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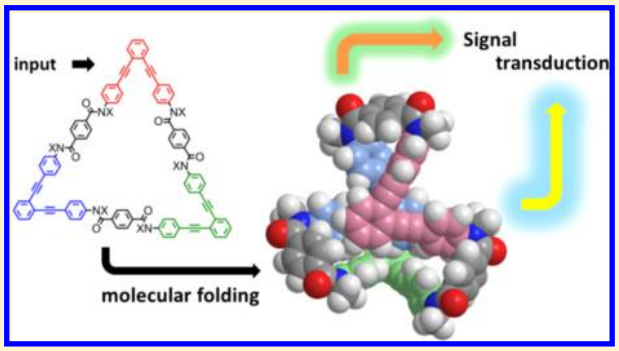
A Foldable Cyclic Oligomer: Chiroptical Modulation through Molecular Folding upon Complexation and a Change in Temperature

Ryo Katoono,* Yuki Tanaka, Kenshu Fujiwara, and Takanori Suzuki*

Department of Chemistry, Faculty of Science, Hokkaido University, Sapporo 060-0810, Japan

Supporting Information

ABSTRACT: A foldable cyclic oligomer **1** consisting of three terephthalamide units spaced with a 3-fold *o*-phenylene unit presented a dynamic pair of enantiomeric forms through molecular folding, to which the external chirality on a ditopic guest [(*S*,*S*)-**2** or (*R*,*R*)-**2**] was supramolecularly transferred to prefer a particular sense of dynamic helicity [(*M*,*M*)-/(*P*,*P*)-**1** and (*M*,*M*,*P*)-/(*P*,*P*,*M*)-**1**]. In the macrocycle, the terephthalamide units acted as exotopic binding sites to fold into helical forms upon complexation. The internal chirality associated with a host [(*R*,*R*,*R*,*R*,*R*)-**1b**] had no preference in a helical sense in the absence of a guest. Instead, the internal chirality was responsible for the signal modulation that it was cooperatively or competitively transferred in response to the external chirality on a guest (*S*,*S*)-**2** or (*R*,*R*)-**2**. During the diastereomeric complexation, a particular sense of dynamic helicity was favored due to cooperative transmission of chirality when the helical preference was matched between the host and guest. Alternatively, the host complexed with an antipodal guest underwent a drastic change in conformation upon a change in temperature.

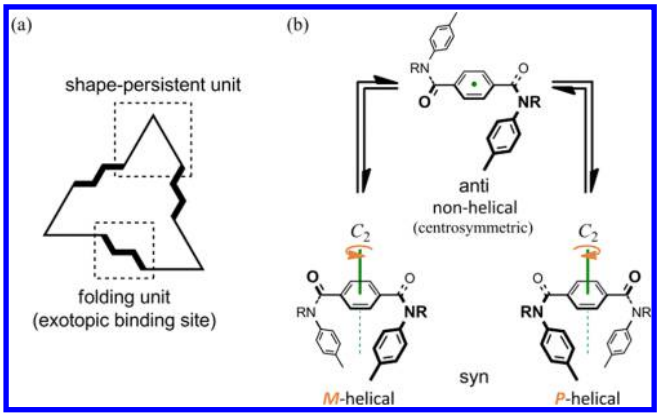


INTRODUCTION

Change in conformation of a host molecule in response to recognition of a guest molecule is one of the central issues to study signal transduction and amplification.[1] Such a dynamic host molecule is designed to accompany some spectral modulation upon the change in conformation.[2] In an advanced system, a host molecule gives a specific response to an analyte, e.g., each of the enantiomeric guests, through a specific change in conformation.[3] Circular dichroism (CD) signals are useful to find a change in conformation of a molecule to be chiral.[4] There has been particular interest in foldamers[5,6] with a goal of inducing a change in conformation from random to helical forms in response to a change in the environment, such as temperature[5a−c] or solvent,[5c−f] as well as with the addition of a guest.[7,8] They are designed to prefer a helical form under a specific condition due to well-defined intramolecular interactions, but adopt a random conformation under other conditions.

We considered how a foldable oligomer acts in a cyclic structure that either is highly flexible or does not have a specific programmed intramolecular interaction among repeating components. We were interested in a foldable cyclic oligomer consisting of two components that are alternatively arranged to form a cyclic structure (Scheme 1a). One component is a shape-persistent chromophoric unit that enables detection of a change in conformation by spectroscopy. The other component is a flexible part that can transform with the addition of a guest. In such a macrocycle, the molecule could show various patterns of folding rather than folding into a single pair of right- or left-handed helices. To promote various types of folding, which are important in terms of signal modulation, it would be better to adopt an exotopic type of recognition of a guest rather than an endotopic recognition such as the encapsulation of a guest in a cavity presented by a single pair of right- or left-handed helices.[8] To generate an exotopic binding site upon folding, we

Scheme 1. (a) A Foldable Cyclic Oligomer Consisting of a Shape-Persistent Unit and a Folding Unit (Exotopic Binding Site) and (b) Dynamic Interconversion between a Nonhelical (Anti) Form and Helical (Syn) Forms of a Terephthalamide Unit



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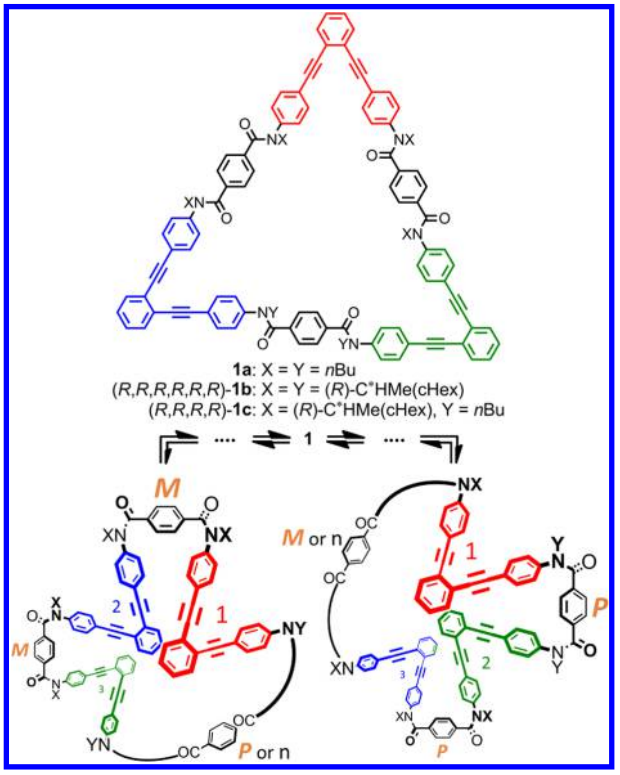
used a terephthalamide derivative (Scheme 1b). A syn-form terephthalamide unit can capture a ditopic guest at the two amide carbonyls through the formation of hydrogen bonds.[9] In a syn-form, two helical forms are present, in terms of the direction of twisting of the two amide groups, while an anti-form is no longer helical due to a local center of symmetry.[10]

We envisioned a trimeric macrocycle, in which three shape-persistent *o*-phenylene units, often used in the design of helical molecules,[11−13] and dynamic terephthalamide units are linked through triple bonds (Scheme 2). A helically foldable

Scheme 2. Chemical Structures of 1 and Dynamic Helicity [(*M*)/(*P*), (*M*,*M*)/(*P*,*P*), or (*M*,*M*,*P*)/(*P*,*P*,*M*)] Generated through Molecular Folding at a Terephthalamide Unit(s)



terephthalamide unit with a particular sense of (*M*)- or (*P*)-helicity is arranged by spacing with the V-structure, and it acts as a binding site when it adopts a syn-form. Otherwise, it might adopt a nonhelical anti-form and might act as just a linker unit. In a folded macrocycle, replacement of the two neighboring V-shaped units with each other, such as 1 and 2, or 2 and 3 depicted in Scheme 2, gives a mirror image, and the two forms before and after replacement are considered to be an enantiomeric pair [(*M*)/(*P*), (*M*,*M*)/(*P*,*P*), or (*M*,*M*,*P*)/(*P*,*P*,*M*), etc.], which may be classified as dynamic helical molecules[13] rather than chiral triangular molecules.[14] The biasing of helicity would be controlled by a preference for a particular sense of local dynamic helicity of the syn-form terephthalamide unit(s). The control of helicity in a syn-form would be enabled by the formation of a complex with a chiral ditopic guest at the two amide carbonyls through the supramolecular transmission of chirality, and/or by the attachment of a chiral auxiliary to each amide nitrogen through the intramolecular transmission of chirality.

