*Russian Chemical Reviews* **70** (1) 23 – 44 (2001) © 2001 Russian Academy of Sciences and Turpion Ltd

DOI 10.1070/RC2001v070n01ABEH000608

# Rotaxanes and polyrotaxanes. Their synthesis and the supramolecular devices based on them

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**Abstract. Various approaches to the synthesis of rotaxanes and polyrotaxanes are considered. The principles employed in the design of highly organised structures comprising rod-shaped polymeric molecules, *viz*., macromolecular inclusion complexes, are discussed. In addition to the conventional (step-by-step) methodology which consists of polymerisation of monomers in the presence of macrocycles, molecular self-assembly is gaining an ever increasing significance. The main emphasis is laid on the preparation and characterisation of inclusion complexes which are based on cyclodextrins and linear synthetic polymers. The bibliography includes 138 references.**

## I. Introduction

Supramolecular chemistry as a new line of research has evolved and has developed intensively in the past few years. This interdisciplinary science encompasses the chemistry of noncovalent interactions, molecular physics and molecular biology. Its main attention is focussed on the systems which are capable of self-organisation, *i.e*., spontaneous production of definite structures by self-assembly of constituents into supramolecular assemblies. The synthesis of such structures is based on the molecular recognition principle and is effected by the cooperation of various non-covalent interactions, *e.g*., electrostatic, hydrophobic, hydrogen bonding, *etc*.

The principle of molecular recognition can be exemplified in the formation of complexes of the 'host – guest' type. The role of 'hosts', *i.e*., receptors, is played by cyclic molecules, *e.g*., cryptands, crown ethers, cyclodextrins and calixarenes. The chemical nature of 'guests' is extremely diverse, they include both small particles (*e.g*., inert gas atoms, metal ions, *etc*.) and complex bulky molecules of the fullerene type. In the past few years, supramolecular chemistry has been enriched by systems with polymers as the 'guest' molecules, which underlies the supramolecular chemistry of polymers.

This approach has made it possible to obtain such compounds as polyrotaxanes, catenanes, 'molecular necklaces', dendrimers, *etc*., which possess novel, previously unknown structures and remarkable properties. This review is devoted to one type of polymeric supramolecular assemblies, *viz*., polyrotaxanes. In the latter, the macrocycles are 'threaded' onto a polymeric molecule with bulky terminal groups. In addition to polyrotaxanes, their topological analogues, *viz*., pseudopolyrotaxanes including 'molecular necklaces', are reviewed. Since these structures are synthesised using essentially the same procedures as for rotaxanes, the strategy of rotaxane synthesis is also discussed.

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Received 2 June 2000
*Uspekhi Khimii* **70** (1) 28 – 51 (2001); translated by R L Birnova

## II. Rotaxanes

Rotaxanes (Rt) represent complexes comprising cyclic molecules (C) threaded onto linear molecules (L). Their characteristic feature is the lack of covalent binding between the components C and L. In order to prevent the dissociation of the complex into constituents, the 'stoppers' (S), *i.e*., bulky molecules which are covalently linked to the ends of linear molecules, are used (Fig. 1 *a*, *b*). Similar structures in which the molecules S are absent are called pseudorotaxanes (pseudo-Rt) (Fig. 1 *c*). The nomenclature used to describe such compounds takes account of the number of components involved in the complexation. Thus [2]-Rt (see Fig. 1 *a*) contains one L and one C molecule; [3]-Rt is comprised of one L and two C molecules (see Fig. 1 *b*), *etc*.

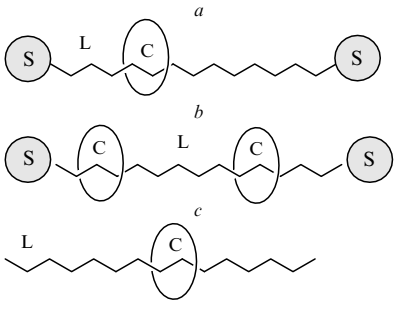
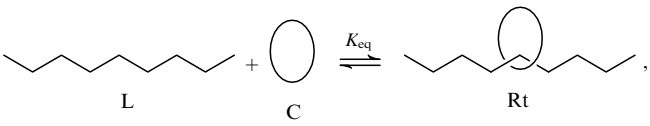



**Figure 1.** A schematic representation of rotaxanes: (*a*) [2]-Rt, (*b*) [3]-Rt, (*c*) pseudo-Rt.

### 1. General approaches to the rotaxane synthesis

It should be noted that the threading of cyclic molecules onto linear components, which forms the basis for all the strategies of the rotaxane synthesis (Fig. 2), is a reversible process which is described by the equilibrium constant $K_{eq} = [Rt]/[L][C]$.




Therefore, the creation of conditions where the equilibrium of the reaction is shifted towards complex formation is the key event in the assembly of rotaxane molecules. Quantitatively, this process can be described by standard thermodynamic equations:

$$RT\ln K_{eq} = -\Delta G = -(\Delta H - T\Delta S), \quad (1)$$

$$\ln K_{eq} = -\frac{\Delta H}{RT} + \frac{\Delta S}{R}. \quad (2)$$

As can be seen from Eqn (2), two extreme cases are thermodynamically possible. First, the so-called statistical threading, *i.e.*, a random collision and interaction of molecules of different nature (*e.g.*, L and C). The enthalpy of such a reaction, $\Delta H$, is close to zero or is positive, *i.e.*, the threading is determined by the entropy factor. Second, template-directed threading, which is based on the principle of molecular self-assembly where the reaction is energetically favourable due to the existence of specific non-covalent interactions between the particles L and C ($\Delta H < 0$).

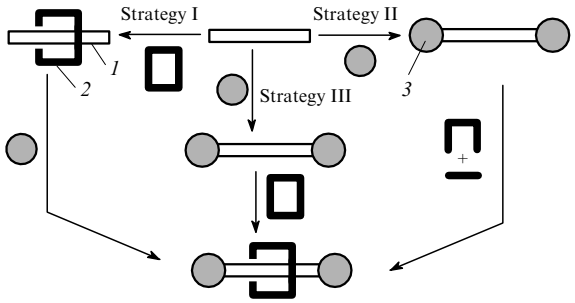



**Figure 2.** The strategies of the chemical synthesis of rotaxanes: (*1*) rod molecule, (*2*) macrocycle, (*3*) 'stopper'.

When considering the strategies of chemical synthesis of rotaxanes (see Fig. 2), one can distinguish three general approaches: [1]

(1) threading of a macrocycle onto a rod molecule and subsequent interaction of the complex formed with the blocking reagents (strategy I);

(2) cyclisation in the presence of compounds having a dumbbell-like structure (strategy II);

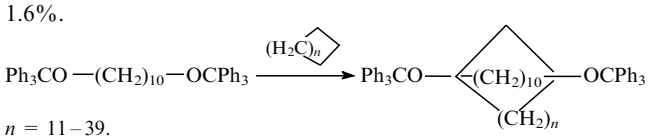
(3) temperature-induced 'slipping' of the macrocycle onto bulky terminal groups of the dumbbell-shaped molecule (strategy III).

## 2. The statistical approach to the rotaxane synthesis

The first attempts to synthesise rotaxanes were based on statistical threading of a cyclic component onto linear molecules. The first report on a successful synthesis of such complexes,[2] which consisted of random threading of a macrocyclic acyloin onto decane-1,10-diol using bulky trityl groups as stoppers, was published in 1967. After a 70-fold passage of the reaction mixture containing components L and S through a column with an immobilised cyclic component (C) and subsequent chromatographic separation of the eluate, the yield of rotaxane was as low as 6%. Further experiments [3,4] were aimed at establishing a correlation between the efficiency of statistical threading, the properties of the reactants C, L and S and reaction conditions.

The synthesis of rotaxanes from various dibenzocrown ethers, ethylene oxide oligomers (EOO) and trityl chloride by their joint fusion has been described.[4] In this case, the efficiency of threading depended on the size of the ring, the L : C ratio, the length of the chains of the L-molecules and the total volume of the reaction mixture, whereas temperature had no effect on the course of the reaction. The maximum degree of threading was achieved when a mixture of an ethylene oxide oligomer having a molecular mass (MM) of 1000 and crown ethers (on average, dibenzo-58.2-crown-19.4) is used. Mixing of EOO (MM = 400) with dibenzo-58.2-crown-19.4 at 130 °C and subsequent addition of triphenylchloromethane gave the corresponding [2]-Rt in 15% yield. The introduction of bromomethyl substituents into each phenyl group of the blocking reagent and the reaction in the presence of the Zn/Cu couple in DMF resulted in [4]-Rt in 8% yield.[5]

The experiments [3] with statistical threading of cyclic hydrocarbons onto 1,10-bis(triphenylmethoxy)decane at 120 °C revealed that only rotaxanes comprising $C_{29}$ rings were more or less stable at this temperature, although their yields did not exceed 1.6%.




$n = 11-39$.

Later, it was found [4] that a macrocycle which has to be threaded onto the methylene groups should contain no less than 22 carbon atoms. It was shown also that terminal trityl groups can hold the rings which contained no more than 29 carbon atoms. Bulkier tris(*p*-butylphenyl)methyl groups prevent the dissociation of the rings containing 42 carbon atoms.

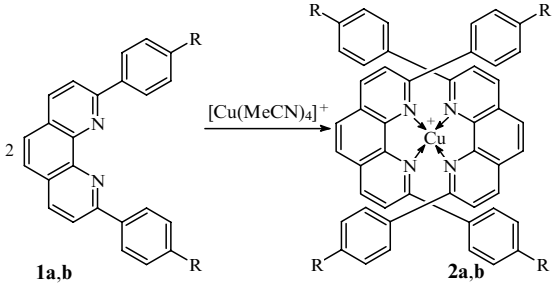
Thus, the statistical approach affords a mixture of starting compounds and rotaxanes; the isolation of the latter often presents a problem.[2–5] The efficiency of threading and the yields are controlled by varying the concentrations of the reactant and their molar ratios and by matching the geometric parameters of the molecules L, C and S. It is noteworthy that this approach gives relatively low yields of reaction products which at best do not exceed 15%. On the other hand, one of the benefits of the statistical approach to the rotaxane synthesis is the possibility of using a vast diversity of linear and cyclic molecules of different chemical nature which significantly expand the range of the structures that can be synthesised by this method.

## 3. Template synthesis of rotaxanes

Yet another approach to the rotaxane synthesis is based on the use of the fundamental principle of supramolecular chemistry, namely, the self-organisation of molecules due to specific non-covalent interactions. This approach is named template or directed synthesis, since in this case the process is directed by molecular recognition between two or more complementary fragments of the interacting molecules. Depending on the type of bonding, the following main routes to the rotaxane synthesis may be distinguished: (1) the formation of metal–ligand coordination bonds; (2) donor–acceptor interactions; (3) combined interactions which are observed in the formation of inclusion complexes based on cyclodextrins.

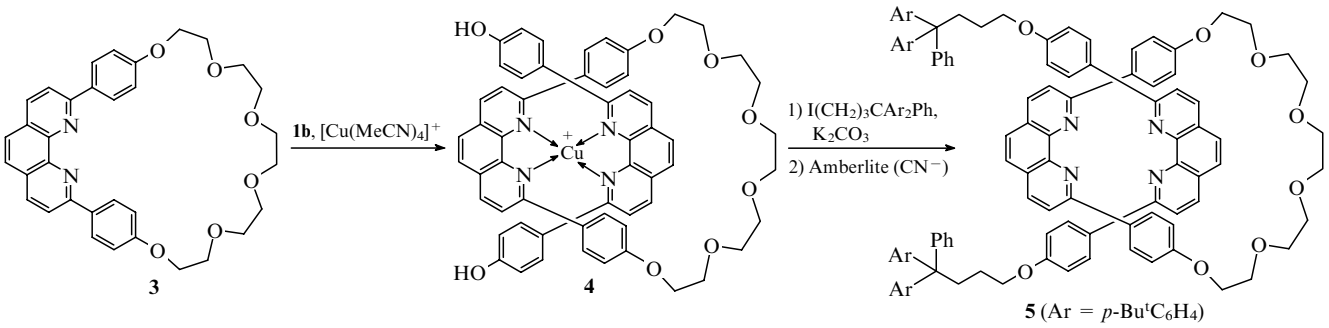
### a. The synthesis of rotaxanes using transition metal ions

This strategy is based on the assembling and 'orientational' properties of transition metals. The complexation of two 2,9-disubstituted 1,10-phenanthrolines **1a**,**b** with the copper(I) ion was




R = OMe (**a**), OH (**b**).

Scheme 1

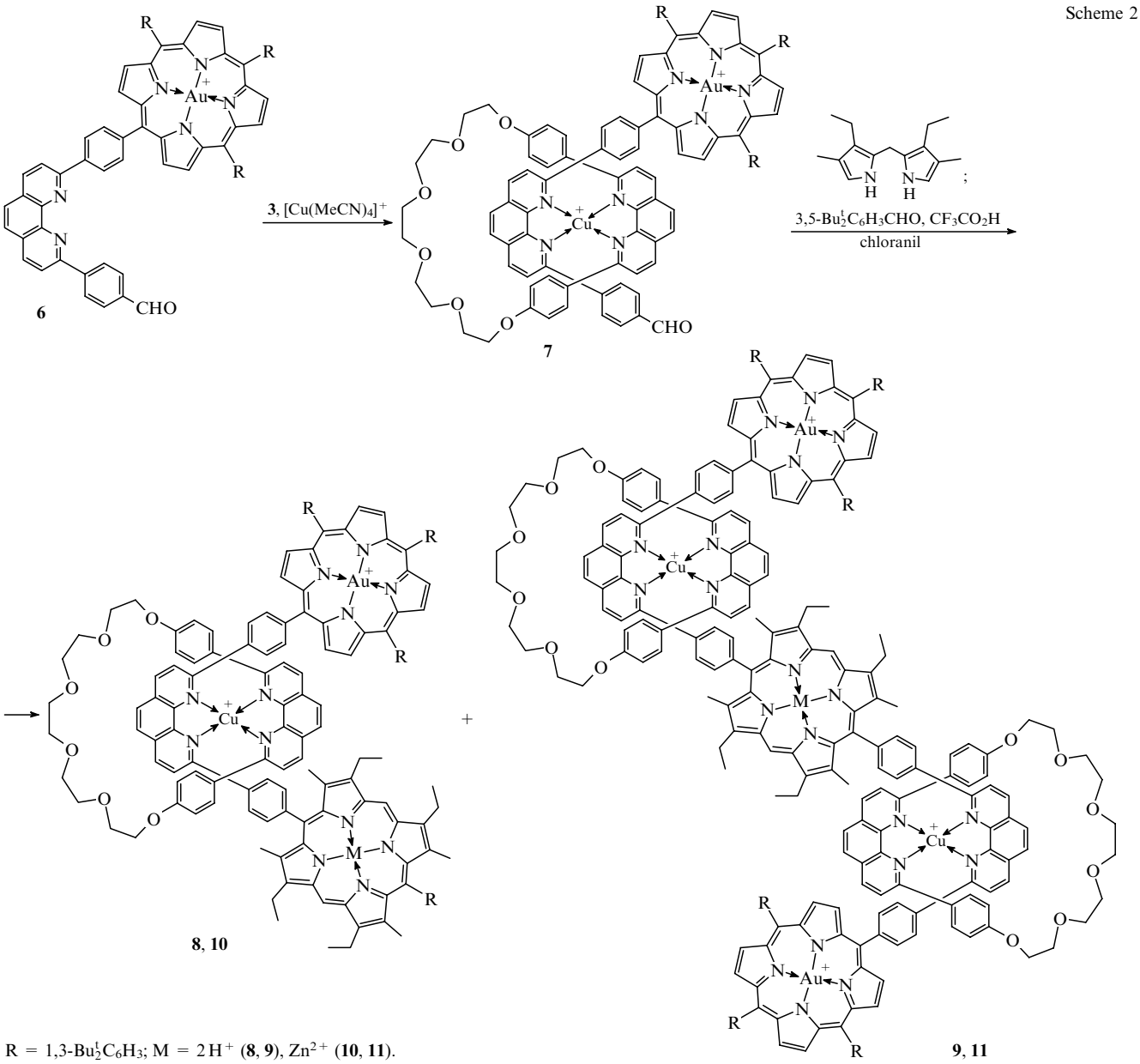



first proposed as the template-based reaction.[6] The complexes **2a**,**b** formed have an ideal spatial structure for the synthesis of rotaxanes based on them.

The synthesis of the macrocycle **3** incorporating one bidentate centre has been described.[7] The reaction of compound **3** with $[Cu(MeCN)_4]^+[BF_4]^-$ and 2,9-bis(4-hydroxyphenyl)phenanthroline **1b** affords the pseudorotaxane **4** (Scheme 1).[7] Reactive phenolic groups can react with different stoppers. Modification of the terminal groups of the complex **4** with alkyl iodide containing the bulky triarylmethyl group has led to [2]-Rt **5**.[8] In order to remove $Cu^I$, the complex formed was passed through an ion-exchange resin. The structure of the individual [2]-Rt **5** isolated in 21% yield was confirmed by $^1H$ NMR spectroscopy and mass spectrometry.

