

Interlocked and Intertwined Structures and Superstructures

David B. Amabilino and J. Fraser Stoddart*

School of Chemistry, The University of Birmingham, Edgbaston, Birmingham B15 2TT, UK

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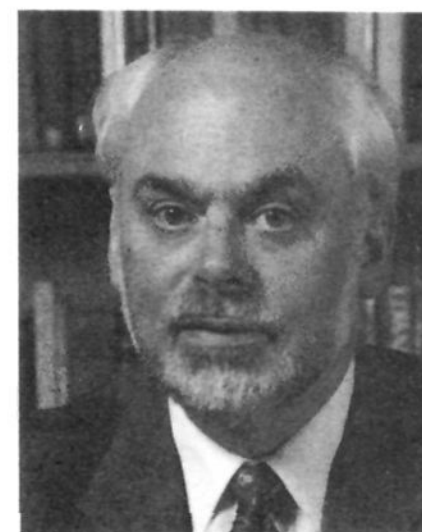
I. Introduction

"How can anyone not find these beautiful molecules fascinating?!"¹

Scientists draw great inspiration² from the objects that surround them in the world at large, whether they come from mother nature, or art³ or architecture,⁴ or wherever else. Comparisons with everyday objects often aid us in understanding and communicating about systems in action, as well as in the conception and realization of new chemical designs.⁵ The "chair" and "boat" forms of the cyclohexanes,⁶



David B. Amabilino was born and raised in Hertfordshire, close to the northernmost outskirts of London, England. His B.Sc. (1988) and Ph.D. (1991) were earned at Royal Holloway and Bedford New College (University of London), the latter in the research laboratories of Dr. M. C. Grossel (now at the University of Southampton). The subject of his Thesis was the synthesis and properties of dendritic macromolecules and podands. Dr. Amabilino then worked for three years as a postdoctoral fellow in the research laboratories of Professor J. F. Stoddart at the University of Birmingham, where he studied the self-assembly of catenanes and rotaxanes. His major achievement during this period was the self-assembly of the [5]catenane olympiadane. Presently, he is concerned with the metal ion-templated synthesis of photoactive interlocked compounds as models of photosynthesis in the research laboratories of Dr. J.-P. Sauvage at the Université Louis Pasteur in Strasbourg.



J. Fraser Stoddart was born and educated in Edinburgh, Scotland. He has been Professor of Organic Chemistry at the University of Birmingham since 1990. He was appointed Head of the School of Chemistry there in 1993. Previously, he was a Reader in Chemistry at the University of Sheffield for eight years, where he was also Lecturer from 1970 to 1982. From 1978 to 1981, he was seconded from the University of Sheffield to the ICI Corporate Laboratory in Runcorn. He gained his B.Sc. in 1964, his Ph.D. in 1966, and his D.Sc. in 1980, all from the University of Edinburgh. He was elected to the Fellowship of the Royal Society of London in 1994. He has received many awards, including the International Izatt–Christensen Award in Macrocyclic Chemistry in 1993, and has been a distinguished lecturer in many universities all around the world. Professor Stoddart has published more than 350 communications, papers, reviews, and monographs and has wide ranging interests in supramolecular science. He is at present developing the transfer of concepts such as self-assembly between the life sciences and materials science.

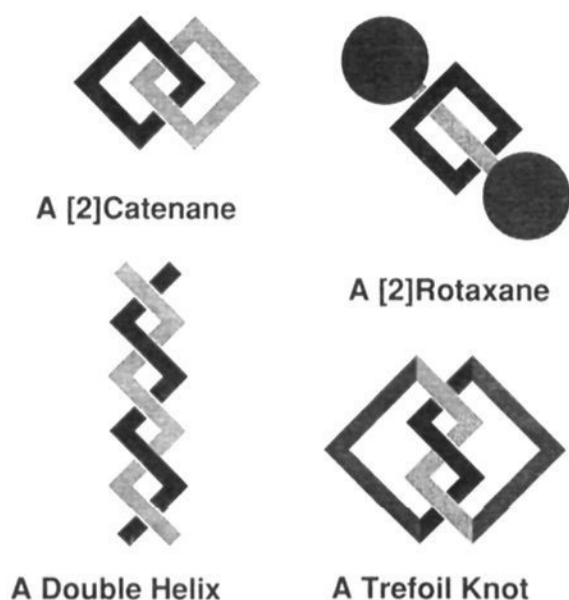


Figure 1. A simple collection of interlocked molecules and intertwined supermolecules.

and Emil Fischer's "lock-and-key" hypothesis of enzyme action⁷ are two examples of well-established teaching aids. Dendrimers⁸ and arborols⁹ cannot fail but to be likened to the trees of the natural world, while fullerenes⁴ derive their name from architecture and C₆₀, sometimes referred to as "footballene", is most easily envisioned as a soccer ball. There has even been a suggestion¹⁰ of "molecular shish-kebabs"! Interlocking and intertwining objects are all around us. The laces on our shoes contain threads which are woven together to form the laces, which we then tie in the form of a "knot" (in layman's terms!). Chains of all kinds are commonplace. Yet, until relatively recent times, the existence of interlocked and intertwined structures at the molecular level had not been realized in the laboratory. Catenanes,¹¹ rotaxanes,¹² knots,^{13,14} and helices¹⁵ (Figure 1) have captured the imaginations of a wide spectrum of the scientific community. This interest is not only because of their undisputed beauty,¹⁶ but also a result of the potential applications that might be addressed by incorporating the aspect of entanglement into chemical systems. Perhaps for this reason, as well as for the improved methods of their synthesis, the last few years have witnessed an explosion in research carried out into the creation of interlocked and intertwined chemical structures and superstructures.

Catenanes,¹⁷ from the Latin *catena* meaning chain, are molecules which contain two or more interlocked rings, which are inseparable without the breaking of a covalent bond. Rotaxanes, from the Latin *rota* meaning wheel, and *axis* meaning axle, are comprised of a dumbbell-shaped component, in the form of a rod and two bulky stopper groups, around which there are encircling macrocyclic component(s). The stoppers of the dumbbell prevent the macrocycle(s) unthreading from the rod. When these stopper groups are absent from the ends of the rod, or if the bulky groups are of insufficient size to stop equilibration of the bead, we refer to the corresponding complexes as *pseudorotaxanes*. Schill has pointed out¹¹ that a wide range of interlocked structures is accessible from such entities (Figure 2). Other groups refer to this type of structure as a prerotaxane or precatenane,¹⁸ depending on the target compound. The nomenclature employed with these systems involves placing (in square brackets) the number of the components before the name of the compounds

or complexes. Thus, a [2]catenane is comprised of two interlocked macrocycles, a [2]rotaxane is comprised of one dumbbell component and one macrocycle, and a pseudo[2]rotaxane is comprised of one macrocycle with a rodlike molecule inserted through its center. The nomenclature for polymeric systems is also defined in Figure 2.

The concept of chemical topology is highly relevant when considering interlocked structures. Many excellent discussions have appeared concerning this subject, by van Gulick,¹⁹ Frisch and Wasserman,²⁰ and Sokolov,²¹ and more, recently, by Lipatov, Lipatova, and Kosyanchuk,²² Walba²³, Chambron, Dietrich-Buchecker, and Sauvage,²⁴ and Liang and Mislow.²⁵ Therefore, only the key concepts need be mentioned in this review. A compound is said to be topologically nontrivial if, by a continuous deformation of the bonds between the atoms, it cannot be converted into another isomer of the compound although the connectivity may be the same. They possess nonplanar molecular graphs when embedded in three-dimensional space.²³ Catenane molecules are "topological isomers"²⁰ of the separated component rings (Figure 3). Each of the rings in the catenane is homeomorphic with the ring in isolation, but they are not isotopic. This property is apparent when their molecular structures are analyzed. A [2]catenane cannot be drawn on a piece of paper without at least two crossing points, *i.e.* the structure has a nonplanar graph when embedded in three-dimensional space,²³ meaning that it cannot be converted into the constituent rings without physically breaking one of the macrocycles, and then re-forming the cycle in the absence of the other. Con-

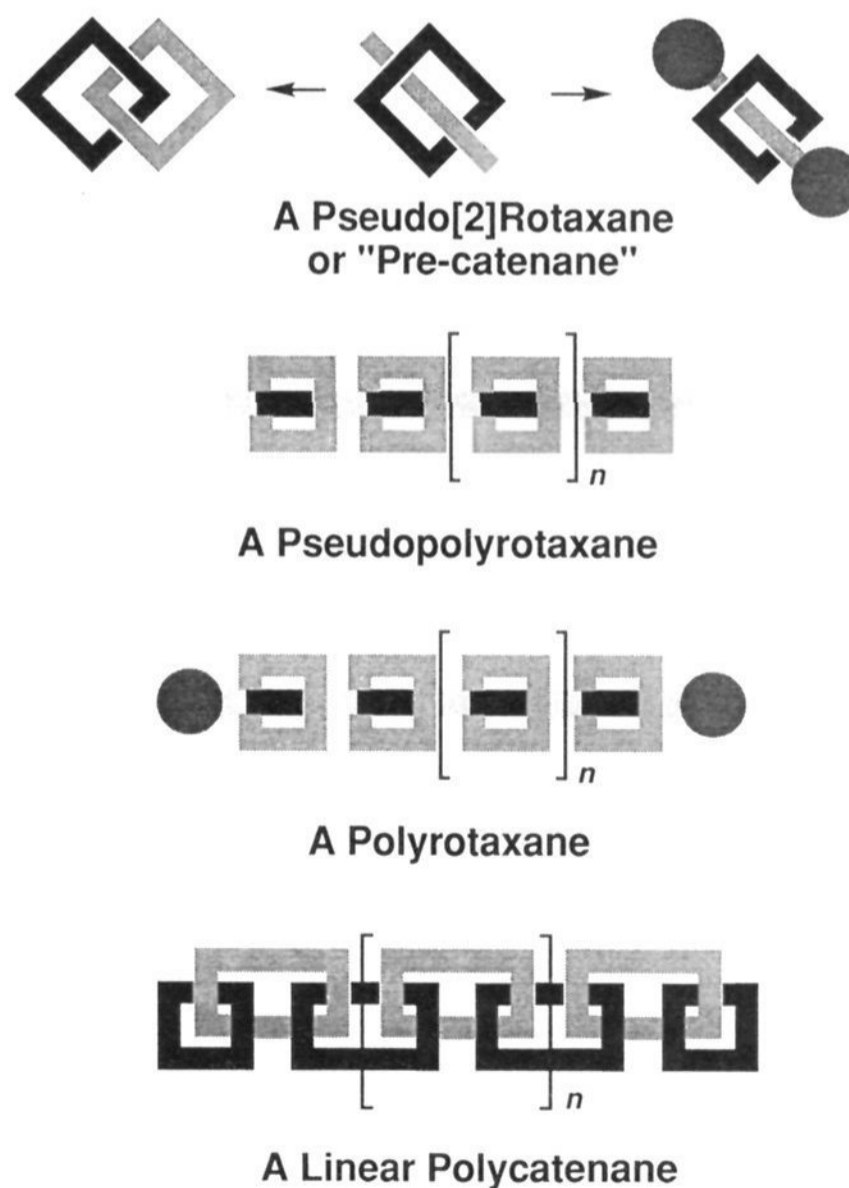


Figure 2. Some examples of nomenclature in operation.

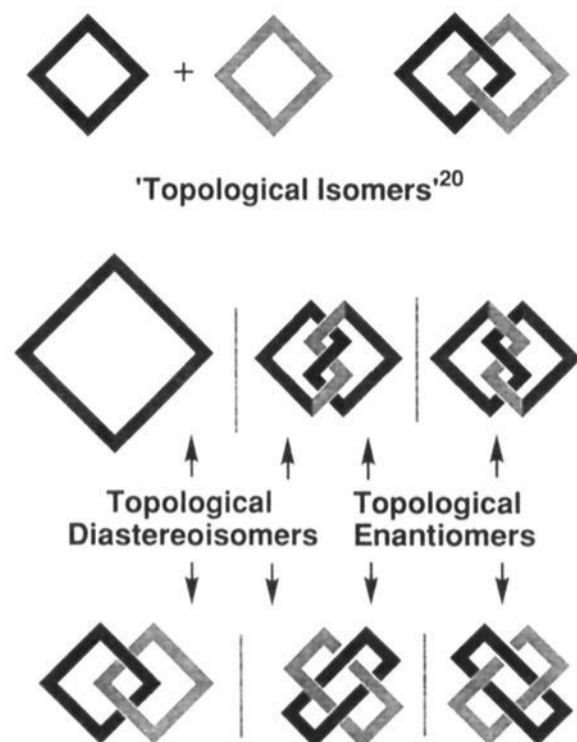


Figure 3. Topological isomerism²⁰ as it relates to a [2]-catenane, a trefoil knot, and a doubly interlocked [2]-catenane.

versely, rotaxanes are not topological isomers of their component parts. Deformation of the macrocyclic component of a [2]rotaxane allows it to be removed from the dumbbell component, *i.e.* the [2]rotaxane can be drawn as a planar graph when embedded in three-dimensional space. In reality, [2]rotaxanes can be prepared with sufficiently large blocking groups such that the components are inseparable, illustrating that covalent bonds are not able to be stretched infinitely! To all intents and purposes, the chemical components are interlocked (or reversibly threaded). Clearly, helices are not topological isomers of their component threads, since they can be unravelled from one another. However, by linking the termini of a double helix in the correct manner, a range of topological stereoisomers can be generated.¹³ The simplest of these is the trefoil knot, which is a topological diastereoisomer of the corresponding macrocycle since the two are not mirror images. In addition, the trefoil knot is chiral and so can exist as two topological enantiomers (Figure 3). It may also be noted that a singly interlocked [2]catenane is a topological diastereoisomer of the two homeomorphic topologically enantiomeric doubly interlocked [2]catenanes.

It has been pointed out by Sauvage and Dietrich-Buchecker,²⁶ in one of the most recent comprehensive reviews concerning catenanes, that the tremendous advances in analytical chemistry, complemented by the remarkable developments in synthetic methodology—particularly in the field of supramolecular chemistry²⁷—not to mention the emergence of self-assembly,²⁸ have allowed the creation and characterization of chemical structures and superstructures, which, until not so long ago, had been merely wild dreams in the minds of the chemists. This review discusses research which relates to the creation of molecules and supermolecules that have made some of these wild dreams come true. Each family of chemical species is discussed in sections, each genre being introduced, as far as possible, in chronological order, before being updated to its “state-of-the-art”.

II. Early Attempts at the Chemical Synthesis of Interlocked Compounds

In order to put the more recent advances in research into catenanes and rotaxanes into perspective, only a résumé of the early successes in the synthesis and isolation of interlocked rings is given here, in the knowledge that this area has been reviewed extensively elsewhere.^{11,26} A number of different conceptual approaches toward the synthesis of catenanes were discussed¹⁷ by Lüttringhaus *et al.* in 1958, along with the first, apparently unsuccessful, deliberate attempt at the synthesis of a compound containing two interlocked rings. The latter will be discussed in section IV. The former will be summarized in this section.

A. Statistical Methods for Catenane and Rotaxane Synthesis

The chance formation of one macrocycle, while being threaded through another, has been termed²⁶ the “statistical” approach. It was this approach that was responsible for providing the first experimental evidence for the formation of a [2]catenane. Wasserman’s historic “preparation of interlocking rings” was achieved²⁹ in less than 1% yield by the cyclization (Figure 4) of a diethyl tetratriacontanedioate, to form

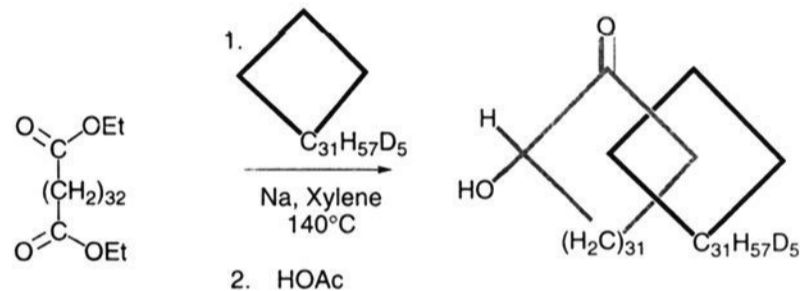


Figure 4. The synthesis²⁹ of a [2]catenane in less than 1% yield by the statistical approach.

a cyclic acyloin, in the presence of an excess of a pentadeuterated C_{34} cycloalkane, which was introduced with the solvent (xylene) into the reaction mixture. The [2]catenane’s existence was established using chemical methods. The presence in one of the products of the reaction of the pentadeuterated macrocycle, after cleavage of the acyloin ring from the material rendered free from the starting pentadeuterated macrocycle, could only arise, it was argued, from a compound composed of two interlocking rings.

The first synthesis (Figure 5) of a [2]rotaxane was reported by Harrison and Harrison³⁰ in 1967. They called it a “hooplane”. A cyclic ketone with a pendant

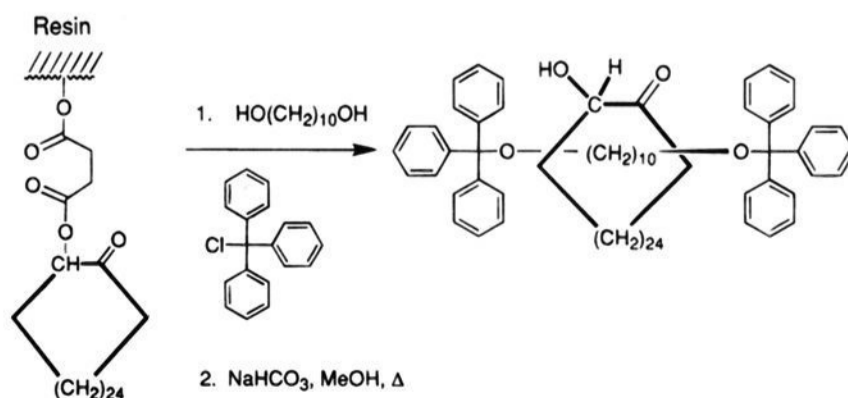


Figure 5. The synthesis³⁰ of a [2]rotaxane in 6% yield by the statistical method repeated 70 times on the surface of a resin.

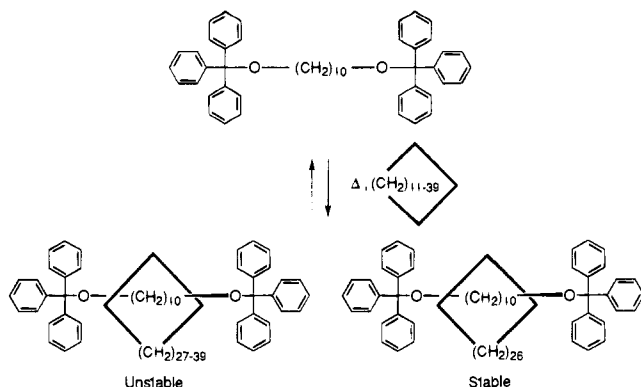


Figure 6. The preparation³¹ of [2]rotaxanes using the “statistical slipping” methodology.

carboxylic acid function was coupled to a Merrifield resin, which was treated on a column repeatedly (70 times!) with decane-1,10-diol and triphenylmethyl chloride. Cleavage of the rings from the resin, followed by purification, yielded the [2]rotaxane in 6% yield. It was characterized by IR spectroscopy and degradation studies. Later, I. T. Harrison³¹ reported (Figure 6) the “statistical slipping” of a mixture of cyclic hydrocarbons over the end groups of the dumbbell-shaped 1,10-bis(triphenylmethoxy)decane at 120 °C. Heating of the “slipped” rotaxane caused the reverse reaction to take place. The rotaxane incorporating the “slipped” C₂₉ macrocycle was stable at ambient temperature, while those greater in size than C₃₃ were extremely labile. The synthesis of the [2]rotaxanes was also achieved³² by reversible bond breaking and bond formation involving the stopper groups of the dumbbell component with acid in the presence of a variety of macrocycles. The largest yield obtained using this method was only 1.6%.

The “statistical” methods of Zilkha and Agam³³ brought the yields of “rotaxanes” up to more respectable figures. The reason for placing “statistical” in quotation marks is that the method might involve a small amount of molecular recognition associated with it and so may be a little more than just statistical. The reason for placing “rotaxanes” in quotation marks is that none of the species produced can formally be regarded as rotaxanes since the threading components remained unstoppered. Even so, the results that the authors describe in their publications^{33,34} of 1976 are highly significant. In their first series of experiments, pseudopolyrotaxanes were prepared by “statistical threading” of dibenzo crown ethers on to poly(ethylene glycols) at elevated temperatures, followed by polymerization of the assemblies with naphthalene-1,5-diisocyanate to form polyurethanes. Although purification of the polymers was not achieved, the degree of threading on to the polyurethane chain was evaluated by absorbing the reaction product on to silica gel and back-extracting the free crown ether. It was assumed that unthreading was only significant toward the ends of the polymer chains, it being suggested that coiling up of the polymer chain would trap the rings near the central part of the chains. The extent of threading was found to be dependent upon (i) the proportions of the two components, (ii) the sizes of the rings, (iii) the lengths of the threads, and (iv) the total volume of the reaction mixture. Degrees of threading of up

to approximately 60% were achieved with poly(ethylene glycol) 1000 and dibenzo-58.2-crown-19.4 (a mixture of crowns!). After mixing neat poly(ethylene glycol) 400 and dibenzo-58.2-crown-19.4 at 130 °C, followed by addition of triphenylchloromethane and pyridine, the researchers isolated (Figure 7) a “[2]rotaxane” in 15% yield, although it must be pointed out that the trityl stoppers at the ends of the poly(ethylene glycol) chains would be much too small to prevent unthreading of the large crown ether rings. Despite this potential drawback, the neat isolated “rotaxane” was decomposed by only 30% after heating for 10 h at 130 °C. Dissociation of the dumbbell from the bead in solution was found to be dependent on the nature of the solvent; it is slow in *o*-xylene and relatively fast in 2-octanol. The heat of the reaction for the rotaxane going to ring plus chain is 9.5 kcal mol⁻¹, a value which the authors considered to be the approximate magnitude of the dipole interactions between the poly(ethylene oxide) moieties in each component. Such a scenario would perhaps explain the relatively high yield obtained in the synthesis. In addition, the activation energy required for the threading process is approximately 3.4 kcal mol⁻¹, whereas the activation energy for decomposition is approximately 15.9 kcal mol⁻¹. It was argued that, since the threading process does not require the breaking of electrostatic interactions, it would be expected to be associated with a lower energy barrier. The incorporation of a bromomethyl group into each of the trityl groups in the “[2]rotaxane” also provided a route to the synthesis (Figure 8) at high dilution of a [2]catenane in 14% yield.³⁴ The structure of the [2]catenane was confirmed by hydrolysis of the trityl groups and analysis of the product. The zinc/copper couple in DMF, the reaction conditions which gave rise to the [2]catenane, also afforded a compound whose structure was proposed to be a “[4]rotaxane”, in 8% yield. Remarkably, the further reaction of this “[4]rotaxane” to form a polyrotaxane was not reported.

The “statistical” approach of Harrison was also applied by Schill and co-workers³⁵ to the preparation of [2]rotaxanes in which triarylmethanethiol blocking groups on the termini of an alkyl thread were equilibrated using *p*-toluenesulfonic acid in the presence of cycloalkanes. Yields of up to 11.3% were achieved with the optimum ring size for the cycloalkane and the appropriate chain length in the dumbbell component. The reactions were followed by HPLC. More recently, the same kind of statistical approach is claimed to have afforded³⁶ a [2]rotaxane in 49% yield. Reaction of 1,12-bis(triphenylmethoxy)dodecane with *p*-toluenesulfonic acid in the presence of [2.18]paracyclophane in a bomb at 100 °C for 1 h yielded a mixture which was treated with triethylamine before being subjected to column chromatog-

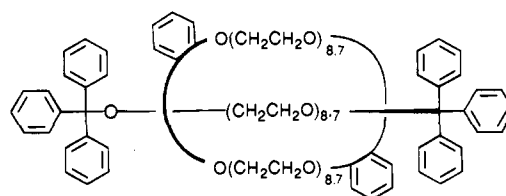


Figure 7. A “[2]rotaxane” prepared from poly(ethylene glycol) and a mixture of dibenzo crown ethers.³³

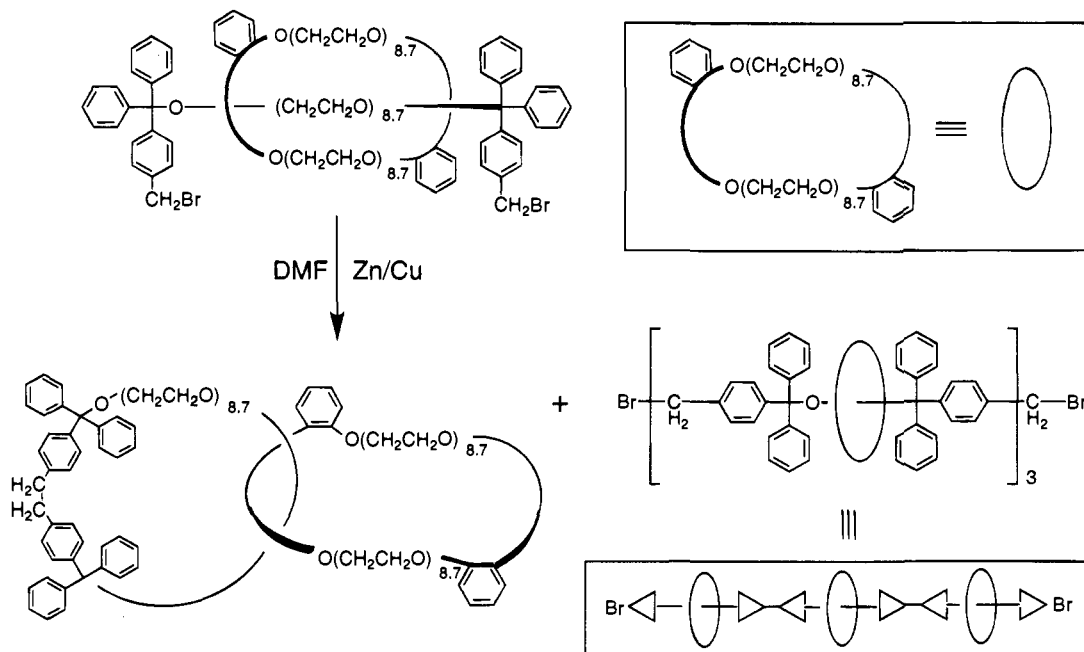


Figure 8. The synthesis³⁴ of a [2]catenane and a “[4]rotaxane”.

raphy. Broad signals resonating at δ 0.8–0.9 in the ^1H NMR spectrum of the product indicated the location of part of the aliphatic chain of the dumbbell in the shielding zone of the aromatic residues of the cyclophane. No mass spectroscopic evidence for the product was presented in the communication.

B. Cylinders, Möbius Strips, Macrocycles, and Catenanes

It was Frisch and Wasserman^{20a} who first recognized that the formation of catenanes is possible as a result of cleavage of the links (Figure 9) in a doubly twisted striplike molecule. The observation³⁷ of large carbon macrocycles in the products of the transition metal-catalyzed metathesis of cyclic olefins led to the hypothesis that Möbius strips, catenanes and knots may be present in these reaction mixtures. Indeed, this proposal proved to be correct. It was substantiated independently and simultaneously by Wolovsky³⁸ and by Ben-Efraim, Batich, and Wasserman.³⁹ In both papers, the presence of the catenated hydrocarbons in the metathesis reaction products was inferred directly from mass spectroscopic evidence. The proposed mechanism of formation of interlocked structures is surprising in view of the current theory regarding metathesis reactions of this type (carbene mechanism).

The first synthesis of a molecular Möbius strip compound, an “isomer” (Figure 9) of a cylinder which has one side and one edge, was achieved by Walba and his co-workers,⁴⁰ and was reported in 1982. The synthesis was developed from an earlier preparation⁴¹ of cylindrical macropolycyclic hosts comprised of fused crown ethers incorporating the tetrakis-(hydroxymethyl)ethylene (THYME) residue.⁴² The THYME diol ditosylate **1** was cyclized under high dilution conditions to yield (Figure 10) the cylindrical compound **2** and the chiral molecular Möbius strip derivative **3** in 24% and 22% yields, respectively. The identity of the chiral⁴³ Möbius strip derivative **3**, which contains no tetrahedral stereogenic centers,

and is not rigid, was confirmed by addition of Pirkle’s reagent [(+)-2,2,2-trifluoro-9-anthrylethanol] to a solution of the compound. Two distinct olefinic carbon resonances were evident in the ^{13}C NMR spectrum of the chiral Möbius strip compound **3**, while the spectrum of the cylindrical compound **2**

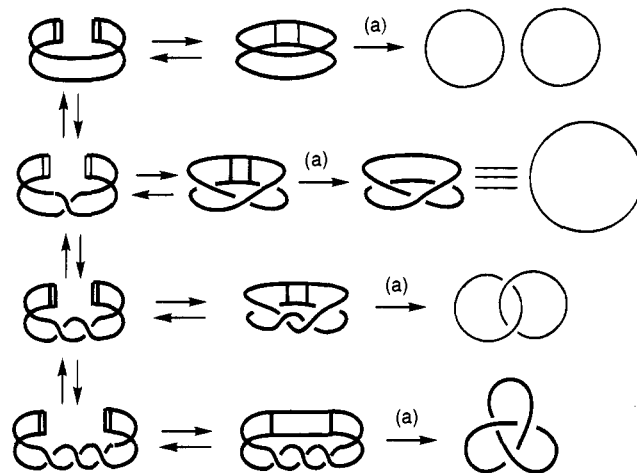


Figure 9. Possible approaches^{20a} to the synthesis of a [2]catenane and a trefoil knot by cleaving links in twisted striplike molecules.

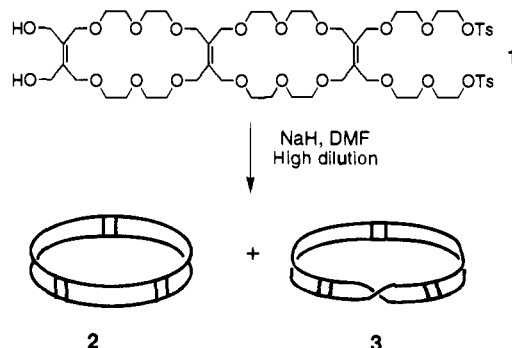


Figure 10. The cyclization of THYME diol ditosylate **1** to give a cylindrical compound **2** and the molecular Möbius strip **3**.⁴⁰

shows only one. The authenticity of **3** was also confirmed chemically.⁴⁴ Ozonolysis of **2** and **3** independently produced two separate homologous macrocycles, a smaller triketone from the double-edged cylinder compound **2**, and a larger hexaketone from the single-edged strip derivative **3**. A problem was encountered in the isolation of these materials because of the ease of decomposition of the macrocyclic ketones. This problem was overcome⁴⁵ by treating the macrocyclic ketones with lithium-free methylenetriphenylphosphorane to afford the corresponding crown ethers. The polymethyleneated products were stable and easy to characterize. The possibilities of preparing catenanes, from doubly half-twisted strip compounds, or knots, from triply half-twisted strip compounds, are limited presently by the statistical nature of the twisting required in the precursors. The efficient syntheses of compounds with interlocked structures in a straightforward manner is always going to require an element of direction!

C. "Directed" Synthesis of Catenanes and Rotaxanes

Clearly, the "statistical" approach for the creation of molecular structures with aspects of interlocking or entanglement has extreme limitations since the yields obtained using this method are associated with chance events and so must always be low. The use of a template,^{46,47} or "auxiliary linkage",¹¹ is essential for the efficient synthesis of compounds with interlocked structures. Figure 11 shows the principle behind this general approach. The components of the rings that are to become incorporated into a [2]- or [3]catenane are brought together in relative orientations such that the most favored outcome from linking the (appropriate) termini of the oriented components is that of interlocked rings. It is clear that the template could be, for example, (i) a covalent bond, (ii) a coordinative bond, or (iii) a noncovalent bond.

Six years after the first reported attempt to make a [2]catenane, Lüttringhaus and Schill⁴⁸ reported the use of covalent bonds as templates in what they

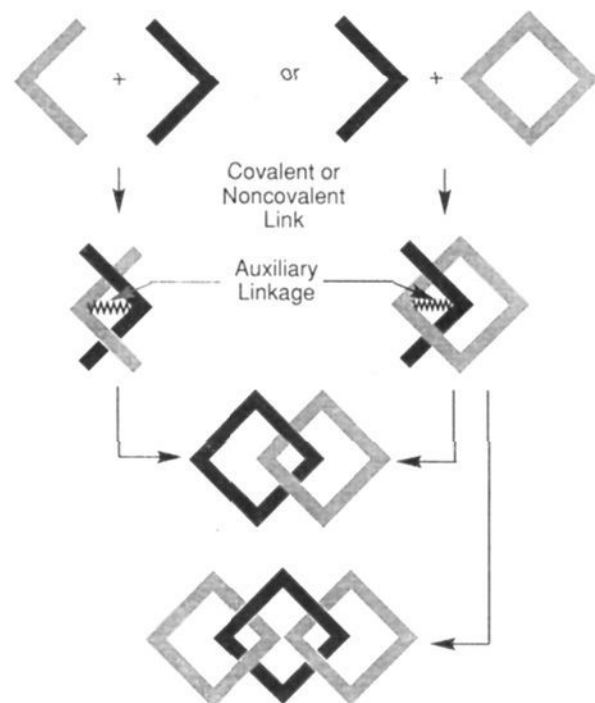


Figure 11. Approaches to the synthesis of [2]- and [3]catenanes employing auxiliary linkages associated with a covalent, a coordinative, or a noncovalent bond.

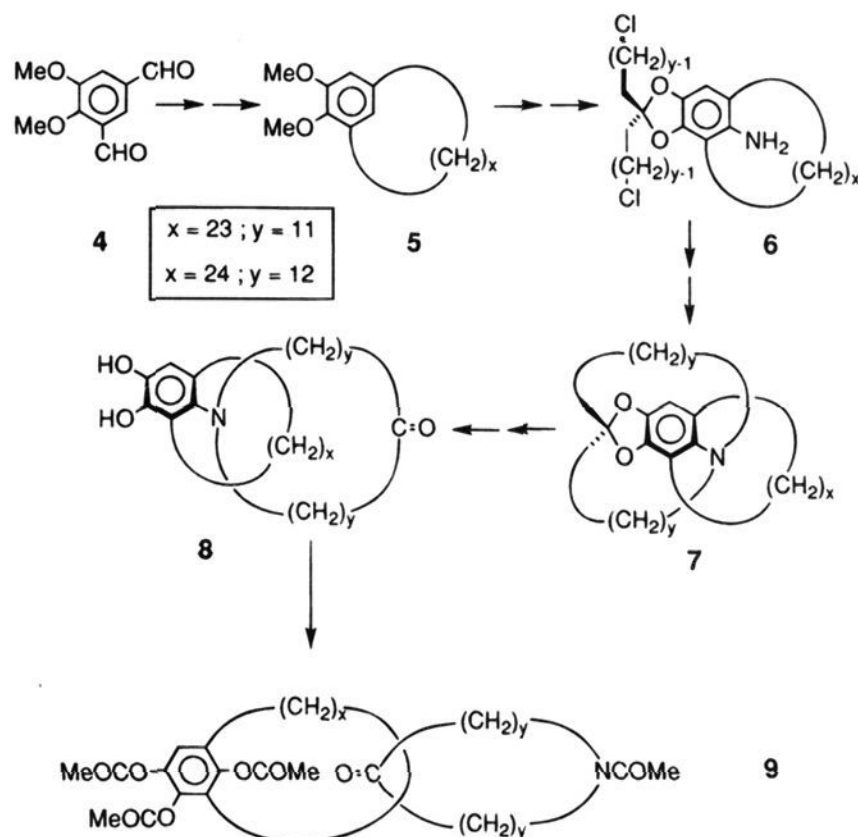


Figure 12. The "directed" synthesis⁵⁰ of the [2]catenane **9**.

described as "directed" catenane syntheses. This approach involves incorporation of a relatively labile covalent linkage between one moiety from a component of each of the rings, such that the reactive termini from each component are directed away from one another. Steric control prevents unfavorable cyclizations which would normally be more favored when using the "statistical" method.⁴⁹ In this situation, the steric effect is acting as a negative template.⁴⁷ Many ingenious and elaborate synthetic schemes have been designed and executed by Schill and his co-workers, many of which are presented¹¹ in his book, *Catenanes, Rotaxanes and Knots*. Rather than retrace the historically important work presented therein, the directed approach to the synthesis of catenanes and rotaxanes using covalent bonds as templates will be illustrated with a few recent and interesting examples.

In 1981, the syntheses (Figure 12) of two new [2]catenanes were reported.⁵⁰ This research epitomizes the elegant strategy that has been developed over the years by the Schill group,⁵¹ whereby the size and functionality of the component rings have been varied systematically. The bisaldehyde **4** was converted into a bisalkyne using a four-step procedure starting with a Wittig reaction, followed by subsequent cyclization of the bisalkyne and reduction, in a manner similar to that employed by Isele and Scheib⁵² in analogous systems, to afford the macrocycles **5**. Demethylation of the phenol methyl ether functions paved the way for ketal formation, which was followed by nitration of the aromatic ring. Catalytic reduction of the nitro compound produced the aromatic amine **6**, which was cyclized to form the double ansa compound **7**. In this synthesis, the chains emanating from the ketal are held perpendicular to the plane of the aromatic ring in **6**, so that the nucleophilic attack by the amine function at each of the two carbon atoms α to the chlorine atoms at the ends of the long chains of **6** must take place on opposite faces of the aromatic ring. Hydrolysis of the ketal "auxiliary" linkage with HBr in acetic

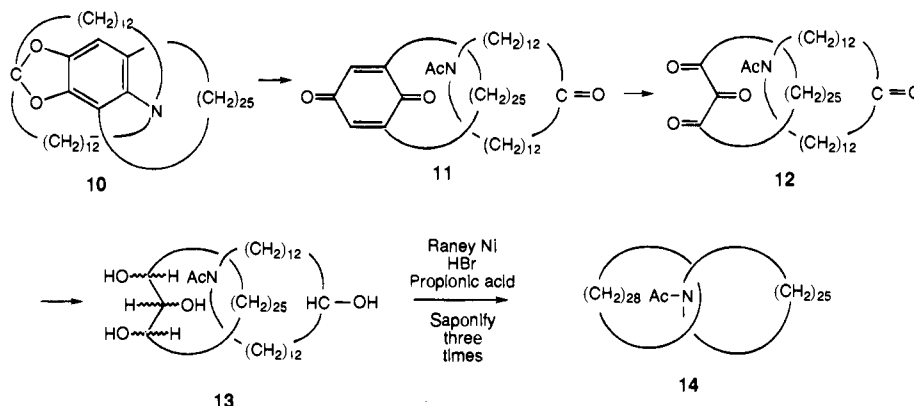


Figure 13. The "directed" synthesis⁵⁴ of the [2]catenane 14 from the bisansa compound 10.

acid, to form the ketone 8, followed by cleavage of the nitrogen aromatic ring bond,⁵³ liberates the [2]catenanes 9.

In 1978, Schill's group reported⁵⁴ the synthesis of a [2]catenane incorporating cyclooctacosane and azacyclohexacosane from the bisansa compound 10 which was transformed (Figure 13) in the first instance into 11 by cleavage of the ketal and aromatic nitrogen bonds. Exhaustive ozonolysis of 11 gave the tetraketone 12, which was reduced directly with sodium borohydride to afford the tetrol 13 as a mixture of stereoisomers. Repeated treatment of 13 with Raney nickel in HBr and propionic acid gave the [2]catenane 14. Purification of this compound was troublesome on account of side reactions involving the hydrocarbon ring during ozonolysis.

The initial characterization of catenanes often relies heavily upon mass spectrometry. Two seminal papers^{55,56} describing the development of this technique toward the characterization of interlocked macrocycles involved the analysis of compounds prepared using the Schill "directed" synthetic methodology. The mass spectrum of a variety of [2]catenanes was observed⁵⁵ to be very different from that of the precursors in which the component macrocycles were linked by a covalent bond, yet resembled more the sum of the spectra of the two macrocycles. The [2]catenanes give molecular ion peaks at high m/z values, which are accompanied by fragmentation peaks similar to those observed for the component macrocycles in isolation. Few fragmentation peaks are observed at lower mass until one of the macrocycles is broken apart from the other macrocycle. Also prevalent⁵⁶ in the fragmentations at high m/z values are peaks corresponding to the transfer of a hydrogen atom from one of the macrocycles to a functional group on the other macrocycle.

Both the ¹H and ¹³C NMR spectra of the [2]catenane 14 reveal shifts to low field in the resonances arising from the nuclei in the component macrocycles in the interlocked structure⁵⁴ when compared to those in the corresponding free macrocycles.⁵⁷ The reason for these chemical shift changes was attributed to van der Waals interactions between the two ring components. High-field chemical shift changes arising from solvent effects were also noted in the ¹H NMR spectra of the catenane. Spin-lattice relaxation time (T_1) measurements⁵⁸ on the C₂₈ macrocycle in the [2]catenane 14 revealed diminished T_1 values for its protons compared with those of the

free macrocycle, confirming that the motions of the interlocked rings are more restricted than the motions of the free components.

Schill and his team⁵⁹ have also used the "directed" approach for the synthesis of mechanically modified dumbbell-shaped molecular components carrying entrapped macrocycles—compounds to which he gave the name, *rotaxanes*. Their syntheses are very similar to those of the catenanes.⁶⁰ For example, the bisansa compound 15 was formed (Figure 14) in which two substituent chains, bearing functional end groups, protrude either side of the central benzene ring. Introduction of bulky groups at the termini of these chains to form 16, followed by cleavage of the orienting covalent bonds, afforded the [2]rotaxane 17. The mass spectra of the compounds gave molecular

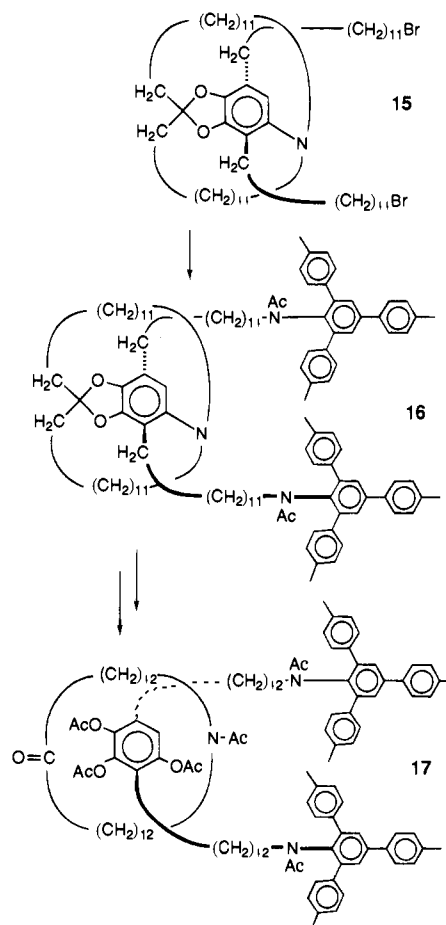


Figure 14. The "directed" synthesis⁵⁹ of the [2]rotaxane 17 from the bisansa compound 15.

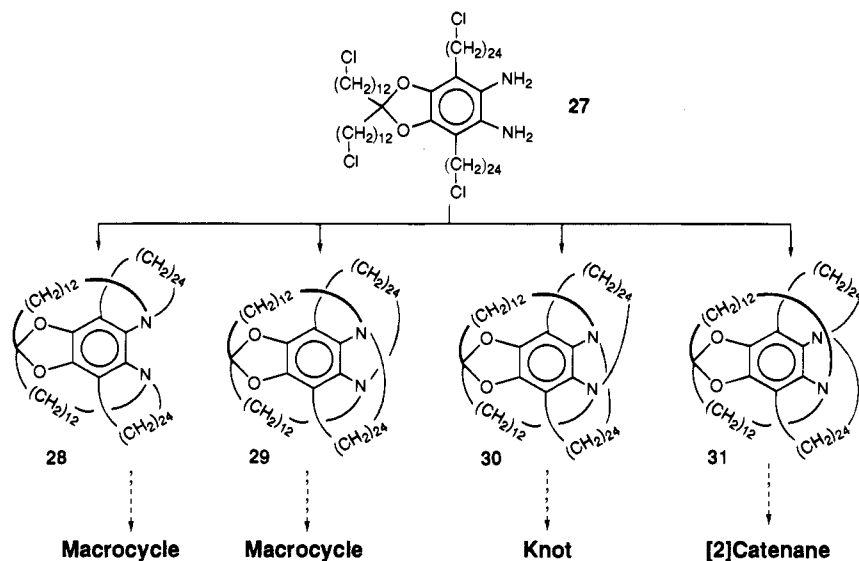


Figure 17. Possible synthetic routes to knots and catenanes via triply cyclized intermediates.⁶⁸

time. It was assumed that the barrier to interconversion between **24** and **25** was sufficiently large at room temperature to allow their separation. Glaser coupling of the translational isomers **24** and **25** yielded a [2]rotaxane and a [2]catenane, respectively.⁶⁵ Reduction of the alkyne units and removal of the redundant blocking groups from the [2]catenane yielded the all-hydrocarbon [2]catenane **26**. A similar treatment of the [2]rotaxane afforded the separate cycloalkanes.

Schill *et al.* also used a covalently directed method for the attempted synthesis of knots,⁶⁶ through both Möbius strip-like⁶⁷ and multiple cyclization⁶⁸ approaches. Although the attempts were elegant in synthetic terms, they were unsuccessful owing to the relatively poor efficiencies in the key steps associated with the long synthetic routes. In the multiple cyclization approach, triple cyclization (Figure 17) of **27** (itself prepared in nine steps) afforded⁶⁸ a mixture of three isomeric products in only 1.7% yield. There are four possible triply cyclized products, namely **28** and **29**, which should afford macrocycles upon cleavage of the ketal and amine auxiliary linkages, **30**, which should give a knot, and **31**, which should yield a [2]catenane. Separation of the three compounds, followed by NMR spectroscopy, suggested that **30** might have been formed, although the identity of the isomers was not established. The final step, to generate the cyclic, catenated, or knotted products, was not reported.⁶⁸

The construction of catenanes, rotaxanes, and knots using covalent bonds as templates has been extremely well exemplified by Schill's ingenious synthetic strategies in research that was much ahead of its time. However, the synthetic routes demand a great deal of technical expertise and manipulation. The construction of interlocked molecular structures is probably much simpler using coordinative and/or noncovalent bonding interactions to act as the sources of the templates.

III. Helices, Catenanes, and Knots from the Natural World

The natural world is replete with examples of molecular intertwining. Because of the breadth and

depth of this field in science, it is clearly beyond the scope of this review to discuss all the intertwined and interlocked structures that have been uncovered so far in biological systems. Despite the fact that their importance in determining the superstructures and molecular recognition properties of many biopolymers is far-reaching, single helices will not be discussed at all, since they do not by themselves constitute intertwined superstructures. Instead, an overview of the variety of entangled structures will be presented here—the emphasis being placed on molecular recognition.

The double helix, formed by deoxyribonucleic acid (DNA),⁶⁹ is the intertwined structure which illustrates the benefits of molecular entanglement for function. The four simple base-pair building blocks, adenine (A), cytosine (C), guanine (G), and thymine (T), attached to the sugar-phosphate backbone of the nucleic acid determine the information that is stored and then relayed from each strand of DNA in the form of the genetic code.⁷⁰ The incredible simplicity and stability of the double helix is adequate demonstration of the perfection in superstructure terms to which synthetic chemists must aspire. The formation of the double helix, the so-called secondary structure of DNA, is determined (Figure 18) by the primary structure of each strand in the helix, since A binds noncovalently with T, and C binds noncovalently with G. Generally, the most stable form of the DNA double helix is the right-handed B-form, which crystallizes as fibers whose diffraction patterns led originally to the proposal of the double helical superstructure by Watson and Crick.⁶⁹ The helix has the base pairs buried around the central axis that hold it together, with the phosphate groups of the backbone facing out toward the external environment. As a result, two so-called grooves spiral their way down the double helix, namely the major one and the minor one. The grooves result from the differential angles (*ca.* 75° and 285°) between the glycosyl bonds of the DNA.

While the right-handed double helical B-form of DNA is the best known one, at high salt concentrations, certain sequences of base pairs exist as a left-handed double-helical superstructure known as the

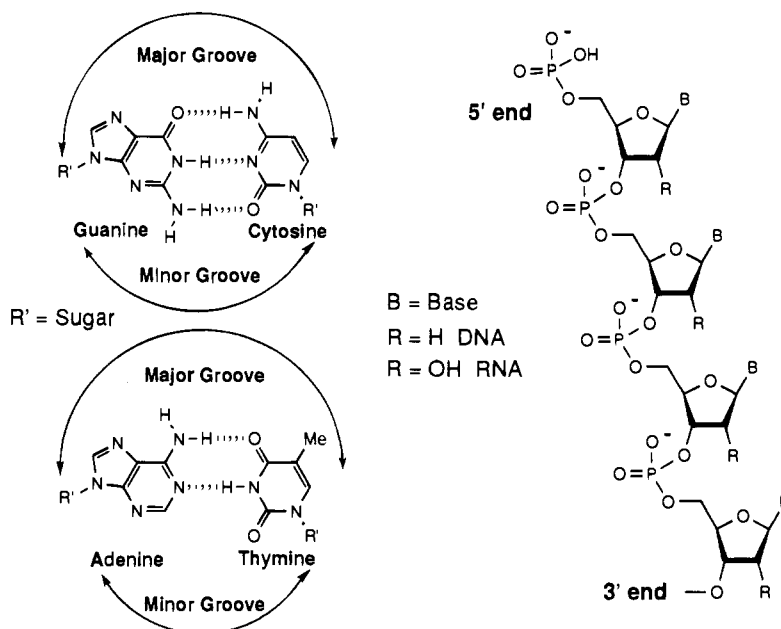


Figure 18. The primary structures of DNA and RNA and how it relates through base-pairing in DNA to the major and minor grooves in the secondary structure of DNA.

Z-form of DNA.⁷¹ Atomic resolution X-ray crystal structures are usually obtained from crystals of DNA containing short complementary sequences. The first crystal structure of the Z-form of DNA was obtained⁷² from a fragment with the sequence d(CpGpCpG-pCpG), which was known to exist in the alternative double-helical form. The structure of this double helix has similar gross features to that of B-DNA, with Watson-Crick base pairs aligned parallel to one another, but tilted with respect to the helical axis, with a left-handed sense and with a "zigzag" shape to the backbone, hence, the name Z-DNA. Whereas the repeating unit in B-DNA is a mononucleoside, in Z-DNA it is a dinucleoside on account of the alternating conformations in the sugar residues. Perhaps the most striking feature of Z-DNA is the absence of a discernable major groove, while the narrow minor groove is considerably deeper than in the corresponding regions in the B-form. In addition, the left-handed helix is more extended. Over a distance of 44.6 Å, the B-form has 13 base pairs, while the Z-form has only 12, and the diameters of the duplexes are 20 and 18 Å, respectively. Combinations of complementary enantiomorphous DNA strands, where the natural D-deoxyribose is replaced⁷³ with L-deoxyribose, result in *left-handed* B-DNA, and also result in Z-DNA at high salt concentrations. A crystal structure⁷⁴ of a racemic duplex containing D- and L-strands showed pairs of right-handed double helices in the Z-form from the L-L pairing and left-handed Z-DNA from the D-D pairing.

The major and minor grooves in B-DNA are both capable of forming complexes with other molecular species.^{70,75} This capability has permitted the formation of a number of triple-helical superstructures between linear homopurine/homopyrimidine duplexes and the corresponding homopyrimidine strands.⁷⁶ Moreover, it has led to the creation of site-specific cleavers of DNA.⁷⁷ The additional strands are bound to the Watson-Crick-paired duplex by Hoogsteen hydrogen bonds⁷⁸ in the major groove

(Figure 19). Triple helices have also been observed in supercoiled plasmid DNA⁷⁹ and in the binding⁸⁰ of single strands of purine- or pyrimidine-rich DNA using a circular DNA molecule which is either pyrimidine- or purine-rich, respectively. The binding is achieved by the circular DNA molecules wrapping themselves round the host, as depicted schematically in Figure 20. The minor groove of DNA has also been the object of recognition and site-specific cleavage—this time by noncovalently paired peptide dimers,⁸¹ where the peptide hydrogen atoms are involved in noncovalent interactions with the lone pairs on the N-3 atom in purine or on the O-2 atom of the pyrimidine in the host DNA. Very recently, Dervan's group has prepared⁸² a covalently linked peptide heterodimer, which exhibits sequence specific recognition in the minor groove of duplex DNA.

Beyond the helical forms, a third level of DNA structure results from the bending of the axis running through the duplex.⁸³ Circular DNA, common in bacteria and viruses, is comprised of two intact DNA macrocycles, and theoretically can exist as four possible topological stereoisomers, although the right-handed helix with antiparallel edges is the only one to be considered. In addition to these circular duplexes, a further family of topological stereoisomers⁸⁴ is also present in nature—namely supercoils,⁸⁵ catenanes,⁸⁶ and knots (Figure 21). Walba²³ and

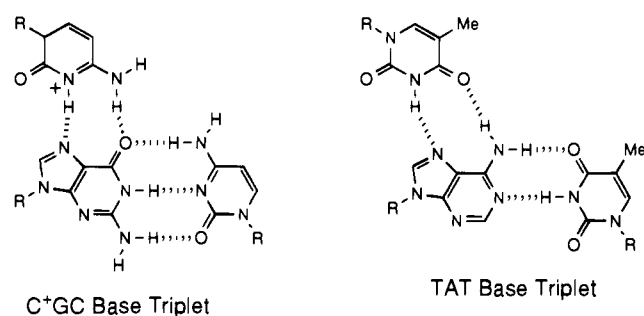


Figure 19. The recognition motifs that give rise to triple-helical superstructures in DNA.

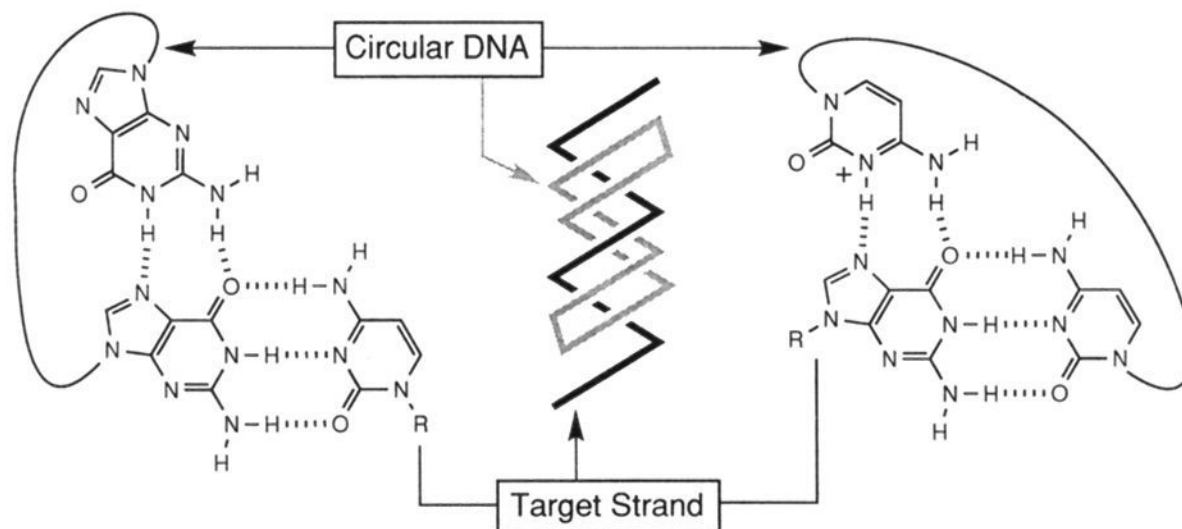


Figure 20. The binding of circular DNA by single-stranded DNA.

Wasserman and Cozzarelli⁸⁴ have produced detailed discussions of the topological isomers that are afforded upon cyclization of the DNA. A summary and more recent developments will be presented here.

The existence of catenated circular DNA *in vivo* was discovered by Vinograd and co-workers.⁸⁷ The dimeric forms of DNA from mitochondria were separated and viewed under an electron microscope, which revealed that two circular duplex DNA molecules were mechanically interlocked. Further studies⁸⁸ indicated the presence of catenated trimers, *i.e.* a [3]catenane, comprised of three circular duplex DNA molecules. In the same year, Wang and Schwartz⁸⁹ reported a synthetic approach to the catenation of DNA. At high concentrations, as in synthetic chemical situations, linear aggregates of DNA are formed, while, at low concentrations, cyclization is favored although interpenetration decreases. In fact, the team used labeled bacteriophage 1 DNA in the presence of a high concentration of

preformed 186 DNA rings. The two types of DNA were chosen because they are incompatible chemically. Density gradient centrifugation was used to separate the interlocked ring compounds. Later reports showed the existence of catenanes in plasmid DNA,⁹⁰ as well as in viruses.⁹¹ Some of the most stunning images⁹² of twisted and catenated DNA are of kinetoplast DNA from cells of *Leishmania tarentolae*, where electron micrographs show mixtures of simple [2]catenanes through to incredibly huge, complex, and beautiful mechanically linked assemblies.

Although the catenanes and knots formed in biological systems by DNA are extremely beautiful when viewed using an electron microscope, they are of rather more profound interest when one considers their functions. During the later stages of the replication of simian virus 40 (SV40) DNA, 20 discrete catenated dimeric species have been identified⁹³ in which two circular duplex DNAs are linked by one or more intertwining events. It was proposed that a specific enzyme is necessary to uncatenate the daughter chromosomes *in vivo*. These enzymes, which are responsible for the formation of intertwined and interlocked DNA by carrying out the transient breakage of either one or both strands of DNA, before passing single or double-stranded through the break, and then resealing the break in the DNA, are called the topoisomerases.⁹⁴ They are crucial to replication, transcription, and recombination of the genetic information store. While the topological transformations are being carried out, type I topoisomerases break single strands of DNA,⁹⁵ and the type II enzymes break both strands of the double helix. This fact was dramatically shown⁹⁶ in 1987, when a group working with SV40 blocked the topoisomerases extracted from HeLa cells with either specific inhibitors or with antibodies. The rate of DNA synthesis was decreased by a factor of 15–20. The replication was fully restored upon addition of purified topoisomerase II. The products in this case were monomeric daughter molecules: but when the blocked cells were treated with topoisomerase I, multiply intertwined and catenated daughter molecules were found. The authors concluded that, although either enzyme may unlink DNA, for the segregation of freshly synthesized daughter molecules to occur, topoisomerase II is essential. Similar results were obtained⁹⁷ by inhibition of topoisomerase IV in partitioning bacterial replicons: inhibition of the enzyme leads to the formation of right-handed

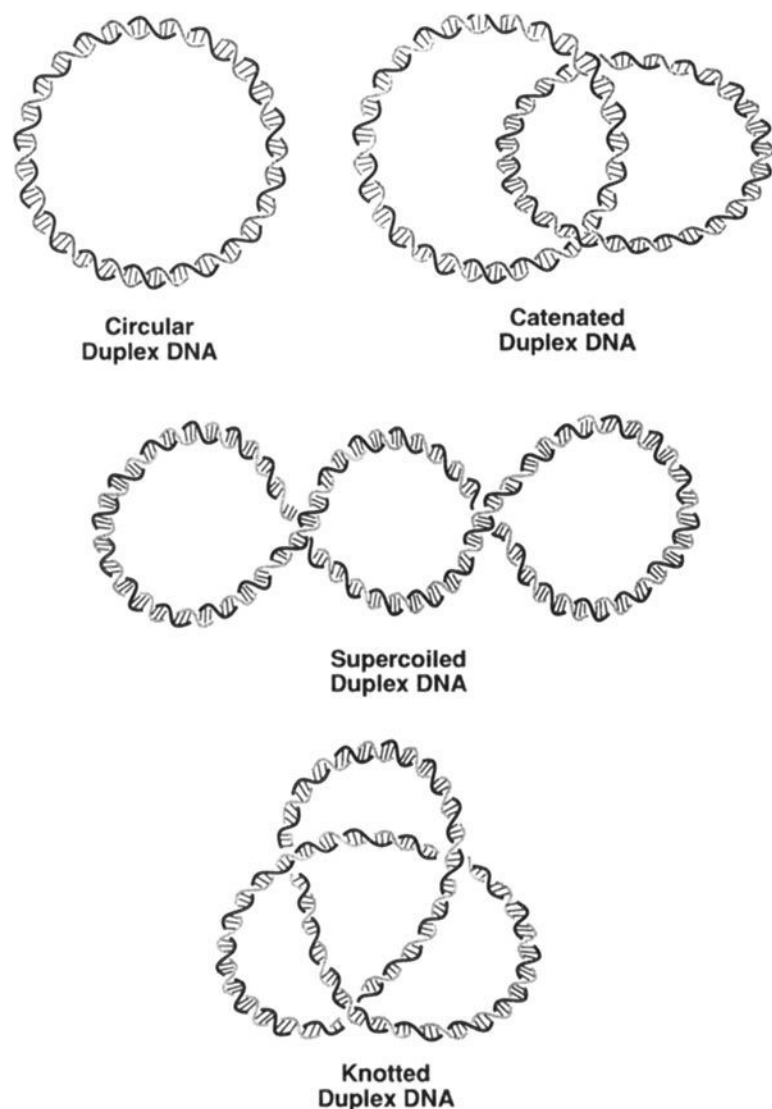


Figure 21. Diagrammatic representations of circular, catenated, supercoiled, and knotted double-stranded DNA.

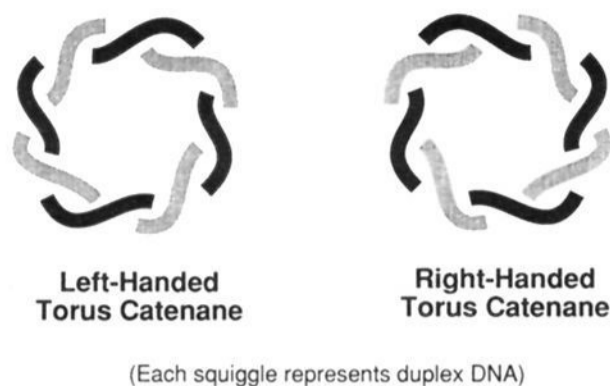


Figure 22. Cartoon representations of left-handed and right-handed torus catenanes formed by DNA.

and parallel catenanes with a torus form (Figure 22) with from two to more than 32 crossing points. One of the catenanes observed under the electron microscope contained a macrocycle as one component and a trefoil knot as the other. The buildup of these structures support the model of a two-stage unwinding mechanism,⁹⁸ which has also been proposed for ATP-dependent topoisomerases.⁹⁹

The observation¹⁰⁰ of a knotted single-stranded DNA ring was first made in 1976, when circular fd DNA was treated with *Escherichia coli* (*E. coli*) ω . The resulting mixture of products was separated by sedimentation. The fraction which sedimented more quickly, on account of its more compact nature, was characterized by electron microscopy to be a product with a knotted structure, which had very similar properties to normal circular DNA, and could be equilibrated back to the more usual state upon treatment with the enzyme under dilute conditions. The trefoil knots formed by duplex DNA can have two forms, containing either left-handed (-) supercoils or right-handed (+) supercoils (Figure 23). The three crossing points, or nodes, of a trefoil knot all have the same sign. In 1983, a method was reported¹⁰² to distinguish between the two types of node by staining with *E. coli* RecA protein and observing the resulting superstructures in an electron microscope. It was found that knots generated by topoisomerase I were a mixture of (+) and (-) knots, the topoisomerase I family are known to be unselective toward the sign and orientation of crossing segments.

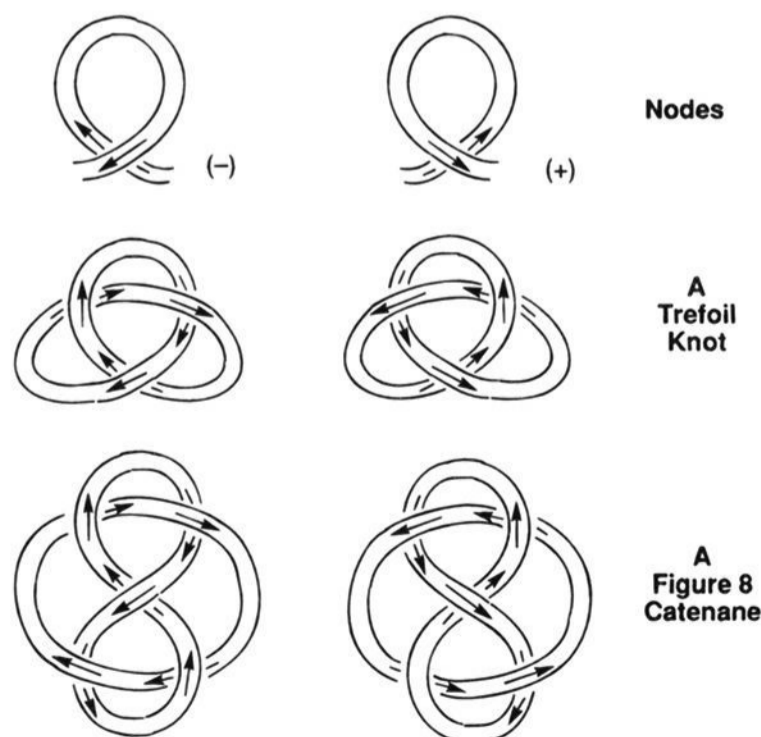


Figure 23. The definition of nodes. Diagrammatic representation of a trefoil knot and a figure-eight catenane formed by duplex DNA.

However, figure-eight catenanes were generated in a stereospecific way using the resolvase of transposon Tn3. The catenanes had (+) nodes. Approximately 99% of the recombinants in this latter experiment were singly linked [2]catenanes, which were subsequently studied and found to have exclusively (-) nodes.¹⁰³ Stereoselectivity, as performed by enzymes on "normal" chemical substrates, is usually relatively easily explained. It is not so obvious how the formation of catenanes by Tn3 resolvase is stereoselective. The reason for the selectivity is more clear when the effect of catenation upon the twisting in the duplex DNA rings is considered. In the catenated state, the double helix is unwound by approximately two-thirds for every right-handed supercoil in the catenated form compared with the cyclic form, an effect that is believed to be of key importance to the unwinding of DNA during replication.¹⁰⁴ The action of Tn3 resolvase on cyclic DNA to produce the catenated form therefore removes four negative supercoils. In relaxed or nicked DNA, this reaction is slower. In Figure 24, the resolution sites are represented as arrows, which define the directions of the component rings. Fusion, the reversal of resolution, introduces four negative supercoils into the DNA. When one considers the fusion of a (+2)

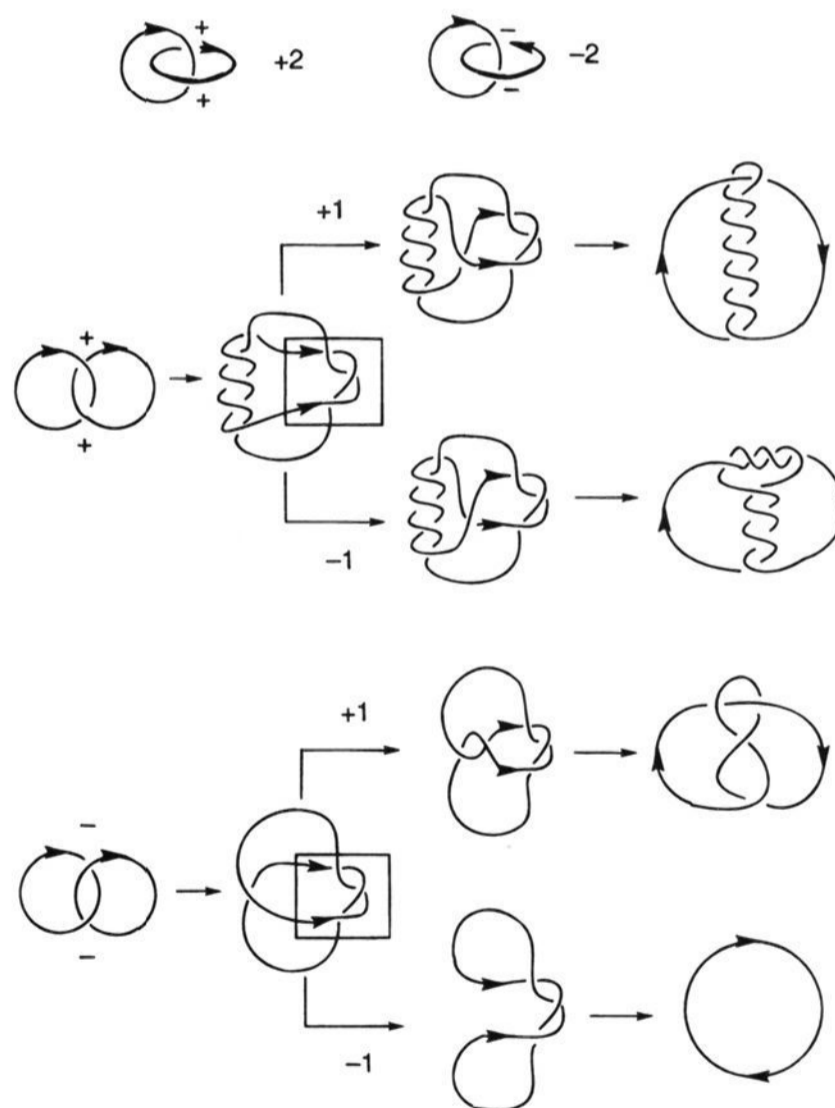


Figure 24. This figure illustrates the reason for selection between topological diastereomers during resolution.¹⁰³ The black arrows in the [2]catenanes (top) represent the directions of the *res* recombination sites in double-stranded DNA. The two [2]catenanes differ only by the relative direction of one site. The two schemes show the effects of synapsis and strand exchange, given that the *res* sites are aligned in the enzyme. The products of the right-handed (+1) and left-handed (-1) strand exchange are shown. The diagrams show clearly that synapse of the (+2) catenane is energetically very unfavorable, while the (-2) catenane requires relatively little flexing to act as a substrate; it can form a four-noded knot or a trivial circular product.

catenane by the enzyme, it is necessary that an eight-noded knot is formed for the resolution sites to adopt their correct position in the enzyme, a thermodynamically unfavorable situation. On the other hand, recombination of the (-2) catenane produces either a macrocycle or a four-noded structure. The actual effect of Tn3 or Tn21 resolvases is not only to produce macrocyclic DNA duplexes, but also small quantities of the four-noded material, an outcome which supports the proposed mechanism of action, although the exact interactions between the enzyme and the DNA have yet to be established.

The complete *E. coli* DNA topoisomerase I is a metalloprotein, of molecular weight 97K, which achieves DNA cleavage through transesterification of a tyrosyl residue of the enzyme with a DNA phosphodiester bond.¹⁰⁵ The covalently linked intermediate is then attacked by the severed DNA, rejoining it and freeing the enzyme. Some clues as to how the enzyme achieves its topological transformations were provided by the crystal structure¹⁰⁶ of its 67K N-terminal fragment. (Although the fragment is incapable of relaxing supercoiled DNA, it can cleave single-stranded oligonucleotides.) The crystal structure reveals an elongated toroid-shaped molecule, with a hole sufficiently large so as to be able to accommodate the B-form DNA with no steric encumbrance. In addition, a hole, running parallel to the large hole of the toroid, houses the active site of the enzyme. It was suggested that this small hole may receive a single strand of DNA and deliver it to the active site. A mechanism for passage of part of a complete DNA ring through the cleaved DNA (covalently bound to the enzyme) into the large void in the enzyme has been proposed: it requires that part of the enzyme acts as a hinge.

Liang and Mislow have recently uncovered the presence of both catenanes¹⁰⁷ and knots¹⁰⁸ in protein structures. These discoveries have led the authors to speculate that topological chirality may be present in a wide range of conjugated proteins. Both classes of structure are restrained by disulfide cross-links and include the presence of cofactor. In the catenated forms of quinoprotein methylamine dehydrogenases, the cofactors are covalently bound cross-linkers of either a pyrroloquinoline quinone or tryptophan tryptophylquinone nature. In the case of the knot found in the structure of ascorbate oxidase, this cofactor, which forms part of the knotted cycle, is a copper(II) ion.¹⁰⁸ Liang and Mislow^{107,108} have also speculated that the inclusion of hydrogen bonds as edges of a molecular graph of a protein molecule could give other interlocked structures. This speculation raises a point which we will return to at the end of this review—namely, when is an interlocked structure interlocked? More precisely, which kind of bonds can you include on a molecular graph and which ones can you discount?

Perhaps the most abundant triple helical structure in the natural world is found in a group of proteins we call collagen.¹⁰⁹ All varieties of collagen, which constitutes the extracellular framework present in all multicellular organisms, are comprised of a coiled coil of three polypeptide α -chains, each containing a three-residue per turn left-handed helix wound together to form a right-handed superhelix.¹¹⁰ The

superhelix that results has a diameter of approximately 1.4 nm and exists as self-assembled fibrils of 10–200 nm in diameter and are eventually covalently cross-linked.¹¹¹ The most striking feature of the primary structure of each of the α -chains in collagen is the presence of a glycine every third residue. The principal reason for this particular feature of the primary structure is that glycine is the only amino acid small enough to be incorporated into the center of the triple helical superstructure. Approximately one-third of the remaining amino acid residues present in collagen are proline and 4-hydroxyproline, which are apparently there in order to assist in strengthening and rigidifying each strand, as well as to form hydrogen bonds between the strands in the triple helix.¹¹² Approximately 90 4-hydroxyproline residues are required in each α -chain in order that the collagen triple helix becomes a stable entity at physiological temperatures.¹⁰⁹

The structural information so far reported for collagen has been largely derived from fiber diffraction patterns. However, very recently, the crystal structure of a 30 amino acid peptide trimer has been solved and refined to 1.9 Å resolution.¹¹³ The protein sequence most common in collagen is proline-hydroxyproline-glycine (Pro-Hyp-Gly). The decamer containing this sequence forms a stable triple helix.¹¹⁴ When a single Gly to alanine (Ala) substitution is made in the center of this decamer, then the triple helix which forms has lower thermal stability than that of the nonmutated structure.¹¹⁵ Yet, it was the mutant which crystallized! The triple helix which forms is 87 Å in length and 10 Å in diameter. Either the carbonyl groups or the imino acid rings of all residues are exposed to the solvent, a feature which is believed to play a vital role in the formation of this type of protein aggregate. Water molecules form hydrogen-bonded bridges at the site of Ala substitution where there is some distortion of the triple helix on account of the direct hydrogen bonding between the amino acids of each helical thread being precluded for steric reasons. The alanine residues in each strand are located inside the triple helix, where the glycine residues they replace would be expected to reside. The Pro carbonyl groups and Gly amide functions form a total of 46 interchain hydrogen bonds (60 are possible) in the form of the Rich and Crick¹¹⁶ model II. Six of the residues that do not form hydrogen bonds are located at the termini of the triple helix, which is slightly unwound and disordered. The triple helices pack laterally some 14 Å apart, leaving this gap to be bridged by a highly ordered network of water molecules in which the Hyp residues play an important part. The self-assembled triple helix is thus, at least in the first instance, held together through hydrogen bonding as a result of the chemical information present in each of the component strands. Collagen's strength and versatility as a material in the body is partly a consequence of the intertwining of polypeptide chains that occurs at the molecular level: it is similar to a rope!

Certain naturally occurring polysaccharides which show great versatility in living organisms have intertwined superstructures in the solid and solution states. The family of carrageenans, which are extracted from red algae, are comprised of repeating

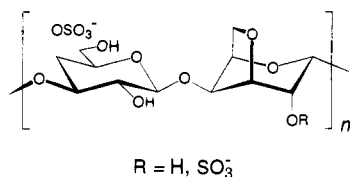


Figure 25. The repeating units present in κ -carrageenan and ι -carrageenan.

units of alternate 1,3-linked β -D-galactopyranose and 1,4-linked 3,6-anhydro- α -D-galactopyranose units (Figure 25). Two polymers from this family, κ -carrageenan ($R = H$) and ι -carrageenan ($R = SO_3^-$) have double-helical conformations, a superstructural feature first revealed by X-ray diffraction¹¹⁷ of stretched films of their salts. In each double helix, one complete turn of the helix corresponds to three disaccharide units (*ca.* 25 Å). It was proposed that these helices are held together by hydrogen bonds between the hydroxyl groups in each strand. The sulfate groups appear to be oriented toward the outside of the double helices. Similar duplexes are believed to be present in aqueous solutions of the polysaccharides, as determined by temperature¹¹⁸ and concentration¹¹⁹ studies carried out on the aggregates. Further association of the helices is believed to be promoted by cations in solution.¹²⁰ In addition, recent computational studies¹²¹ have confirmed the preference of this type of disaccharide unit to form helical conformations.

Hyaluronic acid is another important biopolymer which is capable of adopting a double helical structure.¹²² This polysaccharide is based on a disaccharide repeating unit comprised of alternating D-glucuronic acid and *N*-acetyl-D-glucosamine moieties. At pH 2.5, the polysaccharide forms a putty with a high proportion of crystallinity. An X-ray diffraction study of a stretched film of the material extracted from human umbilical cord led the authors¹²² to propose the existence of a left-handed double helix with antiparallel strands. The pitch length of 33.7 Å in the double helix is equivalent to a repeating unit composed of four of the disaccharide residues. Interestingly, in the proposed double helix, some of the carbonyl groups of the acid and acetyl functions of the disaccharide are directed toward the center of the superstructure, perhaps providing sites for metal ion or water binding. A very similar structure, reported in the subsequent paper,¹²³ for the potassium salt of hyaluronic acid was determined using the same technique as that for the structure of the parent polymer. A number of other conformations, whose interconversion is achieved readily in solution, are known to exist. The mechanism of interconversion of the different forms has been proposed to take place via a randomly coiled structure.¹²³ The ease of conversion of the double-helical form into other conformational states implies that it is not favored dramatically in solution. As well as forming double helices, polysaccharides have also been found¹²⁴ to possess triple-helical structures in the solid state. The naturally occurring (1 \rightarrow 3)- β -D-xylan¹²⁵ and, more recently, the (1 \rightarrow 3)- β -D-glucan¹²⁶ both form right-handed helices which are stabilized by hydrogen bonds around the inner edge of the three strands between the O(2) hydroxyl groups. The hydroxymethyl groups present in the glucan do not affect the helix as they are located on the periphery.

The remainder of this review will be given over to the attempts of synthetic chemists to use molecular recognition to construct interlocked and intertwined chemical objects. Nature informs us about the considerable benefits that might await the realization of such systems, while providing the inspiration for designing totally new and novel synthetic materials. The first compounds which have been exploited for the construction of rotaxanes by molecular recognition are produced naturally and are comprised of α -1,4 linked D-glucopyranose residues: they are the cyclodextrins.

IV. The Chemical Synthesis of Catenanes and Rotaxanes Incorporating Cyclodextrins

Cyclodextrins¹²⁷ are cyclic oligosaccharides that are probably the most obvious and readily available starting materials to employ in the assembly of interlocked molecular compounds¹²⁸ such as catenanes and rotaxanes.¹²⁹ The α -, β -, and γ -cyclodextrins, containing six, seven, and eight α -D-glucopyranose residues, respectively, have a rigid, cylindrical, hydrophobic cavity, which is capable of binding a vast range of rod-shaped guests in aqueous solution.¹³⁰ Indeed, many of these complexes can be regarded as pseudorotaxanes, *i.e.* rotaxanes in which no stoppers are present in order to prevent unthreading of the host from the guest. Lüttringhaus *et al.*,¹⁷ in the first planned experiment to prepare a catenane, tried linking the thiol-functionalized termini of a thread-like molecule (Figure 26), incorporating a hydroquinone residue, while the guest was surrounded by α -cyclodextrin in aqueous solution. Their efforts failed, possibly as a result of the lengths of the aliphatic chains in the guests being insufficient, or the conformations of the aliphatic chains in the guests being inappropriate.

In 1976, Ogata, Sanui, and Wada¹³¹ reported the synthesis of "inclusion polyamides"—pseudopolyrotaxanes! When β -cyclodextrin was stirred with aliphatic diamines (hexamethylenediamine, *p*-xy-

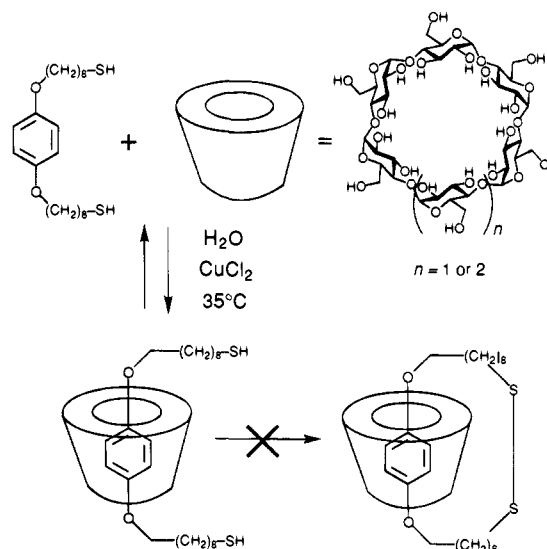


Figure 26. The first unsuccessful attempt to make a [2]-catenane (involving a cyclodextrin) reported¹⁷ in the literature.

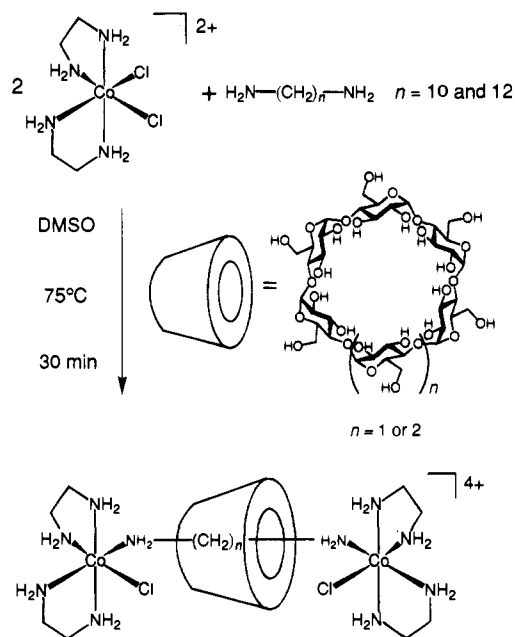


Figure 27. The preparation of a cyclodextrin-based [2]-rotaxane with metalloorganic stoppers using a threading procedure.¹³⁷

lylenediamine) in water, precipitates were formed and they were characterized as inclusion compounds. Subsequent condensation of these included diamines with isophthaloyl or terephthaloyl chloride afforded polyamides, which were surrounded by many of the cyclodextrins—“like a train passing through many tunnels”, to quote the authors. The solubilities and moisture absorptions exhibited by the pseudopolyrotaxanes were greater than those of the naked polymer thread. Differential thermal analyses of the threaded and naked polymer showed that there were no significant amounts of unthreaded polyamide in the pseudopolyrotaxane. The authors concluded that similar materials “will develop a new broad field of polymer materials”.

Maciejewski and co-workers^{132–136} have reported several attempts at the preparation of polyrotaxanes in the solid state, by, for example, radiation polymerization of crystalline monomeric adducts of β -cyclodextrin and vinylene dichloride, allyl chloride, and methyl methacrylate. In the case of polyvinylene dichloride, stable polymers ($M_w \approx 20\,000$) were reported, containing 80 wt % β -cyclodextrin and 20 wt % polymer chain. Polyrotaxanes were suspected to be formed, although the possibility of covalent bonding between beads and threads was not ruled out. Polymerization of the crystalline adduct of β -cyclodextrin with methyl methacrylate did not produce a stable polymer.

The first well-characterized low molecular weight rotaxanes incorporating both α - and β -cyclodextrins as the bead components were reported by Ogino¹³⁷ in 1981. The [2]rotaxanes were prepared (Figure 27) by dissolving a diaminoalkane in a small volume of DMSO which was then saturated with the cyclodextrin, followed by addition of *cis*-[CoCl₂(en)₂]Cl. The threaded dumbbell and free dumbbell compounds were separated by column chromatography, which was also used for their characterization, along with optical rotation, electronic spectra, and ¹³C NMR spectroscopic measurements. The rotaxanes were

isolated in 2–19% yields, the more efficient reactions being with the smaller cyclodextrins.¹³⁸ Using a similar approach and characterization methods, Yamanari and Shimura¹³⁹ have prepared rotaxanes composed of the same bead components and a dumbbell incorporating similar cobalt(II) stopper complexes, but where the rod contains a thiol coordinated to the stopper (Figure 28). The [2]rotaxanes were prepared by reacting a thiol-derivatized cobalt(II) complex with a dibromoalkane in the presence of either α - or β -cyclodextrin. Here, the formation of the rotaxanes incorporating the Δ form of the complex was found to be favored over those incorporating the Λ form. The best yield obtained was 28% for the [2]-[$\Delta\Delta$ -(en)₂Co{H₂N(CH₂)₂S(CH₂)₁₂S(CH₂)₂NH₂}Co(en)₂Cl₆]-[α -cyclodextrin]-rotaxane. The same research group¹⁴⁰ went on to incorporate a mercaptoacetic acid residue into each blocking complex, although it actually proved to be less stable than the 2-aminoethanethiol analogs. Once again, the threads incorporating the Δ complexes formed a rotaxane with α -cyclodextrin preferentially. The unsymmetrical [2]-[(en)₂Co{O₂CCH₂S(CH₂)₁₂S(CH₂)₂NH₂}Co(en)₂Cl₆]-[α -cyclodextrin]-rotaxane, where the two stoppers of the dumbbell were different, was also prepared. Rotaxane formation was confirmed by thorough circular dichroism and ¹³C NMR spectroscopic studies.

The self-assembly (Figure 29) in 71% yield of a “threaded molecular loop” was reported in 1990 by the group of Lawrence.¹⁴¹ Substitution of biphenol with an ammoniumpropyl chain provides an ideal substrate for inclusion within the cavity of heptakis-(2,6-di-*O*-methyl)- β -cyclodextrin. Although the chloride salt of the substrate is only sparingly soluble in aqueous solution, addition of the substituted cyclodextrin renders the former completely soluble, in the form of a pseudorotaxane. Addition of an aqueous solution of sodium tetraphenylboron yielded a precipitate, which was characterized as the “threaded molecular loop”, in essence a pseudorotaxane. Although the complex is stable in acetone, even at reflux, addition of triethylamine to the solution

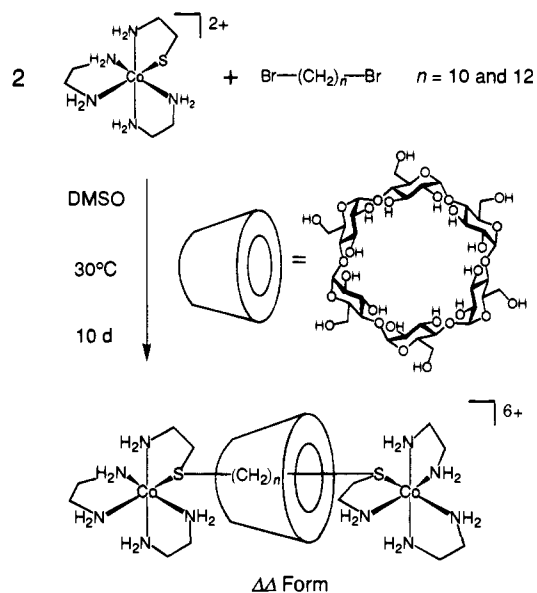


Figure 28. The preparation of a cyclodextrin-based [2]-rotaxane with chiral metalloorganic stoppers using a threading procedure.¹³⁹

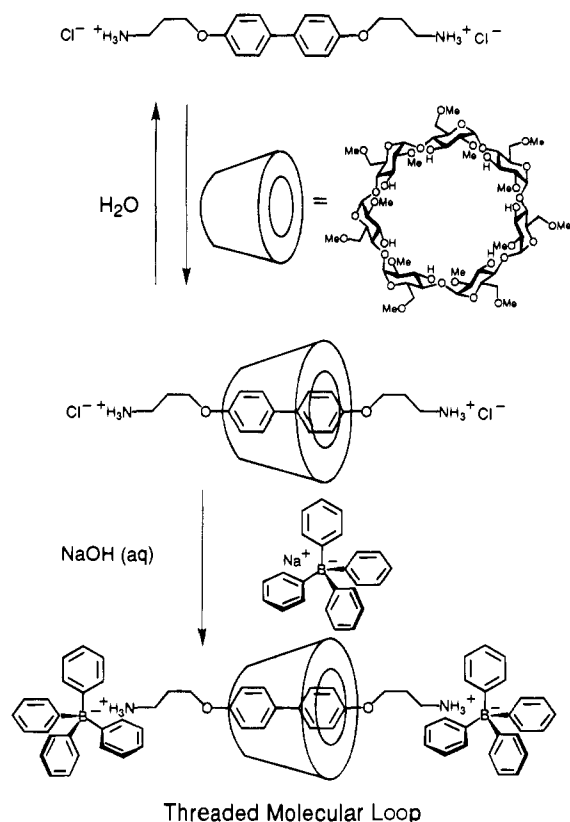


Figure 29. The self-assembly of a threaded molecular loop.¹⁴¹

causes dissociation of the "loop". The same cyclodextrin was also used for the self-assembly (Figure 30) of a [3]pseudorotaxane containing a tetra-aryloxy-alkylammonium porphyrin in the rod component, upon which two of the cyclodextrins are accommodated.¹⁴² The authors proposed that two sodium ions were trapped between the two cyclodextrin rings in this superstructure which has been compared¹⁴³ to heme-containing proteins, where a potential binding site is surrounded by a hydrophobic sheath. The groups of Waggon¹⁴⁴ and Czarnik¹⁴⁵ have prepared similar [3]pseudo- and [4]pseudorotaxanes, but without ionic blocking groups. The latter incorporates a substituted 1,4,5,8,9,12-hexaazatriphenylene core with three appended phenylene residues which are each surrounded by an heptakis(2,6-di-*O*-methyl)- β -cyclodextrin.

