Vol. 80 Commemorative Accounts

Symmetry Driven Self-Assembly of Metallo-Supramolecular Architectures

Markus Albrecht*[1] **and Roland Fröhlich**[2]

[1]Institut für Organische Chemie, RWTH Aachen, Landolweg 1, D-52074 Aachen, Germany

[2]Organisch-Chemisches Institut, Universität Münster, Corrensstrasse 40, D-48149 Münster, Germany

Received January 10, 2007; E-mail: markus.albrecht@oc.rwth-aachen.de

The self-assembly of well-defined metallosupramolecular aggregates highly depends on the symmetry of the ligands as well as of the metals. Approaches in which symmetry considerations allow the stepwise—"hierarchical"—assembly of helicate-type complexes from very simple catechol derivatives are described. In addition helicates and meso-helicates are stereoselectively obtained by the use of linear ligands possessing the relevant symmetry element for the formation of either diastereomer (even–odd principle). In case of helicates, this allows the preparation of enantiomerically pure complexes. Finally, the self-assembly of tetrahedral M_4L_4 complexes is described using either constrained flexible or highly predisposed rigid ligands.

Introduction

Self-assembly processes allow the specific formation of well-defined (multi)nanometer-sized objects and therefore open up an entry into a chemical bottom up approach towards nanotechnology. For effective self-assembly the interaction between molecular building blocks should be non-covalent (and thus reversible). This is important to correct mistakes which occur during aggregation.[1–4]

In metallosupramolecular chemistry the non-covalent interactions are coordinative bonds between donor ligands and acceptor metals. In fact, this kind of bond can not really be considered as non-covalent due to a high covalency of the interaction. However, in case of ligand/metal ion systems in which thermodynamically stable but kinetically labile complex units are involved, the reversibility of the complex formation enables "self-assembly." Well-defined multinuclear metallosupramolecular aggregates are only obtained, if the ligands as well as the complex geometries complement one another to finally form one thermodynamically favoured object. Therefore, in metallosupramolecular chemistry, we have to consider the preferred coordination mode of metal ions, as well as the symmetry of the ligands.[5–9]

Following Alfred Werners early concept of coordination chemistry, different metal ions prefer different coordination environments like square planar, tetrahedral, or octahedral (as shown in Fig. 1).[10] This geometrical preference at the metal can be used to control the spatial orientation of coordinating ligands. In one approach ligands are introduced which posses several monodentate binding sites. This leads either to coordination polymers[11] or, as described by Fujita,[12] Stang et al.,[13] and others,[14,15] to big soluble supramolecular species. However, very often not monodentate but chelating complex units are used preferably because they often result in more stable compounds.

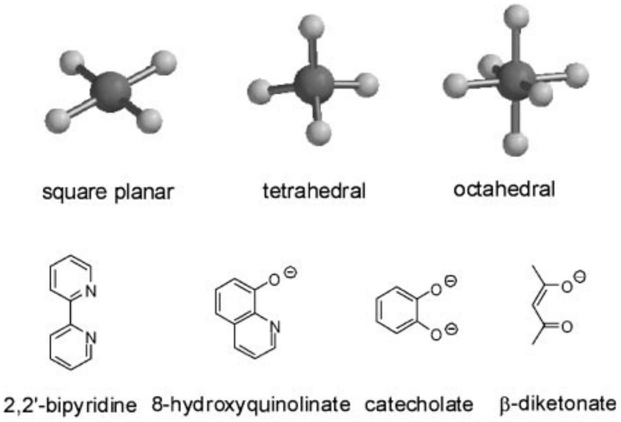


Fig. 1. Schematic representations of square planar, tetrahedral, or octahedral metal complexes and chelating ligands which are frequently used in metallosupramolecular chemistry.

2,2′-Bipyridine is probably the most prominent bidentate complex unit in metallosupramolecular chemistry.[16] This will not be the topic of this article but we will present our recent results on the symmetry driven formation of oligonuclear coordination compounds, using 8-hydroxyquinolinate,[17] catecholate,[18] or β-diketonate[19,20] chelating units.

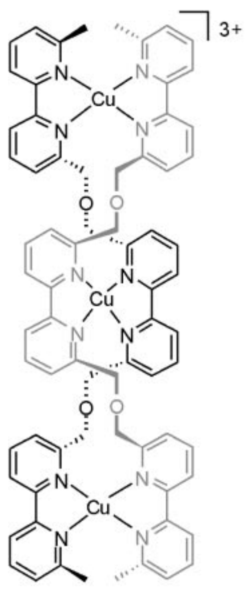
Published on the web May 14, 2007; doi:10.1246/bcsj.80.797

An Introduction to Helicates

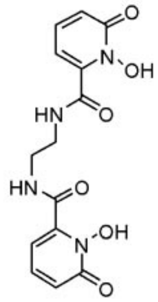
In 1987, Lehn et al. introduced the term "helicate" for di- or oligonuclear complexes, in which two or three linear oligodonor ligands wrap around two or more metal centres. The complexes are formed in self-assembly processes by simple mixing of the components. The trinuclear copper(I) complex $[Cu_3(\mathbf{1})_2]^{3+}$ was the first structurally characterized double-stranded helicate (Fig. 2).[21] Already two years earlier, when the term "helicate" was not even introduced, Raymond et al. described the dinuclear triple-helical complex $[Fe_2(\mathbf{2})_3]$.[22]

In principle, helicates are Werner-type coordination compounds with two (or more) complex moieties connected by spacers. E.g., double-stranded helicates are formed from linear ligand strands with bidentate chelating units and tetrahedrally coordinated metal ions, whereas appropriate metal centres for triple-stranded helicates possess, e.g., octahedral coordination geometry.[23–25]

Due to the simplicity of helicates, they developed over the years to a kind of metallosupramolecular chemists "drosophila." They allow the study of fundamental mechanistic principles. Those can not so easily investigated with more complicated systems. In the following, some symmetry aspects of helicate assembly will be described, that (1) result in the hierarchical formation of non-covalently connected helicates, (2) allow to control the stereoselectivity during the complex formation, and (3) prevent the formation of a helicate but cause the formation of an interesting cluster complex. Based on this, a strategy is developed, how molecular tetrahedra can be made from rigid as well as from flexible triangular ligands.



$[Cu_3(\mathbf{1})_2]^{3+}$



$\mathbf{2}$-H_2

Fig. 2. The first structurally characterized trinuclear double-stranded helicate $[Cu_3(\mathbf{1})_2]^{3+}$ and ligand $\mathbf{2}$-H_2 which forms a dinuclear triple-stranded helicate $[Fe_2(\mathbf{2})_3]$.

Hierarchical Assembly of Dinuclear Helicate-Type Complexes

There are two different methodologies, to afford helicates. The first and more common approach is to prepare linear ligand strands and then mix those with metal ions to get the desired complexes (vide infra). Alternatively, coordination compounds with additional binding sites or reactive units are prepared, so that in a second reaction step appropriate spacers can be introduced between two (or more) complex moieties.

Following the latter strategy, dinuclear titanium(IV) complexes $[Li_3\{Ti(\mathbf{3})_3\}_2]^-$ were synthesized. Ligands **3** do not only possess the catecholate but in addition a salicylate binding site. The catecholate is appropriate for a three-fold pseudooctahedral coordination to a titanium(IV) ion. If this proceeds in the presence of lithium cations, each of the latter can be chelated by two salicylate units. In this way two Ti-complexes are triply bridged to obtain $[Li_3\{Ti(\mathbf{3})_3\}_2]^-$ (see Figs. 3 and 4). The complex formation with titanium(IV) can be considered as the first recognition, while the dimerization by three lithium ions represents the second recognition event. Those two steps define the hierarchy of the assembly process.

Figure 4 shows the X-ray structure of the dimeric anion $[Li_3\{Ti(\mathbf{3a})_3\}_2]^-$. The side view (left) presents the two pseu-

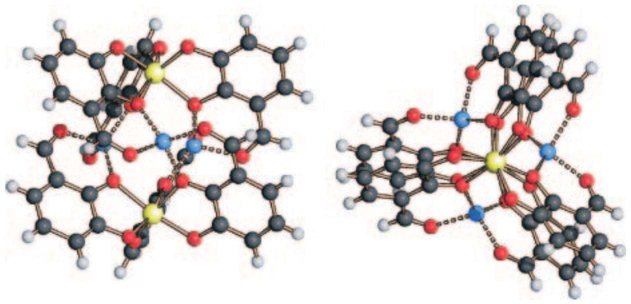


Fig. 4. Two different views of the X-ray structural analysis of $[Li_3\{Ti(\mathbf{3a})_3\}_2]^-$.