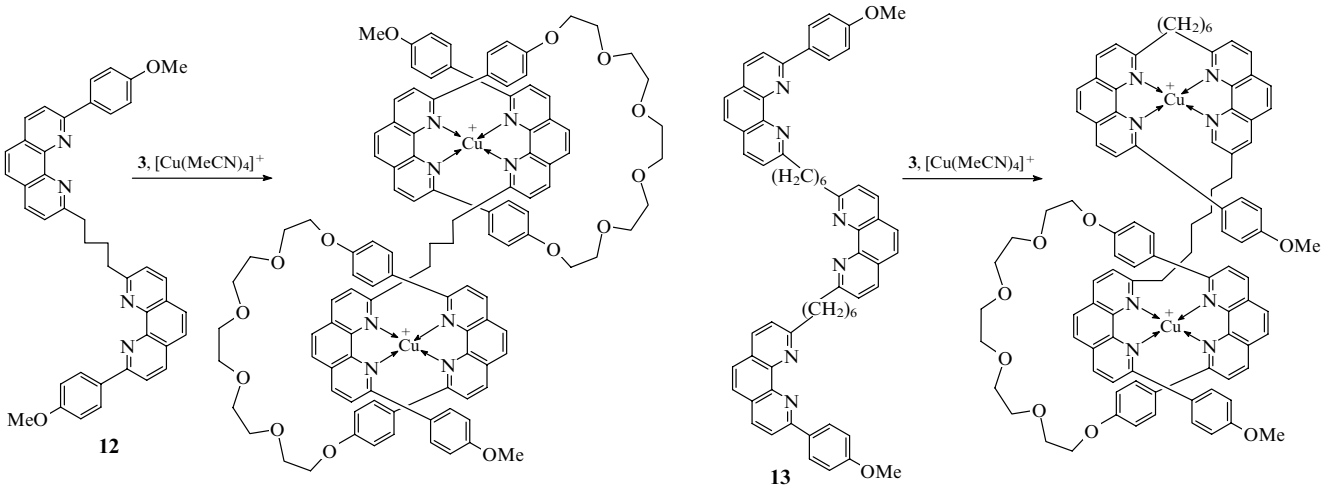
Later, data on the synthesis of porphyrin-containing rotaxanes have been documented (Scheme 2).[9–12] Initially, compound

Scheme 2




R = 1,3-$Bu^t_2C_6H_3$; M = $2H^+$ (**8**, **9**), $Zn^{2+}$ (**10**, **11**).

Scheme 3



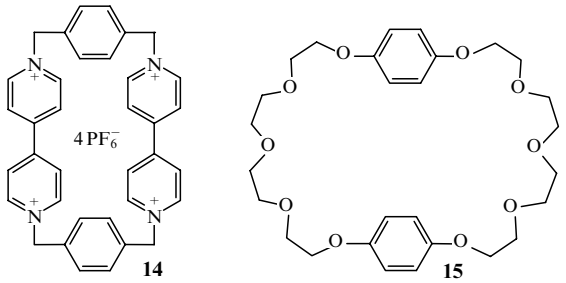

**6** which contained a porphyrin–gold(III) complex as a stopper was prepared. This complex was added to the macrocycle **3** in the presence of a copper(I) complex. The intermediate product **7** formed reacted with 3,5-di-*tert*-butylbenzaldehyde and bis-(3-ethyl-4-methylpyrrol-2-yl)methane in the presence of trifluoroacetic acid. The intermediate porphyrinogen was oxidised with chloranil. Chromatographic separation gave [2]-Rt (**8**) and [3]-Rt (**9**) in 25% and 32% yields, respectively.[11] The rotaxanes **8** and **9** were converted into their Zn-analogues **10** and **11** by treatment with $Zn(OAc)_2 \cdot 2H_2O$. A $^1H$ NMR spectroscopic study showed that demetallation of the phenanthroline moiety of [2]-Rt by ion exchange with KCN changes its structure so that the phenanthroline fragment of the macrocycle lies outside the 'cleft' formed by the porphyrin fragments.[12]

Several modifications of this synthetic procedure are known. In one of them, the blocking groups are represented by fullerenes.[13]

It was suggested [14] to use linear molecules incorporating two (**12**) or three (**13**) 1,10-phenanthroline fragments for the synthesis of structurally more elaborate rotaxanes. Their interactions with the macrocycle **3** in the presence of $[Cu(MeCN)_4]^+ [BF_4]^-$ have been studied (Scheme 3). It was shown that [3]-pseudo-Rt formed on the basis of compound **12** has the composition $L : Cu^I : C = 1 : 2 : 2$. Compound **13**, which contains three phenanthroline fragments, yields a complex with the composition $L : Cu^I : C = 1 : 2 : 1$, *i.e.*, [2]-Rt in which two phenanthroline fragments of the rod molecule interact both with each other and with $Cu^I$, rather than the expected complex with a $L : Cu^I : C$ ratio of 1 : 3 : 3. This phenomenon was attributed to the flexibility of the stretched rod molecule. The ability for self-complexation must be taken into consideration in the synthesis of [3]- and [4]-Rt by this method.

**b. Rotaxane syntheses based on donor-acceptor interactions of L and C molecules**

This method consists in the interaction of electron-donor and electron-acceptor molecules or their fragments and results in π-bonding. Cyclobis(paraquat-*p*-phenylene) **14**,[15] which reacts with a variety of aromatic electron-donor substrates, and bis-*p*-phenylene-34-crown-10 (**15**),[16] which forms a complex with paraquat bis(hexafluorophosphate), have received especially wide acceptance as receptors. Using X-ray diffraction analysis, it was shown [17,18] that the complexes prepared on the basis of these compounds and the corresponding ligands have ordered structures both in solution and in the solid phase and represent pseudorotaxanes. The aromatic rings of the 'guest' molecules are accommodated inside the 'host' molecules between the rings of the receptor, which are stacked parallel to one another. The complexes have box-like structures, which are ideal for their conversion into rotaxanes.



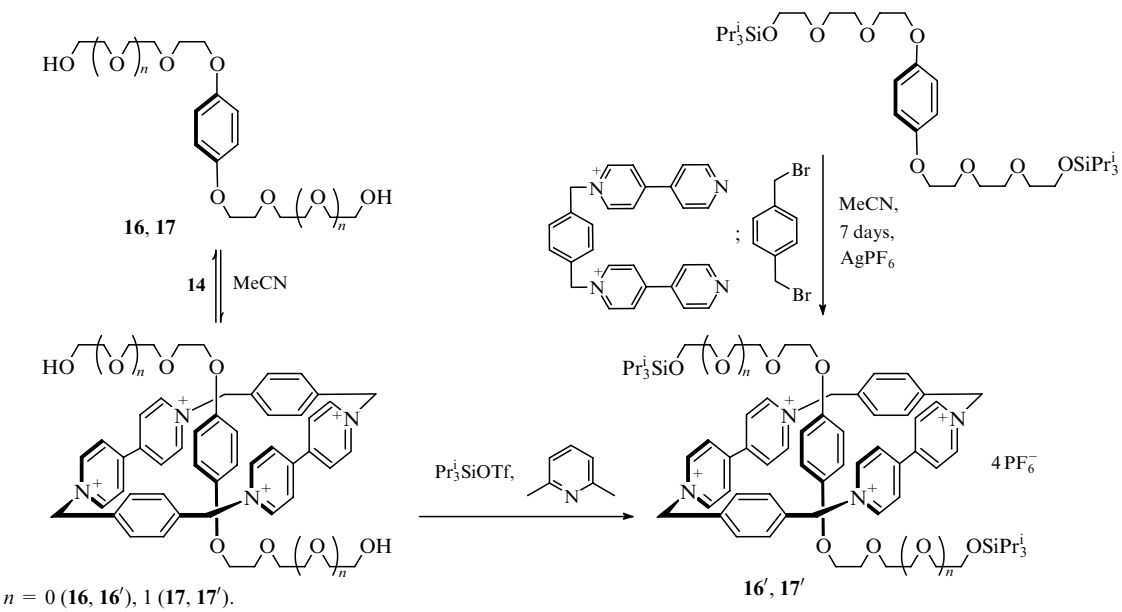

The interaction of compounds **16** and **17** (Scheme 4) with the macrocycle **14** in acetonitrile followed by a reaction with triisopropylsilyl triflate was studied.[19] After purification of the reaction mixture by column chromatography on silica gel, [2]-Rt **16′** and **17′** were isolated in equal yields (22%).

A similar compound, *viz.*, [2]-Rt **17′**, was obtained in 14% yield using strategy II (see Scheme 2, Fig. 2).[20] It was noted [19] that the reduction in the length of the oligoethylene oxide fragments of the rod molecules changes the arrangement of the *p*-dioxyphenylene fragments relative to the plane of cyclophane and results in the increase in the distance between the complementary aromatic fragments of the L and C molecules.

An increase in the number of electron-donor fragments in the rod molecule not only increases the yields due to the self-organisation of rotaxanes, but also enables the synthesis of the so-called molecular shuttles,[21–27] *viz.*, the complexes in which the macrocycle can migrate from one part of the rod molecule to another (the so-called translocation isomers). For the first time, such rotaxanes were synthesised in 1991 [21] by the reaction of the tetracationic cyclophane **14** with the dumbbell-shaped compound **18** (Scheme 5) containing two *p*-dioxyphenylene fragments. The corresponding rotaxane was obtained in 32% yield. A $^1H$ NMR spectroscopic study revealed that the cyclophane migrated between the two aromatic fragments of the L molecule at a rate of 500 $s^{-1}$. The activation free energy of the migration observed ($\Delta G$) is $\sim$ 13 kcal $mol^{-1}$.

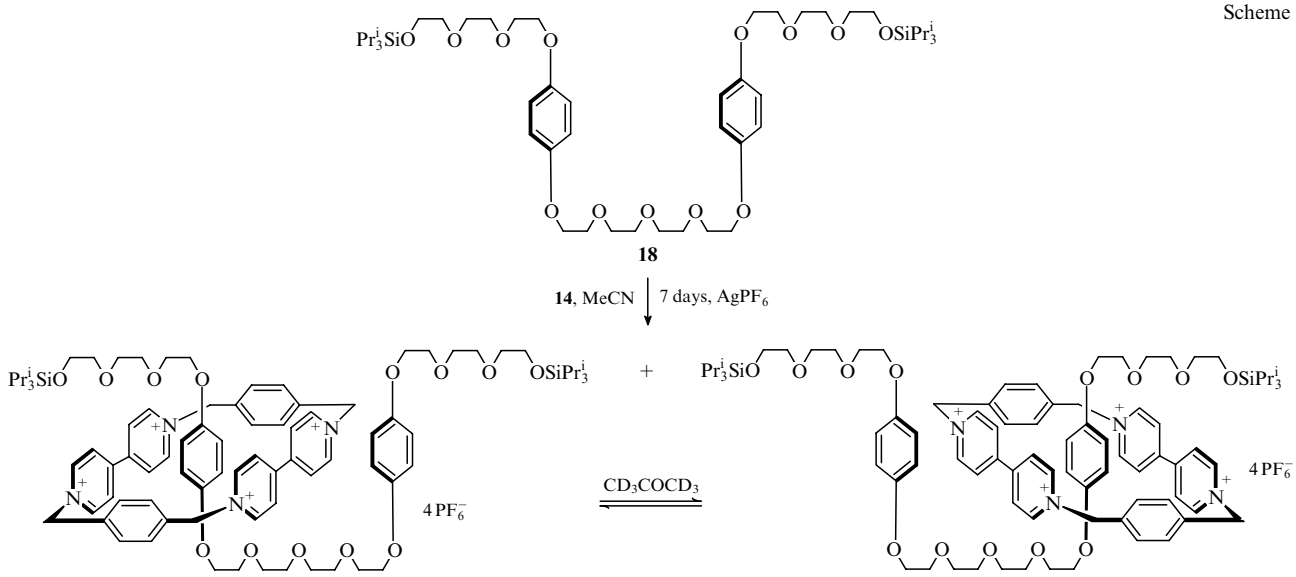
Strategy II was also used for the synthesis of a series of [2]-Rt **19–22** (yields 1%, 25%, 29% and 40%, respectively).[22] It is remarkable that in neither case [3]-Rt was obtained. Of the four rotaxanes isolated, only complex **22** exists in the form of two translocation isomers. Similar 'molecular shuttles' were obtained by substitution of electron-donor (*e.g.*, tetrathiofulvalene,[23–25] 4,4′-bisphenol, benzidine [26,27]) fragments for one of the *p*-dioxyphenylene fragments of the rod molecule; the yields of the isolated rotaxanes did not exceed 9%. Presumably, this can be attributed

Scheme 4

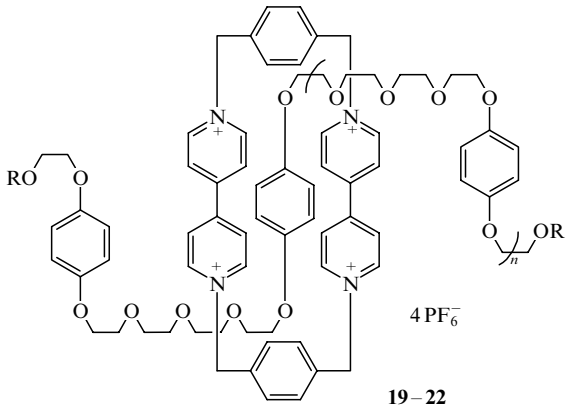


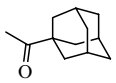

$n$ = 0 (**16**, **16′**), 1 (**17**, **17′**).

Scheme 5




to the fact that in these cases the complexation largely involves one binding centre of the rod molecule.



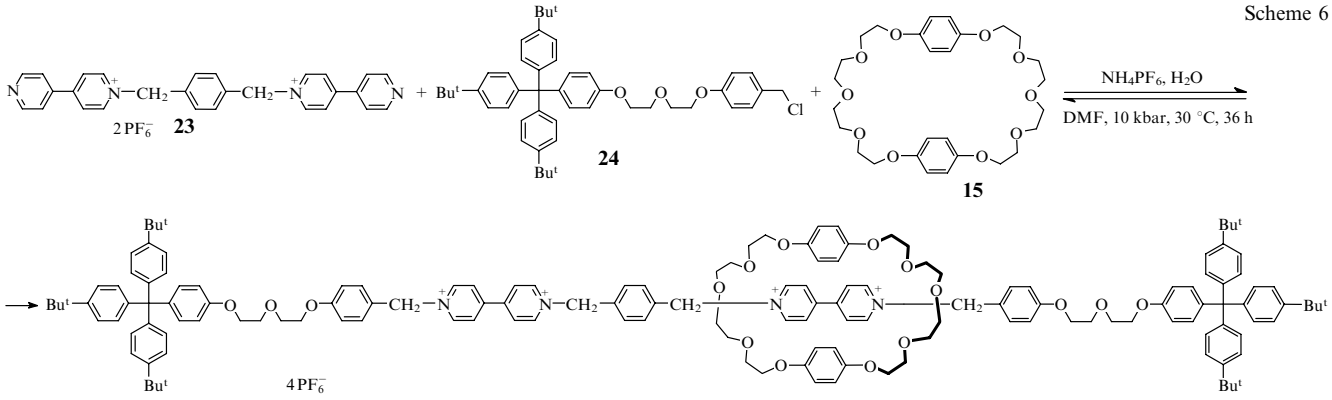

R =  ; $n$ = 0 (**19**), 1 (**20**), 2 (**21**), 3 (**22**).

The synthesis of rotaxanes based on crown ether **15** was carried out using strategies I and III.[28] Thus the reaction of the dication **23** with the bulky blocking reagent **24** in the presence of an equimolar amount of the macrocycle **15** under high pressure (strategy I) (Scheme 6) has been described. The yield of the target product, *viz.*, [2]-Rt, was 23%. Noteworthy, the rate of the translocation of the macrocycle between the two dications in this complex is $\sim 300\,000\ s^{-1}$, which markedly exceeds that of rotaxanes based on cyclobis(paraquat-*p*-phenylene).

