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Synthesis and enantioselective recognition of an (*S*)-BINOL-based colorimetric chemosensor for mandelate anions

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ABSTRACT

New chiral receptors **1** and **2** based on (*S*)-BINOL and thiourea units were synthesized. The chiral recognition of receptors for chiral anions were studied by fluorescence, UV–vis, and ^{1}H NMR spectra. The results of the non-linear curve fitting indicated that the receptors and guest anions formed a 1:1 stoichiometric complex. The obvious color change of receptor **2** can be observed by the naked eye when the enantiomers of mandelate anions were added, which demonstrates that receptor **2** may be used as a colorimetric sensor for mandelate anions.

1. Introduction

The development of chiral artificial receptors, which have the properties of chiral recognition and chiral catalysis, has attracted considerable attention,[1] because recognition and catalysis are fundamental characteristics of biochemical systems, and could contribute to the development of pharmaceuticals, enantioselective sensors, catalysts, enzyme models, and other molecular devices.[2] Many artificial receptors of different kinds have been synthesized for selective anion recognition, which include chiral macrocyclic and acyclic polyamines, chiral calixarenes, and chiral cyclodextrin derivatives.[3] For the molecular design of chemosensors, how to achieve the specific recognition of a certain molecule and how to transfer the recognition event into a signal are crucial points. UV–vis based chemosensors are very useful for detecting and discriminating between enantiomers, and have attracted the interest of chemists.[4]

Mandelate is incorporated in some selective media used for the isolation of bacteria.[5] L-Mandelic acid can act as a metabolite of phenylalanine in mammalian cells, which plays an important role in biological systems, as well as being a component of various pharmaceutical formulations.[6] In Nature, under most physiological conditions, the predominant form of mandelic acid is the mandelate ion.[7] Therefore, the synthesis of enantioselective receptors for mandelate anion has attracted considerable attention.[8] Many receptors for mandelate anions have been designed and synthesized.[9] Their enantioselective recognition abilities have been tested by ^{1}H NMR and fluorescence spectra, and the different signals within the ^{1}H NMR spectrum and changes of fluorescence spectra toward D/L-mandelate indicate that these receptors have selective recognition toward the guest. However a colorimetric chemosensor for mandelate is rare. Herein, we report the synthesis of new chiral receptors **1** and **2** containing (*S*)-BINOL and thiourea units. Their enantioselective recognition ability for chiral carboxylate anions has been investigated by fluorescence, UV–vis, and ^{1}H NMR spectra. The results reveal that receptor **2** has a good enantioselective recognition ability ($K_{ass(L)}/K_{ass(D)}$ = 13.6) for the enantiomers of mandelate anion.

2. Results and discussion

2.1. Synthesis

Chiral receptors **1** and **2** were efficiently synthesized by the reaction of intermediates **3a** and **3b** with *p*-nitrophenyl isothiocyanate, respectively (Scheme 1). These compounds were characterized by IR, MS, ^{1}H NMR, ^{13}C NMR, and elemental analysis.

2.2. Fluorescence and absorption spectra

The fluorescence and absorption spectra were recorded from a solution of receptors **1** and **2** (5.0×10^{-5} mol L^{-1}) in DMSO in the absence or presence of chiral anions (such as D- and L-phenylglycine anion, D- and L-mandelate, D- and L-malate); in each case the anions were used as their tetrabutylammonium salts.

Figure 1 shows the fluorescence emission spectra of the interaction between receptor **1** and D- or L-mandelate anion, with the addition of D- or L-mandelate anion to the solution of receptor **1** in DMSO (5.0×10^{-5} mol L^{-1}), the fluorescence emission intensities of the receptor **1** at 439 nm (λ_{ex} = 368 nm) are decreased with a slight red shift. The quenching efficiency was about 50% with the addition of 0.8 equiv of L-mandelate, while it was 48% with 0.8 equiv of D-mandelate (Fig. 1). The similar quenching efficiencies

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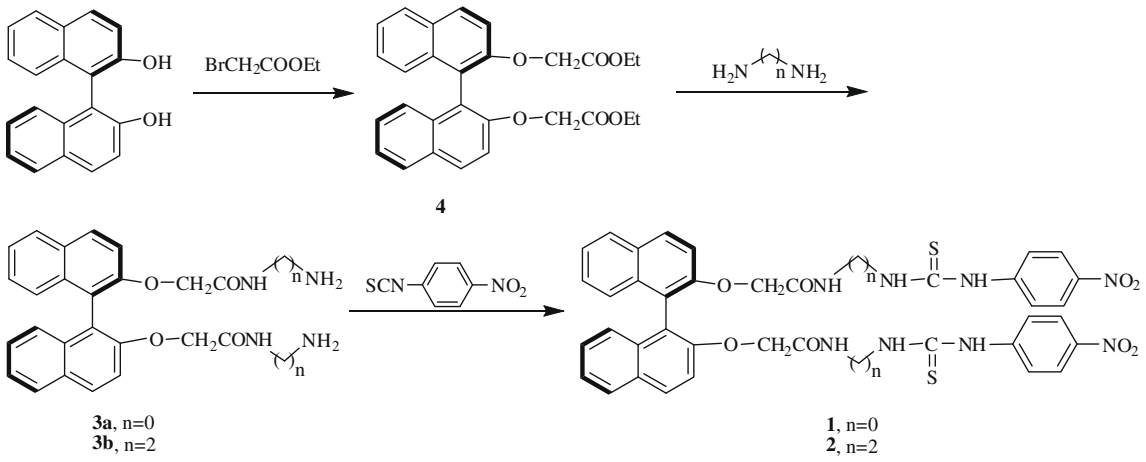

Scheme 1. The synthesis of receptors **1** and **2**.

