Specific Recognition of Chiral Amino Alcohols via Lanthanide Coordination Chemistry: Structural Optimization of Lanthanide Tris(β-diketonates) toward Effective Circular Dichroism/Fluorescence Probing

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Lanthanide tris(β-diketonates) formed stable, 1:1 highly coordinated complexes with amino alcohols, and the resulting complexes exhibited large enhanced fluorescence and intense induced circular dichroism (CD) signals. The stability constants of the highly coordinated complexes were determined for various combinations of lanthanide centers, β-diketonate ligands, and organic substrates. These revealed that amino alcohol coordinated with the lanthanide center much more strongly than monoamine, monoalcohol, or diol derivative. On the basis of the highly coordinated complexation, several lanthanide tris(β-diketonates) acted as CD/fluorescence probes specific for amino alcohols. Tris(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octadionato)europium(III) showed enhanced fluorescence in the presence of amino alcohols, while the corresponding ytterbium complex exhibited chirality-dependent CD signals for amino alcohols. In particular, the observed CD spectral profiles related well with the absolute configuration and optical purity of the bound amino alcohol, indicating that the structural optimization of lanthanide tris(β-diketonates) offered specific sensing of amino alcohols and precise determination of their enantiomer excess percentages.

Introduction

Lanthanide tris(β-diketonates) are one of the representatives of rare earth metal complexes exhibiting interesting properties.[1] Although these are electrically neutralized by three β-diketonate ligands, one or more additional substrates usually bind to the central lanthanide cation, increasing the coordination number to more than 6. On the basis of such highly coordinated complexation, various lanthanide tris(β-diketonates) and related complexes were widely employed as shift reagents in NMR spectroscopy and catalysts in organic synthesis.[2] They also have two other promising features as sensing and/or probing devices. Their fluorescence and circular dichroism (CD) spectroscopic profiles can be modified upon highly coordinated complexation with specific substrates.[3−5] Typically, europium tris(β-diketonate) **1b** was reported to become highly luminescent because of complexation with phosphate esters in the noncoordinating solvents,[3c] while praseodymium tris(β-diketonate) **2a** gave split-type Cotton effects in CD spectra upon addition of chiral 1,2-diols.[4a] Recently we demonstrated that lanthanide tris(β-diketonates) **1f** and **4** extracted zwitterionic amino acids from neutral aqueous solutions into CH_2Cl_2 solutions and offered characteristic CD spectra.[6] Since such lanthanide tris(β-diketonates) exhibit variable and versatile coordination modes,[7] the highly coordinated complexation apparently involves the reorganizations of diketonate−chelate rings and the following

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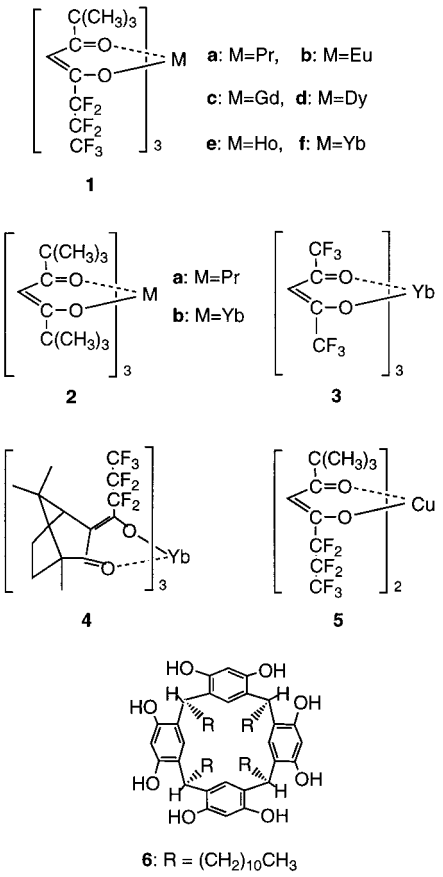

Figure 1. Lanthanide tris(β-diketonates) and reference probes.

