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Enantioselective fluorescent recognition of mandelate by substituted BINOL in aqueous solutions

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The fluorescent photo-induced electron transfer chemosensors (*R*)-**1**, (*R*)-**2**, (*S*)-**1** and (*S*)-**2** based on the 3,3′-positions of 1,1′-bi-2-naphthol were designed for their recognition of mandelate. The binding properties for mandelate were examined by the fluorescence spectra. The high fluorescence sensitivity and enantioselectivity make compound (*R*)-**2** a practically useful sensor for the recognition of mandelate in CH_3OH/H_2O system (1:1, 0.01 M Tris–HCl buffer, pH 7.4).

Keywords: chiral receptor; fluorescence; enantioselectivity recognition

1. Introduction

Nowadays, as one of the most fundamental and significant processes in natural systems, enantioselective recognition is receiving increasing focus from researchers (*1*). However, enantioselective recognition still remains a major challenge for host–guest chemists (*2*). Using fluorescence in enantioselective recognition has the advantages of real-time response, high sensitivity and many modes of detection (*3*). A proper host requires a compatible configuration with the guest. The binaphthyl unit was especially eye-catching for its stable chiral configuration and tunable dihedral angle between the two naphthalene rings. Over the last two decades, 1,1′-bi-2-naphthol (BINOL) and its derivatives have been shown to exhibit excellent enantioselectivities and turnovers in several types of asymmetric reactions (*4*), often matching the enantioselectivities traditionally regarded as being reserved for the enzyme realm. Mandelic acid is among the most attractive targets for enantioselectivity recognition and sensing since they are the key structural moieties of many bioactive molecules. However, most known mandelic acid receptors only function in aprotic solvents, such as DMSO, $CHCl_3$, CH_3CN (*3d*, *5*), and they are inappropriate to be used in biochemical or physiological investigation. Thus, design and synthesis of water-soluble artificial receptors are a challenging and attractive task in supramolecular chemistry. In this study, we have designed and synthesised chiral BINOL-based fluorescent chemosensors for the enantioselective fluorescent recognition of mandelate in CH_3OH/H_2O system ($c = 0.05$, 1:1, 0.01 M tris(hydroxymethyl)aminomethane–HCl buffer, pH 7.4). The receptors showed good binding ability towards mandelates and showed high sensitivity and high enantioselectivity in the fluorescent recognition of the mandelates.

2. Results and discussion

2.1 Synthesis

The starting materials binaphthyl dialdehydes were prepared from BINOLs (*6*). Condensation of (*R*)- or (*S*)-binaphthyl dialdehydes with *S*-alaninol or *S*-phenylalaninol followed by reduction afforded the four disubstituted BINOL (Scheme 1), respectively. These target compounds are soluble in DMSO, CH_3OH or CH_2Cl_2. The structures of these compounds were characterised by IR, ^1H and ^{13}C NMR spectroscopy, ESI-MS and elemental analysis. Furthermore, their solubility in CH_3OH/H_2O system is good even when the water content in the mixed solvent is as high as 90%. To investigate the binding properties of neutral receptors towards mandelates in aqueous solution, the CH_3OH/H_2O system (1:1, 0.01 M Tris–HCl buffer, pH 7.4) was employed to ensure that the receptors are completely dissolved in the titration experiments.

2.2 Fluorescence spectra

The properties of enantioselective recognition of receptors were investigated for *R*- or *S*-mandelate. Because there is almost no change on the UV–vis spectra of (*R*)-**1**, (*R*)-**2**, (*S*)-**1** or (*S*)-**2** upon addition of mandelate even when guest anions are far excess ([anion]/[1 or 2] > 100), the properties of enantioselective recognition of (*R*)-**1**, (*R*)-**2**, (*S*)-**1** or (*S*)-**2** were only investigated for *R*- or *S*-mandelate by the fluorescence spectra.

