JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

Removal of Acidic or Basic α-Amino Acids in Water by Poorly Water Soluble Scandium Complexes

Nobuyuki Hayashi,*,† Shigeki Jin,‡ and Tomomi Ujihara§

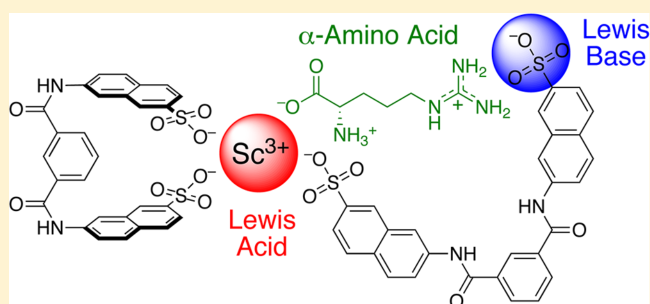
†National Food Research Institute, National Agriculture and Food Research Organization (NARO), 2-1-12 Kannondai, Tsukuba, Ibaraki 305-8642, Japan

‡Faculty of Health Science, Hokkaido University, Kita 12, Nishi 5, Kita-ku, Sapporo, Hokkaido 060-0812, Japan

§National Institute of Vegetable and Tea Science, National Agriculture and Food Research Organization (NARO), 2769 Kanaya, Shimada, Shizuoka 428-8501, Japan

Ⓢ Supporting Information

ABSTRACT: To recognize α-amino acids with highly polar side chains in water, poorly water soluble scandium complexes with both Lewis acidic and basic portions were synthesized as artificial receptors. A suspension of some of these receptor molecules in an α-amino acid solution could remove acidic and basic α-amino acids from the solution. The compound most efficient at preferentially removing basic α-amino acids (arginine, histidine, and lysine) was the receptor with 7,7′-[1,3-phenylenebis(carbonylimino)]bis(2-naphthalenesulfonate) as the ligand. The neutral α-amino acids were barely removed by these receptors. Removal experiments using a mixed amino acid solution generally gave results similar to those obtained using solutions containing a single amino acid. The results demonstrated that the scandium complex receptors were useful for binding acidic and basic α-amino acids.



■ INTRODUCTION

α-Amino acids are a class of extremely important compounds for living systems. They constitute proteins that form the structures of organisms or catalyze biological reactions and are precursors of a variety of biomolecules.[1] In addition, some α-amino acids are neurotransmitters[2] or taste substances.[3] In biosynthetic processes and signal transductions, the chemical structures of α-amino acids are recognized by enzyme and receptor proteins.[1−4] Mimicking these biochemical events using artificial molecules that sense α-amino acids is attractive from the perspective of molecular recognition chemistry. In the past three decades, numerous studies on the recognition of α-amino acids and their derivatives by artificial receptors have been reported using various receptor molecules. In most reported studies, the recognition of the α-amino acid derivatives was performed in organic solvents,[5−17] where the amino or carboxyl groups of the α-amino acids were protected, although actual biochemical recognition processes for native α-amino acids occur in aqueous systems. Even in the case of targeting native α-amino acids, although some studies have been performed in water,[18−28] organic or aqueous organic solvents often have been used to take advantage of electrostatic interactions, including hydrogen bonding, as the major intermolecular binding force.[29−39] Although nonpolar interactions can be utilized for easy and effective complexation in water, not all α-amino acids are nonpolar enough to form a stable complex with artificial receptor molecules in water through nonpolar interactions. Therefore, using electrostatic interactions as the main alternative intermolecular binding force is the natural approach. Because electrostatic interactions exert a greater effect in low-polarity organic solvents than in aqueous solutions, organic solvents have been used in many studies, where the amino or the carboxyl group of the α-amino acids was protected to increase the solubility in the low-polarity organic solvents.

To recognize native α-amino acids with highly polar side chains in water, the electrostatic interactions between the α-amino acids and the receptor molecules must be maintained in water. The present study focuses on scandium compounds as the receptor molecules. Because scandium compounds can maintain Lewis acidity even in aqueous media,[40] the complex composed of the receptor and α-amino acid should be stable even in water, due to the electrostatic interaction between the metal portion of the receptor molecule and the Lewis basic portion of the α-amino acid. This article describes the preferential molecular recognition of acidic and basic α-amino acids with highly polar side chains by scandium complex receptors in water.

■ RESULTS AND DISCUSSION

The concept of the receptor design is shown in Figure 1. If two ligands with two anionic portions in one molecule coordinate to a trivalent scandium cation, the resulting complex will have

Received: August 15, 2012
Published: October 10, 2012

 © 2012 American Chemical Society

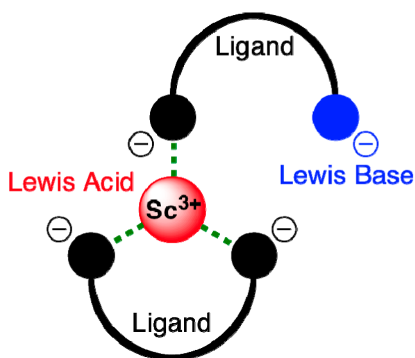


Figure 1. Concept of the scandium complex type receptor.

both Lewis acidic and Lewis basic portions within the same molecule. For this purpose, a ligand with two sulfonate groups was prepared. The sulfonate group is a good linker for coordinating the ligands to a scandium ion, as described in a previous study on a Lewis acid−surfactant combined catalyst (LASC).[41] In fact, four ligands (**1−4** in Scheme 1) were synthesized from isophthaloyl chloride and four amino-naphthalenesulfonic acids. To an aqueous solution of each ligand was added the aqueous scandium triflate solution at ambient temperature to obtain poorly water soluble solids. The ^{1}H and ^{45}Sc NMR spectra confirmed that all of the solids consisted of the ligand molecules and scandium atoms. The absence of resonance signals in the ^{19}F NMR spectra indicated that sulfonate ligands had replaced the triflates on the scandium

Scheme 1. Synthesis of Scandium Complex Receptors 5−8

ion. MALDI-TOF-MS analysis detected an m/z value of 1193 for all four solids. High-resolution MS analyses determined that these m/z values fit the mass of a complex composed of two ligands and one scandium ion. Therefore, the structures of these solid samples were determined as **5**–**8**, as shown in Scheme 1.[42]

