetylenes will also be described in the following section.

4.1. HYDROCARBONS

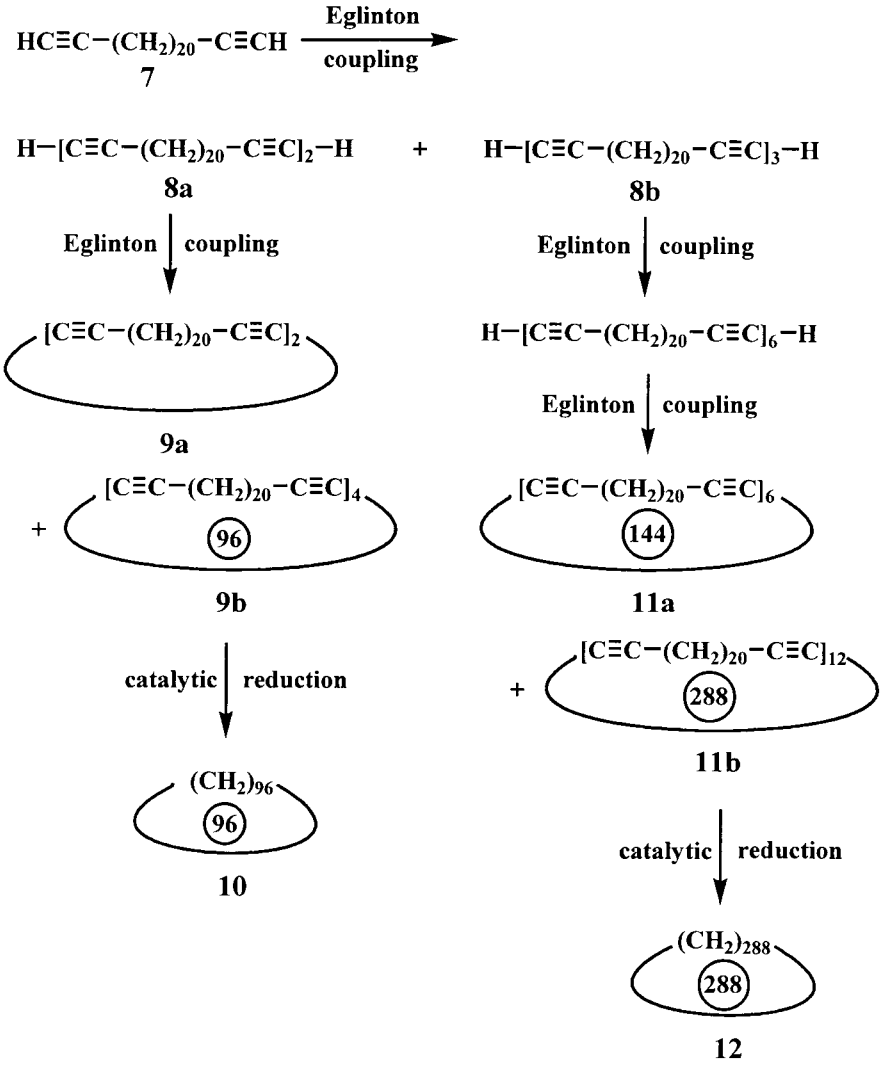
Cycloalkanes are one of the best known cyclic compounds in organic chemistry which are able to form ring systems with very high ring numbers. For that reason, we will start our review article with a focus on simple cyclic hydrocarbons. Until 1977 the largest isolated and purified cycloalkane was the 54-membered gigantocycle cyclotetrapentacontane $C_{54}H_{108}$. In 1978 Schill *et al*. reported on the synthesis of cycloalkanes with up to 96 methylene groups (Scheme 3) [16]. Starting from



Scheme 2.

1,23-tetracosadiyne **7**, the authors obtained the 1,ω-diynes **8a** and **8b** by Eglinton coupling with copper(II)acetate in pyridine. The precursor **8a** was transformed into the cyclic species **9a** and **9b**. Catalytical reduction of **9b** led to the 96-membered cycloalkane **10**. The ultracycles **11a** and **11b** were obtained by a two step Eglinton coupling starting from the precursor **8b**. Lee and Wegner described the reduction of the diacetylene **11b** to the ultracyclic 288-membered cycloalkane **12** in 1985 [17].

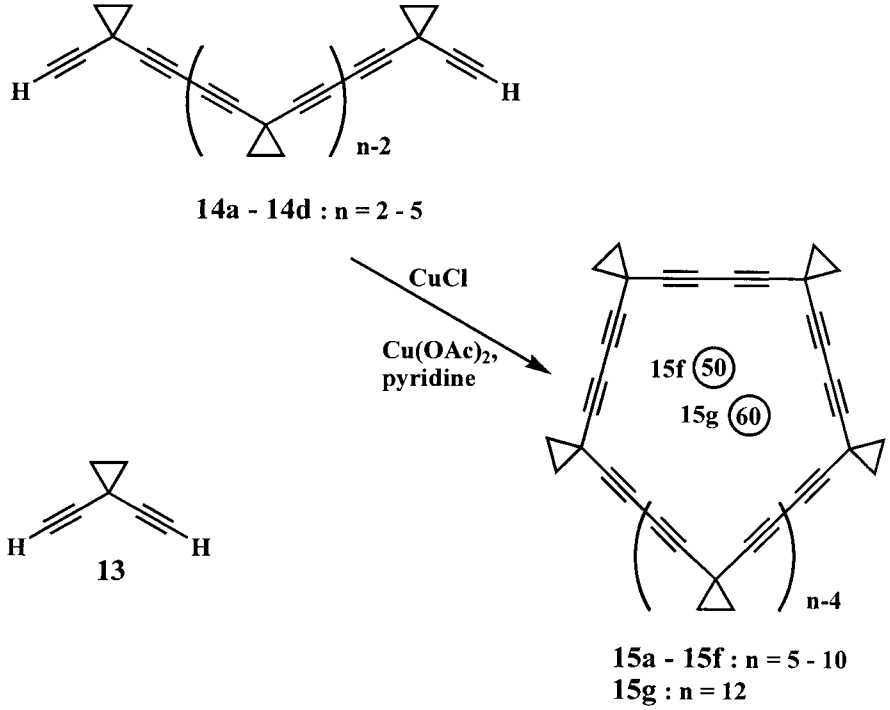
Schill *et al*. observed a correlation between ring size and ^{13}C shifts of the cycloalkanes. With increasing ring sizes up to 96 ring atoms the ^{13}C chemical shifts of the cycloalkanes and the shifts of the 'inner' carbon atoms of *n*-alkanes come



Scheme 3.

closer to each other. This property adds some justification for the distinction and division medium rings/gigantocycles/ultracycles.

Gigantocyclic high-energy hydrocarbons have been synthesized by de Meijere *et al*. in 1995 [18]. The oxidative coupling of several open-chain dehydrooligomers **14a**–**14d** of 1,1-diethylcyclopropane **13** led to the family of completely spiro-cyclopropanated macro- and gigantocyclic polydiacetylenes **15a** to **15g** (Scheme 4). These so-called [n]rotanes with n = 5–12 show a strong electronic interaction between the cyclopropane and the acetylene units. The HOMO of a cyclopropane ring is close in energy to the π-MO of an acetylene unit. Thus, the authors observed homoconjugative effects, such as a significant shortening of distal and lengthening



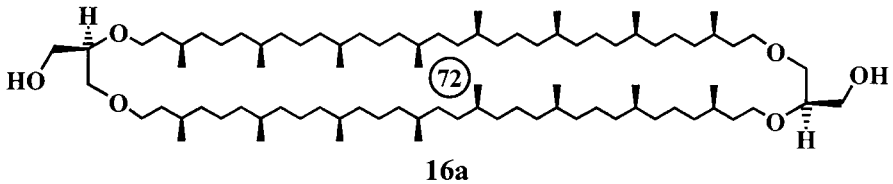
Scheme 4.

of cyclopropane bonds. The gigantocycle **15f** with 50 ring atoms and the 60-membered gigantocycle **15g** were obtained in 0.2% and 1% yield, respectively. All cyclic compounds were characterized by ^{1}H- and ^{13}C-NMR spectra.

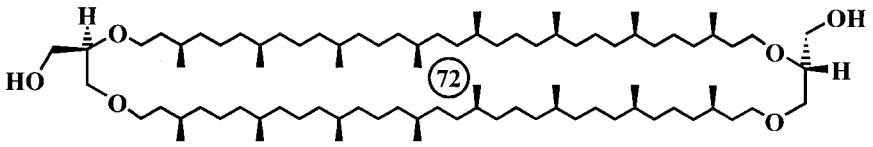
4.2. NATURAL GIGANTOCYCLES AND SYNTHETIC ANALOGUES

Biologically relevant gigantocyclic systems have been isolated from different *Archaea* organisms and tested on stereochemical characteristics and physical properties. *Archaea* consists of microorganisms, growing in unusual habitats like low or high pH, high temperatures or high ion strength. Their core lipids are distinguished from those of eukaryotes and bacteria by the absence of fatty acid glycerolesters. Instead, the archaeal lipids consist of ethers formed by condensation of polyols or glycol and two isoprenoid alcohols.

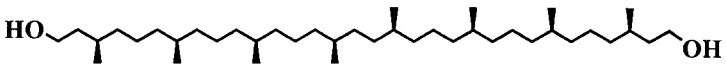
The detection of regioisomeric isoprenoid glycerolethers in the membrane core lipids of *Methanobacterium thermoautotrophicum*, *Thermoplasma acidophilum* and *Sulfolobus solfataricus* was published by Gräther and Arigoni in 1995 [19]. The authors observed a nearly statistical mixture of regioisomeric tetraethers **16a** and **16b** in the three different archaeal species (Scheme 5). The proof for the configuration of the stereocentres in the biphytanyl units of **16a** has been provided by a stereorational synthesis of the corresponding diol **17**.



