Supramolecular Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713649759

Synthesis and enantioselective fluorescent sensors for amino acid derivatives based on BINOL

Kuo-Xi Xu[ab]; Li-Rong Yang[c]; Yu-Xia Wang[b]; Jin Zhao[b]; Chao-Jie Wang[b]
[a] Institute of Fine Chemical and Engineering, Henan University, Kaifeng, Henan, P.R. China [b] Key Lab of Natural Medicinal and Immunal Engineering, Henan University, Kaifeng, Henan, P.R. China [c] Institute of Molecule and Crystal Engineering, Henan University, Kaifeng, Henan, P.R. China

First published on: 19 August 2010

To cite this Article Xu, Kuo-Xi , Yang, Li-Rong , Wang, Yu-Xia , Zhao, Jin and Wang, Chao-Jie(2010) 'Synthesis and enantioselective fluorescent sensors for amino acid derivatives based on BINOL', Supramolecular Chemistry, 22: 10, 563 — 570, First published on: 19 August 2010 (iFirst)
To link to this Article: DOI: 10.1080/10610271003713920
URL: http://dx.doi.org/10.1080/10610271003713920

Supramolecular Chemistry
Vol. 22, No. 10, October 2010, 563–570

Taylor & Francis
Taylor & Francis Group

Synthesis and enantioselective fluorescent sensors for amino acid derivatives based on BINOL

Kuo-Xi Xu[a,b], Li-Rong Yang[c], Yu-Xia Wang[b], Jin Zhao[b] and Chao-Jie Wang[b]*

[a]*Institute of Fine Chemical and Engineering, Henan University, Kaifeng, Henan 475004, P.R. China;* [b]*Key Lab of Natural Medicinal and Immunal Engineering, Henan University, Kaifeng, Henan 475004, P.R. China;* [c]*Institute of Molecule and Crystal Engineering, Henan University, Kaifeng, Henan 475004, P.R. China*

(*Received 18 July 2009; final version received 8 February 2010*)

Four novel derivatives of 1,1′-bi-2-naphthol have been prepared and the structures of these compounds characterised by IR, MS, ^{1}H and ^{13}C NMR spectroscopy and elemental analysis. The enantioselective recognition of these sensors has been studied by fluorescence titration and ^{1}H NMR spectroscopy. The sensors exhibited different chiral recognition abilities towards *N*-Boc-protected amino acid anions and formed 1:1 complexes between the host and the guest. Sensors exhibit excellent enantioselective fluorescent recognition ability towards the amino acid derivatives.

Keywords: anions; fluorescence sensor; enantioselective recognition; NMR spectroscopy

1. Introduction

Chiral recognition of racemic compounds exists extensively in nature. To understand biological process, synthetic chiral receptors were prepared to bind the chiral guest selectively (*1*), these have the ability of discriminating the enantiomers. 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 (*2*). Many efforts involve the covalent linking of an optical signalling unit (a chromophore or a fluorophore) to a specific receptor for the chiral molecules (*3*). 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. Over the last two decades, 1,1′-bi-2-naphthol (BINOL) and its derivatives have been extensively used in chiral recognition and asymmetric catalysis (*4*). Because of the fluorescence properties of the naphthalene groups in these compounds, their fluorescence responses towards various chiral molecules have also been investigated (*5*, *6*). Enantioselective recognition of amino acid and its derivatives is important in asymmetric synthesis and drug discovery (*7*). Herein, we describe the development of four novel BINOL derivatives (Scheme 1); their chiral recognition ability towards amino acid derivatives, the enantiomers of the *N*-Boc-protected alanine or phenylalanine anions by fluorimetric titration in $CHCl_3$. ^{1}H NMR experiments suggested that the hydrogen-bonding interaction between the host and guest was the main factor in the recognition process.

2. Results and discussion

2.1 Synthesis

The synthesis of sensors (***S***)-**1**, (***S***)-**2** and (***R***)-**1**, (***R***)-**2** was started from commercially available *S*- or *R*-1,BINOL, as shown in Scheme 1. The hydroxyl groups of BINOL were protected as methoxymethyl (MOM) ethers to get 2,2′-Bis-methoxymethoxy-1,1′-binaphthyl, (***S***)-**4** (*8*). The resulting compound (***S***)-**4** was subjected to ortholithiation, followed by carboxylation to give the corresponding 3,3′-dicarboxylic acid derivatives (***S***)-**5** or (***S***)-**6**, which was hydrolysed by the treatment with hydrogen chloride in absolute C_2H_5OH to give sensors. In order to understand the functions of the aryl hydroxyl groups in the chiral recognition in (***S***)-**1**, we synthesised compound (***S***)-**3** where the hydroxyls are selectively protected with methyl groups (Scheme 1). In this compound, the two aryl hydroxyls are protected. In order to study how the aryl hydroxyls and BINOL groups in (***S***)-**1** and (***S***)-**2** influenced the enantioselective fluorescent recognition, (***R***)-**1** and (***R***)-**2**, the enantiomers of (***S***)-**1** and (***S***)-**2**, were also prepared. The structures of all these compounds were characterised by IR, MS, ^{1}H and ^{13}C NMR spectroscopy and elemental analysis. They are readily soluble in common organic solvents such as $CHCl_3$, CH_2Cl_2, CH_3OH, DMSO and DMF.

