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Fluorescent sensors for amino acid anions based on calix[4]arenes bearing two dansyl groups

Shun-ying Liu, Yong-bing He,* Guang-yan Qing, Kuo-xi Xu and Hai-juan Qin

Department of Chemistry, Wuhan University, Wuhan, Hubei 470072, China

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Abstract—Two novel types of chiral calix[4]arenes containing hydrazide and dansyl groups were synthesized and examined for their enantioselective recognition abilities by the fluorescence and ^{1}H NMR spectra in $CHCl_3$. The results indicate that both **4a** and **4b** have excellent enantioselectivities to the *N*-protected alanine or phenylalanine anions.

1. Introduction

Molecular recognition, and in particular chiral recognition, is one of the most fundamental and significant processes in living systems.[1] Chiral recognition can contribute to the understanding of biochemical systems and offer new perspectives for the development of pharmaceuticals, enantioselective sensors, catalysts, and other molecular devices.[2]

Among the several kinds of host molecule for recognition, calixarenes offer a number of advantages in terms of selectivity and efficiency of binding.[3] The introduction of an amino acid could lead to the chirality of the artificial receptors. Due to the important role played by amino acid units in several recognition processes of natural and artificial systems,[4] chiral discrimination,[5] and stereoselective synthesis, synthetic calix[4]arenes containing amino acid have been extensively studied.[6]

For the molecular designs of chemosensors, that is, how to achieve the specific recognition of a certain molecule and how to transduce the recognition event into a signal are crucial points. Fluorescent molecular sensors for the detection of ions or molecules have attracted considerable interest because of their high sensitivity and potential applications in analytical, biological, and clinical biochemical environments.[7] Chiral recognition in luminescence has been studied over the past two decades.[8] Molecule-based fluorescent sensors are generally composed of a fluorophore and a binding site. By introducing chirality into the binding site, the resulting fluorescent sensor can carry out the enantioselective recognition of chiral molecules. The dansyl group is an excellent fluorophore[9] and hydrazide is valuable as binding site.[10] Only a few samples containing dansyl groups based on calix[4]arenes for cations have so far been reported.[11]

To the best of our knowledge, chiral calix[4]arenes acting as enantioselective fluorescent sensors for amino acid anions have hardly been reported. Herein, we report the synthesis of novel chiral calix[4]arene containing hydrazide and dansyl groups, and found that these chiral artificial receptors exhibit excellent enantioselective recognition toward amino acid anions.

2. Results and discussion

2.1. Synthesis

The synthetic route of receptors **4a** and **4b** is shown in Scheme 1. The intermediates **2a**, **2b**, **3a**, and **3b** were all obtained in high yield (79–93%). Compounds **3a** and **3b** were allowed to react with dansyl chloride and give target molecules **4a** and **4b**. Receptors **4a** and **4b** are easily soluble in common organic solvents, such as $CHCl_3$, CH_3OH, DMSO, and DMF.

The stereogenic centers of receptors **4a** and **4b** disturb the planar symmetry of the parent rings, which results

