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Supramolecular chiroptical switching of helical-sense preferences through the two-way intramolecular transmission of a single chiral source associated with a dynamic helical loop

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We demonstrate a chiroptical switching system with a simple molecule. The molecule contains a pair of chromophores of diphenylacetylene that are linked with a diyne bond and arranged to exert exciton coupling in helically folded forms with (M)- or (P)-helicity. A tertiary amide group is attached to each end of the looped molecule. The amide carbonyls were used to capture a ditopic hydrogen-bonding guest. A chiral auxiliary group on the amide nitrogen acted as a chiral handle to control the helical-sense preference of dynamic helical forms of the loop. The helical-sense preference is brought about by an intramolecular transmission of point chirality associated with the loop. The preferred sense was switched upon complexation with an achiral additive through the formation of hydrogen bonds. In both states, before and after complexation, the helical-sense preferences were controlled through two-way transmission of the single chiral source.

Introduction

Molecules with dynamic chirality have attracted considerable attention since the chiral-sense preference for a particular stereochemistry can be controlled through the transmission of some chiral element.1,2 Especially, dynamic molecules equipped with exciton-coupled chromophores3-8 that interconvert between two enantiomeric forms have often been studied as chirality-sensing molecules because a particular sense of dynamic chirality could be favored to show a strong spectral output through noncovalent association6,7 or covalent bond formation8 with a chiral analyte. In most cases, for these purposes it would be enough for the sensing molecule to adopt dynamic chiral forms at least during interaction with the analyte.6b,9 Instead, if the chiral sense of a dynamic chiral molecule with exciton-coupled chromophores could be switched in response to a change in the environment between two states, e.g., presence or absence of an analyte, a rare detecting as well as molecular switching system could be constructed even though the analyte is not chiral. In this case, the host molecule should predominate dynamic chiral forms regardless of whether or not an analyte is present.10,11 In the absence of an analyte, the host should prefer a particular sense of dynamic chirality, and the original chiral-sense preference should be reversed in the presence of an analyte. We envisioned a simple system in which a single chiral source exists in a looped molecule with exciton-coupled chromophores.

Scheme 1. Two-way control of helical-sense preferences through the intramolecular transmission of point chirality (⋆) associated with a dynamic helical loop in the (a) absence or (b) presence of an achiral additive.

Fig. 1 Chemical structures of dynamic helical loops (R,R)-1, 3 and 5, ditopic guests 2, (S,S)-4 and (R,R)-4.
(Scheme 1). In the uncomplexed and complexed states, different senses of dynamic chirality would be preferred through two-way intramolecular transmission of the single chiral source associated with the host.

Thus, we designed a helical loop in which two chromophores are arranged helically to exert exciton coupling. We attached a chiral auxiliary to each end of the loop \((R,R)-1\) as a single chiral source to control the helical-sense preferences (Fig. 1). A successful intramolecular transmission of point chirality \((R)\) to dynamic helical forms with \((M)\)- or \((P)\)-helicity of 1 led to a helical-sense preference in the absence of any guest. Next, complexation with an achiral ditopic guest \(2\) induced the helical loop \((R,R)-1\) to reverse its original helical-sense preference, which was also based on the intramolecular transmission of point chirality associated with the loop even in a complexed state. A conformational preference for helically folded forms of the dynamic loop in both the absence and presence of a guest was investigated with an achiral reference loop 3, which does not possess any chiral source other than dynamic helicity when it adopts folded forms. The details of the two-way intramolecular transmission of point chirality are described below.

**Results and Discussion**

**Preparation and dynamic structures of \((R,R)-1\) and 3**

We prepared dynamic helical loops \((R,R)-1\) and 3 through a two-fold Sonogashira coupling reaction of known acetylenes on diphenylbutadiyne \(6\) with the corresponding \(N\)-benzoylated iodoaniline derivatives \(7a/b\) (Scheme 2).

![Scheme 2. Preparation of dynamic helical loops \((R,R)-1\) and 3.](image)

![Fig. 2 Energy-minimized structures for a model \(1^*\) [NMe]: (a) a helically folded form (rel. 0 kJ mol\(^{-1}\)) and (b) an extended form (+28.4 kJ mol\(^{-1}\)), and for a parent hydrocarbon \(5\) (c) a helically folded form (rel. 0 kJ mol\(^{-1}\)) and (d) an extended form (+16.2 kJ mol\(^{-1}\)), obtained by conformational searches using MacroModel software (v9.9 OPLS_2005, Monte Carlo Multiple Minimum method, non-solvated, 50 000 steps for \(1^*\) and 20 000 steps for \(5\)). Only one enantiomeric form with \((M)\)-helicity is depicted in (a) and (c).](image)

A conformational search for a model \(1^*\) [NMe] predicted that a helically folded form was the most energy-minimized structure (rel. 0 kJ mol\(^{-1}\)) and an extended form existed at a higher energy level (+28.4 kJ mol\(^{-1}\)) (Fig. 2a and 2b). Notably, a similar prediction was made for the parent hydrocarbon \(5\) (Fig. 2c and 2d), although an extended form has often been seen in crystals of related compounds.\(^{6c,13b,14}\) Such an inherent preference for helically folded forms of these loops would be suitable for realization of the two-way intramolecular transmission of chirality.