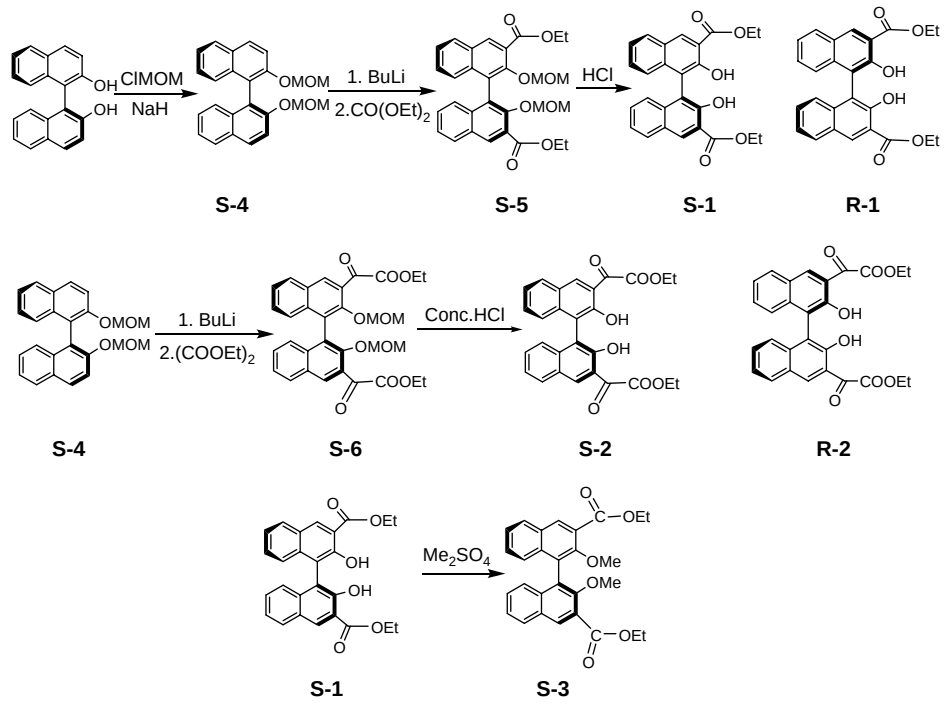
2.2 Fluorescence spectra study

The properties of the chiral recognition of sensors (***S***)-**1** and (***S***)-**2** were investigated in the absence and the presence of the *S*- and *R*-*N*-Boc-protected alanine anion

*Corresponding author. Email: wcjaxq@henu.edu.cn

ISSN 1061-0278 print/ISSN 1029-0478 online

DOI: 10.1080/10610271003713920
http://www.informaworld.com



Scheme 1. Synthesis of the sensors ***S*-1**, ***S*-2**, ***R*-1** and ***R*-2**.

(Ala) and *N*-Boc-protected phenylalanine anion (Phe), in which 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 sensor and guest by hydrogen bondings. Because there was almost no change observed on the UV–vis spectra of sensors upon the addition of guest anions, the interaction between the host and the anion was only evaluated by fluorescent spectra.

Figures 1 and 2 show the fluorescence emission spectra of the sensor (***S*)-1** with different concentrations of *R*- or *S*-Ala anions in $CHCl_3$. Gradually increasing the concentration of the *R*-enantiomer caused the fluorescence emission intensities of (***S*)-1** (1.25×10^{-5} M) at 369 nm ($\lambda_{ex} = 282$ nm) to decrease remarkably (Figure 1). The quenching efficiency was 5.91% with 10 equiv. of *R*-Ala anion, when 500 equiv. of *R*-Ala anion was added, the fluorescence quenching efficiency was 59.35%. Upon the addition of *S*-Ala anion, the quenching efficiency was 30.18% with 10 equiv. of *S*-Ala anion. When 500 equiv. of *R*-Ala anion was added, the fluorescence quenching efficiency was 67.33% (Figure 2). The different quenching efficiencies indicated excellent enantioselective recognition ability of the sensor (***S*)-1** between *R*- and *S*-Ala anion. Such a large difference in fluorescence quenching implies that the sensor (***S*)-1** can be used as a sensitive enantioselective fluorescent sensor for Ala anions.

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. For a complex of 1:1 stoichiometry, the association constant (K_{ass}) can be calculated using Equation (1) from the Origin 7.0 software package (*9*).

$$I = I_0 + (X_{lim} - X_0)/2C_0\Big\{C_H + C_G + 1/K_{ass} - [(C_H + C_G + 1/K_{ass})^2 - 4C_H C_G]^{1/2}\Big\}, \quad (1)$$

where I represents the fluorescence intensity, C_H and C_G are the host and the guest concentrations and C_0 is the initial concentration of the host (*10*). The association constants (K_{ass}) and correlation coefficients (R) obtained by a nonlinear least squares analysis of I vs. C_H and C_G are listed in Table 1.

The continuous variation methods were also employed to determine the stoichiometric ratio of the sensor (***S*)-1** with guests (*S*- and *R*-Ala anions). The total concentration of the host and the guest was constant (1.0×10^{-6} M) in $CHCl_3$, with a continuously variable molar fraction of the host ([H]/([H] + [G])). Figure 3 shows the Job plots of the receptor (***S*)-1** with *S*- and *R*-Ala anion (at 369 nm, $\lambda_{ex} = 282$ nm). When the molar fraction of the host was 0.50, the fluorescence intensity reached a maximum, which demonstrated that the sensor (***S*)-1** formed a 1:1 complex with *S*- and *R*-Ala anions, respectively (*11*).

