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Stepwise Helicity Inversions by Multisequential Metal Exchange

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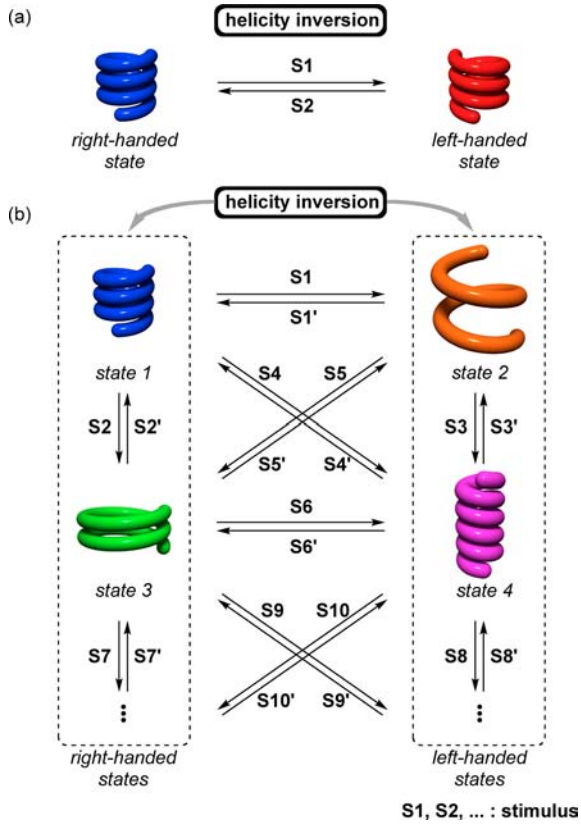
Supporting Information

ABSTRACT: Development of artificial helical molecules that can undergo responsive helicity inversion has been a challenging research target in functional molecular chemistry. However, most reported helicity inversions are based on a single-mode transition, i.e., the conversion between right- and left-handed states. We report here the first molecular system that allows stepwise multisequential helicity inversion utilizing metal exchange of helical complexes derived from a hexaoxime ligand, H_6L^1. The ligand H_6L^1 underwent a four-step conversion ($H_6L^1 \rightarrow L^1Zn_3 \rightarrow L^1Zn_5 \rightarrow L^1Zn_3Ba \rightarrow L^1Zn_3La$) upon sequential metal addition (Zn^{2+}, Ba^{2+}, then La^{3+}). Associated with the conversion, three-step helicity inversion took place (L^1Zn_3, right-handed $\rightarrow$ L^1Zn_5, left-handed $\rightarrow$ L^1Zn_3Ba, right-handed $\rightarrow$ L^1Zn_3La, left-handed). This is the first example of stepwise multimode helicity inversion of a discrete molecule, which could be useful as a platform for construction of dynamic regulation systems with multiple asymmetric functions.

Helical structures are widely seen in biological systems, such as the DNA double helix and the protein α-helix. It is known that DNAs and proteins can adopt several types of helical structures, such as A-, B-, and Z-DNA[1] or α-, β-, 3_{10}-, and π-helix.[2] These helical structural motifs work differently in living systems according to their structural feature. In this context, it would be important to design and synthesize a molecule that can adopt different types of helical structures in different situations. To date, various artificial helical molecules[3] have been developed and their biorelated and bioinspired functions such as enantioselective catalysis, chirality sensing, and chiral information processing have been investigated. Since these functions could be regulated by structural transformations including helicity inversion, development of artificial helical molecules that can undergo responsive helicity inversion has been a challenging research target in functional molecular chemistry.[4−13] However, most of the reported helicity inversions are based on a *single-mode* transition (Scheme 1a), i.e., the conversion between right- and left-handed states. If a *sequential and multistep* conversion feature[14] is incorporated into the helicity inversion system (Scheme 1b), it would work as a multifunction control system that can switch different kinds of asymmetric functions upon each helicity inversion. We report here the first molecular system that allows the stepwise *multisequential* helicity inversion utilizing metal exchange of helical complexes derived from a hexaoxime ligand, H_6L^1 (Scheme 2).

