Inorganic Chemistry
Article

Inorg. Chem. **2009**, *48*, 11921–11928 **11921**
DOI: 10.1021/ic901496s

Asymmetric Twisting and Chirality Probing Properties of Quadruple-Stranded Helicates: Coordination Versatility and Chirality Response of Na^+, Ca^{2+}, and La^{3+} Complexes with Octadentate Cyclen Ligand

Hitomi Misaki, Hiroyuki Miyake, Satoshi Shinoda, and Hiroshi Tsukube*

Department of Chemistry, Graduate School of Science, Osaka City University, Sugimoto, Sumiyoshi-ku, Osaka 558-8585, Japan

Received July 28, 2009

A series of Na^+, Ca^{2+}, and La^{3+} complexes with octadentate cyclen ligand were prepared and structurally characterized in the crystal and solution states. The employed cyclen ligand formed 6-, 7-, and 9-coordinated, crystalline complexes with Na^+, Ca^{2+}, and La^{3+} cations, respectively, in which the parent cyclen ring and quinoline-functionalized side arms were cooperatively coordinated. These three metal cations provided the quadruple-stranded helicates in CH_3CN-C_2H_5OH solutions. In each helicate, four quinoline-functionalized side arms were arranged in a propeller-like fashion to yield an enantiomer-pair of Δ- and Λ- forms. Addition of a chiral anion to the cyclen$-Ca^{2+}$ complex solution induced circular dichroism (CD) signals around the quinoline chromophore, which indicated that 1:1 diastereomeric complexation between the Ca^{2+} complex and the chiral anion imposed the stereoisomeric equilibrium. The intensity and sign of the observed CD signal were significantly dependent on both the absolute configuration and the enantiomeric purity of the added anion. The corresponding cyclen$-Na^+$ complex rarely induced a CD signal, while the La^{3+} complex exhibited complicated anion-induced spectral changes. Thus, the octadentate cyclen ligand employed was demonstrated to form the quadruple-stranded helicate with the Ca^{2+} cation in the solution state, which functioned as an effective CD probe for the determination of enantiomer excess (ee%) of the chiral anions.

Introduction

Helical metal complexes, "helicates", are one of the most fundamental motifs in inorganic chemistry, in addition to synthetic, material, supramolecular, and nanoscale chemistry.[1] When a stereogenic element on a coordinating unit, bridging moiety, chiral template, or in the environment is combined with an inert metal center, the resulting helicate is composed of diastereomers that can be resolved by recrystallization or related separation techniques.[2] Interconversion between these stereoisomers rarely occurs, so that helicates containing inert metal centers have severe limitations in the development of dynamic chirality induction and switching systems. In contrast, helicates containing labile metal centers usually provide dynamic equilibrium mixtures of the stereoisomers, but some chiral ligands and counter-anions have been reported to define the sense of the dynamic helicates.[3−6] Lisowski et al. reported helicity inversion of lanthanide(III) complexes with chiral macrocyclic ligands.[4] Kuroda et al.[5] and we[6] recently presented chiral helicates including Co(II) centers, and some of these have exhibited further time-programmed helicity inversion. These studies emphasize the

---

*To whom correspondence should be addressed. E-mail: tsukube@sci.osaka-cu.ac.jp.

(1) (a) Rigault, S.; Piguet, C.; Bernardinelli, G.; Hopfgartner, G. *Angew. Chem., Int. Ed.* **1998**, *37*, 169. (b) Albrecht, M. *Chem. Rev.* **2001**, *101*, 3457. (c) Nabeshima, T.; Hashiguchi, A.; Saiki, T.; Akine, S. *Angew. Chem., Int. Ed.* **2002**, *41*, 481. (d) Mamula, O.; von Zelewsky, A. *Coord. Chem. Rev.* **2003**, *242*, 87. (e) Seeber, G.; Tiedemann, B. E. F.; Raymond, K. N. *Top. Curr. Chem.* **2006**, *265*, 147. (f) Lehn, J.-M. *Chem. Soc. Rev.* **2007**, *36*, 151. (g) Saalfrank, R. W.; Maid, H.; Scheurer, A. *Angew. Chem., Int. Ed.* **2008**, *47*, 8794. (h) Haino, T.; Shio, H.; Takano, R.; Fukuzawa, Y. *Chem. Commun.* **2009**, 2481. (i) Warr, R. J.; Willis, A. C.; Wild, S. B. *Inorg. Chem.* **2008**, *47*, 9351. (j) Crassous, J. *Chem. Soc. Rev.* **2009**, *38*, 830.

(2) (a) Lacour, J.; Linder, D. *Chem. Rec.* **2007**, *7*, 275. (b) Amouri, H.; Gruselle, M. *Chirality in Transition Metal Chemistry: Molecules, Supramolecular Assemblies Materials*; John Wiley & Sons: Chichester, 2008.

(3) (a) Pfeiffer, P.; Quehl, K. *Chem. Ber.* **1931**, *64*, 2667. (b) Nordén, B.; Tjerneld, F. *FEBS Lett.* **1976**, *67*, 368. (c) Kirschner, S.; Ahmad, N.; Munir, C.; Pollock, R. J. *Pure Appl. Chem.* **1979**, *51*, 913. (d) Zahn, S.; Canary, J. W. *Science* **2000**, *288*, 1404. (e) Lacour, J.; Jodry, J. J.; Monchaud, D. *Chem. Commun.* **2001**, 2302. (f) Yeh, R. M.; Ziegler, M.; Johnson, D. W.; Terpin, A. J.; Raymond, K. N. *Inorg. Chem.* **2001**, *40*, 2216. (g) Huang, X.; Fujioka, N.; Pescitelli, G.; Koehn, F. E.; Williamson, R. T.; Nakanishi, K.; Berova, N. *J. Am. Chem. Soc.* **2002**, *124*, 10320. (h) Hiraoka, S.; Harano, K.; Tanaka, T.; Shiro, M.; Shionoya, M. *Angew. Chem., Int. Ed.* **2003**, *42*, 5182. (i) Habermehl, N. C.; Angus, P. M.; Kilah, N. L.; Norén, L.; Rae, A. D.; Willis, A. C.; Wild, S. B. *Inorg. Chem.* **2006**, *45*, 1445. (j) Laleu, B.; Bernardinelli, G.; Chauvin, R.; Lacour, J. *J. Org. Chem.* **2006**, *71*, 7412. (k) Winkelmann, O.; Linder, D.; Lacour, J.; Näther, C.; Lüning, U. *Eur. J. Org. Chem.* **2007**, 3687. (l) Bonnot, C.; Chambron, J.-C.; Espinosa, E.; Graff, R. *J. Org. Chem.* **2008**, *73*, 868.

(4) Gregoliński, J.; Lisowski, J. *Angew. Chem., Int. Ed.* **2006**, *45*, 6122.

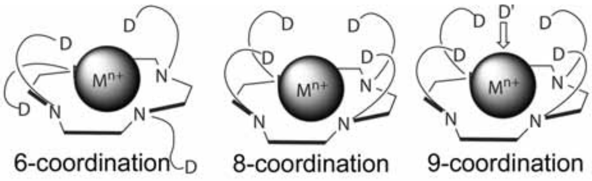
(5) Telfer, S. G.; Kuroda, R. *Chem.—Eur. J.* **2005**, *11*, 57.

