INCLUSION COMPOUNDS

1. Introduction

The history of inclusion compounds (1,2) dates back to 1823 when Michael Faraday reported the preparation of the clathrate hydrate of chlorine. Other early observations include the preparation of graphite intercalates in 1841, the β-hydroquinone H_2S clathrate in 1849, the choleic acids in 1885, the cyclodextrin inclusion compounds in 1891, and the Hofmann's clathrate in 1897. Later milestones of the development of inclusion compounds refer to the tri-*o*-thymotide benzene inclusion compound in 1914, phenol clathrates in 1935, and urea adducts in 1940.

Perhaps the first turning point in understanding the nature of inclusion compounds occurred in the late 1940s with pioneering x-ray crystal studies on the β-hydroquinone clathrates (3). At this time the term clathrate, derived from the Latin word *clathratus* meaning enclosed by the bars of a grating, was coined to describe the principle of these systems possessing cage-like structures for the accommodation of a secondary species (4). The more general term inclusion compound (from the German *Einschlu*βverbindung) was introduced in 1952 by the German chemist Cramer (5) who gave the following definition: "All these compounds namely have in common the ability to incorporate into the cavities of their own molecules, or within their lattices, other molecules of suitable size, spatially to enfold them, that is to hold them, though not by main or secondary valence forces, but mostly by physical imprisonment." A scheme for this process is given in Figure 1.

The real breakthrough in inclusion chemistry, however, is attached to the discovery of crown compounds by Pedersen (6) in the mid-1960s. From this time, a tremendous variety of compounds and materials all having the attribute of inclusion were developed giving rise to what is called host–guest chemistry (7,8), a typical feature of which is accommodation of a complementary guest species into a concave host framework involving a molecular recognition process (9–11) such as imaged by the complementarity of a lock and a key (12) (see Fig. 1). For their pioneering studies in this field, the triumvirate Pedersen (13), Cram (14), and Lehn (15) were awarded the 1987 Nobel Prize in chemistry (16). Logically a new broad area of chemistry grew up on this basis during the last two decades. It is called supramolecular chemistry (17–20) and means the chemistry beyond the molecule (15). Here, noncovalent bonds and spatial fit between molecular individuals that form a specific supramolecular complex (inclusion complex) are in the foreground. This new direction of science and thinking where concave frameworks and containers rather than convex molecular structures are the top target and which is understood as the third important phase of chemistry, is expected to have its culminating point ahead.

Notwithstanding the immense number and great variety of inclusion compounds (21,22), all of them may be classified into three main categories (2) being either a complex, a cavitate, or a clathrate according to the criteria given in Figure 2. Typical examples for each class of inclusion compounds are the crown complexes, the calix–cavitates, and the hydroquinone clathrates but in many of the recently known inclusion situations there are borderline cases treated as complex–clathrate hybrids (coordinatoclathrates or clathratocomplexes

depending on the dominant inclusion character). By way of contrast, the description addition compound (adduct) may be used to the best advantage if a cavity does not exist either at the host molecule or in the lattice build-up. Inclusion compound, therefore, is the generic term of choice which refers to the presence of any not precisely defined cavity. In a more detailed topological characterization (23), there are two-dimensional open intercalates (layer- or sandwich-type inclusions), one-dimensional open channel inclusions (tubulates), and totally enclosed cage inclusions (cryptates).

2. Intramolecular Cavity Inclusions: Cavitates

2.1. Crown Macroring Inclusion Compounds (Coronates). Prototypical crown macrorings are cyclic oligoethers such as given by formulae (**1–4**) (Fig. 3). Inside the ring they make available a negatively polarized cavity capable of accommodating metal ions to form crown cation inclusion complexes (coronates) (24–26). In particular alkali and alkaline earth metal ions that match the ring interior in size and give rise to high ion–dipole interaction are involved and make these compounds unique (eg, Li^+/12-crown-4 [294-93-9] (**1**), Na^+/15-crown-5 [33100-27-5] (**2**), Ba^{2+}/18-crown-6 [17455-13-9] (**3**), K^+/18-crown-6 (**3**), Cs^+/21-crown-7[33089-36-0] (**4**). Ammonium cations and uncharged organic molecules suitable to form crown–guest hydrogen bonds are also complexed. Oxygen donor atoms have been replaced by nitrogen, sulfur, and other heteroatoms to give hetero crown ethers (27). They are efficient complexants of soft transition metal ions (Ag^+, Hg^{2+}, etc).

2.2. Cryptates. They are inclusion complexes of quasispherical analogues of crown macrorings (cryptands) having bi- or oligocyclic frameworks (28,29). Important examples of different topology are illustrated with formulae (**5–8**), and (**9,10**) (Fig. 3). Compared with the monocyclic crown hosts they provide enforced cavities, thus giving rise to increased stability and selectivity of inclusion complexes, eg, bicyclic cryptands (**5–8**) preferably accommodate H^+, Li^+, Na^+, and K^+, in this order. The spherical cryptand (**9**), (soccer ball molecule) with tetrahedral orientation of nitrogen atoms strongly complexes the ammonium cation; the cylindrical cryptand (**10**) is well suited to give dinuclear cryptates with size matching diammonium cations.

2.3. Podates. Acyclic analogues of crown ethers/coronands and cryptands (podands, eg, (**11**) (30) are also capable of forming inclusion compounds (podates) with cations and uncharged organic molecules, the latter being endowed with a hydrogen bond functionality. Podates normally are less stable than coronates and cryptates but have favorable kinetics.

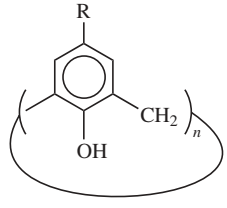
2.4. Inclusions of Other Crown Analogues. A variety of crown analogues and hybrid modifications (24–28) with other topological features (lariat ethers (31,32), octopus molecules (33), spherands (eg, (12) (34), torands (35)) including chiral derivatives (36) have been prepared and demonstrated to show particular inclusion properties such as chiroselective inclusion (Fig. 4) (37) or formation of extremely stable complexes ($K_s'' > (Li^+)$ for (12) $> 7 \times 10^{16}$ in $CDCl_3$ saturated with D_2O at 25°C) (34).

For thermodynamic (stability constants) and kinetic data involving crown-type inclusion complexes see References r38 and r39; structural results in References r40–r42 (see also CHELATING AGENTS).

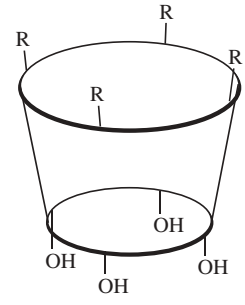
2.5. Cyclophane Host Inclusion Compounds. Cyclophane-type hosts are determined by a polycyclic framework composed of rigid aromatic groups and linkers rather than by the presence of a set of donor heteroatoms typical of crown compounds and their analogues (43–45). Today, they represent the central class of synthetic receptors in molecular recognition and inclusion. Inclusion phenomena involve all kinds of *ortho-, meta-*, and *para*-bridged aromatic host topologies including macrorings, intercalands, pockets, open vessels, and macrocages. They may have *exo-* or *endo*-polar groups and additional functions for solubilization and/or complexation. Typical examples of this host design and of respective inclusion compounds are given by formulae (**15–18**) (Fig. 5) showing that hydrogen bonds, π-π-stacking interactions, and steric fit all play important roles. Complementary guest species to be included are shapely molecules of suitable size involving hydrogen bond donors and acceptors or aromatic compounds. Certainly, the case of inclusion having the highest level of imprisonment is shown with formula (**17**). According to the topological image, hosts of this type have been called carcerands and their inclusion compounds are named carceplexes (46). Incarceration of the guest is permanent here. Escape from the host interior is impossible without cleavage of covalent bonds of the container shell. Other namings for particular types of cyclophane hosts based on structural features are cryptophane (aromatic cryptands) (47) or collarene (collar-like hosts) (48,49). Moreover, macrocyclic heteroaromatic analogues containing the bipyridino–paraquat building block, were designed that form charge-transfer type inclusion complexes with aromatic guests having electron-donating substituents (50). The principle has been used masterfully to make formation of self-organized host–guest rotaxanes and catenanes possible (51). Chiral analogues of cyclophane hosts for chiroselective inclusion of guest molecules are also available (44).

2.6. Calixarene Inclusion Compounds. Calixarenes are a particular class of metacyclophane hosts bearing protonizable hydroxy groups (52,53). In the original sense, they are cyclic oligomers produced by condensation of *p*-substituted phenols with formaldehyde (19). The class name calixarene was chosen due to the characteristic cone- or calix-like conformation (20), especially of such molecules with four aromatic moieties (calix[4]arene); the higher homologues (calix[6]arene and calix[8]arene) are more flexible. An enormous variety of such compounds with different ring sizes and substituents have been synthesized since the early 1970s. Although broad in variation, most of these compounds derive from the two prototypes *p-t*-butylcalix[4]arene [60705-62-6] (21) and *C*-methylcalix[4]resorcinarene [74708-10-4] (22) having hydroxy groups either at the lower or upper rims of the calix. Compound (21) is the one-pot cyclocondensation product of 4-*t*-butylphenol [98-54-4] with formaldehyde, (22) of resorcinol with acetaldehyde. Special calixarenes where the *t*-butyl groups of (21) (and higher ring analogues) are removed and replaced by other functional groups or more sophisticated constructions involving different phenolic or resorcinol units require a stepwise synthesis. The same is true for compounds with bridged *p*-positions and systems where two calixarenes are connected via their

p-positions. Note that carcerate (17) and cavitate (18) of Figure 5 are based on calix[4]resorcinarene (22) as the supporting frame. Modification of the phenolic hydroxyl makes special calixarenes available (54).



(**19**)



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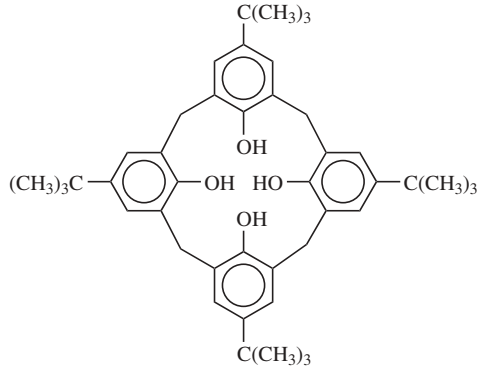
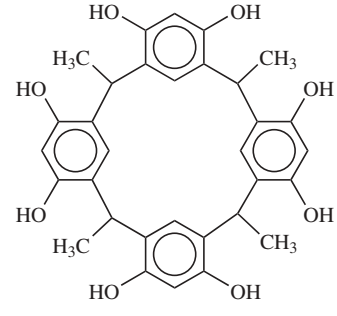


(**21**)



(**22**)

Many calixarenes show a spontaneous ability to retain the solvent from which they are crystallized (eg, benzene, toluene, xylene, anisole, chloroform) to give a solid state inclusion compound (52,53). They may be divided into three main categories: intramolecular, cage-type, and intermolecular. In the 1:1 inclusion compound between (**21**) and toluene, the guest is accommodated into the hydrophobic pocket of the host cone conformation. Anisole yields a 2:1 cage inclusion compound with (**21**) where the guest is enclosed in the cage formed by two facing intramolecular cavities of two calixarenes. In the case of the 1:1 inclusion compound between the bulkily substituted *p*-(1,1,3,3-tetramethylbutyl)calix[4]arene and toluene partial filling of the cone cavity by *t*-butyl groups of neighboring hosts is observed. On the other hand, the bulky chains give rise to interstitial lattice space including the guest, a clathrate type inclusion compound. Reference r53 depicts these three inclusion compounds described.

Amalgamation of structural units typical of crowns and calixarenes has led to the development of calixpodands, calixcrowns, and calixspherands (55). Naturally they behave as cation complexants rather than inclusion hosts for uncharged molecules.

2.7. Cyclodextrin Inclusion Compounds. Cyclodextrins comprise a family of cyclic oligosaccharides obtained from starch by enzymatic degradation (56,57). Three of them, the so-called α-, β-, and γ-cyclodextrins (**23**) Fig. 6**a**), are of great importance. They are composed of 6, 7, and 8 glucose units, respectively, and form cone structures similar to the calixarenes (Fig. 6**b**). Thus, the cyclodextrins may be understood as natural analogues of the artificial calixarenes. Dimensions of the cone-shaped molecular cylinders of α-, β-, and γ-cyclodextrin are given in Table 1. In contrast with the calixarenes, the cavities are lined on both rims with hydroxyl groups. The interior of the cavity is hydrophobic whereas the outside is hydrophilic. These unique properties explain some of the unusual features of the cyclodextrins. They are easily soluble in water and form inclusion compounds with a wide variety of guest species in solution and in the solid state. Nobel gases, paraffins, alcohols, carboxylic acids, aromatic dyes, benzene derivatives, salts, etc, are included, just to name a few of a long list of potential substances; the only obvious requirement is that the guest must fit into the cavity even if only partly. It has been confirmed via x-ray crystallography that the central cavities of α-and β-cyclodextrin contain two and nine water molecules, respectively. On formation of inclusion compounds, the water molecules are displaced by the guests.