In fluorimetric study, when the solution of (*R*)-**1** (2.5×10^{-5} M) in CH_3OH/H_2O system (1:1, 0.01 M Tris–HCl buffer, pH 7.4) was excited at 320 nm, (*R*)-**1** gave a characteristic emission spectrum with monomeric BINOL maximum at *ca.* 368 nm. Subsequently, the binding behaviours of (*R*)-**1** with *R*-mandelate in CH_3-

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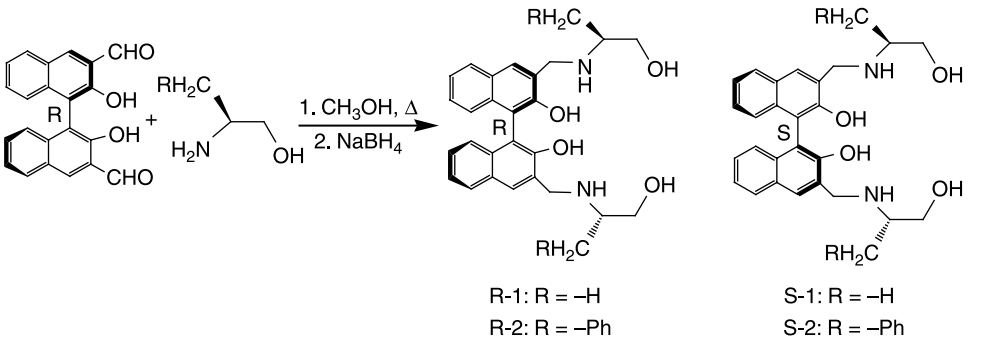

Scheme 1. Synthesis of the compounds (*R*)-**1**, (*R*)-**2**, (*S*)-**1** and (*S*)-**2**.

OH/H_2O system (1:1, 0.01 M Tris–HCl buffer, pH 7.4) were investigated by means of titration fluorimetry (*vide supra*).

Figures 1 and 2 show the fluorescence emission spectra of a mixture of (*R*)-**1** and different concentrations of *R*- or *S*-mandelate in CH_3OH/H_2O system (1:1, 0.01 M Tris–HCl buffer, pH 7.4), respectively. When gradually increasing the concentration of mandelate, the fluorescence emission intensities of (*R*)-**1** at 368 nm increased obviously. The enhancement efficiency was about 52% with the addition of 14.4 equiv. of *R*-mandelate (Figure 1), while it was 34% by 14.4 equiv. of *S*-mandelate (Figure 2). The extent of increasing, though small, is of great significance. Much stronger increases occurred when the titrations were performed in aprotic solvents. The different enhancement efficiencies ($\Delta I_R/\Delta I_S \approx 1.53$) indicated that receptor (*R*)-**1** has a good enantioselective recognition ability between *R*- and *S*-mandelates.

Since there were no changes in the UV–vis spectra of receptors when treated with *R*- or *S*-mandelate, the increase in fluorescence intensity of the excimer upon addition of the anion is similar to the anion-induced fluorescence enhancement reported previously (*7*). In the absence of anions, the photo-induced electron transfer (PET) between the binaphthyl group and weak electron-withdrawing amino substituents might result in decreased fluorescence intensity. When exogenous anions were added to the solution, the interaction of the anions with the receptor unit could erase this specific PET process and led to fluorescence enhancement (*8*). Indeed, the anion-induced fluorescence enhancement was observed (*9*).