Scheme 1. Concept of Multisequential Helicity Inversions: (a) *Single-Step* Helicity Inversion between the Right- and Left-Handed States and (b) *Sequential and Multistep* Helicity Inversions among Multiple States



To incorporate such a multisequential conversion feature into a functional molecular system, metal coordination has a great advantage: we can convert one state to another simply by changing the metal ions based on labile coordination bonds. The oligo(salamo) ligands[15−19] such as H_6L^2 [17] (Scheme 2) are good candidates to create a multisequential inversion system. We can obtain dynamic and controllable helical structures upon the multiple complexation of these ligands with labile metal ions, and we can convert one complex to another by site-selective metal exchange according to the affinity order.[17a,18] If we select suitable metal ions so that the metal complexes before and after each conversion have opposite helicities, we can

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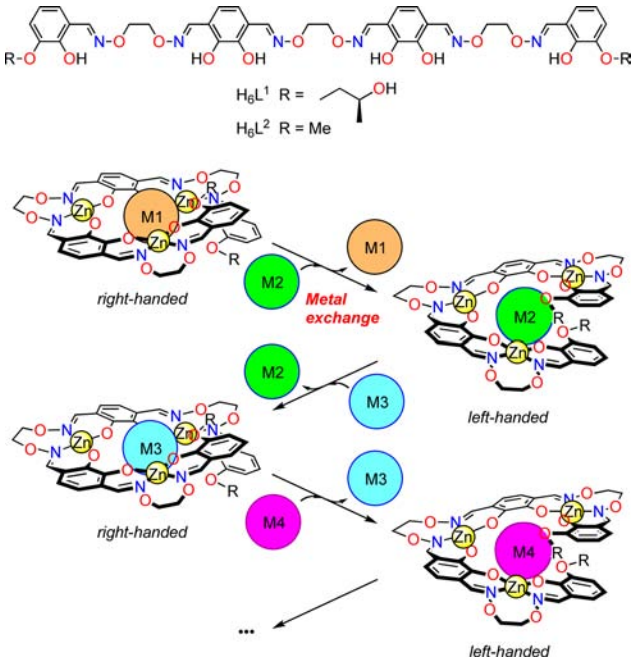
Scheme 2. Design of Oligooxime Ligands H_6L^1 and H_6L^2 for Stepwise Helicity Inversions Based on Multisequential Metal Exchange



convert helicity in a *multistep* way. Here we use a chiral ligand, H_6L^1, bearing (*S*)-2-hydroxypropyl groups (Scheme 2).[19] The ligand H_6L^1 was synthesized (Figure 1a, see also Supporting Information Figures S1 and S2) from a chiral salicylaldehyde oxime[19] in a manner similar to that of the achiral analogue