Packing of the cyclodextrin molecules (α, β, β) within the crystal lattice of inclusion compounds (58,59) occurs in one of two modes, described as cage and channel structures (Fig. 7). In channel-type inclusions, cyclodextrin molecules are stacked on top of one another like coins in a roll producing endless channels in which guest molecules are embedded (Fig. 7**a**). In crystal structures of the cage type, the cavity of one cyclodextrin molecule is blocked off on both sides by neighboring cyclodextrin molecules packed crosswise in herringbone fashion (Fig. 7**b**), or in a motif reminiscent of bricks in a wall (Fig. 7**c**).

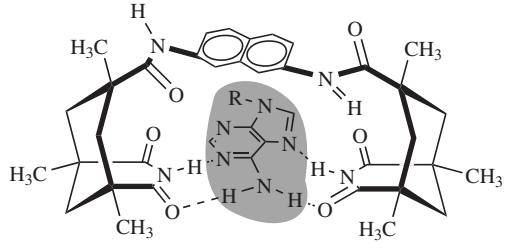
Thermodynamics and kinetics of cyclodextrin inclusion compounds have been reported and mechanisms have been suggested by which the guests are enclosed in the cyclodextrin ring (60). These factors and others have led to structural modifications involving the addition of flexible and rigid caps to one end of the cyclodextrin cylinder (61) or linkage of two cyclodextrins (duplex cyclodextrin) (62) which proved efficient in enhancement of the guest binding. More sophisticated functional systems based on cyclodextrins as models for several enzymes (63) have also been constructed.

2.8. Amylose Inclusion Compounds. Like cyclodextrins (Fig. 6**a**) amylose also consists of glucose units (5). However, amylose is not macrocyclic in structure and its mol wt is much higher (300,000–1 million, depending on the starch source from which it is derived). Amylose forms inclusion compounds mostly with long-chain fatty acids but also with iodine to give the well-known blue starch–iodine complex (64). These inclusion compounds of amylose apparently are of channel character (Fig. 8). In the latter case, iodine atoms are joined together to form a long, straight polyiodide chain spirally wrapped by the amylose polymer. Neither the helical configuration of the starch molecule nor the chain of iodine atoms is stable except for inclusion structures of this general type (see CARBOHYDRATES; STARCH).

2.9. Cucurbituril Inclusion Compounds. Cucurbituril [80262-44-8] (**24**) is a nonadecacyclic cage molecule readily produced by self-assembly from

urea, glyoxal, and formaldehyde (Fig. 9**a**) (65). The designated trivial name derives from the general resemblance of models of the molecule to a pumpkin (of botanical family Cucurbitaceae) (66). The most notable feature as regards molecular inclusion is the presence of an internal cavity of approximately 0.55 nm diameter within the rigid macrocyclic structure, to which access is provided by a 0.4 nm diameter occulus situated among the carbonyl groups on both the top and the bottom of the molecule. The cavity inside of cucurbituril can hold small organic molecules with a particular preference for alkylammonium ions (Fig. 9**b**). This has been established crystallographically and in solution by nmr spectroscopy. Solid complexes of (**24**) with dye-stuffs (67) as well as the synthesis of the next lower analogue (decamethylcucurbit[5]uril) (68) have been reported.

2.10. Molecular Cleft Inclusion Compounds. Nonmacrocyclic hosts for the inclusion of uncharged guests that contain preorganized molecular clefts aligned with binding sites are a promising new development (69–71). Owing to structural mimicry and depending on the origin they are called molecular clefts, clips, or tweezers. One example (**25**) shows the host design and illustrates the binding and inclusion principles for adenines as guest molecules. Specific host–guest hydrogen bonds and π-π-stacking interactions are decisive factors for inclusion here. This general receptor design for the docking of guests appears to be a clever approach to making enzyme mimics and catalytic systems (11).



(**25**)

2.11. Anionic Guest Inclusion Compounds. Artificial inclusion hosts for anions (72–75) should contain cationic or electron-deficient binding sites to complement and neutralize the negative charge of these guests, opposite to the way cations are complexed (crown compounds). Cationic centers can be included in the covalent framework of the host (eg, ammonium, guanidinium, or phosphonium groups) and may also incorporate hydrogen bond donor groups, or (similar to metallo enzymes) cationic substructures of so-called cascade complexes may serve as anchor groups for anionic guests. Electron-deficient binding sites are provided by Lewis acid centers (boron, mercury, and tin) incorporated in the host frame. Representative examples for each category are illustrated in Figure 10. The hexaprotonated bis-tren cryptand of (**26**) selectively includes the linear azide anion which ideally matches the cavity and is held by the two arrays of three $N^+-H \cdots N^-$ hydrogen bonds. In a cascade type of inclusion (**27**) two dien dicobalt substructures of a macroring complex to oxalate. In (**28**) a fluoride anion is cryptated by a tin-containing host. Since anions display important roles

in biology, inclusion chemistry of anions is promising, not least for the potential applications in medicine.

3. Extramolecular Cavity Inclusions: Lattice-Type Inclusion Compounds, Clathrates

3.1. Hydrate Inclusion Compounds. These compounds are characterized by a host lattice constructed wholly or principally from hydrogen-bonded water molecules closely analogous to that of ice (76–79). No less than four different categories can be classified although a species termed as clathrate hydrate is most frequent. Here the guests are trapped inside isolated cavities of the water matrix. The substances with which water forms clathrate hydrates are largely gases or liquids of low boiling point. This is why the clathrate hydrates are historically known as gas hydrates. Such hydrates fall into two groups (80). The first usually contains six guest molecules combined with 46 water molecules; the second contains one guest molecule for each 17 water molecules. The guests in the first group are small molecules such as Cl_2, Br_2, SO_2, H_2S, CH_4, C_2H_6, CH_3Cl, or CH_2Cl_2; in the second group of gas hydrates slightly larger guest molecules are found, among them $CHCl_3$, C_2H_5Cl, CH_3I, CF_2BrCl, and C_3H_8.

The structural feature common to all but a few clathrate hydrates is a pentagonal dodecahedron of oxygen atoms arising from hydrogen-bonded water molecules (Fig. 11**a**) (76). They are the main building blocks of the clathrate structure. Since space cannot be filled completely by any packing arrangement of dodecahedrons, some interstitial space must remain. It is in these spaces where the guest molecules are held. Actually other polyhedra (14-hedra and 16-hedra) do occur which, together with the regular 12-hedra, allow a periodical 3D arrangement. In the first group of clathrate hydrates (see above), the host framework is composed of 12- and 14-hedra in the ratio of 1/3 (Fig. 11**b**). When only the larger voids are occupied, the composition is as given (46 $H_2\dot{O}6$ guest). The second group of clathrate hydrates formed with larger guests are composed of 12- and 16-hedra. The unit cell consists of 136 water molecules oriented as dodecahedra enclosing 24 interstitial spaces, 8 of which are larger than the other 16. If only the larger voids are occupied, the composition is 136 $H_2\dot{O}8$ guest. However, in both cases and if appropriately sized guests are present, both types of holes may be occupied to give mixed clathrate hydrates. Mention should also be made of the existence of alkylonium salt hydrates and amine hydrates involving other structures and more complex polyhedra than those specified above (76). Proteins also form highly hydrated crystals that may be seen as modified clathrate structures (81).

3.2. Hofmann- and Werner-Type Inclusion Compounds. There is a wide range of clathrates having as the host component inorganic coordination compounds represented by the general formulae $M(NH_3)_2\ M'(CN)_4$ and $M''\ X_2Y_4$. The first formula is typical of Hofmann-type clathrates (79,82) where M stands for Mn, Fe, Co, Ni, Cu, Zn, or Cd and M′ denotes Ni, Pd, or Pt. The second specifies the Werner-type (83,84) clathrates for M″ being a divalent cation (Fe, Co, Ni, Cu, Zn, Cd, Mn, Hg, Cr), X an anionic ligand (NCS^-, NCO^-, CN^-,

NO_3^-, NO^{-2}, Cl^-, Br^-, I^-) and Y an electrically neutral ligand such as pyridine, substituted pyridines, or isoquinoline.

In Hofmann clathrates two guests usually belong to one host complex; the guest is benzene, thiophene, furan, pyrrole, aniline, or phenol. The prototype is $Ni(NH_3)_2Ni(CN)_4 \cdot 2\,C_6H_6$ (Hofmann's compound) (85). The structure consists of planar layers containing the metal atoms and the cyanide groups with the NH_3 groups protruding above and below these layers. The ammonia groups then define the void wherein the guest molecule resides. As a consequence of the essentially fixed host lattice, a selectivity towards the length of the guest molecule is provided; thus benzene can be accommodated but the longer toluene molecule cannot. Extensive studies of these host lattices have been made with respect to structure, stability, and selectivity, and several interesting modifications have been performed by using diamines as bridging units or tetrahedral M′(CN)4 moieties replacing the planar complexes (86).

A wide variety of guest molecules may be trapped by the Werner-type crystalline host lattice, ranging, eg, from noble gases to condensed aromatic hydrocarbons. These clathrates may be formed from solution or by sorption. Kinetics of sorption–desorption have been studied (83).

3.3. Inclusion Compounds of Urea, Thiourea, and Selenourea

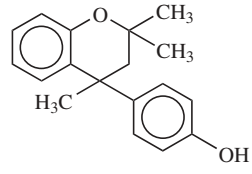
They are characteristic of channel host structures (87,88). Each channel in crystalline urea is formed by three interpenetrating spirals of molecules held together by hydrogen bonding between thenitrogen and oxygen atoms, thus forming long tubular cavities in which the guest molecules reside (Fig. 12**a**) (79,89,90). The spirals are randomly right- or left-handed. The inside diameter of the channels is about 0.5 nm which is just the right size to accommodate the straight-chain hydrocarbons (*n*-alkanes and *n*-alkenes). Any such substance can pack into the channels provided that the hydrocarbon has six or more carbon atoms. Urea[57-13-6] forms inclusion compounds not only with hydrocarbons but also with ethers, aldehydes, ketones, esters, carboxylic acids, alcohols, amines, nitriles, thiols, and sulfides, that exceed the lower limit of carbon atoms. Aromatic compounds also form inclusions if the benzene ring carries a long chain substituent (eg, octadecylbenzene).

Channels in crystals of thiourea [62-56-6] (87) are comparable but, as a consequence of the larger size of the sulfur atom, have larger cross-sectional areas (0.7 nm) and can trap branched-chain, alicyclic, and other molecules of similar dimensions including polychlorinated hydrocarbons. But they do not include the straight-chain hydrocarbons that work so well with urea.

Selenourea [630-10-4] like urea and thioruea can form channel inclusion compounds (87) with a variety of hydrocarbons. Though the difference in channel diameter between thiourea and selenourea is small, selenourea seems to be much more selective for the inclusion of certain guest molecules (eg, cis/trans isomers).

3.4. Inclusion Compounds of Phenolic Hosts. Inclusion compounds involving phenols, hydroquinone, Dianin's compound, and related molecules (91) mostly consist of cage-like structures with the guest molecules lying trapped in the cavities, a feature that initially prompted the term clathrate. The principle in forming these cages is the linkage of the OH groups of six host molecules, eg, phenol, by hydrogen bonds such that the oxygen atoms form a hexagon and alternate aromatic groups point above and below this hexagon (Fig. 13**a**) (79,88,92).

In this way, a large open structure is created, which may be visualized as consisting of two interpenetrating cups, each cup formed by three phenolic molecules. The networks, however, do not fill the available space but remain a roughly spherical cavity for accommodation of the guests. In case of hydroquinone, both ends of the molecule are similarly involved, and a three-dimensional hydrogen-bonded network results (Fig. 13**b**) (4). An important feature of Dianin's compound[472-41-3] (29) in addition to the hexameric unit, is the existence of a waist halfway up the cavity formed by six inward pointing methyls whereas the lateral packing leaves no significant space (93). This has given rise to structural modifications of Dianin's compound (thiachroman, noranalogue, etc) for controlling cavity shape (91).



(**29**)

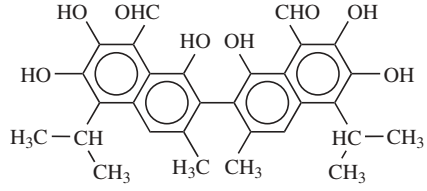
Host lattices of phenol and simple substituted phenols (91,93) usually provide an extra (relatively large) lattice space, in addition to the hydrogen-bonded cage (~1.5 nm effective length and 0.4–0.45 nm free diameter, and 0.45 nm free diameter, respectively, in the case of phenol). Both cavities are capable of including suitably sized guest molecules involving noble gases or other volatile species such as H_2S, SO_2, CO_2, CS_2, HCl, HBr, CH_2Cl_2, and CH_2CHF.

