Enantioselective fluorescent sensors for chiral carboxylates based on BINOL — Synthesis and chiral recognition

Kuo-xi Xu, Yu-xia Wang, Shu-yan Jiao, Jin Zhao, and Chao-jie Wang

Abstract: The four novel derivatives of 1,1′-bi-2-naphthol (BINOL) have been prepared, and the structures of these compounds have been characterized by IR, MS, ^{1}H and ^{13}C NMR spectroscopy, and elemental analysis. The enantioselective recognition of these receptors has been studied by fluorescence titration and ^{1}H NMR spectroscopy. The receptors exhibited different chiral-recognition abilities towards some enantiomers of chiral materials and formed 1:1 complexes between host and guest. The receptors exhibit excellent enantioselective fluorescent-recognition ability towards the amino acid derivatives.

Key words: receptor, fluorescence, enantioselective recognition, anions, NMR spectroscopy.

Résumé : On a préparé quatre nouveaux dérivés du BINOL et on en a déterminé les structures par analyse élémentaire et par spectroscopies infrarouge, de masse et RMN du ^{1}H et du ^{13}C. On a étudié les propriétés de reconnaissance énantiosélective de ces récepteurs par titrage de fluorescence et par spectroscopie RMN du ^{1}H. Les récepteurs présentent diverses capacités à reconnaître la chiralité de quelques énantiomères de produits chiraux et ils forment des complexes 1:1 entre molécules hôtes et invitées. Les récepteurs présentent une capacité excellente de reconnaître une fluorescence énantiosélective vis-à-vis des dérivés d'acides aminés.

Mots-clés : récepteur, fluorescence, reconnaissance énantiosélective, anions, spectroscopie RMN.

[Traduit par la Rédaction]

Introduction

Molecular recognition, and in particular chiral recognition, is a fundamental characteristic in the biochemical systems. The study of synthetic model systems could contribute to the understanding of these processes and, at the same time, offer new perspectives for the development of pharmaceuticals, enantioselective sensors, catalysts, and other molecular devices.[1] The basis of any chiral recognition event is the formation of diastereomeric complexes composed of a chiral receptor and a chiral substrate possessing different stabilities.[2] The crucial points in the molecular design of chemosensors are how to achieve the specific recognition of a certain molecule and how to transduce the recognition event into a signal.[3] Many efforts involve the covalent linking of an optical signaling unit (a chromophore or a fluorophore) to a specific receptor for the chiral molecuales.[4] Compared with other detection methods, such as NMR, HPLC, CD, or capillary electrophoresis, fluorescence techniques have often been used to study the interaction between enantiomers and receptors because of their sensitivity, selectivity, and versatility.[5] On the basis of their respective advantages, we attempt to design some receptors with optical response to the enantiomers in the recognition interaction, which may offer a simple method to explore the recognition process for more information. The binaphthyl unit was especially eye-catching for its stable chiral configuration and tunable dihedral angle between the two naphthalene rings. Over the last two decades, binaphthyl derivatives have been shown to exhibit excellent enantioselectivities and turnovers in several types of asymmetric reactions, often matching the enantioselectivities traditionally regarded as being reserved for the enzyme realm.[6] As a naturally occurring chiral source, amino acids generally exhibit biological activity, and their recognition, in particular chiral recognition, attracts considerable interest.[7] Furthermore, they can be easily modified at the amino and carboxylic groups, which can also act as binding sites to form coordinate bonds with chiral molecules, so they were often used in the design and synthesis of artificial chiral receptors,[8] such as different types of acyclic compounds[9] as host molecules. We chose several familiar amino acids (e.g., alanine, phenylalanine) as chiral building blocks and introduced them into the 1,1′-bi-2-naphthol (BINOL) framework to construct the fluorescent receptors (Scheme 1). Herein, we describe the development of BINOL

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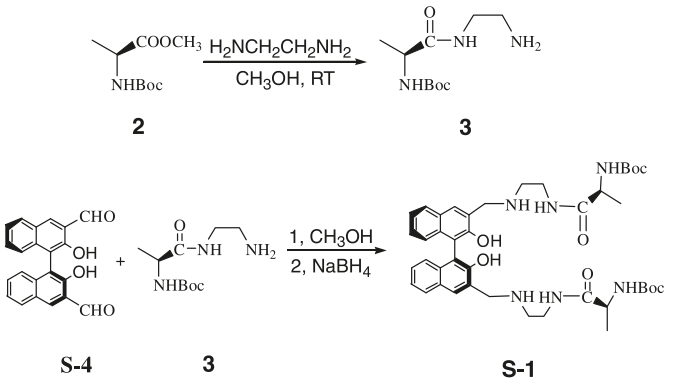
Scheme 1. Synthesis of the receptor **S-1**.



derivatives bearing amino acid units, and their bonding properties with some enantiomers of chiral materials have been examined by using fluorescence titration experiments in $CHCl_3$. Receptors exhibited good enantioselective recognition abilities towards chiral materials and formed 1:1 complex with the guests in $CHCl_3$. ^1H NMR experiments suggested that hydrogen-bonding interactions between the host and guest were the main factor in the recognition process.

Results and discussion

Synthesis

The synthesis of receptor **S-1** is outlined in Scheme 1. The starting materials binaphthyl dialdehydes were prepared from BINOL.[10] *N*-Boc-protected alanine methyl ester (**2**) were synthesized according to the literature with high yield,[11] and then reacted with excess amount of ethylenediamine to obtain the compound (*S*)-*tert*-butyl-1-(2-aminoethylamino)-1-oxopropan-2-ylcarbamate (**3**). To avoid the partial racemization of **3** in this reaction, the compound **2** and ethylenediamine were dissolved in large amount of methanol and stirring was continued at room temperature. Especially at the end of reaction, the solvent and ethylenediamine should be evaporated under high vacuum at about 30 °C, because a little higher temperature may lead the racemization of compound. Condensation of *S*-binaphthyl dialdehydes with compound **3**, followed by reduction, afforded the disubstituted BINOL **S-1** (Scheme 1). To study how the BINOL and amino acid units in **S-1** influenced the enantioselective fluorescent recognition, **R-1**, **S-5**, and **R-5** were also prepared (Fig. 1). They are readily soluble in common organic solvents, such as $CHCl_3$, CH_2Cl_2, CH_3OH, DMSO, and DMF. The structures of all these compounds were characterized by IR, MS, ^1H and ^{13}C NMR spectroscopy, and elemental analysis.

