# 1. Introduction

Shape persistent macrocycles have been developed into a field of major scientific importance over the last two decades.[1] In contrast to flexible, monodisperse cycles like the famous [(CH$_2$)$_n$]-series they do not attain coiled conformations similar to those of polymer chains but rather have a non-collapsable framework.[2] Typically this framework is hexagonal. In order to ensure the reduced conformational rigidity, these hexagons' backbones consist of unsaturated atoms, commonly sp$^2$ and sp-hybridized carbons. Because of these structural characteristics, shape-persistent macrocycles have an interior and an exterior which by the specific substitution with functional groups or complexation sites can be selectively addressed. Like for the wealth of liquid crystalline compounds, the rigid part of macrocycles can be considered a mesogen and causes them to form ordered mesophases. This led to the expectation that hexagonal macrocycles of the described sort should have a tendency to form, e.g., columnar phases in bulk.
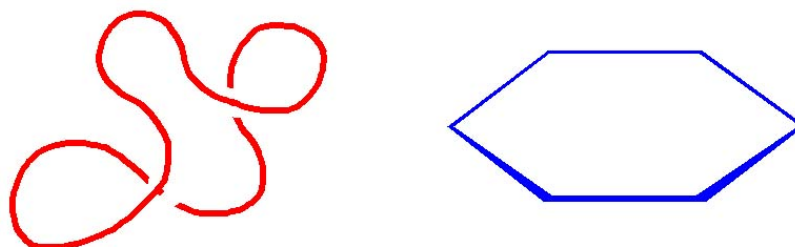


Figure 1.      Cartoon representation of a flexible, e.g., polymethylene cycle (left) and its hexagonal, shape-persistent siliby with its distinctly different interior and exterior (right).

Transition metal mediated cross-coupling reactions, like the Suzuki, Stille, or Sonogashira reaction allow for C-C bond formation between unsaturated carbons and are therefore ideal tools for the synthesis of macrocycles.[3] They have thus been widely and successfully applied. All these approaches can be divided into two main classes which differ by the number and size of building blocks used for the cycle synthesis: (a) the statistical reaction between two or more building blocks is most oftenly encountered. It gives isolated product yields of around 15-40%, and (b) the cyclization of a bisfunctionalized oligomer, a direct cycle precursor, giving significantly higher yields of macrocycles (75-90%) (Figure 2).[1b-d]
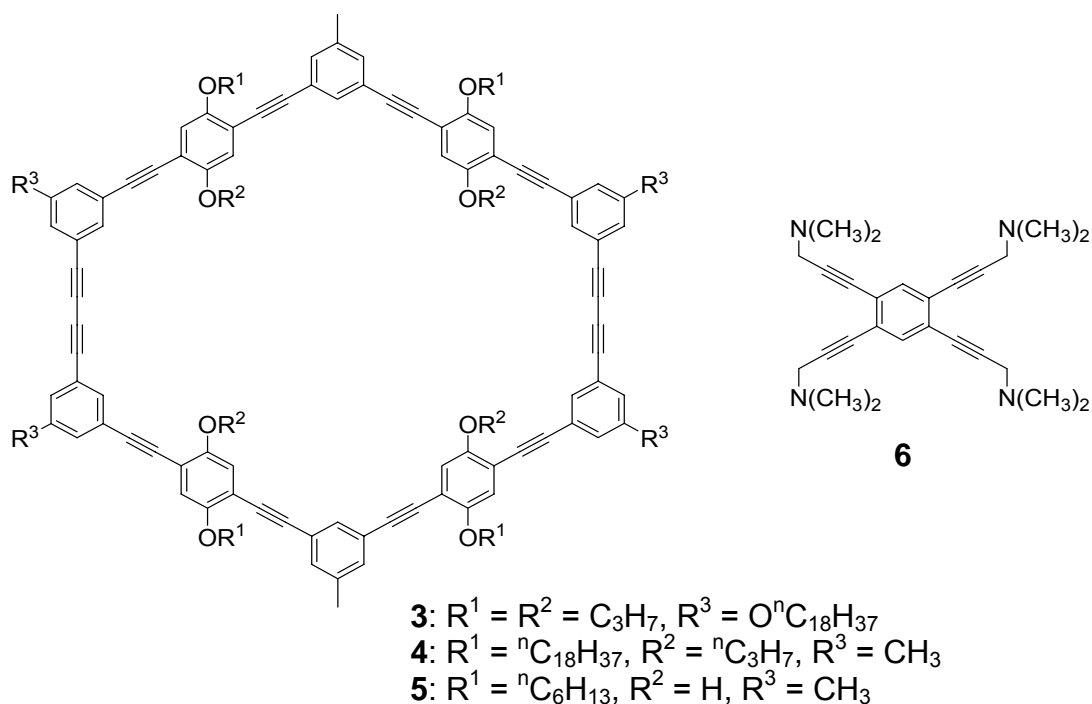
Figure 2.      Ring closure reaction from (a) two (or more) precursors and (b) from one precursor.