($\Delta I_L/\Delta I_D \approx 1.04$) indicated that receptor **1** has only weak enantioselective recognition ability for the enantiomers of mandelate. Figure 2 shows the changes in the fluorescence spectra of receptor **2** (5.0×10^{-5} mol L^{-1}) with the addition of D- or L-mandelate in DMSO. The quenching efficiency at 442 nm (λ_{ex} = 372 nm) was about 33% with the addition of 9 equiv of L-mandelate, while it was only 10% for 9 equiv of D-mandelate (Fig. 2). The different quenching efficiencies ($\Delta I_L/\Delta I_D$ = 3.3) indicated that receptor **2** has a good enantioselective recognition ability for the enantiomers of mandelate.

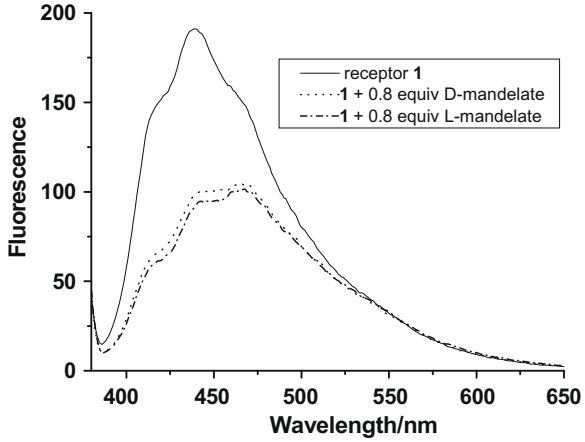

Figure 1. Fluorescence spectra of receptor **1** (DMSO, 5.0×10^{-5} mol L^{-1}) in DMSO with addition of D- and L-mandelate anion in DMSO, λ_{ex} = 368 nm.

When either D- or L-mandelate anions were added into the solution of receptor **1** or **2**, the fluorescence quenching phenomena was observed. In the presence of mandelate anion, the fluorescence quenching of receptors **1** and **2** most likely arose from the change of the free energy ($-\Delta G_{PET}$) of electron transfer between the excited fluorophore and the receptor.[10] When the mandelate anion interacted with either receptor **1** or **2**, the reductive potential of the amide and thiourea groups increased along with the ratio of the electron transfer from the HOMO orbit of receptors to the excited binaphthyl group, which in turn led to a more facile intramolecular photoinduced electron transfer (PET) process,[11] and so fluorescence quenching was observed.

The UV–vis absorption spectra of **1** upon addition of D- or L-mandelate anions are, respectively, shown in Figures 3 and 4. With the addition of either D- or L-mandelate anion to the solution of receptor **1** in DMSO (5.0×10^{-5} mol L^{-1}), the absorption at 336 nm was decreased gradually, and the peak at 278 nm was increased gradually, and a new absorption peak at 412 nm was dra-

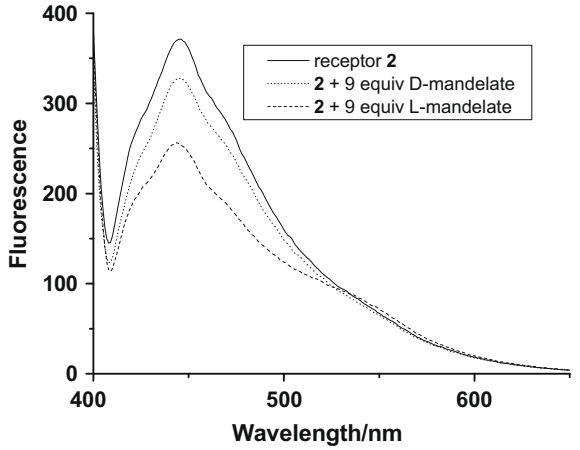

Figure 2. Fluorescence spectra of receptor **2** (DMSO, 5.0×10^{-5} mol L^{-1}) in DMSO with addition of D- and L-mandelate anion in DMSO, λ_{ex} = 372 nm.

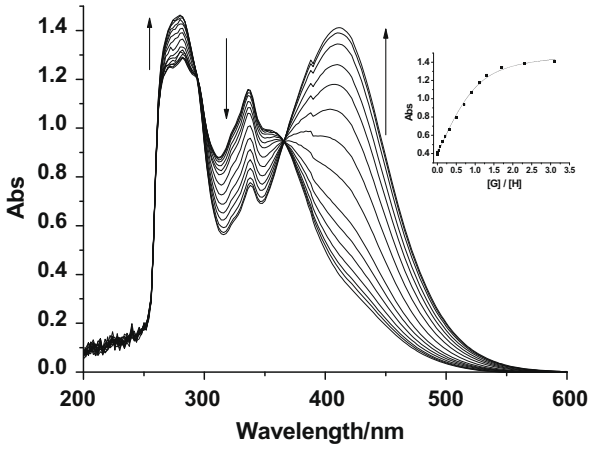

Figure 3. UV–vis absorption spectra of receptor **1** (DMSO, 5.0×10^{-5} mol L^{-1}) upon the addition of various amounts (0→3.11) of D-mandelate anion in DMSO. The nonlinear fitting curve of change in absorption at 412 nm with respect to the amount of D-mandelate is shown in the inset.