Thus, we designed a tristerephthalamide host **1a** to investigate whether or not it could give a dynamic helical pair through molecular folding upon complexation and could prefer a particular sense of dynamic helicity through supramolecular transmission of the external chirality of a chiral ditopic guest,[9] such as (*R*,*R*)-**2** and (*S*,*S*)-**2** (Figure 1). We considered how the

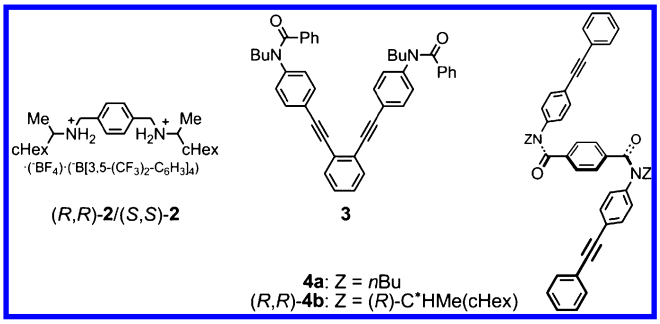
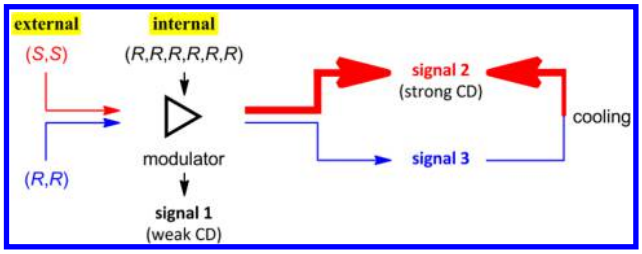


Figure 1. Chemical structures of chiral ditopic guests (*R*,*R*)-**2** and (*S*,*S*)-**2**,[9a] and substructures **3** and **4a**[9b]/**4b**.

internal chirality could be intramolecularly transferred in a macrocycle (*R*,*R*,*R*,*R*,*R*,*R*)-**1b** with a chiral auxiliary (*R*) on each amide nitrogen. There was no preferred helical sense in the absence of a guest (described later). However, it should act as a chiral handle to prefer a particular sense of dynamic helicity through the intramolecular transmission of chirality, once dynamic helicity is generated in the macrocycle through molecular folding upon complexation. We then investigated the signal modulation upon transmission of the internal and external chirality to dynamic helicity generated in the macrocycle through molecular folding. We examined diastereomeric complexation of (*R*,*R*,*R*,*R*,*R*,*R*)-**1b** with each of the enantiomeric guests (*R*,*R*)-**2** and (*S*,*S*)-**2**, while varying the equivalent ratios of guest to host, and the temperature (Scheme 3), since an equilibrium is perturbed by such parameters. When

Scheme 3. Chiroptical Modulation by a Foldable Cyclic Oligomer through Intramolecular (Signal 1) Transmission of Chirality, and Cooperative (Signal 2) or Competitive (Signal 3) Transmission of Chirality upon Complexation and a Change in Temperature



the preference for a particular sense of dynamic helicity is matched, both internal and external chirality would be cooperatively transferred to produce strong CD signals. This was true for a combination of (*R*,*R*,*R*,*R*,*R*,*R*)-**1b** and (*S*,*S*)-**2**. Alternatively, each preference competed during transmission of internal and external chirality in a complex of (*R*,*R*,*R*,*R*,*R*,*R*)-**1b** with (*R*,*R*)-**2**, and resulted in production of different signals from those obtained with (*S*,*S*)-**2**. The host underwent a drastic change in conformation with a decrease in temperature to accompany a drastic change in CD signals.

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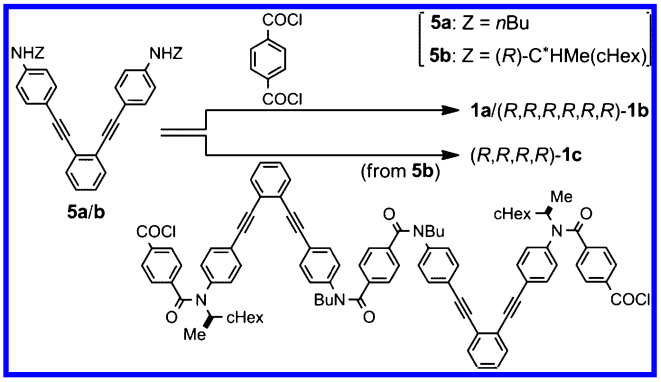
RESULTS AND DISCUSSION

Preparation and ^{1}H NMR Characterization of Tristerephthalamides 1a–c. We prepared hosts **1a** and **1b** [X = Y] in one step through a 3-fold condensation reaction of a V-shaped dianiline **5a**/**b** and terephthaloyl chloride,[15] and prepared a derivative **1c** with both chiral and achiral substituents on the amide nitrogens [X = (*R*)-C*HMe(cHex) and Y = *n*Bu] through a condensation reaction of dianiline **5b** and an acid chloride (Scheme 4), which was derived from 1,2-

Scheme 4. Preparation of Tristerephthalamides 1a, (*R*,*R*,*R*,*R*,*R*)-1b, and (*R*,*R*,*R*)-1c



diethynylbenzene[16] in a stepwise manner (Scheme S1 in the Supporting Information). We also prepared a V-shaped substructure **3**, and double-armed substructures **4a**[9b]/**b** (Figure 1), the latter of which prefers a nonhelical anti-form in the absence of a guest and adopts helical arm-crossing syn-forms in a 1:1 complex with a ditopic guest.[9b]

In the ^{1}H NMR spectra of **1a** and **1b**, measured at room temperature, we observed a single set of averaged resonances that was assigned to D_{3h} for **1a** or C_3 for **1b** (Figure S1 in the Supporting Information). These observed symmetries should be due to dynamic interconversion among conformations,[13a,b,17] because we observed decoalesced resonances in the spectra of **1b** measured at low temperatures (Figure S3a in the Supporting Information). It seems reasonable if we consider that the molecules should avoid a planar and triangular structure with six *trans*-amides, as depicted in Scheme 2, due to the *cis*-preference in *N*-alkylbenzanilides.[18,19] In the spectrum of **1c**, two sets of averaged resonances were present in a 1:2 ratio as if we superimposed the two spectra of **1a** and **1b**.