Fluorescence spectra study

The properties of the chiral recognition of receptors **S-1** were investigated in the absence and presence of various chiral carboxylates (Fig. 2), such as (*S*)- and (*R*)-mandelate, the α-phenylglycine anion, *N*-Boc-protected alanine anion (Ala), and *N*-Boc-protected phenylalanine anion (Phe), in which the amino groups were protected by the *tert*-butyloxycarbonyl functionality. In each case, tetrabutylammonium was used as the counter cation, which could increase the reaction

Fig. 1. Structures of the receptors **R-1**, **S-5**, and **R-5.**

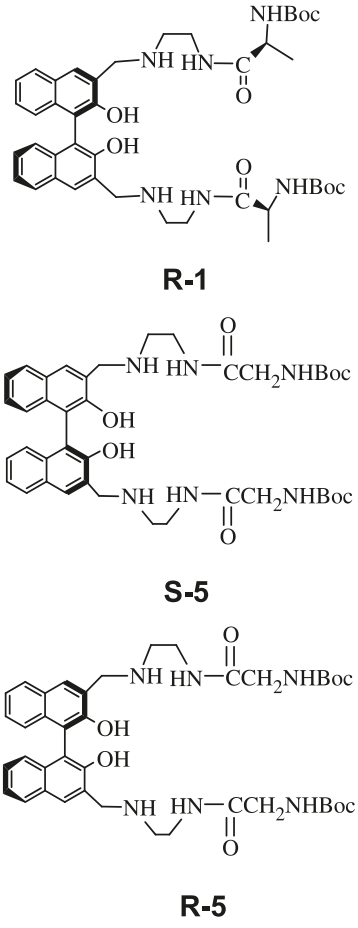
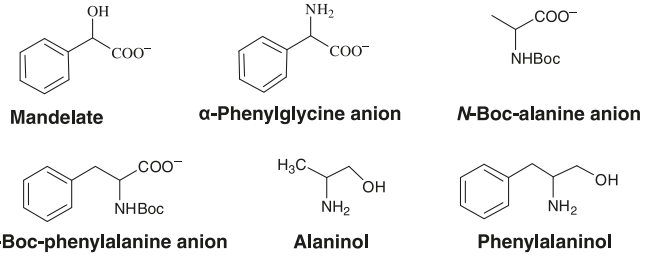


Fig. 2. Structures of the guests.



between the receptor and guest by hydrogen bondings.[1c] We also chose two amino alcohols, namely, alaninol and phenylalaninol, as guests to compare the associated abilities of the hosts to bind with neutral molecules.

The fluorescence spectra were recorded from a solution of sensor **S-1** (1.22×10^{-5} mol L^{-1}) in $CHCl_3$ in the absence or presence of various enantiomers, (*R*)-, (*S*)-Ala, and Phe anions. Because there was almost no change observed on the UV–vis spectra of receptors upon addition of the anions, the interaction between host and anion was only evaluated by fluorescent spectra.

Upon addition of (*S*)- or (*R*)-Ala or Phe anions, different fluorescent-quenching degrees of **S-1** were observed. The quenching efficiencies of (*S*)-amino acid anions were much higher than the (*R*)-amino acid anions. Figure 3 and Fig. 4 show the fluorescence emission spectra of a mixture of **S-1**

Fig. 3. Fluorescence spectra of receptor **S-1** (1.22×10^{-5} mol L^{-1}) with (*S*)-Ala anion in $CHCl_3$. The anion equivalents are: 0, 2, 4, 6, 8, 10, 20, 40, 60, 80, 100, 150, 200, 300, and 500. λ_{ex} = 278 nm. Inset: changes in the fluorescence intensity of **S-1** at 371 nm upon addition of (*S*)-Ala anion. The line shown is a line-fitted curve. The correlation coefficient (*R*) of the nonlinear curve fitting is 0.9994.

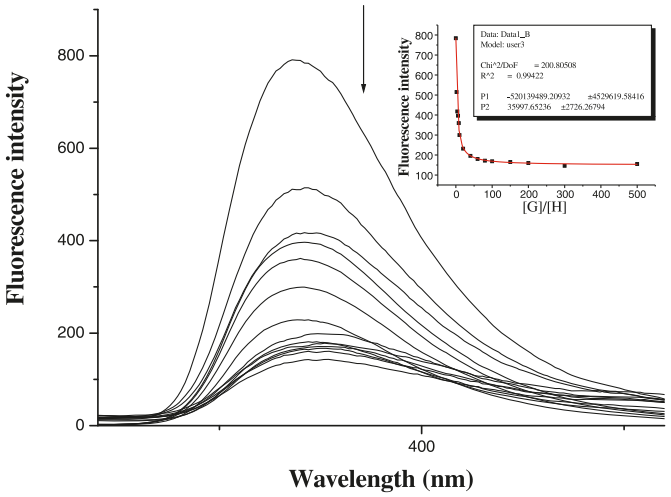
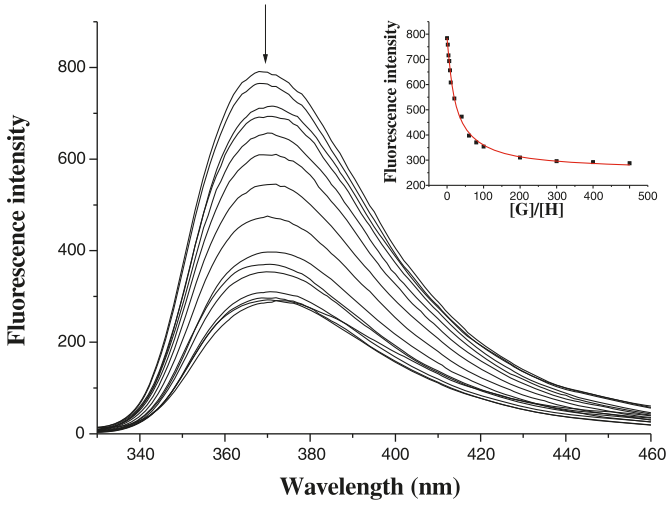