Although the second route provides the highest cyclization yields, it has not been used so oftenly. Its main drawback lies in the necessity to prepare the relative complex final precursor for cyclization. This is a time consuming process which involves repetitive protecting, deprotecting and coupling steps. The synthesis of macrocycles from two precursors, however, is more often used since fewer synthetic steps to the precursors are required making this procedure more time-efficient. High dilution techniques are used in both syntheses in order to favour cyclization over linear oligomerization.[1c] Hensel et al. used the two different approaches for construction of macrocycle **2**, and they can be easily compared.[4] The first route, when two precursors **1b** were combined, provided **2** in 17% yield, whereas the cyclization of precursor **1c** gave the same macrocycle **2** in 68% yield (Scheme 1). The total yields calculated from the last common intermediate **1a** amount to 11% and 24% which favour the later route involving six instead of four steps.



**1a**: X = TMS, n = 3

**1b**: X = I, n = 3

**1c**: X = I, n = 6

R = $C_6H_{13}$

**2**
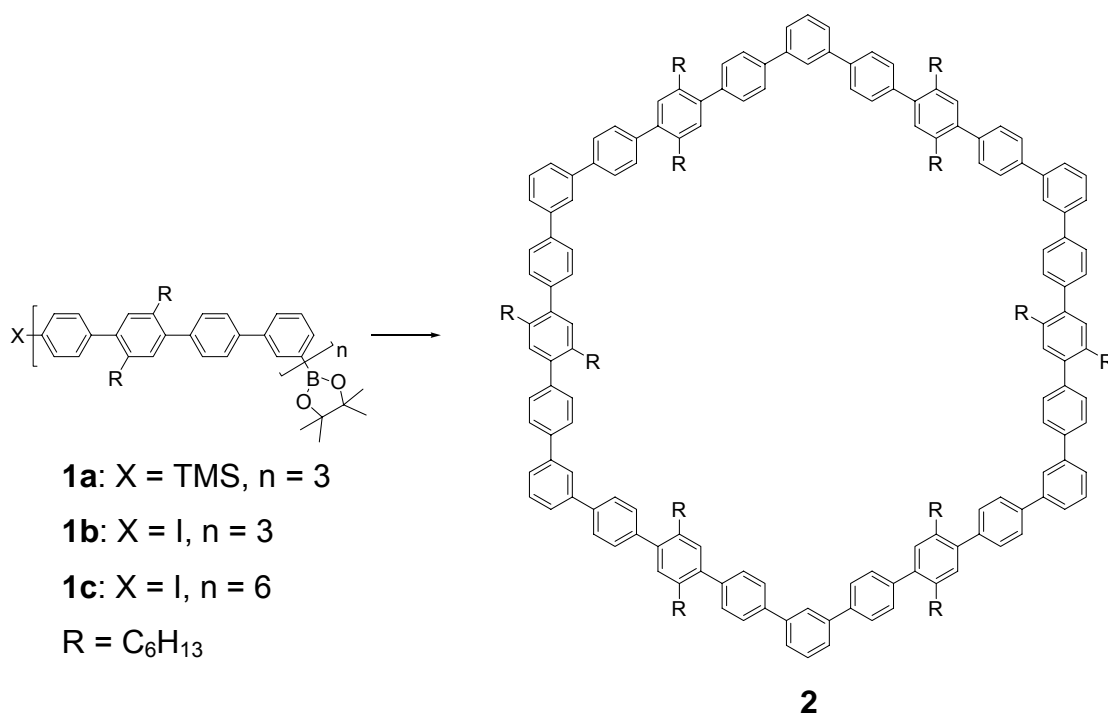
Scheme 1.    Hensel's approach to macrocycle **2**.

The properties of shape-persistent macrocycles depend on the nature of both their interior and exterior substitution patterns. Of utmost importance in this regard is their peripheral substitution with flexible chains in order to keep the cycles soluble, characterizable, and processable. This is why all representatives of this class of compounds, irrespective of their anticipated use or function, carry at least a few flexible chains like straight or branched alkyl, oligoethyleneoxy, and alike. The pronounced influence the substitution pattern can have on properties is nicely illustrated by the macrocycles **3** and **4** published by Höger (Scheme 2). [5] Both compounds match the design principle of discotic liquid crystals, but only one of them, **4**, actually