Supramolecular Transmission of External Chirality to Dynamic Helicity upon Complexation of 1a with a Chiral Ditopic Guest 2. We first investigated the complexation of **1a** with a ditopic guest **2** by monitoring continuous changes in the chemical shift by ^{1}H NMR spectroscopy. We confirmed that the host and guest formed a complex by an upfield shift for both the phenylene protons of a terephthalamide unit in **1a** and the phenylene protons in **2** (Figure 2a). These upfield shifts indicated that a ditopic guest was captured at the two amide carbonyls. For some other protons in **1a**, far from the binding site, a small change in the chemical shift was also induced.[20] A Job plot, based on relatively large changes in the chemical shift for guest protons, revealed that the stoichiometry was 1:2 (Figure 2b), which verified the presence of two syn-form terephthalamide units in the macrocycle under the condition ([**1**] + [**2**] = 2 mM). The complexation-induced chemical shifts broke the continuity when the guest was excessively added

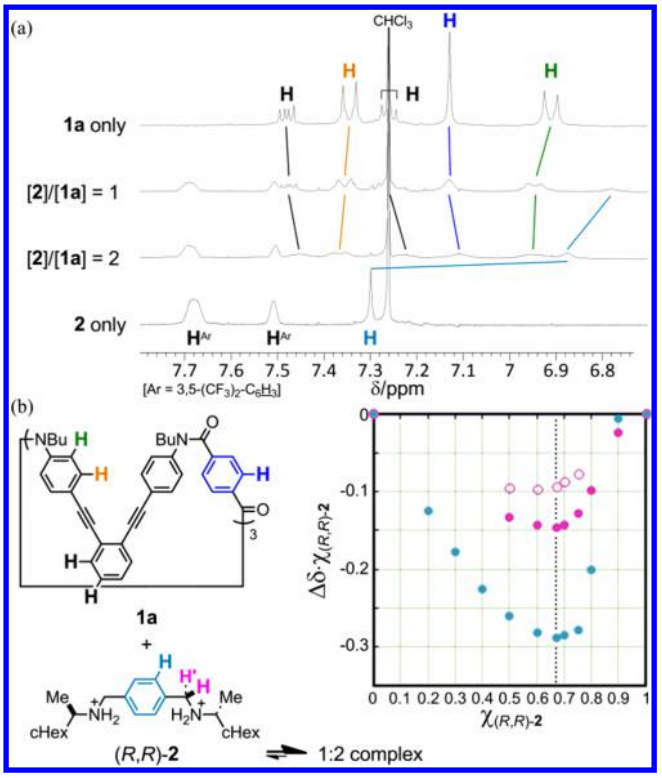


Figure 2. (a) ^{1}H NMR spectra (300 MHz) of **1a** in the presence of (*R*,*R*)-**2** [0 (**1a** only), 1, and 2 equiv], and ^{1}H NMR spectrum of (*R*,*R*)-**2**. (b) Job plot for the complexation of **1a** with (*R*,*R*)-**2**, using continuous changes ($\Delta\delta = \delta_{1a\cdot2} - \delta_2$) in the chemical shift for phenylene (pale blue) or benzyl protons (pink) of **2** ([**1**] + [**2**] = 2 mM). All spectra were measured in $CDCl_3$ at 303 K.

(0.75 < χ_2), which might indicate a further change in conformation.

We then monitored the complexation of **1a** with each of an enantiomeric pair of (*R*,*R*)-**2** and (*S*,*S*)-**2** by UV and CD spectroscopy. The UV spectrum of **1a** showed two major absorptions that could be assigned to the diphenylacetylene unit (290 nm) and longer conjugation through the *o*-phenylene group (around 330 nm sh) (Figure 3a),[21] and the latter was attenuated in the presence of **2** (Figure 3b), which might reflect a change in conformation such as reduction of effective conjugation due to generation of twisting upon complexation.

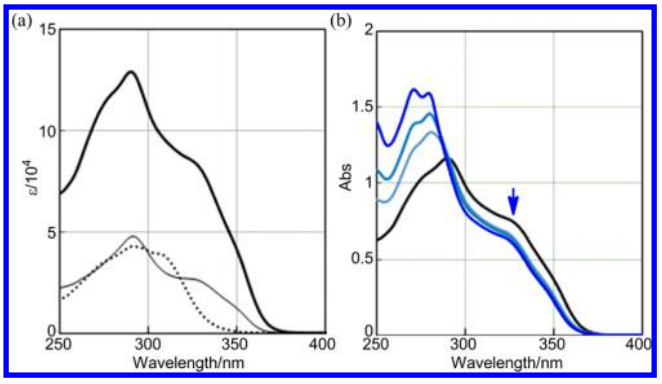


Figure 3. (a) UV spectra of **1a** (bold line), **3** (thin line), and **4a** (dashed line). (b) UV spectra of **1a** (9.0×10^{-5} M) in the presence of (*R*,*R*)-**2** [0 (**1a** only, black line), 3, 6, and 12 equiv (blue lines)]. All spectra were measured in CH_2Cl_2 at room temperature.

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The two major absorptions were commonly seen in the spectrum of V-shaped substructure **3** (293 nm and 330 sh nm), and only the former was found for a double-armed **4a** (291 nm). In the CD spectrum of **1a**, we found a pair of mirror images with bisignated Cotton effects in the absorption region of **1a** [321 nm ($\Delta\varepsilon$ −15) and 286 (+11) for a solution of **1a** in the presence of (*R*,*R*)-**2**], which continuously increased with the addition of up to 6 equiv of **2** (Figure 4a). When the guest

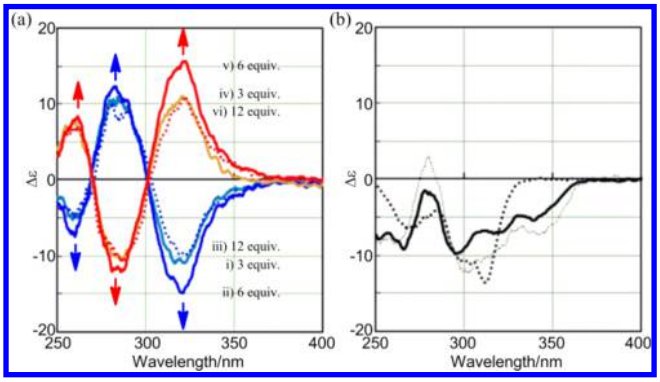

Figure 4. (a) Continuous changes in the CD spectrum of **1a** (1×10^{-4} M) upon complexation with (*R*,*R*)-**2** [blue lines, (i) 3, (ii) 6, and (iii) 12 equiv] or (*S*,*S*)-**2** [red lines, (iv) 3, (v) 6, and (vi) 12 equiv]. (b) CD spectra of (*R*,*R*,*R*,*R*,*R*,*R*)-**1b** (bold line), (*R*,*R*,*R*,*R*)-**1c** (thin dashed line), and (*R*,*R*)-**4b** (bold dashed line). All spectra were measured in CH_2Cl_2 at 293 K.

was further added (12 equiv), the induced Cotton effects were reduced [321 nm ($\Delta\varepsilon$ −10) and 286 (+9)], and we considered the change as a result of cancellation of local helicity in the terephthalamide units [e.g., (*M*,*M*,*P*)/(*P*,*P*,*M*)]. The shapes of the induced Cotton effects for the complexes of **1a** with **2** were similar to that for a 1:1 complex of the double-armed host **4a** with **2**, where Cotton effects continuously increased with an increase in equivalents of the guest throughout the addition [312 nm ($\Delta\varepsilon$ +12) and 283 (−4)], although the sign was reversed (Figure S4 in the Supporting Information).[22] These results showed that a dynamic helical pair was generated in a syn-form terephthalamide unit (Scheme 2), and a particular sense was preferred through the supramolecular transmission of guest chirality. The chirality in **2** was transferred to the dynamic helicity of the host to show their own preference under cyclic or acyclic conditions.

Intramolecular Transmission of Internal Chirality Associated with Hosts 1b and 1c. The CD spectra of (*R*,*R*,*R*,*R*,*R*,*R*)-**1b** and (*R*,*R*,*R*,*R*)-**1c** were similar and showed several negatively signed Cotton effects [341 nm ($\Delta\varepsilon$ −8), 318 (−11), 295 (−16), 280 (−4), and 265 (−14) for **1b**; 342 nm ($\Delta\varepsilon$ −7), 315 (−11), 302 (−12), 280 (+3), and 260 (−9) for **1c**] (Figure 4b),[23] and they were totally different from that of **1a** in the presence of (*R*,*R*)-**2** or (*S*,*S*)-**2** (Figure 4a). A local chiral auxiliary on the amide nitrogen has some effects even though a molecule does not adopt a helical form, as shown by the nonhelical structure of (*R*,*R*)-**4b** in the absence of a guest (Figure 4b). Thus, we considered that the difference in the shape of the Cotton effects was the result of a failure in generation of helical forms through intramolecular transmission of chirality (*R*) to **1b** or **1c**.