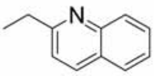
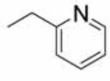
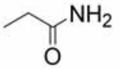
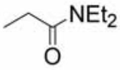
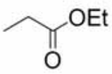
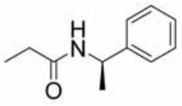
(6) Miyake, H.; Kamon, H.; Miyahara, I.; Sugimoto, H.; Tsukube, H. *J. Am. Chem. Soc.* **2008**, *130*, 792.

promising potential of helicates as dynamic chirotopic devices.

Octadentate cyclen ligands, characterized by a cyclen ring and four metal-ligating side arms, form quadruple-stranded helicates with alkali, alkaline earth, and lanthanide metal cations.[7] Figure 1 lists examples of octadentate cyclen ligands that form the crystalline complexes containing these metal cations. When the cyclen forms complexes with large-sized metal cations, the four ligating side arms stand up in the same direction and are twisted around the metal center in a propeller-like fashion. Wainwright et al., Parker et al., and other researchers have demonstrated that cyclen ligands **3**−**7** afford mostly crystalline, 8-coordinated Na^+ and Ca^{2+} complexes exhibiting Δ- and Λ-stereoisomers,[7d,g,h] while 9-coordinated lanthanide complexes are favored with the aid of external ligands.[7i−k,m,8] Pyridine-armed cyclen **2** provided versatile coordination modes in the crystal state. Nishihara et al. isolated several 9-cooordinated lanthanide complexes,[7e] while we have reported a crystal structure of the 7-coordinated Na^+ complex.[7d] The coordinative pyridine moieties of cyclen **2** cause steric hindrance around the metal center, so that 7- or 9-coordination is sterically preferred to 8-coordination.

In this work, we report the coordination versatility and chirality response of Na^+, Ca^{2+}, and La^{3+} complexes with octadentate cyclen ligand **1**. The introduced quinoline side arm can act as an effective coordination site and an intense chromophore, although this may cause more severe steric hindrance upon coordination than the pyridine-functionalized side arm. Crystal structure determination revealed that cyclen **1** formed 6-, 7-, and 9-coordinated complexes with Na^+, Ca^{2+}, and La^{3+} cations: however, quadruple-stranded helicates were predominantly afforded in the solution state with propeller-like arrangement of the four quinoline moieties. The resulting helicates exist as the racemic mixtures of enantiomers in solution, but addition of an external chiral anion dynamically imposes diastereomeric equilibrium to induce the circular dichroism (CD) signals. Although the observed chirality induction behavior is controlled by the nature of metal center, the cyclen **1**−Ca^{2+} complex forms 1:1 complexes with external chiral anions and functions well as an effective CD chirality probe. The results indicate that further combination of the designed ligand and a functional metal center would afford sophisticated helicates that exhibit dynamic functions.



Ligand	—D	M^{n+}	CN*	Ref
1		Na^+	6	this work
		Ca^{2+}	7	
		La^{3+}	9	
2		Na^+	7	7d
		Tb^{3+}, Nd^{3+}, Eu^{3+}	9	7e
3		Na^+	7,8	7f, 7g
		La^{3+},Tb^{3+}	9	8
4		Ca^{2+}	8	7h
		Pr^{3+}, Eu^{3+} Gd^{3+},Yb^{3+}	9	7i, 7j, 7k
		La^{3+}	10	7l
5		Na^+	8	7d
6		Na^+	8	7d
7		Pr^{3+}, Nd^{3+}, Gd^{3+}, Tb^{3+}, Dy^{3+}, Er^{3+} Yb^{3+}, Lu^{3+}	9	7m

CN*: Coordination number in crystal state.

Figure 1. Coordination modes of crystalline helicates with octadentate cyclens.

Results and Discussion

1. Crystal Structures of Na^+, Ca^{2+}, and La^{3+} Complexes with Cyclen 1.

Cyclen **1** has four cyclen and four quinoline nitrogen atoms that function as an octadentate ligand. The three metal cations examined here have high lability for ligand exchange and similar ionic radii for metal complexation:[9] 1.02−1.18 Å for 6-, 7-, and 8-coordinated Na^+ complexes; 1.06−1.12 Å for 7- and 8-coordinated Ca^{2+} complexes; and 1.16−1.22 Å for 8- and 9-coordinated La^{3+} complexes. Pyridine-functionalized cyclen **2** formed 7-coordinated Na^+ complex and 9-coordinated lanthanide complexes in the crystal state,[7d,e] while other octadentate cyclens **4**−**6** with carbonyl-functionalized side arms formed 8-coordinated complexes with Na^+ and Ca^{2+} cations.[7d,h] Considering the steric bulkiness of the nitrogen-aromatic ring upon metal complexation, cyclen **1** seems to prefer 7- or 9-coordination to 8-coordination.

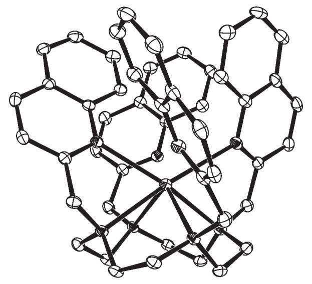
---

(7) (a) Damsyik, A.; Lincoln, S. F.; Wainwright, K. P. *Inorg. Chem.* **2006**, *45*, 9834. (b) Montgomery, C. P.; New, E. J.; Parker, D.; Peacock, R. D. *Chem. Commun.* **2008**, 4261. (c) Michinobu, T.; Shinoda, S.; Nakanishi, T.; Hill, J. P.; Fujii, K.; Player, T. N.; Tsukube, H.; Ariga, K. *J. Am. Chem. Soc.* **2006**, *128*, 14478. (d) Tsukube, H.; Mizutani, Y.; Shinoda, S.; Okazaki, T.; Tadokoro, M.; Hori, K. *Inorg. Chem.* **1999**, *38*, 3506. (e) Wada, A.; Watanabe, M.; Yamanoi, Y.; Nankawa, T.; Namiki, K.; Yamasaki, M.; Murata, M.; Nishihara, H. *Bull. Chem. Soc. Jpn.* **2007**, *80*, 335. (f) Buøen, S.; Dale, J.; Groth, P.; Krane, J. *J. Chem. Soc., Chem. Commun.* **1982**, 1172. (g) Custelcean, R.; Vlassa, M.; Jackson, J. E. *Angew. Chem., Int. Ed.* **2000**, *39*, 3299. (h) Maumela, H.; Hancock, R. D.; Carlton, L.; Reibenspies, J. H.; Wainwright, K. P. *J. Am. Chem. Soc.* **1995**, *117*, 6698. (i) Bombieri, G.; Marchini, N.; Ciattini, S.; Mortillaro, A.; Aime, S. *Inorg. Chim. Acta* **2006**, *359*, 3405. (j) Zhang, S.; Michaudet, L.; Burgess, S.; Sherry, A. D. *Angew. Chem., Int. Ed.* **2002**, *41*, 1919. (k) Amin, S.; Voss, D. A., Jr.; Horrocks, W. D., Jr.; Lake, C. H.; Churchill, M. R.; Morrow, J. R. *Inorg. Chem.* **1995**, *34*, 3294. (l) Amin, S.; Morrow, J. R.; Lake, C. H.; Churchill, M. R. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 773. (m) Parker, D.; Puschmann, H.; Batsanov, A. S.; Senanayake, K. *Inorg. Chem.* **2003**, *42*, 8646.