To evaluate the ability of these receptor molecules to recognize α-amino acids in water, the removal ratio of the α-amino acids in suspensions of the receptors was investigated. This evaluation method is reasonable, because all of the receptor molecules were poorly water soluble. An equimolar amount of receptor **5**, **6**, **7**, or **8** was added to each deuterium oxide solution (0.700 mL) of 2.00 mM α-amino acid in a 2 mL microcentrifuge tube, and the resulting suspensions were stirred by a microtube mixer for 30 min at 25 °C. After centrifugation, the amount of amino acid remaining in the supernatant was determined by integration of the ^{1}H NMR spectrum. The bar graphs in Figure 2 illustrate the removal ratios of the α-amino acids in the supernatants. Receptor **5** showed greater selectivity for removal of the basic amino acids (arginine (Arg), histidine (His), and lysine (Lys)), with a removal ratio of >70%. Receptors **7** and **8** demonstrated a tendency to remove preferentially both the acidic amino acids (aspartic acid (Asp) and glutamic acid (Glu)) and basic amino acids. However, the removal ratio of His by **8** was less than those of Asp, Glu, Arg, and Lys, and receptor **7** did not remove His. Interestingly, **8** removed approximately 30% of the neutral α-amino acid tryptophan (Trp). The removed amino acids were found in the precipitates recovered after the removal experiments. This was confirmed by the ^{1}H NMR spectra of the DMSO-d_6 solutions of the recovered precipitates. Receptor **6** did not possess significant ability to remove any of the α-amino acids.

In complexes of the receptors and α-amino acids, the carboxyl groups (carboxylate form) of the amino acids probably coordinate to the scandium ions of the receptors. In the case of a carboxyl group with an amino group on the vicinal carbon, the amino group (ammonium form) may form a hydrogen bond with the sulfonate group coordinated to scandium. Such secondary interactions would contribute to stabilizing the complexes. The high removal ratios of the basic amino acids by **5** and **8** can be explained by stabilization of the complexes by interactions between functional groups on the side chains of the α-amino acids and the receptors, because the guanidinium group (Arg), imidazolium group (His), and ammonium group (Lys) of the basic amino acids can interact electrostatically with the Lewis basic portions (sulfonate groups) of the receptor molecules. However, it is difficult to determine which carboxyl group of the acidic α-amino acids interacts with the scandium ion of the receptor molecules. When a carboxyl group with an amino group on the α-position coordinates with the scandium, and the carboxyl group of the side chain of the amino acid is in the carboxylate form, the Lewis basic portions (sulfonate groups) of the receptor molecules have no effect on the stabilization of the complex through interaction with the carboxyl groups (carboxylate form) on the side chains because of the negative charges of both. However, depending on the chemical structure of the receptor molecule, the carboxyl group (carboxylate form) of the side chain might interact with the amide group of the receptor ligand through hydrogen bonding to stabilize the complex. If the carboxyl group of the side chain is in the carboxylic acid form, it will promote stabilization of the complex by hydrogen bonding with the Lewis basic portion (sulfonate group) of the receptor. In contrast, the carboxyl groups (carboxylate form) on the side chains of the amino acids might coordinate to the scandium. In this case, the amino groups (ammonium form) of the amino acid can interact with the Lewis basic portions (sulfonate groups) of the receptors. Thus, because both the acidic and the basic α-amino acids can interact with the receptors at multiple points through ionically electrostatic interactions, the resulting complexes will have greater stability than complexes with fewer interaction points.

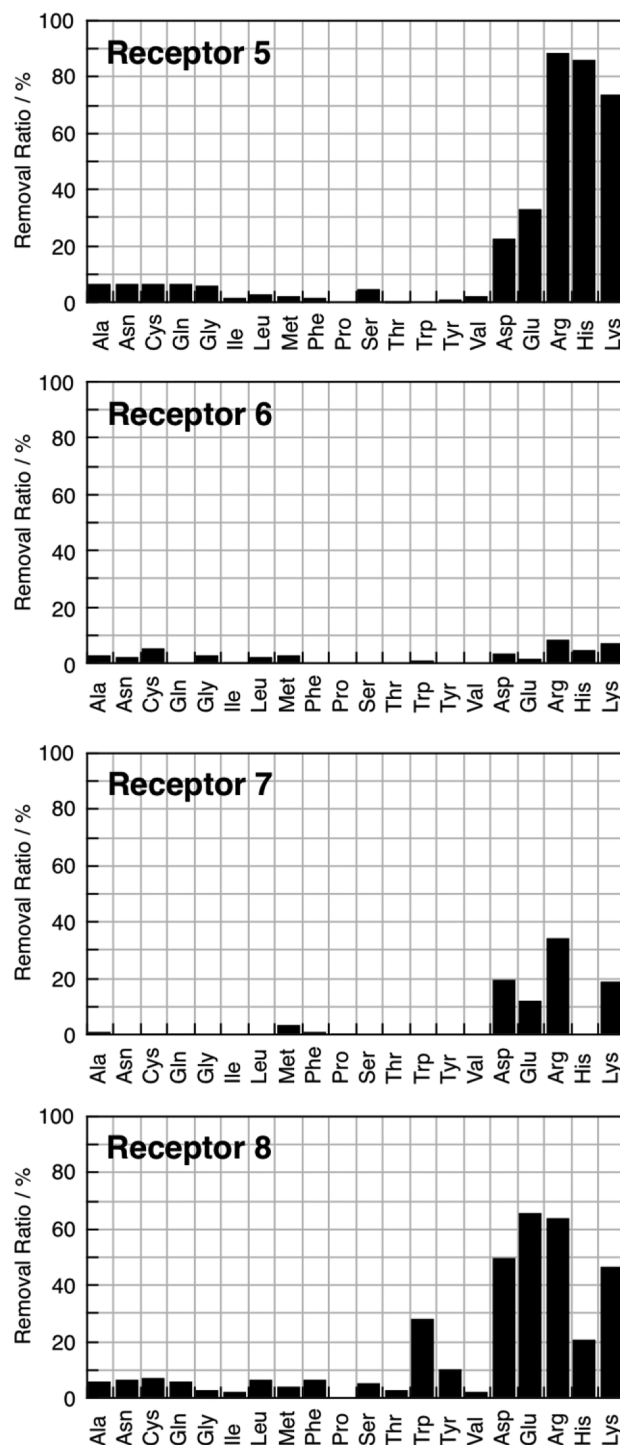


Figure 2. Removal ratio of α-amino acids by receptors **5**–**8**.

