JOC The Journal of Organic Chemistry

Article

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Dynamic Figure Eight Chirality: Multifarious Inversions of a Helical Preference Induced by Complexation

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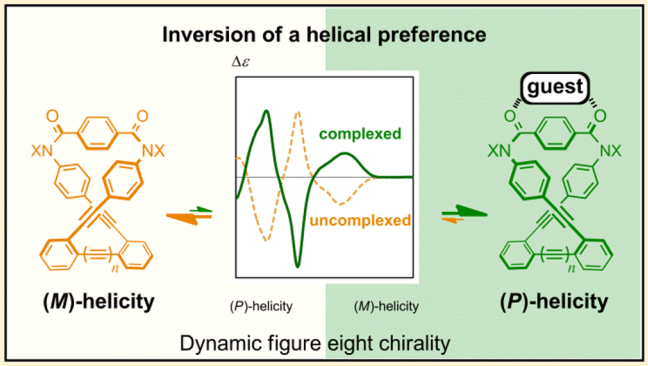
Supporting Information

ABSTRACT: We demonstrate two types of inversion of a helical preference upon the 1:1 complexation of a dynamic figure eight molecule with a guest molecule through the controlled transmission of point chirality. We designed a series of macrocycles that prefer a nonplanar conformation with figure eight chirality. These macrocycles are composed of a chirality-transferring unit (terephthalamide) and a structure-modifying unit (two *o*-phenylene rings spaced with a varying number of triple bonds). The former unit provides a binding site for capturing a guest molecule through the formation of hydrogen bonds. The attachment of chiral auxiliaries to the former unit induces a helical preference for a particular sense through the intramolecular transmission of point chirality. For relatively small-sized macrocycles, the preferred sense was reversed upon complexation with an achiral guest. Contrary preferences before and after complexation were both seen for chiral auxiliaries associated with a figure eight host through two-way intramolecular transmission of the single chiral source. Alternatively, the helical preference induced in relatively large-sized macrocycles was reversed only when a figure eight host formed a 1:1 complex with a particular enantiomeric guest through the supramolecular transmission of point chirality in the guest. This stereospecific inversion of a helical preference is rare.



INTRODUCTION

Figure eight molecules have attracted much attention regarding the design of novel π-conjugated molecules with a nonplanar structure[1] and have been considered to provide synthetic precursors to carbon allotropes. In addition to pioneering work based on hydrocarbons,[1] molecules containing heteroatoms[2] have also been explored and have demonstrated not only beautiful figure eight shapes but also characteristic supramolecular[2a−g] or electrochemical[2h] features. Chirality is of particular interest in the field of figure eight molecules. Chiroptical properties have often been investigated through the successful separation of enantiomers,[1h,i,2i−o] whereas only a few studies on dynamic molecules with labile stereochemistry have shown a promising approach to the transmission of chirality to control the labile stereochemistry of a figure eight molecule.[2a−c] Lability in dynamic chiral molecules presents a fascinating challenge regarding how we might induce a preferred sense of dynamic chirality as well as how we could reverse this preference in response to a change in environmental conditions, such as an electrical field,[3] temperature,[4] solvent,[5] or photoirradiation.[6] The addition of a guest can offer a solution to this task,[5g] allowing us to envision more advanced systems in which a helical preference is specifically reversed upon complexation because we can select various guests with different structures in terms of shape,[5g] size,[7f] and chirality. Here, we report the inversion of a helical preference upon complexation of a dynamic figure eight molecule with a guest molecule through the controlled transmission of point chirality (Scheme 1). We assumed a dynamic molecule with figure eight chirality and two enantiomeric conformations with (*M*)- or (*P*)-helicity interconvert to each other. When we attach a chiral auxiliary to the figure eight molecule (host), a particular sense of dynamic figure eight chirality would be favored over the other through the intramolecular transmission of chirality. In a simple case of the complexation-induced inversion of helical preference, the host molecule would favor the other sense over the original in a complex with an achiral guest (Scheme 1a). In both the absence and presence of the achiral guest, a preferred sense is brought about by the single chiral source associated with the host to exhibit contrary preferences before and after complexation. An achiral guest has no preference with respect to the direction of the twisting toward (*M*)- or (*P*)-helicity. In an advanced case, the host molecule would reverse its original helical preference only when it forms a complex with a particular enantiomeric guest, and would retain its original preference or make it marginal in a diastereomeric complex with the antipodal enantiomer (Scheme 1b). Chiral guests should have their own preferences with respect to the direction of twisting, and the chirality would be supramolecularly transferred if the preference of the chiral guest matched the

Received: May 29, 2015
Published: July 16, 2015

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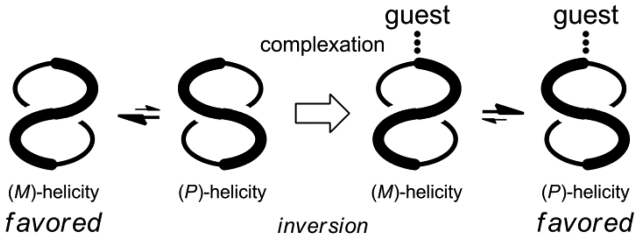
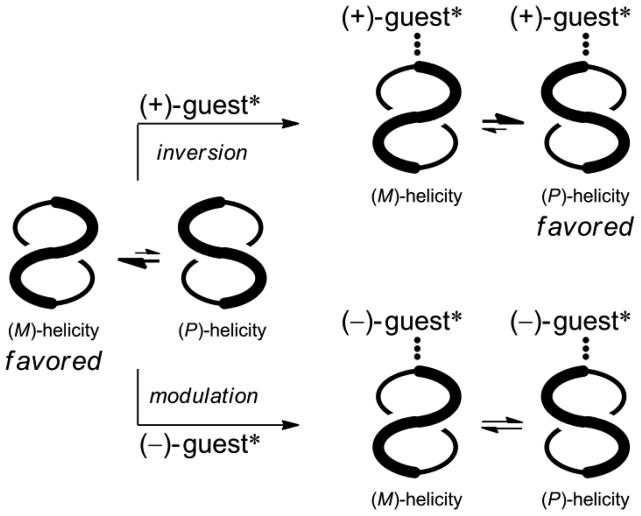
DOI: 10.1021/acs.joc.5b01206
J. Org. Chem. 2015, 80, 7613−7625

Scheme 1

(a) Complexation-induced inversion of a helical preference



(b) Stereospecific inversion of a helical preference upon complexation with a chiral guest



preference of the internal chirality associated with the host in a complexed state.

Thus, we designed a series of figure eight macrocycles **1** and **2** that are composed of a chirality-transferring unit and a structure-modifying unit (Figure 1) as a new category of dynamic helical molecules based on terephthalamides.[8] The former unit is terephthalamide, in which the two amide groups create local chiral conformations when they are twisted in a conrotatory manner with respect to the central benzene ring. They dynamically interconvert to each other through rotation about the $C_{C=O}-C_{central}$ bonds. These two amide carbonyls are suitable for capturing a hydrogen-bonding ditopic guest. When a guest is chiral, the chirality would lead to a preference in the direction of twisting and favor a particular sense of the local chirality of the unit (supramolecular transmission of chirality). The attachment of a chiral auxiliary to each amide nitrogen is also a promising approach to control the local chirality in the unit (intramolecular transmission of chirality). We assumed that the motility of the two amide groups in the unit and/or the transmission of chirality to the dynamic unit would be affected by the attributes of the macrocyclic framework. The structure-modifying unit enabled the framework to vary in size because the number (n) of triple bonds between the two *o*-phenylene rings varied from zero to three. The two *o*-phenylene rings would induce the macrocycle to prefer a nonplanar figure eight form[1a−h,2f−i] in concert with the twisting of the two amide groups in the chirality-transferring unit. These two units are linked by rigid triple bonds. The substituent X on each amide nitrogen is an *n*-butyl group with no asymmetric element for

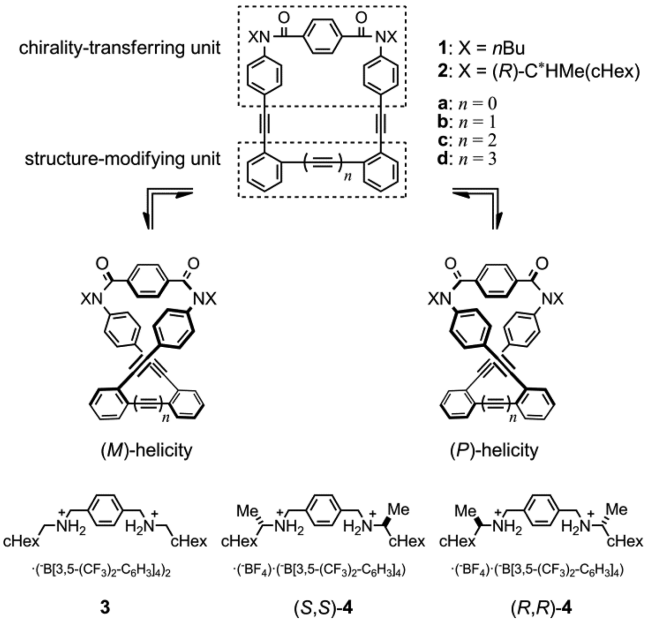


Figure 1. Chemical structures of macrocycles **1**/**2**, ditopic guests **3**[9e]/**4**,[7j,9b−d,g] and dynamic interconversion between the two enantiomeric forms with figure eight chirality.

macrocycle **1** and an (*R*)-C*HMe(cHex) group as a chiral auxiliary for **2** in the chirality-transferring unit, and the number of triple bonds in the structure-modifying unit (0−3) is indicated as **a**−**d**, respectively (Figure 1).

In this article, we describe dynamic chiroptical features based on a series of figure eight macrocycles that showed the reversal of a helical preference upon complexation with a guest molecule through the controlled transmission of point chirality. First, we demonstrated the supramolecular transmission of chirality upon 1:1 complexation using a host **1** with no asymmetric element other than dynamic figure eight chirality and a chiral ditopic guest with point chirality, according to our previous reports.[2a,9a−d] Second, we characterized the intramolecular transmission of chirality through the observation of Cotton effects from a host (*R*,*R*)-**2** with chiral auxiliaries in addition to dynamic figure eight chirality in the absence of any guest molecule.[9f] Next, we investigated the complexation-induced inversion of a helical preference of (*R*,*R*)-**2** in the presence of either an achiral guest without any chiral element or chiral guests (Scheme 1). We found here two types of complexation-induced inversion of a helical preference. A preferred sense of figure eight chirality was reversed upon complexation with whatever guest formed a 1:1 complex with **2** (Scheme 1a). This was the case for (*R*,*R*)-**2a** or (*R*,*R*)-**2b**. In such a complex, we considered that the internal chirality determined the helical preference. Contrary preferences before and after complexation both originated in the chiral auxiliaries (*R*,*R*) associated with a figure eight host through two-way intramolecular transmission of the single chiral source. In contrast, a helical preference induced in a dynamic figure eight host was reversed in a stereospecific manner upon complexation with enantiomeric guests (Scheme 1b). This is a rare case regarding the stereospecific inversion of a helical preference and was realized with both (*R*,*R*)-**2c** and (*R*,*R*)-**2d**. They exhibited inversion of a helical preference only when they formed a 1:1 complex with a particular enantiomeric guest through the supramolecular transmission of point chirality in the guest.

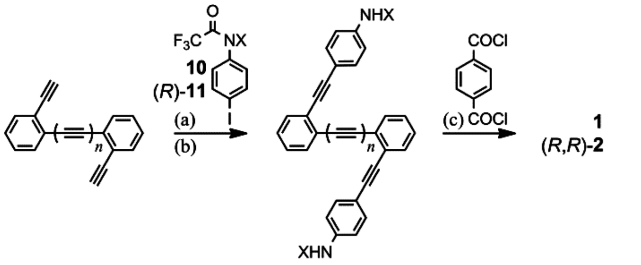
DOI: 10.1021/acs.joc.5b01206
J. Org. Chem. 2015, 80, 7613−7625

Alternatively, in a diastereomeric complex, they did not show any preference even though they could form a complex similarly to the antipodal guest regarding the binding affinity.

RESULTS AND DISCUSSION

Preparation of Figure Eight Macrocycles 1 and 2. We prepared a series of macrocycles **1a**−**1d** and (*R*,*R*)-**2a**−(*R*,*R*)-**2d** through a condensation reaction of terephthaloyl chloride with the corresponding dianilines[10] **8a**−**8d** and (*R*,*R*)-**9a**−(*R*,*R*)-**9d**, respectively. The ring-closing precursors **8** and (*R*,*R*)-**9** were obtained by a Sonogashira coupling reaction of an *N*-trifluoroacetylated iodoaniline derivative[9c] **10** or (*R*)-**11** with the corresponding diynes[1g,11] **5a**−**5d**, followed by deprotection of the trifluoroacetyl groups in **6** or (*R*,*R*)-**7** with sodium hydride in methanol-containing tetrahydrofuran (Scheme 2).