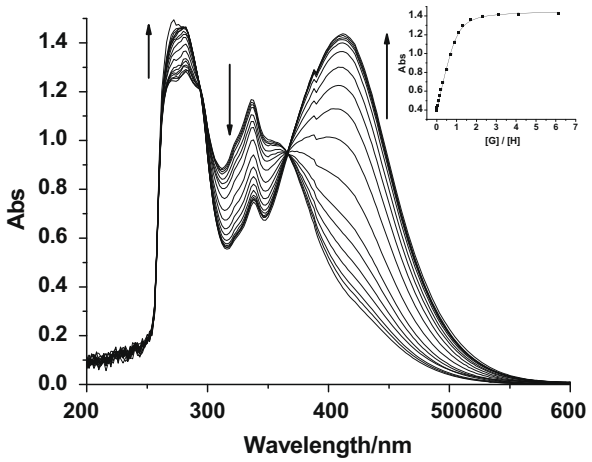

Figure 4. UV–vis absorption spectra of receptor **1** (DMSO, 5.0×10^{-5} mol L^{-1}) upon the addition of various amounts (0→6.11) of L-mandelate anion in DMSO. The non-linear fitting curve of change in absorption at 412 nm with respect to the amount of L-mandelate is shown in the inset.

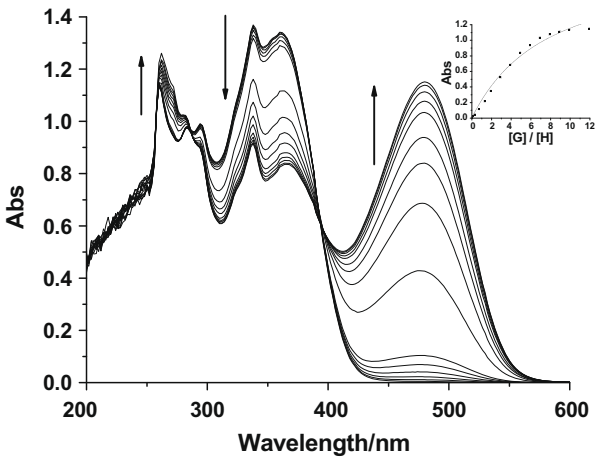

Figure 6. UV–vis absorption spectra of receptor **2** (DMSO, 5.0×10^{-5} mol L^{-1}) upon the addition of various amounts of L-mandelate anion in DMSO. The equivalents of anion are 0→11.9. The non-linear fitting curve of change in absorption at 480 nm with respect to the amount of L-mandelate is shown in the inset.

matically enhanced. Two clear isobestic points at 296 nm and 366 nm were observed, which indicated that there is a balance between the complex and host, guest in solution.[12] At the same time, the color of the solution of receptor **1** in DMSO was changed from pale yellow to dark yellow, which could be observed visually.

Figures 5 and 6 show the absorption spectra of the interaction between receptor **2** and D- or L-mandelate anion. With the addition of D- or L-mandelate anion to the solution of receptor **1** in DMSO (5.0×10^{-5} mol L^{-1}), the absorption at 336 nm was decreased gradually, and the peak at 266 nm was increased gradually; a new absorption peak at 480 nm was dramatically enhanced. Two obvious isobestic points were observed at 284 nm and 394 nm. In particular, the remarkable and obvious color changes were observed when either D- or L-mandelate anion was added into receptor **2** in DMSO. Upon a gradual increase of the concentration of D-mandelate, when 30 equiv of D-mandelate anion was added into the receptor **2** (5.0×10^{-5} mol L^{-1}) in DMSO, the color of the solution of receptor **2** changed from light yellow to light orange (Fig. 7), while the color of the solution of receptor **2** with the same amount of L-mandelate changed from light yellow to red (Fig. 7), which

Figure 7. Effect of the anion (as Bu_4N^+ salts) on color changes of receptor **2** in DMSO. From left to right **2** (5.0×10^{-5} mol L^{-1}), **2** (5.0×10^{-5} mol L^{-1}) + 30 equiv D-mandelate, **2** (5.0×10^{-5} mol L^{-1}) + 30 equiv L-mandelate.