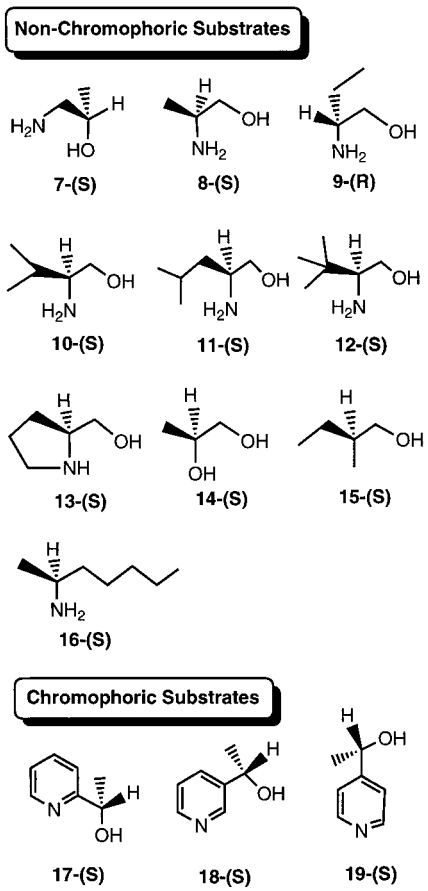

Figure 2. Employed organic substrates.

several processes to attain the most stable complex geometry. Thus, the observed fluorescence and CD spectral changes often had time- and concentration-dependent natures and were not applicable in the practical sensing and probing systems.

We present systematic studies of highly coordinated complexation between lanthanide tris(β-diketonates) and neutral organic substrates (Figures 1 and 2) and optimize their structures as CD/fluorescence probes specific for chiral amino alcohols.[8] The employed lanthanide tris(β-diketonates) **1**−**4** include praseodymium, europium, gadolinium, dysprosium, holmium, and ytterbium ions as trivalent lanthanide centers. Chiral amino alcohols **7**−**13** were chosen as target substrates for probing. These amino alcohols are silent in the fluorescence and CD spectra (>250 nm) but are useful chiral building blocks in organic synthesis as well as biological substrates for ethanolamine ammonia-lyase, reacting to yield aldehydes and ammonia via common enzyme-bound intermediates.[9] Chiral diol **14**, monoalcohol **15**, and monoamine **16** were also examined for comparison. The stability constants of the highly coordinated complexes with various combinations of lanthanide centers, β-diketonate ligands, and organic substrates were determined by UV and CD titration experiments. The lanthanide tris(β-diketonates) having fluorinated moieties are demonstrated below to specifically form very stable 1:1 complexes with amino alcohols in $MeOH/CH_2Cl_2$ (1/99) solutions and offer steady fluorescence and CD signals depending on the structure and chirality of the bound amino alcohols.

Results and Discussion

1. Probe Characteristics of Lanthanide Tris(β-diketonates). A variety of lanthanide tris(β-diketonates) **1**−**4** were examined as fluorescence and CD probes, while copper bis(β-diketonate) **5** was chosen to elucidate the effect of the central metal cation on the probe functions (Figure 1). Since their central lanthanide ions have larger ionic radii (0.99−1.13 Å)[10] and higher coordination numbers (7−12) than those of transition metal cations, these lanthanide tris(β-diketonates) usually include one or more solvent molecules in addition to three β-diketonate ligands.[7] They also have three different types of chromophoric β-diketonate ligands: nonfluorinated ligands, fluorinated ligands, and chiral fluorinated ligands. Among them, the fluorinated ligands are expected to increase the Lewis acidity of the lanthanide center, to stabilize the highly coordinated complexes, and to enhance the solubility of the complex species.

There are two possible ways to detect nonfluorescent or nonchromophoric substrates using the fluorescence or CD spectroscopic method:[11] derivatization and complexation. Many successful examples of the derivatization method have been reported in the literature, but this requires laborious tasks including coupling reaction with the chromophore, purification of the resulting derivative, and recovery of the chiral substrate via bond cleavage. The complexation method is a promising alternative that has great advantages over the derivatization method: only several micrograms of the substrate is required; neither coupling reaction nor purification is needed; and recovery