Similar phenomena were observed when *S*- or *R*-Phe anions were added into a solution of sensor (***S*)-1**. The result of a nonlinear curve fitting (at 369 nm) indicates that

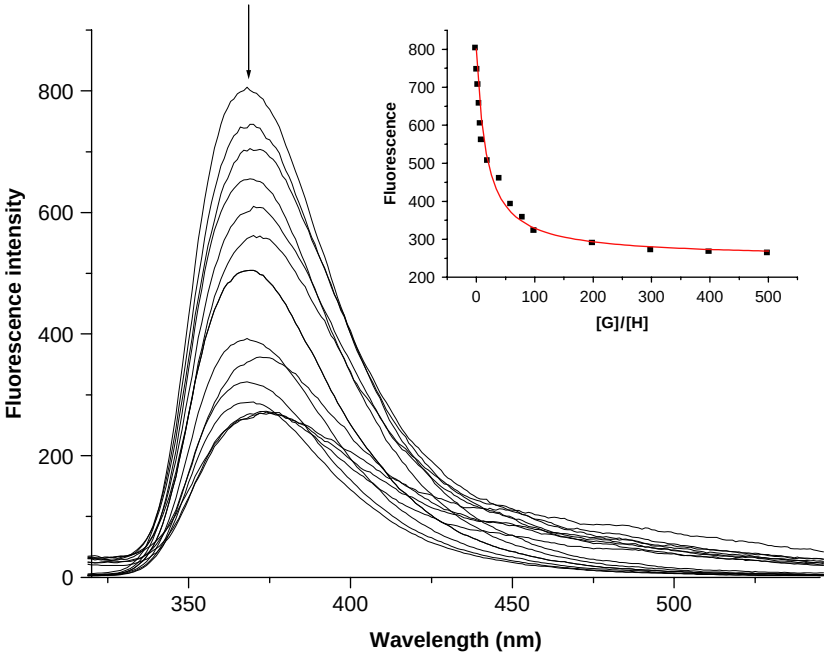


Figure 1. Fluorescence spectra of the receptor (***S***)-**1** (1.25×10^{-5} M) with *S*-Ala anion in $CHCl_3$. The anion equivalents are: 0, 2, 4, 6, 8, 10, 20, 40, 60, 80, 100, 200, 300, 400 and 500, $\lambda_{ex} = 282$ nm. Inset: changes in the fluorescence intensity of (***S***)-**1** at 369 nm upon the addition of *S*-Ala anion. The line shown is a line-fitted curve. The correlation coefficient (*R*) of the nonlinear curve fitting is 0.9957.

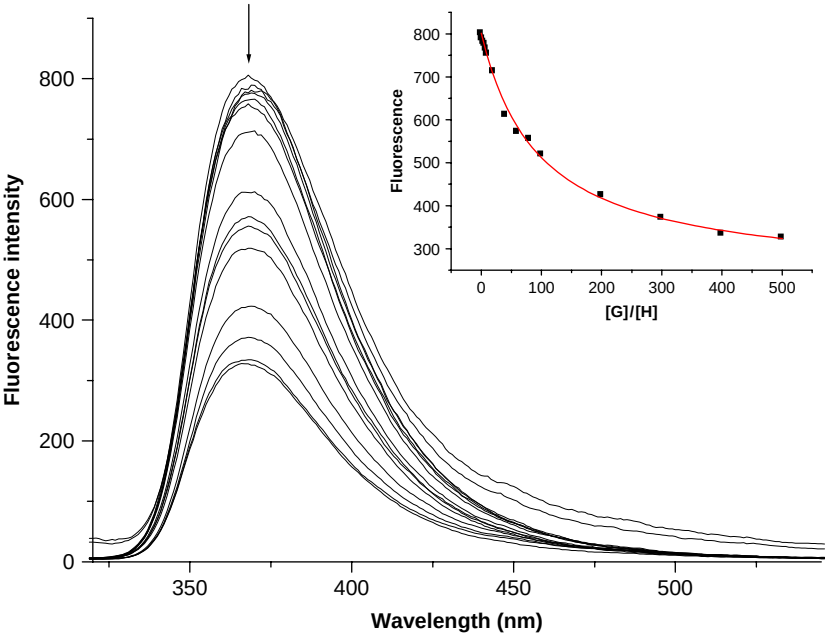


Figure 2. Fluorescence spectra of the receptor (***S***)-**1** (1.25×10^{-5} M) with *R*-Ala anion in $CHCl_3$. The anion equivalents are: 0, 2, 4, 6, 8, 10, 20, 40, 60, 80, 100, 200, 300, 400 and 500, $\lambda_{ex} = 282$ nm. Inset: changes in the fluorescence intensity of (***S***)-**1** at 369 nm upon the addition of *R*-Ala anion. The line shown is a line-fitted curve. The correlation coefficient (*R*) of the nonlinear curve fitting is 0.9943.

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 sensors (***S***)-**1**, (***S***)-**2** and (***R***)-**1**, (***R***)-**2** with *S*-/*R*-guests in $CHCl_3$ at 25°C.

Entry	Host	Guest[a]	K_{ass} (M^{-1})[b,c]	R	$K_{ass(S)}/K_{ass(R)}$	$-\Delta G_0$ (kJmol^{-1})	$\Delta\Delta G_0$ (kJmol^{-1})
1	(***S***)-**1**	*S*-Ala	$(4.91 \pm 0.42) \times 10^4$	0.9957		26.78	
2	(***S***)-**1**	*R*-Ala	$(8.93 \pm 0.51) \times 10^3$	0.9943	5.50	22.55	−4.23
3	(***S***)-**1**	*S*-Phe	$(3.87 \pm 0.36) \times 10^4$	0.9925		26.19	
4	(***S***)-**1**	*R*-Phe	$(7.68 \pm 0.48) \times 10^3$	0.9986	5.04	22.18	−4.01
5	(***S***)-**2**	*S*-Ala	$(5.89 \pm 0.24) \times 10^4$	0.9937		27.23	
6	(***S***)-**2**	*R*-Ala	$(1.86 \pm 0.19) \times 10^4$	0.9926	3.17	24.37	−2.86
7	(***S***)-**2**	*S*-Phe	$(4.53 \pm 0.37) \times 10^4$	0.9947		26.58	
8	(***S***)-**2**	*R*-Phe	$(1.61 \pm 0.08) \times 10^4$	0.9954	2.81	24.02	−2.56
9	(***R***)-**1**	*S*-Ala	$(1.27 \pm 0.51) \times 10^4$	0.9921		23.43	
10	(***R***)-**1**	*R*-Ala	$(4.69 \pm 0.27) \times 10^4$	0.9938	1/3.69	26.67	3.24
11	(***R***)-**1**	*S*-Phe	$(4.02 \pm 0.29) \times 10^4$	0.9941		26.28	
12	(***R***)-**1**	*R*-Phe	$(1.11 \pm 0.24) \times 10^4$	0.9957	1/3.62	23.09	3.19
13	(***R***)-**2**	*S*-Ala	$(2.51 \pm 0.19) \times 10^4$	0.9914		25.12	
14	(***R***)-**2**	*R*-Ala	$(5.97 \pm 0.38) \times 10^4$	0.9961	1/2.39	27.26	2.14
15	(***R***)-**2**	*S*-Phe	$(2.93 \pm 0.68) \times 10^4$	0.9939		25.00	
16	(***R***)-**2**	*R*-Phe	$(5.01 \pm 0.63) \times 10^4$	0.9922	1/1.71	26.83	1.83