Fig. 4. Fluorescence spectra of receptor **S-1** (1.22×10^{-5} mol L^{-1}) with (*S*)-Ala anion in $CHCl_3$. The anion equivalents are: 0, 2, 4, 6, 8, 10, 20, 40, 60, 80, 100, 200, 300, 400, and 500. λ_{ex} = 278 nm. Inset: changes in the fluorescence intensity of **S-1** at 371 nm upon addition of (*S*)-Ala anion. The line shown is a line-fitted curve. The correlation coefficient (*R*) of the nonlinear curve fitting is 0.9994.



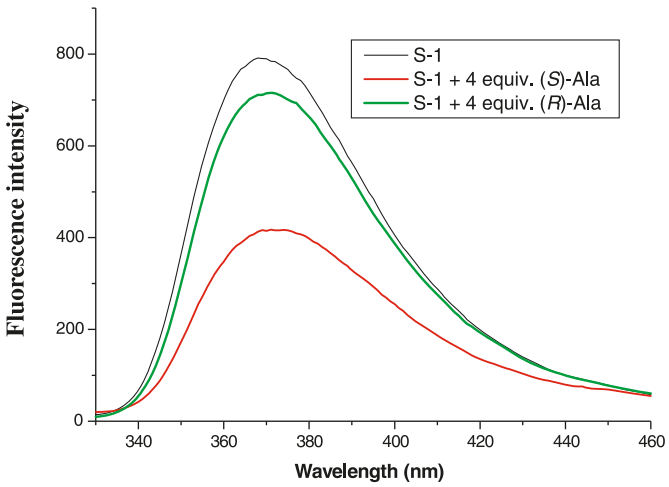
and different concentrations of the (*S*)- or (*R*)-Ala anion in $CHCl_3$ (λ_{ex} = 278 nm), respectively. The graphs in the top right corners of Figs. 3 and 4 illustrate the fluorescence intensity change of receptor **S-1** upon addition of (*S*)- and (*R*)-Ala anions, respectively. Figure 5 shows the different fluorescence intensity changes when the same equiv. of (*S*)- or (*R*)-Ala anion were added to the host **S-1**, the quenching efficiency was 46.7% when 4 equiv. of (*S*)-Ala anion was added to the solution of **S-1**, while the quenching efficiency was only 8.7% when 4 equiv. of (*R*)-Ala anion was added. The quenched efficiencies ($\Delta I_S/\Delta I_R$ = 5.37) indicated that the host **S-1** has a good enantioselective recognition ability between the (*S*)- and (*R*)-Ala anions, respectively. Satisfactory nonlinear curve fitting (the correlation coefficient is over 0.99) confirmed that **S-1** and the (*S*)- or (*R*)-Ala formed a 1:1 complex (see the insets of Fig. 3 and Fig. 4). For a complex of 1:1 stoichiometry, the association constant (K_{ass}) can be calculated by using eq. [1] from the Origin 7.5 software package[12,13]

$$[1] \quad X = X_0 + (X_{lim} - X_0)/2C_0\{C_H + C_G + 1/K_{ass} - [(C_H + C_G + 1/K_{ass})^2 - 4C_HC_G]^{1/2}\}$$

where *X* represents the fluorescence intensity, C_H and C_G are the host and guest concentrations, respectively, and C_0 is the initial concentration of the host. The association constants (K_{ass}) and correlation coefficients (*R*) obtained by a nonlinear least squares analysis of *X* vs. C_H and C_G are listed in Table 1.

The association constant for the interaction of **S-1** with the (*S*)- and (*R*)-Ala anion is (3.60 ± 0.27) × 10^4 and (3.54 ± 0.19) × 10^3 M^{-1}, respectively. Receptor **S-1** gives an enantioselectivity $K_{ass((S)\text{-Ala})}/K_{ass((R)\text{-Ala})}$ = 10.17. The dramatically different fluorescent responses and quenching efficiencies observed for the two enantiomers indicate that **S-1** has excellent enantioselective fluorescent-recognition ability towards the Ala anion. Similar phenomena were observed

Fig. 5. Fluorescence spectra of host **S-1** (2.13×10^{-6} mol L^{-1}) with 4.0 equiv. of (*S*)- and (*R*)-Ala anion in $CHCl_3$.



when (*S*)- or (*R*)-Phe anions were added into a solution of **S-1**. The result of a nonlinear curve fitting (at 371 nm) indicates that a 1:1 complex was formed between receptor **S-1** and (*S*)- or (*R*)-Phe (see Table 1). In addition, the association constants (K_{ass}) were different (see Table 1) ($K_{ass(S)}$ = (3.17 ± 0.11) × 10^4 M^{-1}, ΔG_0 = –25.69 kJ mol^{-1}; $K_{ass(R)}$ = (3.09 ± 0.08) × 10^3 M^{-1}, ΔG_0 = –19.92 kJ mol^{-1}), yielding an *S*/*R* selectivity [$K_{ass(S)}/K_{ass(R)}$] of 10.26 for the Phe anions and a $\Delta\Delta G_0$ value of –5.77 kJ mol^{-1}, demonstrating that **S-1** has good chiral recognition ability towards the enantiomers of Phe anions.