* Corresponding author. Fax: +86 27 68754076; e-mail: ybhe@whu.edu.cn

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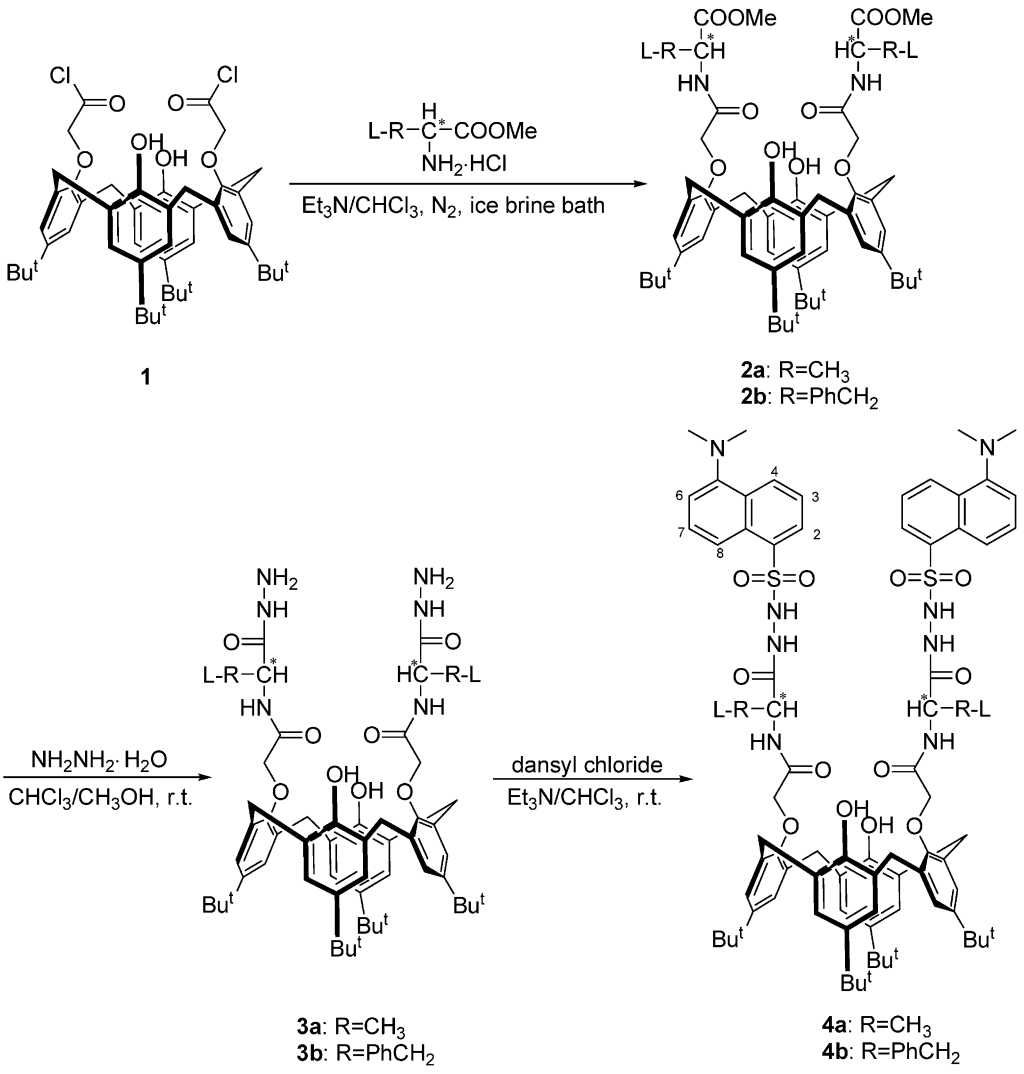

Scheme 1. Synthesis of receptors **4a** and **4b**.

in more aromatic carbon signals appearing in the ^{13}C NMR spectra of receptors **4a** and **4b**. This pattern is similar to that which has been observed in other chiral calix[4]arenes.[12] The ^{1}H NMR spectra of **4a** and **4b** show two sets of AB quartets for the bridging methylene protons and two sets of singlets for the *tert*-butyl group. This indicates that the two receptors are in the cone conformation in $CHCl_3$. The ^{1}H NMR spectra of **4a** and **4b** also exhibit one set of doublets for the $ArOCH_2$ protons. This splitting pattern may relate to the introduction of the chiral moieties in the molecules, as seen in other chiral calix[4]arenes.[12]

2.2. Fluorescence spectra

In order to investigate the properties of the chiral recognition of **4a** and **4b**, Boc alanine and phenylalanine tetrabutylammonium salts (L-Ala anions, D-Ala anions, L-Phe anions, and D-Phe anions) were chosen as the guests, which could increase the reaction between the receptor and guest by hydrogen bondings. The amino group was protected by di-*tert*-butyldicarbonate.

The fluorescence spectra of receptor **4a** were studied from a solution (5.0×10^{-5} mol L^{-1}) of **4a** in $CHCl_3$ in the absence and presence of various enantiomers, D-, L-Ala, and Phe anions. Upon addition of D- or L-amino acid anions, the different fluorescent quenching degree of **4a** was observed. The quenching efficiencies of L-amino acid anions were much higher than the D-amino acid anions. Figures 1 and 2 show fluorescence emission spectra of **4a** (at 515 nm) and its L- or D-Ala anions complexes following excitation at 361 nm, respectively. The graph in the top right corner of Figure 1 illustrates the fluorescence intensity change of receptor **4a** upon addition of L-Ala anions at 515 nm. Upon addition of L-Ala anions, the fluorescent intensity of **4a** was decreased gradually with a slight blue shift. While adding D-Ala anions to the solution of **4a**, no blue shift was observed. The quenching efficiency was 50% by 100 equiv of L-Ala anions while it was 10% by 100 equiv of D-Ala anions. The different quenching efficiencies ($\Delta I_L/\Delta I_D = 5.0$) indicate that receptor **4a** has a good enantioselective recognition between L- and D-Ala anions. When upon addition of 100 equiv of L-Phe anions or D-Phe anions