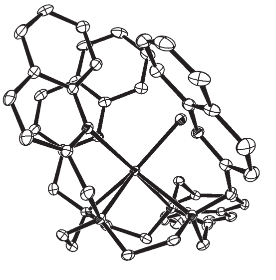
(8) In the crystal of 9-coordinated Tb^{3+} complex with cyclen **3**, CH_3O^- anion and H_2O molecule coordinated as external ligands, though in La^{3+} complex, only H_2O was coordinated as an axial external ligand: Thompson, M. K.; Lough, A. J.; White, A. J. P.; Williams, D. J.; Kahwa, I. A. *Inorg. Chem.* **2003**, *42*, 4828.

(9) Shannon, R. D. *Acta Crystallogr.* **1976**, *A32*, 751.

(a) **1**-NaI (6-coordination)



(b) **1**-Ca(OH_2)I_2 (7-coordination)



(c) **1**-La(OCH_3)I_2 (9-coordination)

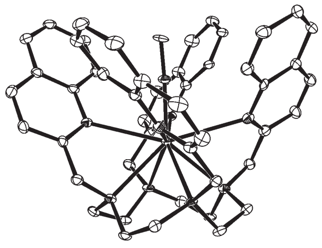


Figure 2. Crystal structures of cyclen **1**−NaI, Ca(OH_2)I_2, and La(OCH_3)I_2 complexes. H atoms, I atoms, and solvent molecules are omitted for simplification. All the I^- atoms located apart from metal coordination sphere (Na−I = 7.0 Å, Ca−I > 7.1 Å, La−I > 7.2 Å). Thermal ellipsoids are shown at the 50% probability level.

Cyclen **1** readily formed Na^+ and Ca^{2+} complexes by mixing with NaI and CaI_2 in CH_3CN at room temperature, while reflux in CH_3OH was required to yield the La^{3+} complex. After several recrystallizations, single crystals suitable for X-ray structure determination were obtained. Figure 2 illustrates the crystal structures of the cyclen **1**−NaI, Ca(OH_2)I_2, and La(OCH_3)I_2 complexes. The cyclen **1** gave a 6-coordinated Na^+ complex and a 7-coordinated Ca^{2+}complex. In both complexes, two quinoline moieties provide effective coordination with the metal centers, and most of the non-coordinated quinolines locate nearby the metal centers: N(coordinated quinoline)−Na^+ = 2.53 and 2.67 Å; N(non-coordinated quinoline)−Na^+ = 3.23 and 3.69 Å; N(coordinated quinoline)−Ca^{2+} = 2.55 and 2.71 Å; and N(non-coordinated quinoline)−Ca^{2+} = 3.58 and 5.45 Å. The La^{3+} complex was isolated as a 9-coordinated **1**−La(OCH_3)I_2, in which cyclen **1** provided 8-coordination and CH_3O^- also coordinated with the La^{3+} center. Thompson et al. reported a similar 9-coordinated Tb^{3+} complex with cyclen **3**, in which the octadentate cyclen ligand and CH_3O^- group similarly coordinated the lanthanide cation.[8] Nishihara et al.[7e] recently found that cyclen **2** forms 9-coordinated Eu^{3+}, Nd^{3+}, and Tb^{3+} complexes with the aid of external Cl^-, NO_3^-, and $CF_3SO_3^-$ anions.

The three complexes isolated here have enantiomer pairs in the crystal state. The 9-coordinated La^{3+} complex has quadruple helical arrangement of the four side arms, in which the four quinoline rings are twisted by about 25°. The distances between the least-squares mean planes defined by atoms of quinoline rings and 8-positioned hydrogens of the neighboring quinoline rings were found to be 2.38−2.52 Å, which indicates C−H---π stabilization between the quinoline moieties.[10] Although cyclen **1** did not function as an octadentate ligand for Na^+ and Ca^{2+} cations, the resulting complexes gave racemic mixtures of enantiomers in the crystal state. In these complexes, most of the quinoline rings were standing in the same direction and some exhibited C−H---π interaction to form loose helical structures (Supporting Information, Figure S1).

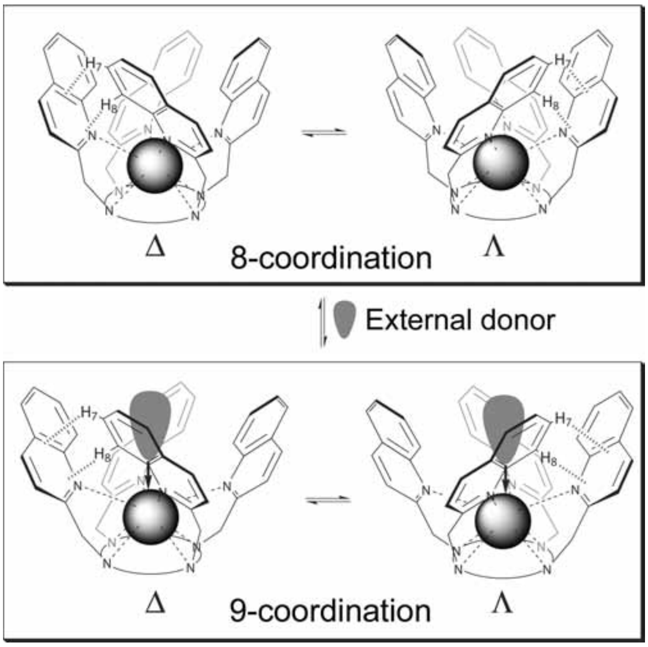


Figure 3. Solution mixture of a quadruple-stranded metal complex with octadentate cyclen **1**.

2. Solution Structures of Na^+, Ca^{2+}, and La^{3+} Complexes with Cyclen 1. ^{13}C- and ^1H NMR experiments revealed that three kinds of cyclen **1**−metal complexes had quadruple-stranded coordination structures in CD_3CN-C_2D_5OD (1:1 = v/v) solutions. Typically, the **1**−Ca^{2+} complex exhibited one signal for quinoline-methylene carbons and nine signals for quinoline-ring carbons in the ^{13}C NMR spectrum, corresponding to chemical shiftes of 61.6, 123.7, 127.2, 128.0, 129.4, 130.0, 130.5, 141.2, 147.7, and 161.5 ppm. Two signals were separately observed for the cyclen-ring carbons at 52.1 and 52.5 ppm; therefore, both the Δ- and Λ-stereoisomers were confirmed to slowly exchange at room temperature, while the four quinoline moieties were simultaneously coordinated. The corresponding **1**−La^{3+} complex also exhibited similar ^{13}C NMR spectral patterns with different chemical shifts; however, the **1**−Na^+ complex exhibited one broadened peak for the cyclen-ring carbons. When achiral cyclen **1** forms a quadruple-stranded complex with a metal cation in solution, an equilibrium mixture of 8- and 9-coordinated complexes

---

(10) C-H---π interaction was discussed in several pyridine derivatives: (a) Moriuchi, T.; Ikeda, I.; Hirao, T. *Organometallics* **1995**, *14*, 3578. (b) Yamanari, K.; Nozaki, T.; Fuyuhiro, A.; Kushi, Y.; Kaizaki, S. *J. Chem. Soc., Dalton Trans.* **1996**, 2851.

