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Title	Supramolecular chiroptical switching of helical-sense preferences through the two-way intramolecular transmission of a single chiral source
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Description	アクセプト後にタイトル変更あり、著者最終稿は変更前のタイトル"Supramolecular chiroptical switching of helical-sense preferences through the two-way intramolecular transmission of a single chiral source associated with a dynamic helical loop"
Citation	Organic & biomolecular chemistry, 16(7), 1167-1171 https://doi.org/10.1039/c7ob03057f
Issue Date	2018-02-21
Doc URL	https://hdl.handle.net/2115/72699
Type	journal article
File Information	manu_OB-ART-12-2017-003057.pdf

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Journal Name

ARTICLE

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Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

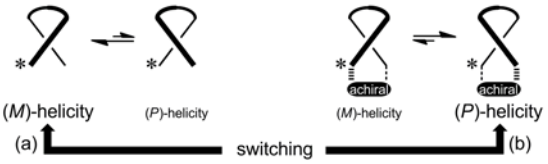
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Ryo Katoono,*[a] Keiichi Kusaka,[a] Yuki Tanaka,[a] Kenshu Fujiwara[a] and Takanori Suzuki[a]

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 condrol 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 chromophores[3-8] 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 association[6,7] or covalent bond formation[8] 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 this 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.

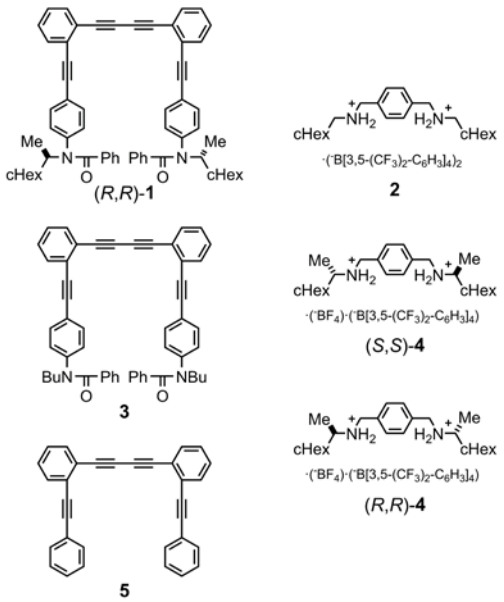


Fig. 1 Chemical structures of dynamic helical loops (*R*,*R*)-**1**, **3** and **5**, ditopic guests **2**, (*S*,*S*)-**4** and (*R*,*R*)-**4**.

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Electronic Supplementary Information (ESI) available: [details of NMR, UV and CD spectroscopic data (Fig. S1-S3), and experimental details of new compound preparation]. See DOI: 10.1039/x0xx00000x

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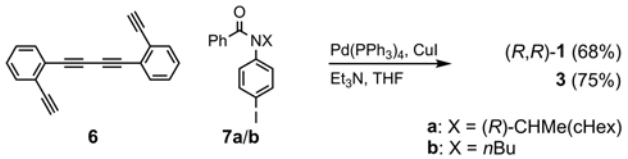
(Scheme 1). In the uncomplexed and complexed states, different senses of dynamic chirality would be preferred through two-way intramolecular transmission of the single chiral source associated with the host.

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**][11h] 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**[9b] 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**[12] with the corresponding *N*-benzoylated iodoaniline derivatives[11g] **7a/b** (Scheme 2).



Scheme 2. Preparation of dynamic helical loops (*R*,*R*)-**1** and **3**.