Scheme 2. Preparation of Macrocycles 1 and 2[a]



	(a)		(b)		(c)		
Product	**6**	(*R*,*R*)-**7**	**8**	(*R*,*R*)-**9**	**1**	(*R*,*R*)-**2**	
Yield	100%	98%	77%	67%	95%	87%	**a**: $n = 0$
	97%	99%	99%	86%	94%	90%	**b**: $n = 1$
	98%	96%	93%	84%	73%	66%	**c**: $n = 2$
[a]See Experimental and Supporting information							**d**: $n = 3$[a]

[a]Reagents: (a) $Pd(PPh_3)_4$, CuI, Et_3N, THF. (b) NaH, MeOH, THF. (c) Et_3N, toluene.

Among the macrocycles **1** and (*R*,*R*)-**2**, only (*R*,*R*)-**2a** was obtained as a mixture. Successful separation by HPLC gave two components, and they changed over several days at room temperature ($t_{1/2}$ = ∼10 h at 298 K) to give a mixture, which was close to the original as-prepared mixture (details are described later). We used diammonium salts **3**, (*R*,*R*)-**4**, and (*S*,*S*)-**4** as a hydrogen-bonding ditopic guest (Figure 1), which formed a 1:1 complex at the two amide carbonyls of terephthalamide in the chirality-transferring unit. We also prepared acyclic references (*R*,*R*)-**12a**−(*R*,*R*)-**12c**, and compared their electronic and chiroptical properties with those of the macrocycles. The details of the preparation of intermediates and references are summarized in Scheme S1 in the Supporting Information.

Molecular Structures of Macrocycles 1 and 2. Single-crystal X-ray analyses of macrocycles **1** revealed that every macrocycle adopted a helical form with figure eight chirality (Figure 2) and appeared as a racemate of two helical forms with (*M*)- or (*P*)-helicity in a crystal. In each macrocycle, the two amide groups were twisted in a conrotatory manner, and the two *o*-phenylene rings had a significant dihedral angle to prefer a nonplanar structure, as expected.

The ^{1}H NMR spectrum of **1b** (n = 1), measured in chloroform-*d* at 303 K, exhibited a single set of averaged resonances that were assigned to C_{2v} symmetry. The observed symmetry was maintained during VT measurements at 223−323 K (Figure 3a) and was attributed to averaging through dynamic interconversion between two equivalent species with C_2 symmetry if we considered the results of X-ray analyses (Figure 2) and the VT measurements. At a lower temperature, a sequential change in appearance (broadening and split) was observed for butyl protons, which are closest to the nitrogen atom, to indicate the presence of a diastereotopic situation (H^D and $H^{D'}$) in the molecule. Similar changes were observed for some *p*-phenylene protons (H^A, H^B, and H^C) and were considered to be the result of slow local rotations on the NMR time-scale. Notably, there were almost no significant changes in the chemical shift during the VT measurements, which showed that the macrocyclic framework was only allowed to convert to the equivalent form. We estimated an activation energy at the coalescence temperature ($\Delta G^{\neq}$ = 48 kJ mol^{-1} at 253 K) for the dynamic interconversion between two equivalent forms based on the coalescence of diastereotopic protons H^D and $H^{D'}$ ($\Delta\delta$ = 287 Hz).[1c,2e,f,11a,12] Similar observations were noted with other macrocycles (**1a**, **1c**, and **1d**) that showed dynamic interconversion between two equivalent forms in solution, although there were differences in the chemical shift and

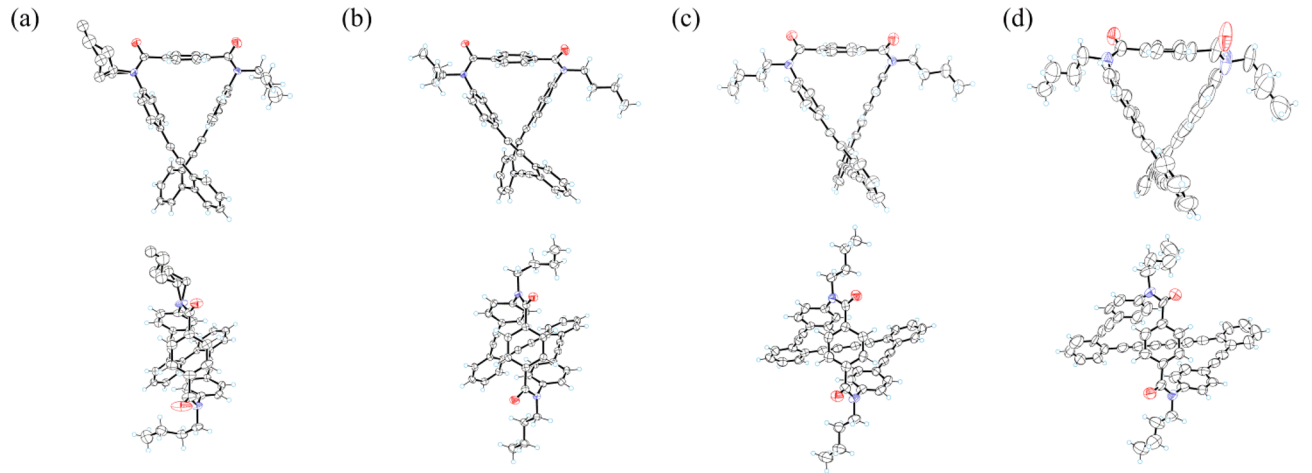


Figure 2. X-ray structures of (*P*)-**1** in *rac*-**1** crystals. Only one enantiomer is depicted in (a) **1a**, (b) **1b**, (c) **1c**, and (d) **1d** (upper: front view; lower: top view). Thermal ellipsoids are shown at the 50% probability level.

DOI: 10.1021/acs.joc.5b01206
J. Org. Chem. 2015, 80, 7613−7625

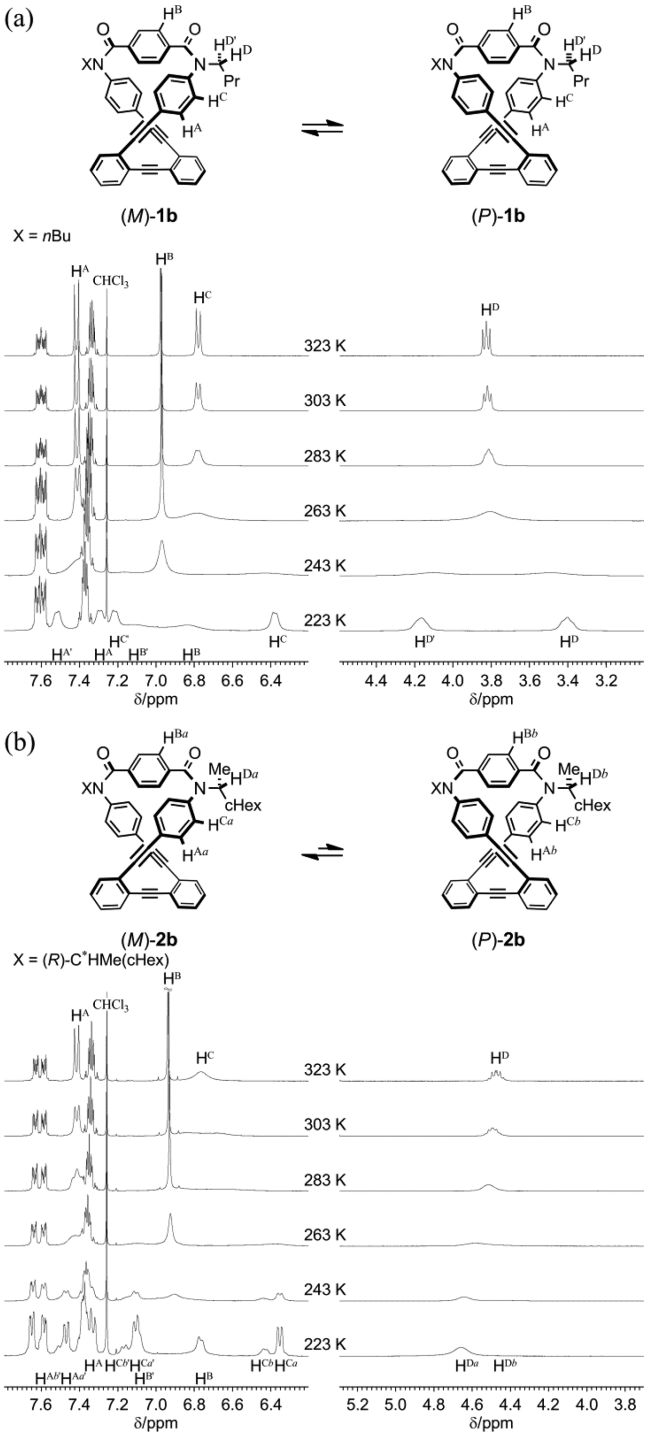


Figure 3. Partial VT-^{1}H NMR spectra (400 MHz) of (a) **1b** and (b) (*R*,*R*)-**2b** measured in $CDCl_3$ at 223−323 K. Two protons (H and H′, or H^a and H^b) in a pair of split resonances are tentatively assigned. There is less information in the aliphatic region.

coalescence temperatures (Figure S1, Supporting Information).[13]

Quantitative ^{1}H NMR spectroscopy was useful when we investigated the dynamic equilibrium between two nonequivalent conformers in a solution of macrocycles with a chiral auxiliary on each nitrogen. We considered the spectra of (*R*,*R*)-**2b** (n = 1) as a representative example (Figure 3b). At an elevated temperature (323 K), we observed a single set of averaged resonances that were assigned to C_2 symmetry. With a decrease in temperature, two step changes in appearance (broadening and split) were recorded for *p*-phenylene protons H^A and H^C. The first step at ∼283 K was due to slow local rotation about the *p*-phenylene ring because splitting gave two equivalent resonances, as with **1b** or (*R*)-**14**,[7j] which is a diphenylacetylene derivative with the same chiral auxiliary. Alternatively, the second step at ∼243 K proved, upon averaging on the NMR time-scale, to be a dynamic interconversion between two nonequivalent species with C_2 symmetry. We considered the two nonequivalent resonances (H^{Ca} and H^{Cb}) to be the result of the intramolecular transmission of chirality (*R*) to dynamic figure eight chirality (*M*) and (*P*)[14] and estimated an activation energy of $\Delta G^{\neq}$ = 55 kJ mol^{-1} for the dynamic interconversion between two diastereomeric forms based on the coalescence of H^{Ca} and H^{Cb} ($\Delta\delta$ = 31 Hz) at 260 K.[12] The populations of H^{Ca} and H^{Cb} at the coalescence temperature were determined from a plot of ln *K* versus 1/*T* (Figure S3, Supporting Information), where *K* is the equilibrium constant between the two diastereomeric forms, obtained at lower temperatures. We confirmed a similar dynamic interconversion between two diastereomeric forms in solutions of macrocycles (*R*,*R*)-**2a**, (*R*,*R*)-**2c**, and (*R*,*R*)-**2d** (Figure S1, Supporting Information).[15] There were almost no significant changes in the chemical shift during the VT measurements.

Macrocycle **2a** in dichloromethane showed absorption at 295 (log ε 4.77) and 315 (sh, 4.59) nm, similar to acyclic reference **13** [290 (4.78) and 306 (4.68)][9a] and diphenylacetylene derivative **14** [291 (4.47) and 307 (4.45)][7j] (Figure 4a). This similarity in the appearance of these spectra indicated that diphenylacetylene was an effective chromophore in each molecule. In the spectrum of acyclic reference **12a**, in which two diphenylacetylene chromophores are directly conjugated, the corresponding absorption was bathochromically shifted and slightly enhanced [303 (4.69) and 313 (4.70)] (Figure 4a). There seemed to be a slight difference between macrocycle **2b** and the acyclic reference **12b** at a longer absorption region (>320 nm) (Figure 4b), and the spectrum of the latter was similar to that of the parent hydrocarbon.[16] In the spectra of macrocycles **2c** and **2d**, the absorption characteristic of α,ω-diphenylpolyynes[17] was present (Figure 4c,d). The observations for a series of **1** were comparable to those for **2** and indicated that the electronic structures of the macrocycles were not affected by the substituent on the amide nitrogen.

Complexation of Figure Eight Macrocycles 1 with Chiral Ditopic Guest 4. We first investigated the complexation of a macrocyclic host **1b** (n = 1), which exhibited average resonances at room temperature, with a ditopic guest **4**[18] by ^{1}H NMR spectroscopy. When **1b** and **4** were mixed in chloroform-*d*, significant upfield shifts were induced for both the phenylene protons H^B in **1b** and the phenylene protons H^a in **4** (Figure 5a), which indicated that they were assembled through the formation of hydrogen bonds at the two amide carbonyls. We confirmed that the stoichiometry for the assembly was 1:1 by a Job plot based on a continuous change for **4** (Figure 5b). Also, in a titration experiment, we found an obvious transition point at a ratio of around 1:1 (Figure 5c).[19] During complexation, almost no changes in the chemical shift were induced for other protons far from the binding site, which indicated that the host did not deform into any other structure in a complexed state.