Examples of the hydroquinone inclusion compounds (91,93) are those formed with HCl, H_2S, SO_2, CH_3OH, HCOOH, CH_3CN (but not with C_2H_5OH, CH_3COOH or any other nitrile), benzene, thiophene, CH_4, noble gases, and other substances that can fit and remain inside the 0.4 nm cavities of the host crystals. That is, clathration of hydroquinone is essentially physical in nature, not chemical. A less than stoichiometric ratio of the guest may result, indicating that not all void spaces are occupied during formation of the framework. Hydroquinone clathrates are very stable at atmospheric pressure and room temperature. Thermodynamic studies suggest them to be entropic in nature (88).

Crystals of Dianin's compound (91,93) have been shown to accommodate more than 50 diverse guest species into the hour-glass shaped cages of about 1.1 nm length and 0.43 nm width, for example argon, I_2, SO_2, SF_6, NH_3, CH_3OH *n*-heptanol, glycerol, di-*t*-butylnitroxide, $CHCl_3$, CCl_4, decalin, aromatic hydrocarbons, and derivatives. The host:guest ratio ranges from a low of 2:1 up to 9:1, depending on the size relationship, with 6:1 being the most frequent ratio observed. Analogues of Dianin's compound (91,93) provide increased maximum diameters of the cage (0.71 nm for analogue with a methyl group removed) and reduced cavity length (0.8 nm for 8-methyl-substituted derivative of the thia-analogue) thus giving rise to selective clathration properties.

3.5. Inclusion Compounds of Gossypol. The oligophenolic compound gossypol[303-45-7] (30), a natural product and biologically active compound, has proved to be an efficient inclusion host for a variety of low molecular weight organic substances (94). It forms clathrates of all possible types: cage, channel,

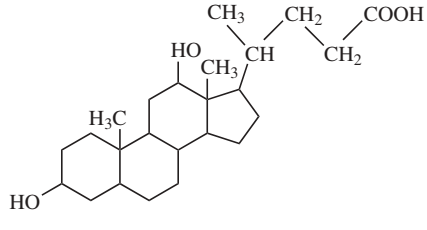
and layer inclusions (95). Twenty groups of gossypol isostructural clathrates have been established. For the crystal forms of gossypol, spatial isolation of hydrophilic and hydrophobic areas is observed leading to the availability of hydrophobic and hydrophilic inclusion cavities. Gossypol itself possesses unusual polymorphism (95), consisting in the formation of eight crystallographically identified polymorphs.



(**30**)

3.6. Inclusion Compounds of Deoxycholic Acid (Choleic Acids)

Deoxycholic acid[83-44-3] (DCA) (**31**) forms stable inclusion compounds with a wide variety of guests involving aliphatic, alicyclic, and aromatic hydrocarbons, alcohols, ketones, fatty acids, esters, ethers, phenols, azo dyes, nitriles, peroxides, and amines (96). The guests are generally trapped in channels that run through the host lattice (88,90). These inclusion compounds are called choleic acids . They can be grouped into three crystal systems: orthorhombic (most commonly observed and showing superior inclusion property), tetragonal, and hexagonal (96). The characteristic structural unit of the orthorhombic and tetragonal inclusion crystals is a bilayer developed by two rows of head-to-tail hydrogen-bonded molecules that are interconnected via hydrogen bonds. They assemble, related to a 2_1 or 4_1 axis, to give rise to channel space (Fig. 14**a**), which may have a variable size and shape depending on the mutual positions of the bilayers. This accounts for the ability of the (orthorhombic) host lattice to accommodate guest molecules of very different dimensions. The hexagonal host lattice is characterized by the packing of hollow helices of deoxycholic acid molecules, generated by a 6_5 axis (Fig. 14**b**). The cavity of the helix has a diameter of about 0.4 nm, which allows the inclusion only of small size or thread-like guest molecules. According to the nature of the inner channel surface, being either hydrophobic or hydrophilic, the hexagonal host can be utilized to receive polar guest molecules while the orthorhombic one prefers apolar guests. This is in line with the packing diagrams for the two crystal systems shown in Figure 14, the guest compounds being phenanthrene and dimethyl sulfoxide–water, respectively.



(**31**)

3.7. Inclusion Compounds of Macrocyclic and Oligocyclic Lattice Hosts. As a common feature, all these hosts (Fig. 15) belong to the trigonal class of symmetry and most inclusions are of channel structure.

Perhydrotriphenylene[15074-91-6] (**32**) comprises four cyclohexane chairs anellated in such a way as to give D_3 symmetry which makes the molecule chiral. Inclusion formation (79,97) is broad involving a great number of linear aliphatic hydrocarbons, ethers, alcohols, acids, and esters, but also branched compounds such as 2,2,4-trimethylpentane as well as cyclic compounds such as benzene, toluene, cyclohexane, dioxane, or spherical and quasispherical molecules such as CCl_4, $CHCl_3$, etc. It has been stated that it took longer to find a simple compound which would not form an inclusion than forming one. The stoichiometry of perhydrotriphenylene inclusions is not, in general, simple or even-numbered, typical of a channel structure with different repeat distances for the occluded guests. In case of the *n*-heptane inclusion compound c(98), the structure is composed of stacks of superimposed host molecules leaving channel cavities of about 0.5 nm diameter that contain the guests.

Hosts of cyclotriphosphazenez type are tribladed paddle wheel-shaped molecules (see Fig. 16) of which [311-03-5] (**33**) is the prototype and other substitution products between hexachlorophosphazene and aromatic diols or diamines are structural variations. The cyclotriphosphazenes, eg, (**33**), have been shown to form inclusion compounds with a wide variety of guest molecules (99,100). Examples include aliphatic and aromatic hydrocarbons, ethers, esters, ketones, nitriles, carbon disulfide, and ethanol. The guest molecular dimensions vary from those of small molecules (see above) to larger species such as decalin, norbornadiene, or short polymer molecules. A particular feature of (**33**) is that inclusions are formed both by crystallization from the guest solvent and by direct exposure of the host to the vapor or liquid guest. Replacement of the included guest has also been demonstrated. A typical host lattice of (**33**) consists of alternating layers of molecules. Superposition of the layers leads to tunnels (0.45–0.5 nm in diameter) in which the guests reside (Fig. 16). However, there are also structures with guests trapped in cavities rather than in tunnels.

Cyclotriveratrylene[1180-60-5] (**34**) is a cyclocondensation product of veratrole with formaldehyde. It possesses a stable trigonal crown conformation and forms crystalline inclusion compounds with benzene, chlorobenzene, toluene, thiophene, decalin, chloroform, acetone, carbon disulfide, acetic acid, and butyric acid (101). Their structures consist of columns of cyclotriveratrylene molecules that are not amenable to close packing and provide channels into which the guests are accommodated. A number of modified host structures, derived from prototype (**34**) have been prepared. The hexaphenol analogue cyclotricatechylene also yields well-defined channel inclusions (101). They involve mostly polar guests and the structures are held by hydrogen bonding.

Tri-*o*-thymotide[2281-45-0] (**35**) and its derivatives are cyclocondensation products of salicyclic acids, and adopt an asymmetric propeller-like conformation. Inclusion compounds of thymotides, involving benzene, aliphatic ethers, alkyl halides, alcohols, and ketones, crystallize in a variety of space groups and display different modes of guest accommodation: cages, quasiuniform channels, and channels of noticeably variable section (79,102). The parameters governing the crystal form include primarily the size of the guest and, to a lesser extent,

the chemical nature and the experimental conditions. It has been observed that guest molecules of length less than 0.9 nm give rise to cage-type crystals, whereas those of greater length are accommodated in uniform section channels; larger molecules (eg, stilbene) induce crystallization in channels of variable section. A host:guest stoichiometric ratio of 2:1 is usual but not general. Once formed, the inclusion compounds of (**35**) prove to be thermally stable. Tri-*o*-thymotide clathrates are reported to undergo spontaneous resolution, thus being attractive optical resolving agents for included guest species (102). Trianthranilides, the nitrogen analogues of (**35**), have also been synthesized (103). They exist in propeller and helical conformations. Their inclusion properties are less studied.

3.8. Designed Organic Host Lattices. As contrasted with the previous clathrate hosts, which have mostly been observed accidentally, these new hosts are designed compounds unrelated to any known host lattice but which would be expected to act as host lattices (2). A collection of these compounds is shown in Figure 17. They follow different design strategies to oppose the usual close packing in crystals and to create rigid open host structures.

Thus, by analogy with the hydrogen-bonded hexamer unit present in most of the phenol-type clathrates (see Fig. 13), the synthesis of molecules with sixfold symmetry was undertaken, and a new range of inclusion hosts, named hexahosts was discovered (93,104). They feature benzenoid compounds with six substituents such as SAr, CH_2OAr, CH_2SAr, and CH_2SCH_2Ar, where Ar is an aromatic nucleus. The prototype of this vast family of molecules endowed with inclusion properties is hexabis(benzylthiomethyl)benzene[61040-51-5] (**36**). Guest species of hexahost clathrates mainly involve aromatic and alicyclic hydrocarbons, aryl and alkyl halides, dioxane, and acetone. A special merit of this host-type is that the inclusion cavity is easy to tune to the geometric and steric requirements of the guest enclosure by altering the bulk of the side arms. Using a central naphthalene moiety instead of the benzenoid ring leads to corresponding octahosts (104).

Another strategy which orients along the overall molecular shape of a host is picturesquely called the wheel-and-axle host concept (105). Such hosts, eg, 1,1,1,6,6,6-hexabis(phenyl)-2,4-hexadiyne>[90507-76-9] (**37**) (R = H) contain a long molecular axis made of *sp* carbons with sp^3 carbons at each end that bear large, relatively rigid groups (106). These act as spacers which prevent the host molecules from a close-packed structure in the crystal and give rise to inclusion properties, mostly towards nonpolar aromatic and alicyclic hydrocarbon guests. Bulky frameworks that resemble a pair of scissors (107) or a roof (108) are other basic structures of the geometrical host concept (109).

Attachment of polar groups at selected positions of the bulky host frameworks led to a broad new type of clathrate hosts that follow the principle of coordinatoclathrate formation (110) which deals with concerted action of van der Waals nonpolar steric shielding and polar Coulomb attraction or hydrogen bonding by the host, thus yielding increased chemical guest selectivity and higher stability of inclusion compounds than under van der Waals conditions alone (111,112). Representative coordinatoclathrate hosts are shown, eg, 1,1′-binaphthalene-2,2′-diol[602-09-5] (**38**) and the dicarboxylic acid[116841-20-4] (**39**), and a typical packing diagram of a respective inclusion compound indicating defined

host–guest interaction is illustrated in Figure 18**a**. Inclusion strategies via coordinatoclathration seem to be universal and prove very efficient even when relatively simple host structures, such as 9-phenyl-9-fluorenol[25603-67-2] (**40**), are involved (113). Guests matching the voids of the host lattice and that have groups complementary to the host functions are usually preferred and form stable inclusions (114,115). This means, eg, that size conformable alcohols and formamides or sulfoxides are favored by carboxylic hosts (112) whereas amines show a tendency for binding to hydroxy hosts (116).

Although a number of chiral hosts (eg, (**38**)), based on the given principles have been found good for enantioselective guest inclusion (105,106,117), the development of optically pure clathrate hosts for enantioseparations of guests is more advanced. The new strategy consists in addition of bulky and rigid substituents (clathratogenic groups) to a natural chiral compound thus giving an optically pure lattice host (118). Tartaric and lactic acids transformed in this way (**41**) [93379-48-7], (**42**) (119,120) show efficient clathration and excellent enantioseparation properties involving a variety of guest compounds such as chiral alcohols, ketones, amines, sulfoxides, sulfoximines, and oxiranes.

Also among hydrogen-bonded network type of clathrate hosts there is a promising development leading to a class of helical tubulands of which [147318-38-5] (**43**) shows a prototypical structure (121). The building principle of clathrates formed by this family of diol hosts is a series of tight spiral spines of hydrogen bonds (Fig. 18**b**) (122). Host molecules radiate from and interconnect these spines such that a hexagonal arrangement of the spines enclose a channel which may contain trapped solvent molecules of a variety of functional group classes (hydrocarbons, aryl halides, ethers, esters, ketones, amines, nitriles, and sulfides). Variation of the diol molecular structure (eg, bridging of (**43**), equatorial orientation of the hydroxy groups) results in considerable modification of the channel topology and dimensions with altered inclusion properties (123).

4. Preparation and Characterization of Inclusion Compounds

There are several ways to prepare inclusion compounds. In solution (25,44), they may simply be formed by dissolving together host and guest in a common solvent. This solvent should compete minimally with the guest or, preferably, the bulk solvent should be the guest compound. Inclusion formation in solution applies only for intramolecular cavity inclusions and complexes. Crystalline inclusion compounds (21) may be prepared by crystallization from the guest solvent or by cocrystallization of host and guest from an inert solvent. Solid inclusion compounds are also formed by direct exposure of the host to the vapor or liquid guest or, sometimes (124,125), by grinding solid host and guest together. Moreover, replacement of an included guest has been demonstrated in particular cases (99,100).