Cooperative and Competitive Transmission of Chirality to Dynamic Helicity. We further investigated the intra- and intermolecular transmission of chirality to dynamic helicity in a macrocyclic host by CD spectroscopy. When we gradually added up to 3 equiv of a chiral guest (*S*,*S*)-**2** to a solution of (*R*,*R*,*R*,*R*,*R*,*R*)-**1b**, the Cotton effects changed continuously [320 nm ($\Delta\varepsilon$ +40), 283 (−97), and 256 (+27)] (Figure 5a),

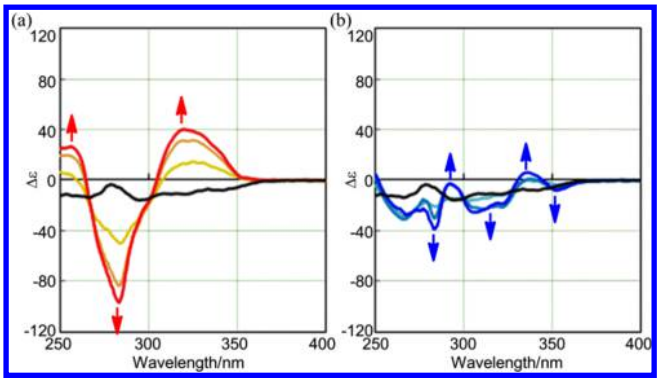

Figure 5. Continuous changes in the CD spectrum of (*R*,*R*,*R*,*R*,*R*,*R*)-**1b** (1.1×10^{-4} M) upon complexation with (a) (*S*,*S*)-**2** (red lines) or (b) (*R*,*R*)-**2** (blue lines) [0 (**1b** only, black line), 1, 2, and 3 equiv], measured in CH_2Cl_2 at 293 K.

and the spectral shape of the induced effects was identical to that for the complex of **1a** with (*S*,*S*)-**2** (Figure 4a). We considered that the successful chiroptical enhancement was the result of the cooperative transmission of the internal (*R*) and external (*S*,*S*) chirality to dynamic helicity generated in the complex. Alternatively, the Cotton effects fluctuated upon the addition of (*R*,*R*)-**2** (Figure 5b) and indicated a competitive transmission of chirality to a flexible conformation in the macrocycle. Also in the cases of using (*R*,*R*,*R*,*R*)-**1c** instead of (*R*,*R*,*R*,*R*,*R*,*R*)-**1b**, we observed similar responses to each of the enantiomers (Figure S5 in the Supporting Information). The shape of the induced Cotton effects for a complex of (*R*,*R*,*R*,*R*)-**1c** with (*S*,*S*)-**2** (3 equiv) [318 nm ($\Delta\varepsilon$ +30), 282 (−48), and 257 (+13)] was common with that for complexes **1a**/**1b** with (*S*,*S*)-**2**. The result indicated that these hosts adopted a common structure in each complex and every terephthalamide unit with X or Y groups can act as a binding site or a linker unit.

Most notably, we found a remarkable difference in the chiroptical response between the diastereomeric complexes when we added greater amounts of each of the guests (up to 6 equiv) and changed the temperature (263−313 K) (Scheme 3). For the complex of (*R*,*R*,*R*,*R*,*R*,*R*)-**1b** with (*S*,*S*)-**2**, the induced Cotton effects were further enhanced with an increase in guest equivalents (6 equiv), and with a decrease in temperature to 263 K, and attenuated with an increase in temperature to 313 K (Figure 6a). This continuous change while maintaining the spectral shape can be explained as follows: (1) a dynamic pair of helical forms such as (*M*,*M*)-**1b** and (*P*,*P*)-**1b** is in equilibrium, and the population of the major component increases with a decrease in temperature,[24] and (2) the formation of complexed species is also favored with a decrease in temperature.[25]

For a solution of (*R*,*R*,*R*,*R*,*R*,*R*)-**1b** in the presence of (*R*,*R*)-**2**, the spectral shape changed discontinuously upon addition of the guest up to 6 equiv (Figure 6b, black line) from those obtained with less than 3 equiv (Figure 5b), and showed ultimately a response similar to that of the complex with (*S*,*S*)-**2** upon lowering the temperature (Figure 6b, purple line). These changes demonstrated that the internal chirality (*R*) associated with **1b** could be predominantly transferred to dynamic helicity,

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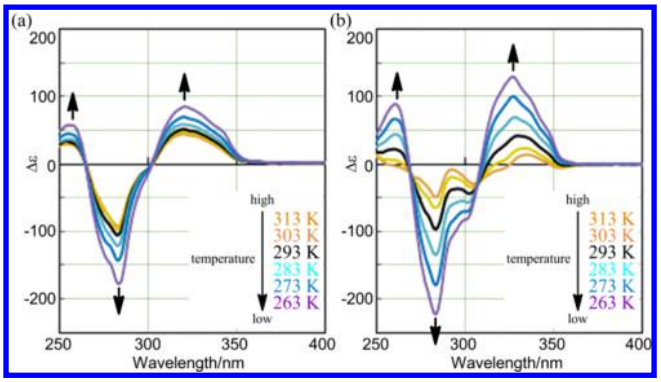

Figure 6. VT-CD spectra of (*R*,*R*,*R*,*R*,*R*,*R*)-**1b** (1.1×10^{-4} M) in the presence of (a) (*S*,*S*)-**2** or (b) (*R*,*R*)-**2** (6 equiv), measured in CH_2Cl_2 at 263−313 K.

once a helical form was sufficiently induced in the macrocycle by complexation. Alternatively, it was competitive with the supramolecular transmission of chirality (*R*,*R*) in the guest, which would promote the opposite preference (Figure 4a), at elevated temperatures or under lower equivalents of guest to host (<3 equiv). During the complexation, the host underwent a drastic change in conformation through molecular folding to produce a drastic change in chiroptical signals upon a change in temperature.

CONCLUSION

We have demonstrated a foldable cyclic oligomer, in which a shape-persistent unit and a folding unit are repeatedly arranged. A helically folded (syn-form) terephthalamide unit provided a dynamic pair of enantiomeric forms in the macrocycle, and the helical preference was successfully controlled through supramolecular transmission of the guest chirality. In addition, the guest chirality was modulated with the internal chirality through cooperative or competitive transmission to dynamic helicity generated by molecular folding. The external chirality (*S*,*S*) on a guest was enhanced with the internal chirality (*R*) on a host. For the combination of internal (*R*,*R*,*R*,*R*,*R*,*R*) and external chirality (*R*,*R*), the internal chirality competed with the external chirality upon transmission under conditions of lower equivalents of guest to host or elevated temperatures, and the internal chirality was predominantly transferred to dynamic helicity once a helical form was sufficiently generated in the complex. Thus, we demonstrated that a difference in the structure of a guest triggered different signaling pathways.

EXPERIMENTAL SECTION

Preparation of 1a [X = Y = *n*Bu]. To an ice-cooled solution of **8a** (1.0 g, 1.6 mmol) in MeOH/THF (33 mL/33 mL) was added 60% NaH in oil (0.65 g, 16 mmol), and the mixture was stirred at room temperature for 1 h and then diluted with chloroform. The diluted solution was washed with water and brine, dried over $MgSO_4$, and then purified by column chromatography on SiO_2 (0.5:2.5:7 triethylamine/chloroform/hexane) to give **5a** (0.67 g) as a brown solid in 98% yield. The product was immediately subjected to the next reaction without further purification [deprotection of TFA].

