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Supramolecular chemistry of cucurbiturils

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Abstract. The main principles of the design of supramolecular compounds starting from organic macrocyclic cavitands, *viz*., cucurbit[*n*]urils $[C_6H_6N_4O_2]_n$ ($n = 5-10$), are considered. The presence of the hydrophobic inner cavity along with polar carbonyl groups forming the cucurbituril portals are responsible for high specificity of the formation of host – guest complexes. The unique ability of cucurbiturils to act as synthetic molecular containers is discussed. In these containers, bimolecular reactions between specially selected guests proceed with high regio- and stereoselectivity. The review surveys new data on the directed construction of supramolecular organic – inorganic compounds through the formation of an extensive network of hydrogen bonds between the portal oxygen atoms of cucurbiturils and water molecules of metal aqua complexes. The bibliography includes 108 references.

I. Introduction

Supramolecular chemistry is a new extensively evolving area of research focused on the association of individual molecules giving rise to more complex chemical systems formed through intermolecular (non-covalent) interactions.[1–3] Supramolecular chemistry concerns various phenomena in different fields of science (organic, coordination and physical chemistry, biology, physics) and has a broad spectrum of possibilities due to the mutual enrichment of these areas of scientific exploration. Supramolecular chemistry deals with supramolecular ensembles, which are spontaneously self-assembled from complementary (*i.e*., characterised by geometric and chemical compatibility) fragments in much the same fashion as spontaneous self-assembly of very complicated spatial structures in leaving cells. The directed construction of such systems and the design of highly ordered supramolecular compounds with desired structures and properties from molecular building blocks are fundamental problems of modern chemistry.

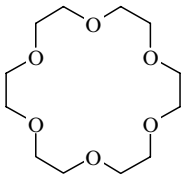
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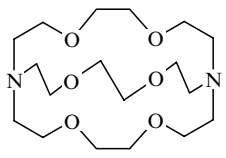
Intermolecular interactions holding the fragments together, *viz*., Coulombic interactions, hydrogen bonds and van der Waals interactions, are, on the whole, much weaker than the covalent bonds in the molecule itself. To increase the strength of these bonds, their directionality and specificity, it is necessary to use rather large molecular building blocks capable of creating an extensive network of bonds due to a large contact interface.

Examples of compounds with a large number of bonded non-covalent interactions are host – guest complexes in which the inner cavity of the host molecule (or cavitand)[4] can include a guest molecule of suitable size. Numerous complexes containing such macrocyclic organic molecules as crown ethers (**1**), cryptands (**2**), calixarenes (**3**) or cyclodextrins (**4**) as the host are presently available.

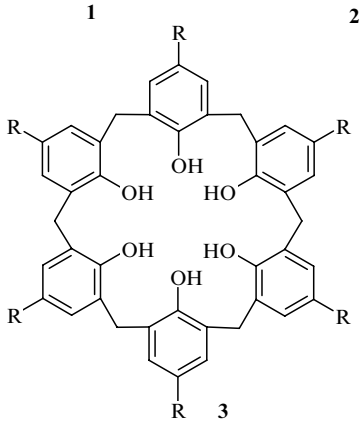
The encapsulation of inert gases, metal ions or organic molecules in the cavities of these molecules gives rise to stable compounds having unusual structures and exhibiting interesting properties. The present review surveys the synthesis and structures of supramolecular compounds prepared with the use of macrocyclic cavitands having the trivial name cucurbiturils.



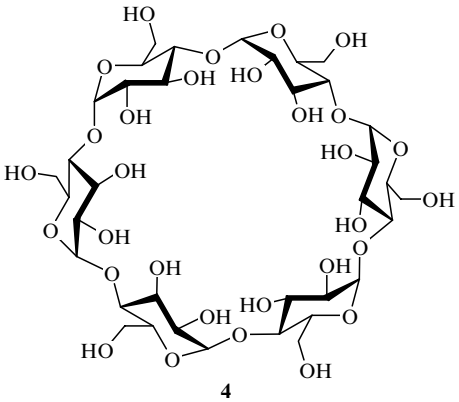
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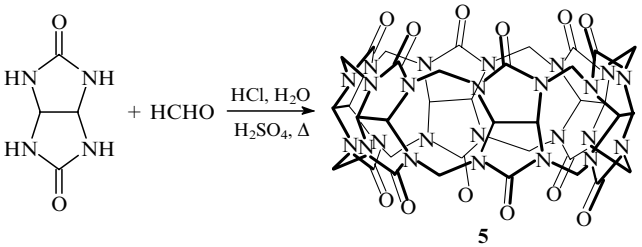


3



4

Cucurbituril with composition $C_{36}H_{36}N_{24}O_{12}$ [cucurbit[6]uril (**5**)] consisting of six methylene-linked glycoluril fragments has been studied the most. This compound is the first example of cucurbiturils. It was prepared by Behrend *et al.*[5] in 1905 by condensation of formaldehyde with glycoluril (condensation product of urea and glyoxal) in acidic medium. At that time, however, the procedures available did not allow one to determine correctly its composition and structure.



5

In 1981, Freeman, Mock and Shih[6] reproduced the synthesis developed by Behrend and obtained a colourless crystalline compound whose structure was established by X-ray diffraction analysis. Cucurbituril **5** is a barrel-shaped macrocyclic cavitand containing carbonyl oxygen atoms (portals) at the top and bottom of the barrel. This cavitand received its trivial name for the visual similarity of its molecular shape to *Cucurbitaceae* (pumpkin family). According to the nomenclature of Chemical Abstracts, the systematic name of this compound is dodecahydro-1*H*,4*H*,14*H*,17*H*-2,16 : 3,15-dimethano-5*H*, 6*H*, 7*H*,8*H*,9*H*,10*H*,-11*H*,12*H*,13*H*,18*H*,19*H*,20*H*,21*H*,22*H*,23*H*,24*H*,25*H*,26*H*-2,3,-4*a*,5*a*,6*a*,7*a*,8*a*,9*a*,10*a*,11*a*,12*a*,13*a*,15,16,17*a*,18*a*,19*a*, 20*a*, 21*a*,-22*a*,23*a*,24*a*,25*a*,26*a*-tetraoxaazabispentaleno [1‴,6‴ : 5″,6″,7″]-cycloocta(1,2,3-*cd* : 5,6,7-*c*′*d*′)dipentaleno-1,4,6,8,10,12,14,17,-19,21,23,25-dodecane. Hereinafter, cucurbiturils consisting of *n* glycoluril fragments will be abbreviated to Q*n* or referred to as cucurbit[*n*]uril.

The dimensions of the inner cavity of cucurbit[6]uril (**5**) (the height is 6 Å and the inner diameter is 5.5 Å) allow the molecule to accommodate small guest organic molecules or ions and the portals formed by the carbonyl groups (the diameters of the portals are 4 Å) can bind cations. The structure determination of Q6 gave impetus to investigations of its ability to act as a macrocyclic cavitand. Cucurbit[6]uril (**5**) whose cavity is similar in size to those of α-cyclodextrin and 18-crown-6 has higher negative charges on the donor oxygen atoms resulting in the enhancement of stability of its adducts with positively charged ions.[7,8] Yet another difference between cucurbituril Q6 and other cavitands is its structural rigidity. Thus, this cucurbituril virtually retains its shape upon the inclusion of different guests and, consequently, exhibits higher selectivity in the formation of inclusion compounds.[7]

Cucurbit[6]uril (**5**) is a colourless crystalline compound, which is insoluble in water and organic solvents but is readily soluble in some mineral acids (HCl, H_2SO_4, CF_3SO_3H), carboxylic acids (for example, HCOOH) and aqueous solutions of alkali salts. Cucurbit[6]uril serves as a convenient starting compound for the preparation of various supramolecular compounds due to its unique structure, the simplicity of the synthesis procedure and thermal stability (it does not decompose upon heating to 400 °C; see Ref. 9). Presently, cucurbit[6]uril is a readily available reagent (in particular, it can be purchased from Merck).

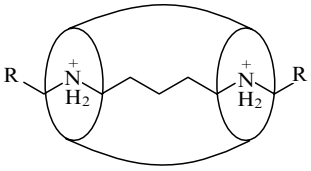
The results of studies devoted to the synthesis, examination of structures and properties of supramolecular compounds of cucurbiturils and investigations of thermodynamic and kinetic aspects of formation of these systems are summarised in reviews.[7,10–13] The present review surveys the recent advances in the chemistry of cucurbiturils achieved, primarily, in the latter half of the 1990s. Considerable attention is given to the studies aimed at the directed construction of supramolecular organic–inorganic hybrid materials, which have been performed in the last five years.

II. Host–guest cucurbit[6]uril compounds

The presence of the rather rigid inner cavity is responsible for the ability of cucurbit[6]uril (**5**) to accommodate small guest molecules. The formation of inclusion compounds was established by crystallographic methods as well as by different physicochemical methods because absorption, fluorescence and NMR spectra of guests are changed as the guest molecules go from the solvent environment (generally, from weakly acidic aqueous solutions) to the non-polar cavity of cucurbituril. Cucurbit[6]uril (**5**) forms stable inclusion compounds with amines, diamines, alkylammonium ions, benzylammonium ions and dye molecules.

1. Inclusion compounds with alkylammonium ions

Inclusion compounds of cucurbit[6]uril (**5**) with alkylammonium ions have received the most study. The hydrocarbon radical of the alkylammonium cation is encapsulated in the cavity of Q6 displacing the solvent molecules and is held in this cavity through van der Waals forces, whereas the nitrogen atom is fixed at the portal through Coulombic interactions of the cation with the oxygen atoms of the carbonyl groups. As a result, high specificity of binding of alkylammonium ions to cucurbit[6]uril is achieved.



X-Ray diffraction analysis of the supramolecular compound of Q6 with *p*-xylylenediammonium chloride carried out by Freeman[14] in 1984 showed that the hydrocarbon fragment of the diammonium cation $H_3N^+CH_2C_6H_4CH_2N^+H_3$ is located in the cavity, whereas two protonated nitrogen atoms are located at the portals of the macrocycle. The formation of host–guest compounds with composition 1 : 1 was also evidenced by X-ray diffraction data and solution NMR spectroscopic studies of supramolecular compounds of cucurbit[6]uril with alkyldiamines containing four, five or six methylene units between the nitrogen atoms.[14–16]

The incorporation of alkylammonium cations into cucurbit-[6]uril was examined by solution NMR spectroscopy in the 1980–1990s.[15–20] It was found that the most stable inclusion compounds with cations of primary amines $H(CH_2)_nNH_3^+$ and diamines $H_3N^+(CH_2)_nNH_3^+$ are formed at $n = 4$ and $n = 5$, 6, respectively. An increase in the length of the hydrocarbon chain either hinders coordination of both amino groups of the alkyldiamine to the portals of cucurbit[6]uril or causes the hydrophobic alkyl fragment of the amine to interact with the second hydrophilic portals. A decrease in the length of the hydrocarbon chain leads to a decrease in the number of van der Waals contacts as a result of which two ammonium groups cannot be simultaneously

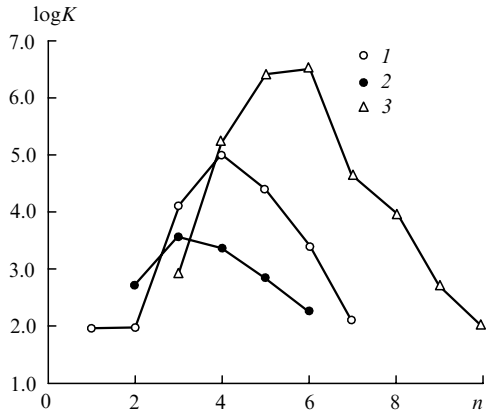
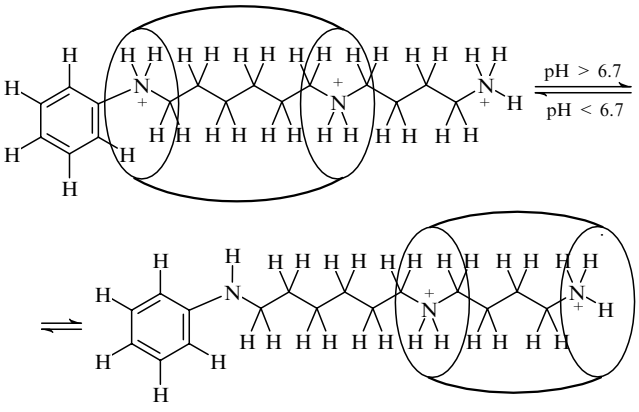


Figure 1. Logarithm of the formation constant (K) of inclusion compounds of cucurbit[6]uril with amines *vs.* the number of CH_2 groups in the chain; (*1*) alkylamines, (*2*) alkydiamines, (*3*) amino alcohols.

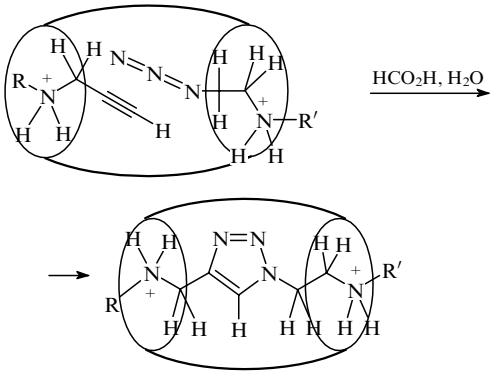
located at the portals. The plots of the formation constants of inclusion compounds with composition 1 : 1 *versus* the chain length for alkylamines,[17] alkyldiamines [17] and amino alcohols [18] are shown in Fig. 1. In the case of amino acids, no influence of the number of methylene groups on the stability constants was observed.[18]

The $PhNH(CH_2)_6NH(CH_2)_4NH_2$ ligand containing three amino groups was specially synthesised and its binding with cucurbit[6]uril (**5**) was studied.[19] An important characteristic feature of this guest molecule is the presence of two nitrogen atoms involved in the diaminoalkyl fragment. Their basicity is 10^6 times as high as that of the nitrogen atom bound to the phenyl group. In addition, the formation constant of the supramolecular compound of the hexanediammonium cation with cucurbit[6]uril is approximately 100 times larger than that for the butanediammonium ion, *i.e.*, different fragments of the triamine behave differently in binding to Q6. In aqueous solutions, the constant pK_a of the nitrogen atom of the aniline fragment in this triamine is 4.7 and it is increased to 6.7 in the presence of stoichiometric amounts of Q6. The behaviour of each region of the triamine depends on pH. In acidic solutions, the hexanediammonium fragment (more complementary to the cavity in size) is located inside the cavitand. By contrast, the butanediammonium end of the triamine is bound to Q6 at pH > 6.7 because the nitrogen atom of the aniline fragment is deprotonated. This system is a molecular 'switch', *i.e.*, Q6 can be moved along the triamine molecule by changing the pH.