The formation of such materials may be monitored by several techniques. One of the most useful methods is ^{1}H- and ^{13}C-nmr spectroscopy where stable complexes in solution may give rise to characteristic shifts of signals relative to the uncomplexed species (43). Solution nmr spectroscopy has also been used to detect the presence of solid inclusion compound (after dissolution) and to

determine composition (host:guest ratio) of the material. Infrared spectroscopy (126) and combustion analysis are further methods to study inclusion formation. For general screening purposes of solid inclusion structures, the x-ray powder diffraction method is suitable (123). However, if detailed structures are required, the single crystal x-ray diffraction method (127) has to be used.

Appropriate guest molecules are those that have a suitable size and shape to accommodate the host cavity and that complement the host cavity chemically. Host cavities lined only with apolar groups may prefer apolar guest entrapment and polar host cavities favor polar guests. Host cavity (cage) free diameters usually range between 0.4 and 0.8 nm. Host channels are inclined to accommodate linear guests; host cages have affinity to entrap spherical guests. Cage inclusions are generally more stable than channel or layer inclusions.

Stabilities of inclusion compounds span a wide range. Some are very stable at ambient conditions and require heating to considerable temperatures or treatment under high vacuum to cause decomposition. Others are only stable when in contact with mother liquor or excess guest solvent from which the inclusion compound was grown. A simple yet informative way for estimation of inclusion stabilities is to relate the decomposition point of the inclusion compound to the usual boiling point of the respective guest liquid (110). However, thermodynamic and kinetic properties including stabilities of inclusion compounds have also been studied on a more scientific base (44,128,129). Stability data of crown cation and uncharged molecule complexes of macrocyclic and oligocyclic hosts in solution are available in numerous cases (38,39).

5. Uses

Inclusion compounds open up a wide area of applications (1,2,17–28). An important aspect in this connection is the specific microenvironment created by the host enclosure of the guest which exerts an influence on the physical, spectroscopic, chemical, and other properties of the guest.

5.1. Retardation and Control. This influence may manifest itself in a reduced volatility and therefore lower possible storage and handling problems of a compound when included; toxic and hazardous substances become safer. As most inclusion compounds dissociate in a solvent or decompose under intensified conditions, it is easy to recover the guest. 18-crown-6 ((**3**) Fig. 3), for example, forms a solid inclusion complex with dimethyl sulfate that makes this dangerous compound easy to handle and to dose (130). The hydroquinone clathrate of krypton can be used as a way of handling radioactive krypton (^{85}Kr) turned into a solid, thus providing a safe and useful radioactive source (131). Moreover, odorous substances and flavoring compounds may be solidified via inclusion and reduced in their vapor pressure and volatility which makes controlled, retarded, and suppressed release possible. Cyclodextrin inclusions (Fig. 7) are most useful in this sense and aroused great value for many industries including cosmetology, food industry, laundering, pharmacy, agriculture, and others (57,132,133). For instance, cyclodextrins can be used to trap clinging and unpleasant odors (fish, garlic, cigarettes, alcohol). They can be used in the form of liquids, powders, tablets, chewing gums, toothpastes, sprays, and mouthwashes (133). Interesting

examples of prolonged release obtained with cyclodextrins concern drugs (134), pesticides (135), and pheromones (136). An extreme form of molecular imprisonment and environmental shielding is found in carceplexes (see (**17**) Fig. 5) that can release guest molecules only by breaking covalent bonds of the container shell (46).

Enclosure also changes the redox properties of a compound, its color, and other physical properties (1,2). On this basis nonlinear optical materials, luminescence markers, controlled light switches, and other high-tech devices might be designed and prepared (15,17,137).

5.2. Shielding and Stabilization. Inclusion compounds may be used as sources and reservoirs of unstable species. The inner phases of inclusion compounds uniquely constrain guest movements, provide a medium for reactions, and shelter molecules that self-destruct in the bulk phase or transform and react under atmospheric conditions. Clathrate hosts have been shown to stabilize molecules in unusual conformations that can only be obtained in the host lattice (138) and to stabilize free radicals (139) and other reactive species (1) similar to the use of matrix isolation techniques. Inclusion compounds do, however, have the great advantage that they can be used over a relatively wide temperature range. Cyclobutadiene, pursued for over a century has been generated photochemically inside a carcerand container (see (**17**) Fig. 5) where it is protected from dimerization and from reactants by its surrounding shell (140).

Improved stability of included guest molecules leading to protection from environmental factors such as heat, light, and oxygen is also economical. In the food industry, spices and fruit flavors included and transformed into powder by cyclodextrins ((**23**), Fig. 6) exhibit good stability when they are heated during industrial food processing (133). So it is possible to use smaller amounts and such flavors last for a longer period. Similarly, oxidation of vitamins is considerably slowed down (141) and insecticides such as pyrethroids included in cyclodextrins show higher resistance to ultraviolet light and oxygen (142). Clathrates of fatty acids have been used to protect them from oxidation (88). Numerous dyes form stable inclusion complexes with cucurbituril ((**24** Fig. 9) which leads to stabilization of such molecules (65) and has importance in the textile industry (143).

5.3. Solubilization and Activation. Compounds included in a host take solubility properties of the host shell and thus become more soluble when trapped in polar or apolar media, depending on the nature of the host. This leads to important uses in chemical synthesis known as the phase-transfer principle (144). Salt-type reagents (nucleophiles, bases, etc) including a metal ion that are only poorly soluble in organic solvents may be drastically enhanced in their solubility via complexation with crown compounds or cryptands (see Fig. 3) when used in solid–liquid and liquid–liquid (aqueous–organic solvent) phase-transfer systems (see CATALYSIS, PHASE-TRANSFER). Complexation of the cation and transfer of the reagent into a lipophilic medium causes activation of poorly solvated anions (naked anions) that work miracles in reactivity (145–147). Very resistant esters can be saponified or problematic oxidation and substitution reactions can be performed using this method. The other way round, cyclophane type hosts (Fig. 5) (43,44) and cyclodextrins (Fig. 6) (56,57) enhance hydrosolubilities of organic molecules. Furthermore, increased compound solubility occupies an important place in pharmacy, cosmetics, or the food industry (139). For instance,

sweetening agents which precipitate easily by cooling, no longer precipitate after addition of β-cyclodextrin (**23b**, Fig. 6) (133); complexed flurbiprofen becomes more soluble in water (148).

5.4. Organized Media Effects. Another general reason for using host–guest inclusion chemistry in synthesis is controlled selectivity and artificial enzyme mimicry (149–151). Anisole included in α-cyclodextrin ((**23a**), Fig. 6) gives a considerably higher ratio of *p*-chlorination than under usual conditions (152). Cyclodextrins and cyclophane hosts (see Fig. 5) carrying catalytic groups show efficiency in hydrolysis or C–C coupling reactions (43,44,153). The same types of host also work as molecular reaction vessels via cooperative binding of reactants, eg, to perform an accelerated Diels-Alder reaction (152). The organizing principle of crystalline inclusion compounds make topochemistry (154) and crystal engineering (155) possible. Evidently, channel complexes (see Fig. 16) can act as templates for stereoregular inclusion polymerizations (156,157). Photoreactions of clathrates give rise to regio- and stereo-controlled products different from solution reaction (105). Enantioselective product formation via solid state reaction (158) can be performed in bulk from achiral material under absolute asymmetric conditions.

5.5. Separation and Retrieval. Separation of chemical species that differ in shape and size is another important field of application. All kinds of metal ions, anions, and uncharged molecules that match a specific cavity structure, thus forming a stable inclusion complex, make a distinction from nonmatching materials possible. Crown compounds and analogues (see Fig. 3) are efficient in separating individual metal ions such as alkali and alkaline-earth metal ions, and also transition metals if the host donor sites are suitable (159,160). They are useful for recovery of noble metals, for decontamination of wastewaters, and other concentration processes based on solvent extraction (161) and membrane separation techniques (162,163). Efficiency and convenience is high if the host is attached to an insoluble support (164). Hosts for molecular species are able to separate aromatic from aliphatic compounds (107), substituted from unsubstituted compounds (105), linear from branched isomers (5), positional isomers (165), diastereomers, and enantiomers (117,166–168). Racemate resolution using clathrates (eg, of (**38**), (**41**), and (**42**); Fig. 17) are noticed increasingly (105,107,118,169). Dyes, alkaloids, carbohydrates, nucleotides, or barbiturates are particular examples of compounds separated in bulk amounts (11,44).

Analytically, the inclusion phenomenon has been used in chromatography both for the separation of ions and molecules, in liquid and gas phase (1,79,170,171). Peralkylated cyclodextrins enjoy high popularity as the active component of hplc and gc stationary phases efficient in the optical separation of chiral compounds (57,172). Chromatographic isotope separations have also been shown to occur with the help of Werner clathrates and crown complexes (79,173).

5.6. Sensing. Crown compounds modified by responsible chromogenic groups (chromoionophores) (174) proved valuable tools for measuring metal ions (175,176) and even enantiomeric guest concentrations in solution (177). Ion selective electrodes based on crown compounds and podands (see Fig. 3) as the sensitive component (178,179) have broad analytical applications from industrial wastewater control to clinical bedside monitoring of blood

(162). Moreover, cyclodextrins and other cavity hosts gain increasing influence as sensitive coatings of chemical sensor devices (180–183) for organic solvents and vapors (184,185). Quite recently, it appeared that clathrate forming hosts such as shown in Figure 17 are also useful in this field (186–188).

BIBLIOGRAPHY

"Clathration" in *ECT* 3rd ed., Vol. 6, pp. 179–189, by E. C. Makin, Monsanto Chemical Intermediates Co.

CITED PUBLICATIONS

1. J. E. D. Davies and co-workers, *J. Incl. Phenom.* **1**, 3 (1983).
2. E. Weber, in E. Weber, ed., *Molecular Inclusion and Molecular Recognition—Clathrates I,* Springer, Berlin-Heidelberg, 1987, p. 1.
3. H. M. Powell, *J. Chem. Soc.,* 61 (1948).
4. H. M. Powell, in L. Mandelcorn, ed., *Non-stoichiometric Compounds,* Academic Press, Inc., New York, 1964, "Chapt. 7."
5. F. Cramer, *Angew. Chem.* **64**, 437 (1952).
6. C. J. Pedersen, *J. Am. Chem. Soc.* **89**, 7017 (1967).
7. F. Vögtle and E. Weber, eds., *Host-Guest Complex Chemistry—Macrocycles,* Springer, Berlin-Heidelberg, 1985.
8. J. F. Stoddart, *Ann. Rep. Progr. Chem.* **85**, 353 (1988).
9. G. Van Binst, ed., *Design and Synthesis of Organic Molecules Based on Molecular Recognition,* Springer, New York, 1986.
10. H.-J. Schneider, *Angew. Chem.* **103**, 1419 (1991); *Angew. Chem. Int. Ed. Engl.* **30**, 1417 (1991).
11. A. D. Hamilton, in H. Dugas, ed., *Frontiers in Bioorganic Chemistry,* Vol. **2**, Springer, Berlin, 1991, p. 115.
12. E. Fischer, *Ber. Dtsch. Chem. Ges.* **27**, 2985 (1894).
13. C. J. Pedersen, *Angew. Chem.* **100**, 1053 (1988); *Angew. Chem. Int. Ed. Engl.* **27**, 1021 (1988); C. J. Pedersen, *J. Incl. Phenom.* **6**, 337 (1988).
14. D. J. Cram, *Angew. Chem.* **100**, 1041 (1988); *Angew. Chem. Int. Ed. Engl.* **27**, 1009 (1988); D. J. Cram, *J. Incl. Phenom.* **6**, 397 (1988).
15. J.-M. Lehn, *Angew. Chem.* **100**, 91 (1988); *Angew. Chem. Int. Ed. Engl.* **27**, 89 (1988); J.-M. Lehn, *J. Incl. Phenom.* **6**, 351 (1988).
16. E. Weber and F. Vögtle, *Nachr. Chem. Techn. Lab.* **35**, 1149 (1987).
17. F. Vögtle, *Supramolecular Chemistry—An Introduction,* John Wiley & Sons, Inc., Chichester, U.K., 1991.
18. V. Balzani and De Cola, eds., *Supramolecular Chemistry,* Kluwer, Dordrecht, 1992.
19. G. W. Gokel, ed., *Advances in Supramolecular Chemistry,* Vol. **1**, JAI-Press, Greenwich, Conn., 1990.
20. E. Weber, ed., *Supramolecular Chemistry I—Directed Synthesis and Molecular Recognition,* Springer, Berlin-Heidelberg, 1993.