To a solution of **5a** (673 mg, 1.60 mmol) in Et_3N/toluene (3 mL/3 mL) was added terephthaloyl chloride (357 mg, 1.76 mmol) at 85 °C, and the mixture was stirred at that temperature for 30 min and then diluted with chloroform. The diluted solution was washed with water and brine, dried over $MgSO_4$, and then purified by column chromatography on SiO_2 (1:3 ethyl acetate/chloroform) to give two fractions: one was a mixture containing **1a**, and the other gave **6a**[3b] (282 mg, 32%) as a white solid. The former fraction containing **1a** was further purified by GPC to give **1a** (71 mg) as a white solid in 8% yield. An analytical sample of **1a** was obtained as a white solid by further purification through GPC, followed by recrystallization from ethyl acetate.

*Data of **1a** [X = Y = nBu]:* mp 199.5−202.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ = 7.48 (6H, dd, J = 3.3, 5.7 Hz),[26] 7.35 (12H, d, J = 8.4 Hz), 7.26 (6H, dd, J = 3.3, 5.7 Hz),[26] 7.13 (12H, s), 6.91 (12H, d, J = 8.4 Hz), 3.85 (12H, br t), 1.55 (12H, quin, J = 7.5 Hz), 1.31 (12H, sext, J = 7.5 Hz), 0.87 (18H, t, J = 7.5 Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 169.2, 143.1, 137.2, 132.4, 132.0, 128.2, 127.6, 125.2, 121.6, 92.5, 89.3, 50.1, 29.8, 20.1, 13.8 ppm; IR (KBr) 3055, 2956, 2926, 2871, 2211, 1650, 1601, 1561, 1511 cm^{-1}; FD-LRMS m/z (%) 1656.1 (4) $[M + 5]^+$, 1655.1 (11) $[M + 4]^+$, 1654.1 (31) $[M + 3]^+$, 1653.1 (65) $[M + 2]^+$, 1652.1 (100) $[M + 1]^+$, 1651.1 (81) $[M]^+$; UV (CH_2Cl_2) λ_{max} (log ε) 330sh (4.90), 290 (5.11), 276sh (5.06) nm; FD-HRMS[29] m/z calcd for $C_{114}H_{102}N_6O_6$ 1650.78608 $[M]^+$; found 1650.78573.

Preparation of (*R*,*R*,*R*,*R*,*R*,*R*)-1b [X = Y = (*R*)-C*HMe(cHex)]. To an ice-cooled solution of **8b** (809 mg, 1.12 mmol) in MeOH/THF (22 mL/22 mL) was added 60% NaH in oil (1.80 g, 45.0 mmol), and the mixture was stirred at room temperature for 1 h and then diluted with dichloromethane. The diluted solution was washed with water and brine and then dried over $MgSO_4$. After removal of a solid by filtration, the filtrate was passed over a short column of Al_2O_3 eluted with 1:2 dichloromethane/hexane and then concentrated to give **5b** (581 mg) as a yellow amorphous solid in 98% yield. The product was immediately subjected to the next reaction without further purification [deprotection of TFA].

To a solution of **5b** (229 mg, 0.433 mmol) in Et_3N/toluene (0.6 mL/1 mL) was added terephthaloyl chloride (105 mg, 0.517 mmol) at 85 °C, and the mixture was stirred at that temperature for 4 h and then diluted with chloroform. The diluted solution was washed with water and brine, dried over $MgSO_4$, and then purified by column chromatography on SiO_2 (1:5 ethyl acetate/chloroform) to give two fractions: one was a mixture containing **1b**, and the other gave **6b** (103 mg, 35%) as a yellow solid. The former fraction containing **1b** was further purified by repeated preparative TLC on SiO_2 (1:5 ethyl acetate/chloroform), followed by GPC, to give **1b** (9 mg) as a white solid in 3% yield. An analytical sample of **6b** was obtained as a white solid by GPC and recrystallization from toluene.

*Data of (R,R,R,R,R,R)-**1b** [X = Y = (R)-CH*Me(cHex)]:* mp 202−204 °C (dec); $[\alpha]_D^{25}$ = −158.5 (c = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) [333 K] δ = 7.45 (6H, dd, J = 3.2, 5.6 Hz),[26] 7.34 (12H, d, J = 8.4 Hz), 7.22 (6H, dd, J = 3.2, 5.6 Hz)[26] 7.08 (12H, s), 6.89 (12H, d, J = 8.4 Hz), 4.33 (6H, br s), 2.05 (6H, br d), 1.84−1.42 (30H, br m), 1.37−1.04 (24H, br m), 1.15 (18H, d, J = 7.2 Hz), 1.02−0.89 (6H, br m) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 169.7, 141.6, 137.8, 132.1, 132.0, 129.5, 128.3, 127.9, 125.1, 122.0, 92.4, 89.5, 59.3, 41.4, 30.8, 30.3, 26.2, 26.0, 26.0, 16.7 ppm; IR (KBr) 3058, 2970, 2928, 2851, 2216, 1650, 1600, 1556, 1510 cm^{-1}; FD-LRMS m/z (%) 1980.99 (3) $[M + 6]^+$, 1980.02 (8) $[M + 5]^+$, 1978.99 (20) $[M + 4]^+$, 1977.99 (46) $[M + 3]^+$, 1976.99 (82) $[M + 2]^+$, 1975.99 (100) $[M + 1]^+$, 1974.98 (62) $[M]^+$; UV (CH_2Cl_2) λ_{max} (log ε) 327sh (4.87), 287 (5.08), 272sh (5.02) nm; CD (CH_2Cl_2) λ 341 ($\Delta\varepsilon$ −8), 318 (−11), 295 (−16), 280 (−4), 265 (−14) nm; FD-HRMS[29] m/z calcd for $C_{138}H_{138}N_6O_6$ 1975.06778 $[M]^+$; found 1975.06423.

*Data of (R,R)-**6b** [Z = (R)-CH*Me(cHex)]:* mp 206−208 °C (dec); $[\alpha]_D^{25}$ = −60.0 (c = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ = 7.51 (2H, dd, J = 3.2, 6.0 Hz),[26] 7.35 (2H, dd, J = 3.2, 6.0 Hz),[26] 7.27 (4H, d, J = 8.4 Hz),[26] 7.08 (4H, s), 6.85 (4H, d, J = 8.4 Hz),[26] 4.34 (2H, br dq), 1.98 (2H, br d), 1.83−1.52 (10H, br m), 1.29−1.06 (8H, br m), 1.22 (6H, d, J = 6.8 Hz), 1.02−0.90 (2H, br m) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 169.5, 142.2, 137.9, 131.7, 130.0, 128.3, 128.2, 128.1, 126.9, 121.2, 93.6, 88.5, 60.5, 41.2, 30.7, 30.6, 26.2, 26.0, 25.9, 16.8 ppm; IR (KBr) 3053, 2970, 2932, 2850, 2216, 1644, 1599, 1556, 1510 cm^{-1}; FD-LRMS m/z (%) 661.4 (5) $[M + 3]^+$, 660.4 (17) $[M + 2]^+$, 659.4 (55) $[M + 1]^+$, 658.4 (100) $[M]^+$; UV (CH_2Cl_2) λ_{max} (log ε) 263 (4.58) nm; CD (CH_2Cl_2) λ 306 ($\Delta\varepsilon$ −2), 284 (+1), 272

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(0) nm; elemental analysis calcd (%) for $C_{46}H_{46}N_2O_2$ C 83.85, H 7.04, N 4.25; found C 83.60, H 7.00, N 4.03.

Preparation of (*R*,*R*,*R*,*R*)-1c [X = (*R*)-C*HMe(cHex), Y = *n*Bu]. To a refluxed solution of **13** (1.05 g, 0.763 mmol) and $BnNEt_3Cl$ (5 mg, 0.02 mmol) in CH_2Cl_2 (15 mL) was added $SOCl_2$ (0.15 mL, 2.1 mmol), and the mixture was further refluxed for 1 h. After removal of the solvent by evaporation, the residual solid (**13′**) was dried *in vacuo* and dissolved in toluene (20 mL) [acid chloride preparation].