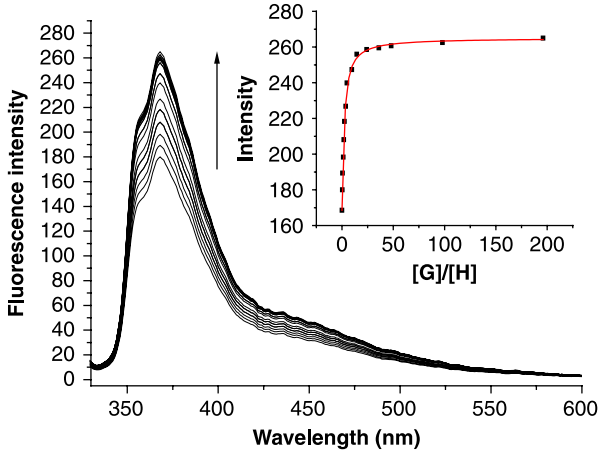

Figure 1. Fluorescence spectra of receptor (*R*)-**1** (2.5×10^{-5} M CH_3OH/H_2O, 1:1, 0.01 M Tris–HCl buffer, pH 7.4) upon the addition of various amounts of substrate *R*-mandelate in CH_3OH/H_2O system (1:1, 0.01 M Tris–HCl buffer, pH 7.4). $\lambda_{ex} = 320$ nm. Equivalent of Bu_4N^+ (*R*-mandelate): 0, 0.28, 0.56, 1.2, 1.8, 2.4, 3.6, 4.8, 9.6, 14.4, 24, 36, 48, 98 and 196. Inset: changes of fluorescence intensity of (*R*)-**1** at 368 nm upon addition of *R*-mandelate. The line is fitting curve. The correlation coefficient (*R*) of nonlinear curve fitting is 0.9981.

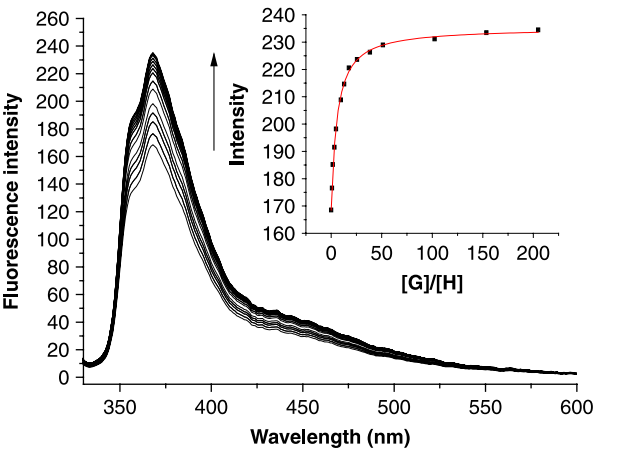

Figure 2. Fluorescence spectra of receptor (*R*)-**1** (2.5×10^{-5} M CH_3OH/H_2O, 1:1, 0.01 M Tris–HCl buffer, pH 7.4) upon the addition of various amounts of substrate *S*-mandelate in CH_3OH/H_2O system (1:1, 0.01 M Tris–HCl buffer, pH 7.4). $\lambda_{ex} = 320$ nm. Equivalent of Bu_4N^+ (*R*-mandelate): 0, 0.28, 0.56, 1.2, 1.8, 2.4, 3.6, 4.8, 9.6, 14.4, 24, 36, 48, 98 and 196. Inset: changes of fluorescence intensity of (*R*)-**1** at 368 nm upon addition of *R*-mandelate. The line is fitting curve. The correlation coefficient (*R*) of nonlinear curve fitting is 0.9989.

Table 1. Association constants (K_{ass}), correlation coefficients (R), enantioselectivities ($K_{ass\,(R)}/K_{ass\,(S)}$), Gibbs free energy changes ($-\Delta G_0$) and $\Delta\Delta G_0$ calculated from ΔG_0 for the complexation of receptors (*S*)-**1**, (*S*)-**1**, (*R*)-**2** and (*R*)-**2** with *R*-/*S*-mandelates in CH_3OH/H_2O system (1:1, 0.01 M Tris–HCl buffer, pH 7.4) at 25°C.

Host	Guest	K_{ass} $(M^{-1})^{a,b}$	R	$K_{ass\,(R)}/K_{ass\,(S)}$	$-\Delta G_0$ (kJ/mol)	$\Delta\Delta G_0$ (kJ/mol)
(*R*)-**1**	*R*[c]	$(2.25 \pm 0.13) \times 10^4$	0.9981		24.83	
(*R*)-**1**	*S*[c]	$(7.54 \pm 0.33) \times 10^3$	0.9989	2.98	22.12	−2.71
(*R*)-**2**	*R*[c]	$(1.38 \pm 0.17) \times 10^4$	0.9914		23.62	
(*R*)-**2**	*S*[c]	$(3.74 \pm 0.32) \times 10^3$	0.9954	3.69	20.38	−3.24
(*S*)-**1**	*R*[c]	$(7.32 \pm 0.68) \times 10^3$	0.9947		22.05	
(*S*)-**1**	*S*[c]	$(1.14 \pm 0.10) \times 10^4$	0.9949	1/1.56	23.14	1.09
(*S*)-**2**	*R*[c]	$(7.56 \pm 0.36) \times 10^3$	0.9989		22.13	
(*S*)-**2**	*S*[c]	$(2.13 \pm 0.29) \times 10^4$	0.9914	1/2.82	24.69	2.56

[a] The data were calculated from the results of fluorescence titrations in CH_3OH/H_2O system (1:1, 0.01 M Tris–HCl buffer, pH 7.4).
[b] All error values were obtained from nonlinear curve fitting.
[c] *R* and *S* represent *R*- and *S*-mandelates, respectively.

