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Chiroptical Control in Helical Receptor–Anion Complexes

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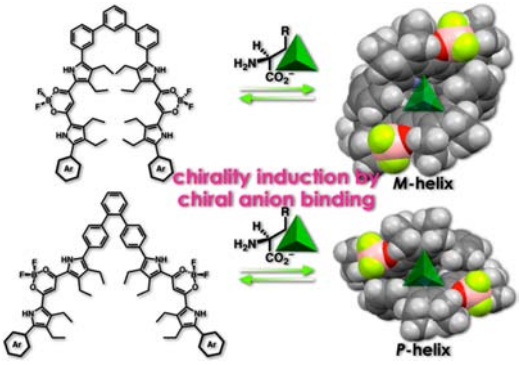
ABSTRACT



Dimers of appropriately arranged anion-responsive π-conjugated moieties form helical structures by interaction with chiral anions. Terphenyl-bridged dimers of dipyrrolyldiketone boron complexes show chirality induced by binding L-amino acid anions, as observed by circular dichroism (CD) and circularly polarized luminescence (CPL). The preferred configurations of helical structures depend on the geometries of the terphenyl spacer moieties.

Chirality can be induced by asymmetric factors[1] and also infrequently by symmetrical breaking[2] even from achiral molecules. As observed in biotic systems, wherein DNA and proteins exhibit folding structures correlated with their surrounding conditions,[3] it is important to design and synthesize the molecules forming helical structures that are responsive to noncovalent interactions with guest species.[4] In particular, some anions including chiral species are useful to construct helical structures.[5] Control of helical structures and their resulting chiroptical properties have attracted considerable attention for fabricating useful electronic and optical materials.[6] Arrangement of multiple π-conjugated moieties as chromophores and fluorophores in helical structures can exhibit various

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(1) Selected examples of chirality sensing with achiral indicators: (a) Shundo, A.; Labuta, J.; Hill, J. P.; Ishihara, S.; Ariga, K. *J. Am. Chem. Soc.* **2009**, *131*, 9494–9495. (b) Labuta, J.; Ishihara, S.; Shundo, A.; Arai, S.; Takeoka, S.; Ariga, K.; Hill, J. P. *Chem.—Eur. J.* **2011**, *17*, 3558–3561.

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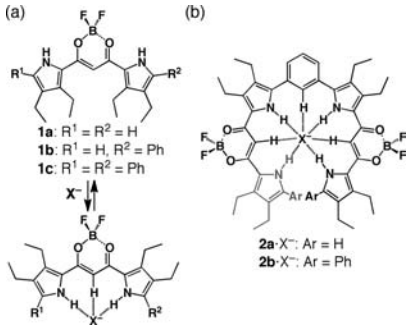

Figure 1. (a) Anion receptors **1a**–**c** and their anion-binding mode and (b) schematic halide-driven helical structures of **2a**,**b** (drawn in *M*-forms).

spectroscopic features according to their relative locations. A fascinating chiroptical property is circularly polarized luminescence (CPL) that can be observed in chiral emissive species. CPL is essential for biological probing and display technologies because it provides two pieces of information derived from left- and right-handed circularly polarized photons.[7] Achievement of desired chiroptically active systems that can be modulated by anions requires (i) introduction of emissive π-conjugated linear motifs that show affinities for anions and (ii) appropriate arrangement of multiple anion-responsive units. A combination of these factors seems simple, but it is not easy as seen in a few examples of helical structures containing multiple anion-responsive emissive moieties.

Dipyrrolyldiketone boron complexes (e.g., **1a**–**c**, Figure 1a) are π-conjugated anion-responsive linear motifs and show a highly emissive property that can be controlled by anion binding.[8] For example, *meta*-phenylene-bridged dimers **2a**,**b** (Figure 1b) effectively bind small anions such as halides, resulting in the emergence of CPL from the halide-driven helices, whose chirality was induced by ion pairing with chiral cations.[8d] In contrast to