The binding of **S-1** with mandelate and α-phenylglycine anion was also carried out, and the association constants of the host **S-1** with mandelate and α-phenylglycine anion are also listed in Table 1. When **S-1** interacted with α-phenylglycine anion, the receptor **S-1** exhibited weak enantioselective recognition ability to α-phenylglycine anion that have been

Table 1. Association constants (K_{ass}), correlation coefficients (R), enantioselectivities ($K_{ass(S)}/K_{ass(R)}$), Gibbs free energy changes ($-\Delta G_0$), and $\Delta\Delta G_0$ calculated from ΔG_0 for the complexation of receptors **S-1** and **R-1** with *S*-/*R*- guests in $CHCl_3$ at 25 °C.

Entry	Host	Guest	K_{ass} (M^{-1})[a,b]	R	$K_{ass(S)}/K_{ass(R)}$	$-\Delta G_0$ (kJ mol^{-1})	$\Delta\Delta G_0$ (kJ mol^{-1})
1	**S-1**	(*S*)-Ala[c]	$(3.60\pm0.27)\times10^4$	0.9971		26.01	
2	**S-1**	(*R*)-Ala[c]	$(3.54\pm0.19)\times10^3$	0.9984	10.17	20.26	–5.75
3	**S-1**	(*S*)-Phe[c]	$(3.17\pm0.11)\times10^4$	0.9927		25.69	
4	**S-1**	(*R*)-Phe[c]	$(3.09\pm0.08)\times10^3$	0.9928	10.26	19.92	–5.77
5	**S-1**	(*S*)-Mandelate	$(5.81\pm0.26)\times10^4$	0.9908		27.2	
6	**S-1**	(*R*)-Mandelate	$(1.04\pm0.13)\times10^4$	0.9946	5.87	22.93	–4.27
7	**S-1**	(*S*)-Phenylglycine	$(6.64\pm0.26)\times10^4$	0.9923		27.53	
8	**S-1**	(*R*)-Phenylglycine	$(3.91\pm0.19)\times10^4$	0.9931	1.70	26.22	–1.31
9	**S-1**	(*S*)-Alaninol	$(6.72\pm0.31)\times10^2$	0.9924		16.14	
10	**S-1**	(*R*)-Alaninol	$(4.31\pm0.05)\times10^2$	0.9902	1.56	15.04	–1.1
11	**S-1**	(*S*)-Phenylalaninol	$(5.98\pm0.21)\times10^2$	0.9944		15.85	
12	**S-1**	(*R*)-Phenylalaninol	$(1.99\pm0.15)\times10^2$	0.9919	3.01	13.12	–2.73
13	**R-1**	(*S*)-Ala[c]	$(3.26\pm0.22)\times10^3$	0.9903		20.06	
14	**R-1**	(*R*)-Ala[c]	$(3.02\pm0.13)\times10^4$	0.9912	1/9.26	25.57	5.51
15	**R-1**	(*S*)-Phe[c]	$(3.47\pm0.26)\times10^3$	0.9941		20.21	
16	**R-1**	(*R*)-Phe[c]	$(3.29\pm0.24)\times10^4$	0.9937	1/9.48	25.79	5.58
17	**R-1**	(*S*)-Mandelate	$(1.75\pm0.11)\times10^4$	0.9952		24.22	
18	**R-1**	(*R*)-Mandelate	$(7.81\pm0.51)\times10^4$	0.9917	1/4.46	27.93	3.71
19	**R-1**	(*S*)-Phenylglycine	$(2.98\pm0.22)\times10^4$	0.9962		25.54	
20	**R-1**	(*R*)-Phenylglycine	$(5.07\pm0.19)\times10^4$	0.9933	1/2.41	26.86	1.34
21	**R-1**	(*S*)-Alaninol	$(3.51\pm0.14)\times10^2$	0.9917		14.53	
22	**R-1**	(*R*)-Alaninol	$(6.94\pm0.29)\times10^2$	0.9951	1/1.98	16.22	1.69
23	**R-1**	(*S*)-Phenylalaninol	$(1.51\pm0.07)\times10^2$	0.9903		12.44	
24	**R-1**	(*R*)-Phenylalaninol	$(8.81\pm0.44)\times10^2$	0.9927	1/5.64	16.81	4.37
25	**S-5**	(*S*)-Ala[c]	$(4.53\pm0.18)\times10^4$	0.9989		26.58	
26	**S-5**	(*R*)-Ala[c]	$(9.71\pm0.52)\times10^3$	0.9946	4.67	22.76	–3.82
27	**S-5**	(*S*)-Phe[c]	$(4.19\pm0.24)\times10^4$	0.9938		26.39	
28	**S-5**	(*R*)-Phe[c]	$(8.62\pm0.29)\times10^3$	0.9913	4.86	22.47	–3.92
29	**S-5**	(*S*)-Mandelate	$(4.97\pm0.26)\times10^4$	0.9931		26.81	
30	**S-5**	(*R*)-Mandelate	$(1.54\pm0.39)\times10^4$	0.9911	3.23	23.91	–2.90
31	**S-5**	(*S*)-Phenylglycine	$(6.77\pm0.43)\times10^4$	0.9956		27.58	
32	**S-5**	(*R*)-Phenylglycine	$(4.34\pm0.39)\times10^4$	0.9931	1.56	26.47	–1.11
33	**S-5**	(*S*)-Alaninol	$(6.53\pm0.35)\times10^2$	0.9907		16.07	
34	**S-5**	(*R*)-Alaninol	$(3.37\pm0.39)\times10^2$	0.9916	1.94	14.43	–1.64
35	**S-5**	(*S*)-Phenylalaninol	$(6.01\pm0.35)\times10^2$	0.9907		15.86	
36	**S-5**	(*R*)-Phenylalaninol	$(2.32\pm0.39)\times10^2$	0.9921	2.59	13.50	–2.36
37	**R-5**	(*S*)-Ala[c]	$(1.27\pm0.10)\times10^4$	0.9934		23.43	
38	**R-5**	(*R*)-Ala[c]	$(4.02\pm0.18)\times10^4$	0.9940	1/3.17	26.28	2.85
39	**R-5**	(*S*)-Phe[c]	$(9.78\pm0.41)\times10^3$	0.9941		22.78	
40	**R-5**	(*R*)-Phe[c]	$(3.99\pm0.22)\times10^4$	0.9913	1/4.08	26.27	3.49
41	**R-5**	(*S*)-Mandelate	$(1.99\pm0.26)\times10^4$	0.9919		24.54	
42	**R-5**	(*R*)-Mandelate	$(4.82\pm0.39)\times10^4$	0.9934	1/2.42	26.73	2.19
43	**R-5**	(*S*)-Phenylglycine	$(3.98\pm0.43)\times10^4$	0.9926		26.26	
44	**R-5**	(*R*)-Phenylglycine	$(6.27\pm0.39)\times10^4$	0.9915	1/1.58	27.39	1.13
45	**R-5**	(*S*)-Alaninol	$(4.03\pm0.35)\times10^2$	0.9923		14.87	
46	**R-5**	(*R*)-Alaninol	$(5.99\pm0.39)\times10^2$	0.9908	1/1.49	15.86	0.99
47	**R-5**	(*S*)-Phenylalaninol	$(2.53\pm0.35)\times10^2$	0.9912		13.72	
48	**R-5**	(*R*)-Phenylalaninol	$(5.74\pm0.39)\times10^2$	0.9903	1/2.27	15.75	2.03