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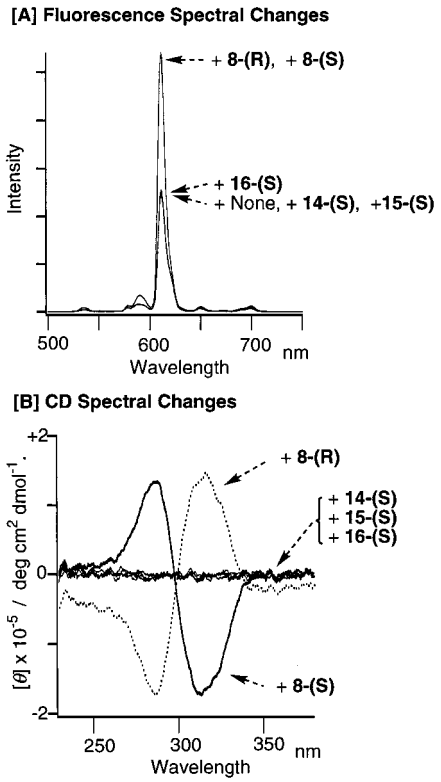

Figure 3. Fluorescence and CD spectral changes of probe **1b** upon complexation with chiral substrates (**8**, **14**, **15**, and **16**): [**1b**] = 3.50×10^{-5} mol/L; [substrate] = 3.50×10^{-4} mol/L; in MeOH/CH_2Cl_2 (1/99). Fluorescence spectra were obtained by excitation at 294 nm and uncorrected.

of the substrate is very easy. Macrocycle **6** is a typical CD probe that has chromophoric groups and offers selective CD response based on complexation with chiral diols.[12a]

When europium tris(*β*-diketonate) **1b** was dissolved in a MeOH/CH_2Cl_2 (1/99, v/v) solution, the fluorescence observed at 611 nm was enhanced by 2.2 times upon addition of 10 equiv of (*S*)- or (*R*)-2-amino-1-propanol **8** (Figure 3A). In contrast, the fluorescence spectral changes were rarely induced by diol, monoalcohol, or monoamine substrates **14**−**16** under the same conditions. Some europium tris(*β*-diketonates) were reported to form 1:2 highly coordinated complexes with monoalcohol and monoamine substrates in CCl_4 and other noncoordinating solvents,[3b,c] but these highly coordinated complexes were very unstable in the polar solvents. Although the solution examined here included a large number of methanol molecules competing with organic substrates in the coordination, bidentate amino alcohol **8** was confirmed to form the highly coordinated complex, which was stable enough and gave a much stronger emission.

Figure 3B illustrates that europium tris(*β*-diketonate) **1b** exhibited a split Cotton effect in the CD spectrum upon addition of (*S*)- or (*R*)-2-amino-1-propanol **8** though both europium complex **1b** and chiral amino alcohol **8** are themselves CD-silent under the employed conditions (>250 nm). Since chiral diol, monoalcohol, and monoamine **14**−**16** did not induce any CD spectral changes, complex **1b** worked as a chemoselective probe of amino alcohols not only in fluorescence but also in CD spectroscopy. Furthermore, this complex afforded symmetrical CD spectra in the presence of enantiomers of amino alcohol **8**. There are several possible stereoisomers in the solution, but the bidentate coordination from chiral amino alcohol is thought to induce asymmetric deformation of three chromophoric *β*-diketonate ligands in the coordination sphere of the europium center. Nakanishi and Dillon earlier demonstrated that praseodymium tris(*β*-diketonate) **2a** interacted with 1,2-glycols to give CD signals specific to the chirality of the bound 1,2-diols.[4a,b] The characteristic CD spectra were recorded in the anhydrous, noncoordinating solvents and often had time-dependent natures. We similarly observed unsteady CD spectral behaviors for combinations of amino alcohols and probes **2a** and **2b**. In contrast, the employed europium complex **1b** having fluorinated *β*-diketonates offered definite CD signals upon addition of chiral amino alcohols. Although the resulting highly coordinated complexes should have variable and versatile coordination modes in the solutions,[7] the fluorinated moieties introduced to the *β*-diketonate ligands are suggested to increase the stability of the highly coordinated complexes, which give high sensitivity and reproducibility in the CD probing process. Therefore, the lanthanide tris(fluorinated *β*-diketonates) have potential as useful probes for the complexation method in detection and chirality sensing of amino alcohols if the probe structures are optimized to offer both steady CD signals and high substrate selectivity.

2. Chirality Probing of Amino Alcohols with Lanthanide Tris(*β*-diketonates). Although resorcinol cyclic tetramers, calixarenes, polymer helices, porphyrins, and diboronic acid derivatives have already been developed as CD probes for chirality sensing, the number of effective probes and target substrates is still limited.[12,13] The lanthanide tris(*β*-diketonates) are viewed as new, effective CD probes having many advantages of easy preparation, versatile structure, and tunable selectivity.