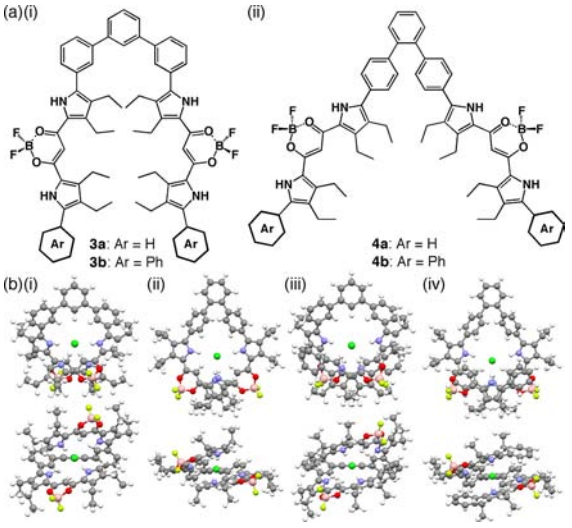

Figure 2. (a) Anion receptor dimers (i) **3a**,**b** and (ii) **4a**,**b** and (b) DFT-optimized structures (top and side view) of (i) $\mathbf{3a}^{M}\cdot Cl^{-}$, (ii) $\mathbf{4a}^{P}\cdot Cl^{-}$, (iii) $\mathbf{3b}^{M}\cdot Cl^{-}$, and (iv) $\mathbf{4b}^{P}\cdot Cl^{-}$.

halides, binding of anionic chiral auxiliaries to induce asymmetric helical structures needs larger anion-binding cavities than those of the dimers bridged by a *meta*-phenylene spacer. Candidates for the spacers between two receptor units are acute-angled terphenyl groups such as *meta-meta-meta*- and *para-ortho-para*-linked ones. They can make suitable arrangements of the receptor units and binding cavities for anionic species that possesses a point chirality.

Essential key intermediate species, *meta-meta-meta*- and *para-ortho-para*-linked terphenylbisboronic acids **3′** and **4′**, respectively, were prepared by Suzuki coupling of differentially protected benzenediboronic acids[9] and diiodobenzenes. Subsequent coupling reactions of **3′**/**4′** and an α-iodo-β-tetraethyl-substituted receptor[8a] provided the corresponding terphenyl-bridged dimers **3a** and **4a** (Figure 2a) in 23% and 21% yields, respectively. In a similar way, Suzuki coupling of **3′**/**4′** and an α-phenyl-substituted α′-iodo-β-tetraethyl receptor[8e] gave α-phenyl-substituted **3b** and **4b** in 12% and 16% yields, respectively. UV/vis absorption maxima (λ_{max}) of **3a** and **4a** in CH_2Cl_2 were 489 and 479 nm, respectively, and those of both **3b** and **4b** were 502 nm. These observations suggested no significant π-extension compared to the corresponding monomers **1b** (476 nm) and **1c** (499 nm),[8a] owing to the distortion of terphenyl moieties in **3a**,**b** and **4a**,**b**. Furthermore, **3a**,**b** and **4a**,**b** showed fluorescence emission (with emission quantum yields Φ_F) at 508 (0.82), 522 (0.77), 536 (0.81), and 547 (0.93) nm, respectively, in CH_2Cl_2. The exact structure of **4b** was elucidated by single-crystal X-ray analysis,[10] indicating the contribution of N–H···F hydrogen bonding to the packing structure.

(5) Selected examples for anion-assisted helical structures: (a) Sánchez-Quesada, J.; Seel, C.; Prados, P.; de Mendoza, J. *J. Am. Chem. Soc.* **1996**, *118*, 277–278. (b) Chang, K.-J.; Kang, B.-N.; Lee, M.-H.; Jeong, K.-S. *J. Am. Chem. Soc.* **2005**, *127*, 12214–12215. (c) Meudtner, R. M.; Hecht, S. *Angew. Chem., Int. Ed.* **2008**, *47*, 4926–4930. (d) Hua, Y.; Flood, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 12838–12840. (e) Suk, J.-m.; Naidu, V. R.; Liu, X.; Lah, M. S.; Jeong, K.-S. *J. Am. Chem. Soc.* **2011**, *133*, 13938–13941.

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(7) Selected reviews of CPL: (a) *Comprehensive Chiroptical Spectroscopy*; Berova, N., Polavarapu, P. L., Nakanishi, K., Woody, R. W., Eds.; John Wiley & Sons: NJ, 2012. (b) Riehl, J. P.; Richardson, F. S. *Chem. Rev.* **1986**, *86*, 1–14. (c) Carr, R. C.; Evans, N. H.; Parker, D. *Chem. Soc. Rev.* **2012**, *41*, 7673–7686. (d) Maeda, H.; Bando, Y. *Pure Appl. Chem.* **2013**, *85*, 1967–1978.