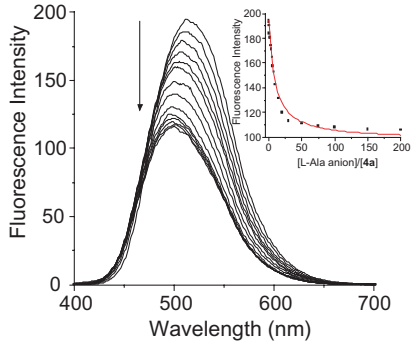

Figure 1. Fluorescence spectra of receptor **4a** ($CHCl_3$, 5.0×10^{-5} mol L^{-1}) upon the addition of various amounts of L-Ala anions in $CHCl_3$. Equivalents of L-Ala anions: 0, 2, 4, 6, 8, 10, 15, 20, 30, 50, 75, 100, 150, and 200. λ_{ex} = 361 nm.

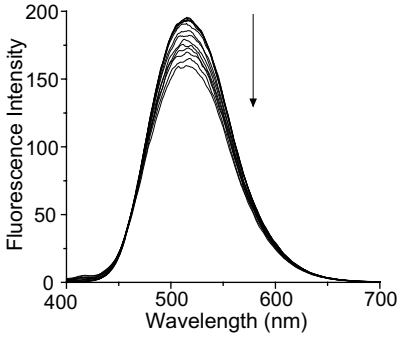

Figure 2. Fluorescence spectra of receptor **4a** ($CHCl_3$, 5.0×10^{-5} mol L^{-1}) upon the addition of various amounts of D-Ala anions in $CHCl_3$. Equivalents of D-Ala anions: 0, 2, 4, 6, 8, 10, 20, 40, 60, 100, 150, 200, 250, and 300. λ_{ex} = 361 nm.

to a solution (5.0×10^{-5} mol L^{-1}) of **4a**, the enantioselectivity fluorescence response was 2.5 ($\Delta I_L/\Delta I_D$).

Similar phenomena were observed when L- or D-Ala and Phe anions were added into a solution (5.0×10^{-5} mol L^{-1}) of **4b**. The emission spectra of **4b** appeared at 517 nm when it was excited at 363 nm. The quenching efficiencies of receptor **4b** were 46% and 43% by 100 equiv of L-Ala and L-Phe anions with a slight blue shift while 8% and 17% by D-Ala and D-Phe anions with no blue shift in $CHCl_3$. Enantioselective fluorescence responses were observed, which gave $\Delta I_L/\Delta I_D = 5.7$ for Ala anions and $\Delta I_L/\Delta I_D = 2.5$ for Phe anions.

Upon the addition of 500 equiv of the *N*-protected Ala or Phe derivatives (not as tetrabutylammonium salts) into a solution of **4a** or **4b** in $CHCl_3$, the fluorescence intensity of **4a** or **4b** was slightly quenched (about 10%) by both L- and D-amino acid derivatives. This indicates that hydrogen bonding plays an important role in the interaction between the host and guest and leads to the easier signal transductions of chiral recognition by fluorescence method.

In the presence of amino acid anions, the fluorescence quenching of receptors **4a** and **4b** most likely arises from the change of the free energy (ΔG_{PET}) of electron transfer between the excited fluorophore and the receptor.[13] When the anion was introduced into a solution of either receptor **4a** or **4b**, the reductive potential of the amide group increased along with the ratio of the electron transfer from the HOMO orbit of the receptors to the excited naphthalene group, which in turn leads to the intramolecular PET (photo-induced electron transfer) process being more easy.[7a,14]

Assuming the complex stoichiometry was 1:1, then the complexation of guest *N*-protected amino acid anions (G) with host calix[4]arene derivatives (H) could be expressed by Eq. 1. The association constant (K_{ass}) of the complex was calculated from the changes in fluorescence intensity (I) of host upon stepwise addition of G to the solution of host in $CHCl_3$, using the nonlinear least squares method.[15]

$$I = I_0 + \frac{I_{lim} - I_0}{2c_0}\left\{c_H + c_G + 1/K_{ass} - \left[(c_H + c_G + 1/K_{ass})^2 - 4c_H c_G\right]^{1/2}\right\} \quad (1)$$

where I represents the fluorescence intensity; I_0 represents the fluorescence intensity of pure host; c_H and c_G are the corresponding concentrations of host and guest and K_{ass} is the association constant. The nonlinear curve fitting results of the fluorescence intensity (at 515 nm for **4a** and 517 nm for **4b**) of the interaction between **4a** or **4b** and L-, D-amino acid anions are shown in Table 1. The fitting curves all have large correlation coefficients (R >0.99), which indicate that the 1:1 complex between **4a** or **4b** and the amino acid anion has been formed.[15,16] According to Table 1, both **4a** and **4b** have good enantioselectivities to Ala and Phe anions. Compound **4a** gives an enantioselectivity $K_{ass(L\text{-Phe})}/K_{ass(D\text{-Phe})} = 10$. The association constants of **4a** or **4b** with L-amino acid anions are much higher than that of **4a** or **4b** with D-amino acid