Next, we monitored the 1:1 complexation of **1** with the chiral guests (*R*,*R*)-**4** and (*S*,*S*)-**4** in dichloromethane to investigate the supramolecular transmission of chirality. To a set of

DOI: 10.1021/acs.joc.5b01206
J. Org. Chem. 2015, 80, 7613−7625

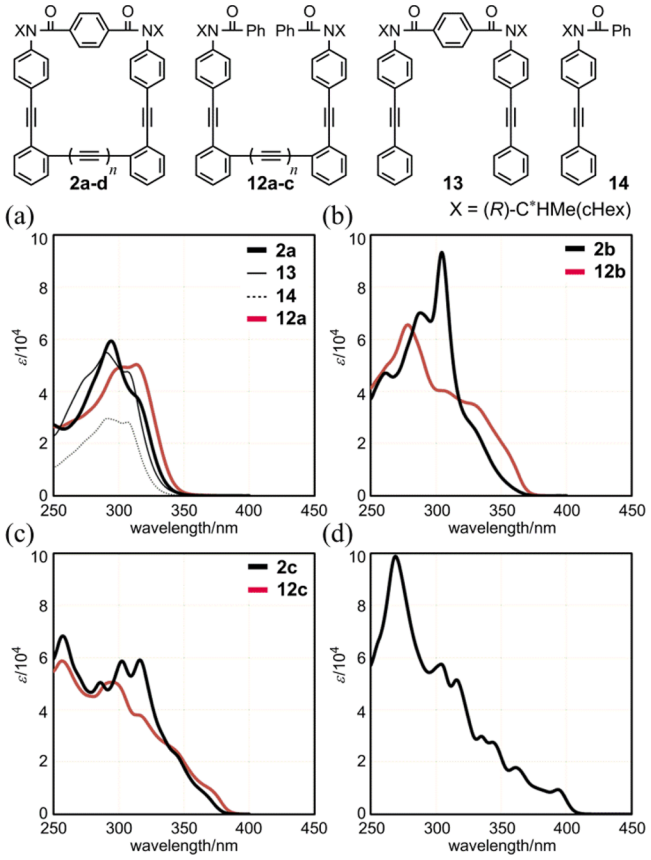


Figure 4. UV spectra of (a) **2a**, **12a**, **13**, and **14**, (b) **2b** and **12b**, (c) **2c** and **12c**, and (d) **2d**. All spectra were measured in CH_2Cl_2 at room temperature.

solutions containing **1a** (1.9×10^{-4} M), which contained an equivalent mixture of two forms with (*M*)- or (*P*)-helicity, we added one, two, or four equiv of (*R*,*R*)-**4** at room temperature, and each solution was left to stand for 2 days at a constant temperature. We measured the CD spectrum of each solution and found that a single pair of bisignated Cotton effects was induced in the absorption region of **1a** (Figure 6a, blue lines). When we used (*S*,*S*)-**4** instead of (*R*,*R*)-**4**, a set of mirror images emerged (Figure 6a, red lines). Notably, in such a diluted solution, the changes were saturated with the addition of only two equiv.[19] In the cases of **1b**, **1c**, and **1d**, we gradually added up to four equiv of (*R*,*R*)-**4** or (*S*,*S*)-**4** to a solution of **1**, and measured the spectrum after each addition.[19] We found that mirror images were continuously induced in the spectra of **1b**, **1c**, and **1d** (Figure 6b, c, and d, respectively). These spectra exhibited compositive Cotton effects in each absorption region of **1** due to multiple transition moments in the framework. These mirror-imaged Cotton effects indicated that a host preferred a particular sense of dynamic chirality in response to the chirality in each guest, and which we considered to be the result of successful supramolecular transmission of chirality in the guest to the dynamic figure eight chirality in the host.

We further confirmed the dynamic equilibrium in a complexed state through VT-measurements at 263 and 313 K. For a solution of **1b**, **1c**, and **1d** containing four equiv of a guest[19] in which the equilibrium immediately reached the steady state in response to a change in the environment, we found that Cotton effects were enhanced with a decrease in temperature and attenuated with an increase in temperature,

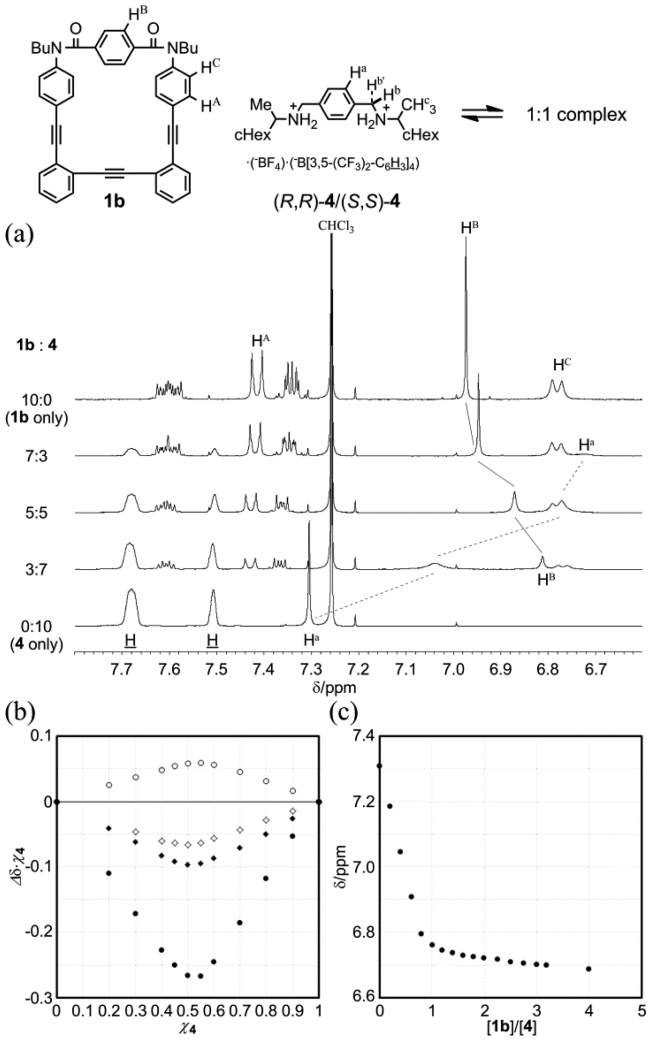


Figure 5. (a) ^{1}H NMR spectra (400 MHz) of **1b** in the presence of a 1:1 mixture of ditopic guests (*R*,*R*)-**4** and (*S*,*S*)-**4**, (b) Job plot ([**1b**] + [**4**] = 2 mM), and (c) a titration curve ([**1b**] = 0–8 mM, [**4**] = 2 mM) for the complexation of **1b** with (*R*,*R*)-**4**/(*S*,*S*)-**4** using continuous changes ($\Delta\delta = \delta_{1b\cdot4} - \delta_4$) in the chemical shift for phenylene protons H^a (circles), methylene protons H^b, and $H^{b\prime}$ (diamonds) and methyl protons H^c (outlined circles) of **4**. All spectra were measured in $CDCl_3$ at 303 K.

while the shape of the spectrum was maintained (Figure S5, Supporting Information), which showed the existence of two nonequivalent complexes [(*M*)-**1**·(*R*,*R*)-**4** and (*P*)-**1**·(*R*,*R*)-**4**] as well as unbound (*M*)-**1** and (*P*)-**1** that were in dynamic equilibrium. These observations can be explained by one or both of the following considerations. Some supramolecular assemblies, such as hydrogen-bonded complexes driven by a gain of enthalpy, are often favored at lower temperatures.[20] A preferred conformer is more favored at lower temperatures in an equilibrium between two nonequivalent conformers,[21] as demonstrated in the VT ^{1}H NMR measurements for (*R*,*R*)-**2b** and (*R*,*R*)-**2d**.

For a pair of mirror-imaged complexes of **1a** with (*R*,*R*)-**4** or (*S*,*S*)-**4**, in which we assumed a simple pair of transition moments that were parallel to the longitudinal diphenylacetylene chromophores,[22] we considered a preferred sense of dynamic figure eight chirality in the complex according to the exciton coupling method,[9a,23] and assigned it to (*P*)-**1a**·(*R*,*R*)-**4**

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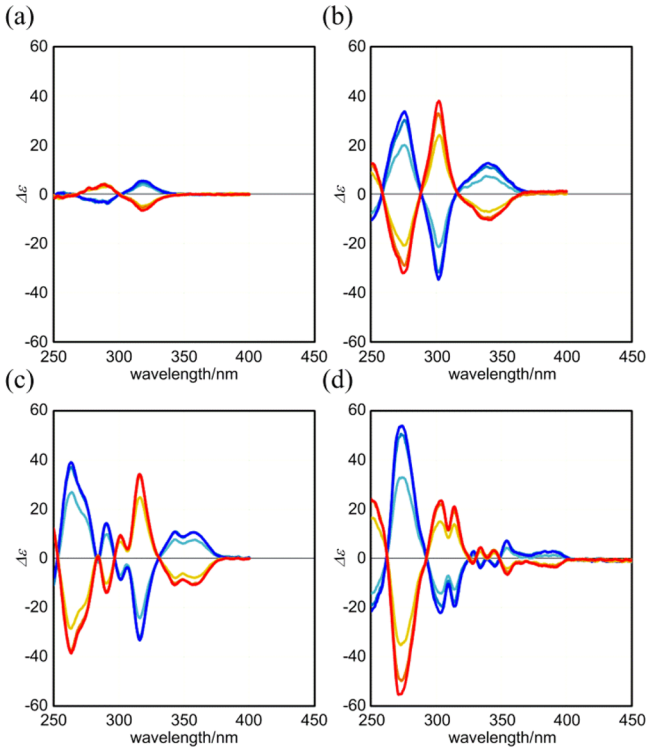

Figure 6. CD spectra of (a) **1a** (1.9×10^{-4} M), (b) **1b** (1.5×10^{-4} M), (c) **1c** (1.6×10^{-4} M), and (d) **1d** (9.7×10^{-5} M) in the presence of chiral ditopic guest (*R*,*R*)-**4** (blue lines) or (*S*,*S*)-**4** (red lines) (1, 2, and 4 equiv). All spectra were measured in CH_2Cl_2 at 293 K. Molar CDs ($\Delta\varepsilon$) of (*R*,*R*)-**4** or (*S*,*S*)-**4** were less than |0.2| throughout the absorption region of 250−450 nm.

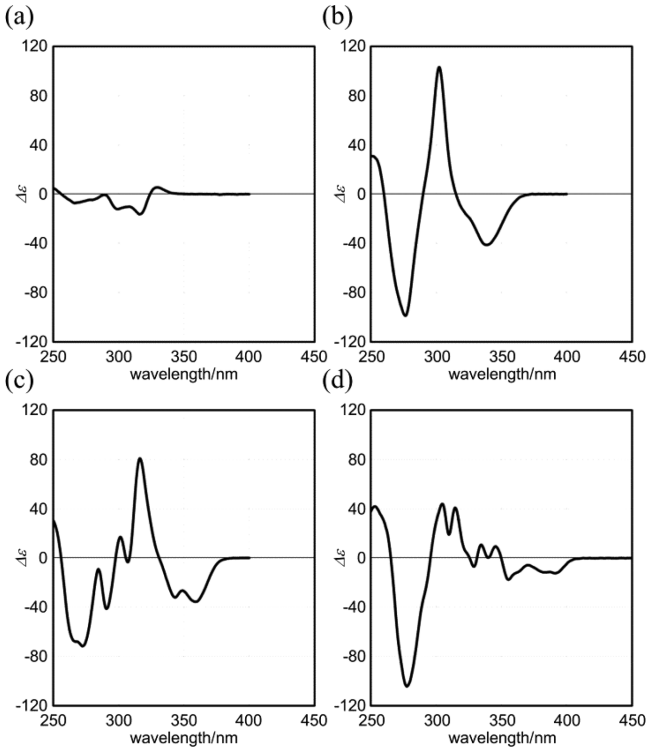

Figure 7. CD spectra of (a) (*R*,*R*)-**2a** (5.6% de), (b) (*R*,*R*)-**2b** (3.2% de), (c) (*R*,*R*)-**2c**, and (d) (*R*,*R*)-**2d** (13% de). All spectra were measured in CH_2Cl_2 at 293 K in the steady state. For reference, we noted a value of diastereomeric excess (%) at room temperature in parentheses.

and (*M*)-**1a**·(*S*,*S*)-**4**. During this monitoring, we did not find any significant changes in the appearance of the absorption of **1** (Figure S6, Supporting Information), which indicated that the host maintained the framework in a complexed state.

Attachment of a Chiral Auxiliary to Figure Eight Macrocycles 2. To investigate the intramolecular transmission of local point chirality to dynamic figure eight chirality, we measured the CD spectra of macrocycles (*R*,*R*)-**2** with a chiral auxiliary (*R*) on each amide nitrogen (Figure 7). A solution of (*R*,*R*)-**2a** was left to stand for 2 days prior to the measurement, which we discuss later in detail. The spectra of (*R*,*R*)-**2b**, (*R*,*R*)-**2c**, and (*R*,*R*)-**2d**, but not the spectrum of (*R*,*R*)-**2a**, exhibited Cotton effects very similar in appearance to those induced for each complex of **1** with (*S*,*S*)-**4** (Figure 6, red lines). Also, with a change in temperature, we found a similarity to the corresponding complexes **1**·**4** (Figure S7, Supporting Information). These results showed that there was a dynamic equilibrium between two nonequivalent forms with (*M*)- or (*P*)-helicity, and a particular sense was favored over the other through the intramolecular transmission of local point chirality (*R*) to dynamic figure eight chirality (*M*)/(*P*) in **2**.