For the complex of 1:1 stoichiometry, an association constant K_{ass} can be calculated using the following equation (*8*):

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

where I represents the fluorescence intensity, C_H and C_G are the host and guest concentrations, respectively and C_0 is the initial concentration of the host. The association constants (K_{ass}) and correlation coefficients (R) obtained by a nonlinear least-squares analysis of I versus C_H and C_G are listed in Table 1. Satisfactory nonlinear curve fitting (the correlation coefficient is over 0.99) confirmed that the receptors and the mandelate formed a 1:1 complex (see the inset of Figures 1 and 2).

Figures 3 and 4 show the changes in the fluorescence spectra of receptor (*R*)-**2** (5.0×10^{-5} M) with the addition of *R*- or *S*-mandelate. When *R*- or *S*-mandelate was introduced to the solution of (*R*)-**2** in CH_3OH/H_2O system (1:1, 0.01 M Tris–HCl buffer, pH 7.4), the fluorescence emission of (*R*)-**2** was increased gradually. The enhancement efficiency was 61% with the addition of 12.8 equiv. of *R*-mandelate (Figure 3), while it was 22% by 12.8 equiv. of *S*-mandelate (Figure 4). The different enhancement efficiencies ($\Delta I_R/\Delta I_S \approx 2.8$) indicated that receptor (*R*)-**2** has an excellent enantioselective recognition ability

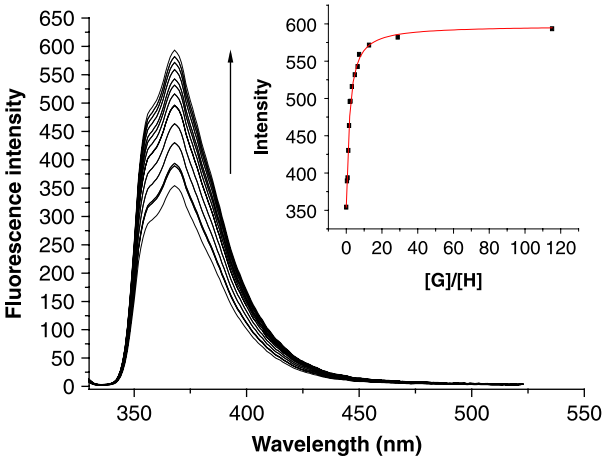

Figure 3. Fluorescence spectra of receptor (*R*)-**2** (5.0×10^{-5} M CH_3OH/H_2O, 1:1, 0.01 M Tris–HCl buffer, pH 7.4) upon the addition of various amounts of substrate *R*-mandelate in CH_3OH/H_2O system (1:1, 0.01 M Tris–HCl buffer, pH 7.4). $\lambda_{ex} = 320$ nm. Equivalent of Bu_4N^+ (*R*-mandelate): 0, 0.4, 0.8, 1.2, 1.6, 2.0, 2.4, 3.2, 4.8, 6.4, 7.2, 12.8, 28.8 and 115.2. Inset: changes of fluorescence intensity of (*R*)-**2** at 368 nm upon addition of *R*-mandelate. The line is fitting curve. The correlation coefficient (R) of nonlinear curve fitting is 0.9914.