[a] Ala and Phe tetrabutylammonium salts, the amino group was protected by a *tert*-butyloxycarbonyl function.
[b] The data were calculated from results of fluorescence titrations in $CHCl_3$.
[c] All error values were obtained from nonlinear curve fitting.

a 1:1 complex was formed between the sensor (***S***)-**1** and *S*- or *R*-Phe (see Table 1). In addition, the association constants (K_{ass}) were different (see Table 1) ($K_{ass(S)} = (3.87 \pm 0.36) \times 10^4\,M^{-1}$, $\Delta G_0 = -26.19\,kJ\,mol^{-1}$, $K_{ass(R)} = (7.68 \pm 0.48) \times 10^3\,M^{-1}$ and $\Delta G_0 = -22.18$ kJmol^{-1}), yielding a *S*/*R* selectivity [$K_{ass(S)}/K_{ass(R)}$] of 5.04 for the Phe anions and a $\Delta\Delta G_0$ value of $-4.01\,kJmol^{-1}$, demonstrating that sensor (***S***)-**1** has good chiral recognition ability towards the enantiomers of Phe anions.

The decrease in fluorescence intensity of the excimer upon the addition of the anion is similar to the anion-induced fluorescence decrease reported previously (*12*).

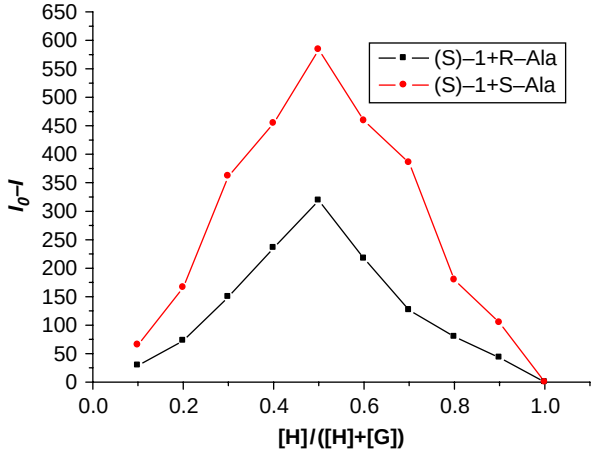


Figure 3. Job plots of the receptor (***S***)-**1** with *S*- and *R*-Ala anions (369 nm, $\lambda_{ex} = 282$ nm). The total concentration of the host ([H]) and the guest ([G]) is 1.0×10^{-6} M in $CHCl_3$. I_0, fluorescence intensity of (***S***)-**1** and I, fluorescence intensity of (***S***)-**1** in the presence of the guest.

Similar phenomena were observed when *R*- or *S*-Ala, Phe anions were added into a solution ($1.25 \times 10^{(5}$ M) of sensor (***S***)-**2**, respectively. Upon the addition of *R*- or *S*-guest, the different fluorescent quenching degree of the sensor (***S***)-**2** was observed. The quenching efficiencies of *S*-*N*-Boc-protected amino acid anions were much higher than the *R*-*N*-Boc-protected amino acid anions. Satisfactory nonlinear curve fitting (the correlation coefficient is over 0.99) confirmed that the sensor (***S***)-**2** formed a 1:1 complex with the *R*- and *S*-guest anion (*13*).

The fluorescence responses of sensor (***S***)-**3** and in the presence of both enantiomers of Ala and Phe were investigated. When (***S***)-**3** was treated with them, no fluorescence quenching was observed, this demonstrates that the interaction of the hydroxyl protons with the amino acid anion is essential for the fluorescence quenching of (***S***)-**1**. This also indicates that hydrogen bonding plays an important role in the interaction between the host and the guest and leads to the easier signal transductions of chiral recognition by fluorescence method.

We also prepared (***R***)-**1** and (***R***)-**2**, the enantiomers of (***S***)-**1** and (***S***)-**2**, and studied its interaction with *S*- or *R*-Ala, Phe anions, which showed the opposite enantioselectivity. That is, the enantiomer of *R*-Ala, Phe anion, quenched the fluorescence of (***R***)-**1** and (***R***)-**2** more efficiently than *S*-guest. The result of fluorescence titration indicated that the enantiomers of guest anions interacted with (***R***)-**1**, (***R***)-**2** and (***S***)-**1**, (***S***)-**2** in a similar fashion.

According to Table 1, it indicates that the interaction of sensors (***S***)-**1**, (***S***)-**2** with the *S*-Ala or *S*-Phe anions is better than that with the *R*-Ala or *R*-Phe anions, which is probably due to the *S*-amino acid anions having a more complementary structure with sensors (***S***)-**1**, (***S***)-**2**.