NMR spectroscopic studies demonstrated that the rate of formation of adducts with cucurbit[6]uril (**5**) depends on the diameter of the ammonium molecules and it is independent of thermodynamic stability of the resulting complexes.[20] Linear hydrocarbon chains with a diameter that is no larger than the diameter of the portals of Q6, readily penetrate into the cavity, whereas the inclusion of cyclic or branched hydrocarbons is, apparently, accompanied by deviation of the oxygen atoms at the portals from their normal positions. Studies devoted to investigations of the thermodynamic and kinetic aspects of the inclusion of bulky ligands [21–23] demonstrated that the formation of host–guest supramolecular compounds depends, in particular, on the acidity of the medium. The formation of compounds with cucurbit[6]uril is the first example of the pH-controlled kinetics of encapsulation of organic guests into the host cavity. The inclusion of a protonated guest into the cavity of the cavitand is slow due to formation of an intermediate upon interaction of the guest with the polar oxygen atoms at the portals, whereas an unprotonated molecule is encapsulated directly in the cavity and the rate constant of this reaction is 20 times larger.[23]

High specificity of binding of Q6 with ammonium ions made it possible to perform unique azide–alkyne cyclisation in which both starting components, *viz.*, propargylamine and azidoethylamine, are included in the cavity of cucurbit[6]uril and cyclisation proceeds within the cavitand.[24, 25]



Under standard conditions, azide–alkyne cyclisation proceeds in solutions rather slowly ($k_0 \sim 10^{-6}$ mol^{-1} s^{-1}) to give two isomeric products in equal amounts. Due to interactions of the ammonium groups of the starting reagents with the opposite portals of Q6, only a certain arrangement of the components in the cavity is possible resulting in regiospecificity of this reaction (only the 1,4-addition product is generated). Besides, the reaction is substantially accelerated in the presence of catalytic amounts of cucurbit[6]uril ($k_0 \sim 10^{-2}$ mol^{-1} s^{-1}).

2. Inclusion of dye and other guest molecules

Examples of inclusion of other guest molecules into the cavity of cucurbit[6]uril (**5**) are few in number. The sizes of the cavity allow tetrahydrothiophene, tetrahydrofuran, benzene, cyclopentanone and furan to be accommodated, which was proved by shifts of the signals in the solution NMR spectra of these compounds.[17, 26] The *para*-substituted benzene ring can also be included into the cavity of cucurbit[6]uril (if the substituents are directed toward the portals). However, the size of this ring is somewhat larger than the size of the cavity resulting in distortions of both the guest and host molecules. Calorimetric titration showed that the stability of inclusion compounds of Q6 with aliphatic alcohols as well as with acids and nitriles is unaffected by the presence of polar groups and the number of methylene units in the guest molecule.[27]

Various dye molecules form stable inclusion compounds with cucurbit[6]uril.[7, 28–30] Most of the dyes are hydrophobic and their molecules (or molecular fragments of suitable size) can interact rather strongly with the inner cavity of the cavitand. In some cases, the encapsulation in cucurbit[6]uril leads to substantial stabilisation of dye molecules. For example, Phenol Blue ($^-OC_6H_4NC_6H_4NMe_2$) decomposes in a 0.1 M HCl solution during 3 min. If this dye is incorporated into cyclodextrin, it decomposes under the same conditions during 7 min. If this dye is

encapsulated in Q6, it is stable for 7 h.[28] Higher stabilities of inclusion compounds of dye molecules with cucurbit[6]uril in dilute solutions of formic acid as compared to inclusion compounds with c β-cyclodextrin were also confirmed by spectrophotometric measurements.[29] The formation of inclusion compounds of cucurbit[6]uril with dyes is used for example, in textile industry for efficient absorption of dissolved, dispersed or emulsified dyes from industrial wastes.[7, 30]

Cucurbit[6]uril can bind surfactants and polyethylene glycols,[31] fluorescent compounds,[32] and volatile organic compounds from the gas phase.[33] The ^{129}Xe and ^{1}H NMR spectroscopic data provided evidence for the reversible inclusion of xenone into Q6 and the formation of a 1 : 1 complex in an aqueous solution.[34, 35] In spite of the absence of Coulombic or hydrophobic interactions, the stability of this compound is comparable with the stabilities of Q6 complexes with alkylammonium ions.

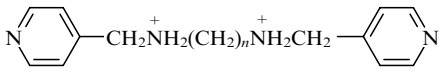
3. Synthesis and structures of nanosized rotaxanes

The ability of cucurbit[6]uril (**5**) to form host–guest compounds with alkyldiammonium salts provided the basis for the directed construction of nanosized rotaxanes (coordination polymers), which are not only of interest from the viewpoint of structural chemistry but also possess a series of unique properties due to which they show promise as materials, for example, for molecular electronics.[12, 13] Rotaxanes are supramolecular compounds in which cyclic molecules (beads) are threaded onto linear molecules containing bulky terminal groups, which keep the beads from sliding off.[36] Analogous structures devoid of bulky terminal groups are called pseudorotaxanes. Such macrocycles as cryptands, crown ethers, cyclodextrins and calixarenes are rather widely used in the synthesis of rotaxanes.[37] Compounds containing the Q6 molecule as a bead were first prepared and structurally characterised by K Kim and co-workers.[38] Two protonated nitrogen atoms of the $RN^+H_2(CH_2)_4N^+H_2R$ molecule [R = $(CH_2)_3NHC_6H_3(NO_2)_2$-2,4] are fixed at both portals of cucurbit[6]uril thus holding a chain of four polymethylene groups in its cavity, whereas two bulky 2,4-dinitrophenyl groups are located at the ends of the molecule. In addition, a pseudorotaxane compound was prepared in the cited study by the replacement of the 2,4-dinitrophenyl groups with the carbamate groups. In this case, Q6 does not move along the chain due to rather strong interactions between the protonated nitrogen atoms and the carbonyl groups at the portals of cucurbit[6]uril. In crystals, these pseudorotaxanes are linked in chains through hydrogen bonds between the carbamate groups of the adjacent fragments to form one-dimensional polymers.

The formation of pseudorotaxanes in solutions containing diammonium ions and cucurbit[6]uril has been proved by different methods, *viz*., by IR and NMR spectroscopy and mass spectrometry.[39–44] It has been demonstrated that pseudorotaxanes can act as molecular switches, *i.e*., an increase in pH of solutions, as in the case of diamines, leads to deprotonation of the ammonium nitrogen atoms responsible for binding with Q6 and causes the movement of the macrocycle along the chain. In some cases, however, not only an increase in acidity of the medium but also heating are required for the reverse reaction to occur.[43] The use of fluorenyltriamine as the guest molecule made it possible to prepare a unique highly sensitive molecular switch in which the reversible movement of Q6 along the chain is accompanied by changes in the colour of the solution and fluorescence intensity.[44] At pH 1.0, a yellow fluorescent solution of the Q6 complex with the hexanediamine fragment of fluorenyltriamine is formed. As the pH is increased to 7, Q6 moves to the butanediamine fragment of the guest molecule due to deprotonation of the aniline nitrogen atom. This process is accompanied by a change in the colour of the solution to violet and the fluorescence intensity decreases. The use of cucurbit[6]uril as a catalyst for azide–alkyne cyclisation within the cavity made it possible to prepare a polyrotaxane with desired composition[45] from which the Q6 molecules were removed by increasing the pH of the medium. As a result, oligotriazoles containing up to nine triazole-linked monomeric units were obtained.[46]

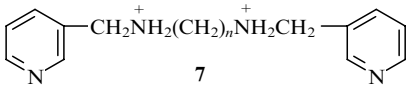
K Kim and co-workers[12, 13] developed an original approach to the synthesis of cucurbituril-containing polyrotaxanes, which allowed them to prepare first coordination-linked polymers. Initially, Q6 are threaded onto a small organic molecule with the diamine hydrocarbon chain containing suitable terminal functional groups. Then these fragments are linked to form a coordination polymer through bonds between the donor atoms of the terminal groups of the resulting pseudorotaxanes and the metal atoms. The above-described method has particular advantages over the previously known procedures giving rise to polyrotaxanes in which such macrocycles as cyclodextrins or crown ethers are threaded onto organic polymers. First, the resulting polyrotaxanes are characterised by high structural regularity, *i.e*., cyclic beads are present in each repeated structural unit of the polymer chain. Second, these polyrotaxanes were obtained as single crystals and characterised by X-ray diffraction analysis, whereas single crystals of cyclodextrin-containing polyrotaxanes suitable for X-ray diffraction studies are difficult to prepare because of the existence of numerous isomers with different orientations of the cone-like macrocycle.

Coordination of the donor atoms of the terminal groups of pseudorotaxanes to transition metal atoms [Cu(II), Co(II), Ni(II), Ag(I), Cd(II)] gives rise to one- and two-dimensional polyrotaxanes depending on the coordination number of the metal atom, the structure of pseudorotaxane, the size and the coordination ability of the counterion of the starting metal salt. The products of the reactions of different metal salts with the pseudorotaxanes (PR*nm*) are shown in Fig. 2. In these compounds, the cucurbit[6]uril molecule accommodates the molecule of dipyridylamines **6** or **7**, which contain chains of *n* methylene units (*n* = 4, 5) and the *para*- (*m* = 4) or *meta*-substituted (*m* = 3) terminal pyridine rings.



6

n = 4, 5; *m* = 4.



7

n = 4, 5; *m* = 3.

The reactions of pseudorotaxanes of the PR44 (*n* = 4, *m* = 4) and PR43 (*n* = 4, *m* = 3) types with aqueous solutions of cobalt(II) nitrates[47] and nickel(II) nitrates[48] afforded chain polymers. In these polymers, pseudorotaxanes can be in either the *trans* or *cis* positions at the octahedrally coordinated metal atoms to form linear chains (PR44) (see Fig. 2, structure **A**) and zigzag chains (PR43) (see Fig. 2, structure **B**), respectively. The size of the repeated zigzag fragment in the structure **B** is larger than 23 Å. The reaction of PR44 with $Cu(NO_3)_2$ also gave rise to zigzag chains where two pseudorotaxane molecules are coordinated to the copper atom in a square-pyramidal environment.[49] Silver(I) compounds tend to form linear two-coordinate complexes. The reaction of PR44 with silver tosylate [$Ag(MeC_6H_4SO_3)$] resulted in the *trans* coordination of two pseudorotaxane molecules to the metal atom giving rise to a virtually linear chain structure.[50] One-dimensional helical polymers were synthesised by the reactions of $AgNO_3$ (see Ref. 51) and $Cd(NO_3)_2$ (see Ref. 47) with pseudorotaxane PR53 in which the organic molecule encapsulated in cucurbituril contains five methylene groups and the *meta*-substituted terminal pyridine rings. Two silver ions and two pseudorotaxanes coordinated to these ions comprise one turn of the helix (see Fig. 2, structure **C**), the length of one fragment being equal to 17.9 Å. In the compound with cadmium, each turn of the helix (50.5 Å) consists of four pseudorotaxanes PR53 and four metal ions (see Fig. 2, structure **D**). The space between the chains in polyrotaxanes is filled with water molecules and anions linked

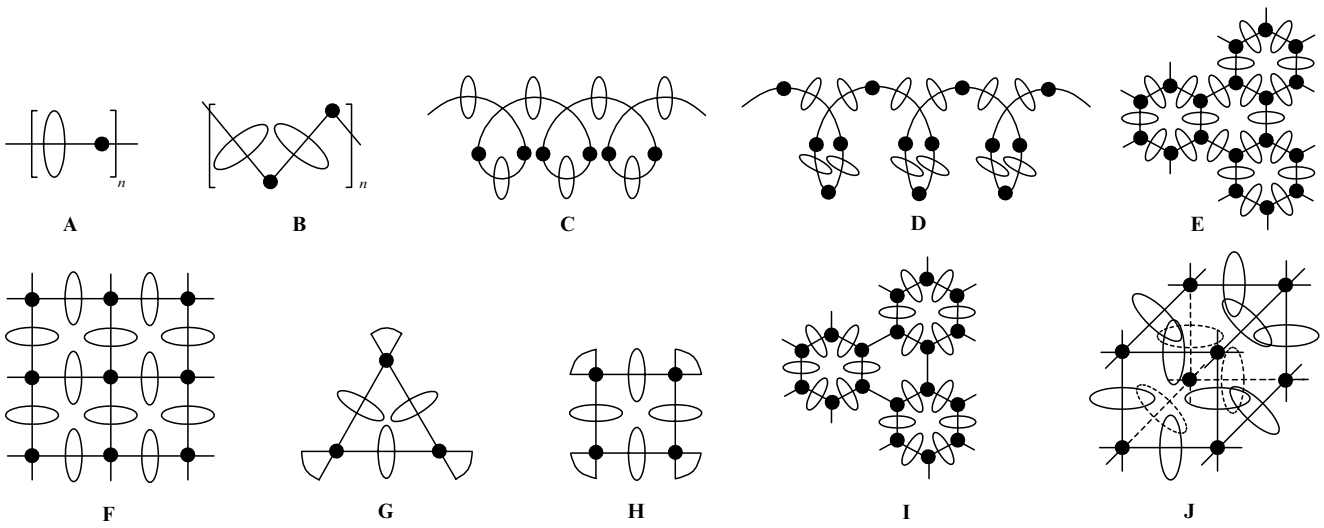


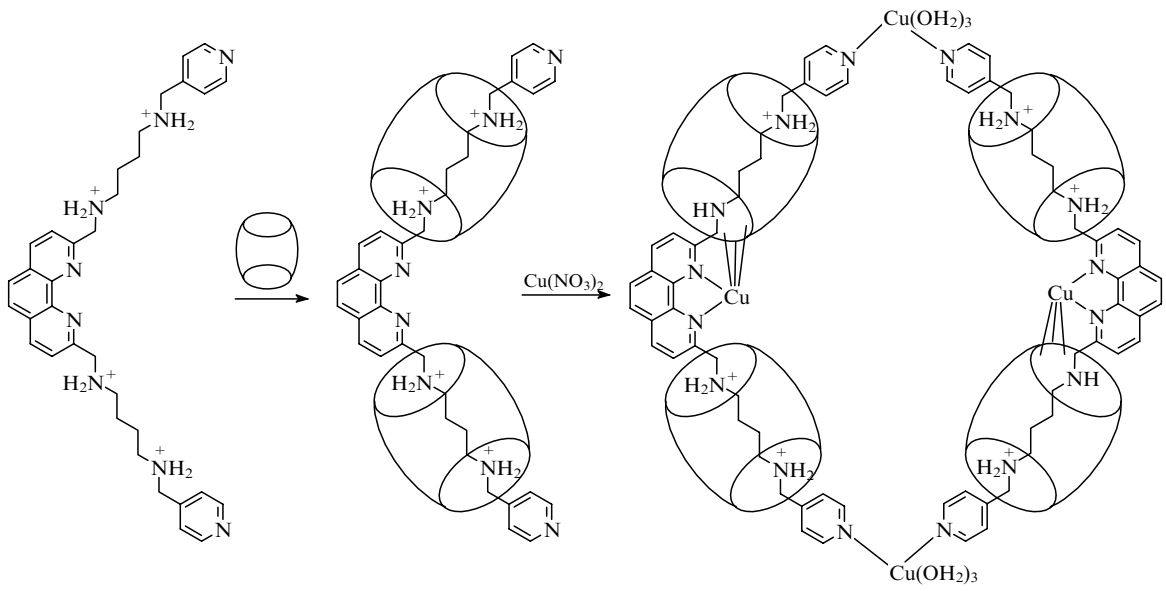
Figure 2. Formation of one-, two- and three-dimensional polyrotaxanes **A** – **J** (see the text) in the reactions of pseudorotaxanes with solutions of metal salts.

through an extensive network of hydrogen bonds resulting in additional stabilisation of the structure.