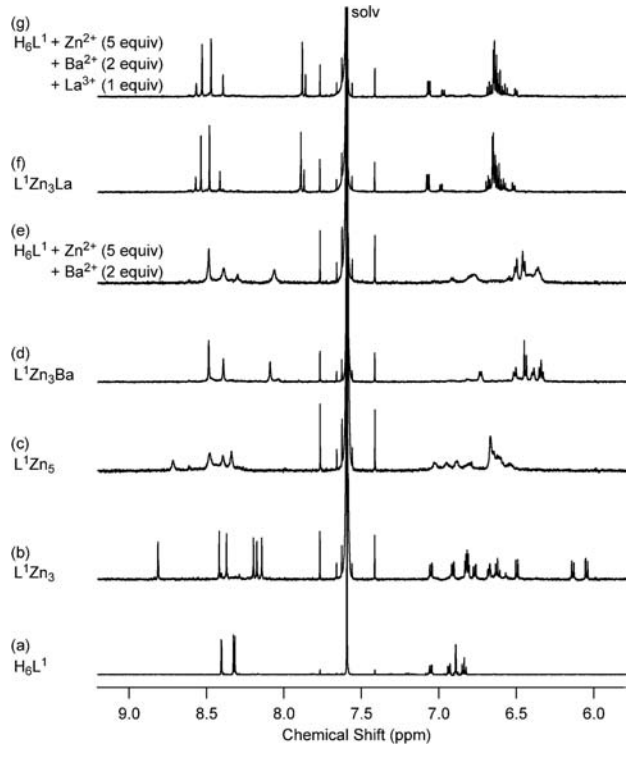
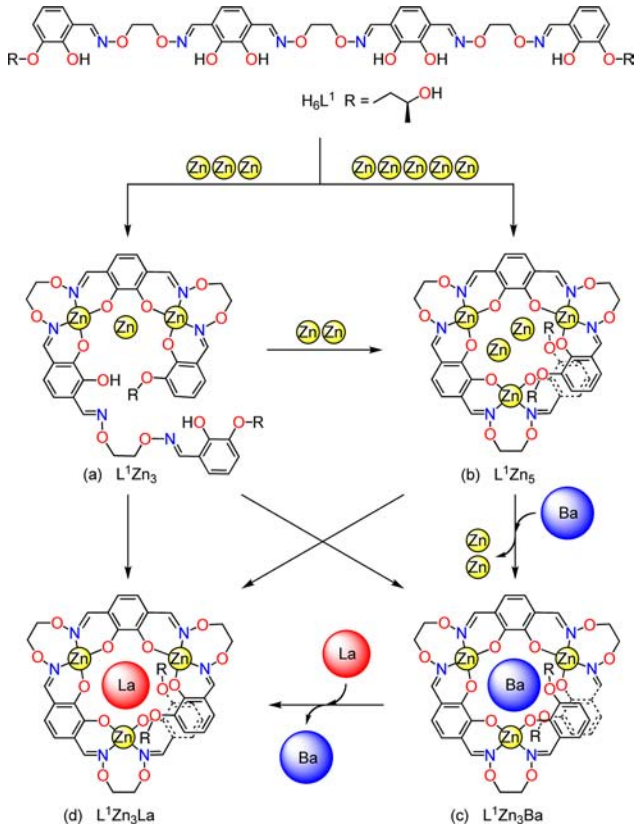


Figure 1. ^{1}H NMR spectra of H_6L^1 and the helical structures prepared from the H_6L^1 ligand (600 MHz, 0.20 mM, $CDCl_3/CD_3OD$ (1:1)).

H_6L^2. The multistep conversion feature of the metal complexes of H_6L^1 was studied by spectroscopic techniques.

Since this type of oligo(salamo) ligands can form complexes with multiple Zn^{2+} ions, we investigated the complexation behavior of the ligand H_6L^1. When 3 equiv of zinc(II) acetate was added to the ligand H_6L^1, a trinuclear complex L^1Zn_3 was formed, which was clearly evidenced by the ESI-MS (*m*/*z* 1082.3 for $[L^1Zn_3 + H]^+$) and ^{1}H NMR spectrum (Figures 1b, S3, and S4). The well-resolved but unsymmetrical feature of the ^{1}H NMR spectrum is attributable to a structure in which the two neighboring salamo coordination sites formed a zinc(II) trinuclear core[18a] while the other site remained vacant (Scheme 3a). When 5 equiv of zinc(II) acetate was added, a pentanuclear

Scheme 3. Four-Step Conversion ($H_6L^1 \rightarrow L^1Zn_3 \rightarrow L^1Zn_5 \rightarrow L^1Zn_3Ba \rightarrow L^1Zn_3La$) by Metal Addition



species L^1Zn_5 was formed (Scheme 3b), which was confirmed by the mass spectrum (*m*/*z* 604.9 for $[(L^1 - 2H)Zn_5]^{2+}$) and ^{1}H NMR spectrum (Figures 1c, S5, and S6). These observations clearly indicate the two-step feature ($H_6L^1 \rightarrow L^1Zn_3 \rightarrow L^1Zn_5$) of the complexation with zinc(II) acetate.

