Enantioselective Fluorescent Sensors for *N*-Boc-Protected Amino Acid Anions Based on BINOL

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The four novel derivatives of BINOL have been prepared and the structures of these compounds 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 *N*-Boc-protected amino acid anions and formed 1∶1 complexes between host and guest. Receptor**s** exhibit excellent enantioselective fluorescent recognition ability towards the amino acid derivatives.

Keywords receptor, fluorescence, enantioselective recognition, anions

Introduction

Chiral recognition of racemic compounds exists extensively in nature. It is of particular significance for understanding the interactions of biological molecules and for the designing of asymmetric catalysis systems.[1] With the increasingly successful application to smart artificial systems, chiral recognition which is a broader and more commonly used 'tool' for academic research and industry[2] has gained greater scientific maturity.

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 molecule.[4] Compared with other detection methods, such as capillary electrophoresis,[5] HPLC,[6] absorption spectrometry,[7] and electrochemistry,[8] fluorescence techniques have often been used to study the interaction between enantiomers and receptors because of their sensitivity, selectivity, and versatility.[9]

The binaphthyl unit was especially eyecatching for its stable chiral configuration and tunable dihedral angle between the two naphthalene rings. Over the last two decades, the 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.[10] The molecular recognition of amino acids by synthetic receptor molecules has been attracting much attention due to the frequent use of the basic amino acids (*e.g*., Lys, Arg, His and Ala) for biological processes and therapeutic drugs made from chiral amino acids intermediates.[11] Herein, we describe the development of 1,1'-bi-2-naphthol (BINOL) derivatives bearing amino acid units (Scheme 1), and their bonding properties with *N*-Boc-protected amino acid derivatives 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 $CHCl_3$. ^{1}H NMR experiments suggested that hydrogen-bonding interaction between the host and guest was the main factor in the recognition process.

Results and discussion

Synthesis

The synthesis of receptors *S*-**1a**, *S*-**1b** and *R*-**1a**, *R*-**1b** is outlined in Scheme 1. The starting materials binaphthyl dialdehydes were prepared from 1,1'-bi-2-naphthol (BINOL).[12] *N*-Boc-protected amino acid methyl ester (**2**) was synthesized according to the literature with high yield,[13] and then reacted with excess amount of diamine to obtain the compounds **3**. To avoid the partial racemization of **3** in this reaction, the material **2** and diamine were solved in large amount of

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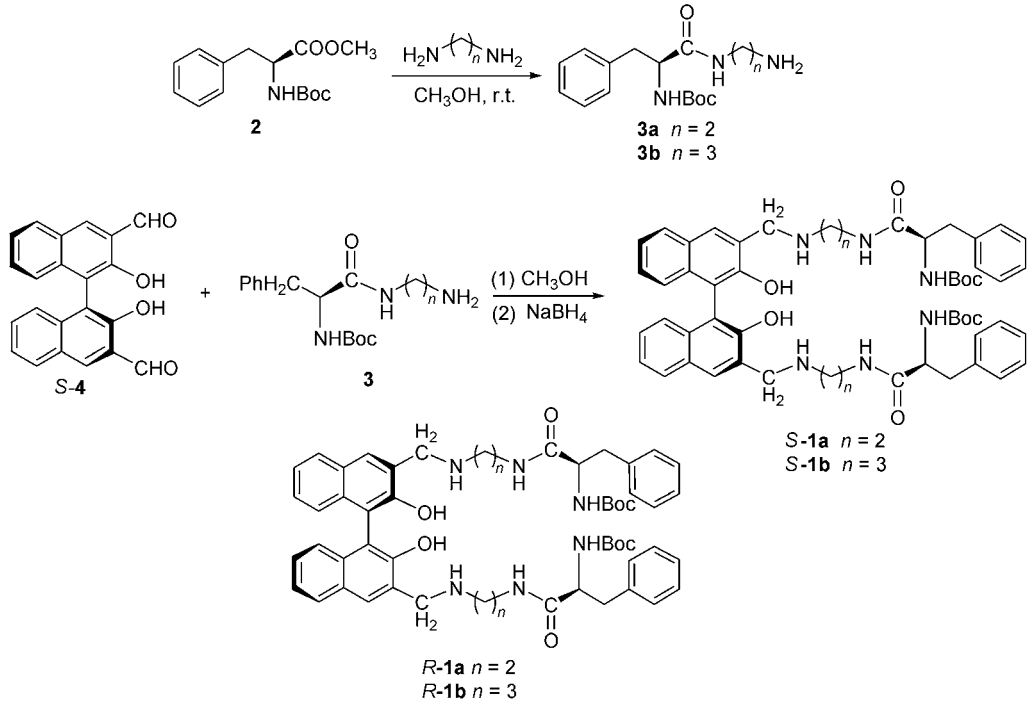
Scheme 1 Synthesis of the receptors *S*-**1**, *R*-**1**