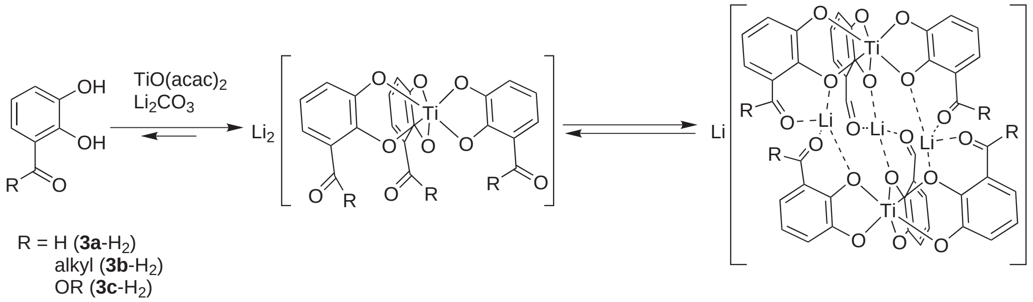


Fig. 3. Hierarchical assembly of dinuclear titanium(IV) complexes by lithium cation-templated dimerization of tris[(3-carbonyl)-catecholate] complexes.

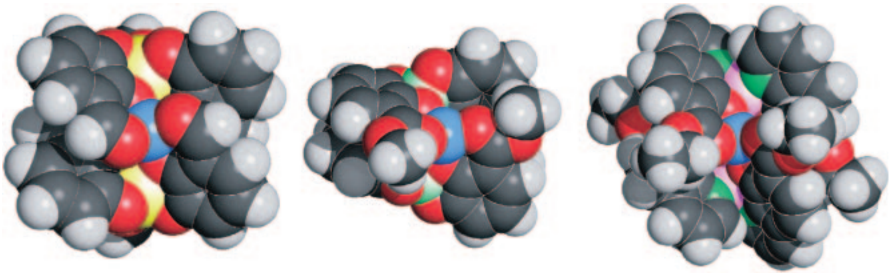


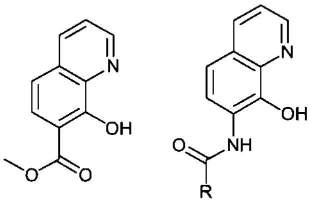
Fig. 5. Comparison of the X-ray structures of the lithium-bridged dimeric helicate-type complexes $[Li_3\{Ti(\mathbf{3a})_3\}_2]^-$ (left), $[Li_2\{B(\mathbf{3c})_2\}_2]^-$ (centre), and $[Li_3\{Ni(\mathbf{4a})_3\}_2]^-$ (right).

dooctahedral complex units which are triply bridged by lithium bis-salicylate spacers. The high symmetry of this complex is seen by the view along the Ti–Ti axis (right). The assembly process is highly stereoselective and only the helicate is formed. This means that two complexes possessing the same configuration afford the dimer, while the heterochiral meso-complex is not found. This chiral recognition in some respects is related to the formation of a sphere (e.g. an apple) from two chiral halves in "La coupe du roi."[26] Due to the dynamic behaviour of the mononuclear titanium complexes, the selection of the second unit proceeds out of an equilibrating mixture of stereoisomers.

Due to the non covalent nature of the lithium bis-salicylate bridge in the spacer the helicate formation is reversible. In solution monomeric as well as dimeric species are observed. The dimerization strongly depends on different factors: (1) The donor ability of the substituent at the catechol ligand is very important. With a good donor group lithium is bound more strongly than with a poor donor. Therefore, the stability of the dimer increases in the sequence aldehyde < ketone < ester. In addition, sterical demands at the ester or at the ketone can destabilize the dimer. (2) Solvents which are able to solubilize lithium cations reduce the stability of the dimer. DMSO effectively competes with the carbonyls at the ligands for lithium binding. It results in the observation of the monomer as the major component. Poorly lithium solvating solvents like acetone lead to a strong preference of the dimer. (3) Lithium cations are attracted stronger by highly negative-charged monomeric units resulting in more stable dimers (e.g. $[Ga(\mathbf{3})_3]^{3-}$ forms more stable dimers than $[Ti(\mathbf{3})_3]^{2-}$).

Thorough investigations of the dimerization process reveal that it is enthalpically as well as entropically favoured. The latter is due to the liberation of solvent molecules from the solvation sphere of lithium upon fixation of three of the cations as the spacers of the dimer. On the first view, the observed monomer–dimer equilibrium and the hierarchical assembly of dinuclear helicate-type complexes $[Li_3\{Ti(\mathbf{3a})_3\}_2]^-$ seems to be unprecedented. However, Figures 5 and 6 show further cases of related systems which document the versatility of this process.[27]

In Fig. 5, the structure of the triple-stranded catecholate complex $[Li_3\{Ti(\mathbf{3a})_3\}_2]^-$ is compared to a related double-stranded dinuclear boron $[Li_2\{B(\mathbf{3c})_2\}_2]$ complex (centre). Here, boron(III) is coordinated to two ligands **3c** in a pseudo-tetrahedral fashion and two lithium cations bridge two complex units $[B(\mathbf{3c})_2]^-$. The coordination geometries at the lithium cations are strongly distorted in the solid phase owing to release of strain arising during the dimerization. In solution, on the other hand, a symmetric (probably fluxional) structure is observed by NMR.



4a

R = C_8H_{17},
S-NHCH(CH_3)Ph
4b

Chart 1.

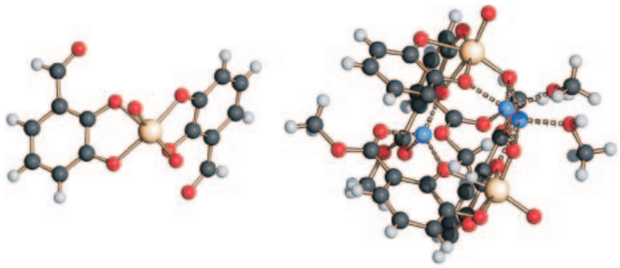


Fig. 6. Parts of the X-ray structures of monomeric $[MoO_2(\mathbf{3a})_2]^{2-}$ (left) and dimeric $[Li_3\{MoO_2(\mathbf{3c})_2\}_2]^-$ (right).

Substitution of the catechol ligands **3c** by 8-hydroxyquinoline ligands **4a** (Chart 1) with an ester group in 7-position allows the hierarchical formation of dinuclear complexes with metal ions like zinc(II), cobalt(II), or nickel(II). The structure of the nickel complex $[Li_3\{Ni(\mathbf{4a})_3\}_2]^-$ is depicted in Fig. 5 (right). A prerequisite for the formation of the dimer is the negative charge at the monomeric complex units. If neutral complexes (e.g. $Al(\mathbf{4a})_3$) are present, no dimerization can take place even if an excess of lithium salts is added.[28]

Figure 6 shows a further example of dimerization through lithium cations. The substitution of titanium(IV) by the dioxomolybdenum(VI) unit enables the coordination of only two catecholate units to the metal. In solution still monomer–dimer equilibria are observed. In the case of the aldehyde **3a** the monomeric $[MoO_2(\mathbf{3a})_2]^{2-}$ crystallizes. It possesses anti orientation of the coordinating ligands. A lithium- and DMF-bridged coordination polymer is observed. With the ester-type ligand **3c** the dimer $[Li_3\{MoO_2(\mathbf{3c})_2\}_2]^-$ is found by X-ray structure analysis (Fig. 6). One lithium cation bridges two ligands **3c**. The lack of the third ligand enforces the involvement

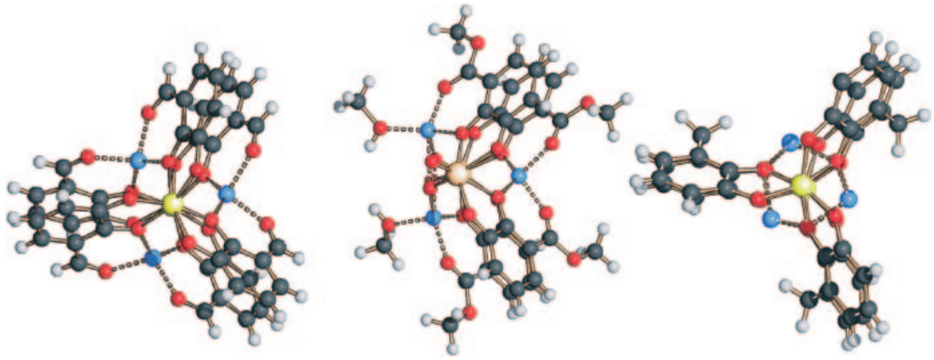


Fig. 7. Comparison of helicate-type complexes with three-coordinated lithium cations. Left: $[Li_3\{Ti(\mathbf{3a})_3\}_2]^-$, centre: $[Li_3\{MoO_2(\mathbf{3c})_2\}_2]^-$, right: $[Li_3\{Ti_2(\mathbf{5a})_3\}]^{4-}$.