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(10) See the details in the Supporting Information.

Formation of helical structures of **3a**,**b** and **4a**,**b** by anion binding was predicted by DFT calculations (Figure 2b).[11] In fact, anion-binding behaviors of **3a** and **4a** were suggested by ^{1}H NMR spectral changes upon the addition of 1 equiv of Cl^- as a tetrabutylammonium (TBA) salt in CD_2Cl_2 (1 mM) at −50 °C. ^{1}H NMR signals of two kinds of pyrrole NH, one terphenyl inner CH, and one receptor-bridging CH in **3a** at 9.54, 9.43, 7.84, and 6.43 ppm were shifted to 11.66, 11.06, 9.15, and 7.78 ppm, respectively, suggesting the formation of a [1 + 1]-type anion-binding helical structure. The proximal arrangement of the terminal α-CH (6.96 ppm) resulted in an upfield-shifted signal (5.76 ppm) by Cl^- binding. **4a** showed similar spectral changes by Cl^- binding. The addition of $CH_3CO_2^-$ as a TBA salt resulted in the formation of [1 + 1]-type complexes, as observed in the similar shifts of the corresponding signals. The formation of [1 + 1]-type anion complexes by **3a** and **4a** was also supported by ROESY. Formation of a [1 + 1]-type anion-binding helical complex of α-phenyl **3b** and **4b** was also examined by ^{1}H NMR, wherein the signals of terminal α-phenyl moieties were shifted upfield, due to the proximal arrangement of phenyl rings by Cl^- binding.

Anion-binding constants (K_a) of **3a**,**b** and **4a**,**b** at rt were estimated by UV/vis absorption spectral changes of diluted CH_2Cl_2 solutions (0.5−5 μM) upon the addition of TBA salts. In the case of α-unsubstituted receptor dimers, the K_a values for Cl^-, Br^-, and $CH_3CO_2^-$ binding were 7.3×10^6, 2.7×10^5, and 1.3×10^7 M^{-1}, respectively, for **3a** and 1.4×10^6, 2.7×10^5, and 2.7×10^6 M^{-1}, respectively, for **4a**. These K_a values are much higher than those for **1b** (4200, 600, and 9.8×10^4 M^{-1}, respectively), but the two receptor units in **3a** and **4a** do not work cooperatively for anion binding because the values of ln K_a(**3a**) and ln K_a(**4a**) are comparable or slightly smaller than 2 × ln K_a(**1b**). Unlike **3a**, the dimer **4a** showed drastic UV/vis spectral changes by anion binding, wherein λ_{max} at 479 nm was shifted to 461 nm by Cl^- binding, due to the remarkable change in the exciton coupling between receptor chromophore units in **4a**. Anion-binding affinities were affected by the terminal α-phenyl substituents, as observed in the K_a values for Cl^- of 6.0×10^4 and 4.9×10^5 M^{-1} for **3b** and **4b**, respectively. UV/vis absorption spectral changes of **3a**,**b** and **4a**,**b**, as detected by stopped-flow measurements, exhibited time-resolved anion-driven conformational changes with kinetic parameters k of $(3.1–9.9) \times 10^6$ M^{-1} s^{-1} for [1 + 1] binding with Cl^-.

Chirality induced by interactions with chiral anions can be achieved even with the addition of a small amount of salts to the solutions of receptor dimers. The chirality induction for the dimers **3b** and **4a**,**b** (Figure 3) by the L-phenylalanine anion (L-Phe^-), with K_a values of 8.2×10^4, 2.0×10^7, and 6.0×10^5 M^{-1}, respectively, were examined by circular dichroism (CD) spectral changes. The addition of L-Phe^- as a TBA salt to the CH_2Cl_2 solution of **3b** (5 μM) enhanced positive and negative Cotton effects at 509 and 478 nm, respectively (Figure 4a). In this study,

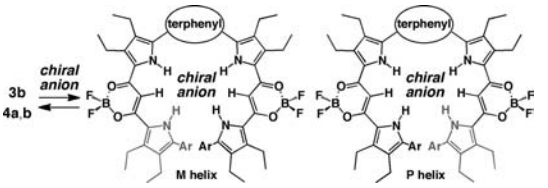

Figure 3. Chiral-anion-driven formation of helical structures of terphenyl-bridged dimers as unequivalent amounts of *M*- and *P*-type diastereomers.