As mentioned above, the macrocycle (*R*,*R*)-**2a** was present as a mixture of two components in solution at room temperature. We separated them by HPLC (Figure S8, Supporting Information) and calculated the populations of the two components in the steady state with each area in the chromatogram (5.6% de). Each of the two separated fractions was immediately diluted and subjected to CD measurement. We found a simple pair of bisignated Cotton effects in each spectrum (Figure 8a,b). Although they were pseudo mirror-imaged, we tried to assign the first fraction to (*M*)-**2a** and the second fraction to (*P*)-**2a**, which were considered to be similar in appearance to those for complexes of **1a**·(*S*,*S*)-**4** and **1a**·(*R*,*R*)-**4**, respectively.

We monitored a change in the spectrum of (*M*)-**2a** with time at a constant temperature (Figure 8a,b) and found that the molar CDs continuously decreased to give a spectrum close to the steady state. On the basis of a change in the molar CD at 319 nm, which was observed in the initial state, we plotted a value of ln ($\Delta\varepsilon/\Delta\varepsilon_0$) versus time *t* and found a process that obeyed first-order kinetics [rate constant $k/s^{-1} = 1.2 \times 10^{-5}$ (293 K), 1.9×10^{-5} (298 K), and 3.4×10^{-5} (303 K)] (Figure 8c,d).[1f,h,24] On the basis of these data, the activation energy $\Delta G^{\ddagger}$ for the interconversion between two pseudo enantiomeric forms with (*M*)- or (*P*)-helicity was estimated to be 77 kJ mol^{-1}.

Complexation-Induced Inversion of a Helical Preference. We describe here two types of complexation-induced inversion of a helical preference (Scheme 1). In solution, figure eight macrocycles (*R*,*R*)-**2** with a chiral auxiliary on each amide nitrogen exist as a mixture of two pseudo enantiomeric forms with (*M*)- or (*P*)-helicity in dynamic equilibrium, and a particular form is favored through such intramolecular transmission. The induced helical preference was reversed in two ways upon 1:1 complexation with a ditopic guest, as follows.

First, we demonstrate the cases of (*R*,*R*)-**2a** and (*R*,*R*)-**2b** (Scheme 1a). To a set of solutions containing (*R*,*R*)-**2a** (1.7×10^{-4} M) in dichloromethane was added 1, 2, or 4 equiv of achiral guest **3**.[19] Each solution was left to stand for 2 days and then subjected to a CD measurement. In these spectra, we

DOI: 10.1021/acs.joc.5b01206
J. Org. Chem. 2015, 80, 7613−7625

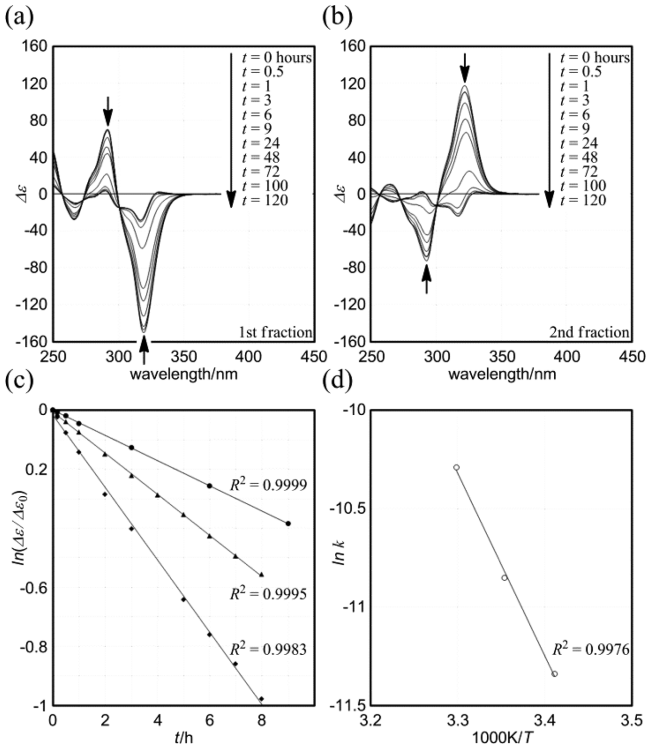

Figure 8. Continuous changes in the CD spectra of (a) (*M*)-**2a** (first fraction) and (b) (*P*)-**2a** (second fraction) with time *t* (0−120 h) measured in CH_2Cl_2 at 293 K. (c) Plots of ln ($\Delta\varepsilon/\Delta\varepsilon_0$) versus time *t* (0−9 h), $\Delta\varepsilon$ at 319 nm in the CD spectrum of (*M*)-**2a** (circle: 293 K; triangle: 298 K; and diamond: 303 K), and (b) plot of ln *k* versus 1/*T* (Arrhenius plot). The rate constants *k* were obtained in each observation at 293, 298, and 303 K.

found that the achiral guest induced the host to exhibit pseudo mirror-imaged Cotton effects (Figure 9a). This result showed

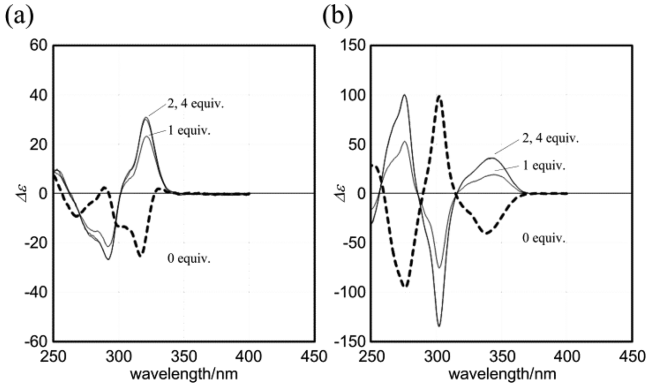

Figure 9. Continuous changes in the CD spectra of (a) (*R*,*R*)-**2a** (1.7 × 10^{-4} M) and (b) (*R*,*R*)-**2b** (1.1 × 10^{-4} M) upon 1:1 complexation with achiral ditopic guest **3** (solid lines) [0 (**2** only, dashed line), 1, 2, and 4 equiv]. All spectra were measured in CH_2Cl_2 at 293 K.

that the helical preferences in dynamic chirality both before and after complexation were determined by the single chiral source (*R*) associated with the host through intramolecular transmission because the achiral guest has no preference with respect to the direction of twisting. To examine a supramolecular transmission of chirality in the guest, we again used (*R*,*R*)-**4** and (*S*,*S*)-**4** instead of achiral **3** as an external chiral source (Figure S9a, Supporting Information). The addition of (*R*,*R*)-**4** in a manner similar to that described above led to an inversion of the preference, and the diastereomeric excess was enhanced in the complex (*R*,*R*)-**2a**·(*R*,*R*)-**4**, where chirality in the guest might be cooperatively transferred to dynamic chirality in collaboration with the internal chirality, if we considered that (*R*,*R*)-**4** induced host **1a** to exhibit a positive couplet. When we used (*S*,*S*)-**4**, pseudo mirror-imaged Cotton effects were also observed and were indistinguishable from those of a complex with **3**. This result showed that chirality in (*S*,*S*)-**4** did not exert its own preference at all, whereas the internal chirality was dominantly responsible for determining the preference even in a complexed state. We noted similarities in the changes upon the additions of a guest to a solution of (*R*,*R*)-**2b** (Figure 9b and Figure S9b, Supporting Information). We considered that (*R*,*R*)-**2a** and (*R*,*R*)-**2b** provided a nice framework to which the intramolecular transmission of chirality was effective in both uncomplexed and complexed states.[25]

Next, we discuss the cases of (*R*,*R*)-**2c** and (*R*,*R*)-**2d** (Scheme 1b). To a solution of (*R*,*R*)-**2c** in dichloromethane was gradually added up to four equiv of achiral guest **3**. In contrast to the above observations with (*R*,*R*)-**2a** or (*R*,*R*)-**2b**, the original preference did not reverse, but rather its strength was attenuated to be marginal (Figure S11, Supporting Information). This result indicated that the intramolecular transmission of chirality in a complexed state was mostly negated due to perturbation of the local chirality around the binding site. When we added (*R*,*R*)-**4** (Figure 10a), the helical

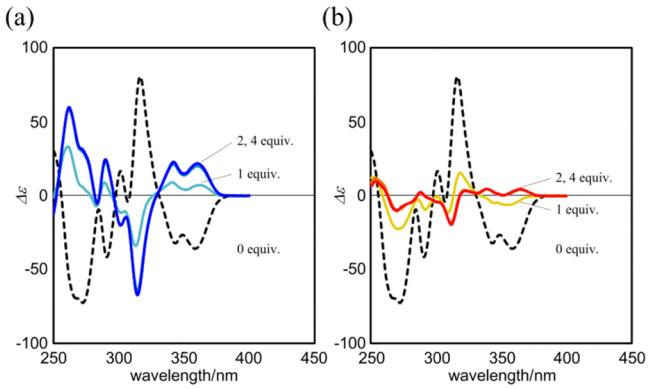

Figure 10. Continuous changes in the CD spectrum of (*R*,*R*)-**2c** (2.0 × 10^{-4} M) upon 1:1 complexation with a chiral ditopic guest (a) (*R*,*R*)-**4** (blue lines) or (b) (*S*,*S*)-**4** (red lines) [0 (**2** only, black dashed line), 1, 2, and 4 equiv]. All spectra were measured in CH_2Cl_2 at 293 K.

preference, which was induced through intramolecular transmission in the absence of any guest, was reversed to exhibit pseudo mirror-imaged Cotton effects, which were similar to the Cotton effects seen in the spectrum of **1c**·(*R*,*R*)-**4**. We considered that the supramolecular transmission of external chirality in the guest was essential for this inversion. Alternatively, addition of antipodal guest (*S*,*S*)-**4** led to marginal effects similar to those induced by achiral **3** (Figure 10b). Notably, in the spectral changes in the molar CD, both were similarly saturated when only two equiv of each guest were added.[19] Thus, we identified a rare system in which a helical preference was stereospecifically reversed upon complexation with an enantiomeric guest, although the diastereomeric excess in a complexed state was reduced to some extent.[26]

DOI: 10.1021/acs.joc.5b01206
J. Org. Chem. 2015, 80, 7613−7625

CONCLUSIONS

We have discussed dynamic figure eight chirality based on macrocycles that prefer nonplanar figure eight forms, which exhibited dynamic chiroptical properties, including not only a helical preference of the dynamic figure eight chirality [**1** and chiral guests (*R*,*R*)-**4**/(*S*,*S*)-**4**], but also two types of complexation-induced inversion of the helical preference through the controlled transmission of point chirality [(*R*,*R*)-**2** and achiral guest **3**, or chiral guests (*R*,*R*)-**4**/(*S*,*S*)-**4**]. We found a two-way intramolecular transmission of chirality of a single chiral source, which exhibited contrary preferences before and after complexation [(*R*,*R*)-**2a**/**b** and achiral guest **3**]. Alternatively, the internal chiral source was only effective in the absence of a guest (one-way intramolecular transmission) and was negated in a complexed state [(*R*,*R*)-**2c**/**d**]. This one-way transmission imparted an unprecedented stereospecific inversion to the macrocycle upon complexation with enantiomeric guests (*R*,*R*)-**4** and (*S*,*S*)-**4**. Although quantitative analyses and a detailed mechanism of the complexation-induced inversion are required to be further considered, we identified multifarious inversions of a helical preference through systematic modulation of the figure eight framework and showed the potential of dynamic figure eight molecules in addition to chiral molecules that are stereochemically stable.

EXPERIMENTAL SECTION

Preparation of 6a [X = *n*Bu, *n* = 0]. To a solution of **5a** (128 mg, 0.634 mmol) and **10**[9c] (600 mg, 1.62 mmol) in Et_3N/THF (6 mL/6 mL) were added $Pd(PPh_3)_4$ (147 mg, 0.127 mmol) and CuI (29 mg, 0.15 mmol) under an argon atmosphere, and the mixture was stirred at 55 °C for 15 h. The reaction mixture was diluted with chloroform, which was washed with water and brine. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on SiO_2 (1:1 dichloromethane/hexane) to give **6a** (436 mg) as a pale yellow amorphous solid in 100% yield. An analytical sample was obtained as a white amorphous solid by further purification with GPC (chloroform). **6a**: mp 50.0−52.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 7.69 (2H, dd, J = 1.6, 7.2 Hz), 7.54 (2H, dd, J = 1.6, 7.2 Hz), 7.47 (2H, dt, J = 1.6, 7.2 Hz), 7.43 (2H, dt, J = 1.6, 7.2 Hz), 7.25 (4H, d, J = 8.4 Hz), 7.08 (4H, d, J = 8.4 Hz), 3.68 (4H, t, J = 7.6 Hz), 1.53−1.46 (4H, m), 1.30 (4H, sext, J = 7.2 Hz), 0.89 (6H, t, J = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.4 (C(=O)CF_3), 143.3, 138.5, 132.2, 132.1, 130.3, 128.2, 128.1, 127.6, 124.3, 122.3, 116.3 (CF_3), 91.1, 90.7, 51.5, 28.9, 19.8, 13.6. IR (KBr): 3064, 2965, 2938, 2871, 2221, 1698, 1511 cm^{-1}. FD-LRMS m/z (%): 691.3 (2) $[M + 3]^+$, 690.3 (11) $[M + 2]^+$, 689.3 (45) $[M + 1]^+$, 688.3 (100) $[M]^+$. FD-HRMS (m/z):[31] $[M]^+$ calcd for $C_{40}H_{34}F_6N_2O_2$, 688.25245; found, 688.25129.