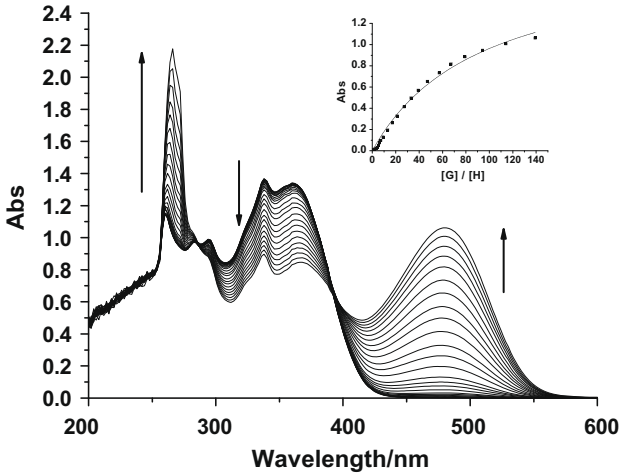

Figure 5. UV–vis absorption spectra of receptor **2** (DMSO, 5.0×10^{-5} mol L^{-1}) upon the addition of various amounts of D-mandelate anion in DMSO. The equivalents of anion are 0→139.1. The non-linear fitting curve of change in absorption at 480 nm with respect to the amount of D-mandelate is shown in the inset.

could be visually observed. This color change could be attributable to the appearance of a long-wavelength peak at 480 nm. The new absorption of the receptors **1** and **2** in the visible region can be ascribed to charge-transfer interactions between the electron-rich donor nitrogen atom of the thiourea units and the electron-deficient *p*-nitrophenyl moieties. When receptor **1** or **2** interacted with mandelate anion, hydrogen bonds were constructed to form stable complexes, and the electron density in the supramolecular system was considerably increased; this enhanced the charge-transfer interactions between the electron-rich and -deficient moieties, which resulted in a visible color change.[13] When a protic solvent, such as methanol or water, was added to the solution of **1** or **2** and a mandelate mixture in DMSO, the color of the mixture changed to light yellow. These phenomena illustrate that hydrogen bonding interactions occur between receptor **1** or **2** with mandelate anion.[3e,14]

When the enantiomers of malate and phenylglycine anions were, respectively, added into a solution of receptor **1** or **2** in DMSO, the changes of fluorescence emission spectra and UV–vis absorption spectra were similar, but there were no enantioselectivity for these chiral guests. The association constants (K_{ass}) and correlation coeffients (R) of the interaction between host and guest are listed in Table 1.

The continuous variation methods were used to determine the stoichiometric ratios of receptors **1** and **2** with mandelate anions.

Table 1
Association constants (K_{ass})[a,b], correlation coefficients (R), enantioselectivities ($K_{ass(L)}/K_{ass(D)}$), Gibbs free energy changes ($-\Delta G_0$) of receptor **1** or **2** with L/D guests in DMSO at 25 °C

Guest[c]	Receptor **1**				Receptor **2**			
	K_{ass}[a,b] (M−1)	R	$K_{ass(L)}/K_{ass(D)}$	$-\Delta G_0$ (KJ mol^{-1})	K_{ass}[a,b] (M^{-1})	R	$K_{ass(L)}/K_{ass(D)}$	$-\Delta G_0$ (KJ mol^{-1})
D-Mandelate	$(9.98 \pm 0.60) \times 10^4$	0.9988		28.49	$(2.15 \pm 0.2) \times 10^2$	0.9968		13.30
L-Mandelate	$(2.09 \pm 0.09) \times 10^5$	0.9989	2.1	30.33	$(2.92 \pm 0.23) \times 10^3$	0.9942	13.6	19.75
D-Malate	$(3.25 \pm 0.45) \times 10^5$	0.9960		30.03	$(8.35 \pm 0.25) \times 10^2$	0.9937		16.65
L-Malate	$(4.05 \pm 0.19) \times 10^5$	0.9981	1.25	30.52	$(9.41 \pm 0.21) \times 10^2$	0.9968	1.12	16.95
D-Phenylglycine	$(1.85 \pm 0.42) \times 10^5$	0.9921		30.03	$(1.98 \pm 0.32) \times 10^3$	0.9963		18.78
L-Phenylglycine	$(1.69 \pm 0.35) \times 10^5$	0.9937	0.91	29.78	$(2.20 \pm 0.38) \times 10^3$	0.9945	1.11	19.05

[a] The data were calculated from fluorescence titration in DMSO.
[b] All error values were obtained by the results of non-linear curve fitting.
[c] The anions used were their tetrabutylammonium salts.

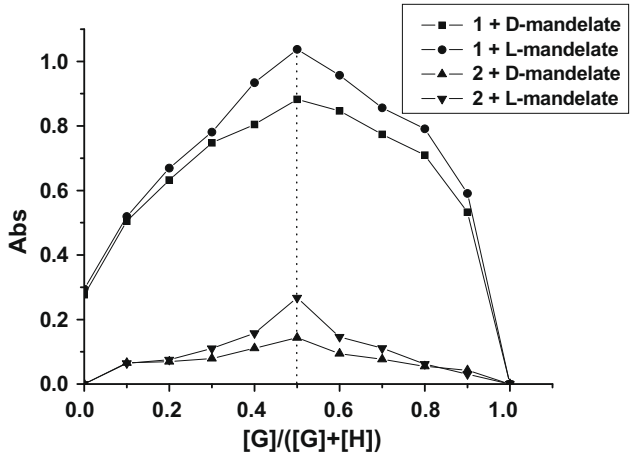

Figure 8. The Job plots of receptors **1** and **2** with D-/L-Mandelate anions (at 412 nm and 480 nm, respectively). The total concentration of host and guest is 1.0×10^{-4} mol L^{-1}.