Unlike the acidic and basic α-amino acids, the neutral α-amino acids do not have side chains that can effectively contribute to stabilizing complexes with the receptors through

Table 1. Removal Ratios of α-Amino Acids in the Mixture Solutions and in the Corresponding Single Amino Acid Solutions

		mixture system								single system					
		amino acid (AA)			removal ratio/%					removal ratio/%			pH		
entry	rec[a]	AA1	AA2	AA3	AA1	AA2	AA3	total	pH	AA1	AA2	AA3	AA1	AA2	AA3
1	**5**	Ala	Glu	Asp	5.3	24.9	15.8	46.0	4.8	6.3	32.8	22.1	4.0	4.5	4.3
2	**7**	Ala	Glu	Asp	0.9	18.6	17.6	37.1	4.4	0.5	11.7	19.3	2.8	3.5	3.3
3	**8**	Ala	Glu	Asp	4.0	67.1	31.6	102.7	4.4	5.6	65.3	49.6	3.5	3.8	3.7
4	**5**	Ala	Glu	Arg	*b*	15.1	93.7	108.8	5.3	6.3	32.8	88.4	4.0	4.5	5.5
5	**7**	Ala	Glu	Arg	5.9	30.0	54.5	90.4	5.0	0.5	11.7	33.8	2.8	3.5	5.1
6	**8**	Ala	Glu	Arg	1.1	53.9	57.0	112.0	5.0	5.6	65.3	63.9	3.5	3.8	4.4
7	**5**	Ala	Glu	His	5.5	10.4	72.1	88.0	4.4	6.3	32.8	85.6	4.0	4.5	5.6
8	**7**	Ala	Glu	His	2.7	23.3	34.8	60.8	5.2	0.5	11.7	*b*	2.8	3.5	4.9
9	**8**	Ala	Glu	His	8.8	65.4	25.0	99.2	5.0	5.6	65.3	20.7	3.5	3.8	4.7
10	**5**	Ala	Glu	Lys	1.4	18.5	62.8	82.7	5.1	6.3	32.8	73.7	4.0	4.5	5.0
11	**7**	Ala	Glu	Lys	*b*	27.0	36.4	63.4	5.0	0.5	11.7	18.6	2.8	3.5	4.6
12	**8**	Ala	Glu	Lys	*b*	58.8	18.2	77.0	5.2	5.6	65.3	46.3	3.5	3.8	4.4
13	**5**	Ala	Asp	Arg	0.1	16.4	84.7	101.2	5.2	6.3	22.1	88.4	4.0	4.3	5.5
14	**7**	Ala	Asp	Arg	1.1	26.3	46.0	73.4	4.9	0.5	19.3	33.8	2.8	3.3	5.1
15	**8**	Ala	Asp	Arg	8.4	33.6	52.5	94.5	4.8	5.6	49.6	63.9	3.5	3.7	4.4
16	**5**	Ala	Asp	His	1.5	14.4	84.1	100.0	5.5	6.3	22.1	85.6	4.0	4.3	5.6
17	**7**	Ala	Asp	His	1.1	25.1	33.6	59.8	5.0	0.5	19.3	*b*	2.8	3.3	4.9
18	**8**	Ala	Asp	His	6.5	44.2	65.6	116.3	4.8	5.6	49.6	20.7	3.5	3.7	4.7
19	**5**	Ala	Asp	Lys	3.3	17.5	65.1	85.9	5.3	6.3	22.1	73.7	4.0	4.3	5.0
20	**7**	Ala	Asp	Lys	*b*	31.7	35.0	66.7	4.8	0.5	19.3	18.6	2.8	3.3	4.6
21	**8**	Ala	Asp	Lys	3.2	44.0	28.7	75.9	4.6	5.6	49.6	46.3	3.5	3.7	4.4
22	**8**	Ala	Glu	Trp	*b*	69.3	20.3	89.6	4.2	5.6	65.3	28.0	3.5	3.8	3.6

[a]Receptors. [b]Actual calculated values were from −0.2 to −1.9.

electrostatic interactions. This weakens the interaction between these amino acids and the receptors; therefore, the neutral amino acids are more difficult to remove in water by the receptor molecules. For example, the removal ratios of asparagine (Asn) and glutamine (Gln), neutral α-amino acids that are the amide derivatives of Asp and Glu, respectively, were 6.2% (Asn) and 6.5% (Gln) for **5**, 0% (Asn) and 0.2% (Gln) for **7**, and 6.0% (Asn) and 5.8% (Gln) for **8**, which were lower than those of Asp and Glu. Interestingly, the aromatic amino acids Trp, phenylalanine (Phe), and tyrosine (Tyr) were barely removed except for removal of Trp by **8**, although these amino acids appear to have advantages when forming complexes with receptor molecules in water because of interactions between the aromatic rings. This might be due to ineffective intermolecular interactions between the side chains of Trp, Phe, and Tyr and the ligands of scandium because of incompatible conformations.

The molecular recognition abilities of the receptors were tested by performing experiments using a solution of mixed amino acids (mixture systems). The receptor **5**, **7**, or **8** was added to the mixture solution containing three amino acids in equal molar amounts. As shown in Table 1, the removal ratios of the amino acids in these mixture systems were generally similar to those in the experiments using a single amino acid (single systems). However, interestingly, the removal ratios in some mixture systems were greater than that in each single system, although the mole number of the receptor molecule per α-amino acid decreased. These results cannot be explained simply on the basis of variations in the abundance ratios of the chemical species of the amino acids caused by changes in solution pH between the mixture and single systems. For example, in entry 5, although the abundance ratio of the chemical species of Arg is almost the same in the mixture system (pH 5.0) and in the single system (pH 5.1), where >99% of the chemical species exists as the guanidinium/$-NH_4^+/-CO_2^-$ form, the removal ratio in the mixture system was approximately 20% greater than that in the single system. Similar phenomena were apparent in entries 8 and 17. In the single system, His was not removed. Nevertheless, in the mixture systems, 30% of His was removed. In entry 8, the abundance ratio of the chemical species of His was calculated as 86.3% for the imidazolium/$-NH_4^+$/-CO_2^- form and 13.7% for the imidazoyl/$-NH_4^+/-CO_2^-$ form in the mixture system at pH 5.2, and 92.6% for the imidazolium/$-NH_4^+/-CO_2^-$ form and 7.4% for the imidazoyl/$-NH_4^+/-CO_2^-$ form in the single system at pH 4.9. In entry 17, the abundance ratio of the chemical species of His in the mixture system at pH 5.0 was 90.9% for the imidazolium/$-NH_4^+/-CO_2^-$ form and 9.1% for the imidazoyl/$-NH_4^+/-CO_2^-$ form; values in the single system at pH 4.9 were the same.