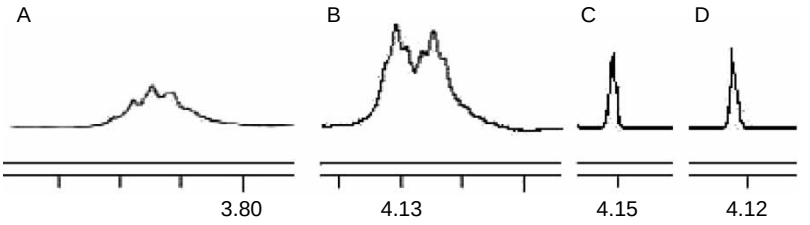


Figure 4. The changes in ^{1}H NMR spectra of CH proton of the guest in the absence and the presence of the host at 25°C ([(***S***)-**1**] = [guest] = 4.0×10^{-3} M) in $CDCl_3$ at 400 MHz. (A) The methine proton signals of racemic Ala anion; (B) the methine proton signals of racemic Ala anion in the presence of an equimolar amount of the sensor (***S***)-**1**; (C) the methine proton signals of *S*-Ala anion in the presence of an equimolar amount of the sensor (***S***)-**1** and (D) the methine proton receptor on signals of *R*-Ala anion in the presence of an equimolar amount of the sensor (***S***)-**1**.

The Phe anion has a structure similar to that of the Ala anion, but the association constants for the association of the receptors with the Phe anion are smaller than those for the Ala anion, which could be attributed to the greater steric hindrance of the phenyl ring relative to the methyl group. The sensors (***S***)-**1**, (***S***)-**2** and (***R***)-**1**, (***R***)-**2** all exhibit good chiral recognition ability towards the enantiomers of the Ala and Phe anions, which indicates that the preorganised structure of the chiral centre of binaphthyl unit plays important roles in the enantioselective recognition process.

2.3 ^{1}H NMR study

^{1}H NMR experiments were undertaken to assess the chiral recognition properties between the sensor (***S***)-**1** and chiral anionic guest because NMR spectroscopy can provide structural and dynamic information directly (*14*). Chiral recognition studies were carried out with a 400-MHz NMR spectrometer using the sensor (***S***)-**1** by ^{1}H NMR in $CDCl_3$ as chiral solvating agent at room temperature.

Ala anions were chosen as the probe. The spectra of the sensor (***S***)-**1** and its complex with equimolar amounts of racemic Ala anions are shown in Figure 4. When treated with equimolar amounts of the sensor (***S***)-**1**, the CH proton of racemic Ala anion cleaved into a more complicated signal pattern (Figure 4(B)) with a downfield shift (from $\delta = 3.83$ to 4.13 ppm). The interaction of the sensor (***S***)-**1** with *S*-Ala shows that the CH proton has a larger downfield shift (from $\delta = 3.83$ to 4.15 ppm, $\Delta\delta = 0.32$ ppm, Figure 4(C)) than that of the CH proton of *R*-enantiomer (from $\delta = 3.83$ to 4.12 ppm, $\Delta\delta = 0.29$ ppm, Figure 4(D)). Moreover, the signals of the —OH proton in the ^{1}H NMR spectra of the sensor (***S***)-**1** downfield shifted and almost disappeared, 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 linked to the Boc moiety was also clearly downfield shifted from $\delta = 5.91$ to 6.04 ($\Delta\delta = 0.13$ ppm) for the *S*-Ala anion, whereas the *R*-Ala anion downfield shifted from $\delta = 5.91$ to 5.98 ($\Delta\delta = 0.07$ ppm) for the *R*-Ala anion, suggesting that the amide group of the Ala anion participated in the association process. 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 the guest also happened by multiple hydrogen bondings.

3. Conclusion

In summary, four novel chiral fluorescent sensors (***S***)-**1**, (***S***)-**2** and (***R***)-**1**, (***R***)-**2** were synthesised and their enantioselective recognition was studied by fluorescence titration and ^{1}H NMR spectroscopy. The sensors (***S***)-**1**, (***S***)-**2** and (***R***)-**1**, (***R***)-**2** exhibit different chiral recognition abilities towards some enantiomers of amino acid derivatives and form 1:1 complexes with the guest molecules (*15*). It is clear that the nature of the sensor, good structural preorganisation, multiple hydrogen-bonding interactions and complementary chiral-centre interactions inducement may be responsible for the enantiomeric recognition of anionic guests. The sensors (***S***)-**1**, (***S***)-**2** and (***R***)-**1**, (***R***)-**2** are promising in their use as fluorescence sensors for amino acid derivatives. The remarkably different fluorescent responses that result from complexation reveal that (***S***)-**1**, (***S***)-**2** and (***R***)-**1**, (***R***)-**2** could be used as fluorescent chemosensors for the *N*-Boc-protected alanine anion or *N*-Boc-protected phenylalanine anion in the future.

4. Experimental

4.1 Materials and methods

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 ESI recorded on an Esquire 3000 LC-MS mass instrument. Optical rotations were taken on a Perkin-Elmer Model 341

polarimeter. Fluorescence spectra were obtained with an F-7000 FL spectrophotometer. Elemental analyses were performed by the Vario Elemental CHSN-O microanalyser. 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 synthesised according to a literature method (*16*).

4.2 General procedure for the synthesis of compounds (S)-5, (R)-5 and (S)-6, (R)-6

Under nitrogen, 2,2′-Bis-MOM-1,1′-binaphthyl, (***S***)-**4** or (***R***)-**4** (5.0 mmol, 1.87 g) was dissolved in ether (100 ml) in a flask equipped with a side arm and a magnetic stirring bar. The solution was cooled to 0°C, and *n*-BuLi (25.0 mmol, 2.5 M in hexane, 10 ml) was added dropwise. The reaction mixture was stirred for about 3 h at 0°C, then dry carbonic acid diethyl ester or oxalic acid diethyl ester (25.0 mmol) was slowly added. The reaction was allowed to warm to room temperature overnight. Saturated aqueous NH_4Cl solution was added to quench the reaction. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate (20 ml × 3). The combined organic extracts were washed with brine, and dried over Na_2SO_4. After the removal of the solvent, the residue was purified by column chromatography on silica gel. Elution with hexane–ethyl acetate (50:1), $R_f = 0.5$ (hexane–ethyl acetate = 10:1), gave the compound (***S***)-**5**, (***R***)-**5** or (***S***)-**6** or (***R***)-**6**, as a yellow solid.