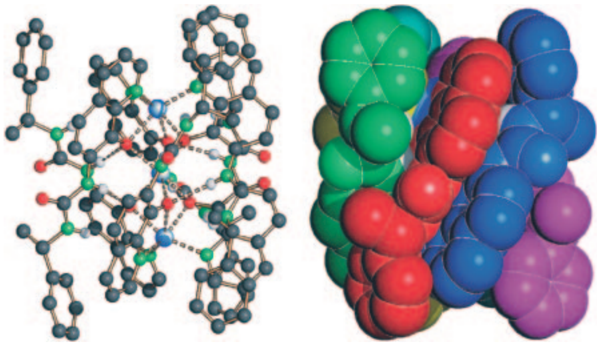


Fig. 8. Structure of the hierarchically assembled trinuclear zinc(II) complex $[Zn\{Zn(\mathbf{4b})_3\}_2]$. The representation on the right shows the hexa-stranded helical arrangment.

of two Mo=O functions coordinating to the additional two bridging lithium cations. Again only complex units with the same configuration can afford a homochiral dimer.[29]

Figure 7 shows the similarity of the positions of lithium cations in the hierarchically formed complexes $[Li_3\{Ti(\mathbf{3a})_3\}_2]^-$ (left), $[Li_3\{MoO_2(\mathbf{3c})_2\}_2]^-$ (centre), and the triply methylene-bridged complex $[Li_3\{Ti_2(\mathbf{5a})_3\}]^{4-}$ (right).[30,31] Two lithium cations of the molybdenum complex, which coordinate two oxo-units of the complex moieties, are pentacoordinated. Solvent molecules are filling up the remaining coordination site.

In case of $[Li_3\{Ti_2(\mathbf{5a})_3\}]^{4-}$ all three lithium cations are pentacoordinated binding DMF molecules as coligands (not shown in Fig. 7).

Introducing a secondary amide in 3-position of catechol or in 7-position of 8-hydroxyquinoline suppresses the assembly of the dimer due to an unfavourable conformation of the amide caused by intramolecular hydrogen bonding to the coordinated phenolate. Inverting the amide in 7-position of 8-hydroxyquinoline or attaching an urea moiety (ligands **4b**) afford a different class of hierarchically assembled helicates upon coordination with zinc(II) ions. Now one central zinc atom bridges two syn arranged monomeric complex units $[Zn(\mathbf{4b})_3]^-$ by coordination to the quinolinate oxygen atoms.[32]

Figure 8 presents the result of an X-ray structure analysis of a trinuclear zinc complex $[Zn\{Zn(\mathbf{4b})_3\}_2]$ with a *S*-phenylethylurea substituent in 7-position of the ligand. Due to the chiral information at the ligand side chain, the complex is formed in enatiomerically pure form. A right-handed helical twist of the coordination compound is induced by the *S*-configuration of the ligand.[33]

The reported examples show, that the hierarchical assembly of oligonuclear helicate-type complexes is not a curiosity of coordination chemistry but seems to be a general approach to obtain such compounds. Some additional examples are found in the literature.[34–40] Therefore, this strategy should be appropriate in order to make functional compounds in which the implementation of special properties is predetermined by substituents at the ligand and by judicious choice of the metal.

Stereoselective Formation of Helicates and *meso*-Helicates

In the "classical" way helicates are obtained by coordination of covalently bridged oligo-topic ligands to metal cations. Figure 9 shows some representative examples of alkyl-bridged catechol **5** as well as 8-hydroxyquinoline ligands **6**.

Ligand **6b**-H_2 contains an iso-butenylidene spacer, which is easily introduced following the Hiratani-double-Claisen rearrangement.[41–43]

The stereochemistry of helicate-type complexes is highly dependent on the length of the alkyl spacer. In Fig. 9 (centre) the general principle of the stereocontrol is illustrated: linear alkyl groups prefer a zigzag conformation due to the minimization of steric interaction within the chain. This results in case of an even number of carbon atoms in a structure possessing a C_2 axis (an element of chirality) as the relevant symmetry. With an odd number of carbon atoms a conformation with a mirror plane (σ) is obtained. Therefore, ditopic ligands with an even number of methylene units in the spacer are predisposed to form chiral helicates, while an odd number of carbon atoms results in the preference of the heterochiral *meso*-helicate. In a thermodynamically controlled system the weak influence of the zigzag arrangement of the alkyl chain is decisive to determine high diastereoselectivities in the assembly of either the helicate or the *meso*-helicate.[44] However, if other controlling forces (e.g. templating effects) override the influence of conformation, the relative stereochemistry between the two metal complex units can be inverted.[45]

Figure 10 shows the results of X-ray structure analyses of titanium(IV) complexes with ligands **5**-H_4. Following the described principle, ligands **5a** (CH_2 spacer) and **5c** ($(CH_2)_3$ spacer) form the *meso*-helicates $[Ti_2(\mathbf{5a}/\mathbf{5c})_3]^{4-}$.[46] In the solid state only two of the ligands **5c** of $[Ti_2(\mathbf{5c})_3]^{4-}$ feature the

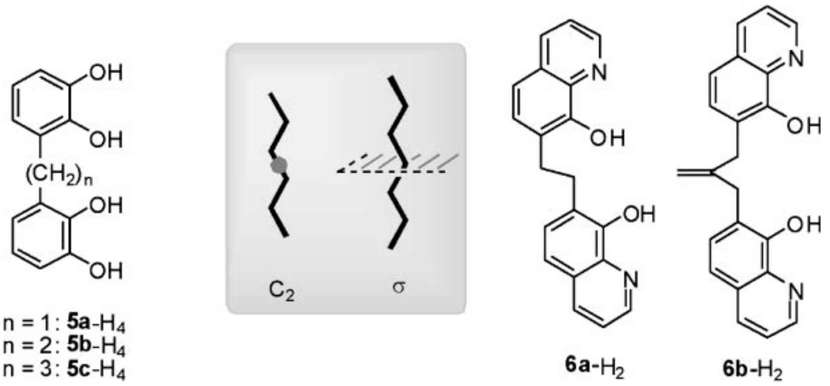


Fig. 9. Alkyl-bridged dicatechol (**5a**–**5c**-H_4) and di(8-hydroxyquinoline) ligands (**6a**,**b**-H_2). The inset shows the relevant symmetry elements of the alkyl chain, which controls the formation of the helicate (C_2) versus the *meso*-helicate (σ).

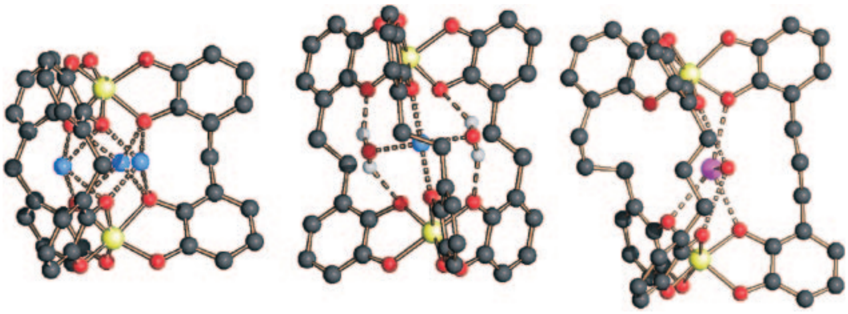


Fig. 10. Self-assembled dinuclear titanium(IV) catecholate complexes. Left: $[Li_3\{Ti_2(\mathbf{5a})_3\}]^-$ (*meso*-helicate), centre: $[\{Li(H_2O)_2\}\{Ti_2(\mathbf{5b})_3\}]^{3-}$ (helicate), right: $[\{Na(H_2O)\}\{Ti_2(\mathbf{5c})_3\}]^{3-}$ (*meso*-helicate).

zigzag conformation. Due to packing effects of the complex and co-crystallizing solvent molecules, one of the ligands strands is not able to adopt this conformation. Anyhow, the two complex units possess the proposed opposite configuration of the *meso*-helicate. In solution, the *meso*-compounds ΔΛ-$[Ti_2(\mathbf{5a}/\mathbf{5c})_3]^{4-}$ are the only detectable species by NMR. The central methylene units act as stereochemical probes which allow discrimination between the diastereomeric complexes.[47] With two carbon atoms in the spacer, the homochiral helicate $[Ti_2(\mathbf{5b})_3]^{4-}$ is found (Fig. 10, centre) as the racemic mixture of the left- (ΛΛ) and right-handed (ΔΔ) helices.[48]