Preparation of 1a [X = *n*Bu, *n* = 0]. To an ice-cooled solution of **6a** (95 mg, 0.14 mmol) in THF (6 mL) were added 60% NaH in oil (62 mg, 1.5 mmol) and MeOH (6 mL), and the mixture was stirred at room temperature for 40 min. The reaction mixture was diluted with dichloromethane, which was washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on Al_2O_3 (1:9 ethyl acetate/dichloromethane) to give **8a** (53 mg) as a yellow solid in 77% yield, which was immediately subjected to the following reaction without further purification.

To a solution of **8a** (31 mg, 0.062 mmol) in toluene (21 mL) containing Et_3N (0.10 mL) was added terephthaloyl chloride (17 mg, 0.084 mmol), and the mixture was stirred at 85 °C for 45 min. The reaction mixture was diluted with dichloromethane, which was washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on SiO_2 (1:7 ethyl acetate/dichloromethane) to give **1a** (37 mg) as a white solid in 95% yield. An analytical sample was obtained as a white solid by further purification with GPC (chloroform). A single crystal was obtained by recrystallization from ethyl acetate with a diffused vapor of methanol. **1a**: mp 223.0−224.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 7.69−7.67 (2H, m), 7.42 (2H, dt, J = 1.6, 7.6 Hz), 7.39 (2H, dt, J = 1.6, 7.6 Hz), 7.34−7.31 (2H, m), 7.21 (4H, d, J = 8.4 Hz), 7.01 (4H, s), 6.78 (4H, d, J = 8.4 Hz), 4.00−3.93 (2H, m), 3.74−3.67 (2H, m), 1.57−1.49 (4H, m), 1.32 (4H, sext, J = 7.6 Hz), 0.87 (6H, t, J = 7.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): 169.6, 142.5, 142.5, 137.3, 132.6, 131.8, 130.8, 128.6, 127.8, 127.7, 127.6, 122.6, 122.1, 92.0, 91.3, 49.4, 29.7, 20.1, 13.7. IR (KBr): 3058, 2959, 2932, 2865, 2216, 1649, 1511 cm^{-1}. FD-LRMS m/z (%): 629.4 (3) $[M + 3]^+$, 628.4 (14) $[M + 2]^+$, 627.4 (52) $[M + 1]^+$, 626.4 (100) $[M]^+$. UV (CH_2Cl_2): λ_{max} (log ε) 313 (sh, 4.61), 295 (4.79) nm. FD-HRMS:[31] $[M]^+$ calcd for $C_{44}H_{38}N_2O_2$, 626.29333; found, 626.29336.

Preparation of 6b[9c] [X = *n*Bu, *n* = 1]. To a solution of **5b** (72 mg, 0.32 mmol) and **10** (310 mg, 0.836 mmol) in Et_3N/THF (3 mL/3 mL) were added $Pd(PPh_3)_4$ (76 mg, 0.066 mmol) and CuI (15 mg, 0.079 mmol) under an argon atmosphere, and the mixture was stirred at 55 °C for 17 h. The reaction mixture was diluted with dichloromethane, which was washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on SiO_2 (2:1 dichloromethane/hexane) to give **6b** (221 mg) as a yellow amorphous solid in 97% yield.

Preparation of 1b [X = *n*Bu, *n* = 1]. To an ice-cooled solution of **6b** (198 mg, 0.278 mmol) in THF (11 mL) were added 60% NaH in oil (113 mg, 2.82 mmol) and MeOH (11 mL), and the mixture was stirred at room temperature for 40 min. The reaction mixture was diluted with dichloromethane, which was washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on Al_2O_3 (dichloromethane) to give **8b** (144 mg) as a yellow solid in 99% yield, which was immediately subjected to the following reaction without further purification.

To a solution of **8b** (144 mg, 0.276 mmol) in toluene (90 mL) containing Et_3N (0.40 mL) was added terephthaloyl chloride (62 mg, 0.31 mmol), and the mixture was stirred at 85 °C for 30 min. After removal of the solvent by evaporation, the residue was dissolved in dichloromethane, which was washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on SiO_2, followed by Al_2O_3 (1:4 ethyl acetate/dichloromethane) to give **1b** (169 mg) as a white solid in 94% yield. An analytical sample was obtained as a white solid by further purification with GPC (chloroform). A single crystal was obtained by recrystallization from ethyl acetate with a diffused vapor of methanol. **1b**: mp 213.0−214.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 7.64−7.57 (2H × 2, m), 7.42 (4H, d, J = 8.8 Hz), 7.38−7.31 (2H × 2, m), 6.98 (4H, s), 6.78 (4H, br.d), 3.82 (4H, t, J = 7.2 Hz), 1.51 (4H, quin, J = 7.2 Hz), 1.32 (4H, sext, J = 7.2 Hz), 0.86 (6H, t, J = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0, 142.7, 137.4, 132.7, 132.6, 132.4, 128.4, 128.3, 128.2, 127.3, 125.4, 125.0, 121.7, 92.3, 91.6, 89.7, 49.1, 29.7, 20.1, 13.8. IR (KBr): 3059, 2954, 2930, 2868, 2213, 1653, 1601, 1510 cm^{-1}. FD-LRMS m/z (%): 653.4 (3) $[M + 3]^+$, 652.4 (14) $[M + 2]^+$, 651.4 (52) $[M + 1]^+$, 650.4 (100) $[M]^+$. UV (CH_2Cl_2): λ_{max} (log ε) 325 (sh, 4.22), 304 (4.89), 288 (4.78), 261 (4.59) nm. FD-HRMS (m/z):[31] $[M]^+$ calcd for $C_{46}H_{38}N_2O_2$, 650.29333; found, 650.29522.

Preparation of 6c [X = *n*Bu, *n* = 2]. To a solution of **5c** (39 mg, 0.16 mmol) and **10** (153 mg, 0.412 mmol) in Et_3N/THF (2 mL/2 mL) were added $Pd(PPh_3)_4$ (38 mg, 0.033 mmol) and CuI (8 mg, 0.04 mmol) under an argon atmosphere, and the mixture was stirred at 55 °C for 18 h. The reaction mixture was diluted with dichloromethane, which was washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on SiO_2 (3:2 dichloromethane/hexane) to give **6c** (113 mg) as a white amorphous solid in 98% yield. An analytical sample was obtained as a white amorphous solid by further purification with GPC (chloroform). **6c**: mp 51.0−53.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 7.62 (4H, d, J = 8.4 Hz), 7.59−7.56 (2H × 2, m), 7.40 (2H, dt, J = 1.2, 8.0 Hz), 7.35 (2H, dt, J = 1.2, 8.0 Hz), 7.12 (4H, d, J = 8.4 Hz), 3.67 (4H, t, J = 7.6 Hz), 1.53−1.45 (4H, m), 1.30 (4H, sext, J = 7.2 Hz), 0.89 (6H, t, J = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): 156.4 (C(=O)CF_3), 138.9, 134.7 (dec), 132.8, 132.6, 131.7, 129.9 (dec), 129.1, 128.4, 128.3, 127.9 (dec), 126.7, 124.6, 123.9, 116.3 (CF_3), 93.0, 89.4, 81.5, 78.0, 51.6, 28.8, 19.8, 13.6. IR (KBr): 3064, 2959,

DOI: 10.1021/acs.joc.5b01206
J. Org. Chem. 2015, 80, 7613−7625

2932, 2871, 2216, 1698, 1506 cm^{-1}. FD-LRMS m/z (%): 739.3 (2) $[M + 3]^+$, 738.3 (13) $[M + 2]^+$, 737.3 (50) $[M + 1]^+$, 736.3 (100) $[M]^+$. FD-HRMS (m/z):[31] $[M]^+$ calcd for $C_{44}H_{34}F_6N_2O_2$, 736.25245; found, 736.25221.

Preparation of 1c [X = *n*Bu, *n* = 2]. To an ice-cooled solution of **6c** (82 mg, 0.11 mmol) in THF (5 mL) were added 60% NaH in oil (47 mg, 1.2 mmol) and MeOH (5 mL), and the mixture was stirred at room temperature for 1 h. The reaction mixture was diluted with dichloromethane, which was washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on Al_2O_3 (dichloromethane) to give **8c** (57 mg) as a yellow solid in 93% yield, which was immediately subjected to the following reaction without further purification.

To a solution of **8c** (57 mg, 0.10 mmol) in toluene (35 mL) containing Et_3N (0.20 mL) was added terephthaloyl chloride (24 mg, 0.12 mmol), and the mixture was stirred at 85 °C for 30 min. After removal of the solvent by evaporation, the residue was dissolved in dichloromethane, which was washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on SiO_2 (1:4 ethyl acetate/dichloromethane) to give **1c** (52 mg) as an off-white solid in 73% yield. An analytical sample was obtained as a white solid by further purification with GPC (chloroform). A single crystal was obtained by recrystallization from ethyl acetate with a diffused vapor of methanol. **1c**: mp 224.0−225.0 °C. ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 7.59−7.56 (2H × 2, m), 7.42 (4H, d, J = 8.4 Hz), 7.38 (2H, dt, J = 1.6, 7.6 Hz), 7.31 (2H, dt, J = 1.6, 7.6 Hz), 7.03 (4H, s), 6.84 (4H, d, J = 8.4 Hz), 3.88 (4H, t, J = 7.6 Hz), 1.56−1.48 (4H, m), 1.31 (4H, sext, J = 7.2 Hz), 0.87 (6H, t, J = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): 169.4, 143.3, 137.3, 133.1, 132.3, 131.8, 129.0, 128.2, 128.1, 127.8, 126.4, 124.3, 121.3, 93.2, 88.7, 81.0, 77.4, 49.5, 29.7, 20.1, 13.8. IR (KBr): 3058, 2954, 2932, 2871, 2211, 1660, 1517 cm^{-1}. FD-LRMS m/z (%): 677.3 (3) $[M + 3]^+$, 676.3 (15) $[M + 2]^+$, 675.3 (54) $[M + 1]^+$, 674.3 (100) $[M]^+$. UV (CH_2Cl_2): λ_{max} (log ε) 367 (sh, 3.90), 344 (sh, 4.40), 317 (4.81), 303 (4.79), 285 (4.71), 258 (4.83) nm. Elemental Anal. Calcd (%) for $C_{48}H_{38}N_2O_2$: C, 85.43; H, 5.68; N, 4.15. Found: C, 85.12; H, 5.60; N, 4.14.

Preparation of (*R*,*R*)-7a [X = (*R*)-CHMe(cHex), *n* = 0]. To a solution of **5a** (230 mg, 1.14 mmol) and (*R*)-**11**[9c] (1.21 g, 2.85 mmol) in Et_3N/THF (12 mL/12 mL) were added $Pd(PPh_3)_4$ (266 mg, 0.231 mmol) and CuI (52 mg, 0.27 mmol) under an argon atmosphere, and the mixture was stirred at 55 °C for 12 h. The reaction mixture was diluted with chloroform, which was washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on SiO_2 (1:1 dichloromethane/hexane) to give (*R*,*R*)-**7a** (893 mg) as a yellow amorphous solid in 98% yield. An analytical sample was obtained as a white amorphous solid by further purification with GPC (chloroform). (*R*,*R*)-**7a**: mp 91.5−93.0 °C. $[\alpha]_D^{23}$ −37.3 (c 1.0 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 7.70 (2H, dd, J = 1.2, 7.6 Hz), 7.54 (2H, br.d), 7.49−7.41 (2H × 2, br.m), 7.24 (4H, br.d), 7.05 (4H, br.d), 4.37 (2H, dq, J = 7.2, 10 Hz), 1.93 (2H, br.d), 1.80−1.59 (8H, br.m), 1.43−0.87 (12H, br.m), 1.06 (6H, d, J = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.8 (C(=O)CF_3), 143.2, 135.5, 132.1, 131.7, 131.5, 130.6, 130.3, 129.2, 128.1, 127.6, 124.5, 122.3, 116.4 (CF_3), 91.2, 90.8, 59.8, 40.2, 30.6, 29.7, 26.1, 25.9, 25.7, 16.3. IR (KBr): 3064, 2932, 2849, 2221, 1693, 1511 cm^{-1}. FD-LRMS m/z (%): 799.4 (3) $[M + 3]^+$, 798.4 (15) $[M + 2]^+$, 797.4 (56) $[M + 1]^+$, 796.4 (100) $[M]^+$. Elemental Anal. Calcd (%) for $C_{48}H_{46}F_6N_2O_2$: C, 72.35; H, 5.82; N, 3.52. Found: C, 72.18; H, 5.79; N, 3.44.