Table 1. Association constants K_{ass} (M^{-1}) of receptors **4a** and **4b** with amino acid anions

N-protected amino acid anions	**4a**		**4b**	
	K_{ass} (M^{-1})	R	K_{ass} (M^{-1})	R
L-Ala[a]	$(2.30 \pm 0.19^{b}) \times 10^4$	0.9941	$(1.08 \pm 0.14^{b}) \times 10^3$	0.9995
D-Ala[a]	[c]		[c]	
L-Phe[a]	$(1.32 \pm 0.14^{b}) \times 10^4$	0.9904	$(1.94 \pm 0.15^{b}) \times 10^3$	0.9938
D-Phe[a]	$(1.01 \pm 0.13^{b}) \times 10^3$	0.9912	$(0.73 \pm 0.06^{b}) \times 10^3$	0.9963

[a] The anions were used as their tetrabutylammonium salts.
[b] All error values were obtained by the results of nonlinear curve fitting.
[c] The association constants are too small to calculate.

anions, which is probably due to the L-amino acid anions having a more complementary structure with receptors **4a** and **4b**. Due to the receptors having a good preorganization property and relative rigidity structure, receptors **4a** and **4b** showed a high enantioselective recognition for L- and D-Ala anions.[17] However because of the π–π stack interactions of the aryl rings between the host and the guest, **4a** and **4b** showed relatively lower enantioselective recognitions for L- and D-Phe anions. At the same time, the association constants of **4a** with amino acid anions are higher than that of **4b**. This is perhaps due to the bigger steric hindrance of **4b** over that of **4a**.

2.3. ^{1}H NMR study

Preliminary experiments were undertaken to confirm the enantioselective recognition properties of receptors **4a** and **4b** by ^{1}H NMR in $CDCl_3$ at room temperature. The spectra of receptors **4a** and its complex with equimolar amounts of racemic Ala or Phe anions are shown in Figure 1. When treated with equimolar amounts of receptor **4a**, the CH proton of racemic Ala anion cleaved into more complicated signals (Fig. 3C) with a downfield shift (from δ 3.91 to 4.04) while that of the host with an upfield shift (from δ 4.76 to 4.64). When