As also is shown in Fig. 10, the tetraanionic dinuclear complexes $[Ti_2(\mathbf{5a}\text{–}\mathbf{5c})_3]^{4-}$ provide some inner room for counter cations.[49] Those are attracted by the negative charge and are coordinating to the internal oxygen atoms. In case of $[Ti_2(\mathbf{5a})_3]^{4-}$ this space is too small to encapsulate the cations and they are coordinating from the outside of the cavity. In fact, the incorporated alkaline metal cations act as templates and control the formation of the dinuclear complexes. If instead of the alkaline metals non-appropriate cations (e.g. $[Ph_4P]^+$) are added, only mixtures of oligomeric coordination compounds are obtained.[50]

This templating effect can be well studied in case of the hydroxyquinoline ligands **6**-H_2, which form neutral complexes with trivalent cations such as aluminium(III), gallium(III), or iron(III).[51] In the absence of templating cations only mixtures of oligomeric compounds are observed. Akaline metal salts can be added during complex formation and in a template-directed self-assembly process the helicates are formed in quantitative yield.[52] The same product can be found by adding salts to the oligomers in solution and heating the mixtures for some time. Following the principle of "dynamic combinatorial chemistry,"[53] the preformed mixture ("library") is transformed into one defined species. Crosswise dependence of the size of the template and the length of the spacer is seen. The stereochemistry of the formation of dinuclear compounds from quinoline ligands **6** is controlled by the same even–odd principle as it was described for the catecholates **5**.[54]

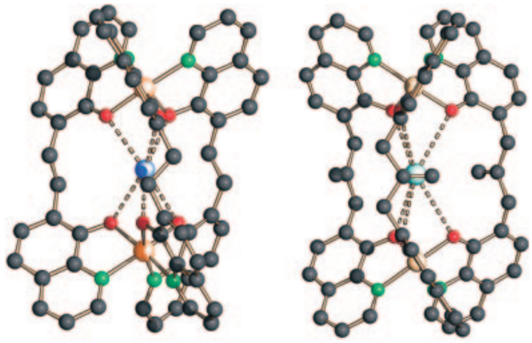


Fig. 11. Dinuclear gallium(III) complexes. Left: $[KGa_2(\mathbf{6a})_3]^+$ (helicate), right: $[CsGa_2(\mathbf{6b})_3]^+$ (*meso*-helicate).

Figure 11 shows the results of X-ray structure analyses of complexes $[Ga_2(\mathbf{6a}/\mathbf{6b})_3]$. In $[KGa_2(\mathbf{6a})_3]^+$ three of the ethylene-bridged ligands wrap in a helical fashion around two metal centers forming the chiral helicate. A potassium cation acts as template and stabilizes the dinuclear complex. If a related ligand with the spacer attached in 3-position of the quinoline is introduced, no internal oxygen atoms are present in the

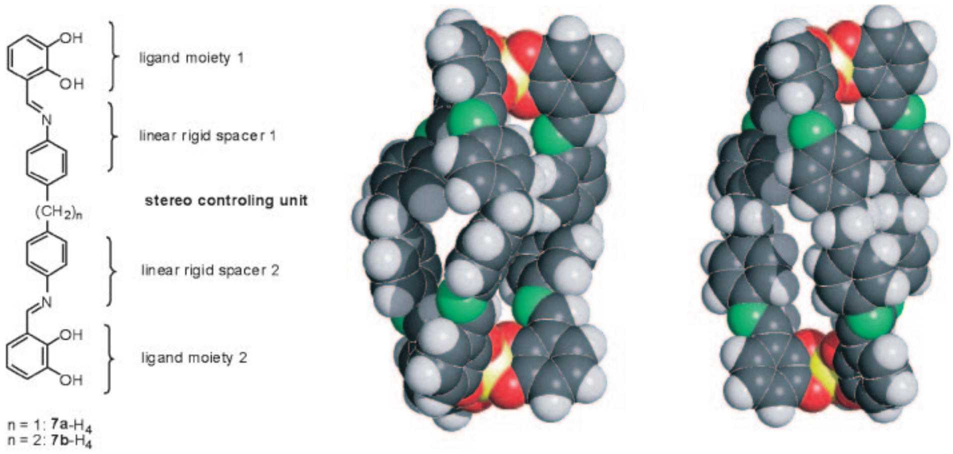


Fig. 12. Formation of a *meso*-helicate and a helicate from rigid ligands **7a**,**b**-H_4 with 2 nm length, possessing a small stereo controlling unit.

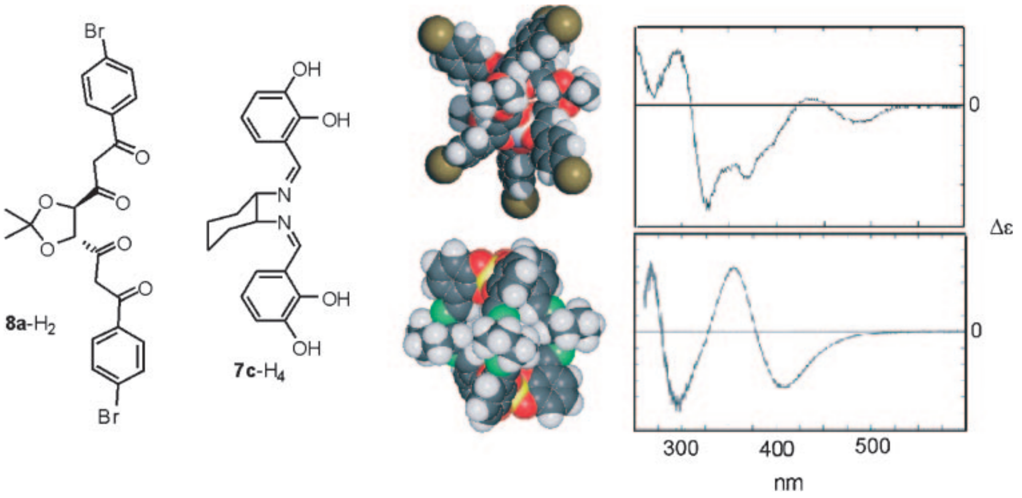


Fig. 13. Enantiomerically pure helicates $[Fe_2(\mathbf{8a})_3]$ (top) and $[Ti_2(\mathbf{7c})_3]^{4-}$ (bottom) and corresponding CD spectra.

gallium(III) complex cavity. Consequently, no templating by alkaline metal cations can occur and no defined coordination compounds are obtained.

In $[CsGa_2(\mathbf{6b})_3]^+$ the three ligands with three carbon atoms in each spacer form the *meso*-helicate. A cesium cation acts as the template in the structure presented in Fig. 11 (right). The relative stereocontrol between the two metal complex units in catechol $[Ti_2(\mathbf{5})_3]^{4-}$ as well as in 8-hydroxyquinolinate complexes $[Ga_2(\mathbf{6})_3]$ can be influenced by the preferred zigzag conformation of alkyl spacers (even versus odd). The question arose, if this control is still effective, when the distance between the complex moieties gets very large with only a small stereo controlling unit in the spacer.

Ligands **7a**-H_4 and **7b**-H_4 were prepared by imine condensation of 2,3-dihydroxybenzaldehyde with the appropriate diamines.[55] They possess two catechol coordination sites which bear linear and rigid phenyl imine units in 3-position. Two of those are connected through the para position of the phenyl rings to a central stereo controlling unit: methylene to obtain the meso helicate or ethylene for helicate formation. Reaction of the ligands with titanium(IV) ions (in the presence of alkaline metal carbonate as base and template) leads to the dinuclear coordination compounds $\Lambda\Delta$-$[Ti_2(\mathbf{7a})_3]^{4-}$ and $\Lambda\Lambda/\Delta\Delta$-$[Ti_2(\mathbf{7b})_3]^{4-}$. In those 2 nm sized complexes the stereocontrol is still effective (see Fig. 12). Hereby the chiral information of one complex moiety is transferred through the rigid spacer to the stereo controlling unit. The latter is located about 1 nm from the first stereo centre apart and controls the stereochemistry of the second complex unit, which again is 1 nm away from the stereo controlling unit. This example shows, that stereo control over long distances in supramolecular chemistry can be achieved by very simple mechanisms.[56,57]

The described self-assembly processes of helicates are highly diastereoselective. However, it is important to obtain the helicates not as racemic mixtures but as the enantiomerically pure left- or right-handed helices. In most cases the separation of the enantiomers is not possible due to a low racemization barrier.[58–60] Enantiomerically pure helicates can be made by introducing chiral substituents either at the termini of the complexes[61] or in the spacer.[62,63]