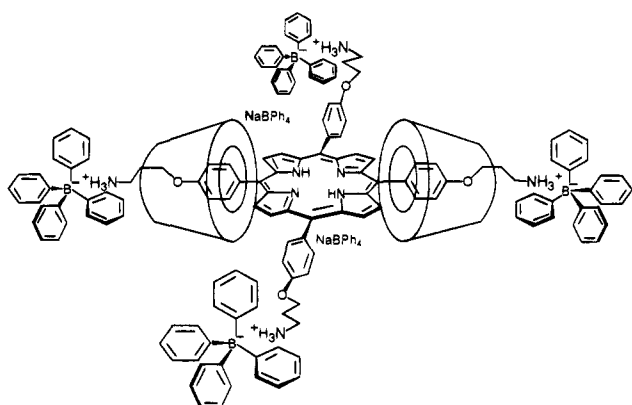


Figure 30. The self-assembly of a [3]pseudorotaxane involving heptakis(2,6-di-*O*-methyl)- β -cyclodextrin as the two rings.¹⁴²

The complexation of (ferrocenylmethyl)dimethylamine derivatized with *n*-alkyl chains of varying lengths¹⁴⁶ within the cavities of α -, β -, and γ -cyclodextrins paved the way for the synthesis (Figure 31) of a zwitterionic rotaxane in 15% yield.¹⁴⁷ The [2]-rotaxane was prepared by 1-[3-(dimethylamino)propyl]-3-ethyl-carbodiimide (EDC) coupling of potassium 5-amino-2-naphthalenesulfonate with either dimethyl(7-oxoheptyl)(ferrocenylmethyl)ammonium cation or dimethyl(7-oxoundecyl)(ferrocenylmethyl)ammonium cation in the presence of 2 equiv of α -cyclodextrin in water. The unsymmetrical nature of the dumbbell component in these compounds means that two isomers of each [2]rotaxane are possible. In both cases, they were identified by ¹H NMR spectroscopy. In the case of the rotaxane incorporating the heptyl thread,¹⁴⁸ the ratio of these isomers was 6:4. The isomeric rotaxanes were separated using reverse-phase TLC. An intriguing fact about the isomers is that those with the wider primary face of the cyclodextrin facing the naphthalenesulfonate stopper undergo slow unthreading at a rate which was found to be dependent on the solvent. The other isomers are completely stable.

In 1991, Ritter and Born¹⁴⁹ reported the first side-chain polyrotaxane, which incorporates heptakis(2,6-di-*O*-methyl)- β -cyclodextrin as the bead. A "semirotaxane" (pseudorotaxane) was formed (Figure 32) between an aliphatic amine terminated with a triarylmethane blocking group and the torus-shaped host. It was characterized by FABMS, ¹H NMR spectroscopy, and DSC. This complex was reacted with an anhydride-activated copolymer of MMA and 11-(methacryloylamino)undecanoic acid. The resulting polyrotaxane was subjected to ¹H NMR and IR

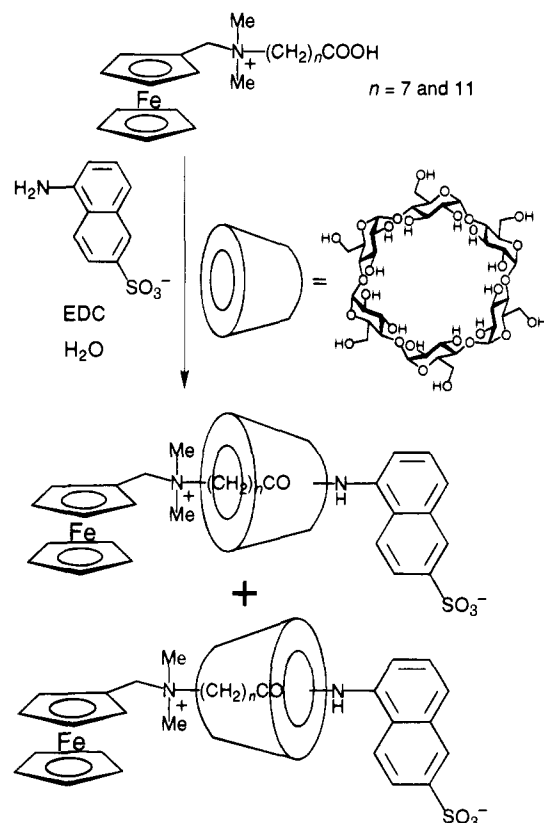


Figure 31. The synthesis of orientational isomers of a [2]-rotaxane where α -cyclodextrin is the ring and one of the stoppers is a ferrocenyl group.¹⁴⁶⁻¹⁴⁸

spectroscopies, which showed that virtually all the copolymer side chains were attached rotaxanes, and ruled out the presence of any free cyclodextrin. The polyrotaxane has a lower viscosity than the native polymer because of the lack of any interchain hydrogen bonding. Polymerization¹⁴⁹ of a diene-terminated pseudorotaxane, whose existence was confirmed spectroscopically, did not lead to a similar comblike polymer under standard conditions. The same group has recently reported¹⁵⁰ similar side-chain polyrotaxanes, utilizing the same semirotaxane to that described in Figure 32. However, the semirotaxane is covalently linked to a polymer bearing side arm with two reactive groups. The resulting poly(bis[2]-rotaxane) was characterized by elemental analysis and NMR spectroscopy and showed modified thermal behavior to that of the native polymer containing no threaded cyclodextrin.

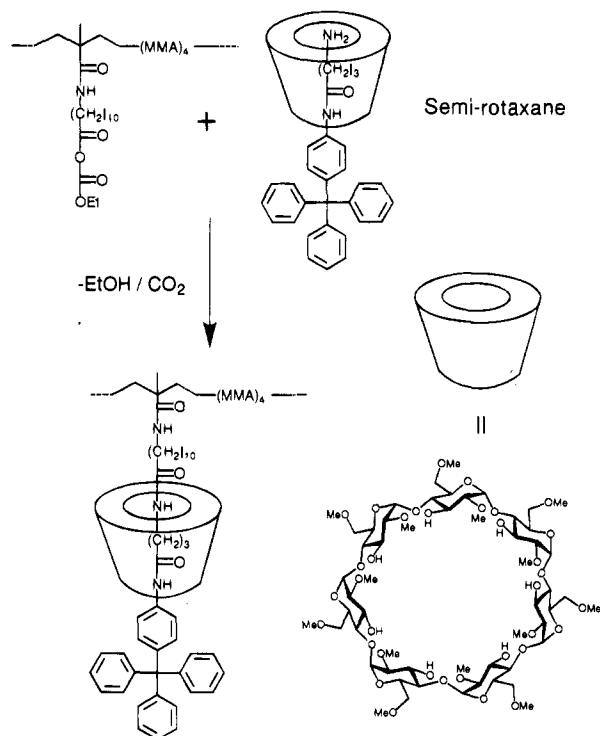


Figure 32. The preparation of a side-chain polyrotaxane by a threading procedure.¹⁴⁹

In a manner similar conceptually to that of the Ogino research, Wylie and Macartney¹⁵¹ have achieved the self-assembly (Figure 33) of [2]rotaxanes incorporating an α -cyclodextrin threaded on to an 1,1'-(α,ω -alkanediyl)bis-(4,4'-bipyridinium) dicationic ligand and stoppered with labile $[\text{Fe}(\text{CN})_5\text{OH}_2]^{3-}$ ions. The rotaxane, which is formed efficiently in solution, is not kinetically inert, and was not isolated. This lability is emphasized by the fact that, when the dumbbell component $[(\text{NC})_5\text{Fe}(\text{bpy}(\text{CH}_2)_n\text{bpy})\text{Fe}(\text{CN})_5]^{4-}$ is mixed with α -cyclodextrin, rotaxane formation takes place by slow dissociation of the blocking groups, and then their recombination after threading of the bead by the "semirotaxane".¹⁵² Similar rotaxanes incorporating pyrazinium moieties, rather than bipyridinium groups, were reported¹⁵³ to be more kinetically stable than the 4,4'-bipyridine analogs.

The ability of heptakis(3-*O*-acetyl-2,6-di-*O*-butyl)- β -cyclodextrin to complex the pyridinium group of a

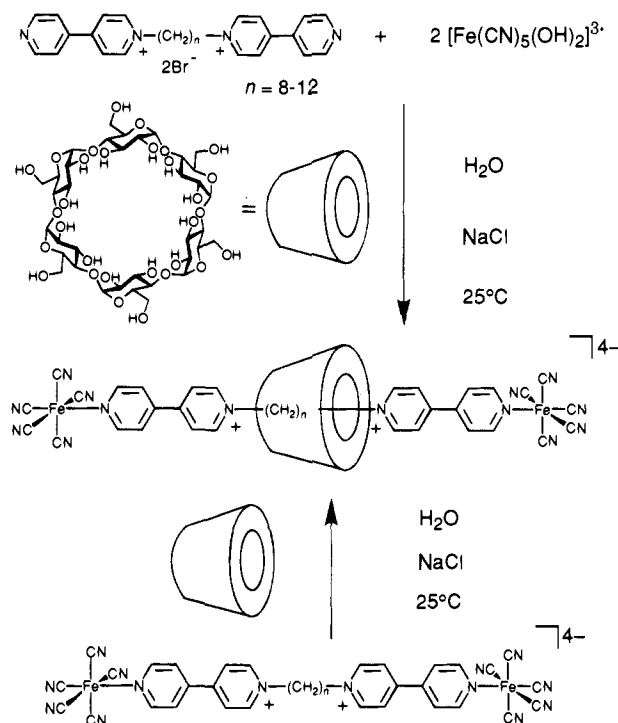


Figure 33. The self-assembly of a kinetically labile [3]-rotaxane.¹⁵¹

monostoppered 4,4'-bipyridine unit in CD_3CN encouraged Wenz *et al.*¹⁵⁴ to believe that treatment with a benzylic bromide attached to a stopper group would yield a [2]rotaxane. Their hopes were dashed on account of the more rapid rate of reaction of the pyridyl ring and benzylic bromide groups outside the cavity of the cyclodextrin. However, extension of the alkyl spacer between the reactive groups and the triarylmethane stopper in each component of the dumbbell, followed by reaction in the presence of the lipophilic cyclodextrin, yielded 19% of a [2]rotaxane (Figure 34). The failure of the first attempt was attributed to steric interactions between the blocking group and the host. A slight modification of this

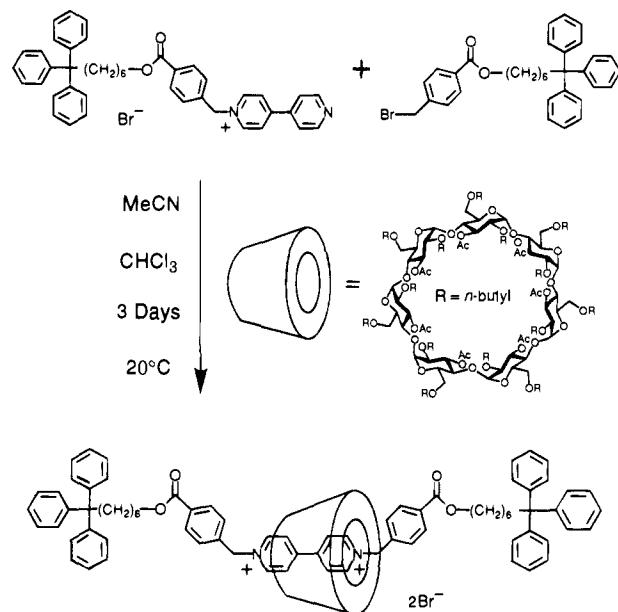


Figure 34. The self-assembly in organic solvents by a threading procedure of a [2]rotaxane incorporating a lipophilic cyclodextrin.¹⁵⁴

original system (replacing an ester spacer in the dumbbell with an ether linkage) enabled the Mainz group (now in Karlsruhe) to prepare a [2]rotaxane¹⁵⁵ in 36% yield in acetonitrile–chloroform (3:1). The efficiencies of rotaxane formation were found to be highly solvent dependent, the yields in chloroform or DMSO–chloroform (3:1) being much lower than those in acetonitrile–chloroform (3:1). Similarly, the ring size of the cyclodextrin is crucial to the efficiency of the reaction. No rotaxane was isolated with the smaller α -cyclodextrin derivative, while the yield with the larger γ -cyclodextrin derivative is only 15%, possibly on account of its poorer preorganization.

When the bis(hydrochloride) of 4,4'-diaminostilbene and an excess of β -cyclodextrin were dissolved in aqueous sodium bicarbonate, a complex is formed which can be capped¹⁵⁶ with a trisulfonic acid-substituted trichloro-*s*-triazine at 25 °C (Figure 35). Reaction of the remaining chloro functions on the triazine nuclei with aniline at elevated temperatures yielded a [2]rotaxane in 28% yield. The temperature-dependent reactivity of the three chloride groups of 2,4,6-trichloro-*s*-triazine allowed this control in the synthesis. The constitution of the rotaxane was confirmed by the perturbation of the π - π^* absorption band of the stilbene chromophore by the threaded cyclodextrin.

Pseudopolyrotaxanes and polyrotaxanes, in which cyclodextrins are incorporated as the ring component, were associated with a surge of interest¹⁵⁷ in 1992. Both poly(iminoundecamethylene) and poly(iminotrimethylene-iminodecamethylene) accommodate α -cyclodextrin and heptakis(2,6-di-*O*-methyl)- β -cyclodextrin.¹⁵⁸ The threading of α -cyclodextrin onto poly-

(iminoundecamethylene) takes place at a rate which is slow on the ¹H NMR time scale in heavy water at pH < 6. It has been proposed that the cationic groups present a barrier to the motion of the bead along the chain. The ¹H NMR spectrum of this mixture was stable after 1.5 h, while equilibration required 170 h when poly(iminotrimethylene-iminodecamethylene) was used as the polymeric thread. Following the equilibration by viscosity measurements gave very similar times for the steady states to be reached. Mixing either of the polymers with the larger substituted cyclodextrin, *i.e.* heptakis(2,6-di-*O*-methyl)- β -cyclodextrin, resulted in virtually instantaneous equilibration upon mixing the components. The long reaction times for the α -cyclodextrins were attributed to the difficulty of threading the cyclodextrins all the way on to the middle of the polymeric chain once they had found their way on to the ends of the polymer. The equilibration hypothesis was confirmed by removal of cyclodextrin from the fully threaded polymer by dialysis. To unthread the α -cyclodextrin from poly(iminoundecamethylene) took 15 h, while removal of the rings from poly(iminotrimethylene-iminodecamethylene) was not complete after 2 weeks! Conclusive proof of the threading of α -cyclodextrin on to poly(iminotrimethylene-iminodecamethylene) was achieved by the arbitrary stoppering of the polymeric backbone of the pseudopolyrotaxane with the hydrochloride salt of nicotinoyl chloride, to form a polyrotaxane. Dialysis of the reaction products released only the cyclodextrins not positioned between two stoppers. The amount of unthreading upon dialysis decreased with the amount of reacted stopper group. A polyrotaxane

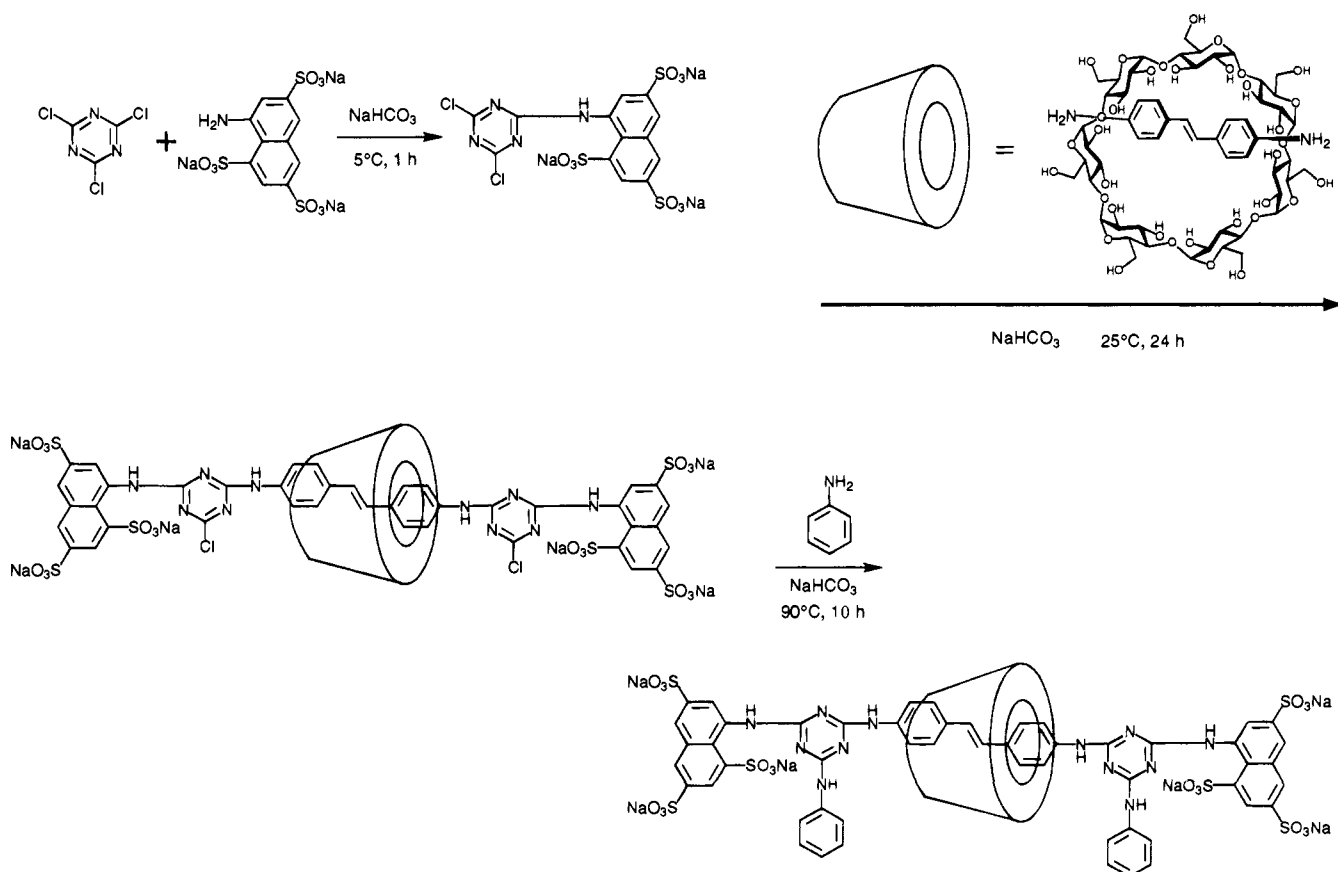


Figure 35. The self-assembly of a [2]rotaxane incorporating β -cyclodextrin by a threading procedure.¹⁵⁶

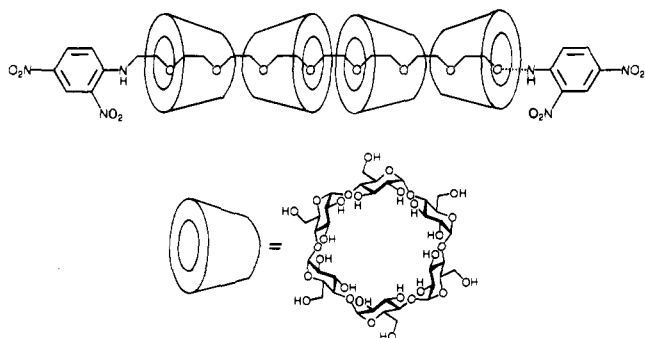


Figure 36. The self-assembly of a polyrotaxane with poly(ethylene glycol) bisamine as the thread and α -cyclodextrin as the ring by a threading procedure.¹⁵⁹ The cyclodextrin rings are believed to be threaded in a head-to-head/tail-to-tail fashion.

was isolated with a degree of polymerization of 55 ± 5 with 37 threaded cyclodextrins, and an average molecular weight of $55\,000 \pm 5\,000 \text{ g mol}^{-1}$, as determined by low-angle laser light scattering.

In a similar vein, the pseudopolyrotaxane formed in water between poly(ethylene glycol) bisamine (mass 3350) and a vast excess of α -cyclodextrin was isolated and then stoppered in DMF, this time selectively at the termini of the polymeric thread, with 2,4-dinitrofluorobenzene (Figure 36).¹⁵⁹ Purification by washing and chromatography yielded a product with dramatically different solubility characteristics to either of the two components. The polyrotaxane, which the authors refer to as a molecular necklace, was isolated in a crude 60% yield and was characterized by elemental analysis, ^1H and ^{13}C NMR spectroscopies, and gel chromatography. It has an average molecular mass of approximately 25 000 and carries in the region of 20–23 threaded cyclodextrins. The fact that the polyrotaxane is insoluble in water, yet soluble in 0.1 N sodium hydroxide suggested the presence of strong hydrogen bonds between the cyclodextrins, leading to the claim that an alternate orientation of the rings on the thread was present (Figure 36).

Later, Harada reported¹⁶⁰ the same reaction carried out starting with poly(ethylene glycol) of average

molecular weight 2000. Fractionation of the product allowed identification of “polyrotaxanes” with different numbers of α -cyclodextrins per molecule. Up to 37 molecules of α -cyclodextrin were accommodated on to one poly(ethylene glycol) thread! The products were clearly polydisperse. The X-ray powder patterns of the poly(ethylene glycol) (molecular weight = 3350) bisamine-derived rotaxane showed the material to be crystalline, with a pattern similar to those observed for complexes of cyclodextrins with extended column structures, confirming the rotaxane topography. When the 28-mer of poly(ethylene glycol) bisamine (molecular weight = 1248) was used as the thread,¹⁶¹ only 16% crude yield of the “polyrotaxane” was isolated, in which 12 cyclodextrins were threaded on to the linear component, indicating that the structure has the cyclodextrin beads relatively close packed. The reasons for the discrepancies in the occupancy of the poly(ethylene glycol) dumbbells by the cyclodextrins is partially a result of the fact that glycols between 600 and 2000 molecular weight are complexed most efficiently.

The polyrotaxane synthesized from poly(ethylene glycol) (mass 1450) has been used¹⁶² as a template for the construction of a tubular polymer (Figure 37). The hydroxyl groups of the threaded α -cyclodextrins were reacted with epichlorohydrin to “link up the lampshades”. The stopper groups of the resulting “jumbo”-sized [2]rotaxane (since the beads are joined!) were cleaved with strong base. The molecular tube, which had an average molecular weight of 20 000 as determined by size exclusion chromatography, was isolated in 92% yield. The signals in the ^1H NMR spectrum of the molecular tube were broad, presumably owing to the random substitution of the cyclodextrin. UV-visible spectroscopic experiments, involving mixing $\text{KI}-\text{I}_2$ with either randomly cross-linked α -cyclodextrin or the molecular tube, indicated that I_3^- ions were oriented in the molecular tube. Thus, the polyrotaxane has been used as a scaffold for a nanometer-scale structure which would otherwise have been inaccessible. Most recently, the same group¹⁶³ have claimed the double-stranded inclusion

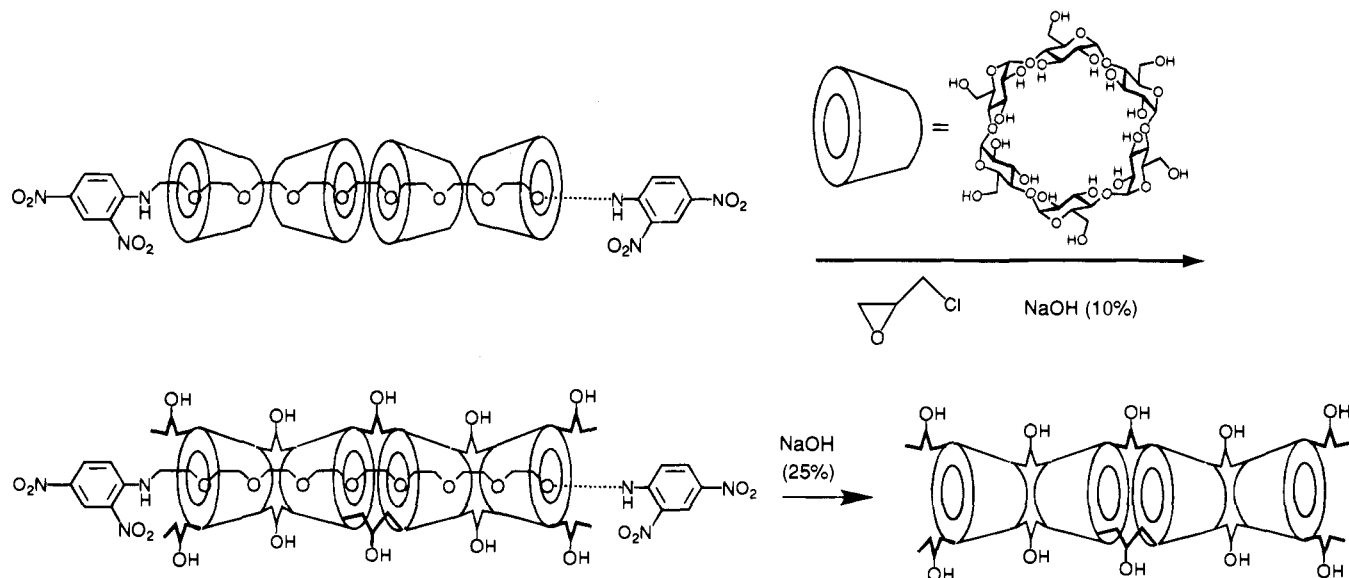


Figure 37. The synthesis¹⁶² of a tubular polymer of linked α -cyclodextrin units from the polyrotaxane described in Figure 36.

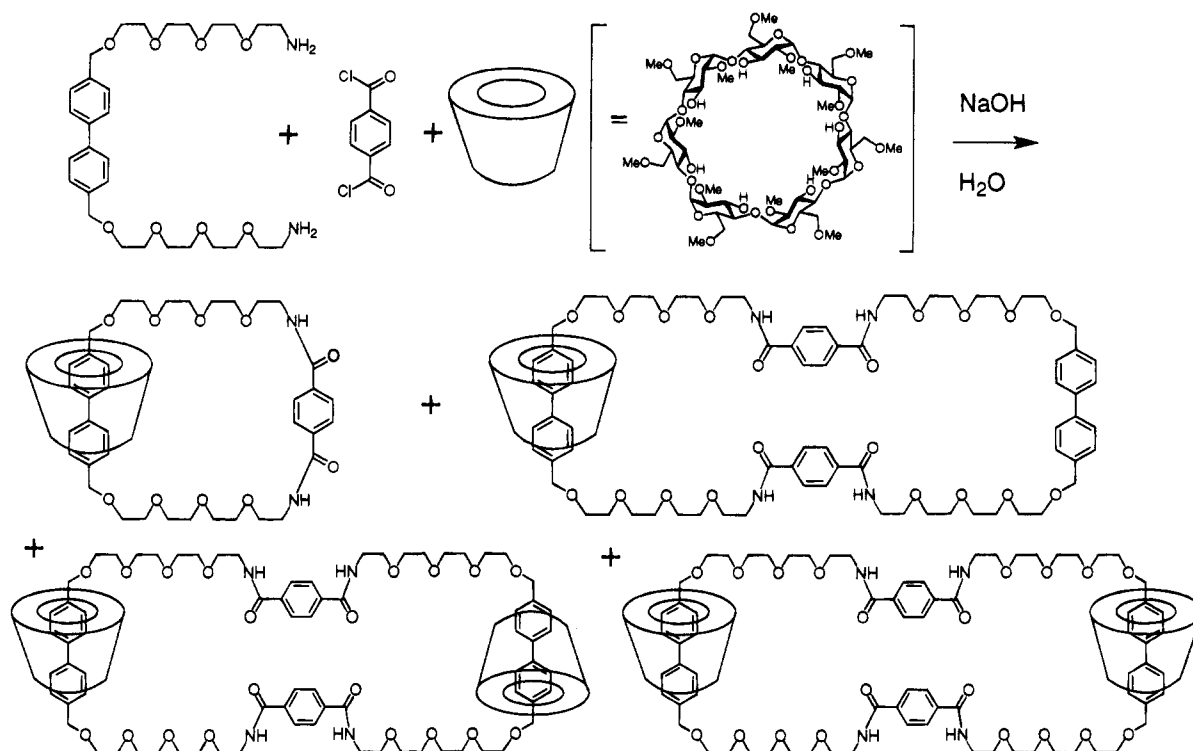


Figure 38. The self-assembly of two [2]catenanes and two isomeric [3]catenanes, involving heptakis(2,6-di-*O*-methyl)- β -cyclodextrin as one or two of the rings, in aqueous solution under Schotten–Baumann conditions.^{164–166}

of poly(ethylene glycol) chains, derivatized with aromatic residues at the termini, within the cavities of γ -cyclodextrin hosts. The proposed inclusion of two guest strands within two cyclodextrins was supported by emission spectra, which showed excimer bands not present in the guest alone. Folding back of one strand within the cavities of the cyclodextrins was ruled out by monosubstitution of the poly(ethylene glycol) chain. The excimer band for the dimer remained, proving that two of the aromatic probes from different molecules were in close proximity. It has been proposed that such complexes, which were compared to the inclusion of DNA's double helix by DNA polymerases, may be used for the construction of polycatenanes.

The first catenated cyclodextrins^{164,165} were reported 35 years after the team headed by Lüttringhaus had attempted to reach this goal. Heptakis(2,6-di-*O*-methyl)- β -cyclodextrin was chosen as the preformed ring, owing to its rigid and extended torus-shaped cavity (compared with the native β -cyclodextrin) and good solubility in a variety of solvents including water. The strong binding of extended bitolyl units within the cavity of the modified cyclodextrin suggested using this aromatic unit as a building block for the other macrocycle. A bitolyl unit, extended by tetraethylene glycol chains and terminated with amino groups, was reacted (Figure 38) under Schotten-Baumann conditions with terephthaloyl chloride (0.01 N sodium hydroxide solution) in the presence of heptakis(2,6-di-*O*-methyl)- β -cyclodextrin. The highest yielding products were the 1:1 and 2:2 macrocyclic amides formed between the two acyclic reagents. The [2]catenanes related to the 1:1 and 2:2 macrocycles were formed in 3.0 and 0.8% yields, respectively. In addition, two isomeric [3]catenanes were obtained as an equimolar mixture in 1.1% yield. They were separated¹⁶⁶ using reverse-

phase HPLC and assigned to the head-to-head and head-to-tail isomers on the basis of their ¹³C NMR spectra. The relative yields of the macrocycles and catenanes strongly suggest that the presence of the bound cyclodextrin around the macrocycle precursor inhibits the latter's ring closure. None of the dynamic processes taking place in these catenanes could be slowed down on the ¹H NMR time scale. An X-ray crystal structure (two views are shown in Figure 39) was obtained for the [2]catenane incorporating one modified cyclodextrin and one 1:1 macrocycle. The structure reveals that the bitolyl residue of the macrocycle which is formed during the Schotten-Baumann reaction occupies the cavity of the heptakis(2,6-di-*O*-methyl)- β -cyclodextrin, while the bislactam component nestles alongside the cyclic oligosaccharide. Somewhat surprisingly, no hydrogen-bonding interactions between the two macrocycles could be observed in the solid-state structure. However, the molecules pack in a pseudo cone-in-cone arrangement such that the lower polyether strand of one [2]catenane is inserted partially into the upper orifice of another [2]catenane molecule. This packing arrangement extends throughout the crystal.

When a constitutionally asymmetric diamine was employed¹⁶⁶ as the substrate during the catenation, orientational isomers of a [2]catenane were formed and isolated without being identified one from the other unambiguously. In general, the catenated cyclodextrin derivatives shown in Figures 38 and 39 are soluble in halogenated and aromatic hydrocarbons as well as in hydroxylic solvents. The existence at long last of these intriguing new compounds gives us potentially a unique insight into the nature of the noncovalent bonding interactions that cyclodextrins employ in binding substrate molecules.

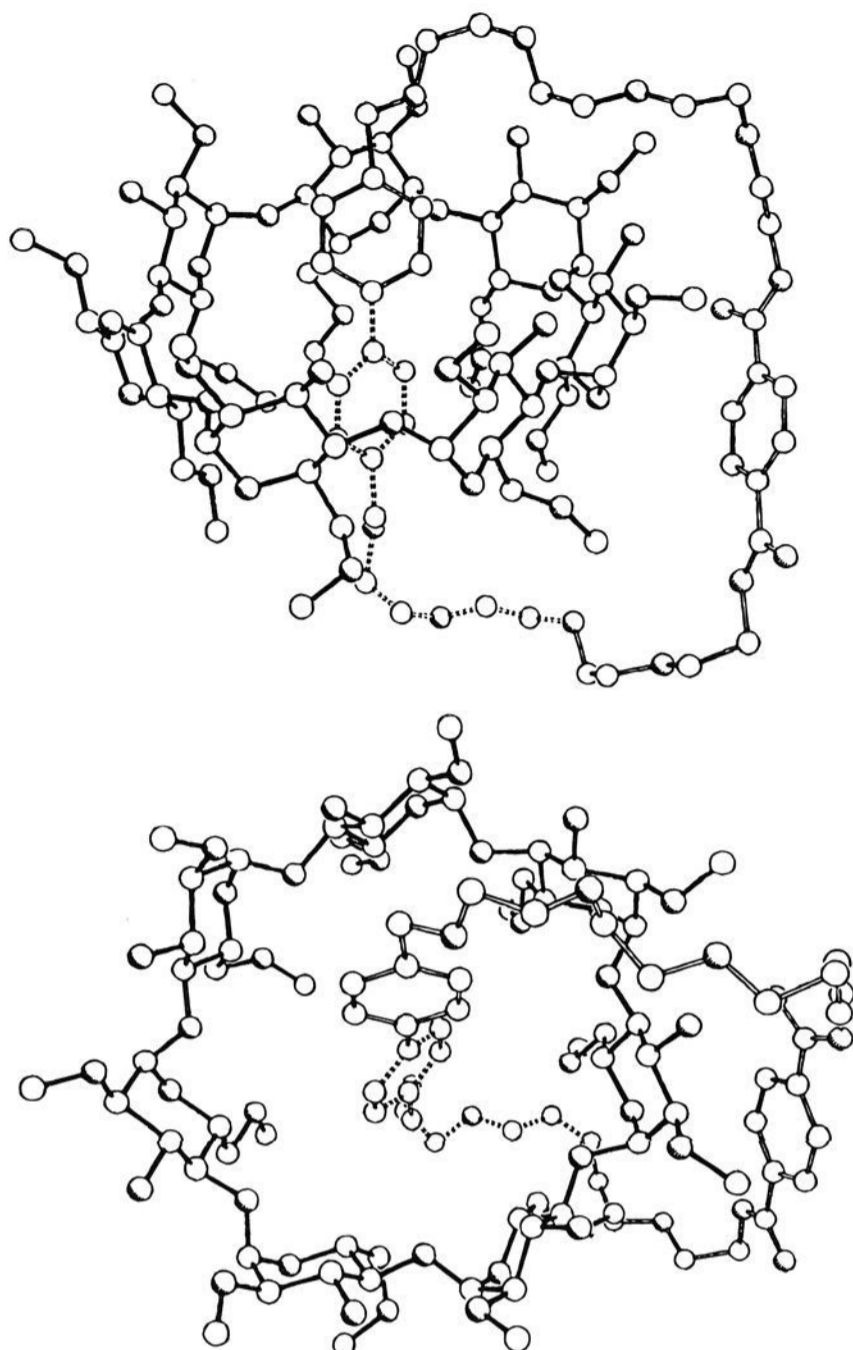


Figure 39. A side-on view and a plane view of the X-ray crystal structure of the smaller [2]catenane illustrated in Figure 38.¹⁶⁶

V. Synthetic Double and Triple Helices

The synthetic chemical mimicry of the double-helix structural motif has been an area of intense research activity in recent years. The occurrence of single helices¹⁶⁷ is not uncommon in the realm of synthetic organic chemistry, where it endows stereochemistry,¹⁶⁸ for instance, with propellers¹⁶⁹ and helicenes.¹⁷⁰ However, examples of double and triple helices are extremely rare in this area of chemistry. In order to generate double- and triple-helical structures, control over the directionality of noncovalent bonding and the conformations of the components is essential. For this reason, the creation of entirely synthetic double- and triple-helical structures has been dominated by examples which are templated by transition metal ions,¹⁵ since they have well-defined and varied coordination geometries while a wide range of ligands are accessible to the chemist. Mononuclear transition metal complexes by themselves are the beginnings of helices, as demonstrated by their existence as antipodes.¹⁷¹ Indeed, the resolution of the antipodes of mononuclear transition metal complexes was first achieved¹⁷² in the early part of this century. Moreover, it is highly probable that multinuclear double helices were formed by multidentate ligands long before they were recognized.

The ligand bis(2-thiobenzaldimino)-2,6-diacetylpyridine forms a single helix around zinc(II).¹⁷³ Using

a similar ligand (**32** in Figure 40), Webster and Palenik¹⁷⁴ reported the preparation and crystal structure of a dimeric zinc complex by deprotonation of the pentagonal-bipyramidal (single-helical) complex $\text{Zn}(\text{H}_2\text{dapp})(\text{H}_2\text{O})\text{Cl}_2$ ($\text{dapp} = 2,6\text{-diacetylpyridine bis-2-pyridylhydrazone}$). The structure of the resulting deprotonated complex, $[\text{Zn}_2(\text{dapp})_2]_2\text{CHCl}_3 \cdot \text{H}_2\text{O}$, has a geometry (Figure 40) where the two dianionic dapp^{2-} ligands wind round both zinc ions which have distorted octahedral coordination geometries with the central pyridine atom of each ligand coordinating to both metal centers.¹⁷⁵ Several years later, a derivative (**33**) of this ligand was shown to form complexes with a wide variety of transition metal ions¹⁷⁶ and, in particular, to form a double-helical complex with silver(I). The two 2,6-diacetylpyridine bis(6-chloro-2-pyridylhydrazone) ligands surround the two silver ions such that the coordination around the metal ion is a distorted tetrahedron, with one of the terminal pyridyl rings of each ligand being uncoordinated (Figure 40). The ligand geometry is stabilized by $\pi-\pi$ stacking interactions between the uncoordinated terminal pyridyl rings of one ligand and the central pyridine ring of the other.¹⁷⁷ The silver ions are 3.14 Å apart.

In 1976, Fuhrhop and co-workers¹⁷⁸ showed that dehydrated zinc octaethyl formyl biliverdinate forms a double-helical dimer (Figure 41). The monomeric zinc octaethyl formyl biliverdinate forms brown crystals, which were separated manually from those of the green dehydrated dimeric complex that cocrystallizes in acidic media. Each zinc ion has a distorted tetrahedral coordination involving two nitrogen atoms from each ligand. The distance between the zinc ions is 3.37 Å, while the total length of the helix is 5.2 Å. Similar tetrapyrrolic metal ion complexes have been studied because of their similarity to bilirubin, the naturally occurring bile pigment, as well as on account of their intermediacy in the synthesis of corrinoid and porphyrinoid macrocycles. The X-ray crystal structure of the zinc(II)

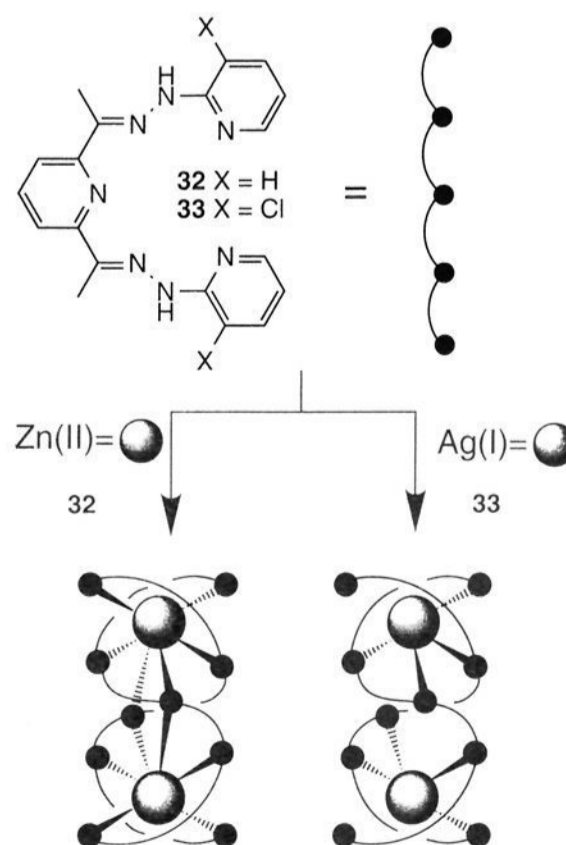


Figure 40. The double-helical complexes formed when two dianionic dapp^{2-} ligands [$\text{dapp} = 2,6\text{-diacetylpyridine bis-}(2\text{-pyridylhydrazone})$] wrap themselves around zinc(II) and silver(I) ions.^{175,176}

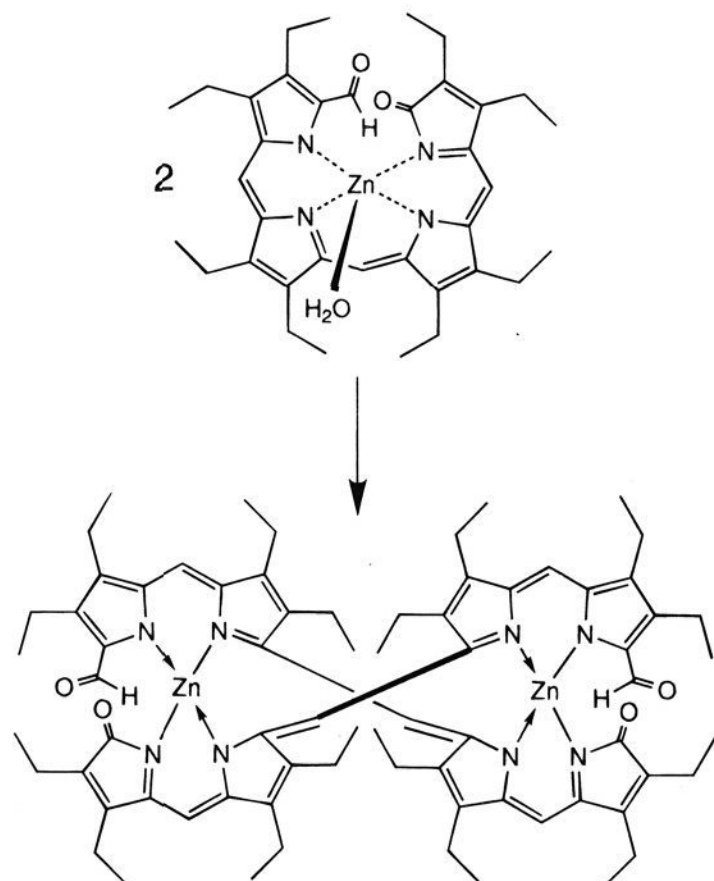
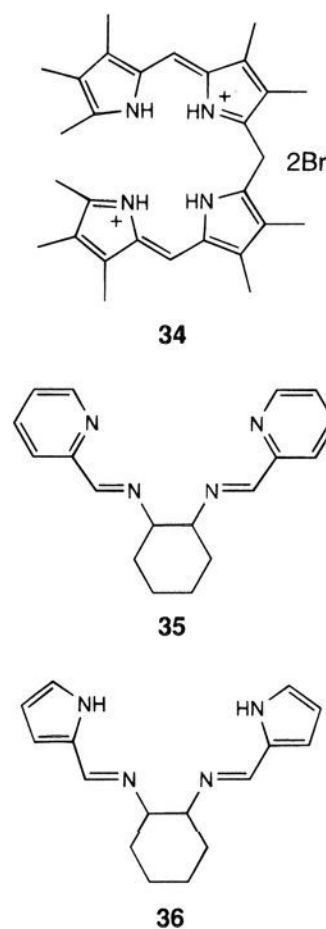


Figure 41. The formation of a double-helical dimer by dehydrated zinc octaethylformyl biliverdinate.¹⁷⁸

complex of decamethylbiladiene (**34**) reveals¹⁷⁹ a similar double-helical arrangement of the dimeric complex to that described by Fuhrhop. The zinc ions are coordinated as a distorted tetrahedron. No solution state studies were reported. The nickel(II) complex of a bilindione derivative, on the other hand, forms a 1:1 complex¹⁸⁰ in which the ligand is forced to adopt a single-helical arrangement around the central metal ion, as is the case for related ligands in this series.¹⁸¹

The quadridentate ligands **35**, where the cyclohexyl ring has the (*RS*) configuration, were shown by van Koten and co-workers¹⁸² to react with $[M(O_3SCF_3)]$ [$M = Ag(I)$ or $Cu(I)$] to form dimeric double-helical complexes in both the solid and solution states. The dimeric complexes are preferred over the monomeric ones, partially because of the preferences of the two metal ions for nonplanar coordination geometries, and also because of the strain that would be placed on the ligand if it was forced into a 1:1 complex. The solid-state structural analysis of the complex formed by **35** and silver(I) revealed its double helical geometry, where the metal ion centers are 3.25 Å apart and coordinated by two donor atoms from each ligand. The structure was denoted *endo*-DSR-*RSD*. Support for the existence of a similar structure in solution was forthcoming from a comprehensive multinuclear ($^{107,109}Ag$, 1H , ^{15}N , ^{13}C) NMR spectroscopic investigation, though clearly, the enantiomer *endo*-LRS-*SRL* may also be present in solution.¹⁸³ The dissociation and recoordination of the complexes are slow on the 1H NMR time scale from 210 to 310 K. As a result of efforts to obtain solution-state structural and dynamic information, concerning the pyrrole-containing complexes described earlier, the same group¹⁸⁴ prepared the ligand **36**—once again as the (*RS*) isomer, and then reacted it with $ZnSO_4$ in the presence of KOH to afford neutral dinuclear complexes. The stoichiometries of the complexes were confirmed using field-desorption mass spectrometry, and a helical arrangement of the ligands around the

metal centers was suggested on the basis of NMR spectroscopic evidence. The intramolecular and intermolecular exchange processes between complexes were slow on the 1H NMR time scale. Indeed, when an ethyl spacer was used instead of the cyclohexyl spacer in **36**, the resulting complex was dynamic on the 1H NMR time scale, even at 213 K.



The first triple-stranded helix incorporating two metal ion centers (Figure 42) was reported by the group of Shanzer¹⁸⁵ in 1987. Circular dichroism showed that the chiral ligand **37** forms a right-handed triple-helical structure when two iron(III) ions are bound to the host. The complex is stabilized by interstrand hydrogen bonds between the periph-

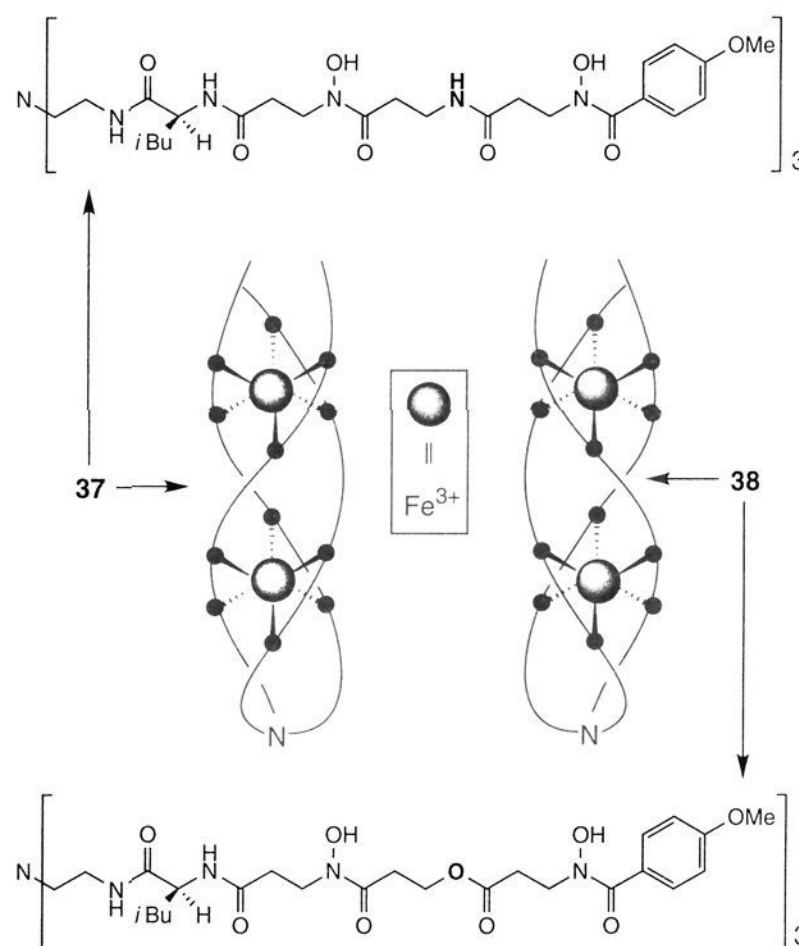


Figure 42. Two tethered triple-stranded helices incorporating two iron(III) ions.¹⁸⁵

eral amide functions in the ligand, which, together with the three chiral centers, help to determine the handedness of the complex. The reduced Cotton effects in polar solvents support this conclusion. The formation of a left-handed helix was achieved by replacing the noncovalently active amide bonds in **37** with ester bonds, thus producing ligand **38**, in which the remaining amide bonds determine the handedness of the complex. This research demonstrates the tremendous selectivity that relatively weak hydrogen bonds can afford in the construction of helical arrangements.

The research groups of Constable and Potts have approached the formation of helicates, helices incorporating metal ions, by exploiting the limited rotations that occur about intraannular C–C bonds between aromatic rings in order to control the twisted conformations of their ligands.¹⁵ The observation¹⁸⁶ that oligopyridine ligands¹⁸⁷ are forced to be nonplanar when some of the rings are coordinated and others are not, has led these two research groups to the realization of several helicates incorporating these ligands and a variety of metal ions.

The simplest member of the family of oligopyridines that has only recently been shown to form helicates is terpyridine. Realizing that π - π stacking interactions are very important in the formation of helicates by this family of ligands, Potts and co-workers¹⁸⁸ designed the ligand **39**—6,6'-disubstituted with phenyl rings—which, upon mixing with tetrakis-(acetonitrile)copper(I) forms an orange solution, from which dark red crystals of the 2:2 complex crystallize out. The X-ray crystal structure of the complex, shown schematically in Figure 43, illustrates how the ligand strands wrap around one another and the two copper ions, which occupy, respectively, distorted tetrahedral coordination and linear coordination geometries. This example was the first reported complex with two copper(I) centers having different coordination numbers. The helix has a pitch of only 8 Å, with the copper–copper distance being only 2.63 Å. Four sets of aromatic stacks are formed by π - π stacking interactions, two between the middle pyridine ring of one ligand and the two phenyl ring

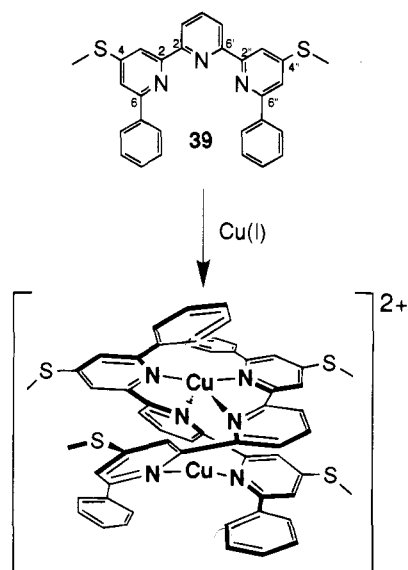


Figure 43. The formation of a double helicate around two copper(I) ions of two substituted terpyridine ligands.¹⁸⁸

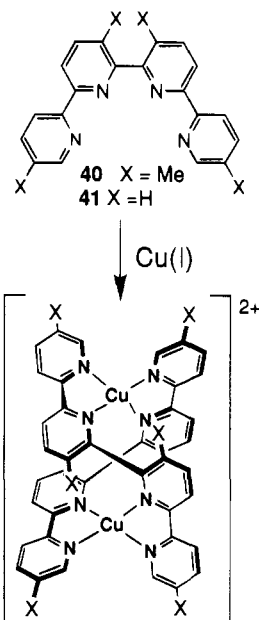


Figure 44. The formation of dinuclear double helicates around two copper(I) ions by two quaterpyridine ligands.^{190,194}

termini of the crystallographically equivalent second ligand, and the other two between the remaining pyridine rings in each ligand. The dinuclear double helical complex was also stable in solution wherein it adopts an averaged geometry in contrast with the ligand in which the phenyl substituents are not present which does not form a stable complex. Constable¹⁸⁹ has, more recently, described a similar structure, where the methylthio groups present in **39** are absent, in which the metal–metal distance is 2.57 Å. In this structure, the copper(I) center, which is two-coordinate, exhibits long-range interactions with the central pyridine nitrogen atom of the ligand.

One of the earliest approaches that was devised to create double helicates around templating metal ions involved the exploitation of a quaterpyridine derivative. Lehn and co-workers¹⁹⁰ introduced methyl groups onto two of the pyridine rings of such a derivative, generating the ligand **40** (Figure 44) so that the methyl groups can act as a conformational lock in between the two 2,2'-bipyridine units. When this ligand was combined with copper(I), a dinuclear double helicate was formed, a fact confirmed by the X-ray crystal structure of the complex in which the two copper(I) centers are held apart by 3.90 Å. The methyl groups do provide the steric barrier to prevent planarity of the ligand, an observation that is demonstrated¹⁹¹ by the mononuclear cupric complex, in which the twist angle of 26° between the two inner pyridine rings is found to be greater than the other twist angles present in the ligand. Reduction of the cupric complex was achieved readily and the species which was formed was the dimeric helicate structure. The copper(I) ion in this double helicate is stabilized¹⁹² to oxidation by 1 V when compared with the [Cu(2,2'-bipyridine)₂]⁺ cation. However, it transpired that the presence of the methyl substituents proved to be unnecessary for double helicate formation,¹⁹³ since the unsubstituted 2,2':6',2'':6'',2''':6'''-quaterpyridine (**41** in Figure 44) crystallizes with both copper(I) and silver(I) ions to form binuclear double helicates. The pitch of the cuprous helicate formed with

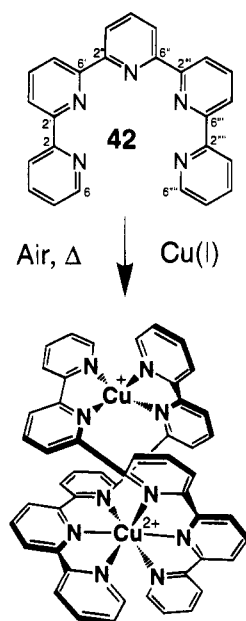


Figure 45. The formation of a double helicate with two nonequivalent copper ions—a six-coordinate copper(II) center and a four-coordinate copper(I) center—and two quinquepyridine ligands.¹⁹⁸

41 is substantially shorter—copper—copper distance of 3.17 Å—than that of the double helicate formed with **40**. It appears, therefore, that the methyl substituents control the pitches of the helices. The distance between the same metal ions in a double helicate¹⁹⁴ incorporating two 4,4'-methylthio-substituted quaterpyridine ligands is 3.32 Å. In all the crystalline helicate complexes, both right-handed and left-handed double helicates are formed.

When 2,2':6',2''':6'',2''':6''',2''':6''''-quinquepyridine (**42** in Figure 45) is combined¹⁹⁵ with a range of transition metal ion [Cu(II), Co(II), Zn(II), Ni(II)] acetates in boiling methanol, complexes are formed whose stoichiometries were proved by mass spectrometry to be 2:2. In the case of the copper(II) complex, crystals were obtained in which the complex was shown to exist as a double helix with the two nonequivalent copper ions separated by 4.50 Å. The ligand is terdentate, assuming a very distorted octahedral geometry with respect to one copper(II) ion and is bidentate in relation to the other. The coordination sphere of the latter copper(II) ion is satisfied by an acetate counterion, leading to a distorted trigonal-bipyramidal arrangement around the metal. The ligand twists about the C—C bond which links its terdentate and bidentate sections. The bidentate section of one ligand π - π stacks with the terdentate section of another ligand with an interplanar separation of approximately 3.3 Å. Both enantiomers of the double helix are present in its crystals. A very similar solid-state structure was identified¹⁹⁶ for the corresponding nickel(II) complex, the principal difference from the copper(II) complex being that the coordinated acetate ion is bidentate. Similar structures to these ones were obtained for substituted quinquepyridines in the solid state.^{194,197} When [Cu(MeCN)₄][PF₆]₂ is combined with **42**, the double helix which forms is very similar to that of the exclusively copper(II) complex, except that the absence of the acetate ion leads (Figure 45) to one six-coordinate copper(II) center and one four-coordinate copper(I)

center in the helix.¹⁹⁸ By contrast, when silver(I) ions are crystallized with the same ligand, a near-planar ligand geometry is observed in the 1:1 complex.¹⁹⁹ Whereas quaterpyridine forms a 1:1 complex with palladium(II), wherein the metal ion has a distorted square-planar coordination, a binuclear double helix is formed²⁰⁰ between palladium(II) and quinquepyridine. This latter complex has an X-ray crystal structure in which each metal center displays an irregular five-coordinate geometry, with four close contacts to ligating nitrogen atoms. The pronounced twisting ($\approx 70^\circ$) between the bi- and tridentate parts of each ligand results in a large intermetal distance of 4.96 Å. The double helicate structure is stabilized to a large extent by π - π stacking interactions between the ligands (interplanar separations of approximately 3.4 Å). Ferrocenyl groups have also been incorporated at the 4' and 4''' positions of **42** and it has been shown that this modification does not hinder the formation of either mononuclear helical or binuclear double-helical complexes.²⁰¹ It has also been demonstrated that charge proximity to the ligand alone does not cause helication,²⁰² since the ligand adopts a planar *cis,trans,trans,cis* arrangement in its protonated form.

The complexes formed by derivatives of **42** emerge as either 1:1 or 2:2 complexes with cobalt(II) in the solid state.²⁰³ In the 1:1 complexes,^{204,205} which dominate in solution, the ligand is monohelical and the cation is seven coordinate. However, crystals have also been obtained of a binuclear double helix, corresponding to the complex [Co₂(**42**)₂(OAc)]³⁻ in which both metal ion centers are six coordinate, yet nonequivalent.²⁰⁶ As in the nickel(II) complex, the acetate group is coordinated in a bidentate fashion to one metal ion, the distance between the metals being 4.46 Å.

When silver(I) or copper(I) salts are added to methanolic or ethanolic solutions of the 1:1 complex of quinquepyridine and cobalt(II), heterobinuclear double-helical complexes (Figure 46) are formed.²⁰⁷

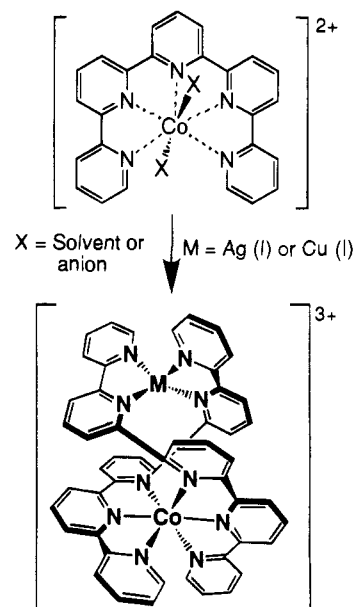


Figure 46. The formation of heterobinuclear double-helical complexes from the 1:1 complex of quinquepyridine and cobalt(II) when silver(I) or copper(I) salts are added.²⁰⁷

The self-assembly of these mixed-metal complexes is driven by the cobalt(II) ion achieving a pseudooctahedral coordination, while the other component metal ion occupies a pseudotetrahedral geometry. Mixing the monohelical silver(I) and cobalt(II) complexes of **42** also resulted in the formation of the corresponding heterobinuclear double-helical complex in near quantitative yield. The observation of a $\text{Co}^{\text{III}}/\text{Co}^{\text{II}}$ couple at 0.40 V in the bimetallic complex contrasts with the mononuclear monohelical complex of the cobalt(II) with the same ligand, strongly suggesting a six-coordinate site for the cobalt(II) in the former. Indeed, this structural feature was confirmed when the crystal structure of $[\text{CoAg}(\mathbf{42})_2](\text{ClO}_4)_3 \cdot 2\text{H}_2\text{O}$ was solved.²⁰⁸ The cobalt ion resides in the terpyridyl section of the ligand, while the silver ion is surrounded by the bipyridyl section. The intermetal distance in the two independent double helicates present in the crystal are 4.17 and 4.22 Å, respectively. Once again, π - π stacking interactions occur between pyridine rings in each section of the two ligands—and, in addition, between pyridine rings in *different* complexes, so that a head-to-head dimer is formed in the crystal with a silver(I) to silver(I) distance of 3.82 Å. Thus, π - π stacking exists along the whole length of the dimeric helicate.

The next higher homolog of oligopyridine, namely 2,2':6',2'':6'',2''':6''',2''':6''',2''':6''',2''':6'''-sexipyridine (**43** in Figure 47), also displays a rich coordination chemistry, as well as an ability to form mononuclear²⁰⁹ and dinuclear²¹⁰ single helicates and binuclear double helicates. Specifically, the binuclear double helical cadmium(II) complex (Figure 47), where each metal center is six coordinate, has been crystallized²¹¹ as its tetrakis(hexafluorophosphate) salt. Once again, π - π stacking interactions are considered to be very important in the formation of the complex between the two ligands and help to ensure that the metal ions are held 4.17 Å apart in the helix. The copper(II) dinuclear double helix with 4,4''-bis(methylthio)-sexipyridine shows¹⁹⁷ very similar features, but with a metal-metal distance of 4.89 Å. Solutions of copper(I) and derivatives of sexipyridine ligands

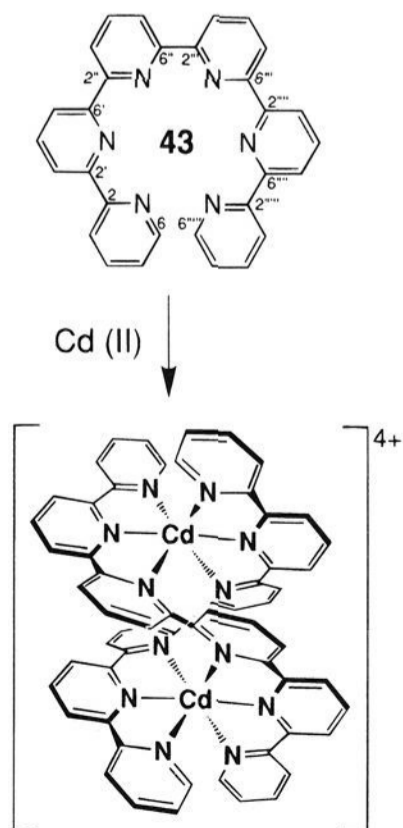


Figure 47. The formation of a binuclear double-helical cadmium(II) complex with sexipyridine as the two ligands.²¹¹

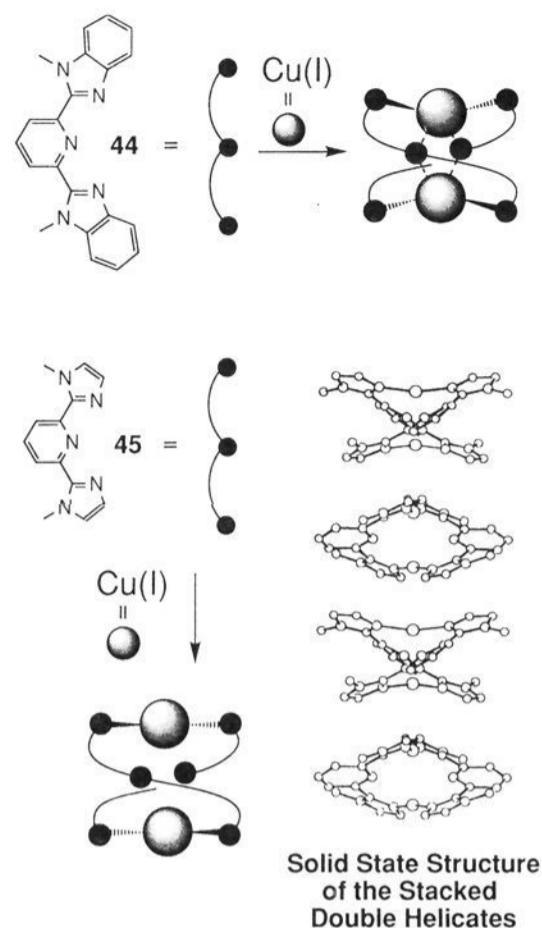


Figure 48. (Top) The formation of a binuclear double helicate around copper(I) ions by two of the tridentate ligands **44**;²¹⁵ (bottom) the formation of a double helicate around copper(I) ions by two of the ligands **45**, and a view of the infinite double-helical array they form in the crystal.²¹⁷

contain trinuclear double helices of the type $[\text{Cu}_3(\mathbf{43})_2][\text{PF}_6]_3$, in which the proposed geometry for each metal ion center is a distorted tetrahedron. An ^1H NMR spectrum of the cuprous complex with **43** revealed 10 well-resolved resonances, in accord with an averaged D_2 solution state symmetry.²¹² Furthermore, it was found to be possible to oxidize electrochemically the dark brown trinuclear copper(I) species to the green dinuclear copper(II) species with the ejection of a copper ion. Potts and co-workers¹⁹⁷ have noted similar phenomena in substituted sexipyridine complexes, while Constable and Chotalia²¹³ have used the templating effect, which results in the formation of helicates, for the preparation of the ligands themselves. The formation of a dinuclear nickel(II) double helicate, by dimerization of a terpyridine ligand substituted at its 6-position with a bromine atom with a suspension of $[\text{Ni}(\text{PPh}_3)_n]$ ($n = 3, 4$) in dimethylformamide, proceeds in an overall yield of 50% after isolation of the tetrakis(hexafluorophosphate) salt. The reaction was reported to constitute a facile synthesis for the even-ring oligopyridines, which are obtained subsequently in quantitative yield by demetalation of the helicate following treatment with KCN.

The combination of pyridine and benzimidazole moieties into ligands has proved to be a very fruitful area for the creation of double and triple helicates by Piguet, Bernardinelli, and Williams.^{214–227} In their first report,²¹⁵ the tridentate ligand 2,6-bis(1-methylbenzimidazol-2-yl)pyridine (**44** in Figure 48) was crystallized with copper(I) to form a binuclear double helicate in which each metal ion is coordinated almost linearly by a benzimidazole moiety from each strand. The pyridine moiety is coordinated weakly to the two metal ions, which are separated by an extremely short distance of 2.62 Å. The benzimida-

zole rings of a given strand are π - π stacked with the same moieties in the other strand (interplanar separation of 3.4 Å). This helicate is remarkable on account of its low number of binding sites per ligand for each metal ion and for the fact that it is stable in polar aprotic solvents. When the pyridine ring is replaced by a benzene ring substituted in the same manner, a nonhelical structure is formed in which, once again, the copper ion is coordinated linearly by the nitrogen atoms of each benzimidazole group.²¹⁶ One way to extend the helix formed by these complexes is to increase the number of binding sites in the ligand. Another way is to generate an infinite one-dimensional helix by the formation of a monomer unit and then to achieve subsequent association of these units into a linear aggregate. The latter approach has been demonstrated²¹⁷ using the ligand **45** (Figure 48), which was designed to test the importance of π - π stacking to this type of helicate structure. The helix that forms upon reacting **45** and copper(I) has a solid-state structure in which each metal ion is ligated linearly by a nitrogen atom from each imidazole group of **45**, with any interaction from the bridging pyridine nitrogen atom being very weak. The distances between the copper ions in the two distinct complexes present in the crystal were both approximately 2.82 Å. The packing of the helices in the crystal is such that an infinite double-helical array is generated (Figure 48). Although no stacking within each single dimer is present, the imidazole planes of adjacent complexes do overlap (interplanar separation of approximately 3.4–3.5 Å). The inter-complex copper–copper distances are 3.29 and 3.43 Å. The binuclear double helicates mesh together to form the infinite double helicate array, each parallel stack having a different helicity to the next. Although this aggregate is not maintained in solution, monomeric double helicates are present.

The same research group went on²¹⁸ to use the bisbidentate ligand (**46A** in Figure 49) for the formation of a dinuclear triple helix, something which

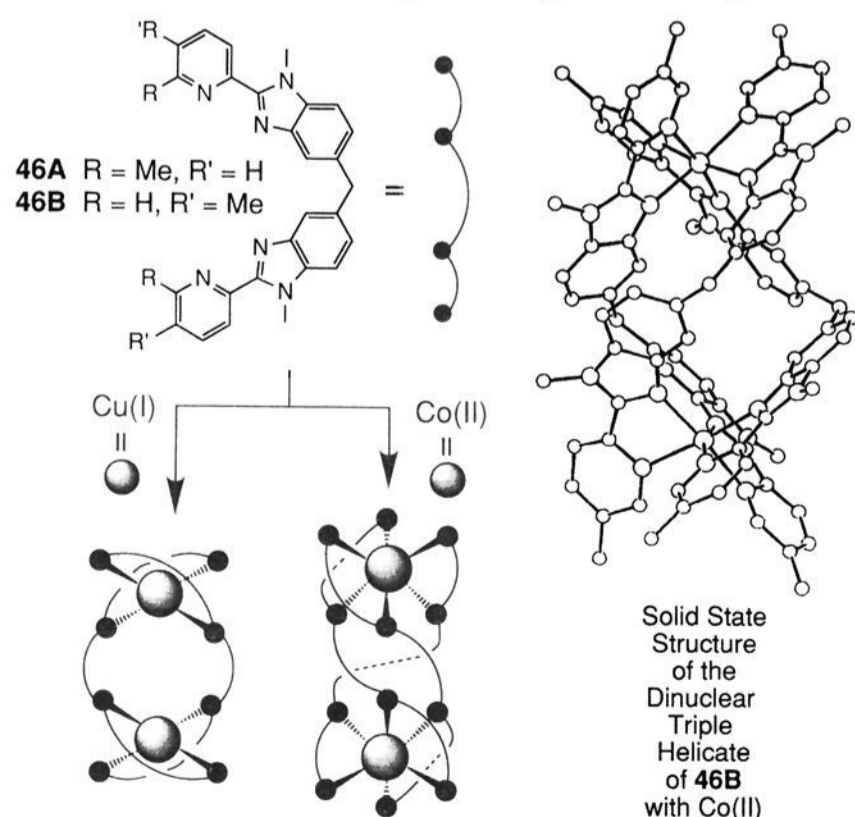


Figure 49. (Left) The formation of binuclear double helicates with copper(I) ions and dinuclear triple helicates with cobalt(II) ions when the bisbidentate ligands **46** are present; (right) the solid-state structure of the dinuclear triple helicate of **46B** with cobalt(II).^{218,219}

happens when it complexes with cobalt(II). The rigid spacer in **46** prevents folding back of the coordination sites, while steric repulsion between the benzimidazole units disfavors a planar structure, rendering the ligand well-suited to act in a bisbidentate mode. When the ligand **46B** was mixed in a 3:2 (ligand/metal ion) stoichiometrically with cobalt(II) perchlorate, red-orange crystals were formed. X-ray crystallography shows that each cobalt ion has a flattened octahedral coordination with the ligand exhibiting a wide range of torsion angles, suggesting that it is fairly flexible. The π - π stacking interactions noted in other complexes were not observed in this complex. The same ligand also forms a binuclear double helicate when combined with copper(I) in polar aprotic solvents.²¹⁹ The double-helical nature of the complex was confirmed by ¹H NMR spectroscopy, as well as by analysis of metal-to-ligand charge transfer bands in the visible spectrum, indicating a pseudotetrahedral geometry around the metal ions. Titration experiments indicated that the cuprous helicate was not the only complex present in solution and that there were significant amounts of the mononuclear complex involving two ligands. Zinc(II) forms a mixture of helicates in solution with **46A**, including binuclear double and triple helicates, on account of its ability to adopt both pseudotetrahedral and pseudooctahedral coordination geometries. In the case of **46A**, the outcome regarding the particular type of helix formation is therefore determined by the coordination geometries that are preferred by the metal ions.

A consequence of using the strict self-assembly strategy, which entails the system reaching a thermodynamic minimum by trial and error, for the preparation of helicates is that the ligand–metal complex should be relatively kinetically labile, a property which prevents the straightforward resolution of the complexes into enantiomeric forms. One way to address resolving enantiomers is to render the complex kinetically inert, something which should be possible with the cobalt(II) complex of **46A** by oxidizing it. Unfortunately, this complex did not oxidize, but a related cobalt(II) complex with the ligand **46B** could be oxidized with bromine to the cobalt(III) complex in 67% yield.²²⁰ The crystal structure of the cobalt(III) complex reveals an octahedral coordination to the metal ion, which is approximately 0.2 Å closer to the ligating nitrogen atoms than is the metal ion in the analogous cobalt(II) complex. The ¹H NMR spectrum of the complex confirmed its helical nature in D₂O solution, since addition of the chiral salt, Na₂Sb₂[(-)-C₄O₆H₂]₂·5H₂O, caused clear splitting of appropriate signals arising from the enantiomers of the complex. They were separated successfully by elution of the racemic modification from a Sephadex SP-C25 column with aqueous Na₂Sb₂[(-)-C₄O₆H₂]₂·5H₂O. The successful resolution of the enantiomeric complexes was confirmed by circular dichroism performed on the two complexes.

The bisterdentate ligand (**47** in Figure 50) was synthesized²²¹ in the hope that it would form triple-helical structures with metal ions of coordination number nine. This design feature was successful in so far as the ligand self-assembled around two europium(III) ions to form the first dinuclear triple-helical lanthanide complex. The complex, which was

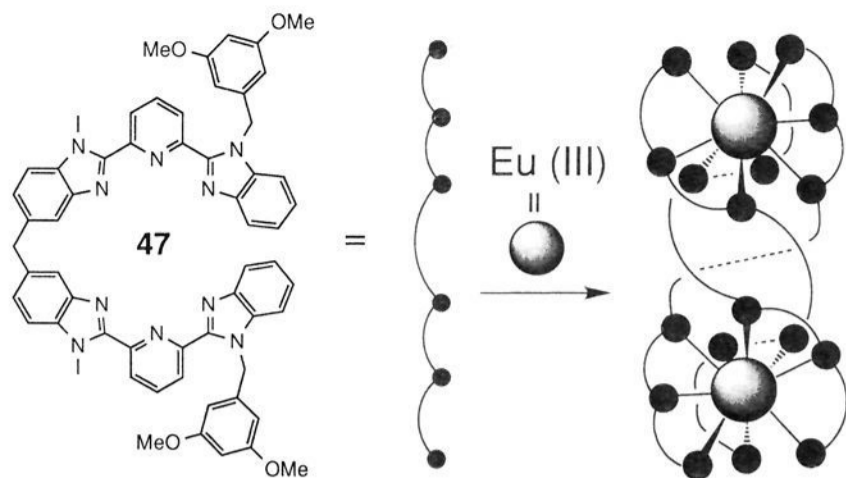
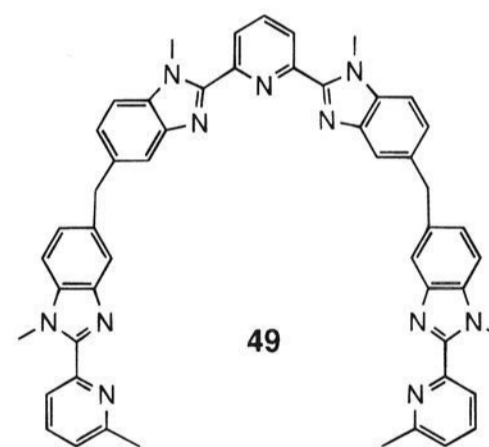
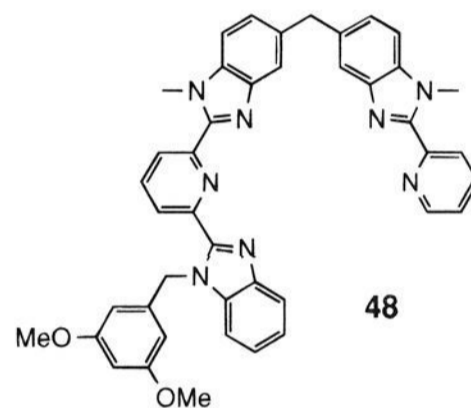


Figure 50. The formation of a binuclear triple helicate with europium(III) ions in the presence of the bisterdentate ligand **47**.^{221–223}

isolated in 80% yield from europium(III) perchlorate and **47**, was characterized in the first instance by fast-atom bombardment (FAB) mass spectrometry. Later, electrospray mass spectrometry (ESMS) was also used to characterize similar complexes,²²² since the results could be obtained more easily than by using FAB mass spectrometry. ESMS also gives a qualitative feel for the species present in solution. The crystal structure of the triple helicate reveals the close to D_3 symmetry of the helix, which is approximately 15 Å long with a pitch of 12 Å. The metal ions are coordinated in distorted tricapped trigonal prisms, with three pyridine nitrogen atoms occupying the capping points leaving the benzimidazole nitrogen atoms at the vertices. There are π - π stacking interactions observed between the benzimidazole moieties of the ligands, albeit they are relatively weak ones. The authors²²¹ proposed that the driving force for helix formation is the coordination geometry of the metal ions. In addition, ^1H NMR spectroscopic experiments reveal that the triple-helical structure also exists in solution, and that this structure is the only complex formed, indicating a cooperative mechanism in the self-assembly process. The triple helicate also forms with other lanthanides,²²³ although those with the heavier lanthanides, namely Tb and Lu, are less stable, at least as determined by competition experiments between these ions and europium(III) ions. The larger the size of the lanthanide, the greater is the interference within the complex from solvent molecules as a result of the less compact nature, and thus poorer π - π stacking, of the ligand. This effect has also been observed²²⁴ in mononuclear triple-helical structures of a similar type. It was anticipated that the helicates might operate as light-conversion devices.²²³ Efficient intramolecular energy transfer does take place between the ligand's $^3\pi\pi^*$ excited state and the excited levels of both europium(III) and terbium(III) templates at low temperatures. At room temperature, however, the luminescence undergoes significant quenching, as a result of the flexibility of the ligand. The heterodinuclear complex, formed by **47** and terbium(III) and europium(III), was used to study metal-to-metal energy transfers, because the ions are well protected from the environment, thus ensuring that the processes are intramolecular. The observed yield for the energy transfer supports a dipole-dipole mechanism for this process. It is hoped that additional modifications of the ligand will lead to further investigations of intramolecular energy

transfer processes in these supramolecular systems with the aim, ultimately, of creating light-conversion devices.

The group from Geneva have most recently prepared²²⁵ the segmental ligands **48** and **49** with bidentate and tridentate ligating sections. The ligand **48** forms 2:1 ligand/metal ion complexes with iron(II), zinc(II), and cobalt(II), with its terdentate sections surrounding the cations in a pseudo-octahedral geometry. It is also capable of forming²²⁶ a 2:2 double-helical complex with zinc(II). Meanwhile, the iron(II) mononuclear complex of **48**, when treated with silver(I) ions forms a heterodinuclear double helicate, albeit of very low stability—only 27% of the complex was formed at 1:1 complex/silver(I) stoichiometry. However, a heterodinuclear triple helix forms in solution when **48** is combined with zinc(II) and either lanthanum(III) or europium(III), as indicated by ^1H NMR spectroscopy.²²⁵ The trileptic ligand **49** forms a trinuclear complex with a 2:2:1 ligand/silver(I)/iron(II) stoichiometry, with the iron(II) ion occupying the central position of the ligand.



An investigation of the complex using ^1H NMR spectroscopy indicated the presence either of a double-helical complex or of a catenated structure (Figure 51): they have the same point group. Solid-state structures of the two crystalline forms of the complex showed that they were the chiral and meso forms of the catenated superstructure.²²⁶ The two chiral forms rapidly interconvert with the meso form of the catenate in solution, as witnessed by ^1H NMR spectroscopy. Generally, these ligands are relatively poor in terms of their selectivity and it is proposed to modify the ligating atoms and the chelate bite angle to circumvent this problem.

Several research groups have explored the possibilities of using bipyridine ligating groups, separated by a relatively rigid spacer, for the formation of double and triple helicates. However, in some instances, folding back of the ligand to generate²²⁷ a mononuclear complex has been observed. In the course of their studies on oligopyridines, Constable

and co-workers²²⁸ have described the synthesis and helicate formation involving a ligand (**50**) in which two 2,2'-bipyridine residues are separated by a 1,3-disubstituted benzene ring, a structure related to quinquipyridine, where the central ligating nitrogen atom is not present. An X-ray crystal structure²²⁹ revealed that a binuclear double helicate does form between a bismethylthio derivative of the ligand with nickel(II) ions as the template and where the octahedral coordination of the metal ion is satisfied by two bidentate acetate ions at each end of the helix axis. There is no $\pi-\pi$ stacking in this structure and consequently the metal ions are a long 5.87 Å apart. Dinuclear double helices are also formed²²⁹ by the ligand **50**, particularly with distorted tetrahedrally coordinated copper(I) and silver(I) ions as indicated by mass spectrometry and ¹H NMR spectroscopy.

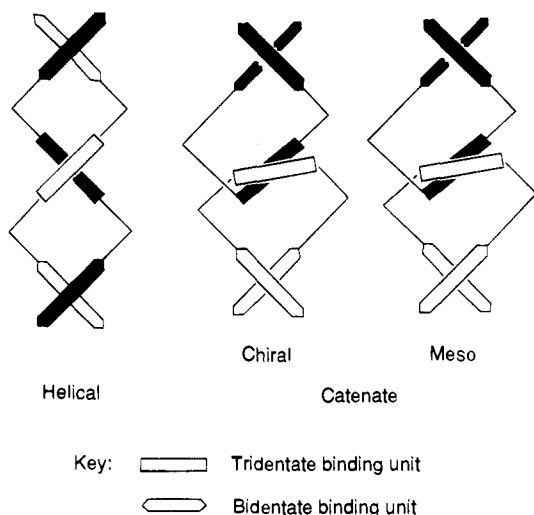
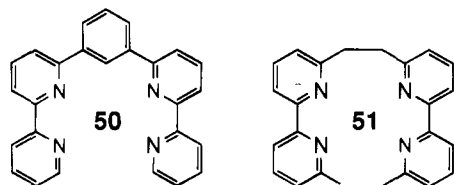


Figure 51. The double-helical complex and catenated compounds formed when two trileptic ligands **49** complex with one iron(II) ion in the "middle" and two silver(I) ions on the "outside".^{225,226}

The linking of two 6-methyl-2,2'-bipyridine residues at the 6'-positions with an ethylene unit yielded the ligand **51** which does form a helicate with copper(I) ions.²³⁰ An X-ray crystal structure of the complex reveals that the copper ions are coordinated in a distorted tetrahedral geometry, the distance between them being 5.93 Å. This structure is maintained in solution, as witnessed by ¹H NMR spectroscopy. When the same ligand is combined with cobalt(II), a folded back ligand coordinates a single metal ion. In contrast, when two 4-methyl-2,2'-bipyridine residues are linked by an ethylene unit at the ligand's 4'-positions, a face-to-face complex is formed with iron(II) in which three ligands are coordinated to two pseudo-octahedral metal centers.²³¹



The Lehn group in Strasbourg has exploited the self-assembly of extended ligands around several metal ions to form extended double helicates which display "intelligent" self-assembly. The ligand strands

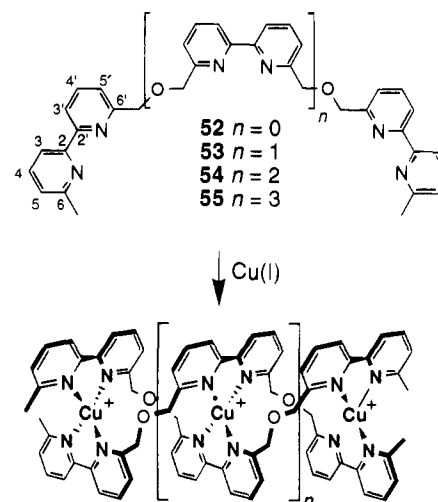


Figure 52. The self-assembly of a homologous series of double helicates around two to five copper(I) ions by ligands **52–55**, which contain two to five 6,6'-dimethyl-2,2'-bipyridine ligands.^{232,235}

52–55 (Figure 52), containing between two and five 6,6'-dimethyl-2,2'-bipyridine moieties, when combined with copper(I), form double-stranded helicates with between two²³² and five²³³ metal ion centers. The double helicates were prepared (Figure 52) quantitatively either (i) by combinations of solutions/suspensions of the ligands in chloroform with acetonitrile solutions of the copper(I) salts (perchlorate, trifluoroacetate, or trifluoromethanesulphonate), or (ii) by reduction of a mixture of aqueous copper(II) salt solutions and acetonitrile suspensions of the ligand. The dramatic changes in the ¹H NMR spectra of the ligands, upon complexing with the metal ions, bear witness to double-helicate formation. The singlets for the CH₂OCH₂ protons in the free ligands are shifted downfield by 1 ppm and are separated into AB systems in the double helicates as a result of the protons lying in the deshielding zone of the aromatic units of the intertwined ligands. The bipyridine unit's ability to bind copper(I) in a distorted tetrahedral geometry was confirmed²³² by the crystal structure of the double helicate, incorporating two **53** ligands wrapped around three copper(I) ions, two views of which are illustrated in Figure 53. The length of the double helicate is between 16.5 and 17 Å, with one and a half turns of each ligand strand over this distance. The double helix is bent in the solid state, a feature which implies that a dynamic process in which the double helicate bends and twists takes place in solution. The presence of enantiomeric double helicates, formed by **54** and **55** in solution, was confirmed by the addition of (Eu(tfc)₃ [tfc = [(trifluoromethyl)hydroxymethylene]-(+)-camphorato] in an experiment which led to the splitting of appropriate proton resonances in their ¹H NMR spectra. The tetra- and pentanuclear double-stranded helicates were estimated to contain two and two and a half turns, and to be 22 and 27 Å in length, respectively. Although silver(I) is less strongly and less selectively bound by bipyridine, similar double helicates are obtained²³⁴ by using this metal ion as the template for the same series of ligands. The cooperativity leading to the formation of double helicates was suggested on the basis of titration experiments of the silver salts into ligand solutions

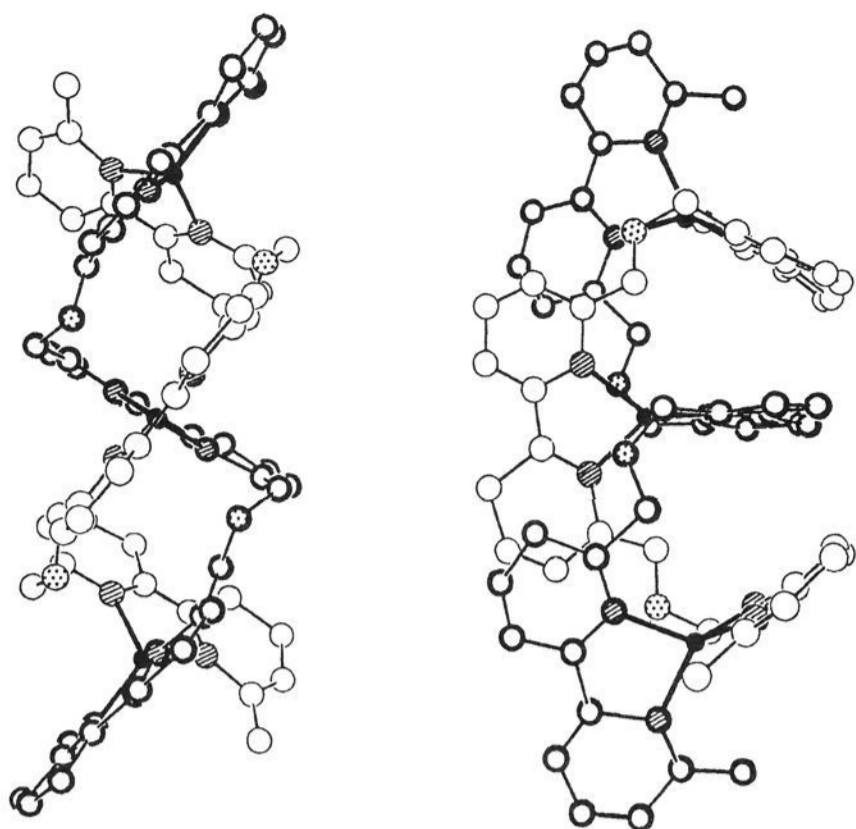


Figure 53. Two views of the ball-and-stick representation of the X-ray crystal structure of the trinuclear double helicate formed when two ligands **53** self-assemble with three copper(I) ions.²³²

where the double helicates are formed uniquely. An X-ray crystal structure (Figure 54) of the trinuclear silver(I) complex shows that this double helicate is also bent in the solid state. It is 9.8 Å in width and 20 Å in length. The positive cooperativity leading to the double helicates—*i.e.* binding, followed by enhanced rate of growth through sequential binding—was confirmed²³⁴ by Scatchard and Hill plots, obtained from treatment of the data collected from spectrophotometric titrations. Subsequently, Newkome and co-workers²³⁵ have reported the utilization of the helicate ligands developed by Lehn *et al.* for the preparation of a macromolecular helical complex. We also note with interest the very recent report²³⁶

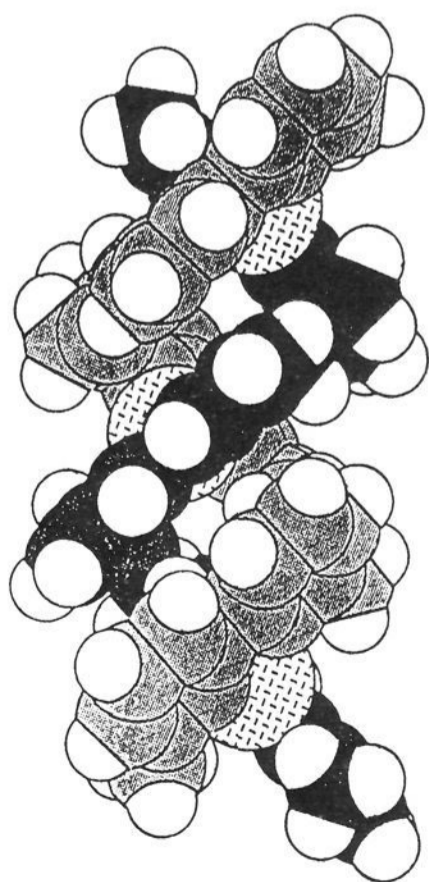
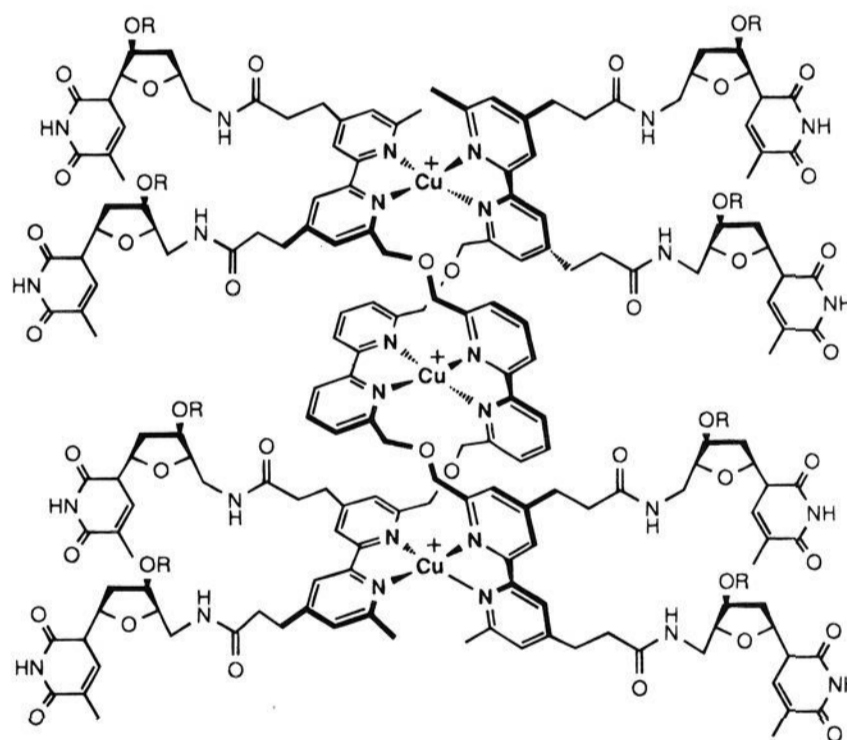


Figure 54. A space-filling representation of the X-ray crystal structure of the trinuclear double helicate formed when two ligands **53** self-assemble with three silver(I) ions.²³⁴

of double-helix formation from an optically pure tetra(tertiary phosphine) ligand and silver(I). A left-handed double helix, as well as a side-by-side helix conformer, were characterized.