For the acidic amino acids, similar increases in the removal ratio were observed for some mixture systems. In entry 5 (involving receptor **7**), the removal ratio of Glu changed from 11.7% in the single system to 30.0% in the mixture system. The chemical species ratios of Glu were calculated as 15.1% for the $-CO_2H/-NH_4^+/-CO_2^-$ form and 84.9% for the $-CO_2^-/-NH_4^+/-CO_2^-$ form in the mixture system at pH 5.0 and 4.0% for the $-CO_2H/-NH_4^+/-CO_2H$ form, 81.5% for the $-CO_2H/-NH_4^+/-CO_2^-$ form, and 14.5% for the $-CO_2^-/-NH_4^+/-CO_2^-$ form in the single system at pH 3.5. It might appear that the increase in the $-CO_2^-/-NH_4^+/-CO_2^-$ form of Glu in the mixture system contributed to the change in the removal ratio. However, in entry 9 (involving receptor **8**), although the difference in pH between the mixture system (pH 5.0) and single system (pH 3.8) of Glu was similar to that in entry 5, the removal ratio of Glu was almost the same in the

mixture and the single systems of Glu, unlike the case in entry 5. Here, the chemical species ratio of Glu at pH 3.8 was calculated to be 17.8% for the $-CO_2H/-NH_4^+/-CO_2H$ form, 72.5% for the $-CO_2H$ $/-NH_4^+/-CO_2^-$ form, and 25.7% for the $-CO_2^-/-NH_4^+/-CO_2^-$ form.

In some mixture systems (entries 3, 4, 6, 13, and 18 in Table 1), the totals of the removal ratios of the amino acids exceeded 100%. These results suggest that the receptors do not necessarily form a 1:1 complex with the amino acids. This may be related to the coordination number of scandium, which can vary between 3 and 7.[43] Therefore, one factor that increased the removal ratios in mixture systems in comparison to the corresponding single systems may be multiple complex formation by the receptor molecule and a few α-amino acids.

In conclusion, poorly water soluble scandium complexes with Lewis acidic and basic portions were investigated as artificial receptors for recognizing the α-amino acids with the highly polar side chains in water. Some of the synthesized receptors could preferentially remove acidic or basic amino acids from the aqueous solution. These results suggest that this methodology is useful for binding such α-amino acids. In the future, water solubilization of receptor molecules and elaboration of ligand design may expand the applicable scope of this type of receptor.

■ EXPERIMENTAL SECTION

General Information. All reactions were performed in short-neck Kjeldahl flasks fitted with a polyethylene stopper containing a few holes made by a needle in an air atmosphere. Solutions were magnetically stirred during the reactions. Special reagent-grade organic solvents and reagents were used without further purification. Pure water was obtained using a water purification apparatus.

The ^1H, ^{13}C, and ^{45}Sc nuclear magnetic resonance (NMR) spectra were recorded on a 500 or 400 MHz spectrometer. Chemical shifts in ^1H NMR spectra are reported in ppm, referenced to the proton resonance of the residual proton of dimethyl sulfoxide (DMSO-d_6; δ 2.49 ppm). Chemical shifts in ^{13}C NMR spectra are reported in ppm, referenced to the carbon resonances of DMSO-d_6 (δ 39.50 ppm). Chemical shifts in ^{45}Sc NMR are reported in ppm, using scandium chloride (δ 0.00 ppm) in deuterium oxide as an external standard, which was inserted into an NMR tube (o.d. 5 mm) with a coaxial cell. Data are presented as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, dd = double doublet, t = triplet, m = multiplet, and br = broad), and coupling constant in Hz. Proton signals were assigned by double quantum filtered COSY, HMQC, HMBC, and NOESY methods. Hydrogen multiplicity information was obtained from HMQC spectra.

Infrared (IR) spectra were recorded on a FT-IR spectrometer. The MS analyses were performed in negative-ion mode. Measurement conditions of the ESI-TOF-MS were as follows: needle voltage, −2.5 kV; orifice voltage, −70 V; desolvation temperature, 80 °C; sample flow rate, 10 μL min^{-1}; solvent, H_2O. Reserpine was used as the calibrant for high-resolution measurements. The MALDI-TOF-MS was measured under the following conditions: accelerating voltage, −20 kV; pulse delay time, 145 ns; grid voltage, 67%. Sinapinic acid was used as a matrix. Sinapinic acid, angiotensin I, and angiotensin II were used as calibrants for high-resolution measurements.

Disodium 7,7′-[1,3-Phenylenebis(carbonylimino)]bis(2-naphthalenesulfonate) (1). A solution of isophthaloyl chloride (2.00 g, 9.85 mmol) in chloroform (100 mL) and 2.00 M aqueous sodium carbonate (Na_2CO_3) (4.98 mL) were added to a solution of sodium 7-amino-2-naphthalenesulfonate (4.83 g, 19.7 mmol) in pure water (380 mL) at ambient temperature (25 °C). The reaction mixture was stirred vigorously at ambient temperature for 18 h to generate a precipitate, which was separated by centrifugation (10 000*g*, 15 min, 15 °C). After recrystallization of the precipitate from hot water and centrifuge separation (47 000*g*, 20 min, 15 °C), the solid was freeze-dried to give compound **1** (2.35 g, 38%) as a solid: mp (**1** did not change in appearance up to 300 °C); ^1H NMR (500 MHz, DMSO-d_6) δ 10.68 (2H, s, N-*H*), 8.66 (1H, t, *J* = 1.9 Hz, C2-*H*), 8.41 (2H, dd, *J* = 1.6 Hz, C8′-*H*), 8.22 (2H, dd, *J* = 1.9, 8.0 Hz, C4-*H* and C6-*H*), 8.04 (2H, d, *J* = 1.5 Hz, C1′-*H*), 7.93 (2H, dd, *J* = 1.6, 8.9 Hz, C6′-*H*), 7.91 (2H, d, *J* = 8.9 Hz, C5′-*H*), 7.82 (2H, d, *J* = 8.6 Hz, C4′-*H*), 7.74 (1H, t, *J* = 8.0 Hz, C5-*H*), and 7.63 (2H, dd, *J* = 1.5, 8.6 Hz, C3′-*H*); ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.3 (C), 146.0 (C), 137.1 (C), 135.1 (C), 132.4 (C), 130.8 (CH), 129.8 (C), 128.7 (CH), 128.0 (CH), 127.1 (CH), 127.0 (CH), 123.6 (CH), 122.9 (CH), 121.4 (CH), and 117.2 (CH); IR (neat) 1648, 1541, 1172, 1096, 1031 cm^{-1}; HR-ESI-TOF-MS, calcd for $C_{28}H_{19}N_2O_8S_2$ (M − $2Na^+$ + H^+) 575.0588, found 575.0577.