Unlike the above-described reaction with silver tosylate giving rise to a chain structure, the reaction of the pseudorotaxane PR44 with an aqueous solution of silver nitrate afforded a two-dimensional polyrotaxane.[50] The reaction with the use of another counterion afforded a polymeric structure in which the cucurbituril beads are threaded onto a network of face-sharing chair-shaped hexagons with silver ions occupying each vertex (see Fig. 2, structure **E**). Each face consists of two silver ions coordinated by two nitrogen atoms of the terminal pyridine rings of the pseudorotaxane. The length of the face is 20.9 Å and the average distance between two opposite angles is 38.0 Å. In the crystal, these two-dimensional polyrotaxane networks form superimposed interpenetrating layers with complete linkage of the hexagons. The resulting compound is the first example of polycatenane – polyrotaxane networks (catenanes are compounds consisting of interpenetrating rings). When the positions of the nitrogen atoms of the terminal pyridine rings of the pseudorotaxane are changed with the simultaneous change of the counterion, the reaction of PR43 with (CF_3SO_3) affords a two-dimensional polyrotaxane of another type, which can be described as networks consisting of squares with cucurbituril molecules threaded onto all sides of these squares (see Fig. 2, structure **F**).[47] The networks are packed in layers (the distance between the layers is 12.7 Å). In this case, the catenane structure is not formed. A compound prepared by the reaction of the pseudorotaxane PR43 with copper nitrate $Cu(NO_3)_2$ has an analogous layered structure.[47]

The *cis*-coordination of pseudorotaxanes to the metal atoms in a planar-square coordination makes it possible to prepare the so-called molecular necklaces in which several cyclic molecules are threaded onto a larger-size ring. Thus, the coordination of the ethylenediamine ligand in the $[Pt(en)(NO_3)_2]$ complex (en is ethylenediamine) is such that pseudorotaxanes can occupy only *cis* positions on reaction with this complex to give nanocycles with three (PR44) (see Fig. 2, structure **G**) or four (PR43) (see Fig. 2, structure **H**) threaded cucurbit[6]uril molecules.[52] A molecular necklace consisting of four rotaxane fragments was also prepared in the reaction of copper(II) nitrate with a polyrotaxane, whose angular form is dictated by the phenanthroline derivative that links two Q6 molecules.[53] The ring is formed upon *cis* coordination of the copper atom by the nitrogen atoms of the terminal

Scheme 1

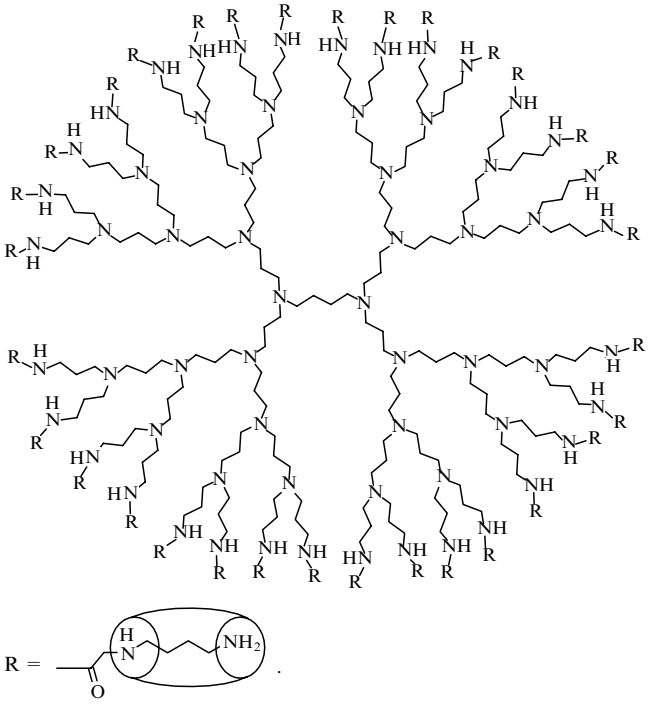


pyridine groups of two angular pseudorotaxanes. The distance between the metal atoms in these nanocycles is ~20 Å (Scheme 1).

The use of molecular necklaces as large building blocks for the design of supramolecular compounds is of obvious interest. The reaction of PR53 with $Cu(NO_3)_2$ in the presence of oxalate ions afforded a supramolecular structure in which molecular necklaces consisting of six copper-bound pseudorotaxanes are linked to each other through the coordinated oxalate ions (see Fig. 2, structure **I**).[53] Each planar ring is bound to six other rings giving rise to two types of cavities in the polymer structure. The cavities of one type are located within the hexagons (the diameter is 5 Å), whereas the cavities of another type formed by oxalate ions are located between the hexagons (the diameter is 14 Å). These cavities form channels occupied by the NO_3^- ions and water molecules. The sizes of the channels are sufficiently large and allow NO_3^- ions to be replaced by the PF_6^- and tosylate ions in aqueous solutions. The replacement by bulkier anions, such as tetraphenylborate, does not occur, which is indicative of the rather high selectivity of the polyrotaxane compound in these reactions.

Three-dimensional polyrotaxanes can be prepared upon coordination of the terminal groups of pseudorotaxanes by lanthanide atoms, which typically have large coordination numbers.[54] Under hydrothermal conditions, the reaction of the pseudorotaxane PR43 containing the terminal 3-carboxyphenyl groups with $Tb(NO_3)_3$ afforded a supramolecular compound with a three-dimensional coordination network as the framework. Each lattice node is occupied by two Tb^{3+} cations (see Fig. 2, structure **J**; one solid circle in each lattice node corresponds to two terbium atoms) coordinated by six pseudorotaxane molecules through the carboxylate groups, with four carboxylate groups serving as bridges between the terbium atoms. As a result of a change in the position of the carboxylate group in the benzene ring, the reaction of $Tb(NO_3)_3$ with the pseudorotaxane PR44 yielded a two-dimensional polymer in which each terbium centre is coordinated by three pseudorotaxane fragments. The polycatenane-polyrotaxane structure of this compound is analogous to the structure of the two-dimensional polyrotaxane formed in the reaction of $AgNO_3$ with a pseudorotaxane containing the terminal pyridine groups (see Fig. 2, structure **E**).

Cucurbit[6]uril (**5**) has found an interesting application in the chemistry of dendrimers. In the last decade, these three-dimensional organic compounds have attracted the attention of researchers because of their successful use in various fields of science and technology (medicine, catalysis and agriculture).[55] In the reaction of Q6 with a dendrimer containing terminal alkyldiammonium groups, the macrocycles are threaded onto these terminal groups to give a dendrimer with terminal pseudorotaxane fragments.



The use of a bulky bead as a component of the terminal groups imparts rigidity to the structure of the dendrimer. The resulting compound has a globular structure and can hold guests within its cavity. If the pH of the solution is increased, Q6 is removed and the dendrimer becomes conformationally flexible and releases the guest molecule. This reversible inclusion of molecules opens up new possibilities for using dendrimers for the transport, for example, of pharmaceuticals.

Hence, rotaxanes and pseudorotaxanes based on cucurbit[6]uril (**5**) have proved to be convenient building blocks for the construction of supramolecular compounds. Cucurbit[6]uril is rigidly fixed at the hydrocarbon chain through Coulombic and van der Waals interactions and the resulting rotaxanes and pseudorotaxanes are linked to each other through bonds between the donor atoms of the terminal groups and the metal atoms to form nanosized supramolecular compounds.

III. Supramolecular compounds of cucurbit[6]uril with metal aqua complexes

The ability of cucurbit[6]uril (**5**) to bind metal ions in aqueous solutions was discovered by Behrend and co-workers in 1905.[5] The presence of more polar oxygen atoms in cucurbit[6]uril as compared to those in crown ethers or cryptands is responsible for the formation of stronger interactions between these oxygen atoms and metal cations. The formation constants of metal complexes with Q6 are much higher than the formation constants of complexes with the above-mentioned organic macrocycles.[8] Besides, the rigidity of Q6 hinders its conformational changes upon complex formation, in contrast, for example, to metal complexes with crown ethers.[56] The metal cations are coordinated by the oxygen atoms located in the planes of the portals of cucurbit[6]uril rather than are included into the cavity of the cavitand. Hence, due to the unique structure of cucurbit[6]uril, it can form not only inclusion compounds with organic molecules but also mixed organic – inorganic compounds with metal cations.

In the late 1990s, interesting supramolecular compounds of Q6 with the sodium, potassium, rubidium and cesium cations were prepared.[26, 57–59] Cucurbit[6]uril is insoluble in water but its solubility is noticeably increased in the presence of salts of these metals. These compounds were obtained as single crystals by slow diffusion of organic solvents into aqueous solutions and characterised by X-ray diffraction analysis. Metal aqua complexes are bound to the carbonyl oxygen atoms of the Q6 portals to form lids, which efficiently close the cavitand from both sides.

In the compound of cucurbit[6]uril with a sodium aqua complex (**8**), each portal of the macrocycle is coordinated to two metal cations linked to each other through a bridging water molecule (the symbol $\subset$ designates the inclusion into the cavity of the cavitand).[26]

$$\{[Na_4(H_2O)_{10}](C_4H_8O\subset C_{36}H_{36}N_{24}O_{12})\}(SO_4)_2\cdot 10\,H_2O$$

8

Each sodium atom is bound to two carbonyl oxygen atoms of Q6 and three water molecules. Due to formation of supramolecular compounds of the type 'barrel with two lids', the cavity of the cavitand can include and hold the tetrahydrofuran molecule (Fig. 3). However, an increase in acidity leads to protonation of the carbonyl groups at the Q6 portals, removal of the lids and release of the guest from the cavity of the cavitand. After the addition of Na_2CO_3, tetrahydrofuran is again included into the cavity because the barrel is again efficiently closed by the lids. According to the ^1H NMR spectroscopic data, other guests, such

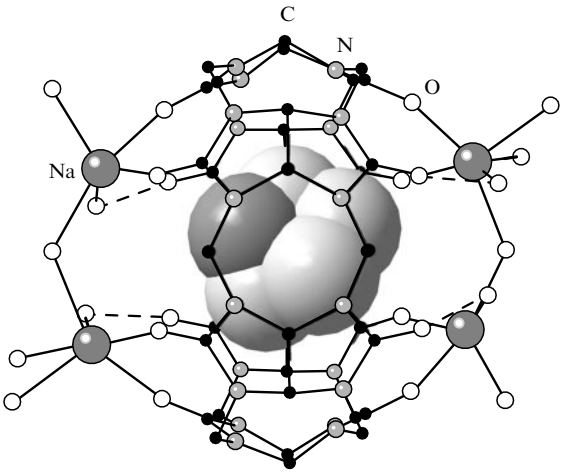


Figure 3. Structure of the supramolecule $\{[Na_4(H_2O)_{10}](C_4H_8O\subset C_{36}H_{36}N_{24}O_{12})\}(SO_4)_2 \cdot 10\,H_2O$ (**8**). The cavity of the cavitand encapsulates the tetrahdyrofuran molecule.

as benzene, cyclopentanone and furan, behave analogously. The supramolecular compound of Q6 with the sodium aqua complex is the first example of a molecular container into which guests can be reversibly included through the formation and cleavage of the bonds between the metal aqua complex and macrocycle.

In the compounds with potassium (**9**)[57] or rubidium (**10**),[58] the portals of Q6 are also closed by the bridging binuclear aqua complexes serving as the lids.

$\{[K_2(OH)_2](C_4H_8O\subset C_{36}H_{36}N_{24}O_{12})\} \cdot 18\,H_2O$

9

$\{[Rb_2(OH)_2(CH_3OH)_2(H_2O)_2](C_{36}H_{36}N_{24}O_{12})\} \cdot 17\,H_2O$

10

Each metal atom is coordinated by four oxygen atoms at the portals of two Q6 molecules (two oxygen atoms from each molecule) (Fig. 4). This leads to the formation of hybrid

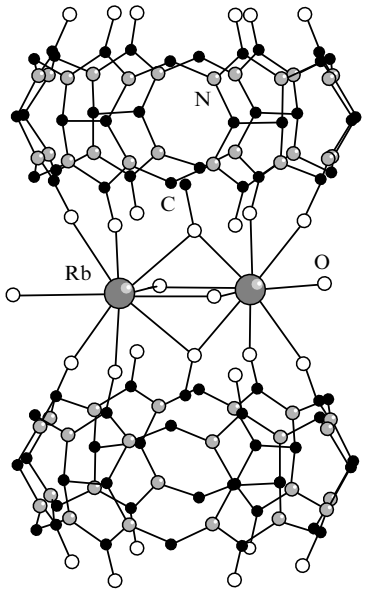


Figure 4. Structure of the supramolecular compound $\{[Rb_2(OH)_2(CH_3OH)_2(H_2O)_2](C_{36}H_{36}N_{24}O_{12})\} \cdot 17\,H_2O$ (**10**) (view along the axis *a*).

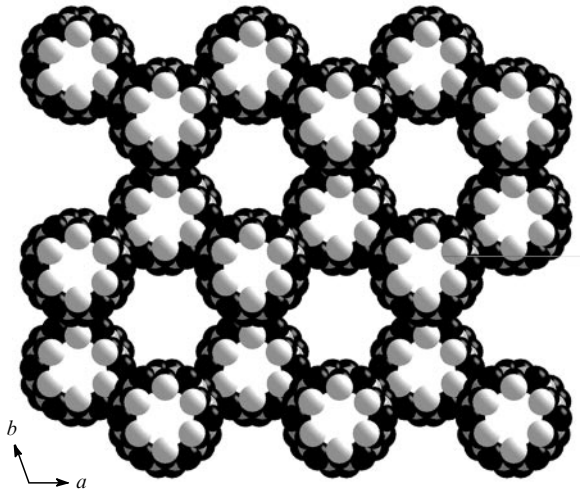


Figure 5. Formation of the honeycomb-like structure in the supramolecule **9** (view along the axis *c*).

organic–inorganic polymers consisting of alternating metal aqua complexes and cucurbit[6]uril. The structures of these compounds are stabilised by van der Waals interactions due to complementarity of the chain folds, *i.e.*, the convexities of one chain match the concavities of the adjacent chains. The polymer chain surrounded by three adjacent chains is shifted by half of the translation along the axis *c* to form a honeycomb-like packing containing large channels (Fig. 5). The resulting compounds are promising for the design of porous materials, which find use in separation processes, supramolecular catalysis and optoelectronics. In the honeycomb-like structure of the compound with the rubidium ion **10**, the diameter of the channels filled with water molecules of solvation is $\sim$10 Å and the volume of these chains comprises 23% of the total volume of the structure.[58] Upon the addition of THF or ethylenediamine, the molecules of these compounds are included only into the cavity of the cavitand, the channels remaining unoccupied.[57, 58]

Each portal of cucurbit[6]uril in the supramolecular compound $\{[Cs_2(H_2O)_2](H_2O\subset C_{36}H_{36}N_{24}O_{12})\}Cl_2 \cdot 2\,H_2O$,[59] like those in the above-described compounds with sodium (**8**), potassium (**9**) and rubidium (**10**), is coordinated to the metal aqua complexes. However, due to the larger ionic radius of the cesium cation, the barrel can be closed by a mononuclear cesium complex serving as the lid. The cesium atom is bound to four carbonyl oxygen atoms of cucurbituril and three water molecules. The addition of tetrahydrofuran gave rise to the inclusion compound $\{[Cs(H_2O)_2Cl](C_4H_8O\subset C_{36}H_{36}N_{24}O_{12})\} \cdot 5\,H_2O$ (**11**) in which the barrel is closed only by one lid, whereas the oxygen atom of the guest THF molecule is coordinated to the cesium ion (Fig. 6). In this case, the inclusion of tetrahydrofuran, as in the case of the sodium complex **8**, is also reversible and depends on the acidity of the medium.