(***S***)-**5**: 54% yield (1.46 g); $[\alpha]_D^{20} = -89.6$ ($c = 0.50$, $CHCl_3$); (***R***)-**5** was also prepared from (***R***)-**4** with the same procedure. (***R***)-**5**, 51% yield (1.38 g); $[\alpha]_D^{20} = +87.7$ ($c = 0.24$, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.39 (s, 2H, Ar-H), 7.74–7.71 (m, 2H, Ar-H), 7.25–7.21 (m, 4H, Ar-H), 7.12–7.08 (m, 2H, Ar-H), 5.04 (d, $J = 6.4$ Hz, 2H), 4.99–4.95 (m, —CH_2—, 6H), 3.11 (s, 6H, —CH_3), 1.49 (t, $J = 6.8$ Hz, —CH_3, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 184.2, 153.6, 134.8, 132.1, 131.4, 129.8, 129.1, 127.5, 124.2, 124.0, 100.1, 58.1, 57.6, 56.9, 18.4; IR (KBr/cm^{-1}): 3449, 3067, 2934, 1759, 1658, 1392, 1238, 751; ESI-MS *m/z*: 542 ((M + Na + 1)$^+$, 100); $C_{30}H_{30}O_8$: calcd. C 69.49, H 5.83; (***S***)-**5**, found C 69.32, H 5.88; (***R***)-**5**, found C 69.37, H 5.86.

(***S***)-**6**: 71% yield (2.04 g); $[\alpha]_D^{20} = +77.9$ ($c = 0.25$, $CHCl_3$); (***R***)-**6** was also prepared from (***R***)-**5** with the same procedure. (***S***)-**5**, $[\alpha]_D^{20} = -75.8$ ($c = 0.50$, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.47 (s, 2H, Ar-H), 7.91–7.87 (m, 2H, Ar-H), 7.26–7.21 (m, 4H, Ar-H), 7.14–7.10 (m, 2H, Ar-H), 5.09 (d, $J = 6.4$ Hz, 2H), 5.04–5.00 (m, —CH_2—, 6H), 3.17 (s, 6H, —CH_3), 1.51 (t, $J = 6.8$ Hz, —CH_3, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 197.1, 179.6, 159.3, 137.6, 134.1, 133.2, 131.9, 130.8, 128.9, 125.7, 125.1, 101.4, 59.7, 58.3, 57.8, 18.5; IR (KBr/cm^{-1}): 3454, 3071, 2937, 1764, 1748, 1662, 1397, 1239, 750; ESI-MS *m/z*: 598 ((M + Na + 1)$^+$, 100); $C_{32}H_{30}O_{10}$: calcd. C 66.89, H 5.26; (***S***)-**6**, found C 66.72, H 5.31; (***R***)-**6**, found C 69.75, H 5.30.

4.3 General procedure for the synthesis of compound (S)-1, (R)-1 and (S)-2, (R)-2

After compound (***S***)-**5**, (***R***)-**5**, (***S***)-**6** or (***R***)-**6** (2.0 mmol) was dissolved in 20 ml absolute ethanol and conc. HCl (5 ml), the mixture was stirred at room temperature overnight. The resulting yellow solution was concentrated with a rotary evaporator. Water (10 ml) was then added, and the solution was extracted with ethyl acetate (20 ml × 3). The combined extract was dried over Na_2SO_4. After the removal of the solvent, the residue was purified by column chromatography on silica gel eluted with hexane–ethyl acetate (30:1), to give (***S***)-**1**, (***R***)-**1** or (***S***)-**2**, (***R***)-**2**, as a yellow solid.

(***S***)-**1**: 84% yield (0.72 g); $[\alpha]_D^{20} = -97.9$ ($c = 0.24$, $CHCl_3$). The optical purity of (***S***)-**1** was 94% ee as determined using HPLC-Chiralcel OD column (solvent: hexane–^{i}PrOH 9/1). (***R***)-**1** was also prepared from (***R***)-**5** with the same procedure. (***R***)-**1**, 79% yield (0.68 g); $[\alpha]_D^{20} = +95.2$ ($c = 0.24$, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 10.83 (s, 2H, —OH), 8.70 (s, 2H, Ar-H), 7.94–7.92 (m, 2H, Ar-H), 7.35–7.33 (m, 4H, Ar-H), 7.17–7.15 (m, 2H, Ar-H), 4.52 (q, $J = 6.4$ Hz, 2H), 4.97 (q, $J = 7.2$ Hz, —CH_2—, 4H), 1.51 (t, $J = 6.8$ Hz, —CH_3, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 186.4, 154.7, 135.2, 132.6, 132.1, 130.1, 129.6, 128.2, 124.6, 124.1, 100.2, 56.9; IR (KBr/cm^{-1}): 3449, 3067, 2934, 1759, 1658, 1392, 1238, 751; ESI-MS *m/z*: 453 ((M + Na)$^+$, 100); $C_{26}H_{22}O_6$: calcd. C 72.55, H 5.15; (***S***)-**5**, found C 72.47, H 5.19; (***R***)-**5**, found C 72.49, H 5.18.