16a



16b



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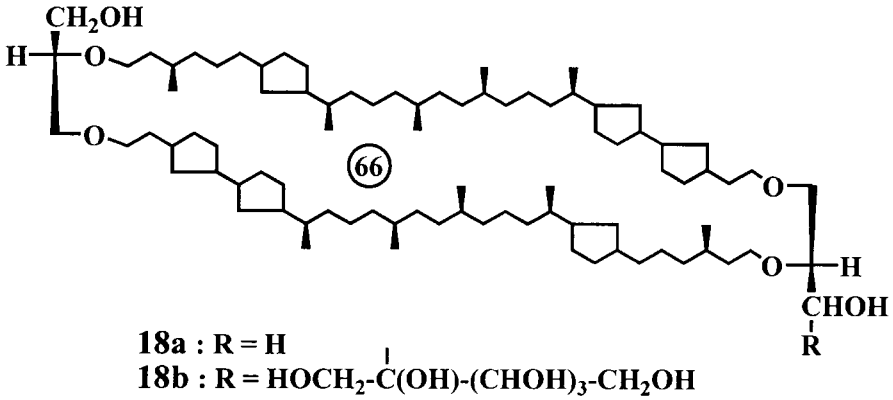
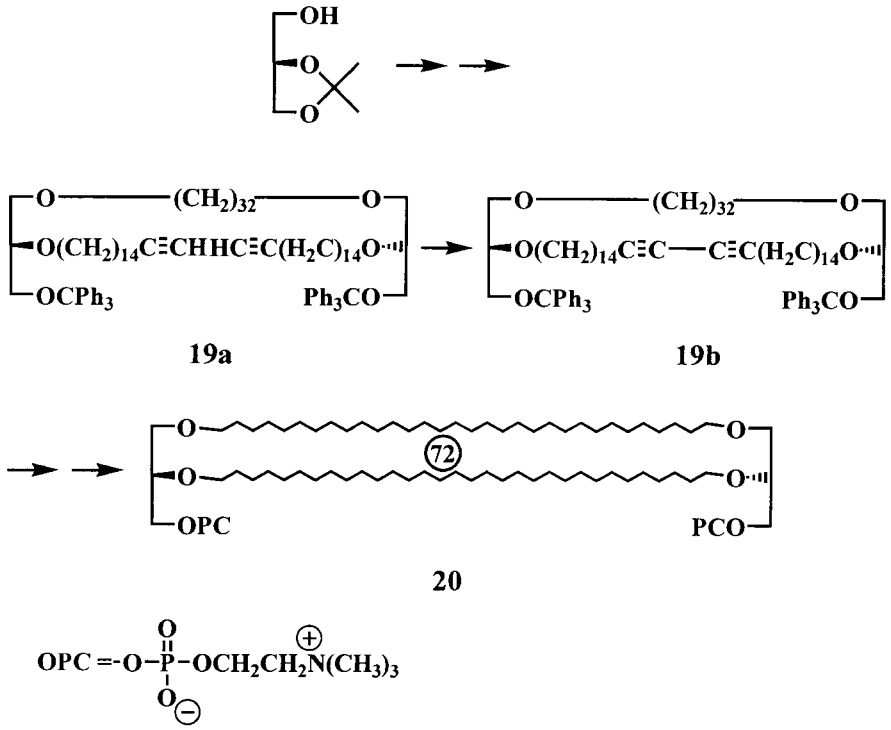
Scheme 5.



Scheme 6.

Long distance proton conduction by *Sulfolobus solfataricus* bolaform lipids has been investigated by Gliozzi *et al.* in 1996 [20]. By hydrolysis of the cytoplasma membrane the authors extracted the two fractions **18a** and **18b** and dissolved them in chloroform (Scheme 6). The monolayer obtained was tested on lateral proton conduction by interfacial fluorescence experiments. The structural organisation of these bolaamphiphiles at the air/water interface can be related to the lateral proton conduction.

In 1996 Menger and Chen published the synthesis of the 72-membered gigantocyclic phospholipid pair **20** (Scheme 7) [21]. This ‘double-phospholipid’ should be a synthetical unimolecular analogue to the bilayer assembly which is found in most biological membranes. **20** belongs to the class of bolaamphiphiles because



Scheme 7.

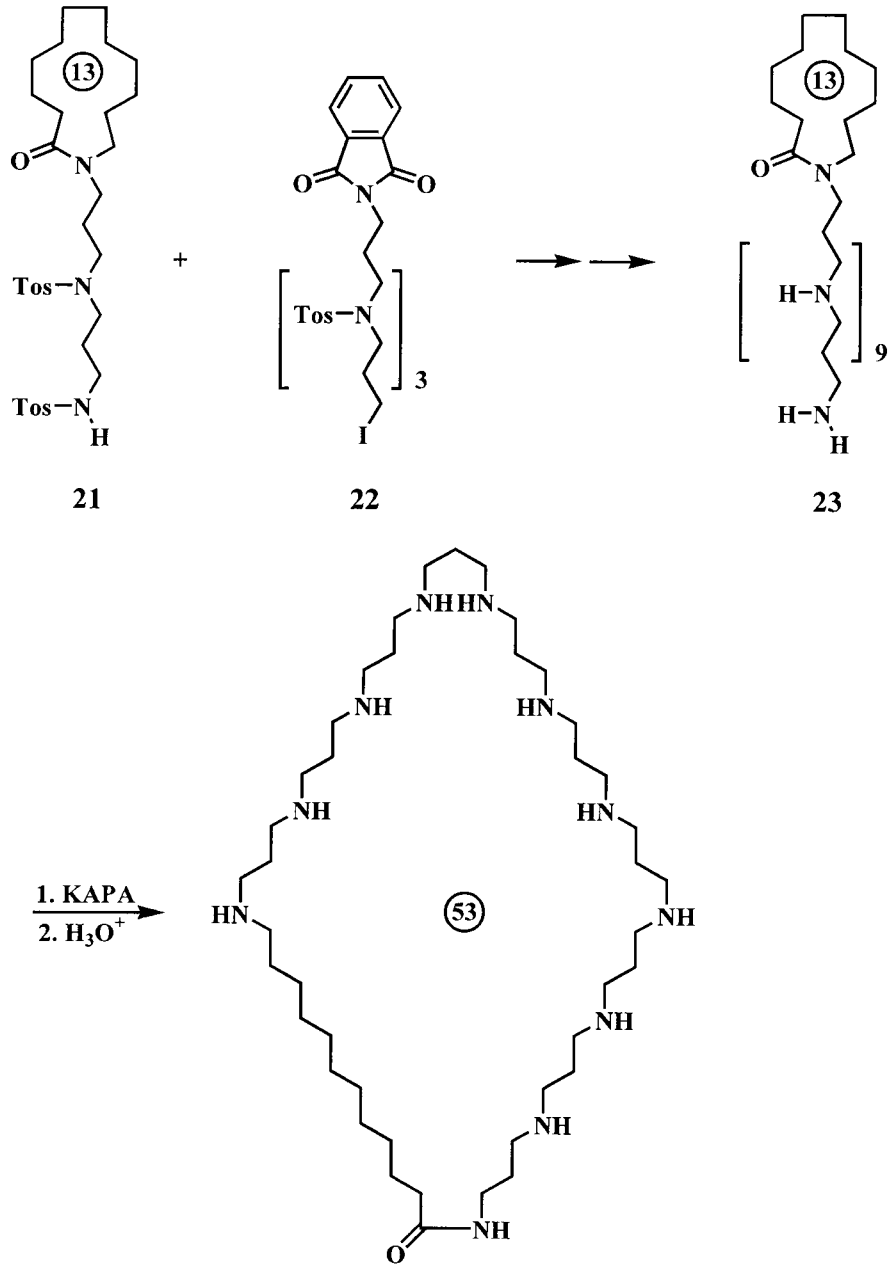
of its two separated polar groups. The particularly difficult reactions in the 12-step synthesis of **20** were an intramolecular macrocyclization of **19a** via Glaser coupling and reduction of the resulting diyne **19b** to the saturated system **20**.

4.3. LACTAMS

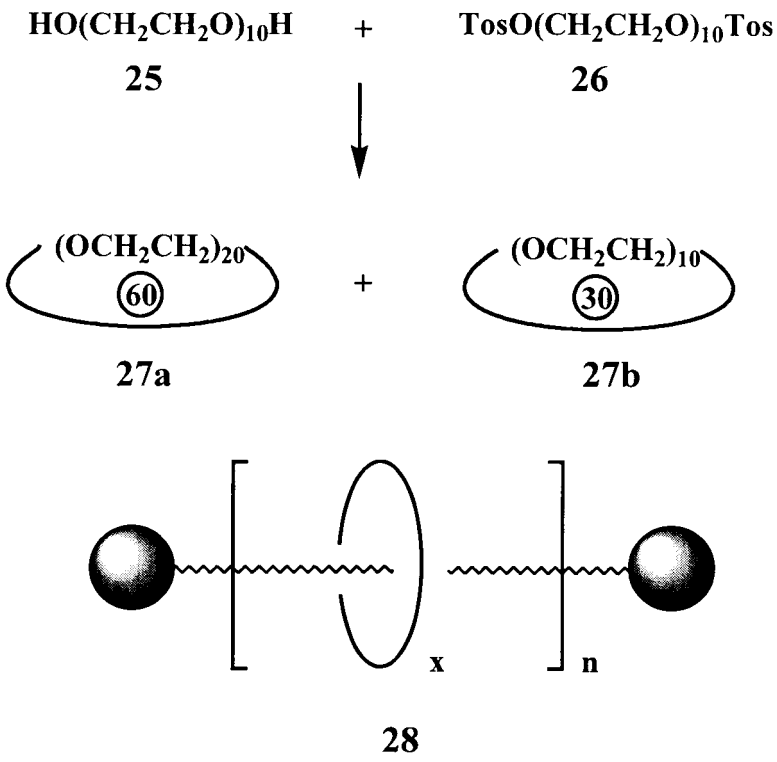
The 'Zip' ring enlargement reaction can be used to convert *N*-(*ω*-aminoalkyl)lactams into polyaminolactams with gigantocyclic dimensions. In 1979 Hesse *et al.* reported on the synthesis of the 53-membered polyaminolactam **24** [22] starting from the 13-membered lactam **21** and the open-chained precursor **22** (Scheme 8). Several steps led to the decaamine **23** which could be transformed into the isomeric target molecule **24**. **23** and **24** were characterized by IR, ^{1}H-NMR and MS spectra. Furthermore, decaacyl derivatives of **23** and **24** were synthesized and characterized.

4.4. ALIPHATIC CROWN ETHERS

A synthetic approach to very large aliphatic crown ethers (>21-membered) was reported by Gibson *et al.* in 1994 [23]. They synthesized the gigantocyclic species **27a** and the smaller homologous **27b** from deca(ethylene glycol) **25** and its dito-


13
O
N
Tos–N
Tos–N
H
+
O
N
O
Tos–N
3
I
13
O
N
H–N
9
H–N
H
21
22
23
1. KAPA
2. H3O+
NH HN
NH
HN
NH
HN
HN
NH
53
NH
NH
NH
O

Scheme 8.