We first investigated the dynamic structure of a reference loop 3 [NBu] in solution by \(^1\)H NMR spectroscopy. The spectrum measured at room temperature showed a single set of averaged resonances. Some chemical shifts changed with
temperature (Fig. 3a). These results indicated that several conformers with different forms, e.g., folded and extended, were involved in equilibrium and were dynamically interconvertible. The populations of these contributors changed with temperature.

Also, when a ditopic hydrogen-bonding guest (R,R)-4\textsuperscript{11h} was added to a solution of 3, some chemical shifts changed through the formation of hydrogen bonds at each carbonyl of 3 (Fig. 3b). The similarity of these changes indicated that the major contributor in a complexed state was identical to that in an uncomplexed state seen at lower temperatures. Through an NMR titration experiment, the 1:1 binding constant was estimated to be 3.5×10\textsuperscript{11} M\textsuperscript{-1} (Fig. S2a).\textsuperscript{16,17}

Next, we monitored the complexion of helical loop 3 with a chiral ditopic guest (R,R)-4 or (S,S)-4 by UV and CD spectroscopy.\textsuperscript{12,16} In the UV spectrum of 3 (λ\textsubscript{max} (log ε) 372 (shoulder, 4.03), 346 (sh., 4.42), 319 (sh., 4.60), 297 (4.73) and 259 (4.76) nm),\textsuperscript{19} several absorbances at a longer wavelength region were reduced upon the addition of a guest (Fig. 4a). This result indicated that the population of an extended form was decreased upon complexation. In the absorption region of 3, when a chiral guest (R,R)-4 was added, composite bisignated Cotton effects were induced (Fig. 4b).\textsuperscript{20} Addition of the antipodal ditopic guest (S,S)-4 induced mirror images. These complexion-induced CD spectra were different in shape from those of the chiral guest itself (Fig. 4c), and we considered that these induced Cotton effects were attributed to biased populations of dynamic helical forms of the loop through complexation. This was supported by VT measurements of an induced CD spectrum (Fig. 4d). The intensity changed with temperature, increased at a lower temperature and decreased at a higher temperature, while maintaining a spectral appearance. In a control experiment, no change was found in either the UV or CD spectra of 3 upon mixing a monotopic guest (R)-8\textsuperscript{11h} with the same chiral auxiliary group (Fig. S4). These results showed that the host 3 with a pair of chromophores could adopt dynamic helical forms and a particular helical sense was preferred in a 1:1 complex with a chiral ditopic guest through the supramolecular transmission of point chirality.

Two-way intramolecular transmission of a single chiral source associated with a dynamic helical loop

First, we demonstrate the intramolecular transmission of point chirality in the helical loop (R,R)-1 without any guest molecule. In the absorption region of (R,R)-1 (λ\textsubscript{max} (log ε) 371 (sh., 3.97), 343 (sh., 4.39), 316 (sh., 4.58), 300 (4.70), 290 (4.70) and 256 (4.77) nm),\textsuperscript{11h} which was similar to that of 3, the CD spectrum showed composite Cotton effects (Fig. 5a). This spectral appearance closely resembled that of a cyclic reference (R,R)-9 with dynamic figure-eight chirality, and CD spectra of (a) (R,R)-1 (bold solid line) and (b) (R,R)-9, measured in dichloromethane at 293 K.

![Fig. 5 Chemical structures of a substructure (R)-10 with the same chiral auxiliary and a cyclic reference (R,R)-9 with dynamic figure-eight chirality, and CD spectra of (a) (R,R)-1 (bold solid line) and (b) (R,R)-9, measured in dichloromethane at 293 K.](image)

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helical sense was switched between before and after complexation. Since no preference was induced by achiral helical sense was switched between before and after complexation. The molecule can be linked and helically arranged. Fortunately, we found that two triple bonds were suitable for the linker in the present system. This chiroptical switching phenomenon, where chirality is twice transmitted to dynamic helical forms in one molecule under different conditions, is a fascinating feature in dynamic chiral chemistry.

Conflicts of interest
There are no conflicts to declare.

Notes and references
3 N. Harada and N. Berova, Complementary Chirality, 2012, 8, 449.

14 (a) G. Huang, Y.-Q. Sun, Z. Xu, M. Zeller and A. D. Hunter, Dalton Trans., 2009, 5083; (b) F. Körte, C. Bruhn and R. Faust, Synlett, 2015, 26, 1620.

15 Similar results were obtained with (R,R)-1 (Fig. S1). In this case, the two helically folded forms with (M)- or (P)-helicity are diastereomers. The chemical shifts of averaged resonances changed with temperature regardless of whether or not we assume that an extended form was involved.

16 S. Akine, TitrationFit, program for analyses of host-guest complexation, Kanazawa University, Kanazawa, Japan, 2013.

17 For the estimation, we used data obtained with the addition of 0-1 equivalents. Later in titration, we might have to assume the formation of a competitive 1:2 complex through two-fold single hydrogen bonds at each carbonyl group of 3. For the complexation of (R,R)-1 with 2, we did not estimate the binding constant due to the lack of accuracy in identifying the peak of widely-broadened resonances (Fig. S2b).


19 The observed absorption seemed to follow the pattern seen for the parent 5.

20 Titration curves for this complexation were shown in Fig. S3.