(***S***)-**2**: 81% yield (0.79 g), $[\alpha]_D^{20} = +91.8$ ($c = 0.25$, $CHCl_3$). The optical purity of (***S***)-**2** was 97% ee as determined using HPLC-Chiralcel OD column (solvent: hexane–^{i}PrOH 20/3). (***R***)-**2** was also prepared from (***R***)-**6** with the same procedure. (***R***)-**2**, 76% yield (0.74 g); $[\alpha]_D^{20} = -88.3$ ($c = 0.25$, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 10.89 (s, 2H, —OH), 8.77 (s, 2H, Ar-H), 7.99–7.97 (m, 2H, Ar-H), 7.38–7.36 (m, 4H, Ar-H), 7.19–7.17 (m, 2H, Ar-H), 4.97 (q, $J = 7.2$ Hz, —CH_2—, 4H), 1.53 (t, $J = 6.8$ Hz, —CH_3, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 194.7, 175.8, 157.8, 136.7, 133.5, 132.6, 130.7, 129.9, 128.5, 124.8, 124.4, 57.1, 18.5; IR (KBr/cm^{-1}): 3454, 3071, 2937, 1764, 1748, 1662, 1397, 1239, 750; ESI-MS *m/z*: 509 ((M + Na)$^+$, 100); $C_{28}H_{22}O_8$: calcd. C 69.13, H 4.56; (***S***)-**1**, found C 69.07, H 4.61; (***R***)-**1**, found C 69.10, H 4.59.

4.4 Synthesis of compound (S)-3

Under nitrogen and ice bath, the solution of Me_2SO_4 (2.5 mmol) in anhydrous $CHCl_3$ (10 ml) was added dropwise to the stirred solution of compound (***S***)-**1**

(0.43 g, 1.0 mmol) in anhydrous $CHCl_3$ (20 ml), and the mixture was stirred at room temperature overnight. Water (30 ml) was then added. The organic layer was separated and dried over Na_2SO_4. After the removal of the solvent, the residue was purified by column chromatography on silica gel eluted with hexane–ethyl acetate (30:1), to give (***S***)-**3**, as a yellow solid. Seventy-nine percentage yield (0.36 g); $[\alpha]_D^{20} = -92.6$ ($c = 0.20$, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ (ppm) 8.38 (s, 2H, Ar-H), 7.76–7.72 (m, 2H, Ar-H), 7.27–7.23 (m, 4H, Ar-H), 7.15–7.11 (m, 2H, Ar-H), 4.99 (q, $J = 7.2$ Hz, —CH_2—, 4H), 2.58 (s, 6H), 1.54 (t, $J = 6.8$ Hz, —CH_3, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ (ppm) 184.1, 153.2, 134.4, 131.9, 131.5, 130.0, 129.1, 126.7, 124.1, 123.8, 60.4, 56.9, 18.4; IR (KBr/cm^{-1}): 3444, 3063, 2931, 1757, 1659, 1392, 1241, 753; ESI-MS *m*/*z*: 481 ($(M + Na)^+$, 100). $C_{28}H_{26}O_6$: calcd. C 73.35, H 5.72; found C 69.27, H 5.69.

4.5 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 *N*-Boc-protected alanine or phenylalanine in methanol, and stock solutions of the salts were prepared in $CHCl_3$. The resulting syrup was dried under high vacuum for 24 h, analysed by NMR spectroscopy and stored in a desiccator. The compounds (***S***)-**1**, (***S***)-**2**, (***S***)-**3**, (***R***)-**1** and (***R***)-**2** were prepared as stock solutions in $CHCl_3$. The test solutions were prepared by adding different volumes of anionic 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 analysed immediately.

4.6 Experimental procedure for the Job plots

Stock solutions of the host (***S***)-**1** and the *S*-Ala, *R*-Ala tetrabutylammonium salts in $CHCl_3$ system (the total concentration of the host and the guest is 1.0×10^{-6} M) were freshly prepared. The compound (***S***)-**1** and Phe 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 were measured immediately.

Acknowledgements

We thank the National Natural Science Foundation of China (Grant No. 20872027/B0206) and the Education Department of Henan Province of China (2010B150004) for financial support.

References

(1) (a) Ragusa, A.; Rossi, S.; Hayes, J.M.; Stein, M.; Kilburn, J.D. *Chem. Eur. J.* **2005**, *11*, 5674–5688. (b) Rossi, S.; Kyne, G.M.D.; Turner, L.; Wells, N.J.; Kilburn, J.D. *Angew. Chem., Int. Ed.* **2002**, *41*, 4233–4236. (c) Wong, W.L.; Huang, K.H.; Teng, P.F.; Lee, C.S.; Kwong, H.L. *Chem. Commun.* **2004**, *7*, 384–385. (d) Li, Z.B.; Pu, L. *J. Mater. Chem.* **2005**, *15*, 2860–2864.

(2) Hembury, G.A.; Borovkov, V.V.; Inoue, Y. *Chem. Rev.* **2008**, *108*, 1–73.

(3) (a) Demirtas, H.N.; Bozkurt, S.; Durmaz, M.; Yilmaz, M.; Sirit, A. *Tetrahedron* **2009**, *65*, 3014–3018. (b) Xu, K.X.; Qiu, Z.; Zhao, J.J.; Zhao, J.; Wang, C.J. *Tetrahedron: Asymmetry* **2009**, *20*, 1690–1696.

(4) (a) Pu, L. *Chem. Rev.* **1998**, *98*, 2405–2494. (b) Kocovsky, P.; Vyskocil, S.; Smrcina, M. *Chem. Rev.* **2003**, *103*, 3213–3245. (c) Chen,Y.; Yekta, S.; Yudin, A.K. *Chem. Rev.* **2003**, *103*, 3155–3211. (d) Brunel, J.M. *Chem. Rev.* **2005**, *105*, 857–897.