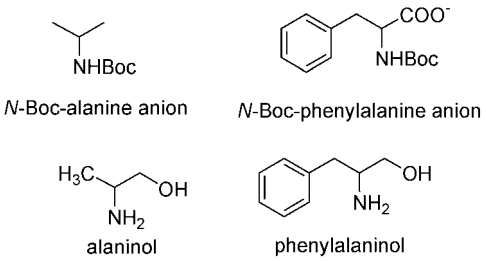
methanol and continued to stir at room temperature, especially at the end of reaction, the solvent and diamine should be evaporated under high vacuum at about 30—40 ℃, because a little higher temperature may lead the racemization of compound. Condensation of *S*- or *R*-binaphthyl dialdehydes with compounds **3** followed by reduction afforded the disubstituted BINOL *S*-**1a** or *S*-**1b** (Scheme 1), respectively. In order to study how the BINOL and amino acid units in *S*-**1a** or *S*-**1b** influenced the enantioselective fluorescent recognition, the *R*-**1a** or *R*-**1b**, diastereoisomeric compounds of *S*-**1a** or *S*-**1b**, were also prepared. They are all 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*-**1a** and *S*-**1b** were investigated in the absence and presence of *S*- and *R*-*N*-Boc-protected alanine anion (Ala) and *N*-Boc-protected phenylalanine anion (Phe), whose amino groups were protected by the *tert*-butyloxycarbonyl functionality. In each case tetrabutylammonium was used as the counter cation, which could increase the reaction between the receptor and guest by hydrogen bondings. We also chose two amino alcohols, namely alaninol and phenylalaninol, as guests to compare the association abilities of the hosts to bind with neutral molecules (Scheme 2).

The fluorescence spectra were recorded from a solution of receptor *S*-**1a** or *S*-**1b** (1.25×10^{-5} mol/L) in $CHCl_3$ in the absence or presence of various enantiomers, *L*-, *D*-Ala, and Phe anions. Because there was almost no change observed on the UV-vis spectra of receptors upon addition of *L*- or *D*-Ala or Phe anions, the interaction between host and anion was only evaluated by fluorescent spectra.

Scheme 2 Structures of the guests



Upon addition of *L*- or *D*-Ala or Phe anions, the different fluorescent quenching degree of *S*-**1a** was observed. The quenching efficiency of *L*-amino acid anions was much higher than the *D*-amino acid anions. Figures 1 and 2 show the fluorescence emission spectra of a mixture of *S*-**1a** and different concentrations of the *L*- or *D*-Ala anion in $CHCl_3$ (λ_{ex}=278 nm), respectively. The graphs in the top right corner of Figure 1 and Figure 2 illustrate the fluorescence intensity change of receptor *S*-**1a** upon addition of *L*- and *D*-Ala anions, respectively. Figure 3 shows the different fluorescence intensity changes when the same equiv. of *L*- or *D*-Ala anion was added to the host *S*-**1a**. The quenching efficiency was 70% when 20 equiv. of *L*-Ala anion was added to the solution of *S*-**1a**, while the quenching efficiency was only 30% when 20 equiv. of *D*-Ala anion was added. The quenched efficiencies ($\Delta I_S/\Delta I_R$=2.33) indicated that the host *S*-**1a** has a good enantioselective

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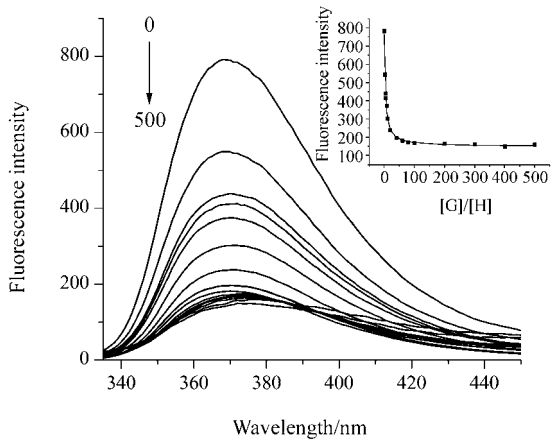

Figure 1 Fluorescence spectra of receptor *S*-**1a** (1.25×10^{-5} mol/L) with *L*-Ala anion in $CHCl_3$. The anion equivalents are 0, 2, 4, 6, 8, 10, 20, 40, 60, 80, 100, 200, 300, 400 and 500, $\lambda_{ex}=278$ nm. Inset: changes in the fluorescence intensity of *S*-**1a** at 371 nm upon addition of *L*-Ala anion. The line shown is a line-fitted curve. The correlation coefficient (*R*) of the nonlinear curve fitting is 0.9972.