To a solution of **5b** (412 mg, 0.779 mmol) and Et_3N (1.1 mL, 7.9 mmol) in toluene (56 mL) was added the freshly prepared toluene solution (20 mL) containing the acid chloride **13′** at 85 °C, and the mixture was stirred at that temperature for 2 h and then diluted with chloroform. The diluted solution was washed with water and brine, dried over $MgSO_4$, and then purified by column chromatography on SiO_2 (1:4 ethyl acetate/chloroform), preparative TLC on SiO_2 (1:3 ethyl acetate/chloroform), and GPC to give **1c** (150 mg) as a slightly colored solid in 11% yield.

*Data of (R,R,R,R)-**1c** [X = (R)-CH*Me(cHex), Y = nBu]:* mp 190−192 °C (dec); $[\alpha]_D^{26}$ = −113.3 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ = 7.59−7.40 (6H, br m), 7.40−7.29 (8H, br m), 7.35 (4H, d, *J* = 8.0 Hz), 7.26−7.21 (6H, br m), 7.12 (4H, s), 7.07 (8H, br s), 6.92 (4H, d, *J* = 8.0 Hz), 6.88 (8H, br s), 4.44 (4H, br s), 3.85 (4H, br t), 2.07 (4H, br d), 1.88−1.45 (20H+4H, br m), 1.39−0.78 (12H+20H, br m), 1.31 (4H, sext, *J* = 7.2 Hz), 0.88 (6H, t, *J* = 7.2 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 169.8, 169.0, 143.1, 141.6 (br), 137.8, 137.8, 137.1, 132.4, 132.0 (br), 129.5 (br), 128.2, 127.8 (br), 127.5, 125.2, 122.0 (br), 121.6, 92.4, 89.5, 89.3, 59.2, 50.2, 41.5, 30.8, 30.3, 29.8, 26.2, 26.0, 26.0, 20.1, 16.7, 13.8 ppm; IR (KBr) 3052, 2928, 2851, 2216, 1650, 1600, 1559, 1510 cm^{-1}; FD-LRMS *m*/*z* (%) 1871.94 (7) $[M + 5]^+$, 1870.93 (19) $[M + 4]^+$, 1869.93 (45) $[M + 3]^+$, 1868.92 (81) $[M + 2]^+$, 1867.92 (100) $[M + 1]^+$, 1866.92 (68) $[M]^+$; UV (CH_2Cl_2) λ_{max} (log ε) 327sh (4.89), 288 (5.10), 272sh (5.04) nm; CD (CH_2Cl_2) λ 342 ($\Delta\varepsilon$ −7), 315 (−11), 302 (−12), 280 (+3), 260 (−9) nm; FD-HRMS[29] *m*/*z* calcd for $C_{130}H_{126}N_6O_6$ 1866.97388 $[M]^+$; found 1866.97714.

Preparation of 3. To a solution of **5a** (305 mg, 0.725 mmol), DMAP (1 mg, 0.007 mmol), and Et_3N (0.20 mL, 1.4 mmol) in toluene (10 mL) was added benzoyl chloride (0.34 mL, 2.9 mmol), and the mixture was stirred at 80 °C for 2 h. The reaction mixture was treated with 1 N NaOH aq and extracted with diethyl ether. The organic layer was washed with water and brine, dried over $MgSO_4$, and then purified by column chromatography on SiO_2 (1:2 ethyl acetate/hexane) to give **3** (397 mg) as a yellow amorphous solid in 87% yield. An analytical sample of **3** was obtained as a white solid by recrystallization from methanol, followed by GPC.

*Data of **3**:* mp 134.0−134.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ = 7.51 (2H, dd, *J* = 3.2, 5.6 Hz),[26] 7.36 (4H, d, *J* = 8.8 Hz),[26] 7.33−7.28 (6H, m), 7.25−7.16 (6H, m), 6.97 (4H, d, *J* = 8.8 Hz), 3.94 (4H, t, *J* = 7.6 Hz), 1.62 (4H, quin, *J* = 7.6 Hz), 1.38 (4H, sext, *J* = 7.6 Hz), 0.93 (6H, t, *J* = 7.6 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.1, 143.6, 136.0, 132.3, 131.8, 129.7, 128.7, 128.2, 127.8, 127.5, 125.4, 121.2, 92.6, 89.0, 50.1, 29.9, 20.1, 13.8 ppm; IR (KBr) 3055, 2959, 2928, 2865, 2211, 1649, 1600, 1560, 1510 cm^{-1}; FD-LRMS *m*/*z* (%) 631.3 (5) $[M + 3]^+$, 630.3 (16) $[M + 2]^+$, 629.3 (54) $[M + 1]^+$, 628.3 (100) $[M]^+$; UV (CH_2Cl_2) λ_{max} (log ε) 330sh (4.41), 291 (4.68) nm; FD-HRMS[29] *m*/*z* calcd for $C_{44}H_{40}N_2O_2$ 628.30898 $[M]^+$; found 628.31138; elemental analysis calcd (%) for $C_{44}H_{40}N_2O_2$ C 84.04, H 6.41, N 4.46; found C 83.64, H 6.43, N 4.39.

Preparation of (*R*,*R*)-4b [Z = (*R*)-C*HMe(cHex)]. To a solution of **9b** (584 mg, 0.741 mmol) and phenylacetylene (0.18 mL, 1.6 mmol) in Et_3N/THF (20 mL/20 mL) were added $Pd(PPh_3)_4$ (77 mg, 0.067 mmol) and CuI (27 mg, 0.14 mmol) under an argon atmosphere at 40 °C, and the mixture was stirred for 20 h. After removal of a solid by filtration through a Celite pad, the filtrate was concentrated and purified by column chromatography on SiO_2 (dichloromethane−1:10 ethyl acetate/dichloromethane) and GPC to give **4b** (429 mg) as a white solid in 79% yield. An analytical sample was obtained as a white solid by recrystallization from ethanol.

*Data of (R,R)-**4b** [Z = (R)-C*HMe(cHex)]:* mp 209.0−209.5 °C; $[\alpha]_D^{25}$ = −180.5 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ = 7.54−7.50 (4H, m), 7.37 (4H, br d), 7.34−7.28 (6H, m), 7.01 (4H, br s), 6.84 (4H, br d), 4.47 (2H, br s), 2.09 (2H, br d), 1.85−1.53 (10H, br m), 1.33−1.07 (8H, br m), 1.12 (6H, d, *J* = 6.8 Hz), 1.05−0.91 (2H, br m) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 170.1, 141.1, 137.9, 132.0, 131.6, 129.5, 128.4, 128.3, 127.5, 122.8, 121.9, 90.7, 88.5, 58.6, 41.4, 30.8, 30.3, 26.2, 26.0, 25.9, 16.7 ppm; IR (KBr) 3060, 2970, 2932, 2851, 2221, 1649, 1594, 1555, 1509 cm^{-1}; FD-LRMS *m*/*z* (%) 739.39 (4) $[M + 3]^+$, 738.39 (18) $[M + 2]^+$, 737.38 (59) $[M + 1]^+$, 736.38 (100) $[M]^+$; UV (CH_2Cl_2) λ_{max} (log ε) 306 (4.68), 290 (4.78), 273 (4.65) nm; CD (CH_2Cl_2) λ 312 ($\Delta\varepsilon$ −13), 300 (−11), 284 (−4), 267 (−6) nm; elemental analysis calcd (%) for $C_{52}H_{52}N_2O_2$ C 84.75, H 7.11, N 3.80; found C 84.60, H 7.05, N 3.78.

Preparation of 8a [Z = *n*Bu]. To a solution of **7**[16] (955 mg, 7.57 mmol) and **15a** (6.18 g, 16.7 mmol) in Et_3N (62 mL) were added $PdCl_2(PPh_3)_2$ (0.58 g, 0.83 mmol) and CuI (0.32 g, 1.7 mmol) under an argon atmosphere, and the mixture was stirred at 40 °C for 16 h. After removal of a solid by filtration through a Celite pad, the filtrate was concentrated and dissolved in chloroform. The solution was washed with water and brine, dried over $MgSO_4$, and then purified by column chromatography on SiO_2 (chloroform) to give **8a** (4.64 g) as a brown oil in 100% yield. An analytical sample was obtained as a colorless oil by further purification through GPC (chloroform, detected by UV 254 nm and RI).