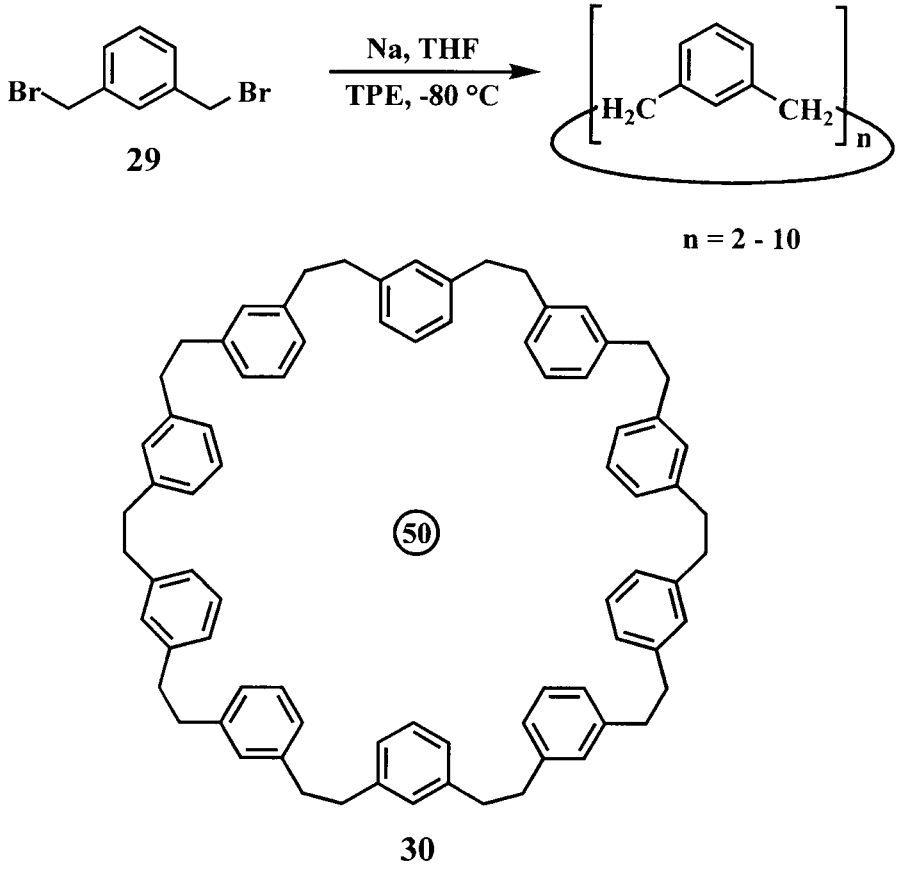
Scheme 9.

sylate **26** in a one-pot process (Scheme 9). **27a** was recrystallized from acetone and characterized by ^{1}H-, ^{13}C-NMR spectra and elemental analysis. The aim of synthesizing very large crown ethers was the fact that these rings are ideally suited for the synthesis of polyrotaxanes **28**.

A larger gigantocyclic crown ether, the 81-membered cyclic heptacosa(oxyethylene), was described by Yang *et al*. in 1996 [24]. They prepared the huge molecule from linear 1-hydro-ω-hydroxy-heptacosa(oxyethylene) by reaction with tosyl chloride under alkaline conditions. After purification the cyclic oligomer crystallized as a twice folded ring.

5. Gigantocycles and Ultracycles with Aromatic Units

The following chapter is focused on gigantocyclic systems which consist of alternating aromatic and aliphatic units. Because of its balanced rigidity these compounds are playing an important role especially in supramolecular chemistry. Although the synthetic routes to the presented examples also led to larger ring systems, we just describe the isolated, purified and well characterized compounds.



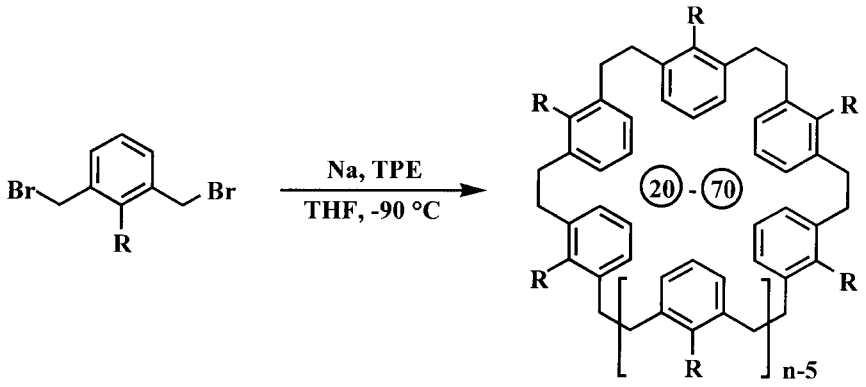
Scheme 10.

5.1. CYCLOPHANES

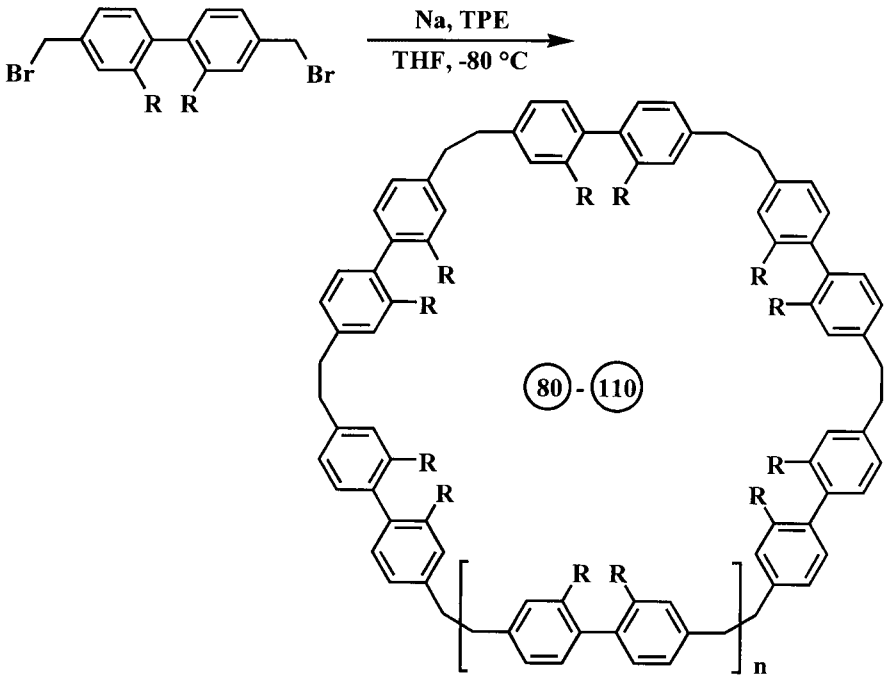
In 1969 Paioni and Jenny isolated a series of [2_n]metacyclophanes [25] in the pure state by Müller-Röscheisen cyclization of α,α'-dibromo-*m*-xylene **29** (Scheme 10). The decamer **30** contains 50 ring atoms and thus may be considered as a gigantocyclic hydrocarbon at the lower borderline. Furthermore, the authors reported on some physical properties, such as melting points and conformational geometries.

In our research group *all*-homocalix[n]arenes [13] **31a**–**31k** with up to 70 ring atoms and biphenylophanes [26] **32a**–**32d** with ring sizes up to 110 ring members have been synthesized (Scheme 11). These cyclic compounds are attractive host systems which can easily be fitted to ionic guests by functionalisation of the methoxy groups. The purification and isolation of a gigantocyclic species was achieved in the case of the 80-membered biphenylophane **32a**.

To create new materials by combining nano-scaled rigid building blocks, Moore and Zhang synthesized the gigantocyclic toroid **33** by ring-closure reaction of a 1,ω-unsymmetrical difunctionalized phenylacetylene precursor in 1992 (Scheme



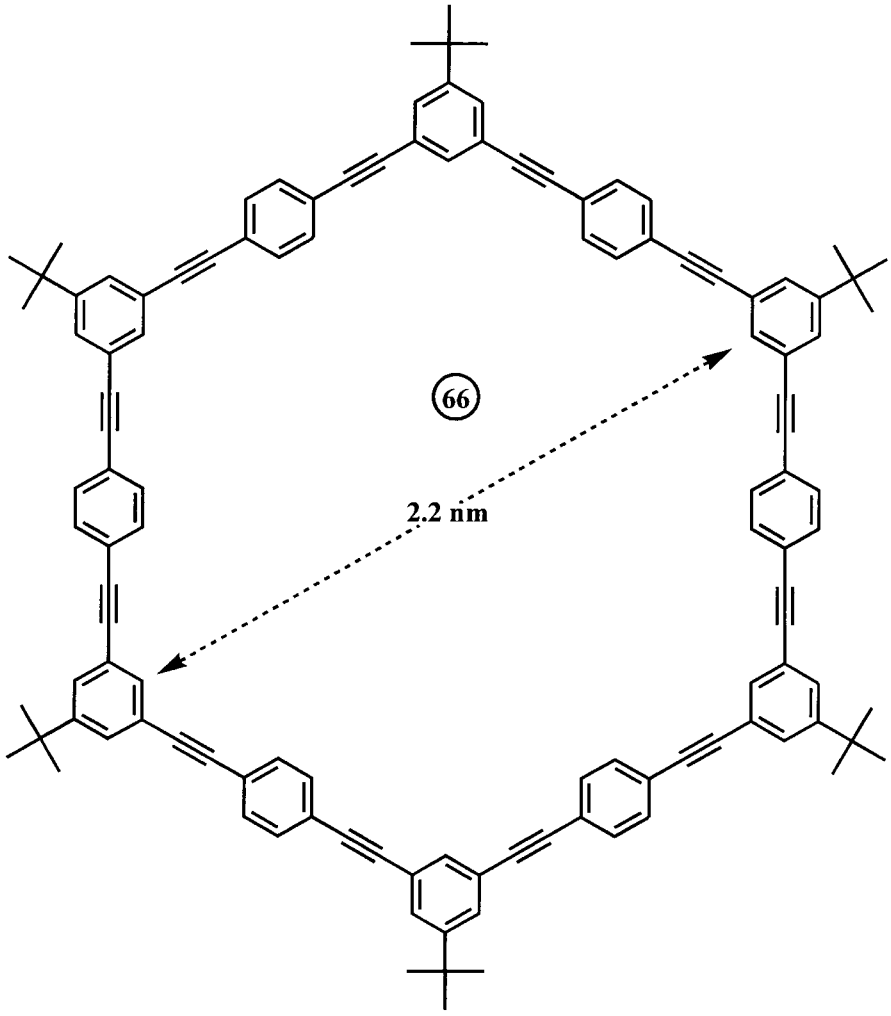
31a - 31k : n = 4 - 14



R = OCH_3
TPE = Tetraphenylethane

32a - 32d : n = 3 - 6

Scheme 11.