Lanthanide tris(fluorinated *β*-diketonates) **1a**−**1f** gave the induced CD signals with the same sign for various amino alcohols **7**−**13** of the same configuration,[8] while secondary amino alcohol **13** exhibited modest CD amplitude.[14] Figure 4 illustrates the bidentate coordination modes of amino alcohols **7-(S)**, **8-(R)**, and **8-(S)** with lanthanide centers. When **7-(S)** coordinates with the lanthanide center in a bidentate fashion, an "anticlockwise" conformation should be more energetically favored than a "clockwise" conformation for steric reasons. **8-(S)** may also have predominantly the "anticlockwise" conformation, though its substituent is attached at a different position from that in amino alcohol **7**. These (*S*)-amino alcohols are thought to have the same "anticlockwise" conformations, though both similarly offered first negative and then positive CD signs: reversed S-shaped CD signals. In the case of amino alcohol **8-(R)**, the "clockwise" conformation must be more stable than the "anticlockwise" one. Since it gave an S-shaped CD signal, the sign of the induced CD signal related well with the favorable conformation of the target amino alcohol in the bidentate fashion. We also compared CD spectral changes in the presence of three geometrical isomers of chiral pyridylethanols **17**−**19**.

(12) Examples of CD probes: (a) Kikuchi, Y.; Kobayashi, K.; Aoyama, Y. *J. Am. Chem. Soc.* **1992**, *114*, 1351. (b) Morozumi, T.; Shinkai, S. *J. Chem. Soc., Chem. Commun.* **1994**, 1219. (c) Crossley, M.; Mackay, L. G.; Try, A. C. *J. Chem. Soc., Chem. Commun.* **1995**, 1925. (d) Mizutani, T.; Kurahashi, T.; Murakami, T.; Matsumi, N.; Ogoshi, H. *J. Am. Chem. Soc.* **1997**, *119*, 8991. (e) Yashima, E.; Natsusihima, T.; Okamoto, Y. *J. Am. Chem. Soc.* **1997**, *119*, 6345. (f) Huang, X.; Rickman, B. H.; Borhan, B.; Berova, N.; Nakanishi, K. *J. Am. Chem. Soc.* **1998**, *120*, 6185.

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(14) Chiral diamines such as (*S*)-2-pyrrolidinemethylamine gave the induced CD signals with smaller amplitudes than those with corresponding amino alcohols. Since the resulting complexes exhibited markedly different UV spectra from those of parent lanthanide tris(*β*-diketonates), their *β*-diketonate ligands were suggested to exchange with diamines.

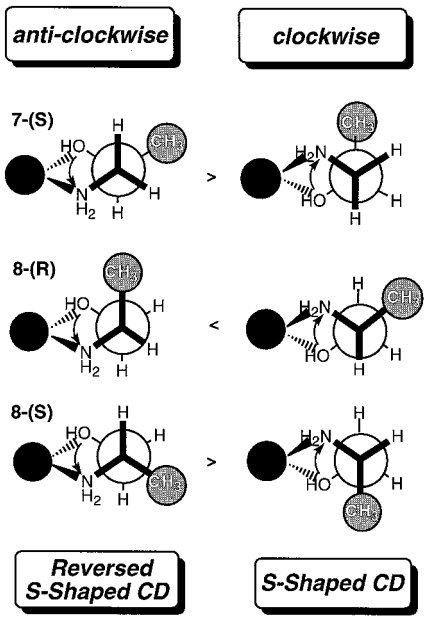

Figure 4. Preferred conformations of bidentate amino alcohols **7-(S)**, **8-(R)**, and **8-(S)**.

Only **17-(S)** gave the induced CD signal, and 3- and 4-substituted **18-(S)** and **19-(S)** exhibited negligible CD spectral changes in the presence of **1f**. This means that bidentate chelation of nitrogen and oxygen atoms in the amino alcohol plays an important role in the induction of Cotton effects.