The supramolecular compound of cucurbit[6]uril with the calcium aqua complex $\{[Ca(HSO_4)_2]_2(C_{36}H_{36}N_{24}O_{12})\} \cdot 13\,H_2O$ is the first example of the structurally characterised cucurbituril compound. The structure of this compound, which was established by Freeman and co-workers[6] in 1981 and refined by Freeman at a later time,[14] is a polymer consisting of the alternating Q6 molecules linked to the calcium cations through the carbonyl groups. In the presence of methanol, the coordinated CH_3OH molecule is included into the cavity of the cavitand, the shape and packing of the supramolecules remaining virtually unchanged.[60] The structure of the fragment of the chain in the $\{[Ca(H_2O)_3(HSO_4)(CH_3OH)]_2(C_{36}H_{36}N_{24}O_{12})\}(HSO_4)_2 \cdot 4\,H_2O$ complex (**12**) is shown in Fig. 7. Each Q6 molecule is bound to four calcium cations and each calcium cation is bound to two Q6

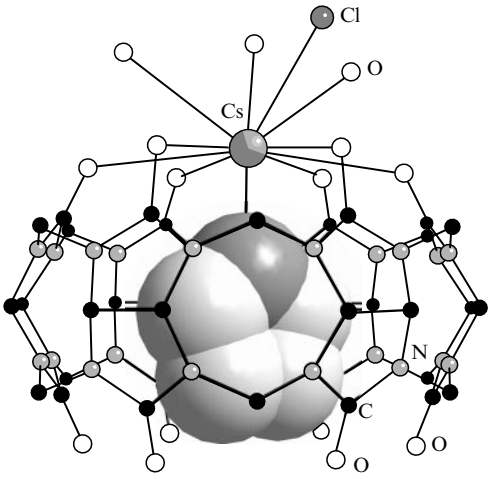


Figure 6. Structure of the supramolecule $\{[Cs(H_2O)_2Cl](C_4H_8O\subset C_{36}H_{36}N_{24}O_{12})\}\cdot 5\,H_2O$ (**11**). The cavity of the cavitand encapsulates the tetrahdyrofuran molecule.

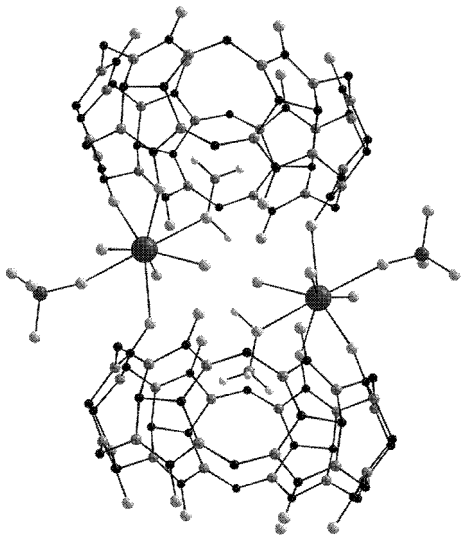


Figure 7. Fragment of the chain of the compound of cucurbit[6]uril with the calcium aqua complex $\{[Ca(H_2O)_3(HSO_4)(CH_3OH)]_2(C_{36}H_{36}N_{24}O_{12})\}(HSO_4)_2\cdot 4\,H_2O$ (**12**). The cavity of the cavitand encapsulates the methyl group of MeOH.

molecules (one carbonyl group of one molecule and two carbonyl groups of another molecule). In addition to the carbonyl groups of the Q6 molecules, the calcium ions are coordinated by three water molecules, the hydrosulfate anion, and the methanol molecule whose methyl group is located in the hydrophobic cavity of the cavitand.

In the crystals, the polymer molecules form molecular cylinders linked to each other through hydrogen bonds and the channels are occupied by the water molecules of crystallisation and HSO_4^- anions (Fig. 8).

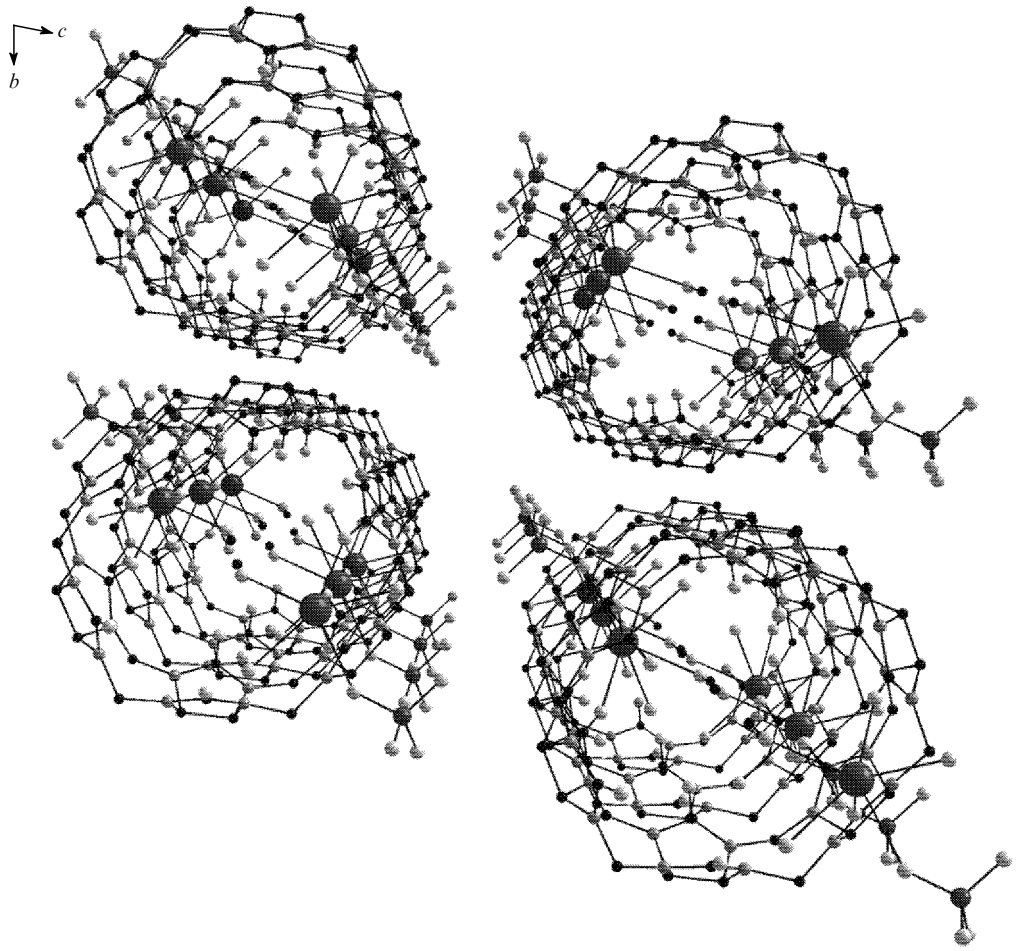


Figure 8. Formation of molecular cylinders (view along the *a* axis) in the supramolecular compound **12**. Water molecules of crystallisation and sulfate anions are omitted.

Unlike the compounds of cucurbit[6]uril (**5**) with aqua complexes of Groups 1 and 2 metals in which there are direct interactions between the metal atoms and oxygen atoms at the portals of Q6, coordination of Group 13 metals by the macrocycle occurs through hydrogen bonding between the portal oxygen atoms and coordinated water molecules of the aqua complexes. It should be noted that in the latter type of compounds, Q6 acts as an outer-sphere ligand. In supramolecular compounds with cucurbit[6]uril, distortions in the aqua complexes are much smaller than those in the case of insertions of the ligands into the first coordination sphere. Consequently, the structural information for compounds with Q6 corresponds better to the compositions and structures of aqua complexes that are actually present in solution.

In the compounds of cucurbit[6]uril with aqua and chloro aqua complexes of indium and aluminium, the metal complexes are located between the Q6 molecules and are linked to each other through a complex network of hydrogen bonds involving the portal oxygen atoms and water molecules. The complex *trans*-$[InCl_2(H_2O)_4]^+$ and *cis*- and *trans*-$[InCl_4(H_2O)_2]^-$ ions were isolated and structurally characterised in the investigation of the reaction of cucurbit[6]uril with indium nitrate in hydrochloric acid solutions.[61] In the compound with composition $\{[InCl_2(H_2O)_4]_3(Cl\subset C_{36}H_{36}N_{24}O_{12})\}2\,Cl\cdot 4\,H_2O$ (**13**), the macrocyclic molecules form a hexagonal one-layer packing (Fig. 9), the crystallographic positions occupied by the macrocycles in this structure having the highest symmetry D_{6h} possible for cucurbit[6]uril. The cavity of the cavitand contains the Cl^- anion disordered over 12 positions. The structure of the $(H_3O)_3\{[InCl_4(H_2O)_2]_3(C_{36}H_{36}N_{24}O_{12})_2\}\cdot 17\,H_2O$ compound is composed of both the *trans* and *cis* isomers of the $[InCl_4(H_2O)_2]^-$ complex. In this crystal structure, the Q6 molecules form a parquet-like packing. The reactions of Q6 with aluminium chloride and indium nitrate in aqueous solutions afforded supramolecular compounds with the aqua complexes $[Al(H_2O)_6]^{3+}$ and $[In(H_2O)_6]^{3+}$ with compositions $\{[Al(H_2O)_6].(C_{36}H_{36}N_{24}O_{12})\}Cl_3\cdot 18\,H_2O$ and $\{[In(H_2O)_6](C_{36}H_{36}N_{24}O_{12})\}.(NO_3)_3\cdot 9\,H_2O$, respectively.[61] In the structure of the former compound, the centres of the Q6 molecules follow the body-centered law. In the structure of the latter compound, the molecules of the macrocycle form a parquet-like packing.

In studies of the $M^{3+}-HCl-Q6$ systems, the isostructural compounds with composition

$$(H_7O_3)_4\{[MCl_4]_2(C_{36}H_{36}N_{24}O_{12})\}Cl_2\cdot n\,H_2O,$$

where (M = Ga, n = 2;[62] M = Fe, n = 3 [63]), were obtained. In the structures of these complexes, the Q6 molecules alternating with the $[MCl_4]^-$ anions are also linked through a system of hydrogen bonds between the portal oxygen atoms and water molecules.

The reactions of lanthanide(III) nitrates and sulfates with Q6 in aqueous solutions afforded supramolecular compounds in which (according to the X-ray diffraction data) the aqua complexes are bound to the macrocycle through both the direct coordination of the metal atom by the oxygen atoms and hydrogen bonding between the coordinated water molecules and portal oxygen atoms of cucurbit[6]uril.[64] In the resulting compounds, the aqua complex : cucurbit[6]uril ratio is 1 : 1, 2 : 2 or 2 : 3. In complexes **14**–**17** with composition 1 : 1, the metal atom together with its ligand environment forms the lid that closes the Q6 molecule from one side.

$\{[La(H_2O)_6(SO_4)](C_{36}H_{36}N_{24}O_{12})\}(NO_3)\cdot 12\,H_2O$
14

$\{[Gd(NO_3)(C_2H_5OH)(H_2O)_3](C_{36}H_{36}N_{24}O_{12})\}(NO_3)_2\cdot 5.5\,H_2O$
15

$\{[Ho(NO_3)(H_2O)_4](C_{36}H_{36}N_{24}O_{12})\}(NO_3)_2\cdot 7\,H_2O$
16

$\{[Yb(NO_3)(H_2O)_4](C_{36}H_{36}N_{24}O_{12})\}(NO_3)_2\cdot 6_2O$
17

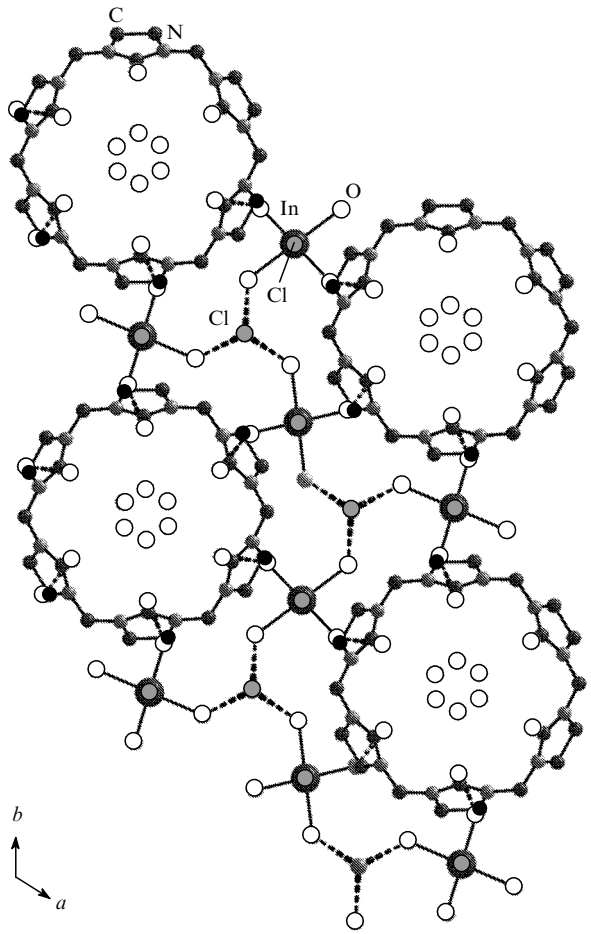


Figure 9. Crystal structure of $\{[InCl_2(H_2O)_4]_3(2\,Cl\subset C_{36}H_{36}N_{24}O_{12})\}Cl\cdot 4\,H_2O$ (**13**).

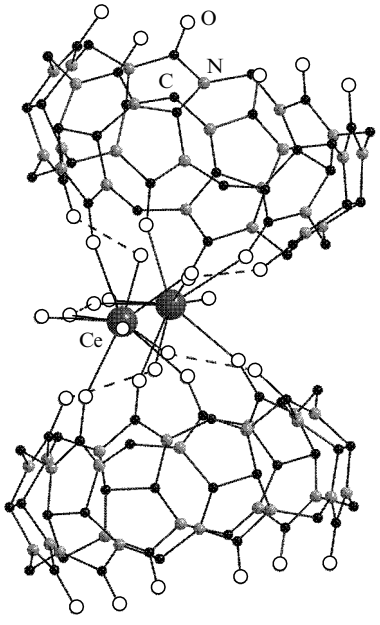


Figure 10. Fragment of the $\{[Ce(H_2O)_5]_2(C_{36}H_{36}N_{24}O_{12})_2\}Br_6\cdot 26\,H_2O$ structure (**18**): formation of the sandwich-type compound.

