Tetrahedron: *Asymmetry* 19 (2008) 2051–2057

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Preparation of a metal–ligand fluorescent chemosensor and enantioselective recognition of carboxylate anions in aqueous solution

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ARTICLE INFO

Article history:
Received 1 July 2008
Accepted 24 July 2008

ABSTRACT

Two chiral fluorescent chemosensors **1** and **2** were synthesized, and the structure characterized by IR, ^{1}H NMR, ^{13}C NMR, MS spectra and elemental analysis. Their recognition ability was studied in aqueous solution (Tris–HCl buffer pH 7.4, MeOH/H_2O = 1:1) through fluorescence spectra. Receptors **1** and **2** showed a good binding ability to the copper ion. The host **1**-Cu^{2+} complex showed a chiral recognition ability to mandelate anions with a preferable binding to L-mandelate than D-mandelate anions. The host **1**-Cu^{2+} complex and L- or D-mandelate anions formed 1:1 stoichiometric complex. The binding constant for L-mandelate is 576 M^{-1}, whereas that for D-mandelate is only 38 M^{-1}, which can be distinguished by the different change of fluorescence intensity.

1. Introduction

Anions play an important role in a range of chemical, biological and environmental processes. For this, the recognition of anions has attracted much interest from chemists in the supramolecular field to design and synthesize different receptors for the detection of different anions.[1]

Chiral recognition of racemic compounds exists extensively in nature. To understand biological process, synthetic chiral receptors were prepared to bind the chiral guest selectively;[2] these have the ability of discriminating the enantiomers. Many receptors have already been reported; their binding ability to both chiral and achiral anion guests has been studied by ^{1}H NMR, UV–vis spectra, fluorescence and electrochemical analysis.[3] Most of the receptors have mainly been studied in organic solvents such as chloroform, CH_3CN and DMSO.[4] For the competing effect of water, receptors of these kinds based on hydrogen bonding have little interaction with guests in aqueous solution.[5] The synthesis and study of water soluble receptors has become challenging work in the recent years.

Since many anion recognition processes occur in neutral aqueous solution in bio-systems, much work has been carried out in this area.[6] Unlike the traditional hydrogen binding in uncompetitive solvents, many new receptors based on strong binding ability have been synthesized to minimize the competing effect of water and other highpolarity solvents.[7] Receptors of this purpose are usually based on the electrostatic interaction between the host and guest,[8] such as guanidinium, boronic acid[9] and metal–anion coordination.[10]

The binding of the receptor to anions such as halogen,[11] tartrate,[12] ppi,[13] ATP,[14] saccharate[15] and peptide[16] has been studied. These receptors exhibit good binding properties to the anion guest in aqueous solution. However, receptors for chiral anion recognition in aqueous solution are still rare.[17]

To develop a receptor for chiral recognition in aqueous solution we designed a ligand–metal complex. At first, in order to find a metal which can form a complex with ligand **1** and **2** so as to be used in the anion binding, it is interesting to note that the ligands **1** and **2** have a special selective binding to Cu^{2+}, meaning that receptors **1** and **2** can be used as an efficient sensor for Cu^{2+}. As a result, the complex **1**-Cu^{2+} and **2**-Cu^{2+} were chosen as host binding anions.

Many receptors for mandelate anions have been designed and synthesized,[18] and their enantioselective recognition ability tested by ^{1}H NMR and fluorescence in the uncompetitive organic solvents such as $CHCl_3$ and DMSO. However, the recognition of mandelate in aqueous solution still remains rare. Herein, we report two hosts **1**-Cu^{2+} and **2**-Cu^{2+} for anions, their binding properties towards carboxylate anions were examined by fluorescence and CD spectra in aqueous solution. The host **1**-Cu^{2+} exhibited excellent enantioselective recognition abilities for the enantiomers of mandelate, the enantioselectivity: $K_{ass}(L)/K_{ass}(D)$ = 15.2. The difference of the fluorescence response indicates that host **1**-Cu^{2+} could be used as an enantioselective fluorescent chemosensor for mandelate under physiological pH conditions.

2. Results and discussion

2.1. Synthesis

The synthesis routine of receptors **1**, **2** and **1**-Cu^{2+} is outlined in Scheme 1. The terminal compounds **1** and **2** were obtained in the

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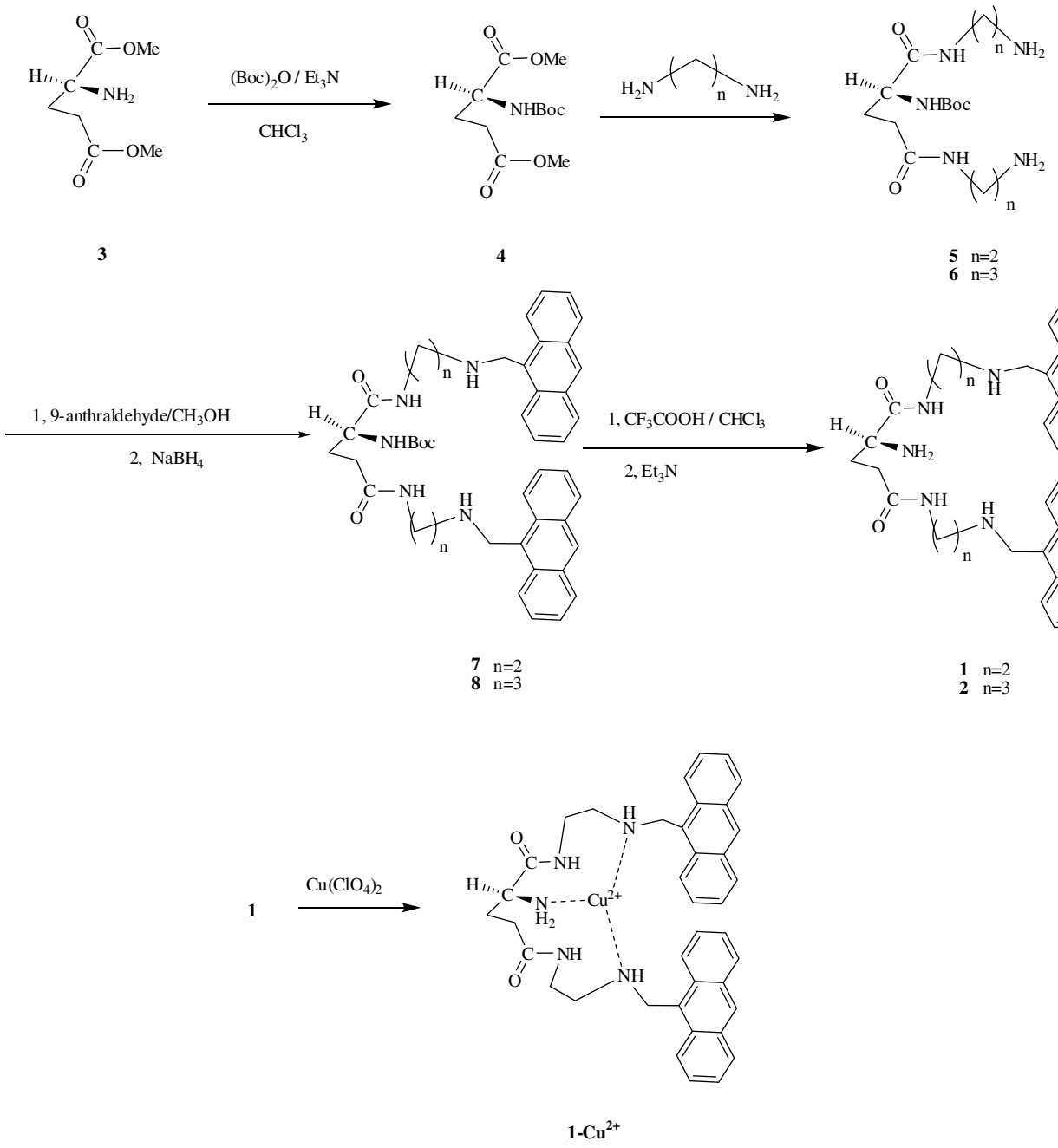
doi:10.1016/j.tetasy.2008.07.038