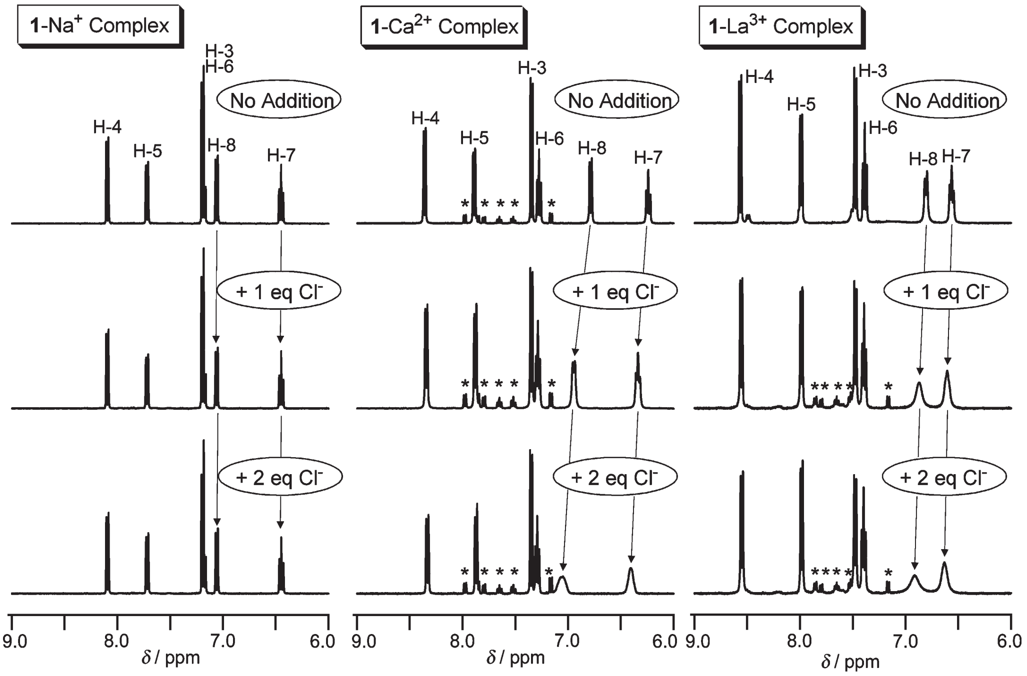


Figure 4. ^{1}H NMR spectral changes of cyclen **1**$-$Na$^+$, Ca^{2+}, and La^{3+} complexes upon addition of chloride anion. Conditions; [**1**-M^{n+} Complex] = 3.5×10^{-3} mol/L, [*n*-Bu$_4$NCl] = 0, 3.5×10^{-3} or 7.0×10^{-3} mol/L in CD$_3$CN-C$_2$D$_5$OD (1:1 = v/v). The signals marked by * were due to the free cyclen **1**.

is assumed, as schematically illustrated in Figure 3.[11] In addition to the cyclen structure, the nature of the metal center and the co-existing coordinative ligand have significant influences on the structures of the major species and the dynamics of interconversion between the isomers. The quinoline moieties of cyclen **1** cause severe sterical problems, so that the highly charged Ca^{2+} and La^{3+} cations are thought to favor 9-coordination; however, the monovalent Na$^+$ cation seems to be coordinatively satisfied by the octadentate cyclen ligand.

Figure 4 indicates ^{1}H NMR signals for quinoline protons of **1**$-$Na$^+$, **1**$-$Ca^{2+}, and **1**$-$La^{3+} complexes in CD$_3$CN-C$_2$D$_5$OD (1:1 = v/v) solutions. When the **1**$-$Na$^+$ complex was dissolved in the solution, one set of signals was recorded for the quinoline protons. The signals for two $-$CH$_2-$ protons in the cyclen ring were not observed separately, which indicates that rapid interconversion between two enantiomers (Δ- and Λ-forms) occurred in the solution. Several quinoline protons appeared at much lower frequency than those of free ligand **1**; 7.19 (H-3), 6.45 (H-7), and 7.06 ppm (H-8) for the Na$^+$ complex, and, 7.76 (H-3), 7.63 (H-7), and 7.95 ppm (H-8) for free ligand **1**. These quinoline protons are thought to give shifted signals because of the ring current of the neighboring quinoline ring,[12] so that the four quinoline rings located closely to each other form a quadruple-stranded structure in the solution. The addition of 1 or 2 equiv of Cl$^-$ anion to the **1**$-$Na$^+$ complex solution had no significant effect on the ^{1}H NMR signals. In the electrospray ionization mass spectrometry (ESI-MS) spectrum, the signal due to [**1** + Na]$^+$ was observed as the largest peak; however, no signal for solvated species such as [**1** + Na + C$_2$H$_5$OH]$^+$ was detected. Although 6-coordination was confirmed in the crystal state, the Na$^+$ cation was satisfied by 8-coordination from the octadentate cyclen **1** in solution.

Cyclen **1**$-$Ca^{2+} and La^{3+} complexes exhibited similar patterned ^{1}H NMR spectra. The signals for the 8-positioned protons of quinoline were observed at lower frequency than that of the Na$^+$ complex (Figure 4); 7.06 ppm for the Na$^+$ complex, 6.77 ppm for the Ca^{2+} complex, and 6.81 ppm for the La^{3+} complex. Both the Ca^{2+} and La^{3+} complexes exhibited separated NMR signals for the quinoline $-$CH$_2-$ protons, while the Na$^+$ complex offered a broad singlet signal; 4.00 ppm for the Na$^+$ complex, 3.75 and 4.45 ppm for the Ca^{2+} complex; and 3.94 and 4.94 ppm for the La^{3+} complex. Thus, the Ca^{2+} and La^{3+} complexes have different coordination structures from the Na$^+$ complex, which offer slower exchange rates between the Δ- and Λ-isomers than the Na$^+$ complex. When the coordinative Cl$^-$ anion was added to a solution of the Ca^{2+} or La^{3+} complex, broadened and shifted signals were recorded for the 7- and 8-positioned quinoline-protons. Therefore, both complexes were thought to further bind one Cl$^-$ anion and form 9-coordinated ternary complexes in which the quinoline rings had restricted mobility. The ESI-MS spectra also suggested that the cyclen **1**$-$Ca^{2+} and La^{3+} complexes formed ternary complexes with the Cl$^-$ anion (Supporting Information, Figures S2 and S3).

3. Induced CD Profiles of Cyclen 1$-$Ca^{2+} Complex upon Addition of Chiral Anions. A variety of chiral

---

(11) Some octadentate cyclens formed the ternary complexes between cyclens, metal cations, and guest anions, but their chirotopic behavior was not reported: (a) Smith, C. B.; WallWork, K. S.; Weeks, J. M.; Buntine, M. A.; Lincoln, S. F.; Taylor, M. R.; Wainwright, K. P. *Inorg. Chem.* **1999**, *38*, 4986. (b) Winschel, C. A.; Kalidindi, A.; Zgani, I.; Magruder, J. L.; Sidorov, V. *J. Am. Chem. Soc.* **2005**, *127*, 14704.