This type of lanthanide complex exhibited higher CD probing sensitivity for chiral amino alcohols than common probe **6**. Resorcinol cyclic tetramer **6** was reported as a CD probe for chiral polyols and chiral amino alcohols[12a] (Figure 1). Under the same concentration conditions, its amplitudes of the induced CD signals for amino alcohols were much lower than those with lanthanide tris(β-diketonates) **1a**−**1f**. Copper bis(β-diketonate) **5** was also examined but exhibited no CD signal in the presence of chiral amino alcohols. The CD signals with split Cotton effects were frequently observed with chiral transition metal complexes, when achiral original ligands were exchanged with chiral substrates.[11b] In contrast, the employed lanthanide tris(β-diketonates) formed the highly coordinated complexes without loss of β-diketonate ligands, in which three chromophoric β-diketonates might be asymmetrically oriented on the lanthanide center to give the induced CD signals. In both cases, the sign of the Cotton effect correlates with the absolute structure of the mixed-ligand complex.

3. Quantitative Studies of Highly Coordinated Complexation with Lanthanide Tris(β-diketonates). We carried out titration experiments in the MeOH/CH_2Cl_2 (1/99, v/v) mixed-solvent system and estimated stability constants (log *K*) for amino alcohols **8**−**12** on the basis of changes in CD amplitude (Amp = {[θ at first λ] − [θ at second λ]} × 10^{-5}/deg cm^2 dmol^{-1}). The titration curves based on changes in CD amplitudes gave good fits for 1:1 complexation, and log *K* values were calculated by a nonlinear least-squares treatment, which were similar to those obtained based on changes in UV absorbance. We also performed NMR titration experiments with diol, monoalcohol, and monoamine **14**−**16** because their CD spectral changes were negligible (see Figure 3B). The log *K* value of the 1:1 highly coordinated complex was estimated as 1.37 for a combination of diol **14** and probe **1f**, while substrates **15** and **16** were suggested to give mixtures of much less stable complexes with 1:1 and 1:2 stoichiometries. Such large differences in the log *K* values between these substrates can explain why lanthanide tris(β-diketonates) act as chemoselective probes of amino alcohols.

Table 1. The log *K* Values of Highly Coordinated Complexes between Probes **1a**−**1f** and Amino Alcohols **8**−**12**[a]

probe (Ln)	amino alcohol	first λ/nm second λ/nm	log *K*	Amp[b]
1a (Pr)	**10-(S)**	288 315	4.19	+0.91
1b (Eu)	**10-(S)**	286 313	4.45	+1.76
1c (Gd)	**10-(S)**	285 314	4.53	+2.15
1d (Dy)	**10-(S)**	286 313	4.88	+2.13
1e (Ho)	**10-(S)**	285 313	4.76	+2.74
1f (Yb)	**10-(S)**	284 312	4.67	+2.90
1f (Yb)	**10-(R)**	284 312	4.59	−2.71
1f (Yb)	**8-(S)**	284 312	4.22	+1.86
1f (Yb)	**9-(S)**	285 314	4.28	+2.12
1f (Yb)	**11-(S)**	284 313	4.40	+2.26
1f (Yb)	**12-(S)**	284 312	4.82	+3.33

[a] Conditions: **1a**−**1f**, 8.00 × 10^{-5} mol/L; in MeOH/CH_2Cl_2 (1/99). [b] The saturated Amp values {Amp = [θ at first λ] − [θ at second λ](10^{-5}/deg cm^2 dmol^{-1})} were calculated under the conditions that all probes formed complexes with amino alcohols.