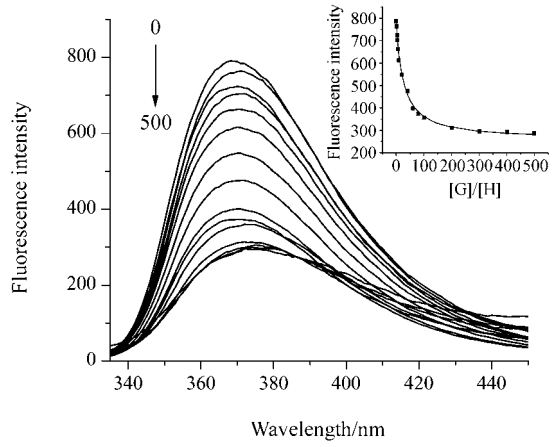

Figure 2 Fluorescence spectra of receptor *S*-**1a** (1.25×10^{-5} mol/L) with *D*-Ala anion in $CHCl_3$. The anion equivalents are 0, 2, 4, 6, 8, 10, 20, 40, 60, 80, 100, 200, 300, 400 and 500, $\lambda_{ex}=$ 278 nm. Inset: changes in the fluorescence intensity of *S*-**1a** at 371 nm upon addition of *D*-Ala anion. The line shown is a line-fitted curve. The correlation coefficient (*R*) of the nonlinear curve fitting is 0.9980.

recognition ability between the *L*- and *D*-Ala anions, respectively. Satisfactory nonlinear curve fitting (the correlation coefficient is over 0.99) confirmed that *S*-**1a** and the *L*- or *D*-Ala formed a 1∶1 complex (see the insets of Figure 1 and Figure 2). For a complex of 1∶1 stoichiometry, the association constant (K_{ass}) can be calculated by using Eq. (1) from the Origin 7.0 software package,[14,15] where X represents the fluorescence intensity, respectively, C_H and C_G are the host and guest concentrations, 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 versus C_H and C_G are listed in Table 1.

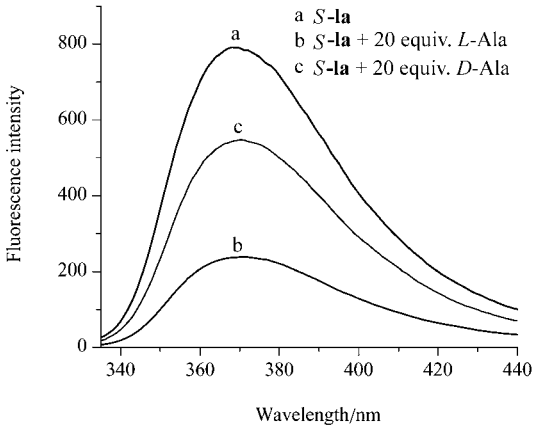

Figure 3 Fluorescence spectra of host *S*-**1a** (1.25×10^{-5} mol/L) with 20 equiv. of *L*- and *D*-Ala anion in $CHCl_3$.

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

The association constants for the interaction of *S*-**1a** with the *L*- and *D*-Ala anion are $(2.99\pm0.21)\times10^4$ and $(3.34\pm0.19)\times10^3$ L/mol, respectively. Compound *S*-**1a** gives an enantioselectivity $K_{ass(S\text{-Ala})}/K_{ass(R\text{-Ala})}=8.95$. The dramatically different fluorescent responses and quenching efficiencies observed for the two enantiomers indicate that *S*-**1a** has excellent enantioselective fluorescent recognition ability towards the Ala anion. Similar phenomena were observed when *L*- or *D*-Phe anions were added into a solution of *S*-**1a**. The result of a non-linear curve fitting (at 371 nm) indicates that a 1∶1 complex was formed between receptor *S*-**1a** and *L*- or *D*-Phe (see the Table 1). In addition, the association constants (K_{ass}) were different (see the Table 1) [$K_{ass(S)}=(3.17\pm0.11)\times10^4$ L/mol, $\Delta G_0=-25.69$ kJ/mol; $K_{ass(R)}=(3.09\pm0.08)\times10^3$ L/mol, $\Delta G_0=-19.92$ kJ/mol], 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, demonstrating that *S*-**1a** has good chiral recognition ability towards the enantiomers of Phe anions.

The binding of *S*-**1a** with alaninol or phenylalaninol is also listed in Table 1. Upon the addition of alaninol or phenylalaninol into a solution of *S*-**1a** in $CHCl_3$, the fluorescence intensity of *S*-**1a** was slightly quenched by both *L*- and *D*-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.