While the salamo coordination sites of the ligand H_6L^1 have an affinity toward Zn^{2+}, the central O_8 site favors alkaline earth or rare earth metals; a binding affinity trend in the order of $Zn^{2+} < Ba^{2+} < La^{3+}$ [18b] was observed in the related ligand systems. Thus, the metal exchange of the homonuclear complex L^1Zn_5 was investigated. When 2 equiv of Ba^{2+} was added, L^1Zn_5 was converted almost completely to L^1Zn_3Ba. The conversion was confirmed by ESI-MS (*m*/*z* 609.8 for $[L^1Zn_3Ba]^{2+}$) and ^{1}H NMR spectrum (Figures 1d,e, S7, and S8). The minor signals in Figure 1e could be assigned to the remaining L^1Zn_5 or related complexes. In this process, two Zn^{2+} ions in the O_8 site were substituted by one Ba^{2+} (Scheme 3c). The heteronuclear

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complex L^1Zn_3Ba was also formed by the reaction of trinuclear complex L^1Zn_3 with Ba^{2+} in place of L^1Zn_5. This heteronuclear complex L^1Zn_3Ba was further converted to L^1Zn_3La by the addition of 1 equiv of La^{3+} (Scheme 3d). Complete conversion was confirmed by the ^1H NMR and ESI-MS (m/z 406.9 for $[L^1Zn_3La]^{3+}$) (Figures 1f,g, S9, and S10). In the ^1H NMR spectrum of L^1Zn_3La, two sets of signals were observed in a 74:26 ratio, which can be assigned to the left- and right-handed diastereomers. In the conversion process from the L^1Zn_3Ba, the Ba^{2+} ion of the O_8 site was replaced with a La^{3+}. This L^1Zn_3La complex was also generated directly by the reaction of L^1Zn_3 or L^1Zn_5 with La^{3+}. Consequently, we can convert one complex to another among four complexes according to the affinity order. If the order of the metals is appropriate, up to four-step conversion ($H_6L^1 \rightarrow L^1Zn_3 \rightarrow L^1Zn_5 \rightarrow L^1Zn_3Ba \rightarrow L^1Zn_3La$, Scheme 3) could be possible upon sequential addition of these metal ions.

The helical handedness of these four complexes was investigated by CD spectroscopy (Figures 2 and S11).

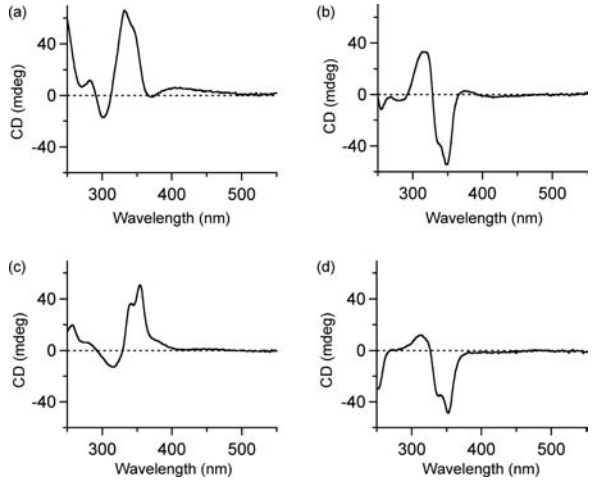

Figure 2. CD spectra of (a) L^1Zn_3, (b) L^1Zn_5, (c) L^1Zn_3Ba, and (d) L^1Zn_3La (0.20 mM, chloroform/methanol (1:1)).