Figure 13 shows two dinuclear helicates $[Fe_2(\mathbf{8a})_3]$ and $[Ti_2(\mathbf{7c})_3]^{4-}$ which are the $\Delta\Delta$-enantiomers. The sense of helicity is induced by the R,R-configurated substitution at the central five-membered ring of the bis-β-diketonate ligand **8a**[64] and

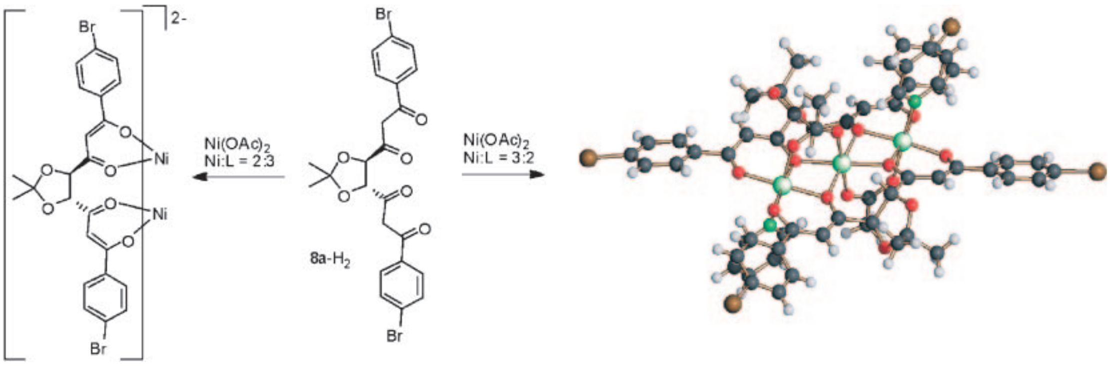


Fig. 14. Stoichiometry-controlled formation of $[Ni_2(\mathbf{8a})_3]^{2-}$ and $[Ni_3(\mathbf{8a})_2(OAc)_2(pyridine)_2]$.

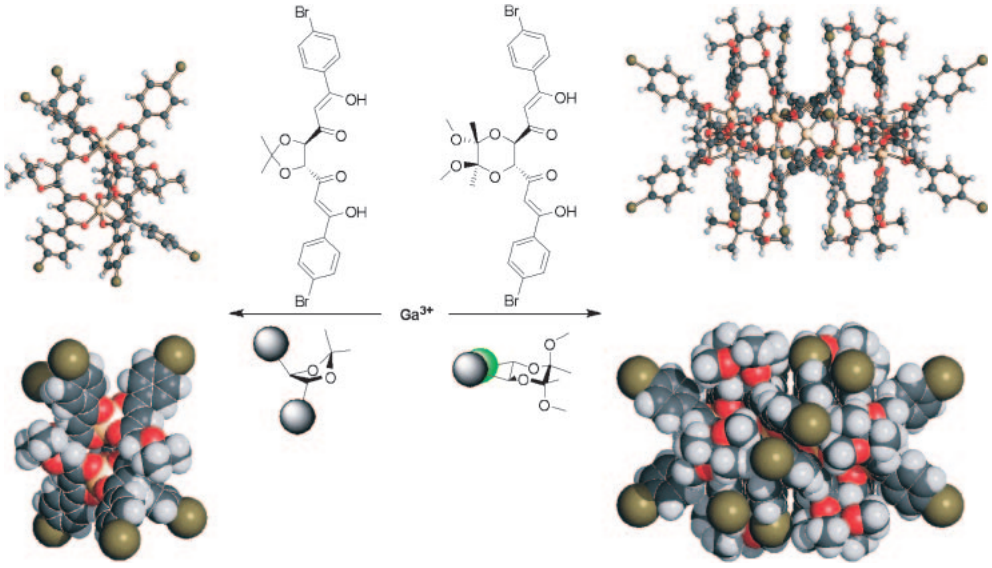


Fig. 15. Formation of the helicate $[Ga_2(\mathbf{8a})_3]$ and the nonanuclear cluster $[Ga_9(\mathbf{8b})_8(OH)_{10}]^+$.

of the six-membered ring of the iminocatechol **7c**. The compounds were investigated by CD spectroscopy and the assignment of the stereochemistry at the complex units of $[Ti_2(\mathbf{7c})_3]^{4-}$ was confirmed in solution by computational methods.[65]

In general, the self-assembly of helicates or *meso*-helicates is highly stereoselective. Hereby the transfer of symmetry features of the ligands onto the dinuclear coordination compounds is very effective. As was discussed above, the diastereoselectivity of this process can be used to get not only racemic mixtures of helicates. Enantiomerically pure compounds are formed by introduction of chiral information in the ligand.

Commensurate versus Incommensurate Ligand Geometries for the Formation of Helicates

Ligands which are able to form helicate-type complexes have to adopt a special conformation in order to afford the dinuclear compounds. However, the rotation around σ-bonds might lead to conformations which favour other structures then helicates.[66] E.g., the bis-β-diketonate ligand **8a** forms with nickel(II) ions either a dinuclear triple-stranded helicate $[Ni_2(\mathbf{8a})_3]^{2-}$ or a trinuclear double-stranded complex $[Ni_3(\mathbf{8a})_2(OAc)_2(pyridine)_2]$ (Fig. 14). The assembly of the respective compounds is controlled by the stoichiometry of the reactants.[67]

In the case of nickel complexes $[Ni_2(\mathbf{8a})_3]^{2-}$ and $[Ni_3(\mathbf{8a})_2(OAc)_2(pyridine)_2]$ the ligand **8a** can adopt a twisted conformation, which is in favour for helicate formation, while a planar arrangement of the binding sites favours the trinuclear complex.

The situation changes by switching from ligand **8a** with a 5-membered ring in the spacer to the corresponding ligand **8b** with a 6-membered bridge.[68]

Ligand **8b** is incommensurate for the assembly of triple-stranded helicates. Due to a different dihedral angle of the chelating units at the bridging ring system (approx. 95° at the five- and 53° at the six-membered ring) ligand **8a** forms a triple-stranded helicate $[Ga_2(\mathbf{8a})_3]$ with gallium(III) ions (and also iron(III) or nickel(II) ions). On the other hand, ligand **8b** can not form the triple-stranded complex. The reaction stops at the double-stranded hydroxide-bridged intermediate $[Ga_2(\mathbf{8b})_2(\mu\text{-}OH)]^+$, which is observed by ESI-MS and which is isolated as building block of the nonanuclear cluster $[Ga_9(\mathbf{8b})_8(OH)_{10}]^+$ (Fig. 15). This cluster exhibits a connecting central $[Ga(OH)_4]^-$ moiety and two bridging hydroxides in addition to four $[Ga_2(\mathbf{8b})_2(\mu\text{-}OH)]^+$ units. The building block $[Ga_2(\mathbf{8b})_2(\mu\text{-}OH)]^+$ as well as the cluster $[Ga_9(\mathbf{8b})_8(OH)_{10}]^+$ can be considered as analogues to intermediates in the formation of helicates like e.g. $[Ga_2(\mathbf{8a})_3]$.[69]

Tripodal Triscatechol Ligands for the Formation of Mononuclear as well as Tetranuclear Complexes

Helicates and *meso*-helicates are more or less cylindrical objects. Thus, the main axis of the molecule is orientated in only one dimension. In order to obtain three-dimensional structures, the linear oligo-donor ligands which are used for the formation of helicates have to be substituted by more complex ligands that span up faces of geometric bodies.[70] A possible geometry of such a ligand is the triangle (C_3-symmetry), which in combination with appropriate metal ions can form a tetrahedron.[71,72]

Our approach was to use triangular ligands with catechol corners and octahedrally coordinating metal ions to obtain tetrahedra.[73–77] In the investigations the problem was addressed, if the ligands have to be rigid and highly preorganized, or if flexible ligands also can be manipulated in such a way that they lead to the desired oligonuclear structure and not only to mononuclear complexes (Fig. 16).[78]

Flexible ligands should favour the mononuclear compounds, while rigid ligands should lead to tetrahedra. However, if constrains are induced in a flexible system, the formation of the mononuclear coordination compound might be prevented and tetrahedra could be available.