Table 1 summarizes log *K* values and the saturated CD amplitudes of the highly coordinated complexes for various combinations of lanthanide complexes **1a**−**1f** and amino alcohols **8**−**12**. The natures of lanthanide centers had interesting effects on log *K* values and the saturated CD amplitudes. Their ionic radii decrease in the order Pr^{3+} (1.13 Å) > Eu^{3+} (1.07 Å) > Gd^{3+} (1.05 Å) > Dy^{3+} (1.03 Å) > Ho^{3+} (1.02 Å) > Yb^{3+} (0.99 Å) when octadentate geometry is assumed.[10] The estimated log *K* values for amino alcohol **10-(S)** in the MeOH/CH_2Cl_2 (1/99) solutions exhibited a different trend from that of ionic radii: Pr^{3+} (log *K* = 4.19) < Eu^{3+} (log *K* = 4.45) < Gd^{3+} (log *K* = 4.53) < Dy^{3+} (log *K* = 4.88) ≥ Ho^{3+} (log *K* = 4.76) > Yb^{3+} (log *K* = 4.67). This probably means that smaller lanthanide center provides shorter and stronger coordination from amino alcohol but larger steric repulsion between the amino alcohol and β-diketonate ligands. In contrast, the saturated CD amplitudes of the highly coordinated complexes are clearly dependent on the ionic radii, and the largest CD signal was observed with the smallest ytterbium ion: Pr^{3+} (Amp = +0.91) < Eu^{3+} (Amp = +1.76) < Gd^{3+} (Amp = +2.15) = Dy^{3+} (Amp = +2.13) < Ho^{3+} (Amp = +2.74) < Yb^{3+} (Amp = +2.90). The nature of the attached substituent to the asymmetric carbon of amino alcohol also influenced both CD amplitude and the log *K* value. When **1f** was employed as a CD probe, the same order was observed for CD amplitudes and log *K* values: **12-(S)** (Me_3C−, Amp = +3.33, log *K* = 4.82) > **10-(S)** (Me_2CH−, Amp = +2.90, log *K* = 4.67) > **11-(S)** (Me_2CH−CH_2−, Amp = +2.26, log *K* = 4.40) > **9-(S)** (Me-CH_2−, Amp = +2.12, log *K* = 4.28) ≥ **8-(S)** (H−CH_2−, Amp = +1.86, log *K* = 4.22). Empirical calculations using PALLAS for Windows (version 3.0, Compu Drug Chemistry Ltd.) predicted the pK_a values of these amino alcohols as follows: 9.37 and 15.41 for **8**; 9.50

Table 2. Highly Coordinated Complexes between Various Yb Probes and Amino Alcohol **10-(S)**[a]

probe	log *K*	first λ/nm second λ/nm third λ/nm[c]	Amp[b]
1f	4.67	284 312	+2.90
3	4.95	292 329	+1.56
2b	*d*	288 311	*d*
(+)-4[c]	3.68	248 298 338	+0.65
(−)-4[c]	3.90	245 299 332	+0.99

[a] Conditions: Yb complex, 8.00×10^{-5} mol/L; in MeOH/CH_2Cl_2 (1/99). [b] The saturated Amp values {Amp = [θ at first λ] − [θ at second λ] for **1f** and **3**; Amp = [θ at second λ] − [θ at third λ] for **4** ($\times 10^{-5}$/deg cm^2 dmol^{-1})} were calculated under the conditions that all probes formed complexes with amino alcohols. [c] In these cases, three peaks were observed in their CD spectra. [d] The observed CD changes were too small to be used.

and 15.47 for **9**; 9.61 and 15.51 for **10**; 9.47 and 15.45 for **11**; 9.75 and 15.57 for **12**. Since the amino groups of the substrates have similar pK_a values, the more bulky substituent neighboring the amino group is thought to enforce asymmetric arrangement of three chromophoric β-diketonates more strongly and to offer a more intense CD signal.

Table 2 indicates the effects of the ligand structures on the stability constants of highly coordinated complexes between amino alcohol **10-(S)** and several ytterbium probes. When ytterbium tris(non-fluorinated β-diketonate) **2b** was employed, the observed UV and CD changes were too small to use for quantitative studies. Since their spectra also had time-dependent fluctuations, coexisting water molecules or another solvating species may occupy the coordination sites and disturb the bidentate chelation in the non-fluorinated ligand system. In other words, non-fluorinated β-diketonate ligands offered much more unstable highly coordinated complexes that exhibited unsteady CD spectra. The fluorinated β-diketonate ligands generally exhibited larger log *K* values and steady CD signals (see **1f**, **3**, and **4**), although ytterbium complex **4** having camphor-derived ligands gave 10 times smaller *K* values than one having acyclic β-diketonates **1f**. Chiral recognition was attained for a combination of amino alcohol **10-(S)** and camphoratoytterbium **4**. These ytterbium complexes having chiral β-diketonate ligands themselves exhibited CD signals around 300 nm, which overlapped with the CD signals derived from the highly coordinated complexes. Thus, the log *K* values indicated in Table 2 were estimated on the basis of differential CD data between those in the absence and those in the presence of amino alcohol **10-(S)**. The table indicates that the ytterbium complex (−)-**4** exhibited a larger log *K* value for amino alcohol **10-(S)** than (+)-**4**, but other amino alcohols such as 2-phenylglycinol, *cis*-1-amino-2-indanol, and 2-amino-1,2-diphenylethanol were nonstereoselectively bound by chiral ytterbium complex (+)- or (−)-**4**.[15]