The total concentration of host and guest was constant (1.0×10^{-4} mol L^{-1}) in DMSO, with a continuously variable molar fraction of guest ($[G]/([H]+[G])$). Figure 8 shows the Job plots of receptors **1** and **2** with a D/L-mandelate anion (at 412 nm or 480 nm). When the molar fraction of the guest was 0.50, the UV–vis absorption of the host reached a maximum, which demonstrated that the host (receptor **1** or **2**) and the guest (D/L-mandelate anion) formed a 1:1 complex. Using the same method, receptors **1** and **2**, and other anions (phenylglycine anion and malate) also formed 1:1 complexes.[3e,15]

2.3. Determination of the association constants (K_{ass}) of the complexes

In a supramolecular system, for a complex with a 1:1 stoichiometry, the association constants (K_{ass}) can be calculated according to the following relation:[16]

$$A = A_0 + \frac{A_{lim} - A_0}{2C_0}\left\{C_H + C_G + 1/K_{ass} - \left[(C_H + C_G + 1/K_{ass})^2 - 4C_H C_G\right]^{1/2}\right\}$$

where A represents the absorption intensity, C_G and C_H represent the corresponding concentration of anion guest and host. The association constants and correlation coefficients (R) were obtained by a non-linear least square analysis of A versus C_H and C_G, the results are listed in Table 1. The correlation coefficients of the non-linear curve fitting were all larger (>0.99), which indicated that the 1:1 complex between receptors **1** and **2** and the anions had been formed.[17] From Table 1, we can see that (1) receptor **2** exhibited highly enantioselective recognition between the enantiomers of mandelate anion, which gave the enantioselectivity $K_{ass(L)}/K_{ass(D)} = 13.6$, (2) the association constants (K_{ass}) of **1** with anions were much higher than those of **2** with anions, which is probably due to the fact that receptor **1** has a larger rigid structure than receptor **2**.

2.4. ^{1}H NMR study

^{1}H NMR experiments were undertaken to assess the chiral recognition properties between receptor **2** and the mandelate anion because it can provide structural and dynamic information directly. Chiral recognition studies were carried out with a 300 MHz NMR spectrometer in DMSO at room temperature using receptor **2** as chiral-solvating agents.

The mandelate anion was chosen as a probe. The ^{1}H NMR spectra of receptor **2** (4.0×10^{-2} mol L^{-1}) and its complex with equimolar amounts of D- or L-mandelate anions (4.0×10^{-2} mol L^{-1}) in DMSO-d_6 are shown in Figure 9. Figure 9a shows the ^{1}H NMR spectra of racemic mandelate anions, with only one singlet ($\delta = 4.35$ ppm) being exhibited for the CH proton resonance. Upon the addition of racemic mandelate anion to a solution of **2**, the proton signal of CH was shifted downfield and overlapped with the proton signals of OCH_2 in receptor **2**; and the proton resonances ($\delta = 10.10$, 8.11 ppm, Fig. 9b) of two characteristic thiourea NH of receptor **2** were also shifted downfield ($\delta = 10.89$, 9.40 ppm) as seen in Figure 9c. Moreover, when the D-mandelate anion was added to the solution of **2**, the proton chemical shifts of two characteristic thiourea NH of receptor **2** shifted downfield ($\delta = 10.23$, 9.20 ppm, Fig. 9d). When the L-mandelate anion was added to the solution of **2**, the proton chemical shifts of two characteristic thiourea NH of receptor **2** shifted downfield ($\delta = 10.97$, 9.39 ppm, Fig 9e). The different downfield shifts of the two characteristic thiourea NH show that receptor **2** has a different recognition ability to the enantiomers of mandelate. However, when racemic D-/L-mandelate anions was added into receptor **2** in DMSO, the changes of the proton chemical shift of amide NH ($\delta = 7.45$ ppm) were slight (Fig. 9c–e). The ^{1}H NMR spectra of **1** have the similar changes when racemic, D- or L-mandelate anion were added to the solution of **1**.

The results of the ^{1}H NMR investigation indicate that multiple hydrogen bonding plays a major role in the formation of complexes between receptors and anions, while receptor **2** has a good enantioselective recognition ability for the enantiomers of mandelate.

In addition, the good enantioselectivity of receptor **2** for L-mandalate over D-mandelate can be understood via molecular modeling studies; the energy-minimized structures of the complex formed from receptor **2** and L-/D-mandelate anions are, respectively, shown in Figure 10. The method of calculation is a torsion angle conformation search with a energy function of molecular mechanic force field and solvation. The results indicate that the