Disodium 6,6′-[1,3-Phenylenebis(carbonylimino)]bis(1-naphthalenesulfonate) (2). An aqueous solution of 2.00 M Na_2CO_3 (9.96 mL) and a solution of isophthaloyl chloride (2.00 g, 9.85 mmol) in chloroform (100 mL) were added to sodium 6-amino-1-naphthalenesulfonic acid (4.40 g, 19.7 mmol) in pure water (250 mL) at ambient temperature (25 °C). The reaction mixture was stirred vigorously at ambient temperature for 18 h to generate a precipitate, which was separated by centrifugation (10 000*g*, 15 min, 15 °C) and filtered using a Kiriyama funnel. After recrystallization from hot water, the precipitate was divided into six centrifuge tubes and centrifuged (28 000*g*, 15 min, 15 °C). The supernatants were removed, and pure water (10 mL) was added to each aliquot. The precipitate was washed and separated by centrifugation (28 000*g*, 15 min, 15 °C). The washing processes were repeated three times. The precipitate was freeze-dried to give sulfonate **2** (5.27 g, 86%) as a solid: mp (**2** did not change in appearance up to 300 °C); ^1H NMR (500 MHz, DMSO-d_6) δ 10.64 (2H, s, N-*H*), 8.80 (2H, d, *J* = 9.2 Hz, C8′-*H*), 8.67 (1H, t, *J* = 1.8 Hz, C2-*H*), 8.50 (2H, d, *J* = 2.5 Hz, C5′-*H*), 8.22 (2H, dd, *J* = 1.8, 7.6 Hz, C4-*H* and C6-*H*), 7.85 (2H, dd, *J* = 1.3, 7.1 Hz, C2′-*H*), 7.84 (2H, dd, *J* = 1.3, 8.0 Hz, C4′-*H*), 7.82 (2H, dd, *J* = 2.5, 9.2 Hz, C7′-*H*), 7.73 (2H, t, *J* = 7.6 Hz, C5-*H*), and 7.41 (2H, dd, *J* = 7.1, 8.0 Hz, C3′-*H*); ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.3 (C), 143.9 (C), 136.3 (C), 135.1 (C), 134.0 (C), 130.8 (CH), 129.1 (CH), 128.6 (CH), 128.1 (CH), 127.0 (CH), 126.0 (C), 125.0 (CH), 123.3 (CH), 120.4 (CH), and 116.6 (CH); IR (neat) 1635, 1542, 1185, 1063 cm^{-1}; HR-ESI-TOF-MS, calcd for $C_{28}H_{19}N_2O_8S_2$ (M − $2Na^+$ + H^+) 575.0588, found 575.0557.

Disodium 4,4′-[1,3-Phenylenebis(carbonylimino)]bis(1-naphthalenesulfonate) (3). A solution of isophthaloyl chloride (2.00 g, 9.85 mmol) in chloroform (100 mL) and 2.00 M aqueous Na_2CO_3 (4.98 mL) were added to a solution of sodium 4-amino-1-naphthalenesulfonate tetrahydrate (6.25 g, 19.7 mmol) in pure water (100 mL) at 0 °C. The reaction mixture was stirred vigorously at ambient temperature (25 °C) for 23 h to generate a precipitate, which was separated by centrifugation (28 000*g*, 15 min, 15 °C) and then filtered through a Kiriyama funnel. After recrystallization from hot water, the precipitate was divided into two centrifuge tubes and centrifuged (28 000*g*, 15 min, 15 °C). The supernatants were removed, and pure water (10 mL) was added to each aliquot. The precipitate was washed and separated by centrifugation (28 000*g*, 15 min, 15 °C). The washing processes were repeated two times. The precipitate was freeze-dried to give sulfonate **3** (3.68 g, 60%) as a solid: mp (**3** did not change in appearance up to 300 °C); ^1H NMR (500 MHz, DMSO-d_6) δ 10.64 (2H, s, N-*H*), 8.92−8.88 (2H, m of ABMX spin system, C8′-*H*), 8.81 (1H, t, *J* = 1.5 Hz, C2-*H*), 8.30 (2H, dd, *J* = 1.5, 7.7 Hz, C4-*H* and C6-*H*), 7.57−7.52 (2H, m of ABMX spin system, C5′-*H*), 7.99 (2H, d, *J* = 8.0 Hz, C2′-*H*), 7.75 (1H, t, *J* = 7.7 Hz, C5-*H*), 7.56 (2H, d, *J* = 8.0 Hz, C3′-*H*), and 7.57−7.52 (4H, m of ABMX spin system, C6′-*H* and C7′-*H*). ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.8 (C), 142.4 (C), 134.73 (C), 134.70 (C), 130.9 (CH), 129.8 (C), 129.4 (C), 128.7 (CH), 127.9 (CH), 127.3 (CH), 125.6 (CH), 125.5 (CH), 124.1 (CH), 123.1 (CH), and 122.3 (CH); IR (neat) 1646, 1511, 1196, 1061 cm^{-1}; HR-ESI-TOF-MS, calcd for $C_{28}H_{19}N_2O_8S_2$ (M − $2Na^+$ + H^+) 575.0588, found 575.0571.

Disodium 8,8′-[1,3-Phenylenebis(carbonylimino)]bis(2-naphthalenesulfonate) (4). An aqueous solution of 2.00 M Na_2CO_3 (9.96 mL) and a solution of isophthaloyl chloride (2.00 g, 9.85 mmol) in chloroform (100 mL) were added to a solution of

sodium 8-amino-2-naphthalenesulfonic acid (4.40 g, 19.7 mmol) in pure water (100 mL) at ambient temperature (25 °C). The reaction mixture was stirred vigorously at ambient temperature for 18 h to generate a precipitate, which was separated by centrifugation (28 000*g*, 15 min, 15 °C) and filtered through a Kiriyama funnel. After recrystallization from hot water, the precipitate was divided into four centrifuge tubes and was centrifuged (28 000*g*, 15 min, 15 °C). The supernatants were removed, and pure water (5 mL) was added to each aliquot. The precipitate was washed and separated by centrifugation (28 000*g*, 15 min, 15 °C). This washing process was repeated two times. The precipitate was freeze-dried to give sulfonate **4** (1.73 g, 28%) as a solid: mp (**4** did not change in appearance up to 300 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.77 (2H, s, N-*H*), 8.76 (1H, t, *J* = 1.2 Hz, C2-*H*), 8.30 (2H, dd, *J* = 1.2, 7.7 Hz, C4-*H* and C6-*H*), 8.29 (2H, d, *J* = 1.6 Hz, C1′-*H*), 7.92 (2H, d, *J* = 8.6 Hz, C4′-*H*), 7.85 (2H, dd, *J* = 1.3, 7.3 Hz, C5′-*H*), 7.78 (2H, t, *J* = 7.7 Hz, C5-*H*), 7.74 (2H, dd, *J* = 1.6, 8.6 Hz, C3′-*H*), 7.59 (2H, dd, *J* = 1.3, 7.3 Hz, C7′-*H*), and 7.56 (2H, t, *J* = 7.3 Hz, C6′-*H*); ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.9 (C), 145.5 (C), 134.9 (C), 134.6 (C), 133.6 (C), 130.8 (CH), 128.7 (C and CH), 127.7 (CH), 127.4 (CH), 126.1 (CH), 126.0 (CH), 124.7 (CH), 124.1 (CH), and 119.7 (CH); IR (neat) 1647, 1524, 1495, 1174 cm^{-1}; HR-ESI-TOF-MS, calcd for $C_{28}H_{19}N_2O_8S_2$ (M − 2Na$^+$ + H$^+$) 575.0588, found 575.0579.