Scheme 1. Synthesis of receptor **1**, **2** and **1**-Cu^{2+}.

total yield of 73% and 55%, respectively. At first, compound **3** was synthesized according to the literature.[4d] After being treated with $(Boc)_2O$ in chloroform at room temperature, the protected compound **4** was reacted with diamine in dry methanol to afford **5** or **6**. Compound **5** or **6** was then reacted with 9-anthraldehyde to afford the Schiff's base, which was directly reduced without purification to afford intermediate **7** or **8**. Finally intermediate **7** or **8** was deprotected in trifluoroacetic acid to get the target molecule **1** or **2**. Compound **1**-Cu^{2+} was directly obtained by mixing compound **1** and copper perchlorate in methanol to afford a blue precipitation. Compounds **1** and **2** have a good solubility in many organic solvents, such as $CHCl_3$, DMF, DMSO, CH_3CN and 1,4-dioxane. Compound **1**-Cu^{2+} also has a solubility in H_2O/MeOH (v/v 9:1). The structures of these compounds were characterized by IR, ^1H NMR, and ^{13}C NMR, electrospray ionization mass spectroscopy (ESI-MS) and elemental analysis.

2.2. Binding study of the receptors to metal ions[19]

The binding study of receptors **1** and **2** to metal ions was studied by fluorescence and UV–vis spectra by gradually titrating the guest to the host solution in aqueous solution (Tris–HCl buffer pH 7.4, MeOH/H_2O = 1:1) at room temperature. The emission spectra of the corresponding titration curves revealed the dependence of the fluorescence behavior of the receptor on the guest concentration.

Figure 1 shows the fluorescence emission spectra of a mixture of receptor **1** (5×10^{-5} mol L^{-1}) and different concentrations of the guest Cu^{2+} (λ_{ex} = 369 nm). By gradually increasing the concentration of copper ions, the fluorescence emission intensity of receptor **1** at 415 nm dramatically decreased. When 1.1 equiv of copper ion was added, the fluorescence intensity was quenched about 57%. The quench efficiency was 68% when 2.0 equiv of copper ion

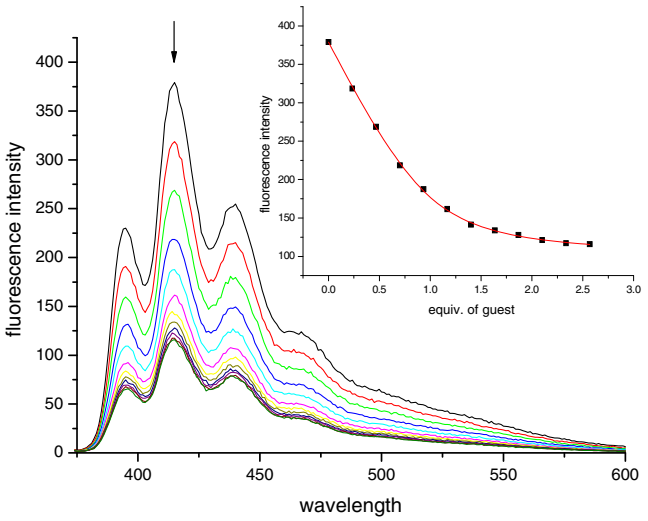


Figure 1. Fluorescence spectra of receptor **1** (5.0×10^{-5} mol L^{-1}) upon the addition of various amounts of Cu^{2+} in 1:1 MeOH/H_2O Tris–HCl buffer pH 7.4. The equivalents of guest are 0, 0.23, 0.47, 0.70, 0.93, 1.17, 1.40, 1.63, 1.87, 2.10, 2.33, 2.57, λ_{ex} = 366 nm. Inset: changes of fluorescence intensity of **1** at 415 nm upon addition of Cu^{2+}. The correlation coefficient (R) of non-linear curve fitting is 0.9998.

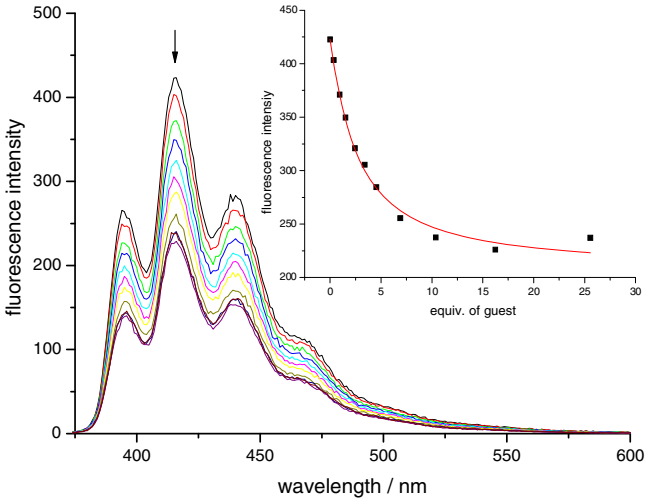


Figure 2. Fluorescence spectra of receptor **2** (5.0×10^{-5} mol L^{-1}) upon the addition of various amounts of Cu^{2+} in 1:1 MeOH/H_2O Tris–HCl buffer pH 7.4. The equivalents of guest are 0, 0.35, 0.93, 1.52, 2.45, 3.38, 4.55, 6.88, 10.38, 16.22, 25.55, λ_{ex} = 366 nm. Inset: changes of fluorescence intensity of **2** at 415 nm upon addition of Cu^{2+}. The correlation coefficient (R) of non-linear curve fitting is 0.9959.

was added to the solution of receptor **1**; the fluorescence intensity required no further quenching when additional copper ion was added. While other metal ions were added to the solution of receptor **1**, such as Zn^{2+}, Cd^{2+}, K^+, Ca^{2+}, Mg^{2+}, Fe^{2+}, Co^{2+}, Ni^{2+}, La^{3+}, there was little to no fluorescence response. The association constants of receptor **1** to metal ions are listed in Table 1.

Table 1
The association constants of receptors **1** and **2** with metal ions in aqueous solution (1:1 MeOH/H_2O Tris–HCl buffer pH 7.4) at 20 °C

Entry	Receptor **1** K_{ass} (M^{-1})	Receptor **2** K_{ass} (M^{-1})
Cu^{2+}	$(1.8 \pm 0.1) \times 10^5$	$(9.1 \pm 0.9) \times 10^3$
Zn^{2+}	324	*c*
Ni^{2+}	87	*c*
Cd^{2+}	220	*c*

c: The constant is too small to be calculated.