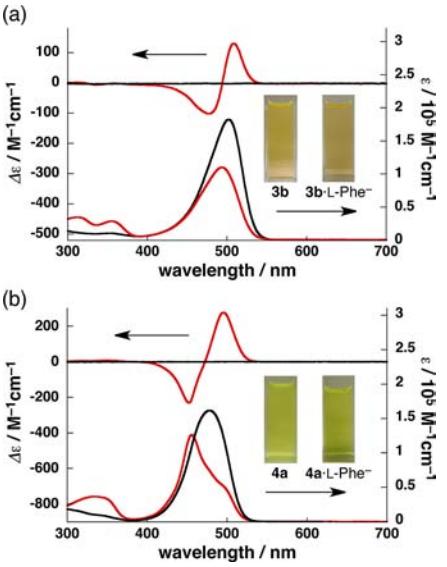

Figure 4. Spectral changes for (a) **3b** and (b) **4a** (5 mM in CH_2Cl_2 at 20 °C) in CD (top) and UV/vis absorption as a reference (bottom) upon addition of L-Phe^- as a TBA salt (10 equiv for **3b**, 2 equiv for **4a**) (anion-free dimers: black line; L-Phe^- complexes: red line) along with corresponding solution photographs (insets).

L-Phe^- was used as a representative amino acid anion after preliminary examinations of other amino acids. Under the same conditions, **4a** showed enhanced positive and negative Cotton effects at 495 and 452 nm, respectively (Figure 4b). In an analogous fashion, **4b** showed positive and negative CD signals at 522 and 480 nm, respectively. D-Phe^- binding exhibited opposite CD patterns. In contrast to **3b** and **4a**,**b**, L-Phe^- binding by **3a** showed very small CD spectral changes. The CD spectral changes suggested the predominant formation of either the *M*- or *P*-type helical configuration by binding the amino acid anion. The anisotropic factors g_{abs}, which were defined as $\Delta\varepsilon/\varepsilon$, of L-$Phe^-$ complexes of **3b** and **4a**,**b** were estimated to be 1.6×10^{-3} (502 nm), 7.0×10^{-3} (495 nm), and 5.2×10^{-3} (522 nm), respectively, at 20 °C. At −50 °C, the L-Phe^- complexes of **3b** and **4a**,**b** showed enhanced g_{abs} values of 1.9×10^{-3} (513 nm), 7.5×10^{-3} (500 nm), and 5.5×10^{-3} (524 nm), respectively. The enhancement of the g_{abs} values at low temperatures can be ascribable to (i) the more tightly

(11) (a) Frisch, M. J., et al. *Gaussian 03*, revision C.01; Gaussian, Inc.: Wallingford, CT, 2004. (b) Frisch, M. J., et al. *Gaussian 09*, revision B.01; Gaussian, Inc.: Wallingford, CT, 2009.

curled helical structures of the receptor−anion complexes and/or (ii) the changes in the ratios of *M*- and *P*-helices. Examination of the chirality induced in **4a** by other L-amino acid anions provided g_{abs} values of $(2.5-7.0) \times 10^{-3}$.

Theoretical studies such as ZINDO calculations of **4a**,**b** as their helical model structures[11] suggested that the *P*-type helices were predominantly induced by the interaction with L-amino acid anions. On the other hand, in the case of **3a**,**b**, binding with L-Phe$^-$ resulted in similar CD patterns, which were surprisingly ascribable to the preferred formation of *M*-type helices by ZINDO. These observations suggest that a point chirality of L-Phe$^-$ could induce opposite helical chiralities according to the different geometries of the terphenyl spacer units. Furthermore, L-Phe$^-$ complexes of **2a**,**b** showed CD patterns with first negative and second positive Cotton effects by the formation of *M*-helices, in sharp contrast to the *P*-helices of **4a**,**b**.[12] It is noteworthy that, in contrast to **2a**,**b** and **4a**,**b**, the empirical assignments of the predominant helical configurations of **3a**,**b** by the observed CD patterns may not be consistent with those suggested by the theoretical study. This situation is similar to a biflavone system reported by Harada et al.: the biflavone with *M*-helicity exhibited a plus-to-minus sequence in CD intensity in ascending energy terms.[13]

^{1}H NMR of **4a**,**b** in the presence of 1 equiv of L-Phe$^-$ as a TBA salt in CD_2Cl_2 (1 mM) at −50 °C showed a single set of signals of two pyrrole NH, one receptor-bridging CH, and one α-CH similar to the chemical shifts by Cl$^-$ binding.[14] These observations may suggest the possibilities of (i) almost the same chemical shifts corresponding to both *M*- and *P*-type diastereomers, (ii) fast interconversion between *M*- and *P*-type helices, or (iii) the homochirality of *M*- or *P*-type helices. In any case, it is noteworthy that the top and bottom parts of the helices **4a**·L-Phe$^-$ and **4b**·L-Phe$^-$ cannot be distinguished by ^{1}H NMR.