Figure 17**A** shows the preferred conformation of coordinated catecholamides.[79] The amide proton forms a hydrogen bond to the internal catecholate oxygen atom. Due to this fixation, flexible tripodal catecholamides (like trencam)[80] are ideal for the binding of metal ions. In case of catechol imines the situation is different. For the formation of a 1:1 complex the imine nitrogen atoms have to be orientated towards the catecholate oxygens **B**. Due to the repulsion between the electron pairs at O and N, the nitrogen atom directs "outwards" **C**. This would lead to a spreading out of the deprotonated ligands **9**, what predisposes them for the formation of tetranuclear rather than mononuclear complexes. However, if appropriate cationic templates (alkaline metal ions, protons) are present, they compensate the repulsion between the electron pairs and enable the "inward" orientation of the imine **D**. In order to obtain tetrahedral complexes, the conformation **C** has to be the favoured one.[81]

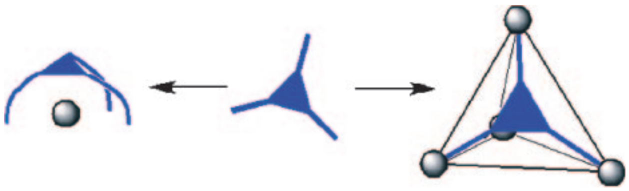


Fig. 16. Schematic representation of the coordination behaviour of triangular ligands leading either to a mononuclear complex or to a tetranuclear molecular tetrahedron.

To investigate the coordination chemistry of tripodal flexible catechol imines, the ligands **9a**,**b**-H_6 were prepared. **9a**-H_6 represents a chiral version of **9b**-H_6.[82] However, the bulky isopropyl groups of **9a**-H_6 prevent from "spreading out" of the ligand and only mononuclear complexes can be obtained with gallium(III) or titanium(IV) ions.

The repulsion between the imine and the catecholate lone pairs leads to a high basicity at the catechol imine units, which consequently take up protons (e.g. from solvent) to compensate this repulsion.

Figure 18 (left) shows the X-ray structure analysis of [Ga(**9a**-H_3)]. Ligand **9a** coordinates in a hexadentate fashion to the gallium center and forms a cap, in which three protons are encapsulated. To reduce repulsion between the three protons, the catechol imines adopt an enaminone/chinomethine mesomeric structure. In the presence of sodium cations all three protons can be removed to afford [Ga(Na**9a**)]$^+$. Now sodium is coordinated to the catechol imines and stabilizes the mononuclear gallium complex.[83]

The X-ray structure of [Ti(Na**9b**)]$^-$ (Fig. 18, centre) shows that sodium fits perfectly into the cavity of the coordination compound. Performing the coordination of titanium(IV) ions with **9b** in the presence of potassium carbonate does not lead to defined compounds. However, it is possible to crystallize one complex from the mixture of compounds in DMF. The X-ray structure of [Ti_3O_2(K**9b**)$_2$]$^{2-}$ reveals that potassium cat-

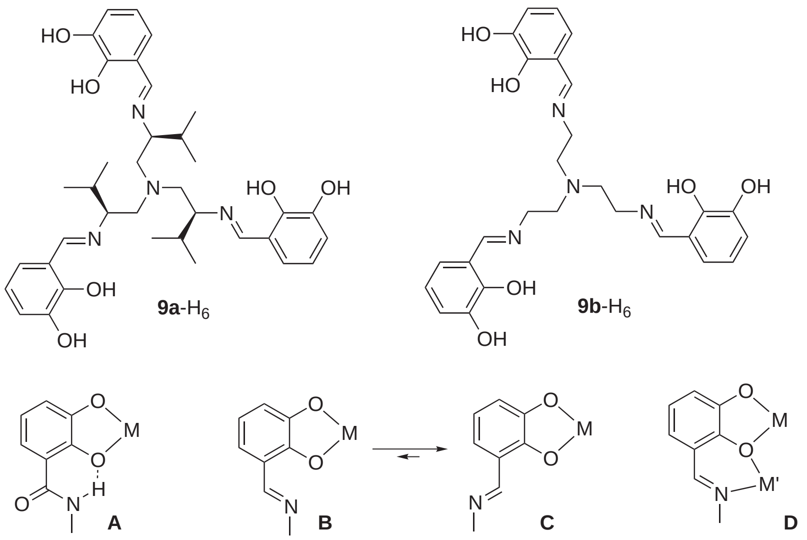


Fig. 17. Flexible ligands **9a**,**b**-H_6 and the preferred conformation at coordinated catechol amides **A** and catechol imines **B**–**D**.

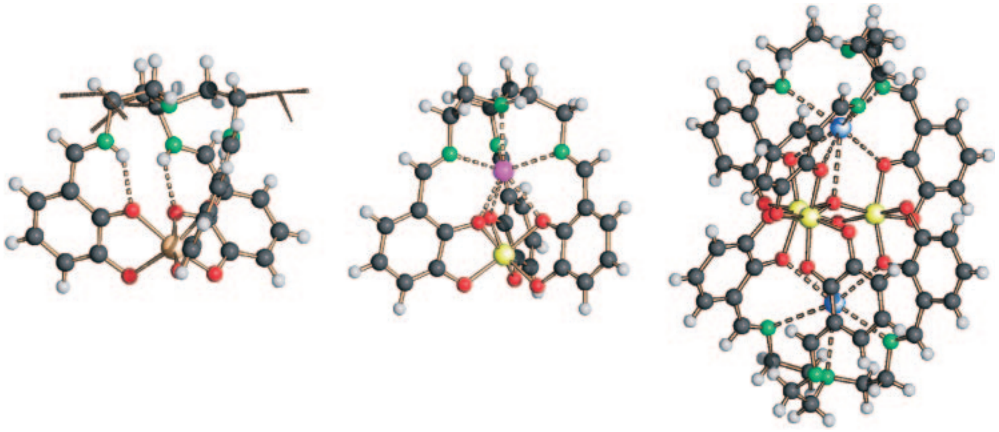


Fig. 18. X-ray structures of complexes [Ga(**9a**-H$_3$)] (left), [Ti(Na**9b**)]$^-$ (centre), and [Ti$_3$O$_2$(K**9b**)$_2$]$^{2-}$ (right) based on flexible tripodal ligands.

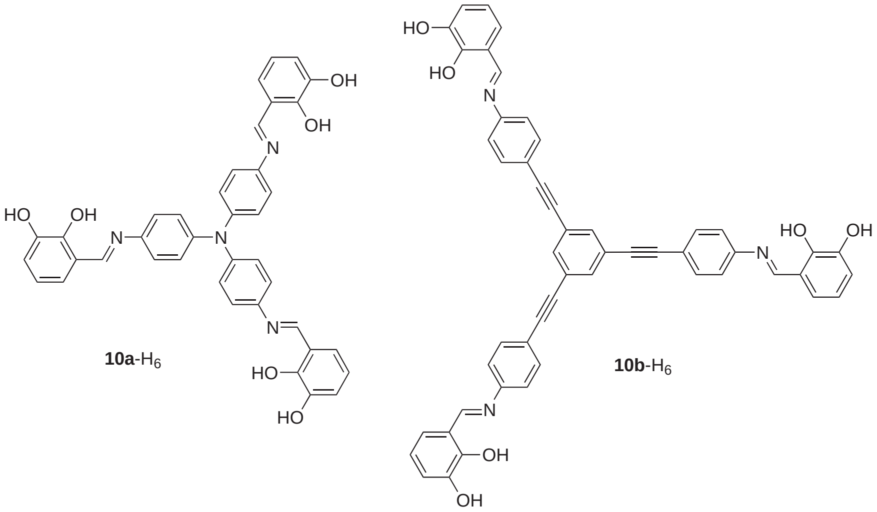


Fig. 19. Rigid triangular ligands **10a**,**b**-H$_6$.

ions also can be bound to coordinated ligand **9b**. In contrast to sodium, the bigger size of potassium in the "cap" prevents the binding of the ligand to only one metal center. Therefore, two (K**9b**)$^{5-}$ units coordinate to a trinuclear dioxo-tris-titanium cluster.

Dissolution of the reaction product of ligand **9b** with titanium(IV) ions and potassium carbonate in the strong donor solvent DMSO causes the removal of potassium from the coordination compound. Within a few hours the tetranuclear complex [Ti$_4$(**9b**)$_4$]$^{8-}$is built. It was characterized by NMR and ESI-MS. In this example, repulsion between the imine and the oxygen lone pairs becomes effective, resulting in the metallo-supramolecular tetrahedron [Ti$_4$(**9b**)$_4$]$^{8-}$.[84]

To enforce the binding of three coordination sites of triangular ligands to three different metal centres, the rigid derivatives **10a**,**b**-H$_6$ were prepared (Fig. 19). Mixing of those compounds with titanium(IV) ions in the presence of potassium carbonate as base leads to the metallosupramolecular tetrahedra [Ti$_4$(**10a**/**10b**)$_4$]$^{8-}$. The complexes [Ti$_4$(**10a**/**10b**)$_4$]$^{8-}$ are stable in solution, what is demonstrated by ESI-MS. Moreover, high symmetry spectra are measured by NMR.