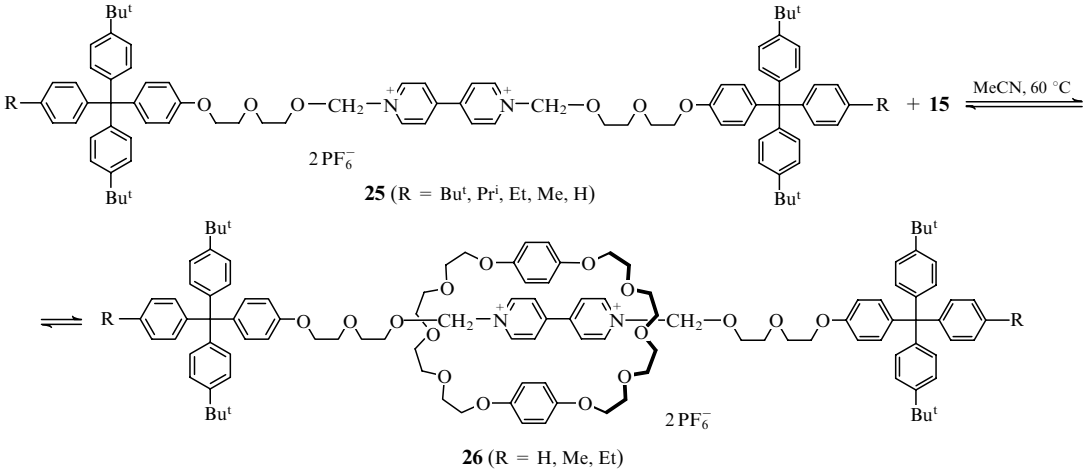
By varying the size of the blocking group in the dumbbell-shaped molecule **25** (Scheme 7), it became possible to synthesise rotaxanes using thermodynamically more favourable slipping of the macromolecule **15** onto the bulky terminal groups of compound **25** (strategy III, see Fig. 2). Compound **25** in which the terminal *tert*-butyl groups were replaced severally by isopropyl, ethyl and methyl groups as well as by hydrogen atoms were heated in acetonitrile with four equivalents of the macrocycle **15** at 60 °C.[29] This resulted in the self-organisation of [2]-Rt of the type **26** (see Scheme 7) in 47%, 45% and 51% yields for R = Et, Me and H, respectively. The isopropyl groups appeared to be too bulky for the slipping of the macrocycle. All the rotaxanes thus prepared were stable at room temperature.

Strategy III was also employed in the synthesis of [2]- and [3]-Rt containing two bipyridine fragments.[30] It should be noted that such rotaxanes cannot be synthesised using strategies I and II,

Scheme 6




Scheme 7




whereas slipping allows one to obtain them in 20% and 55% yields, respectively.

An illustrative example of a successful application of strategy III has been described.[31] Heating of a mixture containing compound **27** and the macrocycle **15** affords [2]-Rt **28** (yield 19%), [3]-Rt **29** (yield 41%) and [4]-Rt **30** (yield 22%) (Fig. 3). Such branched supramolecular assemblies are the first examples of dendritic rotaxanes.

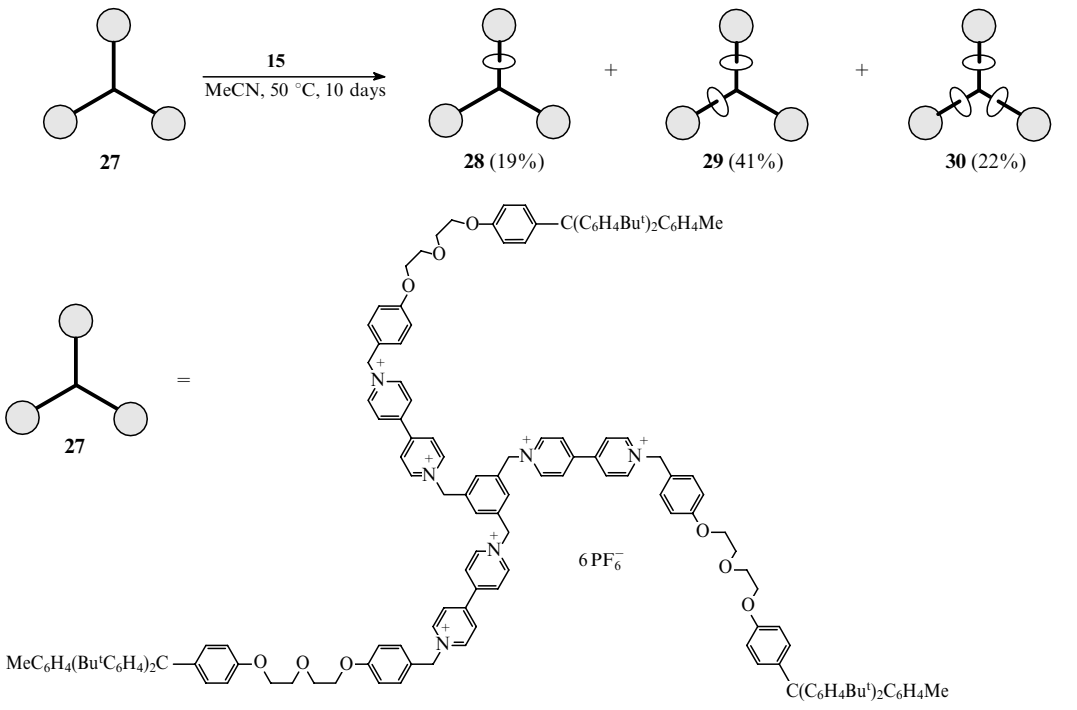



**Figure 3.** The synthesis of dendrimeric rotaxanes using strategy III.[31]

**c. The synthesis of cyclodextrin-containing rotaxanes**

The use of cyclodextrins (CD) as cyclic components has marked a new step in the synthesis of rotaxanes. These compounds were first discovered in 1891 [32] and represent cyclic oligosaccharides built up of D-glucopyranose units linked together by α-1,4-glucoside bonds. The shape of the cyclodextrin molecules resembles a torus. The structure of α-, β- and γ-cyclodextrins is schematically represented in Fig. 4. The presence of a cylindrical hydrophobic cavity determines the ability of cyclodextrins to form inclusion complexes with molecules of different chemical nature in aqueous solutions. The synthesis and characteristics of such complexes have been outlined in numerous reviews and monographs.[33–39] Suffice it to say that the driving forces of this complexation are Coulombic, dipole–dipole, hydrophobic and van der Waals interactions as well as hydrogen bonds between the CD and 'guest' molecules. Matching of the geometrical characteristics of the cyclodextrin cavity and those of the 'guest' molecule is an important prerequisite for the formation and stability of the inclusion complexes. The unique capacity of cyclodextrins to interact selectively with the substrate molecules which are complementary in size makes them attractive subjects of the supramolecular chemistry.

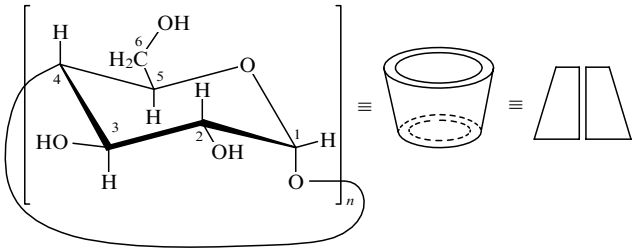
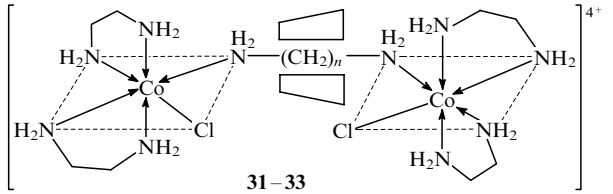


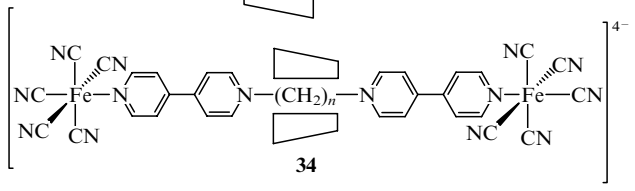
**Figure 4.** The structural formula of α- ($n$ = 6), β- ($n$ = 7) and γ-cyclodextrins ($n$ = 8).

Initially, syntheses of cyclodextrin-containing rotaxanes were based on the ability of CD molecules to be threaded onto polymethylene chains. It should be noted that the cavity of one macrocycle accommodates approximately five methylene units. The blocking groups were introduced into pseudorotaxanes by the reaction with the terminal functional groups of the rod molecules. The role of stoppers was played by transition metal complexes. This approach was used in the synthesis of [2]-Rt **31**–**33** based on α- and β-CD.[40] The maximum yield of the rotaxanes (19%) was obtained for the systems comprising α-cyclodextrin and linear molecules whose alkyl chains contained 12 carbon atoms ($n$ = 12). Similarly, [2]-Rt **34** was prepared by the reaction of the α-CD–1,1′-nonamethylenebis(4,4′-bipyridine) complex with cyanoferrate(II) in an aqueous solution.[41] The rotaxane formed was kinetically labile, so it could not be isolated from the solution.



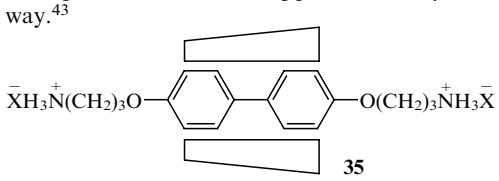
**31**–**33**

$n$ = 8 (**31**), 10 (**32**), 12 (**33**); = α-CD, β-CD.

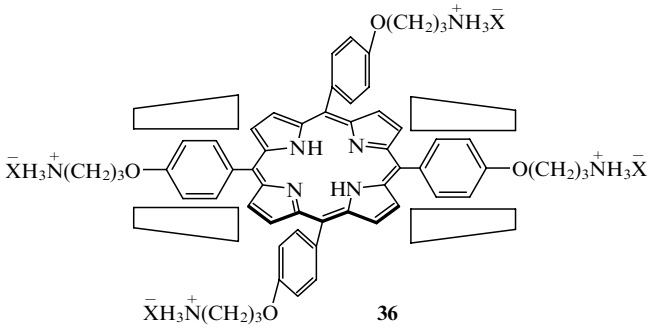


**34**

Ion-to-ion interactions were used to stabilise cyclodextrin-containing pseudorotaxanes.[42] The role of the thread was played by molecules carrying terminal ammonium groups, heptakis(2,6-di-*O*-methyl)-β-cyclodextrin (DM-β-CD) was used as the cyclic component. Pseudorotaxane **35** was precipitated from the solution by addition of tetraphenylborate; after isolation and purification, its yield was 71%. [3]-Rt **36** which can be regarded as an analogue of heme-containing proteins was synthesised in a similar way.[43]



**35**

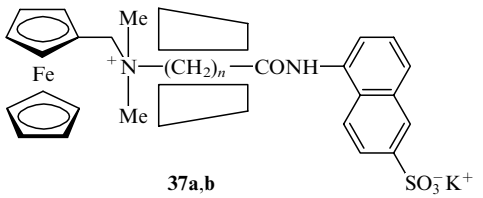


**36**

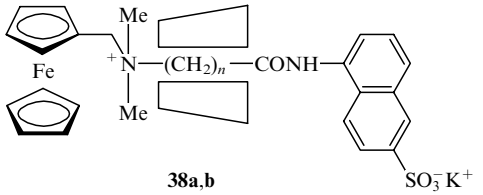
X = $Ph_4B^-$; = DM-β-CD.

Stable rotaxanes can only be obtained in those cases where stoppers are covalently bound to the termini of the 'guest' molecule. The main difficulty is related to the choice of a solvent which must serve as a suitable medium for the chemical reaction of the terminal groups of the pseudorotaxane and simultaneously ensure stabilities of the inclusion complexes. Water, which is the best solvent for the interaction of cyclodextrins with the substrate, is most often inappropriate for the introduction of terminal groups, since these reagents are usually poorly soluble in water or undergo hydrolysis. To overcome this problem, it was suggested [44] to use strong nucleophiles (*e.g.*, $NH_2$) as the functional groups of the stoppers and aliphatic carboxylic acid derivatives as the rod molecules.

This approach was used in the synthesis of two [2]-Rt, *viz.*, **37a**,**b**, and their orientational isomers **38a**,**b** in 15% yield.[45]



**37a**,**b**



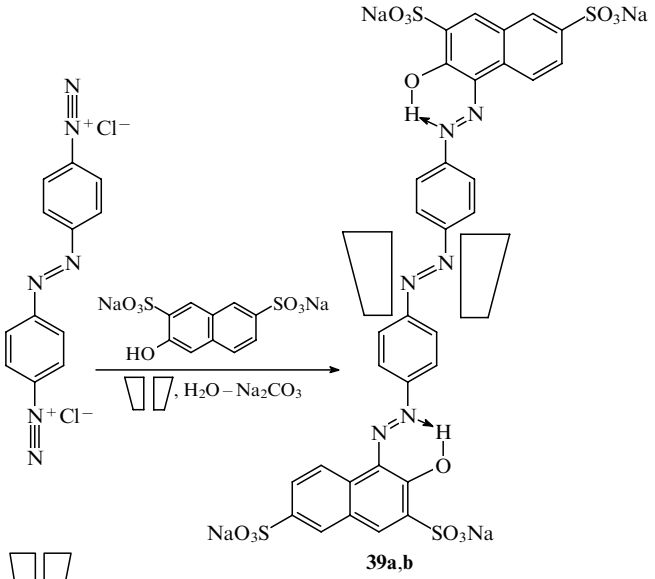
**38a**,**b**

$n$ = 7 (**a**), 11 (**b**).

It is remarkable that the isomer **37a** remained stable, whereas the complex **38a** dissociated into constituents. This example illustrates the strong dependence of the stability of the rotaxanes on the spatial orientation of the CD molecules threaded onto the 'guest' molecules. A similar strategy of the rotaxane synthesis in aqueous solutions on the basis of rod molecules carrying terminal $NH_2$ groups and di-*O*-methyl- and tri-*O*-methyl-α-cyclodextrins

was used by Harada and Kamachi.[46] In this study, 1,12-diaminododecane complexes with methylated cyclodextrins reacted with an aqueous solution of trinitrobenzenesulfonic acid, which resulted in the corresponding rotaxanes isolated in 42% and 48% yields.

The formation of inclusion complexes based on cyclodextrins is often used for stabilisation of photosensitive compounds.[34–36] The conversion of such complexes into rotaxanes is a logical sequel of these studies. Thus an azo dye was synthesised from a bisdiazonium salt and a β-naphthol derivative in the presence of various cyclodextrins.[47] Rotaxanes **39a**,**b** were prepared from α- and β-CD in 12% and 15% yields, respectively. The formation of such water-soluble rotaxanes illustrates the possibility of an increase in the stabilities and solubilities of practically important synthetic dyes using this simple approach. It has thus been demonstrated that molecular self-assembly is an efficient tool for the design of new structures.




## III. Polyrotaxanes

The strategies of rotaxane synthesis can also be applied to the development of procedures for the preparation of structurally more elaborate compounds, *viz*., polyrotaxanes (PRt or [*n*]-Rt) which represent supramolecular assemblies where multiple macrocycles are non-covalently bound with the polymeric chains. Two main types of such complexes are distinguished, *viz*., linear polyrotaxanes where the macrocycles are threaded onto the main chain (Fig. 5 *a*) and comb-like polyrotaxanes (Fig. 5 *b*).

There are several main approaches to the synthesis of polyrotaxanes, namely, the formation of a polymer in the presence of a macrocycle (method 1); the formation of a ring in the presence of a macromolecule (method 2); polymerisation or polycondensation of a stable pseudorotaxane (method 3); self-organisation of a pseudopolyrotaxane (pseudo-PRt) due to specific non-covalent interactions (method 4) and temperature-induced slipping of the macrocycles onto the stoppers, *viz*., terminal groups or those pertaining to the main chain (method 5). It should be noted that cyclisation is usually performed in dilute solutions. However, if polyrotaxanes are synthesised by the method 2, the Le Chatelier principle requires that the polymer was used as a solvent or was taken in excess. This results in a significant increase in the viscosity of the reaction mixture and, correspondingly, in a decrease in the rate of the reaction. For this reason, method 2 is virtually inapplicable to the synthesis of polyrotaxanes. The role of macrocycles is usually played by synthetic or natural cyclic molecules, *e.g*., crown ethers [48–59] or cyclodextrins.[60–117]

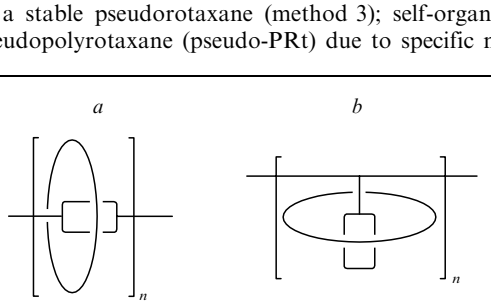
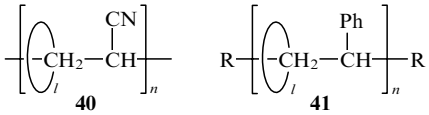


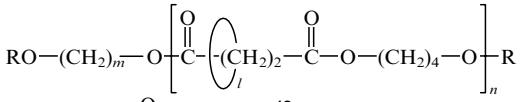

**Figure 5.** A schematic representation of polyrotaxanes: (*a*) linear, (*b*) comb-like.

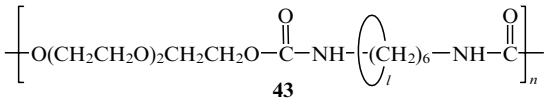
### 1. Linear polyrotaxanes based on crown ethers

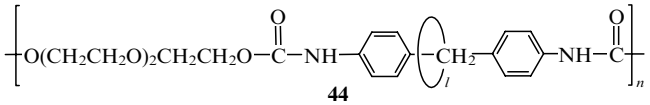
The procedures used for the synthesis of polyrotaxanes which incorporate crown ethers have been studied in sufficiently great detail.[48–59] They are based on the statistical threading of macrocycles onto the rod molecule in the course of polymerisation (method 1). The possibility of the use of virtually all (as regards their chemical nature) linear molecules for the rotaxane synthesis allows the design of a great diversity of pseudopolyrotaxanes. 36-Crown-12, 42-crown-14, 48-crown-16 and 60-crown-20 are usually used as crown ethers.