Similar phenomena were observed when *L*- or *D*-Ala and Phe anions were added into a solution (1.25×10^{-5} mol/L) of *S*-**1b**. The emission spectra of *S*-**1b** appeared at 371 nm when it was excited at 278 nm. The quenching efficiencies of receptor *S*-**1b** were 62% and 57% by 20 equiv. of *L*-Ala and *L*-Phe anions while 37% and 31% by *D*-Ala and *D*-Phe anions in $CHCl_3$, respectively. Enantioselective fluorescence responses were observed, which gave $\Delta I_S/\Delta I_R=1.68$ for Ala anions and

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 *L*-/*D*-guests in $CHCl_3$ at 25 ℃

Entry	Host	Guest	$K_{ass}{}^{a,b}$/(L•mol^{-1})	R	$K_{ass(S)}/K_{ass(R)}$	$-\Delta G_0$/(kJ•mol^{-1})	$\Delta\Delta G_0$/(kJ•mol^{-1})
1	*S*-**1a**	*L*-Ala[c]	$(2.99\pm0.21)\times10^4$	0.9972		25.55	
2	*S*-**1a**	*D*-Ala[c]	$(3.34\pm0.19)\times10^3$	0.9980	8.95	20.12	−5.43
3	*S*-**1a**	*L*-Phe[c]	$(3.17\pm0.11)\times10^4$	0.9927		25.69	
4	*S*-**1a**	*D*-Phe[c]	$(3.09\pm0.08)\times10^3$	0.9928	10.26	19.92	−5.77
5	*S*-**1a**	*L*-Alaninol	$(6.72\pm0.31)\times10^2$	0.9924		16.14	
6	*S*-**1a**	*D*-Alaninol	$(4.31\pm0.05)\times10^2$	0.9902	1.56	15.04	−1.1
7	*S*-**1a**	*L*-Phenylalaninol	$(5.98\pm0.21)\times10^2$	0.9944		15.85	
8	*S*-**1a**	*D*-Phenylalaninol	$(1.99\pm0.15)\times10^2$	0.9919	3.01	13.12	−2.73
9	*S*-**1b**	*L*-Ala[c]	$(3.07\pm0.27)\times10^4$	0.9971		25.62	
10	*S*-**1b**	*D*-Ala[c]	$(3.16\pm0.19)\times10^3$	0.9984	9.72	19.98	−5.64
11	*S*-**1b**	*L*-Phe[c]	$(3.04\pm0.27)\times10^4$	0.9947		25.59	
12	*S*-**1b**	*D*-Phe[c]	$(3.09\pm0.08)\times10^3$	0.9974	9.84	19.92	−5.67
13	*S*-**1b**	*L*-Alaninol	$(5.60\pm0.31)\times10^2$	0.9954		15.69	
14	*S*-**1b**	*D*-Alaninol	$(1.11\pm0.05)\times10^2$	0.9919	5.05	11.68	−4.01
15	*S*-**1b**	*L*-Phenylalaninol	$(5.81\pm0.21)\times10^2$	0.9928		15.78	
16	*S*-**1b**	*D*-Phenylalaninol	$(1.91\pm0.15)\times10^2$	0.9913	3.04	13.02	−2.76
17	*S*-**1a**	*L*-Ala[c]	$(3.26\pm0.22)\times10^3$	0.9903		20.06	
18	*S*-**1a**	*D*-Ala[c]	$(3.02\pm0.13)\times10^4$	0.9912	1/9.26	25.57	5.51
19	*S*-**1a**	*L*-Phe[c]	$(3.47\pm0.26)\times10^3$	0.9941		20.21	
20	*S*-**1a**	*D*-Phe[c]	$(3.29\pm0.24)\times10^4$	0.9937	1/9.48	25.79	5.58
21	*S*-**1a**	*L*-Alaninol	$(3.51\pm0.14)\times10^2$	0.9917		14.53	
22	*S*-**1a**	*D*-Alaninol	$(6.94\pm0.29)\times10^2$	0.9951	1/1.98	16.22	1.69
23	*S*-**1a**	*L*-Phenylalaninol	$(1.51\pm0.07)\times10^2$	0.9903		12.44	
24	*S*-**1a**	*D*-Phenylalaninol	$(8.81\pm0.44)\times10^2$	0.9927	1/5.64	16.81	4.37
25	*S*-**1b**	*L*-Ala[c]	$(2.88\pm0.09)\times10^3$	0.9972		19.75	
26	*S*-**1b**	*D*-Ala[c]	$(2.69\pm0.11)\times10^4$	0.9961	1/9.34	25.29	5.54
27	*S*-**1b**	*L*-Phe[c]	$(2.41\pm0.13)\times10^3$	0.9935		19.31	
28	*S*-**1b**	*D*-Phe[c]	$(2.08\pm0.15)\times10^4$	0.9922	1/8.63	24.65	5.34
29	*S*-**1b**	*L*-Alaninol	$(1.35\pm0.11)\times10^2$	0.9942		12.16	
30	*S*-**1b**	*D*-Alaninol	$(7.03\pm0.27)\times10^2$	0.9929	1/5.21	16.25	4.09
31	*S*-**1b**	*L*-Phenylalaninol	$(2.84\pm0.09)\times10^2$	0.9918		14.01	
32	*S*-**1b**	*D*-Phenylalaninol	$(8.29\pm0.32)\times10^2$	0.9909	1/2.92	16.66	2.65

[a] The data were calculated from 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.

$\Delta I_S/\Delta I_R=1.84$ for Phe anions.