[a]The data were calculated from the results of fluorescence titrations in $CHCl_3$.

[b]All error values were obtained from nonlinear curve fitting.

[c]Ala and Phe tetrabutylammonium salts, the amino group was protected by a *tert*-butyloxycarbonyl function.

tested (see Table 1). Upon the addition of alaninol or phenylalaninol into a solution of in $CHCl_3$, the fluorescence intensity of **S-1** was slightly quenched by both (*S*)- and (*R*)-enantiomers (see Table 1). This indicates that hydrogen bonding plays an important role in the interaction between the host and guest and leads to the easier signal transductions of chiral recognition by fluorescence method.

The continuous variation methods were also employed to determine the stoichiometric ratio of the receptor **S-1** with guests [(*S*)- and (*R*)-Ala anions]. The total concentration of

host and guest was constant (1.0×10^{-6} mol L^{-1}) in $CHCl_3$, with a continuously variable molar fraction of host ([H]/([H] + [G])). Figure 6 shows the Job plots of receptor **S-1** with (*S*)- and (*R*)-Ala anion (at 371 nm, λ_{ex} = 278 nm). When the molar fraction of the host was 0.50, the fluorescence intensity reached a maximum, which demonstrated that receptor **S-1** formed a 1:1 complex with (*S*)- and (*R*)-Ala anions, respectively.[14]

The decrease in fluorescence intensity of the excimer upon addition of the anion is similar to the anion-induced fluorescence decrease reported previously.[15] Because of the similar structure of **S-1**, the fluorescent variations of **S-1** showed the same trend. Since there were no changes in the UV–vis spectra of the receptors when treated with (*S*)- or (*R*)-anions, a photoinduced electron transfer (PET) process might be responsible for the fluorescent quenching.[16] In the absence of anions, PET between the binaphthyl unit and the electron-withdrawing amide substituents might result in quenched fluorescence. In the presence of guest anions, the fluorescence quenching of receptors **S-1** most likely arose from the change of the free energy (ΔG_{PET}) of the electron transfer between the excited fluorophore and the receptor.[17] Therefore, fluorescence quenching was observed.

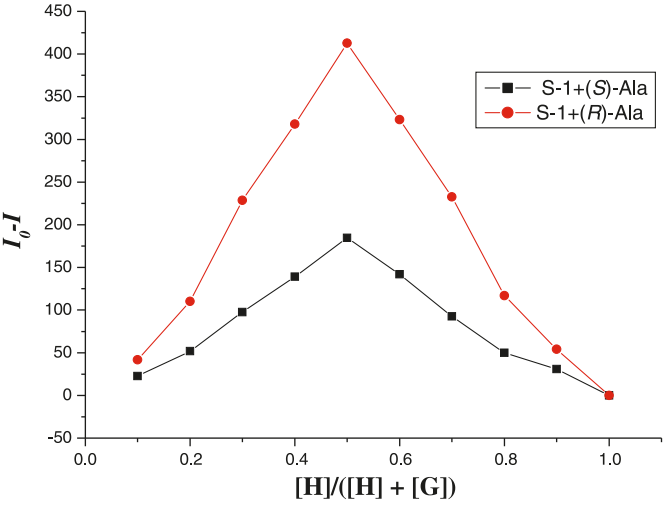
To study how the chirality of the amino acid unit and BINOL groups in **S-1** influenced the enantioselective fluorescent recognition, **R-1**, the diastereomeric compounds of **S-1**, **S-5**, and **R-5** were also prepared by similar methods. We also studied its interaction with mandelate, phenylglycine, Ala and Phe anions, alaninol, and phenylalaninol, which showed the opposite enantioselectivity. That is, the (*R*)-guest enantiomer quenched the fluorescence of **R-1** more efficiently than (*S*)-guest. The result of fluorescence titration indicated that a matched chirality between the guest anions center and the chiral BINOL unit led to the enantioselective recognition. The enantiomers of guest anions interacted with **R-1** and **S-1** in the same fashion.

According to Table 1, the interaction of **S-1** with the (*S*)-Ala and (*S*)-Phe anions is better than that with the (*R*)-Ala and (*R*)-Phe anions, which is probably due to the (*S*)-amino acid anions having a more complementary structure with receptors **S-1**. The receptors **S-1** and **R-1** all exhibit good chiral recognition ability towards the enantiomers of the Ala and Phe anions, which indicates that the preorganized structure of the chiral center of the binaphthyl unit plays important roles in the enantioselective recognition process.