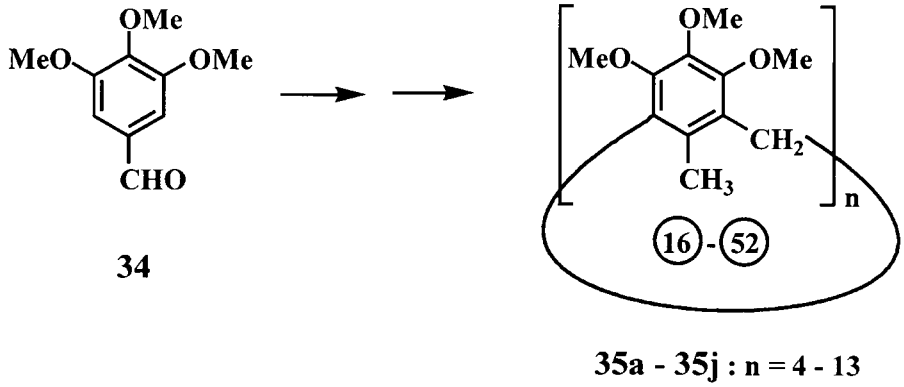
33

Scheme 12.

12) [27]. This preorganized material was obtained in a several step synthesis and yielded the 66-membered gigantocycle **33** in 70%. In comparison to that the one-pot synthesis of **33** led to the cyclic product in only 5% yield.

5.2. CALIXARENES

Usual calixarenes with 4 to 8 phenolic units and 16 to 32 ring members, respectively, are too small to be dealt with in this review. But some calixarene analogues and higher aggregated calixarenes occur in giganto- and ultracyclic dimensions.



Scheme 13.

In 1995 Schilling *et al*. prepared a series of ten persubstituted inverse calixarenes **35a**–**35j** [28] starting from 3,4,5-trimethoxybenzaldehyde **34** (Scheme 13). A conformational analysis was carried out by variable ^{1}H-NMR spectroscopy and MM2 calculations. The 52-membered inverse calix[13]arene **35j** was conformationally highly flexible even at low temperatures.

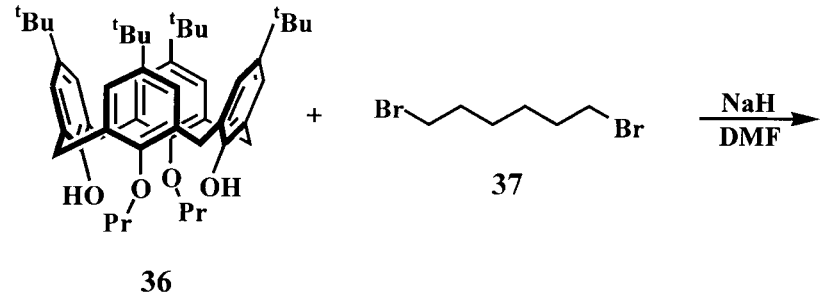
A series of remarkable gigantocyclic and ultracyclic calixarene aggregates [29] was generated by Shinkai et al., in 1996. Three to eight calix[4]arene subunits had been connected to a cyclic array by hexamethylene spacers. The synthesis was carried out in DMF in the presence of NaH starting with 5,11,17,23-tetra-*tert*-butyl-25,27-dihydroxy-26,28-dipropoxy-calix[4]arene **36** and 1,6-dibromohexane **37** (Scheme 14). These reaction conditions are known to produce just *cone* conformation. The 136-membered compound **38f** was isolated in 4% yield, the smaller cycles **38a** to **38e** were obtained in higher yields. Their structures were proved by the combination of NMR, MS and GPC.

5.3. CROWN ETHERS

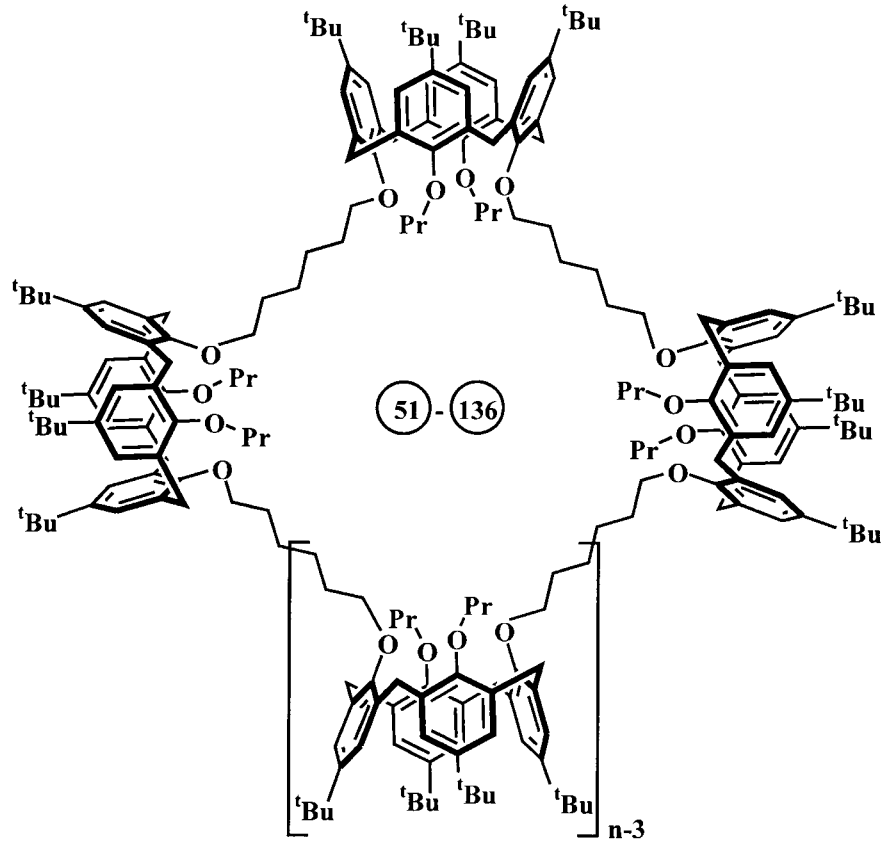
Crown ethers are one of the most important neutral ligands for molecular recognition and for use as building blocks in supramolecular chemistry. Although a variety of crown compounds had been synthesized until now, there are still some peculiarities to be found.

For the synthesis of [2]catenanes Stoddart *et al*. prepared the 66-membered crown ether **40a** in 1995 (Scheme 15) [30]. The formation was achieved by reacting hydroquinone in the presence of tetraethylene glycol bitosylate. After purification the resulting polyether **39** was reacted with resorcinol to give **40a** and **40b** in 11% and 51% yield, respectively.

In the same year Jenneskens *et al*. isolated huge cyclic oligomers by polycondensation of 1,5-bis(1-hydroxy-3,6,9-trioxanonyl)naphthalene **41** and terephthaloyl chloride **42** (Scheme 16) [31]. The crownophanes **43a**–**43e** were formed in