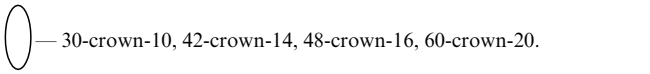
Radical polymerisation was used for the synthesis of pseudopolyrotaxanes **40** based on polyacrylonitrile.[48,49,59] Polystyrene-based polyrotaxanes **41** were synthesised by anionic polymerisation of styrene in the presence of 36-crown-12 and 42-crown-14.[50] Pseudopolyrotaxanes and polyrotaxanes based on various polyesters (compound **42**) and polyurethanes (compounds **43** and **44**) were obtained by polycondensation and polyesterification.[51–58]



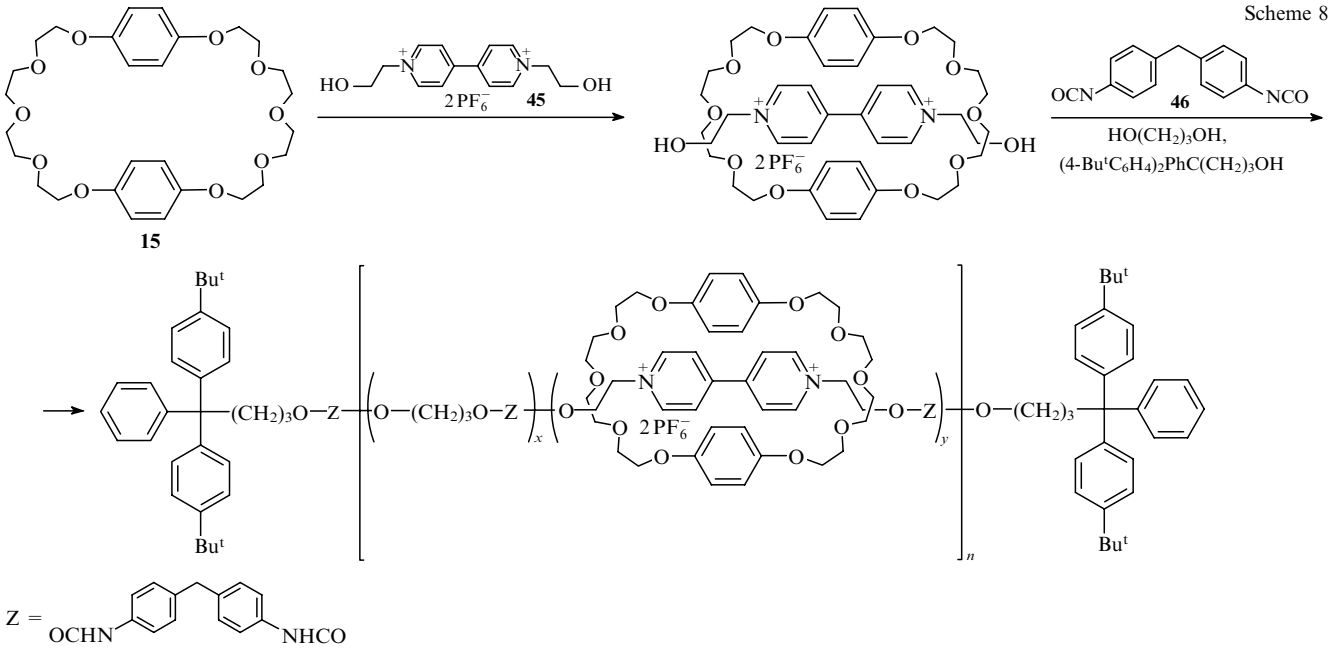




The isolation and purification of the polymers thus formed were carried out by multiple precipitation of the macrocycles using selective solvents. To ensure invariable composition, it is sufficient to repeat the procedure once or twice even in the case of pseudopolyrotaxanes. This suggests that the folded conformation of the macromolecules prevents the dissociation of the complex into the constituents. The properties of the polymers synthesised were studied by NMR spectroscopy, gel permeation chromatography (GPC), viscosimetry and differential scanning calorimetry (DSC). It was found that the molecular mass of the polyrotaxane formed and the degree of threading of the crown ether increase with an increase in the concentration of the macrocycle and depend on the ratio of the components in the original mixture. The maximum efficiency of threading of crown ethers is achieved where the latter are used as solvents or co-solvents for monomers in the course of polymerisation.

Scheme 8



The possibility of a template synthesis of polyrotaxanes was also studied using crown ether **15** as a template. Co-polymerisation of *N*,*N*′-bis(2-hydroxyethyl)-4,4′-bipyridinium bis(hexafluorophosphate) (**45**) with bis(*p*-isocyanatophenyl)methane (**46**) in the presence of the macrocycle **15** (Scheme 8) afforded a polyrotaxane with a high (54%) content of cyclic molecules.[51, 55] To increase the flexibility of the synthetic polymer, small amounts of an ethylene oxide oligomer were added to the reaction mixture. It was found that the molecular mass and the amount of the macrocycle in polyrotaxane depend on the ratio of the starting components as well as by the amount of the stopper added.

The incorporation of macrocycles into polymers causes significant changes in the physicochemical properties (*e.g.*, solubility, thermal and mechanical characteristics) of the rotaxanes formed in comparison with the starting compounds. Some authors [48–59] consider crown-ether-based polyrotaxanes as specific copolymers of the cyclic and linear components. The solubilities of polyurethane- and polyester-based rotaxanes depend on their composition as well as on the nature and size of the macrocycle. For example, the incorporation of 60-crown-20 increases the polarities of polyurethane-based rotaxanes so that these compounds, contrary to the original polymers, become soluble in polar solvents. In some cases, synthetic polyrotaxanes were water-soluble producing micellar structures.[55, 56] Treatment of polyurethane-based rotaxanes with solvents which are selective with respect to the incorporated polymer was accompanied by the aggregation and even crystallisation of the cyclic component which was attributed [55, 56] to the free migration of the crown ethers along the rod molecule.

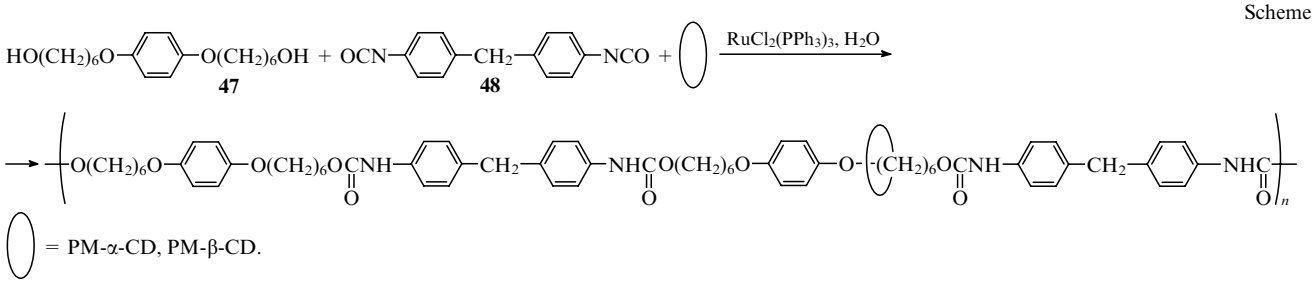
Studies of the thermal characteristics of polyrotaxanes by DSC revealed that phase-transition temperatures strongly depend on the nature of the interacting components and the composition of the supermolecules formed. For example, the polymer based on poly(butane-1,4-diyl sebaceate) and 60-crown-20 produced two endothermal peaks at 40 and 60 °C, which corresponded to the melting of the cyclic and linear components, respectively. These values are several degrees lower than those for the corresponding individual crown ethers and the polyester, which suggests a decrease in the crystallinity of each of the polyrotaxane components.[53] The glass transition of polyurethane-based rotaxanes is also observed at a lower temperature range in comparison with the glass transition temperatures for the original components.[59]

According to Gibson *et al.*,[48–59] the properties of polyrotaxanes formed by polymerisation of monomers can be changed directionally by varying their compositions. The feasibility of incorporation of crown ethers into polymers as plasticisers was also considered.[56]

## 2. Linear polyrotaxanes based on cyclodextrins

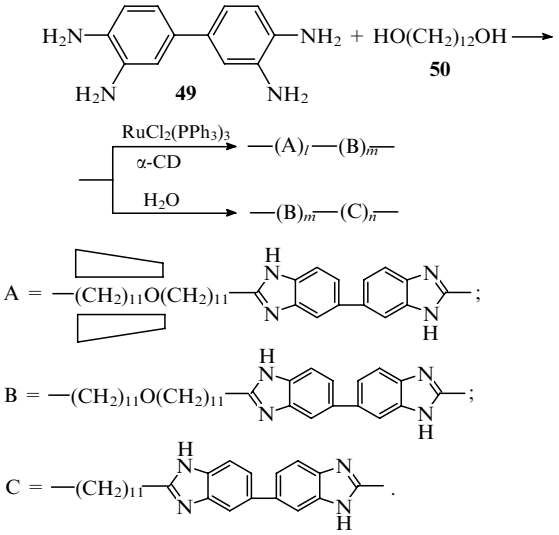
The procedure for the preparation of cyclodextrin-containing polyrotaxanes by the method 1 included polycondensation of 1,4-bis(ω-hydroxyhexyloxy)benzene (**47**) and 4,4′-methylenediphenylisocyanate (**48**) (Scheme 9) in the presence of permethylated α- and β-cyclodextrins (PM-α-CD and PM-β-CD).[60] This approach was used to synthesise a series of polyurethane-based pseudopolyrotaxanes in high yields (85% – 92%) with the starting components taken at different ratios. It was found that the compositions of the synthetic polymers depend on the PM-CD : monomer ratio. The maximum content of the macrocycles for PM-α-CD and PM-β-CD is one molecule of a cyclodextrin per four and five repeating fragments of the polymer, respectively. A $^1$H NMR spectroscopic study revealed that in the polymers synthesised PM-α-CD fragments are accommodated on the polymethylene groups, whereas PM-β-CD, which has a larger cavity, is predominantly localised on the aromatic groups of the

Scheme 9



rod macromolecule. As in the case of the polyrotaxanes containing crown ethers, the glass transition temperature of cyclodextrin-based polyurethane pseudopolyrotaxanes was lower than that of the native polymer. This is attributed to partial destruction of polyurethane-specific intramolecular hydrogen bonds as a result of shielding of polar NH-groups of the polymer by the cyclic macromolecule.

A similar strategy was used in the polycondensation of monomers which contained either binding centres or blocking groups in the presence of a macrocycle.[61] It was shown that catalytic oxidative polycondensation of compounds **49** and **50** in the presence of α-CD resulted in the formation of irregular polyrotaxanes which comprised block copolymers incorporating the structural fragments A and B in a 16 : 84 ratio.




It is of note that the polyrotaxanes synthesised contain no structural fragments of the C type, whereas in the absence of cyclodextrin the polycondensation affords a polymer which contains ~ 20% of such blocks.

An alternative strategy of the polyrotaxane synthesis consisted in preliminary synthesis of inclusion complexes of a series of diamines with β-cyclodextrin and their subsequent polycondensation with isophthaloyl or terephthaloyl chlorides[62] (method 3). The conclusion concerning the formation of the macromolecular cyclodextrin – polymer complex was made on the basis of the results of elemental and differential thermal analyses. Radical polymerisation was used in the synthesis of cyclodextrin-containing homopolymers and copolymers based on inclusion complexes of β-CD with vinylidene chloride, allyl chloride, styrene and methyl methacrylate.[63] In this case, the reaction was accompanied by the chain transfer to cyclodextrin. The attempts to characterise unambiguously the compositions and structures of the resulting complexes failed owing to their poor solubilities and the presence of by-products.[62, 63] For this reason, the synthesis of supramolecular structures incorporating polymers and cyclodextrin from the inclusion complexes of the corresponding monomers did not acquire popularity.

**a. Water-insoluble cyclodextrin-containing polyrotaxanes**

Two independent groups of investigators[64–85] demonstrated the possibility of applying the molecular self-assembly principle (method 4) to the synthesis of polyrotaxanes. This method consists in the direct interaction of cyclodextrin and polymers in aqueous solutions.

A group of Japanese investigators[64–80] carried out a detailed study of interactions of poly(ethylene oxides) (PEO) with α-cyclodextrin. It was shown that mixing of aqueous solutions of the polymer and CD resulted in the precipitation of a weakly soluble product. It was assumed that in this case 'self-organisation' of the inclusion complex occurred in which cyclodextrin molecules are threaded onto the polymeric chain. This type of complexes have acquired the name of 'molecular necklaces' (MN). As a matter of fact, these structures represent pseudopolyrotaxanes which can be converted into polyrotaxanes by modification of their terminal groups.

Studies of complexation of poly(ethylene oxides) with α-cyclodextrin by the nephelometric method revealed that the lowest molecular mass of a polymer necessary for the formation of insoluble complexes is 300. However, in a more recent publication by these authors it was shown that 'molecular necklaces' can be prepared from tetra(oxyethylene) dibromide (MM = 176).[78] The rate of complexation reaches a maximum at the average molecular mass ($M_n$) of 1000 and shows a tendency to decrease with a further increase in $M_n$.[68] This result is attributed to a decrease in the number of terminal groups with an increase in the molecular mass of the polymer, which in its turn is due to the inclusion nature of the complexes. Evidence for the formation of MN can be obtained from the results of elemental and thermogravimetric studies as well as from $^1$H and $^{13}$C NMR spectroscopy and X-ray diffraction data. Thus $^1$H NMR spectroscopy was used to determine the compositions of the complexes synthesised. Irrespective of the molecular mass of PEO and the molar ratios of the reagents, the complexes formed had strictly stoichiometric compositions where one molecule of α-cyclodextrin corresponded to two ethylene oxide units. Molecular simulation revealed that the diameter of the PEO chain matches perfectly the width of the inner cavity of α-CD, whereas the length of two ethylene oxide fragments is practically equal to the height of the cyclodextrin cone. Additional evidence in favour of MN formation can be derived from the fact that in the case where PEO molecules contained bulky terminal groups (2,4-dinitrophenyl or 3,5-dinitrobenzoyl groups), the sizes of which exceed that of the inner cavity of α-CD, cyclodextrin loses its ability to be threaded onto the polymeric chain and no inclusion complex is formed. It was suggested that the driving force of self-organisation of the complexes are hydrophobic interactions between the cyclodextrin cavity and the polymer fragments as well as the formation of hydrogen bonds between the OH groups of the neighbouring CD molecules.

Further studies showed that similar complexes could be prepared with other cyclodextrin – polymer pairs (Table 1). These data suggest that hydrophobic polymers can be used for complexation along with hydrophilic ones. Although the formation of complexes based on hydrophobic polymers takes much more time and requires preliminary sonication of the reaction mixture, the pseudopolyrotaxanes produced possess strictly stoichiometric compositions and they can be obtained in sufficiently high yields. It should be noted that the dependences of the yields of MN on the molecular mass of the polymer differ substantially for the complexes prepared from hydrophilic or hydrophobic polymers and cyclodextrin. Thus for the α-CD – PEO complex, this dependence is described by a curve which consists of two parts. First, the yield of the polymer increases with an increase in the molecular mass and then is independent of the molecular mass. For hydrophobic polymers, this dependence is bell-shaped;[65, 71, 74] in some cases, *e.g.*, for poly(isobutylene),[73] the product yield decreases monotonically. The observed regularities can be explained as follows. In aqueous solutions, hydrophobic polymers exist in an aggregated state. Since the tendency for aggregation increases with an increase in the molecular mass, the accessibility of the terminal groups of the polymer for the interaction with cyclodextrin is expected to decrease; therefore, only part of the macromolecules can find their 'partners'. Some polymers, *e.g.*, poly(oxytrimethylene), form pseudopolyrotaxanes with both α- and β-cyclodextrins (see Table 1), which was attributed[72] to different conformations of the polymer incorporated.

