

Spontaneous formation of a chiral supramolecular superhelix in the crystalline state using a single-stranded tetranuclear metallohelicate†

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An unprecedented one-handed coiled-coil structure was formed in the crystal of a Zn_3La tetranuclear metallohelicate, in which the handedness of both the helical component and the helical array was well controlled by the chiral auxiliary of the flexible acyclic ligand.

The superhelix is a hierarchical structure in which a helix is coiled to produce a more ordered helix. The structure plays an important role in biopolymers such as supercoiled DNAs¹ and the α -helical coiled-coil² structure of proteins. There are also artificial coiled-coil structures, and some synthetic helical polymers form a higher-ordered spiral liquid crystal, which is observable by an electron microscope.³ In such cases, the higher-ordered structure is maintained by many simultaneous weak interactions among the chains.

Recently, a non-covalent strategy has been frequently employed to make artificial molecular helices, including a wide range of metallohelicates with double and triple helical structures.⁴ Functional metallohelicates were also used to invert the handedness in response to external stimuli.⁵ However, an artificial coiled-coil structure based on the supramolecular self-assembly of discrete helical subunits has been rarely explored, mainly due to the difficulty of controlling the handedness of both the higher-ordered helix and the helical subunits.⁶ In this *communication*, we report an unprecedented hierarchical supramolecular superhelix, in which an array of helical metal complexes with a chiral auxiliary forms the coiled-coil structure in the crystal (Fig. 1). The chiral auxiliary, introduced into the acyclic oligoimine ligand, effectively regulates the handedness of the single-stranded tetranuclear metallohelicate. The chiral moiety also contributes to the formation of a one-handed helical array of the helical subunits in the crystalline state.

We used a tetranuclear single-stranded metallohelicate $[L^1Zn_3La]^{3+}$ as the basic framework of the helical subunit. The heteronuclear complex can be spontaneously formed by the complexation of the acyclic oligoimine ligand (H_6L^1) with two kinds of metal ions.^{7,8} We introduced a chiral salen unit having a *trans*-1,2-diphenylethylene group into the framework

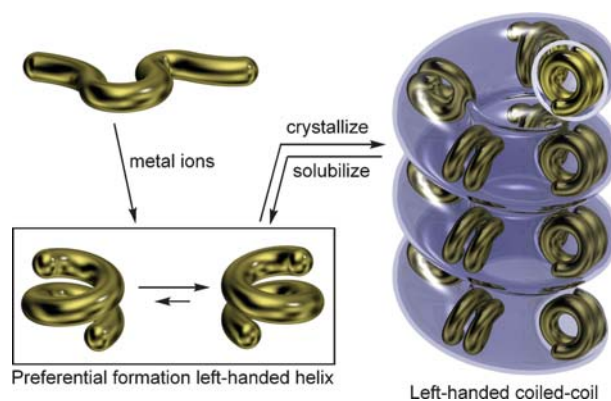
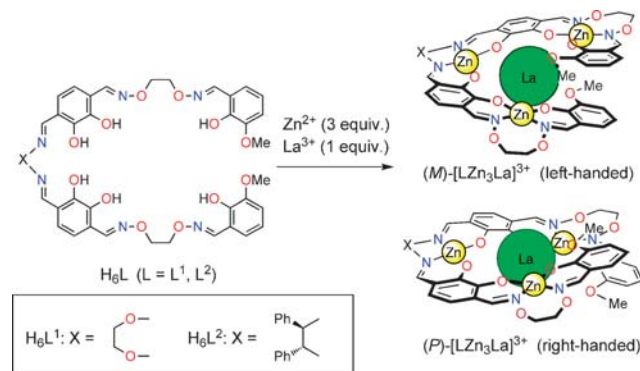


Fig. 1 Supramolecular superhelix formed by crystallization of a chiral metallohelicate.

in order to obtain the one-handed helix (Scheme 1).^{9,10} Salen-metal analogues with such a chiral auxiliary have been utilized as an excellent enantioselective catalyst for organic reactions.¹¹ This chiral salen moiety is placed in the middle of the acyclic oligoimine framework, taking into consideration the reactivity of the imine and oxime $C=N$ bonds; the former suffers from recombination of the $C=N$ bonds while the latter does not.¹² If the salen moiety is introduced into other positions, the recombination of the imine $C=N$ bonds may produce a mixture of several compounds with different chain lengths. The target ligand H_6L^2 was prepared by the reaction of a commercially available chiral diamine with 2 equiv. of the terminal unit (ESI†).

The complexation of the chiral ligand H_6L^2 with zinc(II) acetate produced a mixture of soluble zinc(II) complexes, which were not characterized. However, when 1 equiv. of



Scheme 1 Single-stranded tetranuclear metallohelicate bearing a chiral auxiliary.