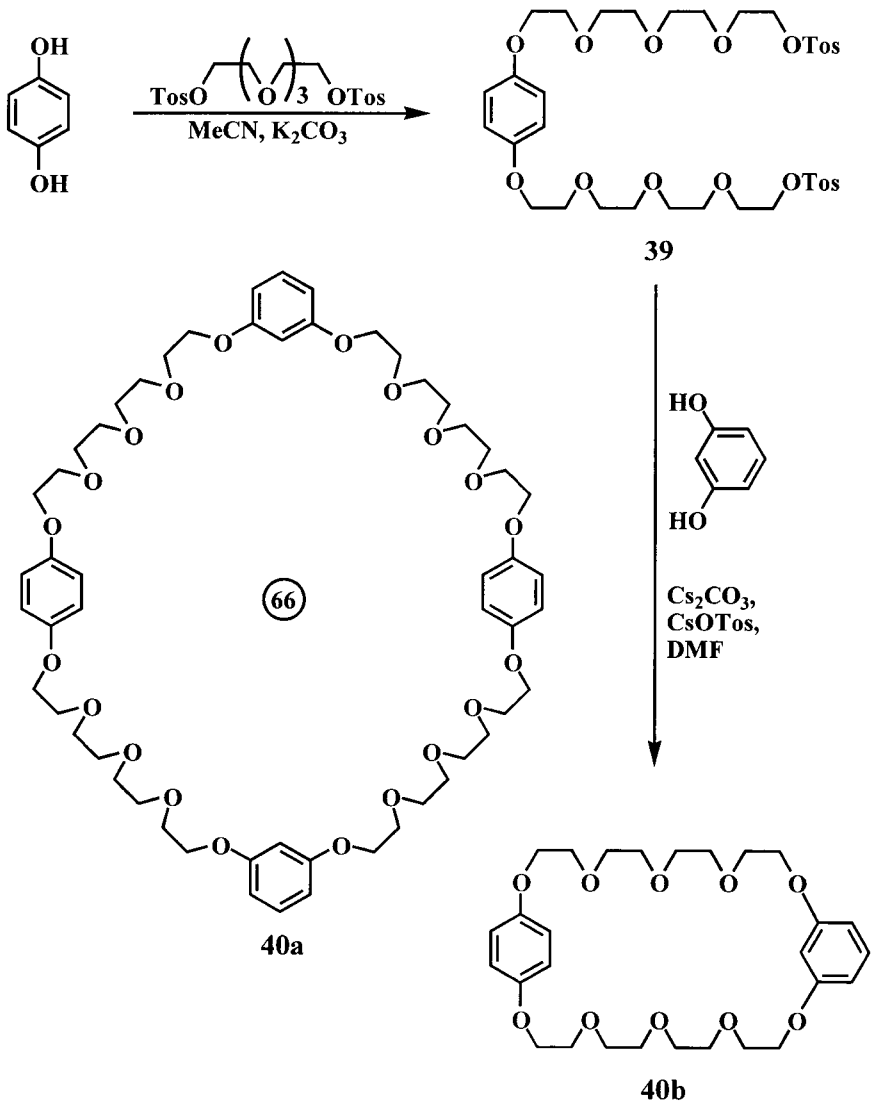


36 **37**



38a - 38f : n = 3 - 8

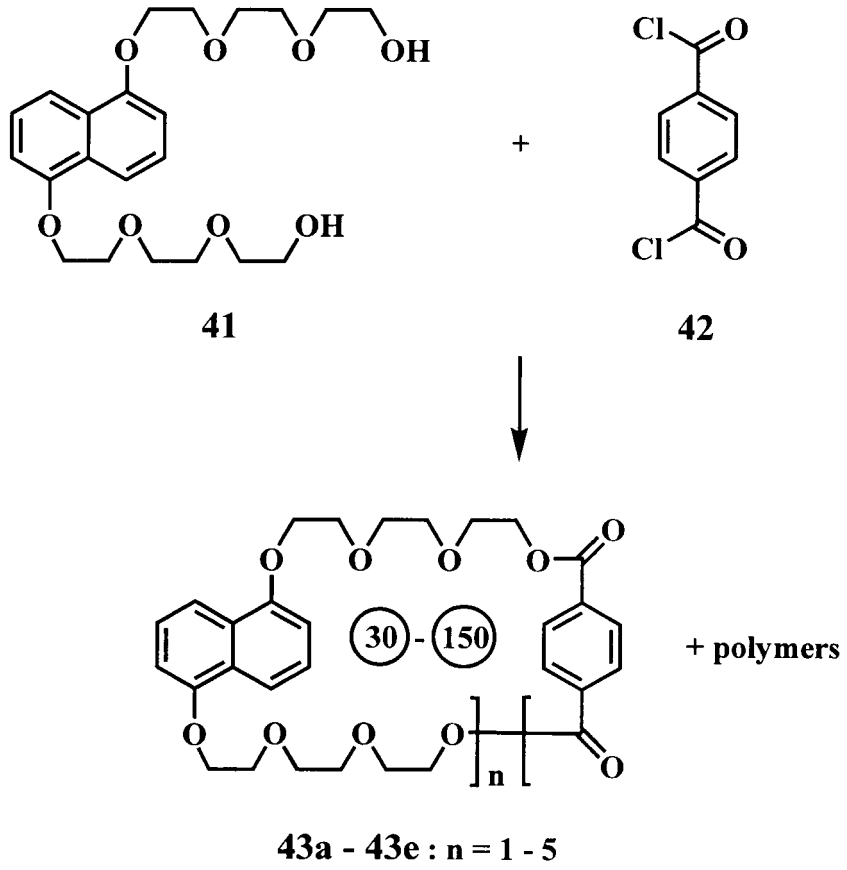
Scheme 14.



Scheme 15.

considerable yields without working under high dilution conditions. Purification was carried out with HPLC. A rationalization for the high overall yield of the very large cycles was given by ^{1}H-NMR conformational analysis: The O-CH_2-CH_2-O units of **41** were presented in a *gauche* conformation. This led to the favourable pre-orientation for an intramolecular ring-closure. The authors explained the high packing ratio in the crystal structure of **43a** (72%) by arene-arene interactions.

Chiral poly(9,9′-spirobifluorene)crown ethers were synthesized by Prelog *et al*. in 1985 [32]. Under phase transfer conditions the condensation of 2,2′-

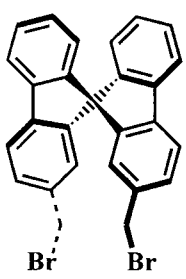


Scheme 16.

bis(bromomethyl)-9,9′-spirobifluorene **44** and the dihydroxyethers **45a** and **45b** mainly produced crown ethers with 26 and 32 ring atoms. As by-products the gigantocyclic and ultracyclic species **46a** and **46b** were obtained in 2% and 0.1% yield, respectively (Scheme 17). These compounds belong to the class of chiral and highly symmetrical molecules with a C_n point symmetry. They are believed to be enantioselective host compounds.

5.4. LACTAMS

In 1992 Hunter and Purvis synthesized the tetrameric gigantocycles **47** and **48** (Scheme 18) [33]. ^{1}H-NMR data for these 64-membered compounds suggested that they adopt very different conformations in solution. So gigantocycle **47** adopts an open structure with all the *i*-phthaloyl subunits in *transoid*-conformation. In contrast, the pyridyl species **48** adopts a folded conformation. This folding gener-



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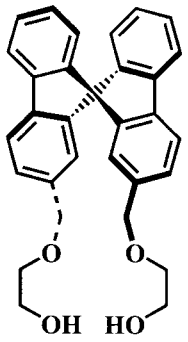
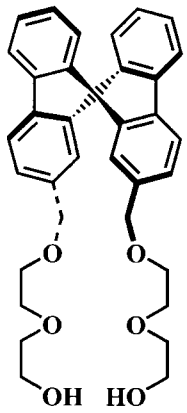
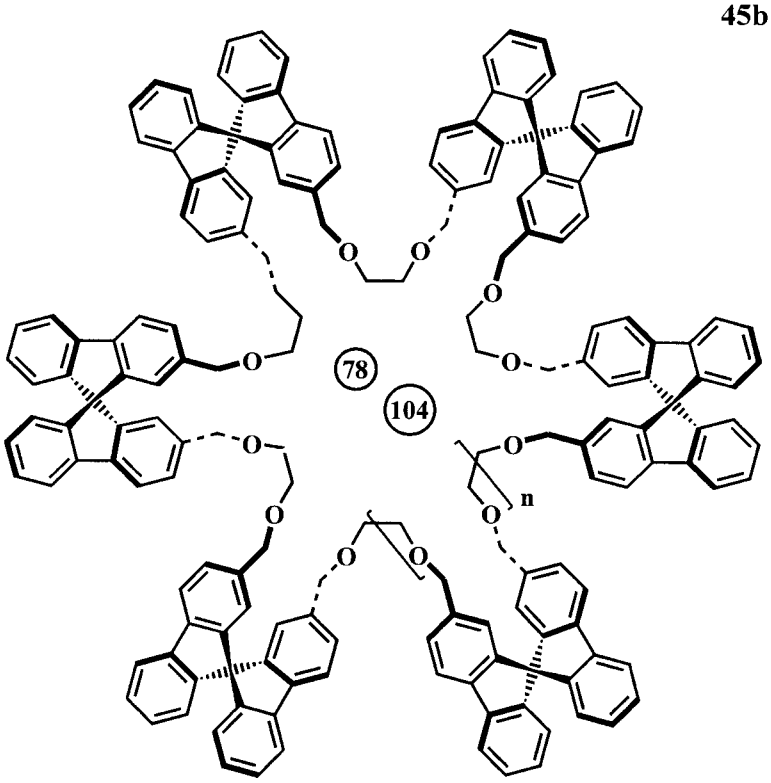


45a

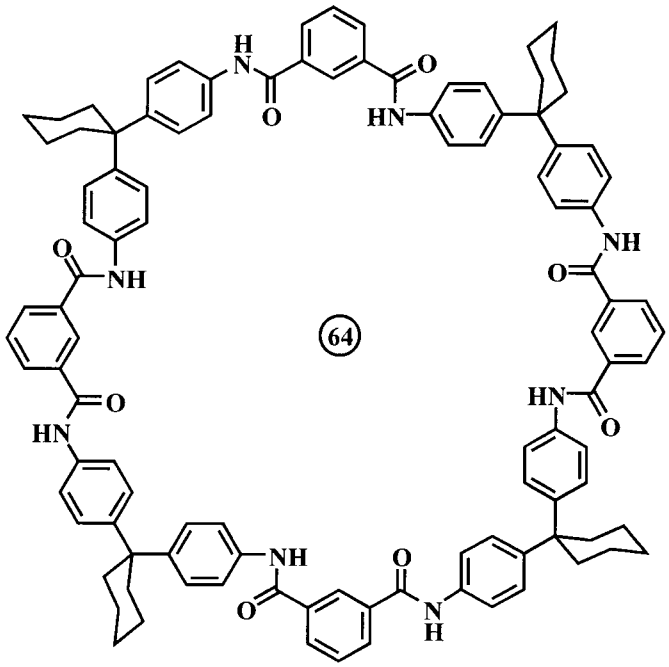


45b

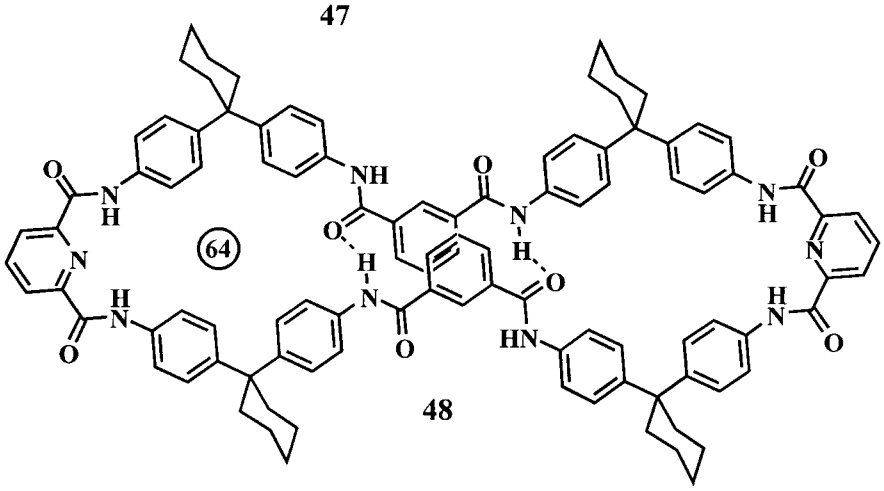


46a : n = 1
46b : n = 3

Scheme 17.



47

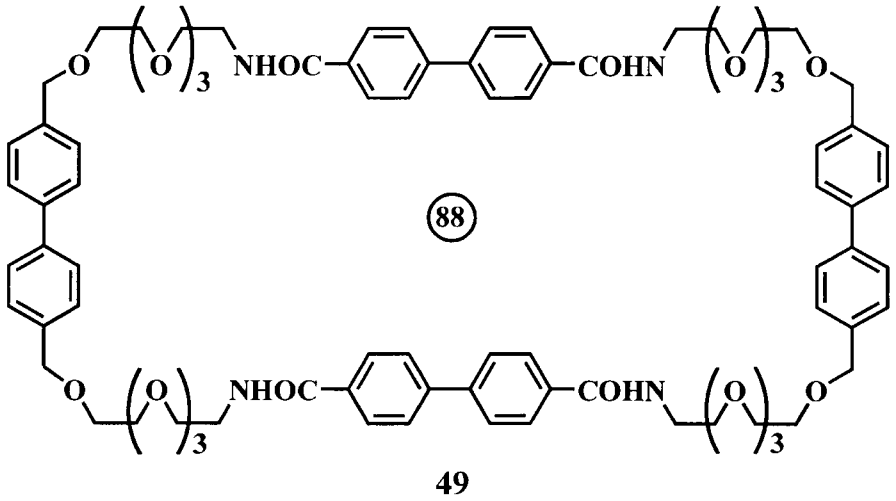


48

Scheme 18.

ates two cavities which are complementary to *p*-benzoquinone serving as a guest. Indeed, the authors observed a complex of **48** and two quinone molecules.