(12) Ring current effects were reported in several quinoline systems: (a) Maurizot, V.; Dolain, C.; Leydet, Y.; Léger, J.-M.; Guionneau, P.; Huc, I. *J. Am. Chem. Soc.* **2004**, *126*, 10049. (b) Abella, D.; Blanco, V.; Pía, E.; Chas, M.; Platas-Iglesias, C.; Peinador, C.; Quintela, J. M. *Chem. Commun.* **2008**, 2879.

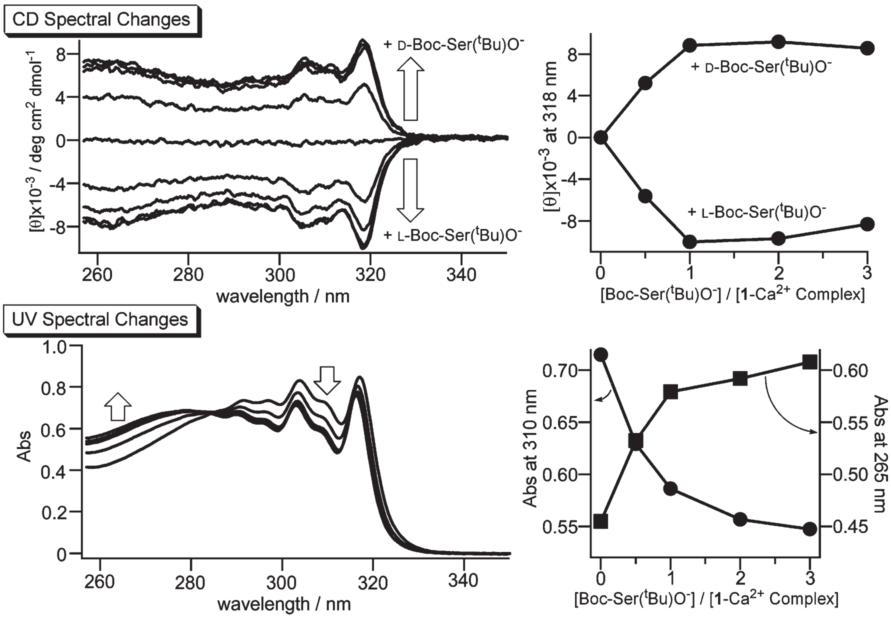


Figure 5. CD and UV spectral changes of the cyclen $\mathbf{1}-Ca^{2+}$ complex upon addition of chiral Boc-Ser(^{t}Bu)O^- anion. Conditions; [$\mathbf{1}-Ca^{2+}$ Complex] = 1.0×10^{-4} mol/L, [D- or L-Boc-Ser(^{t}Bu)OH·DCHA] = $0.50-3.0 \times 10^{-4}$ mol/L in CH_3CN-C_2H_5OH (1:1 = v/v). Addition of L- and D-Boc-Ser(^{t}Bu)O^- anions gave almost the same UV spectral changes of the cyclen $\mathbf{1}-Ca^{2+}$ complex.

armed cyclen ligands were reported to form propeller-like quadruple-stranded helicates with alkali, alkaline earth, and lanthanide cations both in solution and in crystal states.[13,14] Some of these exhibited characteristic CD signals based on one-handed helical arrangements of the side arm-chromophores around the metal centers.[14] The cyclen **1** employed has no chiral element; therefore, its quadruple-stranded metal complex exists as a racemic mixture of two enantiomers and that exhibits no CD signal in the solution state. Addition of the chiral dicyclohexylamine salt of D-Boc-Ser(^{t}Bu)OH to the $\mathbf{1}-Ca^{2+}$ complex solution induced a positive-signed CD signal around 318 nm, while L-Boc-Ser(^{t}Bu)O^- anion exhibited a negative-signed CD signal (Figure 5). The sign of the observed CD signal correlates well with the stereochemistry of the added anion, so that the combination of chiral anion with the $\mathbf{1}-Ca^{2+}$ complex dynamically defines the major stereoisomer (Figure 3). Figure 5 clearly demonstrates that 1 equiv of the chiral anion is sufficient to induce intense CD and UV spectral changes, which indicates 1:1 complexation between the cyclen $\mathbf{1}-Ca^{2+}$ complex and the chiral anion.

Figure 6 show the ^{1}H NMR spectral changes of the cyclen $\mathbf{1}-Ca^{2+}$ complex upon addition of the D-Boc-Ser(^{t}Bu)O^- anion, in which the concentration of the Ca^{2+} complex was 35-times higher than that employed in the CD experiment. Broad signals for the quinoline protons were observed in the presence of 1 equiv of chiral anion, indicating that 1:1 ternary complex was formed between the $\mathbf{1}-Ca^{2+}$ complex and chiral anion. Since the signals for 7- and 8-positioned protons were largely downfield shifted by addition of the chiral anion, quinoline moieties are rearranged upon chiral anion-coordination.

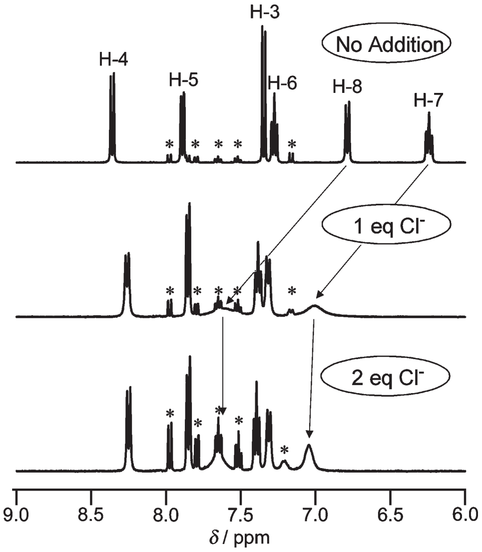


Figure 6. ^{1}H NMR spectral changes of the cyclen $\mathbf{1}-Ca^{2+}$ complex upon addition of chiral Boc-Ser(^{t}Bu)O^- anion. Conditions; [$\mathbf{1}-Ca^{2+}$ Complex] = 3.5×10^{-3} mol/L, [D-Boc-Ser(^{t}Bu)OH·DCHA] = 0, 3.5×10^{-3}, or 7.0×10^{-3} mol/L in CD_3CN-C_2D_5OD (1:1 = v/v). The signals marked by * were due to the free cyclen **1**, and their intensity was increased by addition of chiral anion. Since we observed no ^{1}H NMR spectral change of 2-methylquinoline in the presence of dicyclohexylamine salt of chiral anion, a possibility of the quinoline protonation of the cyclen **1** with chiral anion salt was not assumed.