Substitution²³⁷ at the 4- and 4'-positions of the ligand strands of **53** has led to the self-assembly of what has been described²³⁸ as deoxyribonucleo helicates (DNH). The double helicate **56** and the homolog containing five metal ion centers, which were prepared in an analogous way to those described previously, were characterized by fast-atom bombardment mass spectrometry as well as by NMR spectroscopy. In complete contrast to DNA, the structures have a coating of 6'-amino-3'-deoxythymidine residues protruding from the central positively charged nucleus of the double-helicate strands. It was proposed that the self-assembled double helicates may be able to recognize other structures via their thymidine residues, one possible target being the major groove of DNA itself. In fact, subsequently, it was proven that the helicates derived from **52–55** without these substituents interact with the DNA double helix.²³⁹ Although the presence of the chiral nucleosides could theoretically have induced handedness in the double-helical complex **56**, this control has not been shown to occur.



56 R = ^tBuMe₂Si

Induction of helicity in the complexes formed between optically pure bipyridine-containing ligands and copper(I) or silver(I) ions has been achieved by using simpler asymmetric ligands.²⁴⁰ The methylene units attached to the central bipyridine units were substituted in *C*₂ symmetric fashion with methyl groups in the simple three and five unit ligands to give the optically pure **57** and **58**, which both have the (*SS*) configuration. The ¹H NMR spectra of the resulting complexes (Figure 55) strongly suggested double-helicate formation, as the chemical shift changes were similar to those for the previously self-assembled double helicates. An extremely large and positive Cotton effect exhibited by the double helicates indicates the presence of only a single diastereoisomer. The helicity induction was extremely high, *i.e.* >95%. Although no direct experimental evidence has been obtained, molecular modeling

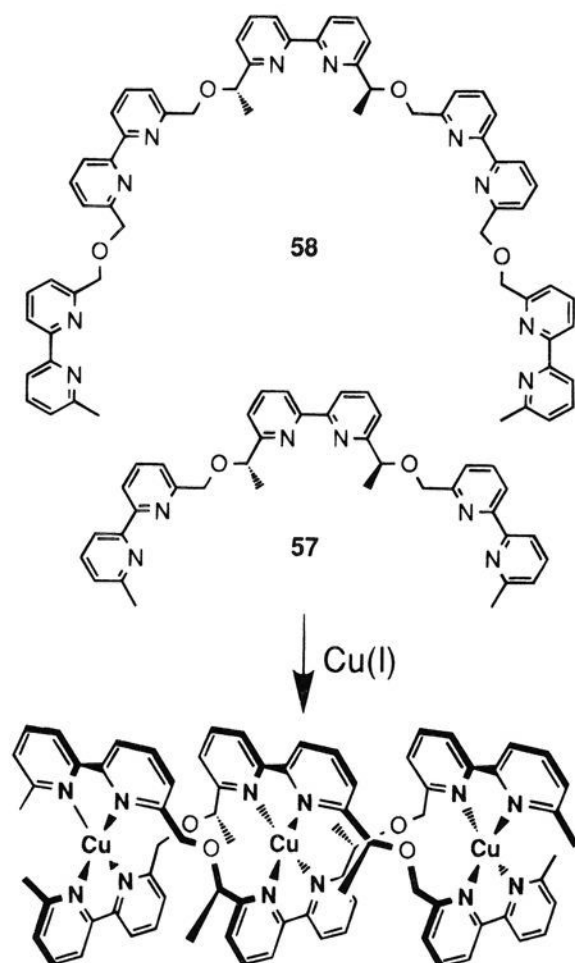


Figure 55. Chiral bispyridine-containing ligands **57** and **58** with the (*SS*)-configuration and the self-assembly of a trinuclear double helicate of ligand **57** with three copper(I) ions.²⁴⁰

strongly suggests the formation of right-handed double helicates.

The coordination number of copper(I) is not suitable for triple helicate formation, and neither are the 6,6'-disubstituents patterns on the 2,2'-bipyridine units, since they offer a steric barrier to entwining. By modifying the coordination "algorithm", Lehn and co-workers have prepared²⁴¹ a triple helicate around nickel(II) ions incorporating three 5,5'-disubstituted-2,2'-bipyridine-containing ligands **59** (Figure 56). Mixing the ligand and NiSO₄ in aqueous ethanol, to which a drop of H₂SO₄ had been added, gave a pink complex, which was characterized as the triple helicate by FAB mass spectrometry. Its ¹H NMR spectrum was broad, with resonances between 5 and 160 ppm, indicating that a complex is formed. An X-ray crystal structure (Figure 56) revealed the true beauty of the trinuclear triple-helical complex. The helix has a diameter of 5.3 Å and a shallow twist, six of the octahedral metal centers would be required in order to complete a full helical turn (30–35 Å in length) of the strands. There are essentially no π - π stacking interactions holding the ligands together. The triple helicates align in the crystal and, remarkably, undergo partial spontaneous resolution, *i.e.* any single crystal contains only one enantiomer of the triple helicate. This phenomenon was demonstrated by performing circular dichroism measurements on selected single crystals. The loss of optical activity in solution amounted to only 23% in 24 h at room temperature, showing that the triple helicates are remarkably stable. It was proposed that the crystals containing both enantiomers are comprised of domains of triple helicates with opposite helicities.

The double helicates containing tetrahedral copper(I) ions and the triple helicates incorporating nickel-

(II) ions display a remarkable property—each set of components recognizes itself.²⁴² To illustrate what Lehn has called "the instructed mixture paradigm", derivatives of the ligands **52–55** (Figure 52) were combined in acetonitrile in the presence of an excess of copper(I). A short time after mixing the components together, the ¹H NMR spectrum of the solution was complicated, since a myriad of structures are presumably formed under kinetic control. However, after several days the spectrum showed predominantly the presence of resonances arising from the binuclear double helicate of **52**, the trinuclear double helicate of **53**, the tetranuclear double helicate of **54**, and the pentanuclear double helicate of **55**. Thus, the ligands display self/non-self recognition, as the mixture is allowed to reach a thermodynamically stable state under conditions of strict self-assembly. Furthermore, when the preferentially tetrahedrally coordinating **53** and the preferentially octahedrally coordinating **59** were combined in solution with copper(I) and nickel(II) ions, the trinuclear double helicate incorporating copper(I) ions and the trinuclear triple helicate incorporating nickel(II) ions were formed (Figure 57) exclusively and quantitatively. Therefore, the mixture is preprogrammed, to the extent that its fate is preordained by the chemical code within the components. Recently, Lehn *et al.* have used this preprogramming approach for the multicomponent self-assembly²⁴³ of (i) a cylindrical complex incorporating five ligands and six metal ions, (ii) a grid comprised of six bidentate ligands and nine silver(I) ions, and (iii) a trinuclear rack-type complex.

In 1992, Crane and Sauvage reported²⁴⁴ the synthesis (Figure 58) of a dinuclear double helix from a bis-terpyridine ligand system and using both iron(II) and ruthenium(II) ions as the templates. The

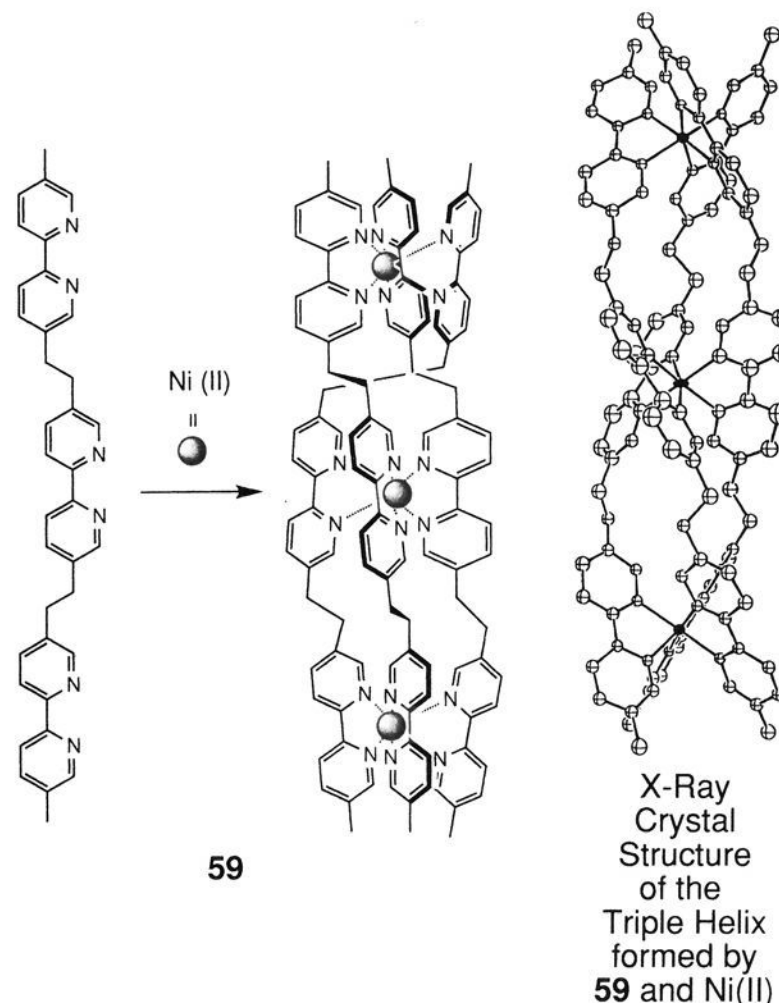


Figure 56. The self-assembly of a triple helicate by three 5,5'-disubstituted 2,2'-bipyridine-containing ligands **59** around three nickel(II) ions (left) and a ball-and-stick representation of the X-ray crystal structure of the same triple helicate (right).²⁴¹

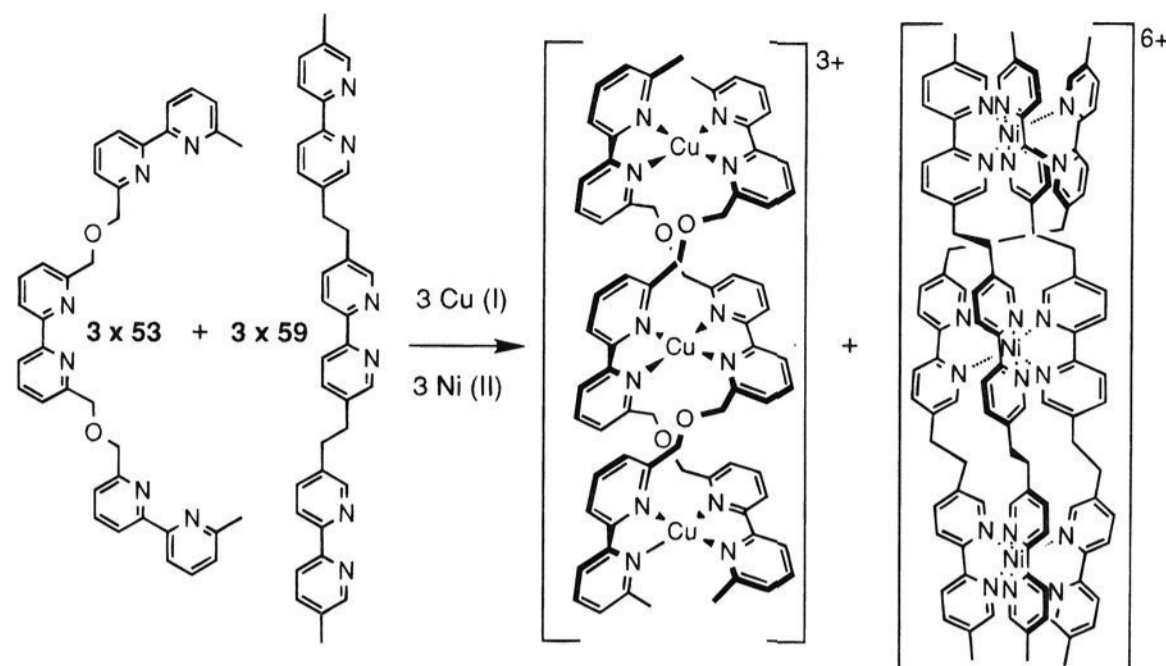


Figure 57. A demonstration of the "instructed mixture paradigm".²⁴²

latter complex was studied by a variety of techniques, including X-ray crystallography. Although a very well-refined structure was not obtained, the double-helical nature of the complex was confirmed. The iron(II) complex was proposed to have a similar structure by analogy.

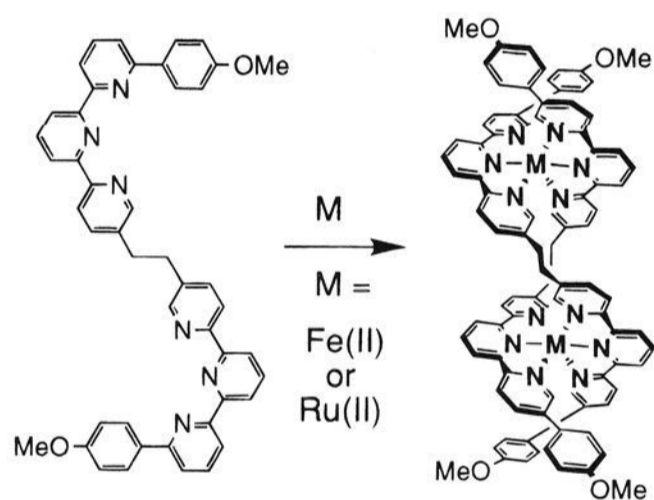
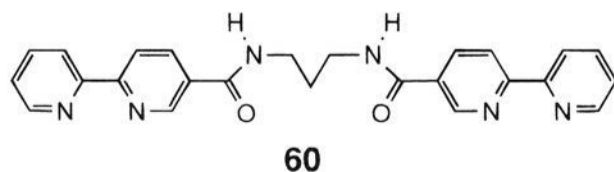


Figure 58. The self-assembly of binuclear double helicates around either iron(II) or ruthenium(II) by a bis-terpyridine ligand.²⁴⁴

The bischelate ligand **60**, derived from 5-carboxy-2,2'-bipyridine, forms²⁴⁵ a 3:2 complex with iron(II) in D₂O. An ¹H NMR spectroscopic study indicated that the binuclear complex is not only triply helical but is also a racemic modification of the $\Delta\Delta$ and $\Lambda\Lambda$ forms. Molecular modeling helped to support this assertion. It also showed the presence of a cavity between the two iron(II) centers in which it is hoped that guest molecules might be bound.



Recently, Enemark and Stack reported²⁴⁶ the stereospecific synthesis of a dinuclear gallium triple helix. Biscatecholamide ligands—in which either (*RR*) or (*SS*) enantiomerically pure spacers were incorporated—were combined with Ga³⁺ and a base. The assembly of the 3:2 ligand/metal complex was apparently cooperative, since only this compound and the free ligand could be detected in solution. The solid-state structure of the complexes confirmed the stereospecific formation of the triple helix. Further

experiments in D₂O revealed that the complexes equilibrate with heterochiral isomers, confirming that the assembly of the system is ruled by thermodynamics.

The torands and heterohelicenes are a group of ligands²⁴⁷ which are related structurally to the cycloarenes and helicenes, where the CH groups of the latter are replaced with heteroatoms, endowing the former with the ability to recognize metal cations. The research group led by Bell has described²⁴⁸ recently the self-assembly of a binuclear double-helical complex of sodium ions (Figure 59). The geometrical requirements of the alkali metal ion are not strict since it is weakly bound and the heterohelicene ligand **61** is rigidly helical, with twists between the adjacent pyridine rings induced by the preference of the bismethylene unit for a staggered conformation. It follows that this system is quite unlike any of the systems so far discussed in this review. When **61** was boiled in methanol containing NaOTf, a complex was isolated which, although it was found to have a 1:1 ratio of ligand/metal ion, mass spectrometry showed it to be a 2:2 complex. With the

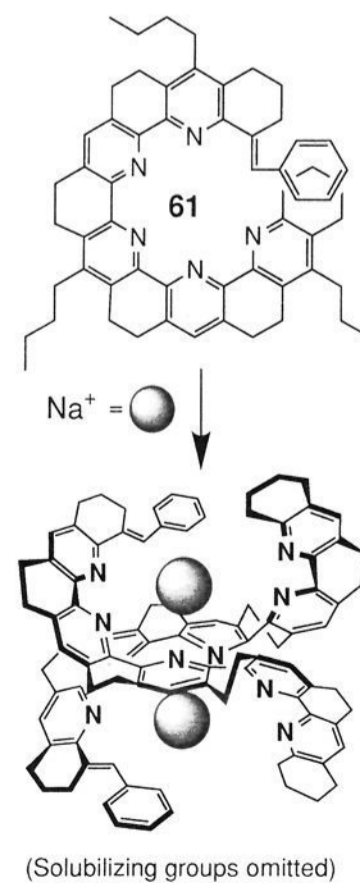


Figure 59. The self-assembly of a binuclear double helix by two heterohelicene ligands (**61**) and two sodium ions.²⁴⁸

greatly increased multiplicities for the resonances arising from the ligand (*cf.* the free ligand), the ^1H NMR spectrum of the complex confirmed its helical structure. In particular, the benzylidene groups of one ligand were located in the shielding zone of the other ligand's pyridine rings. Through-space interactions between protons from each ligand were also evident from a ROESY NMR experiment. A monosodium ion double helix was also observed by mass spectrometry. It is a proposed intermediate in the formation of the double helix, although the detailed mechanism for complex formation has not yet been discussed. This remarkable result, given the relatively weak interactions of the sodium ion with pseudo-cyclic ligands, is the first in which a double helix has been formed around an alkali metal.

A number of cyclic structures with double-helical character²⁴⁹ has also been synthesized recently employing transition metal ions as the templates. The self-assembly²⁵⁰ of a tetranuclear complex (Figure 60) from the ligand **62**, which incorporates a macrocyclic core with two 2,2'-bipyridine units and carries two pendant 1,10-phenanthroline residues, with copper(I) or silver(I) ions, has been achieved. The tetranuclear cuprous complex of **62** was characterized by mass spectrometry, ^1H NMR spectroscopy, and by X-ray crystallography, all of which revealed the coplanar copper(I) ions to be complexed with distorted tetrahedral coordination geometries in each case. The structure was described as a double-stranded helicate. Cram and co-workers²⁵¹ have recently prepared the helically chiral ligand **63**, incorporating two 1,10-phenanthroline ligating groups linked by a binaphthyl hinge, in 41% yield as its racemic modification. Binding studies on the ligand toward alkali metal ions showed poor discrimination with very strong binding associated with $-\Delta G^\circ$ values of up to $15.5 \text{ kcal mol}^{-1}$ in CDCl_3 . In a recent report,²⁵² double-helical macrocyclic complexes were formed by a Schiff base macrocycle **64**, in which two pyridine-2,6-diylidimine moieties converge (Figure 61) on the templating divalent metal ions [Co(II), Ni(II), Zn(II)].

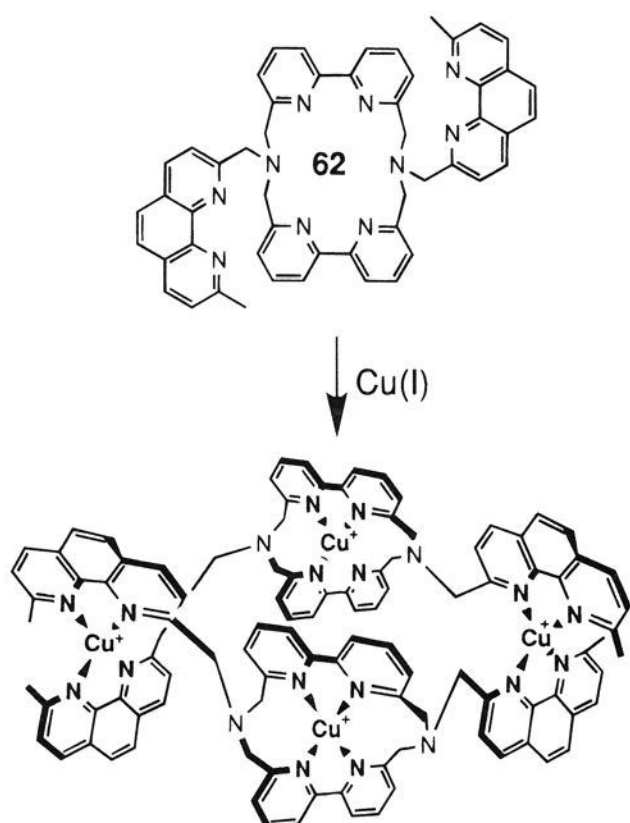


Figure 60. The self-assembly²⁵⁰ of a tetranuclear complex by two of the ligands **62**, containing a macrocyclic core incorporating two 2,2'-bipyridine units and carrying two pendant 1,10-phenanthroline residues, around four copper(I) ions.

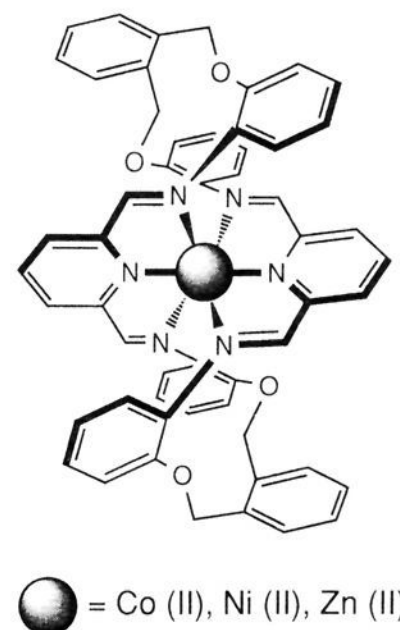
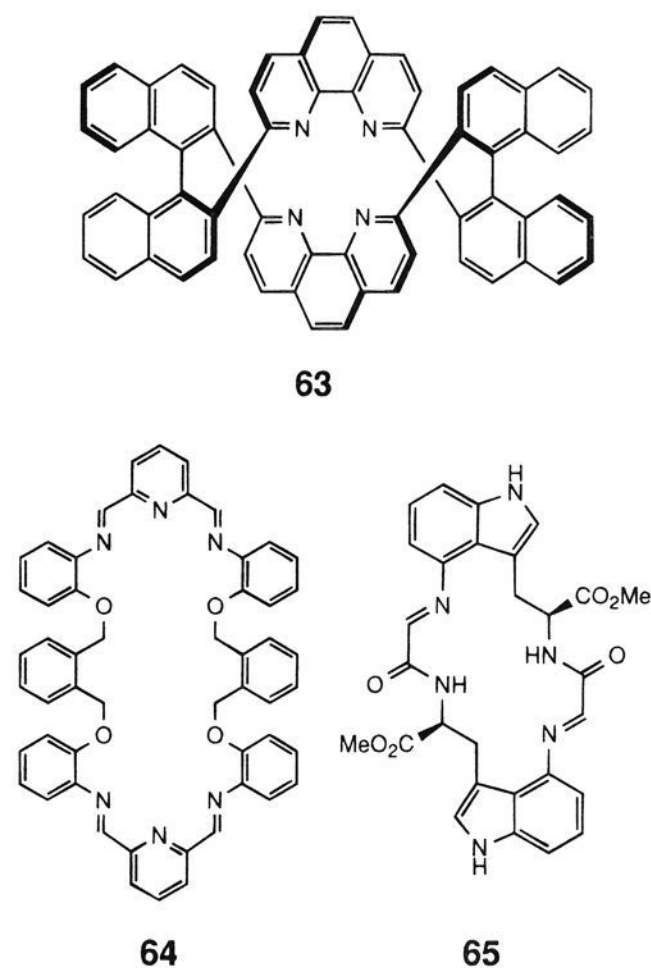


Figure 61. Double-helical macrocyclic complexes formed by the Schiff base macrocycle **64** around divalent metal ions.²⁵²

The X-ray crystal structures of the complexes reveal that the orientations of the two ligating groups induce helicity within the macrocycle in a novel six-coordinate nucleus. The three nitrogen donors of each ligand section are nearly planar, and enter into $\pi-\pi$ stacking interactions with two of the iminophenoxy rings in the rigid macrocycle. In total, there are five pairs of aromatic rings in relative positions which could be considered to be interacting with one another. Evidence was obtained by ^1H NMR spectroscopy for the existence of the helical structure in solution for the zinc(II) complex, although dynamic processes were also evidently taking place.



A double-helical tryptophan-derived azamacrocycle (**65**) has recently been described²⁵³ in which the macrocycle is constrained to adopt a particular conformation on account of hydrogen bonding for the most part. An X-ray crystal structure shows that the left-handed double helix is held in position by strong transannular hydrogen bonds and cannot switch its sense without incurring steric blocking of the ester

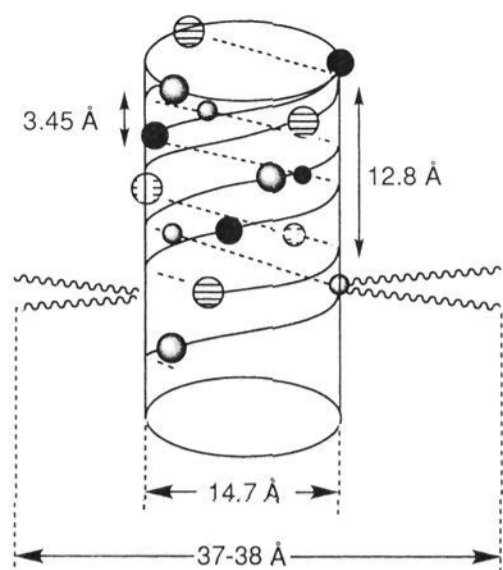


Figure 64. The triple-helical superstructure adopted by the $(LP_2, LU_2)_n$ copolymer portrayed in Figure 63.²⁵⁵ Each dot represents a base pair.

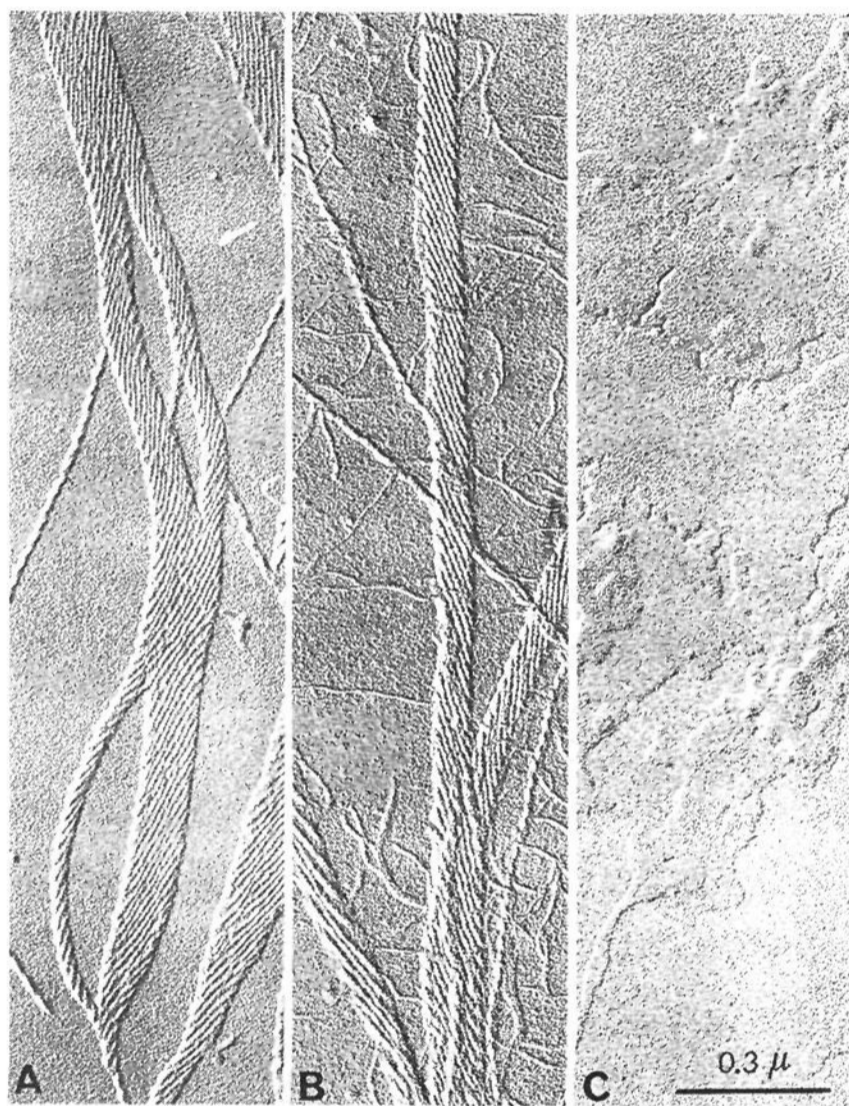
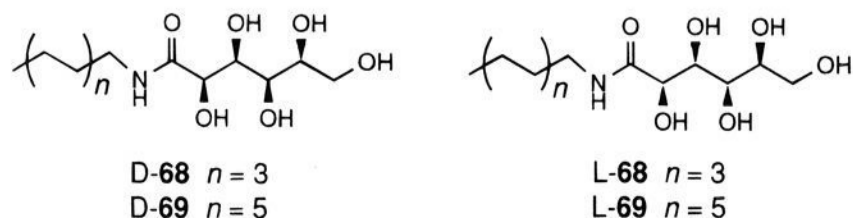


Figure 65. The electron micrographs²⁵⁶ of (A) $LP_2 + LU_2$, (B) $DP_2 + DU_2$, and (C) $MP_2 + MU_2$, showing the two differently handed helical fibers in the two former mixtures, and the absence of these features in the latter. (Reprinted from ref 256a. Copyright 1993 National Academy of Sciences.)

multihelical superstructures incorporating chiral amphiphiles. The research group led by Fuhrhop has achieved the spontaneous aggregation of octyl- and dodecyl-D- and L-gluconamides (D-68/L-68 and D-69/L-69) in water in experiments that resulted in the formation of double-helical fibers which were several micrometers in length.²⁵⁹ Electron micrographs re-



vealed that the double helices were irregular with bulges and crossing points. The width of the crossing points, where the helical strands were in close contact, was equivalent to the lengths of four molecules of the amphiphiles, which were arranged tail-to-tail. The stacking of the amphiphiles in the cylindrical micelles are twisted by the presence of the chiral centers, with the cylinders having a pitch of 238 Å. The *n*-octyl-D-gluconamide forms right-handed double helices, and the L-enantiomer, left-handed ones. The racemic modification did not form fibers. Similar double helices were also observed²⁶⁰ in micellar *n*-octadecylmannonamides. Further investigation²⁶¹ of micrographs, obtained from the amphiphilic gluconamides used for the creation of double helices, revealed additional electron density in the "bulges" of the double helix, and even, with the assistance of image processing, the structure of these complicated fibers could not be deduced. Modeling and geometrical analysis resulted in the proposal that the fibers were actually *quadruple* helices, in which four strands of the micelles twist around one another, while interpenetrating at the tight twisting points. It was also implied that the quadruple helix might contain amphiphiles oriented in a head-to-tail fashion, as they are in their crystalline sheets. Rearrangement of the quadruple helices afforded single helices.

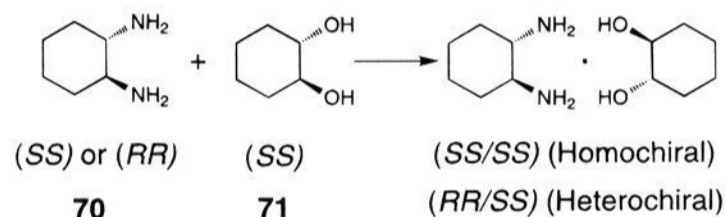


Figure 66. The cocrystallization²⁶² of *trans*-1,2-diaminocyclohexane [(SS) or (RR)] with (SS)-*trans*-cyclohexane-1,2-diol leading to homochiral and heterochiral complexes with triple-helical superstructures as a result of hydrogen bonding.

A remarkable triple helix, completely free of metal ions, is obtained²⁶² in the solid upon cocrystallization (Figure 66) of the diamines **70** and the diol **71**. The hydrogen-bonded superstructure has four vertical "columns", resulting from packing of the cyclohexyl rings on top of one another. Each hydrogen-bonded unit, of which there are eight members, is square planar and includes fully coordinated heteroatoms. One atom from each molecule is used for this purpose, while the others link up so that the heteroatoms are three-coordinated. The homochiral (SS/SS) and heterochiral (RR/SS) complexes both have chiral superstructures, the former being left-handed and the other being right-handed. It has been suggested that **70** is potentially a very versatile "assembler" unit for analogous complexes.

VI. Catenanes, Rotaxanes, and Knots Incorporating Metal Ions

In a manner conceptually similar to that of the "directed" approach of Schill and Lüttringhaus,⁴⁸ coordinating templates can be used to encourage the syntheses of interlocked structures. The use of the templating effect resulting from the coordinative bonding associated with metal ions has been used widely for the synthesis of synthetic macrocycles in which the cations generally reside in the center of the ring that is formed. Perhaps the most utilized

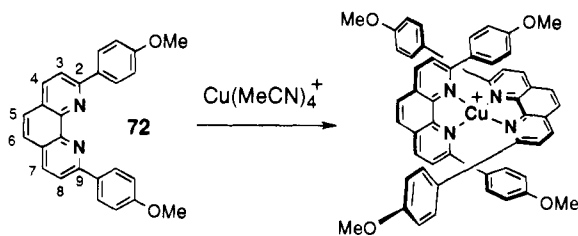


Figure 67. The complex²⁷⁰ formed between two 2,9-dianisyl-1,10-phenanthroline (**72**) ligands and copper(I) ions.

templates are the transition metals,²⁶⁴ which assist in the formation of a rich variety of macropolycyclic hosts. Pedersen's discovery²⁶⁵ that alkali metal ions template the formation of the crown ethers has led to the synthesis of a plethora of macrocycles²⁶⁶ and macrobicycles, *i.e.* cryptands.²⁶⁷ Metal ions can also be used to bring together two ligating moieties such that connection of their termini can afford catenanes. Alternatively, longer thread-like organic ligands can be assembled into the acyclic, yet well-defined, geometries of double and triple helicates,^{15,221,242} which are actually the precursors to a family of knots and catenanes.¹³

Sauvage and his co-workers^{26,268} have pioneered, and continue to lead the field in, the creation of interlocked molecules in which a transition metal ion—generally copper(I)—is used as the template. Indeed, this research actually preceded the major efforts that have been focused upon generating helicates (see section V). Sauvage's approach relies upon the tetrahedral coordination geometry of copper(I) ions, usually by two 2,9-disubstituted 1,10-phenanthroline units.²⁶⁹ The complex²⁷⁰ (Figure 67), formed between 2,9-dianisyl-1,10-phenanthroline **72** and copper(I), reveals the ideal geometry from which to start the construction of a catenane. The methoxyl groups associated with the two perpendicular coordinating strands are directed away from each other, so that the connection of pairs of termini should lead preferentially to a catenane. The term catenane²⁶ is used since the interlocked rings surround a complexed metal ion. In fact, Sauvage and Dietrich-Buchecker²⁷¹ tried the "less risky route" first of all by preparing (Figure 68) the macrocycle **73**, which

incorporates one bidentate coordination site. Treatment of this macrocycle with $\text{Cu}(\text{MeCN})_4^+ \cdot \text{BF}_4^-$ and then with the diphenolic phenanthroline ligand **74** afforded the pseudorotaxane-like complex **75**. Reaction of this complex with the diiodide derived from pentaethylene glycol, in the presence of cesium carbonate acting as the base, afforded²⁷² the [2]-catenane **76** in a remarkable 42% yield, based on the starting macrocycle. The more direct approach, involving the reaction of the copper(I) complex of the diphenol **74** with the same diiodide and under similar conditions to those used previously gave the [2]-catenane in 27% yield, a side product of the reaction being the macrocycle **73** in 20% yield.²⁷³ None of the macrocyclic complex **77** was detected, demonstrating just how well the functional groups are oriented in favor of catenation. The corresponding catenand **78**—the free catenated ligand—was obtained (Figure 69) by decomplexation of **76**, using tetraalkylammonium cyanide or potassium cyanide.²⁷⁴ Evidence from both ¹H NMR spectroscopy and X-ray crystallography reveals²⁷⁵ that the conformation of the ligand is completely different in the catenand, when compared with that present in the distorted tetrahedrally coordinated catenane, *i.e.* the free ligand is not preorganized to form a [2]catenane.

The catenates and catenands have many interesting properties, which arise as a result of the topography associated with their complexation and the topology of the ligand. The air stable copper(I) [2]-catenane **76** could not be demetalated electrochemically (Hg cathode, -1.8 V *vs* SCE), whereas more open complexes (*e.g.* the acyclic complex in Figure 67) are readily decomplexed under similar conditions (Hg cathode, -1.7 V *vs* SCE).²⁷³ The formally copper(0) complex is in fact perfectly stable in an inert atmosphere. The catenates are also remarkably stable to decomplexation with CN^- ion, when compared to complexes in which more simple ligands are coordinated to the metal ion.²⁷⁶ The remarkable kinetic stabilities of the complexes have led to the coining of the term, *catenand effect*. It results from the difficulty encountered by the two ligating moieties in decomplexing from the metal ion while remaining topologically confined within a catenand structure. In the reverse direction, the complexes of

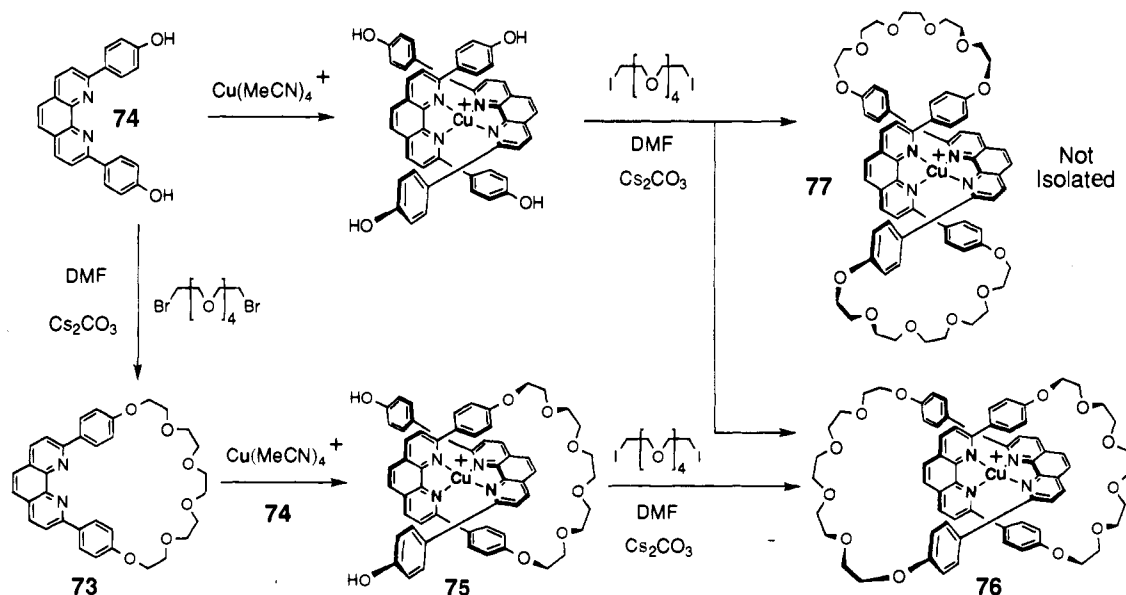


Figure 68. The different synthetic approaches^{271–273} to the self-assembly of the [2]catenane **76**.

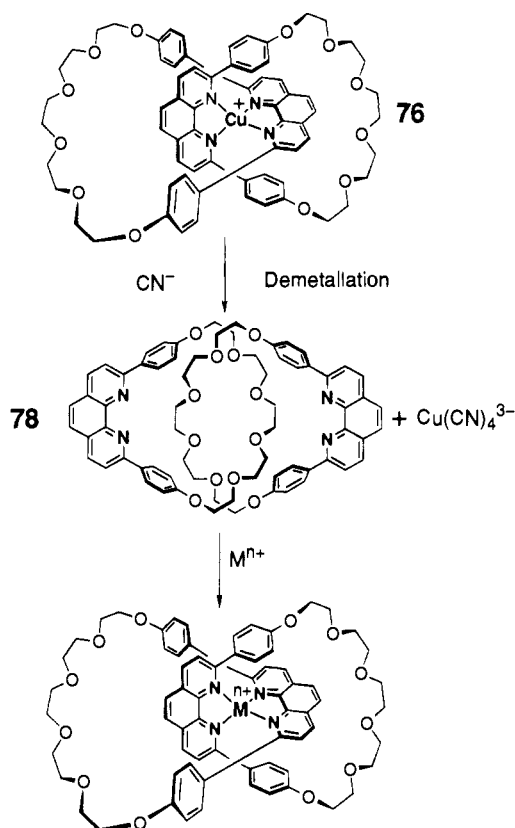


Figure 69. The demetallation²⁷⁴ of the [2]catenate **76** to give the [2]catenand **78**, which can be used to form a wide range of [2]catenates incorporating different metal ions²⁷⁶ (Mⁿ⁺) as well as protons.²⁷⁸

the catenand **78** with copper(I) or silver(I) ions have been shown²⁷⁶ to form according to a classical second-order rate law, as do the model systems **74** and **72**. The formation of the bischelate from the monochelated complex is rate limiting. In contrast, complexation of Li⁺, Cd²⁺, Zn²⁺, and Co²⁺—all with coordination numbers greater than four—by the catenand takes place in two discrete stages, *i.e.* the binding of a cation to one ligating unit is second order and is followed by the coordination of the second ligating unit. Since the first stage only partially desolvates the ions, the importance of solvation of the nontetrahedrally coordinated ions was suspected to be more significant than for the tetrahedrally coordinated copper(I) or silver(I) ions. The energy required to desolvate Li⁺, Cd²⁺, Zn²⁺, and Co²⁺ is greater than that for copper(I) or silver(I), necessitating what has been shown to be a slow conformational rearrangement of the ligand in these cases. Further studies showed²⁷⁷ that the rate constant for the second step decreases as the temperature is increased, the first bimolecular step being a normal one. The temperature dependence of the second step implies two processes: (a) a preequilibrium one, leading to a transient intermediate, which (b) rearranges, according to first order kinetics, to give the catenand. This rearrangement provides a rare example of a process with a negative enthalpy of activation.

The ion which lies at the center of the catenand in Figure 69 can also be a proton.²⁷⁸ The ligand system **78** is several orders of magnitude more basic than open-chain analogs, and when a proton is bound by the chelator, the conformation of the host is very much like that present in the catenand **76**. This

assertion has been proven by both solution-state studies and by X-ray crystallography. Acceptor–donor stacking interactions are present between the phenyl and phenanthroline rings in the proton catenand. The proton is located at a single nitrogen atom in the solid state but equilibrates rapidly between the four nitrogen atoms in solution. In contrast to the facile addition of a single proton to **78**, addition of a *second* proton is *much* harder, but even after this addition, the catenate geometry is retained, possibly because of stronger donor–acceptor interactions. These unique properties are a result of the topology of the ligand.

The catenand **78**, despite its preference for pseudotetrahedral coordination, is able to form, albeit slowly, a [2]catenate with nickel(II) (which prefers a square-planar geometry), while the use of **72** did not give a complex which could be isolated.²⁷⁹ This result demonstrates the importance of the catenand effect. When the nickel(II) catenate is reduced quantitatively to the nickel(I) catenate by electrolysis, the resulting complex has an amazing inertness to re-oxidation. Indeed, it takes days in oxygen-saturated dichloromethane to reoxidize the metal ion, while its complex with **72** is oxidized by air in minutes. The similar topographies of the nickel(I) complex with **73** and the corresponding [2]catenate allow a direct comparison of the catenand effect, that is, oxidation of the d⁹ metal ion is 10⁵ times slower in the catenand than it is with the acyclic analog, a direct result of the topological properties of the ligand. The contrast in the binding between nickel(I) and nickel(II) ions by the catenand has been emphasized by the recent publication²⁸⁰ of the crystal structures of the catenates. In the nickel(I) catenate, the X-ray crystal structure (Figure 70) shows that the geometry of the complex is governed by the metal ion, which has very close to tetrahedral coordination. The nickel(II) complex, on the other hand, contains favorable geometries for both the metal center and the ligand. The metal coordination is a highly distorted metal polyhedron, while the ligand is stabilized by intracomponent stacking interactions between the phenanthroline rings and the phenyl rings.

Treatment of the [2]catenand **78** with Pd(OAc)₂ under reflux in dichloromethane yielded a coordinated monocationic catenate in which *ortho*-metalation of one of the phenanthroline units had also taken place.²⁸¹ The two ligating nitrogen atoms of the metalated unit and one nitrogen atom from the other

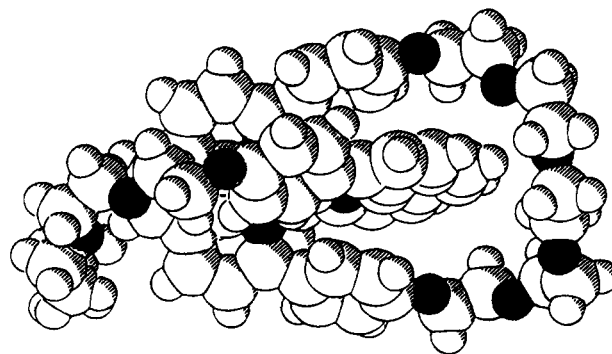


Figure 70. A space-filling representation of the X-ray crystal structure²⁸⁰ of the nickel(I) [2]catenate formed by metal ion complexation with **78**.

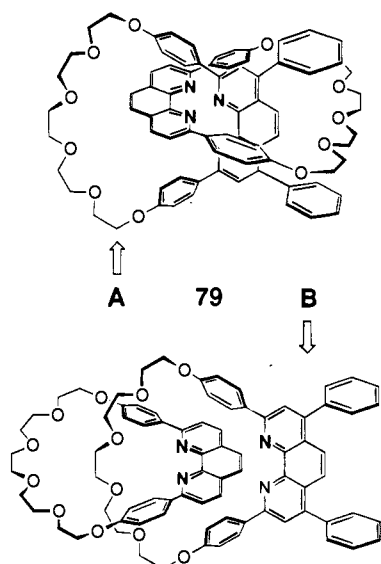


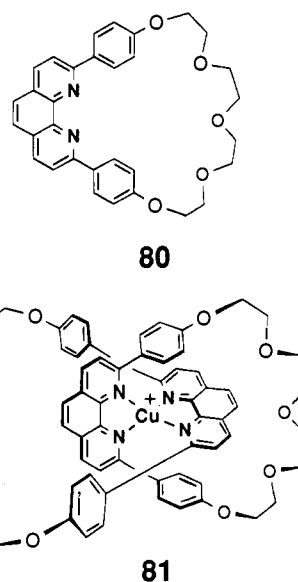
Figure 71. Two translational isomers (A and B) of a [2]-catenate with hindered rotation.²⁸²

macrocyclic component were coordinated to the palladium(II) atom, which had a distorted square-planar coordination geometry. This unusual structure results from the preferences for (i) the metal ion to adopt a square planar coordination geometry and (ii) the ligand to prefer tetrahedral binding geometry.

The catenand **78** exists in rapid equilibration between different geometrical forms in the solution state, since there are essentially no noncovalent interactions to restrain the relative motions of the two components. Sauvage's group have introduced bulky substituents into the 4- and 7-positions of the 1,10-phenanthroline residue in one of the macrocycles in order to endow the catenand with some rotaxane-like character.²⁸² As depicted in Figure 71, two translational isomers (A and B) of **79** can exist. The templated formation of the copper(I) catenate followed a route similar to that depicted in Figure 68, except that the preformed ring was substituted with phenyl groups at the 4- and 7-positions of the ligating moiety. The yield of the corresponding [2]catenate was only 7%, with one of the other products being the [2]catenate **76** in 4% yield. Fortunately, the use of selective decomplexation of the catenates with KCN could be used to separate the two compounds. The separation relies on the fact that the sterically encumbered catenate is substantially more difficult to demetallate.²⁸³ It has been suggested that the difficulty associated with demetalation of the catenate precursor to **79** arises from the lack of conformational mobility in the ligand. Indeed, a comparison of the ¹H NMR spectra for the [2]catenate and the [2]catenand reveals that the free ligand has restricted motion, and that only isomer A, in which the unsubstituted ring passes between the phenyl substituents of the other macrocyclic component, is present in the solution.

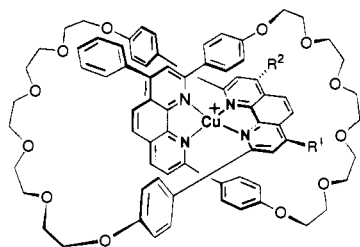
The macrocycle **73** constitutes a 30-membered ring. This size is adequate to allow the comfortable threading through it of a second ligating phenanthroline unit prior to coordination of the templating metal ion. The template-directed synthesis of the [2]catenate, in which both macrocycles have 27-membered rings, on account of incorporating a tetraethylene glycol

residue spacer, is much less efficient than that of the catenate constructed from the larger macrocycles.²⁸⁴ The [2]catenate was synthesized by employing the macrocycle **80**, which was combined with Cu(MeCN)₄⁺·BF₄⁻ and the diphenolic phenanthroline ligand **74** before the resulting complex was cyclized employing the same method as that used for the preparation of the catenate **76**. The major product of the reaction was the macrocycle **80**, with only 3.3% of the [2]catenate **81** being isolated. The effect in **81** of reducing the dimensions of the component macrocycles is to increase dramatically the rigidity of the system compared with that of **76**. Indeed, the [2]-catenate was found to be chiral, on account of the restricted motions of the rings relative to one another. It was proposed that one of the glycol chains of one ring is trapped on one side of the 1,10-phenanthroline unit of the other ring. There is no equilibration between the enantiomers, even at 160 °C.



The first synthesis of a *topologically* chiral [2]-catenand was reported in 1988 by Sauvage and Mitchell.²⁸⁵ In order to build topological chirality into a catenane, the rings must be given *direction*. This directionality was conferred upon a 1,10-phenanthroline unit in a macrocyclic polyether by incorporating one phenyl substituent at the 4-position of the ligating unit. The established template-directed synthesis procedure was used to prepare the racemic [2]catenate **82**. The addition of Pirkle's reagent to a solution of the [2]catenate caused "splittings" of nearly *all* the resonances in the ¹H NMR spectrum of this compound, indicating the presence of stable diastereoisomeric complexes on the ¹H NMR time scale. Removal of the templating metal afforded the racemic mixture of [2]catenands, whose resonances in the ¹H NMR spectrum were no longer separated on addition of the chiral shift reagent. Interestingly, the topologically achiral **83**, which has only one oriented ring, has many of its resonances in its ¹H NMR spectrum "split" in a chiral medium, as a result of the internal enantiotopicities of certain probe protons being rendered diastereotopic in the presence of the chiral complexant. It was pointed out²⁸⁶ that a very careful consideration of the topicities of probe protons is necessary in order to distinguish chiral molecules from achiral ones. The resolution of the

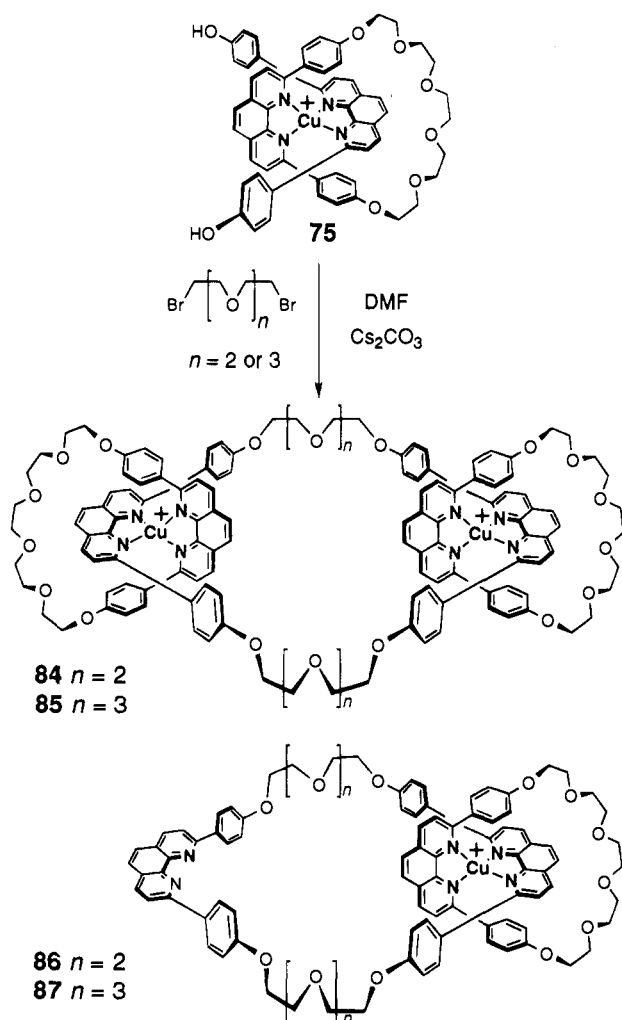
optically active [2]catenates has been achieved²⁸⁷ recently using HPLC on silica gel-coated with amylose tris[(3,5-dimethylphenyl)carbamate]. The CD spectra of the separated catenates proved their optical activity, the first-eluted catenate having a positive Cotton effect centered on 320 nm.



82 [R^1, R^2] = [H, C₆H₅]

83 $R^1 = R^2 = H$

The same metal ion-templated synthesis has been used by the Strasbourg group for the construction of [3]catenates and [3]catenands.²⁸⁸ In their first investigations, the complex **75** was reacted in *N,N*-dimethylformamide in the presence of cesium carbonate with the dibromides of either triethylene glycol or tetraethylene glycol linking units, which are too short to allow efficient cyclizations to afford [2]catenates (Figure 72). The [3]catenates **84** and **85**

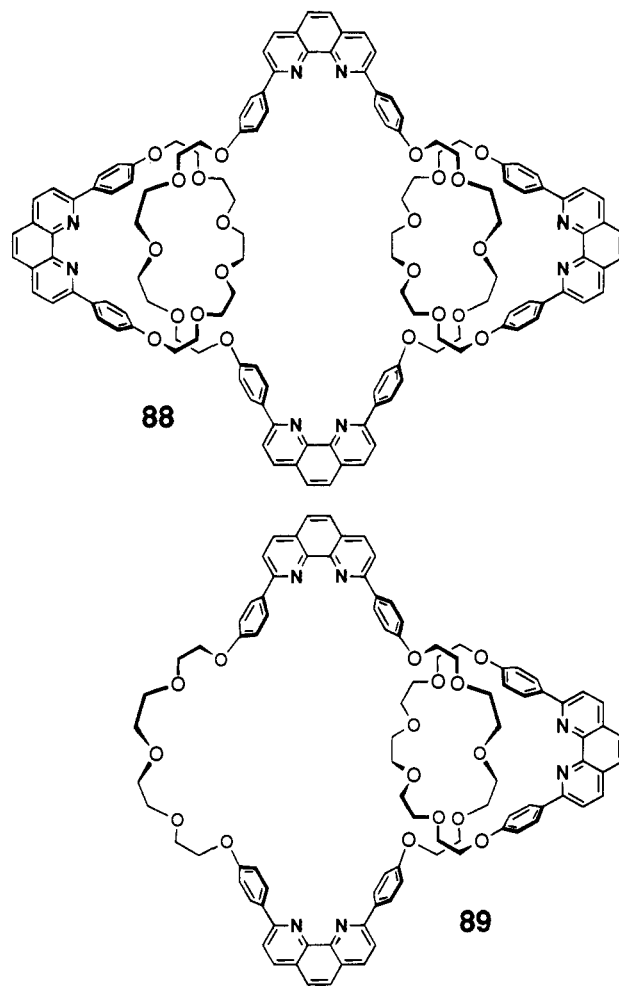


84 $n = 2$
85 $n = 3$

86 $n = 2$
87 $n = 3$

Figure 72. The template-directed synthesis²⁸⁸ of [3]catenates, such as **84** and **85**, with the [2]catenates **86** and **87** being produced in the synthesis as well.

were isolated in 6% and 2% yields, respectively, the reason for the low yields being related to the fact that the corresponding free macrocycles are also formed. In addition, the [2]catenates **86** and **87** were isolated in 5% and 1.2% yields, respectively. Demetalation of the [3]catenates afforded the corresponding [3]catenands. In common with the [2]catenates, the more rigid **84** is more difficult to demetalate than the more flexible **85**. The solid-state structure²⁸⁹ of the [3]catenand **88** revealed an arrangement of the two peripheral macrocycles such that the 1,10-phenanthroline residues within them stack parallel to one another, with an intramolecular interplanar separation of 3.34 Å. In addition, the 1,10-phenanthroline residues in the central macrocycle are stacked with the corresponding residues within another molecule of the [3]catenand in the crystal. Solution-state studies of the [3]catenand **88**, using ¹H NMR spectroscopy, revealed that its gross conformation is very different from that of the [2]catenand **89**. Significant high-field shifts of the resonances associated with the 1,10-phenanthroline residues of the two peripheral macrocycles indicate that an ordered structure may exist in solution which is similar to that characterized in the solid state.



88

89

A more efficient synthesis²⁹⁰ of [3]catenates was achieved subsequently by the Glaser coupling of the complexes such as **90** and **91**, which afford (Figure 73) the [3]catenates **92** and **93** in 68% and 58% yields, respectively.²⁹¹ The greater efficiency of this synthesis results in part from the fact that it requires the oxidative coupling together of only four reactive

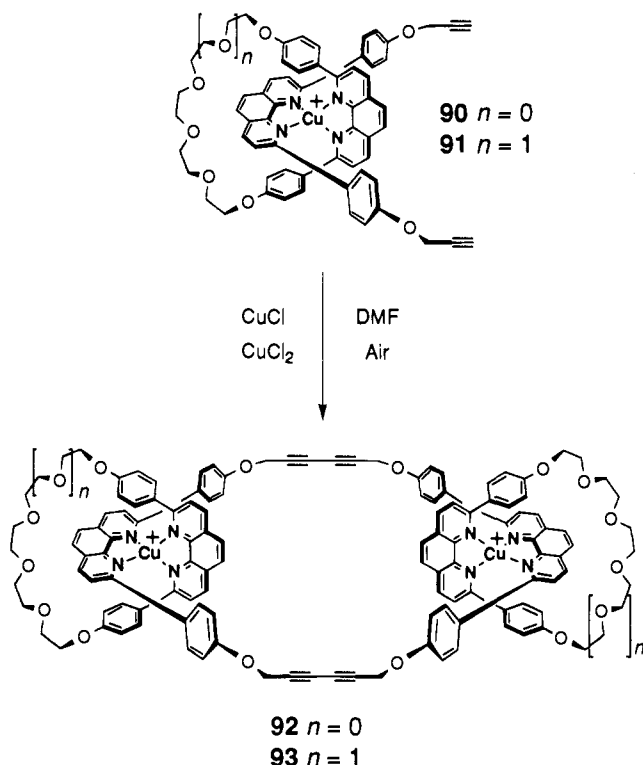


Figure 73. A more efficient template-directed synthesis²⁹⁰⁻²⁹² of [3]catenates **92** and **93** using the Glaser coupling procedure.

groups, while the previously described synthesis (Figure 72) requires substitutions involving eight reactive termini. In addition, the [4]catenates **94** and **95** were isolated in 14% and 22% yields, respectively, from these reactions, bringing the total yields of catenated compounds up to approximately 80%. In a later report,²⁹² the identity of some [5]-, [6]-, and [7]-

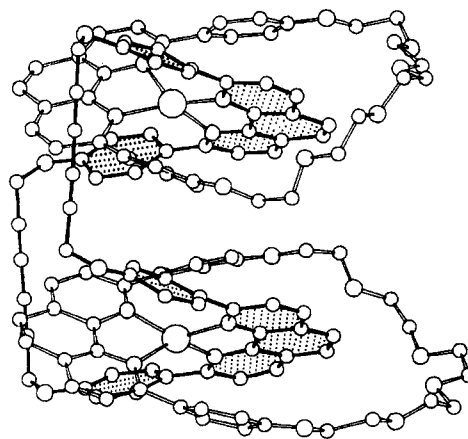
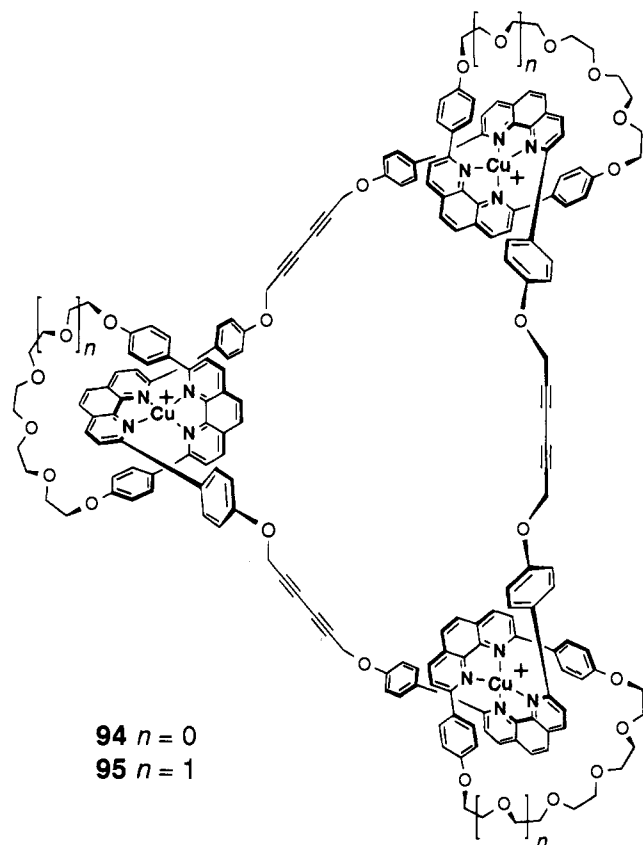


Figure 74. A ball-and-stick representation of the X-ray crystal structure²⁹⁴ of the [3]catenate **93**.

catenates, in which four, five, and six macrocycles **80** were threaded on to one large macrocycle, was confirmed by electrospray mass spectrometry. The largest structure has a mass of approximately 7.8 kDa, as determined by electrospray mass spectrometry.²⁹³ The X-ray crystal structure²⁹⁴ of the [3]catenate **93** reveals (Figure 74) a highly ordered structure in which the phenyl and phenanthroline units of the component macrocycles stack as a result of stabilizing π - π interactions. The globular shape of the [3]catenate is built around the central ring which adopts a boatlike conformation with the copper(I) centers located 8.5 Å apart.²⁹¹ From an ¹H NMR spectroscopic study, this conformation of the central ring is also adopted in the solution state.

Removal of the templating ions²⁹¹ from **92** and **93** affords the corresponding [3]catenands, which have been remetalated with a range of metal ions (Ag^+ , Zn^{2+} , Co^{2+} , Ni^{2+}) in order to study the communication between the cationic centers by electrochemical and photochemical means. The [3]catenates incorporating two Ag^+ ions and two Zn^{2+} ions have collapsed conformations in the solution state similar to those of the Cu^+ analogs. The metal ions in these [3]catenates are more easily reduced in the first reduction wave than are the metal ions in analogous [2]catenates derived from **78**. The reason for this extraordinary shift in potential may be a result of an electrostatic interaction with the second metal ion via the π -stacked aromatic units of the ligand. This hypothesis is supported by the fact that the [3]catenates, in which a more extended conformation is evident from ¹H NMR spectroscopic studies, show no such lowering in the magnitude of the first reduction potential. In particular, ¹H NMR spectroscopy indicates that the [3]catenates incorporating Zn^{2+} have extended conformations in solution, a feature which has been confirmed by electrochemical experiments (Figure 75). In addition to the remetalation of the [3]catenands to afford homonuclear [3]catenates, selective stepwise demetalation of [3]catenates such as **93**, followed by remetalation, affords heteronuclear [3]catenates.²⁹⁵ Studies^{296,297} of **96** reveal that strong fluorescence and phosphorescence bands are completely quenched in the corresponding catenate **93**, with emission being observed as a result of metal-to-ligand charge transfer. The system **97**, which incorporates both catenate and catenand-type substructures, has strongly quenched fluorescence of the free section as a result of the

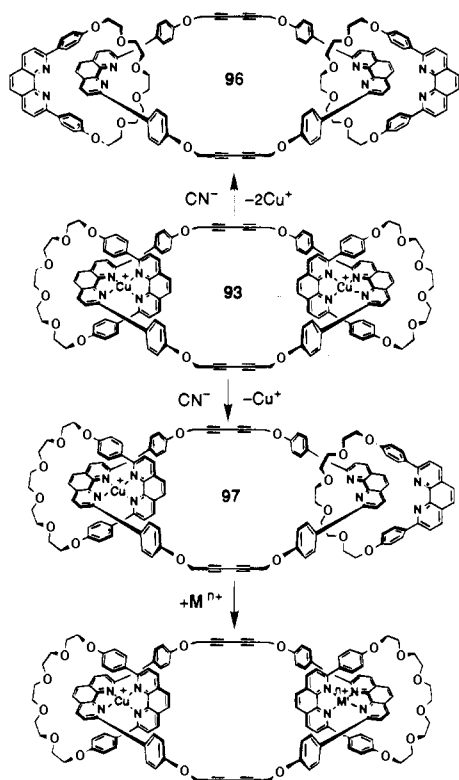


Figure 75. The demetalation of the [3]catenand **93** to give the [3]catenand **96** and also the preparation of heterodimetallic [3]catenates via the partially demetalated intermediate **97**.^{291,295–297}

presence of the remote copper(I) ion. In a heterodimetallic [3]catenand incorporating a copper(I) and a cobalt(II) center, the metal-to-ligand charge transfer of the former is quenched by the presence of the latter. These and other results have demonstrated that the [3]catenates are excellent vehicles for studying the electronic interactions between metal centers in relatively well-defined molecular assemblies. Furthermore, the catenand **96** is believed to form “proton catenates” in the presence of acid,²⁹⁸ a property resulting from the cooperative movement of pairs of the ligands so as to encapsulate the protons.

More recently, the complexation of copper(I) ions by the 1,10-phenanthroline residue has also been utilized for the preparation of rotaxanes. In 1991, Gibson and co-workers²⁹⁹ reported the template-directed synthesis (Figure 76) of a [2]rotaxane, starting from the known complex **75** by simply capping its terminal phenolic functions with the alkyl iodide **98** carrying bulky triarylmethyl groups. Removal of the complexed copper(I) ion was achieved by passing the rotaxane through Amberlite-CN resin. The free [2]rotaxane **99** was isolated in 42% yield. The unthreaded dumbbell compound was also obtained

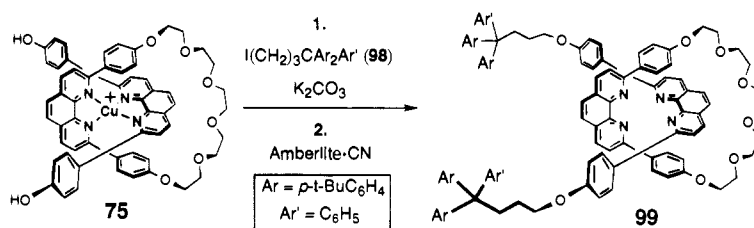


Figure 76. The template-directed synthesis²⁹⁹ of a [2]rotaxane using chelation of copper(I) ions by 1,10-phenanthroline derivatives.

in 9% yield. An ^1H NMR spectroscopic study showed that the bulky stopper groups in **99** lie predominantly in the shielding zones of the phenanthroline residue present in the macrocycle, while the two phenanthroline groups reside in each other's deshielding zone. These observations are consistent with a [2]rotaxane structure, which was confirmed subsequently by mass spectrometry.

Before this “first” [2]rotaxane was reported in the literature, the Strasbourg group had already described³⁰⁰ the synthesis of oblique bisporphyrin dumbbell-shaped compounds incorporating a 1,10-phenanthroline residue as part of an investigation³⁰¹ of intramolecular energy-transfer processes. Subsequently, in 1992 they reported³⁰² the preparation of a porphyrin-stoppered [2]rotaxane. The synthesis was achieved by, first of all, preparing **100** with a relatively inert gold(III) porphyrin stopper in place. This compound was then added to the macrocycle **73** in the presence of copper(I), affording (Figure 77) the intermediate complex **101**. This complex, or “pre-rotaxane”, was reacted with 3,5-di-*tert*-butylbenzaldehyde and bis(3-ethyl-4-methyl-2-pyrryl)methane in the presence of trifluoroacetic acid, after which chloranil was added to oxidize the intermediate porphyrinogen. The whole procedure gave³⁰³ the [2]rotaxane **102** and the [3]rotaxane **103** in 25% and 32% yields, respectively, after chromatography. The free base etioporphyrins were converted into their zinc porphyrin analogs **104** and **105** by treatment with $\text{Zn}(\text{OAc})_2 \cdot 2\text{H}_2\text{O}$. Demetalation of the ligated templating copper(I) ion was achieved in the case of this [2]rotaxane by treatment of it with KCN. The fact that the bisporphyrin dumbbell and the macrocyclic ring remain as one molecular species established the new compound as a true [2]rotaxane. The free phenanthroline ligands in **102** have subsequently been metalated with zinc(II).

The purpose behind constructing these interlocked molecular structures incorporating two different porphyrins was to study their photochemical properties. The Strasbourg group³⁰⁴ has set itself the objective in recent years to mimic the array of tetrapyrrolic chromophores at the heart of bacterial photosynthetic reaction centers. Comparison of the rates of electron transfer upon excitation of the zinc porphyrin in the rotaxanes depicted in Figure 78 with the free bisporphyrin dumbbell reveals a significantly higher rate of electron transfer from the excited state of the zinc porphyrin to the gold(III) porphyrin for the mechanically interlocked structures.³⁰⁵ It is proposed that the extremely rapid rate of electron transfer for **104** is a result of the mediation of the electron transfer by the copper(I) center. Also, the energies of the orbitals in the spacer units are modified according to the nature of the coordinated metal ion. The relatively

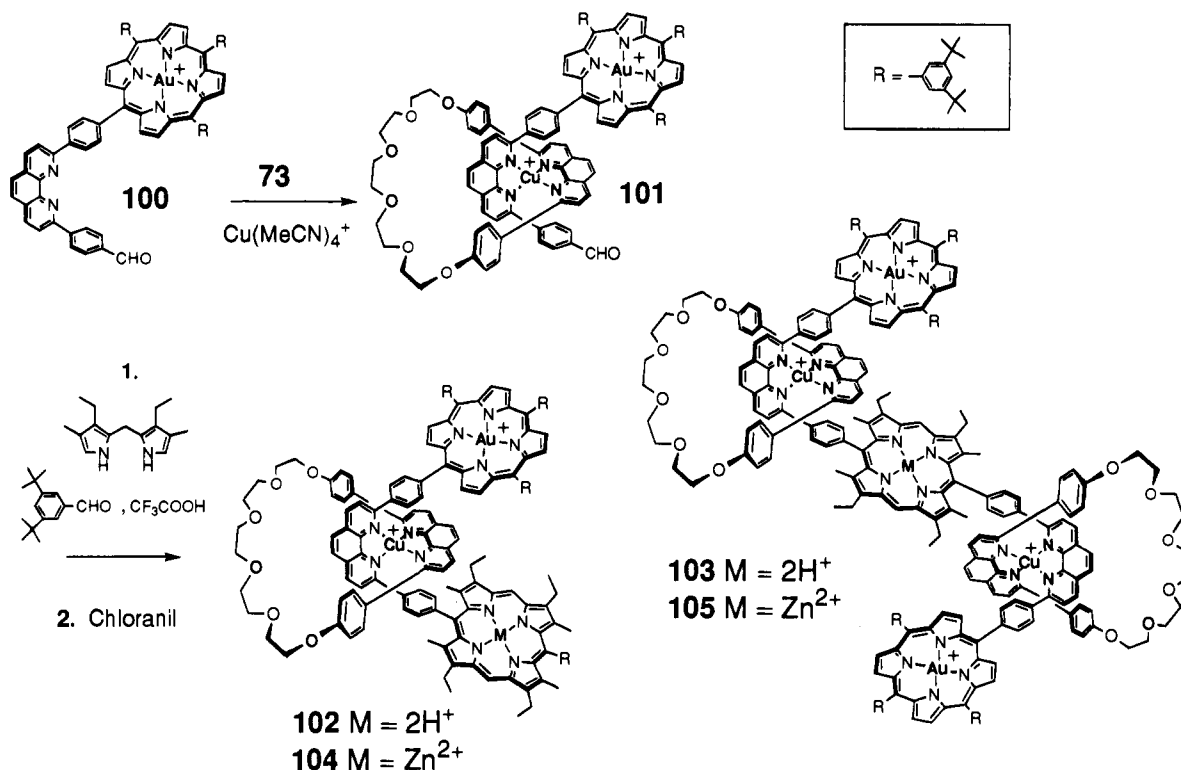


Figure 77. The template-directed synthesis^{302,303} of porphyrin-stoppered [2]- and [3]rotaxanes.

slow back-electron-transfer reaction is not mediated in this way, nor is it affected by the presence of the coordinated metal ion. This observation supports the proposed superexchange mechanism.

The Strasbourg group, in collaboration with Diederich in Zürich, has recently reported³⁰⁶ the synthesis of a rotaxane in which the blocking groups are fullerenes. The oxidation of the copper(I) template

in the rotaxane was considerably more anodic (+0.865 V) than for other similar complexes. It was proposed that the electron-withdrawing effect of the fullerenes destabilizes the copper(II) state.

In a set of studies aimed at determining the viability of making extended rotaxanes using the 1,10-phenanthroline/copper(I) coordination system,³⁰⁷ molecular thread-like molecules incorporating two (107) and three (108) 1,10-phenanthroline residues were combined (Figure 79) with the templating ion

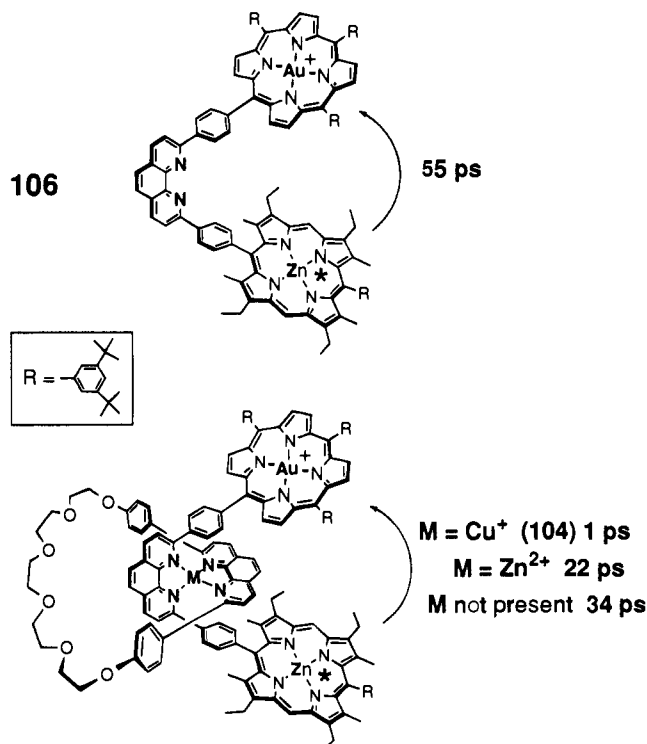


Figure 78. A comparison of the rate of electron transfer from a zinc(II) porphyrin to a gold(III) porphyrin within a dumbbell compound **106** with the rates for the corresponding metalated [2]rotaxanes with copper(I) and zinc(II) as well as in the free [2]rotaxane.³⁰⁵

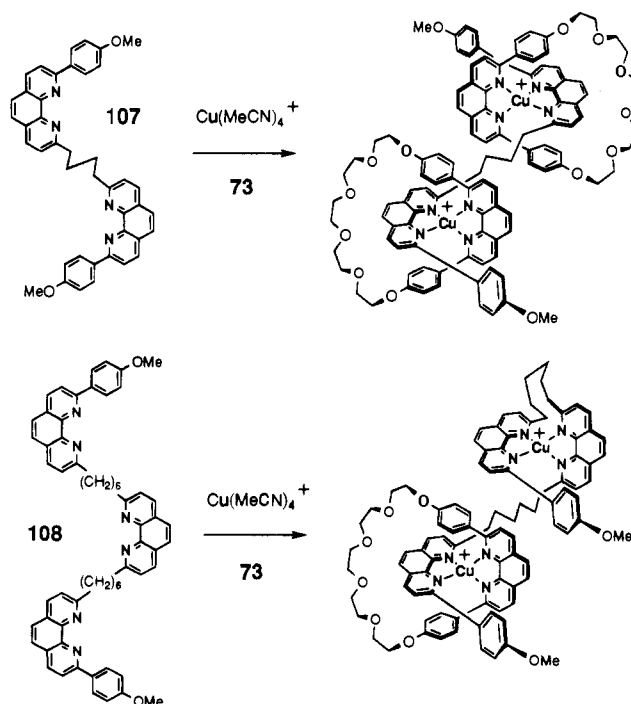


Figure 79. (Top) The template-directed synthesis of a metalated [3]pseudorotaxane; (bottom) the attempt at using the same conditions to prepare a [4]pseudorotaxane.³⁰⁷

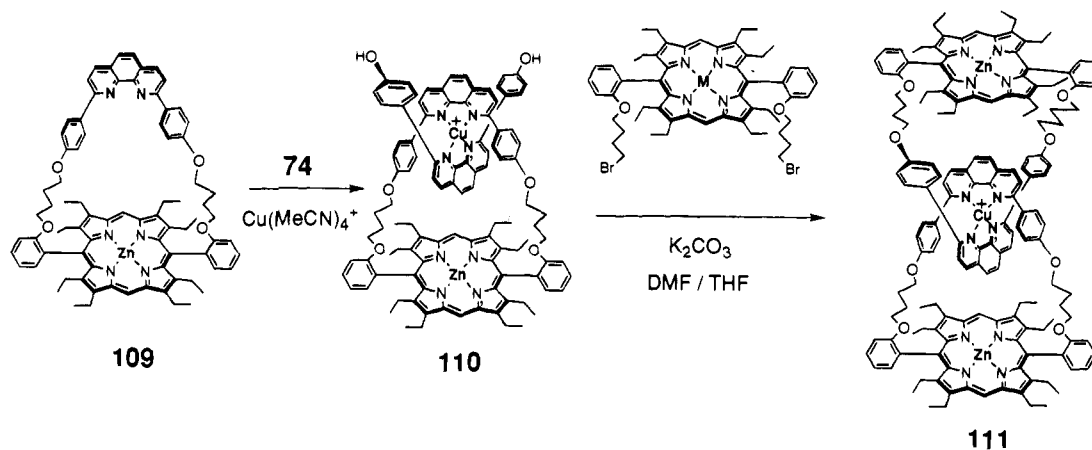


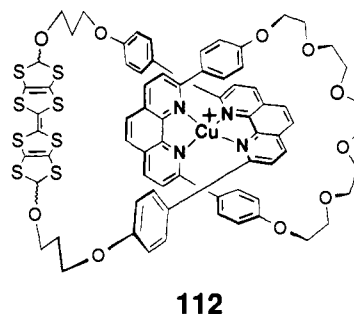
Figure 80. The template-directed synthesis³⁰⁸ of a [2]catenane **111** comprising an “interlocked basket handle porphyrin”.

in the presence of the macrocycle **73**. The thread-like molecule incorporating two phenanthroline residues forms a 1:2:2 complex (thread/metal ion/macrocyclic) with Cu(I) and **73**, in a [3]pseudorotaxane-type assembly. The thread **108** containing three phenanthroline units forms a 1:2:1 complex (thread/metal ion/macrocyclic), in which two phenanthroline units of the thread surround one and the same Cu(I) ion, and not the desired 1:3:3 complex! The flexibility of the spacer in the thread is presumably responsible for this phenomenon, which is important when considering the synthesis of more complex materials.

The same templating concept developed by the Strasbourg group has been used by Momenteau and co-workers³⁰⁸ for the construction of catenates incorporating two porphyrin centers—the so-called “interlocked basket handle porphyrins”. The synthesis of these compounds has been achieved (Figure 80) by preparation of a macrocycle **109**, incorporating one porphyrin and one 1,10-phenanthroline residue, followed by complexation of copper(I) by the macrocycle and **74**, to form the precatenate **110**. Cyclization of this diphenol with a symmetrically disubstituted porphyrin dibromide afforded the [2]catenane **111** in 31% yield. An ¹H NMR spectroscopic study showed the resonances for the phenanthroline unit in the [2]-catenane **111** were shifted dramatically to high field compared with the resonances for the phenanthroline unit of the macrocycle **109**. These observations indicate that the closest distance of the porphyrin to the phenanthroline residue is approximately 4.5 Å. No electron-transfer studies have yet been reported.

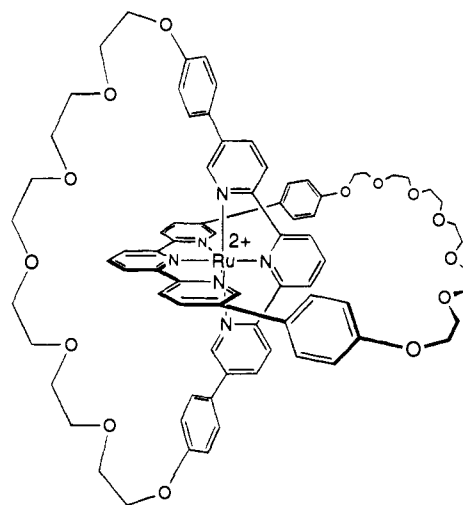
Another report concerning the incorporation of electrochemically addressable components into catenated structures has been published³⁰⁹ recently. A macrocycle containing a substituted tetrathiafulvalene unit (TTF) was prepared by firstly cyclizing a functionalized TTF derivative with **74** in the usual manner. Catenation was achieved by forming the copper(I) complex and cyclizing once again, using established methodology. The resulting [2]catenane **112** can exist as two diastereoisomeric species, because the two stereogenic carbon atoms in the molecule may have either *syn* or *anti* relative configurations. The diastereoisomer which is the predominant one (77%) in the catenated product, is expected to be composed of the TTF-containing macrocycle with the *syn*-configuration. The Strasbourg/Odense team hope to incorporate an electron acceptor

into the other macrocycle as the next step toward forming a donor–acceptor triad.



112

The electrochemical “switching” of a [2]catenane has recently been achieved by the Strasbourg group. It is triggered by the oxidation of a metal ion which causes a rearrangement in the ligands of one macrocyclic component.³¹⁰ Following the successful utilization of terpyridine for the construction³¹¹ of the [2]catenane **113**, templated around an octahedrally



113

coordinated ruthenium(II) ion, the macrocycle **114** was designed and constructed so that it contains one bidentate phenanthroline and one terdentate terpyridine ligating moieties. The Cu(I) catenane **115** was prepared³¹⁰ by treating (Figure 81) **114** with Cu-

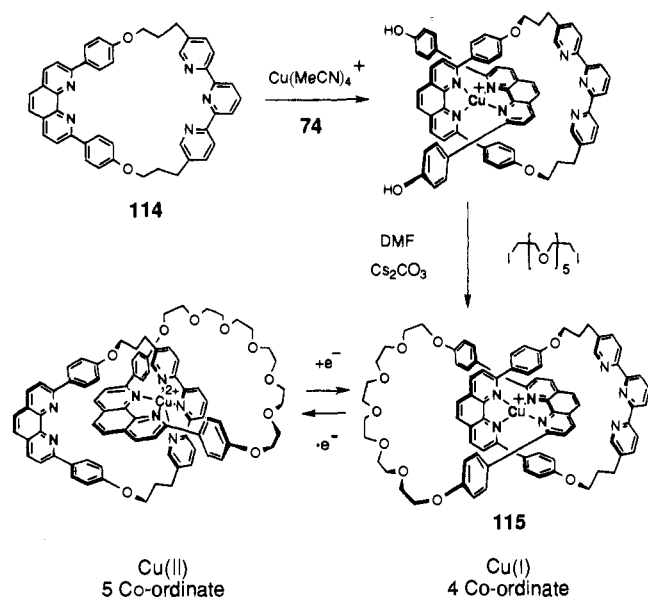


Figure 81. The template-directed synthesis³¹⁰ of a [2]-catenane that can be switched electrochemically on account of the requirements for copper(I) and copper(II) to be four- and five-coordinate, respectively.

(MeCN)₄⁺ and **74**, followed by macrocyclization of the second ring in the usual manner to give in 10% yield the [2]catenane, in which two phenanthrolic moieties are coordinated to the metal ion. Chemical (Br₂) or electrochemical oxidation of the metal ion results in a tetrahedrally coordinated copper(II) catenane, which rearranges slowly to a five-coordinate structure in which one phenanthroline and one terpyridine moiety bind the metal ion. Reduction of the copper(II) catenane regenerates the copper(I) complex and the [2]catenane rearranges rapidly so that the two phenanthroline ligands surround the metal ion once again.

One of the major challenges, which has faced chemists interested in making interlocked molecular

compounds has been the synthesis of a trefoil knot. This milestone was reached in 1989 by Dietrich-Buchecker and Sauvage.³¹² The formation of the trefoil knot is dependent upon the formation of a double-helical complex, which has to be stable under the reaction conditions for the cyclization of appropriate termini. After many efforts, involving the incorporation of various different linkers between the phenanthroline residues, the compound **116** was mixed with copper(I) ions and the resulting binuclear complex was cyclized in the presence of Cs₂CO₃ to afford (Figure 82) the biscopper(I) complex of the knotted system **117** in 3% yield. The major product of the reaction (Figure 83) in 24% yield was characterized as the face-to-face complex **120**. Addition of Pirkle's reagent to a solution of the complexed chiral knot **117** resulted in definite splitting of a number of the resonances in the ¹H NMR spectrum of the compound. Demetalation of the complex **117** with KCN afforded a glass which was characterized as the free knotted ligand **118**. In addition, the dimeric macrocycle **122** was also isolated in 0.5% yield. Although the mass spectra of the topological stereoisomers **118** and **122** were very similar, the NMR spectra of the compounds were very different. Indeed, the ¹H NMR spectrum of the knot displayed extremely broad lines. Complexation of potassium ions by the free knotted ligand **118** once again caused significant splittings of resonances in the spectrum, confirming that the ligating chiral knot was present. Similar experiments, where potassium ions had been added to **121** and **122**, resulted in no splittings of the resonances in the ¹H NMR spectra upon the addition of the chiral shift reagent.