^{1}H NMR study

^{1}H NMR experiments were undertaken to assess the chiral-recognition properties between receptor **S-1** and chiral anionic guest because NMR spectroscopy can provide structural and dynamic information directly.[18] ^{1}H NMR chiral-recognition studies were carried out with a 400 MHz NMR spectrometer using receptor **S-1** in $CDCl_3$ as chiral solvating agent at room temperature. The spectra of receptor **S-1** and its complexes with equimolar amounts of racemic Ala anions are shown in Fig. 7. When treated with equimolar amounts of receptor **S-1**, the signal of the CH proton of the racemic Ala anion cleaved into a more complicated signal pattern (Fig. 7C) with a downfield shift. The interaction of receptor **S-1** with (*S*)-enantiomer showed that the CH proton has a larger downfield shift (from δ = 3.85 to 4.27 ppm, Δδ = 0.42 ppm, Fig. 7D) than that of the CH proton of the (*R*)-enantiomer (from δ = 3.85 to 4.19 ppm, Δδ = 0.34 ppm, Fig. 7E). Moreover, the signals of the –OH proton in the ^{1}H NMR spectra of the receptor **S-1** become weakened obviously and have downfield shift from 6.57 to 6.78 ppm (Δδ = 0.21 ppm, Fig. 7D) or 6.74 ppm (Δδ = 0.17 ppm, Fig. 7E) for (*S*)- or (*R*)-Ala anion, respectively, while the signals of the peaks of binaphthyl fragments are downfield-shifted and broadened with the addition of the guest. The signal of the amide (N*H*) group of Ala linked to the Boc moiety was also clearly downfield-shifted from δ = 5.91 to 5.98 ppm (Δδ = 0.07 ppm, Fig. 7D) and 5.94 ppm (Δδ = 0.03 ppm, Fig. 7E) for (*S*)- and (*R*)-Ala anion, respectively. The above results indicate that **S-1** has a stronger interaction with the (*S*)-Ala anion than with its (*R*)-enantiomer. This indicated that the interaction between the host and guest also happened by multiple hydrogen bondings. The results also illustrate that the nature of the receptor, multiple hydrogen-bonding interactions, and complementary chiral-center interactions maybe responsible for the enantiomeric recognition of the amino acid anion.[19]

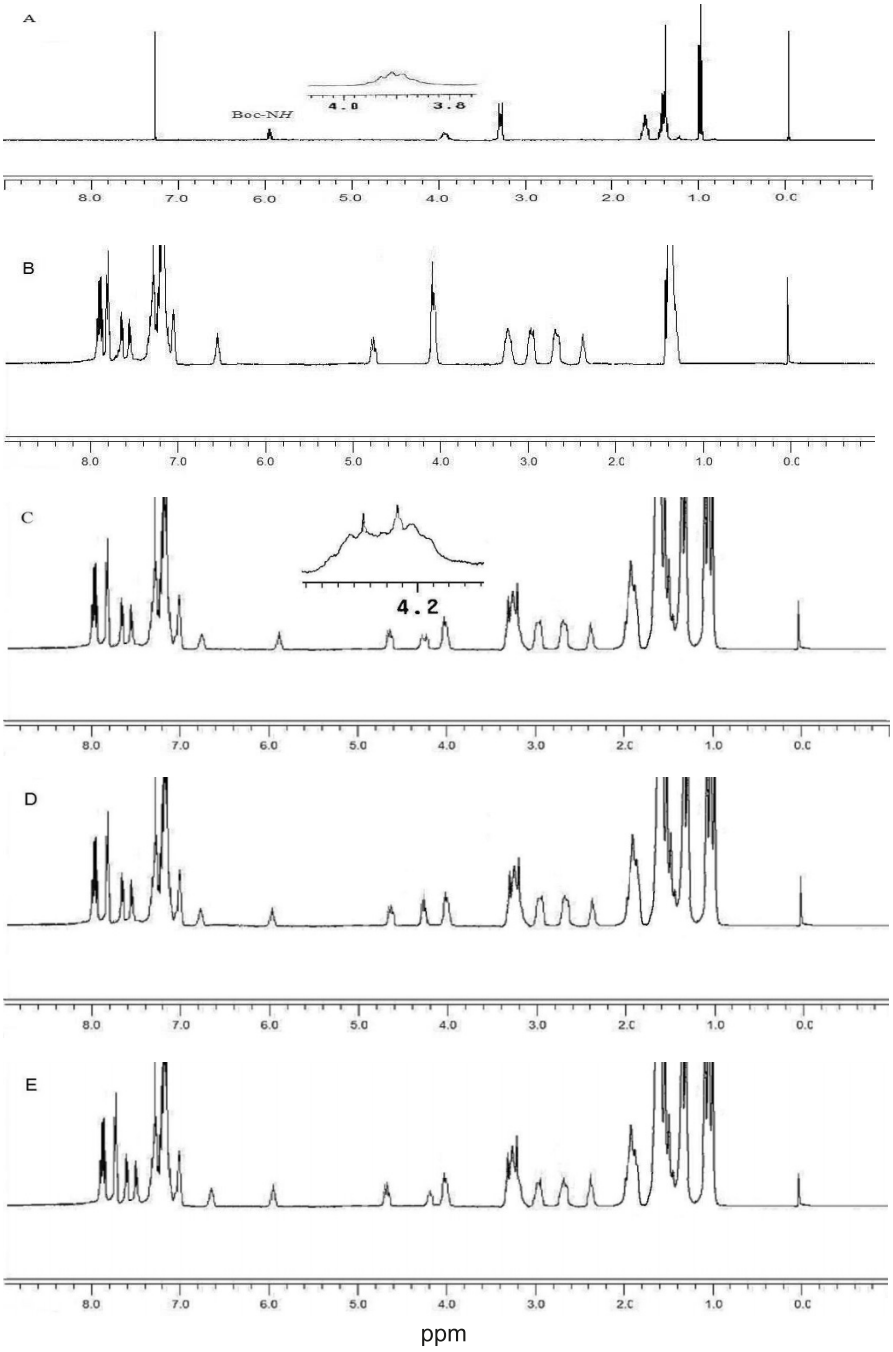
Fig. 6. Job plots of receptor **S-1** with (*S*)- and (*R*)-Ala anions (367 nm, λ_{ex} = 290 nm). The total concentration of the host [H] and guest [G] is 1.0×10^{-6} mol L^{-1} in $CHCl_3$. I_0: fluorescence intensity of **S-1**; I: fluorescence intensity of **S-1** in the presence of the guest.