In the binding process, the fluorescence change phenomenon can be attributed to the classic photoinduced electron transfer (PET) mechanism. When the amine groups of the host formed a complex with the metal, the excited electron state of the anthracene was then transferred to the LUMO of Cu^{2+}, which induced the fluorescence quenching. This phenomenon was confirmed by the UV–vis spectra of the host when the copper ion was added to the solution of **1**. The slight intensity change of the UV–vis absorption bands of the anthracene moiety in the receptor at 348 nm, 366 nm, 386 nm, indicated that a classic PET process occurred when the receptor bound the guest metal ion.

The binding property of receptor **2** was also evaluated by these metal ions, Figure 2 shows the fluorescence emission spectra of a mixture of compound **2** and different concentrations of the guest Cu^{2+} (λ_{ex} = 366 nm). By gradually increasing the concentration of Cu^{2+}, the fluorescence emission intensity of receptor **2** (5×10^{-5} mol L^{-1}) at 415 nm was decreased. When 4.5 equiv of copper ion was added, the fluorescence intensity was quenched at about 33%, when a further 10 equiv of copper ion was added, the fluorescence intensity quenched at about 44% and without much further change by adding more metal ions. There were no fluorescence responses to other metal ions. The slightly changed UV–vis spectra, which occurred by adding Cu^{2+}, illustrated the same PET process as above.

The satisfactory results (the correlation coefficient is over 0.99) of the non-linear curve fitting confirmed that receptors **1** and **2** formed a 1:1 complex with Cu^{2+}, which was also confirmed by the ESI-MS. For a complex with 1:1 stoichiometry, the association constant K_{ass} can be calculated by using the following equation in the ORIGIN 7.0:

$$X = X_0 + (X_{lim} - X_0)/2c_0\{c_H + c_G + 1/K_{ass} - [(c_H + c_G + 1/K_{ass})^2 - 4c_H c_G]^{1/2}\} \quad (1)$$

where X is the absorption intensity and C_H and C_G are the corresponding concentrations of the host and guest anion; C_0 is the initial concentration of the host. The association constants (K_{ass}) and correlation coefficient (R) were obtained by a non-linear least squares analysis of X versus C_H and C_G, the results are listed in Table 1.

From the data in Table 1, the K_{ass} for Cu^{2+} was 1.8×10^5 M^{-1} and 9.1×10^3 M^{-1}, respectively. We found that the receptor **1** and **2** have a selective binding to Cu^{2+}. Since receptor **1** has a shorter chain, resulting in a larger rigidity and a better reorganization ability than receptor **2**, receptor **1** exhibited a larger association constant with Cu^{2+}. Receptor **1** can be used as a sensitive fluorescence chemosensor for Cu^{2+} in aqueous solution.

2.3. Binding study of the receptor-Cu^{2+} complexes to the anion guests

The binding properties of host **1**-Cu^{2+} complex to anions were studied by fluorescence and UV–vis spectra by gradually titrating the guest anions to the host solution in aqueous solution (Tris–HCl buffer pH 7.4, MeOH/H_2O = 1:1) at room temperature.

Figures 3 and 4 show the fluorescence emission spectra of the host **1**-Cu^{2+} under different concentrations of L- or D-mandelate anions in aqueous solution, respectively. By adding L- or D-mandelate anions gradually, the fluorescence intensity of host **1**-Cu^{2+} (5×10^{-5} mol L^{-1}) at 415 nm (λ_{ex} = 366 nm) was enhanced. The enhancement was 27.5% when 5.8 equiv of L-mandelate anion was added to the solution of **1**-Cu^{2+}, while the enhancement was only 5.3% when 5.8 equiv of D-mandelate anion was added. The enhanced efficiencies ($\Delta I_L/\Delta I_D$ = 5.18) indicated that the host **1**-Cu^{2+}

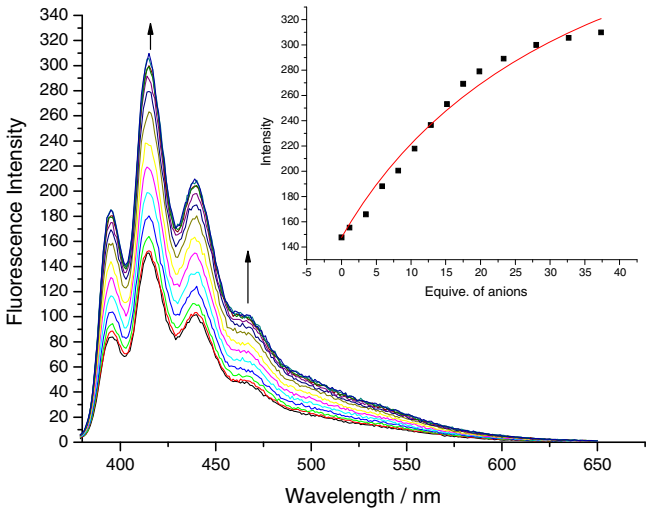


Figure 3. Fluorescence spectra of host **1**-Cu^{2+} (5.0×10^{-5} mol L^{-1}) upon addition of various amounts of L-mandelate anion in 1:1 MeOH/H_2O Tris–HCl buffer pH 7.4. The equivalents of guest are 0→37.3, λ_{ex} = 366 nm. Inset: changes of fluorescence intensity of **1**-Cu^{2+} at 415 nm upon addition of L-mandelate anion. The correlation coefficient (R) of non-linear curve fitting is 0.9910.

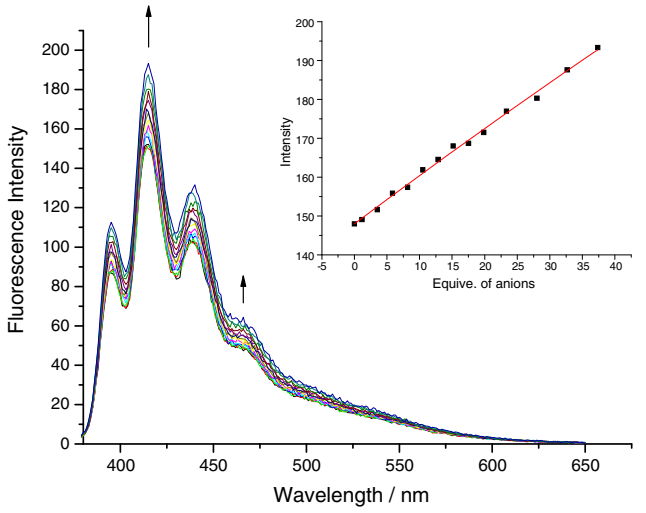


Figure 4. Fluorescence spectra of host **1**-Cu^{2+} (5.0×10^{-5} mol L^{-1}) upon addition of various amounts of D-mandelate anion in 1:1 MeOH/H_2O Tris–HCl buffer pH 7.4. The equivalents of guest are 0→37.3, λ_{ex} = 366 nm. Inset: changes of fluorescence intensity of **1**-Cu^{2+} at 415 nm upon addition of D-mandelate anion. The correlation coefficient (R) of non-linear curve fitting is 0.9982.