4. Optical Purity Determination of Amino Alcohols by Lanthanide Complex Probe. Lanthanide tris(β-diketonates) are applicable as CD probes not only in the chirality sensing of amino alcohols but also in the quantitative determination of their optical purity. When the lanthanide probe was added to a mixture of (*R*)- and (*S*)-amino alcohol, the sign and amplitudes of the observed CD signals exhibited quantitative indication of enantiomer excess percentages of amino alcohol. Figure 5 illustrates plots of the CD amplitudes observed with probe **1f** against enantiomer excess percentages of the employed amino alcohols **8** and **10**: concentration of probe **1f**, 8.00×10^{-5} mol/L; total concentration of enantiomers of amino alcohol, 8.00×10^{-4} mol/L. When total concentrations of the enantiomers were kept constant, the linear correlation coefficients were confirmed to be more than 0.999 for the plots of both amino alcohols. Thus, such relationships can be employed to determine the optical purity of the amino alcohol on a microgram scale.

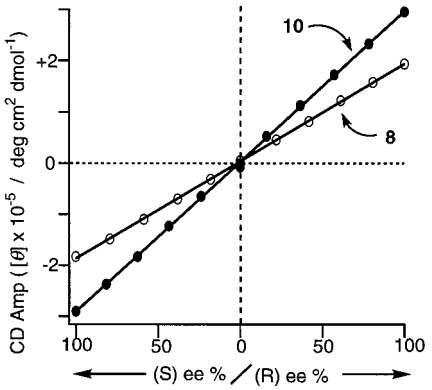

Figure 5. Relationships between enantiomer excess percentages of amino alcohols (**8** and **10**) and CD amplitudes with probe **1f**: [**1f**] = 8.00×10^{-5} mol/L; [**8-(R)**] + [**8-(S)**] or [**10-(R)**] + [**10-(S)**] = 8.00×10^{-4} mol/L; in MeOH/CH_2Cl_2 (1/99).

The lanthanide tris(β-diketonates) **1a**−**1f** caused broadening of ^{1}H NMR signals of the examined amino alcohol, diol, monoalcohol, and monoamine substrates but acted as neither chemoselective nor enantiomer-selective probes in NMR spectroscopy. When they were applied as CD probes, their probe behaviors drastically changed. We demonstrated above that they formed much more stable, highly coordinated complexes with amino alcohol than with the corresponding diol, monoamine, or monoalcohol and worked as specific fluorescence and CD probes of amino alcohols. Although the lanthanide cations are used to label organic molecules in the areas of clinical chemistry and molecular biology and are also employed in immunoassay and nucleic acid hybridization,[1] the structural optimization of lanthanide tris(β-diketonates) done here provides useful fluorescence and CD probing specific for amino alcohols. Further combinations of central lanthanide ions and achiral ligands offer wide variations in the design of a new sensory system for chiral substrates.

Experimental Section

General. ^{1}H and ^{13}C NMR spectra were recorded on JEOL LA-300 and GX-400 spectrometers. Fluorescence spectra were obtained on a Perkin-Elmer LS-50B equipped with a Hamamatsu R-928 photomultiplier, and CD spectra and $[\alpha]_D$ values were recorded with a Jasco J-720 spectrometer and a Jasco DIP-370 polarimeter, respectively.

Materials. Ytterbium tris(β-diketonate) **3** was prepared from ytterbium chloride and the corresponding β-diketone according to the literature[16] and recrystallized from hexane (24%). Anal. Calcd for $C_{15}H_3O_6F_{18}Yb \cdot 2H_2O$: C, 21.71; H, 0.84; Yb, 20.84. Found: C, 21.63; H, 0.83; Yb, 21.07.

(15) The log *K* values were estimated as 3.48 for (*R*)- or (*S*)-2-phenylglycinol, 2.95 for (*R*)- or (*S*)-*cis*-1-amino-2-indanol, and 2.37 for (*R*)- or (*S*)-2-amino-1,2-diphenylethanol in the MeOH/CH_2Cl_2 (1/99) solutions.

(16) Richardson, M. F.; Wagner, W. F.; Sands, D. E. *J. Inorg. Nucl. Chim.* **1968**, *30*, 1275.