(5) (a) Irie, M.; Yorozu, T.; Hayashi, K. *J. Am. Chem. Soc.* **1978**, *100*, 2236–2237. (b) Yorozu, T.; Hayashi, K.; Irie, M. *J. Am. Chem. Soc.* **1981**, *103*, 5480–5484. (c) Avnir, D.; Wellner, E.; Ottolenghi, M. *J. Am. Chem. Soc.* **1989**, *111*, 2001–2003. (d) Iwanek, W.; Mattay, J. *J. Photochem. Photobiol. A: Chem.* **1992**, *67*, 209–226. (e) James, T.D.; Sandanayake, K.R.A.S.; Iguchi, R.; Shinkai, S. *J. Am. Chem. Soc.* **1995**, *117*, 8982–8987. (f) Parker, K.S.; Townshend, A.; Bale, S.J. *Anal. Proc.* **1995**, *32*, 329–332. (g) Kubo, Y. *Synlett* **1999**, *2*, 161–174. (h) Beer, G.; Rurack, K.; Daub, J. *J. Chem. Soc., Chem. Commun.* **2001**, *4*, 1138–1139.

(6) (a) Qin, H.J.; He, Y.B.; Hu, C.G.; Chen, Z.H.; Hu, L. *Tetrahedron: Asymmetry* **2007**, *18*, 1769–1774. (b) Wang, Q.; Chen, X.; Tao, L.; Wang, L.; Xiao, D.; Yu, X.Q.; Pu, L. *J. Org. Chem.* **2007**, *72*, 97–101. (c) Liu, H.L.; Hou, X.L.; Pu, L. *Angew. Chem., Int. Ed.* **2009**, *48*, 382–385. (d) Lu, Q.S.; Dong, L.; Zhang, J.; Li, J.; Jiang, L.; Huang, Y.; Qin, S.; Hu, C.W.; Yu, X.Q. *Org. Lett.* **2009**, *11*, 669–672.

(7) (a) Lin, J.; Rajaram, A.R.; Pu, L. *Tetrahedron* **2004**, *60*, 11277–11281. (b) Ishii, T.; Crego-Calama, M.; Timmerman, P.; Reinhoudt, D.N.; Shinkai, S. *Angew. Chem., Int. Ed.* **2002**, *41*, 1924–1929.

(8) (a) Zhang, H.C.; Huang, W.S.; Pu, L. *J. Org. Chem.* **2001**, *66*, 481–487. (b) Stock, H.T.; Kellogg, R.M. *J. Org. Chem.* **1996**, *61*, 3093–3105.

(9) (a) Kubo, Y.; Ishihara, S.; Tsukahara, M.; Tokita, S. *J. Chem. Soc. Perkin Trans.* **2002**, *12*, 1455–1460. (b) Beer, P.D.; Timoshenko, V.; Maestri, M.; Passaniti, P.; Balzeni, V. *Chem. Commun.* **1999**, 1755–1756. (c) Wu, F.Y.; Li, Z.; Wen, Z.C.; Zhou, N.; Zhao, Y.F.; Jiang, Y.B. *Org. Lett.* **2002**, *4*, 3203–3205.

(10) (a) Valeur, B.; Pouget, J.; Bourson, J. *J. Phys. Chem.* **1992**, *96*, 6545–6549. (b) Bernard, V. *Molecular Fluorescence: Principles and Applications*; Wiley-VCH: Weinheim, 2002. (c) Birks. J.B. *Photophysics of Aromatic Molecules*, Wiley: New York, 1970, p 313.

(11) (a) Connors, K.A. *Binding Constants*; Wiley: New York, 1987. (b) Schneider, H.J.; Yatsimirsky, A.K. *Principles and Methods in Supramolecular Chemistry*; John Wiley & Sons: New York, 2000. (c) Xu, K.X.; He, Y.B.; Qin, H.J.; Qing, Q.Y.; Liu, S.Y. *Tetrahedron: Asymmetry* **2005**, *16*, 3042–3047. (d) Xu, K.X.; Qing, G.Y.; He, Y.B.; Qin, H.J.; Hu, L. *Supramol. Chem.* **2007**, *19*, 403–409. (e) Xu, K.X.;

Chen, P.F.; Wang, Y.X.; Zhao, J.; Wang, C.J. *Supramol. Chem.* **2009**, *21*, 618–623.
(12) (a) Qing, G.Y.; He, Y.B.; Chen, Z.H.; Wu, X.J.; Meng, L.Z. *Tetrahedron: Asymmetry* **2006**, *17*, 3144–3151. (b) Lu, Q.S.; Dong, L.; Zhang, J.; Li, J.; Jiang, L.; Huang, Y.; Qin, S.; Hu, C.W.; Yu, X.Q. *Org. Lett.* **2009**, *11*, 669–672.
(13) (a) Gunnlaugsson, T.; Davis, A.P.; Glynn, M. *Chem. Commun.* **2001**, *4*, 2556–2557. (b) Gunnlaugsson, T.; Davis, A.P.; O'Brien, J.E.; Glynn, M. *Org. Lett.* **2002**, *4*, 2449–2452.
(14) Pirkle, W.H.; Pochapsky, T.C. *Chem. Rev.* **1989**, *89*, 347–362.
(15) (a) Zhang, X.; Guo, L.; Wu, F.Y.; Jiang, Y.B. *Org. Lett.* **2003**, *5*, 2667–2670. (b) Cho, E.J. Moon, J.W.; Ko, S.W.; Lee, J.Y.; Kim, S.K.; Joon, Y.; Nam, K.C. *J. Am. Chem. Soc.* **2003**, *125*, 12376–12377.
(16) (a) Krapcho, A.P.; Kuell, C.S. *Synth. Commun.* **1990**, *20*, 2559–2564. (b) Du, C.P.; You, J.S.; Yu, X.Q.; Liu, C.L.; Lan, J.B.; Xie, R.G. *Tetrahedron: Asymmetry* **2003**, *14*, 3651–3656.