The reason for the poor yield of the knot and for the creation of so many side products is that the

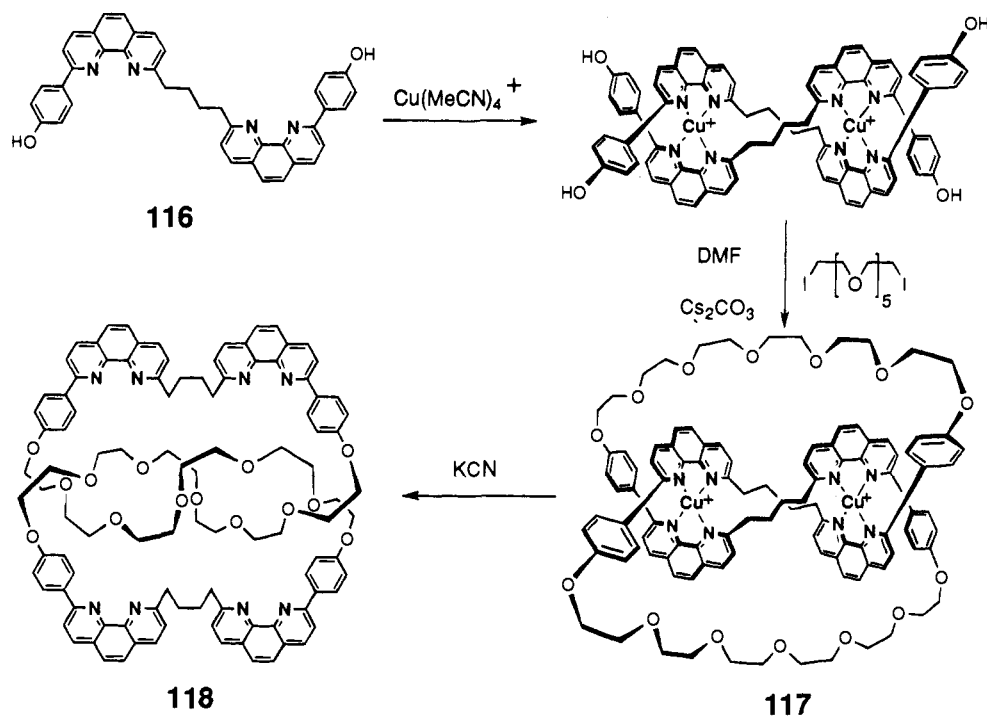


Figure 82. The elegant construction by Dietrich-Buchecker and Sauvage³¹² of a molecular knot, both metalated and "free".

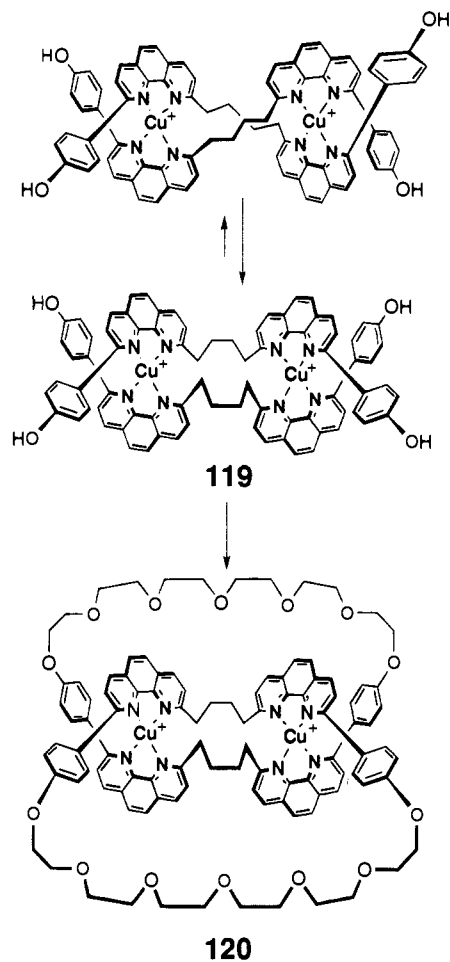


Figure 83. The major face-to-face complex (**120**), resulting³¹³ from the chemistry described in Figure 82.

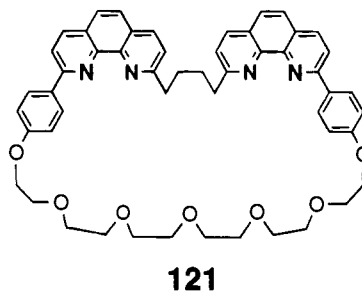
double-helical complex formed by **116** and copper(I) ions is in equilibrium with other structures in solution (Figure 83). The face-to-face complex **119** is the main structure in solution,³¹³ the ratio of this undesired complex to the double helical one being 8:1. Cyclization of the reactive termini of the face-to-face complex **119** should lead *inter alia* to the complex **120** and, after demetalation of the binuclear copper(I) complex, to 2 molar equiv of the macrocycles **121**.

The undisputed beauty of the complexed knot was revealed (Figure 84) in the form of a crystal structure,³¹⁴ which showed the single 86-membered ring with its phenanthroline units spiralling around the two copper(I) ions in a helical fashion, with the termini connected in an end-to-end fashion to form the knot. The two copper ions, which are coordinated in the geometry of a distorted tetrahedron, are located in similar environments, 6.3 Å apart. The presence of folding in the central part of the polyethylene glycol spacer indicates that this link is slightly too long, a design fault which has subsequently been addressed. There are essentially no parallel π - π interactions in the complex in the crystal. Perhaps one of the most appealing aspects of any single crystal of the chiral knot is that it contains only *one enantiomer*, *i.e.* the compound undergoes spontaneous resolution on crystallization. The Strasbourg group hope, by growing sufficiently large crystals, that they will be able to separate the right- and left-handed knots! It should be added that they have also managed to crystallize the face-to-face

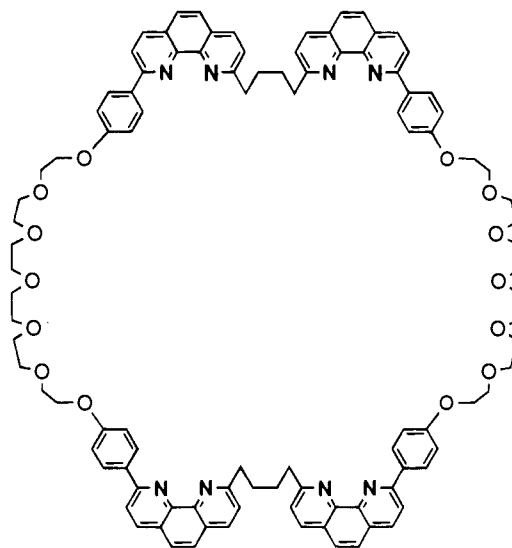
complex **120**, which is comprised of two unconnected and unlinked 43-membered macrocycles.³¹³ The central part of the structure, which also contains a center of symmetry, is quite compact as a result of the two rings being hooked over one another around the two copper(I) ions, which are 7.94 Å apart and have similar coordination geometries to those present in the complexed knot.

The ¹H NMR spectrum of the demetalated knot **118**, while exhibiting broad signals at room temperature, sharpens up considerably upon warming a solution containing the compound.³¹³ Coalescence of resonances arising from protons attached to the phenyl spacers in the knot gave a ΔG_c^\ddagger value of 17.8 kcal mol⁻¹ at 366 K. The wormlike motion of the macrocycle through itself has been described as "molecular reptation". It is estimated that it takes about 2 s for one full reptation to take place in the knot in solution at 298 K.

In an effort to improve the efficiency of the knot formation, the size of the complete ring in the knot has been varied from 80 to 90 atoms.³¹⁵ This range was achieved by altering the length of the alkyl spacer between the two phenanthroline units and the number of bismethyleneoxy units in the linking polyethylene glycol chain (Figure 85). The formation of a double-helical complex is essential for knot formation. No such complex formation was observed when $-(CH_2)_3-$ or $-p-C_6H_4-O-p-C_6H_4-$ spacers were incorporated between the phenanthroline units. When even numbers of methylene groups link the ligating groups, helices are observed, *e.g.* up to 50% of the



121



122

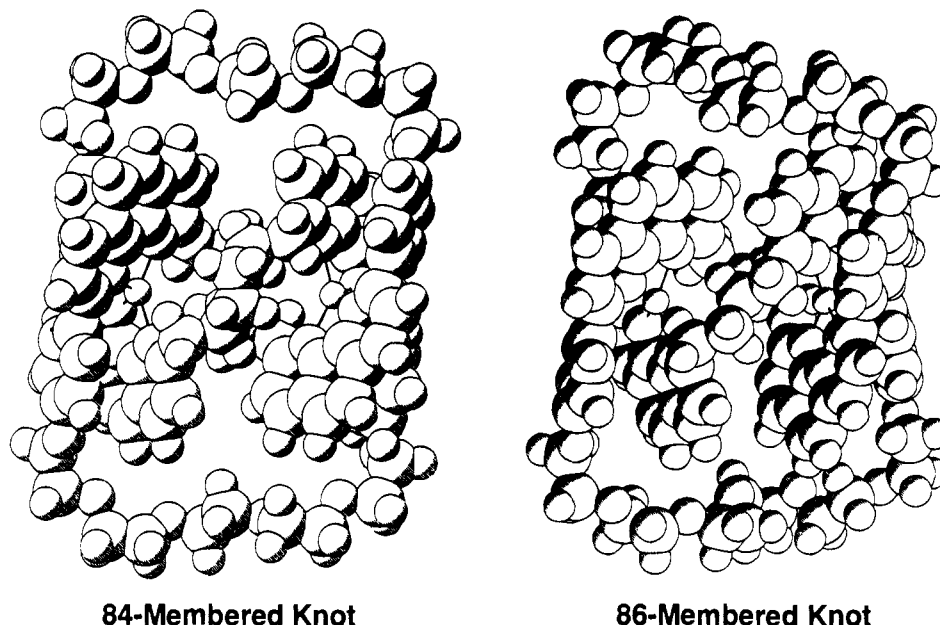


Figure 84. The space-filling representations of the X-ray crystal structures of the knots based on 84- and 86-membered rings as their copper(I) complexes.^{314,316}

total number of complexes for $-(\text{CH}_2)_6-$ spacers. Cyclization of the complexes under the conditions described previously afforded the dicopper(I) knots, the best yield being 8% for the material with $-(\text{CH}_2)_6-$ spacers and a pentaethylene glycol linkage, giving an 84-membered knotted ring. Indeed, this modification proved to be the only successful one. All the others resulted in lower yields of the knots, the major products being the isomeric face-to-face complexes. An X-ray crystal structure of the 84-membered knot complex³¹⁶ reveals (Figure 84) it has a more twisted arrangement compared with the 86-membered knot complex. In addition, the distance between the copper(I) ions in the 84-membered knot complex is 7.03 Å, *cf.* 6.30 Å in the case of the 86-membered knot complex.

Kinetic studies reveal³¹⁶ that the knotted complexes are more difficult to demetalate than the corresponding face-to-face complexes. The knotted structures, it has been suggested, must undergo greater conformational change upon removal of the metal ion. As a result of the greater twisting of the phenanthroline groups around the templating ions afforded when there is a $-(\text{CH}_2)_6-$ spacer between

the pairs of ligating groups, the knots containing 84- and 90-membered rings are harder to demetalate than the 86-membered ring knot complex. The 84-membered knot complex is the most kinetically stable. The copper(I) complexes of the trefoil knots also have electrochemical properties that are dependent upon their structures,³¹⁷ with the $\text{Cu}^{\text{II}}/\text{Cu}^{\text{I}}$ couples having redox potentials ranging from 0.5–0.75 V. The most stable copper(I) complex is the 84-membered knot which is formed most efficiently. This observation is in line with the kinetic data for decomplexation of this complex. The lengths of the oligomethylene spacers and the polyethylene glycol linkers between the phenanthroline units in the knots also have an influence on the photochemical properties of the copper(I) complexes. These properties are determined largely by the geometrical arrangements of the ligands around the metal ions.

Very recently, the synthesis of a trefoil knot has been achieved in a remarkable 30% yield.³¹⁸ The ligand **123**, in which the spacer between the two phenanthroline units is a *m*-phenylene, forms (Figure 86) a double helicate quantitatively when mixed in a 1:1 stoichiometry with copper(I). The crystal structure of the double helix showed that it is perfectly arranged to form the knot **124**, which it does extremely well when combined with the diiodide of hexaethylene glycol. The double helix and the knot are extremely stable to demetalation.

The "correct" cyclization of helices in which an odd number (n) of coordination sites are present provides a route to $(n + 1)$ -crossing [2]catenanes. Sauvage's group has recently extended their system based on copper(I) coordination by 1,10-phenanthroline residues toward this particular objective, and have prepared the first doubly interlocked [2]catenane.³¹⁹ The macrocycle **126** was prepared (Figure 87) in the usual manner from **125** and the diiodide of heptaethylene glycol. The addition of **125** to **126** in the presence of 3 equiv of copper(I) ion afforded a mixture of complexes, including the desired **127**, which was then reacted subsequently with the diiodide of heptaethylene glycol to give a mixture of products

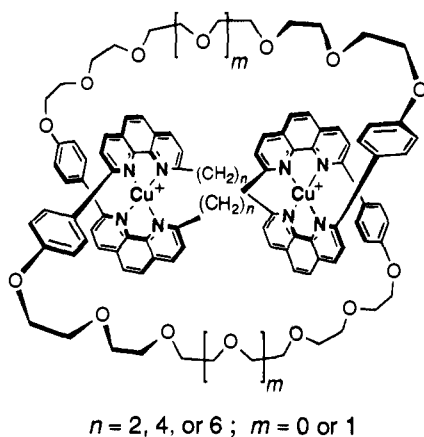


Figure 85. A range of metalated molecular knots that have been isolated and characterized.³¹⁵

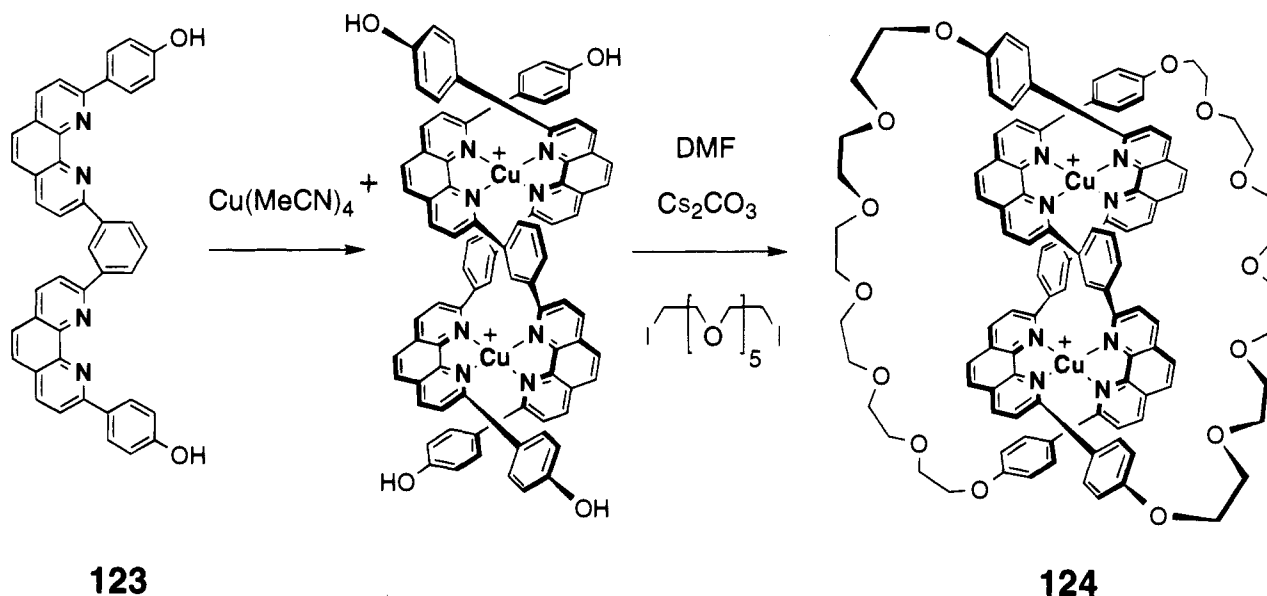


Figure 86. A highly efficient template-directed synthesis (30%) of a trefoil knot complexed with copper(I) ions.³¹⁸

including **128**. Demetalation of this mixture was necessary before performing column chromatography (Figure 88). Following the isolation of "large quantities" of the macrocycle **126**, the [2]catenanes **129** and **130** were obtained in quite meager 2% and 1% yields, respectively. The electrospray mass spectra of the singly (**130**) and doubly (**129**) interlocked [2]catenanes were very similar. Interestingly, by increasing the extraction cone voltage of the spectrometer, the peak corresponding to (**126**·H)⁺, observed as a result of the cleavage of one of the rings in the catenane, is more pronounced³²⁰ in the case of **129**. The ¹H NMR spectra of the two [2]catenanes are very different indeed: that of **130** is quite well-resolved and similar to that of **126**. The ¹H NMR spectrum of the doubly interlocked [2]catenane **129** contains broad peaks at room temperature and undergoes reversible sharpening of the peaks as the temperature of the solution containing the compound is raised. This effect is a result of the "molecular

reptation" observed in the trefoil knots. Although no experiments relating to its chiroptical properties have been reported at the time of writing this review, **129** is a topologically chiral catenane composed of non-oriented rings. The catenanes **129** and **130** are topological diastereoisomers.

The synthesis of a topologically chiral cyclized hook and ladder has been achieved by Walba *et al.*³²¹ They combined the copper(I)-templated catenane synthesis pioneered by Sauvage and their own THYME polyether strategy for making Möbius strips. The macrocycle **131** was synthesized from the standard diphenolic derivative **74** of 1,10-phenanthroline and appropriate "ladder" derivatives (Figure 89). Catenation using the Sauvage methodology afforded **132**, which was demetalated before the ladder was extended to give **133**, which contains the hook (the catenane) and ladder (alkene rungs in the THYME moiety) functions. Cyclization under high dilution conditions afforded the two homologous hook and

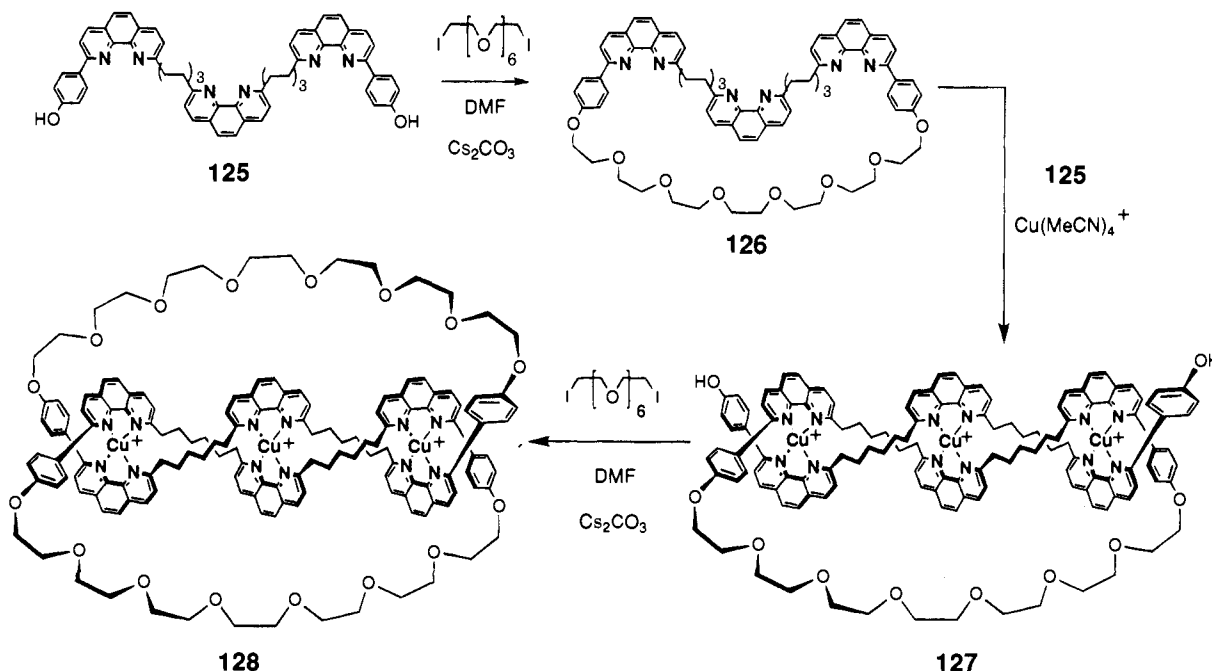


Figure 87. The template-directed synthesis³¹⁹ of a doubly interlocked [2]catenane **128**.

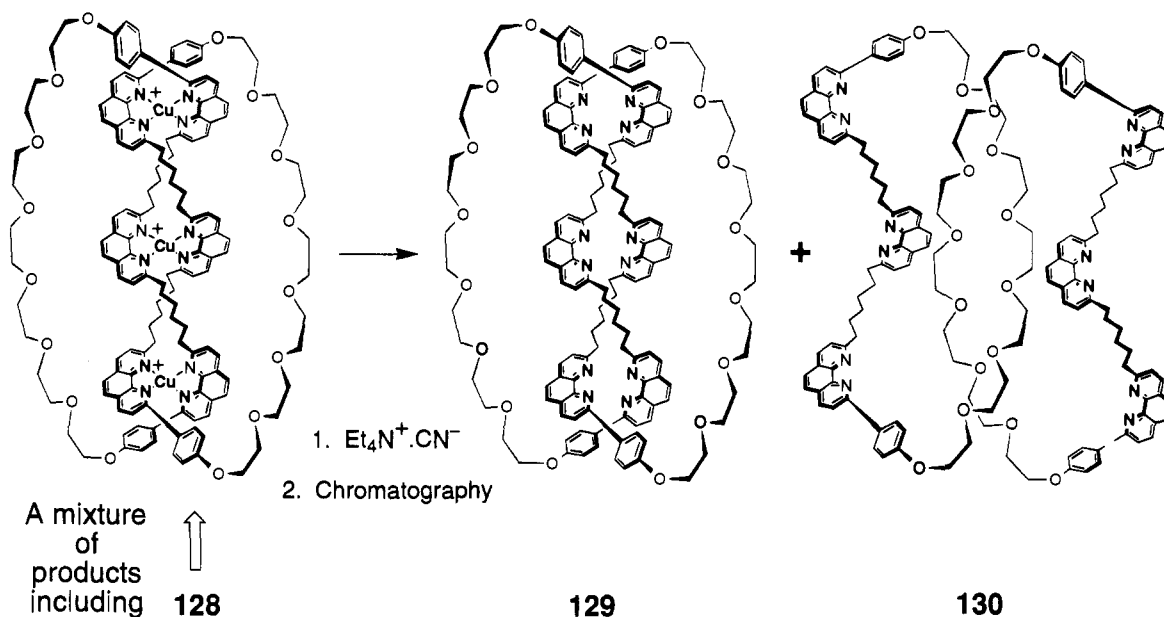


Figure 88. Demetalation³¹⁹ of the doubly interlocked [2]catenate **128** to afford the topologically diastereoisomeric doubly (**129**) and singly (**130**) interlocked [2]catenands.

ladder compounds **134** and **135** in about 60% yields in the final step. The products each contain a one quarter twist, although the possibility of knotted structures was not ruled out. The structures as drawn in Figure 89, have a 2-fold axis of symmetry, a fact which is apparent in their ^1H NMR spectra. When solutions of the cyclized hooks and ladders were warmed up, the two resonances arising from the aromatic residues at room temperature coalesced. From the temperature-dependent spectra, a free energy of activation of approximately 20 kcal mol^{-1} was calculated for both compounds. This energy barrier is associated with the conformational change in the structure which exchanges the protons inside

the hook and ladder with those on the outside. The ultimate goal of this project was the synthesis of a figure-eight knot, a shape which is predicted to be the simplest topological rubber glove.³²²

In a collaborative effort to extend the synthesis of catenanes to multiring systems, the groups of Sauvage and Vögtle used (Figure 90) the macrobicyclic core **136**, incorporating three 1,10-phenanthroline residues, for the template-directed cyclization of three macrocycles,³²³ to form the tris[2]catenate **137** in only 0.5% yield. However, the catenanes **138** and **139** were also produced in 8% and 4% yields, respectively. The low yield of the tris[2]catenate is explained partially by the observation that, when three mac-

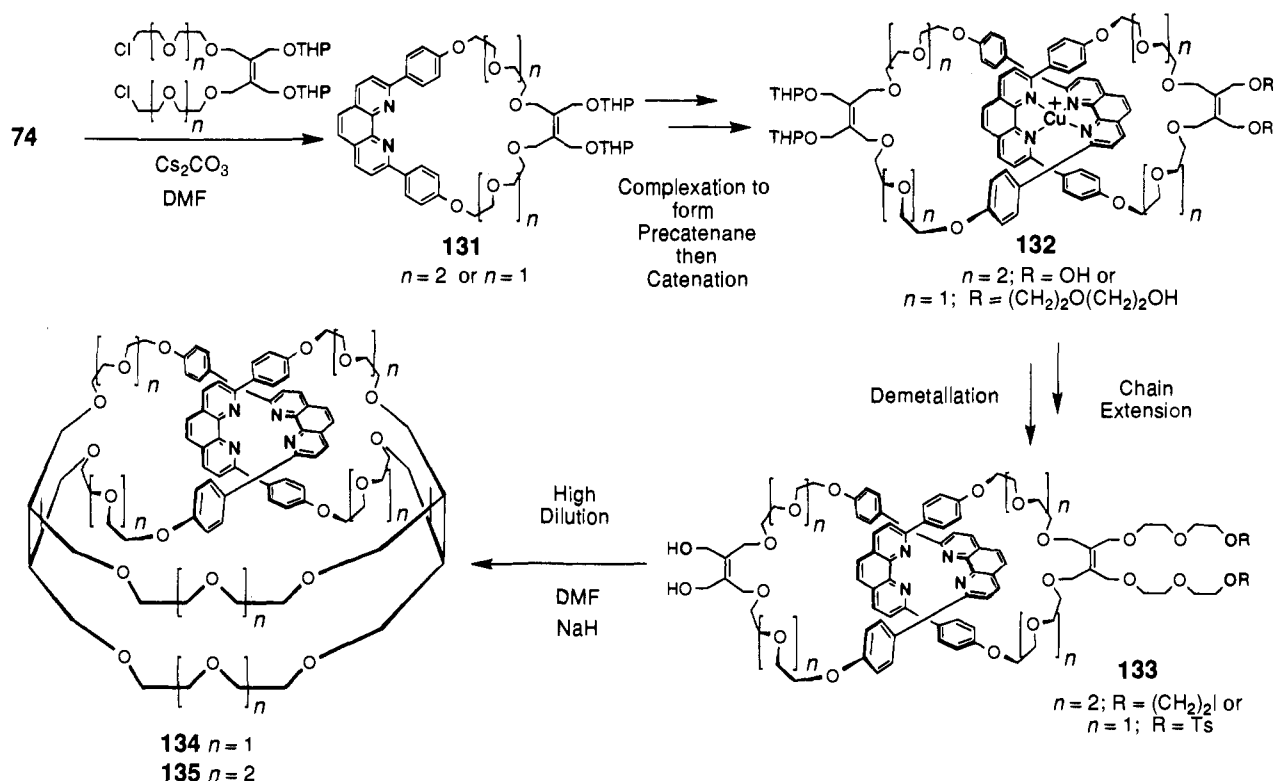


Figure 89. The template-directed synthesis³²¹ of two homologous hook and ladder compounds **134** and **135**.

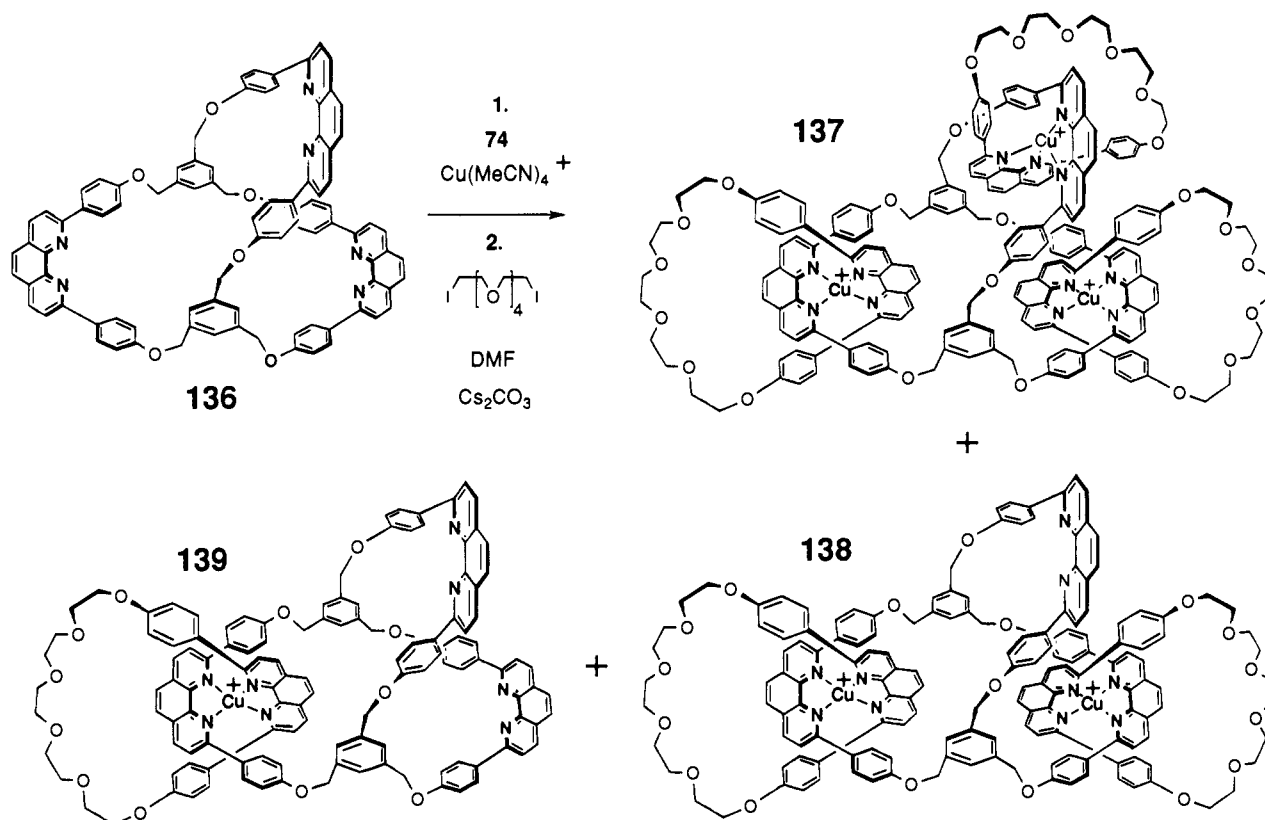


Figure 90. The template-directed synthesis³²³ of a tris[2]catenate **137** along with the related bis- and mono[2]catenates **138** and **139**.

rocycles are linked through the macrobicyclic core, the phenanthroline units, which are forced by their coordination geometry to reside between the two 1,3,5-substituted benzene rings of the core, must stack in order to be accommodated. It is sterically very difficult to template the formation of three macrocycles around all three 42-membered rings in the macrobicyclic core. The steric crowding, together with the loss of the usual geometries found in the simple [2]catenates, was evidenced by the dramatic differences in the ^1H NMR spectra of the three catenated products.

The templating ion for the formation of catenanes and rotaxanes discussed thus far has been copper(I); other metal ions have been incorporated into the structures subsequently. The periodic table is rich with other elements that might be used as templates. Indeed, there are many examples³²⁴ of structures in which metal-containing species are threaded through crown ethers.

Beer and Rothin³²⁵ have combined the strong coordination of copper(I) ions by 2,2'-bipyridine derivatives and the relatively weak "sandwiching" of potassium ions by crown ethers for the preparation of the "catenand" **142** (Figure 91) which was formed by, firstly, treating the ligand **140** with 0.5 molar equiv of $\text{Cu}(\text{MeCN})_4\text{PF}_6$, and then adding an excess of KPF_6 to the resulting air stable complex, giving the "catenand" **141** in unspecified yield. The "catenand", which was obtained in the manner previously reported by Sauvage and co-workers, was characterized by FAB mass spectrometry and ^1H NMR spectroscopy. Presumably, because the alkali metal cation to crown ether noncovalent bonds are weak, the "catenand", better described as a pseudocatenand, could equilibrate with its pseudocyclic components. No observations on this entropically favorable process

were made. The possibility that a noncatenated dimer of **140** binding two potassium ions had been formed was not ruled out either by the authors.

Studies on the interaction of diarylmagnesium compounds with crown ethers led Richey and Kushlan³²⁶ to suggest a threaded orientation for the products. Consideration of the ^1H NMR spectra obtained for $\text{Tol}_2\text{Mg}(18\text{-crown-6})$ and $\text{Tol}_2\text{Mg}(15\text{-crown-5})$ ($\text{Tol} = p\text{-methylphenyl}$) support the proposed geometry. The exchange between free and complexed crown ether was slow on the time scale of the experiment. The lack of reactivity of the complex also supported the proposed structure. While the molecular complex present in crystals of $\text{Me}_2\text{Mg}(15\text{-crown-5})$ did not possess a pseudorotaxane-like structure,³²⁷ when Et_2Mg was added to a solution of 18-crown-6, the crystals that were obtained did reveal a molecular complex with a pseudorotaxane geometry.³²⁸ The magnesium atom was located at the center of the crown ether, and the $\text{Mg}\cdots\text{O}$ distances were quite long, leading the authors to suggest that the complex might be regarded as a clathrate. In the same communication, the pseudorotaxane-like complexation of Et_2Zn with 18-crown-6 in which the metal-oxygen distances were even longer was also described in the solid state.

The formation of an "organometallic rotaxane", based on an organomagnesium compound, has also been described by Bickelhaupt *et al.*,³²⁹ who are interested in the activation of phenylmagnesium compounds by crown ethers.³³⁰ Solid 1,3-xylyl-18-crown-5 **143** was added (Figure 92) to a diethyl ether solution of diphenylmagnesium. The precipitate that formed was crystallized and found to have a rotaxane-like structure in which the magnesium atom was located in the mean plane of the crown ether, making close contacts with two of the ethereal oxygen atoms.

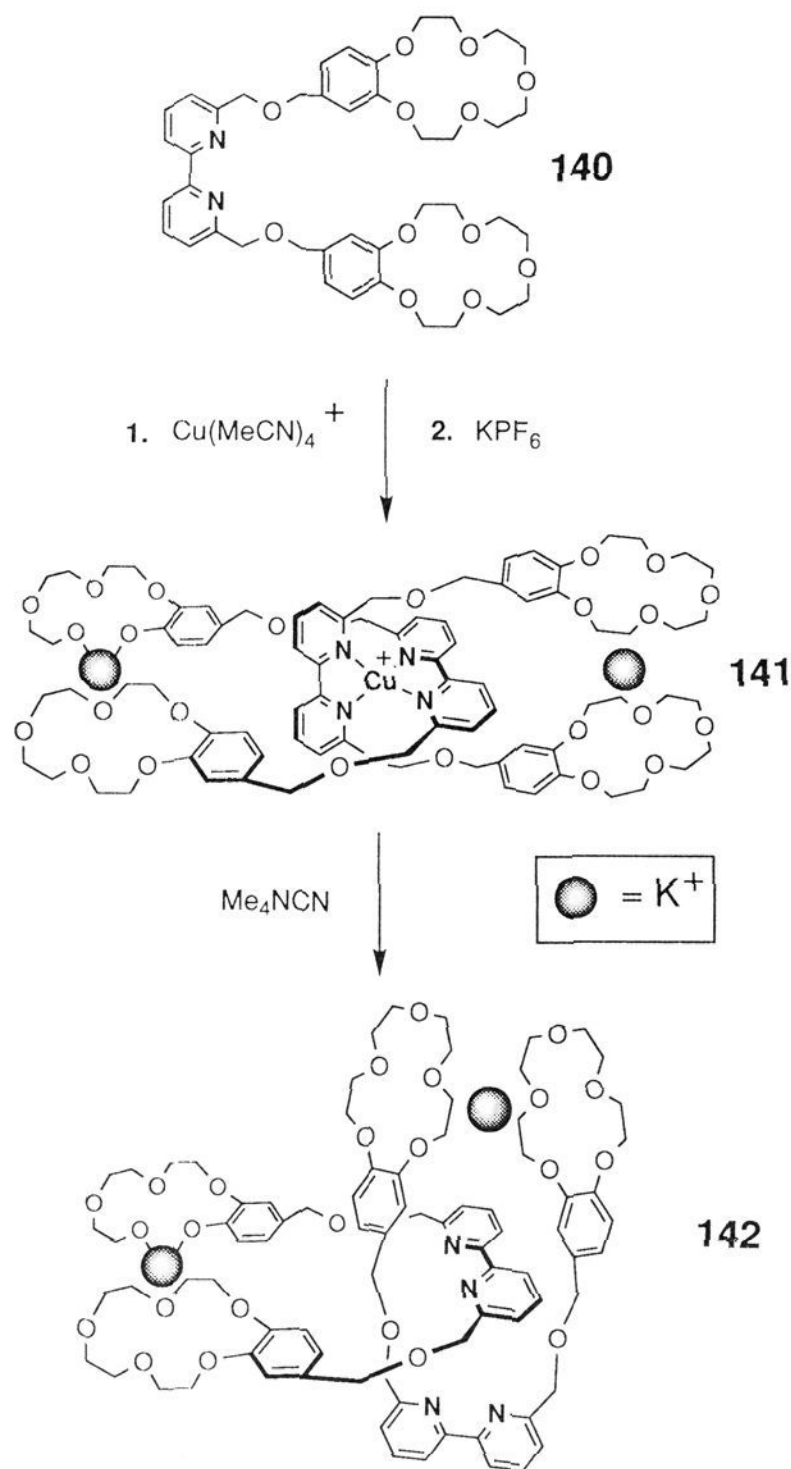


Figure 91. The self-assembly³²⁵ of a pseudo[2]catenand **142** from the novel ligand **140**.

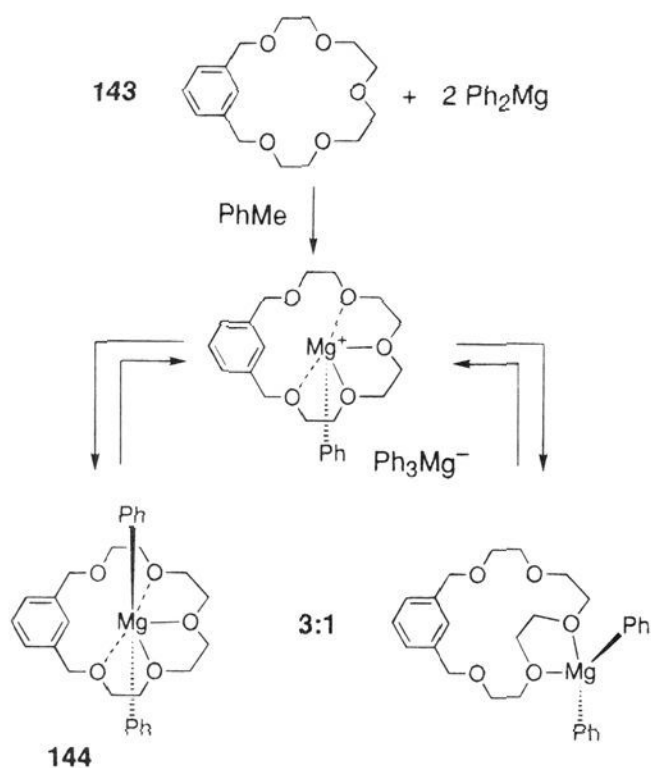


Figure 92. The spontaneous formation³²⁹ of an organometallic [2]rotaxane **144**.

The two phenyl groups are located on opposite sides of the crown ether ring. The rotaxane's formation was proposed to proceed (Figure 92) by dissociation of a phenyl ring from the diphenylmagnesium, com-

plexation of the PhMg^+ cation by the crown ether, followed by recombination of the complex with the phenyl anion from the opposite face, creating the threaded structure **144**. This mechanism was proposed by the authors since they claim very reasonably that the phenyl rings of the magnesium compound are too large to pass through the center of the crown ether. In toluene solution, two different complexes were clearly distinguishable in a 3:1 ratio, while both free starting materials were absent. The major complex was the [2]rotaxane **144**, while the other one was believed to be an external complex³³¹ of the diphenylmagnesium with the crown ether.³²⁹ In THF solution, the complexes dissociate into their components.

Support for the mechanism proposed in Figure 92 has been obtained by the Dutch group, which has also gone on to synthesize "the first organometallic catenane".³³² The interlocked rings were prepared (Figure 93) in a similar manner to the rotaxane by mixing the same crown ether (**143**) with the cyclic organomagnesium compound **145**. The ¹H NMR spectrum of this combination revealed the presence of two complexes in solution. Once again, these complexes were the threaded one, but this time the catenated compound **146**, as well as the side-on complex **147**, was identified. In the equilibrated mixture in deuterated toluene, the side-on complex is favored over the catenated compound, the two species being present in solution in a ratio of 2:1. In common with the rotaxane, the equilibrium between the two complexes is temperature dependent, with the catenane being the more favored structure at lower temperatures.

The self-assembly of a [2]catenane has been achieved³³³ quantitatively from two preformed rings incorporating palladium(II) metal ion centers. The preformed rings were prepared (Figure 94) by the reaction of $(\text{en})\text{Pd}(\text{NO}_3)_2$ with 1 molar equiv of 1,4-bis[(4-pyridyl)methyl]benzene (**148**). Inspection of the ¹H NMR spectrum of the product indicated the presence of one component. By analogy with a similar compound,³³⁴ this product was assigned to the macrocycle. However, at concentrations greater than 50 mM, another product was formed in very high yields. It was identified as the [2]catenane **149**. A

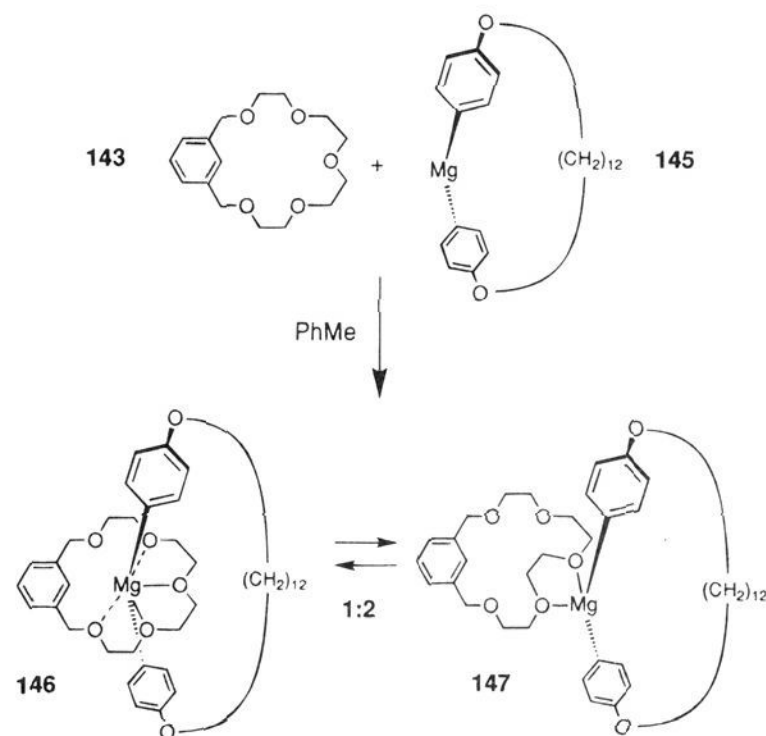


Figure 93. The synthesis³³² of the first organometallic [2]-catenane **146**.

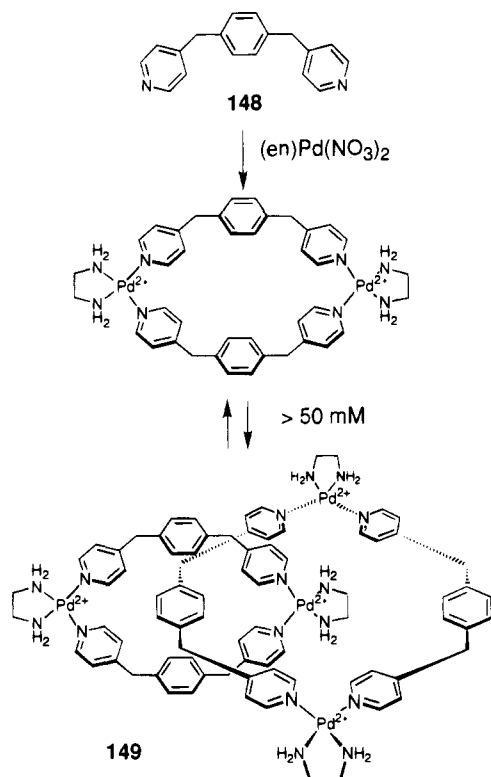


Figure 94. The self-assembly³³³ of a metalloorganic [2]-catenane **149** under conditions of equilibrium control.

combination of ^1H NMR spectroscopy, which revealed resonances for nonequivalent $\text{PyCH}_2\text{C}_6\text{H}_4\text{CH}_2\text{Py}$ groups and a C_6H_4 group shifted markedly to high field, and electrospray mass spectrometry, which revealed peaks characteristic of the proposed [2]-catenane, established its identity. The catenane is formed in a manner "reminiscent of the trick of interlinking 'magic rings'", in which ligating groups are separated from the coordinated metal ion, before being threaded through a preformed macrocycle, and then re-coordinated. This mechanism was confirmed by treating the same ligand with $(\text{en})\text{Pt}(\text{NO}_3)_2$. The platinum(II) complexes are more kinetically stable than the palladium(II) ones. The analogous reaction leads to the formation of the [2]catenane and the macrocycle in a ratio of 1:4 in 60% yield overall. The platinum(II)-containing [2]catenane was prepared in 30% yield when the reaction was performed in a more polar medium (5 M NaNO_3 in H_2O), the ratio of the catenane-to-macrocycle being 9:1. The formation of the [2]catenane is believed to be promoted by "double differential complexation", where the components of the rings are bound in each other's cavity. The more polar the medium, the greater the hydrophobic effect, and so the higher the yield of the catenane.

A recent report³³⁵ has described the catenane incorporating platinum as a "molecular lock". The "lock" is released by heating in the presence of a salt. An X-ray crystal structure confirmed the topology of the catenane incorporating platinum in each of its two rings. Edge-to-face aromatic interactions observed in the crystal are likely to be the driving force for the formation of the catenane in the first place. The group has proposed³³⁶ a mechanism whereby two molecular rings undergo sequential ligand exchanges, such that the intermediate to the [2]catenane is a Möbius strip! The slipping of ligands which was implied from a detailed NMR study, is very much like the initially proposed slipping of magic rings!

The many impressive examples of interlocked chemical compounds that have been created using the strong coordination of metal ions to ligating groups bear witness to the utility of this approach in their synthesis. The transition metal ions' binding geometry directs the formation of connecting groups such that syntheses become predictably efficient. The use of weaker noncovalent interactions, such as π - π stacking and hydrogen bonding, as the forces which enable a template to function for the creation of interlocked structures was not achieved until six years after the first catenane synthesis by Sauvage and Dietrich-Buchecker.

VII. Catenanes and Rotaxanes Based on π -Electron Acceptors and π -Electron Donors

In order to form interlocked molecules without the aid of a coordinating metal ion source, alternate means of template direction are required; otherwise, one is at the mercy of statistics. The components of the potentially interlocked structures must exhibit some mutual attraction or, in other words, display molecular recognition for each other. The catenanes and rotaxanes described in this section began life in an area of host-guest chemistry³³⁷ that was specifically concerned with the search for synthetic receptors for the π -electron deficient herbicides diquat and paraquat.³³⁸

A. Mutual Molecular Recognition between π -Electron Acceptors and π -Electron Donors

The design strategy which was employed for the creation of diquat and paraquat receptors was the incorporation of π -electron-rich aromatic units,³³⁹ such as those derived from dioxybenzenes³⁴⁰ and dioxynaphthalenes,³⁴¹ into macrocyclic polyethers. Many different receptors were prepared³⁴² and one of the best turned out to be bis-*p*-phenylene-34-crown-10 (**150**),³⁴³ which forms quite a strong complex (Figure 95) with the bis(hexafluorophosphate) salt of paraquat in acetone and acetonitrile solutions.³⁴⁴ The X-ray crystal structure of the 1:1 complex reveals (Figure 95) a pseudorotaxane-like incorporation of the guest dication, which is sandwiched in between the parallel aligned hydroquinone rings of the receptor.³⁴⁵ In addition to π - π stacking interactions, the complex is stabilized further by hydrogen bonding between the α -CH hydrogen atoms on the bipyridinium units of the paraquat dication and the oxygen atoms in the macrocycle, and by electrostatic interactions involving the hydroquinone ring oxygen atoms. In addition, the macrocycle is highly preorganized,³⁴⁶ as its conformations in the free and complexed states are remarkably similar. Since these early beginnings, a large number of derivatized 4,4'-bipyridinium dications have been synthesized and have been found to form similar complexes with pseudorotaxane geometries in the solid state.^{347,348}

Similar complexes were formed³⁴⁹ both in the solution and in the solid states by a combination of π -electron-deficient guests with the macrocyclic polyether, 1,5-dinaphtho-38-crown-10 (**151**). However, when the constitution of the macrocycle was enlarged to 1,5-dinaphtho-44-crown-12 (**152**), a rather different crystalline complex was formed³⁵⁰ which actually

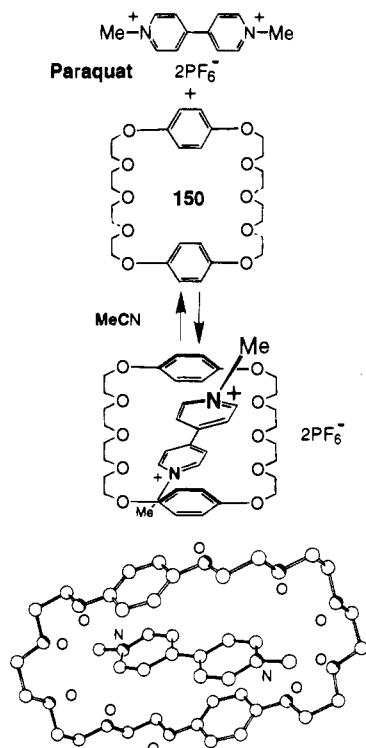


Figure 95. (Top) The formation of the 1:1 complex between bis-*p*-phenylene-34-crown-10 (BPP34C10, **150**) and paraquat bis(hexafluorophosphate); (bottom) a ball-and-stick representation of the X-ray crystal structure of the same 1:1 complex.³⁴⁴

proved to be the inspiration for making the first catenane in the series. The 2:1 complex, which exists as a continuous donor-acceptor stack in the solid state (Figure 96), has one paraquat dication sandwiched between the π -electron-rich aromatic units of one host molecule, while a second paraquat dication is clathrated between adjacent 1:1 complexes. The

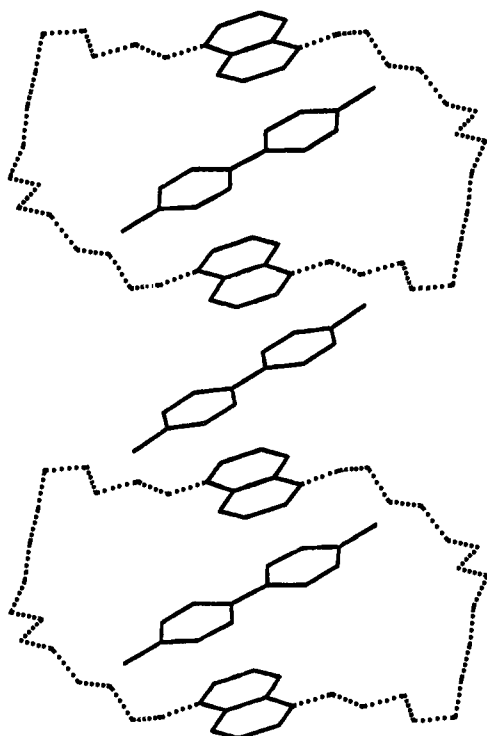
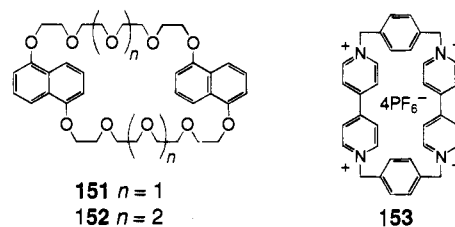


Figure 96. The continuous donor-acceptor stack formed³⁵⁰ in the solid state by paraquat bis(hexafluorophosphate) and 1,5-dinaphtho-44-crown-12 (**152**).

distance (*ca.* 7 Å) between the methyl groups of the two crystallographically independent paraquat dications was just perfect for their connection to be enhanced by *p*-phenylene moieties. The resulting cyclophane that is formed by linking the two pairs of methyl groups is cyclobis(paraquat-*p*-phenylene) (**153**).



The receptor cyclobis(paraquat-*p*-phenylene) (**153**) was reported³⁵¹ in 1988, and has proved, along with related tetracationic cyclophanes,³⁵² to be an ideal receptor for a wide range³⁵³ of aromatic π -electron-rich substrates. The isomeric dimethoxybenzenes are bound within the cavity of **153** in both the solution and solid states. A crystal structure³⁵⁴ (Figure 97) of the 1:1 complex formed between 1,4-dimethoxybenzene and **153** reveals that it has the geometry of a [2]pseudorotaxane. This structure shows π - π stacking (interplanar separation of approximately 3.5 Å) between the π -electron-deficient and the π -electron-rich aromatic rings, as well as T-type interactions between the hydrogen atoms attached to the aromatic guest and the *p*-xylyl spacers of the host, whose geometry is virtually unchanged upon complexation, *i.e.* it is ideally preorganized. The methoxy groups of the guest protrude above and below the upper and lower rims of the tetracationic cyclophane, emphasizing the fact that the guest is threaded through the host. In addition, as the substituents attached to the π -electron-rich 1,4-dioxybenzene ring are increased in length with ethylene glycol repeating units, the free energies of binding for the range of guests in **153** increases³⁵⁵ from approximately 1.7 kcal mol⁻¹ for 1,4-dimethoxybenzene to approximately 4.6 kcal mol⁻¹ for **154**. The oxygen atoms in the polyether "tails" of these thread-like molecules, incorporating a 1,4-dioxybenzene (hydroquinone) ring have approxi-

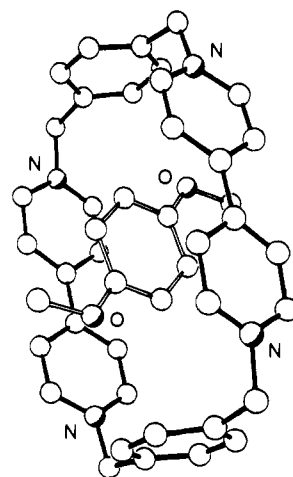
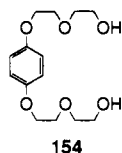


Figure 97. A ball-and-stick representation of the X-ray crystal structure³⁵⁴ of the 1:1 complex formed between cyclobis(paraquat-*p*-phenylene) (**153**) and 1,4-dimethoxybenzene.

mately equal separations from the nitrogen atoms in **153**, formally carrying the positive charges.



B. Catenanes

In 1989, the interlocking of the π -electron-deficient cyclobis(paraquat-*p*-phenylene) tetracationic cyclophane **153** with the π -electron-rich crown ether bis-*p*-phenylene-34-crown-10 (**150**), was achieved.³⁵⁶ The dicationic compound **155**, which is prepared (Figure 98) from *p*-xylylene dibromide (**156**) and an excess of 4,4'-bipyridine, was stirred in acetonitrile with **156** in the presence of a several-fold molar excess of the macrocyclic polyether **150** for 2 days. Following a simple isolation procedure, including counterion exchange to the tetrakis(hexafluorophosphate) salt, the [2]catenane **157** was isolated in a remarkable 70% yield.

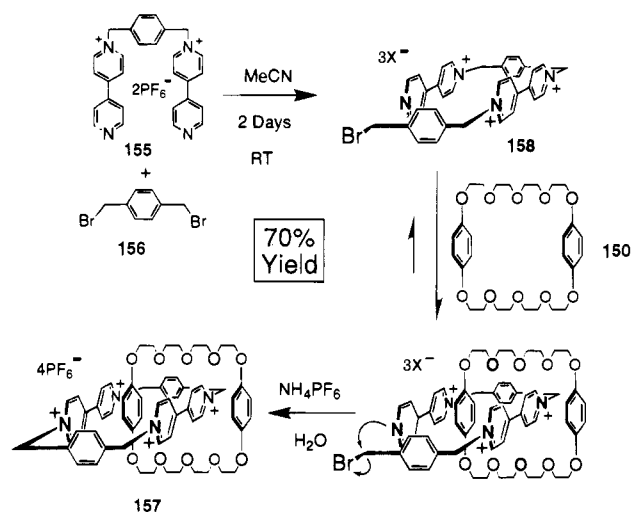


Figure 98. The highly efficient (70%) self-assembly³⁵⁶ of the [2]catenane **157**.

The mass spectrum of the [2]catenane **157**, which is typical of the spectra obtained for this family of interlocked molecules, gave peaks for singly positively charged ions, corresponding to the loss of one, then two, and then three, and so on, hexafluorophosphate counterions from the molecular ion. In the lower mass region, no peaks were observed until one for the ion corresponding to the loss of two hexafluorophosphate counterions from the **153** component, indicating that the polyether ring of the catenane had been broken apart in the spectrometer. The X-ray crystal (Figure 99) structure of the compound shows beautifully the mutual interlocking of the component macrocycles. The relative positions and geometries of the various recognition sites within the components of the [2]catenane are just as they might have been anticipated from the range of crystal structures of complexes formed by the mutually compatible components. One hydroquinone ring resides in the center of the tetracationic cyclophane and shows the same π - π stacking and T-type hydrogen-bonding interactions that were observed in the complexes of cyclobis(paraquat-*p*-phenylene) (**153**). Also, hydrogen-bonding [H \cdots O] distances of 2.60 and 2.64 Å were

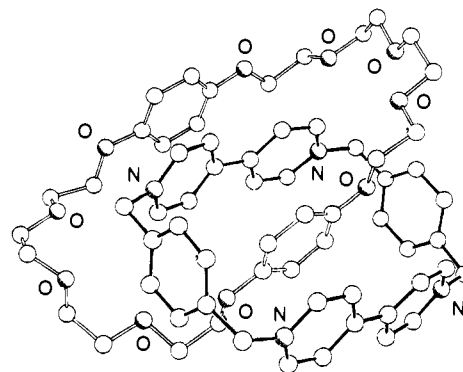


Figure 99. A ball-and-stick representation of the X-ray crystal structure³⁵⁶ of the [2]catenane **157**.

observed between the diametrically opposite oxygen atoms at the centers of the tetraethylene glycol spacers in the neutral crown ether component and α -hydrogen atoms attached to the bipyridinium residues of the tetracationic cyclophane that is sandwiched between the parallel aligned hydroquinone rings of the crown ether. Thus, each of the components of the [2]catenane have an "inside" and an "alongside" environment for their hydroquinone rings and bipyridinium units. In addition, the separation, approximately 3.5 Å, between the planes of these aromatic units is approximately the same, not only within the molecule, but also supramolecularly throughout the polar stacks, *i.e.* they contain one enantiomer, that the [2]catenane molecules form in the solid state, resulting in a π -electron donor/ π -electron acceptor stack all the way along one of the crystallographic directions.

The order that characterizes the [2]catenane intramolecularly in the solid state "lives on" in the molecule in solution. The low-temperature ¹H NMR spectrum of the compound at -65°C indicates the presence of an "inside" and "alongside" bipyridinium unit in relation to the cavity of the crown ether. As the temperature of the solution is raised, the resonances arising from the bipyridinium units of the tetracationic cyclophane indicate that this charged component is spinning around the O-C₆H₄-O axis of the included hydroquinone ring of the crown ether, such that it passes through the center of this neutral macrocycle. This motion, which corresponds to the degenerate process I in Figure 100 and requires the rapid exchange at room temperature of A and B, has a free energy of activation associated with it of 12.2 kcal mol⁻¹. Further warming of the sample resulted in rapid equilibration of the hydroquinone rings of the crown ether within the cavity of the tetracation. This spinning of the neutral component corresponds to the degenerate exchange of C and D according to process II in Figure 100 and has associated with it a free energy of activation of 15.6 kcal mol⁻¹.

Cyclic voltammetry also confirmed the strong interactions that exist between the aromatic residues of the two components of the [2]catenane. Whereas the tetracationic cyclophane **153** has two double electron reduction waves (Figure 101) in the [2]catenane **157**, the first of these waves is split into two single electron reduction waves, and there is considerable broadening of the wave corresponding to the second two-electron reduction of the charged component. The splitting of the first wave is thought to result from the topographical differences between the "inside" and "alongside" bipyridinium units of the

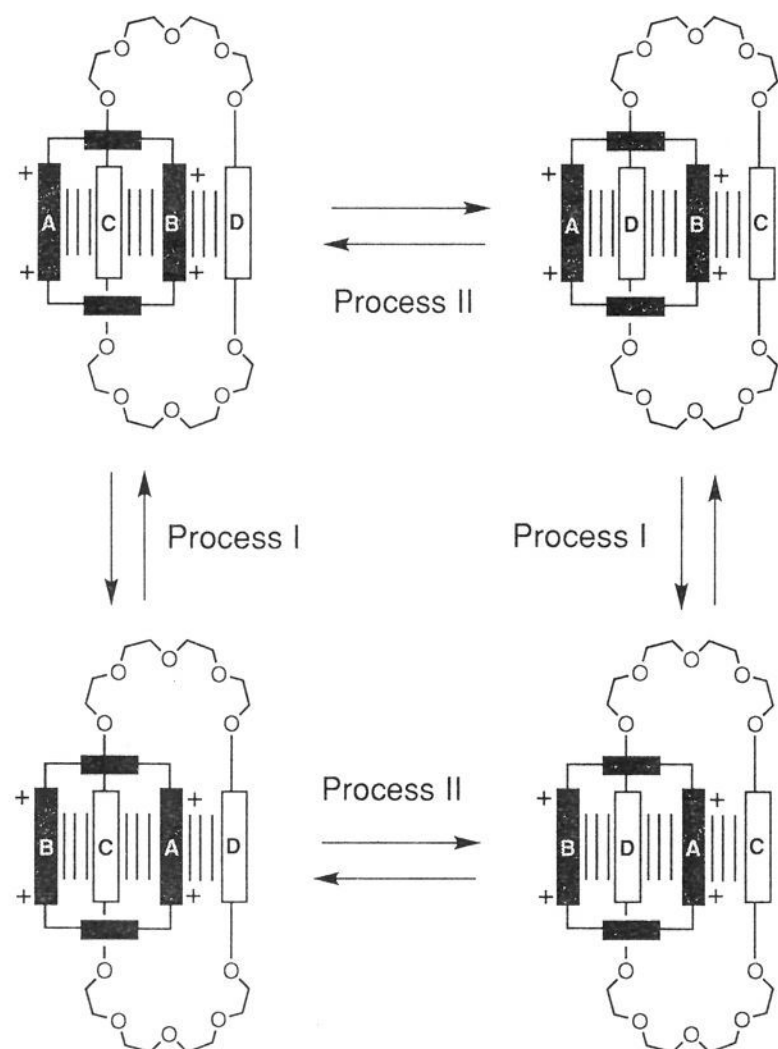


Figure 100. Two of the degenerate dynamic processes (I and II) that take place in solution within the [2]catenane **157** as indicated by ^1H NMR spectroscopy.³⁵⁵

cyclophane, the “inside” unit being stabilized and protected by two adjacent hydroquinone rings. The second two-electron reduction is not split to the same extent, presumably because of the diminished recognition between the two components following partial reduction of the tetracationic cyclophane. Similarly, the oxidation of the hydroquinone rings was split into two waves at very high potential when compared with the results obtained with the free macrocyclic polyether. These results also show that there are appreciable electrochemical gradients within the [2]catenane molecule. The compound is bright red in color, exhibiting a charge-transfer band centered on 478 nm with an ϵ value of 700. In addition, the luminescence of the hydroquinone rings in the neutral component **150** are completely quenched in the [2]catenane.

The mechanism for the formation (Figure 98) of the [2]catenane **157** has been investigated³⁵⁷ by ^1H NMR spectroscopy. Using this technique, the intermediate trication **158** could not be observed. The fact that this material was not observed in the ^1H NMR spectrum implies a fast ring closure to form the [2]catenane. It should also be pointed out that the starting material **155** is not bound appreciably by the macrocyclic polyether, while the trication **158** would be expected to be bound strongly, as a result of the increased molecular recognition afforded by the presence of the dicationic 4,4'-bipyridinium unit in this intermediate. And so, it is proposed that the first alkylation of **155** “turns on” a recognition site in the charged component, which is complexed by the neutral macrocyclic polyether that can then template the ring closure to form the catenated tetracationic cyclophane. The [2]catenane **157** can also be prepared³⁵⁸ with reasonable efficiency in a single step (Figure 102) by reacting 4,4'-bipyridine and *p*-xy-

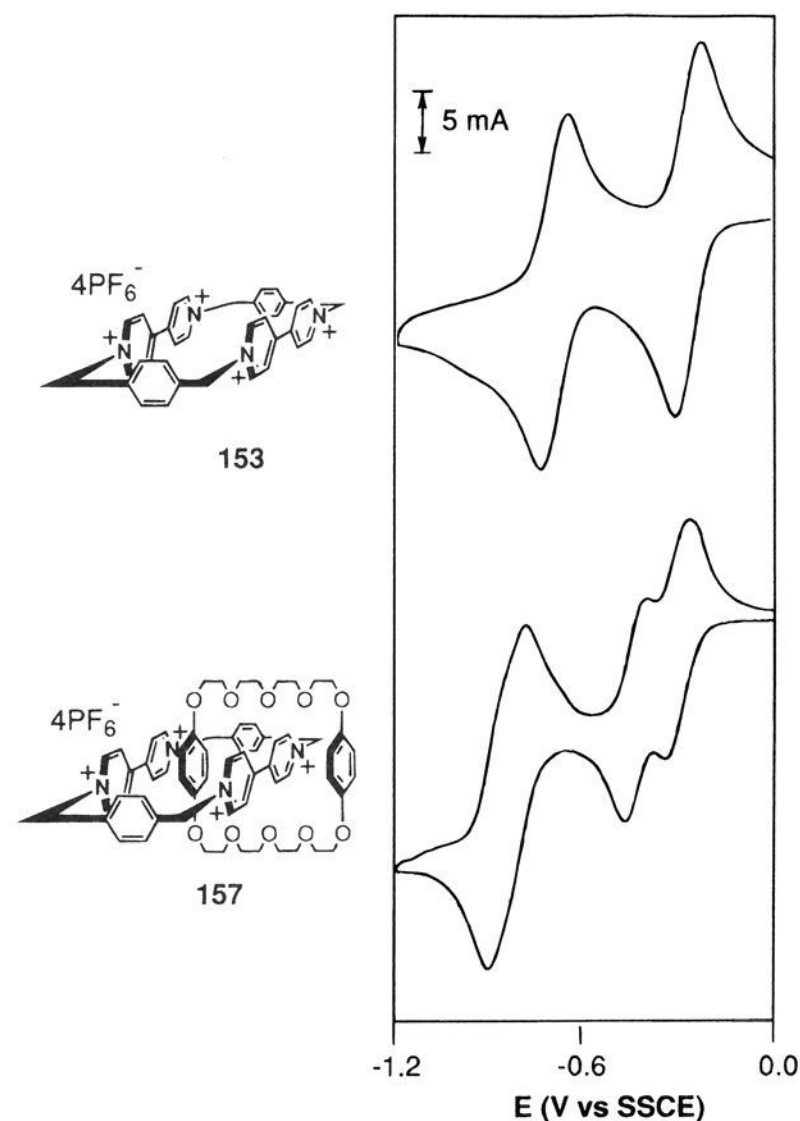


Figure 101. The cyclic voltammograms recorded in 0.1 M tetrabutylammonium hexafluorophosphate/MeCN for (top) cyclobis(paraquat-*p*-phenylene) (**153**) and (bottom) the [2]catenane **157** which incorporates **153** as one of its component rings.³⁵⁵

lylene dibromide in the presence of an excess of the macrocyclic polyether **150**. Under high-pressure conditions (12 kbars), which are known to accelerate the Menschutkin reaction,³⁵⁹ the [2]catenane **157** was isolated in 42% yield, while, at ambient pressure, the same reaction afforded only 18% of the [2]catenane.

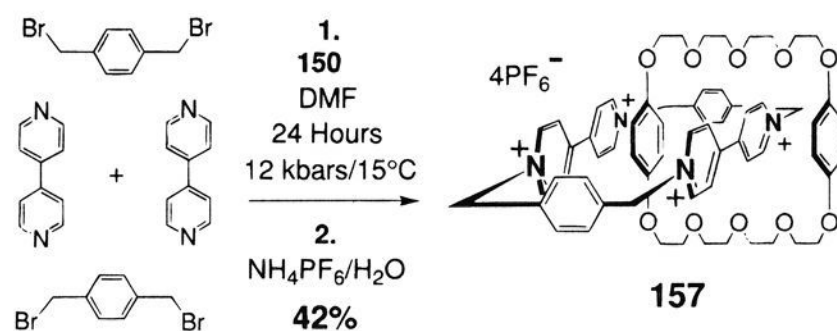
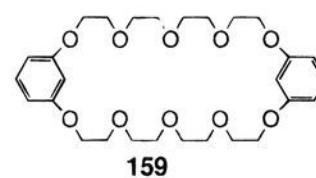


Figure 102. The one-step self-assembly³⁵⁸ of the [2]catenane **157** from bipyridine and *p*-xylylene dibromide in the presence of bis-*p*-phenylene-34-crown-10 (BPP34C10, **150**) at ultrahigh pressure.

A wide range of macrocyclic polyethers have so far acted successfully as templates for **153** to form [2]catenanes. An isomer of **150**, bis-*m*-phenylene-32-crown-10 (**159**), incorporating two resorcinol rings linked by tetraethylene glycol residues, templates the formation of the tetracationic cyclophane to form the [2]catenane **160** in 17% yield.³⁶⁰ The diminished



ability of **159** to act as a template for the tetracationic cyclophane, compared with **150**, is reflected in the dynamic nature of the compound in CD_3COCD_3 solution. In particular, the spinning process of the neutral component through the tetracationic cyclophane component (process II in Figure 100) is associated with a free energy of activation of $13.6 \text{ kcal mol}^{-1}$, *i.e.* approximately 2 kcal mol^{-1} lower in energy than in the case of the isomeric catenane incorporating **150**. An additional dynamic process (III in Figure 103) was also observed in this compound. It corresponds to the dislocation of the π -electron rich residue from the cavity of the tetracationic cyclophane, followed by reorientation of the resorcinol ring, and its return to the thermodynamic energy well associated with its location inside the charged component. The free energy of activation of $12.1 \text{ kcal mol}^{-1}$ governing this process is slightly lower than that required for a complete exchange of two resorcinol rings in the cavity of **153**.

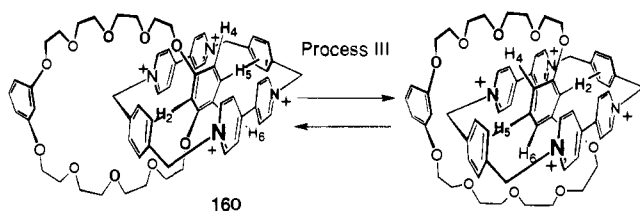
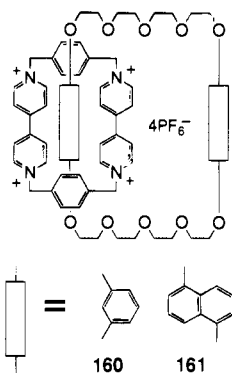


Figure 103. An additional degenerate dynamic process (III) that can be observed³⁶⁰ in the variable-temperature ^1H NMR spectra of the [2]catenane **160**.

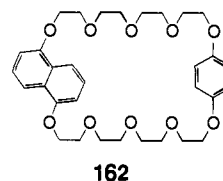
In contrast to the relatively poor intercomponent recognition in **160**, the [2]catenane **161**, self-assembled using 1,5-dinaphtho-38-crown-10 (**151**) as the template for the formation of the tetracationic cyclophane is very highly ordered in both the solution and solid states.³⁶¹ The X-ray crystal structure of this



[2]catenane **161** reveals a similar disposition of the π -electron-rich and π -electron-deficient residues to that observed in the solid-state structure and superstructure of **157**. All four aromatic units are almost parallel with approximately the same intramolecular interplanar separations within the molecule as observed in **157**. However, beyond the molecule, in the polar stacks that this compound also forms in the crystal, the separation between the "alongside" 1,5-dioxynaphthalene residue and the "alongside" bipyridinium residue of adjacent molecules is only 3.3 \AA . The T-type interactions involving the H-4 and H-8 hydrogen atoms of the included 1,5-dioxynaphthalene residue with the *p*-xylyl spacers in the tetracation are very pronounced in this structure (centroid-centroid separations of only 4.7 and 4.8 \AA , respec-

tively). This catenane is highly ordered in solution also. At $-60 \text{ }^\circ\text{C}$, the observable dynamic processes between the components are all slow on the ^1H NMR time scale. In particular, the H-4 and H-8 hydrogen atoms of the included 1,5-dioxynaphthalene residue which are directed toward the *p*-xylyl residues are highly shielded and give rise to a resonance at $\delta 2.4 \text{ ppm}$. The three dynamic processes that have been described (*vide supra*) are also observed in **161**. The spinning (process I) of the tetracationic component through the neutral component is associated with a free energy of activation of approximately $12.7 \text{ kcal mol}^{-1}$, while the free energies of activations for processes II and III are 17.2 and $15.8 \text{ kcal mol}^{-1}$, respectively. The higher energies of activation required for the latter two processes are a reflection of the better intercomponent recognition displayed in **161** in comparison with **160** and **157**.

The presence of two different π -electron-rich aromatic residues within the same macrocyclic polyether component of a [2]catenane incorporating **153** leads to structures which can exist as two translational isomers.⁶³ In principle, the control of this important phenomenon can also be achieved through the introduction of steric or electronic differences into the two π -electron-rich aromatic residues. The macrocyclic polyether 1,5-naphtho-*p*-phenylene-36-crown-10 (**162**),



which incorporates one hydroquinone ring and one 1,5-dioxynaphthalene residue, has been employed³⁶² successfully as a template for the formation of the tetracationic cyclophane, thus allowing the self-assembly of the [2]catenane **163**. In solution, **163** can exist (Figure 104) as the translational isomer **A**, in which the 1,5-dioxynaphthalene residue occupies the cavity of the tetracationic cyclophane component, or as the translational isomer **B**, where the hydroquinone ring resides between the two 4,4'-bipyridinium units in the tetracationic cyclophane. The two translational isomers are interconverted by circumrotation of the neutral component through the charged component. In deuterated acetone at $-40 \text{ }^\circ\text{C}$, the ratio of the isomers **A/B** was 35:65. This result was surprising, given that, when the tetracationic cyclophane **153** was combined with two acyclic thread-like molecules, one incorporating a 1,5-dioxynaphthalene residue and the other a hydroquinone ring, then, in the same solvent at the same temperature, the ratio of naphthalene/benzene derivatives

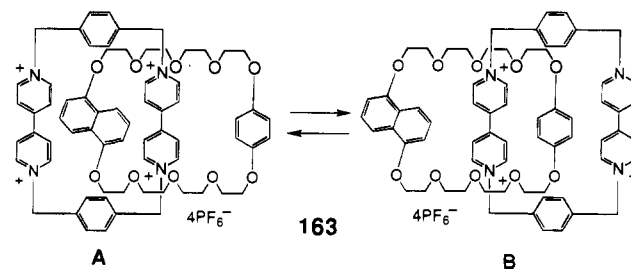
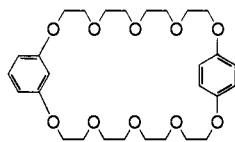


Figure 104. The equilibration between the two translational isomers (**A** and **B**) of the [2]catenane **163**.³⁶²

included in the cavity of the tetracation was 65:35. The implication from these observations is that the relative magnitudes of the binding constants of the two subunits does not determine directly the ratio of translational isomers at least in catenanes of this type. In a search for an explanation of this apparent discrepancy, the translational isomerism observed in the [2]catenane **163** was investigated in a range of solvents. It transpired that the solvent dielectric constant and the ratios of the translational isomers exhibit a sigmoidal relationship for the tetrakis-(hexafluorophosphate) salt of this [2]catenane **163**. The translational isomerism is a balance between π - π stacking interactions and solvation. The positively charged cyclophane favors a shielded situation in relatively nonpolar solvents, such as acetone ($\text{CD}_3\text{-COCD}_3$). The larger π -electron-donating surface area associated with the 1,5-dioxynaphthalene residue is therefore preferably residing on the outside of the tetracationic cyclophane, favoring isomer **B**. In more polar solvents, such as dimethyl sulfoxide ($\text{CD}_3\text{-SOCD}_3$), shielding from the solvent is less important, and the tetracationic cyclophane accepts into its cavity the π -electron-rich unit which is the more strongly bound in its own right.

The macrocyclic polyether *p*-phenylene-*m*-phenylene-33-crown-10 (**164**) contains two π -electron-rich residues of approximately the same dimensions and, as such, provides a test of the steric and electronic preferences for the π -electron-rich residues in the cavity of a tetracationic cyclophane when it is catenated. The catenation³⁶³ of **164** with the components

**164**

of the tetracationic cyclophane resulted in the self-assembly of the [2]catenane **165** in 17% yield. The low yield in this template-directed synthesis may be a result of a mismatch between the structure of the macrocyclic polyether and the molecular recognition requirements of the tetracationic cyclophane. In this catenane, the translational isomerism is extremely selective. In acetone at 0 °C, approximately 98% of the equilibrium mixture has the translational isomer with the hydroquinone ring included inside the cavity (Figure 105). No solvent dependence of this ratio was observed. Also, the same translational isomer exists exclusively in the solid state. An X-ray crystal structure of the [2]catenane **165** showed that the hydroquinone ring of the macrocyclic polyether resides within the cavity of the tetracationic component, despite the observation that the “alongside”

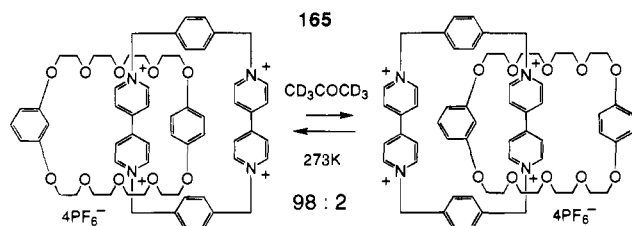


Figure 105. The equilibration between the two translational isomers of the [2]catenane **165**.³⁶³

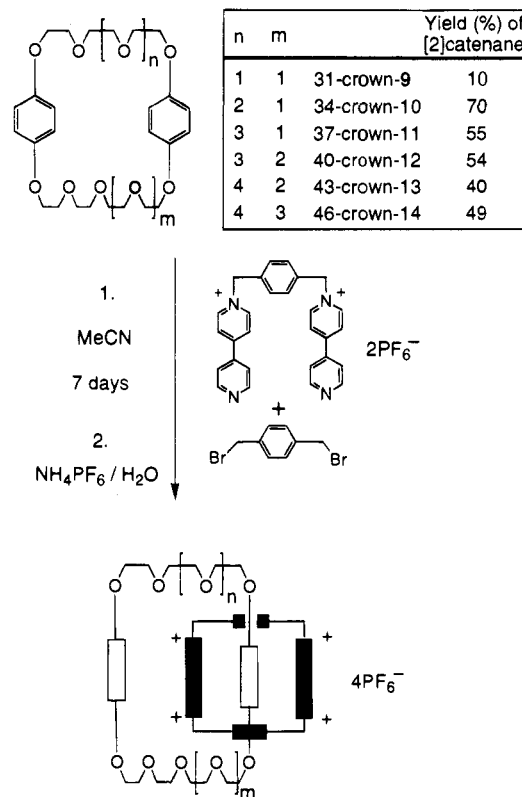


Figure 106. The efficiency of the self-assembly of a range of [2]catenanes as a function of the size of the bis-*p*-phenylene macrocyclic polyether component templating the formation of the interlocked cyclobis(paraquat-*p*-phenylene) (**153**) component.³⁶⁴

resorcinol ring does not occupy an optimal position for π - π stacking with the “inside” bipyridinium unit. This geometry is compensated for in the polar stacks formed by **165**. In them, the “alongside” resorcinol ring π - π stacks with the “alongside” bipyridinium unit of the next molecule in the stack.³⁶³

The significance of the constitution of the spacer unit between the two π -electron-rich residues in the neutral component of these catenanes has also been investigated.³⁶⁴ A range of bis-*p*-phenylene crown ethers from 31-crown-9 to 46-crown-14 (Figure 106) were employed as templates for the components of the tetracationic cyclophane **153** in the self-assembly of a range of [2]catenanes. The highest yield achieved (70%) was with the 34-crown-10 homolog. At the smaller ring size, the 31-crown-9, the cavity is a trifle tight for comfortable inclusion of the paraquat-containing precursor to the [2]catenane, and consequently it was formed in only 10% yield. For the macrocyclic polyethers larger than the bis-*p*-phenylene-34-crown-10 template, the formation of the tetracationic cyclophane occurs with progressively decreasing efficiency as the dimensions of the crown ether component are increased: the yield of the [2]catenanes levels off at approximately 40%. These findings pertain despite the observation that the same macrocyclic polyethers show a dramatic variance in their binding constants with the paraquat dication. The free energies of activation, associated with the dynamic processes taking place in this homologous series of [2]catenanes in solution, reflect the extent of noncovalent bonding interactions between the components. In particular, the ΔG^\ddagger values for process II (Figure 100) are highest for the [2]-

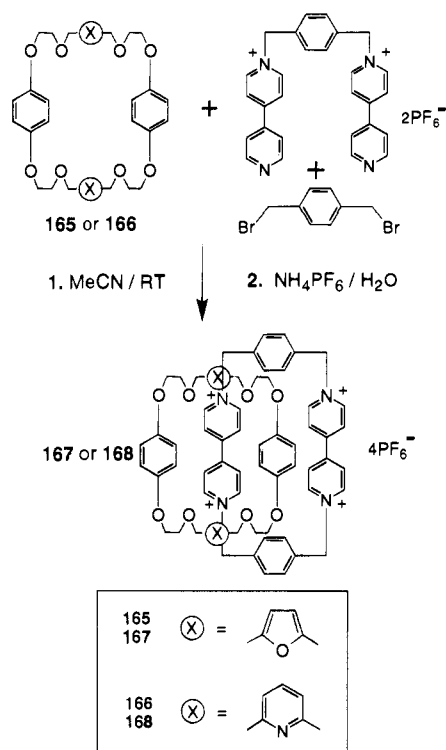


Figure 107. The self-assembly of the [2]catenanes **167** and **168** with the macrocyclic polyether derivatives **165** and **166** incorporating furan-2,5-dimethylenedioxy and pyridine-2,6-dimethylenedioxy residues, respectively.^{365,366}

catenanes incorporating the 31-crown-9 and 34-crown-10 derivatives. When the larger crown ethers are components of the [2]catenanes, the free energies of activation for this process are lower by approximately 2.5 kcal mol⁻¹. Electrochemical studies were also employed to provide useful information concerning the intercomponent recognition in the range of [2]catenanes. The reduction potentials of the bipyridinium units in the tetracationic cyclophane (**153**) components were affected most dramatically upon catenation when the smaller macrocyclic polyethers were implicated. It is believed that poorer intercomponent recognition characterizes the [2]catenanes incorporating the larger macrocyclic polyethers as a result of their inherently greater flexibility and the consequential reduction in the “alongside” interactions of the “outside” hydroquinone rings with the “inside” bipyridinium units.

In order to assess the significance of the central oxygen atom as a hydrogen-bond acceptor in the polyether spacers present in the crown ether component of these [2]catenanes, the central CH₂CH₂OCH₂CH₂ unit has been replaced with furan-2,5-diyl dimethylenedioxy³⁶⁵ and pyridine-2,6-diyl dimethylenedioxy³⁶⁶ residues. As well as modifying the hydrogen-bond donating ability of the heteroatom in the center of the spacer, these moieties also help to rigidify the chain. Incorporation of the two furan-containing residues reduces the extent of intercomponent recognition, as measured by a binding study, yet the macrocyclic polyether **165** acts as a template (Figure 107) for the formation of the tetracationic cyclophane **153**, to give the [2]catenane **167** in 40% yield, at least when an excess of the components of **153** are used in the reaction. Although the pyridine-containing macrocyclic polyether **166** has a free energy of binding for paraquat slightly lower than

that of bis-*p*-phenylene-34-crown-10 (**150**), it still serves as a good template for the formation of the tetracationic cyclophane **153**: the [2]catenane **168** is formed in 31% yield by reaction of 1.1 molar equiv of **166** with 1 molar equiv of the components of **153**. The circumrotation of the neutral component through the charged one (process II) in **168** is associated with a free energy of activation of 13.8 kcal mol⁻¹, a ΔG^\ddagger value significantly lower than that associated with the same process in the [2]catenane **157**. Process I in **168** occurs with a free energy of activation of 11.3 kcal mol⁻¹. The reason for the lower energy barriers for the dynamic processes present in **168**, compared with those present in **157**, is still unclear.

Translational isomerism can also be induced by the introduction of constitutional asymmetry into the tetraethylene glycol chain linking the two π -electron-rich aromatic residues present in the crown ether component. The [2]catenane **169**, which was self-assembled in 16% yield, incorporates a macrocyclic polyether in which catechol rings have been introduced asymmetrically into the spacer of the neutral component.³⁶⁷ Two translational isomers (Figure 108) are possible in the [2]catenane, one (**A**) in which the catechol rings are closer to the “inside” hydroquinone ring, and the other (**B**) in which they are nearer to the “alongside” hydroquinone ring. Although the catechol residues are π -electron rich, they are not located inside the tetracationic cyclophane in this [2]catenane for steric reasons. The ¹H NMR spectrum of the [2]catenane indicated that the translational isomer **A** is slightly favored over isomer **B** in solution, the ratio of the isomers being approximately 64:36 (**A/B**) in CD₃CN solution.

Gunter and co-workers³⁶⁸ have utilized the binding of paraquat to macrocyclic polyethers incorporating a porphyrin unit and π -electron-rich aromatic residues as a basis, using an approach identical to that described for the template-directed synthesis of the [2]catenanes in this section, for the self-assembly of porphyrin-containing [2]catenanes. The macrocycles **170** and **171** were employed³⁶⁹ successfully as templates for the formation of the tetracationic cyclophane **153** to yield (Figure 109) the [2]catenanes **172** and **173** in 20% and 28% yields, respectively.³⁷⁰ These catenanes can be regarded formally as translationally isomeric, although occupation of the porphyrin residue by the tetracation can clearly be ruled out on steric grounds. Both [2]catenanes, in their zinc porphyrin forms, have highly ordered solution-state structures with the free energies of activation associated with process I in **172** and **173** being 14.4 and 12.9 kcal mol⁻¹, respectively. The higher energy required for circumrotation within the catenane with the more tightly strapped porphyrin was ascribed to the steric constraint present in this system. Protonation³⁷¹ of the free base porphyrin analogs of **172** and **173** required much stronger acid than is usually required in the case of unhindered porphyrin analogs, presumably as a result of electrostatic repulsions caused by the proximity of the porphyrin ring to the tetracationic cyclophane in the catenanes. This protonation induces considerable changes in the structures of these [2]catenanes in solution. It was proposed that, on the basis of ¹H NMR spectroscopic experiments, the protonated [2]catenane **175**, incor-

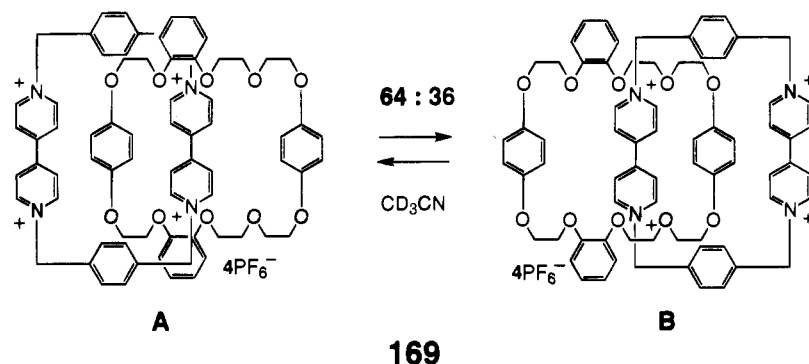


Figure 108. The translational isomerism exhibited³⁶⁷ by the [2]catenane **169** that incorporates a macrocyclic polyether component into which catechol (1,2-dioxybenzene) rings have been introduced into the spacers between the two hydroquinone (1,4-dioxybenzene) rings.