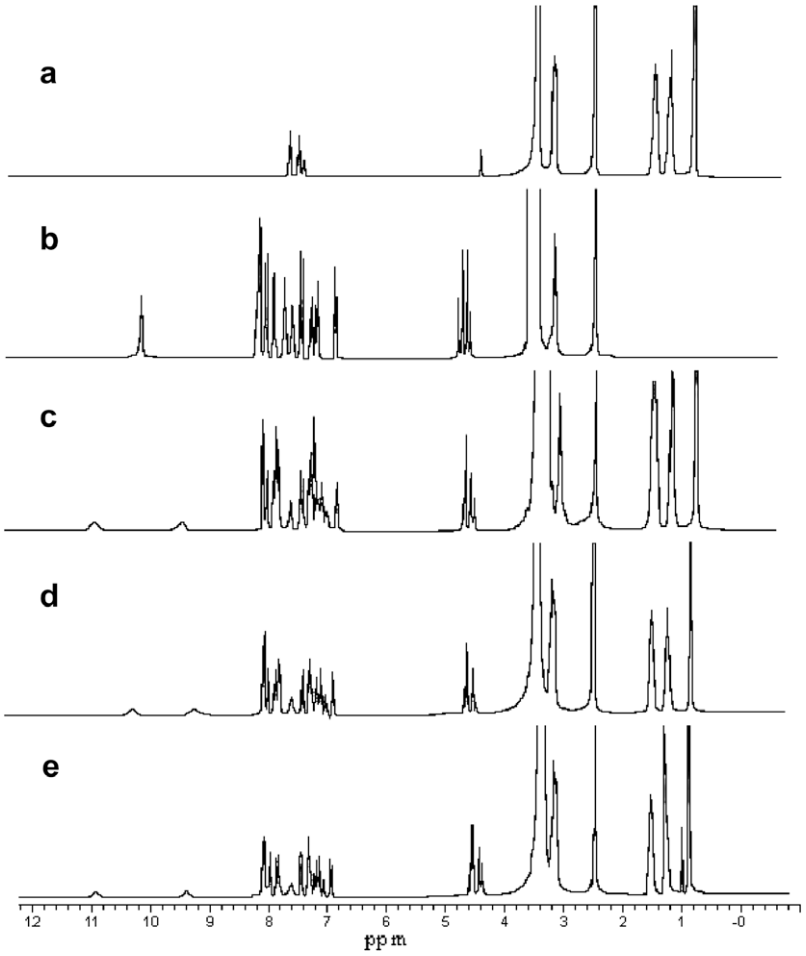

Figure 9. ^{1}H NMR spectra of **2** and its guest complex at 25 °C ([**2**] = [guest] = 4×10^{-2} mol L^{-1}) in DMSO-d_6 at 300 MHz; (a) racemic mandelate; (b) receptor **2**; (c) receptor **2** + racemic mandelate; (d) receptor **2** + D-mandelate; (e) receptor **2** + L-mandelate.

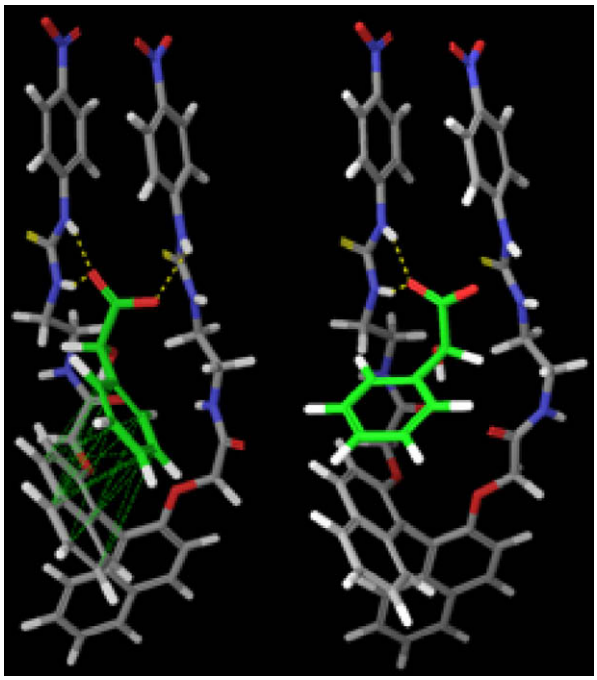

Figure 10. From left to right: calculated energy-minimized structures of the complex formed from receptor **2** and L-/D-mandelate anions.

oxygen atoms of the carboxyl anion in L-mandelate can form three hydrogen bonds with the thiourea NH of receptor **2**; that the π–π stacking interaction between the binaphthyl moiety and benzene cycle of L-mandelate can be found (Fig. 10, left side); that the oxygen atoms of the carboxyl anion in the D-mandelate only form two hydrogen bonds with thiourea NH of receptor **2**, and that there was no π–π stacking interaction due to the spacial structure of the D-mandelate anion (Fig. 10, right side). The relative energies of the complex formed from receptor **2** and D-/L-mandelate anions are 0 kJ/mol, −1.4 kJ/mol, respectively. Other study results support these results.

3. Conclusion

Chiral receptors **1** and **2** containing (*S*)-BINOL and thiourea groups were synthesized. The enantioselective recognition of these receptors was studied by fluorescence, UV–vis, and ^{1}H NMR spectra, and the result indicated that receptors **1** and **2** can form a 1:1 complex between host and guest. Though the association constants of receptor **1** for the anions are much larger than those of receptor **2**, the enantioselective recognition ability of receptor **2** toward the enantiomers of mandelate was much better in comparison to receptor **1**. The steric effects, the relatively rigid structure, and better preorganization properties of receptor **2** may be responsible for the enantioselective recognition of mandelate anions. The different and obvious color

changes upon interaction of receptor **2** with enantiomers of mandelate anions illustrate that receptor **2** may be used as a colorimetric sensor for the enantiomers of mandelate.