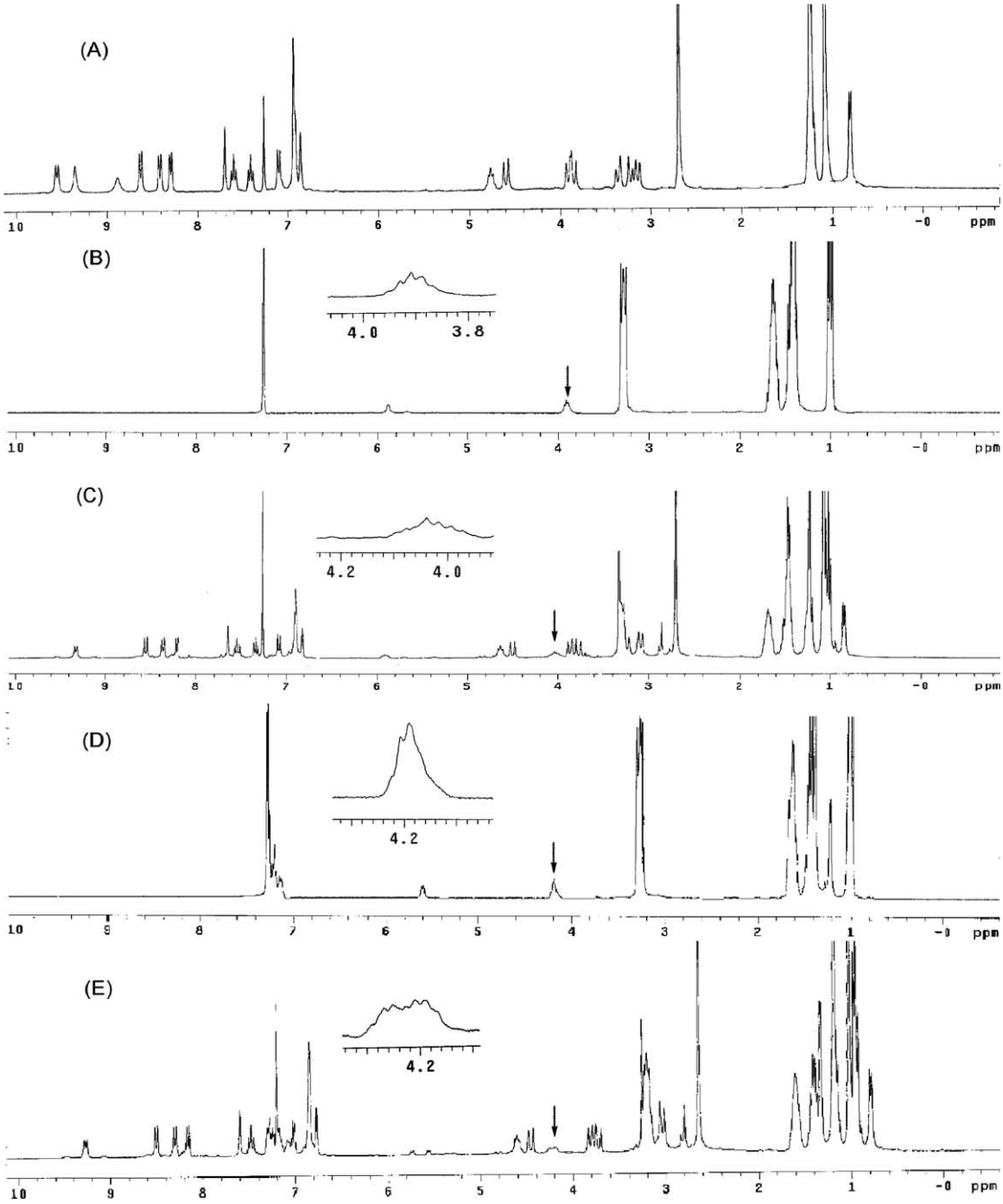

Figure 3. The ^{1}H NMR spectra of receptor **4a** and its guest complex at 25 °C in $CDCl_3$ at 300 MHz. (A) [**4a**] = 2.5×10^{-3} M; (B) [DL-Ala anion] = 2.5×10^{-3} M; (C) [**4a**] = [DL-Ala anion] = 2.5×10^{-3} M; (D) [DL-Phe anion] = 2.5×10^{-3} M; (E) [**4a**] = [DL-Phe anion]=2.5×10^{-3} M. The arrow indicates the CH proton of DL-Ala anion and DL-Phe anion.

adding equimolar amounts of the racemic Phe anion to receptor **4a**, the CH proton of the racemic Phe anion cleaved into more complicated signals (Fig. 3E) with a slight downfield shift (from δ 4.20 to 4.25) while that of the host with an upfield shift (from δ 5.04 to 4.60). This confirmed further that the enantioselective recognition had happened between receptor **4a** and the Ala or Phe anion. Moreover, the signals of the NH proton of the hydrazide in the ^{1}H NMR spectra of receptor **4a** almost disappeared while the signals of other NH protons in receptor **4a** were shifted upfield (about $\Delta\delta$ = 0.3 ppm) with the addition of the guest. This indicated that the interaction between the host and guest also happened by multiple hydrogen bondings.

The similar phenomenon was observed when adding equimolar amounts of the racemic Ala or Phe anion to a solution of **4b** (Fig. 4). The signals of the CH proton of racemic Ala anion and Phe anion were observed with $\Delta\delta$ 0.12 and 0.10 downfield shift, respectively. The signal of the CH of **4b** had an upfield shift while the signals of the hydrazide protons disappeared when the guest was added.