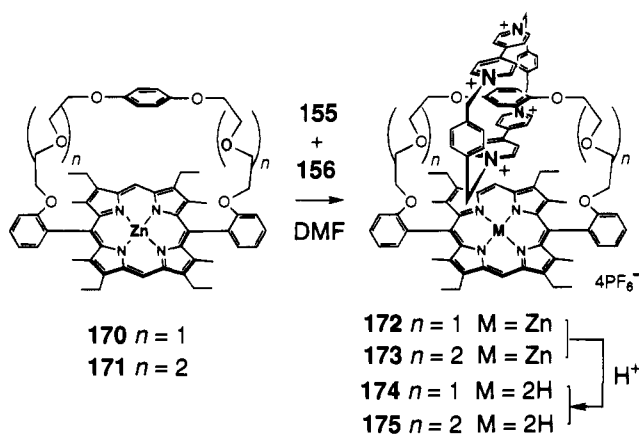


Figure 109. The self-assembly of the two metalated porphyrin-containing [2]catenanes **172** and **173**, and the corresponding free base porphyrin compounds derived from them.³⁷⁰

porating the looser strap across the porphyrin, reorganizes itself such that the unit incorporated between the porphyrin ring and the π -electron-rich residue is a *p*-xylyl spacer rather than a bipyridinium unit in the tetracationic cyclophane. The circumrotation rate associated with process II was not changed significantly upon protonation. In contrast to the free base analog, the protonated form **174** of the [2]-catenane, did not undergo reorientation, but the free energy of activation to process I was significantly decreased from 14.2 kcal mol⁻¹, for the free base porphyrin, to 12.9 kcal mol⁻¹ for the protonated form. The [2]catenane incorporating a 1,5-dioxynaphthalene residue in the porphyrin strap was also prepared in its zinc (45% yield), free base, and protonated forms. The energy barriers associated with processes II and III in this [2]catenane were similar to those observed³⁶¹ in the [2]catenane **161**, in which the neutral component incorporates two 1,5-dioxynaphthalene residues.

The tetracationic cyclophane **153** has also been utilized, along with the ability of thiols to become attached to gold surfaces, for the self-assembly of a surface-attached [2]catenane.³⁷² The thread-like molecule **176**, when combined with **153** in acetonitrile, forms a complex ($K_a = 253 \text{ M}^{-1}$). Exposure of this complex to gold bead electrodes resulted in the attachment of the thiol groups to the gold, thus mechanically trapping the tetracationic cyclophane (Figure 110). The entrapment of the cyclophane by the π -electron-rich "staple" onto the gold surface was confirmed by cyclic voltammetry. A stable and

reversible reduction wave for the bipyridinium units was observed in contrast with a series of control experiments, including the attempted formation of a pseudorotaxane at the gold surface, where they were not observed. The surface coverage for the complex was estimated to be 8% of the maximum possible value. Although the low coverage was explained by the complexity of the attachment process, the relatively low binding constant of the thread with the tetracationic cyclophane was undoubtedly partially responsible.

By increasing the ring size of the crown ether and the number of π -electron-rich aromatic residues in the macrocyclic polyether, it is possible to create higher catenanes. Thus, when tetrakis-*p*-phenylene-68-crown-20 (**177**) is used³⁷³ as a template for the formation of the tetracationic cyclophane, one can imagine the variety of interlocked structures that could result. In fact, at atmospheric pressure, the only catenated product to be formed in this reaction

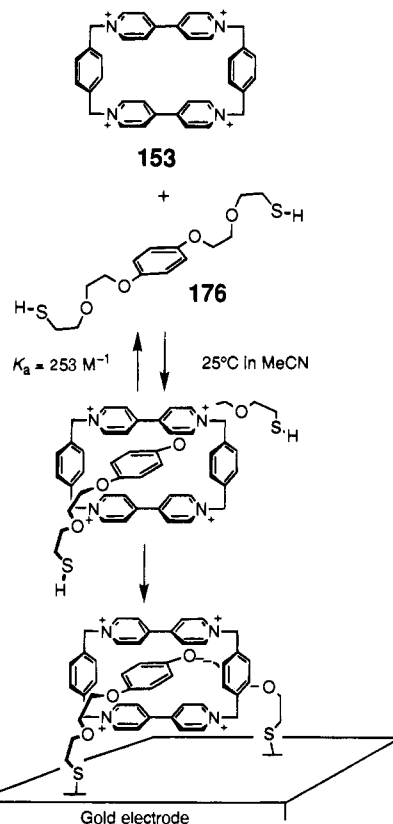


Figure 110. The self-assembly of a [2]catenane attached to a gold surface.³⁷²

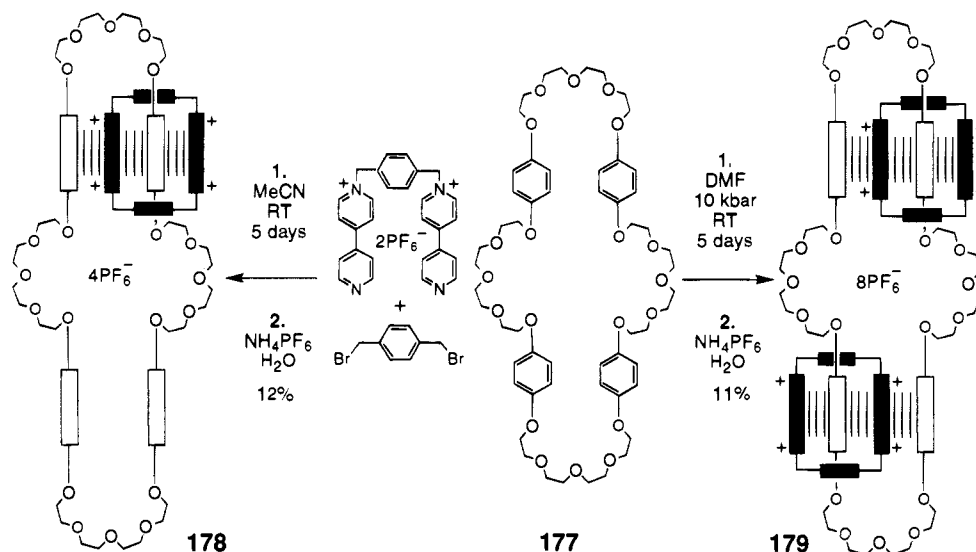


Figure 111. The self-assembly of a [2]catenane **178** at room pressure and a [3]catenane **179** at ultrahigh pressure using tetrakis-*p*-phenylene-68-crown-20 (**177**) as the templating macrocyclic polyether.³⁷³

is the [2]catenane **178** in 12% yield (Figure 111). The variable-temperature ^1H NMR spectrum of this compound, which has been referred to as a “molecular train”, revealed a dynamic process in which the tetracationic component moves from one π -electron-rich “station” to another along the polyether “track”. The energy of activation required for this process of moving the tetracationic “train” around the polyether “track” from “station” to “station” is $14.1 \text{ kcal mol}^{-1}$. Repetition of the template-directed reaction that produced **178**, this time at 10 kbars, resulted in the formation of the [3]catenane **179** in 11% yield. This compound gave a fast-atom bombardment mass spectrum in which peaks were observed corresponding to the singly positively charged ions resulting from the molecular ion minus one through to five hexafluorophosphate counterions. In addition, peaks corresponding to the [2]catenane **178** were observed, indicating that it is formed in the spectrometer by the fracture and loss of one of the tetracationic cyclophanes. The free energy of activation required to move (Figure 112) the two “trains”, which prefer to reside on diametrically opposite “stations” at low temperature, around the four “stations”, is approximately $13.6 \text{ kcal mol}^{-1}$ for each journey between stations. Part of the reason for the lower yields in the self-assembly of **178** and **179** is the low solubility of the macrocycle **177**, as well as its higher flexibility and poorer preorganization when compared with **150**. This reduction in intercomponent recognition is reflected in the lower energies of activation associated with the dynamic processes that take place in these catenanes.

All the catenanes so far discussed in this section have incorporated the tetracationic cyclophane **153**. Increasing or decreasing the dimensions of this cyclophane, as well as building functional groups into it, gives us another way to assess the efficiency and generality of the self-assembly processes operating during the formation of the catenanes, as well as a means of heading toward systems that are addressable in an electrochemical or photochemical manner.

In an effort³⁷⁴ to gain insight into the effects upon the efficiency of the self-assembly process of constitutional change in the tetracationic cyclophane component, the [2]catenanes **180** and **181**, where one

then both of the *p*-xylyl spacers were replaced with *m*-xylyl spacers, were self-assembled. The [2]catenane **180** was obtained using two routes (Figure 113), the first in which the dication **155**, incorporating a *p*-xylyl spacer, was reacted with *m*-xylylene dibromide. This route led to the [2]catenane in 18% yield, while reversal of the substitution patterns in the dication and the dibromide afforded **180** in 40% yield. The results of this experiment show that in the self-assembly process it is better to ring close the *para*-substituted end of the tricationic intermediate

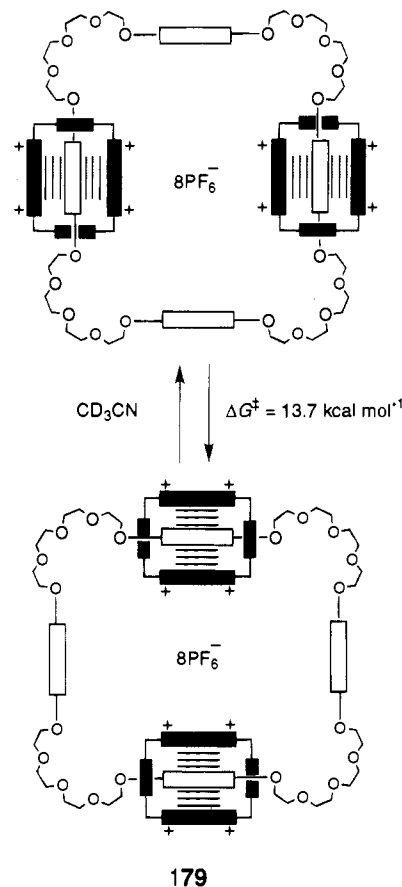


Figure 112. The degenerate shuttling process that takes place in the [3]catenane **179** in solution, as indicated by dynamic ^1H NMR spectroscopy.³⁷³

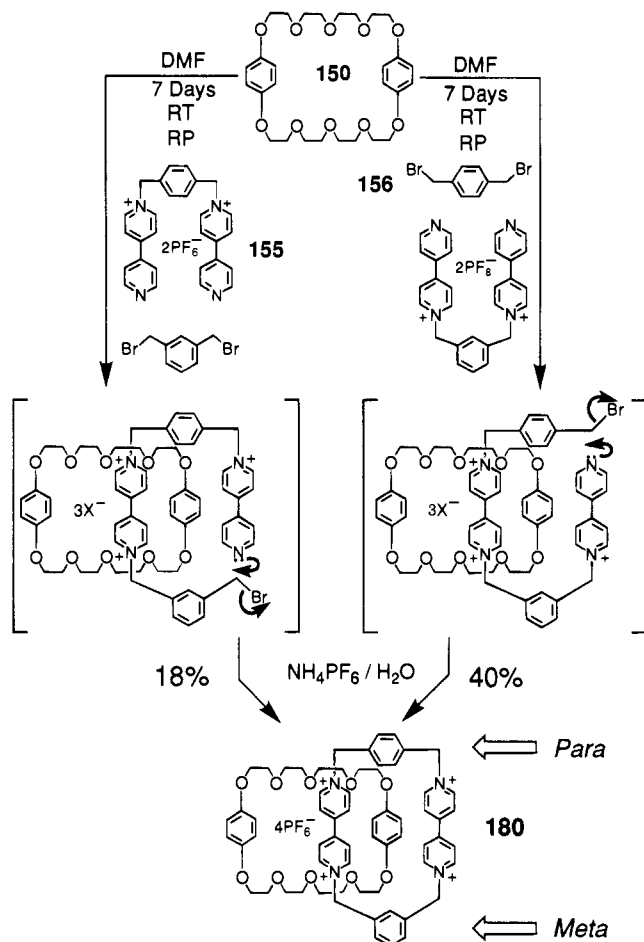
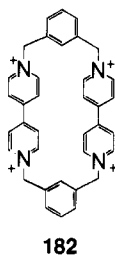


Figure 113. The self-assembly by two different routes of a [2]catenane **180** in which the tetracationic cyclophane component contains one *p*-xylyl spacer and one *m*-xylyl spacer.³⁷⁴ The efficiency of the self-assembly reaction is dependent upon the constitution of the starting materials.

on the way to the [2]catenane **180**. When the dimensions of the tetracationic cyclophane component were reduced still further, so that it contains two *m*-xylyl spacers, the [2]catenane **181** could not be prepared at ambient pressure. Indeed, the tetracationic cyclophane **182** does not bind π -electron-rich aromatic units within its tight cavity at ambient conditions. Yet, when the catenation of the template **150** with the components of **182** was carried out at 10 kbars (Figure 114), a 28% yield of the [2]catenane **181** was achieved. The changes in the constitution



of the tetracationic cyclophane, in addition to affecting the efficiency of the self-assembly process, also alter the solution- and solid-state properties of the resulting [2]catenanes. As the dimensions of the cyclophane are reduced, the free energy of activation ΔG^\ddagger to circumrotation of the neutral component through the cavity of the charged component (process II, Figure 100) is increased from 15.6 kcal mol⁻¹ in

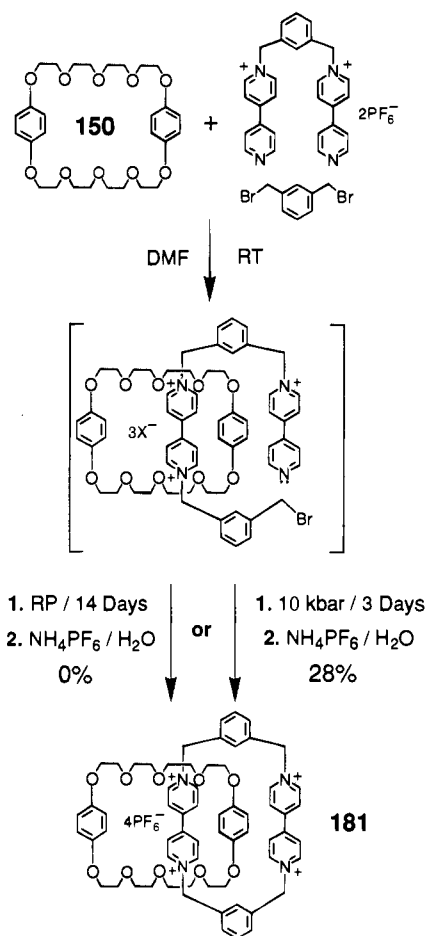


Figure 114. The self-assembly under ultrahigh pressure conditions of the [2]catenane **181** in which the tetracationic cyclophane component contains two bipyridinium units bridged by two *m*-xylyl spacers.³⁷⁴

157, to 16.3 kcal mol⁻¹ in **180**, and to 17.6 kcal mol⁻¹ in **181**. In addition, the mechanism (process IV in Figure 115) by which the hydroquinone ring “rocks” inside the cavity of the tetracationic cyclophane at low temperatures is hindered increasingly as the cavity dimensions of the tetracationic cyclophane component in the [2]catenane is reduced.

The geometry³⁷⁴ of the [2]catenane **180** in the solid state is very similar to that of the isomer **157**. A T-type interaction is observed between a hydrogen atom attached to the included hydroquinone ring and the π -face of the *p*-xylyl spacer in the tetracationic cyclophane. An analysis of the packing diagrams

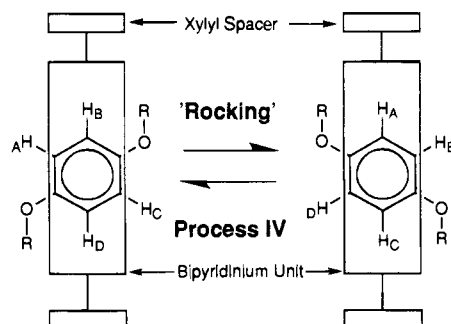


Figure 115. The rocking process (IV) which can be observed by dynamic ¹H NMR spectroscopy in solution at low temperatures for the hydroquinone ring located inside the tetracationic cyclophane components of the [2]catenanes **157**, **180**, and **181**.

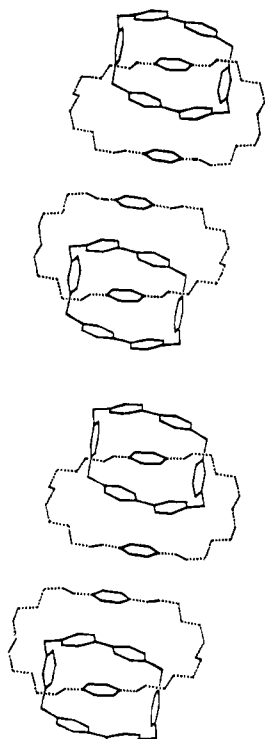
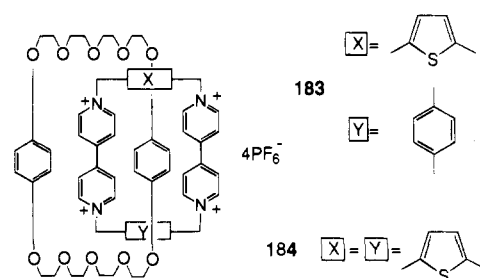


Figure 116. The stacking of enantiomeric pairs of [2]-catenane molecules along one of the crystallographic axes in crystals of the [2]catenane **181** as revealed by X-ray crystallography.³⁷⁴

reveals that the polar stacks of the molecules in the crystals of **180** are also very similar to those of **157**. However, in the crystals of the [2]catenane **181**, the stacking arrangement of the molecules is very different. A continuous stack of alternating donors and acceptors is not observed, possibly as a result of the substantial bowing of the bipyridinium units in the catenane. Rather, two "alongside" hydroquinone rings from an enantiomeric pair of catenane molecules stack (interplanar separation of 3.62 Å) with respect to one another in the crystal (Figure 116).

Very recent research which has also been involved with the variation of the constitution of the spacers between the bipyridinium moieties in the tetra-

catenane components of [2]catenanes of this type has drawn further attention to the effect of constitution upon the efficiency of the self-assembly process, as well as of the dynamic properties of the component with respect to each other.³⁷⁵ One and two thiophene-2,5-diylidimethylenedioxy residues were used in place of the *p*-xylyl spacers in the tetracationic cyclophane component of **157** in the self-assembly of the [2]catenanes **183** and **184**, which were obtained in 59 and 36% yields, respectively, at ambient temperature and pressure. The free energies of activation for processes I and II are approximately the same as those in **157**, but the barrier to the "rocking" (process IV) of the hydroquinone ring inside the cyclophane is increased significantly. An X-ray crystal structure of **184** provides a possible explanation for this observation. There is a significant [S...O] interaction between the sulfur atom in the spacer group of the tetracationic cyclophane component and the oxygen atoms of the included hydroquinone ring in the neutral component.



Vögtle and co-workers³⁷⁶ have incorporated photochemically active azobenzene units into [2]catenanes. The two [2]catenanes **185** and **186** were prepared (Figure 117), in 34% and 16% yields, respectively, along with their component tetracationic cyclophanes. The azobenzene units in these structures were isomerized from the (*E*)-configuration to the (*Z*)-configuration by irradiation at 310 nm wavelength. Their thermal isomerization from (*Z*)- back to (*E*)-configurations was followed by ¹H NMR spectroscopy. The [2]catenanes **185** and **186** have half-lives for their re-isomerizations of 20.5 h and 12 days, respectively, while the component free tetracationic cyclo-

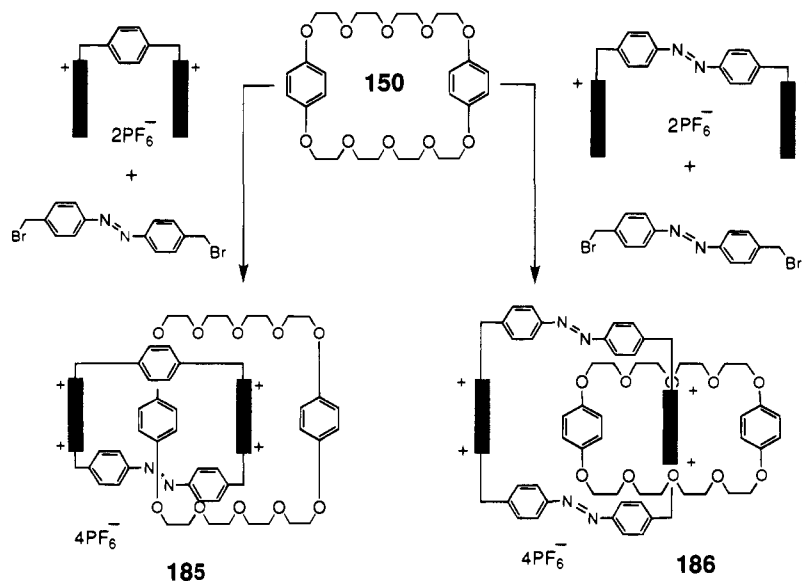


Figure 117. The self-assembly of two [2]catenanes **185** and **186** incorporating one and two photochemically active azobenzene units, respectively, into their tetracationic cyclophane components.³⁷⁶

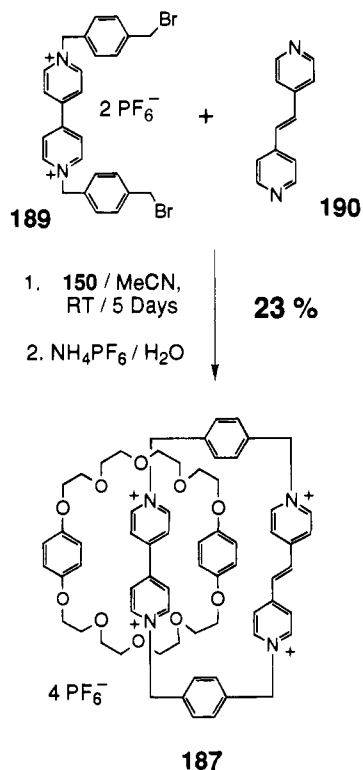


Figure 118. The self-assembly of a [2]catenane **187** in which the tetracationic cyclophane component contains one bipyridinium unit and one *trans*-bis(pyridinium)ethylene unit.³⁷⁷

phanes have half-lives of 8.3 and 14 days. It was proposed that the motion of the hydroquinone ring within the cavities of the tetracations assists the reorganization process. This effect was noticed most dramatically in the [2]catenane **185**, incorporating the smaller tetracationic component. A crystal structure of **185** showed the more open nature of the charged component in the catenane, the "inside" bipyridinium unit being sandwiched by the two hydroquinone rings of the neutral component, while the "alongside" bipyridinium unit is twisted away from the inside hydroquinone ring. Although a detailed dynamic analysis was not presented, this reduced order is also evident from inspection of the ^1H NMR spectrum of the compound.

The incorporation of photoactive groups into the π -electron-deficient units, *i.e.* an active recognition site, in the tetracationic cyclophane has also been achieved.³⁷⁷ The *trans*-bis(pyridinium)ethylene unit was incorporated into the [2]catenanes **187** and **188**, using the self-assembly routes summarized in Figures 118 and 119, in 23% and 15% yields, respectively. The formation of the dissymmetric cyclophane in **187**, in which two different π -electron-deficient units are present, required the preparation of the bipyridinium derivative **189**, which was reacted subsequently with the extended viologen **190** in the presence of **150**. Clearly, the [2]catenane **187** is present in solution as two translational isomers, one in which the neutral component surrounds the bipyridinium unit and the other in which the neutral component encircles the *trans*-bis(pyridinium)ethylene unit. In acetone at -60°C , when process I is slow on the ^1H NMR time scale, the isomer in which the standard bipyridinium unit resides in the center of the neutral component becomes favored to the extent of 92:8. The larger tetracationic cyclophane

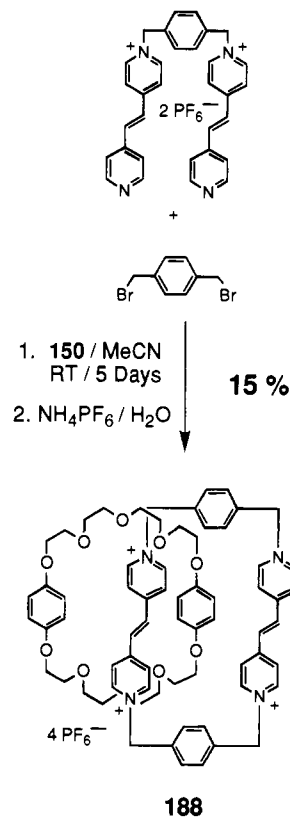


Figure 119. The self-assembly of a [2]catenane **188** in which the tetracationic cyclophane component contains two *trans*-bis(pyridinium)ethylene units.³⁷⁷

components allow lower free energies of activation to the spinning (process II) of the neutral component through the charged one. This process in the [2]catenane **187** is associated with a ΔG_c^\ddagger value of $13.1 \text{ kcal mol}^{-1}$, while the same process in **188** experiences a free energy barrier of $12.6 \text{ kcal mol}^{-1}$. The free energy of activation associated with process I in **188** is $11.1 \text{ kcal mol}^{-1}$, once again lower than the barriers for this process in more highly ordered [2]catenanes. The electrochemistry of the [2]catenanes was extremely informative. The [2]catenane **187** shows four single electron reduction waves. The first reduction occurs in the bipyridinium unit, at a potential very similar to that of the first reduction of **157**, which implies that the standard π -electron-deficient unit does indeed reside predominantly inside the cavity of the neutral component in solution. There follow two single electron reductions for the extended π -electron-deficient unit, before the final one for the bipyridinium unit. The first reduction wave of the extended π -electron-deficient unit in this catenane is very close to that in **188**, which implies that, after a single electron reduction, the translational isomerism is inverted in favor of the site which exhibits the weaker molecular recognition in the original [2]catenane (Figure 120). The molecule is therefore electrochemically switchable.

The self-assembly of a [2]catenane which incorporates two dissymmetric components, giving rise to the possibility of *four* translational isomers (Figure 121), has recently been achieved.³⁷⁸ The [2]catenane **191** was prepared in a manner similar to **187**, but this time using the macrocyclic polyether **162**, which incorporates one hydroquinone ring and one 1,5-dioxynaphthalene residue, as the neutral template. The self-assembly proceeds in 58% yield as a result of the much greater templating ability of the 1,5-

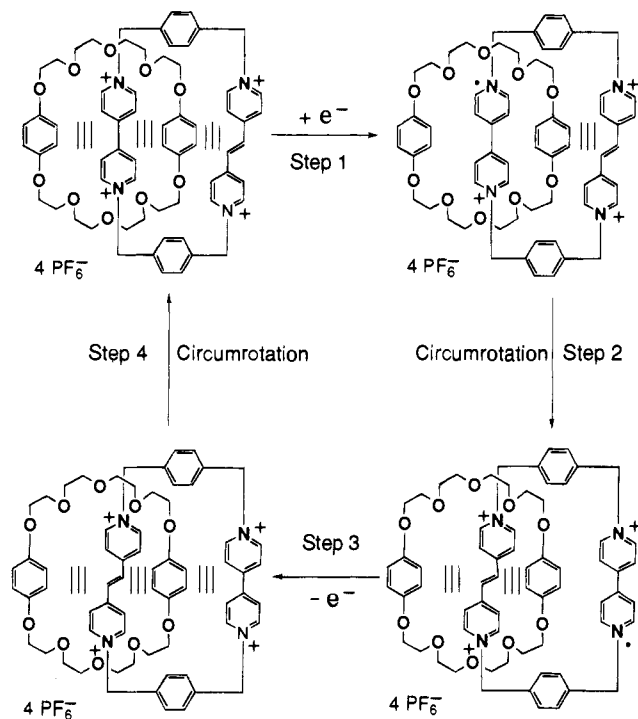


Figure 120. An electrochemical molecular switch.³⁷⁷ The [2]catenane **187** can exist in solution as two different translational isomers with either the bipyridinium unit or the *trans*-bis(pyridinium)ethylene unit of the tetracationic cyclophane component located inside the bis-*p*-phenylene-34-crown-10 component. The predominant isomer in solution is the one represented in the top left-hand corner of this figure, in which the bipyridinium unit occupies the inside position of the macrocyclic polyether, as a result of the dication's greater π -accepting ability when compared with the *trans*-bis(pyridinium)ethylene unit, which occupies the alongside position. However, the molecule can be switched electrochemically by (1) reduction of the [2]-catenane. The first reduction occurs at the inside bipyridinium unit because it has the lower reduction potential and so it becomes a monoradical cation as represented in the top right-hand corner. After reduction, (2) the inside bipyridinium unit is no longer the best π -acceptor, and so circumrotation of the charged component takes place in order to locate the *trans*-bis(pyridinium)ethylene unit between the two hydroquinone rings of the macrocyclic polyether. The predominant translational isomer is now the one represented in the bottom right-hand corner. (3) The process is reversible by oxidation, producing again a tetracationic species as illustrated in the bottom left-hand corner. (4) Finally, a further circumrotation takes place in order to relocate the bipyridinium unit inside the macrocyclic polyether. The isomeric state of the [2]catenane has thus been returned to where it was at the beginning of the experiment.

dioxynaphthalene residue for the formation of the tetracationic cyclophane. Inspection of the ^1H NMR spectrum of the [2]catenane recorded at room temperature in CD_3COCD_3 , when process II is slow and process I is fast on the ^1H NMR time scale, revealed the presence of the isomers in which either the 1,5-dioxynaphthalene residue or the hydroquinone ring occupies the cavity of the charged component, in a ratio of 88:12 in CD_3COCD_3 in favor of the inclusion of the larger aromatic unit. At -40°C , when both processes I and II are slow on the ^1H NMR time scale, the presence of only two of the possible four translational isomers is observed, and they are both isomers in which the 1,5-dioxynaphthalene residue occupies the cavity of the tetracation, in the proportions 95:5 in CD_3COCD_3 . The most favored

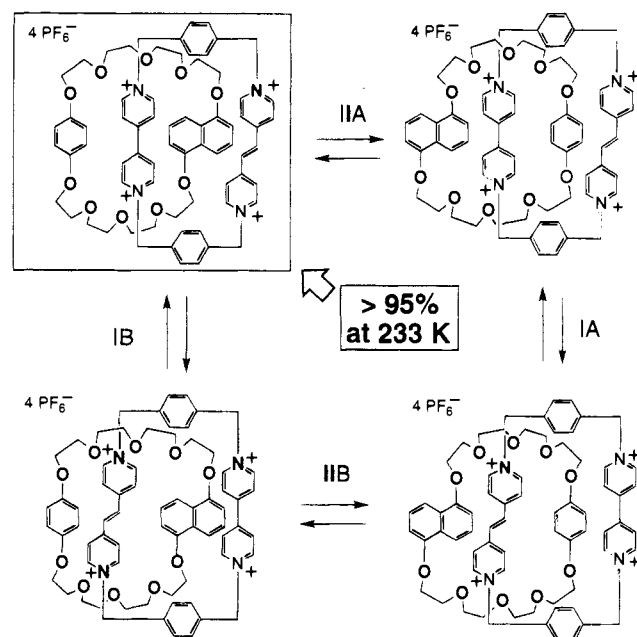


Figure 121. The equilibration between the four different translational isomers of the [2]catenane **191** in CD_3COCD_3 solution as indicated by ^1H NMR spectroscopy.³⁷⁸ The preferred isomer is boxed. The processes involving circumrotation of the charged macrocycle through the neutral one (process I) and circumrotation of the neutral component through the charged one (process II) are designated A and B, since the processes are formally different depending upon which unit is at the center of the other components cavity.

isomer is that in which the bipyridinium residue in the charged component occupies the cavity of the neutral component. Moreover, this isomer is also the only one that is observed in the crystals of **191**. The X-ray crystal structure of the compound clearly shows that the larger π -electron rich unit is located in the center of the tetracationic cyclophane, entering into T-type edge-to-face interactions with its *p*-xylyl spacers. The center of the 1,5-dioxynaphthalene residue is located closer to the bipyridinium unit (3.50 Å) than it is to the extended viologen (3.72 Å). The bipyridinium unit resides inside the neutral component. The [2]catenane also forms polar stacks (Figure 122) in the crystal. An interesting feature of the superstructure is the proximity (3.42 Å) of the center of the double bond in the extended viologen to the "alongside" hydroquinone ring of an adjacent molecule. Indeed, it is the closest π - π interaction in the crystal.

The self-assembly of an optically active [2]catenane has also been achieved recently.³⁷⁹ The incorporation of (*SS*)-hydrobenzoin residues into the dicationic compound **192** was followed by reaction (Figure 123) with *p*-xylylene dibromide in the presence of the macrocyclic polyether **150** to afford the chiral [2]catenane **193** in 8% yield. The low yield of this catenane can be explained by considering the X-ray crystal structure (Figure 124) of the compound. It reveals considerable splaying by the two bipyridinium units in the tetracationic component. The distance between the CH_2N^+ groups at the *p*-xylyl "end" of the cyclophane component is 5.9 Å, while the separation at the opposite end of the cyclophane is 7.3 Å. Despite this distortion, a strong charge transfer band was observed, arising from the π - π stacking interactions. A T-type interaction is once

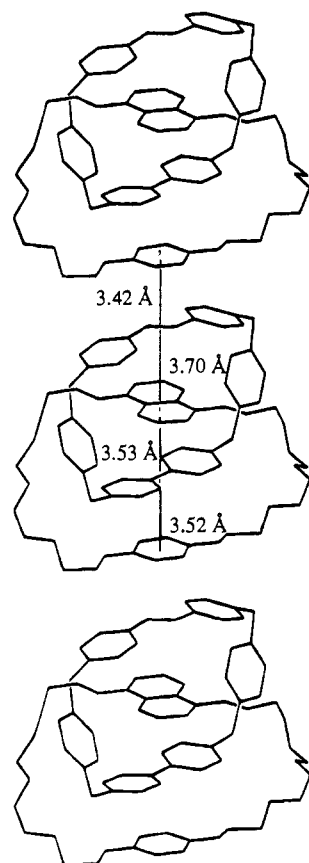


Figure 122. The polar stack formed by molecules of the [2]catenane **191** in the solid state as indicated by X-ray crystallography.³⁷⁸

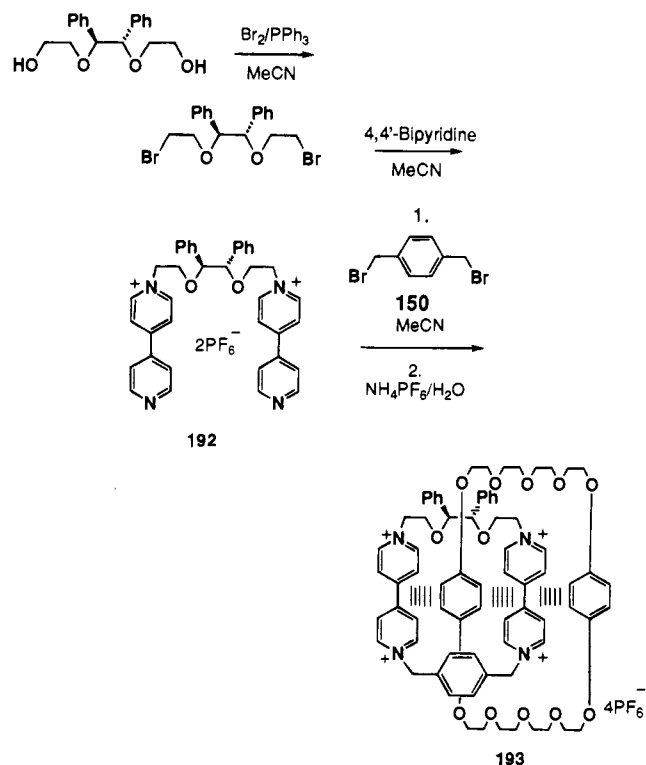


Figure 123. The self-assembly of an optically active [2]catenane (**193**) by incorporating (*SS*)-hydrobenzoin residues into the tetracationic cyclophane component.³⁷⁹

again present and involves one of the included hydroquinone hydrogen atoms and the *p*-xylyl spacer. As a result of the distortions in the molecular

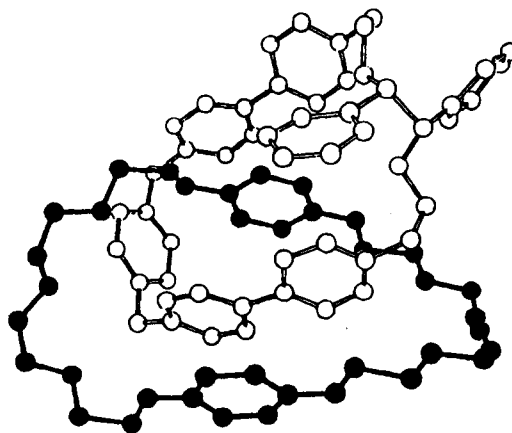


Figure 124. A ball-and-stick representation of the X-ray crystal structure of the optically active [2]catenane **193**.³⁷⁹

structure, no continuous stacking is observed in the crystal.

The appropriate enlargement of the tetracationic cyclophane component in these catenanes allows the simultaneous entrapment of two neutral components to occur during the self-assembly process. This situation was realized by replacing the *p*-xylyl spacer in **153** with a 4,4'-biphenyl unit. The [3]catenanes **194** and **195** were self-assembled (Figure 125) in 25% and 30% yields, respectively.^{364,380} A remarkable

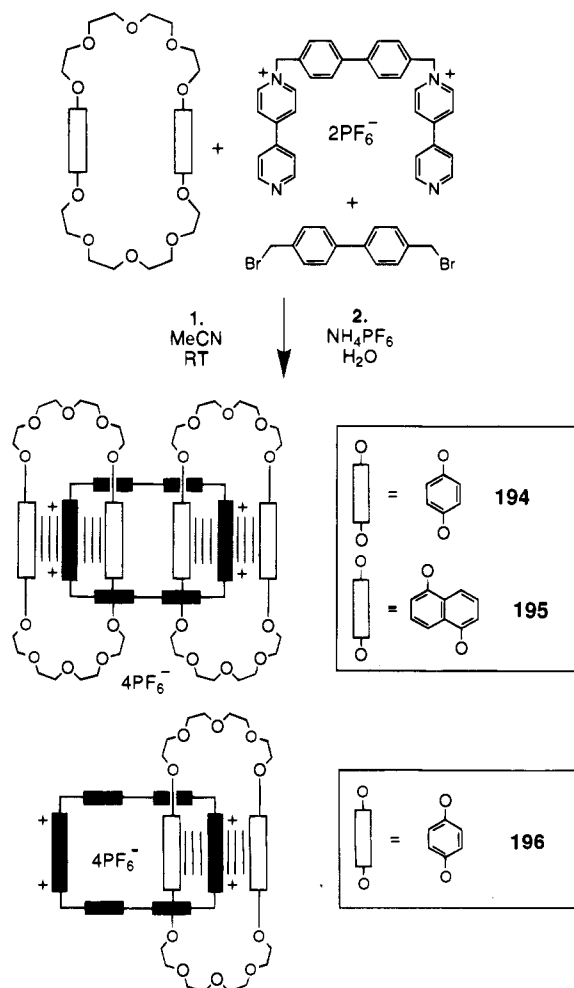
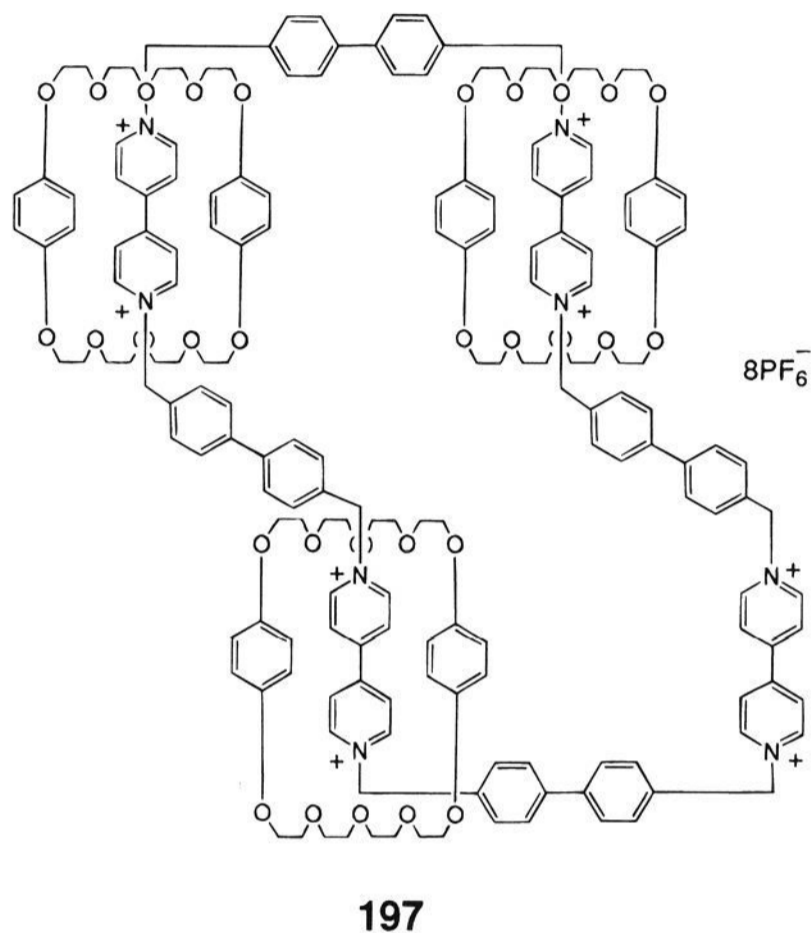


Figure 125. (Top) The self-assembly of two [3]catenanes **194** and **195** incorporating cyclobis(paraquat-4,4'-biphenylene) as the tetracationic cyclophane component;³⁸⁰ (bottom) the minor product of one of the reactions, namely, the [2]catenane **196**.³⁶⁴

feature of the self-assembly process in which this large tetracationic cyclophane is templated is the overwhelming preference for the formation of the [3]catenanes over the formation of the corresponding [2]catenanes, incorporating only one crown ether threaded around the tetracationic cyclophane, *e.g.* **196**. In the case of the template **150**, the [2]catenane was isolated in 2% yield, and a [4]catenane, **197**, incorporating the cyclic dimer of the charged component and three crown ether (**150**) components, was also isolated.³⁶⁴ Moreover, it is easier to form the



[3]catenanes than it is to prepare the tetracationic cyclophane on its own! The [3]catenanes were characterized by fast-atom bombardment and also by electrospray³⁸¹ mass spectrometry—and, in the case of **194**, by X-ray crystallography. The solid-state structure of the [3]catenane shows that the two macrocyclic polyethers are disposed centrosymmetrically with respect to one another, each macrocycle surrounding the 4,4'-bipyridinium residues in the tetracation with parallel alignment of the aromatic residues. The included pair of hydroquinone rings are stacked (interplanar separation of 3.63 Å), as well as being disposed toward the phenylene rings in the spacers, giving rise to T-type interactions. The π -electron donors (D) and π -electron acceptors (A) in the molecule form a DADDAD sequence that extends throughout the crystal forming a continuous stack. Partly as a result of the loss of the DAD sequence, the free energies of activation to the spinning of the macrocyclic polyethers through the cavity of the tetracation in solution is low when it is compared with the analogous free energy barriers in the [2]catenanes incorporating, for example, the tetracationic cyclophane **153**. The ΔG_c^\ddagger values of 10.7 and 13.3 kcal mol⁻¹ for **194** and **195**, respectively, reflect the weaker π - π stacking interactions between the two π -electron donors than between a π -electron donor and a π -electron acceptor.

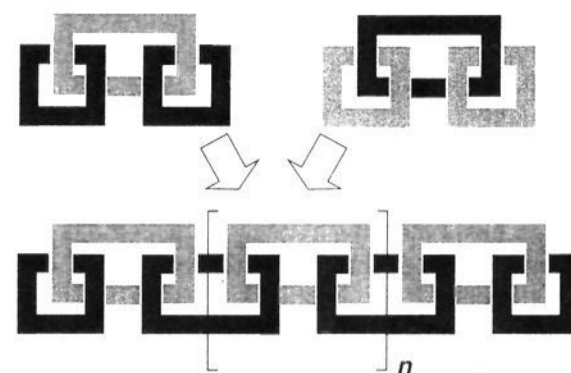


Figure 126. The progression toward polycatenanes at the conceptual level.

We have already noted (Figure 111) that a large macrocycle incorporating four π -electron-rich residues (**177**) can template the formation of two tetracationic cyclophanes. We have just described the entrapment of two macrocyclic polyethers through the center of a large tetracationic cyclophane. One of the objectives of our research is to make polycatenanes. Conceptually, one might conceive of the possibility that the merger of these two approaches might lead to the formation of polycatenanes. This conceptual progression is portrayed schematically in Figure 126. Regrettably, despite numerous attempts, the reaction of **177** with the components of the large tetracationic cyclophane failed to produce any catenated products at all. For some reason, self-assembly does not appear to be prevalent.

In an effort to reach one of our intermediate goals on the way to such polycatenanes, a linear array of five interlocked rings, the chemical equivalent of the symbol signifying the International Olympics movement, the macrocyclic polyether was redesigned. Tris-*p*-phenylene-51-crown-15 (**198**) was first of all tested³⁸² as a template for the formation of the small tetracationic cyclophane **153** at ambient pressure. As in the case of the larger template **177**, only a [2]catenane **199** was formed in 48% yield, but, when the reaction was carried out at high pressure (10 kbar), the [3]catenane **200** was isolated in 15% yield (Figure 127). The critical step in the reaction sequence to the [5]catenane was expected to be that involving the formation of the [3]catenane **201** from **198** and the components of the large tetracationic cyclophane. The reaction did yield the [3]catenane, but only in 3.5% yield (Figure 128), presumably because of the relatively poor preorganization of the macrocyclic polyether. However, this compound provided the opportunity to attempt the self-assembly of a [5]catenane in a reaction under ultrahigh pressure. The [3]catenane **201** was reacted with an excess of the components of **153** at between 11 and 14 kbars for 8 days. Column chromatography gave the [4]catenane (**202**) in 22% yield, but only submilligram quantities of a compound, which liquid secondary ion (LSI) mass spectrometry indicated had the molecular weight of the desired [5]catenane (**203**). The LSI mass spectra of the [4]- and [5]catenane are characteristic of this genre of interlocked molecules. Peaks are observed which correspond to the loss of hexafluorophosphate counterions from the parent

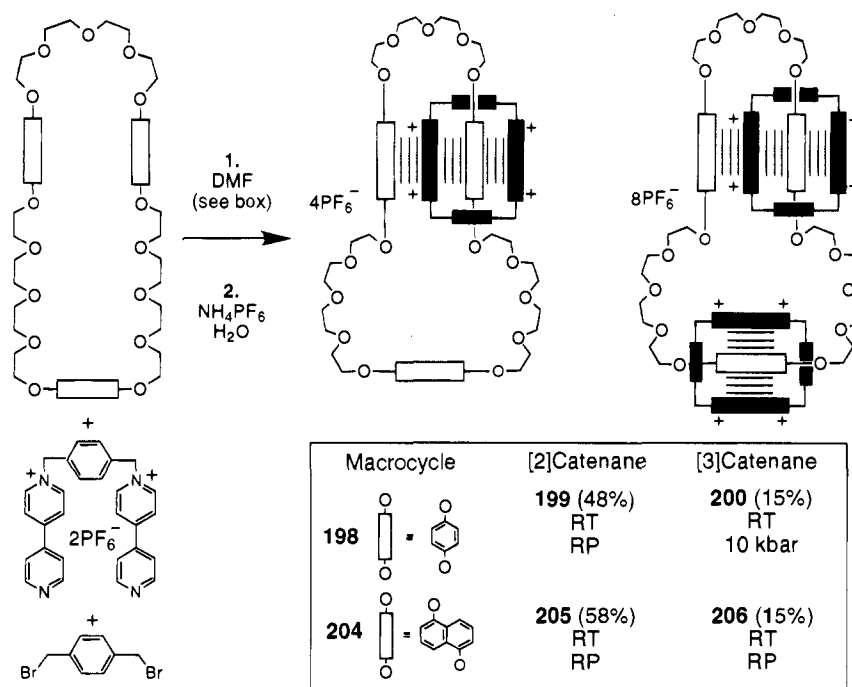


Figure 127. The self-assembly of the [2]catenanes **199** and **205** and the [3]catenanes **200** and **206** using the crown-15 macrocycles **198** and **204** incorporating hydroquinone rings and 1,5-dioxynaphthalene residues, respectively, as the macrocyclic polyether templates.^{382,383}

molecule, and, at lower mass-to-charge ratio, peaks for fragments of the catenated structures, in which some of their macrocycles have been broken apart and lost during the mass spectroscopic procedure, can be identified.

Redesigning the macrocyclic template once again, the hydroquinone rings of **198** were replaced with 1,5-dioxynaphthalene residues, which were known to be better templates for these self-assembly reactions. The crown ether tris-1,5-dioxynaphtho-57-crown-15 (**204**) was employed³⁸³ first of all to template the formation of the small tetracationic cyclophane **153**. At ambient pressure and temperature, the reaction (Figure 127) of 2 molar equiv of the components of **153** with **204** led to the self-assembly of the [2]-catenane **206** in 58% yield, and also to the [3]-catenane **205** in 15% yield. This result bade well for the creation of the [5]catenane at ambient conditions. An X-ray crystal structure⁴² of the [2]catenane **205** revealed (Figure 129) an extremely compact structure in the solid state. All the 1,5-dioxynaphthalene residues are involved in noncovalent π - π stacking interactions with the mechanically linked tetracationic cyclophane. One of the π -electron-rich residues is located inside the π -electron-deficient cavity, another forms a sandwich with a bipyridinium unit, and the remaining one forms an "alongside" interaction with one of the *p*-xylyl spacers in the tetracation (Figure 129). In addition, there are hydrogen bonds between the polyether oxygen atoms and α -CH bipyridinium and *N*-methylene hydrogen atoms in the tetracationic cyclophane. Furthermore, the [2]catenanes form a quiltlike array that is held in two dimensions by a network of π - π stacking interactions between neighboring molecules. It was proposed, on the basis of ¹H NMR spectroscopy, that a similar

superstructure might be present in solution at low temperatures, and that such self-association might contribute to preventing further clipping of the tetracationic cyclophane to the **204** component of the [3]catenane **205** and the [4]catenane **206**.

The reaction³⁸⁴ of **204** with the components of the large tetracationic cyclophane led to the successful self-assembly of the [3]catenane **207** in 6% yield, along with the related [2]catenane in 2% yield (Figure 128). The reaction of the [3]catenane **207** with an excess of the components of the small tetracationic cyclophane **153** was performed at ambient pressure and temperature. After four days, the mixture of products was subjected to column chromatography on silica gel. The [4]catenane **208** was obtained in 31% yield, while the linear [5]catenane **209** was isolated in 5% yield. The remainder of the material was unreacted [3]catenane **207**. The identity of the [4]- and [5]catenanes was confirmed by LSI mass spectrometry. The [5]catenane **209** (Figure 130), which we have named "olympiadane" following van Gulicks' suggestion,¹⁹ displayed a peak in its mass spectrum with *m/z* 5073, corresponding to the $[M-2PF_6]^+$ ion, which was within 5 ppm of the predicted mass. The topology and structure of olympiadane, a molecule with no less than eight crossing points, was confirmed by variable-temperature ¹H NMR spectroscopy. The spectrum of olympiadane in CD₃CN at 70 °C is remarkably simple. It reveals single resonances for all the heterotopic protons except for those associated with the three naphthalene units, which are not completely equilibrated on the ¹H NMR time scale between the two different cavities of the π -electron-deficient cyclophanes at this temperature. At 0 °C, the resonances arising from

the heterotopic protons on the smaller cyclophanes are separated into two, indicating that the naphthalene residues are located within their cavities. All the other resonances remained broad, indicating that the remaining two naphthalene units are vying for the occupation of the cavity in the larger cyclophane. The free energy of activation necessary to dislodge the naphthalene units from the cavity one of the smaller tetracationic cyclophanes is $14.7 \text{ kcal mol}^{-1}$.

An alternative approach to the construction of large interlocked molecular components using the established self-assembly procedure is to exploit increasingly covalent bond formation in addition to nonco-

valent bond formation—and to use polyfunctional starting materials. The preference for the formation of the exclusively *para*-substituted tetracationic cyclophane **153** over that of the tetracationic cyclophane with one *meta*- and one *para*-substituted spacer has been used in the self-assembly—from five components—of a bis[2]catenane in a single step.³⁸⁵ The tetrabromide **210** was combined (Figure 131) with **155** in the presence of an excess of the macrocyclic polyether **150**, and after 10 days and column chromatography on silica gel, the bis[2]catenane **211** was isolated in 13% yield. The molecular weight of this intriguing compound was confirmed by fast-atom

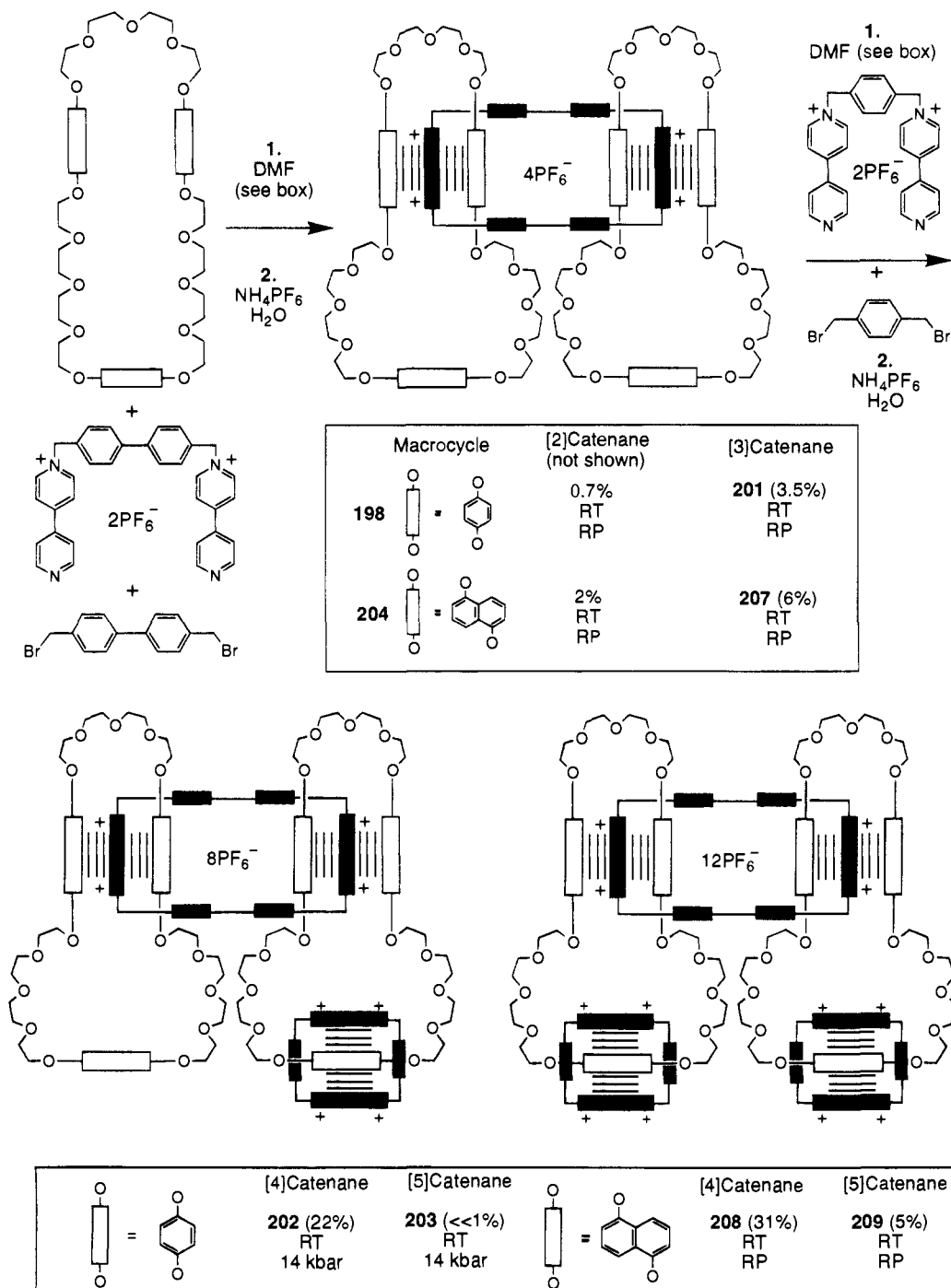


Figure 128. The two-step self-assembly processes leading to the [4]catenanes **202** and **208** and the [5]catenanes **203** and **209**, via the intermediate [3]catenanes **201** and **207**, using the crown-15 macrocycles **198** and **204** incorporating hydroquinone rings and 1,5-dioxynaphthalene residues, respectively, as the macrocyclic polyether templates.^{382,384}

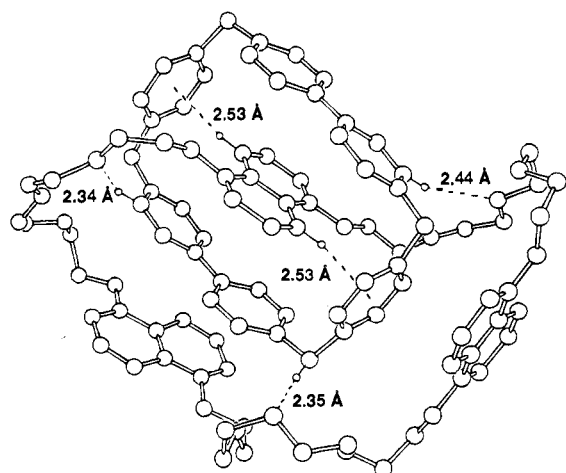


Figure 129. A ball-and-stick representation of the X-ray crystal structure of the [2]catenane **205**.³⁸³

bombardment mass spectrometry. The constitution of the chiral bis[2]catenane, which involves the shared benzene ring in an exclusively *para*-substituted manner with respect to both covalently linked tetracationic cyclophanes, was confirmed by variable-temperature ^1H NMR spectroscopy. The homotopic collection of diastereotopic CH_2N^+ protons gives rise to an AB system. The free energy of activation to the spinning of the two neutral macrocycles through the two fused cavities of the octacationic cyclophane was found by dynamic ^1H NMR spectroscopy to be

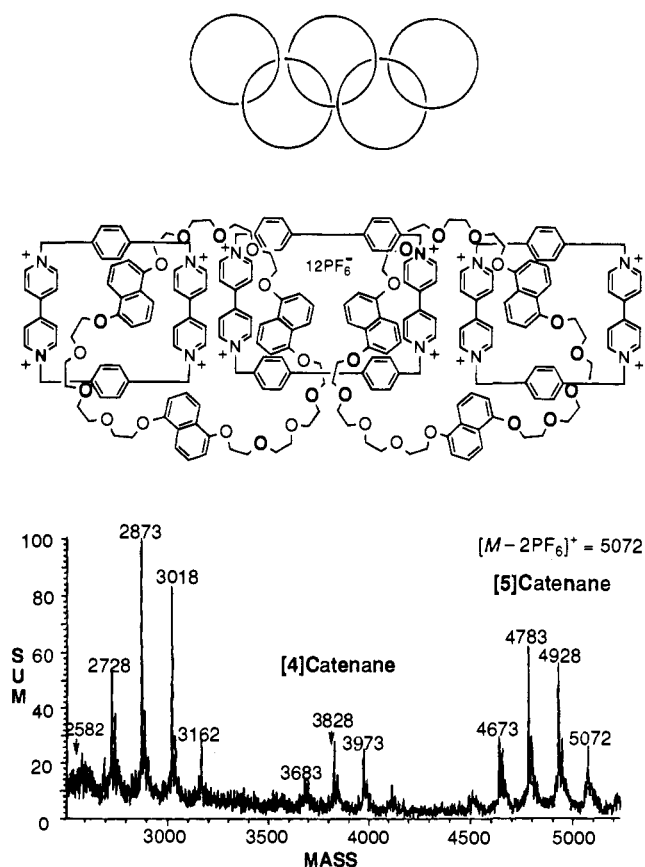


Figure 130. Olympiadane. Its identification by liquid secondary ion mass spectrometry.³⁸⁴ The spectrum is typical of those for catenanes of this type, showing sequential loss of hexafluorophosphate counterions, and then cleavage of the component rings to afford, in this case, the lower catenated intermediates.

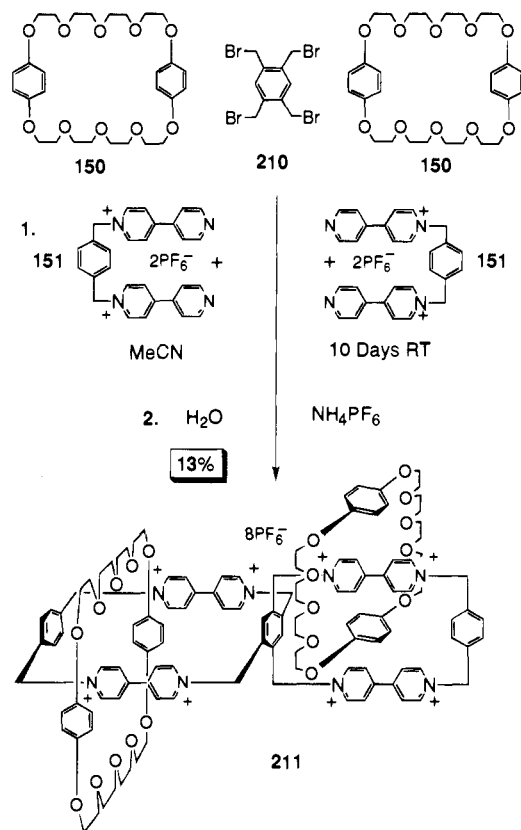


Figure 131. The self-assembly of a chiral bis[2]catenane (**211**) from five components in a single step.³⁸⁵

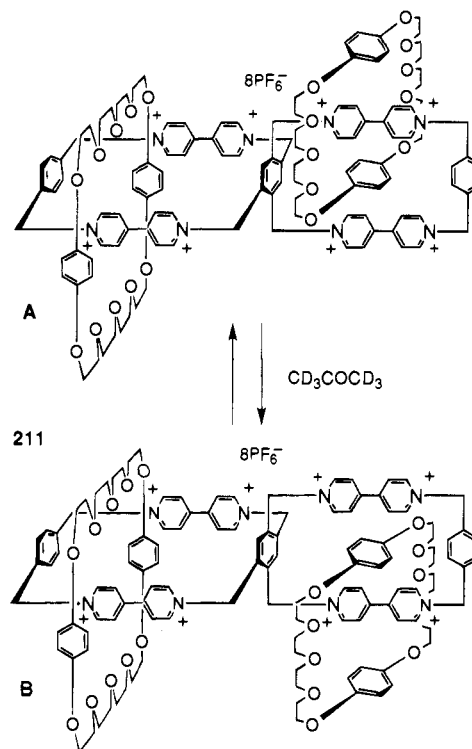
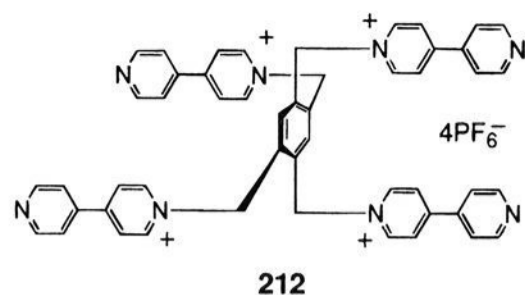


Figure 132. The equilibration between translational isomers **A** and **B** of the chiral bis[2]catenane **211** in $\text{CD}_3\text{-COCD}_3$ solution as studied by dynamic ^1H NMR spectroscopy.³⁸⁵

$16.0 \text{ kcal mol}^{-1}$. At low temperatures, the two translational isomers (**A** and **B**) of the bis[2]catenane were equally populated (Figure 132). Intriguingly, none of **211** was isolated when the tetracation **212** was used as the starting material along with the

other appropriate building blocks. In addition, the



free octacationic cyclophane has not been isolated to date. Hence, the self-assembly of this bis[2]catenane provides yet another example of a situation where it is easier to prepare the catenated compound than one of its components! A higher yield of a bis[2]catenane was obtained when the reactive bromomethyl functions are located much further apart.³⁸⁶ When the tetrabromide **213** was reacted (Figure 133) with **155**

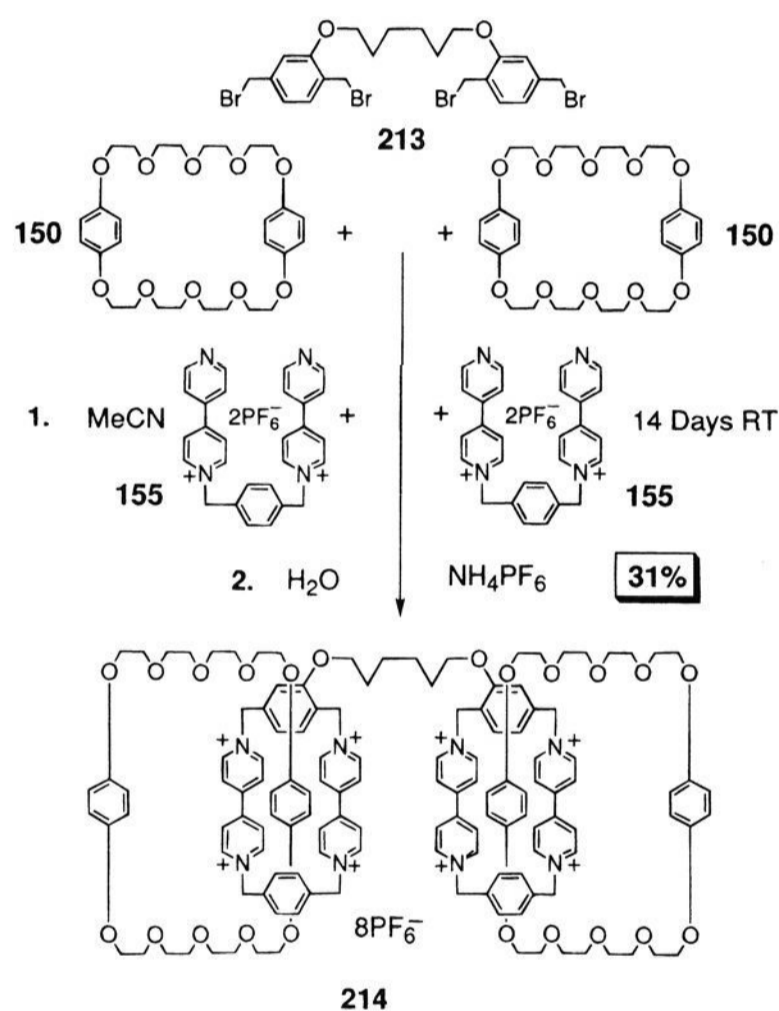


Figure 133. The self-assembly of the bis[2]catenane **214** from five components in a single step.³⁸⁶

and an excess of the macrocyclic polyether **150**, the bis[2]catenane **214** was formed and was isolated in 31% yield. These two biscatenated compounds may be regarded as the forerunners of the type of polymeric catenanes schematically depicted in Figure 134, whose synthesis has been attempted³⁸⁶ with only a limited success at this stage.

During the course of this description of the catenanes derived from donor–acceptor systems, the reader will have noted the marked increase in yields when using 1,5-dioxynaphthalene residues in the templating macrocycle. We were interested to test the relative templating abilities of BPP34C10 (**150**) and DN38C10 (**151**) under competitive conditions.³⁸⁷ Thus, the macrocyclic polyethers were combined in equimolar amounts with the components of either cyclophane A (**153**), B, C, or D in Figure 135. The

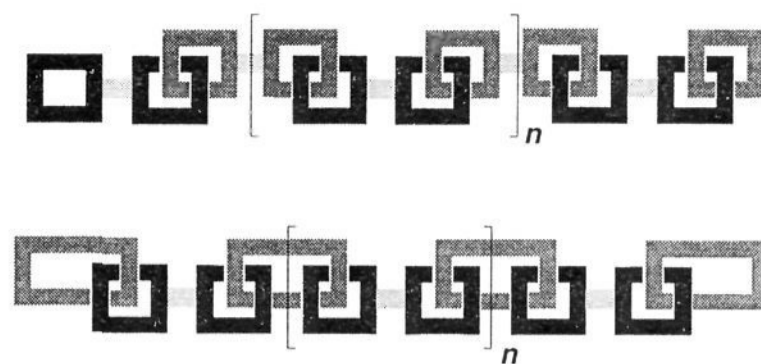


Figure 134. Schematic representations of polymers based on [2]- and [3]catenane linking units within the polymeric chains.

amounts of **150** and **151** which were incorporated into the derived catenanes were analyzed by ¹H NMR spectroscopy. The ratios of the products (Figure 135) again emphasize the marked preference of all cyclophanes for templating by **151**. However, the extent of this preference is dependent on the dimensions of the cyclophane being formed. Since cyclophanes A to C all have bipyridinium dications prior to cyclization to form the catenanes, it would appear that, although the thermodynamics of binding are important, the kinetics of ring closure determines the proportion of either incorporated macrocycle, *i.e.* the Curtin–Hammett principle appears to be displayed. These self-assembly reactions, which occur with intermittent processing,²⁸ are thus interesting complements to systems whose self-assembly is ordained by thermodynamics alone.

C. Pseudorotaxanes

The interactions between molecular thread-like compounds incorporating between three and five π -electron-rich aromatic residues and the π -electron-deficient tetracationic cyclophane **153** has led to the self-assembly of a range of pseudorotaxanes. In the first report³⁸⁸ concerning these intertwined compounds, threads with three π -electron-rich aromatic rings—the central one invariably being a hydroquinone ring—were shown to crystallize with **153**. The solid-state structures of three pseudorotaxanes were obtained by X-ray crystallography. In the first (**153.215**, Figure 136), the three hydroquinone residues of the thread are spaced with tetraethylene glycol units. The X-ray crystal structure of this 1:1 complex shows that the central hydroquinone residue is located in the center of the tetracation, while the terminal hydroquinone residues sustain “alongside” interactions with the outer surface of the bipyridinium units. The complex formed by the thread **216** and **153** has an almost identical superstructure around the cyclophane component and beyond as far as the first 10 atoms emanating from the encircled hydroquinone ring. However, the reduced length of the polyether spacer in the thread does not allow the terminal aromatic rings of the thread to make an optimum overlap with the outer surfaces of the bipyridinium units in the cyclophane. As a consequence of the constitutional modification, a continuous donor–acceptor stack is formed in which the outer π -electron-rich aromatic residues are shared between the two outer surfaces of cyclophane units in different 1:1 complexes (Figure 137).

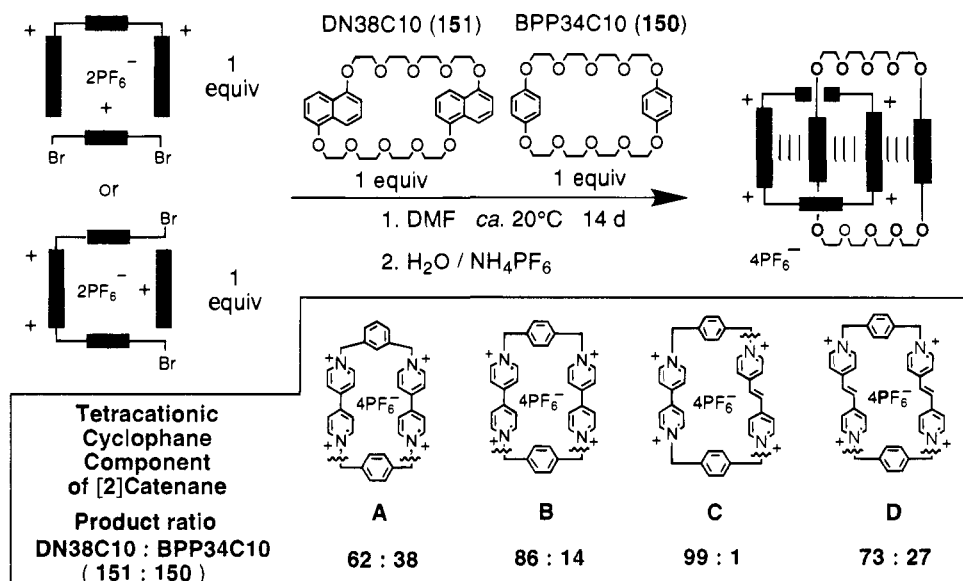


Figure 135. Selectivity at work during the kinetically determined catenations to give [2]catenanes comprised of either **151** (DN38C10) or **150** (BPP34C10) components and a range of different tetracationic cyclophanes.³⁸⁷

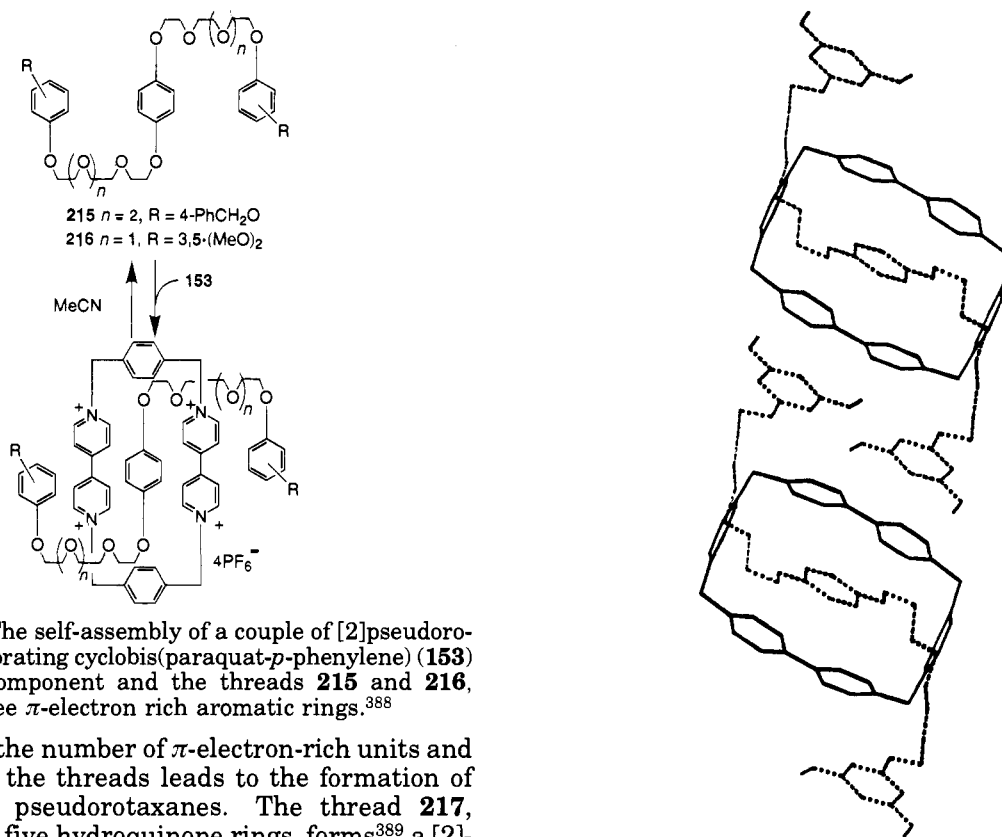


Figure 136. The self-assembly of a couple of [2]pseudorotaxanes incorporating cyclobis(paraquat-*p*-phenylene) (**153**) as the bead component and the threads **215** and **216**, containing three π -electron rich aromatic rings.³⁸⁸

Increasing the number of π -electron-rich units and the length of the threads leads to the formation of higher order pseudorotaxanes. The thread **217**, incorporating five hydroquinone rings, forms³⁸⁹ a [2]-pseudorotaxane when it is combined with 1 molar equiv of the tetracationic cyclophane **153**, while addition of a second molar equivalent of the cyclophane affords a [3]pseudorotaxane (Figure 138). The superstructures were confirmed by ¹H NMR spectroscopy in CD₃COCD₃ solutions at -40 °C, a temperature at which the equilibration of the components is slow on the ¹H NMR time scale. The [3]pseudorotaxane is estimated to be 30 Å in length and 15 Å in diameter.

Replacement³⁹⁰ of the hydroquinone rings in the thread **215** with 1,5-dioxynaphthalene residues followed by addition of the thread to **153**, affords a [2]-pseudorotaxane which forms ordered structures in both the solid and solution states. The solid-state

Figure 137. The continuous donor-acceptor stack formed in the solid state, as indicated by X-ray crystallography, when the [2]pseudorotaxane, obtained from the thread **216** and the cyclophane **153**, crystallizes.³⁸⁸

structure of the complex reveals (Figure 139) that the central naphthalene residue of the thread resides within the center of the cyclophane, with the remaining aromatic units entering into "alongside" π - π stacking interactions with the bipyridinium units of the cyclophane. In addition, the [2]pseudorotaxanes form a quiltlike array in the crystalline state, which is similar to that already discussed for the [2]-catenane **205**, in which the "alongside" naphthalene residues of one complex enter into π - π stacking interactions with the *p*-xylyl spacers in the cyclo-

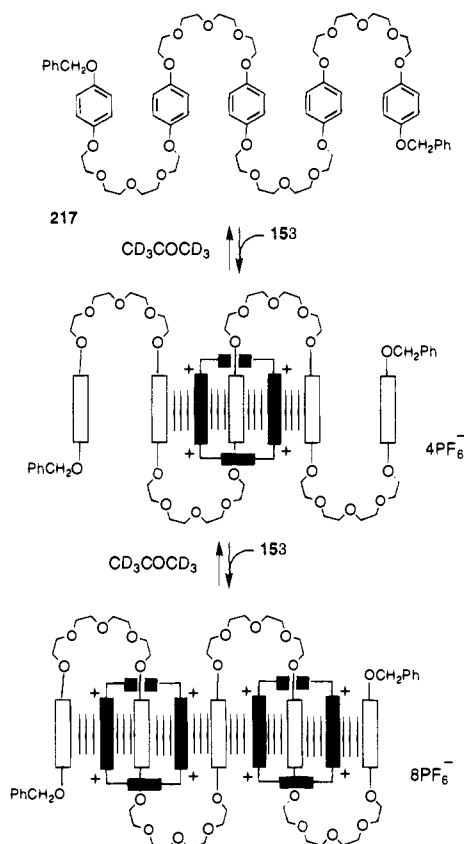


Figure 138. The self-assembly of a [2]pseudorotaxane and a [3]pseudorotaxane incorporating cyclobis(paraquat-*p*-phenylene) (**153**) as the bead component and the thread **217** containing five hydroquinone rings.³⁸⁹

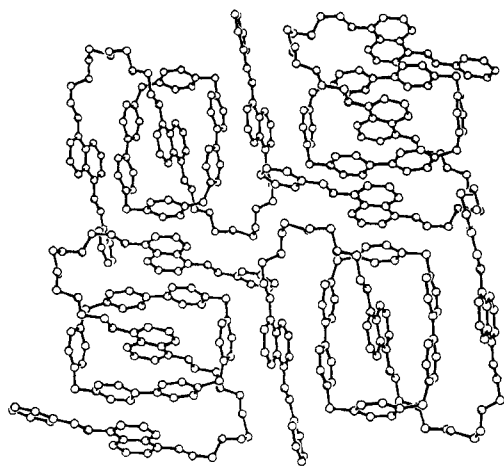


Figure 139. The quiltlike packing in the solid state of [2]pseudorotaxane complexes formed between cyclobis(paraquat-*p*-phenylene) (**153**) as the bead component and a thread, analogous to **215**, but incorporating three 1,5-dioxynaphthalene residues instead of hydroquinone rings.³⁹⁰

phane components of the neighboring complexes (Figure 139). In solution, this 1:1 complex has a K_a value of approximately $11\,000\text{ M}^{-1}$, and the free energy of activation required to dislodge the central naphthalene residue from the middle of the cyclophane is approximately $15.5\text{ kcal mol}^{-1}$. Thus, it has been shown that the two components—**215** and **153**—form a highly stable intertwined supramolecular structure. An attempt³⁹¹ at using these thread-like molecules, comprised of π -electron-rich residues interspersed with tetraethylene glycol units, as complementary strands for thread-like molecules

comprised of 4,4'-bipyridinium units is believed to produce poorly stable double helices in solution, as evidenced by $^1\text{H NMR}$ spectroscopic experiments.

The solid-state structure³⁹² of the 1:1 complex formed between 1,5-dimethoxynaphthalene and **153** led to the design and realization of a crystalline [3]pseudorotaxane-type structure. The linking of two dioxynaphthalene residues with a propyl chain—a design dictated by molecular modeling of the distance between the relevant oxygen atoms in the neighboring 1:1 complexes of **153**/1,5-dimethoxynaphthalene—gave a 2:1 complex with **153**, which is very similar in the solid state to that of the 1,5-dimethoxynaphthalene complex. A polymeric superstructure appears to be present in the solid state for the 2:1 complex, but this picture is clearly a result of the random positioning of the trimethylene spacers in the crystal. This superstructure was described as a “molecular abacus” and it is hoped that polyrotaxane-like structures can be self-assembled one day on the basis of this design.

The pseudorotaxane binding geometry has recently been exploited for the reversible attenuation of conductivity in a conducting macrocyclic polymer.³⁹³ The polythiophene **218** was prepared from the macrocycle **219**, which itself forms a 1:1 complex with paraquat. When the polymer is exposed to a bis(*p*-fluorobenzyl)bipyridinium salt (but not to paraquat), an anodic shift in the redox potential of the polymer is observed. This shift was caused by the formation (Figure 140) of a pseudorotaxane. The reversible changes in the conductivity of the polymer prompted the authors to suggest the use of similar materials as molecular sensors.³⁹⁴

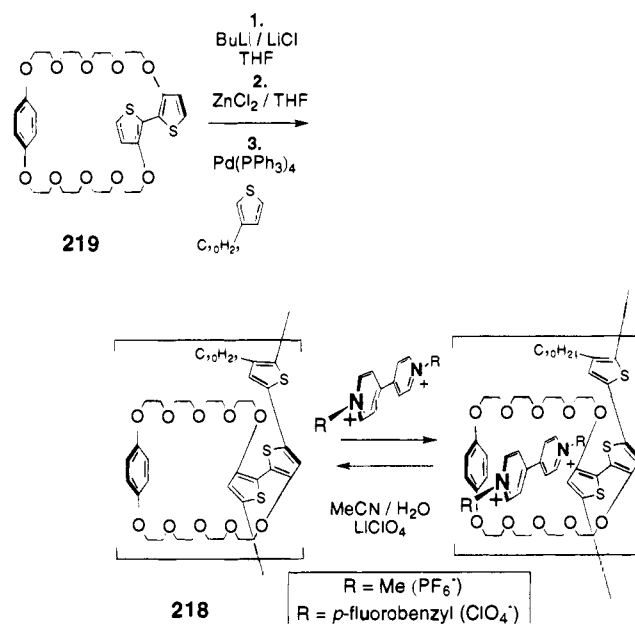


Figure 140. The [2]pseudorotaxane units formed in the polymer **218** when bipyridinium salts are added to it.³⁹³

D. Rotaxanes

The same strategy, based on π -electron-deficient and π -electron-rich aromatic units, that has been used for the self-assembly of the wide range of catenanes, can also be applied to the construction of

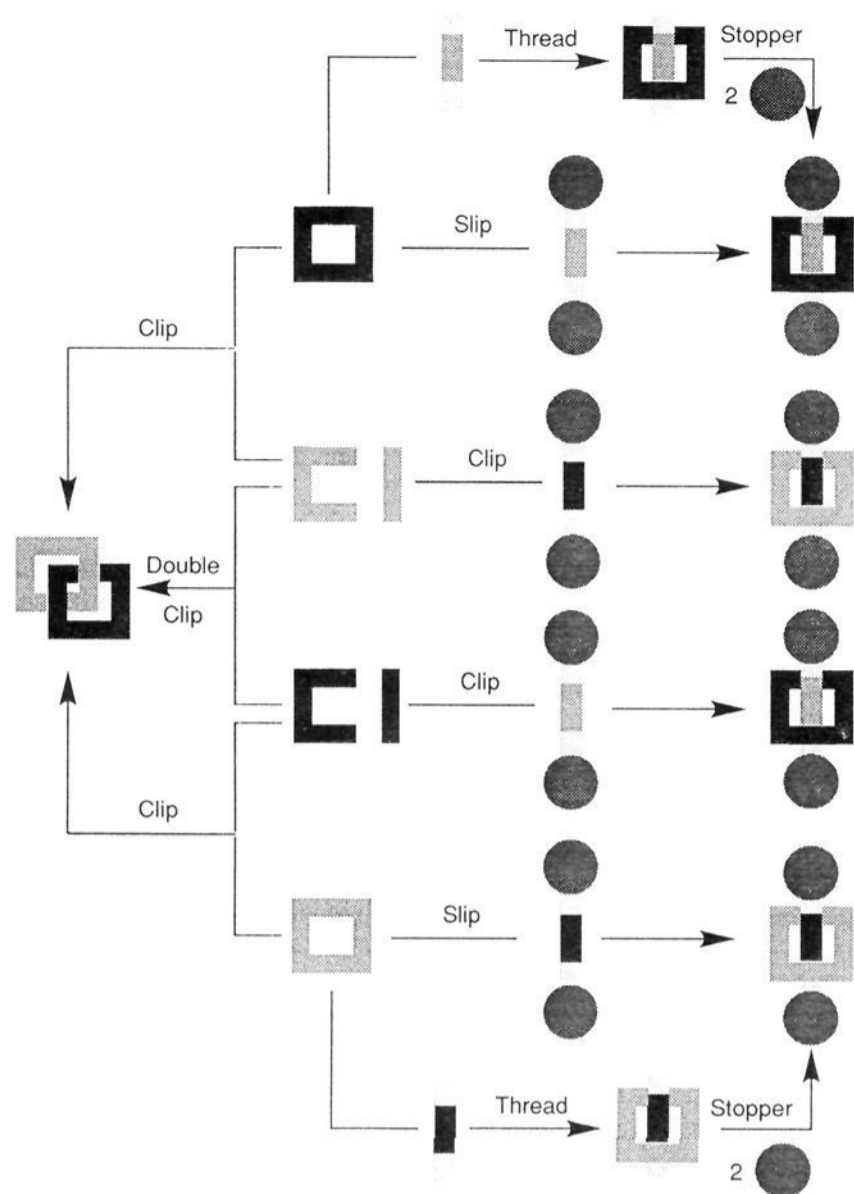


Figure 141. Approaches in principle to the self-assembly of [2]rotaxanes and how they are related to the self-assembly of a [2]catenane.

rotaxanes.³⁹⁵ Furthermore, it is possible to adopt two complementary design logics around this π -donor/ π -acceptor system, and at least three methods of self-assembly (Figure 141). The rotaxanes can incorporate either π -electron-rich and π -electron-deficient aromatic units into the dumbbell components, with the complementary aromatic units located in the “beads”. The self-assembly of the rotaxanes can be achieved (Figure 141) by (i) *threading* a molecule through a preformed ring followed by stoppering the ends of the thread, (ii) *clipping* a macrocycle onto a preformed dumbbell, and (iii) *slipping* a preformed ring over the stoppers of a preformed dumbbell into a thermodynamically favorable site on the rod part of the dumbbell. This approach was first demonstrated by Harrison.³¹

Simple [2]rotaxanes incorporating a hydroquinone ring as the “station” have been prepared³⁵⁵ using both threading and clipping procedures (Figure 142). The two thread-like compounds **154** and **220** were combined independently with the cyclophane **153** in a mixture of lutidine and acetonitrile and triisopropylsilyl triflate was added to the reaction mixture. Purification by column chromatography on silica gel yielded the two [2]rotaxanes **221** and **222**, both in 22% yields. The clipping procedure also afforded (Figure 142) **222** in 14% yield. The X-ray crystal structure of **222** shows a remarkably similar geometry for both the included hydroquinone ring and the polyether chain to those for the 1:1 complexes formed

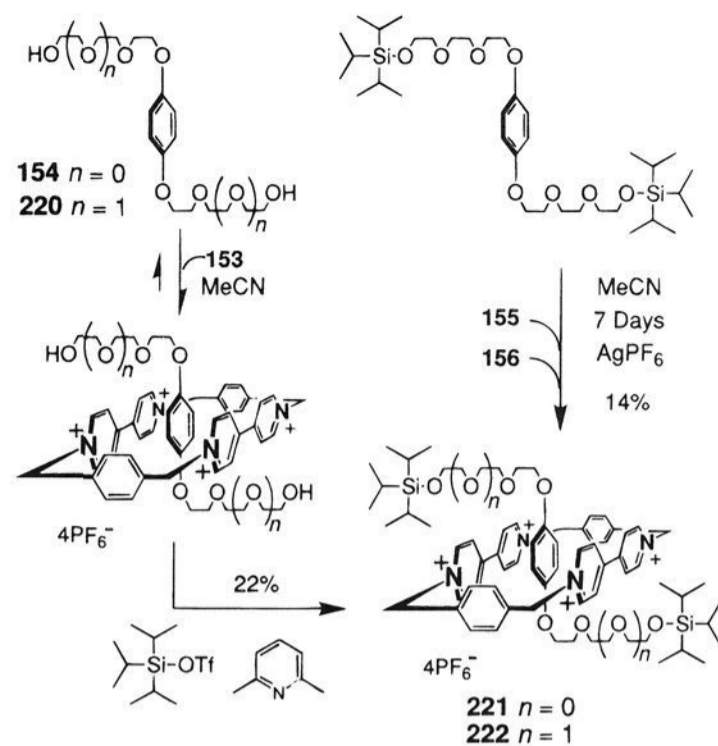


Figure 142. The self-assembly of [2]rotaxanes **221** and **222** by both threading and clipping procedures.³⁵⁵

by **153** with the analogous thread-like compounds. The shorter ethylene glycol chain in **221** results in a near-normal tilt angle of the hydroquinone ring with respect to the plane of the cyclophane, presumably as a result of the reduced distance between the two bulky stopper groups. Also, in this molecular structure, the interplanar separations between the complementary aromatic units are between 3.7 and 3.8 Å—the largest so far observed for this family of compounds. The clipping procedure was also used for the synthesis³⁹⁶ in 10% yield of a [2]rotaxane analogous to **222**, but in which adamantoyl stoppers prevent dethreading of the cyclophane from the dumbbell component. The X-ray crystal structure of this [2]rotaxane reveals a geometry for the included hydroquinone ring which is very similar to that observed in the solid-state structure of the [2]rotaxane **222**.