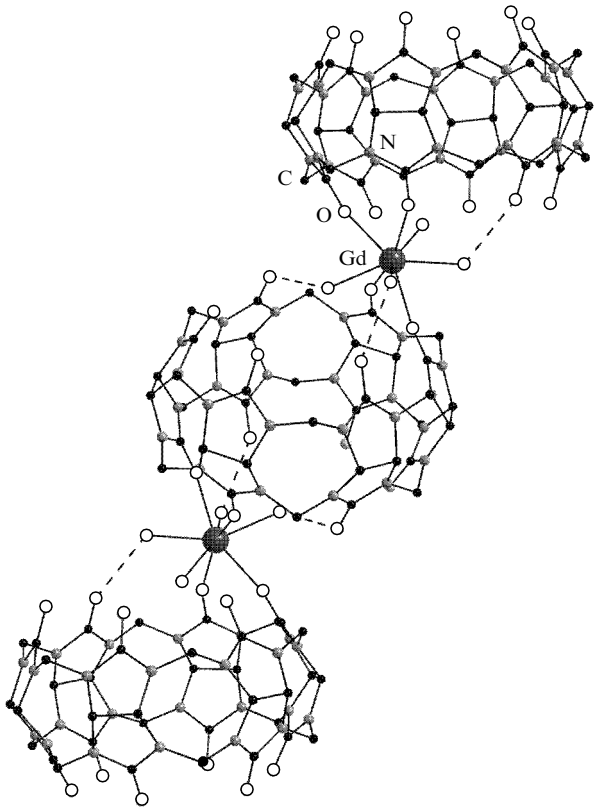


Figure 11. Fragment of the $\{[Gd(H_2O)_4]_2(C_{36}H_{36}N_{24}O_{12})_3\}Br_6 \cdot 45\,H_2O$ structure (**20**): the triple-decker sandwich.

In the $\{[Ce(H_2O)_5]_2(C_{36}H_{36}N_{24}O_{12})_2\}Br_6 \cdot 26\,H_2O$ complex (**18**) with composition 2 : 2, two cerium aqua ions are coordinated by two Q6 molecules to form a sandwich-type compound (Fig. 10).

The crystal structures of compounds **19**[65] and **20**[64] with composition 2 : 3 can be described as packings of nanosized triple-decker sandwiches built from alternating Q6 molecules and metal aqua complexes (Fig. 11).

$\{[Sm(H_2O)_4]_2(C_{36}H_{36}N_{24}O_{12})_3\}Br_6 \cdot 44\,H_2O$

19

$\{[Gd(H_2O)_4]_2(C_{36}H_{36}N_{24}O_{12})_3\}Br_6 \cdot 45\,H_2O$

20

The shape of this supramolecule can be approximated by a skewed cylinder whose largest van der Waals size is 33 Å. In the crystals of lanthanide(III) compounds, the supramolecules are linked in chains or layers or packed in stacks through hydrogen bonding. In these structures, large channels and cavities are occupied by water molecules of crystallisation and counterions.

The possibility of using Q6 for crystallisation of polynuclear aqua complexes was exemplified by the preparation of the mixed uranium(VI) oxochloride complex.[66] The supramolecular compound (**21**), which is composed of the tetranuclear uranium aqua complex and cucurbit[6]uril (**5**), is formed through hydrogen bonding between the coordinated uranium atoms, water molecules and carbonyl oxygen atoms of the Q6 portals (Fig. 12).

$\{[(UO_2)_4O_2Cl_4(H_2O)_6](C_{36}H_{36}N_{24}O_{12})\} \cdot 5\,H_2O$

21

In the crystals, the Q6 molecules and aqua complexes form alternating layers linked to each other through a system of hydrogen bonds. In the aqua complexes, the uranium atoms of four uranyl groups are virtually in a single plane.

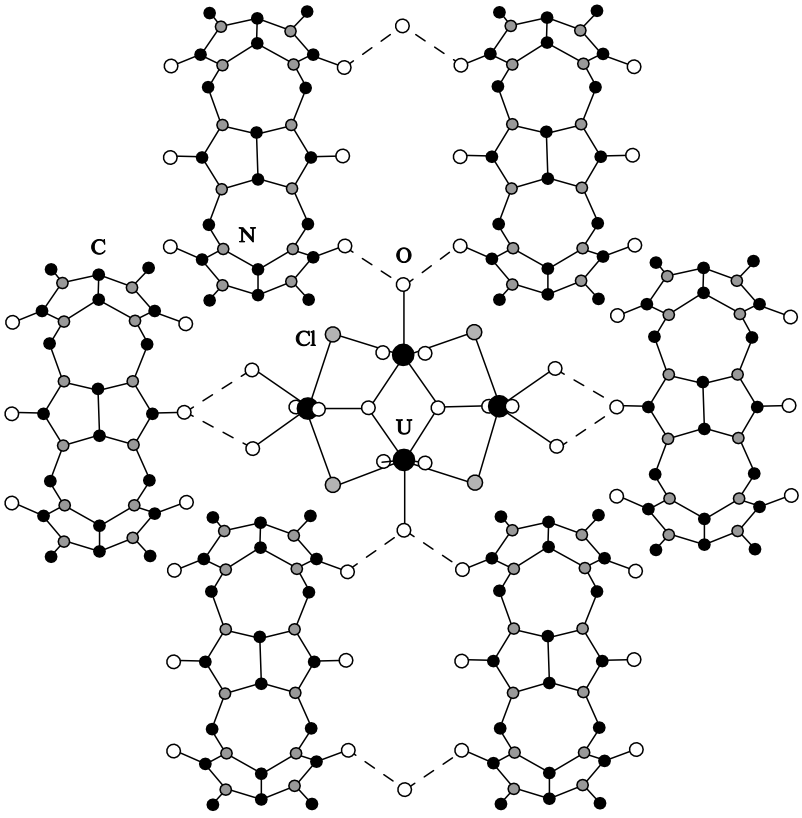
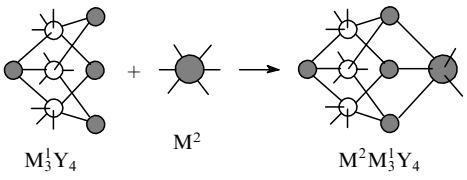


Figure 12. Fragment of the structure of the $\{[(UO_2)_4O_2Cl_4(H_2O)_6](C_{36}H_{36}N_{24}O_{12})\} \cdot 5H_2O$ compound (**21**).

By comparing the modes of binding of cucurbit[6]uril (**5**) to different metals, several conclusions can be made. Thus, the carbonyl oxygen atoms of the Q6 portals are directly coordinated to the metal atoms in supramolecular compounds with alkali, alkaline earth and rare-earth metals. These most electropositive metals have rather large ionic radii (r_{ion} = 0.97, 1.73, 1.03 and 1.14 Å for Na^+, Cs^+, Ca^{2+} and La^{3+}, respectively [67]) and their binding to the ligands should be considered as Coulombic (ion–dipole) interactions. In these cases, cucurbit[6]uril, which is a weak donor but contains polarised C=O groups, competes with other ligands for site in the coordination sphere about the metal atom. Group 13 metal ions have smaller radii (r_{ion} = 0.76 and 0.50 Å for In^{3+} and Al^{3+}, respectively [67]) and their binding to the ligands is predominantly covalent. The larger charges and smaller sizes of Group 13 metal cations lead to an increase in acidity of the coordinated water molecules of aqua ions. Consequently, the protons of the water molecules coordinated to these metal cations can form much stronger hydrogen bonds with the polarised C=O groups due to which the inclusion of water into the first coordination sphere is more favourable than the inclusion of Q6. If the metal–ligand interaction is predominantly Coulombic, Q6 competes with water for sites in the inner coordination sphere of the metal atom. If this interaction is predominantly covalent, the structure is determined primarily by a system of hydrogen bonds between the aqua ligands and cucurbit[6]uril (**5**) as the outer-sphere ligand.

IV. Supramolecular compounds of cucurbit[6]uril with metal cluster aqua complexes

The use of bulky fragments, which retain their geometry and can form extensive networks of hydrogen bonds due to a large contact surface, is an important condition for the directed construction of nanosized complexes or supramolecular compounds. Molybdenum and tungsten cluster aqua complexes are suitable large molecular building blocks for the construction of supramolecular compounds with cucurbit[6]uril (**5**). Studies of interactions of Q6 with trinuclear thio and seleno complexes of these metals and their heterometallic derivatives led to the discovery of a new class of supramolecular compounds. In aqueous solutions, cluster thio and seleno complexes of molybdenum and tungsten produce the stable trinuclear aqua ions $[M^1_3Y_4(H_2O)_9]^{4+}$ (M^1 = Mo or W; Y = S or Se) in which the metal atoms are coordinated by one μ_3-bridging chalcogen atom and three μ_2-bridging chalcogen atoms.[68–71] The coordinatively unsaturated μ_2-bridging chalcogen atoms are readily coordinated to transition and post-transition metal atoms.[72] In this case, the trinuclear cluster (a cube without one vertex) is transformed into the cubane complex $M^2M^1_3Y_4$ and the μ_2-bridging chalcogen atoms are transformed into the μ_3-bridging atoms.



M^1 = Mo, W; M^2 is the transition or main-group metal atom; Y = S, Se.

Each M^1 atom of the cluster core ($M^1_3Y_4$ or $M^2M^1_3Y_4$) is coordinated by three water molecules. Six water molecules are in *cis* positions with respect to the μ_3-bridging chalcogen atom in the trinuclear aqua complexes or with respect to the μ_2-bridging chalcogen atom, which links only the molybdenum (tungsten) atoms, in the cubane heterometallic complexes. These six aqua ligands are virtually in a single plane and are well suited in size and symmetry to six carbonyl groups at each portal of Q6. In addition, the cluster aqua complexes $[M^1_3Y_4(H_2O)_9]^{4+}$ have rather high positive charges due to which they exhibit pronounced acidic properties and act as good donors in hydrogen bonding, whereas the oxygen atoms of the polarised carbonyl groups of Q6 are potential acceptors. This geometric and functional (donor–acceptor hydrogen bond) complementarity gives rise to an extensive network of hydrogen bonds between the macrocycles and the triangular (cubane) aqua complexes. In spite of the fact that the energy of each individual hydrogen bond is low, the presence of a system of these bonds facilitates the formation of stable supramolecular compounds.

The use of Q6 for crystallisation of chalcogenide cluster aqua complexes made it possible for the first time to isolate and structurally characterise more than 20 supramolecular compounds. The compounds were crystallised by slow evaporation (in air) of solutions of cluster aqua complexes and Q6 in dilute hydrochloric acid. The resulting crystals are insoluble or weakly soluble in aqueous solutions of hydrochloric acid in which the starting reagents are readily soluble. If the cluster : cucurbit[6]uril ratio in supramolecular compounds is 1 : 1, only one portal of Q6 is closed by the cluster complex (structural type 'barrel with one lid'). If the cluster : cucurbit[6]uril ratio is 2 : 1, both portals are closed (structural type 'barrel with two lids') (Fig. 13). The distances between the carbonyl oxygen atoms of the macrocycle and aqua ligands in both structural types vary in the range of 2.5–3.1 Å. If the lids are coordinated, the cavity of the cavitand

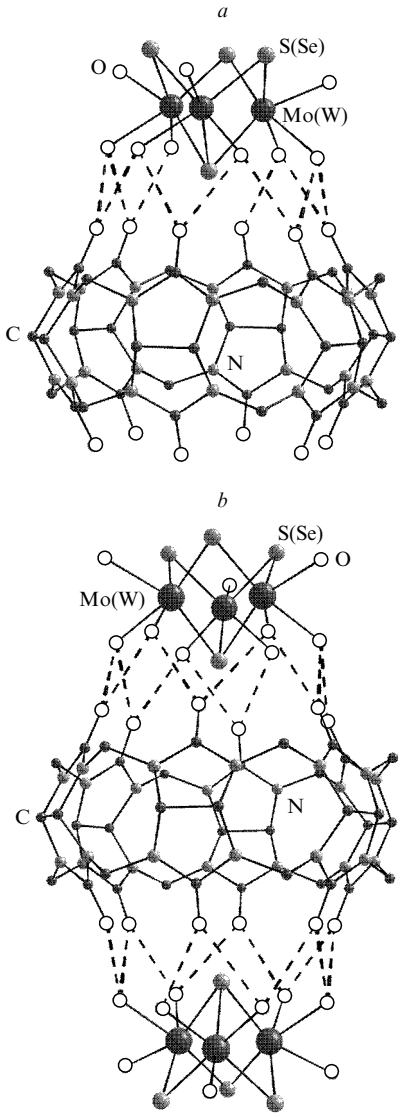


Figure 13. Supramolecular compounds of cucurbit[6]uril with metal cluster aqua complexes: (*a*) barrel with one lid; (*b*) barrel with two lids.

becomes isolated and small molecules can be held in the molecular container. The sizes of supramolecules closed by two lids are 25 – 30 Å.

A wide variety of available supramolecular compounds of Q6 with molybdenum and tungsten cluster aqua complexes is associated with the nature of the chalcogenide cluster, the presence of guests in solution and the concentration of hydrochloric acid in the aqueous solutions in which the reactions proceed.

The reactions of Q6 with the trinuclear tungsten sulfide aqua complex $[W_3S_4(H_2O)_9]^{4+}$ in 2 M HCl afforded products with different compositions and structures depending on the presence of pyridine in the system. The supramolecule $\{[W_3S_4(H_2O)_7Cl_2](C_{36}H_{36}N_{24}O_{12})\}Cl_2 \cdot 10\,H_2O$ (**22**) belongs to the structural type 'barrel with one lid' in which only one portal of Q6 is closed by the cluster complex through a system of complementary hydrogen bonds between six carbonyl groups and six aqua ligands.[73] In the crystal, the supramolecules are linked in zigzag chains through additional hydrogen bonds between the aqua ligands of the cluster and the portal oxygen atoms of Q6 (Fig. 14).

Under the same conditions, the reaction performed in the presence of pyridine led to destruction of the chain structure to form the layered compound $\{[W_3S_4(H_2O)_8Cl](PyH\subset C_{36}H_{36}N_{24}O_{12})\}Cl_4 \cdot 10\,H_2O$.[74] In this compound, the cavity of the Q6 molecule includes the pyridinium cation and both portals are closed by the trinuclear cluster complexes serving as the lids. In the crystal, these supramolecules are packed in layers. Upon the inclusion of the pyridinium cation into the cavity of Q6, both the guest and host molecules adapt to each other in size resulting in distortions of their structures. Thus, the Q6 molecule becomes slightly extended, whereas the pyridine molecule slightly contracts.

However, the inclusion of a guest does not necessarily lead to such dramatic changes in the structure and packing of supramolecules. The conditions of the preparation of selenium-containing tungsten complexes **23**[75] and **24**[76] with cucurbit[6]uril also differ only by the presence of pyridine in the reaction mixture.