Interestingly, the metal ions significantly affect the handedness of the complexes. While L^1Zn_3 and L^1Zn_3Ba showed positive CD peaks at 332 and 354 nm, respectively, L^1Zn_5 and L^1Zn_3La showed negative peaks at 348 and 352 nm, respectively. This indicates that the handedness of the dominant isomer of L^1Zn_3 and L^1Zn_3Ba is opposite to that of L^1Zn_5 and L^1Zn_3La. This also means that each step of the three-step conversion of $L^1Zn_3 \rightarrow L^1Zn_5 \rightarrow L^1Zn_3Ba \rightarrow L^1Zn_3La$ should be associated with helicity inversion.

A plot of the CD intensity at 348 nm upon complexation with the metal ions clearly indicates the emergence and subsequent inversion of CD signal from H_6L^1 to L^1Zn_3La (Figures 3 and S12). Addition of Zn^{2+} (up to 3 equiv) to H_6L^1 induced positive CD signal coming from L^1Zn_3, while the CD signal decreased and turned negative in the presence of an increased amount of Zn^{2+} (>3 equiv) due to the formation of L^1Zn_5. The CD signal turned positive again upon addition of Ba^{2+} associated with the conversion of L^1Zn_5 to L^1Zn_3Ba. Finally, addition of La^{3+} further changed the CD signal from positive to negative, which is associated with the quantitative conversion from L^1Zn_3Ba to L^1Zn_3La. The negative Cotton effect observed at 352 nm for L^1Zn_3La can be ascribed to the

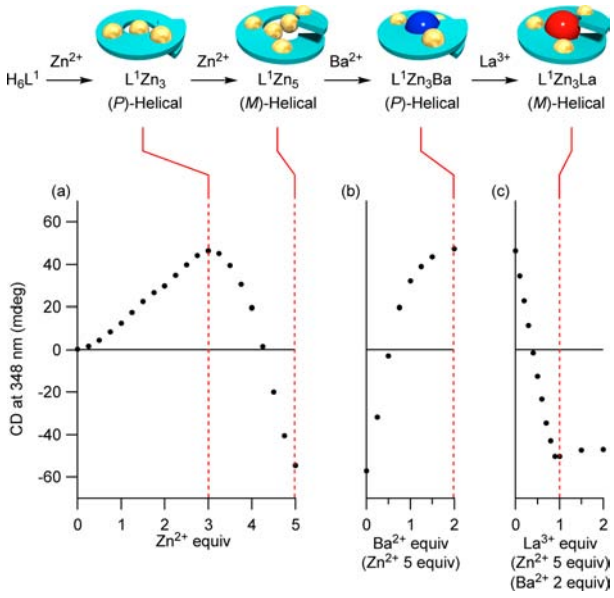

Figure 3. CD intensity changes at 348 nm upon sequential addition of (a) Zn^{2+}, (b) Ba^{2+}, and (c) La^{3+} (0.20 mM, chloroform/methanol (1:1)).

left-handed (M) helix on the basis of comparison with a related complex.[17c]

In this system, the handedness of the organic helical framework changed as $P \rightarrow M \rightarrow P \rightarrow M$, associated with the three-step conversion of $L^1Zn_3 \rightarrow L^1Zn_5 \rightarrow L^1Zn_3Ba \rightarrow L^1Zn_3La$ based on a sequential metal exchange protocol. This is the first example of stepwise *multimode* helicity inversion of a discrete molecule. The labile character of the oligooxime–metal complexes was effective to achieve the stepwise conversion associated with the helicity inversion. The construction of helical molecular systems in which the mode of helicity inversion can be changed in a stepwise fashion would be useful for dynamic regulation systems with multiple asymmetric functions.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Synthesis of ligand; ^1H NMR and mass spectra of H_6L^1, L^1Zn_3, L^1Zn_5, L^1Zn_3Ba, and L^1Zn_3La; spectroscopic titrations for the helicity inversion. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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