The continuous variation methods were also employed to determine the stoichiometric ratio of the receptor *S*-**1a** with guests [*L*- and *D*-Ala anions]. The total concentration of host and guest was constant (1.0×10^{-6} mol/L) in $CHCl_3$, with a continuously variable molar fraction of host ([H]/([H]+[G])). Figure 4 shows the Job's plots of receptor *S*-**1a** with *L*- and *D*-Ala anion (at 371 nm, $\lambda_{ex}=278$ nm). When the molar fraction of the host was 0.50, the fluorescence intensity reached a maximum, which demonstrated that receptor *S*-**1a** formed a 1∶1 complex with *L*- and *D*-Ala anions, respectively.[16]

The decrease in fluorescence intensity of the receptor upon addition of the anion is similar to the anon-induced fluorescence decrease reported previously.[17] Due to the similar structure of *S*-**1a** and *S*-**1b**, the fluorescent variations of *S*-**1a**, *S*-**1b** showed the same trend. Since there were no changes in the UV-vis spectra of receptors when treated with *L*- or *D*-anions, a photoin electron-transfer (PET) process might be responsible for the fluorescent quenching.[18] In the presence of guest anions, the fluorescence quenching of receptors *S*-**1a**, *S*-**1b** most likely arose from the change of the free energy (ΔG_{PET}) of the electron transfer between the excited fluorophore and the receptor units (NH).[19] When the guest anions interacted with receptors *S*-**1a** or *S*-**1b**, the reductive potential of the receptor units increased

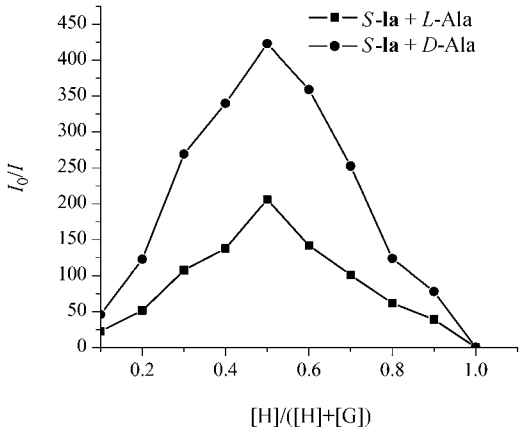

Figure 4 Job's plots of receptor *S*-**1a** with *L*- and *D*-Ala anions (371 nm, λ_{ex}=278 nm). The total concentration of the host ([H]) and guest ([G]) is 1.0×10^{-6} mol/L in $CHCl_3$. I_0: fluorescence intensity of *S*-**1a**; *I*: fluorescence intensity of *S*-**1a** in the presence of the guest.

along with the ratio of the electron transfer from the HOMO orbit of receptor units to the excited binaphthyl group, which in turn led to a more facile intramolecular PET process.[20] Therefore fluorescence quenching was observed.

In order to study how the chirality of the amino acid unit and BINOL groups in *S*-**1a** or *S*-**1b** influenced the enantioselective fluorescent recognition, *R*-**1a** and *R*-**1b**, the diastereoisomeric compounds of *S*-**1a** and *S*-**1b**, were also prepared, and their interactions with Ala, Phe anions, alaninol and phenylalaninol studied were which showed the opposite enantioselectivity (see the Table 1). That is, the enantiomer of *D*-guest, quenched the fluorescence of *D*- more efficiently than *L*-guest. The result of fluorescence titration indicated 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*-**1a**, *R*-**1b** and *S*-**1a**, *S*-**1b** in a same fashion.

Table 1 indicates that the interaction of *S*-**1a** or *S*-**1b** with the *L*-Ala and *L*-Phe anions is better than that with the *D*-Ala and *D*-Phe anions, which is probably due to the *L*-amino acid anions having a more complementary structure with receptors *S*-**1a** or *S*-**1b**.

The receptors *S*-**1a** or *S*-**1b** and *R*-**1a** or *R*-**1b** 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 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*-**1a** and chiral anionic guest because NMR spectroscopy can provide structural and dynamic information directly.[21] Chiral recognition studies were carried out with a 400 MHz NMR spectrometer using receptor *S*-**1a** by ^{1}H NMR in $CDCl_3$ as chiral solvating agents at room temperature. The spectra of receptor *S*-**1a** and its complex with equimolar amounts of racemic Ala anions are shown in Figure 5. When treated with equimolar amounts of receptor *S*-**1a**, the signal of the CH proton of the racemic Ala anion splitted into a more complicated signal pattern (Figure 5C) with a downfield shift. The interaction of receptor *S*-**1a** with *L*-enantiomer shows that the CH proton has a larger downfield shift (from δ 3.85 to 4.27, $\Delta\delta$=0.42, Figure 5D) than the CH proton of *D*-enantiomer (from δ 3.85 to 4.19, $\Delta\delta$=0.34, Figure 5E). Moreover, the signals of the OH proton in the ^{1}H NMR spectra of receptor *S*-**1a** have an downfield shift from δ 6.57 to 6.78 ($\Delta\delta$=0.21, Figure 5D) or 6.74 ($\Delta\delta$=0.17, Figure 5E) for *L*- or *D*-Ala anion, respectively, while the signals of the peaks of binaphthyl fragments are downfield shifted and broadened with the addition of the guest. The above results indicate that *S*-**1a** has a stronger interaction with the *L*-Ala anion than with its *D*-enantiomer. This indicated that the interaction between the host and guest also happened by multiple hydrogen bondings. The above results illustrate that the nature of the receptor, multiple hydrogen-bonding interactions, and complementary chiral-centre interactions maybe responsible for the enantiomeric recognition of amino acid anion.[22]