Scandium Sodium Bis{7,7′-[1,3-phenylenebis(carbonylimino)]bis(2-naphthalenesulfonate)} (5). A solution of trifluoromethanesulfonate scandium (0.282 g, 0.572 mmol) in pure water (2.00 mL) was added to a solution of sulfonate **1** (0.533 g, 0.859 mmol) in pure water (50 mL). The reaction mixture was stirred at ambient temperature (25 °C) for 1 h to generate a precipitate, which was separated by centrifugation (28 000*g*, 10 min, 15 °C). After the supernatant was removed, pure water (6 mL) was added to the centrifuge tube with the precipitate. The mixture was stirred using a spatula and was centrifuged (28 000*g*, 10 min, 15 °C), followed by removal of the supernatant. This washing procedure was repeated two times. The precipitate was freeze-dried to give scandium complex **5** (0.415 mg, 60%) as a solid: mp (**5** did not change in appearance up to 300 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.69 (4H, s, N-*H*), 8.64 (2H, t, *J* = 1.8 Hz, C2-*H*), 8.46 (4H, dd, *J* = 1.9 Hz, C8′-*H*), 8.22 (4H, dd, *J* = 1.8, 7.6 Hz, C4-*H* and C6-*H*), 8.08 (4H, d, *J* = 1.8 Hz, C1′-*H*), 7.94 (4H, d, *J* = 8.9 Hz, C5′-*H*), 7.92 (4H, dd, *J* = 1.9, 8.9 Hz, C6′-*H*), 7.86 (4H, d, *J* = 8.6 Hz, C4′-*H*), 7.74 (2H, t, *J* = 7.6 Hz, C5-*H*), and 7.65 (4H, dd, *J* = 1.8, 8.6 Hz, C3′-*H*); ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.3 (C), 144.9 (C), 137.3 (C), 135.1 (C), 132.4 (C), 130.8 (CH), 130.0 (C), 128.7 (CH), 128.1 (CH), 127.4 (CH), 127.1 (CH), 123.9 (CH), 122.6 (CH), 121.7 (CH), and 117.3 (CH); ^{45}Sc NMR (121 MHz, DMSO-d_6) δ 43.8; IR (neat) 1635, 1528, 1506, 1258, 1144, 1019 cm^{-1}; HR-MALDI-TOF-MS, calcd for $C_{56}H_{36}N_4O_{16}S_4Sc$ (M − Na$^+$) 1193.0574, found 1193.0562.

Scandium Sodium Bis{6,6′-[1,3-phenylenebis(carbonylimino)]bis(1-naphthalenesulfonate)} (6). A solution of trifluoromethanesulfonate scandium (0.267 g, 0.543 mmol) in pure water (2.00 mL) was added to a solution of sulfonate **2** (0.506 g, 0.815 mmol) in pure water (250 mL). The reaction mixture was stirred at ambient temperature (25 °C) for 1 h to generate a precipitate, which was separated by centrifugation (28 000*g*, 10 min, 15 °C). After the supernatant was removed, pure water (5 mL) was added to the centrifuge tube with the precipitate. The mixture was stirred using a spatula and was centrifuged (28 000*g*, 10 min, 15 °C), followed by removal of the supernatant. This washing procedure was repeated two times. The precipitate was freeze-dried to give scandium complex **6** (0.385 mg, 58%) as a solid: mp (**6** did not change in appearance up to 300 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.65 (4H, s, N-*H*), 8.79 (4H, d, *J* = 9.5 Hz, C8′-*H*), 8.66 (2H, t, *J* = 1.9 Hz, C2-*H*), 8.49 (4H, d, *J* = 2.2 Hz, C5′-*H*), 8.22 (4H, dd, *J* = 1.9, 8.0 Hz, C4-*H* and C6-*H*), 7.90−7.86 (8H, m of ABX spin system, C2′-*H* and C4′-*H*), 7.85 (4H, dd, *J* = 2.2, 9.5 Hz, C7′-*H*), 7.74 (4H, t, *J* = 8.0 Hz, C5-*H*), and 7.43 (4H, dd of ABX spin system, *J* = 7.3, 7.9 Hz, C3′-*H*); ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.3 (C), 143.2 (C), 136.4 (C), 135.1 (C), 134.0 (C), 130.8 (CH), 129.5 (CH), 128.7 (CH), 127.9 (CH), 127.1 (CH), 125.9 (C), 125.0 (CH), 123.5 (CH), 120.6 (CH), and 116.7 (CH); ^{45}Sc NMR (121 MHz, DMSO-d_6) δ 44.9; IR (neat) 1635, 1520, 1506, 1257, 1144, 1019 cm^{-1}; HR-MALDI-TOF-MS, calcd for $C_{56}H_{36}N_4O_{16}S_4Sc$ (M − Na$^+$) 1193.0574, found 1193.0553.

Scandium Sodium Bis{4,4′-[1,3-phenylenebis(carbonylimino)]bis(1-naphthalenesulfonate)} (7). A solution of trifluoromethanesulfonate scandium (0.269 g, 0.546 mmol) in pure water (2.00 mL) was added to a solution of sulfonate **3** (0.509 g, 0.820 mmol) in pure water (45 mL). The reaction mixture was stirred at ambient temperature (25 °C) for 23 h to generate a precipitate, which was separated by centrifugation (28 000*g*, 10 min, 15 °C). After the supernatant was removed, pure water (3 mL) was added to the centrifuge tube with the precipitate. The mixture was stirred using a spatula and was centrifuged (28 000*g*, 10 min, 15 °C), followed by removal of the supernatant. This washing procedure was repeated three times. The precipitate was freeze-dried to give scandium complex **7** (0.325 mg, 49%) as a solid: mp (decomposition at ca. 138 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.67 (4H, s, N-*H*), 8.91−8.87 (4H, m of ABMX spin system, C8′-*H*), 8.79 (2H, t, *J* = 1.5 Hz, C2-*H*), 8.31 (4H, dd, *J* = 1.5, 7.6 Hz, C4-*H* and C6-*H*), 8.08−8.04 (4H, m of ABMX spin system, C5′-*H*), 8.01 (4H, d, *J* = 8.0 Hz, C2′-*H*), 7.76 (2H, t, *J* = 7.6 Hz, C5-*H*), 7.58 (4H, d, *J* = 8.0 Hz, C3′-*H*), and 7.60−7.54 (8H, m of ABMX spin system, C6′-*H* and C7′-*H*); ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.9 (C), 141.5 (C), 135.2 (C), 134.7 (C), 130.9 (CH), 129.6 (C), 129.5 (C), 128.8 (CH), 127.7 (CH), 127.4 (CH), 125.9 (CH), 125.7 (CH), 124.4 (CH), 123.3 (CH), and 122.3 (CH); ^{45}Sc NMR (121 MHz, DMSO-d_6) δ 45.0; IR (neat) 1627, 1528, 1506, 1257, 1144, and 1019 cm^{-1}; HR-MALDI-TOF-MS, calcd for $C_{56}H_{36}N_4O_{16}S_4Sc$ (M − Na$^+$) 1193.0574, found 1193.0561.