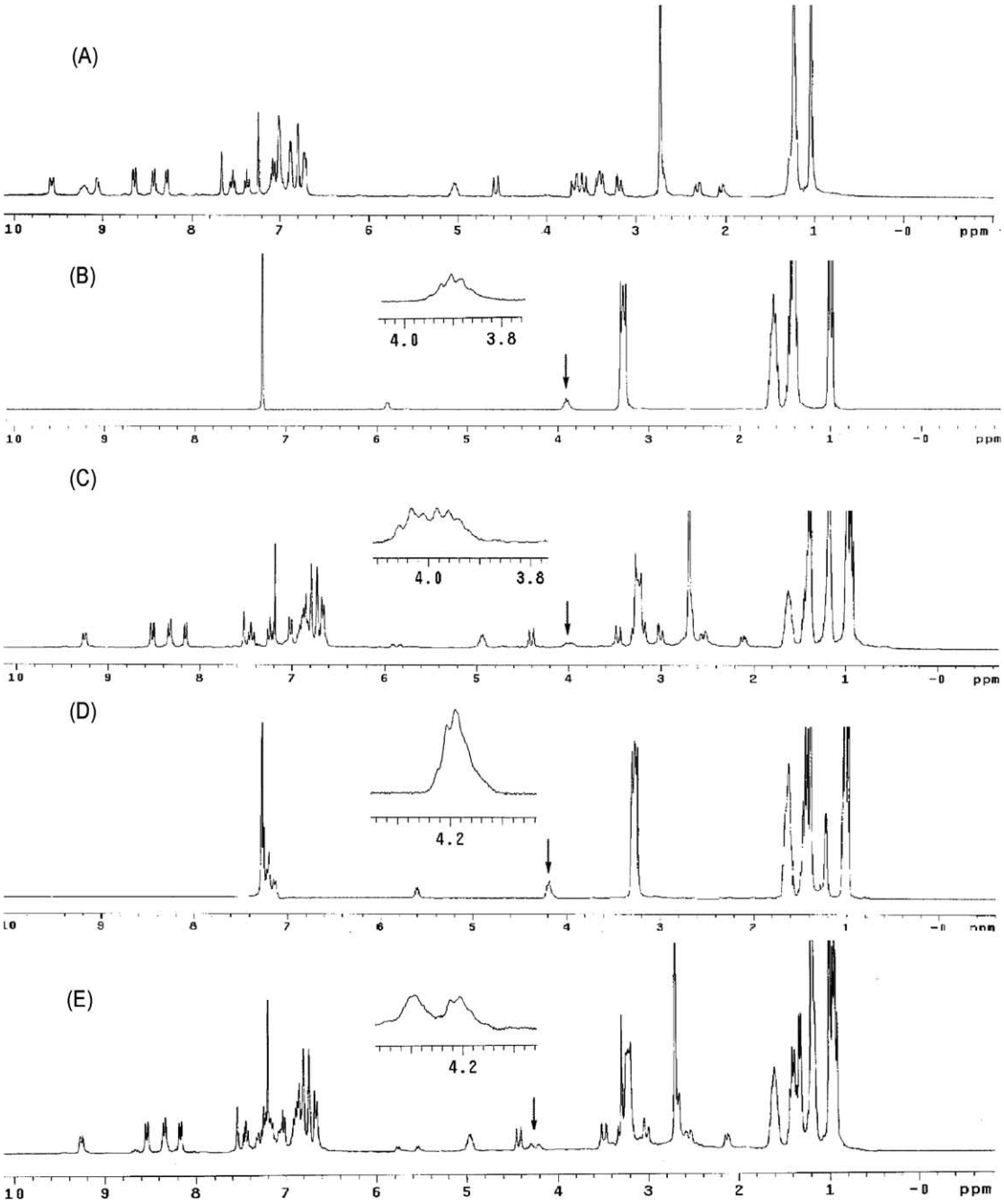

Figure 4. The ^{1}H NMR spectra of receptor **4b** and its guest complex at 25 °C in $CDCl_3$ at 300 MHz. (A) [**4b**] = 2.5×10^{-3} M; (B) [DL-Ala anion] = 2.5×10^{-3} M; (C) [**4b**] = [DL-Ala anion] = 2.5×10^{-3} M; (D) [DL-Phe anion] = 2.5×10^{-3} M; (E) [**4b**] = [DL-Phe anion] = 2.5×10^{-3} M. The arrow indicates the CH proton of DL-Ala anion and DL-Phe anion.

3. Conclusion

Chiral calix[4]arenes containing hydrazide and dansyl groups, were synthesized. The different fluorescence responses and the results of the ^{1}H NMR confirm that both **4a** and **4b** have a good enantiosensitive recognition for L-Ala or Phe anions. The selectivity of **4a** for amino acid anions is better than that of **4b**. It is clear that the cooperative act of the hydrazide and amide in the binding amino acid anion by multiple hydrogen bonds increases the ability of the chiral recognition of **4a** and **4b**. Receptors **4a** and **4b** are promising in their use as fluorescence sensors for chiral anions.