$\{[W_3Se_4(H_2O)_8Cl]_2(C_{36}H_{36}N_{24}O_{12})\}Cl_6 \cdot 12\,H_2O$
23

$\{[W_3Se_4(H_2O)_6Cl_3]_2(PyH\subset C_{36}H_{36}N_{24}O_{12})\}Cl_3 \cdot 18\,H_2O$
24

Both compounds have chain structures in which the supramolecules of the structural type described as a barrel with two lids are linked to each other through short (compared to the sum of the van der Waals radii of 3.9 Å) nonbonded Se···Se interactions (3.59 – 3.72 Å). The cavity of cucurbit[6]uril in compound **24** contains the pyridinium cation (Fig. 15). The chalcogen – chalco-

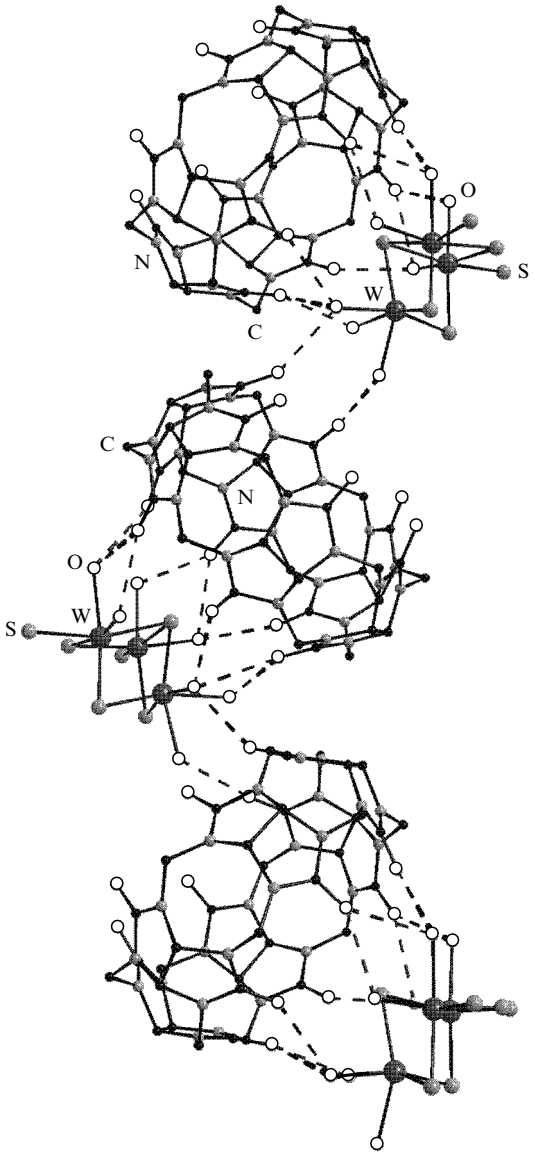


Figure 14. Fragment of the zigzag chain in $\{[W_3S_4(H_2O)_7Cl_2](C_{36}H_{36}N_{24}O_{12})\}Cl_2 \cdot 10\,H_2O$ (**22**).

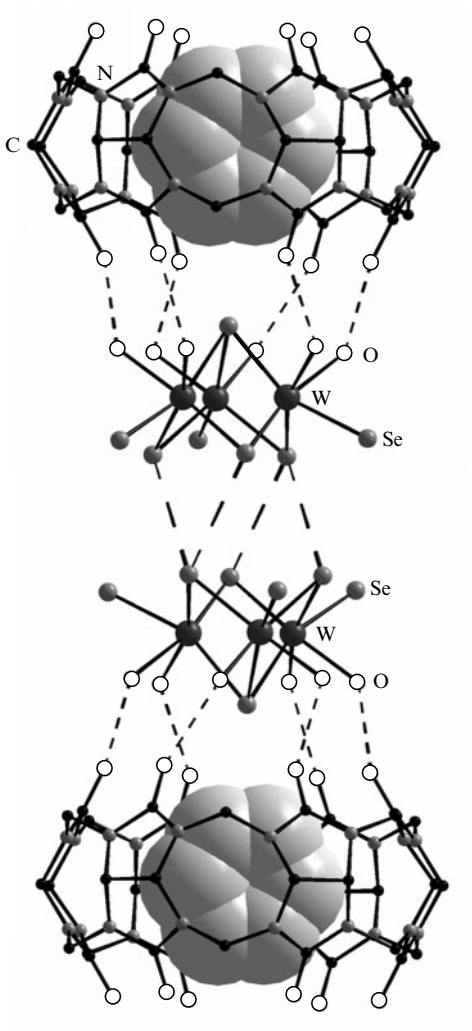


Figure 15. Fragment of the chain structure in $\{[W_3Se_4(H_2O)_6Cl_3]_2(PyH\subset C_{36}H_{36}N_{24}O_{12})\}Cl_3 \cdot 18\,H_2O$ (**24**). The cavity of cucurbit[6]uril accommodates the pyridinium cation.

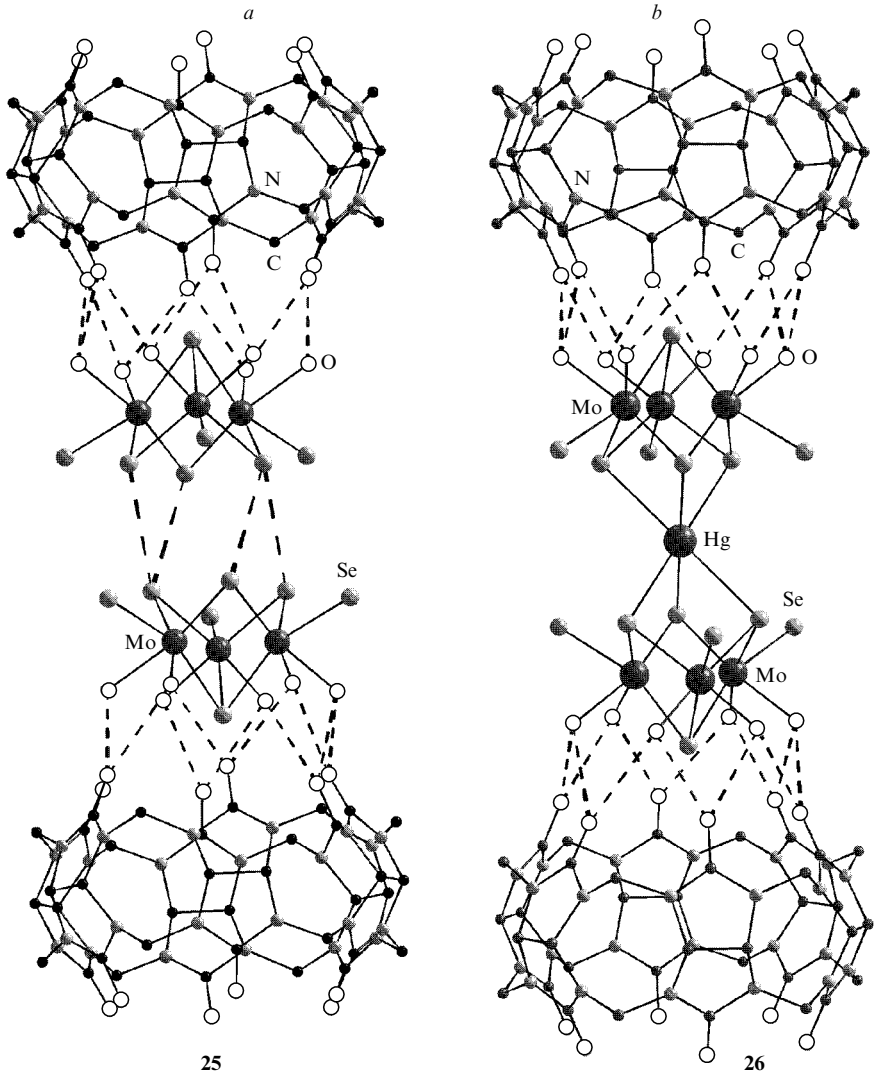


Figure 16. Comparison of the chain structures in $\{[Mo_3Se_4(H_2O)_8Cl]_2(C_{36}H_{36}N_{24}O_{12})\}Cl_6 \cdot 16\,H_2O$ (**25**) (matrix) and $\{[Mo_6HgSe_8(H_2O)_{14}Cl_4](C_{36}H_{36}N_{24}O_{12})\}Cl_4 \cdot 14\,H_2O$ (**26**) (intercalate).

gen interactions between adjacent clusters typical of trinuclear chalcogenide clusters of transition metals are of importance in the structure formation of these complexes.[77] The stronger bonding between the selenide atoms (Se···Se) as compared to that between the sulfur atoms (S···S) [according to the structural data available in the Cambridge Structural Database for $\{M_3Y_4\cdots Y_4M_3\}$ compounds, where Y = Se or S (see Ref. 78)] facilitates the retention of chain structures of the supramolecular compounds of Q6 with selenium-containing tungsten clusters upon the inclusion of a guest molecule. The structures of the selenium-containing complexes differ only by the mode of packing of the chains. In the crystal of compound **23**, the chains are packed to form a hexagonal motif, whereas these chains in the crystal of compound **24** form a distorted square packing.

The chalcogen–chalcogen interactions between the adjacent cluster fragments M_3Y_4 of supramolecular compounds are analogous to interactions between the adjacent layers formed by the chalcogen atoms in the layered transition metal dichalcogenides MY_2 (Y = S, Se).[75] An important property of the layered compounds is their ability to incorporate molecules or atoms between the layers giving rise to intercalates. A comparison of the structures of chain supramolecular compounds **25**[78] and **26**[75,79] shows that these compounds are regarded as a matrix and intercalate from the structural viewpoint. Thus, the mercury atom is included between the chalcogenide clusters M_3Y_4, the principal parameters of the supramolecules remaining virtually unchanged (Fig. 16).

$\{[Mo_3Se_4(H_2O)_8Cl]_2(C_{36}H_{36}N_{24}O_{12})\}Cl_6 \cdot 16\,H_2O$
25

$\{[Mo_6HgSe_8(H_2O)_{14}Cl_4](C_{36}H_{36}N_{24}O_{12})\}Cl_4 \cdot 14\,H_2O$
26

Therefore, the chemistry of supramolecular compounds of chalcogenide clusters is related to the chemistry of layered compounds more closely than one would expect. In both cases, the nonbonded chalcogen–chalcogen interactions play an important role in the structure formation.

Yet another important factor that has an effect on the formation of supramolecular compounds of Q6 with metal cluster aqua complexes is the concentration of hydrochloric acid in dilute solutions in which these reactions proceed. In solutions of HCl, cluster aqua complexes give different mixed chloro aqua complexes $[M_3Y_4(H_2O)_{9-x}Cl_x]^{(4-x)+}$ (Y = Se, S) whose compositions depend on the nature of the metal and chalcogen atoms. As demonstrated above, six *cis*-aqua ligands of the cluster are involved in complementary binding in the compounds of Q6 with Mo and W aqua complexes, whereas up to three Cl^- anions can be located in *trans* positions (for example, in the supramolecular compounds **27**[80] and **24**).[76]

$(H_3O)_{2.5}\{[W_3S_4(H_2O)_6Cl_3]_2(C_{36}H_{36}N_{24}O_{12})\}Cl_{4.5}\cdot 19\,H_2O$

27

$\{[W_3Se_4(H_2O)_6Cl_3]_2(PyH\subset C_{36}H_{36}N_{24}O_{12})\}Cl_3\cdot 18\,H_2O$

24

An increase in the concentration of hydrochloric acid leads to the replacement of the water molecules in aqua complexes by the halide ligands resulting in a sharp weakening of the cluster–cucurbit[6]uril interaction. First, the cluster complex loses a positive charge, *i.e.*, its acidity and ability to act as a donor in hydrogen bonding are decreased. Second, coordination of more than four Cl^- ligands to the cluster core requires the replacement of the *cis*-aqua ligands responsible for binding of the cluster complex to the portals of the macrocycle. Here, crystallisation of a particular form depends on other factors (Y···Y interactions, packing factors, *etc.*). Therefore, cucurbit[6]uril in HCl solutions acts as an outer-sphere ligand with respect to the cluster complex and forms hydrogen bonds only with some of the possible forms of $[M^3Y_4(H_2O)_{9-x}Cl_x]^{(4-x)+}$.

The latter assumption is exemplified by the data on the structure of the $(H_3O)_2[Mo_3Se_4(H_2O)_4Cl_5]_2(C_{36}H_{36}N_{24}O_{12})\cdot 15\,H_2O$ compound (**28**) prepared from a 6 M HCl solution.[78] This compound contains triangular clusters in the $[Mo_3Se_4(H_2O)_4Cl_5]^-$ anionic form. Unlike the chain compound **25** (see Fig. 16), which crystallises from a 2 M HCl solution and contains only one chloride ion per trinuclear cluster, the Mo atoms in the compound **28** are coordinated by three or four Cl^- ligands in *cis* positions with respect to μ_3-Se. As a consequence, the Q6 molecules and the chloro aqua complexes are not involved in a system of complementary hydrogen bonds. The chloro aqua complexes are linked in the dimeric cluster aggregates $\{Mo_3Se_4(H_2O)_4Cl_5\}_2^{2-}$ through short nonbonded Se···Se interactions. In the crystals, these dimers are packed in layers, which alternate with layers consisting of Q6 molecules.

Analogous dimers are present in the isostructural $(H_3O)_4\{[M_3S_7Cl_6]_2(C_{36}H_{36}N_{24}O_{12})\}\cdot 8\,H_2O$ compounds (**29**, M = Mo or W).[81] The $[M_3S_7]^{4+}$ cluster core in which the metal atoms are coordinated by the μ_3-S ligand and three disulfide ligands μ_2-S_2 exhibits a much higher affinity for halide ions than the $[M_3S_4]^{4+}$ core.[82] In a 3 M HCl solution, each metal atom is coordinated by two chloride ligands due to which hydrogen bonding with Q6 becomes impossible. In this case, the structure formation depends primarily on nonbond S···S interactions between the bridging atoms of the disulfide ligands resulting in dimerisation of the $[M_3S_7Cl_6]^{2-}$ anions. The crystal packing consists of alternating layers of dimeric cluster anions and Q6 molecules.