Increasing the number of π -electron-rich residues in the dumbbell component not only increases the yields during the self-assembly processes that form the rotaxanes, but it also enables “shuttling” of the bead along the rod of the dumbbell to occur in a [2]-rotaxane. The first “molecular shuttle”—the [2]-rotaxane **223**—that was described³⁹⁷ which relies upon this design was prepared in 32% yield by clipping (Figure 143) the components of **153** around the two-station dumbbell **224**. Variable-temperature ¹H NMR spectroscopy of the [2]rotaxane clearly reveals the movement of the cyclophane back and forth along the thread portion of the dumbbell. The free energy of activation for this shuttling process (Figure 143) was calculated to be around 13 kcal mol⁻¹. When the CD₃COCD₃ solution of the [2]-rotaxane is cooled down to -50 °C, the shuttling becomes slow on the ¹H NMR time scale, as witnessed by the appearance of an AA'BB' system arising from the “alongside” hydroquinone station (Figure 144), which was employed in a saturation transfer experiment to locate the resonance for the “inside” hydroquinone station at 3.8 ppm. Extension of the number of hydroquinone rings in the dumbbell

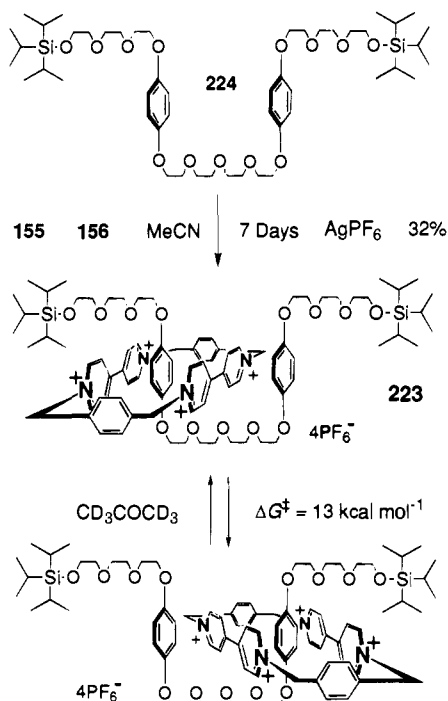


Figure 143. The self-assembly of the [2]rotaxane **223**, which, on account of its two hydroquinone recognition sites, behaves as a molecular shuttle.³⁹⁷

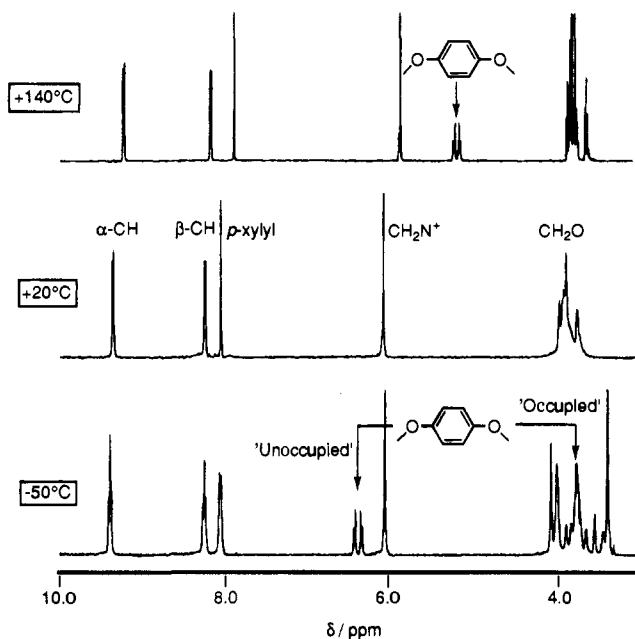
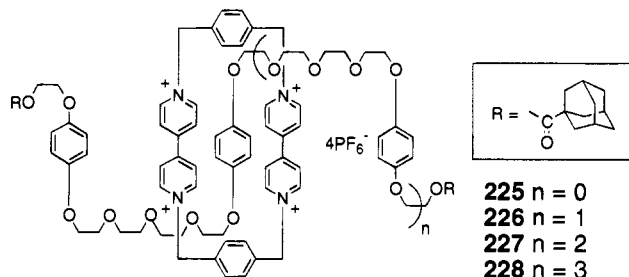


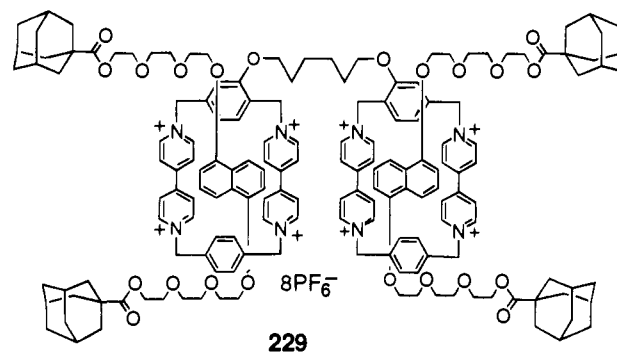
Figure 144. The temperature-dependent ^1H NMR spectra of the [2]rotaxane **223** recorded in CD_3COCD_3 at -50°C and $+20^\circ\text{C}$ and in CD_3SOCD_3 at $+140^\circ\text{C}$.³⁹⁷

component further enhances the yields of the [2]-rotaxanes.³⁹⁸ The series **225**–**228** was prepared by the clipping procedure described previously. The yield for the rotaxane with two stations was only 1% as a result of the proximity of the blocking group to the templating hydroquinone rings.³⁹⁹ The yields for the three-, four-, and five-station [2]rotaxanes were 25%, 29%, and 40%, respectively. Interestingly, no [3]rotaxane was formed by the dumbbell **228**, even at ultrahigh pressures. The observation that higher rotaxanes are not formed is despite the fact that a macrocycle incorporating four hydroquinone rings

does template the formation of two tetracationic cyclophanes to form a [3]catenane. Variable-temperature ^1H NMR spectroscopic studies in CD_3COCD_3 revealed that in the [2]rotaxane incorporating three hydroquinone rings, the two outer “stations” were not occupied at all as indicated by ^1H NMR spectroscopy at -20°C . Similarly, the [2]rotaxane **227** exists as only one translational isomer in solution at low temperatures. However, two translational isomers were observed (Figure 145) for the [2]rotaxane **228**. Each of the three central hydroquinone rings are occupied equally in solution at low temperature, two of them giving rise to degenerate structures, with a translational isomer ratio of 2:1 in CD_3COCD_3 .



The recently reported route to a bis[2]catenane has also been used for the synthesis³⁸⁶ of the bis[2]-rotaxane **229**. This compound was self-assembled in 7% yield from the same cyclophane components as were used for the bis[2]catenane, but employing as the dumbbell component an adamantoyl stoppered 1,5-dioxynaphthalene-containing thread.



The incorporation of two different π -electron-rich residues into the dumbbell component of these [2]-rotaxanes leads⁴⁰⁰ to the creation of potential molecular switches, in which some stimulus—be it chemical, electrochemical, or photochemical—disturbs the equilibrium position of the translational isomers (Figure 146).

In the first attempt⁴⁰¹ at the creation of a controllable [2]rotaxane, one of the hydroquinone rings in the prototypical shuttle **223** was replaced by a *p*-xylyl unit. The dumbbell **230** was reacted with the components of the small tetracationic cyclophane **153**, resulting in the self-assembly (Figure 147) of **231** in only 8% yield, *i.e.* comparable to the low yields achieved where only one templating unit was present in the thread. It was expected that the cyclophane would reside on the hydroquinone ring predominantly and that oxidation of this residue would result in movement of the cyclophane to the *p*-xylyl unit.

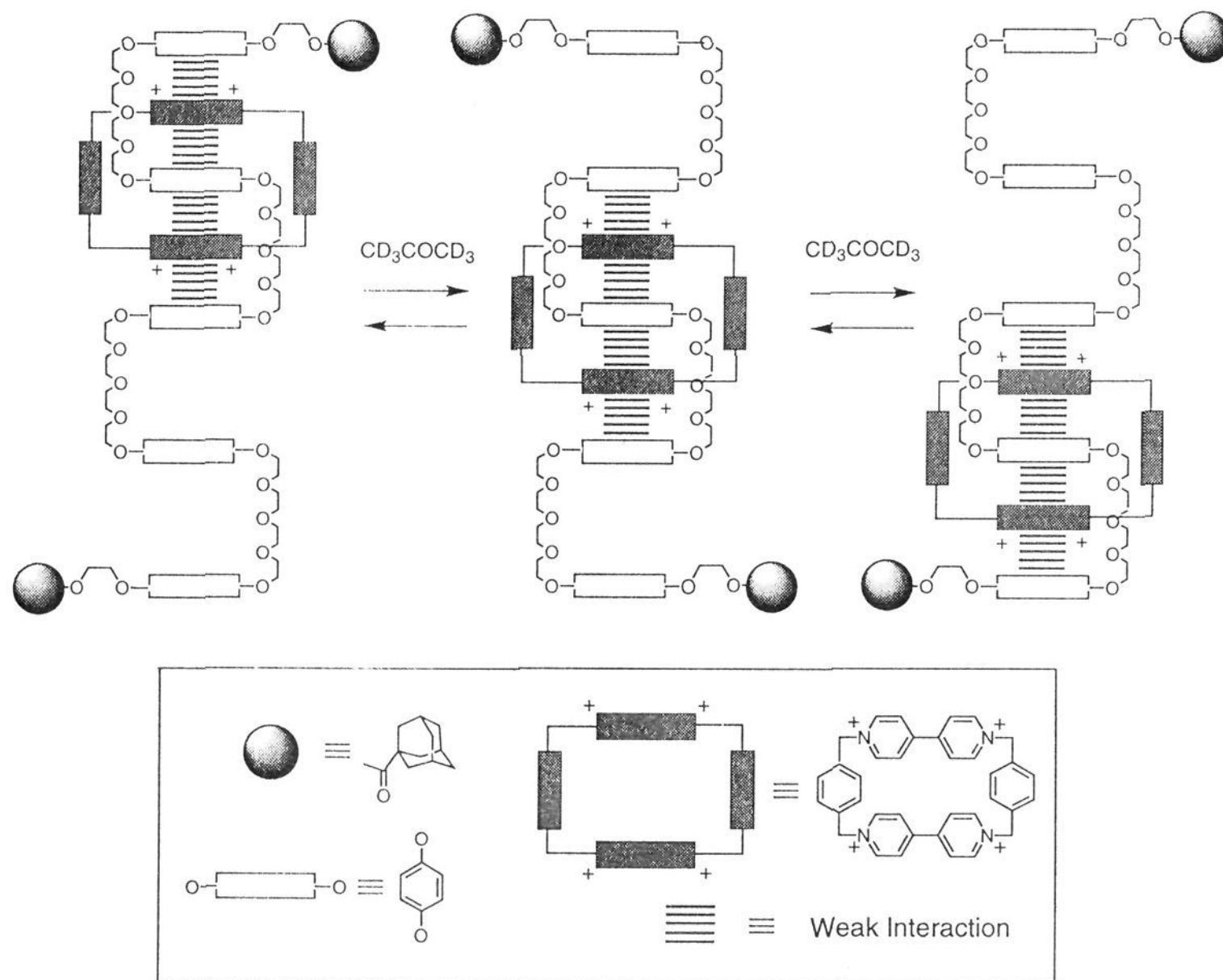


Figure 145. The equilibration in solution between degenerate species and translational isomers of the [2]rotaxane **225**.³⁹⁹

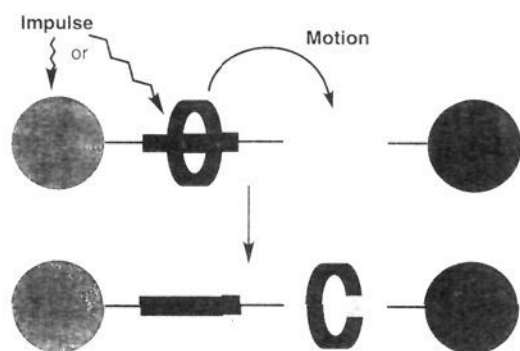


Figure 146. A cartoon indicating the principle for bringing about a switch in action between two translational isomers in a [2]rotaxane that can behave as a molecular shuttle.

However, the ^1H NMR spectrum of the compound in CD_3CN at 233 K showed that the ratio of the translational isomers (Figure 147) is only 70:30 in favor of the more π -electron-rich site. Rapid equilibration of the cyclophane between the two stations can be achieved by warming the sample up to 70°C . Replacement⁴⁰² of the *p*-xylyl residue with the more π -electron-rich indole unit also proved to be less than successful in answering the need for a controllable [2]rotaxane. The dumbbell compound **232** was synthesized by utilizing an efficient Fischer indole synthesis in the final step. The [2]rotaxane **233** was self-assembled (Figure 147) using the clipping method in 9% yield. The [2]rotaxane exists exclusively as the translational isomer in which the cyclophane encircles the hydroquinone ring, a result which is believed reflects the greater steric demands of the indole unit.

Tetrathiafulvalene (TTF) residues are powerful π -electron donors and consequently they are easily oxidized. In addition, the cyclophane **153** forms a

complex⁴⁰³ with TTF which crystallizes with a pseudorotaxane-like geometry. It therefore seemed that a TTF residue was an ideal choice for incorporating into molecular shuttles. The dumbbell component **234** (Figure 148) represents a slightly modified design⁴⁰⁴ with two degenerate stations located on either side of the TTF residue. Following the investigations on pseudorotaxanes, two hydroquinone rings were positioned one each side of the TTF residue in order to ensure that it was the most thermodynamically favorable position for the π -electron-deficient cyclophane to occupy. The self-assembly of the [2]rotaxane **235** was achieved in 8% yield, an efficiency that was disappointing. Preliminary ^1H NMR spectroscopic investigations suggest that the translational isomerism in this [2]rotaxane is highly solvent dependent. In CD_3COCD_3 , the cyclophane occupies exclusively the hydroquinone rings in the dumbbell, while in CD_3SOCD_3 , the TTF residue is the site which is occupied predominantly by the cyclophane.

In the search for alternative pairs of π -electron-rich aromatic "stations", 4,4'-biphenol and the much more π -electron-rich benzidine have been evaluated⁴⁰⁵ as guests for the tetracationic cyclophane **153**. Benzidine forms a much stronger complex ($K_a = 1044 \text{ M}^{-1}$ in MeCN) than 4,4'-biphenol ($K_a = 140 \text{ M}^{-1}$ in MeCN), but ^1H NMR spectroscopic studies indicate that both complexes have pseudorotaxane-like geometries. The two π -donor units have been extended with ethylene glycol chains to afford the diols **236** and **237**, which have been converted (Figure 149) by the threading procedure into the [2]rotaxanes **238**

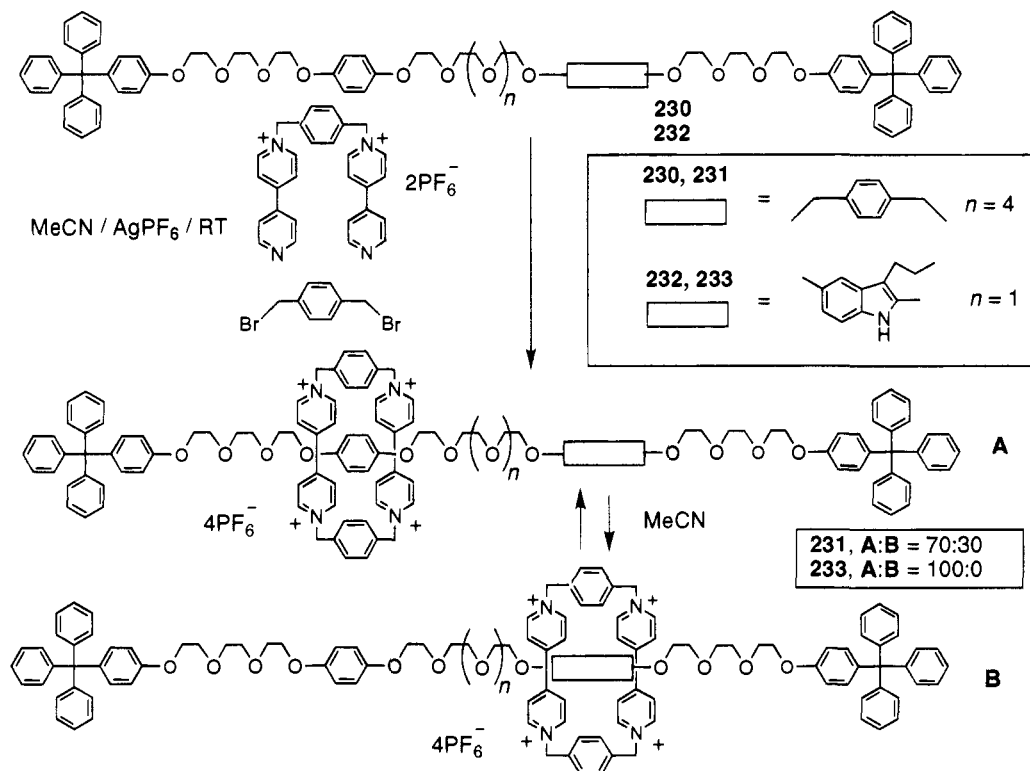


Figure 147. The self-assembly of two potentially controllable [2]rotaxanes **231** and **233** by clipping cyclobis(paraquat-*p*-phenylene) (**153**) around the dumbbell components **230** and **232**, respectively.^{401,402}

and **239** in 5% and 39% yields, respectively. The oxidation of the benzidine residue in **239** is reversible and comes at a higher potential than that of the free unit, as a result of the presence of the cyclophane. It has subsequently been reported⁴⁰⁶ that 1,4-phenylenediamine is also capable of matching the benzidine residue in its ability to template the formation

of an analogous [2]rotaxane. The next step in the research program was to attempt to self-assemble a controllable molecular shuttle. The [2]rotaxane **240** (Figure 150) was prepared⁴⁰⁷ in 19% yield by the same threading procedure as that used previously for the model systems. Its properties are remarkable. The [2]rotaxane **240** exists as two translational

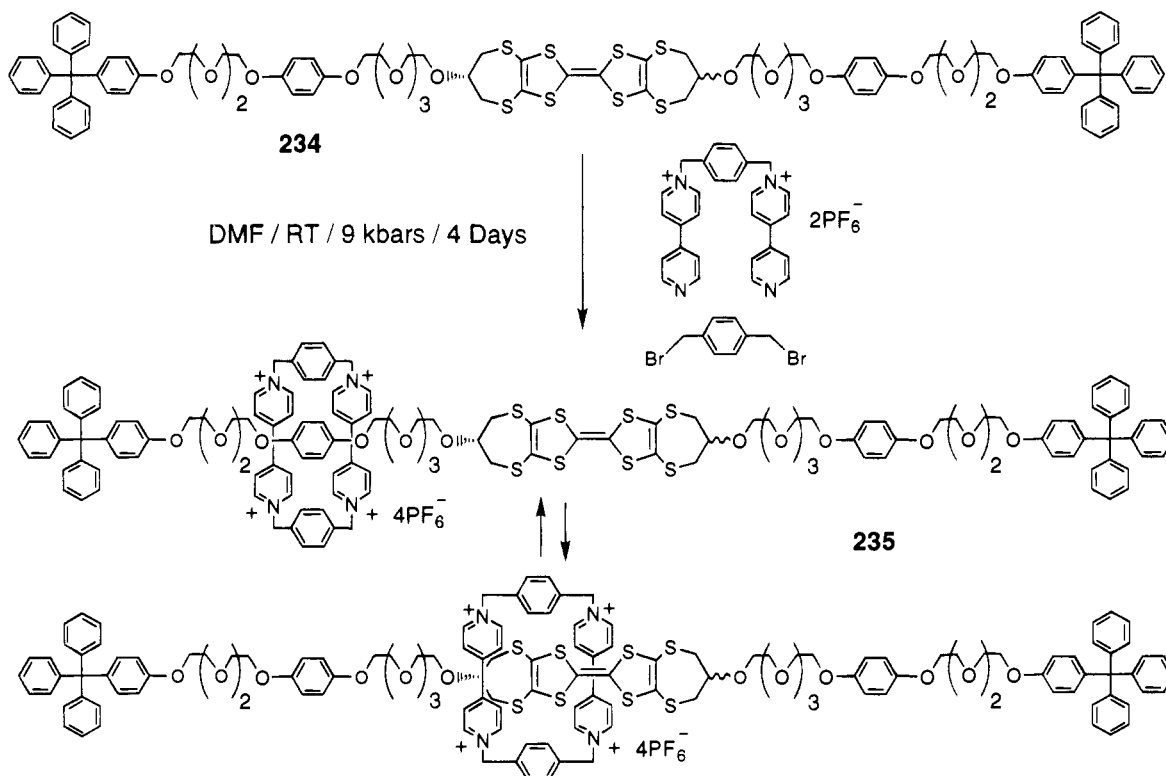


Figure 148. The self-assembly of a potentially controllable [2]rotaxane **235** by clipping cyclobis(paraquat-*p*-phenylene) (**153**) around the dumbbell compound **234**. The [2]rotaxane has two degenerate hydroquinone rings on either side of the TTF residue, rendering it a potentially binary switch.⁴⁰⁴

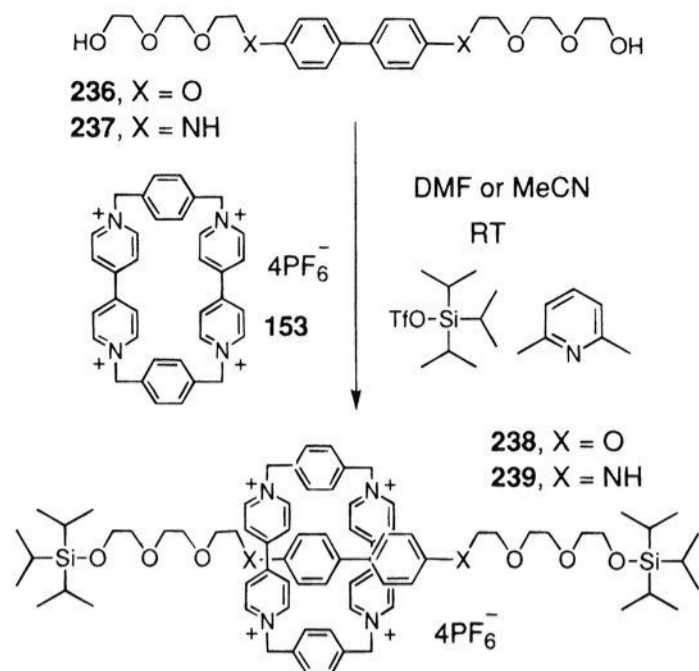


Figure 149. The self-assembly of [2]rotaxanes **238** and **239** by threading cyclobis(paraquat-*p*-phenylene) (**153**) on to the diols **236** and **237**, respectively, and blocking the primary hydroxyl groups with triisopropylsilyl ether protecting groups.⁴⁰⁵

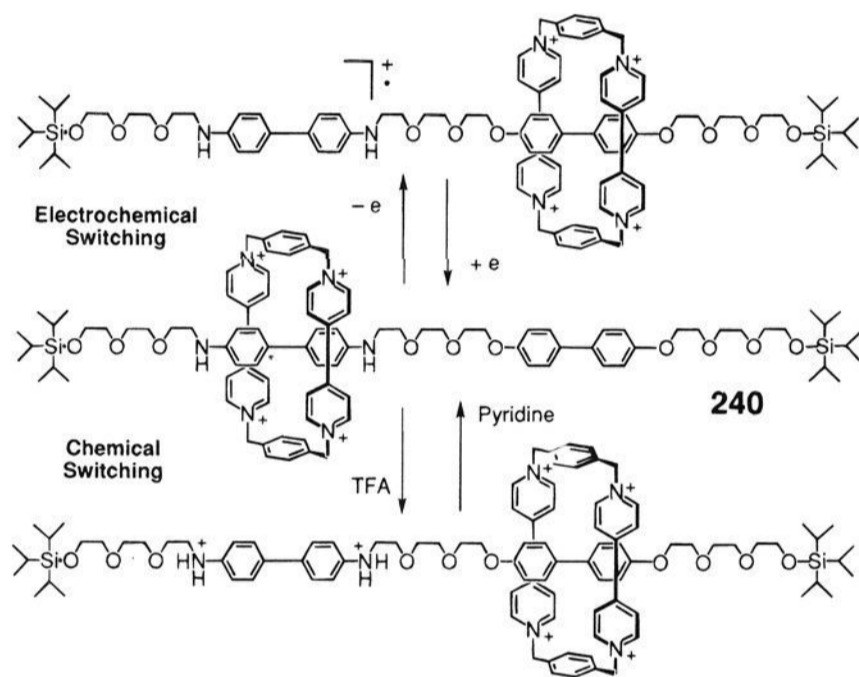
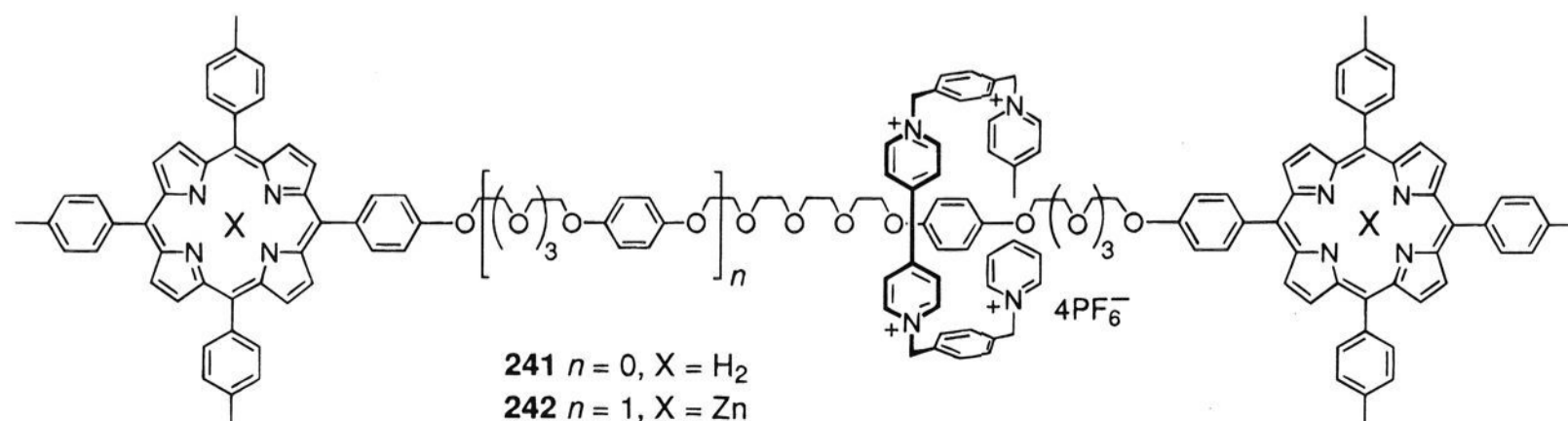


Figure 150. Controlling the molecular shuttle **240** both electrochemically and chemically.⁴⁰⁷

isomers in a ratio of 84:16 in CD_3CN solution at -44°C , with the major isomer being that wherein the benzidine residue is encircled by the cyclophane.⁴⁰⁷ When an excess of deuterated trifluoroacetic acid is added to the solution, only the translational isomer in which the 4,4'-biphenol residue is encircled by the cyclophane can be observed (Figure 149). This change in structure was brought about by protonation of the basic nitrogen atoms associated with the benzidine residue. Addition of deuterated pyridine returns the solution to neutrality, and reinstates the

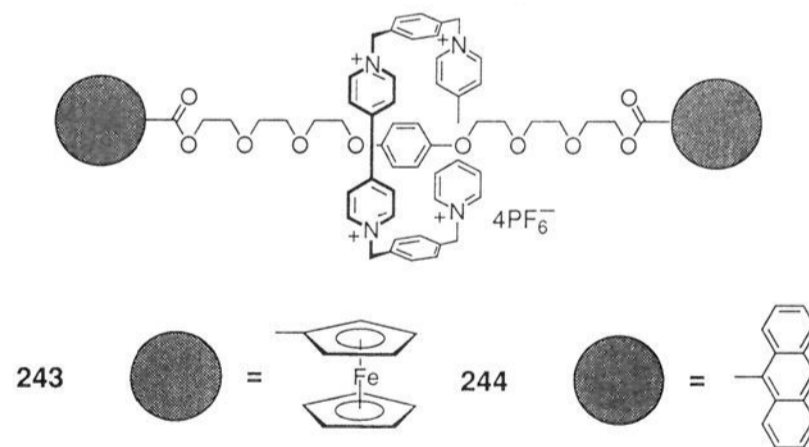
Chart 1



previous distribution of translational isomers. The system is entirely reversible under these conditions. This observation was supported at room temperature by UV-visible spectroscopy. Furthermore, electrochemical oxidation of the more π -electron-rich benzidine residue switches the translational isomer population to the form in which the 4,4'-biphenol unit is occupied (Figure 150). This conclusion was supported by comparison of the electrochemistry of **240** with those of the [2]rotaxane **239** and of a free benzidine thread-like compound. The potential of the first oxidation wave of the benzidine unit in the shuttle lies in between those observed for the simple [2]rotaxane and the free thread. The second oxidation wave, corresponded to the same potential as that observed for the free thread compound, showing that the cyclophane has moved stations after the first oxidation, presumably as a result of coulombic repulsion between the components. The [2]rotaxane **240** behaves therefore both as a chemically and electrochemically controllable molecular shuttle.⁴⁰⁷

The challenge of making a photochemically controllable molecular shuttle is a considerable one. Porphyrins have been incorporated⁴⁰⁸ successfully as the stopper groups into this family of rotaxanes. The [2]rotaxanes **241** and **242** (Chart 1) have been self-assembled using the clipping procedure. The shuttling properties of the [2]rotaxane **242** are very similar to those of the shuttle with the simple stoppers, the free energy of activation to this process being $13.6 \text{ kcal mol}^{-1}$. Thus far, none of the other physical properties of these rotaxanes have been reported in the literature.

Harriman and co-workers have described recently^{409,410} the self-assembly using the clipping method of the simple one-station [2]rotaxanes **243** and **244** incorporating ferrocenyl and anthracenyl stoppers in 6% and 25% yields, respectively. The high



yield of the [2]rotaxane in the case of the anthracenyl-stoppered dumbbell compound was attributed to the

additional templating afforded by the π -donating stoppers. The X-ray crystal structures⁴¹⁰ of both **243** and **244** show that the ferrocenyl and anthracenyl groups enter into "alongside" π - π stacking interactions with the tetracationic cyclophane component. The compounds were prepared in order to study the effects of the molecular entanglement in the structures upon the stabilities of the radical ion pairs formed by illumination of the charge-transfer band. The rotaxanes resemble molecular triads and allow the spatial separation of the primary redox charges. The rotaxane **243** was studied after illumination by a laser pulse at 437 nm. The charge-transfer band was presumed to be centered on 467 nm by analogy to previously reported rotaxanes.³⁵⁵ A species that was presumed to be a radical ion pair was observed. It decays relatively slowly (compared with silyl-stoppered rotaxanes), leaving a residual signal. The residual signal has a transient absorption spectrum very similar to that of the first-formed species and decays very slowly (lifetime 550 ns). It is believed that the radical ion pair was deactivated by rapid charge recombination, but partially by oxidation of one of the ferrocenyl stopper groups. This transfer separates the charges spatially. The ground-state situation is believed to be recovered by slow electron transfer from the radical cation of the cyclophane component to the cationic ferrocenyl stopper. Approximately 25% of the primary redox charge can be sustained for around 500 ns. The sluggishness of the charge recombination was initially proposed⁴⁰⁹ to arise from movement of the cyclophane component along the thread. However, a more recent report⁴¹⁰ suggests that this effect is partly a result of conformational change in the rotaxanes. Nonetheless, this rotaxane is a good example of the way in which combinations of electro- and photochemically active groups can be brought together within the confines of a mechanically linked system for the study of electron transfer phenomena, which may lead ultimately to photo-addressable devices. The anthracenyl-stoppered [2]rotaxane exhibited immediate charge recombination of the radical ion pair upon excitation.⁴¹⁰

The reverse design logic rotaxanes, where the dumbbell component of the rotaxane incorporates π -electron-deficient units and the bead incorporates π -electron-rich units, have also been constructed. The [2]rotaxane **245** was self-assembled⁴¹¹ in 23% yield under high-pressure conditions by the reaction (Figure 151) of the dication **155** with the large functionalized stoppers **246** in the presence of equimolar amounts of the macrocyclic polyether **150**. The shuttling of the π -electron-rich bead along the π -electron-deficient dumbbell is much faster than in the rotaxanes based on the alternative design logic. The movement of **150** was only slowed down on the ¹H NMR time scale at -80 °C. The free energy of activation to the shuttling process is 9.9 kcal mol⁻¹. The rate of movement by the crown ether from one bipyridinium site to another at room temperature is estimated to be around 300 000 s⁻¹.

Tuning the size of the stopper groups in the dumbbells **247** has allowed the preparation⁴¹² of [2]-rotaxanes using a thermodynamically driven slippage of the macrocyclic polyether ring over the bulky

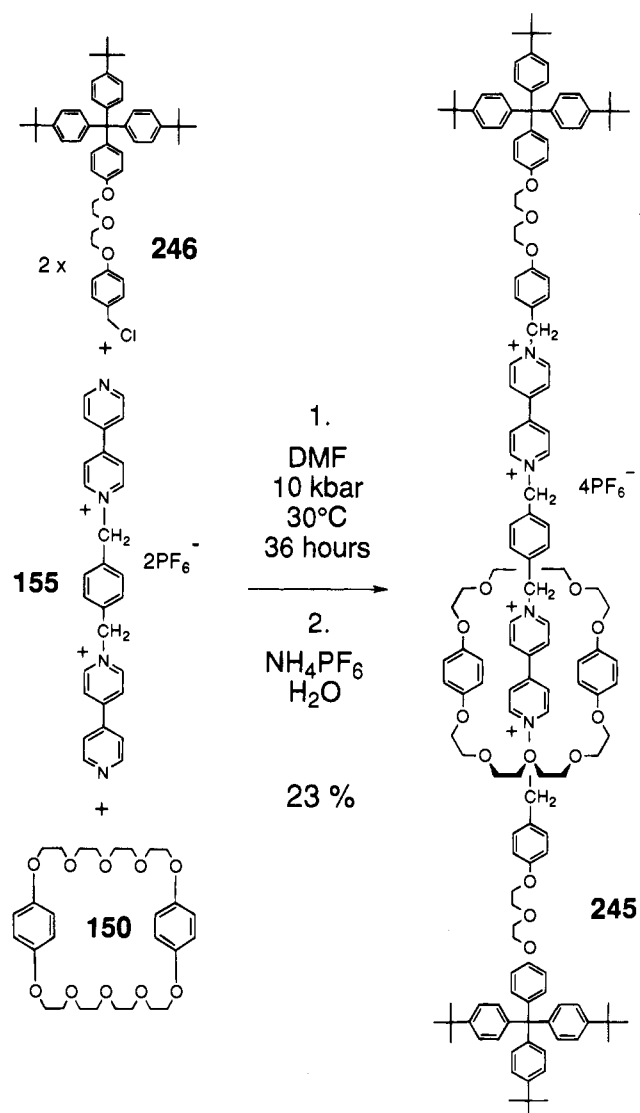


Figure 151. The self-assembly from four components of the [2]rotaxane **245** that behaves as a molecular shuttle.⁴¹¹

stopper groups. The stopper group **246** has three *tert*-butyl groups attached at the available 4-positions on the tetraaryl methane group. This stopper is too large to permit slippage of the macrocyclic polyether **150** when it is incorporated into a dumbbell containing one station. Replacement of one of these *tert*-butyl groups with the progressively smaller isopropyl, ethyl, and methyl groups and finally with a hydrogen atom gives the range of single-station dumbbells **247**. Heating the dumbbell compounds (Figure 152) in acetonitrile at 60 °C with 4 molar equiv of **150** afforded the [2]rotaxanes **248** in 47%, 45%, and 52% for the cases in which the stoppers have ethyl, methyl, and hydrogen at the 4-position (*R*), respectively. The isopropyl group was found to be too large to allow slippage. The yield of the [2]rotaxane with the hydrogen atom at the lone *R*-position (**247**, *R* = H) could be increased to 87% by heating the dumbbell compound with 10 molar equiv of **150**. The [2]-rotaxanes were stable at room temperature, and were purified by chromatography, although the reverse process—slipping off of the bead—was observed for the [2]rotaxane **248** (*R* = H) in CD₃SOCD₃ at 100 °C. The same process was less than 25% complete after heating at 60 °C in acetonitrile for 6 h. The second-order rate constants associated with the formation

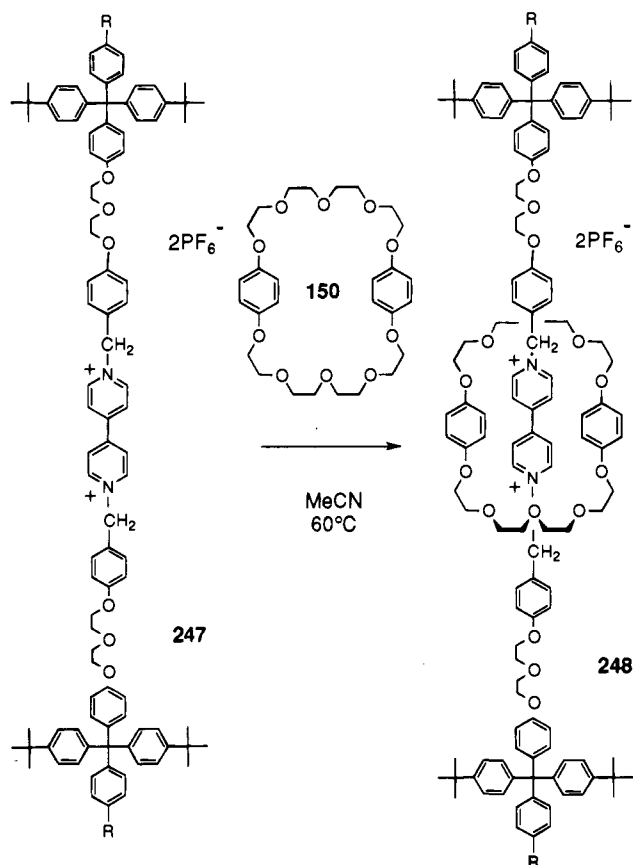
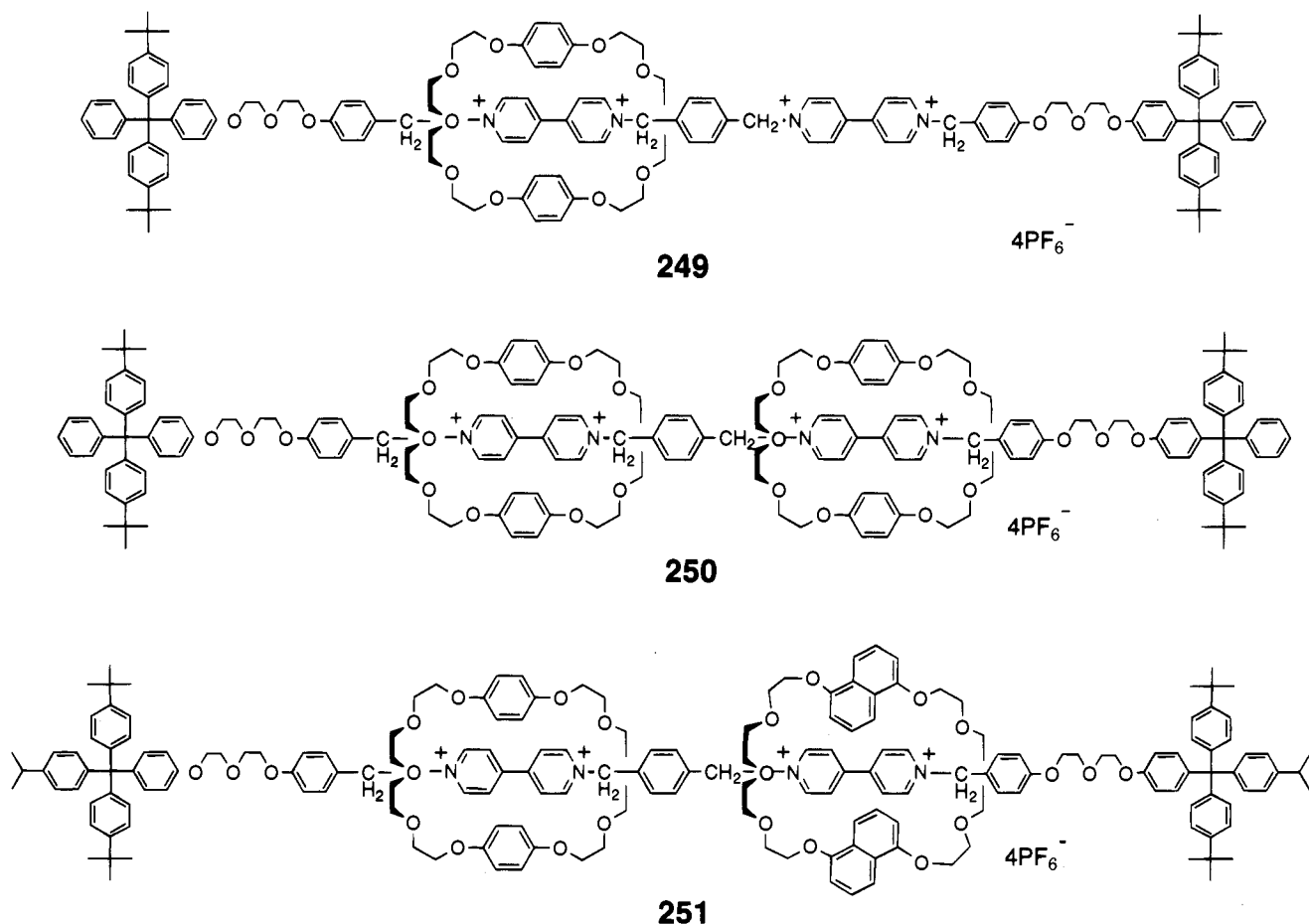


Figure 152. The preparation of the [2]rotaxane **248** from the dumbbell compound **247** and bis-*p*-phenylene-34-crown-10 (**150**) by slippage.⁴¹²

of the [2]rotaxanes were almost identical for the three different slippage processes. The slippage methodology allows those rotaxanes which are not readily accessible using either the clipping or the threading methodologies to be self-assembled rather easily. Gibson and co-workers⁴¹³ have also claimed the synthesis of a similar [2]rotaxane, incorporating one 4,4'-bipyridinium residue, in 94% yield. However, no details are available to our knowledge in the open literature.

The slippage procedure has been applied to the synthesis⁴¹⁴ of the [2]rotaxane **249** and the [3]rotaxane **250** (Chart 2) from the same dumbbell compound incorporating two bipyridinium units. The yields of the [2]- and [3]rotaxanes were 31% and 8%, respectively, when the dumbbell compound was heated with 4 molar equiv of **150** for 10 days at 55 °C. When 10 molar equiv of the crown ether were used in the reaction mixture, the yields of the rotaxanes increased to 20% and 55%. The free energy of activation to the shuttling process was, as expected, the same as that observed in the [2]rotaxane **245**. An interesting feature of this particular synthesis is that once again, a product that cannot be synthesized readily using the threading approach even at ultrahigh pressures, can be obtained in good yield by slippage. The success of the procedure is a result of the size complementarity between the stoppers and the bead component, and the molecular recognition between the rod section of the dumbbell and the macrocyclic polyether.

Chart 2



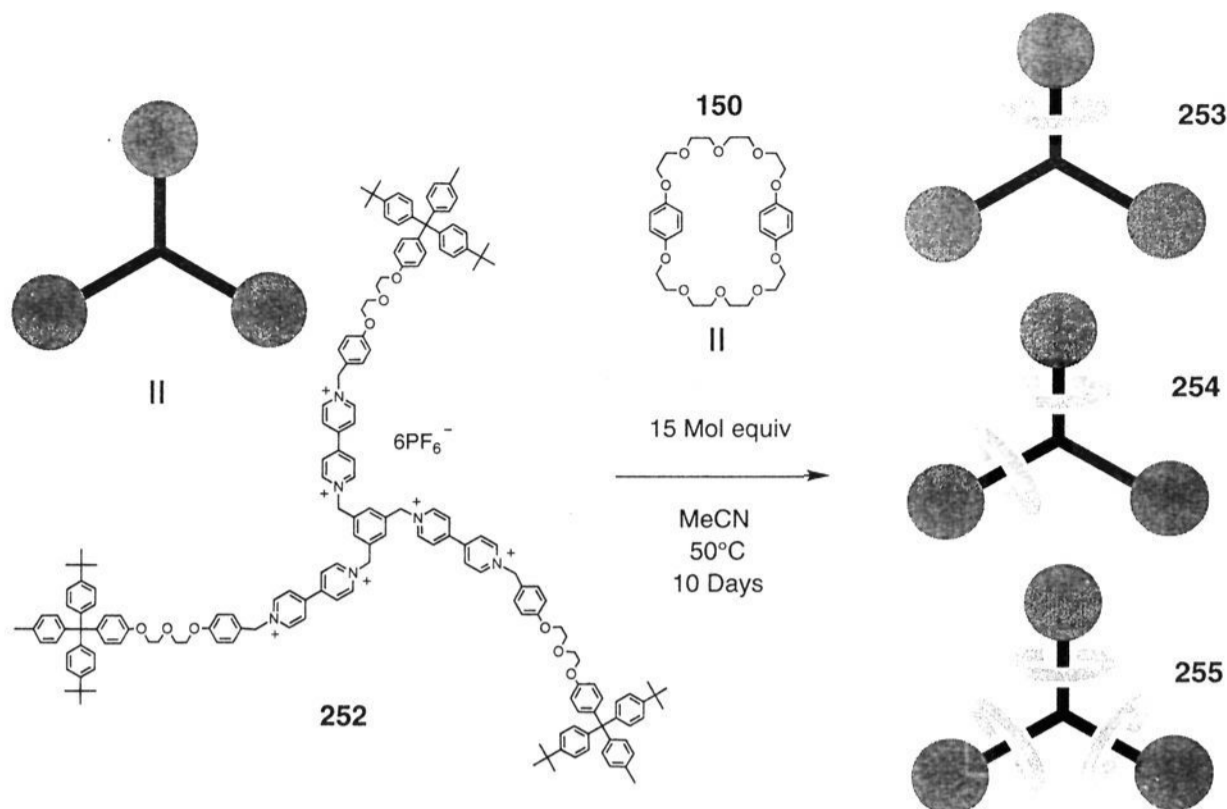


Figure 153. The first step toward dendritic rotaxanes. The preparation of the [2]rotaxane **253**, the [3]rotaxane **254**, and the [4]rotaxane **255** from the common three-way bolas-like compound **252** and bis-*p*-phenylene-34-crown-10 (**150**) by slippage.⁴¹⁶

The attributes of self-assembly using the slippage procedure have been emphasized in the preparation⁴¹⁵ of the [3]rotaxane **251** (Chart 2). It has two *different* bead components which are introduced one after the other using, firstly, threading of the smaller macrocycle, and then secondly, slippage of the larger macrocycle. In addition, the three-way bolas-like compound **252** has been heated with 15 molar equiv of **150** to form⁴¹⁶ (Figure 153) the [2]rotaxane **253**, the [3]rotaxane **254**, and the [4]rotaxane **254** in 19%, 41%, and 22% yields, respectively. These branched rotaxanes have been heralded as the first step toward dendritic rotaxanes!

VIII. Hydrogen Bonding for Catenane and Rotaxane Self-Assembly

A. Amide-Containing Interlocked Compounds

In 1992, Hunter⁴¹⁷ reported the discovery by accident of a new class of catenanes. The macrocycle **256** had been shown to be a receptor for *p*-benzoquinone.⁴¹⁸ Its original preparation was achieved by the reaction of the bis-amine **257** and isophthaloyl chloride. An improvement to this synthesis was sought in the form of a stepwise route, in which the bis-amine **258** was prepared (Figure 154), before being reacted with isophthaloyl chloride under high dilution conditions to yield the desired macrocycle **256** in 51% yield. In addition, however, the [2]-catenane **259** was isolated in a remarkable 34% yield (more recently⁴¹⁹ reported to be 29%). It was characterized by fast-atom bombardment mass spectrometry, as well as by an extensive variable-temperature ¹H NMR spectroscopic study, the findings of which were supported by molecular mechanics calculations.

The geometries of the identical component macrocycles relative to one another are well defined in solution, and reveal the nature of the intermolecular noncovalent interactions that are responsible for the formation of the [2]catenane in the first place. There are several intercomponent hydrogen bonds between

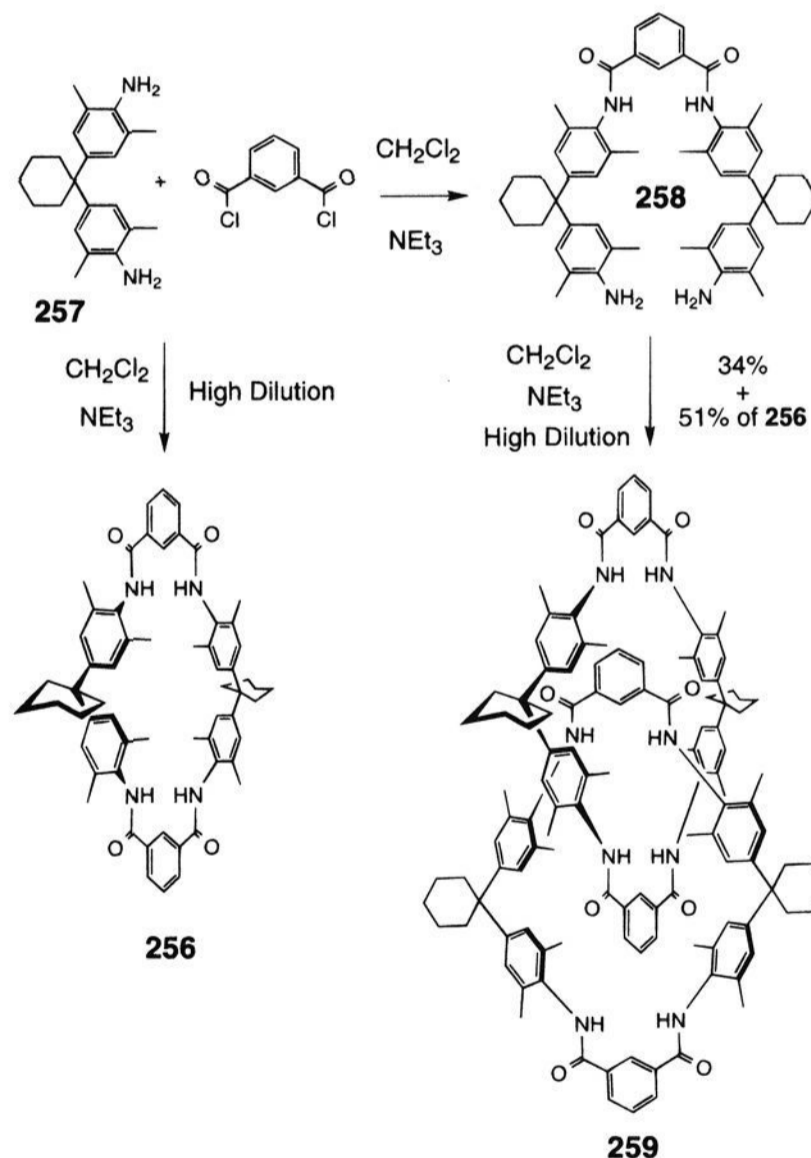


Figure 154. The synthesis of the first amide-based [2]-catenane reported by Hunter.⁴¹⁷

the amide functions as well as interactions between the aromatic rings. Unlike the [2]catenanes discussed in section VII, there is no equilibration between the “inside” and “outside” parts of each macrocycle. This equilibration process is prevented by the presence of cyclohexyl substituents on each macrocycle, which behave as “spokes”. However, a second process (Figure 155) was observed which involves equilibration between the two enantiomeric forms of the catenane. The chiral ground state,

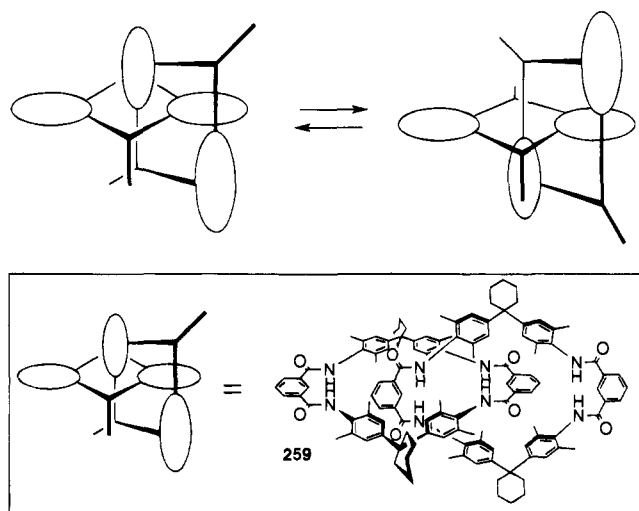


Figure 155. The equilibration between two enantiomeric forms of the [2]catenane **259**.

resulting from the restricted motions of the non-equivalent "inside" isophthaloyl moieties, was revealed by treatment of a $\text{CDCl}_3/\text{C}_2\text{D}_2\text{Cl}_4$ solution of the [2]catenane with two different lanthanide shift reagents, both of which caused increases in the number of resonances arising from appropriate probe protons.

When the bis-amine **258** was reacted⁴¹⁹ with 2,5-pyridinedicarbonyl chloride (Figure 156), it resulted in a 29% yield of the [2]catenane **260**. It was suggested that catenane formation proceeds by the complexation of an intermediate to the cyclic "tetramer" **261** through the center of the cyclic "dimer" of the two starting materials. The main product of the reaction was the cyclic "tetramer" **261**, as a result of the *cis* arrangement of the amide bonds adjacent to the pyridine unit. Replacement of the isophthaloyl group in **258** with a 2,6-pyridinediyl residue, followed by reaction with isophthaloyl chloride resulted in the formation of a cyclic tetramer only. No catenated

products were detected. Catenane formation is believed to be discriminated against by the unfavorable conformation of the two amide bonds adjacent to the pyridine unit.

Shortly after Hunter's first report of the [2]catenane **259**, Vögtle and co-workers⁴²⁰ described the synthesis of a closely related compound, in which methoxy substituents are attached to the 5-positions of the *meta*-substituted aromatic unit. The [2]catenane **262** was prepared (Figure 157) under high dilution conditions in a single step in 8.4% yield, starting from the diamine **257** and the diacid chloride **263**. When the methoxy group in the precursors to **263** were replaced with a nitro substituent, no catenated products were detected, possibly as a result of competitive hydrogen bonding by these appended groups to the amide moieties in the host macrocycle.

Vögtle and co-workers⁴²¹ have used the positioning of substituents on the 1,3-phenylene unit in this range of [2]catenanes to probe the mechanism of their formation. The Bonn group set out to prepare isomeric [2]catenanes in which one substituent on each of the component rings could be directed "in" or "out" with respect to the other interlocked cycle, by virtue of the absence of circumrotation between the rings in these systems. The isomers **264A**, **264B**, and **264C** were prepared in a manner similar to Hunter's original route, except that the OMe substituent was attached either to dicarbonyl chloride or to the diamine building block (Figure 158). The two different routes produced different results. The reaction (Figure 158) of **263** with **258** afforded a much lower yield of catenanes than the corresponding route in which isophthaloyl chloride was reacted with **265**. In the latter case, the "out"–"out" isomer was slightly preferred to the isomer in which one of the substituents was directed at the interlocked macrocycle. It was proposed that steric hindrance disfavored the host–guest complex formed by the first-formed macrocycle and the diacid chloride. A more likely explanation is contained in a footnoted suggestion that the

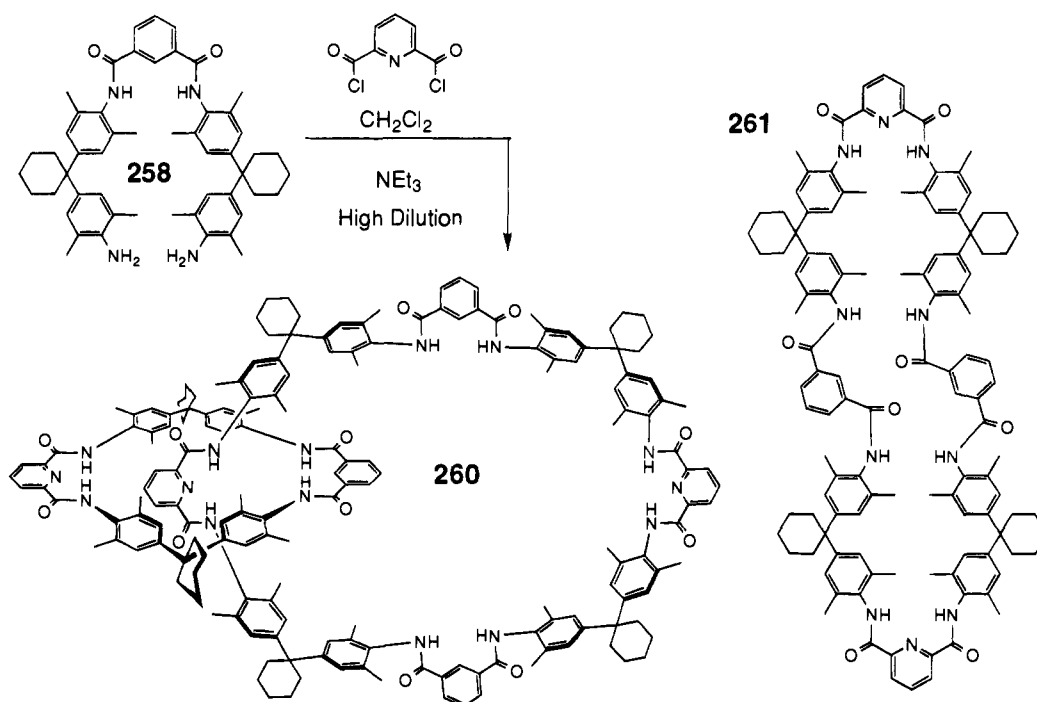


Figure 156. The synthesis⁴¹⁹ of the amide-based [2]catenane **260**, along with the cyclic "tetramer" **261**.

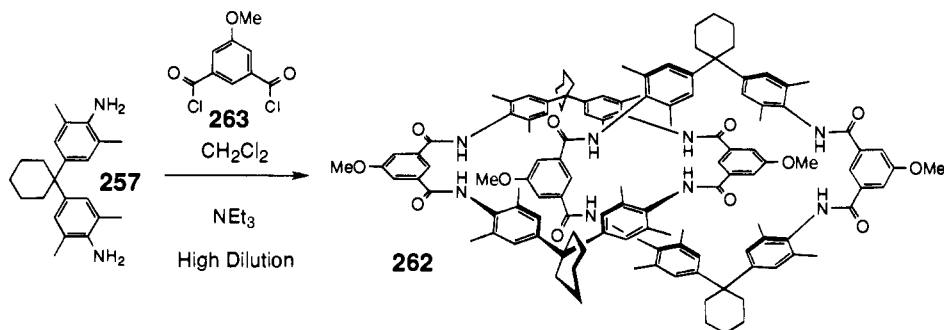


Figure 157. The synthesis of the amide-based [2]catenane **262** reported by Vögtle and co-workers.⁴²⁰

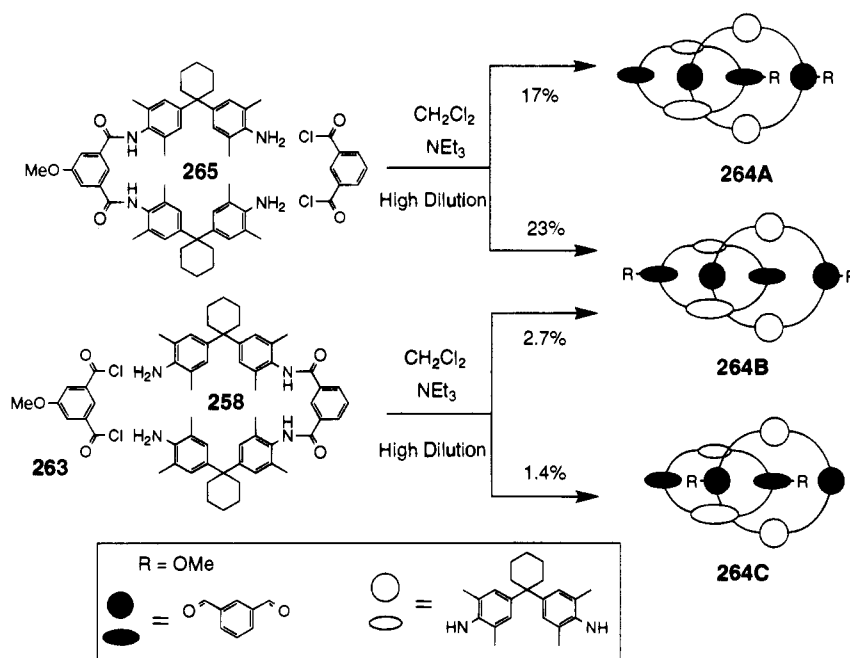
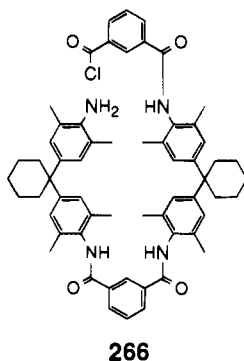


Figure 158. The synthesis of the amide-based [2]catenane **264**, which has been isolated as three different nonequilibrating translational isomers: **A**, **B**, and **C**.⁴²¹

acyclic amine adduct, similar to **266**, is the significant species for binding in the preformed macrocycle prior to catenation. The reaction⁴²¹ of **258** with isophthaloyl



chloride in the presence of the macrocycle **267** gave (Figure 159) the monosubstituted [2]catenane **268** in only 3% yield. Despite the fact that the Hunter [2]-catenane⁴¹⁷ **259** was formed in 34% (or 29%) yield under similar conditions to those used by Vögtle, the Bonn group did not report the isolation of **259** from the reaction.

Hunter⁴²² has subsequently progressed the research of the Sheffield group to the preparation of molecular threads which aggregate in solution, in the

form of “molecular zippers”. It is not clear at present whether these structures are actually intertwined or not.

A spate of publications concerning interlocked compounds of this amide-type has appeared very recently. Vögtle and co-workers have prepared⁴²³ the translationally isomeric amide-based furanocatenanes **269** and **270** (Figure 160) starting from the diamine **271** and isophthaloyl chloride. The [2]-catenanes were isolated in 8% and 20% yields, respectively. Interestingly, when **258** and 2,5-furandicarboxylic acid chloride were used, only the macrocyclic component was isolated. The authors concluded that molecular recognition ensured the *ortho*-substituted benzene ring was preferred by the host macrocycle prior to catenation. An X-ray crystal structure of **269** (Figure 161) has revealed the non-covalent interactions which are presumably responsible for its formation. The isophthaloyl moieties are located at the center of the molecule, each forming offset π -stacking interactions with *m*-xylylene residues. One of each of the carbonyl groups of one of the isophthaloyl units forms a hydrogen bond with the amide proton of the others. The other carbonyl group of the isophthaloyl units forms a bifurcated hydrogen bond with the amide groups attached to the 2,5-furandiyl units, which in turn form hydrogen bonds with the furan oxygen atoms.

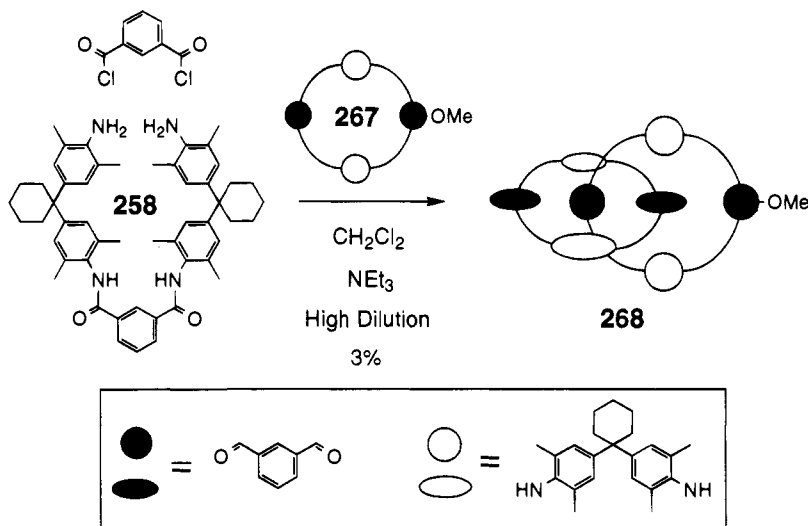


Figure 159. The synthesis of the amide-based monosubstituted [2]catenane **268**.⁴²¹

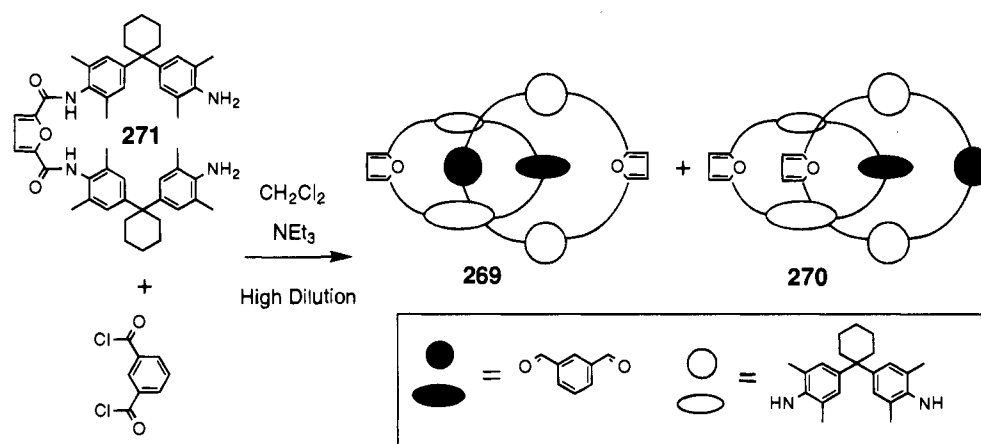


Figure 160. The synthesis of the translationally isomeric (but nonequilibrating) amide-based furano catenanes **269** and **270**.⁴²³

Very shortly after this communication and after several unstable crystals, Hunter finally reported⁴²⁴ the X-ray crystal structure of the [2]catenane **259** which has an extremely similar arrangement and pattern of hydrogen bonds between its components to that of the furanocatenane **269**. One of the oxygen atoms of the "inside" isophthaloyl carbonyl group is directed into the center of the molecule, while the other is directed toward the periphery where it forms the bifurcated hydrogen bond. The oxygen atoms of the "outside" isophthaloyl carbonyl groups are both directed away from the heart of the molecule.

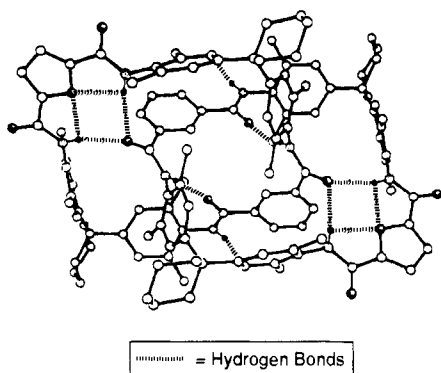


Figure 161. The ball-and-stick representation of the X-ray crystal structure of the amide-based furano catenanes **269**.⁴²³

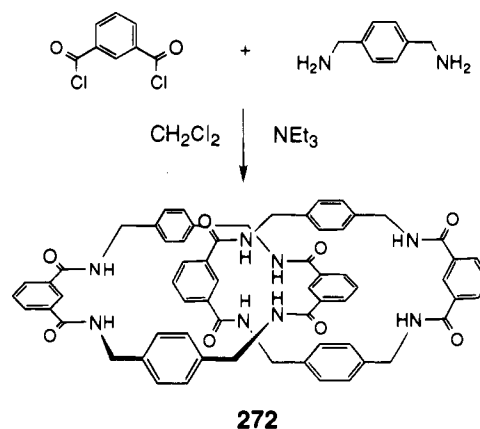


Figure 162. The synthesis of the benzylic amide [2]catenane **272** reported by Leigh and co-workers.⁴²⁵

At the same time, the group led by Leigh have reported⁴²⁵ the serendipitous synthesis of related benzylic amide [2]catenanes from commercially available materials. A condensation between isophthaloyl chloride and *p*-xylylene diamine (Figure 162) formed the [2]catenane **272** in a yield of 20%. As the authors pointed out, this yield is "remarkable for an eight molecule condensation". The X-ray crystal structure of the molecule revealed an extremely similar hydrogen-bonding pattern within each catenane molecule to that of the catenane **259**. In addition, a number

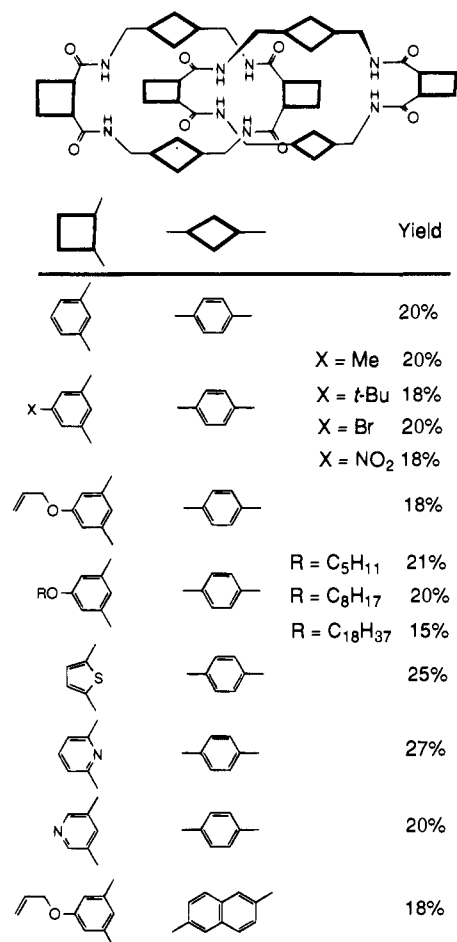


Figure 163. A range of benzylic amide [2]catenanes which have been synthesized.⁴²⁶

of π -stacking and hydrogen-bonding interactions result in a beautiful packing of the molecules to form a layer-like structure. Each layer is connected by hydrogen bonds. In solution, the two identical rings spin through one another rapidly on the ¹H NMR time scale at room temperature, despite the fact that the rings are really quite small.

The same group has illustrated⁴²⁶ the fact that the synthesis is very general, having prepared all the catenanes in Figure 163. In most cases, the starting materials are commercially available. It seems likely that the ease of preparation of these catenanes, particularly those which are functionalized, will lead to a wide variety of catenanes substituted with electro- or photoactive groups. They also open up the way to a variety of catenated polymers.

Vögtle and co-workers have gone on to prepare⁴²⁷ rotaxanes based on this amide hydrogen bond template effect. The [2]rotaxanes **273**, **274**, and **275** were produced according to the route given in Figure 164. The rotaxanes were isolated in 11%, 15%, and 3% yields, respectively. They were convincingly characterized by NMR and mass spectrometry.

The group from Bonn has also prepared⁴²⁸ [2]-catenanes in which sulfonamide groups replace some of the amide groups. The [2]catenane **276** was prepared in 10% yield according to the route shown in Figure 165. The replacement of SO₂NH with SO₂NMe increased the yield of the related [2]catenane to 19%. Interestingly, the [2]catenane **276** is topologically chiral though no resolution into enantiomers has yet been achieved.

B. Ammonium Ions for Rotaxane Construction

The complexation of dialkyl ammonium cations by crown ethers⁴²⁹ has inspired two groups to attempt the synthesis of interlocked compounds using this host-guest phenomena.

Busch and co-workers have prepared a [2]rotaxane in which dibenzo-24-crown-8 surrounds an ammonium ion-containing dumbbell.⁴³⁰ The rotaxane **277** was synthesized (Figure 166) by reaction of the amine **278** and the acylating agent **279**. When the reaction was performed in CHCl₃, a 12% yield of the rotaxane was obtained, while in a mixture of water and CHCl₃, a 22% yield was achieved. It was proposed, therefore, that the complex of the ammonium salt of **278** with dibenzo-24-crown-8 is located at the interface, where this pseudorotaxane is then acylated. An X-ray crystal structure of the [2]rotaxane shows the ammonium center located in the middle of the torus formed by the crown, where its hydrogen atoms form noncovalent bonds with two of the oxygen atoms in the macrocycle. In addition, the anthracene stopper group enters into π - π stacking interactions with one of the benzene rings in the crown ether.

Simultaneously, researchers in our own group had prepared pseudorotaxanes from the same crown ether and dibenzyl ammonium ions.⁴³¹ When a mixture of dibenzo-24-crown-8 and dibenzyl ammonium hexafluorophosphate are combined in solution, a strong complex is formed (Figure 167). X-ray crystallography of a crystallized sample showed (Figure 167) that the ammonium cation resides in the center of the host, with the benzyl groups of the guest protruding from either face of the crown ether.

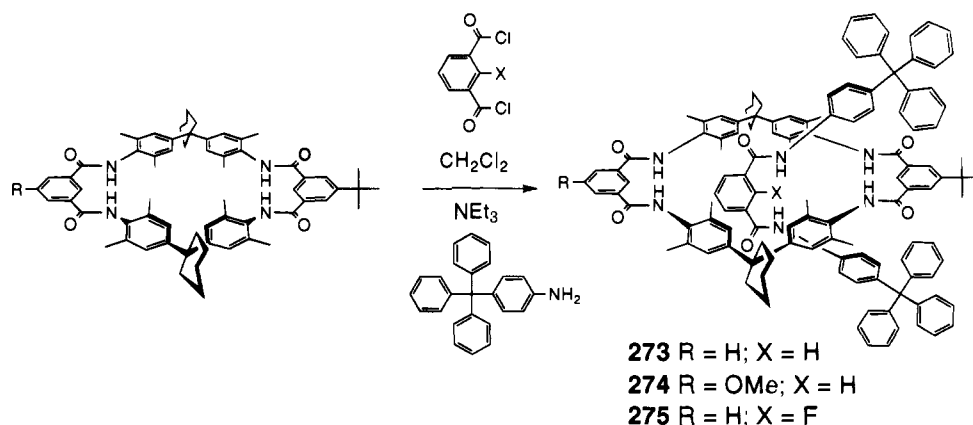


Figure 164. The synthesis of the amide-based [2]rotaxanes **273–275**.⁴²⁷

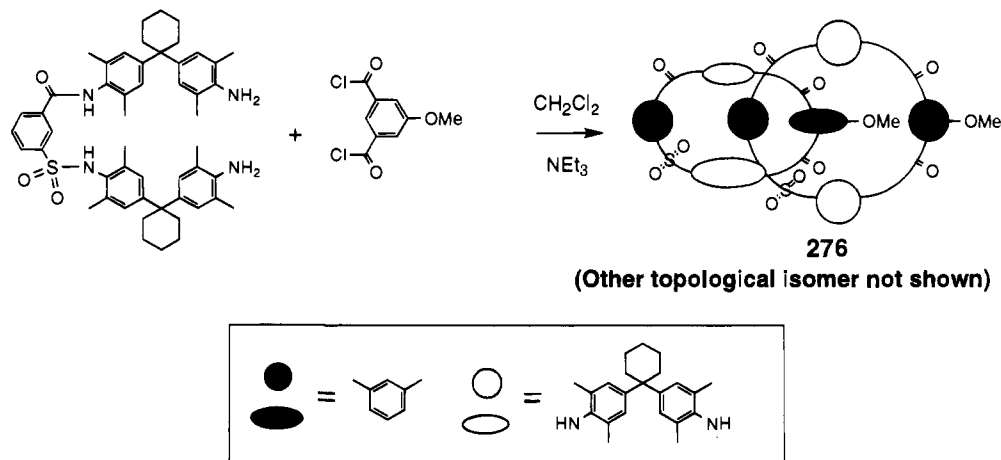


Figure 165. The synthesis⁴²⁸ of the sulfonamide-based [2]catenane **276** (one topological enantiomer shown).

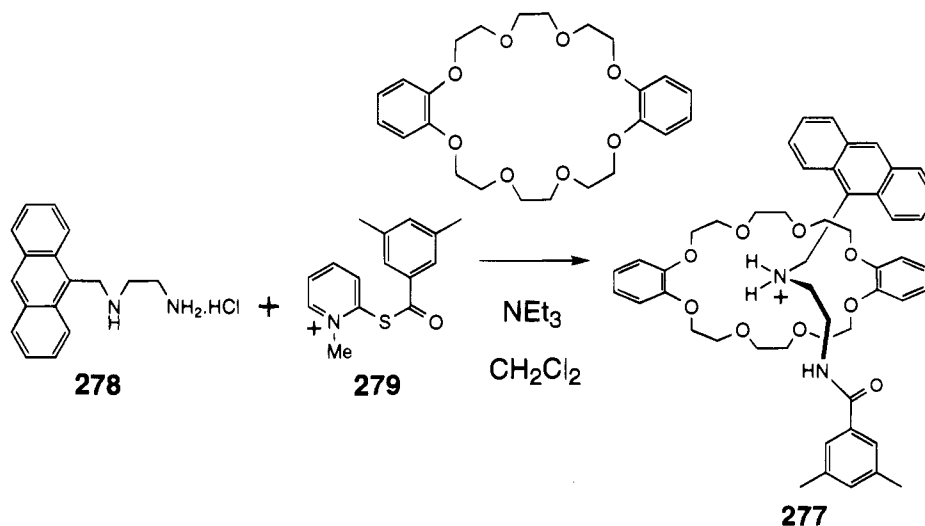


Figure 166. The self-assembly of the [2]rotaxane **277** as a result of surrounding a secondary dialkylammonium center with dibenzo-24-crown-8.⁴³⁰

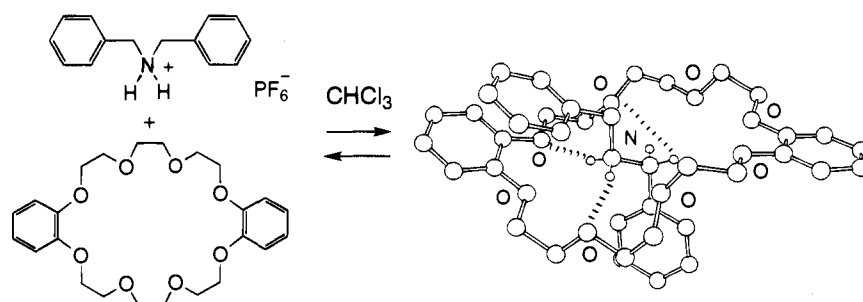


Figure 167. The self-assembly of a [2]pseudorotaxane from dibenzyl ammonium hexafluorophosphate and dibenzo-24-crown-8. The ball-and-stick representation of the X-ray crystal structure of the 1:1 complex reveals its pseudorotaxane nature. This complex is one of the two that are present in equal amounts in the unit cell of the crystal.⁴³¹

Hydrogen bonds between both hydrogen atoms attached to the nitrogen atom; in addition one of the hydrogen atoms, attached to the adjacent methylene group, forms a hydrogen bond with an oxygen atom in the crown ether. The binding constant (K_a) of the complex ranges from 27 000 M^{-1} in $CDCl_3$, to 360 M^{-1} in CD_3COCD_3 to 0 in CD_3SOCD_3 . In addition, dibutyl ammonium hexafluorophosphate forms a similar complex in the solid state, with the quaternary ammonium ion center nestling in the middle of the crown ether. The binding of this guest in the crown ether is weaker than that of the dibenzyl analog.

When dibenzyl ammonium hexafluorophosphate was crystallized⁴³² with the macrocyclic polyether bis-

p-phenylene-34-crown-10 (BPP34C10, **150**), a 2:1 complex resulted in which *two* of the ammonium ions were threaded through the center of the host. The hydrogen atoms attached to the quaternary ammonium form noncovalent interactions with oxygen atoms in the crown ether, although those attached to the adjacent carbon atoms do not. Crystallization⁴³² of the diammonium compound **280** with BPP34C10 (Figure 168) results in a 2:2 complex which is a double-stranded doubly encircled pseudorotaxane. Two of the guests **280** are threaded through two adjacent macrocyclic polyether hosts. The structure is stabilized by nine $[N-H\cdots O]$ and three $[C-H\cdots O]$ hydrogen bonds. These structures

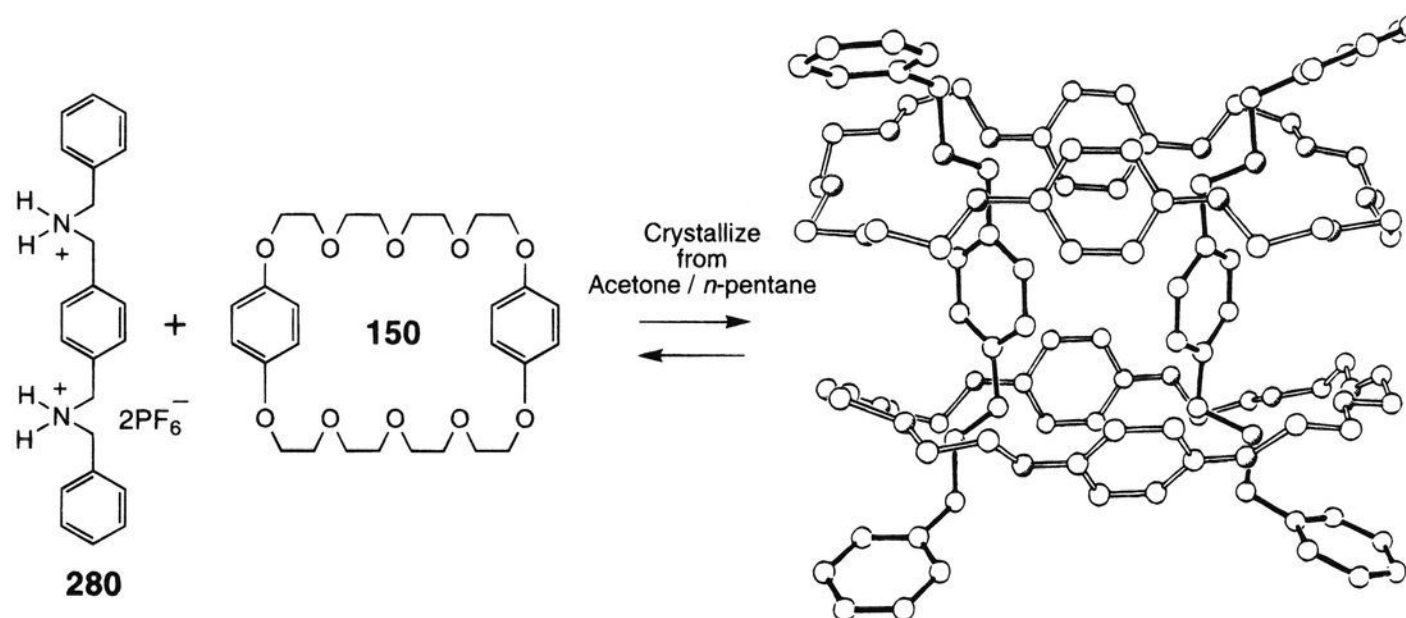


Figure 168. The self-assembly of a 2:2 complex from the dication **280** and bis-*p*-phenylene-34-crown-10 (**150**). The ball-and-stick representation of the X-ray crystal structure of the 2:2 complex emphasizes its double-stranded doubly encircled nature.⁴³²

illustrate the great potential that this recognition partnership has for the construction of interlocked, and indeed, intertwined, systems.

IX. The Construction of Geometrical Objects from DNA

In recent years, Seeman's group has demonstrated in a most impressive manner how DNA can be used for the construction of topologically complex unnatural interlocked structures.⁴³³ The New York team relies upon the specificity of Watson-Crick base pairing for the design of mutually compatible sequences of DNA that are adapted so as to form interlocked structures.

The design and realization of a synthetic knot comprised of a single-stranded DNA molecule was described⁴³⁴ in 1991. Two full turns of a DNA double helix is the starting point for a trefoil knot, which can be prepared by the appropriate connection of the termini of the double helix. Seeman and his co-

workers⁴³⁴ used two complementary 11-mer sequences of bases in a single strand of DNA to achieve their objective. The synthesis is shown schematically at the top of Figure 169. The single strand was designed such that the complementary sequences—A—A' and B—B'—were separated by oligo-T linkers (dT_n, where *n* = 7 or 15), and also so that the 5' and 3' ends of the strand fall between the eighth and ninth nucleotide of the A region. The resultant nick was sealed using a T4 DNA ligase. The strand containing 72 nucleotides (*n* = 7) failed to form a knot, while the strand incorporating 104 nucleotides (*n* = 15) formed a species that was determined, by a denaturing polyacrylamide gel, to be the trefoil knot. The compound had greater mobility than the corresponding circular DNA, and sedimentation studies on ³²P labeled linear strand, circle, and knot forms confirmed the hypothesis that the knot is the most compact form. Its sedimentation velocity is considerably faster than that of the related topological stereoisomers.

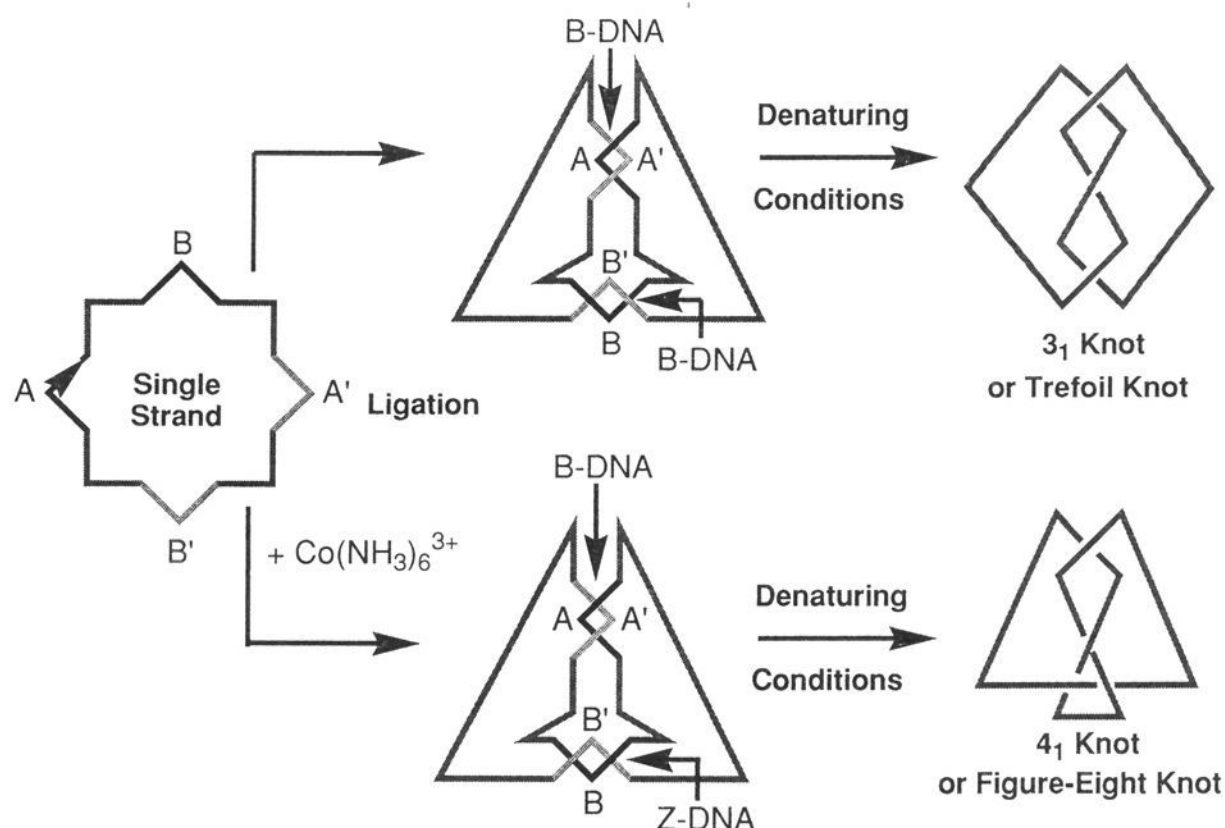


Figure 169. The preparation of a trefoil knot and a figure-eight knot from a single strand of DNA. The topological diastereomers are achieved by cyclization of an intermediate in which one of the double-helical regions contains B-DNA or Z-DNA, respectively.^{434,435}

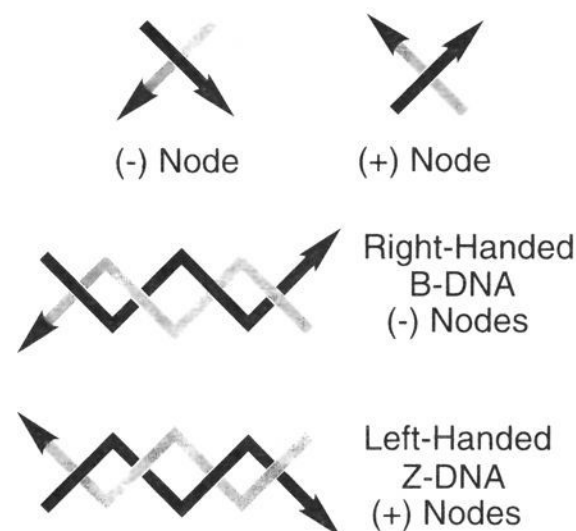


Figure 170. Designation of the nodes in DNA, where the arrows represent the 5' to 3' vector.