Conclusion

In summary, four chiral fluorescent receptors *S*-**1a**, *S*-**1b** and *R*-**1a**, *R*-**1b** were synthesized and their enantioselective recognition was studied by fluorescence titration and ^{1}H NMR spectroscopy. All receptors exhibit different chiral recognition abilities towards *N*-Boc-protected amino acid anions and form 1∶1 complexes with the guest molecules. It is clear that nature of the receptor, good structural preorganization, multiple hydrogen-bonding interactions and complementary chiral-centre interactions induce may be responsible for the enantiomeric recognition of anionic guests.[22] All receptors are promising in their use as fluorescence sensors for *N*-Boc-protected amino acid anions. The remarkably different fluorescent responses that result from complexation reveal that *S*-**1a**, *S*-**1b** and *R*-**1a**, *R*-**1b** could be used as fluorescent chemosensors for the *N*-Boc-protected alanine anion or *N*-Boc-protected phenylalanine anion (Phe) in the future.

Experimental

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 FT-IR spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AV-400 spectrometer. Mass spectra were determined by

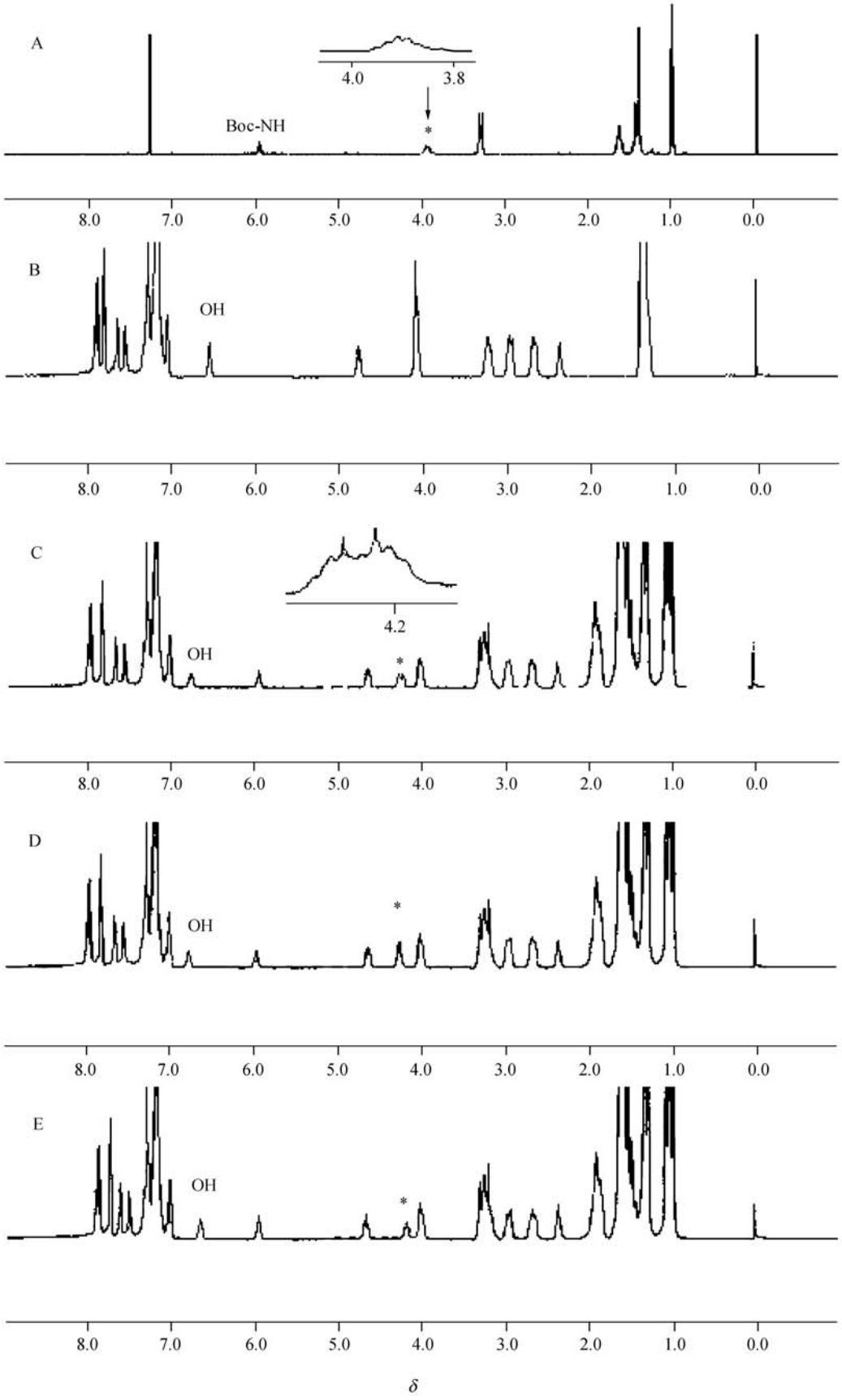

Figure 5 ^{1}H NMR spectra of *S*-**1a** and its guest complexes at 25 ℃ ([*S*-**1a**]=[guest]=4.0×10^{-3} mol/L) in $CDCl_3$ at 400 MHz. (A) Racemic Ala anion; (B) receptor *S*-**1a**; (C) receptor *S*-**1a**+racemic Ala anion; (D) receptor S-**1a**+*L*-Ala anion; (E) receptor *S*-**1a**+*D*-Ala anion.

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ESI recorded on a Esquire 3000 LC-MS mass instrument. Optical rotations were taken on a Perkin-Elmer Model 341 polarimeter. Fluorescence spectra were obtained with a F-7000 FL Spectrophotometer. Elementalanalyses were performed by the Vario Elemental CHSN-O microanalyzer. All other commercially available reagents were used without further purification. 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.[13]

General procedure for the synthesis of compounds 3a and 3b