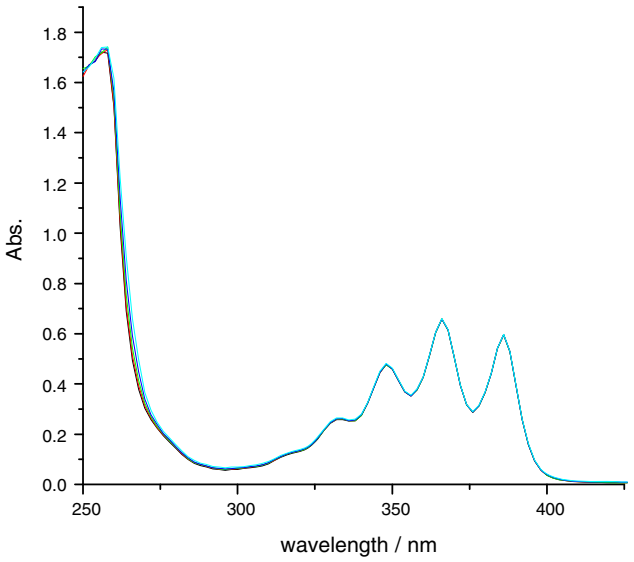


Figure 5. UV–vis absorption spectra of host **1**-Cu^{2+} (5.0×10^{-5} mol L^{-1}) upon the addition of various amounts of L-mandelate anions in 1:1 MeOH/H_2O Tris–HCl buffer pH 7.4. The equivalents of guest are 0→37.3.

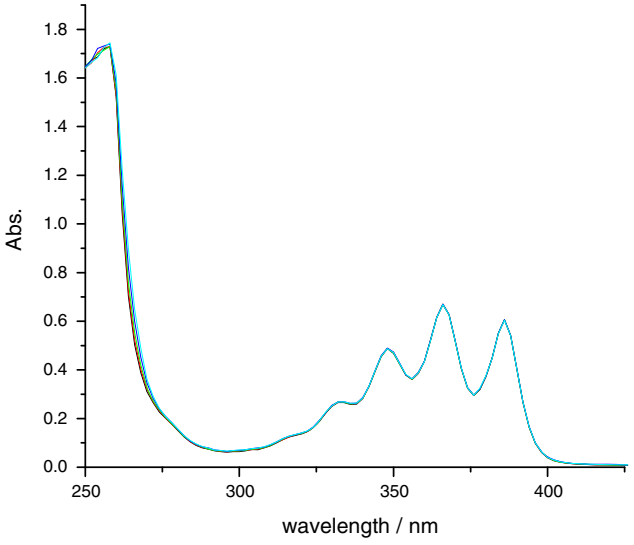


Figure 6. UV–vis absorption spectra of host **1**-Cu^{2+} (5.0×10^{-5} mol L^{-1}) upon the addition of various amounts of D-mandelate anions in 1:1 MeOH/H_2O Tris–HCl buffer pH 7.4. The equivalents of guest are 0→37.3.

complex has a good enantioselective recognition ability between the L- and D-mandelate anions. When the same 37.3 equiv of L- or D-mandelate was added, enhancements in fluorescence intensity of 110% and 32% were seen, respectively.

In the binding with L- and D-mandelate anions, the fluorescence enhancement phenomenal can be attributed to the photoinduced electron transfer (PET) mechanism. In the absence of the guest mandelate anions, the fluorescence quenching of the host **1**-Cu^{2+} complex arose from the change in free energy of electron transfer of the photoinduced anthracene unit and the metal Cu^{2+} unit. When the guest anion binds with the host, the electron of the electron-sufficient anions transferred to the host **1**-Cu^{2+}, which in turn decreased the excited-state anthracene electron transferring to the LUMO of Cu^{2+}, consequently leading to the recovery of the fluorescence intensity of the fluorophore. This PET mechanism can be confirmed by the UV–vis spectra in Figures 5 and 6. When increasing the concentrations of both L- (Fig. 5) and D- (Fig. 6) mandelate anions, no changes in the intensity in the absorption peaks of anthracene at 348 nm, 366 nm, 386 nm were seen, which indicates a classic PET process when the host binds with these anions.[3c,4b]

The association constants of **1**-Cu^{2+} with guests L- and D-mandelate anions were calculated by Eq. 1 listed above using the ORIGIN 7.0 software.

The satisfactory result (emission intensity at 415 nm vs the equivalent of the anion guest, the correlation coefficient is over 0.99) of the non-linear curve fitting was obtained, which indicates that a 1:1 complex was formed between the host and guest. The binding constants were different [$K_{ass(L)}$ = 576 M^{-1}, $K_{ass(D)}$ = 38 M^{-1}], the enantioselectivity was $K_{ass(L)}/K_{ass(D)}$ = 15.2, which demonstrates that the host **1**-Cu^{2+} can be used as an excellent enantioselective fluorescent chemosensor for the enantiomers of mandelate anions in aqueous solution. Figure 7 shows the different

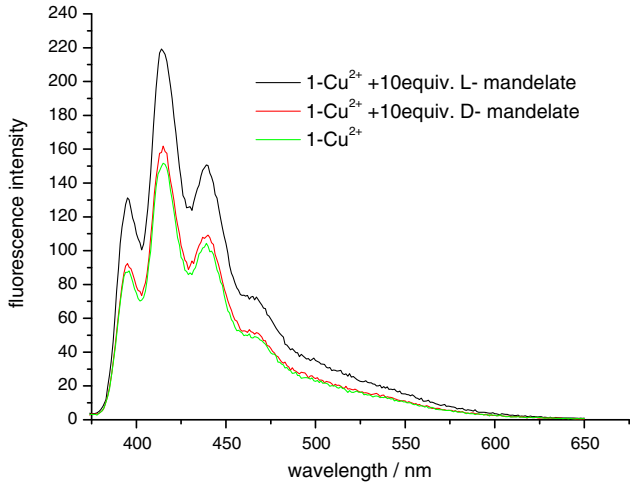


Figure 7. Fluorescence spectra of host **1**-Cu^{2+} (5.0×10^{-5} mol L^{-1}) with 10 equiv of L- and D-mandelate anion in 1:1 MeOH/H_2O Tris–HCl buffer pH 7.4.

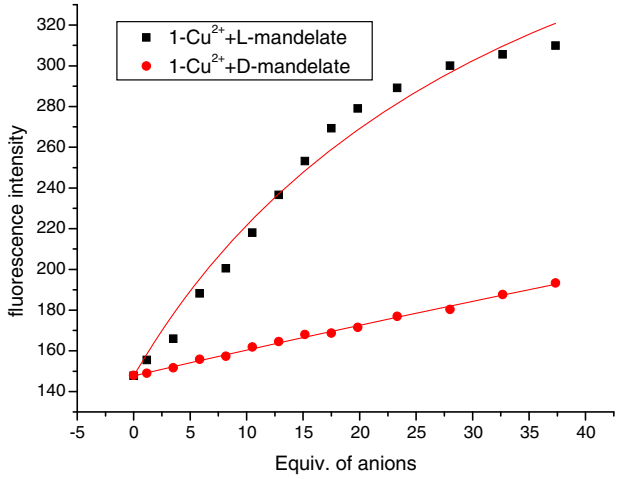


Figure 8. Fluorescence intensity change of host **1**-Cu^{2+} (5.0×10^{-5} mol L^{-1} at 415 nm) with the addition of L- or D-mandelate anions in 1:1 MeOH/H_2O Tris–HCl buffer pH 7.4. The line is a fitting curve.

fluorescence intensity changes when the same equiv of L- or D-mandelate anions were added to the host **1**-Cu^{2+}, and Figure 8 shows the different fluorescence response to the L- or D-mandelate anions. The different fluorescences demonstrate a good enantioselective recognition ability of the host **1**-Cu^{2+} for the enantiomers of mandelate.