The heterometallic molybdenum and tungsten aqua complexes $[L_mM'M_3Y_4(H_2O)_9]^{n+}$ (Y = Se or S) also interact with cucurbit[6]uril to give supramolecular adducts belonging to 'barrels with one lid' or 'barrel with two lids'. In these aqua complexes, the bridging chalcogen atoms are coordinated to the transition and post-transition metal atoms and lose the ability to be involved in nonbonded Y···Y interactions. In the crystals, the supramolecules of heterometallic aqua complexes with cucurbit[6]uril are linked either in chains through additional hydrogen bonds, as in compounds **30**[83] and **31**[84] (Fig. 17), or in layers, as in supramolecular compound **32**.[85]

$\{[Mo_3(NiCl)S_4(H_2O)_8Cl](PyH\subset C_{36}H_{36}N_{24}O_{12})\}Cl_3\cdot 14.5\,H_2O$

30

$\{[Mo_3(PdCl)Se_4(H_2O)_7Cl_2](C_{36}H_{36}N_{24}O_{12})\}Cl\cdot 7\,H_2O$

31

$\{[Mo_3(PdCl)S_4(H_2O)_6Cl_3](PyH\subset C_{36}H_{36}N_{24}O_{12})\}Cl\cdot 14\,H_2O$

32

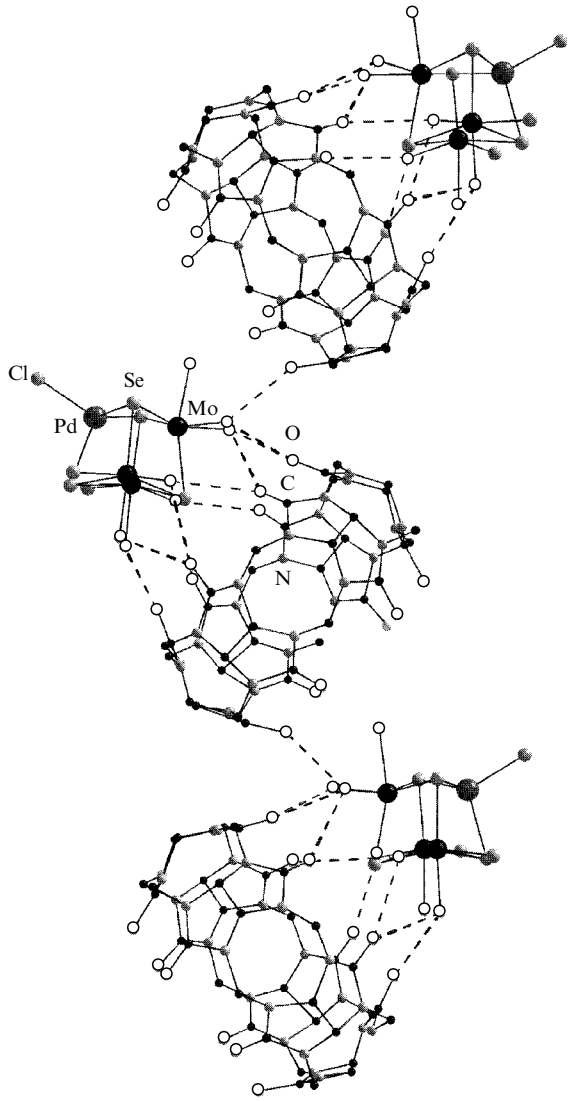


Figure 17. Fragment of the zigzag chain in $\{[Mo_3(PdCl)Se_4(H_2O)_7Cl_2](C_{36}H_{36}N_{24}O_{12})\}Cl\cdot 7\,H_2O$ (**31**).

From a comparison of compounds **31** and **32** in which only one portal of the macrocycle is closed by the cluster lid, it follows that the inclusion of the pyridinium cation into the cavity of Q6 does not lead to substantial changes in the structures of the supramolecules, *i.e.*, not only the cluster : cucurbit[6]uril ratio but also the total charge (+1) remain unchanged. Only the crystal packing undergoes essential changes. The supramolecules **31** form zigzag chains through hydrogen bonds between the aqua ligands of the cluster and the oxygen atoms at the portals of Q6 of the adjacent adduct, whereas the addition of pyridine gives rise to dimers packed in layers.

The use of Q6 for crystallisation of the reaction products of the palladium complex $[Mo_3(PdCl)S_4(H_2O)_9]^{3+}$ with P(III)- or As(III)-containing *n*-donor ligands made it possible to prepare and structurally characterise the $\{[Mo_3(PdE(OH)_3)S_4(H_2O)_6Cl_3]_2.(C_{36}H_{36}N_{24}O_{12})\}Cl_2\cdot n\,H_2O$ compounds [E = P, n = 20 (**33a**); E = As, n = 19 (**33b**)].[86] In these compounds, the Q6 molecules are closed by two cluster lids. The palladium atoms of these clusters are coordinated by the inorganic $P(OH)_3$ or $As(OH)_3$ ligands (Fig. 18). These are the first examples of the structurally characterised tribasic forms of phosphorous and arsenous acids.

Heterometallic indium- and tin-containing supramolecular compounds of cucurbit[6]uril **34**[87] and **35**[78] belong to the structural type described as 'barrels with two lids'.

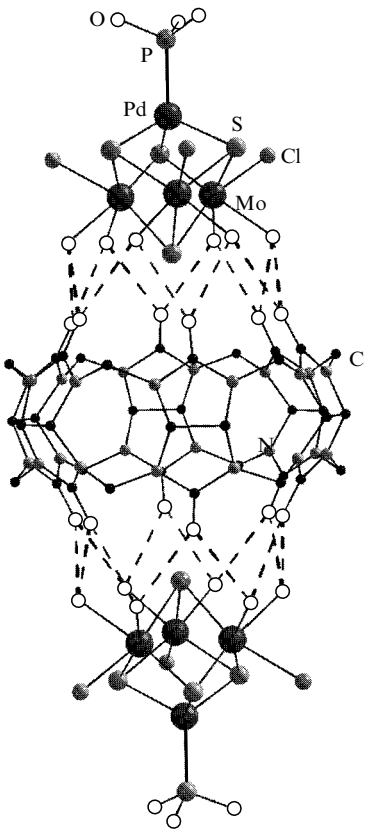


Figure 18. Structure of the supramolecule $\{[Mo_3(PdP(OH)_3)S_4(H_2O)_6Cl_3]_2(C_{36}H_{36}N_{24}O_{12})\}^{2+}$ (**33a**).

$\{[W_3(InCl_3)S_4(H_2O)_9]_2(C_{36}H_{36}N_{24}O_{12})\}Cl_4 \cdot 28\,H_2O$

34

$\{[Mo_3(SnCl_3)Se_4(H_2O)_6Cl_3][Mo_3(SnCl_3)Se_4(H_2O)_7Cl_2].$
$.(C_{36}H_{36}N_{24}O_{12})\}Cl \cdot 26\,H_2O$

35

Among the characteristic features of the crystal structure of the compound **34**, noteworthy are large channels (~7 Å in diameter) occupied by water molecules of solvation and Cl^- counterions. Crystallisation of the tin-containing molybdenum aqua complex with Q6 made it possible for the first time to isolate and structurally characterise the mixed chloro aqua complexes $[Mo_3(SnCl_3)Se_4(H_2O)_6Cl_3]$ and $[Mo_3(SnCl_3)Se_4(H_2O)_7Cl_2]^+$.

Hence, as a result of the good compatibility of the sizes and symmetry of the carbonyl groups at the portals of Q6 with those of the aqua ligands of the triangular (cubane) molybdenum and tungsten chalcogenide aqua complexes, extensive networks of hydrogen bonds are formed and the macrocycle becomes efficiently closed by the cluster lids.

As in the case of the thio and seleno analogues, the trinuclear molybdenum oxo cluster $[Mo_3O_4]^{4+}$ also interacts with Q6 through hydrogen bonds to give the supramolecular compound $\{[Mo_3O_4(H_2O)_6Cl_3]_2(C_{36}H_{36}N_{24}O_{12})\}Cl_2 \cdot 14\,H_2O$ (**36**). In this compound, the portals are closed by two lids formed by the cluster cations (Fig. 19).[88] However, unlike the compounds of Q6 with chalcogenide complexes, the plane of the Mo_3 triangle in the supramolecule **36** is tilted to the plane of the portal of the macrocycle (the tilting angle is 18.5°) and the cluster cation is shifted to one end of the portal resulting in the nonequivalence of the hydrogen bonds that are formed. These differences in the structures are attributed to the smaller size of the oxo cluster as compared to the sizes of the chalcogenide clusters and also to the higher acidity of the oxo complex.

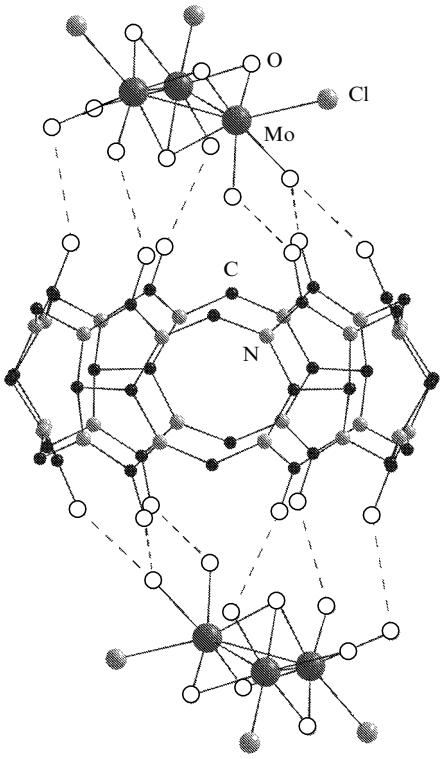


Figure 19. Structure of the supramolecule $\{[Mo_3O_4(H_2O)_6Cl_3]_2(C_{36}H_{36}N_{24}O_{12})\}^{2+}$ (**36**).

In the compound of Q6 with the binuclear niobium aqua complex $\{[Nb_2S_4(H_2O)_8](C_{36}H_{36}N_{24}O_{12})\}Cl_4 \cdot 15\,H_2O$ (**37**) (Fig. 20),[89] the portal of cucurbit[6]uril is incompletely closed by

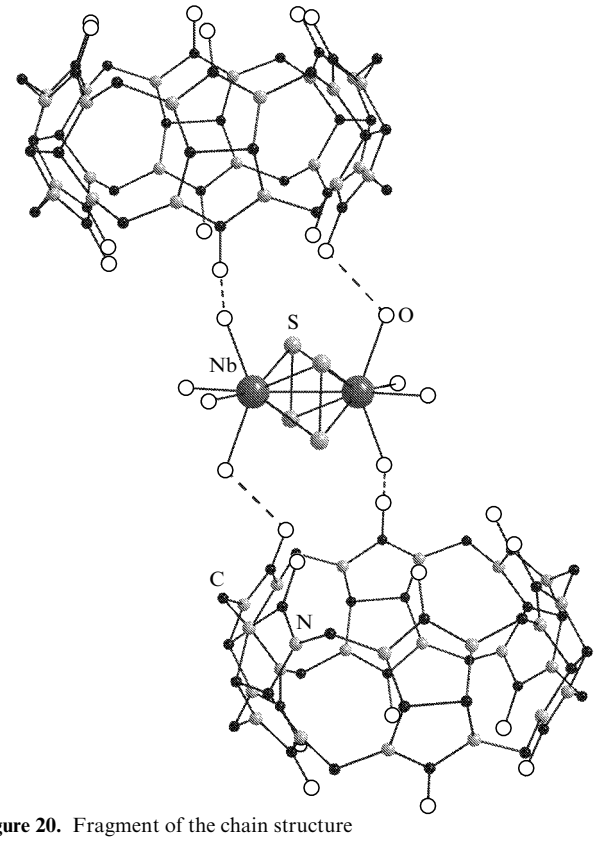


Figure 20. Fragment of the chain structure in $\{[Nb_2S_4(H_2O)_8](C_{36}H_{36}N_{24}O_{12})\}Cl_4 \cdot 15\,H_2O$ (**37**).

the binuclear cluster and the latter is shifted to one end of the portal because of spatial incompatibility. In this case, only two water molecules *trans*-coordinated to the niobium atom are bound directly to the portal oxygen atoms of two Q6 molecules. Several more water molecules present in the hydrophilic region of the portals are involved in additional hydrogen bonds between the aqua complex and macrocycle. In the crystal, the alternating cluster niobium aqua complexes and Q6 molecules are linked in chains.

V. Cucurbit[*n*]urils ($n = 5, 7-10$)

In addition to the above-considered macrocyclic cavitand cucurbit[6]uril (**5**) consisting of six methylene-bound glycoluril fragments, there are also cucurbiturils, which are composed of a smaller or larger number of these fragments and have the shape of barrels with smaller or larger diameters.

Crystals of the cyclic pentamer were first prepared by the reaction of dimethylglycoluril with formaldehyde and structurally characterised in 1992.[90] The decamethylcucurbit[5]uril has a slightly distorted symmetry D_{5h} and its methyl groups are located at the periphery of the molecule. In the cited study, the nomenclature for cucurbiturils was proposed by analogy with that used for calixarenes. According to this nomenclature, the number of glycoluril (or substituted glycoluril) fragments is denoted by the figure in brackets and the number of substituents is represented by the prefix.

In 2000, K Kim and co-workers[91] performed the reaction of glycoluril with formaldehyde in 9 M sulfuric acid and obtained a mixture of cyclisation products ($n = 5-11$) from which five-, seven- and eight-membered homologues of cucurbituril were isolated in very low yields. These compounds were structurally characterised. A comparison of their structural parameters (Table 1) demonstrates that the diameters of the cavity and portals of cucurbiturils increase as the number of glycoluril fragments in the rings is increased. A twofold increase in the inner diameter of the cavity on going from cucurbit[5]uril to cucurbit[8]uril leads to more than a fivefold increase in the volume of the cavity.

Table 1. Comparison of the structural parameters of cucurbit[*n*]urils.

Cucurbit[*n*]uril	Portal diameter /Å	Cavity diameter /Å	Cavity volume /Å^3	Molecule height /Å
$n = 5$	2.4	4.4	82	9.1
$n = 6$	4.0	5.5	164	9.1
$n = 7$	5.4	7.3	279	9.1
$n = 8$	6.9	8.8	479	9.1

Day *et al.*[92] studied the reactions of glycoluril with formaldehyde in H_2SO_4, HCl or HBF_4 solutions by electrospray mass spectrometry and ^{13}C NMR spectroscopy and established the existence of cucurbit[*n*]urils with $n = 5-16$ in solution. Based on the results of investigations into the effects of the nature of acid and its concentration, the concentrations of other reagents and the reaction temperature, a mechanism for the formation of different cucurbit[*n*]urils was proposed and the procedure for their synthesis optimised. Cucurbit[*n*]urils with $n = 5-10$ were isolated in pure form (the yields were 8%, 46%, 24%, 12%, 85% and 5%, respectively). Individual cucurbit[*n*]urils with larger numbers of glycoluril fragments are presently unavailable.

According to the results of theoretical calculations (density functional theory),[93] compounds containing six or seven glycoluril fragments are the most stable homologues of cucurbiturils, and decamethylcucurbit[5]uril is the most stable methyl-substituted derivative. These results agree with both the above-described experimental data and the distortions of the NCN angles at the carbon atoms of the bridging methylene groups that link the glycoluril fragments upon assembly.

As demonstrated above (see Section II), the presence of the hydrophobic cavity along with the polarised carbonyl groups at the portals of cucurbit[6]uril (**5**) are responsible for the formation of numerous inclusion compounds. The smaller cavity in cucurbiturils allows small molecules to be encapsulated and securely held, whereas larger-size molecular containers can accommodate bulkier guest molecules. Besides, an increase in the number of the oxygen atoms at the portals is favourable for the formation of a large number of hydrogen bonds and, correspondingly, more stable supramolecular compounds.

Decamethylcucurbit[5]uril can accommodate a molecule of nitric acid. Due to the fact that the molecular size of nitric acid matches the volume of the cavity, this guest molecule can form rather short contacts and be held in the cavity through both Coulombic interactions with the carbon atoms and hydrogen bonding with the carbonyl oxygen atoms of the macrocycle.[90] It was proved by electrospray mass spectrometric study of the ammonium acetate–decamethylcucurbit[5]uril system that the N_2, O_2, methanol and acetonitrile molecules can be included into the cavity, held in the cavity through the formation of the NH_4^+ lids and released upon the removal of these lids. This ability of the rather rigid macrocycle to accommodate small molecules is of interest for purification or separation of gas mixtures.[94]

The cavity volume of cucurbit[5]uril is insufficient for the inclusion of aromatic molecules. However, according to the data from solution ^1H NMR spectroscopy, the reaction with aliphatic hexylamine afforded an inclusion compound.[95] Hexylamine and 1,6-diaminohexane are not encapsulated into decamethylcucurbit[5]uril. According to the results of X-ray diffraction analysis, the terminal ammonium groups of 1,6-diaminohexane are involved in hydrogen bonds with the portal oxygen atoms of the adjacent macrocycles to form chains.