exhibit LC behavior. In solid state the interior of the macrocycles **3** and **4** are filled with alkyl chains. They point outward in **3** (back folding of the alkyl chains is impossible) and the interior of one ring is filled by the alkyl chains of neighbouring rings, which results in crosslinks of macrocycles. In **4** there is an intramolecular interaction between the rings and the alkyl chains. In this case the molecules become mobile when the alkyl chains melt and can form the liquid crystalline phase by parallel arrangement. In **3** because of the network formation the mechanical coupling of the rings doesn't brake down before it is completely molten (Scheme 2).



**3**: $R^1 = R^2 = C_3H_7$, $R^3 = O^nC_{18}H_{37}$
**4**: $R^1 = {}^nC_{18}H_{37}$, $R^2 = {}^nC_3H_7$, $R^3 = CH_3$
**5**: $R^1 = {}^nC_6H_{13}$, $R^2 = H$, $R^3 = CH_3$

Scheme 2.   Höger's macrocycles with the same backbone but different substitution patterns exhibiting different LC properties.

Because of the cycles' inner void with a diameter on the order of 1 nm to a few nm, they can accommodate guest molecules. Macrocycle **5**, for example, acts as a host and easily forms relatively stable host/guest "inclusion" complexes with guest molecule **6** (Scheme 2). [6] The host's phenol hydrogen bond donor groups and hydrogen bond accepting amine groups of the guests have a near-perfect match.

The introduction of a heteroatom into the macrocycle's backbone should be of particular interest because of the potential biological, chemical, physical functions this may affect. An interesting property of such macrocycles could be the combination of their ability to form complexes with transition metal on one hand and their ability to aggregate in ordered superstructures on the other. This could eventually lead to tubes of macrocycles filled with metal ions. Reduction of the metals inside the tubes opens the exciting possibility to create atomically thin metal wires held together by a confinement provided by the cycles (Figure 3c-e).