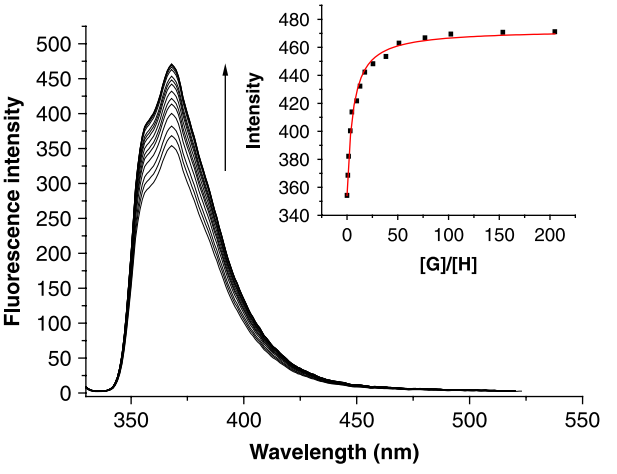

Figure 4. Fluorescence spectra of receptor (*R*)-**2** (5.0×10^{-5} M CH_3OH/H_2O, 1:1, 0.01 M Tris–HCl buffer, pH 7.4) upon the addition of various amounts of substrate *S*-mandelate in CH_3OH/H_2O system (1:1, 0.01 M Tris–HCl buffer, pH 7.4). $\lambda_{ex} = 320$ nm. Equivalent of Bu_4N^+ (*S*-mandelate): 0, 0.8, 1.6, 3.2, 4.8, 9.6, 12.8, 17.6, 25.6, 38.4, 51.2, 76.8, 102.4, 153.6 and 204.8. Inset: changes of fluorescence intensity of (*R*)-**2** at 368 nm upon addition of *R*-mandelate. The line is fitting curve. The correlation coefficient (R) of nonlinear curve fitting is 0.9954.

between *R*- and *S*-mandelates, the enantioselectivity $K_{ass\,(R)}/K_{ass\,(S)}$ is about 3.7.

The continuous variation methods were employed to determine the stoichiometric ratio of the receptor (*R*)-**2** with guests (*R*- and *S*-mandelates). The total concentration of host and guest was constant (1.0×10^{-4} M) in CH_3OH/H_2O system (1:1, 0.01 M Tris–HCl buffer, pH 7.4), with a continuously variable molar fraction of host ([H]/([H] + [G])). Figure 5 shows the job plots of receptor (*R*)-**2** with *R*- and *S*-mandelates (at 368 nm). When the molar fraction of the host was 0.50, the fluorescence intensity reached a maximum, which demonstrated that receptor (*R*)-**2** formed a 1:1 complex with *R*- and *S*-mandelates, respectively (*10*).

Due to the similar core structure of (*R*)-**1** and (*R*)-**2**, the fluorescent variations of (*R*)-**1** and (*R*)-**2** showed the same trend. However, compared with receptor (*R*)-**1**, (*R*)-**2** showed better enantioselective recognition for mandelate. This may be due to a relative bigger hindrance phenyl ring existed in (*R*)-**2**. In addition, as shown in Table 1, the association constants (K_{ass}) were different. For example, the $K_{ass(R)} = 1.38 \times 10^4\ M^{-1}$, $\Delta G_0 = -23.62$ kJ/mol; $K_{ass(S)} = 3.74 \times 10^3$ l/mol, $\Delta G_0 = -20.38$ kJ/mol, yielding a selectivity ($K_{ass(R)}/K_{ass(S)}$) of 3.69 and a $\Delta\Delta G_0$ value of -3.24 kJ/mol for the mandelates. This also demonstrates that receptor (*R*)-**2** has good chiral recognition ability towards the enantiomers of mandelate.

In order to study how the chirality of the amine and BINOL groups in (*R*)-**1** or (*R*)-**2** influenced the enantioselective fluorescent recognition, the (*S*)-**1** and (*S*)-**2**, diastereomeric compounds of (*R*)-**1** and (*R*)-**2**, were also prepared. The specific optical rotation of (*R*)-**1** and (*R*)-**2** was $[\alpha]_D^{20} +25.4°$, $+27.9°$ and that of (*S*)-**1**, (*S*)-**2** was $[\alpha]_D^{20} -26.8°$, $-29.4°$, respectively ($c = 0.05$, CH_3OH/H_2O, 1:1, 0.01 M Tris–HCl buffer, pH 7.4). This indicated that the optical rotations of these compounds were determined by the chirality of the BINOL unit.