Preparation of (*R*,*R*)-2a [X = (*R*)−CHMe(cHex), *n* = 0]. To an ice-cooled solution of (*R*,*R*)-**7a** (771 mg, 0.967 mmol) in THF (20 mL) were added 60% NaH in oil (1.55 g, 38.7 mmol) and MeOH (20 mL), and the mixture was stirred at room temperature for 2 h. The reaction mixture was diluted with dichloromethane, which was washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on Al_2O_3 (1:4 dichloromethane/hexane) to give (*R*,*R*)-**9a** (390 mg) as a yellow solid in 67% yield, which was immediately subjected to the following reaction without further purification.

To a solution of (*R*,*R*)-**9a** (390 mg, 0.645 mmol) in toluene (220 mL) containing Et_3N (1.0 mL) was added terephthaloyl chloride (137 mg, 0.676 mmol), and the mixture was stirred at 85−100 °C for 45 min. To the reaction mixture were added several portions of terephthaloyl chloride [(70 mg, 0.34 mmol), (140 mg, 0.688 mmol), (269 mg, 1.32 mmol), and (338 mg, 1.66 mmol)] every 30 min period at 100 °C. The reaction mixture was diluted with dichloromethane, which was washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on SiO_2, followed by Al_2O_3 (1:9 ethyl acetate/dichloromethane) to give (*R*,*R*)-**2a** (412 mg) as a pale yellow solid in 87% yield. An analytical sample was obtained as a solid by further purification with GPC (chloroform) and preparative TLC (1:7 ethyl acetate/dichloromethane). (*R*,*R*)-**2a**: mp 169.0−170.5 °C. $[\alpha]_D^{23}$ −109 (c 1.0 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, TMS, 296 K): δ 7.71−7.67 (2H, m), 7.45−7.34 (2H × 2, m), 7.34−7.29 (2H, m), 7.28 (2H, br.m), 7.16 (2H, br.m), 6.97 (4H, s), 6.96 (2H, br.m), 6.58 (2H, br.m), 4.54−4.25 (2H, m), 2.16−1.96 (2H, br.m), 1.85−1.39 (10H, br.m), 1.37−0.89 (10H, br.m), [1.17, 1.05] (6H, d, J = 6.8, 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, 295 K): δ [170.6, 170.4, 170.2, 169.9], 142.6, [140.9, 140.6, 140.6, 140.2], [138.4, 138.1, 137.9, 137.5], 132.5, 132.5, 131.9 (br), 130.9 (br), 130.8, 130.8, 129.6 (br), 128.6, 128.2 (br), 127.6, 127.6, 127.3, 127.2, 126.9, [122.6, 122.6, 122.5, 122.5], [122.3, 122.2, 122.2, 122.1], [92.2, 92.1, 92.0, 91.9], [91.5, 91.3, 91.3, 91.2], [58.5, 58.1, 57.9 (br)], [42.0, 41.7, 40.8, 40.5], [30.9, 30.9, 30.6, 30.5, 30.4, 30.3, 30.1, 29.6], 26.2, 26.0, 25.9, 25.9, [17.0, 16.9, 16.6 (br)] [split into four resonances]. IR (KBr): 3058, 2926, 2849, 2216, 1649, 151 cm^{-1}. FD-LRMS m/z (%): 737.5 (4) $[M + 3]^+$, 736.5 (18) $[M + 2]^+$, 735.5 (61) $[M + 1]^+$, 734.4 (100) $[M]^+$. UV (CH_2Cl_2): λ_{max} (log ε) 315 (sh, 4.59), 295 (4.77) nm. CD (CH_2Cl_2): λ 329 ($\Delta\varepsilon$ +5), 316 (−16), 289 (−1), 299 (−12), 266 (−7) nm. FD-HRMS (m/z):[31] $[M]^+$ calcd for $C_{52}H_{50}N_2O_2$: 734.38723; found, 734.38785.

Preparation of (*R*,*R*)-7b[9c] [X = (*R*)-CHMe(cHex), *n* = 1]. To a solution of **5b** (70 mg, 0.31 mmol) and (*R*)-**11** (347 mg, 0.816 mmol) in Et_3N/THF (3 mL/3 mL) were added $Pd(PPh_3)_4$ (73 mg, 0.063 mmol) and CuI (16 mg, 0.084 mmol) under an argon atmosphere, and the mixture was stirred at 55 °C for 17 h. The reaction mixture was diluted with dichloromethane, which was washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on SiO_2 (2:1 dichloromethane/hexane) to give (*R*,*R*)-**7b** (251 mg) as a yellow amorphous solid in 99% yield.

Preparation of (*R*,*R*)-2b [X = (*R*)-CHMe(cHex), *n* = 1]. To an ice-cooled solution of (*R*,*R*)-**7b** (105 mg, 0.128 mmol) in THF (5 mL) were added 60% NaH in oil (206 mg, 5.15 mmol) and MeOH (5 mL), and the mixture was stirred at room temperature for 2 h. The reaction mixture was diluted with dichloromethane, which was washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on Al_2O_3 (dichloromethane) to give (*R*,*R*)-**9b** (69 mg) as a yellow amorphous solid in 86% yield, which was immediately subjected to the following reaction without further purification.

To a solution of (*R*,*R*)-**9b** (69 mg, 0.11 mmol) in toluene (37 mL) containing Et_3N (0.20 mL) was added terephthaloyl chloride (25 mg, 0.12 mmol), and the mixture was stirred at 100 °C for 30 min. To the reaction mixture were added several portions of terephthaloyl chloride [(24 mg, 0.12 mmol), (25 mg, 0.12 mmol), (25 mg, 0.12 mmol), and (25 mg, 0.12 mmol)] every 30 min period at 100 °C. After removal of the solvent by evaporation, the residue was dissolved in dichloromethane, which was washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on Al_2O_3, followed by SiO_2 (1:9 ethyl acetate/dichloromethane) to give (*R*,*R*)-**2b** (75 mg) as a pale yellow solid in 90% yield. An analytical sample was obtained as a white solid by further purification with GPC (chloroform). (*R*,*R*)-**2b**: mp 293.0−295.0 °C (dec). $[\alpha]_D^{25}$ −328 (c 0.11 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, TMS, 303 K): δ 7.64−7.62 (2H, m), 7.60−7.58 (2H, m), 7.41 (4H, br.d), 7.38−7.31 (2H × 2, m), 6.93 (4H, s), 6.76 (4H, br.d), 4.53−4.46 (2H, m), 2.09 (2H, br.d), 1.84−1.61 (8H, br.m), 1.36−0.91 (12H, br.m), 1.08 (6H, J = 6.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.5, 140.8, 137.9, 132.6, 132.4, 132.3 (br), 128.3, 128.2, 127.1, 125.5, 125.1, 121.8, 92.4, 91.6,

DOI: 10.1021/acs.joc.5b01206
J. Org. Chem. 2015, 80, 7613−7625

89.8, 57.6, 41.3, 30.8, 30.2, 26.2, 26.0, 26.0, 16.8. IR (KBr): 3052, 2929, 2850, 2214, 1650, 1510 cm^{-1}. FD-LRMS m/z (%): 761.3 (5) $[M + 3]^+$, 760.3 (20) $[M + 2]^+$, 759.3 (61) $[M + 1]^+$, 758.3 (100) $[M]^+$. UV (CH_2Cl_2): λ_{max} (log ε) 330 (sh, 4.41), 305 (4.97), 288 (4.85), 278 (sh, 4.76), 261 (4.67) nm. CD (CH_2Cl_2): λ 339 ($\Delta\varepsilon$ −41), 302 (+103), 277 (−99) nm. Elemental Anal. Calcd (%) for $C_{54}H_{50}N_2O_2$: C, 85.45; H, 6.64; N, 3.69. Found: C, 85.38; H, 6.58; N, 3.69.

Preparation of (*R*,*R*)-7c [X = (*R*)-CHMe(cHex), *n* = 2]. To a solution of **5c** (41 mg, 0.16 mmol) and (*R*)-**11** (183 mg, 0.431 mmol) in Et_3N/THF (2 mL/2 mL) were added $Pd(PPh_3)_4$ (39 mg, 0.034 mmol) and CuI (10 mg, 0.053 mmol) under an argon atmosphere, and the mixture was stirred at 55 °C for 20 h. The reaction mixture was diluted with dichloromethane, which was washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on SiO_2 (3:2 dichloromethane/hexane) to give (*R*,*R*)-**7c** (133 mg) as a white amorphous solid in 96% yield. An analytical sample was obtained as a white amorphous solid by further purification with GPC (chloroform). (*R*,*R*)-**7c**: mp 89.5−91.0 °C. $[\alpha]_D^{22}$ −106 (c 1.0 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 7.64 (2H, br.d), 7.60−7.55 (2H, br.d + 2H × 2, m), 7.40 (2H, dt, J = 1.6, 7.6 Hz), 7.35 (2H, dt, J = 1.6, 7.6 Hz), 7.10−7.07 (4H, br.m), 4.36 (2H, dq, J = 6.8, 10 Hz), 1.92 (2H, br.d), 1.81−1.53 (8H, br.m), 1.44−0.83 (12H, br.m), 1.01 (6H, d, J = 6.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.8 (C(=O)CF_3), 135.9, 132.5 (br), 132.0, 131.6, 130.7, 129.3, 129.1, 128.5, 126.8, 124.7, 124.0, 116.4 (CF_3), 93.1, 89.6, 81.6, 78.1, 59.7, 40.2, 30.6, 29.7, 26.1, 25.9, 25.7, 16.3. IR (KBr): 3064, 2981, 2932, 2855, 2216, 1693, 1511 cm^{-1}. FD-LRMS m/z (%): 847.4 (4) $[M + 3]^+$, 846.4 (19) $[M + 2]^+$, 845.4 (59) $[M + 1]^+$, 844.4 (100) $[M]^+$. FD-HRMS (m/z):[31] $[M]^+$ calcd for $C_{52}H_{46}F_6N_2O_2$: 844.34635; found, 844.34423.

Preparation of (*R*,*R*)-2c [X = (*R*)-CHMe(cHex), *n* = 2]. To an ice-cooled solution of (*R*,*R*)-**7c** (94 mg, 0.11 mmol) in THF (5 mL) were added 60% NaH in oil (179 mg, 4.46 mmol) and MeOH (5 mL), and the mixture was stirred at room temperature for 1 h. To the reaction mixture were added two portions of 60% NaH in oil [(178 mg, 4.45 mmol) and (178 mg, 4.45 mmol)] every 1 h. The reaction mixture was diluted with dichloromethane, which was washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on Al_2O_3 (dichloromethane) to give (*R*,*R*)-**9c** (61 mg) as a yellow amorphous solid in 84% yield, which was immediately subjected to the following reaction without further purification.

To a solution of (*R*,*R*)-**9c** (61 mg, 0.093 mmol) in toluene (31 mL) containing Et_3N (0.20 mL) was added terephthaloyl chloride (21 mg, 0.10 mmol), and the mixture was stirred at 100 °C for 30 min. To the reaction mixture were added several portions of terephthaloyl chloride [(21 mg, 0.10 mmol), (20 mg, 0.099 mmol), (22 mg, 0.11 mmol), and (23 mg, 0.11 mmol)] every 30 min period at 100 °C. After removal of the solvent by evaporation, the residue was dissolved in dichloromethane, which was washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on Al_2O_3, followed by SiO_2 (1:9 ethyl acetate/dichloromethane) to give (*R*,*R*)-**2c** (48 mg) as a pale yellow solid in 66% yield. An analytical sample was obtained as a white solid by further purification with GPC (chloroform). (*R*,*R*)-**2c**: mp 196.0−198.0 °C. $[\alpha]_D^{23}$ −443 (c 1.0 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 7.60−7.56 (2H × 2, m), 7.40 (4H, br.s), 7.38 (2H, dt, J = 1.6, 7.6 Hz), 7.32 (2H, dt, J = 1.6, 7.6 Hz), 6.98 (4H, s), 6.81 (4H, br.s), 4.47 (2H, br.dq), 2.09 (2H, br.d), 1.83−1.58 (10H, br.m), 1.31−0.91 (10H, br.m), 1.10 (6H, d, J = 6.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 141.9, 137.7, 132.9, 132.0, 131.8, 129.0, 128.2, 127.6, 126.6, 124.2, 121.6, 93.3, 88.8, 81.0, 77.5, 58.6, 41.7, 30.7, 30.4, 26.2, 26.1, 26.0, 16.7. IR (KBr): 3058, 2926, 2849, 2211, 1654, 1511 cm^{-1}. FD-LRMS m/z (%): 785.5 (5) $[M + 3]^+$, 784.5 (21) $[M + 2]^+$, 783.5 (64) $[M + 1]^+$, 782.5 (100) $[M]^+$. UV (CH_2Cl_2): λ_{max} (log ε) 366 (sh, 3.90), 343 (sh, 4.37), 316 (4.77), 302 (4.77), 286 (4.70), 268 (sh, 4.73), 257 (4.84) nm. CD (CH_2Cl_2): λ 359 ($\Delta\varepsilon$ −35), 349 (−27), 343 (−32), 316 (+81), 307 (−3), 301 (+17), 291 (−41), 284 (−10), 272 (−72), 265 (sh, −67) nm. FD-HRMS (m/z):[31] $[M]^+$ calcd for $C_{56}H_{50}N_2O_2$: 782.38723; found, 782.38696.