In our working group the transformation of two opposite *i*-phthalamides into the corresponding thioamides has been achieved [34]. This is an example of one of the few sulphur containing gigantocycles.



Scheme 19.

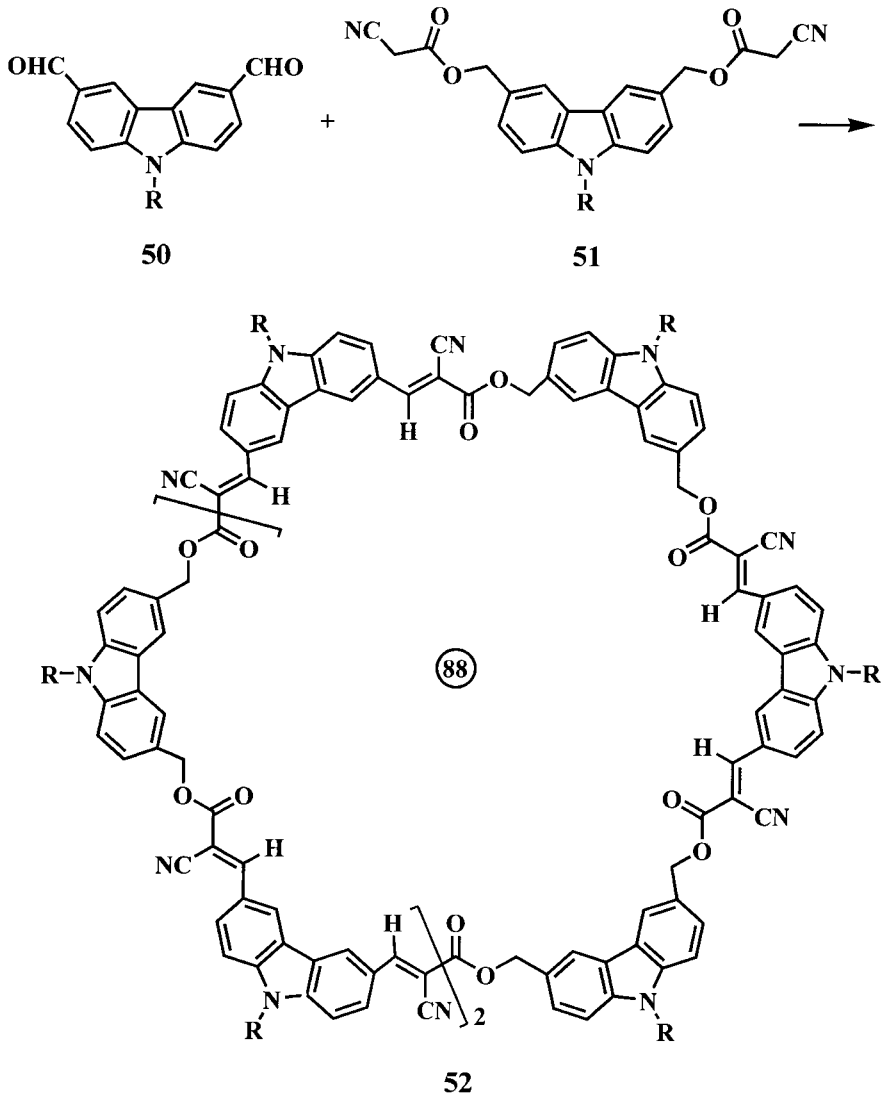
Another lactam-type gigantocycle with 4,4′-biphenyl units was synthesized by Stoddart *et al*. in 1995 [35]. They made a synthetic approach to the construction of water soluble catenanes. Therefore, the formation of [3]catenanes with different partially methylated cyclodextrins was tried out. As a by-product the 88-membered gigantocycle **49** was produced in 2% yield (Scheme 19).

6. Gigantocycles with Heteroaromatic Units

In this section we will report on gigantocycles and ultracycles with nitrogen containing arene units. The introduction of nitrogen by carbazole, porphyrin or phenanthroline moieties leads to fascinating geometries. Thus, examples of rigid structures or the formation of molecular knots will be given.

6.1. CARBAZOLE GIGANTOCYCLES

Polymers and gigantocyclic molecules for nonlinear optics (NLO) and photorefraction have been synthesized by Zhang *et al*. in 1996 [36]. They used carbazole compounds which have multifunctional properties, such as photoconductivity and unique second-order NLO properties. The synthesis of main-chain polymers containing carbazole substituted with two acceptor groups mainly led to the 88-membered molecule **52** (Scheme 20). The starting compounds **50** and **51** were obtained by modification of unsubstituted carbazole. **52** was prepared by Knoevenagel condensation in 94% yield.

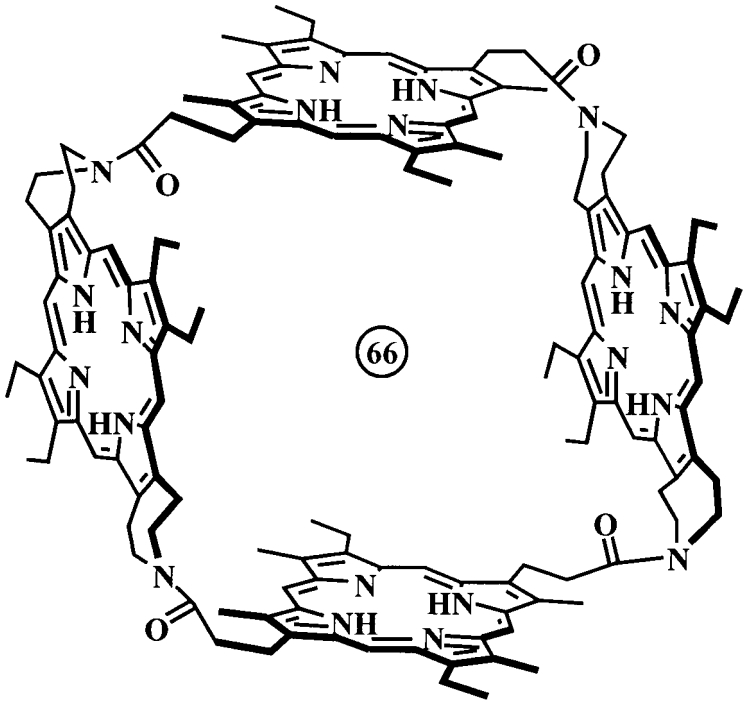


Scheme 20.

6.2. PORPHYRINS

From the multitude of gigantocyclic porphyrin aggregates [37] only two examples will be emphasized.

In 1987 Dubowchik and Hamilton reported on the synthesis of a tetrameric porphyrin with 66 ring atoms [38]. This species can act as a model of multi-tetrapyrrole aggregates in biological systems. The authors prepared **53** by using rigid and doubly functionalized porphyrin spacers (Scheme 21). They chose this arrangement to provide symmetrical structures in which all porphyrin units, and



53

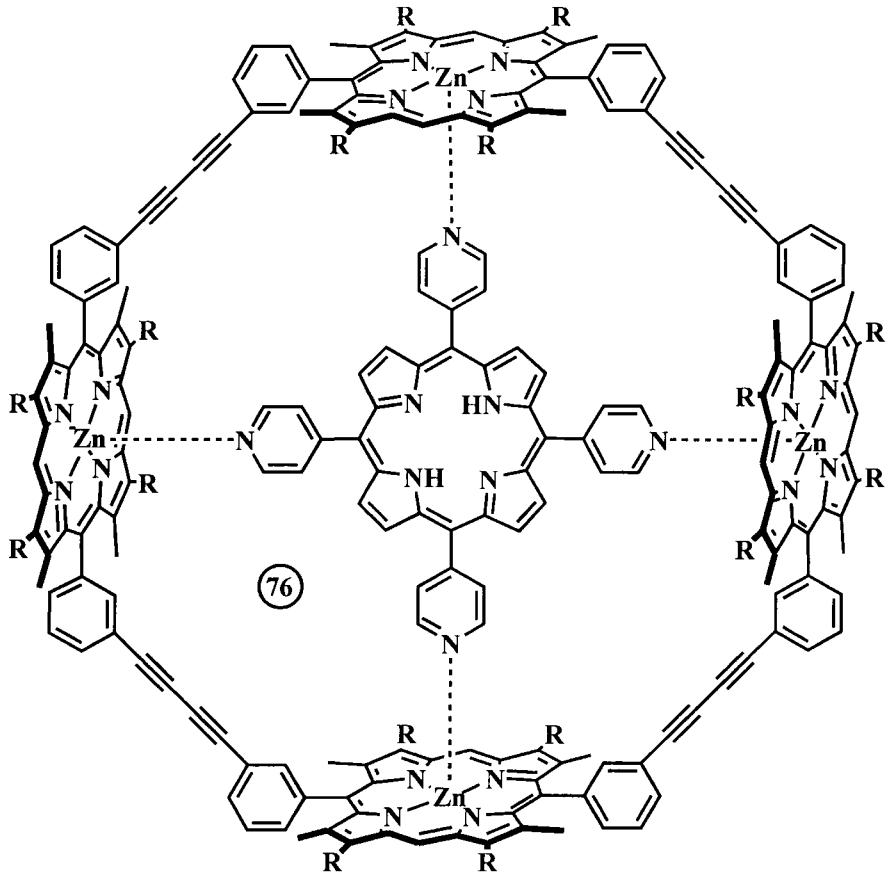
Scheme 21.

thus their chelated metals, can interact. Furthermore, the cavity built is capable of host-guest binding to organic substrates. Yet the cycloporphyrin **53** can exist in a number of possible conformations. In chloroform the central cavity in **53** collapses to a folded or rhombohedral structure.

In 1995 Sanders *et al*. presented a photoactive aggregation of five porphyrins [39]. Their aim was to get further information about energy and electron transfer in natural photosynthetic active reaction centres. Structures with several porphyrin chromophores can act as models for light collecting antennas. For the understanding of photophysical properties rigid compounds are crucial. Thus, the authors synthesized the 76-membered aggregate **54** in high yields by using the central tetrapyridinoporphyrin as a guest template which is finally held in a symmetrical conformation by a multitude of supramolecular interactions (Scheme 22).