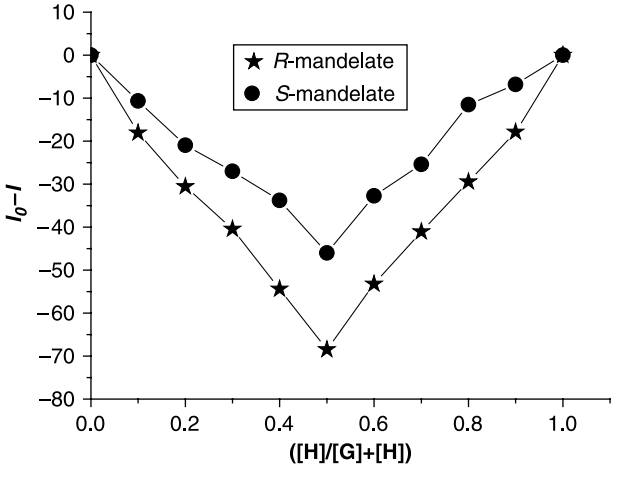

Figure 5. Job plots of receptor (*R*)-**2** with *R*- and *S*-mandelates (368 nm, $\lambda_{ex} = 320$ nm). The total concentration of the host ([H]) and guest ([G]) is 1.0×10^{-4}M in CH_3OH/H_2O system (1:1, 0.01 M Tris–HCl buffer, pH 7.4). I_0: fluorescence intensity of (*R*)-**2**; *I*: fluorescence intensity of (*R*)-**2** in the presence of the guest.

Receptor (*S*)-**1** was interacted with mandelate. This diastereomeric isomer showed much lower enantioselectivity than that of (*R*)-**1**. When (*S*)-**1** (2.1×10^{-5} M in CH_3OH/H_2O, 1:1, 0.01 M Tris–HCl buffer, pH 7.4) was treated with *S*- and *R*-mandelates (CH_3OH/H_2O, 1:1, 0.01 M Tris–HCl buffer, pH 7.4), *S*-mandelate caused about 58% fluorescence enhancement, which was higher than *R*-mandelate with an observed efficiencies ($\Delta I_S/\Delta I_R$) of up to 1.38. In addition, the association constants (K_{ass}) are different; the association constant of (*S*)-**1** with *S*-mandelate is 1.14×10^4; while that of (*S*)-**1** with *R*-mandelate is 7.32×10^3, which corresponds to the *S*/*R*-selectivity ($K_{ass(S)}/K_{ass(R)}$) of 1.56 for mandelates. Receptor (*S*)-**2** gave the enantioselectivities $K_{ass\,(S)}/K_{ass\,(R)} = 2.82$. The result of fluorescence titration indicated a mismatched chirality between the mandelate centres and the chiral BINOL unit led to the enantioselective recognition. The enantiomers of mandelate interacted with (*R*)-**1**, (*R*)-**2** and (*S*)-**1**, (*S*)-**2** in a same fashion.

3. Conclusion

In summary, substituted BINOL (*R*)-**1**, (*R*)-**2**, (*S*)-**1** and (*S*)-**2** have been synthesised and their uses in the fluorescent recognition of mandelates have been examined. We found that compound (*R*)-**2** gave the highest enantioselectivities $K_{ass(R)}/K_{ass(S)} = 3.69$ with $\Delta I_R/\Delta I_S$ up to 2.1, and compound (*R*)-**1** showed up to $K_{ass(R)}/K_{ass(S)}$ about 3 in the presence of mandelates in CH_3OH/H_2O system (1:1, 0.01 M Tris–HCl buffer, pH 7.4). These high fluorescence sensitivity and enantioselectivity make these compounds practically useful receptors for the recognition of the mandelate in H_2O system.

4. Experimental

4.1 Materials and methods

The reagents used were of commercial origin and were employed without further purification. The anions were used as their bis(tetrabutylammonium) salts. Purifications by column chromatography were carried out over silica gel (230–400 mesh). Melting points were measured on Reichert 7905 melting-point apparatus (uncorrected). The IR spectra were performed on a Nicolet 670 FT-IR spectrophotometer. 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. Elemental analyses were performed by the Vario Elemental CHSN-O microanalyzer.

Fluorescence spectra were obtained on a Shimadzu RF-5301 spectrometer. Optical rotations were taken on a Perkin-Elmer Model 341 polarimeter.