*Data of **8a** [Z = nBu]:* ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ = 7.60 (4H, d, *J* = 8.4 Hz), 7.59 (2H, dd, *J* = 3.6, 5.6 Hz),[8] 7.37 (2H, dd, *J* = 3.6, 5.6 Hz),[8] 7.19 (4H, d, *J* = 8.4 Hz), 3.74 (4H, t, *J* = 7.6 Hz), 1.55 (4H, quin, *J* = 7.6 Hz), 1.34 (4H, sext, *J* = 7.6 Hz), 0.91 (6H, t, *J* = 7.6 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.5 (*C*(=O)CF_3), 139.0, 132.5, 131.9, 128.5, 128.5, 125.4, 124.2, 116.4 (CF_3), 92.2, 89.9, 51.6, 28.9, 19.8, 13.6 ppm; IR (neat) 3060, 2961, 2938, 2875, 2221, 1697, 1602, 1510 cm^{-1}; FD-LRMS *m*/*z* (%) 614.17 (8) $[M + 2]^+$, 613.17 (38) $[M + 1]^+$, 612.17 (100) $[M]^+$; elemental analysis calcd (%) for $C_{34}H_{30}F_6N_2O_2$ C 66.66, H 4.94, N 4.57; found C 66.63, H 4.84, N 4.44.

Preparation of 8b [Z = (*R*)-C*HMe(cHex)]. To a solution of **7**[16] (2.09 g, 16.6 mmol) and **15b** (15.5 g, 36.5 mmol) in Et_3N (135 mL) were added $PdCl_2(PPh_3)_2$ (1.28 g, 1.83 mmol) and CuI (0.69 g, 3.6 mmol) under an argon atmosphere, and the mixture was stirred at 40 °C for 22 h. After removal of a solid by filtration through a Celite pad, the filtrate was concentrated and dissolved in chloroform. The solution was washed with water and brine, dried over $MgSO_4$, and then purified by column chromatography on SiO_2 (4:1 chloroform/hexane) to give **8b** (10.1 g) as a dark orange amorphous solid in 85% yield. An analytical sample was obtained as a white solid by further purification through GPC.

*Data of **8b** [Z = (R)-C*HMe(cHex)]:* mp 70.0−71.0 °C; $[\alpha]_D^{26}$ = −31.0 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ = 7.61−7.58 (4H, br), 7.59 (2H, dd, *J* = 3.3, 5.7 Hz), 7.37 (2H, dd, *J* = 3.3, 5.7 Hz),[8] 7.16 (4H, br d), 4.42 (2H, dq, *J* = 6.9, 10.2 Hz), 1.97 (2H, br d), 1.86−1.58 (8H, br m), 1.51−1.33 (2H, br m), 1.30−0.83 (10H, br m), 1.12 (6H, *d*, *J* = 6.9 Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.8 (*C*(=O)CF_3), 136.0, 132.0, 131.9, 130.8, 129.5, 128.5, 125.4, 124.3, 116.4 (CF_3), 92.3, 90.0, 59.8, 40.3, 30.7, 29.7, 26.1, 25.9, 25.8, 16.3 ppm; IR (KBr) 3059, 2981, 2932, 2853, 2221, 1694, 1602, 1510 cm^{-1}; FD-LRMS *m*/*z* (%) 723.3 (4) $[M + 3]^+$, 722.3 (15) $[M + 2]^+$, 721.3 (50) $[M + 1]^+$, 720.3 (100) $[M]^+$; elemental analysis calcd (%) for $C_{42}H_{42}F_6N_2O_2$ C 69.99, H 5.87, N 3.89; found C 69.70, H 5.80, N 3.88.

Preparation of 9b [Z = (*R*)-C*HMe(cHex)]. To a solution of **14b**[3b] (1.69 g, 5.12 mmol) in Et_3N/THF (1 mL/35 mL) was added terephthaloyl chloride (519 mg, 2.56 mmol), and the mixture was refluxed for 22 h. After removal of the solvent, the residue was purified by column chromatography on SiO_2 (dichloromethane−1:20 ethyl acetate/dichloromethane) to give **9b** (1.42 g) as a white amorphous solid in 70% yield. An analytical sample of **9b** was obtained as a white solid by washing in refluxed methanol and hexane, followed by collection through filtration.

*Data of **9b** [Z = (R)-C*HMe(cHex)]:* mp 173.5−175.0 °C; $[\alpha]_D^{25}$ = −113.0 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ =

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7.51 (4H, br d), 7.01 (4H, br s), 6.63 (4H, br d), 4.43 (2H, br s), 2.06 (2H, br d), 1.83−1.52 (10H, br m), 1.33−1.06 (8H, br m), 1.11 (6H, d, J = 7.2 Hz), 1.04−0.89 (2H, br m) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 169.9, 141.0, 137.9, 137.7, 131.3, 127.7, 92.2, 58.8, 41.3, 30.7, 30.3, 26.2, 26.0, 25.9, 16.7 ppm; IR (KBr) 3055, 2928, 2849, 1646, 1581, 1504, 1483 cm^{-1}; FD-LRMS m/z (%) 791.14 (2) [M + 3]$^+$, 790.14 (9) [M + 2]$^+$, 789.13 (42) [M + 1]$^+$, 788.13 (100) [M]$^+$; elemental analysis calcd (%) for $C_{36}H_{42}I_2N_2O_2\cdot(hexane)_{1/6}$ C 55.35, H 5.57, N 3.49; found C 55.18, H 5.30, N 3.24.

Preparation of 11. To a solution of **10′**[3c] (111 mg, 0.232 mmol), which was obtained by deprotection of TMS in **10**,[3c] and **16**[27] (153 mg, 0.510 mmol) in Et_3N/THF (5 mL/5 mL) were added $Pd(PPh_3)_4$ (54 mg, 0.047 mmol) and CuI (9 mg, 0.05 mmol) under an argon atmosphere, and the mixture was stirred at 55 °C for 18 h. The reaction mixture was diluted with chloroform, washed with water and brine, dried over $MgSO_4$, and then purified by column chromatography on SiO_2 (1:10 ethyl acetate/chloroform) to give **11** (166 mg) as a pale yellow solid in 87% yield. An analytical sample was obtained as a white solid by further purification through GPC.

*Data of **11**:* mp 183.0−184.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ = 7.50−7.47 (2H × 2, m), 7.38 (4H, d, J = 8.4 Hz), 7.27−7.25 (2H × 2, m), 7.10 (4H, s), 6.90 (4H, d, J = 8.4 Hz), 3.87 (4H, t, J = 7.6 Hz), 1.56 (4H, br quin), 1.33 (4H, sext, J = 7.6 Hz), 0.89 (6H, t, J = 7.6 Hz), 0.25 (18H, s) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 169.2, 143.1, 137.1, 132.4, 132.3, 131.7, 128.2. 128.2, 128.0, 127.5, 125.7, 125.6, 121.7, 103.4, 98.7, 92.4, 89.2, 50.1, 29.8, 20.1, 13.8, 0.0 ppm; IR (KBr) 3058, 2959, 2926, 2870, 2221, 2152, 1634, 1603, 1563, 1511 cm^{-1}; FD-LRMS m/z (%) 824.36 (3) [M + 4]$^+$, 823.36 (11) [M + 3]$^+$, 822.35 (34) [M + 2]$^+$, 821.35 (73) [M + 1]$^+$, 820.35 (100) [M]$^+$; elemental analysis calcd (%) for $C_{54}H_{56}N_2O_2Si_2$ C 78.98, H 6.87, N 3.41; found C 78.72, H 6.85, N 3.34.