The binding of complex **1**-Cu^{2+} and other chiral guests was also carried out and the association constants of the host **1**-Cu^{2+} and other guest are listed in Table 2. The receptor exhibits moderate enantioselective recognition ability to the chiral guest anions we have tested. From the association constants listed in Table 2, the host **1**-Cu^{2+} has a little chemoselective binding ability to other anions.

The interaction between the host **1**-Cu^{2+} and L-, D-mandelate anions may be the result of the hydrogen bonding, coordination, electrostatic interactions, steric effects and π–π stacking. In addition to the fluorescence study to L-/D-mandelate above, we have also tested the binding property of receptor **1** with anions without the metal Cu^{2+}. The receptor **1** also has a binding ability to anions in the aqueous solution. When binding with D-, L-mandelate anions, there are slight changes in the fluorescence intensity, and the constant is too small to be calculated. When interacting with

Table 2
Association constant (K_{ass}),[a,b] the correlation coefficients (R) and enantioselectivities (K_L/K_D) of host **1**-Cu^{2+} in the aqueous solution (1:1 MeOH/H_2O Tris–HCl buffer pH 7.4) at 20 °C

Anions[c]	K_{ass}	R	K_L/K_D
L-Mandelate	576 ± 52	0.9910	15.2
D-Mandelate	38 ± 13	0.9982	
L-Phenylglycine	(1.2 ± 0.16) × 10^3	0.9954	1.20
D-Phenylglycine	(1.0 ± 0.17) × 10^3	0.9941	
L-Alanine	453 ± 24	0.9948	1.52
D-Alanine	688 ± 51	0.9944	
L-Aspartate	(6.7 ± 0.48) × 10^3	0.9987	0.97
D-Aspartate	(6.9 ± 0.52) × 10^3	0.9986	
L-Glutamate	(1.6 ± 0.17) × 10^3	0.9971	1.23
D-Glutamate	(1.3 ± 0.14) × 10^3	0.9973	

[a] The data were calculated from the fluorescence titration in 1:1 MeOH/H_2O Tris–HCl buffer pH 7.4.
[b] All error values were obained by the results of non-linear curve fitting.
[c] All anions were used as their tetrabutylammonium salts.

phenylglycine and amino acid anions, the fluorescence intensity of receptor **1** was quenched, this can be seen as the interaction of hydrogen bonding between the receptor **1** and guest in the aqueous solution. When receptor **1** binds with other metals such as the zinc ion, the low binding behaviour between receptor **1** and Zn^{2+} made the complex **1**-Zn^{2+} which shows no improvement in the binding with anions. It was confirmed by fluorescence titration that the associate constant calculated was 201 M^{-1} for receptor **1** and 236 M^{-1} for **1**-Zn^{2+} when binding with L-glutamate anions. The same was seen when other metal ions were used, and the weaker binding behaviour between the compound **2** and Cu^{2+} also let complex **2**-Cu^{2+} which has little response to anions. From all of these phenomena, we can conclude that the metal ions were involved and played important roles in the binding process; it was also confirmed by the larger binding constant of **1**-Cu^{2+} with L-asp and L-glutamate anions, which have more binding sites with metal ion than that of alanine and mandelate. There were also π–π stacking interactions between the phenyl group of the guest and the anthracene moieties of the host, which was confirmed by the fluorescence titration. Complex **1**-Cu^{2+} has little response of fluorescence to the OAc^- anion but the response of fluorescence is larger when binding to benzoate anion, and also the binding constants of **1**-Cu^{2+} for phenylglycine and phenyl alanine anions were large than that of the alanine anion, which indicate that π–π stacking occurred in the binding process.

To obtain further information about the interactions between host **1**-Cu^{2+} and the anion guest, the binding of the host **1**-Cu^{2+} complex was studied by the circular dichroism (CD) spectra. In Figures 5 and 6, there was no change in the absorption (250–320 nm) of the host **1**-Cu^{2+} when large amounts of guest L- and D-mandelate anions were added. The CD spectra were taken from 250 to 300 nm in the solution H_2O/MeOH = 1:1 (v/v) (20 °C) at a concentration of 1.0×10^{-5} mol L^{-1}. From Figure 9, receptor **1** displays a strong negative Cotton effect at 259 nm ($\theta = -8.3$ mdeg). When 1 equiv of Cu^{2+} was added to receptor **1**, the CD signal was strongly reversed, a positive Cotton effect at 259 nm ($\theta = 3.0$ mdeg) appeared, which indicated a strong complexation between the receptor **1** and Cu^{2+}. Then the CD spectra of complex **1**-Cu^{2+} with 30 equiv of L- or D- mandelate anions were recorded, respectively. By adding 30 equiv of D-mandelate anions, the positive Cotton effect peak intensity at 259 nm decreased from 3.0 mdeg to 0.93 mdeg, indicating an interaction between the host and guest. When the L-mandelate anion was added to the aqueous solution of complex **1**-Cu^{2+}, the positive peak intensity decreased to 0.26 mdeg. The larger decrease in the intensity of the positive peak at 259 nm by L-mandelate than that of the D-mandelate anion, which indicated a stronger

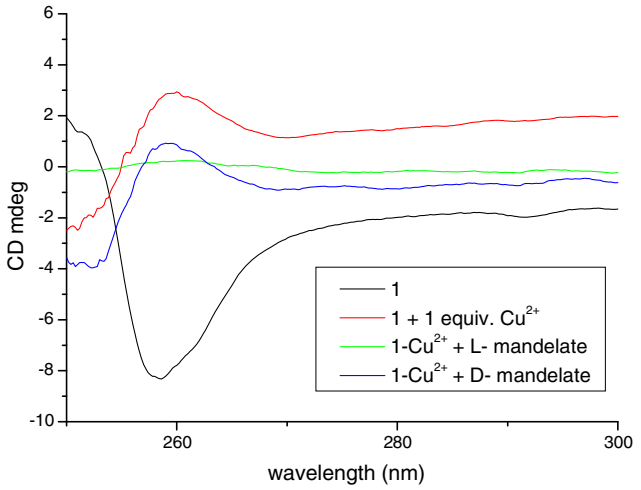


Figure 9. Circular dichroism spectra of receptor **1**, **1**-Cu^{2+} and **1**-Cu^{2+} with 30 equiv of L- or D-mandelate anions in aqueous solution (H_2O/MeOH = 1:1) (20 °C) at the concentration of 1.0×10^{-5} mol L^{-1}.

interaction between the complex **1**-Cu^{2+} with L-mandelate, is in accordance with the result of the fluorescence study.

3. Conclusion

In conclusion, two chiral fluorescent receptors **1** and **2** were synthesized. Receptors **1** and **2** showed a good selective binding ability to Cu^{2+}. The host **1**-Cu^{2+} complex revealed an excellent enantioselective recognition ability for L-/D-mandelate anions in aqueous solution (K_{ass}(L)/K_{ass}(D) = 15.2) and formed a 1:1 stoichiometry complex. The obvious differences in the fluorescence intensity of the interaction between **1**-Cu^{2+} and the enantiomers of mandelate showed that host **1**-Cu^{2+} can be used as an enantioselective fluorescent chemosensor for chiral mandelate anions in physiological pH conditions.