21. J. L. Atwood, J. E. D. Davies, and D. D. MacNicol, eds., *Inclusion Compounds,* Vols. **1**–**3**, Academic Press, Inc., London, 1984; Vols. **4**–**5**, Oxford University Press, Oxford, 1991.
22. E. Weber, ed., *Molecular Inclusion and Molecular Recognition—Clathrates I and II,* Springer, Berlin-Heidelberg, 1987 and 1988.
23. E. Weber and H.-P. Josel, *J. Incl. Phenom.* **1**, 79 (1983).
24. S. Patai and Z. Rappoport, eds., *Crown Ethers and Analogs,* John Wiley & Sons, Inc., Chichester, U.K., 1989.
25. G. W. Gokel, *Crown Ethers and Cryptands, Monographs in Supramolecular Chemistry,* Vol. 3, The Royal Society of Chemistry, Cambridge, 1991.
26. M. Hiraoka, ed., *Crown Ethers and Analogous Compounds,* Elsevier, Amsterdam, 1992.
27. S. R. Cooper, ed., *Crown Compounds Toward Future Applications,* VCH, Weinheim, 1992.
28. B. Dietrich, P. Viout, and J.-M. Lehn, *Macrocyclic Chemistry,* VCH, Weinheim, 1993.
29. J.-M. Lehn, *Acc. Chem. Res.* **11**, 49 (1978).
30. F. Vögtle and E. Weber, *Angew. Chem.* **91**, 813 (1979); *Angew. Chem. Int. Ed. Engl.* **18**, 753 (1979).
31. E. Weber, in Ref. 24, p. 305.
32. G. W. Gokel, in Ref. 21, Vol. 4, p. 283.
33. F. Vögtle and E. Weber, *Angew. Chem.* **86**, 896 (1974); *Angew. Chem. Int. Ed. Engl.* **13**, 814 (1974).
34. D. J. Cram, *Angew. Chem.* **98**, 1041 (1986); *Angew. Chem. Int. Ed. Engl.* **25**, 1039 (1986).
35. J. L. Toner, in Ref. 24, p. 77.
36. J. F. Stoddart, *Top. Stereochem.* **17**, 207 (1987).
37. D. J. Cram and J. M. Cram, *Acc. Chem. Res.* **11**, 8 (1978).
38. Y. Inoue and G. W. Gokel, eds., *Cation Binding by Macrocycles,* Marcel Dekker, Inc., New York, 1990.
39. R. M. Izatt and co-workers, *Chem. Rev.* **92**, 1261 (1992).
40. R. Hilgenfeld and W. Saenger, *Top. Curr. Chem.* **101**, 1 (1982).
41. I. Goldberg, in Ref. 24, p. 359 and 399.
42. E. Weber, in R. M. Izatt and J. J. Christensen, eds., *Synthesis of Macrocycles — The Design of Selective Complexing Agents, Progress in Macrocyclic Chemistry,* Vol. 3, John Wiley & Sons, Inc., New York, 1987, p. 337.
43. F. Diederich, *Angew. Chem.* **100**, 372 (1988); *Angew. Chem. Int. Ed. Engl.* **27**, 362 (1988).
44. F. Diederich, *Cyclophanes, Monographs in Supramolecular Chemistry,* Vol. **2**, The Royal Society of Chemistry, Cambridge, 1991.
45. F. Vögtle, *Cyclophane Chemistry,* John Wiley & Sons, Inc., Chichester, 1993.
46. D. J. Cram, *Nature* **356**, 29 (1992).
47. A. Collet, in Ref. 20, p. 103.
48. F. H. Kohnke, J. P. Mathias, and J. F. Stoddart, *Angew. Chem.* **101**, 1129 (1989); *Angew. Chem. Int. Ed. Engl.* **28**, 1103 (1989).
49. F. H. Kohnke, J. P. Mathias, and J. F. Stoddart, in Ref. 20, p. 1.
50. B. Odell and co-workers, *Angew. Chem.* **100**, 1605 (1988); *Angew. Chem. Int. Ed. Engl.* **27**, 1547 (1988).
51. J. F. Stoddart, in H.-J. Schneider and M. Dürr, eds., *Frontiers in Supramolecular Chemistry and Photochemistry,* VCH, Weinheim, 1991, p. 251.
52. C. D. Gutsche, *Calixarenes, Monographs in Supramolecular Chemistry,* Vol. **1**, The Royal Society of Chemistry, Cambridge, 1989.

53. J. Vicens and V. Böhmer, eds., *Calixarenes—A Versatile Class of Macrocyclic Compounds,* Kluwer, Dordrecht, 1991.
54. A. Arduini and co-workers, in Ref. 18, p. 31.
55. L. C. Groenen and D. N. Reinhoudt, in Ref. 18, p. 51.
56. M. L. Bender and M. Komiyama, *Cyclodextrin Chemistry,* Springer, New York, 1978.
57. J. Szejtli, *Cyclodextrin Technology,* Kluwer, Dordrecht, 1988.
58. W. Saenger, in Ref. 21, Vol. 2, p. 231.
59. K. Harata, in Ref. 21, Vol. 5, p. 311.
60. R. J. Bergeron, in Ref. 21, Vol. 3, p. 391.
61. I. Tabushi, in Ref. 21, Vol. 3, p. 445.
62. R. Breslow, *Supramol. Chem.* **1**, 111 (1993).
63. H.-T. Moon and co-workers, *Supramol. Chem.* **1**, 327 (1993).
64. W. Saenger, *Naturwissenschaften* **71**, 31 (1984).
65. P. Cintas, *J. Incl. Phenom.* **17**, 205 (1994).
66. W. A. Freeman, W. L. Mock, and N. Y. Shih, *J. Am. Chem. Soc.* **103**, 7367 (1981).
67. H.-J. Buschmann and E. Schollmeyer, *J. Incl. Phenom.* **14**, 91 (1992).
68. A. Flinn and co-workers, *Angew. Chem.* **104**, 1550 (1992); *Angew. Chem. Int. Ed. Engl.* **31**, 1475 (1992).
69. J. Rebek, Jr., *Science* **235**, 1437 (1987).
70. J. Rebek, Jr., in Ref. 22, Vol. 149, p. 189.
71. S. C. Zimmerman, in Ref. 20, p. 71.
72. J.-M. Lehn, *Acc. Chem. Res.* **11**, 49 (1978).
73. F. P. Schmidtchen, *Top. Curr. Chem.* **132**, 101 (1986).
74. F. P. Schmidtchen, *Nachr. Chem. Tech. Lab.* **36**, 8 (1988).
75. H. E. Katz, in Ref. 21, Vol. 4, p. 391.
76. G. A. Jeffrey, in Ref. 21, Vol. 1, p. 135.
77. Y. A. Dyadin, I. V. Bondaryuk, and F. V. Zhurko, in Ref. 21, Vol. 5, p. 213.
78. E. D. Sloan, Jr., *Clathrate Hydrates of Natural Gases,* Marcel Dekker, New York, 1989.
79. G. Tsoucaris, in G. R. Desiraju, ed., *Organic Solid State Chemistry,* Elsevier, Amsterdam, 1987, p. 207.
80. G. A. Jeffrey and R. K. MacMillan, *Progr. Inorg. Chem.* **8**, 43 (1967).
81. G. A. Jeffrey and W. Saenger, *Hydrogen Bonding in Biological Structures,* Springer, Berlin-Heidelberg, 1991.
82. T. Iwamoto, in Ref. 21, Vol. 1, p. 29.
83. J. Lipkowski, in Ref. 21, Vol. 1, p. 59.
84. L. R. Nassimbeni and M. L. Niven, in International Union of Crystallography, eds., *Molecular Structure - Chemical Reactivity and Biological Activity,* Oxford University Press, Oxford, 1988.
85. K. A. Hofmann and F. A. Küspert, *Z. Anorg. Allg. Chem.* **15**, 204 (1897).
86. T. Iwamoto, in Ref. 21, Vol. 5, p. 177.
87. K. Takemoto and N. Sonoda, in Ref. 21, Vol. 2, p. 47.
88. S. G. Frank, *J. Pharm. Sci.* **64**, 1585 (1975).
89. F. Cramer, *Einschlußverbindungen,* Springer, Berlin, 1954.
90. W. Schlenk, Jr., *Fortschr. Chem. Forsch.* **2**, 92 (1951); *Acta Crystallogr.* **5**, 224 (1952).
91. D. D. MacNicol, in Ref. 21, Vol. 2, p. 1.
92. J. F. Brown, Jr., *Sci. Am.* **207**, 82 (1962).
93. D. D. MacNicol, J. J. McKendrick, and D. R. Wilson, *Chem. Soc. Rev.* **7**, 65 (1978).
94. A. Gdaniec, B. T. Ibragimov, and S. A. Talipov, *J. Incl. Phenom.* **9**, 231 (1990) and previous papers of this series.
95. B. T. Ibragimov, S. A. Talipov, and P. M. Zorky, *Supramol. Chem.* **3**, 147 (1994).
96. E. Giglio, in Ref. 21, Vol. 2, p. 207.

97. M. Farina, in Ref. 21, Vol. 2, p. 69.
98. G. Allegra and co-workers, *J. Chem. Soc. (B),* 1028 (1967).
99. H. R. Allcock, *Acc. Chem. Res.* **11**, 81 (1978).
100. H. R. Allcock, in Ref. 21, Vol. 1, p. 351.
101. A. Collet, in Ref. 21, Vol. 2, p. 97.
102. R. Gerdil, in Ref. 22, Vol. 140, p. 71.
103. W. D. Ollis and J. F. Stoddart, in Ref. 21, Vol. 2, p. 169.
104. D. D. MacNicol, in Ref. 21, Vol. 2, p. 123.
105. F. Toda, in Ref. 21, Vol. 4, p. 126.
106. H. Hart, L.-T. W. Lin, and D. L. Ward, *J. Am. Chem. Soc.* **106**, 4043 (1984).
107. E. Weber, in Ref. 21, Vol. 4, p. 188.
108. E. Weber, S. Finge, and I. Csöregh, *J. Org. Chem.* **56**, 7281 (1991).
109. I. Goldberg, in Ref. 21, Vol. 4, p. 406.
110. E. Weber and co-workers, *J. Am. Chem. Soc.* **106**, 3297 (1984).
111. E. Weber and M. Czugler, in Ref. 22, Vol. 149, p. 45.
112. E. Weber, *J. Mol. Graphics* **7**, 12 (1989).
113. E. Weber, N. Dörpinghaus, and I. Csöregh, *J. Chem. Soc., Perkin Trans. 2,* 2167 (1990).
114. E. Weber and co-workers, *J. Am. Chem. Soc.* **111**, 7866 (1989).
115. L. J. Barbour and co-workers, *Supramol. Chem.* **1**, 331 (1993).
116. I. Goldberg and co-workers, *J. Chem. Soc., Perkin Trans. 2,* 953 (1990).
117. F. Toda, in Ref. 22, Vol. 140, p. 43.
118. E. Weber, K. Skobridis, and C. Wimmer, *GIT Fachz. Lab.* **36**, 740 (1992).
119. F. Toda and K. Tanaka, *Tetrahedron Lett.* **29**, 551 (1988).
120. E. Weber and C. Wimmer, *Chirality* **5**, 331 (1993).
121. R. Bishop and I. G. Dance, in Ref. 21, Vol. 4, p. 1.
122. R. Bishop and I. G. Dance, in Ref. 22, Vol. 149, p. 137.
123. R. Bishop and co-workers, *Supramol. Chem.* **2**, 123 (1993).
124. F. Toda, K. Tanaka, and A. Sekikawa, *J. Chem. Soc., Chem. Commun.,* 279 (1987).
125. M. C. Etter and G. M. Frankenbach, *Materials* **1**, 10 (1989).
126. J. E. D. Davies, in Ref. 21, Vol. 3, p. 37.
127. G. D. Andreetti, in Ref. 21, Vol. 3, p. 129.
128. N. G. Parsonage and L. A. K. Staveley, in Ref. 21, Vol. 3, p. 1.
129. S. A. Bourne and co-workers, *J. Org. Chem.* **57**, 2438 (1992).
130. F. Vögtle and W. M. Müller, *Naturwissenschaften* **67**, 255 (1980).
131. D. J. Chleck and C. A. Ziegler, *Int. J. Appl. Radiat. Isotop.* **7**, 141 (1959).
132. J. Szejtli, in Ref. 21, Vol. 3, p. 331.
133. D. Duchêne and D. Wouessidjewe, *J. Coord. Chem.* **27**, 223 (1992).
134. J. Szejtli, in V. F. Smolen and L. A. Ball, eds., *Controlled Drug Bioavailability,* Vol. **3**., John Wiley & Sons, Inc., New York, 1985, p. 365.
135. L. Szente and J. Szejtli, *Acta Chim. Acad. Sci. Hung.* **107**, 196 (1981).
136. P. Kondilis and co-workers, in D. Duchêne, ed., *Minutes of the 5th Int. Symp. on Cyclodextrins,* Editions de Santé, Paris, 1990, p. 578.
137. G. A. Ozin, *Adv. Mater.* **4**, 612 (1992).
138. D. D. MacNicol and A. Murphy, *Tetrahedron Lett.* **22**, 1131 (1981).
139. T. Iwamoto, M. Kiyoki, and N. Matsuro, *Bull. Chem. Soc. Jpn.* **51**, 390 (1978).
140. D. J. Cram, M. E. Tanner, and R. Thomas, *Angew. Chem.* **103**, 1048 (1991); *Angew. Chem. Int. Ed. Engl.* **30**, 1024 (1991).
141. J. Szejtli and E. Bolla-Pusztai, *Stärke* **32**, 386 (1980).
142. Y. Katsuda, H. Hirobe, and Y. Minamite, in J. Miyamoto, ed., *Pesticide Chemistry,* Vol. **2**, Pergamon Press, Oxford, 1983, p. 223.
143. H.-J. Buschmann and co-workers, *Textilveredlung* **26**, 160 (1991).