Fluorescence emission can also be modulated by chiral anion binding. For example, **4a**,**b** in CH_2Cl_2 (5 μM) at 20 °C exhibited fluorescence emission with a maximum (λ_{em}) at 521 and 546 nm, respectively, in the presence of L-Phe$^-$ as a TBA salt (2.0 and 2.5 equiv, respectively) by excitation at 479 and 502 nm, respectively. Emission quantum yields (Φ_F) of **4a**,**b** as L-Phe$^-$ complexes were estimated to be 0.68 and 0.62, respectively. Furthermore, **4a**,**b** in CH_2Cl_2 (5 μM) exhibited CPL, whose anisotropic factors g_{lum} (defined as $\Delta I/I = 2(I_{left} - I_{right})/(I_{left} + I_{right})$, wherein I_{left} and I_{right} are the intensities of left- and right-handed polarized luminescence) at the emission maxima were 4.0×10^{-4} (528 nm) and 7.0×10^{-4} (553 nm), respectively, at −50 °C (Figure 5), whereas that of **3b** was 2.5×10^{-4} (536 nm). To the best of our knowledge, this is the first example of CPL from π-conjugated moieties induced by a chiral anion. As observed from these results, point chirality in the anion induced the chirality of helical structures, resulting in attractive chiroptical properties.

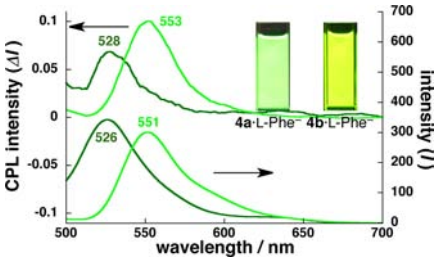

Figure 5. CPL (top) and fluorescence spectra (bottom) for **4a**,**b** (5 mM in CH_2Cl_2 at −50 °C) excited at 480 nm in the presence of L-Phe$^-$ as a TBA salt (2 equiv) (**4a**·L-Phe$^-$: green line; **4b**·L-Phe$^-$: yellow-green line) along with corresponding solution photographs (insets, under $UV_{365\ nm}$, 20 °C).

In summary, terphenyl-bridged dimers of emissive anion-responsive molecules showed chirality induced by binding L-amino acid anions, as observed in CD and CPL spectra. The preferred configuration of *M*- or *P*-type helical structures by binding the chiral anions could depend on the geometries of the terphenyl spacer moieties. The balance between the rigidity and flexibility of the terphenyl units is very important for achieving various helical modes based on the same point chirality. It is noteworthy that introduction of the spacer units gives the basis for the design of promising helical structures with chromophores and fluorophores in desired positions. Furthermore, an improved feature of this study is the CPL induction of prochiral species by a small amount of chiral auxiliary even in micromolar-scale concentrations. Considering the fairly concise synthetic route and the properties depending on chiral guest species, we also see the advantage by using achiral emissive molecular systems as the species that exhibit CPL. Based on this study, stimuli-responsive switching of the geometries of spacing units would provide chiroptically controllable molecular devices based on the anion-responsive π-conjugated moieties.

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Supporting Information Available. Synthetic procedures, theoretical studies, anion-binding properties, a CIF file, and complete ref 11. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.

(12) TD-DFT calculations also provided identical assignment of the preferred helicities. On the other hand, the exciton chirality method could be applied to **2a**,**b** and **4a**,**b**, but the chiralities of **3a**,**b** could not be determined by this method. The point dipole approximation may not be applicable to **3a**,**b** because the dihedral angles of two transition electric dipole moments are almost perpendicular.

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(14) Complicated anion-binding behaviors of **3b** drove us to investigate the anion-binding behaviors in detail only under diluted conditions.