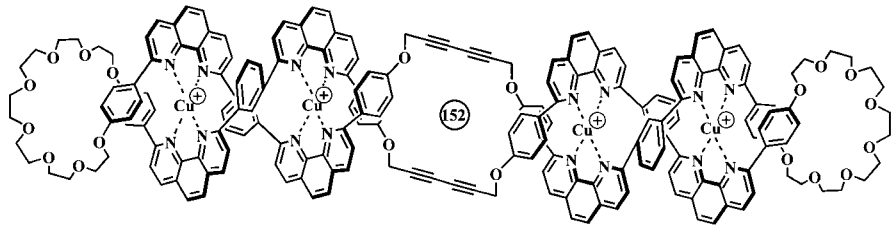
6.3. MOLECULAR KNOTS

Sauvage *et al*. prepared molecular composite knots from copper(I)-assembled 1,10-phenanthroline precursors via Glaser coupling in 1996 [40]. They obtained a variety of gigantocyclic and ultracyclic knotted structures by combining two tied open-chain fragments in a cyclodimerization reaction. Composite knots, as



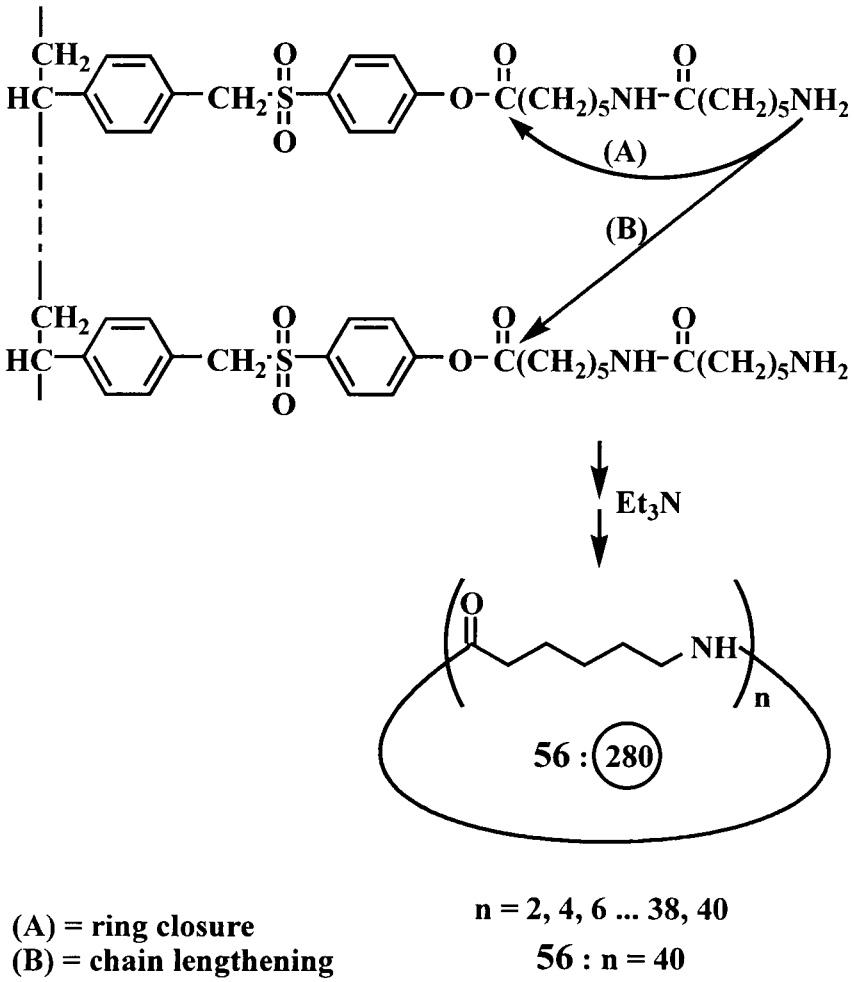
54 : R = $CH_2CH_2CO_2CH_3$

Scheme 22.



55

Scheme 23.



Scheme 24.

opposed to prime knots, consist of two trefoil knot units. The enantiomeric occurrence of the helicoidal dicopper(I) precursor complexes yields various topological diastereomers. Thus, the 152-membered ultracycle **55** is only one possible diastereomer (Scheme 23).

7. Ultracycles in Polymer Chemistry and Nature

Ultracycles, which we would like to define as cyclic molecules with 100 and more ring members, are even less known in structure perfect form than their lower mass analogs. Characteristically, they mainly occur in polymer chemistry or in nature in the form of cyclic proteins, saccharides or circular DNA. Until today the synthesis, isolation and characterization of these molecules challenges many research groups.

7.1. CYCLIC POLYMERS

In 1994 Rothe *et al*., reported on a synthetic route to ultracyclic oligomers [6]. Polycondensation and following cyclization within netted, polymeric carriers led in the case of ϵ-aminocaproyl-ϵ-aminocaproic acid to high-membered cycles (Scheme 24). At the time of the ring closure (A) these molecules were separated from the polymeric carrier. On the other hand linear oligocondensation products, which are formed by the reaction (B), still remained on the carrier. Thus, the separation of cyclic molecules was easily achieved. The largest monodisperse ring molecule the authors isolated and characterized in this reaction was the 280-membered caprolactam cyclo(tetracosamer) **56**. Furthermore, ultracycles with up to 700 ring members were synthesized by Rothe *et al*. by cyclooligomerisation of deca-ϵ-aminocaproic acid. The 700-membered caprolactam hectamer is the largest known ring molecule to date. It has a molecular weight of 11315 g/mol.

Further cyclopolymers with gigantocyclic and ultracyclic dimensions were mainly synthesized by the method Rothe *et al*. used. A review on this class of molecules was published by Semlyen in 1996 [41].

7.2. NATURALLY OCCURRING ULTRACYCLES

From the multitude of cyclic proteins only two examples are given to explain their significance.

In 1981 Wirtz *et al*. reported on the complete primary structure of the phosphatidylcholine-transfer protein from bovine liver [42]. The protein consists of 213 amino acids and contains two disulfide bridges at Cys^{17}- Cys^{63} and Cys^{93}-Cys^{207}. Thus, ultracycles with 143 and 347 ring atoms are formed.

Knossow *et al*. analyzed the X-ray structures of esterase-like catalytic antibodies in 1997 [43]. Both polypeptide chains of each antibody's domains that constitute the catalytic site are internally linked by a disulfide bridge. So both, the light and the heavy chains domains, are ultracyclic rings that encompass about 100 amino acid residues. Each ring is about 300-membered.

A variety of ultracyclic molecules exists in the form of polynucleotides. The occurrence of circular DNA has been known since 1958 [44]. In common viruses and bacteria the genetic information is encrypted on circular polynucleotides. For example, the chromosome of *Escherichia coli* is just one circular DNA molecule with 4.7×10^6 base pairs. An overview on this fascinating research field was published by Stasiak in 1996 [45].

Beside the well known cycloamyloses with up to 26 α(1-4)-linked glucose residues [46] (e.g. cyclodextrins) a multitude of much larger ultracyclic polysaccharides has already been discovered. For instance, the extracellular polysaccharide schizophyllan produced by the fungus *Schizophyllum commune* consists of (1-3)-linked β-D-glucans. A summary on cyclic polysaccharides was published by Brant and McIntire in 1996 [47].

8. Cyclic Coordination Compounds

Although transition metal clusters can reach gigantocyclic sizes we just want to restrict our review on coordination compounds containing palladium or platinum and organic ligands. The following examples are noteworthy because of their rigidity and their appealing structures.

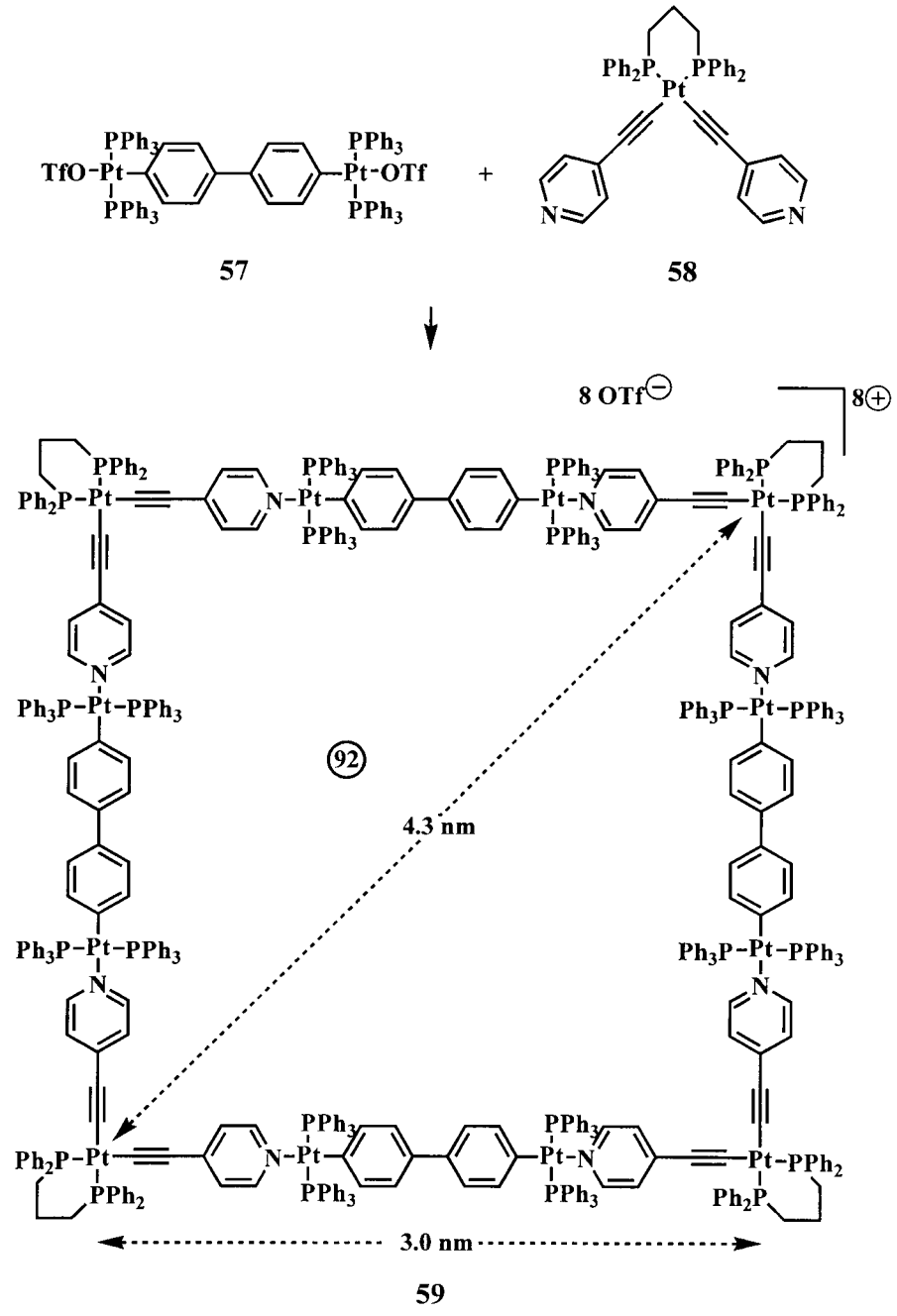
A self-assembly of nanoscale organoplatinum gigantocycles was carried out by Stang *et al*. in 1996. The authors described the synthesis of two 92-membered coordination compounds [48]. The reaction of the bistriflate complex **57** with the free ligand **58** quantitatively yielded the so-called molecular square **59** (Scheme 25). The dimensions of **59** are 3.0 nm along the edge and 4.3 nm diagonally, it is generally planar and rigid. The complex **59** is of interest with regard to its potential nonlinear optical and electronic properties.