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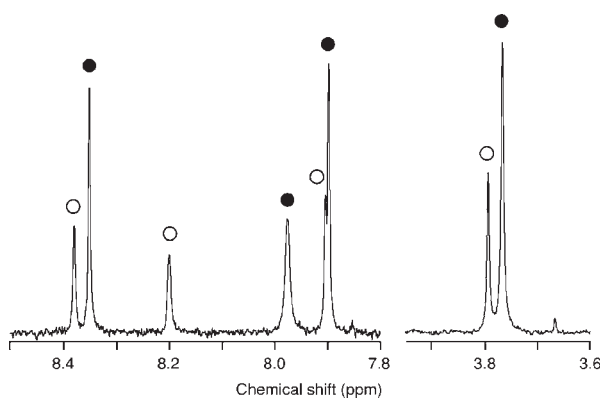


Fig. 2 Part of the ^1H NMR spectrum of $[\text{L}^2\text{Zn}_3\text{La}]^{3+}$ at 400 MHz in $\text{CDCl}_3\text{-CD}_3\text{OD}$ (1 : 1). The two diastereomers are indicated by \circ and \bullet .

lanthanum(III) acetate was present in the mixture, simple and sharp signals were observed in the ^1H NMR spectrum. The results strongly indicate the formation of a single-stranded metallohelicate, similar to the achiral analogue $[\text{L}^1\text{Zn}_3\text{La}]^{3+}$.⁷ The formation of the heterotetranuclear complex $[\text{L}^2\text{Zn}_3\text{La}]^{3+}$ was confirmed by the ESI mass spectrum.

We have already reported that the helix inversion of the achiral helical complex $[\text{L}^1\text{Zn}_3\text{La}]^{3+}$ is very slow on the NMR timescale, even at 353 K in $\text{CDCl}_3\text{-CD}_3\text{OD}$ (1 : 1).⁷ If the helix inversion of the chiral complex $[\text{L}^2\text{Zn}_3\text{La}]^{3+}$ occurs at a similar rate, the right- and left-handed forms must be separately observed in the NMR spectra because they are a diastereomeric pair. Indeed, the ^1H NMR spectrum of $[\text{L}^2\text{Zn}_3\text{La}]^{3+}$ showed two sets of signals (Fig. 2), for example, two singlets for the methoxy protons were observed for the major and minor isomers at 3.76 and 3.79 ppm, respectively. The ratio was 71 : 29, indicating that either of the right- or left-handed diastereomers is preferentially formed. The energy difference between the two forms is estimated to be 2.2 kJ mol^{-1} at 298 K.

From a solution of the isomeric mixture, single crystals of the metallohelicate $[\text{L}^2\text{Zn}_3\text{La}]^{3+}$ were obtained. The ^1H NMR spectrum of the crystals, which was recorded immediately after dissolving, showed only one set of signals. The observed set was found to correspond to the major isomer of the two diastereomers mentioned above. We obtained the pure one-handed isomer by crystallization. However, after the solution was allowed to stand for 4 h at room temperature, we again observed the two sets of signals corresponding to the two isomers in a ratio of 71 : 29, which is exactly the same as that observed for the mixture of H_6L^2 , zinc(II), and lanthanum(III). Obviously, the isomerization took place to afford the equilibrated mixture.

This equilibration process can also be monitored by the change in the CD signals (Fig. 3a). The CD spectrum of $[\text{L}^2\text{Zn}_3\text{La}]^{3+}$ recorded immediately after dissolving in chloroform–methanol (1 : 1) showed negative peaks at 283 and 350 nm and a positive one at 312 nm. The CD intensity at 350 nm gradually decreased to 37% of the initial intensity after the solution was allowed to stand at 22 °C for 4 h. During the isomerization, the maximum wavelength and peak profile did not significantly change and several

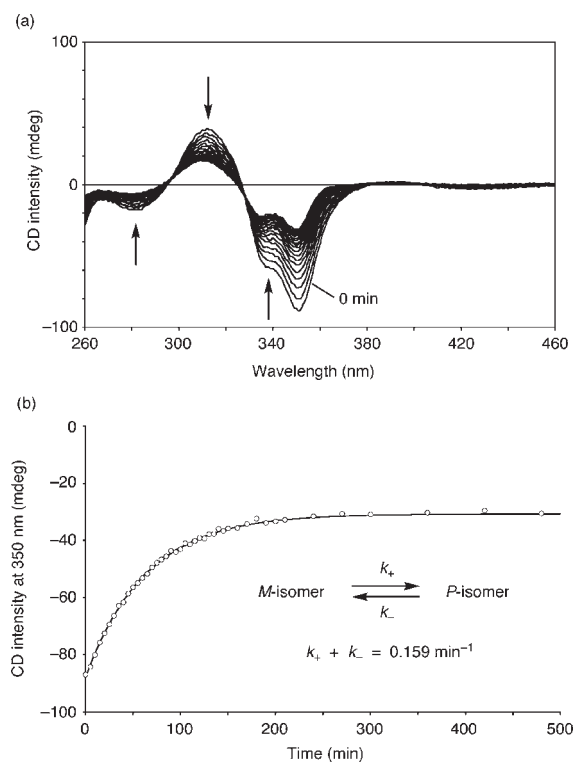


Fig. 3 (a) Change in CD spectra of $[\text{L}^2\text{Zn}_3\text{La}]^{3+}$ recorded every 10 min after dissolving in chloroform–methanol (1 : 1). (b) Change in the CD intensity monitored at 350 nm (\circ). The solid line indicates the exponential decay ($t_{1/2} = 43.7 \text{ min}$) fitted to the observed data.

isodichroic points were observed. This decay obeyed first-order kinetics and the half-life was calculated to be 43.7 min by a nonlinear least-squares analysis (Fig. 3b). The decrease of the intensity can be attributed to the inversion between the right- and left-handed forms of the helical complex. Since it took several days to prepare the single crystals, the minor isomer in the mother liquor probably isomerized to the major one keeping the equilibrium.