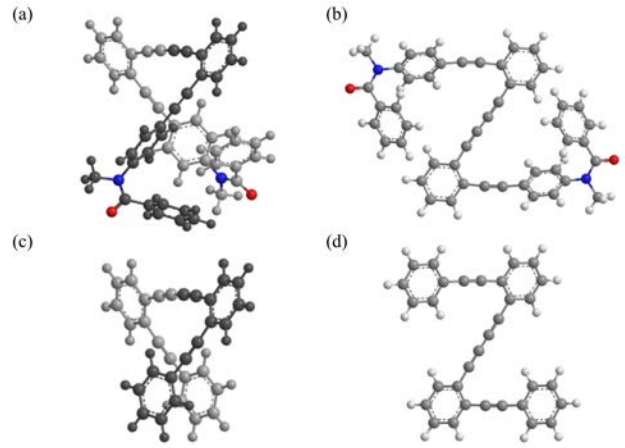


Fig. 2 Energy-minimized structures for a model **1'** [NMe]; (a) a helically folded form (rel. 0 kJ mol^{-1}) and (b) an extended form (+28.4 kJ mol^{-1}), and for a parent hydrocarbon **5**; (c) a helically folded form (rel. 0 kJ mol^{-1}) and (d) an extended form (+16.2 kJ mol^{-1}), obtained by conformational 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).

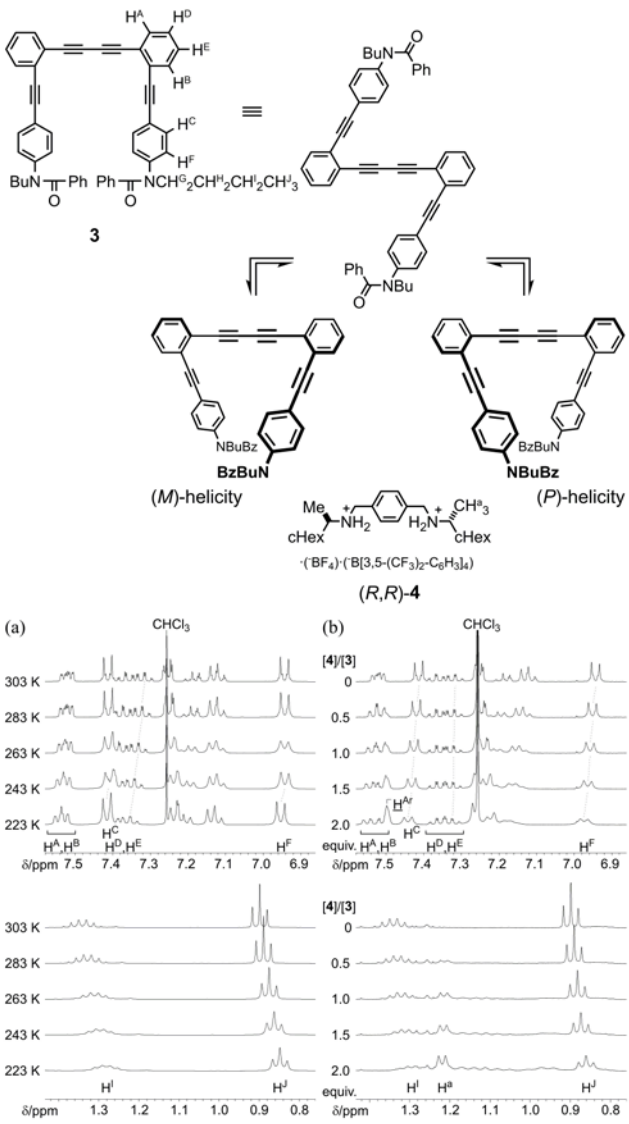


Fig. 3 Partial ^{1}H NMR spectra (400 MHz, upper: aromatic, lower: aliphatic region) of **3** ([**3**] = 1.28 mM), (a) measured at 223-303 K; (b) in the presence of a chiral ditopic guest (*R*,*R*)-**4** (0-2 equiv.), measured at 303 K. All spectra were measured in chloroform-*d*.