4.2 Preparation and characterisation of receptors (R)-1, (R)-2, (S)-1 and (S)-2

A mixture of the (*R*)- or (*S*)-binaphthyl dialdehyde (0.34 g, 1 mmol) and amino alcohol (2.2 mmol) in absolute CH_3OH (30 ml) were degassed with nitrogen. The mixture was heated and stirred under reflux for 24 h. After cooled to room temperature, $NaBH_4$ (0.2 g) was poured into the solution. The mixture was stirred for 6 h under N_2 protection at ambience temperature, then heated to 50°C and stirred for 6 h. The solvent was removed under reduced pressure, the residue was washed with HCl (0.2 M, aq., 30 ml) and then methylene chloride (30 ml) was added. After stirred for 1 h, the organic layer was separated and washed with 0.5 M NaOH aqueous solution, water, brine and dried over $MgSO_4$. The crude product was purified by column chromatography on silica gel using $CHCl_3$/CH_3OH (50/1) as eluant to obtain pure products (*R*)-**1**, (*R*)-**2**, (*S*)-**1** and (*S*)-**2**, respectively.

4.2.1 Compound (R)-1

Yield: 84%; mp: 126–128°C; $[\alpha]_D^{20}+25.4°$ ($c = 0.05$, CH_3OH/H_2O, 1:1, 0.01 M Tris–HCl buffer, pH 7.4); ^1H NMR ($CDCl_3$, 400 MHz) δ 9.26 (d, J = 2.0 Hz, 2H), 9.11 (d, $J = 2.0$ Hz, 2H), 8.74 (s, 2H), 8.40 (d, J = 8.0 Hz, 2H), 7.92 (t, $J = 8.0$ Hz, 2H), 4.31 (s, 4H), 3.68–3.62 (m, 6H), 2.85–2.65 (m, 6H), 1.31 (d, $J = 3.9$ Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 19.5, 51.7, 55.7, 74.1, 116.7, 122.2, 125.6, 126.2, 126.8, 127.4, 127.6, 128.0, 128.4, 128.9, 134.6, 154.3; IR (KBr/cm^{-1}): 3400, 3054, 2928, 1622, 1500, 1427, 1353, 1252, 1147, 1107, 1056, 985, 746; ESI-MS *m/z* (%): 483 ($(M+Na)^+$, 100). Elemental analysis calcd (%) for $C_{28}H_{32}N_2O_4$: C, 73.02; H, 7.00; N, 6.08; found: C, 72.80; H, 7.06; N, 5.99.

4.2.2 Compound (R)-2

Yield: 70%; mp: 144–146°C; $[\alpha]_D^{20}+27.9°$ ($c = 0.05$, CH_3OH/H_2O, 1:1, 0.01 M Tris–HCl buffer, pH 7.4); ^1H NMR ($CDCl_3$, 400 MHz) δ 9.28 (d, $J = 2.0$ Hz, 2H), 9.13 (d, $J = 2.0$ Hz, 2H), 8.81 (s, 2H), 8.41 (d, $J = 8.0$ Hz, 2H), 7.90 (t, $J = 8.0$ Hz, 2H), 7.40–7.20 (m,10H), 4.32 (dd, 4H), 4.01 (q, $J = 4.2$ Hz, 2H), 3.78–3.70 (m, 4H), 2.88–2.64 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 53.6, 58.2, 77.4, 116.8, 122.4, 123.9, 124.9, 125.3, 125.8, 126.0, 126.1, 126.9, 127.1, 127.4, 127.9, 128.3, 128.9, 129.3, 129.9, 134.6, 155.7; IR (KBr/cm^{-1}): 3435, 2930, 1616, 1504, 1431, 1352, 1240, 1111, 751; ESI-MS *m/z* (%): 607 ($(M+Na)^+$, 100). Elemental analysis calcd (%) for $C_{38}H_{36}N_2O_4$: C, 78.06; H, 6.21; N, 4.79; found: C, 77.79; H, 6.27; N, 4.70.