The same pairing strategy, that was used successfully for the construction of the 3_1 knot, has also been employed⁴³⁵ for the creation (Figure 169, bottom) of a figure-eight (4_1) knot, which contains two positive and two negative *nodes*. The designation of a node at a crossing point of an interlocked structure (Figure 170) is determined by the direction in which the strands are aligned in relation to one another. The direction of DNA has been defined as the 5' to 3' vector. The right-handed helix, formed by "normal" B-DNA, has exclusively negative nodes, while the left-handed Z-DNA double helix results in a superstructure with exclusively positive nodes. The undecamer B·B' domain used for the templating of the 3_1 knot, was replaced with a dodecamer duplex sequence [(dCpdGp)₆] which, when treated with Co(NH₃)₆³⁺ favors the Z-form of the DNA duplex. The spacing between the double helical domains employed a dT₁₄ or dT₁₅ sequence. The single strand was utilized by employing the same method used for the 3_1 knot. As determined by gel electrophoretic analysis, the product of the enzymatic ligation is the 4_1 knot with one positive and one negative node DNA base-paired regions. When the Co(NH₃)₆³⁺ was not present in the reaction to form the knot, the topologically stereoisomeric 3_1 knot, containing only negative nodes (B-DNA) was formed. In addition, restriction endonuclease digested both domains of the 3_1 knot, and only one domain of the 4_1 knot. Areas containing left-handed double helical regions are unaffected by the enzyme. Seeman's group has recently prepared⁴³⁶ four topologies—macrocycle, left-handed trefoil knot, right-handed trefoil knot, and a figure-eight knot—from a single strand of DNA. In addition, the group has reported⁴³⁷ the treatment of two synthetic DNA knots with *E. coli* DNA topoisomerases I and III. One of the knots, which both contain 104 nucleotides, was ligated to form cyclic DNA with the topologies of a circle, trefoil knot with negative nodes, or a figure-eight knot, while the other formed these three plus a trefoil knot with positive nodes. The positive or negative nodes derive from left-handed Z-DNA and right-handed B-DNA, respectively. The topoisomerases can be used to catalyze the interconversion of the different topological forms. The outcome of the reaction depends on whether conditions favor B- or Z-DNA.

While DNA double helices are unbranched, it is possible to manipulate the sequences of bases such that helices meet to form a branch point, or junc-

tion.^{438,439} The sequences of the strands that form junctions are designed such that the formation of the normally more favored double helices is precluded.⁴³⁸ Sequence symmetry must be minimized. Junctions⁴⁴⁰ formed by "double crossover" molecules have been studied extensively, since they are precursors to catenanes.⁴⁴¹ Junctions with up to six double-stranded arms have also been prepared.⁴⁴¹ It is possible to combine junctions by the introduction of overhangs of singly stranded DNA at the termini of the duplex—an area referred to as a cohesive or sticky end. Although, in principle, building base complementarity into different sticky-ended junctions opens the doorway into lattices, in practice, the ill-defined geometries of the flexible junctions results in the formation of many different structural types.⁴⁴² Despite this inherent flexibility of the units resulting in poorly controlled directing of the strands, they have been incorporated into designs⁴⁴³ for objects comprised of DNA.

The synthesis (Figure 171) of a quadrilateral has been achieved⁴⁴⁴ using the sticky-ended junction approach. Four different three-arm branched junctions, incorporating a long DNA strand paired with a short DNA strand, were designed such that one arm is an exocyclic one, in the form of a closed hairpin loop. Nonequivalent pairs of cohesive ends were incorporated into the complementary overhangs of each of the four junctions: two 3' overhangs and two 5' overhangs. The associated junctions were fused enzymatically at their cohesive termini, using bacteriophage T4 DNA ligase. The synthesis was carried out in a stepwise manner, since a combination of the four junctions in a single step gave comparatively lower yields of the quadrilateral, owing to the equilibration of the single strands present in the reaction mixture. Each side of the quadrilateral object—a hexatuply linked [2]catenane—contained one and a half turns of the double helix (16 nucleotides). Cleavage of two restriction endonuclease susceptible sites located in the exocyclic hairpins, led to a circular and single stranded DNA. Densitometer scans of an autoradiogram indicated that approximately 15% of the products constituted the cyclic tetramer. The unwanted product, in which only one of the strands was cyclized, was estimated to be produced in 5% yield. Higher cyclized products, *e.g.* a cyclic dimer of the quadrilateral, were not observed.

One of the most important considerations when Seeman's group is planning the syntheses of these more complex geometrical objects starting from DNA is the method of product characterization. Consequently, in the planned synthesis of a duplex DNA cube,⁴⁴⁵ unique sites were incorporated into the edges of the structure for subsequent scission by a restriction endonuclease. The cube was constructed in six main stages. The first two steps (Figure 172) involved the cyclization of phosphorylated 80-mer strands by ligation. Purification of the circles, followed by independent ligation and connection of the sticky ends linked the two squares in such a way as to form a third cycle between them. Purification of the resultant compound yielded a [3]catenane, and then a final ligation, followed by connection of the complementary sticky ends gave the three-dimensional three-connected object. The cube (Figure 172)

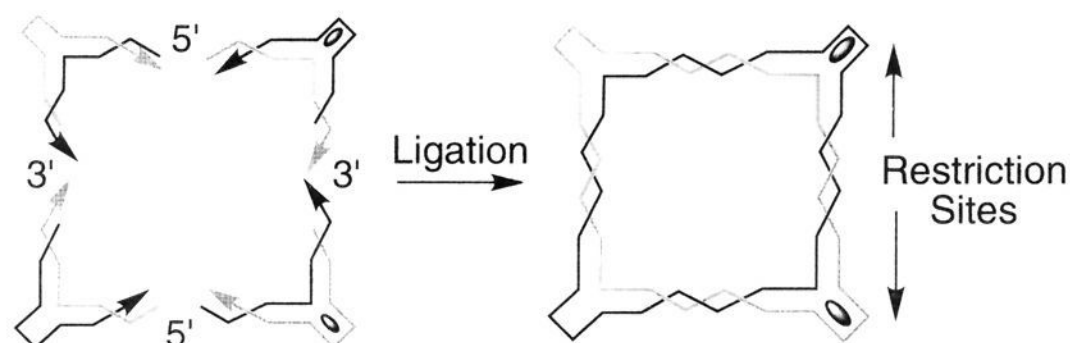


Figure 171. Seeman's synthesis⁴⁴⁴ of a quadrilateral comprised of DNA; it is a hexatuply linked [2]catenane.

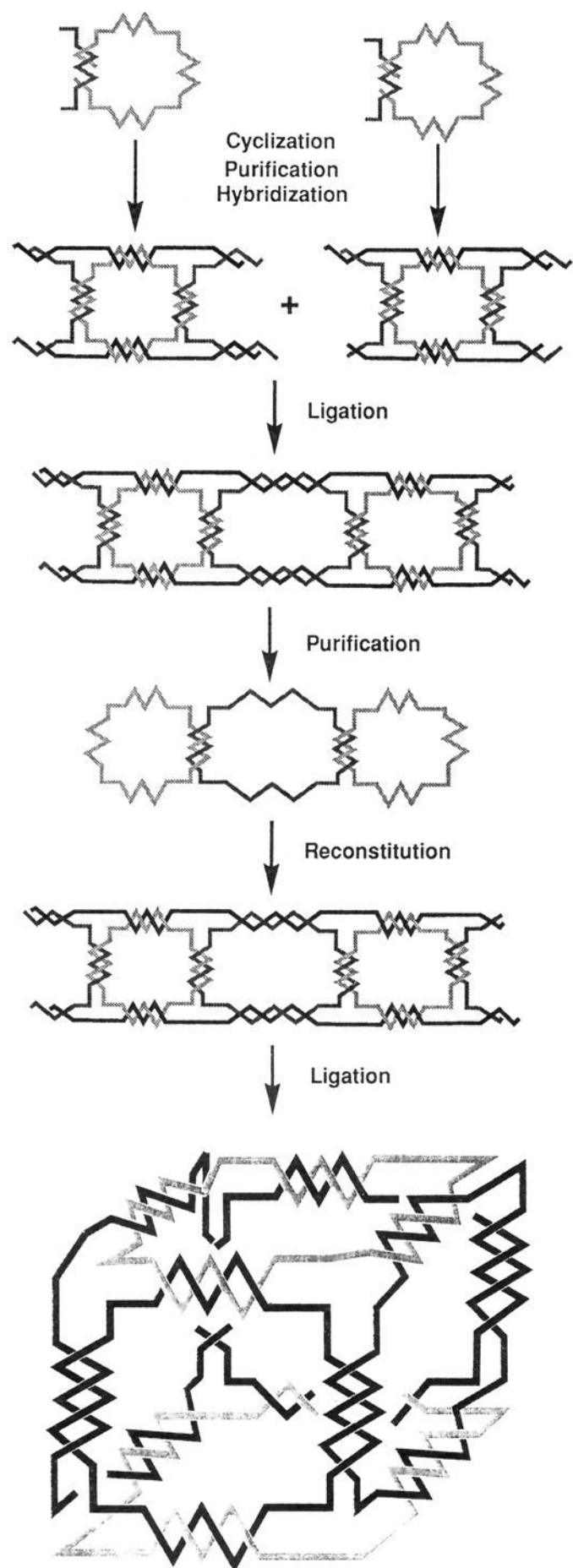


Figure 172. The preparation of a molecular cube constructed from duplex DNA.⁴⁴⁵

is comprised of six linked cycles, each one doubly interlocked with its four neighbors. The squares of the cube contain no duplication of six nucleotide stretches. Indeed, only 28 of the 480 sequences were duplicated in the entire structure. Independent

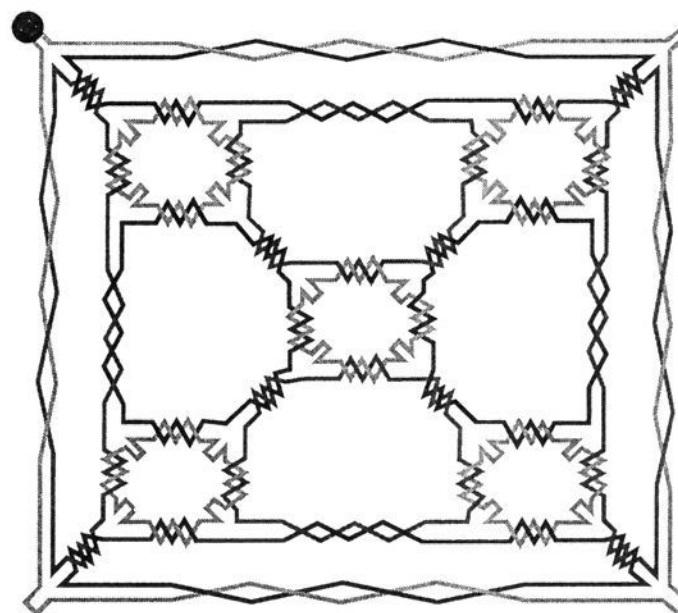


Figure 173. A planar representation of the truncated octahedron constructed using duplex DNA.⁴⁴⁷

restrictions of the individual edges of the cube afforded [4]catenanes and restriction of two independent edges gave a [3]catenane, providing proof for the cube formation.

The synthesis of the cube, while being extraordinarily impressive in comparison to interlocked structures obtained from unnatural sources by truly synthetic means, is not very efficient. The square ligations and the final ring closure proceed in only 10% yield. In an effort to improve the efficacy of the strategy, a solid-support method was developed by the New York group.⁴⁴⁶ The control in this approach is achieved by restriction endonuclease digestion of hairpin loops, which exposes cohesive termini. After formation of a new edge by additive or cyclizing ligation, incorrect products are destroyed by exonuclease. Repetition of these steps builds up the connectivity of the structure, which can then be removed from the support and covalently annealed. The approach was first vindicated for the synthesis of a quadrilateral⁴⁴⁶ and has more recently been applied⁴⁴⁷ to the preparation of an awesome DNA truncated octahedron. The molecule, which is drawn in planar cartoon form in Figure 173, is comprised of cyclic DNA molecules which form the six squares and eight hexagons and a total of 36 edges (each made up of duplex DNA with two full turns) and 24 vertices (DNA junctions) and 24 extra arms coming from each vertex. The complete structure is a [14]-catenane, where each component is doubly interlocked with its neighbors. Each of the extra arms contains a restriction site specific to its square face, and the edges of the structure incorporate seven specific sites for subsequent cleavage by restriction endonuclease. The synthesis of the compound, which contains 2550 nucleotides and weighs approximately 790 kDa, is summarized schematically in Figure 174.

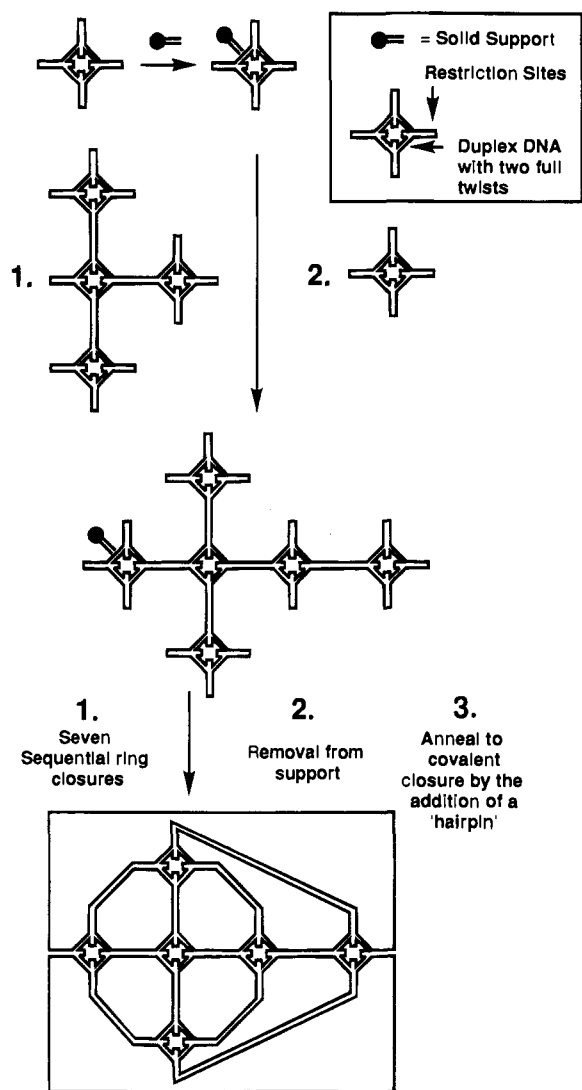


Figure 174. A schematic representation of Seeman's synthesis⁴⁴⁷ of a truncated octahedron comprised of duplex DNA.

First, the squares which were used as the basic building block were prepared, one of them being attached to the solid support. The squares were comprised of two cyclic strands, an inner one, which formed the square in the final object, and an outer strand with appended arms, which were used for ligation to other squares and which finally constitute the hexagons in the truncated octahedron. The components of the squares were designed using the SEQUIN computer program,⁴⁴⁸ so that sequence symmetry was minimized. They were constructed in a manner similar to that described above. The preconstruction of the tetrasquare assembly was necessary because of the inaction of the enzymes required at the restriction sites, when the latter were attached to the support. The yield of the tetrasquare in solution was only 1%, compared with the 10% obtained for the synthesis of each individual square. In contrast, each of the ligations to the solid support proceeded in 30–50% yields. Each of the intermediates in the synthesis of the truncated octahedron were confirmed by removal of a small amount of material from the solid support, followed by cleavage with restriction enzymes, and then scrutinizing the autoradiograms of denaturing gels of the products. The sequential restriction of sites in the edges of the

final structure helped to prove its identity. It was suggested by the authors that the object that they had created is analogous to a zeolite, but with a somewhat larger interior. The edges of the structure were estimated to be 68 Å in length, suggesting that the distance between opposite squares was 192 Å. The total volume of the polyhedron was estimated to be 3557 nm³.

Ultimately, Seeman's goals are the construction of artificial multienzymes, new drug delivery systems, and even mechanical devices and biochips. Yet, the design of these systems will require an intimate knowledge of the structural features of the molecules. Only their connectivities and topologies are accessible at present. Proposed syntheses of complex knots are "well ahead of experimental confirmation", despite the fact—to quote Seeman⁴⁴⁹—the techniques available for DNA manipulation are "readily available to the non-expert".

X. Polyrotaxanes and Polycatenanes

A. Entanglement in Polymers

We have witnessed how the mechanical intertwining and interlocking present in the natural world's macromolecular systems play roles of vital importance—many of these roles having been uncovered only very recently. It is certain that intertwining, and perhaps even interlocking, has been present in many synthetic polymer preparations in the past; even if it has not been recognized. The deliberate chemical synthesis of macromolecules incorporating an aspect of mechanical interlocking is an area of much contemporary interest.^{12,450} It has been reviewed thoroughly by Gibson and co-workers.⁴¹³ The suggestion that mechanical interlocking can exist in polymers is not a new one. Indeed, H. Mark was perhaps the first person to suggest in the literature in 1952, that chemical interlocking existed in polymeric materials.⁴⁵¹ He proposed that a polycatenane-type structure in polysiloxane is responsible for some of its properties. This suggestion was followed up by a more detailed study⁴⁵² which revealed that polysiloxanes are of approximately 1.5 times the dimensions of polystyrenes of similar molecular weight. The authors ruled out an array of interlocked rings, *i.e.* a linear polycatenane, but suggested that arrays of interlocked siloxane macrocycles within the polymer network would prevent it from contracting. Schill¹¹ described this conclusion as "somewhat bold"! However, somewhat remarkably, relatively recent research work⁴⁵³ by J. E. Mark has proved that this hypothesis may be partially correct.

The incorporation of macrocycles into polymer networks has been termed "topological threading". It is not yet possible to state whether macrocycles incorporated into polymers are present in the form of catenanes, *i.e.* in "olympic networks", or whether they are merely trapped in the form of a rotaxane with very large stoppers, *i.e.* the polymer chain. Frisch⁴⁵⁴ has also drawn attention to the possibility of "metastable pseudo-interpenetrating networks", which are intermediate in their properties between straight-chain polymers with random intertwining and catenated interpenetrating networks.⁴⁵⁵

B. Interpenetrating Polymer Networks

In the presence of an already cross-linked polymer, cross-linking a linear polymer can produce a polycatenane or *interpenetrating network*^{456,457} (Figure 175) which merges into itself by mechanical linking rather than by covalent linking alone. In 1960, Millar⁴⁵⁸ reported polymers incorporating two and three interpenetrating networks based on styrene-divinylbenzene copolymers. Formally, independent second and tertiary networks are intermeshed into an existing polymer. The densities and solvent uptakes of the polymers are modified distinctly by incorporation of the second, entangled, network, and it was suggested that such topological features may be responsible for the properties of conventional polymers with a relatively high degree of cross-linking. Frisch, Klemperer, and Frisch⁴⁵⁹ prepared a two-component interpenetrating network by combining linear poly(butadiene-acrylonitrile) with a cross-linked polyether-based poly(urethane-urea) as an aqueous emulsion. Cross-linking agents and stabilizers were also added, films were cast, and the polymer was then cured. Total hydrolysis of the interpenetrating poly(urethane-urea) allowed separation of cross-linked poly(butadiene-acrylonitrile), showing that there is no chemical link between the components, and partially proving the hypothesis that an interpenetrating network is formed. The amount of interpenetration in these polymers was approximated by comparison of the cross-link densities and tensile strength of the interpenetrating network with the mean values for the two cross-linked polymers in isolation. Both these properties give greater values for the interpenetrating network than the mean of the separate cross-linked polymers. Although the degree of interpenetration was considered to be most significant for the polymer system already mentioned, high interpenetration was also observed for polychloropropene/poly(urethane-urea) and poly(butadiene-acrylonitrile)/poly(styrene-butadiene) networks.⁴⁶⁰ Thermal analysis

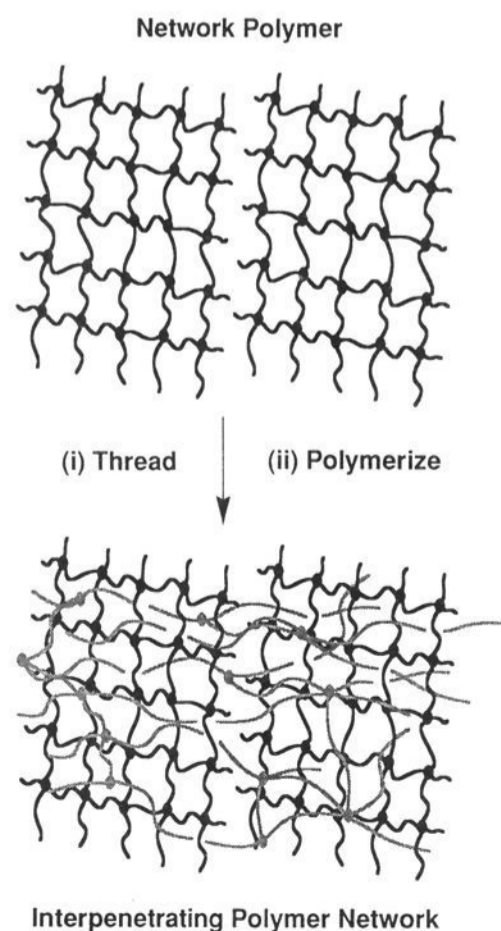


Figure 175. The construction of an interpenetrating polymer network at a conceptual level.

of poly acrylate/poly(urethane-urea) networks also supported the proposed polymer topology.⁴⁶¹

The research of Mark⁴⁵³ and Clarson⁴⁶² on the trapping of cyclic dimethylsiloxanes ($-\text{[Si(Me)}_2\text{O]}_n-$) has established the incorporation of these macrocycles into linear end-linked polymers, following earlier work⁴⁶³ on elastomeric networks which were believed to contain aspects of interlocking. For example, a linear poly(dimethylsiloxane) ($M_n = 7000$ and $14\,800$) with vinyl end groups has been combined⁴⁶⁴ with cyclic dimethylsiloxanes with between approximately 36- and 144-membered rings. After a period of equilibration, $\text{Si[OSi(Me)}_2\text{H]}_4$ was added in order to link up the reactive termini of the linear component tetrafunctionally. None of the 36-membered rings was incorporated into the polymer at all, while approximately 25% of the cyclic dimethylsiloxanes with ring sizes of 116 and 144 were incorporated into both linear strands. It was at this stage that the authors proposed the existence of "olympic networks" which clearly do not rely on cross-linked linear units or covalent trapping. The incorporation of the cycles into the chains was found to reduce the deformation modulus of the polymers.⁴⁶⁵ It was proposed that the entrapped macrocycles introduced constraints on the chains which are more elastic in their absence.

A subsequent study⁴⁶⁶ was concerned with the trapping efficiencies of cyclopoly(dimethylsiloxanes) (PDMS) in the range $31 \leq n_n \leq 517$ during the formation of polymer networks by reacting linear hydroxyl-terminated PDMS ($M_n = 18\,000$) with a cross-linking agent of tetraorthosilicate and stannous 2-ethyl hexanoate as a catalyst. The authors found that the cycles with $n_n < 38$ are not incorporated into the network structures, while 94% of the largest cyclic PDMS is "topologically trapped". The period of time that the components were allowed to undergo mixing prior to the cross-linking did not affect dramatically the amount of trapped macrocycles.⁴⁶⁷ Theoretical methods were also used to study the trapping of the cyclic molecules.⁴⁶⁸ Monte Carlo simulations gave values for the percentage of trapped macrocycles similar to those observed experimentally.

"Polymeric catenanes" have also been prepared⁴⁶⁹ by the cross-linking of poly(2,6-dimethyl-1,4-phenylene oxide) in the presence of cyclic PDMS ($n_n = 92$). Approximately 26% of the macrocycles were reported to have been trapped during the cross-linking process. The physical properties of the polymer are changed significantly upon entrapment of the cyclic PDMS molecules. Notably, greater elasticity and swelling were observed in the "catenane"-type material.

Recently, Lipatov and Nizl'sky⁴⁷⁰ have claimed the formation of "polycatenanes" based on interpenetrating networks formed from diisocyanates. Dissolution of poly(phenylenemethanecarbodiimide) (PCD) in a hexamethylene diisocyanate, followed by polymerization of the latter with (triethylamino)phenyl glycidyl ester as a catalyst yields a "semi-interpenetrating polymer network". The PCD component was cross-linked at either 393 or 523 K to give two different types of interpenetrating networks. Although infrared (IR) spectroscopy indicated that there was no chemical link—"chemical interaction" presumably—between the components of the poly-

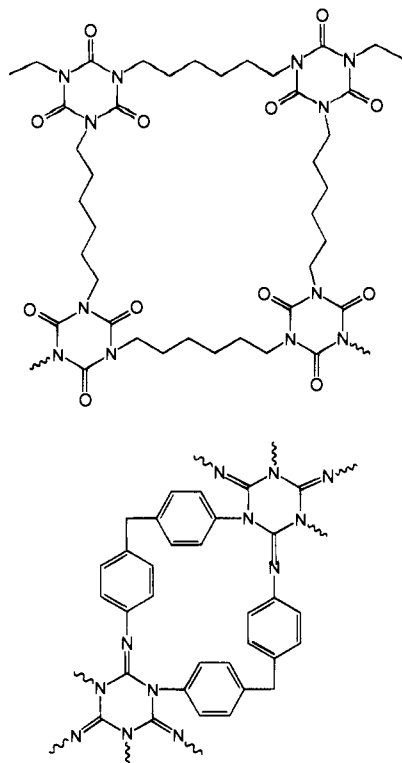


Figure 176. The two polymacrocytic components of the interpenetrating networks formed from diisocyanates.⁴⁷⁰

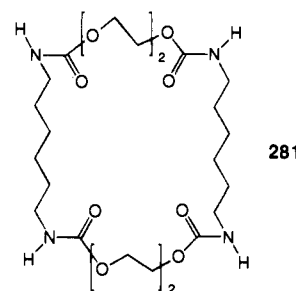
mers, it was claimed that a high degree of complementarity between the two components leads to a homogeneous polymer in which two networks penetrate through each other throughout the system, *i.e.* there are no phase-separated areas. This conclusion was supported by results of differential scanning calorimetry, which gave one thermal transition. The two polymacrocytic components of the proposed interpenetrating network are shown in Figure 176. While the cyclic component comprised of the hexamethylene diisocyanate polymer contains 36 members, that proposed for the cyclotrimerized phenylene methane carbodiimide polycycle is apparently rather small at 24 members. Thus, while the authors propose "thermodynamic compatibility of constituent networks", it is not obvious that there is size compatibility.

C. Polyrotaxanes

We have already discussed some polyrotaxanes which have been prepared by threading and trapping cyclodextrins, as well as the crown-ether based research of Zilkha and co-workers.^{33,34} Here, we discuss the more recent efforts at the synthesis of polyrotaxanes, which have, at least in part, been inspired by these early pieces of work.

After the efforts of Maciejewski,¹³²⁻¹³⁶ Lipatova, Kosyanchuk, and Shilov^{471,472} used a cyclic urethane **281**, rather than a cyclodextrin, as the ring component present during the polymerization of styrene. Styrene was polymerized for 3-4 months in vacuum and in the presence of both (i) the cyclic urethane and (ii) the complex formed between the cyclic urethane and zinc(II) chloride. The polymers were cleaned by several washings to remove free cyclic

urethane and inorganic materials. The molecular masses of the materials produced were 10^5 (no ZnCl_2) and 10^6 (ZnCl_2 complex) as determined by viscometry; we shall see later that threading of rings on to a polymer chain can influence dramatically its viscosity without changing the mass. An X-ray scattering study of the two polymers led the researchers to conclude that, in the absence of zinc(II), one cyclic urethane is incorporated every 18 to 19 monomer units along the backbone, while the complex produced a polymer where one cyclic urethane is incorporated every 6 to 7 monomer units. As a control, when a linear urethane was used in place of the cyclic one, none of the linear urethane was incorporated into the polymer. It was suggested that ordered clusterlike complexes of the macrocycle are responsible for this increase in coverage in the polyrotaxanes upon addition of ZnCl_2 . Since there are degrees of cyclourethane crystallinity in the polymer, the group concluded that areas of high cycle content are present in the polymer,²² while other areas are devoid of them.



The "statistical" approach toward pseudopolyrotaxanes, pioneered by Zilkha and co-workers, has been taken up more recently by Gibson's group,^{413,450} who has used 30-crown-10 and 60-crown-20 for the most part as the cyclic components⁴⁷³ in the synthesis of a wide range of pseudopolyrotaxanes and polyrotaxanes. In its first reports,^{474,475} condensation polymerization of sebacoyl chloride with 1,10-decanol in the presence of 30-crown-10, followed by addition of 3,3,3-triphenylpropionyl chloride, yielded a polyrotaxane of low molecular weight. More efficient (Figure 177) was the transesterification of dimethyl sebacate with triethylene glycol in the presence of the crown ethers, followed by the introduction of a triarylmethane blocking groups.⁴⁷⁶ This method yielded polyrotaxanes which were purified by repeated precipitations, prior to their contents being analyzed by ^1H NMR spectroscopy. One crown ether was incorporated for every four monomer units in the poly(triethyleneoxy sebacate) backbone. Approximately 25 wt % of the polymer, which had M_n between 11 000 (VPO) and 12 200 (GPC), was comprised of threaded portions. The polyrotaxane is a viscous liquid at ambient temperature, whereas the parent thread is a solid. This observation led the authors to conclude that the crown ether was acting as an incorporated solvent or plasticizer. Poly(butylene sebacate) pseudopolyrotaxanes were also prepared. However, the coverage by the macrocyclic polyethers was less than that described in the previous case. The poor compatibility of thread and ring was blamed for this disappointing result. Coverage was slightly higher when 60-crown-20 was used as

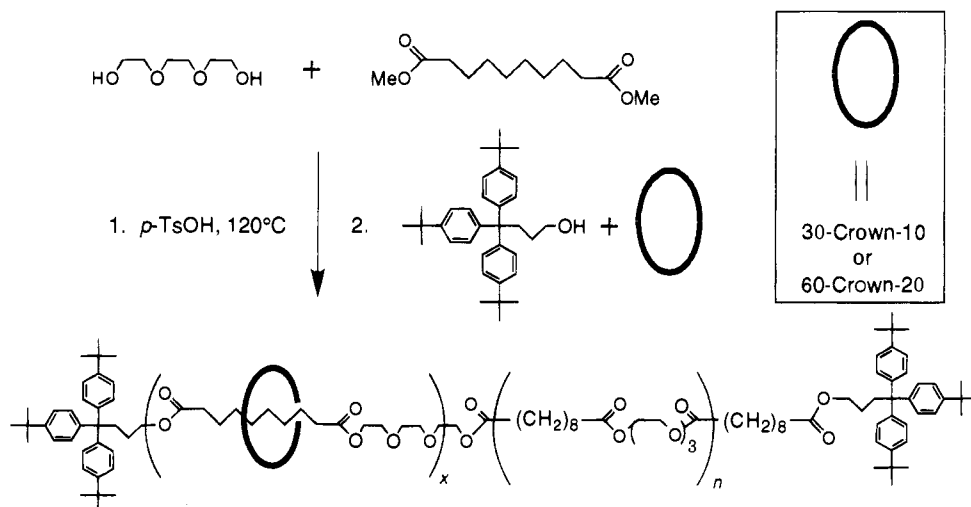


Figure 177. The synthesis of a polyrotaxane from the condensation polymerization of dimethyl sebacate with triethylene glycol in the presence of crown ethers and the chemistry to introduce the triarylmethane blocking groups.⁴⁷⁶

the macrocyclic component, although blocking groups were not attached to the polymer chain termini. The amount of threaded crown ether remained constant through several precipitations. This result indicated that polymer coiling was preventing dethreading of the incorporated rings. The group from Virginia has recently reported⁴⁷⁷ a thorough investigation on the synthesis of these polyester rotaxanes, in which the polymers were prepared in a step-growth fashion. As well as trans-esterification reactions, the polyesters were prepared by reaction of diacid chlorides with appropriate diols in the presence of either 30-crown-10, 42-crown-14, 60-crown-20, or bis-*p*-phenylene-34-crown-10 (**150**). Coverage of the macrocycles on the polymer backbone goes up with increasing ring size and feed ratio, in support of the researchers assertion that the systems follow Le Chetalier's principle. The highest coverage of the polymeric thread, which was achieved using 60-crown-20, corresponded to approximately 33% coverage of the monomer units. The polymer consisted of 55% by weight of the cyclic component. The coverages obtained using **150** were extremely low compared with those obtained with the simple crown ethers. The solubility of the polymers was strongly influenced by the nature and quantity of the threaded macrocycle. In cases where poly-(butylene sebacate) was formed in the presence of 42-crown-14 or 60-crown-20, the resulting polyrotaxanes were observed to possess two phases: a crystalline macrocyclic one and a polyester one. This observation indicated to the authors that the macrocycles are able to move along the thread-like component of the polymer in both the melt and solution states.

Pseudopolyrotaxanes based on polyurethanes, analogous to those of Zilkha *et al.*, were also prepared,⁴⁷⁸ in which (Figure 178) the two crown ethers, 36-crown-12 and 60-crown-20, were employed as solvents for the reaction of methylene di-*p*-phenyl diisocyanate with tetraethylene glycol.⁴⁷⁹ Purification by repeated precipitation gave pseudopolyrotaxanes with M_n values of over 7000 and relatively high coverages, *e.g.* 16% for the smaller crown ether and a massive 57% for the larger macrocycle. Crystallization of the polymer with the higher coverage was observed without dethreading. Once again, incorporation of the crown ethers onto the polymer backbone

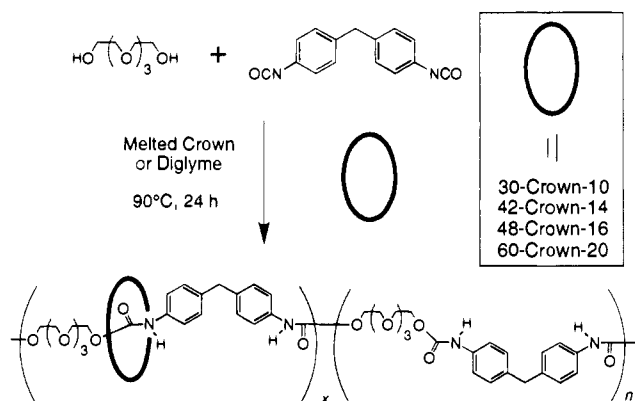


Figure 178. The preparation of pseudopolyrotaxanes based on polyurethanes prepared in the presence of the crown ethers listed in the box.⁴⁸⁰

lowered the glass transition temperatures. Later, the group published⁴⁸⁰ a more complete report of the synthesis of these pseudopolyrotaxanes, where the intermediate 42-crown-14 and 48-crown-16 were used (Figure 178) as the cyclic components during the polymerization. The coverage in the case of these polymers was 29% and 52%, respectively, when the feed ratio of macrocycles:monomers was 1.5. When the same feed ratio was used with 60-crown-20, the coverage was a massive 87%! Thus, as the size of the crown ether ring is increased, so the coverage of the polyurethane backbone goes up. A similar observation of more threading with increasing macrocycle size was made during studies of the gas chromatography of cycloalkanes through polymers by I. T. Hamilton.⁴⁸¹ It has been suggested by Gibson⁴⁸² that intraannular hydrogen bonds between the urethane and the macrocycles provide the enthalpic driving force for the threading of the rings in the case of his materials. The Virginia group also performed experiments in which the feed ratio was lowered to 0.8 and then to 0.5, giving coverages of 58% and 34%, respectively. Interestingly, gel permeation chromatography of the polyrotaxanes in tetrahydrofuran (THF) and 6 mM LiBr in *N*-methylpyrrolidone (NMP) give dramatically different M_n and M_w values. The apparent molecular weights in the more polar solvent are 55% greater for the polymers incorporating 36-crown-12 and 42-crown-14, and 90% greater for the

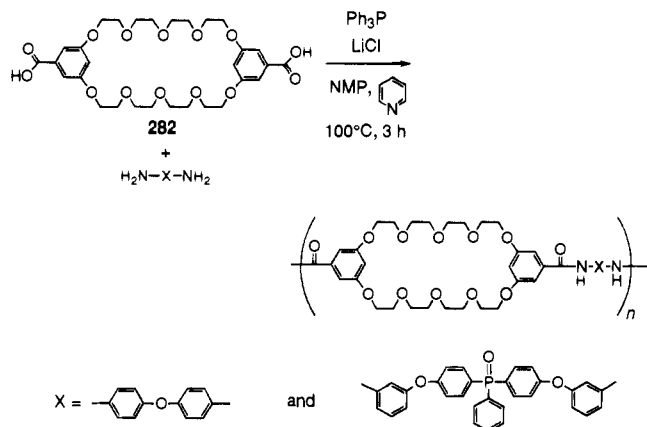


Figure 179. The synthesis of a block copolymer containing a macrocyclic polyether in the repeating unit. The linear part of the monomer is capable of threading through the macrocyclic part of a proximal chain, thus leading to a polyrotaxane.⁴⁸⁶

polymer incorporating 48-crown-16. The polypseudorotaxane has the same size in each solvent while the native polymer increases by only 20%. The results were explained tentatively by (i) the differing solvations of the ring and backbone components in the different solvents, (ii) the relative loadings of the polymers, and possibly (iii) the complexation of the lithium ions.⁴⁸⁰

Notably, attempts⁴⁸² at carrying out similar polyrotaxane syntheses in which the ring component was present during the formation of either polystyrene or polyacrylonitrile were more at the fate of statistics than when polyurethane provided the backbone.⁴⁸³ When 60-crown-20 was present in the radically initiated polymerization of acrylonitrile,⁴⁸⁴ the resulting polymer contained 40% by weight of the macrocycle, even although this composition amounted to a threading efficiency of only 4%, *i.e.* one macrocycle every 25 repeat units of the polymer. Once again, the coverage was highly dependent upon the feed ratio of macrocycle/monomer, and the thermal transitions of the polyrotaxane were similar in magnitude to those of the pure crown. Gibson's group has undertaken additional research on the synthesis of difunctional macrocycles^{485,486} and difunctional stopper groups⁴⁸⁷ for their potential utilization in the synthesis of polyrotaxanes. Although no report of their use in the synthesis of polyrotaxanes has yet been published, polymerization of the macrocycle **282** (Figure 179) with 4,4'-oxydianiline afforded high molecular weight materials which were extremely soluble in all solvents, but which swelled in polar solvents.⁴⁸⁶ The insolubility of the polymers in solvents suitable for analogous materials prompted the authors to suggest threading of the linear section of polymer macromolecules through the macrocyclic section of other macromolecules (Figure 180), producing a "physically cross-linked" polymer.⁴⁸⁶

The changes in the properties of polymer threads, which are encircled by crown ether beads, have been used by Sze and Gibson⁴⁸⁸ for the modulation of the liquid crystalline behavior of polyazomethine. The efficacy of tris(*p*-*tert*-butylphenyl)methane blocking groups for stoppering the rotaxanes was tested on a monomeric [2]rotaxane incorporating a diazomethine moiety as the rod section in the dumbbell component, where 42-crown-14 was the bead component. The [2]-rotaxane **283** was prepared (Figure 181) in 12% yield

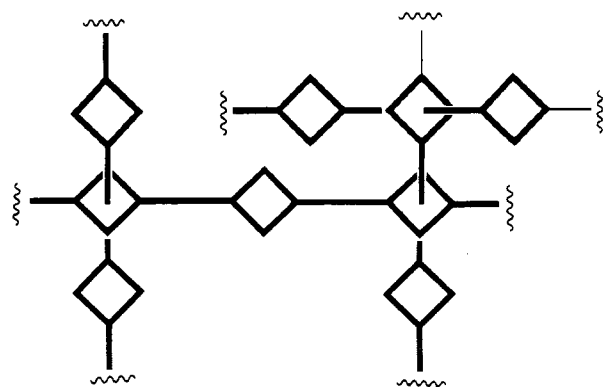


Figure 180. The "physical cross-linked polymer" proposed⁴⁸⁶ by Gibson for the polymer illustrated in Figure 179.

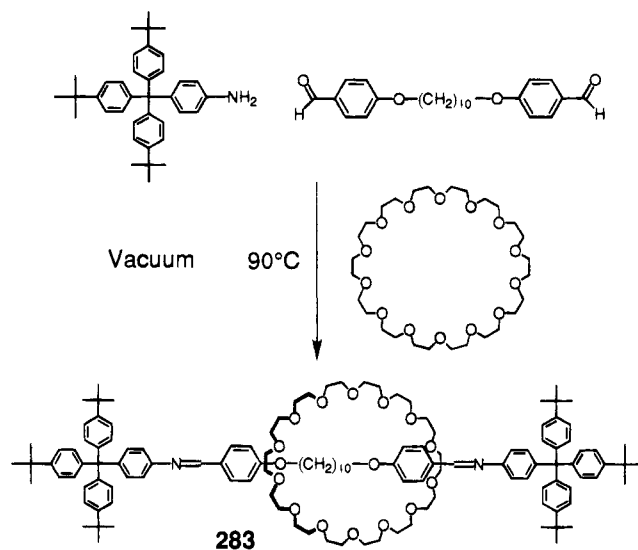


Figure 181. The synthesis of the [2]rotaxane **283** incorporating 42-crown-14 as the bead component.⁴⁸⁸

by using a 10-fold excess of the crown ether relative to the dumbbell components in the threading process. The polyrotaxanes were prepared by reacting 1,10-bis[[[(*p*-hydroxyphenyl)imino]methyl]-*p*-phenoxy]decane, *p*-[tris(*p*-*tert*-butylphenyl)methyl]phenol and either terephthaloyl chloride or 1,8-bis[[*p*-(chloro-carbonyl)phenoxy]carbonyl]octane in a 1:1 mixture of DMAc and 42-crown-14. The degree of polymerization in the resulting materials was approximately 10. One crown ether was incorporated about every eight repeat units of the polymer. The nematic mesophases displayed by the native polymer thread were changed to smectic phases which were exhibited at lower temperatures (by 90–130 °C compared with the parent thread) in the polyrotaxanes. It was proposed⁴⁸⁹ that the liquid crystalline properties of the polymer might be tuned by controlling the amount of threaded macrocycle on the polymer.

Gibson has also exploited the pseudorotaxane-like complexation³⁴⁷ of paraquat residues within the cavity of bis-*p*-phenylene-34-crown-10 (**150**) for the preparation^{478,482} of polyrotaxanes (Figure 182) in which there is a high ratio of macrocycle/repeat unit. The material was prepared by reacting bis(2-hydroxyethyl)-4,4'-bipyridinium bis(hexafluorophosphate) with bis(*p*-isocyanatophenyl)methane in the presence of the macrocycle. Small amounts of either oligo(ethylene glycol) or oligo(tetramethylene oxide) were added to increase the flexibility of the polymer,

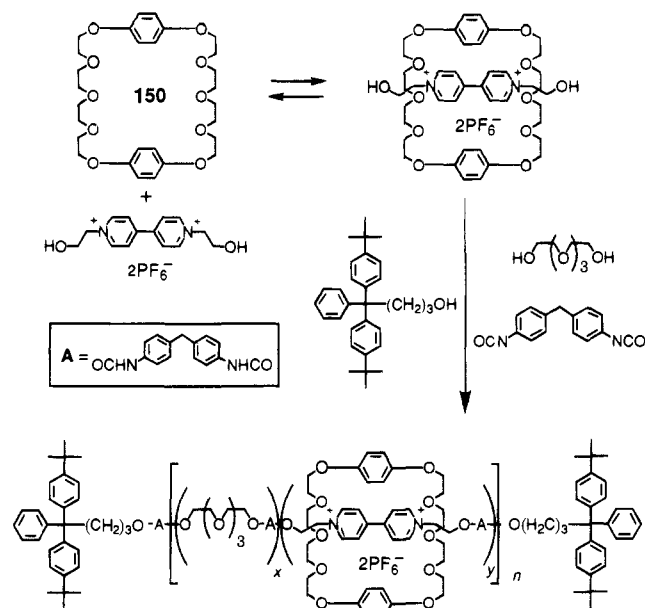


Figure 182. The self-assembly of a polyrotaxane based on a dumbbell component incorporating bipyridinium units and bis-*p*-phenylene-34-crown-10 (**150**) as the bead component.^{478,482}

and the triaryl methane blocking groups were used to cap the ends of the polymer threads. Details of the claimed control of the molecular weight and coverage of the polymer by varying the ratios of the components have not yet been reported.

The recognition logic used by Gibson has been reversed in the synthesis³⁹⁹ (Figure 183) of a pseudopolyrotaxane incorporating cyclobis(paraquat-*p*-phenylene) (**153**) and the polymeric thread **284**, which

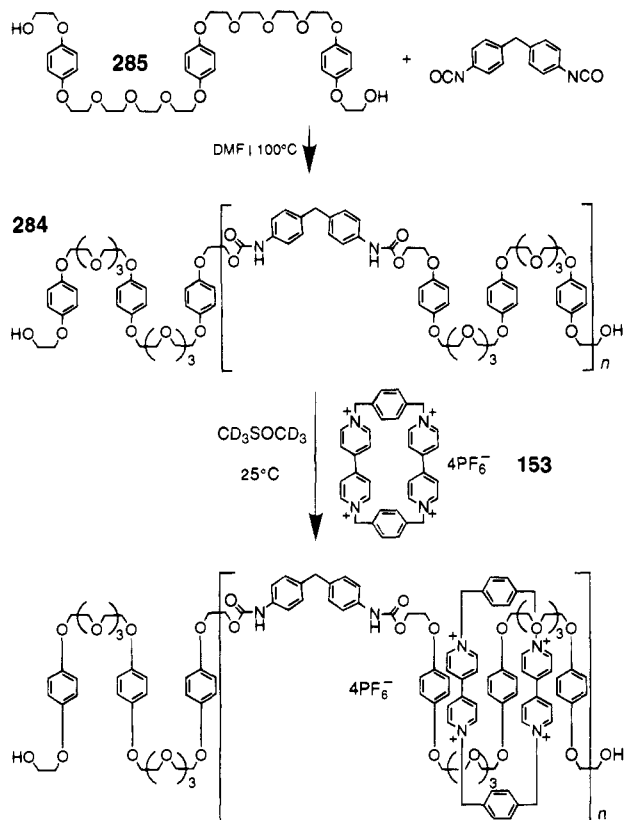


Figure 183. The self-assembly of a pseudopolyrotaxane incorporating cyclobis(paraquat-*p*-phenylene) (**153**) as the bead component along a polymeric thread **284**.³⁹⁹

was prepared from the three hydroquinone residue-containing thread **285** and bis(*p*-isocyanatophenyl)methane. The relatively low molecular weight polymer had approximately nine repeat units, along which the tetracationic cyclophanes shuttle rapidly on the ¹H NMR time scale in CD₃SOCD₃. The tetracationic cyclophane occupies predominantly the hydroquinone residues of the polymer.

D. Polycatenanes

Clearly, the statistical approach for the creation of structures with aspects of interlocking has severe limitations. When the chances of forming two catenated rings is low, the probability of achieving a polycatenated structure is infinitesimally small. Some order, by exploiting molecular recognition, for instance, must be brought to bear on the components of the target catenane in order that efficient interlocking can be achieved.

In 1970, Karagounis and co-workers⁴⁹⁰ published the first in a series of papers⁴⁹¹⁻⁴⁹⁶ in which they described a rather speculative method based upon the orienting of bifunctional bipolar compounds at a surface. The method was directed at preparing "catena compounds". Amphiphilic diols or diamines were spread at a monolayer and, in the presence of dibenzocrown ethers, were reacted with diacid chlorides. The route to the proposed structures is illustrated schematically in Figure 184. As a specific example,⁴⁹⁵ 1,18-octadecanediol was oriented at an air-water interface and was then reacted with tri-

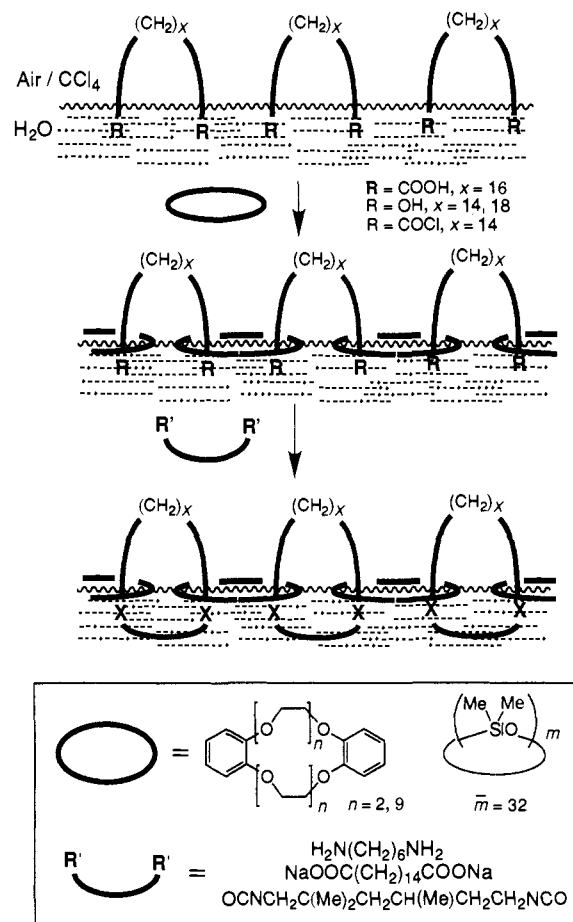


Figure 184. A schematic representation of a method designed to prepare "catena compounds" at surfaces.⁴⁹⁰⁻⁴⁹⁶

methyl hexamethylenediisocyanate in the presence of a mixture of cyclosiloxanes. For some reason, a magnetic field of 18 000 G was applied to the reaction mixture.

The products of the reactions were not studied exhaustively by analytical techniques. The characterization of the isolated materials relied predominantly upon results obtained from infrared (IR) spectroscopy. After thorough extraction of the products of the reactions with solvents in which at least one of the components of the "polycatenanes" were soluble, the IR spectrum of the residual material revealed the presence of both macrocycles. Small frequency shifts in both directions were observed in the bands arising from the individual components, compared with those for the pure compounds. These changes were postulated to have arisen as a result of interannular van der Waals interactions caused by threading. Gas chromatograms of low molecular weight "catenanes" showed that they had different retention times to those of the component macrocycles.

Although all the highly optimistic reports by Karagounis illustrate an idyllic linear chain in representations of the structures, there are a number of more likely outcomes from the reactions that were described, which may explain at least some of the experimental observations. The size of the preformed macrocycles used in the polymerizations were only large enough for the threading of a single chain through their center. Therefore, perhaps the most obvious outcome is the linking of the termini of the bipolar amphiphiles such that pseudopolyrotaxanes are formed at the interface. We have already discussed the fact that pseudopolyrotaxanes have the ability to retain their threaded nature despite the absence of blocking groups at the chain termini as a result of random coiling of the polymer backbone. This phenomenon would result in the presence of both components in the polymeric materials that were produced. Another likely outcome is the formation of a mixture of randomly cross-linked threads along which are trapped macrocycles in a highly polydisperse two-dimensional mesh at the interface. Thus far, no other researchers have reported an evaluation of the method developed by Karagounis to confirm or otherwise the assertions. Probing the products of these reactions with the armory of analytical techniques available to the modern chemist would surely answer some of the unanswered questions arising from this research. Despite the lack of characterization of the materials which were formed in the polymerizations, this approach demonstrates how the principles of self-organization—achieved through hydrophobic interactions—might be used for the synthesis of catenanes. Indeed, since writing the last lines, the method has been proven partially correct by the group of Busch.⁴³⁰

Very recently, Semlyen and co-workers reported⁴⁹⁷ the attempted synthesis of "the first catenated polymers" by attaching 11-bromoundecanoic acid to polymer supports, followed by cyclization (Figure 185). The acid was fixed initially to a basic polymer support, and was then reacted by heating in toluene. The principal products, which were separated by filtering off the resin, were proposed to be cyclic

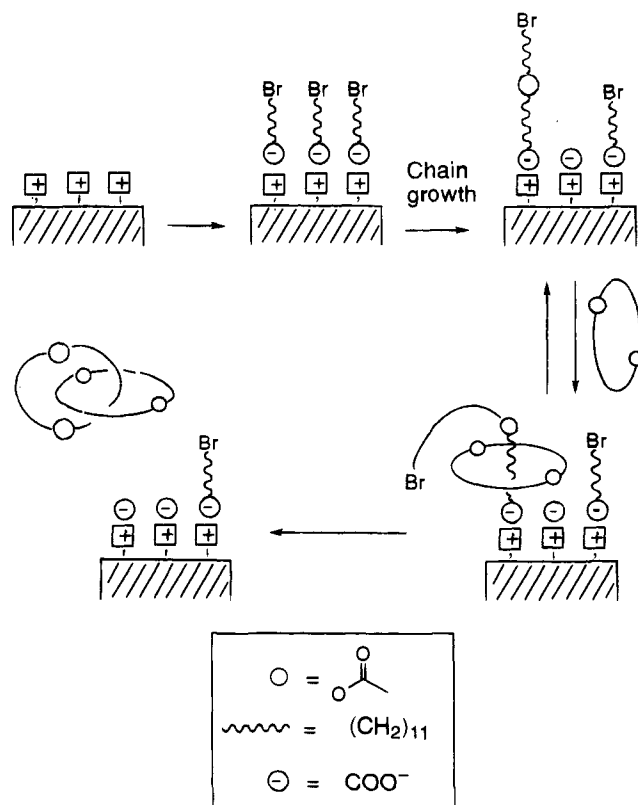


Figure 185. A proposed mechanism for the synthesis of catenated polymers under heterogeneous conditions.⁴⁹⁷

polyesters of the type $[(\text{CH}_2)_{10}\text{CO}\cdot\text{O}]_x$ on the basis of gel permeation chromatography, mass spectrometry, and network trapping. When the reaction was repeated on a small scale in the presence of the prefabricated cyclic polyester, the ^1H NMR spectrum of the product suggested the presence of cyclic polyesters. Gel permeation chromatography showed that these cyclic polyesters have a high molecular mass. The presence of dimeric up to higher order catenanes comprised of cyclic polyester macrocycles was proposed.

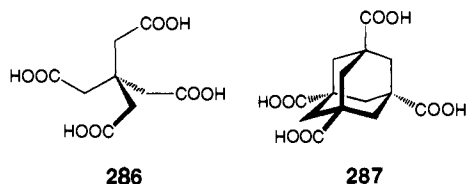
E. Crystals Containing Networks of Interlocking Supramolecular Arrays

Although crystalline formations of interlocked ring structures cannot be regarded strictly as interlocked in a topological sense, unless one considers a noncovalent bond to be a permanent entity, the great number of beautiful structures⁴⁹⁸ that have been described recently by X-ray crystallography are worthy of note.

The crystal structure of trimesic acid (benzene-1,3,5-tricarboxylic acid) shows a two-dimensional chicken-wire-type structure,⁴⁹⁹ where any set of six molecules are held in a 14 Å diameter ring by $\text{O}\cdots\text{H}\cdots\text{O}$ hydrogen bonds. Twisting of some of the hydrogen bonds in the structure means that the sheets are pleated. In addition, the structure is triply catenated, by means of interpenetration of the sheets through one another in the crystal. Indeed, it has only recently been shown that the anhydrous acid can exist in a state where it is not self-filling.⁵⁰⁰

In 1988, Ermer reported^{501,502} two beautiful crystal structures in his search for diamondlike—or diamondoid—networks in the solid state formed by

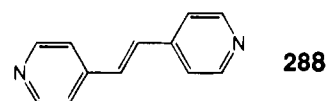
tetrafunctional organic molecules. The mutually interactive functional groups in each molecule were positioned such that their directions described a tetrahedral geometry. The tetracarboxylic acid 3,3'-bis(carboxymethyl)glutaric acid (**286**) does indeed adopt a pseudo-tetrahedral shape and forms⁵⁰¹ elongated diamondoid networks held together by hydrogen bonds, as in the case of trimesic acid. In addition, the hollows in the structure are filled by two identical interpenetrating networks, in a triply catenated manner. The larger and more rigid adamantane-1,3,5,7-tetracarboxylic acid (**287**) also forms hydrogen-bonded diamondoid lattices,⁵⁰² but because of the larger hollows in the structure, *five* equivalent networks interpenetrate one another to form a type of polymeric pentacatenated structure.



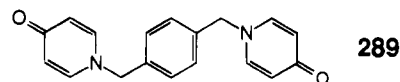
The adamantane-type structure has also been shown to form interpenetrating networks for inorganic materials where the coordination number and geometries of the metal ions are used to determine the form of the assembled lattices. Cadmium cyanide and zinc cyanide form⁵⁰³ infinite frameworks in the solid state, comprised of interpenetrating adamantane-type units as does $K_2[PdSe_{10}]$, which has two interpenetrating networks.⁵⁰⁴ The same has been proposed for frameworks⁵⁰⁵ comprised of BeF_2 and either SiO_2 or GeO_2 . When copper(I) tetrakisacetonitrile hexafluorophosphate was crystallized⁵⁰⁶ with 4,4'-bipyridine, the now familiar diamondoid structure is formed in the solid state. In this structure, the bipyridine ligands link the copper ion junction points in the lattice. This time, however, four equivalent networks interpenetrated one another. On the other hand, crystals of $[Cu_2(Pz)_3SiF_6]_\infty$ obtained in the same manner⁵⁰⁶ give an interpenetrating honeycomb grid, where one network intersects another. When silver(I) triflate is crystallized⁵⁰⁷ with 4,4'-bipyridine, the resulting crystals contain four interpenetrating adamantanoid networks. A similar network was obtained when the tetrafluoroborate salt of the metal ion forms a cocrystal with 4-cyanopyridine. In a similar vein,⁵⁰⁸ crystals of $[Cd(bpy)_2[Ag(CN)_2]_2]$ and $[Cd(pyz)_2[Ag_2(CN)_3][Ag(CN)_2]_2]$ contain doubly and triply interpenetrating framework-type structures, respectively. Three interpenetrating nets form through one another when $Rb[Cd[Ag(CN)_2]_3]$ is crystallized.⁵⁰⁹ Approximately linear $NCAgCN$ connectors coordinate the remaining metal centers in the structure. A set of interpenetrating meshes is observed in crystals of $[Cd(NH_3)_2[Ag(CN)_2]_2]$.⁵¹⁰

The crystal structure⁵¹¹ of a molecular-based magnet showed that it was comprised of a fully interlocked structure. The complex $(rad)_2Mn_2[Cu(opba)]_3 \cdot (DMSO)_2 \cdot 2H_2O$ [where rad^+ is 2-(4-*N*-methylpyridinium)-4,4,5,5-tetramethylimidazolin-1-oyl 3-oxide and *opba* is *o*-phenylenebis(oxamato)] crystallized from DMSO as a structure in which two perpendicularly stacked two-dimensional networks interpenetrate through one another. The mean separation

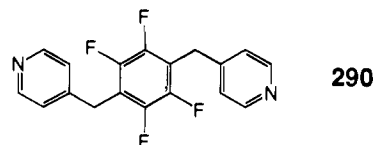
between the corners of the rings, which are comprised of $Mn^{II}_6Cu^{II}_6$ hexagons, is 21.5 Å, the edges of the hexagons being shared between adjacent rings. Three types of spin carrier— $Mn(II)$, $Cu(II)$ antiferromagnetically coupled via oxamato bridges, and rad^+ radical cations which bridge $Cu(II)$ ions—are present in the material which is a magnet below 22.5 K.⁵¹² Another magnetic material reported recently turned out to be an inorganic double helix formed by hydrothermal synthesis.⁵¹³ The vanadium phosphate $[(Me)_2NH_2]K_4[V_{10}O_{10}(H_2O)_2(OH)_4(PO_4)_7] \cdot 4H_2O$ forms crystals in which chiral double helices wind through one another so as to form tunnels and cavities which are occupied by $(Me)_2NH_2^+$ and K^+ cations. The authors proposed that these channels and tunnels might be used for discrimination between enantiomers, since only one enantiomorph is present in any single crystal of this complex structure. Real *et al.* have prepared a spin-crossover system whose structure is of a polycatenane type.⁵¹⁴ The ligand **288** was crystallized from a solution containing half the number of moles of iron(II) thiocyanate. The structure contains two perpendicular networks which are fully interlocked. The material shows a low-spin to high-spin transition between 100 and 250 K.



Crystallization of the simple ligand **289** with $Mn(ClO_4)_2$ produced a polycatenated sheet structure.⁵¹⁵ Each sheet is comprised of a mixture of 34- and 68-membered rings, containing two and four octahedrally coordinated metal ions. Furthermore, this sheet is interwoven with a second sheet so that the $Mn(II)$ centers of one network are located in the middle of one of the 68-membered rings of the other. The layers are thought to be favored as a result of aromatic-aromatic face-to-face and edge-to-face interactions.



The geometrically similar ligand **148** used by Fujita and co-workers for catenane synthesis³³³ has also been employed for the preparation of "interpenetrating molecular ladders and bricks".⁵¹⁶ The single crystal of $[Cd(\mathbf{148})_{1.5}](NO_3)_2$ had a structure in which each cadmium(II) ion was seven-coordinated to pyridyl groups of the ligand. The whole structure had a ladderlike appearance. However, when a fluorinated analog of **148**, specifically **290**, was crystallized with the same metal ion, the similar complex had a completely different structure in which three independent "molecular bricks" interpenetrate through one another, making a sheet approximately 14 Å thick, a section of which is illustrated in Figure 186.



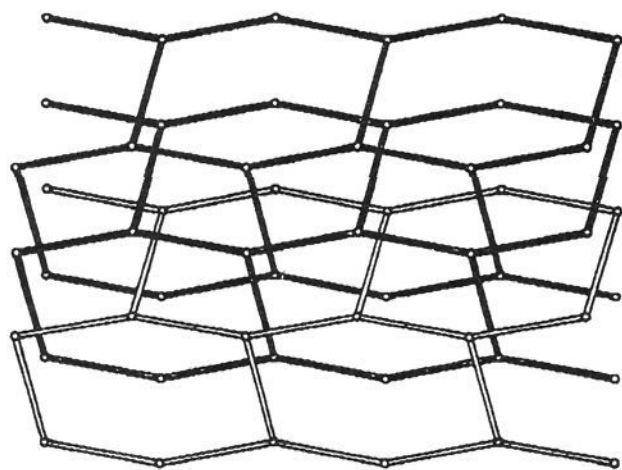


Figure 186. A layer of three interpenetrating "molecular brick" networks of the compound $[\text{Cd}(\mathbf{148})_{1.5}](\text{NO}_3)_2$.⁵¹⁶

Arguably one of the most stunning of these interpenetrating networks is the one reported⁵¹⁷ by the group of Robson. The crystal structure of $\text{ZnAu}_2(\text{CN})_4$ possesses a unit cell with all equivalent zinc centers and gold centers, and two types of cyanide counterions. The $[\text{Au}(\text{CN})_2]^-$ units act as connectors between zinc centers. The topology of the resulting net is identical to quartz, but as a result of the long spacer between the zinc atoms, six identical, but independent, nets interpenetrate through one another.

It is surely certain that further variations of linking units in combination with different metal ions will continue to produce more of this type of beautiful "polycatenane" in the solid state.

XI. Overview and Opportunities

Tremendous progress has been made, from the statistical and serendipitous procedures of bygone days, to the predesigned and predictable syntheses based on molecular recognition phenomena of increasingly intricate interlocked structures and intertwined superstructures of the present day. Arguably, the most impressive molecular structures created so

far have been made possible by utilizing the recognition set provided to us by nature in the form of DNA, which is, in itself, the most awe-inspiring supramolecular system in relation to its form, function, and performance. Yet, all the successful synthetic systems outlined in this review are based on relatively primitive and easily accessible components—such as bipyridinium units, hydroquinone rings, pyridine derivatives, phenanthroline residues, and so on. It is not unreasonable to suggest that synthetic chemistry is capable of creating complex structures from simple building blocks using principles like template direction and self-assembly—concepts borrowed from nature.⁵¹⁸

The conceptual progression from simple recognition processes to a family of more complex interlocked and intertwined structures and superstructures is illustrated in Figure 187. The lower half of the figure traces the progress that is being made in the Strasbourg laboratories by the Sauvage group.²⁴ Their starting point was the simple chelation of metal ions by coordinating ligands. The top part of the figure shows the development of the Birmingham systems^{395,400} based on π -electron donors and acceptors starting from relatively simple host-guest complexes. The development of these systems based on weak noncovalent bonding interactions, and their synthesis using self-assembly techniques, has been aided enormously by structural information from the solid state. It is for this reason that the molecular collage depicts the superstructures in the form of donor-acceptor stacks. In a not dissimilar way, the Whitesides group⁵¹⁹ at Harvard are investing their talents and efforts in the design and creation of huge supermolecules using the mutual hydrogen-bonding interactions between melamine and cyanuric acid derivatives.

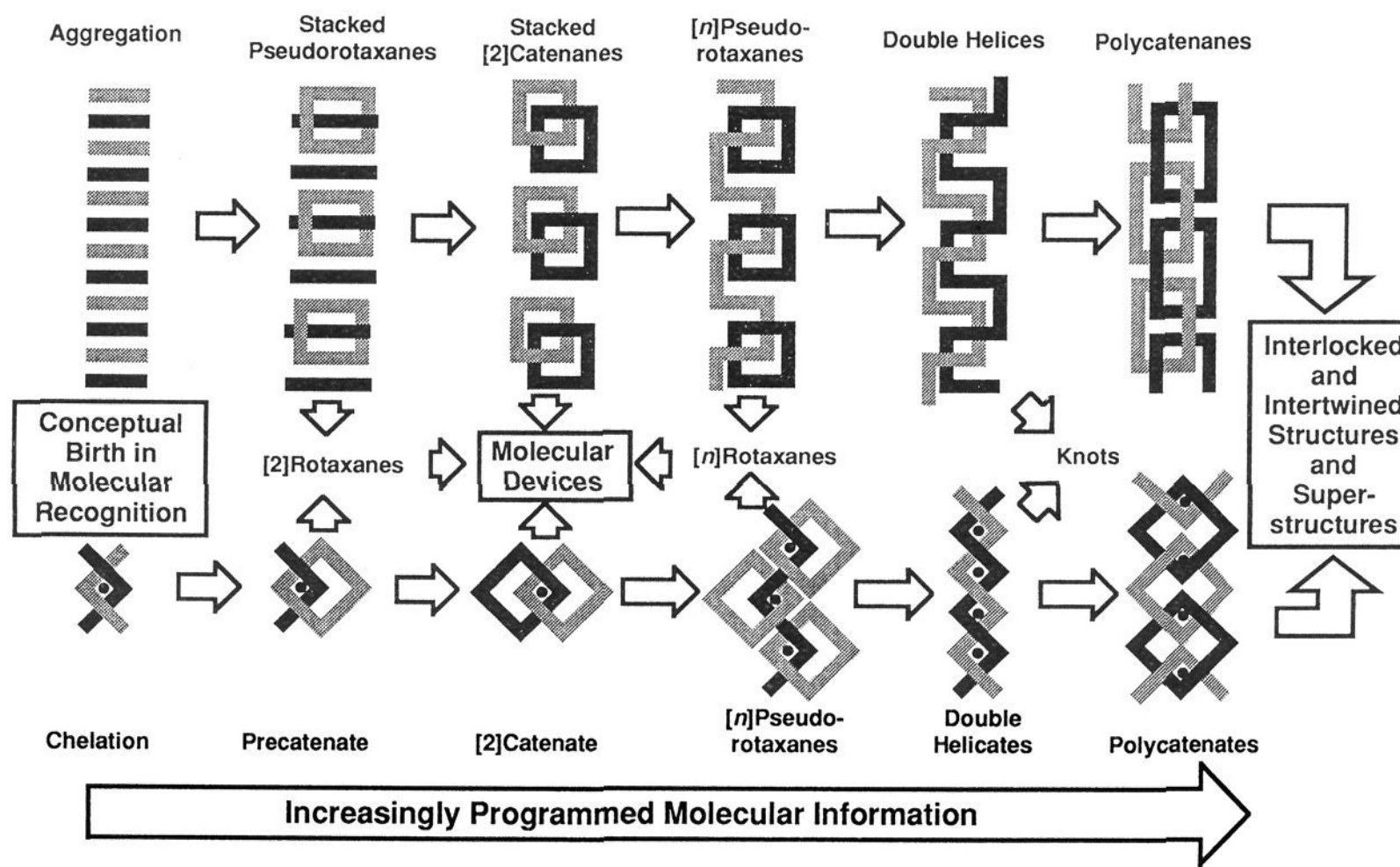


Figure 187. The conceptual progression from simple recognition processes – based on donor-acceptor stacks (top) and metal ion chelation (bottom) – to a family of interlocked and intertwined structures and superstructures.

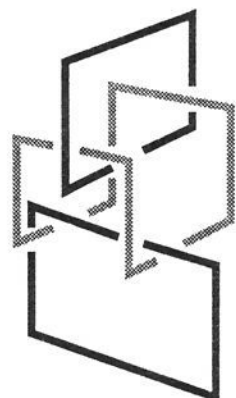
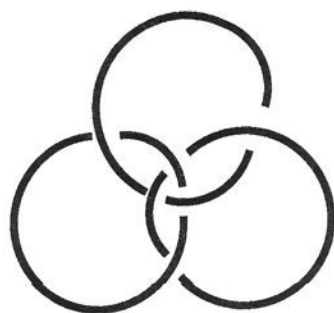
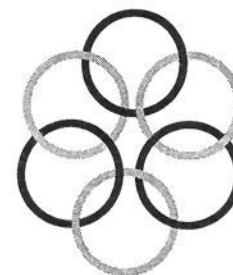


Figure 188. Three representations of the Borromean rings.⁵²²

Recently, Lokey and Iverson⁵²⁰ have reported the formation of a pleated superstructure formed by a preprogrammed macromolecule in aqueous solution. It was inspired by the solid-state structure of the stacking between 1,5-dioxynaphthalene residues and 1,4,5,8-naphthalenetetracarboxylic diimide, which behave as donors and acceptors, respectively. This pleated structure is easily visualized by joining the ends of the aggregate in Figure 187. As progressions such as this one are made successfully to larger and more complex structures and superstructures, the “programming” that has to be incorporated into the molecular components will have to be increasingly more precise—the real challenge provided by this “programming” is the design and synthesis⁵²¹ of the components.

Chemists will continue to search for even greater challenges in the form of new topologically complicated target structures to test their skills in template-directed synthesis. Dietrich-Buchecker and Sauvage²⁴ have achieved the synthesis of trefoil knots using metal ions as templates. This kind of compound remains an elusive one to synthesize using purely organic synthetic building blocks capable of interacting solely in a noncovalent manner. However, the goal has been demonstrated using DNA.⁴³⁴ The formation in solution of purely synthetic organic double helices is a difficult enough task! Yet, as we have seen throughout this review—what is difficult today has a way of becoming easy tomorrow. Perhaps the next fundamental goal to tantalize and tease those chemists practicing template-directed syntheses are the Borromean rings,⁵²² *i.e.* three rings which are linked (Figure 188), yet in which no two individual rings are interlocked. Another aesthetically



A Cyclic [6]Catenane

Figure 189. A challenging goal for the catenane chemists! A cyclic [6]catenane.

appealing structural type, which has yet to be prepared in the laboratory, are the cyclic catenanes (Figure 189). Beyond them lie the vast array of higher knots and other complicated interlocked and intertwined structures and superstructures which have been described⁵²³ as molecular macramé.

In the Introduction, we noted that rotaxanes are, strictly speaking, not topological isomers of their components. In a rotaxane, a bulky group must hinder dethreading, although materials which are clearly pseudorotaxanes—and can be separated by chromatography at room temperature but can be disassembled at relatively high temperatures—can be observed at low temperatures as single threaded species. Problems are encountered in trying to define interlocking. Several researchers have defined interlocking as involving relatively weak metal-to-ligand bonds. The search for sources of interlocking within the structures of proteins and the like must include very weak hydrogen bonds and is certainly of academic interest. However, there is always the need to decide when a bond is a bond! The same situation pertains for rotaxanes formed by slippage, particularly when the energy barrier to dethreading is low. When is a rotaxane a rotaxane and not merely a pseudorotaxane, *i.e.* a complex? A similar problem of definition has been faced in the distinction between stereoisomers which are equilibrated as a result of torsional motions about single covalent bonds.⁵²⁴ The concept, which was introduced by Mislow, is one of “residual stereoisomerism”.⁵²⁵ It is a description which refers to stereoisomers as species which can be differentiated under certain conditions using a specific technique. The situation is not so clear in the case of interlocked systems, where noncovalent bonds are included along the molecular path which is necessary to define interlocking. A similar dilemma is faced when considering what is a topologically significant bond. For example, the axial coordination of bulky ligands to a metalloporphyrin leads, if one discounts the porphyrin-to-metal bonds, to a rotaxane! Two elegant examples of this kind of structure have appeared⁵²⁶ recently. However, appealing to the philosophy adopted by Walba,²³ “rather than make an arbitrary decision concerning the exact weighting necessary for a topologically significant bond” or the energy required to dissociate the two components of a rotaxane, “we choose to leave this point open”.

A critical factor that has permitted the rapid progress toward complex molecular and supramolecular systems is the armory of techniques for synthesis, separation and analysis available to the scientists in their research laboratories today. The invention and development of new analytical methods promises increasingly to take the chemist toward detailed studies of the properties of the structures

and superstructures of interlocked and intertwined systems, respectively. A good example of such a technique in the context of the current systems is the use of scanning force microscopy,⁵²⁷ a technique which has been used, for example, to study DNA supercoiling in three dimensions.⁵²⁸ Indeed, such methods may also be used to manipulate molecules.⁵²⁹ As new information concerning the properties of the novel wholly synthetic interlocked and intertwined systems is uncovered, so the fresh and exciting targets for property-directed synthesis⁵²¹ will be set.

The majority of the interlocked and intertwined structures and superstructures reviewed in this article have been isolated as compounds and complexes with the aim of understanding at a fundamental level the ways in which simple components come together to form larger and more complex assemblies and arrays. The ultimate goal of much of the research is to generate systems that will display a function in some way or another. A few of the systems that have already been prepared exhibit properties which mean that they qualify as simple "devices" at the molecular level.⁵³⁰ Yet, considerable hurdles have to be overcome in the development of such "devices" if we are to be able to address these tiny molecular assemblies or supramolecular arrays. If this goal can be achieved, then the possibility of constructing molecular computers will have begun. Already Adleman⁵³¹ has provided an example of the way in which DNA molecules can be used to carry out computations. As supramolecular science develops and evolves, it too must surely provide more and more sophisticated examples of the acquisition, assessment, transfer, storage, and recall of information at the molecular level.

In the meanwhile, as scientists, we will continue to be amazed at, and excited by, the ways in which molecules and supermolecules recognize each other and react one with another in order to interlock and intertwine.^{532,533}

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XIII. References

- (1) Comment made by Professor A. E. Kaifer in a Chinese restaurant in Birmingham (1992) during a discussion with the authors expressing his amazement at the scepticism shown by some of the scientific community toward interlocked molecular structures.
- (2) Nickon, A.; Silversmith, E. F. *Organic Chemistry-The Name Game*; Pergamon: New York, 1987.
- (3) Schattschneider, D. *Sci. Am.* **1994**, *271*, 48.
- (4) (a) Krätschmer, W.; Lamb, L. D.; Fostiropoulos, K.; Huffman, D. R. *Nature* **1990**, *347*, 354. (b) Kroto, H. W. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 111.
- (5) (a) Turro, N. J. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 882. (b) Milgrom, L. M. *New Sci.* **1988**, 3 Dec, 61. (c) Vögtle, F. *Fascinating Molecules in Organic Chemistry*; Wiley: New York, 1992. (d) Hoffmann, R.; Laszlo, P. *Angew. Chem., Int. Ed. Engl.* **1991**, *32*, 1.
- (6) (a) Sachse, H. *Ber. Dtsch. Chem. Ges.* **1890**, *23*, 1363. (b) Sachse, H. *Z. Phys. Chem.* **1892**, *10*, 203. (c) Mohr, E. *J. Prakt. Chem.* [2] **1919**, *98*, 315. (d) Mohr, E. *Ber. Dtsch. Chem. Ges.* **1922**, *55*, 230. (e) Hassel, O. *Q. Rev.* **1953**, *7*, 221. (f) Barton, D. H. R. *Experientia* **1950**, *6*, 316.
- (7) (a) Fischer, E. *Ber. Dtsch. Chem. Ges.* **1894**, *27*, 2985. (b) Lichtenhaler, F. W. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2364.
- (8) (a) Tomalia, D. A.; Naylor, A. M.; Goddard, W. A., III. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 138. (b) Issberner, J.; Moors, R.; Vögtle, F. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2413. (c) O'Sullivan, D. A. *Chem. Eng. News* **1993**, *71* (Aug 16), 20. (d) Fréchet, J. M. J. *Science* **1994**, *263*, 1710. (e) Seebach, D.; Lapiere, J.-M.; Greiveldinger, G.; Skobridis, K. *Helv. Chim. Acta* **1994**, *77*, 1673. (f) Xu, Z.; Kahr, M.; Walker, K.; Wilkins, C. L.; Moore, J. S. *J. Am. Chem. Soc.* **1994**, *116*, 4537. (g) Jansen, J. F. G. A.; Meijer, E. W.; de Brabender van den Berg, E. M. M. *J. Am. Chem. Soc.* **1995**, *117*, 4417.
- (9) Newkome G. R.; Moorefield, C. N.; Baker, G. R. *Aldrichimica Acta* **1992**, *25*, 31.
- (10) Zhou, Q.-F.; Li, H.-M.; Feng, X.-D. *Macromolecules* **1987**, *20*, 233.
- (11) Schill, G. *Catenanes, Rotaxanes and Knots*; Academic: New York, 1971.
- (12) Amabilino, D. B.; Parsons, I. W.; Stoddart, J. F. *Trends Polym. Sci.* **1994**, *2*, 146.
- (13) (a) Dietrich-Buchecker, C. O.; Sauvage, J.-P. *Bioorg. Chem. Front.* Dugas, H., Ed. **1991**, *2*, 195. (b) Dietrich-Buchecker, C. O.; Sauvage, J.-P. *Supramolecular Chemistry*; Balzani, V., De Cola, L., Eds.; Nato ASI Series 371; Kluwer Academic: Boston, 1992 p 259.

- (14) For a recent series of discussions on knots, see: (a) Weber, C. *New J. Chem.* **1993**, *17*, 627. (b) Schücker, T. *New J. Chem.* **1993**, *17*, 655. (c) Liang, C.; Mislow, K. *J. Math. Chem.* **1994**, *15*, 35. (c) Adams, C. C. *The Knot Book-An Elementary Introduction to the Mathematical Theory of Knots*; W. H. Freeman & Co.: New York, 1994.
- (15) Constable, E. C. *Tetrahedron* **1992**, *48*, 10013.
- (16) Dietrich-Buchecker, C. O.; Sauvage, J.-P. *Bull. Soc. Chim. Fr.* **1992**, *129*, 113.
- (17) For the first reported attempt at a catenane synthesis, see: Lüttringhaus, A.; Cramer, F.; Prinzbach, H.; Henglein, F. M. *Justus Liebigs Ann. Chem.* **1958**, *613*, 185.
- (18) See, for example: Schill, G.; Beckmann, W.; Fritz, H. *Ber. Dtsch. Chem. Ges.* **1982**, *115*, 2683.
- (19) van Gulick, N. *New J. Chem.* **1993**, *17*, 619. See also the preface to this paper: Walba, D. M. *New J. Chem.* **1993**, *17*, 618.
- (20) (a) Frisch, H. L.; Wasserman, J. *Am. Chem. Soc.* **1961**, *83*, 3789. (b) Wasserman, E. *Sci. Am.* **1962**, *207*, 94.
- (21) Sokolov, V. I. *Russ. Chem. Rev.* **1973**, *42* (6), 452.
- (22) Lipatov, Y. S.; Lipatova, T. E.; Kosyanchuk, L. F. *Adv. Polym. Sci.* **1989**, *88*, 49.
- (23) Walba, D. M. *Tetrahedron* **1985**, *41*, 3161.
- (24) Chambron, J.-C.; Dietrich-Buchecker, C. O.; Sauvage, J.-P. *Top. Curr. Chem.* **1993**, *165*, 131.
- (25) Liang, C.; Mislow, K. *J. Math. Chem.* **1994**, *15*, 245.
- (26) Dietrich-Buchecker, C. O.; Sauvage, J.-P. *Chem. Rev.* **1987**, *87*, 795.
- (27) (a) Lehn, J.-M. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 90. (b) Lehn, J.-M. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1304. (c) Schneider, H.-J.; Dürr, H. *Frontiers in Supramolecular Organic Chemistry and Photochemistry*; VCH: New York, 1991. (d) Lehn, J.-M. *Science* **1993**, *260*, 1762. Lehn, J.-M. *Supramolecular Chemistry*; VCH: Weinheim, 1995.
- (28) (a) Lindsey, J. S. *New J. Chem.* **1991**, *15*, 153. (b) Whitesides, G. M.; Mathias, J. P.; Seto, C. T. *Science* **1991**, *254*, 1312. (c) Stoddart, J. F. In *Host-Guest Molecular Interactions; From Chemistry to Biology* (Ciba Found. Symp. 158; Wiley: Chichester, 1991; p 5. (d) Lawrence, D. S.; Jiang, T.; Levett, M. *Chem. Rev.* **1995**, *95*, 2229. (e) Philp, D.; Stoddart, J. F. *Angew. Chem., Int. Ed. Engl.* Submitted.
- (29) Wasserman, E. *J. Am. Chem. Soc.* **1960**, *82*, 4433.
- (30) Harrison, I. T.; Harrison, S. *J. Am. Chem. Soc.* **1967**, *89*, 5723.
- (31) Harrison, I. T. *J. Chem. Soc., Chem. Commun.* **1972**, 231.
- (32) Harrison, I. T. *J. Chem. Soc., Perkin Trans. 1* **1974**, 301.
- (33) Agam, G.; Graiver, D. (in part); Zilkha, A. *J. Am. Chem. Soc.* **1976**, *98*, 5206.
- (34) Agam, G.; Zilkha, A. *J. Am. Chem. Soc.* **1976**, *98*, 5214.
- (35) Schill, G.; Beckmann, W.; Schweickert, N.; Fritz, H. *Ber. Dtsch. Chem. Ges.* **1986**, *119*, 2647.
- (36) Gilliatt, V. J.; Sultany, C. M.; Butcher, J. A., Jr. *Tetrahedron Lett.* **1992**, *42*, 6255.
- (37) Wasserman, E.; Ben-Efraim, D. A.; Wolovsky, R. *J. Am. Chem. Soc.* **1968**, *90*, 3286.
- (38) Wolovsky, R. *J. Am. Chem. Soc.* **1970**, *92*, 2132.
- (39) Ben-Efraim, D. A.; Batich, C.; Wasserman, E. *J. Am. Chem. Soc.* **1970**, *92*, 2133.
- (40) Walba, D. M.; Richards, R. M.; Haltiwanger, R. C. *J. Am. Chem. Soc.* **1982**, *104*, 3219.
- (41) Walba, D. M.; Richards, R. M.; Sherwood, S. P.; Haltiwanger, R. C. *J. Am. Chem. Soc.* **1981**, *103*, 6213.
- (42) Walba, D. M.; Richards, R. M.; Hermsmeier, M.; Haltiwanger, R. C. *J. Am. Chem. Soc.* **1987**, *109*, 7081.
- (43) Walba, D. M.; Simon, J.; Harary, F. *Tetrahedron Lett.* **1988**, *29*, 731.
- (44) Walba, D. M.; Armstrong, J. D., III; Perry, A. E.; Richards, R. M.; Homan, T. C.; Haltiwanger, R. C. *Tetrahedron* **1986**, *42*, 1883.
- (45) Walba, D. M.; Homan, T. C.; Richards, R. M.; Haltiwanger, R. C. *New J. Chem.* **1993**, *17*, 661.
- (46) For discussions on the role of templates in chemical synthesis, see: (a) Busch, D. H.; Stephenson, N. A. *Coord. Chem. Rev.* **1990**, *100*, 119. (b) Busch, D. H. *J. Inclusion Phenom. Mol. Recognit. Chem.* **1992**, *12*, 389. (c) Hoss, R.; Vögtle, F. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 375-384.
- (47) Anderson, S.; Anderson, H. L.; Sanders, J. K. M. *Acc. Chem. Res.* **1993**, *26*, 469.
- (48) Schill, G.; Lüttringhaus, A. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 546.
- (49) Schill, G.; Zürcher, C. *Naturwissenschaften* **1971**, *58*, 40.
- (50) Logeman, E.; Rissler, K.; Schill, G.; Fritz, H. *Ber. Dtsch. Chem. Ges.* **1981**, *114*, 2245.
- (51) (a) Schill, G. *Liebigs Ann. Chem.* **1966**, *695*, 65. (b) Schill, G. *Ber. Dtsch. Chem. Ges.* **1966**, *99*, 2689-2698. (c) Schill, G. *Ber. Dtsch. Chem. Ges.* **1967**, *100*, 2021. (d) Schill, G.; Vetter, W.; *Ber. Dtsch. Chem. Ges.* **1971**, *104*, 3582. (e) Schill, G.; Neubauer, H. *Liebigs Ann. Chem.* **1971**, *750*, 76. (f) Schill, G.; Doerjier, G.; Logeman, E.; Vetter, W. *Ber. Dtsch. Chem. Ges.* **1980**, *113*, 3697.
- (52) Isele, G. L.; Scheib, K. *Ber. Dtsch. Chem. Ges.* **1975**, *108*, 2312.
- (53) Schill, G.; Rissler, K.; Fritz, H. *Ber. Dtsch. Chem. Ges.* **1983**, *116*, 1866.
- (54) Logeman, E.; Schill, G.; Vetter, W. *Ber. Dtsch. Chem. Ges.* **1978**, *111*, 2615.
- (55) Vetter, W.; Schill, G. *Tetrahedron* **1967**, *23*, 3079.
- (56) Vetter, W.; Logemann, E.; Schill, G. *Org. Mass Spectrom.* **1977**, *12*, 351.
- (57) Fritz, H.; Logemann, E.; Schill, G.; Winkler, T. *Ber. Dtsch. Chem. Ges.* **1976**, *109*, 1258.
- (58) Fritz, H.; Hug, P.; Sauter, H.; Logeman, E. *J. Magn. Res.* **1976**, *21*, 373.
- (59) Schill, G.; Zollenkopf, H. *Liebigs Ann. Chem.* **1969**, *721*, 53.
- (60) Schill, G.; Henschel, R. *Liebigs Ann. Chem.* **1970**, *722*, 113.
- (61) Schill, G.; Zürcher, C.; Vetter, W. *Ber. Dtsch. Chem. Ges.* **1973**, *106*, 228.
- (62) (a) Schill, G.; Zürcher, C. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 988. (b) Schill, G.; Murjahn, K.; Vetter, W. *Liebigs Ann. Chem.* **1970**, *740*, 18. (c) Schill, G.; Zürcher, C. *Ber. Dtsch. Chem. Ges.* **1977**, *110*, 2046. (d) Schill, G.; Murjahn, K.; Beckmann, W. *Ber. Dtsch. Chem. Ges.* **1972**, *105*, 3591.
- (63) (a) Schill, G.; Rissler, K.; Fritz, H.; Vetter, W. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 187. (b) Rissler, K.; Schill, G.; Fritz, H.; Vetter, W. *Ber. Dtsch. Chem. Ges.* **1986**, *119*, 1374.
- (64) Schill, G.; Schweickert, N.; Fritz, H.; Vetter, W. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 889.
- (65) Schill, G.; Schweickert, N.; Fritz, H.; Vetter, W. *Ber. Dtsch. Chem. Ges.* **1988**, *121*, 961.
- (66) Boeckmann, J.; Schill, G. *Tetrahedron* **1974**, *30*, 1945.
- (67) Schill, G.; Tafelmair, L. *Synthesis* **1971**, 546.
- (68) Schill, G.; Doerjier, G.; Logeman, E.; Fritz, H. *Ber. Dtsch. Chem. Ges.* **1979**, *112*, 3603.
- (69) Watson, J. D.; Crick, F. H. C. *Nature* **1953**, *171*, 737.
- (70) Blackburn, G. M.; Gait, M. J., Eds. *Nucleic Acids in Chemistry and Biology*; IRL Press: New York, 1990.
- (71) Pohl, F. M.; Jovin, T. M. *J. Mol. Biol.* **1972**, *67*, 375. For a review concerning the different forms of DNA, see: Dickerson, R. E.; Drew, H. R.; Corner, B. N.; Wing, R. M.; Fratini, A. V.; Kopka, M. L. *Science* **1982**, *216*, 475.
- (72) Wang, A. H.-J.; Quigley, G. J.; Kolpak, F. J.; Crawford, J. L.; van Boom, J. H.; van der Marel, G.; Rich, A. *Nature* **1979**, *282*, 680.
- (73) Urata, H.; Shinohara, K.; Ogura, E.; Ueda, Y.; Agaki, M. *J. Am. Chem. Soc.* **1991**, *113*, 8174.
- (74) Doi, M.; Inoue, M.; Tomoo, K.; Ishida, T.; Ueda, Y.; Agaki, M.; Urata, H. *J. Am. Chem. Soc.* **1993**, *115*, 10432. Recently, the effect of linking ribonucleotides with sulfones has been reported, see: Roughton, A. L.; Portman, S.; Benner, S. A.; Egli, M. *J. Am. Chem. Soc.* **1995**, *115*, 7249.
- (75) For two very recent discussions, see: (a) Singleton, S.; Dervan, P. B. *J. Am. Chem. Soc.* **1994**, *116*, 10376. (b) Trapani, T. L.; Ts'o, P. O. P. *J. Am. Chem. Soc.* **1994**, *116*, 10437. The very recent crystal structure of a DNA triplex was reported by: Van Meervelt, L.; Vlieghe, D.; Dautant, A.; Gallois, B.; Precigoux, G.; Kennard, O. *Nature* **1995**, *374*, 742. For the formation of triple helices formed by oligodeoxynucleotides, see: Bolli, M.; Leumann, C.; *Ang. Chem., Int. Ed. Engl.* **1995**, *34*, 694.
- (76) (a) Morgan, A. R.; Wells, R. D. *J. Mol. Biol.* **1968**, *37*, 63. (b) Lee, J. S.; Johnson, D. A.; Morgan, A. R. *Nucleic Acid Res.* **1979**, *6*, 3073.
- (77) (a) Moser, H. E.; Dervan, P. B. *Science* **1987**, *238*, 645. (b) Strobel, S. A.; Dervan, P. B. *J. Am. Chem. Soc.* **1989**, *111*, 7286. (c) Horne, D. A.; Dervan, P. B. *J. Am. Chem. Soc.* **1990**, *112*, 2435. (d) Beal, P. A.; Dervan, P. B. *Science* **1991**, *251*, 1360.
- (78) Cheng, Y.-K.; Pettitt, B. M. *J. Am. Chem. Soc.* **1992**, *114*, 4465.
- (79) Kohwi, Y.; Kohwi-Shigematsu, T. *Proc. Natl. Acad. Sci. U.S.A.* **1988**, *85*, 3781.
- (80) (a) Prakash, G.; Kool, E. T. *J. Am. Chem. Soc.* **1992**, *114*, 3523. (b) Wang, S.; Kool, E. T. *J. Am. Chem. Soc.* **1994**, *116*, 8857. For a further report from the same group, see: Rumney, S., IV; Kool, E. T. *J. Am. Chem. Soc.* **1995**, *117*, 5635.
- (81) (a) Pelton, J. G.; Wemmer, D. E. *J. Am. Chem. Soc.* **1990**, *112*, 1393. (b) Mrksich, M.; Dervan, P. B. *J. Am. Chem. Soc.* **1993**, *115*, 2572.
- (82) Mrksich, M.; Dervan, P. B. *J. Am. Chem. Soc.* **1994**, *116*, 3663.
- (83) For very recent reports containing key references, see: (a) Crothers, D. M. *Science* **1994**, *266*, 1819. (b) Strauss, J. K.; Maher, L. J., III. *Science* **1994**, *266*, 1829.
- (84) Wasserman, S. A.; Cozzarelli, N. R. *Science* **1986**, *232*, 951.
- (85) Cozzarelli, N. R.; Boles, T. C.; White, J. H. In *DNA Topology and its Biological Effects*, Cozzarelli, N. R., Wang, J. C., Eds.; Cold Spring Harbor Laboratory Press: Cold Spring Harbor, 1990; p 139. See also: Boles, T. C.; White, J. H.; Cozzarelli, N. R. *J. Mol. Biol.* **1990**, *213*, 931.
- (86) Wang, J. C. *Acc. Chem. Res.* **1973**, *6*, 252.
- (87) Hudson, B.; Vinograd, J. *Nature* **1967**, *216*, 647.
- (88) Clayton, D. A.; Vinograd, J. *Nature* **1967**, *216*, 652.
- (89) Wang, J. C.; Schwartz, H. *Biopolymers* **1967**, *5*, 953.
- (90) Rush, M. G.; Gordon, C. N.; Novick, R. P.; Warner, R. C. *Proc. Natl. Acad. Sci. U.S.A.* **1968**, *59*, 838.
- (91) (a) Rhoades, M.; Thomas, C. A. *J. Mol. Biol.* **1968**, *37*, 41. (b) Meinke, W.; Goldstein, A. *J. Mol. Biol.* **1971**, *61*, 543. (c) Jaenisch, R.; Levine, A. J. *J. Mol. Biol.* **1973**, *73*, 199.
- (92) Simpson, L.; Da Silva, A. *J. Mol. Biol.* **1971**, *56*, 443.