An equimolar mixture of the $\mathbf{1}-Ca^{2+}$ complex and chiral anion exhibited an intense ESI-MS signal at m/z = 1037, because of the [$\mathbf{1}-Ca$ + Boc-Ser(^{t}Bu)O]$^+$ species (Supporting Information, Figure S4(a)). The L- and D-Boc-Lys(Boc)O^- anions were further examined as chiral anions (Supporting Information, Figure S5), and induced chirality dependent CD signals via 1:1 ternary complexation. The ternary complexation profiles were also followed by monitoring the quinoline fluorescence of the $\mathbf{1}-Ca^{2+}$ complex. This exhibited fluorescence signal

---

[13] Batsanov, A. S.; Beeby, A.; Bruce, J. I.; Howard, J. A. K.; Kenwright, A. M.; Parker, D. *Chem. Commun.* **1999**, 1011.

[14] (a) Govenlock, L. J.; Howard, J. A. K.; Moloney, J. M.; Parker, D.; Peacock, R. D.; Siligardi, G. *J. Chem. Soc., Perkin Trans. 2* **1999**, 2415. (b) Nishimura, T.; Shinoda, S.; Tsukube, H. *Chirality* **2002**, *14*, 555.

around 360 nm, while the Na^+ and La^{3+} complexes rarely showed emission signals. Addition of chiral anion to the solution of the Ca^{2+} complex decreased the fluorescence intensity upon 1:1 ternary complexation. ESI-MS characterization further indicated that the cyclen **1**$-Ca^{2+}$ complex formed 1:1 stoichiometric ternary complexes with these anions (Supporting Information, Figure S4). These observations clearly indicate that the quadruple-stranded Ca^{2+} helicate can accommodate one chiral anion into the coordination sphere and exhibit the characteristic induced CD signals.

The nature of the metal center has a significant influence on the induced CD profile of the employed helicate. The cyclen **1**$-Na^+$ complex exhibited no UV, CD, or NMR spectral changes upon addition of the chiral anion, although the cyclen **1**$-La^{3+}$ complex did exhibit complicated responses. One equivalent of chiral anion induced significant UV and CD changes in the La^{3+} complex, but more than 2 equiv were required to provide saturated spectral changes (Supporting Information, Figure S6). The complicated NMR spectra exhibited upon addition of the chiral anion suggests that several complex species are involved in this La^{3+} complex system (Supporting Information, Figure S7). The ESI-MS spectrum of an equimolar mixture of the cyclen **1**$-La^{3+}$ complex and the chiral anion in CH_3CN-C_2H_5OH (1:1 = v/v) solution also supports the possibility that several species are formed (Supporting Information, Figure S8); for the Boc-Ser(^{t}Bu)O^- anion, [**1**$-$La + OC_2H_5 + Boc-Ser(^{t}Bu)O]$^+$ (m/z = 1181), [**1**$-$La + Boc-Ser(^{t}Bu)O]$^{2+}$ (m/z = 568), and [**1**$-$La + (Boc-Ser(^{t}Bu)O)$_2$]$^+$ (m/z = 1396). For the Boc-Lys(Boc)O^- anion, [**1**$-$La + OC_2H_5 + Boc-Lys(Boc)O]$^+$ (m/z = 1266), [**1**$-$La + Boc-Lys(Boc)O]$^{2+}$ (m/z = 610), and [**1**$-$La + (Boc-Ser(^{t}Bu)O)$_2$]$^+$ (m/z = 1566) are formed.

4. Properties of Cyclen 1$-$Ca^{2+} Complex as a CD Chirality Probe. CD is one of the most effective methods for determination of the absolute stereochemistry and enantiomeric purity of chiral substrates, but is applicable only for chromophoric substrates. Measurement of the optical rotation value $[\alpha]_D$ is an alternative method for the determination of the enantiomeric purity of non-chromophoric substrates. However, this has severe limitations in the case of substrates that exhibit small $[\alpha]_D$ values; therefore, several chirality probes have been developed to form CD-active species with non-chromophoric chiral substrates.[15] We characterize below the cyclen **1**$-Ca^{2+}$ complex as a new class of CD chirality probe for the determination of the enantiomeric excess (ee%) of chiral anions.

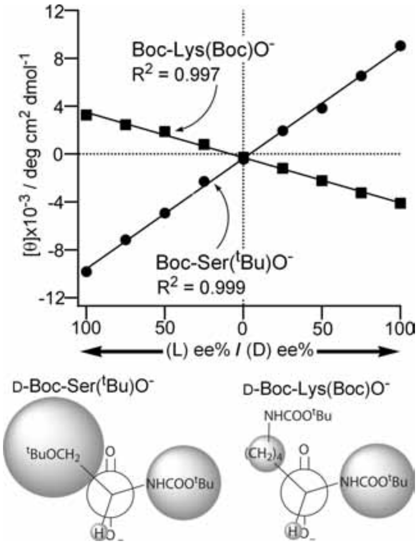


Figure 7. CD chirality probing of non-chromophoric chiral anions with the cyclen **1**$-Ca^{2+}$ complex. Conditions; [**1**$-Ca^{2+}$ Complex] = 1.0 × 10^{-4} mol/L, [D-Boc-Ser(^{t}Bu)OH·DCHA] + [L-Boc-Ser(^{t}Bu)OH·DCHA] = [D-Boc-Lys(Boc)OH·DCHA] + [L-Boc-Lys(Boc)OH·DCHA] = 1.0 × 10^{-4} mol/L in CH_3CN-C_2H_5OH (1:1 = v/v).

Figure 7 illustrates the relationship between ee% of the examined chiral anion and the intensity of the induced CD signal with the **1**$-Ca^{2+}$ complex. Two dicyclohexylamine salts, Boc-Ser(^{t}Bu)O^- and Boc-Lys(Boc)O^- anions, were examined as non-chromophoric chiral substrates. When the D-forms of both anions were dissolved in the cyclen **1**$-Ca^{2+}$ complex solution, the observed CD signals had opposite signs; (+) for the former anion and (−) for the latter. Consideration of these results based on Newman projection suggest that the two D-form anions have different stereochemical configurations upon metal coordination, and therefore induce different arrangements of the four quinoline moieties (see Figure 7).[16] Dicyclohexylamine salts of Boc-Ala, Val, Pro, and Met also exhibited the chirality-dependent CD signals in the presence of the **1**$-Ca^{2+}$ complex (Supporting Information, Figure S9), the sign of which is related well with the stereochemical configuration of the chiral anion upon metal coordination (Figure 7). The Ca^{2+} complex exhibited a linear relationship between the CD intensity and ee% of the examined chiral anion. The $[\alpha]_D$ value of the Boc-Lys(Boc)OH·DCHA was too small (6.1)[17] to use for practical determination; therefore, the proposed CD probe system has the advantage of a simple procedure to amplify the enantiomeric purity information. When the cyclen **1**$-Ca^{2+}$ complex was dissolved in chiral 2-chloropropanol-CH_3CN solution (1:1 = v/v), the resulting mixture exhibited no CD signal. Because a large excess of chiral alcohol rarely induces a CD signal, the cyclen **1**-Ca^{2+} complex probe enables selective probing of chiral anions.