Under nitrogen, excess diamine (10 mmol) in 10 mL of CH_3OH was added dropwise into a solution (20 mL) of compound *S*-*tert*-butoxycarbonylamino-propionic acid methyl ester **2** (2 mmol) in $CHCl_3/CH_3OH$ (1∶10, *V*∶*V*) under an ice-bath. After the addition, the mixture was stirred at room temperature for 48 h. After evaporation of the solvent and the residual diamine under reduced pressure, $CHCl_3$ (30 mL) were added and washed with H_2O (30 mL×3), then the organic layer was separated and dried over Na_2SO_4. After filtration, the solvent was removed under reduced pressure to give **3a** or **3b** as colorless ropy oil.

3a: Yield 92% (0.57 g); $[\alpha]_D^{20}$ +23.61 (*c* 0.05, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 1.49 (s, 9H, CH_3), 1.75 (s, 2H, NH_2), 2.88 (t, *J*=8.0 Hz, 2H, CH_2), 3.09 (t, *J*=8.0 Hz, 2H, CH_2), 3.39 (d, *J*=6.4 Hz, 2H, CH_2), 4.29 (t, *J*=6.7 Hz, 1H, CH), 6.03 (s, 1H, N**H**Boc), 7.33—7.07 (m, 5H, Ph), 7.65 (s, 1 H, CONH); ^{13}C NMR ($CDCl_3$) δ: 27.9, 28.8, 37.2, 41.2, 44.3, 57.8, 79.4, 125.9, 127.1, 128.3, 139.8, 156.8, 174.4; ESI-MS *m/z* (%): 308 (M^++1, 100). Anal. calcd for $C_{16}H_{25}N_3O_3$: C 62.52, H 8.20, N 13.6; found C 62.39, H 8.31, N 13.51.

3b: Yield 95% (0.61 g); $[\alpha]_D^{20}$ +21.06 (*c* 0.05, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ: 1.47 (s, 9H, CH_3), 1.72 (s, 2 H, NH_2), 2.92—3.07 (m, 6H, CH_2), 3.37 (t, *J*=6.7 Hz, 2H, CH_2), 4.32 (t, *J*=6.9 Hz, 1H, CH), 6.08 (s, 1H, N**H**Boc), 7.09—7.35 (m, 5H, Ph), 7.63 (s, 1H, CONH); ^{13}C NMR ($CDCl_3$) δ: 27.9, 28.8, 32.7, 37.9, 43.6, 47.8, 58.2, 79.9, 126.3, 127.4, 128.7, 139.6, 156.9, 174.7; ESI-MS *m/z* (%): 322 (M^++1, 100). Anal. calcd for $C_{17}H_{27}N_3O_3$: C 63.53, H 8.47, N 13.07; found C 63.42, H 8.52, N 12.98.

General procedure for the synthesis of compound *R*-1a, *R*-1b, *S*-1a and *S*-1b

A mixture of the *R*- or *S*-binaphthyl dialdehyde (0.34 g, 1 mmol) and compound **3a** or **3b** (2.2 mmol) in dry $CHCl_3$ (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 nitrogen for another 6 h at 50 ℃. The mixture was poured into 30 mL of 10% $NaHCO_3$ after removing the solvent under reduced pressure, and extracted with $CHCl_3$ for three times. The organic layers were combined and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated under reduced pressure and the residue was purified by column chromatography on a silica gel [eluent: $V(CHCl_3)$∶$V(CH_3CH_2OH)$=50∶1]. The pure product was obtained as a pale yellow solid.