- (93) Sundin, O.; Varshavsky, A. *Cell* **1980**, *21*, 103.
- (94) (a) Wang, J. C. *J. Biol. Chem.* **1991**, *266*, 6659. (b) Gellert, M. *Annu. Rev. Biochem.* **1981**, *50*, 879. (c) Wang, J. C. *Annu. Rev. Biochem.* **1985**, *54*, 665. (d) Uemura, T.; Yanagida, M. *EMBO J.* **1984**, *3*, 1737.
- (95) Tse, Y.-C.; Wang, J. C. *Cell* **1980**, *22*, 269.
- (96) Yang, L.; Wold, M. S.; Li, J. J.; Kelly, T. J.; Liu, L. F. *Proc. Natl. Acad. Sci. U.S.A.* **1987**, *84*, 950. For a very recent report concerning the DNA binding sequence for topoisomerase II see: Spitzner, J. R.; Chung, I. K.; Muller, M. T. *J. Mol. Biol.* **1995**, *270*, 5932.
- (97) Adams, D. E.; Shekhtman, E. M.; Zechiedrich, E. L.; Schmid, M. B.; Cozzarelli, N. R. *Cell* **1992**, *71*, 277.
- (98) Shekhtman, E. M.; Wasserman, S. A.; Cozzarelli, N. R.; Solomon, M. J. *New J. Chem.* **1993**, *17*, 757.
- (99) Hseih, T.-S.; Brutlag, D. *Cell* **1980**, *21*, 115.
- (100) Liu, L. F.; Depew, R. E.; Wang, J. C. *J. Mol. Biol.* **1976**, *106*, 439.
- (101) Dean, F. B.; Stasiak, A.; Koller, T.; Cozzarelli, N. R. *J. Biol. Chem.* **1985**, *260*, 4975.
- (102) Krasnow, M. A.; Stasiak, A.; Spengler, S. J.; Dean, F.; Koller, T.; Cozzarelli, N. R. *Nature* **1983**, *304*, 559.
- (103) Stark, W. M.; Parker, C. N.; Halford, S. E.; Boocock, M. R. *Nature* **1994**, *368*, 76.
- (104) Wasserman, S. A.; White, J. H.; Cozzarelli, N. R. *Nature* **1988**, *334*, 448.
- (105) Lynn, R.; Wang, J. C. *Proteins: Struct., Func., Genet.* **1989**, *6*, 231.
- (106) Lima, C. D.; Wang, J. C.; Mondragón, A. *Nature* **1994**, *367*, 138.
- (107) Liang, C.; Mislow, K. J. *Am. Chem. Soc.* **1994**, *116*, 3588.
- (108) Liang, C.; Mislow, K. J. *Am. Chem. Soc.* **1994**, *116*, 11189. For a full paper related to this work, see: Liang, C.; Mislow, K. J. *Am. Chem. Soc.* **1995**, *117*, 4201.
- (109) Ramachandran, G. N.; Reddi, A. H., Eds. *Biochemistry of Collagen*; Plenum: New York, 1976. Another polypeptide, gramicidin A, has been postulated to form a double helix, see: Veatch, W. R.; Fossel, E. T.; Blout, E. R. *Biochemistry* **1974**, *13*, 5249.
- (110) Eyre, D. R. *Science* **1980**, *207*, 1315.
- (111) Tanzer, M. L. *Science* **1973**, *180*, 561.
- (112) (a) Berg, R. A.; Prockop, D. J. *Biochem. Biophys. Res. Commun.* **1973**, *52*, 115. (b) Jimenez, S.; Harsch, M.; Rosenbloom, J. *Biochem. Biophys. Res. Commun.* **1973**, *52*, 106.
- (113) Bella, J.; Eaton, M.; Brodsky, B.; Berman, H. M. *Science* **1994**, *266*, 75.
- (114) Sakakibara, S.; Inouye, K.; Shudo, K.; Kishida, Y.; Kobayashi, Y.; Prockop, D. J. *Biochim. Biophys. Acta* **1973**, *303*, 198.
- (115) (a) Long, C. G.; Li, M. H.; Baum, J.; Brodsky, B. *J. Mol. Biol.* **1992**, *255*, 10. (b) Long, C. G. *et al. Biochemistry* **1993**, *32*, 11688.
- (116) Rich, A.; Crick, F. H. C. *J. Mol. Biol.* **1961**, *3*, 483.
- (117) Anderson, N. S.; Campbell, J. W.; Harding, M. M.; Rees, D. A.; Samuel, J. W. B. *J. Mol. Biol.* **1969**, *45*, 85.
- (118) McKinnon, A. A.; Rees, D. A.; Williamson, F. B. *J. Chem. Soc., Chem. Commun.* **1969**, 701.
- (119) Bryce, T. A.; Clark, A. H.; Rees, D. A.; Reid, D. S. *Eur. J. Biochem.* **1982**, *122*, 63.
- (120) Morris, E. R.; Rees, D. A.; Robinson, G. J. *J. Mol. Biol.* **1980**, *138*, 349.
- (121) Ueda, K.; Ochiai, H.; Imamura, A.; Nakagawa, S. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 95.
- (122) Dea, I. C. M.; Moorhouse, R.; Rees, D. A.; Arnott, S.; Guss, J. M.; Balazs. *Science* **1973**, *179*, 560.
- (123) Atkins, E. D. T.; Sheehan, J. K. *Science* **1973**, *179*, 562.
- (124) Wu, H. C.; Sarko, A. *Carbohydr. Res.* **1978**, *61*, 7, and 27. Triple helical structures have also been observed in the polysaccharide, schizophyllan. See, along with the references cited therein: McIntire, T. M.; Penner, R. M.; Brant, D. A. *Macromolecules* **1995**, *28*, 6375.
- (125) Atkins, E. D. T.; Parker, K. D. *J. Polym. Sci., Part C* **1969**, *28*, 69.
- (126) Stipanovic, A. J.; Stevens, E. S.; Gekko, K. *Macromolecules* **1980**, *13*, 1471.
- (127) (a) Duchene, D., Ed. *Cyclodextrins and their Industrial Uses*; Editions de Santé: Paris, 1987. (b) Szejtli, J. *Topics in Inclusion Science: Cyclodextrin Technology*; Kluwer Academic: Boston, 1988. (c) Stoddart, J. F. *Carbohydr. Res.* **1989**, *192*, xii.
- (128) Wenz, G. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 803.
- (129) (a) Stoddart, J. F. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 846. (b) Ogino, H. *New J. Chem.* **1993**, *17*, 683.
- (130) For some topical examples, see: (a) Yonemura, H.; Saito, H.; Matsushima, S.; Nakamura, H.; Matsuo, T. *Tetrahedron Lett.* **1989**, *30*, 3143. (b) Harada, A.; Kamachi, M. *J. Chem. Soc., Chem. Commun.* **1990**, 1322. (c) Saito, H.; Yonemura, H.; Nakamura, H.; Matsuo, T. *Chem. Lett.* **1990**, 535. (d) Harada, A.; Li, J.; Suzucki, S.; Kamachi, M. *Macromolecules* **1993**, *26*, 5267. (e) Toki, A.; Yonemura, H.; Matsuo, T. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 3382. (f) Harada, A.; Li, J.; Kamachi, M. *Chem. Lett.* **1993**, 237. (g) Li, J.; Harada, A.; Kamachi, M. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 2808.
- (131) Ogata, H.; Sanui, K.; Wada, J. *J. Polym. Sci., Polym. Lett. Ed.* **1976**, *14*, 459.
- (132) Maciejewski, M.; Panaszewicz, M.; Jarminska, D. *J. Macromol. Sci.-Chem.* **1978**, *A12* (5), 7018.
- (133) Maciejewski, M. *J. Macromol. Sci.-Chem.* **1979**, *A13* (1), 77.
- (134) Maciejewski, M.; Gwizdowski, A.; Peczak, P.; Pietrzak, A. *J. Macromol. Sci.-Chem.* **1979**, *A13* (1), 87.
- (135) Maciejewski, M. *J. Macromol. Sci.-Chem.* **1979**, *A13* (8), 1175.
- (136) Maciejewski, M.; Durski, Z. *J. Macromol. Sci.-Chem.* **1981**, *A16* (2), 441.
- (137) Ogino, H. *J. Am. Chem. Soc.* **1981**, *103*, 1303.
- (138) Ogino, H.; Ohata, K. *Inorg. Chem.* **1984**, *23*, 3312.
- (139) Yamanari, K.; Shimura, Y. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 2283.
- (140) Yamanari, K.; Shimura, Y. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 1596.
- (141) Rao, T. V. S.; Lawrence, D. S. *J. Am. Chem. Soc.* **1990**, *112*, 3614.
- (142) Mankia, J. S.; Lawrence, D. S. *J. Am. Chem. Soc.* **1990**, *112*, 2440.
- (143) Dick, D. L.; Rao, T. V. S.; Sukumaran, D.; Lawrence, D. S. *J. Am. Chem. Soc.* **1992**, *114*, 2664.
- (144) Matile, S.; Hansen, T.; Stocker, A.; Woggon, W.-D. *Helv. Chim. Acta* **1994**, *77*, 1087.
- (145) Rademacher, J. T.; Czarnik, A. W. *J. Am. Chem. Soc.* **1993**, *115*, 3018.
- (146) Isnin, R.; Salam, C.; Kaifer, A. E. *J. Org. Chem.* **1991**, *56*, 35.
- (147) Isnin, R.; Kaifer, A. E. *J. Am. Chem. Soc.* **1991**, *113*, 8188.
- (148) Isnin, R.; Kaifer, A. E. *Pure Appl. Chem.* **1993**, *65*, 495.
- (149) (a) Born, M.; Ritter, H. *Makromol. Chem., Rapid Commun.* **1991**, *12*, 471. (b) Ritter, H. *Macromol. Symp.* **1994**, *77*, 73.
- (150) Born, M.; Ritter, H. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 309.
- (151) Wylie, R. S.; Macartney, D. H. *J. Am. Chem. Soc.* **1992**, *114*, 3136.
- (152) Wylie, R. S.; Macartney, D. H. *Supramolecular Chemistry* **1993**, *3*, 29.
- (153) Macartney, D. H.; Waddling, C. A. *Inorg. Chem.* **1994**, *33*, 5912.
- (154) Wenz, G.; von der Bey, E.; Schmidt, L. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 7835.
- (155) Wenz, G.; Wolf, F.; Wagner, M.; Kubik, S. *New J. Chem.* **1993**, *17*, 729.
- (156) Kunitake, M.; Kotoo, K.; Manabe, O.; Muramatsu, T.; Nakashima, N. *Chem. Lett.* **1993**, 1033.
- (157) Dagani, R. *Chem. Eng. News* **1992**, *70* (Apr. 13), 39.
- (158) Wenz, G.; Keller, B. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 197.
- (159) Harada, A.; Li, J.; Kamachi, M. *Nature* **1992**, *356*, 325. For a very recent report of a similar, biodegradable polyrotaxane, which has been proposed for applications to drug delivery, see: Ooya, T.; Mori, H.; Terrano, M.; Yui, N. *Macromol. Rapid Commun.* **1995**, *16*, 259.
- (160) Harada, A.; Li, J.; Nakamitsu, T.; Kamachi, M. *J. Org. Chem.* **1993**, *58*, 7524.
- (161) Harada, A.; Li, J.; Kamachi, M. *J. Am. Chem. Soc.* **1994**, *116*, 3192.
- (162) Harada, A.; Li, J.; Kamachi, M. *Nature* **1993**, *364*, 516.
- (163) Harada, A.; Li, J.; Kamachi, M. *Nature* **1994**, *370*, 126.
- (164) Armspach, D.; Ashton, P. R.; Moore, C. P.; Spencer, N.; Stoddart, J. F.; Wear, T. J.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 854.
- (165) Armspach, D.; Ashton, P. R.; Spencer, N.; Stoddart, J. F.; Williams, D. J. *Pestic. Sci.* **1994**, *41*, 232.
- (166) Armspach, D.; Ashton, P. R.; Ballardini, R.; Balzani, V.; Godi, A.; Moore, C. P.; Prodi, L.; Spencer, N.; Stoddart, J. F.; Tolley, M. S.; Wear, T. J.; Williams, D. J. *Chem. Eur. J.* **1995**, *1*, 27.
- (167) Meurer, K. P.; Vögtle, F. *Top. Curr. Chem.* **1985**, *127*, 1 and references therein. For more recent examples see: (a) Wilke, G. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 186. (b) Geib, S. J.; Vicent, C.; Fan, E.; Hamilton, A. D. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 119. (c) Williams, D. J.; Colquhoun, H. M.; O'Mahoney, C. A. *J. Chem. Soc., Chem. Commun.* **1994**, 1643. (d) Amelinckx, S.; Bernaerts, D.; Zhang, X. F.; Ivanov, V.; Nagy, J. B. *Science* **1994**, *635*. (e) Noe, C. R.; Miculka, C.; Bats, J. W. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1476.
- (168) Brewster, J. H. *Top. Curr. Chem.* **1974**, *47*, 29.
- (169) Mislow, K.; Gust, D.; Finocchiaro, P.; Boettcher, R. J. *Top. Curr. Chem.* **1974**, *47*, 1.
- (170) Laarhoven, W. H.; Prinsen, W. J. C. *Top. Curr. Chem.* **1984**, *125*, 63. For a recent report containing other references, see: Owens, L.; Thilgen, C.; Diederich, F.; Knobler, C. B. *Helv. Chim. Acta* **1993**, *76*, 2757.
- (171) Bailar, J. C., Jr., Ed. *The Chemistry of Coordination Compounds*; ACS Monograph Series; Reinhold Publ. Co.: New York, 1956.
- (172) (a) Morgan, G. T.; Burstall, F. H. *J. Chem. Soc.* **1931**, 2213. (b) Broomhead, J. A.; Dwyer, F. P. *Aust. J. Chem.* **1962**, *15*, 453. (c) Piper, T. S. *J. Am. Chem. Soc.* **1961**, *83*, 3908. (d) Taylor, L. T.; Busch, D. H. *J. Am. Chem. Soc.* **1967**, *89*, 5372.
- (173) Goedken, V. L.; Christoph, G. *Inorg. Chem.* **1973**, *12*, 2316.
- (174) Wester, D.; Palenik, G. J. *J. Chem. Soc., Chem. Commun.* **1975**, 74.
- (175) Wester, D.; Palenik, G. J. *Inorg. Chem.* **1976**, *15*, 755.
- (176) Constable, E. C.; Holmes, J. M. *Inorg. Chim. Acta* **1987**, *126*, 187.
- (177) Constable, E. C.; Holmes, J. M.; Raithby, P. R. *Polyhedron* **1991**, *10*, 127.

- (178) Struckmeier, G.; Thewalt, U.; Fuhrhop, J.-H. *J. Am. Chem. Soc.* **1976**, *98*, 278. For the recent solid state structure of a metal-free double helix comprised of the oxidation product of a Biliverdin analog, see: Balch, A. L.; Koerner, R.; Olmstead, M. M.; Mazzanti, M.; Safari, N.; St. Claire, T. *J. Chem. Soc., Chem. Commun.* **1995**, 643.
- (179) Sheldrick, W. S.; Engel, J. *J. Chem. Soc., Chem. Commun.* **1980**, 5.
- (180) Bonfiglio, J. V.; Bonnett, R.; Buckley, D. G.; Hamzetash, D.; Hursthouse, M.B.; Malik, K. M. A.; McDonagh, A. F.; Trotter, J. *Tetrahedron* **1983**, *39*, 1865.
- (181) (a) Bonnett, R.; Buckley, D. G.; Namzetash, D. *J. Chem. Soc., Perkin Trans. 1* **1981**, 322. (b) Balch, A. L.; Mazzanti, M.; Noll, B. C.; Olmstead, M. M. *J. Am. Chem. Soc.* **1994**, *116*, 9114.
- (182) van Stein, G. C.; van der Poel, H.; van Koten, G.; Spek, A. L.; Duisenberg, J. M.; Pregosin, P. S. *J. Chem. Soc., Chem. Commun.* **1980**, 1016.
- (183) van Stein, G. C.; van Koten, G.; Vrieze, K.; Brevard, C.; Spek, A. L. *J. Am. Chem. Soc.* **1984**, *106*, 4486.
- (184) van Stein, G. C.; van Koten, G.; Passenier, H.; Steinebach, O.; Vrieze, K. *Inorg. Chim. Acta* **1984**, *89*, 79.
- (185) Libman, J.; Tor, Y.; Shanzer, A. *J. Am. Chem. Soc.* **1987**, *109*, 5880. For the very recent letter describing a switchable system of this type see: Zelikovich, L.; Libman, J.; Shanzer, A. *Nature* **1995**, *374*, 790.
- (186) Potts, K. T.; Gheysen Raiford, K. A.; Keshavarz-K, M. *J. Am. Chem. Soc.* **1993**, *115*, 2793.
- (187) Constable, E. C. *Prog. Inorg. Chem.* Karlin, K. D., Ed. **1994**, *42*, 67.
- (188) Potts, K. T.; Keshavarz-K, M.; Tham, F. S.; Abruña, H. D.; Arana, C. *Inorg. Chem.* **1993**, *32*, 4450.
- (189) Constable, E. C.; Edwards, A. J.; Hannon, M. J.; Raithby, P. R. *J. Chem. Soc., Chem. Commun.* **1994**, 1991.
- (190) Lehn, J.-M.; Sauvage, J.-P.; Simon, J.; Ziessel, R.; Piccini-Leopardi, C.; Germain, G.; Declercq, J.-P.; Van Meerssche, M. *Nouv. J. Chim.* **1983**, *7*, 413.
- (191) Gisselbrecht, J.-P.; Gross, M.; Lehn, J.-M.; Sauvage, J.-P.; Ziessel, R.; Piccini-Leopardi, C.; Arrieta, J. M.; Germain, G.; Van Meerssche, M. *Nouv. J. Chim.* **1984**, *8*, 661.
- (192) Arnaud-Neu, F.; Sanchez, M.; Schwing-Weill, M.-J. *Nouv. J. Chim.* **1986**, *10*, 165.
- (193) Constable, E. C.; Hannon, M. J.; Martin, A.; Raithby, P. R.; Tocher, D. A. *Polyhedron* **1992**, *11*, 2967.
- (194) Potts, K. T.; Keshavarz-K, M.; Tham, F. S.; Abruña, H. D.; Arana, C. *Inorg. Chem.* **1993**, *32*, 4422.
- (195) Constable, E. C.; Drew, M. G. B.; Ward, M. D. *J. Chem. Soc., Chem. Commun.* **1987**, 1600.
- (196) Constable, E. C.; Ward, M. D.; Drew, M. G. B.; Forsyth, G. A. *Polyhedron* **1989**, *8*, 2551.
- (197) Potts, K. T.; Keshavarz-K, M.; Tham, F. S.; Abruña, H. D.; Arana, C. *Inorg. Chem.* **1993**, *32*, 4436.
- (198) Barley, M.; Constable, E. C.; Corr, S. A.; McQueen, R. C. S.; Nutkins, J. C.; Ward, M. D.; Drew, M. G. B. *J. Chem. Soc., Dalton Trans.* **1988**, 2655.
- (199) Constable, E. C.; Drew, M. G. B.; Forsyth, G.; Ward, M. D. *J. Chem. Soc., Chem. Commun.* **1987**, 1450.
- (200) Constable, E. C.; Elder, S. M.; Healy, J.; Ward, M. D.; Tocher, D. A. *J. Am. Chem. Soc.* **1990**, *112*, 4590.
- (201) Constable, E. C.; Martínez-Máñez, R.; Cargill Thompson, A. M. W.; Walker, J. V. *J. Chem. Soc., Dalton Trans.* **1994**, 1585.
- (202) Constable, E. C.; Elder, S. M.; Walker, J. V.; Wood, P. D.; Tocher, D. A. *J. Chem. Soc., Chem. Commun.* **1992**, 229.
- (203) Constable, E. C.; Daniels, M. A. M.; Drew, M. G. B.; Tocher, D. A.; Walker, J. V.; Wood, P. D. *J. Chem. Soc., Dalton Trans.* **1993**, 1947.
- (204) Gheysen, K. A.; Potts, K. T.; Hurrell, H. C.; Abruña, H. D. *Inorg. Chem.* **1990**, *29*, 1589.
- (205) Constable, E. C.; Walker, J. V.; Tocher, D. A.; Daniels, M. A. M. *J. Chem. Soc., Chem. Commun.* **1992**, 768.
- (206) Constable, E. C.; Elder, S. M.; Raithby, P. R.; Ward, M. D. *Polyhedron* **1991**, *10*, 1395.
- (207) Constable, E. C.; Walker, J. V. *J. Chem. Soc., Chem. Commun.* **1992**, 884.
- (208) Constable, E. C.; Edwards, A. J.; Raithby, P. R.; Walker, J. V. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1465.
- (209) Constable, E. C.; Chotalia, R.; Tocher, D. A. *J. Chem. Soc., Chem. Commun.* **1992**, 771.
- (210) Cathey, C. J.; Constable, E. C.; Hannon, M. J.; Tocher, D. A.; Ward, M. D. *J. Chem. Soc., Chem. Commun.* **1990**, 621.
- (211) Constable, E. C.; Ward, M. D.; Tocher, D. A. *J. Am. Chem. Soc.* **1990**, *112*, 1256.
- (212) Constable, E. C.; Ward, M. D.; Tocher, D. A. *J. Chem. Soc., Dalton Trans.* **1991**, 1675.
- (213) Constable, E. C.; Chotalia, R. *J. Chem. Soc., Chem. Commun.* **1992**, 64.
- (214) Williams, A. F.; Piguet, C.; Carina, R. F. *Transition Metals in Supramolecular Chemistry*; Fabbri, L., Poggi, A., Eds.; Kluwer: Boston, 1994; p 409.
- (215) Piguet, C.; Bernardinelli, G.; Williams, A. F. *Inorg. Chem.* **1989**, *28*, 2920.
- (216) Rüttimann, S.; Piguet, C.; Bernardinelli, G.; Bocquet, B.; Williams, A. F. *J. Am. Chem. Soc.* **1992**, *114*, 4230.
- (217) Carina, R. F.; Bernardinelli, G.; Williams, A. F. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1463.
- (218) Williams, A. F.; Piguet, C.; Bernardinelli, G. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1490.
- (219) Piguet, C.; Bernardinelli, G.; Bocquet, B.; Quattropiani, A.; Williams, A. F. *J. Am. Chem. Soc.* **1992**, *115*, 7440.
- (220) Charbonnier, L. J.; Bernardinelli, G.; Piguet, C.; Sargeson, A. M.; Williams, A. F. *J. Chem. Soc., Chem. Commun.* **1994**, 1419.
- (221) Bernardinelli, G.; Piguet, C.; Williams, A. F. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1622.
- (222) Hopfgartner, G.; Piguet, C.; Henion, J. D.; Williams, A. F. *Helv. Chim. Acta* **1993**, *76*, 1759.
- (223) Piguet, C.; Bünzli, J.-C. G.; Bernardinelli, G.; Hopfgartner, G.; Williams, A. F. *J. Am. Chem. Soc.* **1993**, *115*, 8197.
- (224) Piguet, C.; Williams, A. F.; Bernardinelli, G.; Bünzli, J.-C. G. *Inorg. Chem.* **1993**, *32*, 4139.
- (225) (a) Piguet, C.; Bocquet, B.; Hopfgartner, G. *Helv. Chim. Acta* **1994**, *77*, 931. (b) Piguet, C.; Hopfgartner, G.; Williams, A. F.; Bünzli, J.-C. G. *J. Chem. Soc., Chem. Commun.* **1995**, 491.
- (226) (a) Piguet, C.; Hopfgartner, G.; Bocquet, B.; Schaad, O.; Williams, A. F. *J. Am. Chem. Soc.* **1994**, *116*, 9092. (b) Piguet, C.; Bernardinelli, G.; Williams, A. F.; Bocquet, B. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 582.
- (227) Müller, E.; Piguet, C.; Bernardinelli, G.; Williams, A. F. *Inorg. Chem.* **1988**, *27*, 849.
- (228) Constable, E. C.; Hannon, M. J.; Tocher, D. A. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 230.
- (229) Constable, E. C.; Hannon, M. J.; Tocher, D. A. *J. Chem. Soc., Dalton Trans.* **1993**, 1883.
- (230) (a) Youinou, M.-T.; Ziessel, R.; Lehn, J.-M. *Inorg. Chem.* **1991**, *30*, 2144. (b) He, Y.; Lehn, J.-M. *Chem. J. Chin. Univ. (Engl. Ed.)* **1990**, *6*, 183.
- (231) Serr, B. R.; Anderson, K. A.; Elliott, C. M.; Anderson, O. P. *Inorg. Chem.* **1988**, *27*, 4499.
- (232) Lehn, J.-M.; Rigault, A.; Siegel, J.; Harrowfield, J.; Chevrier, B.; Moras, D. *Proc. Natl. Acad. Sci. U.S.A.* **1987**, *84*, 2565.
- (233) Lehn, J.-M.; Rigault, A. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1095.
- (234) (a) Garrett, T. M.; Koert, U.; Lehn, J.-M.; Rigault, A.; Meyer, D.; Fischer, J. *J. Chem. Soc., Chem. Commun.* **1990**, 557. (b) Pfiel, A.; Lehn, J.-M. *J. Chem. Soc., Chem. Commun.* **1992**, 838.
- (235) Eisenbach, C. D.; Schubert, U. S.; Baker, G. R.; Newkome, G. R. *J. Chem. Soc., Chem. Commun.* **1995**, 69.
- (236) Airey, A.-L.; Swiegers, G. F.; Willis, A. C.; Wild, S. B. *J. Chem. Soc., Chem. Commun.* **1995**, 695.
- (237) Harding, M. M.; Koert, U.; Lehn, J.-M.; Marquis-Rigault, A.; Piguet, C.; Siegel, J. *Helv. Chim. Acta* **1991**, *74*, 594.
- (238) Koert, U.; Harding, M. M.; Lehn, J.-M. *Nature* **1990**, *346*, 339.
- (239) Schoentjes, B.; Lehn, J.-M. *Helv. Chim. Acta* **1995**, *78*, 1.
- (240) Zarges, W.; Hall, J.; Lehn, J.-M.; Bolm, C. *Helv. Chim. Acta* **1991**, *74*, 1843.
- (241) Krämer, R.; Lehn, J.-M.; De Cian, A.; Fischer, J. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 703.
- (242) Krämer, R.; Lehn, J.-M.; Marquis-Rigault, A. *Proc. Natl. Acad. Sci. U.S.A.* **1993**, *90*, 5394.
- (243) (a) Baxter, P.; Lehn, J.-M.; De Cian, A.; Fischer, J. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 69. (b) Baxter, P. N. W.; Lehn, J.-M.; Fischer, J.; Youinou, M.-T. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2284. (c) Hanan, G. S.; Arana, C. R.; Lehn, J.-M.; Fenske, D. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1122.
- (244) Crane, J. D.; Sauvage, J.-P. *New J. Chem.* **1992**, *16*, 649.
- (245) Zurita, D.; Baret, P.; Pierre, J.-L. *New J. Chem.* **1994**, *18*, 1143.
- (246) Enemark, E. J.; Stack, T. D. P. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 996.
- (247) (a) Bell, T. W.; Firestone, A.; Ludwig, R. *J. Chem. Soc., Chem. Commun.* **1989**, 1902. (b) Bell, T. W.; Liu, J. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 923. (c) Bell, T. W.; Guzzo, F.; Drew, M. G. B. *J. Am. Chem. Soc.* **1991**, *113*, 3115. (d) Bell, T. W.; Jousselin, H. *J. Am. Chem. Soc.* **1991**, *113*, 6283.
- (248) Bell, T. W.; Jousselin, H. *Nature* **1994**, *367*, 441-444.
- (249) Complexation of a guest, particularly a metal ion, within a cyclic ligand system is often likely to induce helicity into the backbone of the host, and we have restricted the discussion here to recent topical examples. Similarly, metal ion complexation by bicyclic ligands may result in a triple-helical conformation of the host framework. See, for example: Ngwenya, M. P.; Martell, A. E.; Reibenspies, J. *J. Chem. Soc., Chem. Commun.* **1990**, 1207.
- (250) Ziessel, R.; Youinou, M.-T. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 877.
- (251) Judice, J. K.; Keipert, S. J.; Cram, D. J. *J. Chem. Soc., Chem. Commun.* **1993**, 1323.
- (252) Fenton, D. E.; Matthews, R. W.; McPartlin, M.; Murphy, B. P.; Scowen, I. J.; Tasker, P. A. *J. Chem. Soc., Chem. Commun.* **1994**, 1391.
- (253) Mascal, M.; Moody, C. J.; Morrell, A. I.; Slawin, A. M. Z.; Williams, D. J. *J. Am. Chem. Soc.* **1993**, *115*, 813.
- (254) Engel, N.; Gossauer, A.; Gruber, K.; Kratky, C. *Helv. Chim. Acta* **1993**, *76*, 2236.

- (255) Fouquey, C.; Lehn, J.-M.; Levelut, A.-M. *Adv. Mater.* **1990**, *2*, 254.
- (256) (a) Gulik-Krzywicki, T.; Fouquey, C.; Lehn, J.-M. *Proc. Natl. Acad. Sci. U.S.A.* **1993**, *90*, 163. (b) Lehn, J.-M. *Makromol. Chem., Macromol. Symp.* **1993**, *69*, 1.
- (257) Fuhrhop, J.-H.; Helfrich, W. *Chem. Rev.* **1993**, *93*, 1565.
- (258) (a) Nakashima, N.; Asakuma, S.; Kunitake, T. *J. Am. Chem. Soc.* **1985**, *107*, 509. (b) Fuhrhop, J.-H.; Schneider, Boekema, E.; Helfrich, W. *J. Am. Chem. Soc.* **1988**, *110*, 2861.
- (259) Fuhrhop, J.-H.; Schneider, Rosenberg, J.; Boekema, E. *J. Am. Chem. Soc.* **1987**, *109*, 3387.
- (260) Fuhrhop, J.-H.; Svenson, S.; Boettcher, C.; Rössler, E.; Vieth, H.-M. *J. Am. Chem. Soc.* **1990**, *112*, 4307.
- (261) Köning, J.; Boettcher, C.; Winkler, H.; Zeitler, E.; Talmon, Y.; Fuhrhop, J.-H. *J. Am. Chem. Soc.* **1993**, *115*, 693.
- (262) Hanessian, S.; Gomtysan, A.; Simard, M.; Roelans, S. *J. Am. Chem. Soc.* **1994**, *116*, 4495. A full paper has recently appeared on this work. Hanessian, S.; Gomtysan, A.; Simard, M.; Roelans, S. *J. Am. Chem. Soc.* **1995**, *117*, 7630.
- (263) (a) Cram, D. J.; Trueblood, K. N. *Top. Curr. Chem.* **1981**, *98*, 43. (b) Cram, D. J.; Cram, J. M. *Container Molecules and their Guests*, Monographs in Supramolecular Chemistry, Stoddart, J. F., Series Ed.; The Royal Society of Chemistry: Cambridge, 1994.
- (264) (a) Lindoy, L. F. *The Chemistry of Macrocyclic Ligand Complexes*, Cambridge University Press: New York, 1989. (b) Dietrich, B.; Viout, P.; Lehn, J.-M. *Macrocyclic Chemistry*, VCH: New York, 1993.
- (265) Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 7017.
- (266) (a) Pedersen, C. J.; Frensdorff, H. K. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 16. (b) Gokel, G. W.; Durst, H. D. *Synthesis* **1976**, 168. (c) Weber, E.; Vögtle, F. *Top. Curr. Chem.* **1981**, *98*, 1. (d) Gokel, G. W. *Crown Ethers and Cryptands*, Monographs in Supramolecular Chemistry; Stoddart, J. F., Series Ed.; The Royal Society of Chemistry: Cambridge, 1991.
- (267) (a) Dietrich, B.; Lehn, J.-M.; Sauvage, J.-P. *Tetrahedron* **1973**, *29*, 1647. (b) Lehn, J.-M. *Acc. Chem. Res.* **1978**, *11*, 49. (c) Lehn, J.-M. *Pure Appl. Chem.* **1978**, *50*, 871.
- (268) Chambron, J.-C.; Dietrich-Buchecker, C. O.; Heitz, V.; Nierengarten, J.-F.; Sauvage, J.-P. *Transition Metals in Supramolecular Chemistry*; Fabbrizzi, L., Poggi, A., Eds.; Kluwer Academic Publishers: Boston, 1994; p 371.
- (269) Dietrich-Buchecker, C. O.; Marnot, P. A.; Sauvage, J.-P. *Tetrahedron Lett.* **1982**, *23*, 5291.
- (270) Dietrich-Buchecker, C. O.; Marnot, P. A.; Sauvage, J.-P.; Kintzinger, J. P.; Maltese, P. *Nouv. J. Chim.* **1984**, *8*, 573.
- (271) Dietrich-Buchecker, C. O.; Sauvage, J.-P. *Tetrahedron Lett.* **1983**, *24*, 5091.
- (272) Dietrich-Buchecker, C. O.; Sauvage, J.-P.; Kintzinger, J. P. *Tetrahedron Lett.* **1983**, *24*, 5095.
- (273) Dietrich-Buchecker, C. O.; Sauvage, J.-P.; Kern, J.-M. *J. Am. Chem. Soc.* **1984**, *106*, 3043.
- (274) Dietrich-Buchecker, C. O.; Sauvage, J.-P. *Tetrahedron* **1990**, *46*, 503.
- (275) Cesario, M.; Dietrich-Buchecker, C. O.; Guilhem, J.; Pascard, C.; Sauvage, J.-P. *J. Chem. Soc., Chem. Commun.* **1985**, 244.
- (276) (a) Albrecht-Gary, A.-M.; Saad, Z.; Dietrich-Buchecker, C. O.; Sauvage, J.-P. *J. Am. Chem. Soc.* **1985**, *107*, 3205. (b) Albrecht-Gary, A.-M.; Dietrich-Buchecker, C. O.; Saad, Z.; Sauvage, J.-P. *J. Am. Chem. Soc.* **1988**, *110*, 1467.
- (277) Albrecht-Gary, A.-M.; Dietrich-Buchecker, C. O.; Saad, Z.; Sauvage, J.-P. *J. Chem. Soc., Chem. Commun.* **1992**, 280.
- (278) Cesario, M.; Dietrich-Buchecker, C. O.; Edel, A.; Guilhem, J.; Kintzinger, J.-P.; Pascard, C.; Sauvage, J.-P. *J. Am. Chem. Soc.* **1986**, *108*, 6250.
- (279) Dietrich-Buchecker, C. O.; Kern, J.-M.; Sauvage, J.-P. *J. Chem. Soc., Chem. Commun.* **1985**, 760.
- (280) Dietrich-Buchecker, C. O.; Guilhem, J.; Kern, J.-M.; Pascard, C.; Sauvage, J.-P. *Inorg. Chem.* **1994**, *33*, 3498.
- (281) Blake, A. J.; Dietrich-Buchecker, C. O.; Hyde, T. I.; Sauvage, J.-P.; Schröder, M. *J. Chem. Soc., Chem. Commun.* **1989**, 1663.
- (282) Dietrich-Buchecker, C. O.; Sauvage, J.-P.; Weiss, J. *Tetrahedron Lett.* **1986**, *20*, 2257.
- (283) Albrecht-Gary, A.-M.; Dietrich-Buchecker, C. O.; Saad, Z.; Sauvage, J.-P.; Weiss, J. *J. Chem. Soc., Chem. Commun.* **1986**, 1325.
- (284) Dietrich-Buchecker, C. O.; Edel, A.; Kintzinger, J. P.; Sauvage, J.-P. *Tetrahedron* **1987**, *43*, 333.
- (285) Mitchell, D. A.; Sauvage J.-P. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 930.
- (286) Chambron, J.-C.; Mitchell, D. A.; Sauvage J.-P. *J. Am. Chem. Soc.* **1992**, *114*, 4625.
- (287) Kaida, Y.; Okamoto, Y.; Chambron, J.-C.; Mitchell, D. A.; Sauvage J.-P. *Tetrahedron Lett.* **1993**, *34*, 1019.
- (288) Sauvage J.-P.; Weiss, J. *J. Am. Chem. Soc.* **1985**, *107*, 6108.
- (289) Guilhem, J.; Pascard, C.; Sauvage J.-P.; Weiss, J. *J. Am. Chem. Soc.* **1988**, *110*, 8711.
- (290) Dietrich-Buchecker, C. O.; Khémis, A.-K.; Sauvage, J.-P.; *J. Chem. Soc., Chem. Commun.* **1986**, 1376.
- (291) Dietrich-Buchecker, C. O.; Hemmert, C.; Khémis, A.-K.; Sauvage, J.-P.; *J. Am. Chem. Soc.* **1990**, *112*, 8002.
- (292) Bitsch, F.; Dietrich-Buchecker, C. O.; Hemmert, C.; Khémis, A.-K.; Sauvage, J.-P. *J. Am. Chem. Soc.* **1991**, *113*, 4023.
- (293) Bitsch, F.; Hegy, G.; Dietrich-Buchecker, C. O.; Leize, E.; Sauvage, J.-P.; Van Dorsselaer, A. *New J. Chem.* **1994**, *18*, 801.
- (294) Dietrich-Buchecker, C. O.; Guilhem, J.; Khémis, A.-K.; Kintzinger, J.-P.; Pascard, C.; Sauvage, J.-P.; *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 661.
- (295) Dietrich-Buchecker, C. O.; Hemmert, C.; Sauvage, J.-P. *New J. Chem.* **1990**, *14*, 603.
- (296) Armaroli, N.; Balzani, V.; Barigelletti, F.; De Cola, L.; Sauvage, J.-P.; Hemmert, C. *J. Am. Chem. Soc.* **1991**, *113*, 4033.
- (297) Armaroli, N.; Balzani, V.; Barigelletti, F.; De Cola, L.; Flamigni, L.; Sauvage, J.-P.; Hemmert, C. *J. Am. Chem. Soc.* **1994**, *116*, 5211.
- (298) Armaroli, N.; Balzani, V.; De Cola, L.; Hemmert, C.; Sauvage, J.-P. *New J. Chem.* **1994**, *18*, 775.
- (299) Wu, C.; Lecavalier, P. R.; Shen, Y. X.; Gibson, H. W. *Chem. Mater.* **1991**, *3*, 569.
- (300) (a) Noblat, S.; Dietrich-Buchecker, C. O.; Sauvage, J.-P. *Tetrahedron Lett.* **1987**, *28*, 5829. (b) Chardon-Noblat, S.; Sauvage, J.-P. *Tetrahedron* **1991**, *47*, 5123. (c) Heitz, V.; Chardon-Noblat, S.; Sauvage, J.-P. *Tetrahedron Lett.* **1991**, *32*, 197. (d) Pascard, C.; Guilhem, J.; Chardon-Noblat, S.; Sauvage, J.-P. *New J. Chem.* **1993**, *17*, 331.
- (301) (a) Chardon-Noblat, S.; Sauvage, J.-P.; Mathis, P. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 593. (b) Brun, A. M.; Harriman, A.; Heitz, V.; Sauvage, J.-P. *J. Am. Chem. Soc.* **1991**, *113*, 8657.
- (302) Chambron, J.-C.; Heitz, V.; Sauvage, J.-P. *J. Chem. Soc., Chem. Commun.* **1992**, 1131.
- (303) Chambron, J.-C.; Heitz, V.; Sauvage, J.-P. *J. Am. Chem. Soc.* **1993**, *115*, 12378.
- (304) Chambron, J.-C.; Chardon-Noblat, S.; Harriman, A.; Heitz, V.; Sauvage, J.-P. *Pure Appl. Chem.* **1993**, *65*, 2343.
- (305) (a) Chambron, J.-C.; Harriman, A.; Heitz, V.; Sauvage, J.-P. *J. Am. Chem. Soc.* **1993**, *115*, 6109. (b) Chambron, J.-C.; Harriman, A.; Heitz, V.; Sauvage, J.-P. *J. Am. Chem. Soc.* **1993**, *115*, 7419.
- (306) Diederich, F.; Dietrich-Buchecker, C. O.; Nierengarten, J.-F.; Sauvage, J.-P. *J. Chem. Soc., Chem. Commun.* **1995**, 781.
- (307) Chambron, J.-C.; Dietrich-Buchecker, C. O.; Nierengarten, J.-F.; Sauvage, J.-P. *J. Chem. Soc., Chem. Commun.* **1993**, 801. For a recent full paper on this work, see: Chambron, J.-C.; Dietrich-Buchecker, C. O.; Nierengarten, J.-F.; Sauvage, J.-P.; Solladie, N.; Albrecht-Gary, A.-M.; Meyer, M. *New J. Chem.* **1995**, *19*, 409. In addition, Lehn and co-workers have reported analogous systems using bipyridine derivatives in the thread components, which are somewhat more rigid than those of the Sauvage group, the aim being to generate racklike superstructures. See: Sleiman, H.; Baxter, P.; Lehn, J.-M.; Rissanen, K. *J. Chem. Soc., Chem. Commun.* **1995**, 715.
- (308) Momenteau, M.; Le Bras, F.; Loock, B. *Tetrahedron Lett.* **1994**, *35*, 3289. Sauvage and co-workers have subsequently described the preparation of a [3]catenane in which two porphyrins are incorporated into the same central ring. See: Chambron, J.-C.; Heitz, V.; Sauvage, J.-P. *Bull. Soc. Chim. Fr.* **1995**, *32*, 340.
- (309) Jorgensen, T.; Becher, J.; Chambron, J.-C.; Sauvage, J.-P. *Tetrahedron Lett.* **1994**, *35*, 4339.
- (310) Livoreil, A.; Dietrich-Buchecker, C. O.; Sauvage, J.-P. *J. Am. Chem. Soc.* **1994**, *116*, 9399.
- (311) Sauvage, J.-P.; Ward, M. *Inorg. Chem.* **1991**, *30*, 3869.
- (312) Dietrich-Buchecker, C. O.; Sauvage J.-P. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 189.
- (313) Dietrich-Buchecker, C. O.; Sauvage J.-P.; Kintzinger, J.-P.; Maltese, P.; Pascard, C.; Guilhem, J. *New J. Chem.* **1992**, *16*, 931.
- (314) Dietrich-Buchecker, C. O.; Guilhem, J.; Pascard, C.; Sauvage J.-P. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1154.
- (315) Dietrich-Buchecker, C. O.; Nierengarten, J.-F.; Sauvage, J.-P. *Tetrahedron Lett.* **1992**, *33*, 3625.
- (316) Albrecht-Gary, A. M.; Dietrich-Buchecker, C. O.; Guilhem, J.; Meyer, M.; Pascard, C.; Sauvage, J.-P. *Recl. Trav. Chim. Pays-Bas* **1993**, *112*, 427.
- (317) Dietrich-Buchecker, C. O.; Nierengarten, J.-F.; Sauvage, J.-P.; Armaroli, N.; Balzani, V.; De Cola, L. *J. Am. Chem. Soc.* **1993**, *115*, 11237.
- (318) Dietrich-Buchecker, C. O.; Sauvage, J.-P.; De Cian, A.; Fischer, J. *J. Chem. Soc., Chem. Commun.* **1994**, 2231.
- (319) Nierengarten, J.-F.; Dietrich-Buchecker, C. O.; Sauvage, J.-P. *J. Am. Chem. Soc.* **1994**, *116*, 375.
- (320) Dietrich-Buchecker, C.; Leize, E.; Nierengarten, J.-F.; Sauvage, J.-P.; Van Dorsselaer, A. *J. Chem. Soc., Chem. Commun.* **1994**, 2257.
- (321) Walba, D. M.; Zheng, Q. Y.; Schilling, K. *J. Am. Chem. Soc.* **1992**, *114*, 6259.
- (322) (a) Walba, D. M. *Stereochemical Topology*. In *Chemical Applications of Topology and Graph Theory*; King, R. B., Ed.; Elsevier: Amsterdam, 1983; pp 17–32. (b) Flapan, E. *Pac. J. Math.* **1987**, *129*, 57. (c) Walba, D. M. *Topological Stereochemistry: Knot Theory of Molecular Graphs*. In *Graph Theory and Topology in Chemistry*; King, R. B., Ed.; Elsevier: Amsterdam, 1987; pp 23–42.
- (323) Dietrich-Buchecker, C. O.; Frommberger, B.; Lürer, I.; Sauvage, J.-P.; Vögtle, F. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1434.

- (324) (a) Kawasaki, Y.; Matsumoto, T. *J. Inclusion Phenom. Mol. Recognit. Chem.* **1984**, *2*, 171. (b) Bott, S. G.; Elgamal, H.; Atwood, J. L. *J. Am. Chem. Soc.* **1985**, *107*, 1796. (c) Kobiro, K.; Takada, S.; Odaira, Y.; Kawasaki, Y. *J. Chem. Soc., Dalton Trans.* **1986**, 1767. (d) Kobiro, K.; Takahashi, M.; Odaira, Y.; Kawasaki, Y.; Kai, Y.; Kasai, N. *J. Chem. Soc., Dalton Trans.* **1986**, 2613. (e) Pears, D. A.; Stoddart, J. F.; Crosby, J.; Allwood, B. L.; Williams, D. J. *Acta Crystallogr.* **1986**, *C42*, 51. (f) Bott, S. G.; Alvanipour, A.; Morley, S. D.; Atwood, D. A.; Means, C. M.; Coleman, A. W.; Atwood, J. L. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 485. (g) Sibert, J. W.; Lange, S. J.; Stern, C.; Hoffman, B. M.; Barrett, A. G. M. *J. Chem. Soc., Chem. Commun.* **1994**, 1751.
- (325) Beer, P. D.; Rothin, A. S. *Polyhedron* **1989**, *8*, 1251.
- (326) Richey, H. G., Jr.; Kushlan, D. M. *J. Am. Chem. Soc.* **1987**, *109*, 2510.
- (327) Pajerski, A. D.; Parvez, M.; Richey, H. G., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 2660.
- (328) Pajerski, A. D.; BergStresser, G. L.; Parvez, M.; Richey, H. G., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 4844.
- (329) Markies, P. R.; Nomoto, T.; Akkerman, O. S.; Bickelhaupt, F. J. *Am. Chem. Soc.* **1988**, *110*, 4845.
- (330) Markies, P. R.; Nomoto, T.; Akkerman, O. S.; Bickelhaupt, F.; Smeets, W. J. J.; Spek, A. L. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1084.
- (331) Markies, P. R.; Schat, G.; Akkerman, O. S.; Bickelhaupt, F.; Smeets, W. J. J.; Spek, A. L. *Organometallics* **1991**, *10*, 3538.
- (332) Gruter, G.-J. M.; de Kanter, F. J. J.; Markies, P. R.; Nomoto, T.; Akkerman, O. S.; Bickelhaupt, F. *J. Am. Chem. Soc.* **1993**, *115*, 12179.
- (333) Fujita, M.; Ibukuro, F.; Hagihara, H.; Ogura, K. *Nature* **1994**, *367*, 720.
- (334) (a) Fujita, M.; Nagao, S.; Iida, M.; Ogata, K.; Ogura, K. *J. Am. Chem. Soc.* **1993**, *115*, 1574. (b) Fujita, M.; Yazaki, J.; Kuramochi, T.; Ogura, K. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 1837.
- (335) Fujita, M.; Ibukuro, F.; Yamaguchi, K.; Ogura, K. *J. Am. Chem. Soc.* **1995**, *117*, 4175.
- (336) Fujita, M.; Ibukuro, F.; Seki, H.; Kamo, O.; Imanari, M.; Ogura, K. *J. Am. Chem. Soc.*, submitted for publication. We thank Professor Fujita for providing us with a preprint of this work.
- (337) Stoddart, J. F. *Chem. Br.* **1991**, 27, 714.
- (338) Summers, L. A. *The Bipyridinium Herbicides*; Academic Press: New York, 1980.
- (339) Stoddart, J. F. *Pure Appl. Chem.* **1988**, *60*, 467.
- (340) (a) Colquhoun, H. M.; Goodings, E. P.; Maud, J. M.; Stoddart, J. F.; Wolstenholme, J. B.; Williams, D. J. *J. Chem. Soc., Perkin Trans. 2* **1985**, 607. (b) Allwood, B. L.; Shahriari-Zavareh, H.; Stoddart, J. F.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1987**, 1058. (c) Allwood, B. L.; Spencer, N.; Shahriari-Zavareh, H.; Stoddart, J. F.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1987**, 1061.
- (341) Allwood, B. L.; Colquhoun, H. M.; Doughty, S. M.; Kohnke, F. H.; Slawin, A. M. Z.; Stoddart, J. F.; Williams, D. J.; Zarzycki, R. *J. Chem. Soc., Chem. Commun.* **1987**, 1054.
- (342) (a) Anelli, P. L.; Spencer, N.; Stoddart, J. F. *Tetrahedron Lett.* **1988**, *29*, 1569. (b) Anelli, P. L.; Stoddart, J. F.; Slawin, A. M. Z.; Williams, D. J. *Acta Crystallogr.* **1990**, *C46*, 1464. (c) Anelli, P. L.; Stoddart, J. F.; Slawin, A. M. Z.; Williams, D. J. *Acta Crystallogr.* **1990**, *C46*, 1468.
- (343) Helgeson, R. C.; Tarnowski, T. L.; Timko, J. M.; Cram, D. J. *J. Am. Chem. Soc.* **1977**, *99*, 6411.
- (344) Ashton, P. R.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1987**, 1066.
- (345) Allwood, B. L.; Spencer, N.; Shahriari-Zavareh, H.; Stoddart, J. F.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1987**, 1064.
- (346) Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1987**, 10702.
- (347) Ashton, P. R.; Philp, D.; Reddington, M. V.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1991**, 1680.
- (348) Shen, Y. A.; Engen, P. T.; Berg, M. A. G.; Merola, J. S.; Gibson, H. W. *Macromolecules* **1992**, *25*, 2786.
- (349) Ashton, P. R.; Chrystal, E. J. T.; Mathias, J. P.; Parry, K. P.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Williams, D. J. *Tetrahedron Lett.* **1987**, *28*, 6367.
- (350) Ortholand, J.-Y.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 1394.
- (351) Odell, B.; Reddington, M. V.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1547.
- (352) (a) Geuder, W.; Hünig, S.; Suchy, A. *Angew. Chem., Int. Ed. Engl.* **1983**, *27*, 489. (b) Geuder, W.; Hünig, S.; Suchy, A. *Tetrahedron* **1986**, *42*, 1665. (c) Geuder, W.; Hünig, S.; Suchy, A. *Angew. Chem., Int. Ed. Engl.* **1983**, *27*, 489. (d) Brown, C. L.; Philp, D.; Stoddart, J. F. *Synlett* **1991**, 462-464. (e) Benniston, A. C.; Harriman, A. *Synlett* **1993**, 223. (f) Rojas, M. T.; Kaifer, A. E. *J. Am. Chem. Soc.* **1995**, *117*, 5883.
- (353) (a) Bühner, M.; Geuder, W.; Gries, W.-K.; Hünig, S.; Koch, M.; Poll, T. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1553. (b) Goodnow, T. T.; Reddington, M. V.; Stoddart, J. F.; Kaifer, A. E. *J. Am. Chem. Soc.* **1991**, *113*, 4335. (c) Bernardo, A. R.; Stoddart, J. F.; Kaifer, A. E. *J. Am. Chem. Soc.* **1992**, *114*, 10624.
- (354) Ashton, P. R.; Odell, B.; Reddington, M. V.; Slawin, A. M. Z.; Stoddart, J. F.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1550.
- (355) Anelli, P. L.; Ashton, P. R.; Ballardini, R.; Balzani, V.; Delgado, M.; Gandolfi, M. T.; Goodnow, T. T.; Kaifer, A. E.; Philp, D.; Pietraszkiewicz, M.; Prodi, L.; Reddington, M. V.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Vicent, C.; Williams, D. J. *J. Am. Chem. Soc.* **1992**, *114*, 193.
- (356) Ashton, P. R.; Goodnow, T. T.; Kaifer, A. E.; Reddington, M. V.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Vicent, C.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 1396.
- (357) Brown, C. L.; Philp, D.; Spencer, N.; Stoddart, J. F. *Israel J. Chem.* **1992**, *32*, 61.
- (358) Brown, C. L.; Philp, D.; Stoddart, J. F. *Synlett* **1991**, 459.
- (359) (a) Isaacs, N. S. *Liquid Phase High Pressure Chemistry*; John Wiley & Sons: Chichester, 1981. (b) Isaacs, N. S. *Tetrahedron* **1991**, *47*, 8463.
- (360) Amabilino, D. B.; Ashton, P. R.; Stoddart, J. F. *Supramol. Chem.* **1995**, *5*, 5.
- (361) Ashton, P. R.; Brown, C. L.; Chrystal, E. J.; Goodnow, T. T.; Kaifer, A. E.; Parry, K. P.; Philp, D.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1991**, 634.
- (362) Ashton, P. R.; Blower, M.; Philp, D.; Spencer, N.; Stoddart, J. F.; Tolley, M. S.; Ballardini, R.; Ciano, M.; Balzani, V.; Gandolfi, M. T.; Prodi, L.; McLean, C. H. *New J. Chem.* **1993**, *17*, 689.
- (363) (a) Amabilino, D. B.; Ashton, P. R.; Brown, G. R.; Hayes, W.; Stoddart, J. F.; Tolley, M. S.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1994**, 2475. (b) Amabilino, D. B.; Anelli, P. L.; Ashton, P. R.; Brown, G. R.; Córdova, E.; Godínez, L. A.; Hayes, W.; Kaifer, A. E.; Philp, D.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Tolley, M. S.; Williams, D. J. *J. Am. Chem. Soc.* **1995**, *117*, 11142.
- (364) Amabilino, D. B.; Ashton, P. R.; Brown, C. L.; Córdova, E.; Godínez, L. A.; Goodnow, T. T.; Kaifer, A. E.; Newton, S. P.; Pietraszkiewicz, M.; Philp, D.; Raymo, F. M.; Reder, A. S.; Rutland, M. T.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Williams, D. J. *J. Am. Chem. Soc.* **1995**, *117*, 1271.
- (365) Ashton, P. R.; Blower, M. A.; Iqbal, S.; McLean, C. H.; Stoddart, J. F.; Tolley, M. S.; Williams, D. J. *Synlett* **1994**, 1059.
- (366) Ashton, P. R.; Blower, M. A.; McLean, C. H.; Stoddart, J. F.; Tolley, M. S. *Synlett* **1994**, 1063.
- (367) Amabilino, D. B.; Stoddart, J. F. *Recl. Trav. Chim. Pays-Bas* **1993**, *112*, 429.
- (368) (a) Gunter, M. J.; Johnston, M. R. *Tetrahedron Lett.* **1990**, 31, 4801. (b) Gunter, M. J.; Johnston, M. R. *Tetrahedron Lett.* **1992**, *33*, 1771. (c) Gunter, M. J.; Johnston, M. R. *J. Chem. Soc., Perkin Trans. 1* **1994**, 995. (d) Gunter, M. J.; Johnston, M. R.; Skelton, B. W.; White, A. H. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1009.
- (369) Gunter, M. J.; Johnston, M. R. *J. Chem. Soc., Chem. Commun.* **1992**, 1163.
- (370) Gunter, M. J.; Hockless, D. C. R.; Johnston, M. R.; Skelton, B. W.; White, A. H. *J. Am. Chem. Soc.* **1994**, *116*, 4810.
- (371) Gunter, M. J.; Johnston, M. R. *J. Chem. Soc., Chem. Commun.* **1994**, 829.
- (372) Lu, T.; Zhang, L.; Gokel, G. W.; Kaifer, A. E. *J. Am. Chem. Soc.* **1993**, *115*, 2542.
- (373) Ashton, P. R.; Brown, C. L.; Chrystal, E. J. T.; Parry, K. P.; Pietraszkiewicz, M.; Spencer, N.; Stoddart, J. F. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1042.
- (374) Amabilino, D. B.; Ashton, P. R.; Tolley, M. S.; Stoddart, J. F.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1297.
- (375) Ashton, P. R.; Preece, J. A.; Stoddart, J. F.; Tolley, M. S.; White, A. J. P.; Williams, D. J. *Synthesis* **1994**, 1344.
- (376) (a) Vögtle, F.; Müller, W. M.; Müller, U.; Bauer, M.; Rissanen, K. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1295. (b) Bauer, M.; Müller, W. M.; Müller, U.; Rissanen, K.; Vögtle, F. *Liebigs Ann. Chem.* **1995**, 649.
- (377) (a) Ashton, P. R.; Ballardini, R.; Gandolfi, M. T.; Marquis, D. J.-F.; Pérez-García, L.; Prodi, L.; Stoddart, J. F.; Venturi, M. *J. Chem. Soc., Chem. Commun.* **1994**, 177. (b) Ashton, P. R.; Ballardini, R.; Balzani, V.; Credi, A.; Gandolfi, M. T.; Menzer, S.; Pérez-García, L.; Prodi, L.; Stoddart, J. F.; Venturi, M.; White, A. J. P.; Williams, D. J. *J. Am. Chem. Soc.* **1995**, *117*, 11171.
- (378) Ashton, P. R.; Pérez-García, L.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 571.
- (379) Ashton, P. R.; Iriepa, I.; Reddington, M. V.; Spencer, N.; Slawin, A. M. Z.; Stoddart, J. F.; Williams, D. J. *Tetrahedron Lett.* **1994**, *35*, 4835.
- (380) Ashton, P. R.; Brown, C. L.; Chrystal, E. J. T.; Goodnow, T. T.; Kaifer, A. E.; Parry, K. P.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1039.
- (381) Ashton, P. R.; Brown, C. L.; Chapman, J. R.; Gallagher, R. T.; Stoddart, J. F. *Tetrahedron Lett.* **1992**, *33*, 7771.

- (382) Amabilino, D. B.; Ashton, P. R.; Reder, A. S.; Spencer, N.; Stoddart, J. F. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 433.
- (383) Amabilino, D. B.; Ashton, P. R.; Stoddart, J. F.; Menzer, S.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1994**, 2479.
- (384) Amabilino, D. B.; Ashton, P. R.; Reder, A. S.; Spencer, N.; Stoddart, J. F. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1286.
- (385) Ashton, P. R.; Reder, A. S.; Spencer, N.; Stoddart, J. F. *J. Am. Chem. Soc.* **1993**, *115*, 5286.
- (386) (a) Ashton, P. R.; Preece, J. A.; Stoddart, J. F.; Tolley, M. S. *Synlett* **1994**, 789. (b) Amabilino, D. B.; Ashton, P. R.; Preece, J. A.; Stoddart, J. F.; Tolley, M. S. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Sci.)* **1995**, *36* (1), 587. (c) Ashton, P. R.; Huff, J.; Menzer, S.; Parsons, I. W.; Preece, J. A.; Stoddart, J. F.; Tolley, M. S.; White, A. J. P.; Williams, D. J. *Chem. Eur. J.* **1996**, *2*, 123.
- (387) Amabilino, D. B.; Ashton, P. R.; Pérez-García, L.; Stoddart, J. F. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2378.
- (388) Anelli, P. L.; Ashton, P. R.; Spencer, N.; Slawin, A. M. Z.; Stoddart, J. F.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1036.
- (389) Ashton, P. R.; Philp, D.; Spencer, N.; Stoddart, J. F. *J. Chem. Soc., Chem. Commun.* **1991**, 1677.
- (390) Ashton, P. R.; Philp, D.; Spencer, N.; Stoddart, J. F.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1994**, 181.
- (391) Ashton, P. R.; Philp, D.; Spencer, N.; Stoddart, J. F. *Makromol. Chem. Macromol. Symp.* **1992**, *54/55*, 441.
- (392) Reddington, M. V.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Vicent, C.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1991**, 630.
- (393) (a) Marsella, M. J.; Carroll, P. J.; Swager, T. M. *J. Am. Chem. Soc.* **1994**, *116*, 9347. (b) Marsella, M. J.; Carroll, P. J.; Swager, T. M. *J. Am. Chem. Soc.* **1995**, *117*, 9832.
- (394) (a) Swager, T. M.; Marsella, M. J.; Newland, R. J.; Zhou, Q. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Sci.)* **1995**, *36* (1), 546. (b) Zhou, Q.; Ezer, M. R.; Swager, T. M. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Sci.)* **1995**, *36* (1), 607. Some of this more recent work has proved an enhancement in the sensitivity of fluorescent chemosensors; details are described in: Zhou, Q.; Swager, T. M. *J. Am. Chem. Soc.* **1995**, *117*, 7017.
- (395) Amabilino, D. B.; Stoddart, J. F. *Pure Appl. Chem.* **1993**, *65*, 2351.
- (396) Ashton, P. R.; Grognez, M.; Slawin, A. M. Z.; Stoddart, J. F.; Williams, D. J. *Tetrahedron Lett.* **1991**, *32*, 6235.
- (397) Anelli, P. L.; Spencer, N.; Stoddart, J. F. *J. Am. Chem. Soc.* **1991**, *113*, 5131.
- (398) Sun, X.; Amabilino, D. B.; Parsons, I. W.; Stoddart, J. F. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Sci.)* **1993**, *32* (1), 104.
- (399) Sun, X.; Amabilino, D. B.; Parsons, I. W.; Stoddart, J. F.; Tolley, M. S. *Macromol. Symp.* **1994**, *77*, 191.
- (400) Bissell, R. A.; Stoddart, J. F. *Computations for the Nano-Scale*; Blöchl, P. E.; Joachim, C.; Fisher, A. J., Eds.; Kluwer: Boston, 1993; p 141.
- (401) Ashton, P. R.; Bissell, R. A.; Spencer, N.; Stoddart, J. F.; Tolley, M. S. *Synlett* **1992**, 914.
- (402) Ashton, P. R.; Bissell, R. A.; Górski, R.; Philp, D.; Spencer, N.; Stoddart, J. F.; Tolley, M. S. *Synlett* **1992**, 919.
- (403) Philp, D.; Slawin, A. M. Z.; Spencer, N.; Stoddart, J. F.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1991**, 1584.
- (404) Ashton, P. R.; Bissell, R. A.; Spencer, N.; Stoddart, J. F.; Tolley, M. S. *Synlett* **1992**, 923.
- (405) Córdova, E.; Bissell, R. A.; Spencer, N.; Ashton, P. R.; Stoddart, J. F.; Kaifer, A. E. *J. Org. Chem.* **1993**, *58*, 6550.
- (406) Córdova, E.; Bissell, R. A.; Kaifer, A. E. *J. Org. Chem.* **1995**, *60*, 1033.
- (407) Bissell, R. A.; Córdova, E.; Kaifer, A. E.; Stoddart, J. F. *Nature* **1994**, *369*, 133.
- (408) Ashton, P. R.; Johnson, M. R.; Stoddart, J. F.; Tolley, M. S.; Wheeler, J. W. *J. Chem. Soc., Chem. Commun.* **1992**, 1128.
- (409) (a) Benniston, A. C.; Harriman, A. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1459. (b) Benniston, A. C.; Harriman, A.; Lynch, V. M. *Tetrahedron Lett.* **1994**, *35*, 1473.
- (410) Benniston, A. C.; Harriman, A.; Lynch, V. M. *J. Am. Chem. Soc.* **1995**, *117*, 5275.
- (411) Ashton, P. R.; Philp, D.; Spencer, N.; Stoddart, J. F. *J. Chem. Soc., Chem. Commun.* **1992**, 1124. See also: Belohradsky, M.; Philp, D.; Raymo, F. M.; Stoddart, J. F. In *Organic Reactivity: Physical and Biological Aspects*; Golding, B. T., Griffin, R. J., Maskill, H., Eds.; RSC Special Publication No. 148; Royal Society of Chemistry: London, 1995; p 387.
- (412) Ashton, P. R.; Belohradsky, M.; Philp, D.; Stoddart, J. F. *J. Chem. Soc., Chem. Commun.* **1993**, 1269.
- (413) Gibson, H. W.; Bheda, M. C.; Engen, P. T. *Prog. Polym. Sci.* **1994**, *19*, 843.
- (414) Ashton, P. R.; Belohradsky, M.; Philp, D.; Stoddart, J. F. *J. Chem. Soc., Chem. Commun.* **1993**, 1274.
- (415) Amabilino, D. B.; Ashton, P. R.; Belohradsky, M.; Raymo, F. M.; Stoddart, J. F. *J. Chem. Soc., Chem. Commun.* **1995**, 747.
- (416) Amabilino, D. B.; Ashton, P. R.; Belohradsky, M.; Raymo, F. M.; Stoddart, J. F. *J. Chem. Soc., Chem. Commun.* **1995**, 751.
- (417) Hunter, C. A. *J. Am. Chem. Soc.* **1992**, *114*, 5303.
- (418) (a) Hunter, C. A. *J. Chem. Soc., Chem. Commun.* **1991**, 749. (b) Hunter, C. A.; Purvis, D. H. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 792.
- (419) Carver, F. J.; Hunter, C. A.; Shannon, R. J. *J. Chem. Soc., Chem. Commun.* **1994**, 1277.
- (420) Vögtle, F.; Meier, S.; Hoss, R. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1619.
- (421) Ottens-Hildebrandt, S.; Meier, S.; Schmidt, W.; Vögtle, F. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1767.
- (422) Bisson, A. P.; Carver, F. J.; Hunter, C. A.; Waltho, J. P. *J. Am. Chem. Soc.* **1994**, *116*, 10292.
- (423) Ottens-Hildebrandt, S.; Nieger, M.; Rissanen, K.; Rouvinen, J.; Meier, S.; Harder, G.; Vögtle, F. *J. Chem. Soc., Chem. Commun.* **1995**, 777.
- (424) Adams, H.; Carver, F. J.; Hunter, C. A. *J. Chem. Soc., Chem. Commun.* **1995**, 809.
- (425) Johnston, A. G.; Leigh, D. A.; Pritchard, R. J.; Deegan, M. D. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1209.
- (426) Johnston, A. G.; Leigh, D. A.; Nezhath, L.; Smart, J. P.; Deegan, M. D. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1212.
- (427) Vögtle, F.; Händel, M.; Meier, S.; Ottens-Hildebrandt, S.; Ott, F.; Schmidt, T. *Liebigs Ann. Chem.* **1995**, 739.
- (428) Ottens-Hildebrandt, S.; Schmidt, T.; Harren, J.; Vögtle, F. *Liebigs Ann. Chem.* **1995**, 1855. We thank Professor Vögtle for providing us with a preprint of this paper.
- (429) (a) Metcalfe, J. C.; Stoddart, J. F.; Jones, G. *J. Am. Chem. Soc.* **1977**, *99*, 8317. (b) Krane, J.; Aune, O. *Acta Chem. Scand. Ser. B* **1980**, *34*, 397. (c) Tsukube, H. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2685. (d) Abed-ali, S. S.; Brisdon, B. J.; England, R. J. *J. Chem. Soc., Chem. Commun.* **1987**, 1565. (e) Misumi, S. *Top. Curr. Chem.* **1993**, *165*, 163.
- (430) Kolchinski, A. G.; Busch, D. H.; Alcock, N. W. *J. Chem. Soc., Chem. Commun.* **1995**, 1289.
- (431) Ashton, P. R.; Campbell, P. J.; Chrystal, E. J. T.; Glink, P. T.; Menzer, S.; Philp, D.; Spencer, N.; Stoddart, J. F.; Tasker, P. A.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1865.
- (432) Ashton, P. R.; Chrystal, E. J. T.; Glink, P. T.; Menzer, S.; Schiavo, C.; Stoddart, J. F.; Tasker, P. A.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1869.
- (433) Seeman, N. C. *DNA Cell Biol.* **1991**, *10*, 475.
- (434) Mueller, J. E.; Du, S. M.; Seeman, N. C. *J. Am. Chem. Soc.* **1991**, *113*, 6306.
- (435) Du, S. M.; Seeman, N. C. *J. Am. Chem. Soc.* **1992**, *114*, 9652.
- (436) Du, S. M.; Stollar, B. D.; Seeman, N. C. *J. Am. Chem. Soc.* **1995**, *117*, 1194.
- (437) Du, S. M.; Wang, H.; Tse-Dinh, Y.-C.; Seeman, N. C. *Biochemistry* **1995**, *34*, 673.
- (438) Seeman, N. C. *J. Theor. Biol.* **1982**, *99*, 237.
- (439) (a) Kallenbach, N. R.; Ma, R.-I.; Seeman, N. C. *Nature* **1983**, *305*, 829. (b) Wemmer, D. E.; Wand, A. J.; Seeman, N. C.; Kallenbach, N. R. *Biochemistry* **1985**, *24*, 5745.
- (440) (a) Churchill, M. E. A.; Tullius, T. D.; Kallenbach, N. R.; Seeman, N. C. *Proc. Natl. Acad. Sci. U.S.A.* **1988**, *85*, 4653. (b) Lu, M.; Guo, Q.; Seeman, N. C.; Kallenbach, N. R. *J. Mol. Biol.* **1991**, *221*, 1419. (d) Wang, H.; Seeman, N. C. *Biochemistry* **1995**, *34*, 920.
- (441) Fu, T.-J.; Seeman, N. C. *Biochemistry* **1993**, *32*, 3211.
- (442) Ma, R.-I.; Kallenbach, N. R.; Sheardy, R. D.; Petrillo, M. L.; Seeman, N. C. *Nucl. Acids Res.* **1986**, *14*, 9745.
- (443) Seeman, N. C. *J. Biomol. Struct. Dyn.* **1985**, *3*, 11.
- (444) Chen, J.-H.; Kallenbach, N. R.; Seeman, N. C. *J. Am. Chem. Soc.* **1989**, *111*, 6402.
- (445) Chen, J.; Seeman, N. C. *Nature* **1991**, *350*, 631.
- (446) Zhang, Y.; Seeman, N. C. *J. Am. Chem. Soc.* **1992**, *114*, 2656.
- (447) Zhang, Y.; Seeman, N. C. *J. Am. Chem. Soc.* **1994**, *116*, 1661.
- (448) Seeman, N. C. *J. Biomol. Struct. Dyn.* **1990**, *8*, 573.
- (449) Seeman, N. C.; Chen, J.; Du, S. M.; Mueller, J. E.; Zhang, Y.; Fu, T.-J.; Wang, Y.; Wang, H.; Zhang, S. *New J. Chem.* **1993**, *17*, 739.
- (450) Gibson, H. W.; Marand, M. *Adv. Mater.* **1993**, *5*, 11.
- (451) Mark, H. *Monatsh. Chem.* **1952**, *83*, 545.
- (452) Frisch, H.; Martin, I.; Mark, H. *Monatsh. Chem.* **1953**, *84*, 250.
- (453) Mark, J. E. *New J. Chem.* **1993**, *17*, 703.
- (454) Frisch, H. L. *New J. Chem.* **1993**, *17*, 697.
- (455) For two recent papers on this subject, see: (a) Gutowska, A.; Bae, Y. H.; Jacobs, M.; Feijen, J.; Kim, S. W. *Macromolecules* **1994**, *27*, 4167. (b) Pandit, S. B.; Kulkarni, S. S.; Naokarni, V. M. *Macromolecules* **1994**, *27*, 4595.
- (456) Klemmner, D.; Sperling, L. H.; Utracki, L. A., Eds. *Interpenetrating Polymer Networks*; Advances in Chemistry Series 239, American Chemical Society: Washington DC, 1994.
- (457) Sperling, L. H. *Interpenetrating Polymer Networks and Related Materials*; Plenum, New York, 1981.
- (458) Millar, J. R. *J. Chem. Soc.* **1960**, 1311.
- (459) Frisch, H. L.; Klemmner, D.; Frisch, K. C. *J. Polym. Sci. B Polym. Lett.* **1969**, *7*, 775.
- (460) Klemmner, D.; Frisch, H. L.; Frisch, K. C. *J. Polym. Sci. A-2* **1970**, *8*, 921.
- (461) Klemmner, D.; Frisch, H. L. *J. Polym. Sci. B Polym. Lett.* **1970**, *8*, 525.
- (462) Clarson, S. J. *New J. Chem.* **1993**, *17*, 711.

- (463) (a) Mark, J. E. *J. Chem. Educ.* **1981**, *58*, 898. (b) Mark, J. E. *Acc. Chem. Res.* **1994**, *27*, 271.
- (464) Garrido, L.; Mark, J. E.; Clarson, S. J.; Semlyen, J. A. *Polym. Commun.* **1985**, *26*, 53.
- (465) Garrido, L.; Mark, J. E.; Clarson, S. J.; Semlyen, J. A. *Polym. Commun.* **1985**, *26*, 55.
- (466) Clarson, S. J.; Mark, J. E.; Semlyen, J. A. *Polym. Commun.* **1986**, *27*, 244.
- (467) Clarson, S. J.; Mark, J. E.; Semlyen, J. A. *Polym. Commun.* **1987**, *28*, 151.
- (468) DeBolt, L. C.; Mark, J. E. *Macromolecules* **1987**, *20*, 2369.
- (469) Fyvie, T. J.; Frisch, H. L.; Semlyen, J. A.; Clarson, S. J.; Mark, J. E. *J. Polym. Sci., A: Polym. Chem.* **1987**, *25*, 2503.
- (470) Lipatov, Y.; Nizel'sky, Y. *New J. Chem.* **1993**, *17*, 715.
- (471) Lipatova, T. E.; Kosyanchuk, L. F.; Shilov, V. V.; Gomza, Y. P. *Polym. Sci. USSR* **1985**, *27*, 622.
- (472) Lipatova, T. E.; Kosyanchuk, L. F.; Shilov, V. V. *J. Macromol. Sci.-Chem.* **1985**, *A22* (3), 361.
- (473) Bheda, M. C.; Merola, J. S.; Woodward, W. A.; Vasudevan, V. J.; Gibson, H. W. *J. Org. Chem.* **1994**, *59*, 1694. (b) Gibson, H. W.; Bheda, M. C.; Engen, P.; Shen, Y. X.; Sze, J.; Zhang, H.; Gibson, M. D.; Delaviz, Y.; Lee, S.-H.; Liu, S.; Wang, L.; Nagvekar, D.; Rancourt, J.; Taylor, L. T. *J. Org. Chem.* **1994**, *59*, 2186.
- (474) Gibson, H. W.; Engen, P. T.; Lecavalier, P. R. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1988**, *29* (1), 248.
- (475) Lecavalier, P.; Engen, P. T.; Shen, Y. X.; Joarder, S.; Ward, T. C.; Gibson, H. W. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1989**, *30* (1), 189.
- (476) Wu, C.; Bheda, M. C.; Lim, C.; Shen, Y. X.; Sze, J.; Gibson, H. W. *Polym. Commun.* **1991**, *32*, 204.
- (477) Gibon, H. W.; Liu, S.; Lecavalier, P.; Wu, C.; Shen, Y. X. *J. Am. Chem. Soc.* **1995**, *117*, 852.
- (478) Shen, Y. X.; Lim, C.; Gibson, H. W. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1991**, *32* (1), 166.
- (479) Shen, Y. X.; Lim, C.; Gibson, H. W. *Macromolecules* **1992**, *25*, 2058.
- (480) Shen, Y. X.; Xie, D.; Gibson, H. W. *J. Am. Chem. Soc.* **1994**, *116*, 537.
- (481) Harrison, I. T. *J. Chem. Soc., Chem. Commun.* **1977**, 384.
- (482) Gibson, H. W.; Engen, P. T.; Shen, Y. X.; Sze, J.; Lim, C.; Bheda, M.; Wu, C. *Makromol. Chem., Macromol. Symp.* **1992**, *54/55*, 519.
- (483) Gibson, H. W.; Engen, P. T.; Lee, S.-H.; Liu, S.; Marand, H.; Bheda, M. C. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1993**, *34* (1), 64.
- (484) Gibson, H. W.; Engen, P. T. *New J. Chem.* **1993**, *17*, 723.
- (485) Delaviz, Y.; Gibson, H. W. *Macromolecules* **1992**, *25*, 18.
- (486) Delaviz, Y.; Gibson, H. W. *Macromolecules* **1992**, *25*, 4859.
- (487) (a) Liu, S.; Gibson, H. W. *Tetrahedron Lett.* **1994**, *35*, 8533. (b) Liu, S.; Lee, S.-H.; Shen, Y. X.; Gibson, H. W. *J. Org. Chem.* **1995**, *60*, 3155.
- (488) Sze, J. Y.; Gibson, H. W. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1992**, *33* (2), 331.
- (489) Gibson, H. W.; Lee, S.-H.; Engen, P. T.; Lecavalier, P.; Sze, J.; Shen, Y. X.; Bheda, M. *J. Org. Chem.* **1993**, *58*, 3748.
- (490) Karagounis, G.; Pandi-Agathokli, I. *Prakt. Akad. Athenon* **1970**, *45*, 118.
- (491) Karagounis, G.; Pandi-Agathokli, I. *J. Pract. Panellion Chem. Syndriou* **1972**, *2*, 213.
- (492) Karagounis, G.; Pandi-Agathokli, I.; Kontaraki, E. *Chem. Chron.* **1972**, *1*, 130.
- (493) Karagounis, G.; Kontaraki, E. *Prakt. Akad. Athenon* **1973**, *48*, 197.
- (494) Karagounis, G.; Pandi-Agathokli, I.; Kontaraki, E.; Nikolelis, D. *Prakt. Akad. Athenon* **1975**, *49*, 501.
- (495) Karagounis, G.; Pandi-Agathokli, I.; Kontaraki, E. *IUPAC Colloid and Surface Science, International Conference, Selected Papers A* **1975**, *1*, 671.
- (496) Karagounis, G.; Pandezi, M. Proc. 5th Int. Conf. Raman Spectrosc., Freiburg im Breisgau, Freiburg, 1976; p 72.
- (497) Wood, B. R.; Semlyen, J. A.; Hodge, P. *Polymer* **1994**, *35*, 1542.
- (498) Zaworotko, M. J. *J. Chem. Soc. Rev.* **1994**, *23*, 283. For a recent full paper from this group, see: Copp, S. B.; Holman, K. T.; Sangster, J. O. S.; Subramanian, S.; Zaworotko, M. J. *J. Chem. Soc., Dalton Trans.* **1995**, 2233.
- (499) Duchamp, D. J.; Marsh, R. E. *Acta Crystallogr.* **1969**, *B25*, 5.
- (500) Herbstein, F. H.; Kapon, M.; Reisman, G. M. *J. Inclusion Phenom. Mol. Recognit. Chem.* **1987**, *5*, 211.
- (501) Ermer, O.; Eling, A. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 829.
- (502) Ermer, O. *J. Am. Chem. Soc.* **1988**, *110*, 3747.
- (503) Abrahams, B. F.; Hoskins, B. F.; Robson, R. *J. Chem. Soc., Chem. Commun.* **1990**, 60.
- (504) Kim, K.-W.; Kanatzidis, M. J. *J. Am. Chem. Soc.* **1992**, *114*, 4878.
- (505) Proserpio, D. M.; Hoffmann, R.; Preuss, P. *J. Am. Chem. Soc.* **1994**, *116*, 9634.
- (506) MacGillivray, L. R.; Subramanian, S.; Zaworotko, M. J. *J. Chem. Soc., Chem. Commun.* **1990**, 60.
- (507) Carlucci, L.; Ciani, G.; Proserpio, D. M.; Sironi, A. *J. Chem. Soc., Chem. Commun.* **1994**, 2755.
- (508) Soma, T.; Yuge, H.; Iwamoto, T. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1665.
- (509) Hoskins, B. F.; Robson, R.; Scarlett, N. V. Y. *J. Chem. Soc., Chem. Commun.* **1994**, 2025.
- (510) Soma, T.; Iwamoto, T. *Chem. Lett.* **1995**, 271.
- (511) Stumpf, H. O.; Ouahab, L.; Pei, Y.; Grandjean, D.; Kahn, O. *Science* **1993**, *261*, 447.
- (512) Stumpf, H. O.; Ouahab, L.; Pei, Y.; Grandjean, D.; Bergerat, P.; Kahn, O. *J. Am. Chem. Soc.* **1994**, *116*, 3866.
- (513) Soghomonian, V.; Chen, Q.; Haushalter, R. C.; Zubieta, J.; O'Connor, C. J. *Science* **1993**, *259*, 1596.
- (514) Real, J. A.; Andrés, E.; Muñoz, M. C.; Julve, M.; Granier, T.; Bousseksou, A.; Varret, F. *Science* **1995**, *268*, 265.
- (515) Goodgame, D. M. L.; Menzer, S.; Smith, A. M.; Williams, D. J. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 574. For a recent paper on related systems, see: Goodgame, D. M. L.; Menzer, S.; Smith, A. M.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1995**, 1975. We thank Dr Williams for providing us with a preprint of this paper.
- (516) Fujita, M.; Kwon, Y.-J.; Sasaki, O.; Yamaguchi, K.; Ogura, K. *J. Am. Chem. Soc.* **1995**, *117*, 7287.
- (517) Hoskins, B. F.; Robson, R.; Scarlett, V. Y. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1203.
- (518) Eschenmoser, A. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2363.
- (519) Whitesides, G. M.; Simanek, E. E.; Mathias, J. P.; Seto, C. T.; Chin, D. N.; Mammen, M.; Gordon, D. M. *Acc. Chem. Res.* **1995**, *28*, 37.
- (520) Lokey, R. S.; Iverson, B. L. *Nature* **1995**, *375*, 303.
- (521) Gokel, G. W.; Medina, J. C.; Li, C. *Synlett* **1991**, 677.
- (522) Liang, C.; Mislow, K. *J. Math. Chem.* **1994**, *16*, 27.
- (523) Busch, D. H. In *Transition Metals in Supramolecular Chemistry*; Fabbri, L., Poggi, A., Eds.; Kluwer Academic: Boston, 1995; p 55.
- (524) Eliel, E. L.; Willen, S. H. *Stereochemistry of Organic Compounds*; J. Wiley & Sons: New York, 1994.
- (525) Finocchiaro, P.; Gust, D.; Mislow, K. *J. Am. Chem. Soc.* **1973**, *95*, 8172.
- (526) (a) Rao, T. A.; Maiya, B. G.; *J. Chem. Soc., Chem. Commun.* **1995**, 939. (b) Kimura, A.; Funatsu, K.; Imamura, T.; Kido, H.; Sasaki, Y. *Chem. Lett* **1995**, 207.
- (527) (a) Engel, A. *Annu. Rev. Biophys. Chem.* **1991**, *20*, 79. (b) Frommer, J. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1265.
- (528) Samori, B.; Nigro, C.; Armentano, V.; Cimieri, S.; Zucheri, G.; Quagliariello, C. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1461.
- (529) Avouris, P. *Acc. Chem. Res.* **1995**, *28*, 95.
- (530) (a) Willner, I.; Eichen, Y.; Doron, A.; Marx, S. *Israel J. Chem.* **1992**, *32*, 53. (b) Ballardini, R.; Balzani, V.; Gandolfi, M. T.; Prodi, L.; Venturi, M.; Philp, D.; Ricketts, H. G.; Stoddart, J. F. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1301. (c) Seiler, M.; Dürr, H.; Willner, I.; Joselevich, E.; Doron, A.; Stoddart, J. F. *J. Am. Chem. Soc.* **1994**, *116*, 3399.
- (531) Adleman, L. M. *Science* **1994**, *266*, 1021.
- (532) Dagani, R. *Chem. Eng. News* **1994**, *72*, August 29, 28.
- (533) The following work has appeared in the journals between submitting our revised manuscript and receiving the galley proofs. An oligo[2]catenane has been described: (a) Geerts, Y.; Muscat, D.; Müllen, K. *Macromol. Chem. Phys.* **1995**, *196*, 3425. A gold(I) catenane has been crystallized: (b) Mingos, D. M. P.; Yau, J.; Menzer, S.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1894. A double helical dinuclear macrocycle has been discussed: (c) Comba, P.; Faith, A.; Hambley, T. W.; Richens, D. T. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1883. Double helicates have been formed by ferrocene-functionalized sexipyridine: (d) Constable, E. C.; Edwards, E. J.; Martínez-Mañez, R.; Raithby, P. R. *J. Chem. Soc., Dalton Trans.* **1995**, 3253. A titanium(IV) "meso-helicate" has been reported: (e) Albrecht, M.; Kotila, S. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2134. A report of chirality induction in PNA-PNA duplexes has appeared: (f) Wittung, P.; Eriksson, M.; Lyng, R.; Nielsen, P. E.; Nordén, B. *J. Am. Chem. Soc.* **1995**, *117*, 10167. A spectacular crystal structure of a protein bound to DNA reveals a pseudopolymeric superhelical double helix, see: (g) Li, T.; Stark, M. R.; Johnson, A. D.; Wolberger, C. *Science* **1995**, *270*, 262. An interpenetrating network composed of metal complexes held together by hydrogen bonds has been crystallized: (h) Desmarin, P. G.; Williams, A. F.; Bernardinelli, G. *New J. Chem.* **1995**, *19*, 1109. Finally, (i) a number of papers on interlocked and intertwined structures and superstructures have appeared: *Supramolecular Stereochemistry*; Siegel, J. S., Ed.; NATO ASI Series C, Vol. 473; Kluwer Academic: Boston, 1995.