4. Experimental

4.1. Materials and methods

$CHCl_3$, CH_3OH and Et_3N were dried and distilled before using according to the standard procedure. All other commercially available reagents were used without further purification. Melting points were determined with a Reichert 7905 melting-point apparatus and are uncorrected. Optical rotations were taken on a PerkinElmer Model 341 polarimeter. CD spectral were recorded on a JASCO J-810 spectrometer, IR spectra were obtained on a Nicolet 670FT-IR spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 on a Varian Mercury VX-300 MHz spectrometer. Mass spectra were recorded on a Finnigan LCQ advantage mass spectrometer. Elemental analysis was determined with a FlashEA 1112 instrument. Fluorescence spectra were obtained on Schimadzu RF-5301 spectrometer. The UV-spectra were performed with a TU-1901 spectrophotometer. All anions were used as their tetrabutylammonium salts.

4.2. Synthesis

4.2.1. Synthesis of compound 4

Dimethyl L-glutamate **3** (1.89 g, 10 mmol) was dissolved in a solution of 20 mL dry chloroform with 2.0 mL Et_3N, after adding 20 mL dry $CHCl_3$ containing 2.18 g $(Boc)_2O$ in 1 h. The mixture was stirred under nitrogen at room temperature for 16 h. The mixture was washed with 20 mL 10% HCl, saturated $NaHCO_3$ and water, respectively. The organic layer was dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated under reduced pressure to afford the compound **4** 2.80 g as a colourless oil (yield: 97.0%). ^{1}H NMR ($CDCl_3$,300 MHz) δ (ppm): 5.36 (d, J = 7.2 Hz, 1H, NHBoc), 4.12 (br s, 1H, chiral H), 3.56 (s, 3H, OMe), 3.51 (s, 3H, OMe), 2.24 (br s, 2H, CH_2), 2.00–1.73 (br s, 2H, CH_2), 1.25 (d, J = 7.2 Hz, 9H, Boc-CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm): 168.0, 167.6, 150.3, 74.6, 61.8, 47.7, 47.1, 46.5, 24.9, 23.1, 22.4.

4.2.2. General synthesis of compounds 5 and 6

At first, 0.50 g **4** (1.73 mmol) was dissolved in 20 mL of dry methanol, ethylenediamine (1.0 g, 17 mmol) or 1,3-diaminopropane (1.26 g, 17 mmol) was added. The solution was stirred under nitrogen at 50 °C for 3 h. The solvent was evaporated under reduced pressure, and then the excess ethylenediamine or 1,3-diaminopropane was removed under high vacuum to afford **5** or **6**, respectively, as a pale yellow oil in high yield. Compounds **5** and **6** were not purified further and can be used directly in the next step.

4.2.3. General synthesis of compounds 7 and 8

Compound **6** (0.55 g, 1.6 mmol) or **7** (0.63 g, 1.7 mmol) was dissolved in 30 mL of dry methanol; 0.70 g 9-anthraldehyde (3.4 mmol) was added to the stirring solution. After stirring for 24 h under nitrogen at room temperature, a Schiff's base was formed and the precipitated as a yellow solid. $NaBH_4$ (0.38 g, 10 mmol) was then added to the mixture in 3 portions over 1 h, after which it was stirred under nitrogen for another 3 h at 50 °C. The mixture was poured into 10% $NaHCO_3$, and extracted with $CHCl_3$ for three times. The organic layers were combined and dried over anhydrous Na_2SO_4; the solvent was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel using $CHCl_3$/MeOH (30:1) as eluent to obtain pure products **7**, **8**, respectively.

Compound **7**: the pure product was obtained as pale yellow foam (0.92 g) in 80.7% yield, mp 88–90 °C, $[\alpha]_D^{20} = -169$ (c 0.071, $CHCl_3$); IR (KBr, cm^{-1}): ν 3408, 3307, 3081, 3050, 2975, 2931, 2860, 2361, 1705, 1654, 1524, 1447, 1385, 1366, 1249, 1167, 1112, 1050, 883, 863, 835, 789, 734. ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 8.28 (s, 2H, An-H), 8.24 (d, J = 7.5 Hz, 4H, An-H), 7.92 (d, J = 7.5 Hz, 4H, An-H), 7.48–7.40 (m, 8H, An-H), 7.28 (s, 2H, CONH), 5.87 (d, J = 5.1 Hz, 1H, NHBoc), 4.59 (s, 4H, An-CH_2), 4.02 (br s, 1H, chiral H), 3.20 (br s, 4H, CH_2), 2.85 (br s, 4H, CH_2), 1.94–1.62 (m, 4H, CH_2), 1.38 (s, 9H, Boc-CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm): 172.7, 171.9, 155.9, 131.6, 131.1, 130.9, 130.4, 130.3, 130.2, 129.4, 129.3, 127.7, 126.6, 125.3, 124.2, 124.1, 123.9, 80.0, 53.6, 49.2, 45.3, 39.2, 38.7, 33.1, 28.6. Elemental Anal. Calcd for $C_{44}H_{49}N_5O_4$: C, 74.23; H, 6.94; N, 9.84. Found: C, 74.10; H, 6.99; N, 9.77.

Compound **8**: the pure product was obtained as a pale yellow foam (0.83 g) in 69.7% yield, mp 80–82 °C, $[\alpha]_D^{20} = +81.1$ (c 0.074, $CHCl_3$); IR (KBr, cm^{-1}): ν 3412, 3308, 3078, 3056, 2973, 2932, 2867, 2361, 2330, 1704, 1649, 1525, 1447, 1385, 1366, 1281, 1249, 1168, 1106, 1051, 1022, 883, 840, 789, 733. ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm): 8.34–8.32 (m, 2H, An-H), 8.26–8.01 (m, 4H, An-H), 7.94–7.91 (m, 4H, An-H), 7.65 (s, 2H, CONH), 7.53–7.39 (m, 8H, An-H), 5.62 (d, J = 7.8 Hz NHBoc), 4.59 (s, 2H, An-CH_2), 4.45 (s, 2H, An-CH_2), 4.12 (br s, 1H, chiral H), 3.38 (br s, 2H, CH_2), 2.98–2.90 (m, 4H, CH_2), 2.76–2.54 (m, 6H, CH_2), 2.11–1.93 (m, 4H, CH_2), 1.39 (d, J = 7.8 Hz, Boc-CH_3). ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm): 172.9, 172.1, 156.1, 131.7, 131.5, 131.2, 130.5, 129.5, 127.6, 126.5, 125.3, 124.3, 124.2, 79.8, 77.9, 77.7, 77.5, 77.1, 54.2, 48.9, 48.3, 45.8, 39.1, 38.2, 32.7, 29.6, 28.8, 28.6. Elemental Anal. Calcd for $C_{46}H_{53}N_5O_4$: C, 74.67; H, 7.22; N, 9.46. Found: C, 74.44; H, 7.26; N, 9.32.

4.2.4. General synthesis of receptors 1 and 2

Compound **7** (0.40 g, 0.56 mmol) or **8** (0.40 g, 0.54 mmol) was dissolved in 2 mL dry chloroform, after adding trifluoroacetic acid (0.30 g, 2.6 mmol), the mixture was stirred for 1 h at room temperature. The solvent and excess trifluoroacetic acid were evaporated in reduced pressure to afford the TFA salt as pale yellow oil. The TFA salt was then dissolved in 10 mL of chloroform, 1 mL Et_3N was added and stirred for 10 min. The mixture was then poured into water and extracted with chloroform; the organic layer was dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. The residue was then purified on a column of silica gel using $CHCl_3$/MeOH/$NH_3{\cdot}H_2O$ (100:10:1) as eluent to obtain pure products **1** and **2**, respectively.