Scandium Sodium Bis{8,8′-[1,3-phenylenebis(carbonylimino)]bis(2-naphthalenesulfonate)} (8). A solution of trifluoromethanesulfonate scandium (0.267 g, 0.543 mmol) in pure water (2.00 mL) was added to a solution of sulfonate **4** (0.505 g, 0.814 mmol) in pure water (16.5 mL). The reaction mixture was stirred at ambient temperature (25 °C) for 1 h to generate a precipitate, which was separated by centrifugation (28 000*g*, 10 min, 15 °C). After the supernatant was removed, pure water (10 mL) was added to the centrifuge tube with the precipitate. The mixture was stirred using a spatula and was centrifuged (28 000*g*, 10 min, 15 °C), followed by removal of the supernatant. This washing procedure was repeated three times. The precipitate was freeze-dried to give scandium complex **8** (0.387 mg, 59%) as a solid: mp (decomposition at ca. 200 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.82 (4H, s, N-*H*), 8.76 (2H, t, *J* = 1.5 Hz, C2-*H*), 8.34 (4H, dd, *J* = 1.5, 7.6 Hz, C4-*H* and C6-*H*), 8.30 (4H, d, *J* = 1.9 Hz, C1′-*H*), 7.92 (4H, d, *J* = 8.6 Hz, C4′-*H*), 7.90 (4H, m of ABX spin system, C5′-*H*), 7.81 (4H, t, *J* = 7.6 Hz, C5-*H*), 7.77 (4H, dd, *J* = 1.9, 8.6 Hz, C3′-*H*), and 7.62−7.59 (8H, ABX spin system, C6′-*H* and C7′-*H*); ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.9 (C), 144.2 (C), 134.71 (C), 134.68 (C), 133.8 (C), 130.8 (CH), 128.9 (CH), 128.7 (C), 128.1 (CH), 127.5 (CH), 126.5 (CH), 126.4 (CH), 125.0 (CH), 123.8 (CH), and 120.2 (CH); ^{45}Sc NMR (121 MHz, DMSO-d_6) δ 44.0; IR (neat) 1632, 1520, 1495, 1258, 1146, 1102, 1018 cm^{-1}; HR-MALDI-TOF-MS, calcd for $C_{56}H_{36}N_4O_{16}S_4Sc$ (M − Na$^+$) 1193.0574, found 1193.0551.

Removal from a Single α-Amino Acid Solution (Typical Procedure). A receptor compound (1.7 mg, 1.40 μmol) was added to a deuterium oxide solution (0.700 mL) of an α-amino acid (1.40 μmol) in a 2 mL microcentrifuge tube. The reaction mixture was vigorously stirred using a microtube mixer (MT-360, Tomy Seiko Co., Ltd., Tokyo, Japan) for 30 min at ambient temperature (25 °C), followed by centrifugation. The supernatant was filtered through a PTFE membrane filter (pore size, 0.45 μm). The amount of remaining amino acid in the filtrate was quantifed by ^{1}H NMR experiments. Integration of the ^{1}H NMR signals for the α-amino acid was done with reference to the integral value of the methyl group of a deuterium oxide solution of methanol (20 mM), which was inserted into an NMR tube (o.d. = 5 mm) with a coaxial cell. The removal ratio of the α-amino acid was calculated by comparing the integral values of the proton signals of the α-amino acid in the supernatant with those in the original α-amino acid solution that was not treated by the receptor compound.

Removal from a Mixed Solution of α-Amino Acids (Typical Procedure). A receptor compound (1.7 mg, 1.40 μmol) was added to a deuterium oxide solution (0.700 mL) containing three α-amino acids (1.40 μmol each) in a 2 mL microcentrifuge tube. The reaction mixture was vigorously stirred using a microtube mixer (MT-360, Tomy Seiko Co., Ltd., Tokyo, Japan) for 30 min at ambient temperature (25 °C), followed by centrifugation. The supernatant was filtered through a PTFE membrane filter (pore size, 0.45 μm). The amounts of amino acids remaining in the filtrate were quantifed by ^{1}H NMR experiments. Integration of the ^{1}H NMR signals of the α-amino acids was done with reference to the integral value of the methyl group of a deuterium oxide solution of methanol (20 mM), which was inserted into an NMR tube (o.d. = 5 mm) with a coaxial cell. The removal ratios of the α-amino acids were calculated by comparing the integral values of the α-amino acids in the supernatant with those in the original α-amino acid solution that was not treated by the receptor compound.

■ ASSOCIATED CONTENT

Supporting Information

Text giving additional references and figures giving ^{1}H and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: hayn@affrc.go.jp.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by JSPS KAKENHI Grant Number 23550171. The MS analyses were conducted using instruments of the Open Facility, Hokkaido University Sousei Hall.