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**[13] (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

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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.[15]

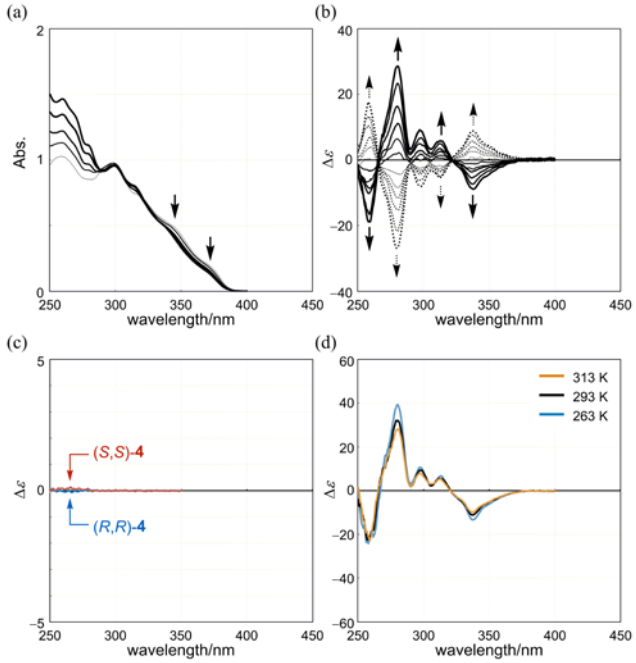


Fig. 4 (a) UV spectrum of **3** (1.79×10^{-4} M) in the presence of (*R*,*R*)-**4** [0 (**3** only, thin line), 1-8 equiv. (bold lines)], measured at room temperature; (b) CD spectra of **3** (1.79×10^{-4} M) in the presence of (*R*,*R*)-**4** (solid lines) or (*S*,*S*)-**4** (dashed lines) (1-8 equiv.), measured at 293 K; (c) CD spectra of (*R*,*R*)-**4** (blue line) or (*S*,*S*)-**4** (red line) itself, measured at room temperature; (d) VT CD spectra of **3** (1.79×10^{-4} M) in the presence of (*R*,*R*)-**4** (16 equiv.), measured at 263 (blue line), 293 (black line) and 313 (orange line) K. All spectra were measured in dichloromethane.

Also, when a ditopic hydrogen-bonding guest (*R*,*R*)-**4**[11h] was added to a solution of **3**, some chemical shifts changed through the formation of hydrogen bonds at each carbonyl group 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^{2} M^{-1} (Fig. S2a).[16,17]

Next, we monitored the complexation of helical loop **3** with a chiral ditopic guest (*R*,*R*)-**4** or (*S*,*S*)-**4** by UV and CD spectroscopy.[1,2,18] In the UV spectrum of **3** [λ_{max} (log ε) 372 (shoulder, 4.03), 346 (sh., 4.42), 319 (sh., 4.60), 297 (4.73) and 259 (4.76) nm],[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, compositive bisignated Cotton effects were induced (Fig. 4b).[20] Addition of the antipodal ditopic guest (*S*,*S*)-**4** induced mirror images. These complexation-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

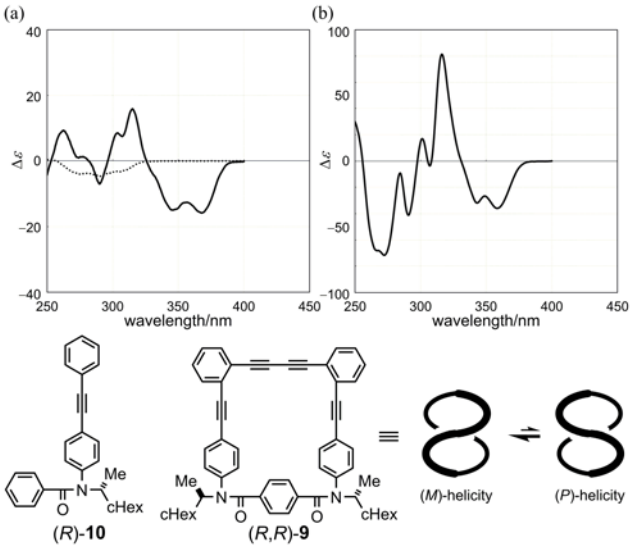


Fig. 5 Chemical structures of a substructure (*R*)-**10** with the same chiral auxiliary and a cyclic reference (*R*,*R*)-**9** with dynamic figure-eight chirality, and CD spectra of (a) (*R*,*R*)-**1** (bold solid line) and (*R*)-**10** (thin dashed line), and (b) (*R*,*R*)-**9**, measured in dichloromethane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