Receptor **1**: the pure product was obtained as a pale yellow solid (0.32 g) in 93.2% yield, mp 74–76 °C, $[\alpha]_D^{20} = -114.2$ (*c* 0.061, $CHCl_3$); IR (KBr, cm^{-1}): *ν* 3412, 3350, 3305, 3081, 3052, 2928, 2840, 1937, 1647, 1551, 1525, 1445, 1384, 1330, 1256, 1155, 1116, 1027, 887, 867, 844, 789, 733. ^{1}H NMR ($CDCl_3$, 300 MHz) *δ* (ppm): 8.40 (s, 2H, An-H), 8.20 (d, *J* = 8.7 Hz, 4H, An-H), 8.00 (d, *J* = 7.8 Hz, 4H, An-H), 7.62 (s, 1H, CONH), 7.52–7.28 (m, 8H, An-H), 7.17 (s, 1H, CONH), 4.67 (s, 2H, An-CH_2), 4.63 (s, 2H, An-CH_2), 3.19 (br s, 1H, chiral H), 3.11–2.72 (m, 8H, CH_2), 2.11–1.81 (m, 4H, CH_2). ^{13}C NMR ($CDCl_3$, 75 MHz) *δ* (ppm): 175.0, 173.0, 131.6, 131.2, 130.3, 129.5, 127.7, 126.5, 125.3, 124.1, 54.6, 49.4, 49.1, 46.1, 45.4, 45.2, 38.8, 33.0, 31.4. MS *m*/*z* (%): 612 (M^++1, 100%). Elemental Anal. Calcd for $C_{39}H_{41}N_5O_2$: C, 76.55; H, 6.77; N, 11.45. Found: C, 76.32; H, 6.81; N, 11.32.

Receptor **2**: the pure product was obtained as a pale yellow solid (0.28 g) in 81.1% yield, mp 82–84 °C, $[\alpha]_D^{20} = +109$ (*c* 0.064, $CHCl_3$); IR (KBr, cm^{-1}): *ν* 3284, 3055, 2932, 2852, 1941, 1809, 1648, 1547, 1446, 1384, 1331, 1260, 1202, 1178, 1158, 1107, 1031, 949, 887, 842, 790.4, 733.5. ^{1}H NMR ($CDCl_3$, 300 MHz) *δ* (ppm): 8.39 (s, 2H, An-H), 8.31 (d, *J* = 7.8 Hz, 4H, An-H), 7.99 (d, *J* = 8.1 Hz, 4H, An-H), 7.67 (s, 2H, CONH), 7.55–7.42 (m, 8H, An-H), 4.72 (s, 4H, An-CH_2), 3.26 (m, 4H, CH_2), 3.09 (br s, 1H, chiral H), 2.99–2.87 (m, 8H, CH_2), 2.08–1.66 (m, 4H, CH_2). ^{13}C NMR ($CDCl_3$, 75 MHz) *δ* (ppm):169.8, 167.9, 129.1, 126.4, 125.7, 125.3, 124.2, 122.6, 122.1, 121.3, 120.1, 118.9, 53.9, 49.3, 43.5, 43.0, 41.0, 40.5, 33.5, 32.6, 27.7, 26.0, 24.3, 23.7. MS *m*/*z* (%): 640 (M^++1, 100%). Elemental Anal. Calcd for $C_{41}H_{45}N_5O_2$: C, 76.95; H, 7.10; N, 10.95. Found: C, 76.82; H, 7.15; N, 10.88.

Synthesis of complex **1**-Cu^{2+}: compound **1** (0.20 g, 0.33 mmol) was dissolved in 10 mL dry methanol, Copper perchloride (0.15 g, 0.40 mmol) in 5 mL of methanol was added dropwise to the solution. The blue solid was precipitated and collected by filtration.

The ESI-MS of complex **1**-Cu^{2+} was taken in methanol and shows a peak at 874 (*m*/*z*), which demonstrating a structure of $[Cu^{II}(l)](ClO_4)_2$.

4.3. Tetrabutylammonium salts

The tetrabutylammonium salts were prepared by adding 2 equiv of tetrabutylammonium hydroxide in methanol to a solution of the dicarboxyl acid and 1 equiv to the monocarboxyl acid derivatives in methanol. The mixture was stirred at room temperature for 4 h and evaporated to dryness under reduced pressure. The residue was dried at high vacuum for 24 h and then stored in a desiccator.

4.4. Binding studies

The study of binding properties was carried out in the aqueous Tris–HCl buffer (0.05 M. pH 7.4, v(MeOH):v(H_2O) = 1:1, 0.1 M NaCl). The fluorescence and UV–vis titration were performed with a series of 5×10^{-5} mol L^{-1} solutions of the receptors. The complex **1**-Cu^{2+} or **2**-Cu^{2+} was tested by adding 1.0 equiv of Cu^{2+} to the solution of receptor **1** or **2**, respectively. Association constants were calculated by means of a non-linear least-square curve fitting with ORIGIN 7.0 (Origin-Lab Corporation).

Acknowledgement

We thank the National Natural Science Foundation for financial support (Grant No. 20572080).