4. Experimental

4.1. General

Melting points were determined with a Reichert 7905 melting-point apparatus and are uncorrected. Optical rotations were taken on a Perkin–Elmer Model 341 polarimeter. IR spectra were obtained on a Nicolet 670 FT-IR spectrophotometer. ^{1}H NMR spectra were recorded in $CDCl_3$, with Me_4Si as the internal standard, on a Varian Mercury VX-300 MHz spectrometer and ^{13}C NMR spectra on a Varian Inova-600 MHz. Mass spectra were recorded on a Finnigan LCQ advantage mass spectrometer. Elemental analysis was determined with a Carlo-Erba 1106 instrument. Fluorescence spectra were obtained on a Shimadzu RF-5301 spectrometer. $CHCl_3$ and Et_3N were dried and distilled from CaH_2. All other commercially available reagents were used without further purification. Compounds **1**, amino acid methyl ether hydrochloride and the *N*-protected amino acid derivatives (by di-*tert*-butyldicarbonate) were synthesized according to the methods reported in the literature,[18–20] respectively.

4.2. Synthesis

General procedure for the synthesis of chiral calix[4]arene derivatives ***2***: To a solution of L-alanine methyl ether hydrochloride or L-phenylalanine methyl ether hydrochloride (3 mmol) and triethylamine (4 equiv for each amino acid methyl ether hydrochloride) in dry $CHCl_3$ (30 mL), **1** (0.5 equiv for each amino acid methyl ether hydrochloride) in dry $CHCl_3$ (20 mL) was dropwise added in ice brine bath under nitrogen atmosphere. After addition, the reaction mixture was stirred at 0 °C for 1 h and then the ice brine bath was removed and kept stirring overnight at room temperature. Then the reaction solution was washed with a dilute aqueous solution of hydrogen chloride (10%), sodium hydrogen carbonate (10%), and brine, respectively. The organic layer was collected and dried over anhydrous Na_2SO_4. After filtration, the solvent was removed under reduced pressure, and the residue purified by column chromatography on silica gel.

4.2.1. 5,11,17,23-Tetra-4-*tert*-butyl-25,27-bis(L-alaninemethylester-*N*-carbonylmethoxy)-26,28-dihydroxycalix[4]arene 2a. Pure product was obtained by column chromatography on silica gel (eluant: $CHCl_3$/CH_3CH_2OH = 100:1 (v/v)) as a white powder (1.30 g) in 93% yield; mp 120–122 °C. IR (KBr/cm^{-1}) *v*: 3423, 3346, 2958, 1751, 1685, 1541, 1484, 1458, 1207, 1159, 1125, 1039, 871; ^{1}H NMR ($CDCl_3$): δH 1.08 (s, 18H, Bu^t), 1.28 (s, 18H, Bu^t), 1.48 (d, *J* = 6.9 Hz, 6H, CCH_3), 3.43, (d, *J* = 13.5 Hz, 2H, $ArCH_2Ar$), 3.47 (d, *J* = 13.5 Hz, 2H, $ArCH_2Ar$), 3.69 (s, 6H, OCH_3), 4.16 (d, *J* = 13.5 Hz, 2H, $ArCH_2Ar$), 4.31 (d, *J* = 13.5 Hz, 2H, $ArCH_2Ar$), 4.53 (d, *J* = 15.3 Hz, 2H, OCH_2CO), 4.67–4.75 (m, 4H, NCHCO and OCH_2CO), 6.95 (d, *J* = 5.1 Hz, 4H, ArH), 7.07 (d, *J* = 5.1 Hz, 4H, ArH), 7.97 (s, 2H, ArOH), 9.46 (d, *J* = 7.5 Hz, 2H, NH).

4.2.2. 5,11,17,23-Tetra-4-*tert*-butyl-25,27-bis(L-phenylalaninemethylester-*N*-carbonylmethoxy)-26,28-dihydroxycalix[4]arene 2b. Pure product was obtained by column chromatography on silica gel (eluant: $CHCl_3$/CH_3CH_2OH = 200:3 (v/v)) as a white powder (1.45 g) in 89% yield; mp 100–102 °C. IR (KBr/cm^{-1}) *v*: 3433, 3313, 3031, 2958, 1750, 1677, 1529, 1484, 1458, 1438, 1206, 1124, 1044, 871, 699; ^{1}H NMR ($CDCl_3$): δH 1.08 (s, 18H, Bu^t), 1.21 (s, 18H, Bu^t), 2.90–3.02 (m, 6H, $ArCH_2Ar$ and $ArCH_2$ CH), 3.41 (d, 2H, $ArCH_2Ar$), 3.54 (s, 6H, OCH_3), 3.94–4.06 (m, 6H, OCH_2CO and $ArCH_2Ar$), 4.92–5.02 (m, 4H, NCHCO and OCH_2CO), 6.77–6.93 (m, 18H, ArH), 7.74 (s, 2H, ArOH), 9.46 (d, *J* = 8.1 Hz, 2H, NH).