It was shown with the help of $^1$H NMR spectroscopy and other analytical methods that the stoichiometric compositions of the complexes are usually independent of the molecular masses of the polymers in the MM range studied and are consistent with the results of molecular simulation studies.[64–68] Violations of this

**Table 1**. Pseuropolyrotaxanes based on α- and β-cyclodextrins and polymers.

| Polymer | MM | Yields of products (%) (number of monomeric units : number of CD molecules) | | | Ref. |
|---|---|---|---|---|---|
| | | α-CD | β-CD | γ-CD | |
| Poly(ethylene oxide) | 300 | 22 (2 : 1) | none | traces | 68 |
| | 400 | 83 | " | " | |
| | 600 | 89 | " | " | |
| | 1000 | 91 | " | " | |
| | 1500 | 93 | " | " | |
| | 2000 | 94 | " | " | |
| | 5000 | 21 | " | " | |
| Poly(propylene oxide) | 400 | none | 1 (2 : 1) | 76 (2 : 1) | 71 |
| | 425 | " | 27 | 74 | |
| | 725 | " | 84 | 77 | |
| | 1000 | " | 96 | 80 | |
| | 2000 | " | 50 | 31 | |
| | 3000 | " | 32 | 20 | |
| | 4000 | " | 27 | 15 | |
| Poly(methyl vinyl ether) | 20 000 | none | none | 67 (3 : 1) | 68 |
| Poly(oligoethylene) | 702 | 67 (3 : 1) | " | none | 70 |
| Poly(isobutylene) | 100 | none | 67 (3 : 1) | " | 73 |
| | 500 | " | 18 | 64 (3 : 1) | |
| | 800 | " | 8 | 90 | |
| | 1350 | " | 4 | 96 | |
| | 2700 | " | 5 | 87 | |
| Poly(oxytrimethylene) | 700 | 87 (1.5 – 2.0 : 1.0) | 52 (2.0 – 2.5 : 1.0) | – | 72 |
| | 1200 | 90 (1.5 – 2.0 : 1.0) | 67 (2.0 – 2.5 : 1.0) | – | |
| | 3100 | 34 (5 : 1) | 55 (4 : 1) | – | |
| Poly(oxytetramethylene) | 250 | 82 (1.5 : 1.0) | – | – | 72 |
| | 1000 | – | – | 100 (2.8 : 1.0) | |
| Poly(ε-caprolactam) | 530 | 82 (1 : 1) | – | – | 74 |

regularity were observed only for the interaction of α- and β-cyclodextrins with poly(oxytrimethylene).[72] When polymers with MM $\leqslant$ 2000 were used, the compositions of MN remained constant and corresponded to one molecule of cyclodextrin per 1.5 – 2 or 2 – 2.5 monomeric units of the polymer for α- and β-CD, respectively. However, with an increase in the molecular mass of the rod macromolecule, the stoichiometry of the complex formed changed (see Table 1). Presumably, the increase in the hydrophobicity with an increase in MM prevents the diffusion of the polymer in the aqueous medium and the involvement of all of the macromolecules in the complex formation.[72] Probably, the precipitation of the complex is accompanied by co-precipitation of the free polymer; therefore, the composition of the pseudopolyrotaxane cannot be calculated exactly.

It was shown [69] that γ-cyclodextrin forms no stable complexes with unmodified PEO, although, like β-cyclodextrin, it forms a 2 : 1 complex with poly(propylene oxide) (PPO) (see Table 1). It was also found that poly(ethylene oxide) which contained bulky terminal substituents, *e.g.*, the 3,5-dinitrobenzoyl substituent, interacted with γ-cyclodextrin to form crystalline complexes in very high yields.[70] A $^1$H NMR spectroscopic study revealed that the cavity of γ-CD accommodates four oxyethylene fragments, which suggests that γ-cyclodextrin is threaded simultaneously onto two polymeric chains. To corroborate this hypothesis, Harada *et al.*[69] obtained a fluorescently labelled polymer, *viz.*, bis(2-naphthylacetyl)poly(ethylene oxide). The MN prepared on the basis of this compound and γ-cyclodextrin also had a stoichiometric composition 1 : 4. Fluorescence spectroscopic studies revealed the presence of excimers, which suggests close contacts between the naphthyl residues and corroborates the hypothesis that the γ-cyclodextrin molecule incorporates two PEO chains (Fig. 6). Similar crystalline double-stranded inclusion complexes based on γ-cyclodextrin and PEO (MM = 1500) were obtained in high (~ 80%) yields;[86] in this case the complexation did not necessitate blocking of the chain termini by bulky substituents.

Later, a group of Japanese investigators synthesised a polyrotaxane **51** based on the molecular necklaces by the reaction of terminal amino groups of bisaminopoly(ethylene oxide) incorporated into α-cyclodextrin with fluoro-2,4-dinitrobenzene.[66] The yield of the reaction product after isolation and purification by GPC was 60%. Subsequent modifications of the polyrotaxane **51** allowed the authors to synthesise oligomers containing cross-linked cyclodextrins, the so-called 'polymeric tubes' (Fig. 7).[80] These compounds were synthesised by treatment of the polymer **51** in 10% NaOH with epichlorohydrin. Using GPC, it was shown that epichlorohydrin cross-linked CD molecules along the polymeric chain with the formation of hydroxypropylene bridges. The blocking groups were removed by hydrolytic cleavage with 25% NaOH which resulted in the release of the polymer enclosed inside the tube. The final product (yield 92%) represented a hollow tube which consisted of about 15 cross-linked cyclodextrin molecules (MM = 20 000) (**52**, see Fig. 7). Probably, such structures can be used for selective separation of substances.

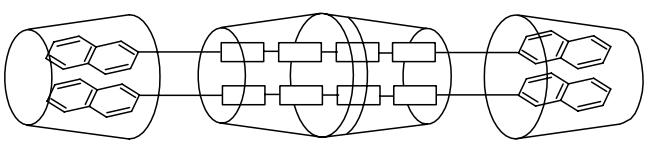


**Figure 6.** A schematic representation of an inclusion complex of γ-cyclodextrin with bis(2-naphthylacetyl)poly(ethylene oxide).[69]

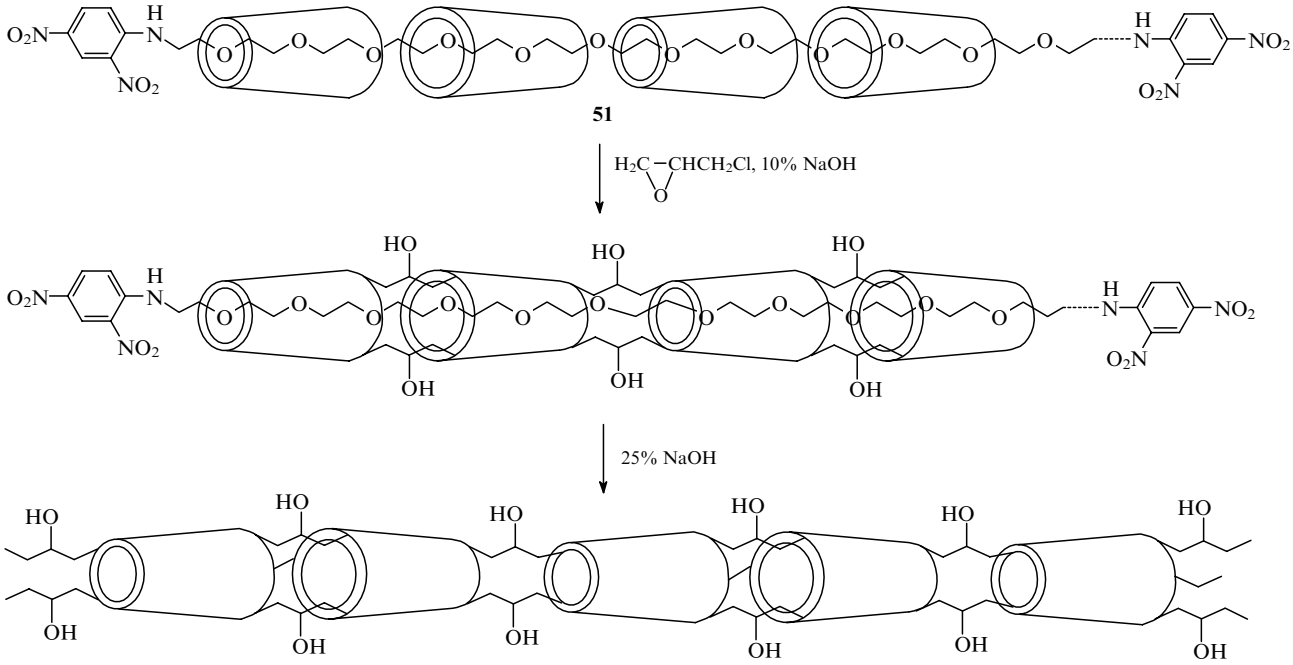
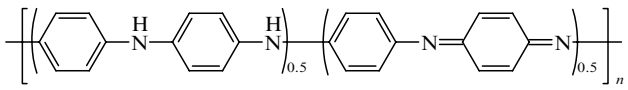



**Figure 7.** A scheme of synthesis of polymeric tubes from polyrotaxanes based on bisaminopoly(ethylene oxide) and α-cyclodextrin.[85]

It was shown[87] that the reaction of cyclodextrin with the conjugated conducting polymer **53** (polyaniline), which contains emeraldine bases,



**53**

afforded a pseudopolyrotaxane in which the polymer was incorporated inside the cavity of the non-conducting cyclic molecules. These structures have been termed as 'insulating molecular wires'. This system was used to demonstrate that cyclodextrins prevent chemical oxidation of the rod macromolecule, *e.g.*, on doping of polyaniline with iodine.

The use of modified CD (particularly, of methylated macrocycles) as 'hosts' allows one to compare processes of molecular recognition involving native CD and their derivatives. Using $^1$H NMR spectroscopy, it was shown than none of the methylated cyclodextrins form complexes with PEO as can be evidenced from the fact that no precipitation occurred even after 2-months' storage of their mixture. A different situation is observed in the interaction of these cyclodextrins with hydrophobic polymers. Complexes of PPO and poly(tetrahydrofuran) (PTHF) with heptakis- and hexakis-(2,6-di-*O*-methyl)cyclodextrins (DM-CD) as well as with heptakis- and hexakis-(2,3,6-tri-*O*-methyl)cyclodextrins (TM-CD) have been described in the literature.[79] It was shown that the addition of DM-β-CD first increases significantly the solubility of PPO in water and then a crystalline complex is formed. However, TM-α-CD, TM-β-CD and DM-α-CD neither favour the solubilisation of PPO in water nor form inclusion complexes. The solubility of PTHF in water increases in the presence of low concentrations of DM-β-CD and DM-α-CD. At high concentrations of these cyclodextrins, the solubility of PTHF decreases and inclusion complexes are precipitated. TM-β-CD also forms inclusion complexes with PTHF. The yields of PTHF – DM-β-CD complexes increase with an increase in the weight-average molecular mass ($M_w$), it is a maximum at $M_w = 1000$. The stoichiometric composition of PTHF – DM-β-CD complexes corresponds to one molecule of the macrocycle per 1.0 – 1.5 monomeric units of the rod macromolecule. Taking into account the number of atoms in the repeating fragment of the polymer per one CD molecule, it appears that the composition of the PTHF – DM-β-CD complex is consistent with the stoichiometric composition of the corresponding MN based on α-CD. The experimental data altogether suggest that hydrophobic interactions between methylated cyclodextrins and hydrophobic polymers make a weighty contribution to the process of molecular recognition.

Based on the geometrical correspondence of the CD molecules to polymeric 'guests', one can postulate the existence of ternary complexes which represent MN with low-molecular-weight 'guests' incorporated into them. Such complexes were obtained in PEO-β-CD – aromatic compound systems.[88] Benzene, its mono-, di- and tri-substituted derivatives were used as aromatic compounds. After mixing of these three components, a complex precipitated from the aqueous solution. Radiolabelled $^3$H-PEO was used for quantitative determination of poly(ethylene oxide) content in the complexes. The content of β-CD was determined polarimetrically, while that of the aromatic compound was established by UV spectroscopy. The composition of the complexes corresponds to one β-CD molecule per two units of PEO and one molecule of the aromatic compound. The ternary complexes precipitate with benzene, benzoic acid and *p*-nitrophenol but do not precipitate in the presence of *o*-nitrophenol and 2,4-dinitrophenol. X-Ray diffraction studies have shown that the structures of the ternary complexes are identical with that of MN. Simulation of the ternary complexes demonstrated that the regular orientation of CD in MN is not disturbed upon incorporation of benzene and its monosubstituted derivatives into their cavities.

The molecular dynamics of MN based on α-CD – PEO[89] and β-CD – PPO[90] complexes has been studied. It was shown that the main driving force of molecular recognition are the van der Waals interactions. Hydrogen bonds provide arrangement of the CD rings in a 'head-to-head' and 'tail-to-tail' fashion. Cyclodextrins in polyrotaxanes exist in a more symmetrical and a less rigid conformation than in the individual state. The formation of polyrotaxanes is accompanied by the transition of the polymers to the stretched conformation due to an increase in the proportion

of *trans*-conformers in comparison with the state of the isolated polymeric chains. The structure- and energy-related reasons for the non-statistical distribution of CD in MN prepared on the basis of PEO – PPO block copolymers were established using the dynamic Monte Carlo method.[91] It was found that the stability of the complexes is determined by both hydrophobic interactions between the 'host' cavity and the 'guest' molecule and the hydrogen bonds between the cyclodextrin molecules.

It should be noted that the interest in MN is generated largely by fundamental problems. According to Tonelli *et al.*,[92–94] the polymeric inclusion complexes are convenient subjects for studying the behaviour of ordered and isolated polymeric chains, which simulates the state of oriented polymers in the crystalline phase.

It was also shown that macromolecular inclusion complexes can be used for the preparation of high-strength oriented fibres. Removal of cyclic molecules from the complexes was carried out by treatment of the polymers with a solvent which is selective with respect to cyclic compounds.[92] The selectivity of formation of crystalline polymeric inclusion complexes incorporating cyclodextrins served as a basis for the development of a new procedure for purification of polymeric materials under laboratory conditions, the so-called extractive crystallisation.[94]

**b. Pseudopolyrotaxanes based on block copolymers**

Considerable progress in the synthesis of supramolecular structures based on CD and polymers is associated with the use of block copolymers (BC) of ethylene oxide and propylene oxide (pluronics) as the 'guest' molecules. Pluronics differ in their compositions, number of blocks and mutual arrangements, which permits the synthesis of MN having different structures and properties. By varying the length of the free component of the complex based on a BC and cyclodextrin, one can obtain both water-insoluble [95–99] and water-soluble [100] polymeric inclusion complexes. For steric reasons, α-CD cannot interact with a poly(ethylene oxide) component of BC of the PPO – PEO – PPO type.

A systematic study of the reactions of α-, β- and γ-CD with different types of PEO – PPO block copolymers [95–99] has been carried out. Their characteristics are listed in Table 2. The interaction of α- and β-CD with BC I and BC II built up of poly(ethylene oxide) and poly(propylene oxide) blocks of virtually equal lengths has been studied.[95] It was found that the addition of solutions of block copolymers to aqueous solutions of the corresponding macrocycles results in the precipitation of water-insoluble complexes. Using the α-CD – BC I system as an example, it was shown that with an increase in the pluronic concentration the mass of the isolated complex increases at first and after reaching a certain maximum remains unchanged, which suggests the formation of a stoichiometric complex. Polarimetric and IR spectroscopic studies of these complexes as well as molecular simulation studies revealed that different pluronic blocks become involved in this process depending on the type of the cyclodextrin (α- or β-CD, which differ in the diameter of their inner cavity) used for the complexation. Thus, the interaction with α-CD involves

**Table 2**. Some characteristics of the block copolymers based on poly(ethylene oxide) (PEO) and poly(propylene oxide) (PPO) used in the synthesis of pseudopolyrotaxanes.[95–99]

| Block copolymer | Type of copolymer | MM | Content of PPO (%) | Degree of polymerisation | |
|---|---|---|---|---|---|
| | | | | PEO | PPO |
| I | PEO – PPO | 3000 | 50 | 30 | 28 |
| II | PEO – PPO | 2000 | 60 | 18 | 20 |
| III | PEO – PPO – PEO | 2700 | 45 | 18 [a] | 19 |
| IV | PEO – PPO – PEO | 6000 | 23 | 52 [a] | 24 |
| V | PPO – PEO – PPO | 3000 | 40 | 40 | 10 [a] |

[a] The degree of polymerisation of one block.