The water solubility of cucurbit[5]uril and decamethylcucurbit[5]uril as well as the solubility of cucurbit[6]uril are substantially increased upon the addition of salts of ammonium, alkali and alkaline earth metals due to formation of complexes with cations,[96] decamethylcucurbit[5]uril giving alkali metal complexes with composition 1 : 1.[97] Cucurbit[5]uril and decamethylcucurbit[5]uril serve as ligands in transition metal complexes (M^{2+} and M^{3+}). The formation constants of these complexes were determined by different experimental methods.[98] It has been also reported that decamethylcucurbit[5]uril in solution exhibits high selectivity toward Pb^{2+} cations.[97] No compounds of cucurbit[5]urils with metal cations have been structurally characterised.

Due to the larger cavity volumes in cucurbiturils consisting of seven or eight glycoluril fragments, these compounds can encapsulate bulky molecules whose sizes are too large to be included into compounds of Q6. Thus, Q7 forms inclusion compounds with *o*-carborane,[99] with the 2,3-diazabicyclo[2.2.2]oct-2-ene molecule, whose size matches excellently the cavity size and fills virtually the entire cavity resulting in a stable supramolecular compound.[100]

The cavity sizes of cucurbit[*n*]urils ($n = 8$, 10) allows smaller macrocycles to be included giving rise to rather rare compounds. Heating of an aqueous solution of Q8 with 1,4,7,10-tetraazacyclododecane (cyclen) and 1,4,8,10-tetraazacyclotetradecane (cyclam) afforded inclusion compounds, which have been structurally characterised. These compounds are stabilised primarily through van der Waals interactions between the inner macrocycle and the cavity of the outer macrocycle.[101] The small and large macrocycles are inclined to one another (the angle between the equatorial planes is $\sim 38^\circ$). The ability of tetraazamacrocycles to coordinate transition metal ions (these complexes are known as catalysts, for example, of epoxidation or DNA hydrolysis) was used in the reactions of the resulting inclusion compounds with Cu^{2+} and Zn^{2+} salts. The compound containing $[Cu(cyclen).(H_2O)]^{2+}$ in the cavity of Q8 was studied by X-ray diffraction analysis. In this compound, the macrocycles are virtually parallel to each other (Fig. 21) and the copper atom present in the inner

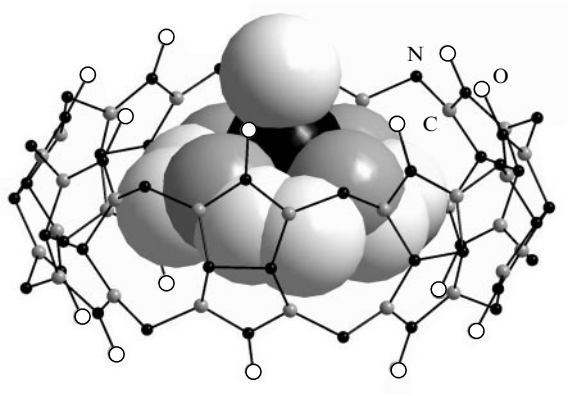


Figure 21. Structure of the compound containing $[Cu(cyclen)(H_2O)]^{2+}$ in the cavity of cucurbit[8]uril. The copper atom is represented by a large solid circle.

macrocycle additionally coordinates the water molecule, which is located in the plane of the portal of Q8 and can be replaced by other ligands. It should be noted that the cyclen coordinated by the metal atom is not encapsulated into cucurbit[8]uril because the formation of the complex with the metal atom enhances its conformational rigidity and hinders its inclusion into the cavity of Q8.

Recently, the unique compound of cucurbit[5]uril encapsulated into cucurbit[10]uril was prepared and characterised by X-ray diffraction analysis (Fig. 22).[102] The molecules of the macrocycles are inclined to each other (the angle between their equatorial planes is 64°). This fact along with the ^1H and ^{13}C NMR spectroscopic data provide evidence that the macrocycles in solution undergo free rotation with respect to each other (molecular analogue of a gyroscope). The cavity of Q5 contains the chloride anion and there is a system of hydrogen bonds between the portal oxygen atoms of both macrocycles and water molecules serving as the lids of the inner pentamer (see Fig. 22). It is believed that Q5 serves as a template for the assembly of larger-size cucurbiturils. Cucurbituril Q10 is as yet unavailable as an individual compound.

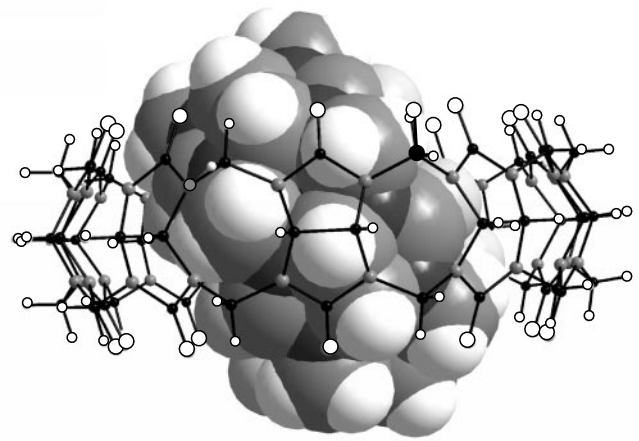


Figure 22. Structure of the inclusion compound of cucurbit[5]uril in cucurbit[10]uril.

A compound of cucurbit[7]uril was prepared in which the inorganic *cis*-$[SnCl_4(OH_2)_2]$ complex is completely encapsulated in the cavity of the macrocycle.[103, 104] A compound of Q7 with the trinuclear anionic chromium complex $[Cr_3O_{10}]^{2-}$ has been synthesised. In this compound, the molecules of the macrocycle are linked in hexagons to form large pores with a diameter of ~17 Å. The Q7 molecules, trinuclear anions and coordinated water molecules are linked through an extensive network of hydrogen bonds.[104]

Like cucurbit[6]uril, larger macrocycles form stable inclusion compounds with organic molecules whose protonated nitrogen atoms are linked to the polarised oxygen atoms at the portals through Coulombic interactions. Due to the larger sizes of the cavities, such bulky molecules as 2,6-bis(4,5-dihydro-1*H*-imidazol-2-yl)naphthalene can be accommodated in these macrocycles. Inclusion compounds with compositions 1:1 and 2:1 were prepared with cucurbit[7]uril and cucurbit[8]uril, respectively.[91] The results of quantum-chemical calculations (density functional theory) of the former compound demonstrated that not only van der Waals interactions and the hydrophobic effect but also hydrogen bonding between the protonated dihydroimidazole substituents and the portal oxygen atoms of Q7 play an important role in the formation of inclusion compounds.[105] Two such bulky molecules are located in an even larger inner cavity of Q8. According to the X-ray diffraction data, the imidazole substituents are located outside and are bound to the portals of Q8. Two naphthalene rings within the cavity are located parallel to each other at a distance of ~3.4 Å, which is indicative of π–π interactions between these rings (Fig. 23).[91]

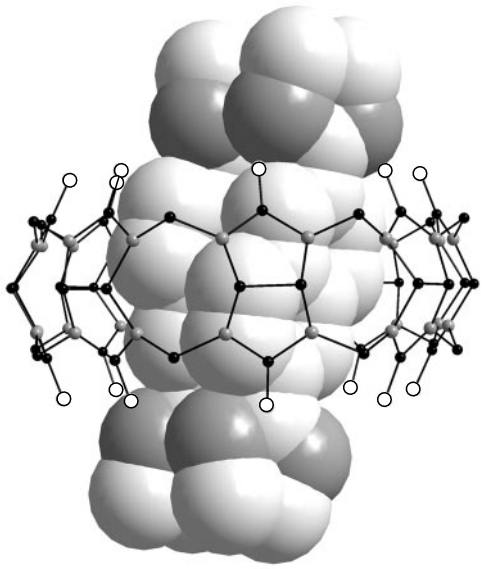
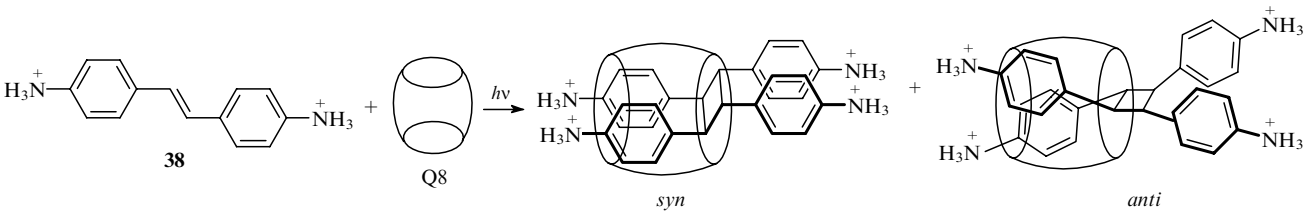


Figure 23. Structure of the inclusion compound of two 2,6-bis(4,5-dihydro-1*H*-imidazol-2-yl)naphthalene molecules in cucurbit[8]uril.

The encapsulation of two or more guest molecules into the cavity of the macromolecule is of great interest in view of the unique possibility of studying new types of stereoisomerism, bimolecular reactions and the behaviour of the molecules in the microenvironment. The Q8 molecule possessing a very large cavity provides rich possibilities for investigating such interactions.

K Kim and co-workers[106] were the first to study the selective encapsulation of two different guests into the cavity of one host. Interactions between two guests are the driving forces for the formation of supramolecular compounds. Two organic molecules, *viz*., the electron-deficient molecule **A** and molecule **B** acting as the electron donor, are accommodated in the cavity of Q8 [**A** is the *N*,*N*′-dimethyl-4,4′-bipyridinium cation (methylviologen $MeN^+C_{10}H_8N^+Me$) and **B** is 2,6-dihydroxynaphthalene or 1,4-dihydroxybenzene]. It should be noted that inclusion compounds with only either molecules **A** or molecules **B** were not obtained. The data from ^1H NMR, emission and UV spectroscopy are unambiguously indicative of strong charge-transfer interactions between the guest molecules due to their tight contact within the cavity. This interaction is much stronger than the interaction

Scheme 2



between these guest molecules if they are not encapsulated in the cavity of the cavitand. The resulting inclusion compounds are rather stable, which enables one to isolate and structurally characterise these compounds. For instance, the structure of the compound of Q8 with the unsymmetrical guest, *viz*., the cation of carboxybenzylviologen $CH_3N^+C_{10}H_8N^+CH_2C_6H_4CO_2H$, was established by X-ray diffraction analysis (Fig. 24). The methylpyridine fragment of this cation and the naphthalene ring of 2,6-dihydroxynaphthalene serving as the electron donor are located in the cavity virtually parallel to each other at a distance of 3.4 Å. This confirms the occurrence of a strong interaction, which was found by spectroscopic methods.

The ability of cucurbit[8]uril to accommodate two closely spaced guests located in particular orientations allows one to use this compound as the synthetic molecular container in which bimolecular reactions between specially selected guests can proceed with high regio- and stereoselectivity. Thus, photodimerisation between two molecules of 4,4′-diammoniostilbene dichloride (**38**) encapsulated into the cavity of Q8 proceeded with a much higher rate and high stereroselectivity (0.5 h, the ratio *syn* : *anti* > 95 : 5) as compared, for example, with this reaction in the presence of γ-cyclodextrin (72 h, the ratio *syn* : *anti* ~ 4 : 1).[107] According to the ^{1}H NMR spectroscopic data, Q8 forms a stable inclusion compound with two molecules **38** in solution even if the starting reagents are taken in a ratio of 1 : 1. In this case, the guests can occupy only particular positions, *viz*., with the parallel orientation of the alkene groups involved in photodimerisation (Scheme 2).

Owing to rather rigid structures and the ability to include various molecules and ions, cucurbiturils are very attractive compounds both as synthetic receptors and convenient building blocks for the construction of supramolecular materials. The detailed study of supramolecular compounds based on the known cucurbiturils is hindered, in particular, by their very low solubilities in water and organic solvents. Because of this, the most promising line of investigation of the chemistry of these compounds is the development of procedures for the preparation of soluble derivatives by the insertion of substituents containing different functional groups. One approach to the solution of this problem involves the synthesis of cucurbiturils by condensation of substituted glycolurils whose bridging CH groups contain either alkyl or aryl substituents instead of hydrogen atoms. However, decamethylcucurbit[5]uril containing peripheral methyl groups, which was synthesised from dimethylglycoluril,[90] also appeared to be a poorly soluble compound. The synthesis of cucurbiturils consisting of five or six cyclohexanoglycoluril fragments [108] is the first success after years of failed attempts. The resulting compounds were reliably characterised by different methods, among them X-ray diffraction analysis. The cyclohexane fragments formed by two carbon atoms of glycoluril and four methylene units are located at the periphery of cucurbiturils. The sizes of the cavities and portals are only slightly different from those in the unsubstituted analogues. These compounds are readily soluble in water, methanol and DMSO and moderately soluble in ethanol, DMF and acetonitrile. Good solubility in organic solvents enables one to use cyclohexanocucurbit[*n*]urils (n = 5, 6) as membrane ion-selective electrodes. Cyclohexanocucurbit[6]uril dissolved in water can be used for highly selective isolation of acetylcholine (neurotransmitter).[108]

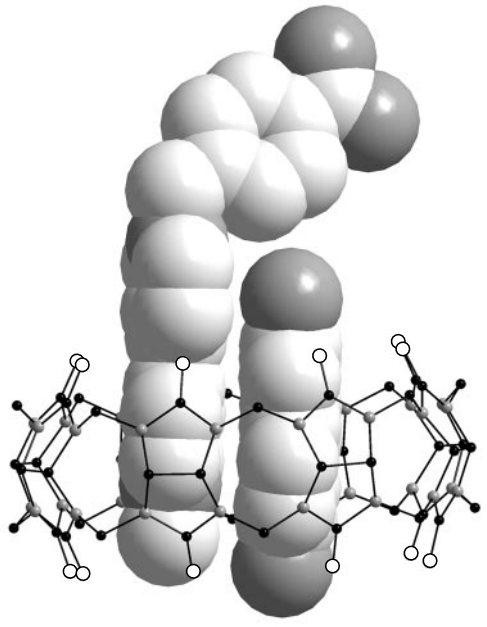


Figure 24. Encapsulation of 'heteroguests', *viz*., electron-deficient (carboxybenzylmethylviologen) and electron-donating (2,6-dihydroxynaphthalene) molecules in cucurbit[8]uril.

* * *

To summarise, the recent advances in the chemistry of cucurbiturils surveyed in the present review provide evidence that these macrocyclic organic molecules can be considered as molecular building blocks for the directed construction of nanosized highly ordered supramolecular compounds. The advantages of cucurbiturils over other macrocyclic cavitands are the presence of a rather rigid hydrophobic inner cavity along with hydrophilic portals, which can form supramolecular compounds with metal aqua complexes through systems of hydrogen bonds. Large cucurbit[*n*]urils (n = 7–10), which became readily available in recent years, show considerable promise. Thus, large molecular containers can encapsulate bulkier guests, and the inclusion of two or more molecules provides a unique possibility for studying new types of stereoisomerism, bimolecular reactions and molecular behaviour in a microenvironment. This review will hopefully be found interesting and useful and contribute to the progress of the chemistry of cucurbiturils.

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