Conclusion

In summary, four chiral fluorescent receptors **S-1**, **R-1**, **S-5**, and **R-5** were synthesized, and their enantioselective recognition was studied by fluorescence titration and ^{1}H NMR spectroscopy. Receptors **S-1** and **R-1** exhibit different chiral-recognition abilities towards some enantiomers of chiral materials and form 1:1 complexes with the guest molecules. It is clear that the nature of the receptor, good structural preorganization, multiple hydrogen-bonding interactions, and complementary chiral-center interactions may be responsible for the enantiomeric recognition of anionic guests.[19] Receptors **S-1**and **R-1** are promising in their use as fluorescence sensors for amino acid anions. The remarkably different fluorescent responses that result from complexation reveal that **S-1** and **R-1** could be used as fluorescent chemosensors for the *N*-Boc-protected alanine anion or *N*-Boc-protected phenylalanine anion in the future.

Fig. 7. The ^{1}H NMR spectra of **S-1** and its guest complexes at 25 °C ([**S-1**] = [guest] = 4.0×10^{-3} mol L^{-1}) in $CDCl_3$ at 400 MHz. (A) Racemic Ala anion; (B) receptor **S-1**; (C) receptor **S-1** + racemic Ala anion; (D) receptor **S-1** + (*S*)-Ala anion; (E) receptor **S-1** + (*R*)-Ala anion.



Experimental section

General

The reagents used were of commercial origin and were employed without further purification. Purifications by column chromatography were carried out over silica gel (230–400 mesh). The IR spectra were performed on a Nicolet 670 FTIR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV-400 spectrometer. Mass spectra were determined by ESI recorded on a Esquire 3000 LC–MS mass instrument. Optical rotations were taken on a PerkinElmer Model 341 polarimeter. Fluorescence spectra were obtained with a F-7000 FL Spectrophotometer. Elemental analyses were performed by the Vario Elemental CHSN-O microanalyzer. The anions were used as their tetrabutylammonium salts. The *N*-protected (by the *tert*-butyloxycarbonyl functionality) amino acid derivatives were synthesized according to a literature method.[20]

The synthesis of compound 3

Under N_2, excess ethylenediamine (0.60 g, 10 mmol) in 10 mL CH_3OH was added dropwise into a solution (20 mL)

of (*S*)-*N*-Boc-protected alanine methyl ester (**2**) (0.41g, 2 mmol) in $CHCl_3/CH_3OH$ (1:10, *v*/*v*) in an ice-bath. After the addition, the mixture was stirred at room temperature for 48 h. The solvent was evaporated, and the residual ethylenediamine was removed under reduced pressure. Then, $CHCl_3$ (30 mL) was added and washed with H_2O (3 × 30 mL); the organic layer was separated and dried over Na_2SO_4. After filtration, the solvent was removed under reduced pressure to give **3** as colorless ropy oil in 86% yield (0.40 g). $[\alpha]_D^{20} + 21.84$ (c = 0.05, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ (ppm): 7.01 (s, 1 H, CON**H**), 5.47 (s, 1 H, N**H**Boc), 4.18 (CH), 3.31 (t, J =6.4 Hz, 2H, CH_2), 2.82 (t, J = 6.4 Hz, 2H, CH_2), 1.72 (s, 2 H, NH_2), 1.44 (s, 9 H, CH_3), 1.35 (t, J = 6.8 Hz, 3 H, CH_3). ^{13}C NMR ($CDCl_3$) δ (ppm): 172.8, 155.2, 77.8, 54.1, 41.2, 40.3, 28.8, 27.9. ESI-MS *m*/*z* (%): 232 (100) $[M + 1]^+$. $C_{10}H_{21}N_3O_3$ calcd.: C 51.93, H 9.15, N 18.17; found: C 51.66, H 9.22, N 18.04.

The preparation of *tert*-butyl-2-(2-aminoethylamino)-2-oxoethylcarbamate

Tert-butyl-2-(2-aminoethylamino)-2-oxoethylcarbamate was prepared by the same method as that of compound **3** by starting with *N*-Boc-protected glycine methyl ester, and it gave 95% yield. ^{1}H NMR ($CDCl_3$) δ (ppm): 7.11 (s, 1H, CON**H**), 5.57 (s, 1H, N**H**Boc), 3.74 (s, 2H, CH_2), 3.39 (t, J = 6.4 Hz, 2H, CH_2), 2.86 (t, J = 8.0 Hz, 2H, CH_2), 1.74 (s, 2 H, NH_2), 1.44 (s, 9 H, CH_3). ^{13}C NMR ($CDCl_3$) δ (ppm): 173.3, 155.9, 78.1, 55.7, 41.9, 40.7, 28.9. ESI-MS: *m*/*z* (%) = 218 (100) $[M + 1]^+$. $C_9H_{19}N_3O_3$ calcd.: C 49.75, H 8.81, N 19.34; found: C 49.57, H 8.89, N 19.22.