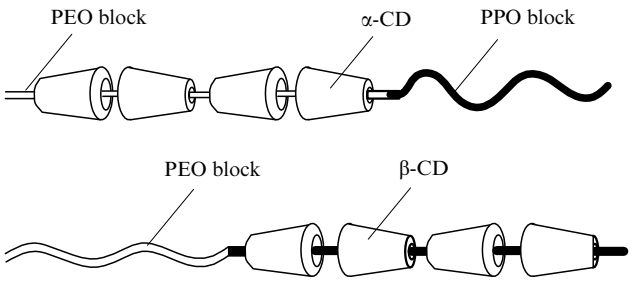



**Figure 8.** A schematic representation of α- and β-cyclodextrin complexes with ethylene oxide and propylene oxide diblock copolymers.[95]

only the PEO block, while the interaction with β-CD, only the PPO block. The stoichiometric compositions of the complexes are similar to those of MN based on homopolymers, *viz*., two monomeric units of ethylene oxide or propylene oxide per one α- or β-CD molecule, respectively. Thus the interactions of α- and β-CD with the PEO – PPO diblock copolymers result in the formation of new BC (Fig. 8) which consist of a rigid block, *viz*., a MN, and a free flexible poly(alkylene oxide).

A study of the interactions of cyclodextrins with PEO – PPO triblock copolymers III – V (see Table 2) revealed that the compositions of the crystalline complexes depend on the position of the interacting block and the reaction conditions.[96–98] If CD is threaded onto the inner block of the copolymer, the complex formed (**54**, Fig. 9) has a stoichiometric composition which is characteristic of cyclodextrin complexes with homopolymers and diblock copolymers. In those cases where CD is threaded onto the peripheral blocks, two types of block structures can be formed depending on the reaction conditions, *viz*., BC with a symmetrical position of MN (Fig. 9, complexes **55** and **56**) and non-symmetrical BC which are composed of three different blocks, one of them being MN (Fig. 9, complexes **57** and **58**). This depends on the concentration of the reagents in the solution. Thus in saturated solutions where the rate of complexation is comparable with the rate of crystallisation, it is the non-symmetrical complexes with one filled block that are formed. In dilute cyclodextrin solutions, *i.e*., under conditions where the rate of crystallisation is much lower than the rate of threading of CD onto the polymeric chains, both peripheral blocks of the complexes represent MN.

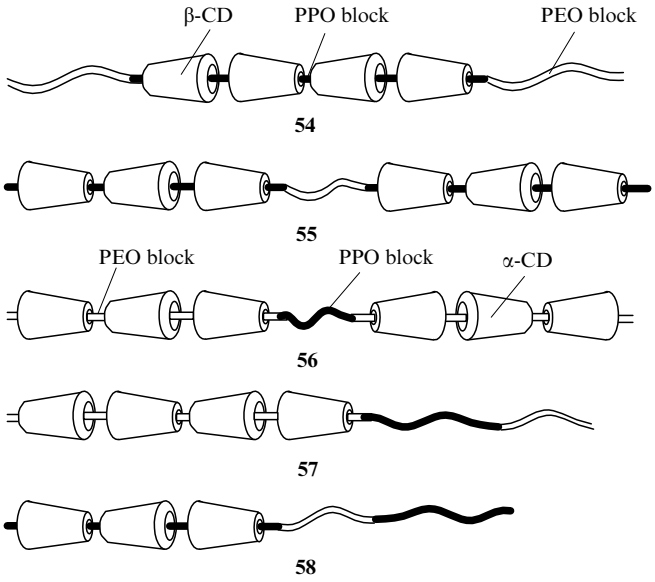



**Figure 9.** A schematic representation of α- and β-cyclodextrin complexes with ethylene oxide and propylene oxide triblock copolymers.

As has been noted above, two types of inclusion complexes of γ-cyclodextrin with poly(alkylene oxides) are possible. These comprise either one PPO chain or two PEO chains. The use of PEO–PPO block copolymers as 'guests' makes it possible to elucidate to which of these blocks γ-CD manifests higher affinity. To answer this question, the complexation of γ-CD with PEO–PPO diblock copolymers was studied where PEO and PPO blocks are sterically equally accessible for the interaction with cyclodextrin.[96–98] An analysis of the compositions of the complexes formed shed some light on the localisation of γ-cyclodextrins, since the number of γ-CD molecules that are threaded onto PEO and PPO blocks differs significantly for the given BC (I or II). It was shown experimentally that the number of γ-CD molecules per one copolymer molecule ($r_{exp}$) represents an intermediate value between the $r_{theor}$ values calculated in the assumption that either PEO or PPO blocks take part in the complexation. This finding suggests that the interaction of γ-CD with PEO and PPO is nonselective.

The use of the γ-cyclodextrin–triblock copolymer couple opens up an opportunity for preparing new non-linear BC. Complexation of γ-CD with pluronics of the PEO–PPO–PEO type which contain peripheral ethylene-oxide blocks affords double-stranded inclusion complexes. It was found[97] that in saturated solutions the composition of the complex formed remains unchanged at any value of the γ-CD : BC IV ratio. This suggests that the interaction of γ-CD with the above block copolymer results in a stoichiometric complex, namely, a double-stranded inclusion complex in which two strands of PEO which belong to different copolymer molecules appear to be incorporated into the channel formed by the macrocycles. Taking account of different accessibility of the PEO blocks with respect to α-CD, it was demonstrated that the interaction of γ-CD with a triblock copolymer of the PEO–PPO–PEO type yields compound **59** (Fig. 10) which is characterised by nonsymmetrical distribution of the free PEO blocks. In dilute solutions, the complexation of γ-CD with the PEO–PPO–PEO copolymer results in pseudopolyrotaxane **60** in which both PEO blocks are coated with the CD molecules (see Fig. 10). Thus, the vast potentials in the design of pluronics and the ability of cyclodextrins to interact selectively with PEO and PPO blocks enable one to use them as a basis for the synthesis of inclusion complexes of different compositions and molecular architecture.

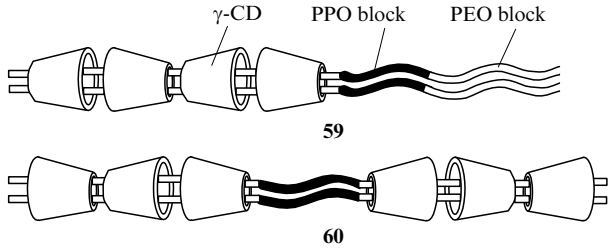
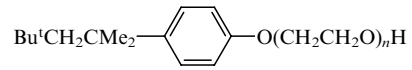



**Figure 10.** A schematic representation of γ-cyclodextrin complexes with the triblock copolymer IV.

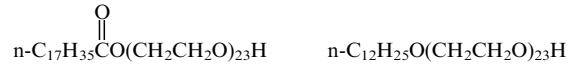
### c. The complexes of nonionic surfactants with cyclodextrins

Poly(ethylene oxide)-containing surfactants can be regarded as particular BC which comprise hydrophilic poly(ethylene oxide) blocks, whereas the hydrocarbon fragments play the role of their hydrophobic 'tails'. PEO surfactants of different chemical nature, *viz*., octylphenyl PEO ethers [Triton X-45 (**61a**) and Triton X-100 (**61b**)], polyethylene glycol-1000 monostearate (**62**) and dodecyl poly(ethylene oxide) ether (**63**) were used as 'guests'.[97, 99, 101, 102]




**61a**,**b**

$n$ = 5 (**a**), 10 (**b**)




**62** **63**

Mixing of saturated aqueous solutions of poly(alkylene oxides) and α-CD resulted in the formation of a crystalline precipitate the structure of which is similar to that of MN based on PEO. The determination of the compositions of the complexes showed that one CD molecule corresponds to two monomeric units; thus, the α-CD molecules are selectively threaded onto the PEO fragments of surfactants. Important information about the type of interaction of PEO surfactants with cyclodextrins in dilute solutions can be derived from an analysis of colloidal and chemical properties of the surfactants, primarily, from the effect of CD on the critical micelle concentration (CMC). The dependences of CMC on the CD : surfactant molar ratio represent curves with saturation, which allows one to determine the stoichiometric compositions of inclusion complexes in solution. It is worth noting that the compositions of such complexes are identical both in solution and in the solid phase. The complexes formed by the interaction of the same surfactant with α-, β- and γ-CD differ drastically both in the structures and their colloidal and chemical properties.[101, 102] The chemical nature of the group linking together the hydrophilic and hydrophobic fragments of surfactants was found to affect critically the localisation and possible migration of CD molecules along the surfactant chains.

The covalent binding of poly(ethylene oxide) fragments to cyclodextrin molecules results in the formation of PEO–CD conjugates which represent bouquet-like structures endowed with amphiphilic properties (Fig. 11).[103–105] The conjugates have molecular masses of 3000–5500 and are characterised by narrow molecular mass distributions; the average degree of substitution is 8 to 12 ethylene oxide units per one glucose residue. A study of the complexation of the conjugates with Triton X-100 (**61b**) revealed that the pseudopolyrotaxanes formed have a stoichiometric composition, *i.e*., one molecule of the conjugate is threaded onto each hydrophilic fragment of the surfactant. These pseudopolyrotaxanes can form micellar structures in aqueous solutions. The architecture of the spherical molecular assemblies consisting of highly branched structural elements resembles that of dendrimers (Fig. 12).

Branched structures of yet another type were obtained[99, 106] as a result of interactions of star-shaped conjugates of PEO and PEO–PPO diblock copolymers with proteins, *e.g*., α-chymotrypsin (ChT). Such conjugates are formed as a result of one-point covalent attachment of the monofunctional derivatives of the polymers to the amino groups of the protein. Mixing of these compounds with cyclodextrin (PEO–ChT–CD and

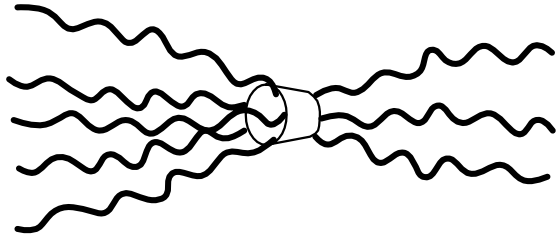


**Figure 11.** The structure of the poly(ethylene oxide)–cyclodextrin conjugate.[104]

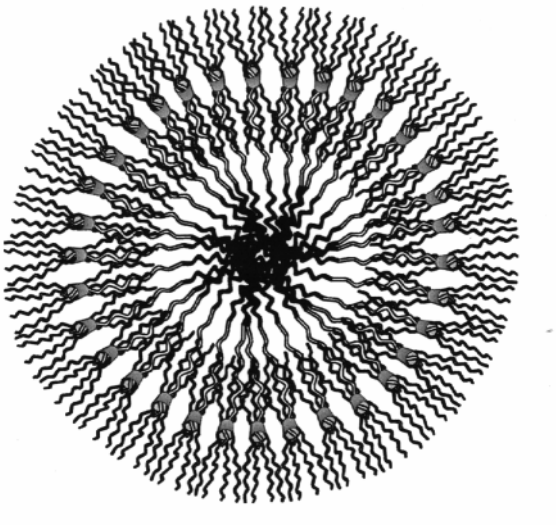


**Figure 12.** The hypothetical dendrimer-like structure based on the poly(ethylene oxide)–cyclodextrin conjugate and a micelle of Triton X-45.[105]

BC–ChT–CD conjugates) results in the formation of precipitates. The determination of their compositions revealed that they are similar to those of the complexes based on linear polymers and the corresponding CD. This implies that all the polymeric chains within the conjugates are accessible for the interaction with the CD. The crystalline structures of the resulting complexes are identical to those of MN. A decrease in the solubility of the complexes in water in comparison with the original polymer–protein conjugates or non-covalent polymer–protein adducts limits their application in biotechnology. The PEO–CD conjugates were used to confer solubility onto the complexes prepared on the basis of polymer–protein adducts and CD.[107, 108] The complexation between PEO chains, which are the components of covalent and non-covalent PEO–ChT and PEO–CD adducts, was studied using a kinetic method based on the analysis of enzymic properties of novel supramolecular structures incorporating these components.[107] For this purpose, the rate constants of thermoinactivation of ChT ($k$) in the adducts of PEO–ChT with PEO–β-CD were determined. A decrease in $k$ suggests that complexation of the constituents occurs. The stoichiometric compositions of the complexes formed were determined from the dependence of $k$ on the PEO–β-CD : $PEO_{(ad)}$ molar ratio, where $PEO_{(ad)}$ is the poly(ethylene oxide) that is involved in the adducts. It was shown that each of the polymeric chains of the PEO–ChT conjugates forms an inclusion complex with PEO–β-CD, whereas in the case of non-covalent PEO–ChT complexes only a half of the polymeric chains of $PEO_{(ad)}$ take part in the formation of the supramolecular structures. The hypothetical structures of supramolecular dendritic assemblies are depicted in Fig. 13.

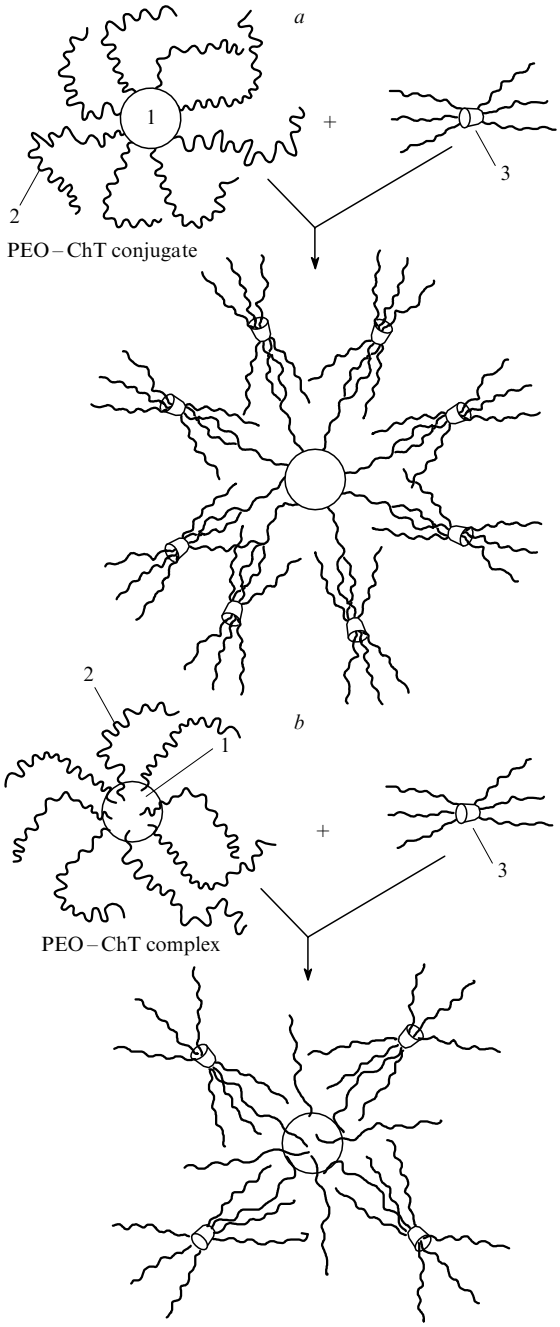



**Figure 13.** The hypothetical dendrimer-like structures of the complexes formed by the covalent (*a*) and non-covalent (*b*) adducts of PEO–ChT and the β-CD–PEO conjugate;
(*1*) α-chymotrypsin, (*2*) poly(ethylene oxide), (*3*) covalent adduct based on PEO and β-cyclodextrin (β-CD–PEO).[107]

**d. Studies of the structural organisation of crystalline pseudopolyrotaxanes based on cyclodextrins**

Supramolecular assemblies can be characterised both by the type of the intermolecular interactions which hold together their constituents and by their spatial configuration, *viz*., their architecture or 'suprastructure'. The phase state and the organisation of macromolecular inclusion complexes are studied using TGA, DSC, X-ray diffraction analysis as well as by optical, scanning electron and scanning tunnelling microscopy.

An X-ray diffraction analysis showed that the precipitates formed by poly(alkylene oxide)–cyclodextrin complexes have crystalline structures and differ from one another and from the original components in the type of the crystal lattice. It should be noted that the method which is commonly employed for the description of the structural organisation of 'molecular necklaces' is based on comparison of the diffractograms of MN and the complexes of the corresponding CD with various low-molecular-weight compounds. According to Saenger's classification,[34] the structures of the CD-based complexes can be divided into two main types, *viz*., cage-type structures in which cyclic molecules form brick network patterns and channel-type structures where the macrocycles are stacked sequentially in a pillar-like fashion. A comparative analysis of the diffractograms revealed [68, 71, 72] that MN belong to channel-like structures. However, this approach discloses only the qualitative differences but cannot provide quantitative evaluation of the parameters of the crystal lattices of macromolecular inclusion complexes.