either the UV or CD spectra of **3** upon mixing a monotopic guest (*R*)-**8**[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_{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],[11h] which was similar to that of **3**, the CD spectrum showed compositive Cotton effects (Fig. 5a). This spectral appearance closely resembled that of a cyclic reference (*R*,*R*)-**9** with dynamic figure-eight chirality (Fig. 5b).[11h] Alternatively, the spectrum of a substructure (*R*)-**10**[11g] with the same chiral auxiliary showed different Cotton effects, which were attributed to a local chiral environment around the auxiliary (Fig. 5a). These results showed that a helically folded form of (*R*,*R*)-**1** was present in solution. The helical-sense preference was brought about through the intramolecular transmission of chirality associated with (*R*,*R*)-**1** (Scheme 1a).

Next, we demonstrate another intramolecular transmission of point chirality in a 1:1 complex with an achiral ditopic guest.

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Upon the addition of **2**, the reduction of absorbance was again monitored in the UV spectrum of (*R*,*R*)-**1** (Fig. 6a). As in the above case with **3** and (*R*,*R*)-**4**, we considered that the population of an extended form was decreased in a complexed state. Notably, upon the addition of **2**, pseudo-mirrored Cotton effects emerged (Fig. 6b), compared to the original Cotton effects. This reversal of the sign showed that the preferred

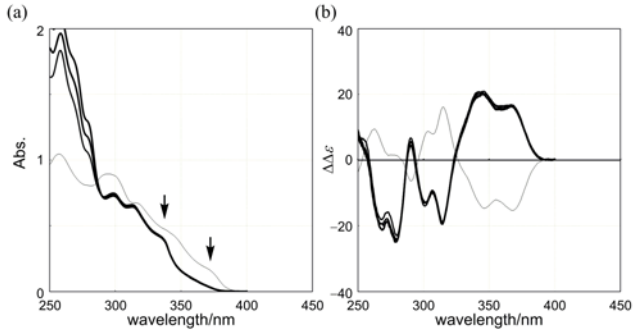


Fig. 6 (a) UV and (b) differential CD spectra ($\Delta\Delta\varepsilon = \Delta\varepsilon_{1\text{-}2} - \Delta\varepsilon_1$) of (*R*,*R*)-**1** ($1.78\times10^{-4}$ M) in the presence of achiral ditopic guest **2** (bold lines) (1, 2, 3 and 4 equiv.), and the CD spectrum ($\Delta\varepsilon_1$) of (*R*,*R*)-**1** itself (thin line). All spectra were measured in dichloromethane at room temperature.

helical sense was switched between before and after complexation. Since no preference was induced by achiral guest **2**, the preferred sense was also induced by the intramolecular transmission of chirality associated with (*R*,*R*)-**1** even in a complexed state (Scheme 1b). These results showed that the chiral auxiliaries (*R*,*R*) attached to each end of the loop acted as a chiral handle to control the helical-sense preference in both uncomplexed and complexed states through the two-way intramolecular transmission of chirality.

Conclusions

We have demonstrated the two-way control of helical-sense preferences before and after complexation with an achiral molecule. To realize this control, several conditions had to be satisfied as listed below, albeit each was easy to achieve except for the last one. First, the molecule is designed to favor dynamic helical forms. One helical sense is preferred over the other through a transmission of chirality. The molecule can capture an achiral guest molecule. In a complexed state, the molecule again adopts dynamic helical forms and again prefers a particular sense. In this regard, however, the preferred senses are opposite.

We used a simple molecule, in which a pair of chromophores are 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.

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