Another vision in the area of shape persistent macrocycles with metal complexation sites is the creation of linear polymers in which the cycles are held together by intermolecularly complexing metal centers (Figure 3f). The orthogonal sequence of macrocycles in such a polymer not only would render its solubility higher than normal but, more importantly, the metal at defined distances should result in materials with an unusually high chargeability. These coordination polymers are interesting for novel applications as electronic and magnetic materials.[7]
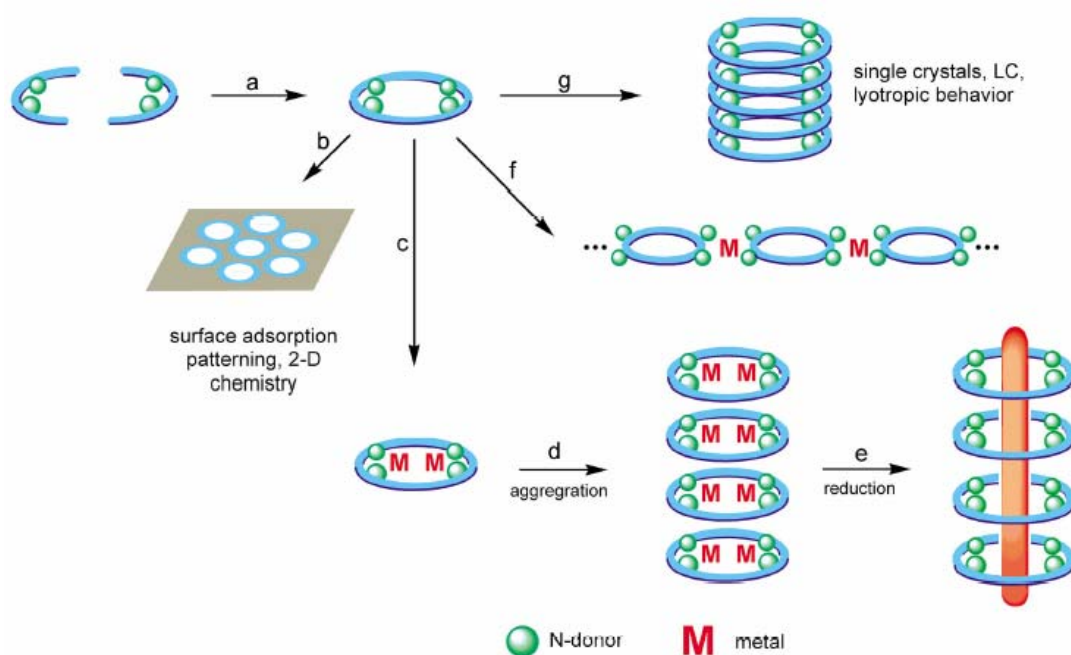


Figure 3.     Directions for research with shape-persistent macrocycles containing donor sides.

As indicated above, shape persistent macrocycles have a high tendency to self-organise through π–π interactions into supramolecular architectures (Figure 3g). Of special interest are columnar structures because they have the potential for unique transport properties or to form a template for atomically thin metal wires. [8]

Most of the shape-persistent macrocycles known today actually form channel structures in the single crystal. Unfortunately, strictly cylindrical arrays where one cycle is positioned directly on top of the other are rather seldomly encountered. Two different stacking motifs are normally observed: offset face to face which is very oftenly the case or face to face quite rare but very interesting because forms structures with empty channels (Figure 4).
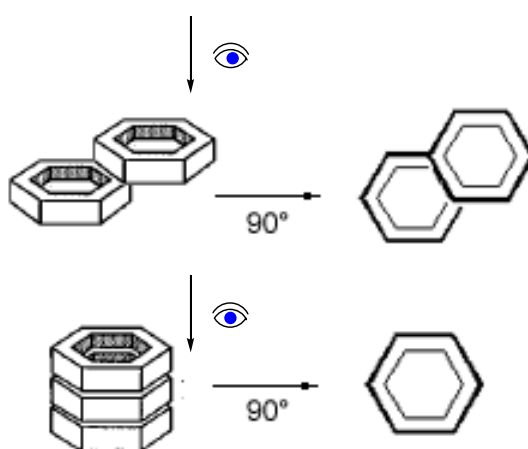


Figure 4.    Two different packing motifs commonly observed in single crystals of shape-persistent macrocycles: offset face to face (top) and face to face (bottom).

Moore and Tobe have shown that phenylacetylene and phenylbutadienyl macrocycles aggregate in solution through π-π interactions.[1d], [9] Not surprisingly this behavior strongly depends on the electronic structure of the macrocycles used and the solvent. Recently, Höger reported a promising approach into cylindrical stacks by attaching flexible oligomeric chains to two opposite corners of hexagonal cycles.[10] A different approach into this matter would be to try to force the cycles into the desired order by attaching them as pendant substituents to a polymer chain. If designed properly the polymer chain could reduce the packing options.

Another very interesting property of these macrocycles is their tendency to give regular 2D structures when a solution of macrocycle is adsorbed to the surface of, e.g., highly oriented pyrolytic graphite (Figure 3b).[1c] For some representatives it

was shown that they can form highly ordered monolayer films. This is to be seen in the on going activity to arrive at surface with regular patterns for applications in, e.g., sensor technology.

Motivated by the novel properties and potential applications of these molecules, some of which are illustrated in Figure 3, much effort has been invested in developing efficient synthetic access. A large variety of shape persistent macrocycles with different size, shape, substituent pattern, and different donor atoms have been reported in the last years.[1c]