Harada *et al*.[76, 77] have succeeded in growing single crystals of α-CD complexes with tetra- and hexa(ethylene oxide) and β-CD with poly(propylene oxide) (MM = 425), which mimic MN, and

the β-CD – poly(oxytrimethylene) complex (MM = 1400) and carried out their detailed X-ray diffraction analysis. It was found that in all these cases the macrocycles are arranged in a 'head-to-head' and 'tail-to-tail' fashion to form hydrogen bonds between all the secondary hydroxy groups of the large bases of the cyclodextrin torus. Water molecules are localised within the structure of α-CD-based [4]-Rt between the minor bases of the macrocycles. The β-CD dimers are shifted relative to one another due to the presence of only one hydrogen bond between the primary OH groups. Rod-like macromolecules are localised inside the narrow channels formed by cyclodextrins and exist in a *trans*-conformation.

The use of single crystals for the disclosure of the structural organisation of rotaxanes allows one to estimate, with a high degree of accuracy, the unit cell parameters, to determine the coordinates of all the atoms within the composition of the complex and to characterise the intermolecular contacts. However, this method has not received wide acceptance in structural studies of high-molecular-weight compounds because of the difficulty and sometimes impossibility of obtaining suitable large-sized single crystals. An approach to the description of the structural organisation of polymeric crystals consists in the use of oriented samples and in the recording and interpretation of X-ray fibre patterns. It was shown [86, 109] that in contrast to ordinary polymers whose orientation demands preliminary treatment, the formation of MN is accompanied by spontaneous formation of oriented structures. An X-ray diffraction analysis which includes a comparison of X-ray fibre patterns and diffractograms enables one to index the observed reflections, to determine the parameters of crystal lattices of the complexes formed and thus to characterise the structure of polymeric inclusion complexes at the molecular level. The results obtained suggest that crystallisation of MN results in the formation of structures in which cyclodextrin molecules are arranged one after another along a common symmetry axis. X-Ray diffraction data suggest the hexagonal, monoclinic and tetragonal packing of MN based on α-, β- and γ-cyclodextrins, respectively.

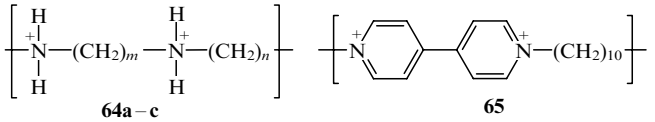
In order to obtain the information about the morphology of the crystallites formed by MN and the nature of their mutual packing in the course of precipitation, cyclodextrin complexes with poly(alkylene oxides) were studied by optical microscopy and scanning electron microscopy.[86, 109] The crystals of the β-CD – PPO complexes have the shape of sharply edged parallelograms, whereas those of the γ-CD – PEO complexes have the shape of rectangular parallelipipeds with an average facet size of the order of several microns, which is consistent with the results of an X-ray diffraction analysis of the symmetry of the crystal lattices of the complexes. The precipitates of cyclodextrin – poly(alkylene oxide) complexes represent lamellar structures the MN in which are located at right angles to the planes of the lamellae.

Isolated MN were visualised by scanning tunnelling microscopy. Japanese investigators [75, 87] have succeeded in photographing α-CD – PEO and β-CD – polyaniline complexes containing discernible rod-like structures. Their lengths correspond to the lengths of the extended molecule of the polymeric 'guest', while their widths match the diameter of the macrocycle.

These results are of fundamental importance for the understanding of the mechanism of the self-assembly of the supramolecular structures formed by polymeric inclusion complexes at different levels of their structural organisation. Three main stages in the formation of the nanostructures in such complexes can be distinguished. The first step consists in the threading of the macrocycles onto the polymeric chains. The driving forces of this process are the cooperation of the hydrophobic interactions between the nonpolar cavity of the cyclic molecule and the fragments of the polymeric 'guest' and the formation of hydrogen bonds between the hydroxy groups of the cyclodextrins. The second step is the crystallisation of MN and the formation of lamellar crystallites the inclusion complexes in which are located at right angles to the planes of the lamellae. In the third step, individual crystallites of the complex are aggregated to form an oriented precipitate. In the precipitation, the lamellae are aligned in parallel to the plane of the support to form an axial pattern of the precipitated material. Thus, polymeric cyclodextrin – poly(alkylene oxide) inclusion complexes can serve as a basis for the design of well-organised supramolecular assemblies.

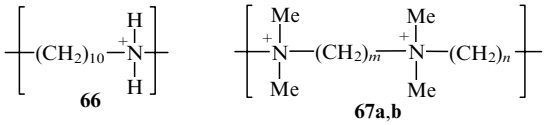
**e. Water-soluble polyrotaxanes**

Cyclodextrin-containing water-soluble pseudopolyrotaxanes were first synthesised by the interaction of CD with polyelectrolytes.[81–85] Self-assembly method was used to obtain inclusion complexes of the so-called poly(iminooligomethylenes) (**64a – c**),[81] *viz*., the polymers containing oligomethylene and quaternary ammonium fragments (**65**,[82] **66**,[83] **67a**,**b**[84, 85]), with α-cyclodextrin. In this case, the threading of CD molecules occurs by virtue of cooperation of hydrophobic and van der Waals interactions between the cyclodextrin cavity and the aliphatic sites of the polymers.



**64a – c** **65**

$m = n = 6$ (**a**); 11 (**b**); $m = 10$, $n = 3$ (**c**).

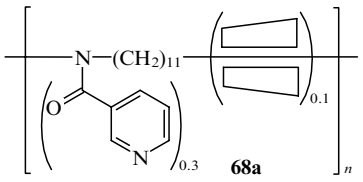


**66** **67a**,**b**

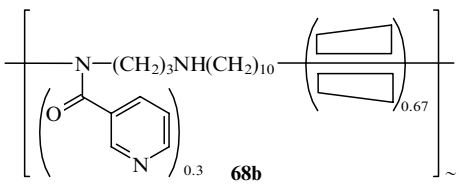
$m = n = 10$ (**a**); $m = 6$, $n = 10$ (**b**).

Using $^1$H NMR spectroscopy, it was shown that α-CD molecules are localised on oligomethylene fragments containing no less than 10 units. Therefore, the short-chain polymer **64a** does not form any complex with α-CD. In contrast with poorly soluble MN, soluble complexes are formed at a very low rate at room temperature, this takes from several hours to several months and even years (in the case of compound **66**). Such a kinetics is attributed to the low rate of migration of CD molecules along the polymeric chain which in turn is due to steric hindrances created by bulky hydrate shells around the charged amino groups. At higher temperatures, slipping of the macrocycles over these 'barriers' occurs (method 5, Section III) resulting in a significant increase in the threading rate.[85]

Polyrotaxanes **68a**,**b** which are also readily soluble in water were prepared on the basis of MN consisting of polymers **64b**,**c** and α-CD, respectively.[81]



**68a**



**68b**

The binding of α-CD molecules to definite sites of the polymeric chain was achieved by acylation of the imino groups by nicotinyl chloride. Using polymers **64c** and **66** as examples, it was demonstrated that β-CD which has a larger cavity does not form any stable inclusion complexes. However, the use of an α- and β-CD mixture made it possible to prepare polyrotaxanes containing 60% β-CD and 7.5% α-CD in which β-CD was

blocked at the ends by α-CD molecules which slip off the chain at a very low rate.[83]

The possibility of formation of a water-soluble pseudopolyrotaxane was also demonstrated for the β-CD – triblock copolymer PEO – PPO – PEO.[100] It was found that the interaction of β-CD with block copolymers of the $PEO_n - PPO_m - PEO_n$ type gives either a crystalline precipitate ($n \ll m$) or a water-soluble complex ($n \gg m$) depending on the composition of the polymer used. The addition of cyclodextrin induces an upfield shift of the methyl and methylene proton signals in the $^1H$ NMR spectra. This suggests the complexation with block copolymers incorporated into the cavity of CD.

Amphiphilic DM-β-CD as a macrocycle and an analogous PEO – PPO – PEO copolymer with blocks of approximately equal sizes ($n \approx m$) were used to study the interactions of cyclodextrin with polymers in a monolayer. This study showed [100, 110] that the polymer passes from the coil to the rod-like conformation during complexation. Hence, one of the approaches to the synthesis of water-soluble MN consists in the introduction, into the starting polymer, of hydrophilic fragments which are not involved in the complexation.

Yet another approach to confer water solubility onto polymeric complexes is based on chemical modification of CD molecules in polyrotaxanes. The synthesis of water-soluble biodegradable polyrotaxanes was carried out by Ooya *et al.*[111–114] These authors used bis[aminopoly(ethylene oxide)] as the polymer and α-cyclodextrin as the cyclic compound. The terminal groups were blocked by an excess of L-phenylalanine (L-Phe) derivatives. The polyrotaxane formed was treated with propylene oxide which alkylated the OH groups of CD. The enhanced solubility of MN in water seems to be due to the destruction of hydrogen bonds. A three-step synthesis including removal of protective groups from the fragment of the stopper is depicted in Scheme 10. The results of light scattering studies [112, 113] suggest that the polyrotaxanes based on hydroxypropylated α-CD and PEO (MM = 2000 for **69a** and 4000 for **69b**) aggregate in aqueous solutions; the degree of aggregation of polyrotaxanes is much lower than that of the original PEO containing the same terminal fragments and is equal to 16 – 23 and 2 for the complexes **69a**,**b**, respectively. It was noted also that these polyrotaxanes preserve their rod-like conformation in solutions. It was found [112, 113] that enzymic hydrolysis of peptide bonds with papain which resulted in the cleavage of the stoppers brought about simultaneous supramolecular destruction of polyrotaxanes **69a**,**b**. This leads to complete dissociation of these polyrotaxanes into constituents irrespective of the degree of their aggregation (Fig. 14).

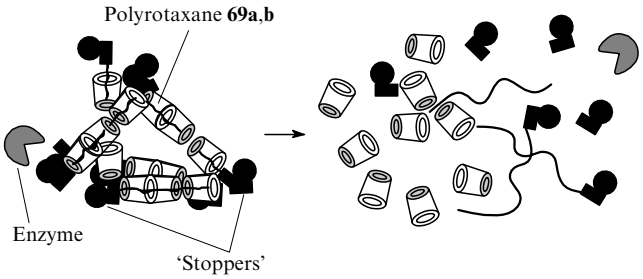
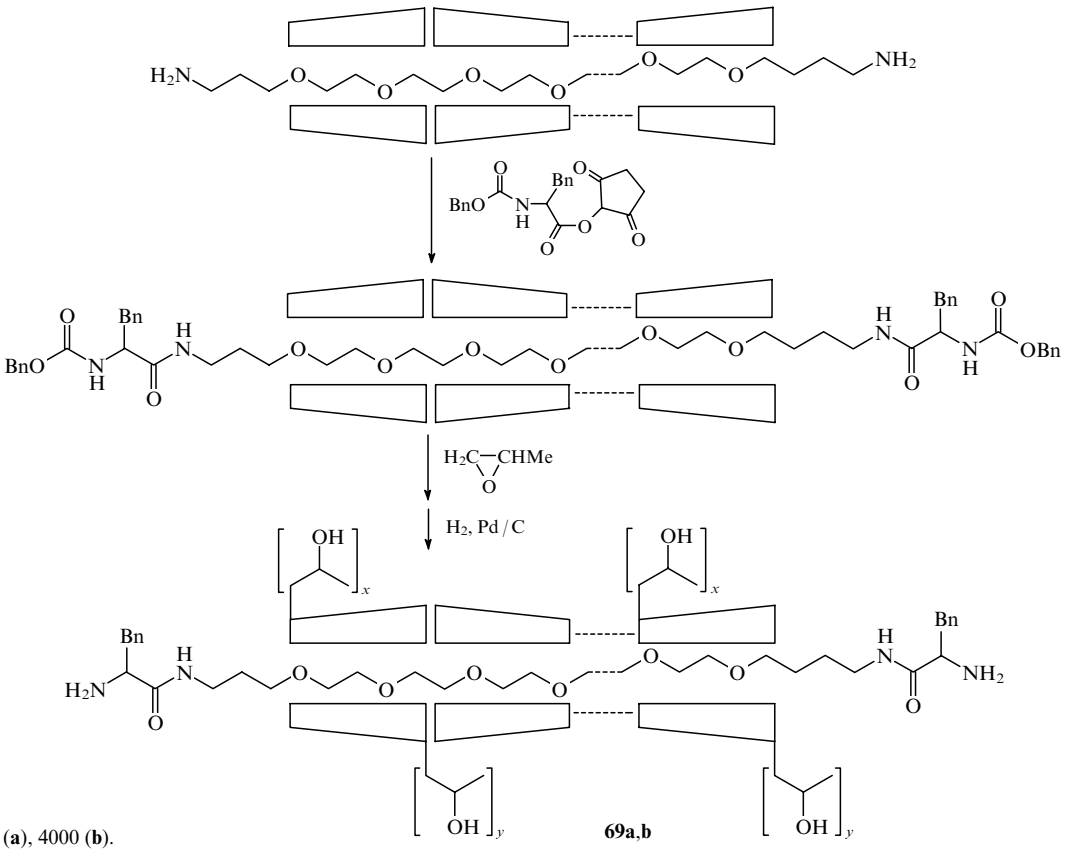



**Figure 14.** The destruction of the polyrotaxanes **69a**,**b** caused by enzymic hydrolysis of terminal L-Phe groups.[113]

It was shown [116, 117] that polyrotaxanes of the type **69a**,**b** can be used in pharmacology and medicine as drug carriers and drug permeation enhancers. The interaction of these polyrotaxanes with blood cells was studied in detail; it was found that hydroxypropylated polyrotaxanes increase the fluidity of membranes and control the level of calcium by inhibiting platelet-induced elevation of $Ca^{2+}$.

The same group of investigators proposed to use this principle in the design of drug conjugates on the basis of polyrotaxanes and were the first to attempt to prepare such conjugates with insulin [112] and theophylline [115] which are covalently linked to CD molecules (Fig. 15).

Scheme 10




MM = 2000 (**a**), 4000 (**b**).

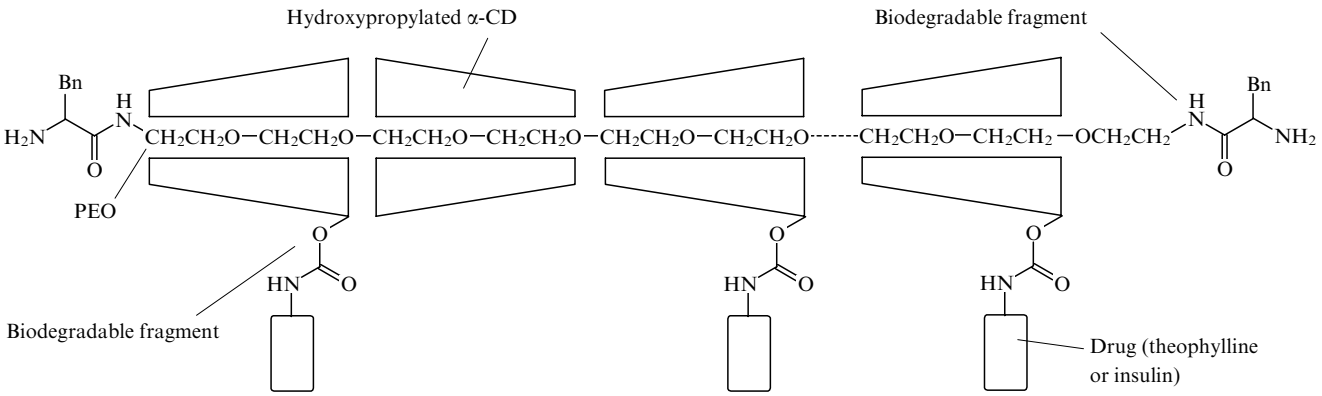



**Figure 15.** The drug–polyrotaxane complex prepared on the basis of poly(ethylene oxide) blocked by L-phenylalanine and hydroxypropylated α-cyclodextrin.

## 3. Comb-like polyrotaxanes

Non-covalent interactions of cyclodextrins with lateral fragments of comb-like polymers is yet another interesting example of molecular recognition. The determination of rate constants for the complexation of cyclodextrin with a series of copolymers of acrylamide with alkyl methacrylates (Table 3)[118] demonstrated the possibility of selective interaction of CD with comb-like polymers resulting in the formation of pseudopolyrotaxanes. In order to design true polyrotaxanes, Ritter *et al.*[119,120] proposed to use the strategy of covalent attachment of preformed pseudorotaxane **70** which is blocked at one end to the activated side fragments of the polymer (Scheme 11).