Conclusion

The coordination versatility and chirality response of three metal complexes with the octadentate cyclen **1** were compared. In contrast to their crystal structures, dynamic quadruple-stranded structures were confirmed in the solution state. Among them, the Ca^{2+} complex formed 1:1 adducts with organic carboxylate anions in solution. This exhibited the intense CD signals around the quinoline chromophore region for the ternary complexes with chiral anions, which

---

(15) (a) Tsukube, H.; Shinoda, S.; Tamiaki, H. *Coord. Chem. Rev.* **2002**, *226*, 227. (b) Hembury, G. A.; Borovkov, V. V.; Inoue, Y. *Chem. Rev.* **2008**, *108*, 1.

(16) Canary et al. determined the stereochemistry of quinoline-functionalized tripod-metal complexes. Although they analyzed the CD signals around 240 nm, our recorded CD spectra contained signals due to the bound I^- anion. Thus, their method is not applicable: Zhang, J.; Holmes, A. E.; Sharma, A.; Brooks, N. R.; Rarig, R. S.; Zubieta, J.; Canary, J. *Chirality* **2003**, *15*, 180.

(17) Keller, O.; Keller, W. E.; Look, G. V.; Wersin, G. *Org. Synth.* **1985**, *63*, 160.

indicated asymmetric twisting was induced in the quadruple-stranded cyclen $\mathbf{1}-Ca^{2+}$ complex. This phenomenon involved chirality transfer from an external anion to the Ca^{2+} center, while the corresponding Na^+ complex exhibited no response for chiral anions, and the La^{3+} complex exhibited a somewhat complicated anion-response. Therefore, the present results imply that further combinations of the designed multidentate ligands and functional metal centers would have wide applications in the development of sensing, switching, and other dynamic devices.

Experimental Section

General Procedures. ^1H and ^{13}C NMR spectra were recorded with a Jeol Lambda-400 spectrometer, and ESI-MS spectra were recorded using a Jeol JMS-700T mass spectrometer. CD experiments were carried out using a Jasco 820 spectrometer.

Materials. Dicyclohexylamine was purchased from Nacalai Tesque Inc., L-Boc-Pro-OH was purchased from Peptide Insutitute Inc., D-Boc-Met-OH and D-Boc-Pro-OH were obtained from Watanabe Chemical Industries, Ltd., the other Boc-amino acids and dicyclohexylamine salts of L-Boc-Ser(^{t}Bu)OH and L-Boc-Lys(Boc)OH were purchased from Kokusan Chemical Co. Ltd., and D-Boc-Ser(^{t}Bu)OH and D-Boc-Lys(Boc)OH were obtained from Bachem AG. They were used without additional purification.

Preparation of 1,4,7,10-Tetrakis(2′-quinolylmethyl)-1,4,7,10-tetraazacyclododecane−NaI Complex [Cyclen 1−Na^+ Complex]. A mixture of cyclen (0.34 g, 2.0 mmol), 2-chloromethylquinoline hydrogen chloride (2.59 g, 12.1 mmol), Na_2CO_3 (4.27 g, 40.3 mmol), and NaI (0.62 g, 4.2 mmol) in CH_3CN (30 mL) was refluxed for 4 h, and the solvent was then evaporated. CH_2Cl_2 was added to the residue, and the solid was filtered. After washing with diethyl ether, recrystallization from CH_3CN/diethyl ether yielded colorless crystals of **1**-NaI (0.37 g, 36%): mp 258−260 °C (decomp); IR (KBr) ν 3407, 2976, 2815, 1619, 1601, 1507, 1428, 1307, and 1093 cm^{-1}; ^1H NMR (CD_3CN-C_2D_5OD (1:1 = v/v), 400 MHz): δ 2.76 (br s, 16H, cyclen ring), 4.00 (br s, 8H, NCH_2Ar), 6.45 (ddd, J = 9.2, 7.8, 1.4 Hz, 4H, H-7), 7.06 (d, J = 8.6 Hz, 4H, H-8), 7.16−7.20 (m, 8H, H-3 and 6), 7.72 (d, J = 8.3 Hz, 4H, H-5), and 8.09 (d, J = 8.3 Hz, 4H, H-4) ppm. ^{13}C NMR (CD_3CN-C_2D_5OD (1:1 = v/v), 100 MHz): δ 51.82, 61.45, 123.08, 127.00, 128.46, 128.71, 129.32, 129.66, 138.14, 148.57, and 160.76 ppm. Anal. Calcd for $C_{48}H_{48}N_8\cdot NaI$: C, 65.01; H, 5.46; N, 12.64. Found: C, 64.85; H, 5.48; N, 12.63.

The cyclen **1**-NaI complex for crystal structure determination was obtained by further recrystallization from CH_3CN/diethyl ether.

1,4,7,10-Tetrakis(2′-quinolylmethyl)-1,4,7,10-tetraazacyclododecane [Cyclen 1]. A solution of **1**-NaI (515 mg, 0.58 mmol) in CH_2Cl_2 (30 mL) was washed three times with deionized water (10 mL), and the organic layer was evaporated. Methanol and then deionized water were added to the residue. The resulting powder was filtered and washed with methanol/water. (414 mg, 96%): mp 206−208 °C (decomp); IR (KBr) ν 3412, 2818, 1618, 1602, 1505, 1427, and 808 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 2.87 (s, 16H, cyclen ring), 3.78 (s, 8H, $ArCH_2N$), 7.48 (ddd, J = 8.1, 7.0, 1.0 Hz, 4H, H-6), 7.65 (ddd, J = 8.4, 7.0, 1.5 Hz, 4H, H-7), 7.70 (d, J = 8.3 Hz, 4H, H-5), 7.75 (d, J = 8.5 Hz, 4H, H-3), 7.85 (d, J = 8.3 Hz, 4H, H-4), and 7.98 (d, J = 8.3 Hz, 4H, H-8) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ 53.72, 62.72, 121.32, 125.97, 127.24, 127.47, 128.90, 129.28, 135.99, 147.48, and 161.06 ppm. Anal. Calcd for $C_{48}H_{48}N_8\cdot 0.3CH_3OH\cdot 0.2H_2O$: C, 77.33; H, 6.66; N, 14.94. Found: C, 77.40; H, 6.63; N, 15.00.

1,4,7,10-Tetrakis(2′-quinolylmethyl)-1,4,7,10-tetraazacyclododecane−CaI_2 Complex [Cyclen 1-Ca^{2+} Complex]. A mixture of **1**-NaI (322 mg, 0.36 mmol) and CaI_2 (155 mg, 0.53 mmol) in CH_3CN (23 mL) was stirred for 20 h at room temperature, and the resulting solution was evaporated. CH_2Cl_2 was added to the residue, and the solid was filtered. Recrystallization from CH_3CN/diethyl ether yielded a pale yellow powder of $\mathbf{1}-CaI_2\cdot 0.5H_2O$ (201 mg, 53%): mp 360−363 °C (decomp); IR (KBr) ν 3435, 2860, 1620, 1602, 1509, 1431, 1307, and 1081 cm^{-1}; ^1H NMR (CD_3CN-C_2D_5OD (1:1 = v/v), 400 MHz): δ 2.52 (d, J = 14.2 Hz, 8H, cyclen ring), 3.40 (t, J = 12.7 Hz, 4H, cyclen ring), 3.75 (d, J = 16.4 Hz, 4H, NCH_2Ar), 3.89 (t, J = 13.5 Hz, 4H, cyclen ring), 4.45 (d, J = 16.6 Hz, 4H, NCH_2Ar), 6.23 (ddd, J = 9.2, 7.8, 1.4 Hz, 4H, H-7), 6.77 (d, J = 8.8 Hz, 4H, H-8), 7.25 (ddd, J = 8.6, 7.6, 1.0 Hz, 4H, H-6), 7.34 (d, J = 8.4 Hz, 4H, H-3), 7.89 (dd, J = 8.3, 1.2 Hz, 4H, H-5), and 8.36 (d, J = 8.3 Hz, 4H, H-4) ppm. ^{13}C NMR (CD_3CN-C_2D_5OD (1:1 = v/v), 100 MHz): δ 52.11, 52.51, 61.61, 123.74, 127.21, 128.01, 129.37, 129.96, 130.48, 141.19, 147.73, and 161.47 ppm. Anal. Calcd for $C_{48}H_{48}N_8\cdot CaI_2\cdot 0.5H_2O$: C, 55.44; H, 4.75; N, 10.78. Found: C, 55.39; H, 4.63; N, 10.70.