The complex with ligand **10a** possesses an edge of 2 nm length while for [Ti$_4$(**10b**)$_4$]$^{8-}$ this is approximately 3 nm. Therefore, the self-assembly of tetrahedra represents an easy approach towards soluble 3-dimensional multi-nanometer-sized aggregates. Furthermore, the complexes provide huge internal cavities, which are appropriate to encapsulate organic molecules as guest species.[85]

The X-ray structure analysis of the octaanion [Ti$_4$(**10a**)$_4$]$^{8-}$ is shown in Fig. 20. Four titanium(IV) cations are located at the corners of the tetrahedron, while the triangular ligands span the faces. In the solid state, four potassium cations as well as twelve DMF molecules are observed in the internal cavity.[86]

While under appropriate conditions flexible ligands can be used for the formation of metallosupramolecular container molecules, analogous rigid systems are easier to introduce. Their coordination behaviour can be better predicted and therefore they are excellent building blocks for the rational design of supramolecular aggregates as artificial receptors or reaction environments.

Conclusion

In this article, a wide variety of supramolecular coordination compounds is described, which are obtained in metal-

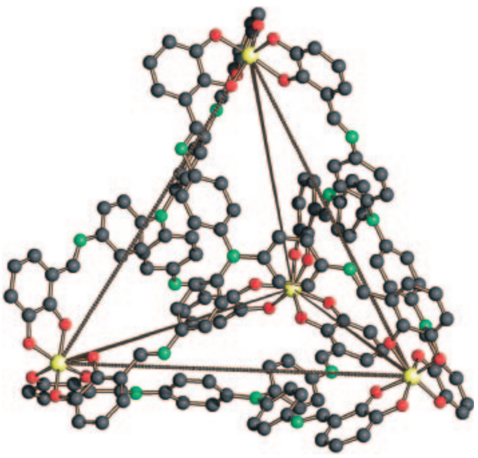


Fig. 20. X-ray structure analysis of the supramolecular tetrahedron $[\mathrm{Ti}_4(\mathbf{10a})_4]^{8-}$.

directed self-assembly processes. Simple mononuclear compounds can be assembled in hierarchical processes to afford complex aggregates. Introducing appropriate bridges as spacers in oligotopic ligands enables the formation of simple helicates or *meso*-helicates as well as huge metallosupramolecular containers.

In all the examples which are reported in this review, symmetry requirements at the ligands and at the metals are the crucial factors for the outcome of the coordination studies. This allows for example the diastereo- and enantioselective preparation of helicates (or *meso*-helicates). On the other hand, incommensurate symmetries or geometries between metals and ligands suppress specific reactions and can result in unprecedented structures such as the described nonanuclear gallium cluster.

In summary, metallosupramolecular chemistry enables the formation of not only aesthetically appealing structures, but it also provides an entry for the preparation of big functional supermolecules. Symmetry considerations help in the design of the ligands and corresponding final aggregates.

We thank all present and former co-workers, which were involved in the different projects. The help by many collaborating partners in the different fields of synthesis, analysis and applications is gratefully acknowledged. Financial support for our chemistry is provided by the Deutsche Forschungsgemeinschaft (e.g. within the Graduiertenkolleg "Methoden der asymmetrischen Synthese" or the Schwerpunktprogramm 1118 and 1166) and the Fonds der Chemischen Industrie.

References

1 J.-M. Lehn, *Supramolecular Chemistry-Concepts and Perspectives*, Wiley-VCH, Weinheim, **1995**.

2 G. M. Whitesides, J. P. Mathias, C. T. Seto, *Science* **1991**, *254*, 1312.

3 D. Philp, J. F. Stoddart, *Angew. Chem.* **1996**, *108*, 1242; *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1154.

4 J. S. Lindsey, *New J. Chem.* **1991**, *15*, 153.

5 S. Leininger, B. Olenyuk, P. J. Stang, *Chem. Rev.* **2000**, *100*, 853.

6 D. L. Caulder, K. N. Raymond, *Acc. Chem. Res.* **1999**, *32*, 975.

7 D. L. Caulder, K. N. Raymond, *J. Chem. Soc., Dalton Trans.* **1999**, 1185.

8 B. J. Holliday, C. A. Mirkin, *Angew. Chem.* **2001**, *113*, 2076; *Angew. Chem., Int. Ed.* **2001**, *40*, 2022.

9 P. J. Steel, *Acc. Chem. Res.* **2005**, *38*, 243.

10 A. Werner, *Z. Anorg. Chem.* **1893**, *3*, 267.

11 K. Biradha, M. Sarkar, L. Rajput, *Chem. Commun.* **2006**, 4169.

12 M. Fujita, *Chem. Soc. Rev.* **1998**, *27*, 417.

13 B. Olenyuk, A. Fechtenkötter, P. J. Stang, *J. Chem. Soc., Dalton Trans.* **1998**, 1707.

14 A. Lützen, *Angew. Chem.* **2005**, *117*, 1022; *Angew. Chem., Int. Ed.* **2005**, *44*, 1000.

15 S. Hiraoka, K. Harano, M. Shiro, Y. Ozawa, N. Yasuda, K. Toriumi, M. Shionoya, *Angew. Chem.* **2006**, *118*, 6638; *Angew. Chem., Int. Ed.* **2006**, *45*, 6488.

16 C. Kaes, A. Katz, M. W. Hosseini, *Chem. Rev.* **2000**, *100*, 3553.

17 P. Baret, C. G. Béguin, H. Boukhalfa, C. Caris, J.-P. Laulhère, J.-L. Pierre, G. Serratrice, *J. Am. Chem. Soc.* **1995**, *117*, 9760.

18 D. Fiedler, D. H. Leung, R. G. Bergman, K. N. Raymond, *Acc. Chem. Res.* **2005**, *38*, 349.

19 J. K. Clegg, L. F. Lindoy, B. Moubaraki, K. S. Murray, J. C. McMurtrie, *Dalton Trans.* **2004**, 2417.

20 A. P. Bassett, S. W. Magennis, P. B. Glover, D. J. Lewis, N. Spencer, S. Parsons, R. M. Williams, L. De Cola, Z. Pikramenou, *J. Am. Chem. Soc.* **2004**, *126*, 9413.

21 J.-M. Lehn, A. Rigault, J. Siegel, J. Harrowfield, B. Chevrier, D. Moras, *Proc. Natl. Acad. Sci. U.S.A.* **1987**, *84*, 2565.

22 R. C. Scarrow, D. L. White, K. N. Raymond, *J. Am. Chem. Soc.* **1985**, *107*, 6540.

23 C. Piguet, G. Bernardinelli, G. Hopfgartner, *Chem. Rev.* **1997**, *97*, 2005.

24 M. Albrecht, *Chem. Rev.* **2001**, *101*, 3457.

25 M. J. Hannon, L. J. Childs, *Supramol. Chem.* **2004**, *16*, 7.

26 F. A. L. Anet, S. S. Miura, J. Siegel, K. Mislow, *J. Am. Chem. Soc.* **1983**, *105*, 1419.

27 M. Albrecht, S. Mirtschin, M. de Groot, I. Janser, J. Runsink, G. Raabe, M. Kogej, C. A. Schalley, R. Fröhlich, *J. Am. Chem. Soc.* **2005**, *127*, 10371.

28 M. Albrecht, M. Fiege, M. Baumert, M. de Groot, R. Fröhlich, L. Russo, K. Rissanen, *Eur. J. Inorg. Chem.* **2007**, 609.

29 M. Albrecht, M. Baumert, J. Klankermayer, M. Kogej, C. A. Schalley, R. Fröhlich, *Dalton Trans.* **2006**, 4395.

30 M. Albrecht, S. Kotila, *Chem. Commun.* **1996**, 2309.

31 M. Albrecht, *Chem. Eur. J.* **1997**, *3*, 1466.

32 M. Albrecht, K. Witt, P. Weis, E. Wegelius, R. Fröhlich, *Inorg. Chim. Acta* **2002**, *341*, 25.

33 M. Albrecht, K. Witt, H. Röttele, R. Fröhlich, *Chem. Commun.* **2001**, 1330.

34 X. Sun, D. W. Johnson, D. L. Caulder, R. E. Powers, K. N. Raymond, E. H. Wong, *Angew. Chem.* **1999**, *111*, 1386; *Angew. Chem., Int. Ed.* **1999**, *38*, 1303.

35 a) X. Sun, D. W. Johnson, D. Caulder, K. N. Raymond, E. H. Wong, *J. Am. Chem. Soc.* **2001**, *123*, 2752. b) X. Sun, D. W. Johnson, K. N. Raymond, E. H. Wong, *Inorg. Chem.* **2001**, *40*, 4504.