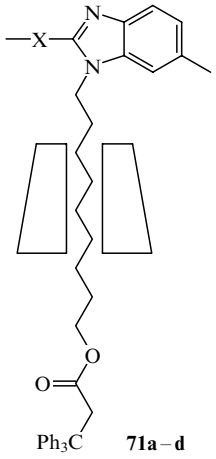
**Table 3**. The constants of complexation ($K$) of cyclodextrins and aliphatic fragments of water-soluble copolymers of acrylamide with alkyl methacrylates.[118]

| Alkyl in alkyl methacrylate | $K$ /litre mol$^{-1}$ | | |
|---|---|---|---|
| | α-CD | β-CD | γ-CD |
| $Bu^n$ | 55 | – | – |
| $Bu^t$ | – | 340 | 57 |
| $Bu^i$ | 36 | – | – |
| n-$C_6H_{13}$ | 290 | 110 | – |
| iso-$C_8H_{17}$ | 303 | 294 | 51 |
| n-$C_{12}H_{25}$ | 990 | 660 | 245 |

A series of polyrotaxanes incorporating DM-β-CD have been synthesised.[119–123] It was found that these polyrotaxanes are less viscous than the starting polymers, apparently due to destruction of the hydrogen bonds between the fragments in the rod macromolecule.

The same group of investigators made an attempt to synthesise comb-like polyrotaxanes by radical polymerisation in aqueous solutions of the corresponding pseudorotaxanes based on β-CD, DM-β-CD and *N*-methacryloyl-11-aminodecanoic acid (method 2). However, this attempt was unsuccessful, since polymerisation was accompanied by elimination of the macrocycle from the side fragments of the polymer being formed.[124]

Alkylation of NH groups of poly(benzoimidazoles) with $Br(CH_2)_{12}OC(O)CH_2CPh_3$ in the presence of TM-β-CD resulted in comb-like polyrotaxane **71a–d**.[125]



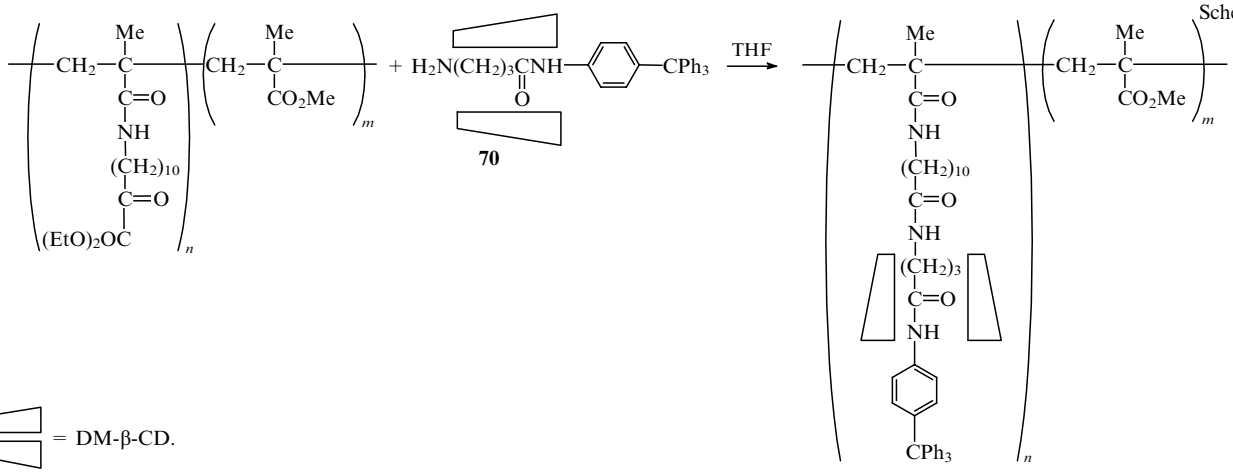

**71a–d**

X = *p*-$C_6H_4$ (**a**),
$(CH_2)_8$ (**b**),
$(CH_2)_{11}O(CH_2)_{11}$ (**c**),
$(CH_2)_{11}$ (**d**);

= TM-β-CD.

It was found that the degree of *N*-alkylation and the amount of the macrocycles incorporated depend on the lengths of the 'spacers' between the benzoimidazole fragments.

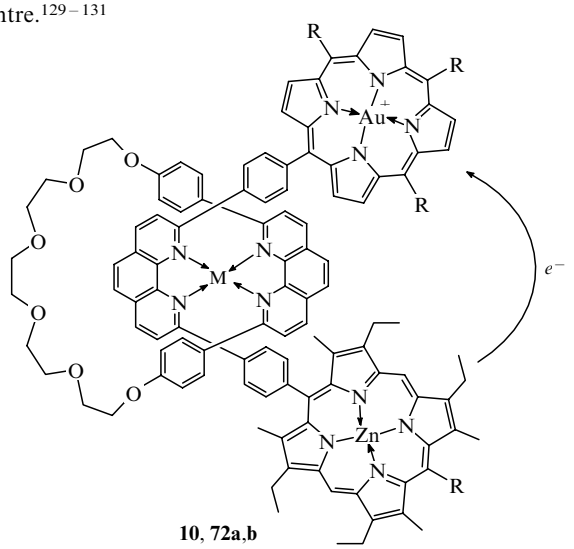
Scheme 11



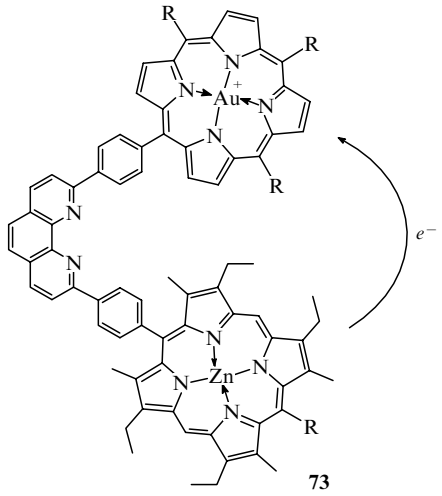
## IV. Supramolecular devices based on rotaxanes and polyrotaxanes

Characteristic physicochemical properties of rotaxane-like structures are determined by both the unusual topology and the nature of their constituents. In the recent years, rotaxanes as molecular assemblies are considered as promising candidates for the construction of supramolecular devices which represent functional, structurally organised systems.[126–128] The feasibility of using rotaxanes in this area is due primarily to the ease of control over molecular directionality which determines the specific spatial configuration of their constituents. The introduction of photo-, electro- or ion-active groups into rotaxane molecules will allow the transfer of energy, electrons or ions as well as the transmission of signals and the storage of information.[12, 126–128]

Rotaxanes [2]-Rt which incorporate two different porphyrins as stoppers can serve as examples. The photophysical properties of [2]-Rt **10** and **72a**,**b** were studied [12, 129–131] and the rates of a photoinduced intramolecular electron transfer from the excited Zn-porphyrin to Au-porphyrin (1, 22 and 34 ps for complexes **10**, **72a** and **72b**, respectively) were compared to that in the dumbbell-shaped bisporphyrin **73** (55 ps). It was found that in the case of rotaxanes, the rate of the electron transfer increases significantly, the maximum increase being observed for complex **10**. This finding was attributed to the presence of copper(I) ions which play the role of mediators and to changes in the energy of the orbitals in the supermolecule under effect of the coordination centre.[129–131]



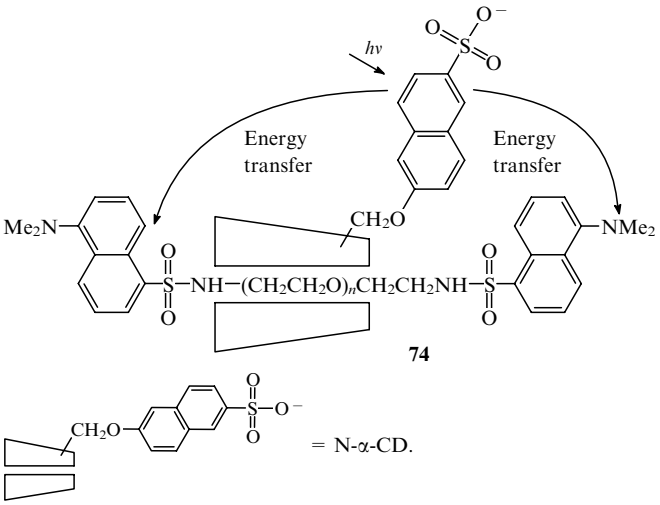

**10**, **72a**,**b**




**73**

M = $Cu^+$ (**10**), $Zn^{2+}$ (**72a**), none (**72b**); R = 1,3-$Bu^t_2C_6H_3$.

The photosensitive rotaxane **74** was prepared on the basis of the naphthalene derivative of α-cyclodextrin (N-α-CD) and poly(ethylene oxide) with dansyl groups as stoppers.[132]




The fluorescence spectra of rotaxane **74** displayed a significant decrease in the intensity of signals elicited by the naphthalene fragments in comparison with the original N-α-CD which is due to the transfer of energy from the excited naphthalene groups of modified CD to the terminal dansyl groups of the rod molecule of PEO. The results of these studies are of interest for the construction of photochemical supramolecular devices which are able to effect directed transfer of electrons and energy.

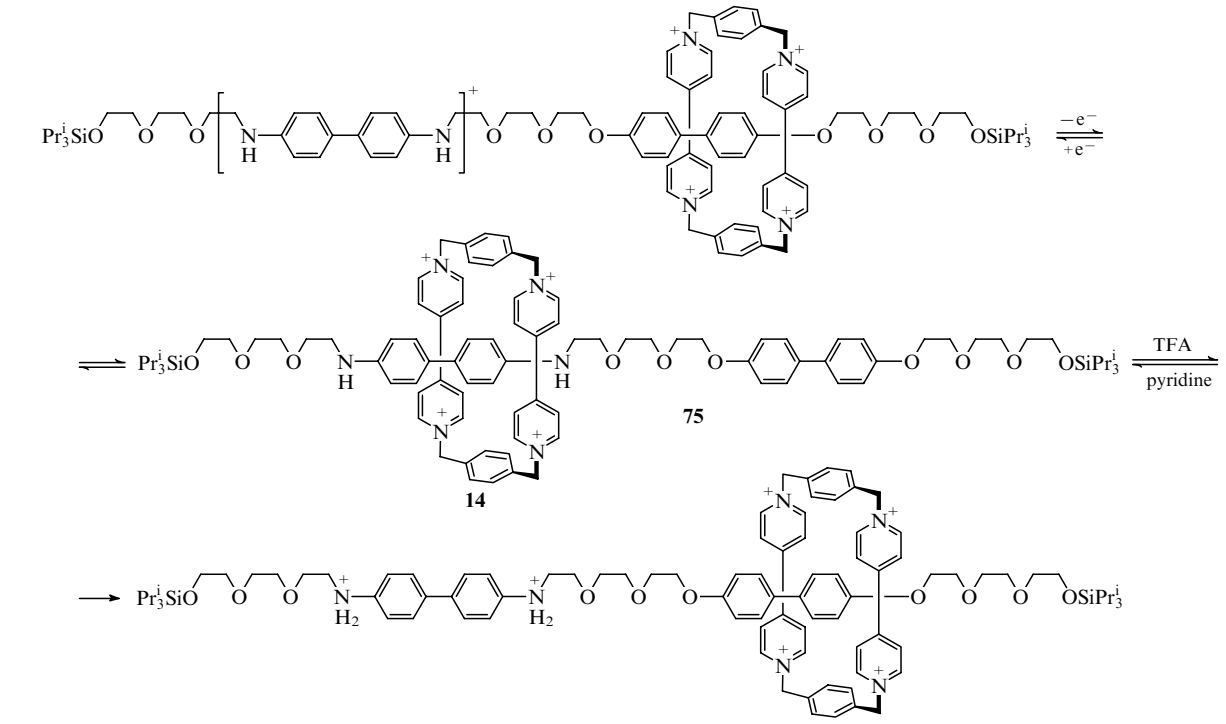
Yet another promising line of investigations is the preparation of controlled 'molecular switches' (or 'shuttles' according to Stoddart). Molecular switch-on/off processes represent reversible transitions of one of the components between the two positions which differ either in structure or in conformation. The recently synthesised [2]-Rt **75** (Scheme 12) can serve as an example of an electrochemical (or chemical) 'molecular shuttle'.[127, 133] In this case, the migration of the macrocycle **14** occurs as a result of a redox reaction or protonation–deprotonation.

The synthesis of a photoreactive molecular switch prepared on the basis of CD-containing [2]-Rt **76** has been carried out (Fig. 16).[134] Here, azobenzene was used as a rod molecule, while 2,4-dinitrophenyl groups were used as stoppers. Irradiation of an aqueous solution of the complex **76** with UV light ($\lambda$ = 360 nm) induced *trans*–*cis*-isomerisation of the azobenzene fragment. This reaction is reversible which was confirmed by the reverse reaction occurring upon irradiation of the solution in the visible region of the spectrum ($\lambda$ = 430 nm). These changes in the configuration of the rod molecule induce the migration of the cyclodextrin molecule from one binding centre to another. A pH-sensitive 'molecular shuttle' was synthesised by self-organisation of aliphatic diamines and a triamine ligand.[135, 136]

Studies with polyrotaxanes based on β-CD and the PEO–PPO–PEO triblock copolymer showed that these polymers also manifest the properties of 'molecular switches'.[137, 138] The transition of polyrotaxanes from the insoluble into the soluble state can occur either upon a rise in the temperature or upon an increase in a pH above 12 due to the destruction of the hydrogen bonds between the CD molecules. As a result, the macrocycles migrate along the rod macromolecule. $^1$H NMR studies of polyrotaxane solutions in 0.1 M NaOH showed that at room temperature CD molecules are distributed statistically along the whole polymeric chain, whereas upon heating the macrocycles are predominantly localised on PPO fragments (Fig. 17). Apparently, by changing such parameters as temperature and permittivity of the medium, one can govern the solubility of polyrotaxanes and the distribution of the CD molecules.

The design of photonic, electroninc and ionic switching devices based on molecular components and their incorporation

Scheme 12



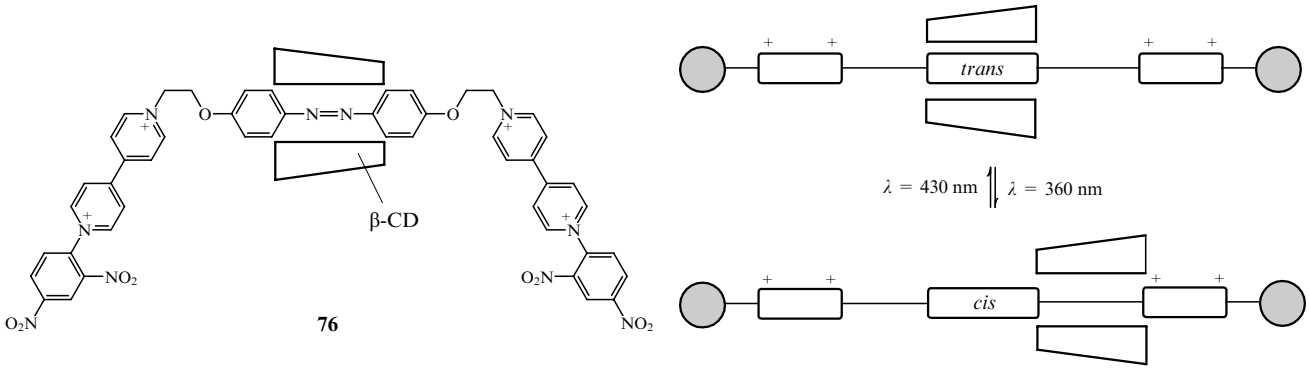




**Figure 16.** A photosensitive 'molecular switch' based on β-cyclodextrin.

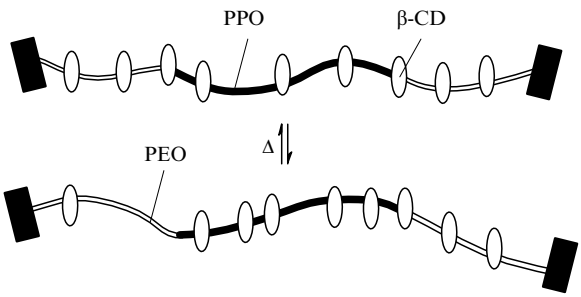



**Figure 17.** A mechanical 'molecular switch' based on polyrotaxane.

into well-organised assemblies is the next step in the development of functional materials on a nanoscale. Further studies in this field will inevitably culminate in the construction on their basis of multifunctional chemical 'machines' as the basis for the development of chemical informatics and an analysis of functioning of these devices in close conjunction with related biological processes.[126]

* * *

Thus, we are witnessing a revival of interest in rotaxane-like structures. New papers are being published and these are devoted to a search for their practical application. The literature data concerning polyrotaxanes consider them as a new type of regulatory polyfunctional rigid-chain polymers. It is these properties that determine the area of their further applications. New opportunities are emerging for the construction of complex polymeric structures which combine the blocks of 'molecular necklaces' with the flexible blocks of free polymers. Therefore, the fundamental problems related to the development of methods of synthesis of new supramolecular assemblies and investigation into their structural organisation and properties still remain in the focus of attention.

This review has been written with the financial support of the Russian Foundation for Basic Research (Project No. 00-03-32770).

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