The cyclen $\mathbf{1}-Ca(OH_2)I_2$ complex for crystal structure determination was obtained by further recrystallization from CH_3CN.

1,4,7,10-Tetrakis(2′-quinolylmethyl)-1,4,7,10-tetraazacyclododecane−$La(OCH_3)I_2$ Complex [1−La^{3+} Complex]. A solution of ligand **1** (277 mg, 0.37 mmol) and LaI_3 (198 mg, 0.38 mmol) in methanol (20 mL) was refluxed for 10 h. After filtration, the residue was evaporated to provide a solid. After filtration, recrystallization from methanol yielded colorless crystals of $\mathbf{1}-La(OCH_3)I_2\cdot H_2O$ (108 mg, 25%): mp 325 °C (decomp); IR (KBr) ν 3434, 2862, 2778, 1619, 1603, 1509, 1431, 1310, and 1082 cm^{-1}; ^1H NMR (CD_3CN-C_2D_5OD (1:1 = v/v), 400 MHz): δ 2.50 (d, J = 13.9 Hz, 4H, cyclen ring), 2.58 (d, J = 14.9 Hz, 4H, cyclen ring), 3.58 (t, J = 14.2 Hz, 4H, cyclen ring), 3.94 (d, J = 17.3 Hz, 4H, NCH_2Ar), 4.04 (t, J = 13.0 Hz, 4H, cyclen ring), 4.94 (d, J = 17.1 Hz, 4H, NCH_2Ar), 6.56 (t, J = 7.6 Hz, 4H, H-7), 6.81 (d, J = 8.6 Hz, 4H, H-8), 7.39 (t, J = 7.5 Hz, 4H, H-6), 7.48 (d, J = 8.5 Hz, 4H, H-3), 7.99 (d, J = 8.0 Hz, 4H, H-5), and 8.57 (d, J = 8.5 Hz, 4H, H-4) ppm. ^{13}C NMR (CD_3CN-C_2D_5OD (1:1 = v/v), 100 MHz): δ 53.16, 53.52, 62.66, 123.40, 128.50, 128.91, 129.36, 129.60, 131.19, 142.04, 147.89, and 161.10 ppm. Anal. Calcd for $C_{48}H_{48}N_8\cdot LaOCH_3I_2\cdot H_2O$: C, 49.93; H, 4.53; N, 9.51; I, 21.53. Found: C, 49.81; H, 4.49; N, 9.61; I, 21.25.

The cyclen $\mathbf{1}-La(OCH_3)I_2$ complex for crystal structure determination was obtained by further recrystallization from CH_3OH.

Crystal Structure Determinations of 1−NaI, CaI_2 and $La(OCH_3)I_2$ Complexes. Data collection was carried out at −173 °C using a Rigaku/MSC Mercury CCD diffractometer equipped with graphite monochromated Mo Kα radiation (λ = 0.71070 Å). Data were processed on a PC using the CrystalClear software (Rigaku). The structures were solved by the direct method using SIR-97[18] for $\mathbf{1}-NaI$ and $\mathbf{1}-La(OCH_3)I_2$, and using the heavy-atom Patterson method (DIRDIF-99)[19] expanded with Fourier techniques. The non-hydrogen atoms were refined anisotropically using the full-matrix least-squares method of SHELXL-97.[20] All hydrogen atoms except for those in the coordinating water molecule were placed at geometrically ideal positions. The crystallographic parameters are summarized in Supporting Information, Table S1.

CD Experiments. Stock solutions of cyclen **1**−metal complexes (3×10^{-4} mol/L in CH_3CN-C_2H_5OH (1:1= v/v)) were prepared. After mixing the stock solution with the chiral anion salt, the concentration of the cyclen $\mathbf{1}-Na^+$, Ca^{2+}, La^{3+} complexes was adjusted to 1.0×10^{-4} mol/L, and the resulting solution was

---

(18) Altomare, A.; Burla, M. C.; Camalli, M.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Moliterni, A. G. G.; Polidori, G.; Spagna, R. *J. Appl. Crystallogr.* **1999**, *32*, 115.

(19) Beurskens, P. T.; Beurskens, G.; de Gelder, R.; Garcia-Granda, S.; Gould, R. O.; Israel, R.; Smits, J. M. M. *The DIRDIF-99 program system*; Crystallography Laboratory, University of Nijmegen: The Netherlands, 1999.

(20) Sheldrick, G. M., *SHELXL-97, Program for the Refinement of Crystal Structures*; University of Göttingen: Göttingen, Germany, 1997.

stirred for 1 h prior to the CD measurement. Errors of induced CD intensities for the cyclen $\mathbf{1}{-}Ca^{2+}$ complex were confirmed to be $<7\%$ and $<11\%$ for addition of the Boc-Ser(^{t}Bu)O^{-} and Boc-Lys(Boc)O^{-} anion systems, respectively. When Boc-Ala-OH, Val, Pro and Met were employed, an equimolar mixture of each amino acid, acid form, and dicyclohexylamine, base form, was added to the stock solution of the $\mathbf{1}{-}Ca^{2+}$ complex for CD measurement. We further confirmed that addition of 0.5 or 1 equiv of Boc-Val, acid form, to the solution of $\mathbf{1}{-}Ca^{2+}$ complex rarely gave UV spectral changes and induced CD spectra, indicating that chiral anion species actually induced characteristic CD signals.

Acknowledgment. This research was supported in part by a Grant-in-Aid for Scientific Research (No. 20245014) from the Japan Society for the Promotion of Science.

Supporting Information Available: C−H---π interactions observed in crystalline $\mathbf{1}{-}Na^{+}$, Ca^{2+}, and La^{3+} complexes, ESI-MS spectra of equimolar mixtures of the $\mathbf{1}{-}Ca^{2+}$ complex and Cl^{-}/chiral anions, UV, CD, ^{1}H NMR, and ESI-MS spectral changes of the cyclen $\mathbf{1}{-}La^{3+}$ complex upon addition of Cl^{-}/chiral anions, the induced CD signals of several Boc-amino acid anions, and X-ray crystallographic data in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.