The other probes **1a**−**1f**, **2a**, **2b**, and **4**−**6** illustrated in Figure 1 were obtained from Dojindo Laboratories (**1a, 1b**, and **2a**), Aldrich Chemical Co. (**1c**, **1d**, **1f**, **2b**, and **4**), Lancaster Synthesis Inc. (**1e**), Gelest Inc. (**5**), and Fluka/RdH (**6**). These were special grade reagents and used without further purification. Three kinds of chiral pyridylethanols **17**−**19** were resolved from racemic mixtures via lipase-catalyzed acetylation,[17] and the optical purity was confirmed by comparing $[\alpha]_D$ values with the reported ones:[18] −28.7 (c = 0.435 g/100 mL, $CHCl_3$) for **17-(S)**; -55.7 (c = 0.815 g/100 mL, $CHCl_3$) for **18-(S)**; −54.7 (c = 0.465 g/100 mL, MeOH) for **19-(S)**. Other amino alcohols and related substrates were received as enantiomerically pure forms from Aldrich Chemical Co. (**8 12** and **13**), Nacalai Tesque Inc. (**10**), Merck KGaA (**7**), Lancaster Synthesis Inc. (**16**) and Tokyo Chemical Ind. Co. (**9**, **11**, **14**, and **15**). Chiral 2-phenylglycinol was purchased from Tokyo Chemical Ind. Co., while *cis*-1-amino-2-indanol and 2-amino-1,2-diphenylethanol were obtained from Aldrich Chemical Co.

Fluorescence, CD, and UV Experiments. Since the spectroscopic profiles of the highly coordinated complexes with low stability constants were sensitive to the natures of the employed solvents, a mixture (1/99, v/v) of MeOH (or CD_3OD) and CH_2Cl_2 (or CD_2Cl_2) was used for quantitative analysis (Tables 1 and 2, Figures 3 and 5). The concentrations of lanthanide tris(β-diketonates) and substrates are shown in each table and figure.

Titration Experiments. For CD titration experiments, we usually prepared more than 10 samples with different ratios of amino alcohols and lanthanide probes. Typically, we pipetted 1.00 mL of a 8.00×10^{-4} mol/L solution of amino alcohol **10-(S)** and 0−8.00 mL of a 8.00×10^{-4} mol/L solution of probe **1f**. By addition of 9.00−1.00 mL of solvent, we adjusted the total volume of the solutions for measurements to be 10.00 mL. The CD and UV spectra of the resulting solutions were recorded after 0.5 h of being stirred at room temperature. Their amplitude values (Amp = $\{[\theta$ at first $\lambda] - [\theta$ at second $\lambda]\} \times 10^{-5}$/deg cm^2 dmol^{-1}) were plotted against substrate/probe ratios to calculate the log K values and the saturated Amp values. Two or three independent experiments were done for each combination, and the calculations were carried out as described below using IGOR Pro (version 3.1, WaveMetric Inc.). The standard deviation parameters (σ) of the estimated log K values were confirmed within 0.03 log unit, except for **1d**−**10-(S)** complex (0.10 log unit). In the NMR titration experiment for the **1f**−**14-(S)** complex, the standard deviation parameter was estimated as 0.05 log unit.

Determination of Stability Constants. The stability constant K for 1:1 highly coordinated complex formation is given by

$$K = \frac{[C]}{([P]_0 - [C])([G]_0 - [C])} \quad (1)$$

where [C], $[P]_0$, and $[G]_0$ represent the concentration of the highly coordinated complex in the equilibrated state and initial concentrations of the lanthanide probe and amino alcohol, respectively. Supposing that the amplitude "A" of the induced CD signal can be related to the saturated amplitude value "A_s" as in

$$A = \frac{[C]A_s}{[P]_0} \quad (2)$$

one can derive eq 3 by substituting eq 1 with eq 2:

$$A = \frac{[P]_0 + [G]_0 + 1/K - \sqrt{([P]_0 + [G]_0 + 1/K)^2 - 4[P]_0[G]_0}}{2[P]_0/A_s} \quad (3)$$

Substituting the measured A, $[P]_0$, and $[G]_0$ in eq 3, we determined the stability constant K with a nonlinear least-squares treatment. The observed spectral changes gave a good fit for each amino alcohol with the computer-calculated titration curve according to eq 3. We determined the stability constants using UV spectral data and obtained similar values for amino alcohols. The NMR method was also applied to determine the log K value for the complex between probe **1f** and diol **14** because its CD and UV changes were so small.

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