144. E. V. Dehmlow and S. S. Dehmlow, *Phase Transfer Catalysis,* 3rd ed., VCH, Weinheim, 1993.
145. G. W. Gokel and H. D. Durst, *Synthesis,* 168 (1976).
146. E. Weber, *Kontakte (Merck),* 38 (1983/1) and previous papers of this series.
147. C. L. Liotta, in Ref. 24, p. 59.
148. M. Otagiri and co-workers, *Acta Pharm. Suec.* **20**, 1 (1983).
149. B. S. Green, Y. Ashani, and D. Chipman, eds., *Chemical Approaches to Understanding Enzyme Catalysis: Biomimetic Chemistry and Transition State Analogs,* Elsevier, Amsterdam, 1982.
150. F. Diederich, *Chem. Uns. Zeit* **17**, 105 (1983).
151. J. F. Stoddart, in M. I. Page and A. Williams, eds., *Enzyme Mechanisms,* The Royal Society of Chemistry, Cambridge, 1987.
152. R. Breslow, in Ref. 21, Vol. 3, p. 473.
153. Y. Murakami, J. Kikuchi, and Y. Hisaeda, in Ref. 21, Vol. 4, p. 448.
154. G. R. Desiraju, ed., *Organic Solid State Chemistry,* Elsevier, Amsterdam, 1987.
155. G. Desiraju, *Crystal Engineering, Materials Science Monographs,* Vol. 54, Elsevier, Amsterdam, 1989.
156. M. Farina, in Ref. 21, Vol. 3, p. 297.
157. M. Miyata, in C. M. Paleos, ed., *Polymerization in Organized Media,* Gordon and Breach, Philadelphia, Pa., 1992, p. 327.
158. F. Toda, in Ref. 22, Vol. 149, p. 211.
159. Y. Takeda, in F. Vögtle and E. Weber, eds., *Host Guest Complex Chemistry III,* Springer, Berlin, 1984, p. 1.
160. T. M. Fyles, in H. Dugas, ed., *Bioorganic Chemistry Frontiers,* Vol. **1**, Springer, Berlin, 1990, p. 71.
161. D. H. Logsdail and M. J. Slater, eds., *Solvent Extraction in the Process Industries,* Vols. **1**–**3**, Elsevier, New York, 1993.
162. E. Weber, *Kontakte (Merck),* 26 (1984/1) and previous papers of this series.
163. J. D. Lamb and J. J. Christensen, in Ref. 21, Vol. 3, p. 571.
164. J. Smid and R. Sinta, in Ref. 159, p. 105.
165. K. Pollmer, *Z. Chem.* **19**, 81 (1979).
166. D. Worsch and F. Vögtle, in Ref. 22, Vol. 140, p. 21.
167. B. S. Green, M. Knossow, and G. Tsoucaris, in Ref. 21, Vol. 3, p. 263.
168. T. H. Webb and C. S. Wilcox, *Chem. Soc. Rev.,* 383 (1993).
169. E. Weber and co-workers, *J. Chem. Soc., Chem. Commun.,* 733 (1992); see also *Chem. Ind. (London),* 364 (1992).
170. E. Blasius and K.-P. Janzen, in Ref. 7, p. 189.
171. D. Sybilska and E. Smolková-Keulemansová, in Ref. 21, Vol. 3, p. 173.
172. W. A. König, *Kontakte (Merck),* 3 (1990/2).
173. N. O. Smith, in Ref. 21, Vol. 3, p. 257.
174. H.-G. Löhr and F. Vögtle, *Acc. Chem. Res.* **18**, 65 (1985).
175. S. Shinkai and O. Manabe, in Ref. 7, p. 245.
176. M. Takagi, in Ref. 38, p. 465.
177. S. Misumi, in Ref. 20, p. 163.
178. D. Amman and co-workers, *Ion-Selective Electrode Rev.* **5**, 3 (1983).
179. K. Kimura and T. Shono, in Ref. 38, p. 429.
180. J. C. Lockhart, in Ref. 21, Vol. 5, p. 345.
181. T. E. Edmonds, ed., *Chemical Sensors,* Blackie, Glasgow, 1988.
182. D. N. Reinhoudt and E. J. R. Sudhölter, *Adv. Mater.* **2**, 23 (1990).
183. K. Cammann and co-workers, *Angew. Chem.* **103**, 519 (1991); *Angew. Chem. Int. Ed. Engl.* **30**, 516 (1991).
184. F. L. Dickert and A. Haunschild, *Adv. Mater.* **5**, 887 (1993).

185. G. Gauglitz and co-workers, *Spektrum der Wissenschaft,* 92 (Jan. 1994).
186. A. Ehlen and co-workers, *Angew. Chem.* **105**, 116 (1993); *Angew. Chem. Int. Ed. Engl.* **32**, 110 (1993); see also *Chem. Ind. (London),* 333 (1993).
187. K. Buhlmann and co-workers, *Fresenius J. Anal. Chem.* **348**, 549 (1994).
188. J. Reinbold and co-workers, *Sensors and Actuators* **B 18–19**, 77 (1994).

EDWIN WEBER
Technische Universität Bergakademie Freiberg

Table 1. **Dimensions of Cone-Shaped Molecular Cylinders of Cyclodextrins**

Cyclodextrin	Molecular weight	Solubility in water, g/100 mL	$[\alpha]_D^{25^\circ}$	Diameter of cavity,[a] nm	Diameter of outer periphery,[a] nm
α-cyclodextrin	972	14.5	150.5 ± 0.5	0.47–0.52	1.46 ± 0.04
β-cyclodextrin	1135	1.85	162.5 ± 0.5	0.60–0.64	1.54 ± 0.04
γ-cyclodextrin	1297	23.2	177.4 ± 0.5	0.75–0.83	1.75 ± 0.04

[a]Measured with CPK-models. The height of all cyclodextrins is 0.79–0.80 nm.

Fig. 1. The principle of formation of an inclusion compound. (**a**) concave host; (**b**) convex guest component; (**c**) host–guest compound.

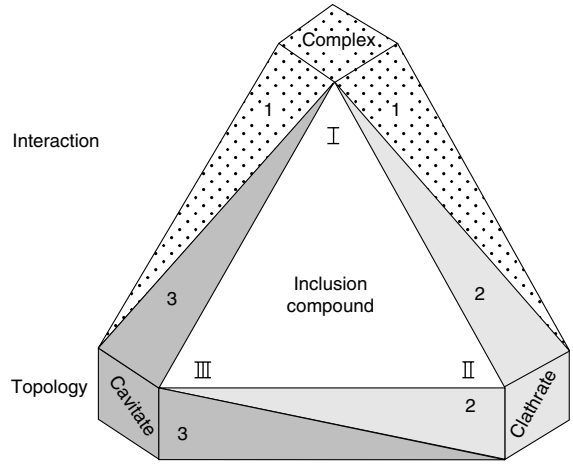
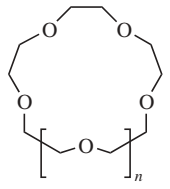
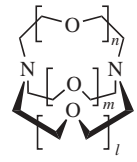


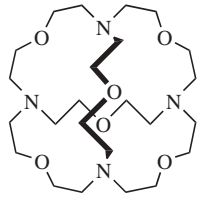
Fig. 2. Classification/nomenclature of host–guest type inclusion compounds, definitions and relations: (*1*) coordinative interaction, (*2*) lattice barrier interaction, (*3*) monomolecular shielding interaction; (I) coordination-type inclusion compound (inclusion complex), (II) lattice-type inclusion compound (multimolecular/extramolecular inclusion compound, clathrate), (III) cavitate-type inclusion compound (monomolecular/intramolecular inclusion compound) (2).



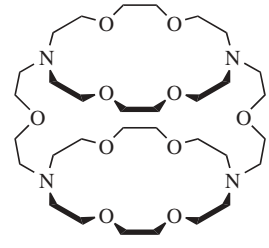
(**1**) $n = 0$ 12-crown-4
(**2**) $n = 1$ 15-crown-5
(**3**) $n = 2$ 18-crown-6
(**4**) $n = 3$ 21-crown-7



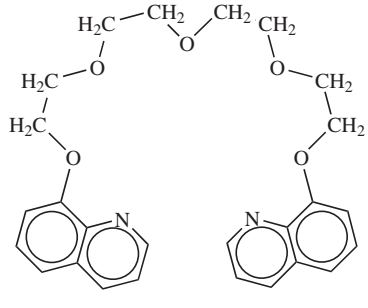
(**5**) $l = m = n = 1$ [1.1.1]
(**6**) $l = 2, m = n = 1$ [2.1.1]
(**7**) $l = m = 2, n = 1$ [2.2.1]
(**8**) $l = m = n = 2$ [2.2.2]



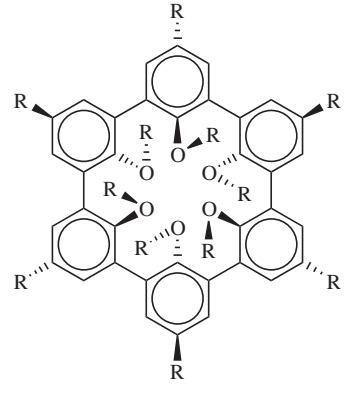
(**9**)



(**10**)

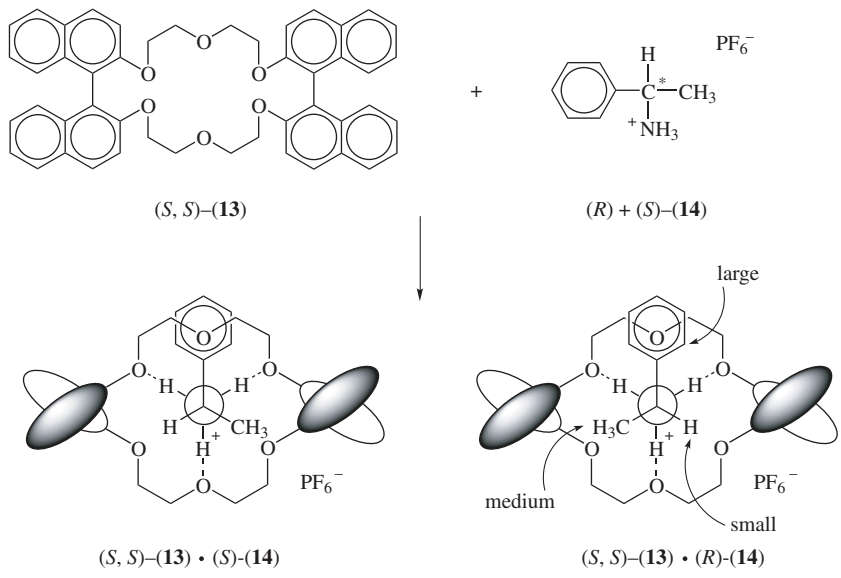


(**11**)



(**12**)

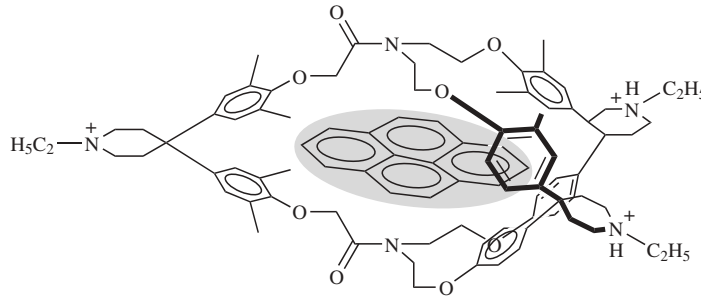
Fig. 3. Crown compounds/cryptands and analogous inclusion hosts. (**1**–**4**) Crown macrorings; bicyclic cryptands (**5**) [37095-49-1], (**6**) [31250-06-3], (**7**) [31364-42-8], (**8**) [23978-09-8]; (**9**) spherical cryptand [56698-26-1]; (**10**) cylindrical cryptand [42133-16-4]; (**11**) a podand [57310-75-5]; and (**12**) a spherand [72526-85-3]. R = methyl.