■ REFERENCES

(1) Meister, A. *Biochemistry of the Amino Acids*; Academic Press: New York, 1965; Vols. *1* and 2.
(2) Rousseaux, C. G. *J. Toxicol. Pathol.* **2008**, *21*, 25−51.
(3) Boughter, J. D., Jr.; Munger, S. D. In *Encyclopedia of Biological Chemistry*; Lennarz, W. J., Lane, M. D., Eds.; Elsevier: Oxford, U.K., 2004; Vol. *4*, pp 158−161.
(4) Ibba, M.; Söll, D. *Annu. Rev. Biochem.* **2000**, *69*, 617−650.
(5) Deniz, P.; Turgut, Y.; Togrul, M.; Hosgoren, H. *Tetrahedron* **2011**, *67*, 6227−6232.
(6) Alfonso, I.; Burguete, M. I.; Galindo, F.; Luis, S. V.; Vigara, L. *J. Org. Chem.* **2009**, *74*, 6130−6142.
(7) Gerbaux, P.; Winter, J. D.; Cornil, D.; Ravicini, K.; Pesesse, G.; Cornil, J.; Flammang, R. *Chem. Eur. J.* **2008**, *14*, 11039−11049.
(8) Murashima, T.; Tsukiyama, S.; Fujii, S.; Hayata, K.; Sakai, H.; Miyazawa, T.; Yamada, T. *Org. Biomol. Chem.* **2005**, *3*, 4060−4064.
(9) Lin, J.; Li, Z.-B.; Zhang, H.-C.; Pu, L. *Tetrahedron Lett.* **2004**, *45*, 103−106.
(10) Hembury, G.; Rekharsky, M.; Nakamura, A.; Inoue, Y. *Org. Lett.* **2000**, *2*, 3257−3260.
(11) Demirtas, H. N.; Bozkurt, S.; Durmaz, M.; Yilmaz, M.; Sirit, A. *Tetrahedron* **2009**, *65*, 3014−3018.
(12) Sdira, S. B.; Felix, C. P.; Giudicelli, M.-B. A.; Seigle-Ferrand, P. F.; Perrin, M.; Lamartine, R. J. *J. Org. Chem.* **2003**, *68*, 6632−6638.
(13) Kuroda, Y.; Kato, Y.; Higashioji, T.; Hasegawa, J.; Kawanami, S.; Takahashi, M.; Shiraishi, N.; Tanabe, K.; Ogoshi, H. *J. Am. Chem. Soc.* **1995**, *117*, 10950−10958.
(14) Konishi, K.; Yahara, K.; Toshishige, H.; Aida, T.; Inoue, S. *J. Am. Chem. Soc.* **1994**, *116*, 1337−1344.
(15) Fokkens, M.; Schrader, T.; Klarner, F.-G. *J. Am. Chem. Soc.* **2005**, *127*, 14415−14421.
(16) Oliva, A. I.; Simón, L.; Hernández, J. V.; Muñiz, F. M.; Lithgow, A.; Jiménez, A.; Morán, J. R. *J. Chem. Soc., Perkin Trans. 2* **2002**, 1050−1052.
(17) Wehner, M.; Schrader, T.; Finocchiaro, P.; Failla, S.; Consiglio, G. *Org. Lett.* **2000**, *2*, 605−608. See also additional references for refs 5−17 in the Supporting Information.
(18) Yi, J.-M.; Zhang, Y.-Q.; Cong, H.; Xue, S.-F.; Tao, Z. *J. Mol. Struct.* **2009**, *933*, 112−117.
(19) Cort, A. D.; Bernardin, P. F.; Schiaffino, L. *Chirality* **2009**, *21*, 104−109.
(20) Arena, G.; Casnati, A.; Contino, A.; Gulino, F. G.; Magrì, A; Sansone, F.; Sciotto, D.; Ungaro, R. *Org. Biomol. Chem.* **2006**, *4*, 243−249.
(21) Miranda, C.; Escartí, F.; Lamarœë, L.; Yunta, M. J. R.; Navarro, P.; García-España, E.; Jimeno, L. *J. Am. Chem. Soc.* **2004**, *126*, 823−833.
(22) Imai, H.; Munakata, H.; Uemori, Y.; Sakura, N. *Inorg. Chem.* **2004**, *43*, 1211−1213.
(23) Silva, E. D.; Coleman, A. W. *Tetrahedron* **2003**, *59*, 7357−7364.
(24) Rensing, S.; Schrader, T. *Org. Lett.* **2002**, *4*, 2161−2164.
(25) Chin, J.; Lee, S. S.; Lee, K. J.; Park, S.; Kim, D. H. *Nature* **1999**, *401*, 254−257.
(26) Liu, Y.; Zhang, Y.-M.; Sun., S.-X.; Li, Y.-M.; Chen, R.-T. *J. Chem. Soc., Perkin Trans. 2* **1997**, 1609−1613.
(27) Chen, H.; Ogo, S.; Fish, R. H. *J. Am. Chem. Soc.* **1996**, *118*, 4993−5001.
(28) Corradini, R.; Dossena, A.; Impellizzeri, G.; Maccarrone, G.; Marchelli, R.; Rizzarelli, E.; Sartor, G.; Vecchio, G. *J. Am. Chem. Soc.* **1994**, *116*, 10267−10274. See also the additional references for refs 17−28 in the Supporting Information.
(29) Ballistreri, F. P.; Pappalardo, A.; Tomaselli, G. A.; Toscano, R. M.; Sfrazzetto, G. T. *Eur. J. Org. Chem.* **2010**, 3806−3810.
(30) Wang, H.; Chan, W.-H.; Lee, A. W. *Org. Biomol. Chem.* **2008**, *6*, 929−934.
(31) Zielenkiewicz, W.; Marcinowicz, A.; Cherenok, S.; Kalchenko, V.; Poznański, J. *Supramol. Chem.* **2006**, *18*, 167−176.
(32) Folmer-Andersen, J. F.; Lynch, V. M.; Anslyn, E. V. *J. Am. Chem. Soc.* **2005**, *127*, 7986−7987.
(33) Shinoda, S.; Okazaki, T.; Player, T. N.; Misaki, H.; Hori, K.; Tsukube, H. *J. Org. Chem.* **2005**, *70*, 1835−1843.
(34) Debroy, P.; Banerjee, M.; Prasad, M.; Moulik, S. P.; Roy, S. *Org. Lett.* **2005**, *7*, 403−406.
(35) Pagliari, S.; Corradini, R.; Galaverna, G.; Sforza, S.; Dossena, A.; Montalti, M.; Prodi, L.; Zaccheroni, N.; Marchelli, R. *Chem. Eur. J.* **2004**, *10*, 2749−2758.
(36) Bell, T. W.; Khasanov, A. B.; Drew, M. G. B. *J. Am. Chem. Soc.* **2002**, *124*, 14092−14103.
(37) Ait-Haddou, H.; Wiskur, S. L.; Lynch, V. M.; Anslyn, E. V. *J. Am. Chem. Soc.* **2001**, *123*, 11296−11297.
(38) Tsukube, H.; Wada, M.; Shinoda, S.; Tamiaki, H. *Chem. Commun.* **1999**, 1007−1008.
(39) Galán, A.; Andreu, D.; Echavarren, A. M.; Prados, P.; Mendoza, J. d. *J. Am. Chem. Soc.* **1992**, *114*, 1511−1512. See also the additional references for refs 29−39 in the Supporting Information.
(40) Kobayashi, S. *Eur. J. Org. Chem.* **1999**, 15−27.
(41) Manabe, K.; Mori, Y.; Wakabayashi, T.; Nagayama, S.; Kobayashi, S. *J. Am. Chem. Soc.* **2000**, *122*, 7202−7207.
(42) Some similarity in the ^{1}H and ^{13}C NMR spectra between scandium complexes and ligand molecules suggests that the ligands might dissociate from the scandium ion in DMSO-d_6.
(43) Cotton, S. In *Lanthanide and Actinide Chemistry*; Wiley: West Sussex, U.K., 2006; Chapter 7.

■ NOTE ADDED AFTER ASAP PUBLICATION

The toc/abstract graphic contained errors in the version published ASAP October 10, 2012; the correct version reposted October 22, 2012.