4. Experimental

4.1. Materials and methods

Ethanol and $CHCl_3$ were dried and distilled before use according to standard procedure. All other commercially available reagents were used without further purification. The tetrabutylammonium salts were used as anionic substrates. Melting points were measured on a Reichert 7905 melting-point apparatus (uncorrected). Optical rotations were taken on a Perkin–Elmer 341 polarimeter. IR spectra were obtained on a Nicolet 670 FT-IR spectrophotometer. The mass spectra were recorded on a Finnigan LCQ advantage mass spectrometer. ^{1}H NMR and ^{13}C NMR spectra were performed on a Varian Mercury VX-300 MHz spectrometer in DMSO-d_6. Fluorescence spectra were obtained on a Shimadzu RF-5301 spectrometer. UV–vis spectra were taken on a TU-1901 spectrometer. Elemental analysis was determined with a Carlo-Erba 1106 instrument. The method on calculation of energy-minimized structures of the complex is torsion angle conformation search with a energy function of molecular mechanic force field and solvation.

4.2. Syntheses

4.2.1. Synthesis of compound 4

A mixture of (*S*)-BINOL (1.0 g, 3.5 mmol), K_2CO_3 (7.0 g, 50 mmol), and ethyl bromoacetate (1.0 ml, 9.01 mmol) in acetone (150 ml) was refluxed overnight under N_2. The reaction mixture was evaporated to dryness under reduced pressure. Water (20 ml) was poured into the residue and extracted with $CHCl_3$. The organic layer was separated and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (eluant: $CHCl_3/CH_3CH_2OH$ 200:1 (v/v)) to give the pure product **4** as a colorless creamy solid (1.30 g) in 81% yield. ^{1}H NMR ($CDCl_3$) δ (ppm): 7.95 (d, J = 8.7 Hz, 2H, biph-H), 7.86 (d, J = 8.4 Hz, 2H, biph-H), 7.17–7.37 (m, 8H, biph-H), 4.54 (s, 4H, $COCH_2$), 4.11 (q, J = 7.2 Hz, 4H, OCH_2), 1.16 (t, J = 7.5 Hz, 6H, CH_3).

IR (KBr/cm^{-1}) v:1756, 1733, 1195, 1289. Elemental Anal. Calcd for $C_{28}H_{26}O_6$: C, 73.34; H, 5.73. Found: C, 73.45; H, 5.82.

4.2.2. Synthesis of compound 3a

A mixture of compound **4** (0.25 g, 0.55 mmol), excess hydrazine hydrate (1.5 ml), and ethanol (20 ml) was stirred for 24 h at room temperature. The reaction mixture was evaporated under reduced pressure and extracted with $CHCl_3$. The organic layer was separated and dried over anhydrous Na_2SO_4. After filtration and evaporation, the compound **3a** was obtained as a white solid (0.21 g) in 91% yield. Mp: 94–96 °C.^{1}H NMR ($CDCl_3$) δ (ppm): 8.06 (d, J = 8.7 Hz, 2H, biph-H), 7.93 (d, J = 8.1 Hz, 2H, biph-H), 7.32–7.45 (m, 6H, biph-H), 7.16 (d, J = 8.1 Hz, 2H, biph-H), 7.05 (s, 2H, NH), 4.65 (d, J_{ab} = 15.3 Hz, 2H, $COCH_2$), 4.52 (d, J_{ab} = 15.3 Hz, 2H, $COCH_2$), 3.52 (s, 2H, NH). IR (KBr/cm^{-1}) v: 3421, 3319, 1676, 1508, 1270, 1218, 751. Elemental Anal. Calcd for $C_{24}H_{22}N_4O_4$: C, 66.95; H, 5.16; N, 13.02. Found: C, 66.79; H, 5.13; N 13.12.

4.2.3. Synthesis of compound 3b

A mixture of compound **4** (0.25 g, 0.55 m mol), excess ethylenediamine (1.0 ml), and anhydrous ethanol (20 ml) was stirred for 24 h at room temperature. After evaporation of the solvent and the excess ethylenediamine under reduced pressure, **3b** was obtained as a white powder (0.24 g) in 91% yield. Mp: 116–118 °C.^{1}H NMR($CDCl_3$) δ (ppm): 8.07 (d, J = 8.7 Hz, 2H, Ar–H), 7.97 (d, J = 8.1 Hz, 2H, Ar–H, 7.90 (s, 2H, NH), 7.32–7.41 (m, 6H, Ar–H, 7.24 (d, J = 8.7 Hz, 2H, Ar–H, 4.62 (d, J_{ab} = 14.7 Hz, 2H, $COCH_2$), 4.50 (d, J_{ab} = 14.7 Hz, 2H, $COCH_2$), 3.38 (s, 2H, NH_2), 2.96 (t, J = 7.2 Hz, 4H, CH_2NH), 2.37(t, J = 7.2 Hz, 4H, CH_2). IR (KBr/cm^{-1}) v: 3460, 3309, 2860, 1730, 1486, 1250, 1132, 765, 726. Elemental Anal. Calcd for $C_{28}H_{30}N_4O_4$: C, 69.11; H, 6.23; N, 11.51. Found: C, 68.83; H, 6.34; N, 11.36.