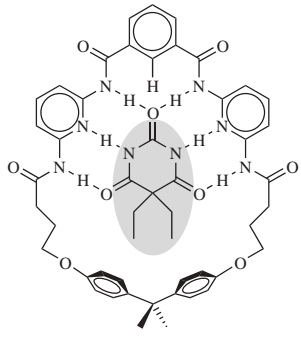
(*S*, *S*)–(**13**) (*R*) + (*S*)–(**14**)

(*S*, *S*)–(**13**) • (*S*)-(**14**) (*S*, *S*)–(**13**) • (*R*)-(**14**)

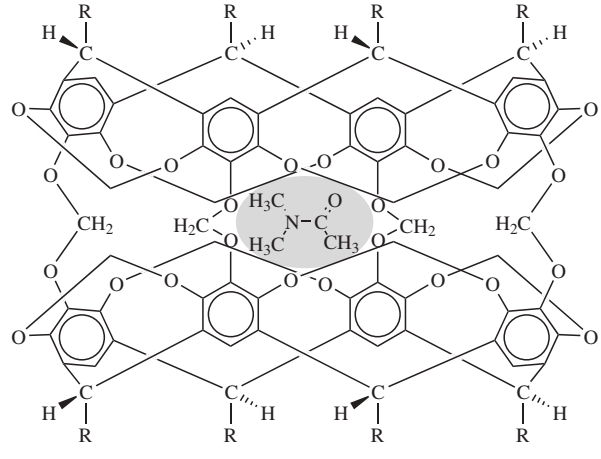
Fig. 4. Chiroselective inclusion formation of racemic 1-phenylethylammonium salt ((R/S)-**14**) using optically active crown compound ((*S,S*)-**13**) [53955-48-9]. The diastereomeric inclusion complex (*S,S*)-(**13**)· (*R*)-(**14**) is more stable than (*S,S*)-(**13**)·(*S*)-(**14**) (top views, dotted lines represent hydrogen bonds) thus making enantio separation of (*R*/*S*)-possible-(**14**) possible. Large, small, and medium refer to phenyl, hydrogen, and methyl, respectively.



(**16**)

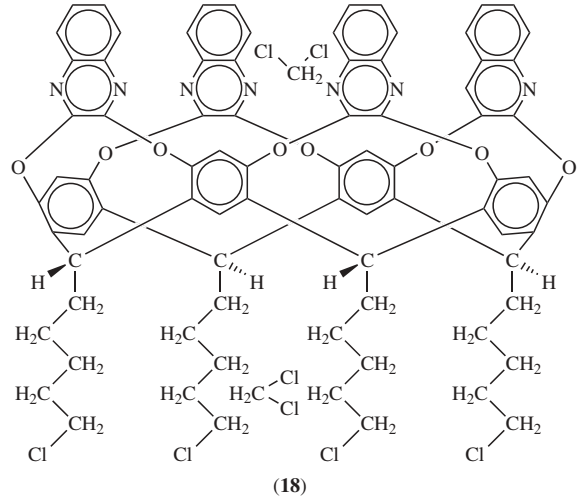


(**15**)



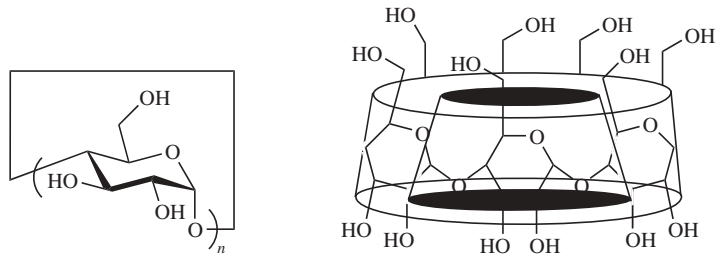
R = $CH_2CH_2C_6H_5$

(**17**)



(**18**)

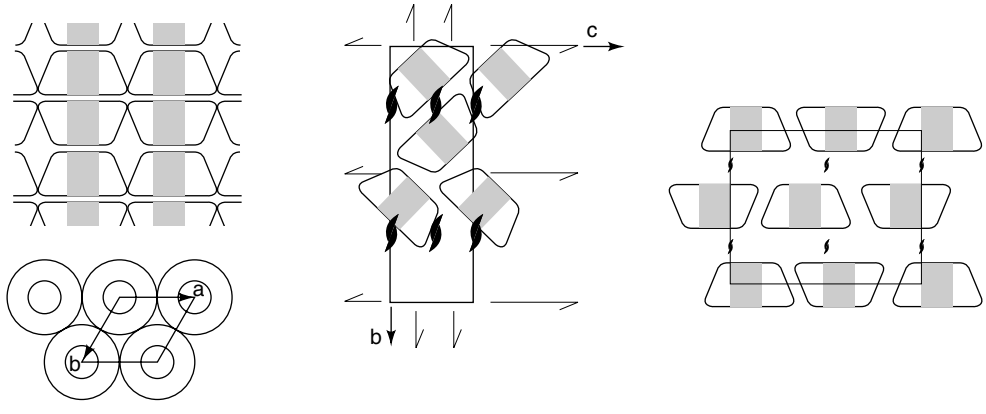
Fig. 5. Cyclophane-type inclusion compounds of different varieties. The guest component is shaded.



(**23**)

(**a**) (**b**)

Fig. 6. Cyclodextrins: (**a**) formula representation for α-cyclodextrin [10016-20-3] (**23**)**a**, $n = 6$, β-cyclodextrin [7585-39-9] (**23**)**b**, $n = 7$, and γ-cyclodextrin [17465-86-0] (**23**)**c** $n = 8$. (**b**) Three-dimensional cone structure of β-cyclodextrin (**23**)**b**.



(**a**) (**b**) (**c**)

Fig. 7. Schemes of crystalline cyclodextrin inclusion compounds: (**a**) channel type; (**b**) cage herringbone type; (**c**) cage brick type (58).

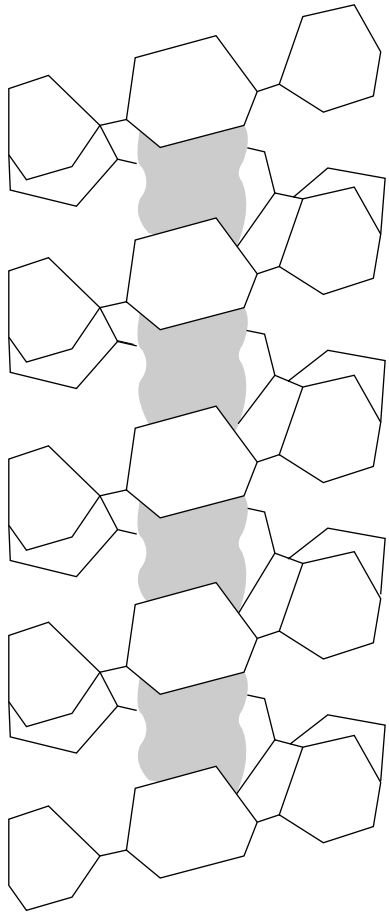
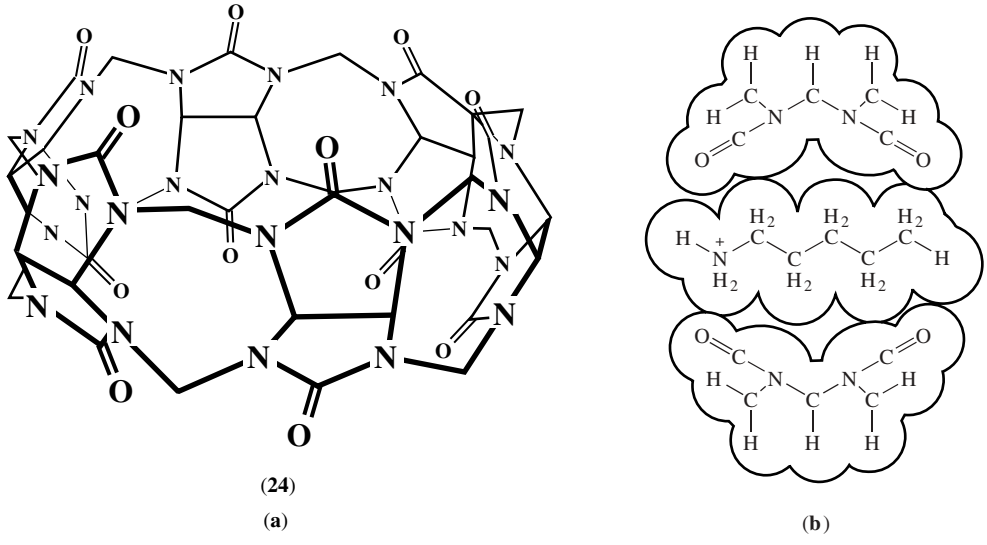


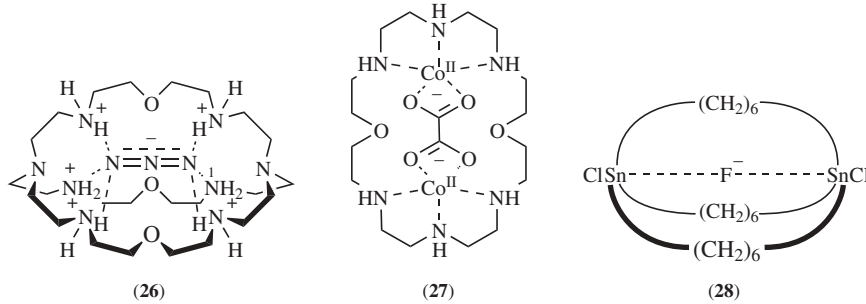
Fig. 8. Amylose inclusion compounds: scheme of the amylose helix showing the inclusion channel. The guest compound is shaded (58).



(**24**)

(**a**) (**b**)

Fig. 9 Cucurbituril inclusion chemistry: (**a**) tridimensional structure of cucurbit[6]uril; (**b**) conjectured cross-sectional representation of a host–guest inclusion compound between curbit[6]uril and *n*-pentylammonium ion.



(**26**) (**27**) (**28**)

Fig. 10. Anionic guest inclusion compounds.

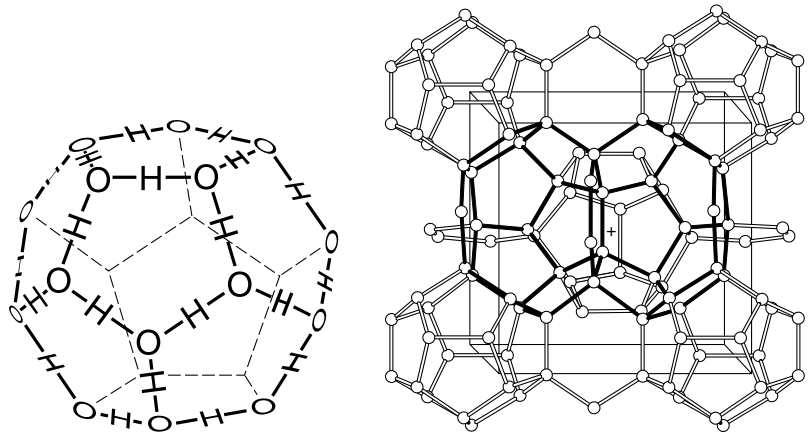


Fig. 11. Clathrate hydrates: (**a**) basic structural component ($H_{40}O_{20}$ pentagonal dodecahedron); (**b**) type I host structure (two face-sharing 14-hedra are shown with solid lines) (76).

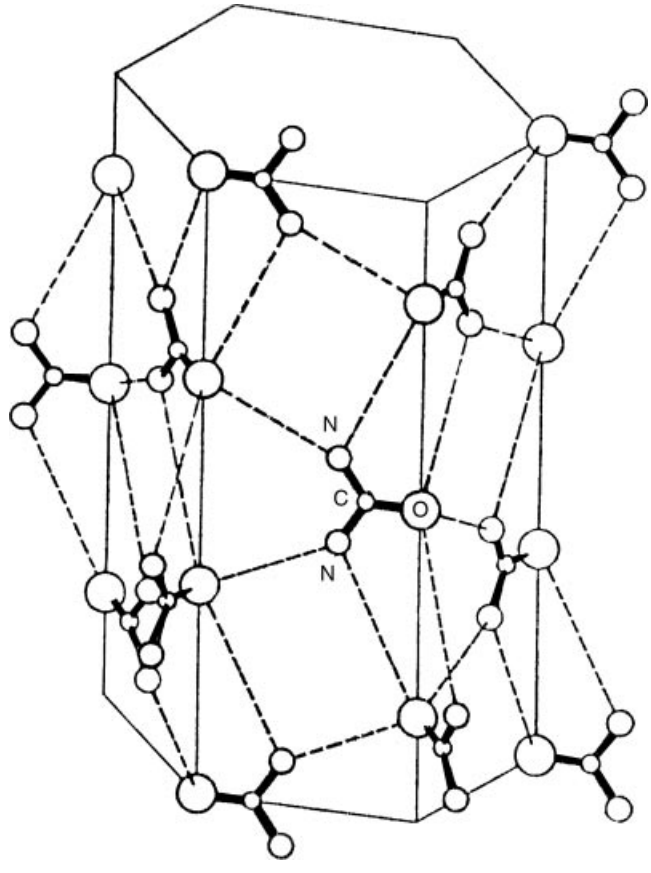


Fig. 12. Hydrogen-bonded network of an urea inclusion channel; (– hydrogen bonds (90)).