36 A. K. Das, A. Rueda, L. R. Falvello, S.-M. Peng, S. Batthacharya, *Inorg. Chem.* **1999**, *38*, 4365.

37 J. Heinicke, N. Peulecke, K. Karaghiosoff, P. Mayer, *Inorg. Chem.* **2005**, *44*, 2137.

38 T. Konno, K. Tokuda, T. Suzuki, K. I. Okamoto, *Bull. Chem. Soc. Jpn.* **1998**, *71*, 1049.

39 T. Konno, K. Tokuda, K. Okamoto, *Chem. Commun.* **1998**, 1697.

40 M. H. W. Lam, S. T. C. Cheung, K.-M. Fung, W.-T. Wong, *Inorg. Chem.* **1997**, *36*, 4618.

41 K. Hiratani, T. Takahashi, K. Kasuga, H. Sugihara, K. Fujiwara, K. Ohashi, *Tetrahedron Lett.* **1995**, *36*, 5567.

42 M. Albrecht, O. Blau, E. Wegelius, K. Rissanen, *New J. Chem.* **1999**, *23*, 667.

43 M. Albrecht, O. Osetska, R. Fröhlich, *Synlett* **2006**, 924.

44 M. Albrecht, *Chem. Eur. J.* **2000**, *6*, 3485.

45 J. Xu, T. N. Parac, K. N. Raymond, *Angew. Chem.* **1999**, *111*, 3055; *Angew. Chem., Int. Ed.* **1999**, *38*, 2878.

46 M. Albrecht, *Chem. Soc. Rev.* **1998**, *27*, 281.

47 M. Albrecht, S. Kotila, *Angew. Chem.* **1995**, *107*, 2285; *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2134.

48 M. Albrecht, S. Kotila, *Angew. Chem.* **1996**, *108*, 1299; *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1208.

49 M. Albrecht, H. Röttele, P. Burger, *Chem. Eur. J.* **1996**, *2*, 1264.

50 M. Albrecht, C. A. Schalley, F. Vögtle, K.-H. Dötz, *Top. Curr. Chem.* **2004**, *248*, 105.

51 M. Albrecht, O. Blau, R. Fröhlich, *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 4867.

52 M. Albrecht, O. Blau, *Chem. Commun.* **1997**, 345.

53 M. Albrecht, *J. Inclusion Phenom. Macrocyclic Chem.* **2000**, *36*, 127.

54 M. Albrecht, O. Blau, R. Fröhlich, *Chem. Eur. J.* **1999**, *5*, 48.

55 M. Albrecht, I. Janser, S. Kamptmann, P. Weis, B. Wibbeling, R. Fröhlich, *Dalton Trans.* **2004**, 37.

56 M. Albrecht, I. Janser, H. Houjou, R. Fröhlich, *Chem. Eur. J.* **2004**, *10*, 2839.

57 M. Albrecht, I. Janser, A. Lützen, M. Hapke, R. Fröhlich, P. Weis, *Chem. Eur. J.* **2005**, *11*, 5742.

58 M. Albrecht, M. Schneider, *Chem. Commun.* **1998**, 137.

59 M. Albrecht, M. Schneider, H. Röttele, *Chem. Ber.* **1997**, *130*, 615.

60 A. V. Davis, T. K. Firman, B. P. Hay, K. N. Raymond, *J. Am. Chem. Soc.* **2006**, *128*, 9484.

61 M. Albrecht, *Synlett* **1996**, 565.

62 W. Zarges, J. Hall, J.-M. Lehn, C. Bolm, *Helv. Chim. Acta* **1991**, *74*, 1843.

63 A. Lützen, M. Hapke, J. Griep-Raming, D. Haase, W. Saak, *Angew. Chem.* **2002**, *114*, 2190; *Angew. Chem., Int. Ed.* **2002**, *41*, 2086.

64 M. Albrecht, S. Schmid, M. deGroot, P. Weis, R. Fröhlich, *Chem. Commun.* **2003**, 2526.

65 M. Albrecht, I. Janser, J. Fleischhauer, Y. Wang, G. Raabe, R. Fröhlich, *Mendeleev Commun.* **2004**, *14*, 250.

66 M. Scherer, D. Caulder, D. W. Johnson, K. N. Raymond, *Angew. Chem.* **1999**, *111*, 1689; *Angew. Chem., Int. Ed.* **1999**, *38*, 1587.

67 M. Albrecht, S. Dehn, G. Raabe, R. Fröhlich, *Chem. Commun.* **2005**, 5690.

68 M. Albrecht, S. Dehn, S. Schmid, M. DeGroot, *Synthesis* **2007**, 155.

69 M. Albrecht, S. Dehn, R. Fröhlich, *Angew. Chem.* **2006**, *118*, 2858; *Angew. Chem., Int. Ed.* **2006**, *45*, 2792.

70 M. Albrecht, *Angew. Chem.* **1999**, *111*, 3671; *Angew. Chem., Int. Ed.* **1999**, *38*, 3463.

71 R. W. Saalfrank, A. Stark, K. Peters, H. G. Von Schnering, *Angew. Chem.* **1988**, *100*, 878; *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 851.

72 D. H. Leung, D. Fiedler, R. G. Bergman, K. N. Raymond, *Angew. Chem.* **2004**, *116*, 981; *Angew. Chem., Int. Ed.* **2004**, *43*, 963.

73 R. M. Yeh, J. Xu, G. Seeber, K. N. Raymond, *Inorg. Chem.* **2005**, *44*, 6228.

74 A. J. Amoroso, J. C. Jefferey, P. L. Jones, J. A. McCleverty, P. Thornton, M. D. Ward, *Angew. Chem.* **1995**, *107*, 1577; *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1443.

75 C. Brückner, R. E. Powers, K. N. Raymond, *Angew. Chem.* **1998**, *110*, 1937; *Angew. Chem., Int. Ed.* **1998**, *37*, 1837.

76 D. Caulder, C. Brückner, R. E. Powers, S. König, T. N. Parac, J. A. Leary, K. N. Raymond, *J. Am. Chem. Soc.* **2001**, *123*, 8923.

77 R. W. Saalfrank, H. Glaser, B. Demleitner, F. Hampel, M. M. Chowdhry, V. Schünemann, A. X. Trautwein, G. B. M. Vaughan, R. Yeh, A. V. Davis, K. N. Raymond, *Chem. Eur. J.* **2002**, *8*, 493.

78 M. Albrecht, I. Janser, R. Fröhlich, *Synthesis* **2004**, 1977.

79 T. J. McMurry, M. W. Hosseini, T. M. Garrett, F. E. Hahn, Z. E. Reyes, K. N. Raymond, *J. Am. Chem. Soc.* **1987**, *109*, 7196.

80 S. J. Rodgers, C. W. Lee, C. Y. Ng, K. N. Raymond, *Inorg. Chem.* **1987**, *26*, 1622.

81 M. Albrecht, I. Janser, R. Fröhlich, *Chem. Commun.* **2005**, 157.

82 C. Moberg, *Angew. Chem.* **2006**, *118*, 4838; *Angew. Chem., Int. Ed.* **2006**, *45*, 4721.

83 M. Albrecht, S. Burk, R. Stoffel, A. Lüchow, R. Fröhlich, M. Kogej, C. A. Schalley, *Eur. J. Inorg. Chem.* **2007**, 1361.

84 M. Albrecht, I. Janser, J. Runsink, G. Raabe, P. Weis, R. Fröhlich, *Angew. Chem.* **2004**, *116*, 6832; *Angew. Chem., Int. Ed.* **2004**, *43*, 6662.

85 M. Albrecht, I. Janser, S. Burk, P. Weis, *Dalton Trans.* **2006**, 2875.

86 M. Albrecht, I. Janser, S. Meyer, P. Weis, R. Fröhlich, *Chem. Commun.* **2003**, 2854.

Markus Albrecht was born in 1964 and studied chemistry in Würzburg and Münster. He obtained his Dr. rer. nat. in 1992 with Prof. Dr. G. Erker. After one year as a postdoctoral fellow in the laboratories of Prof. Dr. K. N. Raymond in Berkeley, he moved to Karlsruhe and received his habilitation in 1997. Since spring 2002, he is Professor of Organic Chemistry at the RWTH Aachen. His work was awarded with the "ADUC-Jahrespreis für Habilitanden," a Heisenberg-fellowship and the "Landeslehrpreis 2002 des Landes Baden-Württemberg."

Roland Fröhlich born in 1952, studied chemistry in Münster and Cologne and received his Dr. rer. nat. in 1982. After postdoctoral studies in the crystallographic insitute of the University of Karlsruhe, he worked as a sales and applications manager for Enraf Nonius. Since 1993, he is a senior scientist at the University of Münster and since 1994, a docent for X-ray crystallography at the University of Jyväskylä.