4.2.4. Synthesis of compound 1

A solution of **3a** (0.25 g, 0.58 mmol) in dry $CHCl_3$ (10 ml) was slowly added dropwise to a solution of *p*-nitrophenyl isothiocyanate (0.21 g, 1.2 mmol) in dry $CHCl_3$ (10 ml) at room temperature. After stirring for 8 h, the precipitate was filtered off, washed with dry $CHCl_3$, and dried in vacuum to give the pure compound **1** (0.38 g) as a light yellow powder in 83% yield. Mp: 174–176 °C. $[\alpha]_D^{20} = +19.75$ (c 0.05. DMSO). ^{1}H NMR (DMSO-d_6) δ (ppm): 10.06 (br, 2H, NHAr), 9.98 (br, 2H, NHCS), 8.15 (d, J = 8.7 Hz, 4H, biph-H), 8.05 (d, J = 8.7 Hz,2H, Ar–H), 7.94 (d, J = 8.7 Hz, 2H, biph-H), 7.80 (d, J = 8.1 Hz, 4H, Ar–H, 7.59 (br, 2H, CONH), 7.34 (t, J = 6.6 Hz, 2H, biph-H), 7.24 (d, J = 6.6 Hz, 2H, biph-H), 6.99 (d, J = 8.7 Hz, 2H, Ar–H, 4.66 (br, 4H, $COCH_2$). ^{13}C NMR (DMSO-d_6) δ (ppm): 181.3, 168.9, 154.4, 146.2, 144.1, 133.9, 130.2, 129.9, 128.7, 127.2, 125.6, 124.5, 119.6, 116.5, 79.8, 67.9, 51.8; IR(KBr/cm^{-1}): 3300, 3058, 2490, 1659, 1534, 1455, 1312, 1136, 1061, 874, 790, 700, 627; ESI-MS m/z (%): 789 ($(M-1)^+$, 100); Elemental Anal. Calcd for $C_{38}H_{30}N_8O_8S_2$: C, 57.70; H, 3.83; N, 14.17. Found: C, 57.52; H, 3.96; N, 13.95.

4.2.5. Synthesis of compound 2

The solution of **3b** (0.24 g, 0.49 mmol) in dry $CHCl_3$ (10 ml) was added dropwise slowly to a solution of *p*-nitrophenyl isothiocyanate (0.18 g, 1.0 mmol) in dry $CHCl_3$ (10 ml) at room temperature. After stirring for 8 h, the solvent was evaporated under reduced pressure. The pure product **2** was obtained by column chromatography on silica gel (eluant: $CHCl_3/CH_3OH$ = 50:1 (v/v)) as a yellow spumous powder (0.32 g) in 76% yield. Mp: 158–160 °C. $[\alpha]_D^{20} = +39.5$ (c 0.05. DMSO). ^{1}H NMR (DMSO-d_6) δ (ppm): 10.10 (s, 2H, NHAr), 8.11 (d, J = 8.7 Hz, 6H, NHCS and biph-H), 8.02 (d, J = 9.0 Hz, 2H, biph-H), 7.90(d, J = 7.8 Hz, 2H, Ar–H), 7.72(d, J = 9.0 Hz, 4H, Ar–H, 7.45 (s, 2H, NHCO), 7.32 (d, J = 9.0 Hz, 2H, biph-H), 7.15 (t, J = 7.2 Hz, 2H, biph-H), 7.02 (t, J = 7.2 Hz, 2H, biph-H), 6.90(d, J = 7.8 Hz, 2H, Ar–H, 4.56 (d, J_{ab} = 15.3 Hz, 2H, $COCH_2$), 4.42 (d, J_{ab} = 15.3 Hz, 2H, $COCH_2$), 3.28–3.17 (m, 4H, CH_2CH_2). ^{13}C NMR (DMSO-d_6) δ (ppm): 180.67, 168.68, 153.93, 146.99, 142.45, 133.84, 130.38, 129.79, 128.78, 127.40, 125.17, 124.61, 121.09, 119.47, 115.93, 68.57, 67.02, 42.01, 36.63. IR(KBr/cm^{-1}): 3303, 3030, 2979, 1691, 1648, 1528, 1450, 1364, 1247, 1173, 1049, 858, 741, 695; ESI-MS m/z (%): 869($(M+Na)^+$, 100), Elemental Anal. Calcd for $C_{42}H_{38}N_8O_8S_2$: C, 59.56; H, 4.52; N, 13.23. Found: C, 59.45; H, 4.75; N, 12.96.

4.3. Tetrabutylammonium salts

All tetrabutylammonium salts were prepared by adding **1** equiv (for a monocarboxylic acid) or **2** equiv (for a dicarboxylic acid) of tetrabutylammonium hydroxide in methanol to a solution of the corresponding carboxylic acid in methanol. The mixture was stirred at room temperature for 2 h and evaporated to dryness under reduced pressure. The resulting syrup was dried under high vacuum for 24 h, analyzed by NMR spectroscopy, and stored in a desiccator.

4.4. Binding studies

The studies on the binding properties of **1** and **2** were carried out in DMSO. The UV–vis titration was performed with a series

of 5×10^{-5} M solutions of receptor **1** or **2** containing different amounts of chiral anions. Association constants were calculated by means of a non-linear least-square curve fitting with Origin 7.0 (Origin-Lab Corporation). ^{1}H NMR studies were recorded as adding equivalent racemic, D- or L-mandelate anions into receptors (4×10^{-2} M).

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