S-**1a**: Yield 72.4%; $[\alpha]_D^{20}$ −31.95 (*c* 0.05, $CHCl_3$). *R*-**1a**: Yield 78.2%; $[\alpha]_D^{20}$ +33.41 (*c* 0.05, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 1.36 (s, 18H, CH_3), 2.36 (s, 2H, NH), 2.64—2.73 (m, 4H, CH_2), 2.92—3.01 (m, 4H, CH_2), 3.16—3.26 (m, 4H, $PhCH_2$), 4.14 (d, *J*=8.0 Hz, 4H, Ar-CH_2), 4.72—4.81 (m, 2H, $CHCH_2$), 6.57 (s, 2H, OH), 7.04—7.07 (m, 2H, ArH), 7.16—7.33 (m, 10H, pH), 7.57 (d, *J*=7.2 Hz, 2H, ArH), 7.64 (d, *J*=2.7 Hz, 2H, NH-Boc), 7.81 (d, *J*=8.1 Hz, 2H, ArH), 7.86 (d, *J*=7.2 Hz, 2H, ArH), 7.88 (d, *J*=8.0 Hz, 2H, ArH), 7.91 (s, 2H, CONH); ^{13}C NMR ($CDCl_3$) δ: 25.35, 39.42, 39.97, 45.51, 47.64, 49.89, 57.12, 57.37, 70.53, 71.80, 124.96, 125.24, 125.64, 125.86, 127.14, 127.17, 128.37, 129.94, 130.14, 130.51, 130.94, 131.29, 132.79, 132.91, 133.76, 133.96, 134.30, 152.53, 153.55, 173.31; IR (KBr) *v*: 3417, 3099, 2954, 1682, 1537, 1263, 1231, 751 cm^{-1}; ESI-MS *m/z* (%): 947 ($M+Na^+$, 100). Anal. calcd for $C_{54}H_{64}N_6O_8$: C 70.11, H 6.97, N 9.08; *S*-**1a**: found C 70.02, H 7.00, N 9.03; *R*-**1a**: found C 69.98, H 7.01, N 9.01.

S-**1b**: Yield 72.4%; $[\alpha]_D^{20}$ −30.07 (*c* 0.05, $CHCl_3$). *R*-**1b**: Yield 78.2%; $[\alpha]_D^{20}$ +32.85 (*c* 0.05, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ: 1.39 (s, 18H, CH_3), 2.38 (s, 2H, NH), 2.56—2.75 (m, 8H, CH_2), 2.94—3.03 (m, 4H, CH_2), 3.18—3.26 (m, 4H, $PhCH_2$), 4.16 (d, *J*=8.0 Hz, 4H, Ar-CH_2), 4.84—4.76 (m, 2H, $CHCH_2$), 6.58 (s, 2H, OH), 7.06—7.09 (m, 2H, ArH), 7.16—7.34 (m, 10H, Ph), 7.59 (d, *J*=7.2 Hz, 2H, ArH), 7.66 (d, *J*=2.7 Hz, 2H, NH-Boc), 7.83 (d, *J*=8.1 Hz, 2H, ArH), 7.89 (d, *J*=7.2 Hz, 2H, ArH), 7.90 (d, *J*=8.0 Hz, 2H, ArH), 7.95 (s, 2H, CONH); ^{13}C NMR ($CDCl_3$) δ: 25.37, 39.42, 41.72, 44.18, 45.50, 47.62, 49.91, 57.11, 57.31, 70.51, 71.87, 124.99, 125.36, 125.67, 125.89, 127.14, 127.23, 128.37, 129.97, 130.33, 130.92, 131.43, 131.35, 132.85, 132.99, 134.17, 134.39, 134.78, 152.83, 154.37, 174.82; IR (KBr) *v*: 3414, 3102, 2951, 1680, 1539, 1263, 1231, 750 cm^{-1}; ESI-MS *m/z* (%): 975 ($M+Na^+$, 100). Anal. calcd for $C_{56}H_{68}N_6O_8$: C 70.56; H 7.19; N 8.82; *S*-**1b**: found C 70.22, H 7.13, N 8.91; *R*-**1b**: found C 70.31, H 7.11, N 8.93.

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 des-

iccator. The compounds *S*-**1a**, *S*-**1b** and *R*-**1a**, *R*-**1b** 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's plots

Stock solutions of host *S*-**1a** and the *L*-Ala, *D*-Ala tetrabutylammonium salts in $CHCl_3$ system (the total concentration of the host and guest is 1.0×10^{-6} mol/L) 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 work solution could be measured immediately.

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