4.2.3 Compound (S)-1

Yield: 76%; mp: 130–132°C; $[\alpha]_D^{20}-26.8°$ ($c = 0.05$, CH_3OH/H_2O, 1:1, 0.01 M Tris–HCl buffer, pH 7.4); ^1H NMR ($CDCl_3$, 400 MHz) δ 9.28 (d, $J = 2.0$ Hz, 2H), 9.12 (d, $J = 2.0$ Hz, 2H), 8.77 (s, 2H), 8.42 (d, $J = 8.0$ Hz, 2H), 7.94 (t, $J = 8.0$ Hz, 2H), 4.29 (s, 4H), 3.68–3.62 (m, 6H), 2.83–2.62 (m, 6H), 1.27 (d, $J = 3.9$ Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 19.5, 51.1, 55.4, 74.3, 116.7, 122.3, 125.4, 125.9, 126.8, 127.3, 127.6, 127.8, 128.4, 128.8, 134.2, 153.9; IR (KBr/cm^{-1}): 3419, 3059, 2930, 1616, 1496, 1424, 1352, 1248, 1143, 1103, 1031, 991, 751; ESI-MS *m/z* (%): 483 ($(M+Na)^+$, 100). Elemental analysis calcd (%) for $C_{28}H_{32}N_2O_4$: C, 73.02; H, 7.00; N, 6.08; found: C, 72.84; H, 7.04; N, 6.00.

4.2.4 Compound (S)-2

Yield: 70%; mp: 148–150°C; $[\alpha]_D^{20}-29.4°$ ($c = 0.05$, CH_3OH/H_2O, 1:1, 0.01 M Tris–HCl buffer, pH 7.4); ^1H NMR ($CDCl_3$, 400 MHz) δ 9.32 (d, $J = 2.0$ Hz, 2H), 9.16 (d, $J = 2.0$ Hz, 2H), 8.81 (s, 2H), 8.44 (d, $J = 8.0$ Hz, 2H), 7.96 (t, $J = 8.0$ Hz, 2H), 7.41–7.22 (m, 10H), 4.29 (dd, 4H), 3.98 (q, $J = 4.2$ Hz, 2H), 3.75–3.69 (m, 4H), 2.83–2.62 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 52.1, 57.3, 76.6, 116.3, 122.1, 123.7, 124.8, 125.5, 125.7, 126.0, 126.4, 126.9, 127.5, 127.8, 127.4, 128.7, 128.9, 129.3, 129.7, 134.0, 154.6; IR (KBr/cm^{-1}): 3424, 2926, 1628, 1500, 1427, 1348, 1242, 1107, 1039, 746, 698; ESI-MS *m/z* (%): 607 ($(M+Na)^+$, 100). Elemental analysis calcd (%) for $C_{38}H_{36}N_2O_4$: C, 78.06; H, 6.21; N, 4.79; found: C, 77.81; H, 6.29; N, 4.68.

4.3 Tetrabutylammonium salts

All tetrabutylammonium salts were prepared by adding 1 equiv. of tetrabutylammonium hydroxide in methanol to a solution of the corresponding mandelic acid (1 equiv.) in methanol. The mixture was stirred at room temperature for 2 h and evaporated to dryness under reduced pressure. The resulting syrup was dried at high vacuum and 50°C for 24 h and stored in a desiccator.

4.4 Binding studies

The studies on the binding properties of (*R*)-**1**, (*R*)-**2**, (*S*)-**1** and (*S*)-**2** were carried out in CH_3OH/H_2O system (1:1, 0.01 M Tris–HCl buffer, pH 7.4). The work solutions were prepared by adding different volumes of mandelate solution to a series of the test tubes, then the same amount of stock solution of host compound was added into each

of test tubes followed by dilution to 3.5 ml by CH_3OH/H_2O system. After being shaken for several minutes, the work solution could be measured immediately (the excited wavelength was 320 nm). Association constants were calculated by means of a nonlinear least-square curve fitting method with Origin 7.0 (Origin-Lab Corporation).

4.5 Experimental procedure for the job plots

The solutions of (*R*)-**2**, (*R*)-mandelate, (*S*)-mandelate in CH_3OH/H_2O system (the total concentration of the host and guest is 1.0×10^{-4} M, 1:1, 0.01 M Tris–HCl buffer, pH 7.4) were freshly prepared. The receptor and mandelate solutions were added to the test tubes in the ratios of 10:0, 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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