Preparation of 18.[27] To a solution of **16**[27] (5.97 g, 15.8 mmol) in acetone (150 mL) were added NBS (3.22 g, 18.1 mmol) and $AgNO_3$ (216 mg, 1.26 mmol),[28] and the mixture was stirred in the dark for 140 min at room temperature. The reaction mixture was quenched with water, diluted with hexane, and then washed with water and brine. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on SiO_2 (hexane) to give **17**[29] (5.70 g) as a yellow oil in 100% yield, which was immediately subjected to the following reaction without further purification.

To a solution of **17** (2.69 g, 7.44 mmol), $Pd(PPh_3)_4$ (436 mg, 0.377 mmol), and CuI (109 mg, 0.570 mmol) in Et_3N (50 mL) was added trimethylsilylacetylene (1.46 g, 14.9 mmol) under an argon atmosphere,[30] and the mixture was stirred at room temperature for 66 h. After removal of the solvent by evaporation, the residue was dissolved in hexane, which was washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on SiO_2 (hexane) to give **18** (1.97 g) as a yellow oil in 70% yield.

Preparation of 19c (*n* = 2). To a solution of **21**[27b] (80 mg, 0.284 mmol) and **17** (102 mg, 0.283 mmol) in Et_3N were added $Pd(PPh_3)_4$ (21 mg, 0.018 mmol) and CuI (10 mg, 0.053 mmol) at room temperature under an argon atmosphere, and the mixture was stirred for 3 h, diluted with hexane, and then washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on SiO_2 (hexane) to give **19c** (144 mg) as a white solid in 90% yield. **19c**: mp 101.5−103.0 °C. ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 7.50−7.45 (2H × 2, m), 7.31−7.24 (2H × 2, m), 1.17 (21H, s). ^{13}C NMR (100 MHz, $CDCl_3$): 132.6, 132.3, 128.5, 127.9, 127.2, 125.0, 104.6, 96.0, 81.0, 78.0, 18.7, 11.3. IR (KBr): 3064, 2941, 2890, 2863, 2157, 1473, 751 cm^{-1}. FD-LRMS m/z (%): 564.3 (22) $[M + 2]^+$, 563.3 (56) $[M + 1]^+$, 562.3 (100) $[M]^+$. Elemental Anal. Calcd (%) for $C_{38}H_{50}Si_2$: C, 81.07; H, 8.95. Found: C, 80.91; H, 8.94.

Preparation of 1d [X = *n*Bu, *n* = 3]. To a solution of $Pd(PPh_3)_4$ (347 mg, 0.300 mmol), CuI (65 mg, 0.34 mmol), and K_2CO_3 (745 mg, 5.39 mmol) in Et_3N/THF/MeOH (270 mL/54 mL/54 mL) was added a solution of **18** (1.02 g, 2.69 mmol) and **17** (1.47 g, 4.07 mmol) in Et_3N (50 mL) via a syringe pump over a period of 3 h under an argon atmosphere, and the mixture was stirred at 50 °C for 6 h. After removal of a solid by filtration through a Celite pad, the filtrate was diluted with hexane and then washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on SiO_2 (hexane) to recover **18** (0.49 g) and to give a mixture (1.39 g) containing **19c** (n = 2), **19d** (n = 3), and tetrayne (n = 4) as a brown oil [Relative Intensity (FD-LRMS): **19c** (n = 2, 100%), **19d** (n = 3, 46%), and tetrayne (n = 4, 8.7%) (Figure S13, Supporting Information)], which was immediately subjected to the following reaction without further purification.

To a solution of the above mixture (1.39 g) in THF (117 mL) was added a 1 M solution (5.1 mL, 5.1 mmol) of TBAF in THF, and the reaction mixture was stirred at room temperature for 20 min. After removal of the solvent by evaporation, the residue was dissolved in ethyl acetate and then washed with brine. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on SiO_2 (1:4 dichloromethane/hexane) to give a mixture (506 mg) containing **5c** (n = 2) and **5d** (n = 3) as a yellow solid, which was subjected to the following reactions without further purification.

To a solution of a mixture (221 mg) of **5c** (n = 2), **5d** (n = 3), and **10** (832 mg, 2.24 mmol) in Et_3N/THF (8 mL/8 mL) under an argon atmosphere were added $Pd(PPh_3)_4$ (199 mg, 0.172 mmol) and CuI (38 mg, 0.20 mmol), and the reaction mixture was stirred at 55 °C for 12 h, diluted with dichloromethane, and then washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on SiO_2 (3:2 dichloromethane/hexane) to give a mixture (632 mg) containing **6c** (n = 2) and **6d** (n = 3) as a pale yellow amorphous solid, which was subjected to the following reaction without further purification.

To an ice-cooled solution of a mixture (150 mg) of **6c** (n = 2) and **6d** (n = 3) in THF (8 mL) were added 60% NaH in oil (82 mg, 2.1 mmol) and MeOH (8 mL), and the reaction mixture was stirred at

DOI: 10.1021/acs.joc.5b01206
J. Org. Chem. 2015, 80, 7613−7625

room temperature for 30 min, diluted with dichloromethane, and then washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on Al_2O_3 (dichloromethane) to give a mixture (103 mg) containing **8c** (n = 2) and **8d** (n = 3) as a yellow solid, which was immediately subjected to the following reaction without further purification.

To a solution of the above mixture (103 mg) containing **8c** (n = 2) and **8d** (n = 3) in toluene (70 mL) and Et_3N (0.52 mL) was added terephthaloyl chloride (42 mg, 0.21 mmol), and the reaction mixture was stirred at 85 °C for 60 min, diluted with dichloromethane, and then washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on SiO_2 (1:4 ethyl acetate/dichloromethane) to give a mixture (116 mg) of **1c** (n = 2) and **1d** (n = 3) as a white solid. Further purification with HPLC gave pure **1d** (n = 3) (28 mg) as a white solid. A single crystal was obtained by recrystallization from chloroform. **1d**: mp 214.0−216.0 °C (dec). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 7.56 (2H × 2, dd, J = 1.2, 7.6), 7.46 (4H, d, J = 8.8 Hz), 7.39 (2H, dt, J = 1.2, 7.6 Hz), 7.31 (2H, dt, J = 1.2, 7.6 Hz), 7.08 (4H, s), 7.00 (4H, br.d), 3.93 (4H, br.s), 1.56 (4H, quin, J = 7.2 Hz), 1.33 (4H, sext, J = 7.2 Hz), 0.88 (6H, t, J = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.3, 143.8, 136.6, 133.1, 132.5, 131.6, 129.5, 128.6, 128.2, 127.7, 127.4, 123.6, 121.2, 93.8, 88.7, 78.1, 77.4, 67.1, 50.1, 29.7, 20.1, 13.8. IR (KBr): 3058, 2959, 2932, 2871, 2216, 2190, 2173, 1649, 1511 cm^{-1}. FD-LRMS m/z (%): 701.4 (4) $[M + 3]^+$, 700.4 (17) $[M + 2]^+$, 699.4 (57) $[M + 1]^+$, 698.4 (100) $[M]^+$. UV (CH_2Cl_2): λ_{max} (log ε) 394 (4.00), 361 (4.29), 344 (4.49), 334 (4.52), 316 (4.75), 304 (4.80), 270 (5.02) nm. FD-HRMS (m/z):[31] $[M]^+$ calcd for $C_{50}H_{38}N_2O_2$: 698.29333; found, 698.29556.

Preparation of (*R*,*R*)-2d [X = (*R*)-CHMe(cHex), *n* = 3]. To a solution of a mixture (214 mg) of **5c** (n = 2), **5d** (n = 3), and (*R*)-**11** (916 mg, 2.16 mmol) in Et_3N/THF (8 mL/8 mL) under an argon atmosphere were added $Pd(PPh_3)_4$ (192 mg, 0.166 mmol) and CuI (32 mg, 0.17 mmol), and the reaction mixture was stirred at 55 °C for 12 h, diluted with dichloromethane, and then washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on SiO_2 (3:2 dichloromethane/hexane) to give a mixture (661 mg) containing (*R*,*R*)-**7c** (n = 2) and (*R*,*R*)-**7d** (n = 3) as a pale yellow amorphous solid, which was subjected to the following reaction without further purification.

To an ice-cooled solution of a mixture (285 mg) of (*R*,*R*)-**7c** (n = 2) and (*R*,*R*)-**7d** (n = 3) in THF (13 mL) were added 60% NaH in oil (529 mg, 13.2 mmol) and MeOH (13 mL), and the reaction mixture was stirred at room temperature for 60 min, diluted with dichloromethane, and then washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on Al_2O_3 (1:1 dichloromethane/hexane) to give a mixture (190 mg) containing (*R*,*R*)-**9c** (n = 2) and (*R*,*R*)-**9d** (n = 3) as a yellow solid, which was immediately subjected to the following reaction without further purification.

To a solution of the above mixture (190 mg) containing (*R*,*R*)-**9c** (n = 2) and (*R*,*R*)-**9d** (n = 3) in toluene (96 mL) and Et_3N (0.80 mL) was added terephthaloyl chloride (65 mg, 0.32 mmol), and the reaction mixture was stirred at 100 °C for 10 min. To the reaction mixture were added several portions of terephthaloyl chloride [(98 mg, 0.48 mmol), (101 mg, 0.498 mmol), and (101 mg, 0.498 mmol)] every 1 h period at 100 °C. The reaction mixture was diluted with dichloromethane and then washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on SiO_2, followed by Al_2O_3 (1:9 ethyl acetate/dichloromethane), to give a mixture (139 mg) of (*R*,*R*)-**2c** (n = 2) and (*R*,*R*)-**2d** (n = 3) as a white solid. A further purification with HPLC gave pure (*R*,*R*)-**2d** (n = 3) (30 mg) as a white solid. (*R*,*R*)-**2d**: mp 178.0−180.0 °C (dec). $[\alpha]_D^{22}$ −310 (c 1.0 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 7.58−7.55 (2H × 2, m), 7.44 (4H, br.s), 7.39 (2H, dt, J = 1.2, 7.6 Hz), 7.31 (2H, dt, J = 1.2, 7.6 Hz), 7.05 (4H, s), 7.00 (4H, br.s), 4.43 (2H, br.s), 2.06 (2H, br.d), 1.84−1.70 (8H, br.m), 1.70−1.61 (2H, br.m), 1.33−1.07 (8H, br.m), 1.18 (6H, br.d), 1.05−0.90 (2H, br.m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.6, 142.8, 137.1, 133.0, 132.2, 131.6, 129.5, 128.5, 128.2, 127.4, 123.5, 121.5, 93.8, 88.7, 78.1, 77.3, 67.1, 60.2, 41.8, 30.6, 26.3, 26.1, 26.0, 16.7. IR (KBr): 3064, 2926, 2855, 2216, 2190, 2174, 1649, 1511 cm^{-1}. FD-LRMS m/z (%): 809.5 (5) $[M + 3]^+$, 808.5 (23) $[M + 2]^+$, 807.5 (66) $[M + 1]^+$, 806.5 (100) $[M]^+$. UV (CH_2Cl_2): λ_{max} (log ε) 394 (3.98), 361 (4.26), 344 (4.44), 335 (4.48), 316 (4.72), 304 (4.76), 269 (5.00), 256 (sh, 4.83) nm. CD (CH_2Cl_2): λ 391 ($\Delta\varepsilon$ −12), 387 (−11), 384 (−12), 370 (−6), 355 (−18), 346 (+9), 340 (+0), 335 (+10), 329 (−7), 315 (+41), 310 (+19), 305 (+44), 278 (−104), 253 (+42) nm. FD-HRMS (m/z):[31] $[M]^+$ calcd for $C_{58}H_{50}N_2O_2$: 806.38723; found, 806.38857.