General procedure for the synthesis of compounds R-1, S-1, R-5, and S-5

A mixture of the (*R*) or (*S*)-binaphthyl dialdehyde (0.34 g, 1 mmol) and compound **3** or *tert*-butyl-2-(2-aminoethylamino)-2-oxoethylcarbamate (2.2 mmol) in CH_3OH (30 mL) was stirred for 48 h under N_2 at room temperature until TLC showed the disappearance of the starting material. $NaBH_4$ (0.19 g, 5 mmol) was then added to the mixture in three portions over 3 h, after which it was stirred under N_2 for another 6 h at 50 °C. The mixture was poured into 30 mL of 10% $NaHCO_3$ after removing the solvent under reduced pressure, and extracted three times with $CHCl_3$. The organic layers were combined and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated under reduced pressur,e and the residue was purified by column chromatography on silica gel [eluent: $CHCl_3/CH_3CH_2OH$, 50:1 (*v*/*v*)]. The pure product was obtained as a pale yellow solid.

S-1 and R-1

Yield (**S-1**): 76.8%; $[\alpha]_D^{20} - 34.72$ (c = 0.05, $CHCl_3$). Yield (**R-1**): 79.3%; $[\alpha]_D^{20} + 117.18$ (c = 0.05, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ (ppm): 7.87 (s, 2H, CONH), 7.83 (d, J = 8.0 Hz, 2H, Ar–H), 7.76 (d, J = 9.6 Hz, 2H, Ar–H), 7.61 (d, J = 8.1 Hz, 2H, Ar–H), 7.28 (d, J = 7.6 Hz, 2 H, Ar–H), 7.19 (d, J = 7.2 Hz, 2H, Ar–H), 7.13–7.16 (t, J = 4.8 Hz, 2H, Ar–H), 6.52 (s, 2H, OH), 4.76–4.68 (m, 2H, C**H**CH_2), 4.10 (d, J = 8.0 Hz, 4H, Ar–C**H**$_2$), 3.00–2.91 (m, 4H, C**H**$_2$), 2.73–2.64 (m, 4H, C**H**$_2$), 2.36 (s, 2H, NH), 1.42 (s, 18H, CH_3), 1.28 (s, 3H, CH_3), 1.22 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ (ppm): 172.39, 152.53, 152.51, 134.32, 133.76, 132.91, 132.69, 131.29, 130.69, 130.54, 130.12, 129.94, 128.34, 127.38, 126.95, 126.07, 125.86, 125.59, 125.22, 124.96, 71.02, 57.31, 57.09, 39.89, 24.95, 14.44, 14.14. ESI-MS *m*/*z* (%): 795 (100) $[M + Na]^+$. $C_{42}H_{56}N_6O_8$ calcd.: C 65.26, H 7.30, N 10.87; found (**S-1**): C 65.11, H 7.21, N 10.99; found (**R-1**): C 65.07, H 7.19, N 11.02.

S-5 and R-5

Yield (**S-5**): 79.6%; $[\alpha]_D^{20} = -68.32$ (c = 0.05, $CHCl_3$). IR (film, cm^{-1}) υ: 3402, 3092, 2969, 1679, 1529, 1268, 1234, 752. ^{1}H NMR ($CDCl_3$) δ (ppm): 7.89 (s, 2H, CONH), 7.87 (d, J = 8.0 Hz, 2H, Ar–H), 7.79 (d, J = 9.6 Hz, 2H, Ar–H), 7.64 (d, J = 8.1 Hz, 2H, Ar–H), 7.22 (d, J = 7.6 Hz, 2H, Ar–H), 7.19 (d, J = 7.2 Hz, 2H, Ar–H), 7.17–7.13 (t, J = 4.8 Hz, 2H, Ar–H), 6.55 (s, 2H, OH), 4.12 (d, J = 8.0 Hz, 4H, Ar–C**H**$_2$), 3.88 (s, 4H, CH_2), 3.03–2.95 (m, 4H, C**H**$_2$), 2.79–2.70 (m, 4H, C**H**$_2$), 2.38 (s, 2H, NH), 1.44 (s, 18H, CH_3). ^{13}C NMR ($CDCl_3$) δ (ppm): 174.03, 153.59, 153.31, 134.99, 133.96, 133.44, 133.17, 132.54, 131.06, 130.86, 130.58, 129.91, 128.71, 127.53, 126.62, 126.01, 125.93, 125.85, 125.73, 124.58, 74.09, 58.39, 58.49, 39.89, 24.92. ESI-MS *m*/*z* (%): 767 (100) $[M + Na]^+$. $C_{40}H_{52}N_6O_8$ calcd.: C 64.50, H 7.04, N 11.28; found (**S-5**): C 64.29, H 7.09, N 11.19; found (**R-5**): C 64.33, H 7.11, N 11.15.

Preparation of samples for fluorescence measurement

All solutions were prepared using volumetric syringes, pipettes, and volumetric flasks. The tetrabutylammonium salts were prepared by adding 1 equiv. of tetrabutylammonium hydroxide in methanol to a solution of the corresponding carboxylic acid in methanol, and stock solutions of the salts were prepared in $CHCl_3$. The resulting syrup was dried under high vacuum for 24 h, analyzed by NMR spectroscopy, and stored in a desiccator. Compounds **R-1** and **S-1** were prepared as stock solutions in $CHCl_3$. The test solutions were prepared by adding different volumes of anion solution to a series of test tubes, and then the same amount of stock solution of the host compound was added to each of the test tubes and diluted to 3.0 mL with $CHCl_3$. After being shaken for several minutes, the test solutions were analyzed immediately.

Job Plots

Stock solutions of host **S-1** and the (*S*)- and (*R*)-Ala tetrabutylammonium salts in $CHCl_3$ system (the total concentration of the host and guest is 1.0×10^{-6} mol L^{-1}) were freshly prepared. The receptor and Ala solutions were added to the test tubes in ratios of 9:1, 8:2 to 0:10, respectively. After being shaken for several minutes, the working solution could be measured immediately.

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