The 84-membered gigantopolycycle **60** was synthesized by Fujita *et al*. in 1995 via self-assembly of four ligands derived from triazine and six palladium cations (Scheme 26) [49]. The crystal structure of a smaller homologue showed a tetrahedral symmetry and a large central void, in which guest molecules can be accommodated. Thus, **60** should also occur in an adamantane-like three-dimensional cage geometry with an intramolecular Pd-Pd distance of about 5 nm.

Another synthetic approach to a new gigantocycle (**63**) with expectedly interesting physical and chemical properties, e.g. liquid-crystalline or catalytic features, is currently under investigation by Praefcke *et al*. (Scheme 27) [50]. Two rodlike bisimines, initially linked by an ortho-metallation reaction [51] gave rise to the very large, flat metal organyl **61** as the starting material in this sequence. The macro*mono*heterocycle **61** was transformed into the *tris*macroheterocycle **62**. The bridging clamps in **62** were opened by a twofold cleavage reaction [52], which was applied to the central 34-membered tetrametalloheterocycle leading to the new 70- or 76-membered giganto-heterocyclic type of molecules **63**.

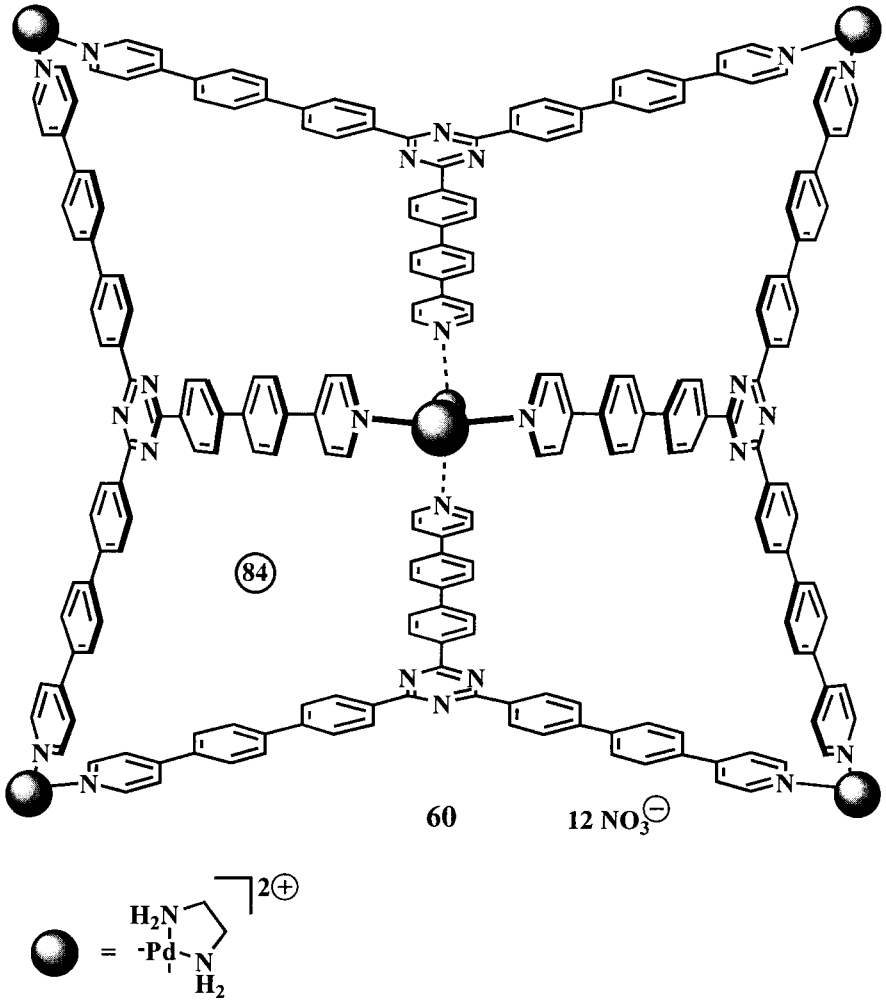
9. Conclusions

In this article we attempted to order a multitude of known cyclic compounds by defining the families of gigantocycles and ultracycles. The rather formal and admittedly imprecise frontiers between them seem to be justified from a heuristical point of view and prove to be not only practical in this review. The presented selection of ring compounds demonstrates the increasing importance of these molecules in different topics of organic chemistry, supramolecular chemistry, biochemistry, biology and polymer sciences. Crown ether gigantocycles, for instance, are needed in the synthesis of catenanes and rotaxanes. New high-membered cyclic host systems are prepared to optimize the complexation selectivity and efficiency towards ionic guests. Moreover, materials with special physical properties, such as nonlinear optics, may consist of giganto- or ultracycles. Models for biological complex systems are developed by preparation of gigantocyclic porphyrin aggregates or phospholipids. Furthermore, investigations in polymer improvement are based on creating


TfO-Pt-OTf
PPh3
Ph2P
PPh2
Pt
N
+
57
58
8 OTf⊖
8⊕
Ph2P-Pt
N-Pt
Pt-N
Pt-PPh2
Ph3P-Pt-PPh3
92
4.3 nm
3.0 nm

59

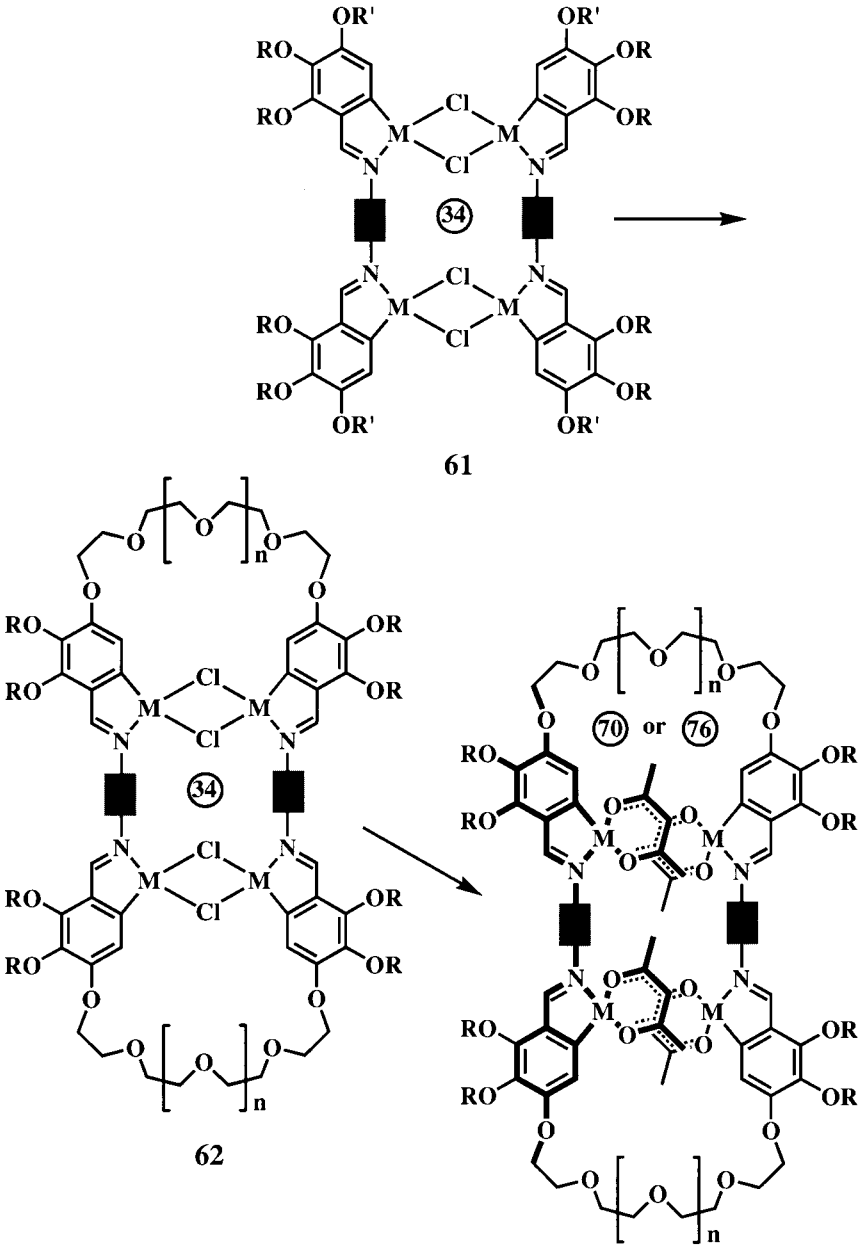
Scheme 25.



Scheme 26.

giganto- and ultracyclic oligomers. Although there are many efforts to synthesize and characterize these compounds, the majority are still found in natural organisms. Examples are cyclic peptides, saccharides and polynucleotides.

There is a variety of gigantocyclic and ultracyclic examples with different, sometimes astonishing properties, but these fascinating molecules have one thing in common: they represent the border area between molecular and nano-scale dimensions. Therefore, they are also important for understanding the fundamental principles of the increasing research field of nanochemistry.


OR'
RO
OR
Cl
M
N
34
70 or 76
61
62
63
R = long alkyl, R' = protecting group, n = 1 or 2,
M = Pd or Pt, = spacer (e.g. 4,4'-terphenylene)

Scheme 27.

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