References

1. (a) Beer, P. D.; Hayes, E. J. *Coord. Chem. Rev.* **2003**, *240*, 167–189; (b) Beer, P. D.; Gale, P. A. *Angew. Chem., Int. Ed.* **2001**, *40*, 486–516; (c) Gale, P. A. *Coord. Chem. Rev.* **2003**, *240*, 17–55; (d) Fabbrizi, L.; Licchelli, M.; Taglitti, A. *Dalton Trans.* **2003**, 3417–3479; (e) Zhang, X. X.; Bradshaw, J. S.; Izatt, R. M. *Chem. Rev.* **1997**, *97*, 3313; (f) Schmidtchen, F. P. *Top. Curr. Chem.* **2005**, *255*, 1–29; (g) Murakakami, Y.; Kikuchi, J.; HIsaeda, Y.; Hayahsida, O. *Chem. Rev.* **1996**, *96*, 721–758; (h) Philp, D.; Stoddart, J. F. *Angew. Chem., Int. Ed.* **1996**, *35*, 1155–1196; (i) Izatt, R. M.; Pawlak, K.; Bradshaw, J. S.; Bruening, R. L. *Chem. Rev.* **1995**, *95*, 2529–2586; (j) Naemura, K.; Tobe, Y.; Kaneda, T. *Coord. Chem. Rev.* **1996**, *148*, 199–219.
2. (a) Ragusa, A.; Rossi, S.; Hayes, J. M.; Stein, M.; Kilburn, J. D. *Chem. Eur. J.* **2005**, *11*, 5674–5688; (b) Yang, D.; Li, X.; Fan, Y. F.; Zhang, D. W. *J. Am. Chem. Soc.* **2005**, *127*, 7996–7997; (c) Rossi, S.; Kyne, G. M. D.; Turner, L.; Wells, N. J.; Kilburn, J. D. *Angew. Chem., Int. Ed.* **2002**, *41*, 4233–4236; (d) Wong, W. L.; Huang, K. H.; Teng, P. F.; Lee, C. S.; Kwong, H. L. *Chem. Commun.* **2004**, 384–385; (e) Li, Z. B.; Pu, L. *J. Mater. Chem.* **2005**, *15*, 2860–2864.
3. (a) Ma, F.; Shen, L.; Ai, X.; Zhang, C. *Org. Lett.* **2007**, *9*, 125–127; (b) Qing, G. Y.; He, Y. B.; Zhao, Y.; Hu, C. G.; Liu, S. Y.; Yang, X. *Eur. J. Org. Chem.* **2006**, 1574–1580; (c) Qin, H.; He, Y.; Hu, C.; Chen, Z.; Hu, L. *Tetrahedron: Asymmetry* **2007**, *18*, 1769–1774; (d) Gasparrini, F.; Misiti, D.; Pierini, M.; Villani, C. *Org. Lett.* **2002**, *4*, 3993–3996; (e) Martínez, R.; Sancenón, F. *Chem. Rev.* **2003**, *103*, 4419–4476.
4. (a) Wang, H.; Chan, H. W.; Lee, A. W. *Org. Biomol. Chem.* **2008**, *6*, 929–934; (b) Qing, G. Y.; He, Y. B.; Chen, Z. H.; Wu, X. J.; Meng, L. Z. *Tetrahedron: Asymmetry* **2006**, *17*, 1769–1774; (c) Xu, K. X.; He, Y. B.; Qin, H. J.; Qing, G. Y.; Liu, S. Y. *Tetrahedron: Asymmetry* **2005**, *16*, 3042–3048; (d) Xu, K. X.; Wu, X. J.; He, Y. B.; Liu, S. Y.; Qing, G. Y.; Meng, G. Y. *Tetrahedron: Asymmetry* **2005**, *16*, 833–839.
5. (a) Gunnaugsson, T.; Glynn, M.; Tocci, G. M.; Kruger, P. E.; Pfeffer, F. M. *Coord. Chem. Rev.* **2006**, *250*, 3094–3117; (b) Liu, S. Y.; Fang, L.; He, Y. B.; Chan, W. H.; Yeung, K. T.; Cheng, Y. K.; Yang, R. H. *Org. Lett.* **2005**, *7*, 5825–5828; (c) Arimori, S.; Bell, M. L.; Oh, C. S.; James, T. D. *Org. Lett.* **2002**, *4*, 4249.
6. (a) Peczuh, M. W.; Hamilton, A. D. *Chem. Rev.* **2000**, *100*, 2479–2494; (b) Zhang, T.; James, T. D. *Org. Lett.* **2007**, *9*, 1627–1629.
7. (a) Liu, Y.; Song, Y.; Chen, Y.; Li, X. Q.; Ding, F.; Zhong, R. Q. *Chem. Eur. J.* **2004**, *14*, 3685–3696; (b) Shinoda, S.; Okazaki, T.; Player, T. N.; Misaki, H.; Hori, K.; Tsukube, H. *J. Org. Chem.* **2005**, *70*, 1835–1843.
8. (a) Gonzalez-Alvarez, A.; Afonso, I.; Diaz, P.; Garcia-Espana, E.; Gotor, V. *Chem. Commun.* **2006**, 1227–1229; (b) Barzzicalupi, C.; Bencini, A.; Bianchi, A.; Borsari, L.; Giorgi, C.; Valtancoli, B. *J. Org. Chem.* **2005**, *70*, 4257–4266.
9. (a) Zhao, J.; Fyles, T. M.; James, T. D. *Angew. Chem., Int. Ed.* **2004**, *43*, 3461–3464; (b) Zhao, J.; Davidson, M. G.; Mahon, M. F.; Kociok-Kohn, G.; James, T. D. *J. Am. Chem. Soc.* **2004**, *126*, 16179–16186; (c) Yang, W.; Yan, J.; Springsteen, G.; Deeter, S.; Wang, B. *Bioorg. Med. Lett.* **2003**, *13*, 1019–1022.
10. (a) Han, M. S.; Kim, D. H. *Angew. Chem., Int. Ed.* **2002**, *41*, 3809–3811; (b) Fabbrizzi, L.; Marcotte, N.; Stomeo, F.; Tagnietti, A. *Angew. Chem., Int. Ed.* **2002**, *41*, 3811–3814; (c) Shao, N.; Jin, J. Y.; Cheung, S. M.; Yang, R. H.; Chan, W. H.; Mo, T. *Angew. Chem., Int. Ed.* **2006**, *45*, 4944–4948; (d) O'Neil, E. J.; Smith, B. D. *Coord. Chem. Rev.* **2006**, *250*, 3068–3080.
11. Wu, J. S.; Wang, F.; Liu, W. M.; Wang, P. F.; Wu, S. K.; Wu, X.; Zhang, X. H. *Sens. Actuators, B* **2007**, *125*, 447–452.
12. (a) Lavigne, J. J.; Anslyn, E. V. *Angew. Chem., Int. Ed.* **1999**, *38*, 3666–3669; (b) Gray, C. W.; Houston, T. A. *J. Org. Chem.* **2002**, *67*, 5426–5428.
13. Lee, D. H.; Kim, S. Y.; Hong, J. *Angew. Chem., Int. Ed.* **2004**, *43*, 4777–4780.
14. (a) Jose, D. A.; Mishra, S.; Ghosh, A.; Shrivastav, A.; Mishra, S.; Das, A. *Org. Lett.* **2007**, *9*, 1979–1982; (b) Li, C.; Numata, M.; Takeuchi, M.; Shinka, S. *Angew. Chem., Int. Ed.* **2005**, *44*, 6371–6374.
15. (a) Zhang, T.; Anslyn, E. V. *Org. Lett.* **2006**, *8*, 1649–1652; (b) Yang, W.; Yan, J.; Fang, H.; Wang, B. *Chem. Commun.* **2003**, 792–793.
16. Hayashida, O.; Ogawa, N.; Uchiyama, M. *J. Am. Chem. Soc.* **2007**, *129*, 13698–13705.
17. (a) Kim, H. J.; Asif, R.; Chung, D. S.; Hong, J. I. *Tetrahedron lett.* **2003**, *44*, 4335–4338; (b) Folmer-Andersen, J. F.; Lynch, V. M.; Anslyn, E. V. *J. Am. Chem. Soc.* **2005**, *127*, 7986–7987.
18. (a) Liu, X. X.; Zheng, Y. S. *Tetrahedron Lett.* **2006**, *47*, 6357–6360; (b) Ma, F.; Ai, L.; Shen, X.; Zhang, C. *Org. Lett.* **2007**, *9*, 125–127; (c) Chen, Z. H.; He, Y. B.; Hu, C. G.; Huang, X. H.; Hu, L. *Aust. J. Chem.* **2008**, *61*, 310–315.
19. (a) Cheung, S. M.; Chan, W. H. *Tetrahedron* **2006**, *62*, 8379–8383; (b) Moletti, A.; Coluccini, C.; Pasini, D.; Taglietti, A. *Dalton Trans.* **2007**, 1588–1592; (c) Shiraishi, Y.; Kohno, Y.; Hirai, T. *J. Phys. Chem. B* **2005**, *109*, 19139–19147; (d) Shiraishi, Y.; Kohno, Y.; Hirai, T. *Ind. Eng. Chem. Res.* **2005**, *44*, 847–851.