Preparation of (*R*,*R*)-12a (*n* = 0). To a solution of **5a** (114 mg, 0.564 mmol) and (*R*)-**20**[9g] (615 mg, 1.42 mmol) in Et_3N/THF (8 mL/8 mL) were added $Pd(PPh_3)_4$ (135 mg, 0.117 mmol) and CuI (25 mg, 0.13 mmol) under an argon atmosphere, and the mixture was stirred at 55 °C for 15 h. The reaction mixture was diluted with dichloromethane and then washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on SiO_2 (1:19 ethyl acetate/dichloromethane) to give (*R*,*R*)-**12a** (426 mg) as a reddish solid in 93% yield. An analytical sample was obtained as a white solid by further purification with GPC (chloroform). (*R*,*R*)-**12a**: mp 161.0−162.0 °C. $[\alpha]_D^{22}$ −113 (c 1.0 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 7.62−7.59 (2H, m), 7.51−7.49 (2H, m), 7.40 (2H, dt, J = 1.6, 7.6 Hz), 7.36 (2H, dt, J = 1.6, 7.6 Hz), 7.22 (4H, br.d), 7.18−7.09 (6H, br.m), 7.01 (4H, d, J = 8.0 Hz), 6.87 (4H, d, J = 8.0 Hz), 4.43 (2H, br.s), 2.12 (2H, br.d), 1.86−1.57 (10H, br.m), 1.35−0.91 (10H, br.m), 1.15 (6H, d, J = 6.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.8, 143.0, 141.7, 137.1, 132.0, 131.6, 130.3, 129.3, 129.2, 128.3, 127.8, 127.7, 127.5, 122.4, 121.8, 91.6, 89.9, 59.3, 41.4, 30.8, 30.4, 26.3, 26.1, 26.0, 16.8. IR (KBr): 3064, 2976, 2932, 2849, 2216, 1644, 1506 cm^{-1}. FD-LRMS m/z (%): 815.5 (6) $[M + 3]^+$, 814.5 (22) $[M + 2]^+$, 813.5 (66) $[M + 1]^+$, 812.5 (100) $[M]^+$. UV (CH_2Cl_2): λ_{max} (log ε) 313 (4.70), 303 (4.69), 266 (4.46) nm. CD (CH_2Cl_2): λ 313 ($\Delta\varepsilon$ −5.4), 308 (−4.7), 299 (−6.1), 282 (−4.8), 274 (−5.4) nm. FD-HRMS (m/z):[31] $[M]^+$ calcd for $C_{58}H_{56}N_2O_2$: 812.43418; found, 812.43454.

Preparation of (*R*,*R*)-12b[9c] (*n* = 1). To a solution of **5b** (97 mg, 0.43 mmol) and (*R*)-**20** (467 mg, 1.08 mmol) in Et_3N/THF (5 mL/5 mL) were added $Pd(PPh_3)_4$ (105 mg, 0.0910 mmol) and CuI (18 mg, 0.095 mmol) under an argon atmosphere, and the mixture was stirred at 55 °C for 15 h. The reaction mixture was diluted with dichloromethane and then washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on SiO_2 (1:24 ethyl acetate/dichloromethane) to give (*R*,*R*)-**12b** (327 mg) as a yellow amorphous solid in 91% yield.

Preparation of (*R*,*R*)-12c (*n* = 2). To a solution of **5c** (22 mg, 0.088 mmol) and (*R*)-**20** (98 mg, 0.23 mmol) in Et_3N/THF (1 mL/1 mL) were added $Pd(PPh_3)_4$ (22 mg, 0.019 mmol) and CuI (4 mg, 0.02 mmol) under an argon atmosphere, and the mixture was stirred at 55 °C for 20 h. The reaction mixture was diluted with dichloromethane and then washed with water. The organic layer was dried over $MgSO_4$, concentrated, and then purified by column chromatography on SiO_2 (1:24 ethyl acetate/dichloromethane) to give (*R*,*R*)-**12c** (52 mg) as a reddish solid in 68% yield. An analytical sample was obtained as a white solid by further purification with GPC (chloroform), followed by preparative TLC. (*R*,*R*)-**12c**: mp 156.0−157.0 °C. $[\alpha]_D^{23}$ −213 (c 1.0 in $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, TMS): δ 7.55−7.51 (2H × 2, m), 7.40 (4H, d, J = 8.4 Hz), 7.37 (2H, dt, J = 1.6, 7.6 Hz), 7.33 (2H, dt, J = 1.6, 7.6 Hz), 7.23−7.21 (4H, br.m), 7.16−7.07 (6H, br.m), 6.92 (4H, d, J = 8.4 Hz), 4.43 (2H, br.s), 2.12 (2H, br.d), 1.84−1.57 (10H, br.m), 1.33−0.91 (10H, br.m), 1.10 (6H, d, J = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.8, 142.1, 137.0, 132.6, 132.3, 131.5, 129.4, 129.3, 129.1, 128.3, 128.2, 127.7, 127.0, 124.5, 121.3, 93.7, 88.8, 81.5, 77.9, 59.2, 41.5, 30.8, 30.5, 26.3, 26.1, 26.0, 16.7. IR (KBr): 3058, 2928, 2849, 2213, 1650, 1510 cm^{-1}. FD-LRMS m/z (%): 863.5 (6) $[M + 3]^+$, 862.5 (26) $[M + 2]^+$, 861.5 (70) $[M + 1]^+$, 860.5 (100) $[M]^+$. UV (CH_2Cl_2): λ_{max} (log ε) 371 (sh, 3.97), 343 (sh, 4.39), 316 (sh, 4.58), 300 (4.70), 290 (4.70), 256 (4.77) nm. CD (CH_2Cl_2): λ 368 ($\Delta\varepsilon$ −15.8), 357 (−12.6), 346 (−14.9), 315 (+15.9), 307 (+7.5), 304 (+8.5), 290 (−6.9), 277 (+1.2), 274 (+1.0), 262

DOI: 10.1021/acs.joc.5b01206
J. Org. Chem. 2015, 80, 7613−7625

(+9.2) nm. FD-HRMS (m/z):[31] $[M]^+$ calcd for $C_{62}H_{56}N_2O_2$: 860.43418; found, 860.43237.

Preparation of (*S*)-15. A mixture of benzaldehyde (0.55 mL, 5.4 mmol), (*S*)-1-cyclohexylethylamine (0.80 mL, 5.4 mmol), and benzene (50 mL) was refluxed for 2.5 h with a Dean−Stark apparatus. After removal of the solvent, the residue (1.14 g) was dissolved in MeOH (20 mL), to which was added $NaBH_4$ (409 mg, 10.8 mmol), and the reaction mixture was stirred at room temperature for 5 h, cooled in an ice-bath, acidified with aq 1 M HCl, and then stirred in aq 1 M NaOH. After extraction with diethyl ether, the organic layer was washed with satd aq $NaHCO_3$, dried over $MgSO_4$, and concentrated to give an *N*-benzylated amine (1.17 g) as a colorless oil in 100% yield.

To a solution of the above amine (1.17 g, 5.39 mmol) in MeOH (16 mL) was added aq 42% HBF_4 (0.82 mL, 5.4 mmol), and the mixture was stirred at room temperature for 10 min. After removal of the solvent with azeotropic benzene, the residue was dried in vacuo, suspended in diethyl ether, and then collected through filtration to give a white salt (*S*)-**15** (1.50 g) as a solid in 91% yield. (*S*)-**15**: mp 105.0−106.0 °C. $[\alpha]_D^{22}$ +2.0 (*c* 1.0 in $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$, TMS): 7.49−7.40 (5H, m), 6.83 (2H, br.s), 4.39 (1H, d, J = 14 Hz), 4.14 (1H, d, J = 14 Hz), 2.90−2.84 (1H, m), 1.80−1.55 (6H, m), 1.30 (3H, d, J = 6.8 Hz), 1.36−0.90 (5H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 129.9, 129.8, 129.5, 129.5, 57.4, 49.2, 40.1, 28.8, 26.4, 25.8, 25.8, 25.5, 12.2. IR (KBr): 3228, 2926, 2855, 2794, 2695, 1577, 1451, 1060 (br), 746, 697 cm^{-1}. FD-LRMS m/z (%): 523.4 (56) [M + (*N*-benzyl-*N*-1-cyclohexylammonium)]$^+$, 218.2 (100) [M − (BF_4^-)]$^+$. UV (CH_2Cl_2): λ_{max} (log ε) 265 (2.28), 260 (2.40), 256 (2.36) nm. CD (CH_2Cl_2): λ 268 ($\Delta\varepsilon$ −0.059), 262 (−0.073), 255 (−0.047) nm. Elemental Anal. Calcd (%) for $C_{15}H_{24}BF_4N$: C, 59.04; H, 7.93; N, 4.59. Found: C, 59.06; H, 7.97; N, 4.59.

■ ASSOCIATED CONTENT

Supporting Information

Supplementary scheme, figures (VT-NMR, energy-minimized structures, NMR titration curves, HPLC chromatogram, and UV/CD in the absence and presence of a guest), $^1H/^{13}C$ NMR spectra of new compounds (**1a−d**, **2a−d**, **6a/c**, **7a/c**, **12a−c**, **15**, and **19c**), and CIF files. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01206.

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Notes

The authors declare no competing financial interest.

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(8) Dynamic helical molecules based on terephthalamides and related compounds are classified into three categories: (1) a molecule undergoes a change in conformation from a nonhelical form to dynamic helical forms upon complexation with a chiral guest and prefers a particular sense in a complexed state due to the supramolecular transmission of chirality in the guest;[2a,9a,b] (2) a molecule adopts dynamic helical forms and prefers a particular sense when it forms a complex with a chiral guest due to the supramolecular transmission of chirality in the guest[9b−d] or in a complexed[9b−e]/uncomplexed[9f] state due to the intramolecular transmission of chirality associated with the molecule (no change in the helical preference even upon complexation with a guest); and (3) a molecule adopts a nonhelical form to which no local chirality is transferred either

DOI: 10.1021/acs.joc.5b01206
J. Org. Chem. 2015, 80, 7613−7625

supramolecularly or intramolecularly, but undergoes a change in conformation from a nonhelical form to dynamic helical forms upon complexation with a chiral guest only when a chiral auxiliary is attached to the host.[7j,9g] The present macrocyclic system can not be classified into any of the above categories.

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(10) Dianiline **8d**/**9d** was obtained as a mixture containing **8c**/**9c**. Details are provided in the Supporting Information (Scheme S1).

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(13) The diastereotopic protons (H^D and $H^{D'}$) in **1a**/**1c** did not coalesce/decoalesce in chloroform-*d* at the temperatures used. For **1d**, the activation energy was estimated in a similar manner (51 kJ mol^{-1}, T_c = 268 K, Δ_δ = 355 Hz).

(14) A figure eight form with (*M*)-helicity was found to be the most energy-minimized structure (rel. 0 kJ mol^{-1}) and was predicted to be more stable than a diastereomeric form with (*P*)-helicity (+1.30 kJ mol^{-1}) in a conformational search for (*R*,*R*)-**2b** (Figure S2, Supporting Information).

(15) With a decrease in temperature, for (*R*,*R*)-**2a**, we found a further split into four species at 263 K, which was also confirmed in the ^{13}C NMR spectrum. For (*R*,*R*)-**2c**, the first-step split was obvious, but the population of the minor component could not be determined due to broadening in the second step. For (*R*,*R*)-**2d**, the activation energy was estimated in a similar manner (53 kJ mol^{-1}, T_c = 259 K, Δ_δ = 78.6 Hz) (Figure S3, Supporting Information).

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(17) We found a set of A, B, and C bands, which are characteristic of α,ω-diphenylpolyynes[16d,e] in the spectra of **2c** and **2d**, and in the latter, each band seemed to be split.

(18) A 1:1 mixture of (*R*,*R*)-**4** and (*S*,*S*)-**4** was used for NMR experiments.

(19) From such a titration curve, we could not estimate an accurate binding constant. Similar titration curves were noted for (*R*,*R*)-**2c**/**d** and (*R*,*R*)-**4**/(*S*,*S*)-**4** (Figure S4b−d, Supporting Information). For reference, we obtained a titration curve under a more severe condition for hydrogen-bonded complexes, and 1:1 fitted it to estimate a binding constant $K_{1:1}$ of 2.9 × 10^3 M^{-1} for the complexation of **1b** with **4** in chloroform-*d* containing 2 vol % acetonitrile-d_3 (Figure S4a, Supporting Information), which would allow us to monitor the complexation in dichloromethane even under a diluted condition. In fact, we could find that complexation-induced changes in the molar CD were saturated only when two or four equiv of a guest were added (Figures 6, 9, and 10).

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(25) In a "supramolecular" figure eight framework, the internal chirality was only sometimes effective in a complexed state. For (*R*,*R*)-**12a**, bisignated Cotton effects emerged upon 1:1 complexation with **3** as well as (*S*,*S*)-**4** (Figure S10a, Supporting Information). For (*R*,*R*)-**12b**, the internal chirality did not contribute to determining the helical preference at all upon 1:1 complexation with a ditopic guest.[9c] For these acyclic references, there was no preference due to achirality of an extended form in the absence of a guest.

(26) We observed similar chiroptical responses for (*R*,*R*)-**2d** upon complexation with **3** (Figure S11b, Supporting Information) or **4** (Figure S12a, Supporting Information). A control experiment with a chiral monotopic guest, (*R*)-**15**[9b] or (*S*)-**15**, showed no change in the spectrum (Figure S12b, Supporting Information) and indicated that ditopic binding was essential for the modulation of a helical preference.

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DOI: 10.1021/acs.joc.5b01206
J. Org. Chem. 2015, 80, 7613−7625