An X-ray crystallographic analysis was carried out using the single crystals of $[\text{L}^2\text{Zn}_3\text{La}(\text{OAc})_3(\text{H}_2\text{O})(\text{MeOH})\cdot 3\text{CHCl}_3\cdot \text{MeOH}]$ (Fig. 4a).^{13,14} The complex crystallizes in the tetragonal, space group $P4_3$, and the unit cell contains four molecules of the left-handed (*M*) isomer of the complex. Consequently, the absolute configuration of the major isomer observed in solution corresponds to the left-handed (*M*) isomer. The three zinc atoms sit in the two types of N_2O_2 sites (two salamo and one salen sites), which surround the central lanthanum atom (La1) forming Zn-O-La μ -phenoxo bridges. The ligand moiety $(\text{L}^2)^{6-}$ forms a single helix and the winding angle of the helix is 419° .¹⁵ The structural feature of $[\text{L}^2\text{Zn}_3\text{La}]^{3+}$ is similar to that of the achiral analogue $[\text{L}^1\text{Zn}_3\text{La}]^{3+}$ (winding angle: 421°).⁷ Thus, the chiral auxiliary (chiral salen unit) can be incorporated into the helical framework without any significant distortion of the molecular structure.

It is worthwhile to point out that the space group $P4_3$ has a 4-fold left-handed screw axis along the crystallographic *c* axis. As a result, a helical array of the helical complex is formed, in which the helix axis of each tetranuclear complex $[\text{L}^2\text{Zn}_3\text{La}]^{3+}$

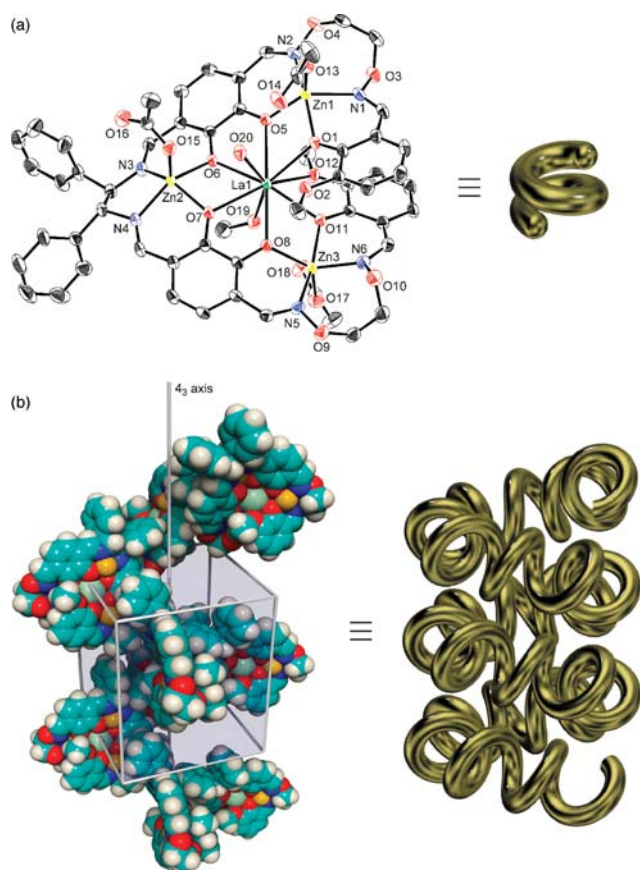


Fig. 4 (a) Molecular structure of $[L^2Zn_3La(OAc)_3(H_2O)(MeOH)]$ with thermal ellipsoids plotted at the 50% probability level. (b) Space filling representation of the crystal structure showing a helical array along the crystallographic c axis.

is tilted from the main axis (c axis) by *ca.* 80° . This makes a coiled-coil structure—a supramolecular superhelix—in the crystal lattice (Fig. 4b). To the best of our knowledge, this is the first example of a coiled-coil structure formed by the folding and assembly of flexible acyclic molecules. The helical arrangement probably results from the weak intermolecular interactions such as the C–H \cdots O and C–H \cdots π ones operating between the helical subunits. The intermolecular interactions may contribute to the exclusive formation of the left-handed isomer during the crystallization process.

In the formation process of the chiral superhelical structure in this study, the *M/M* intermolecular interaction was more favourable than the *P/P* or *M/P* one. Such a system is important from the viewpoint of a self-sorting system for optical purity amplification. The finely designed small subunits lead to the well-controlled secondary structure (helical conformation) and the higher-ordered structure (superhelix), as seen in most of the functional biomolecules. We are now

developing novel superhelices with bio-inspired functions and a self-replication system based on the helical metal complexes.

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