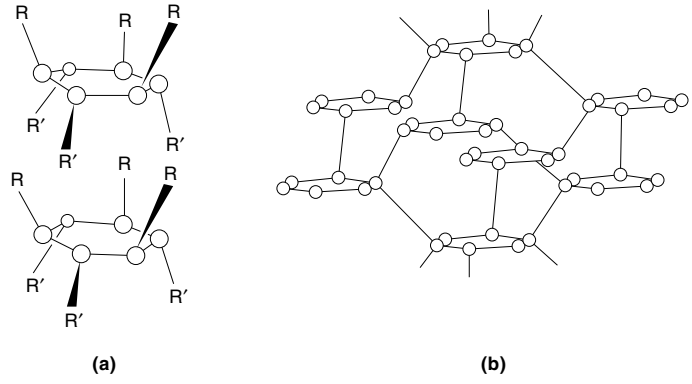


Fig. 13. Phenolic host inclusion chemistry: (**a**) schematic representation of the cage structure (open circles denote oxygen of OH, R corresponds to aryl part of host molecules); (**b**) interpenetrating cagework found in hydroquinone inclusions (91).

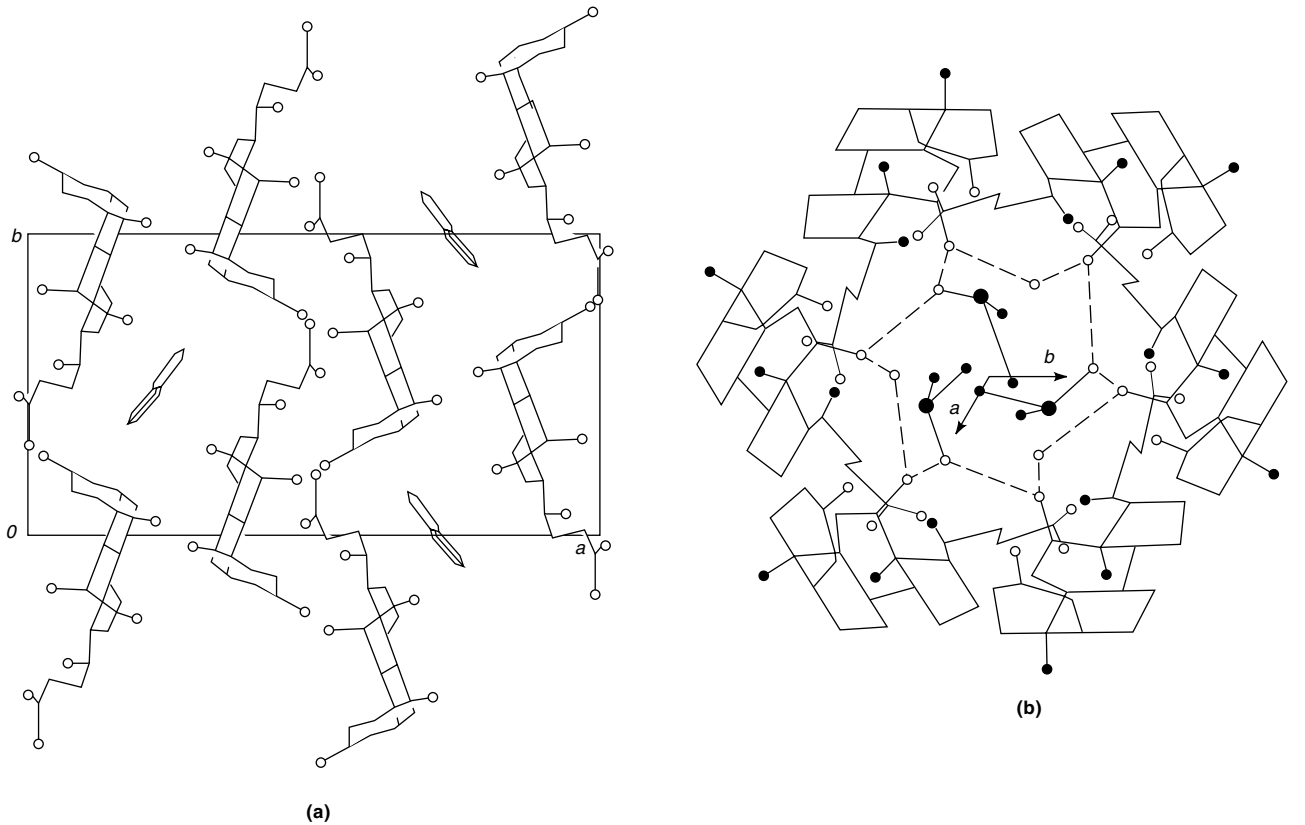
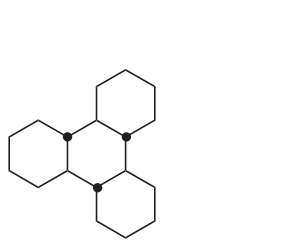
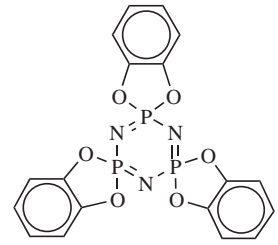


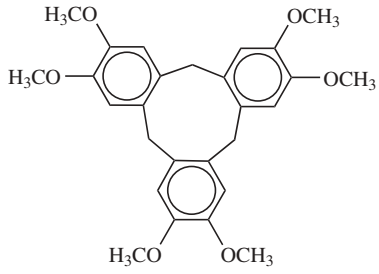
Fig. 14. Choleic acid inclusion chemistry: (**a**) crystal structure of DCA inclusion compound with phenanthrene; (**b**) view along a DCA inclusion helix accommodating DMSO and water guest molecules (oxygen and sulfur atoms and methyl groups are represented by open circles and large and small black circles, respectively). Hydrogen bonds are indicated by broken lines (96).



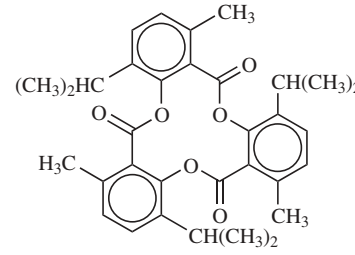
(**32**)



(**33**)



(**34**)



(**35**)

Fig. 15. Macrocyclic and oligocyclic lattice hosts: perhydrotriphenylene (**32**); a cyclotriphosphazene (**33**); cyclotriveratrylene (**34**); tri-*o*-thymotide (**35**).

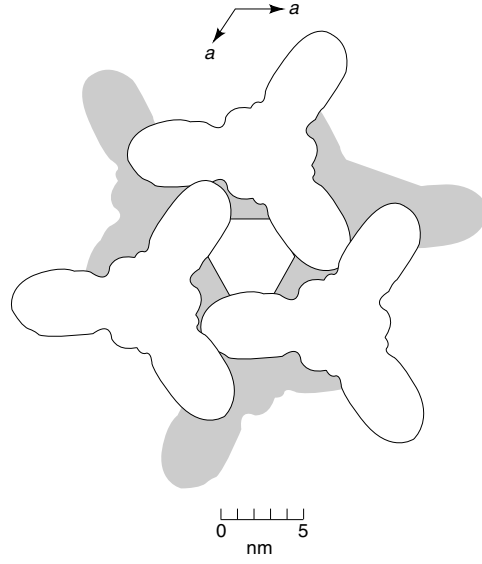
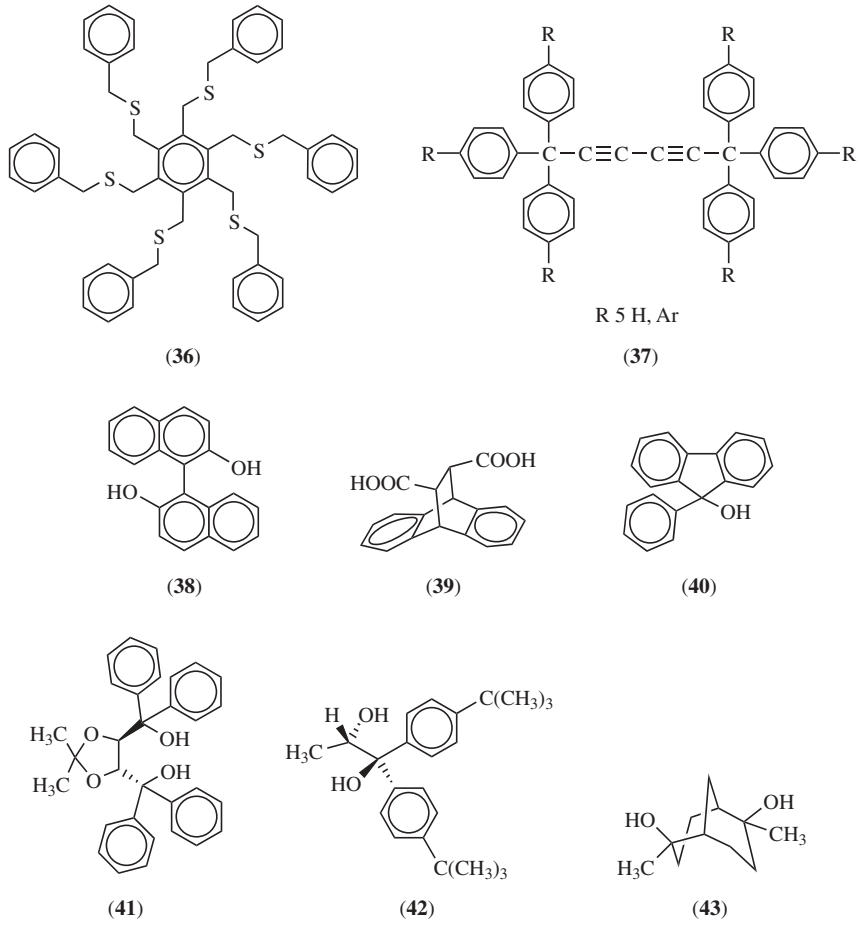
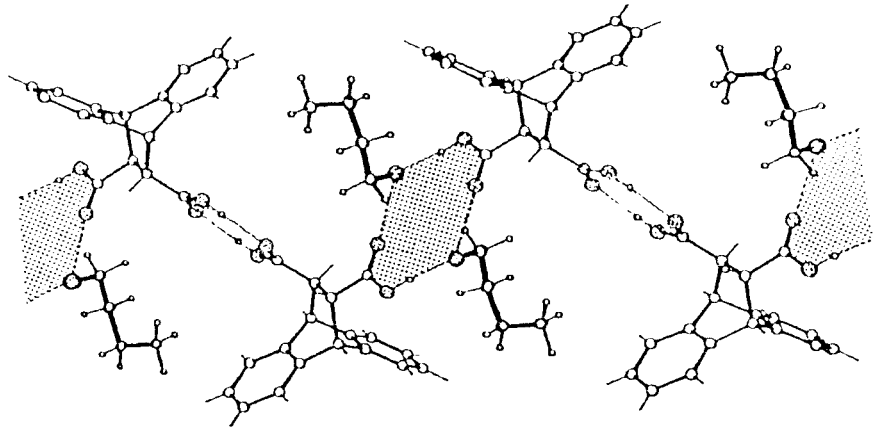


Fig. 16. van der Waals boundaries of (**33**) in hexagonal inclusion compounds (100).

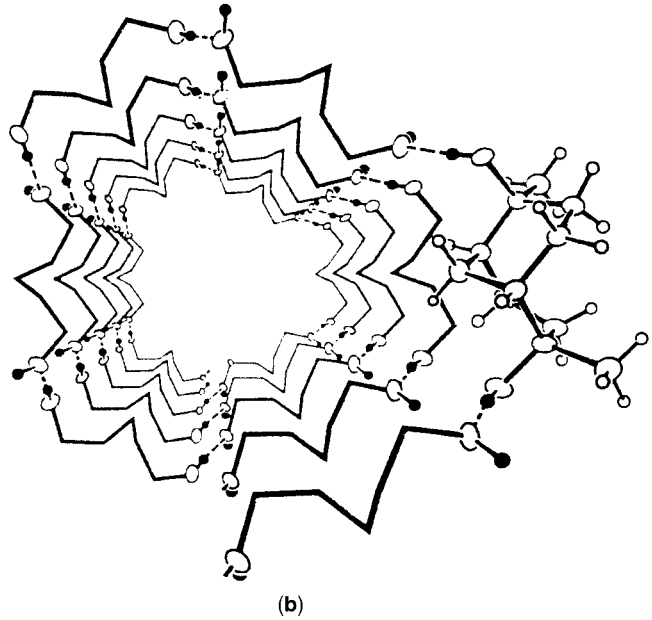


(**36**) (**37**) (**38**) (**39**) (**40**) (**41**) (**42**) (**43**)

Fig. 17. Prototypical host molecules based on more recent clathrate strategies.



(**a**)



(**b**)

Fig. 18. Crystal structures of recent clathrate design: (**a**) coordinatoclathrate between host (**39**) (Fig. 17) and *n*-butanol (host–guest hydrogen bonding in the shaded area); (**b**) perspective view of the helical inclusion channel formed by diol host (43) (Fig. 17; all except one host molecule are represented diagrammatically) (111,122).