Preparation of 12. Under an argon atomosphere, a mixture of **11** (396 mg, 0.482 mmol), THF (10 mL), MeOH (10 mL), and K_2CO_3 (133 mg, 0.964 mmol) was stirred at room temperature for 30 min and then diluted with dichloromethane. The diluted solution was washed with water and brine and then dried over $MgSO_4$. After removal of a solid by filtration, the filtrate was concentrated to give **11′** (324 mg) as a yellow solid in 99% yield, which was subjected to the following reaction without purification [deprotection of TMS].

To a solution of **11′** (324 mg, 0.479 mmol) and **17**[3b] (588 mg, 1.20 mmol) in Et_3N/THF (10 mL/10 mL) were added $Pd(PPh_3)_4$ (111 mg, 96.1 μmol) and CuI (18 mg, 95 μmol) under an argon atmosphere, and the mixture was stirred at 55 °C for 14 h. The reaction mixture was diluted with chloroform, washed with water and brine, dried over $MgSO_4$, and then purified by column chromatography on SiO_2 (chloroform−ethyl acetate/chloroform) to give **12** (648 mg) as a brown amorphous solid in 96% yield. An analytical sample was obtained as a yellow solid by further purification through GPC.

*Data of **12**:* mp 126.0−127.5 °C; $[\alpha]_D^{24}$ = −49.8 (c = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ = 7.82 (4H, br d), 7.55−7.47 (2H × 2, br m), 7.43−7.25 (12H, br m), 7.36 (4H, d, J = 8.4 Hz), 7.13 (4H, s), 6.99 (4H, br d), 6.91 (4H, d, J = 8.4 Hz), 4.50 (2H, br s), 3.87 (4H, br t), 3.84 (6H, s), 2.15 (2H, br d), 1.88−1.63 (10H, br m), 1.57 (4H, br quin), 1.38−1.11 (8H, br m), 1.33 (4H, sext, J = 7.6 Hz), 1.22 (6H, d, J = 7.2 Hz), 1.09−0.95 (2H, br m), 0.89 (6H, t, J = 7.6 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 169.7, 169.1, 166.1, 142.9, 141.4, 141.2, 137.1, 132.9, 132.2, 132.0, 131.9, 131.9, 130.3, 129.4, 128.9, 128.2, 128.1, 128.0, 127.4, 125.1, 125.0, 122.0, 121.4, 92.4, 92.3, 89.3, 89.1, 59.2, 52.0, 49.9, 41.2, 30.7, 30.2, 29.7, 26.1, 25.9, 25.9, 20.0, 16.7, 13.6 ppm; IR (KBr) 3052, 2929, 2851, 2216, 1725, 1649, 1600, 1559, 1510 cm^{-1}; FD-LRMS m/z (%) 1406.62 (7) [M + 4]$^+$, 1405.62 (22) [M + 3]$^+$, 1404.61 (56) [M + 2]$^+$, 1403.61 (100) [M + 1]$^+$, 1402.61 (95) [M]$^+$; FD-HRMS m/z calcd for $C_{94}H_{90}N_4O_8$ 1402.67586 [M]$^+$; found 1402.67838; elemental analysis calcd (%) for $C_{94}H_{90}N_4O_8$ C 80.43, H 6.46, N 3.99; found C 77.97, H 6.25, N 3.82.

Preparation of 13. To a solution of **12** (252 mg, 0.179 mmol) in THF/MeOH (3.6 mL/12 mL) was added a solution of $LiOH\cdot H_2O$ (38 mg, 0.91 mmol) in water (1.2 mL), and the mixture was stirred at room temperature for 5 h. The mixture was diluted with ethyl acetate, acidified with 1 N HCl aq, and washed with brine. The organic layer was dried over $MgSO_4$ and then concentrated to give **13** (238 mg) as a yellow solid in 96% yield. The product was subjected to the next reaction without purification.

Preparation of 15a [Z = *n*Bu]. To a solution of **14a**[28] (4.95 g, 18.0 mmol) and Et_3N (3.81 mL, 27.4 mmol) in CH_2Cl_2 (130 mL) was added TFAA (3.35 mL, 24.0 mmol) at room temperature, and the mixture was stirred for 2 h and then diluted with dichloromethane. The diluted solution was washed with saturated $NaHCO_3$ aq, dried over $MgSO_4$, and then purified by column chromatography on SiO_2 (1:1 dichloromethane/hexane) to give **15a** (6.62 g) as a pale yellow oil in 99% yield. An analytical sample was obtained as a colorless oil by further purification through GPC.

*Data of **15a** [Z = nBu]:* ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ = 7.77 (2H, d, J = 8.8 Hz),[8] 6.96 (2H, d, J = 8.8 Hz), 3.70 (2H, t, J = 7.6 Hz), 1.53 (2H, quin, J = 7.6 Hz), 1.32 (2H, sext, J = 7.6 Hz), 0.91 (3H, t, J = 7.6 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.1 (C(=O)CF_3), 138.6, 138.4, 130.1, 116.1 (CF_3), 94.4, 51.3, 28.6, 19.6, 13.4 ppm; IR (neat) 3065, 2961, 2934, 2874, 1698, 1584, 1486 cm^{-1}; FD-LRMS m/z (%) 371.98 (19) [M + 1]$^+$, 370.97 (100) [M]$^+$; elemental analysis calcd (%) for $C_{12}H_{13}F_3INO$ C 38.83, H 3.53, N 3.77; found C 38.74, H 3.34, N 3.81.

Preparation of 15b [Z = (*R*)-C*HMe(cHex)]. To a solution of **14b**[3b] (11.05 g, 33.57 mmol) and Et_3N (7.1 mL, 51 mmol) in CH_2Cl_2 (250 mL) was added TFAA (6.2 mL, 44 mmol) at room temperature, and the mixture was stirred for 1 h and then diluted with dichloromethane. The diluted solution was washed with saturated $NaHCO_3$ aq, dried over $MgSO_4$, and then purified by column chromatography on SiO_2 (1:1 dichloromethane/hexane) and recrystallization from ethanol to give **15b** (13.63 g) as a white solid in 96% yield.

*Data of **15b** [Z = (R)-CH*Me(cHex)]:* mp 83.5−84.5 °C; $[\alpha]_D^{25}$ = −27.5 (c = 1.0 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ = 7.75 (2H, br d), 6.92 (2H, br d), 4.41 (1H, dq, J = 6.8, 10.2 Hz), 1.94 (1H, br d), 1.85−1.59 (4H, br m), 1.45−1.33 (1H, br m), 1.27−1.06 (4H, br m), 1.09 (3H, d, J = 6.8 Hz), 1.01−0.88 (1H, br m) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 156.7 (C(=O)CF_3), 138.2, 138.0, 135.7, 132.5, 131.2, 116.4 (CF_3), 95.0, 59.5, 40.2, 30.6, 29.7, 26.0, 25.9, 25.7, 16.3 ppm; IR (KBr) 3097, 2987, 2935, 2845, 1685, 1577, 1486 cm^{-1}; FD-LRMS m/z (%) 427.1 (2) [M + 2]$^+$, 426.1 (19) [M + 1]$^+$, 425.0 (100) [M]$^+$; elemental analysis calcd (%) for $C_{16}H_{19}F_3INO$ C 45.19, H 4.50, N 3.29; found C 45.06, H 4.28, N 3.04.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Supplementary figures (NMR/CD spectra in the presence/absence of a guest and energy-minimized structures for **1a′**), supplementary scheme, and ^{1}H/^{13}C NMR spectra of new compounds (**1**, **3**, **4b**, **6b**, **8**, **9b**, **11**, **12**, and **15**). This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Authors

*Tel: (+)81-11-706-3396. Fax: (+)81-11-706-2714. E-mail: katoono@sci.hokudai.ac.jp. E-mail:

*Tel: (+)81-11-706-3396. Fax: (+)81-11-706-2714. E-mail: tak@sci.hokudai.ac.jp

Notes

The authors declare no competing financial interest.

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