General procedure for preparing the hydrazide derivatives ***3***: To a solution (30 mL) of **2a** or **2b** (1.5 mmol) in $CHCl_3$/CH_3OH [1:2 (v/v)], hydrazine hydrate (4 equiv for **2a** or **2b**) was added. The reaction was stirred for 24 h at room temperature. Then the solvent was evaporated under reduced pressure and water (20 mL) poured into the residue. After filtration, the solid was dried in vacuum to obtain pure product.

4.2.3. 5,11,17,23-Tetra-4-*tert*-butyl-25,27-bis(hydrazide-L-alanine-*N*-carbonylmethoxy)-26,28-dihydroxycalix[4]arene 3a. The product was obtained as a white powder (1.22 g) in 87% yield; mp 144–146 °C. IR (KBr/cm^{-1}) *v*: 3432, 3316, 2960, 1750, 1676, 1536, 1484, 1458, 1207, 871; ^{1}H NMR ($CDCl_3$): δH 1.04 (s, 18H, Bu^t), 1.18 (s, 18H, Bu^t), 1.28 (d, *J* = 6.3 Hz, 6H, CCH_3), 3.23, (d, *J* = 13.8 Hz, 2H, $ArCH_2Ar$), 3.42 (d, *J* = 13.8 Hz, 2H, $ArCH_2Ar$), 4.09 (d, *J* = 15.0 Hz, 2H, OCH_2CO), 4.15–4.23 (m, 4H, $ArCH_2Ar$), 4.64–4.69 (m, 2H, NCHCO), 5.16 (d, *J* = 15.0 Hz, 2H, OCH_2CO), 6.87 (s, 4H, ArH), 6.96 (s, 4H, ArH), 8.24 (s, 2H, ArOH), 8.67 (s, 2H, CONHN), 9.85 (d, *J* = 8.4 Hz,2H, CONHC).

4.2.4. 5,11,17,23-Tetra-4-*tert*-butyl-25,27-bis(hydrazide-L-phenylalanine-*N*-carbonylmethoxy)-26,28-dihydroxycalix[4]arene 3b. The product was obtained as a white powder (1.28 g) in 79% yield; mp 128–130 °C. IR (KBr/cm^{-1}) *v*: 3432, 3316, 2958, 1750, 1677, 1529, 1484, 1458, 1439, 1363, 1207, 1124, 871, 699; ^{1}H NMR ($CDCl_3$): δH 1.13 (s, 18H, Bu^t), 1.21 (s, 18H, Bu^t), 2.80–3.02 (m, 4H, $ArCH_2$ CH), 3.16 (d, *J* = 12.9 Hz, 2H, $ArCH_2Ar$), 3.57, (d, *J* = 13.5 Hz, 2H, $ArCH_2Ar$), 4.01 (d, *J* = 15.0 Hz, 2H, OCH_2CO), 4.12 (d,

J = 12.9 Hz, 2H, $ArCH_2Ar$), 4.34, (d, J = 13.5 Hz, 2H, $ArCH_2Ar$), 4.80–4.84 (m, 2H, NCHCO), 5.23 (d, J = 15.0 Hz, 2H, OCH_2CO), 6.99–7.11 (m, 18H, ArH), 8.24 (br, 2H, CONHN), 8.45 (s, 2H, ArOH), 10.12 (d, J = 9.0 Hz, 2H, CONHC).

General procedure for preparing ***4***: To a solution of **3a** or **3b** (1.5 mmol) and triethylamine (4 equiv) in dry $CHCl_3$ (15 mL), dansyl chloride (2 equiv for **3a** or **3b**) in dry $CHCl_3$ (15 mL) was dropwise added. After addition, the reaction mixture was stirred at room temperature overnight and then washed with the aqueous solution of citric acid (10%), sodium hydrogen carbonate (10%), and brine, respectively. The organic layer was collected and dried over anhydrous Na_2SO_4. After filtration, the solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel.

4.2.5. 5,11,17,23-Tetra-4-*tert*-butyl-25,27-bis(*N*-(5-dimethylaminonaphthalene-1-sulfonyl)hydrazide-*N′*-L-alanine-*N″*-carbonylmethoxy)-26,28-dihydroxycalix[4]arene 4a. Pure product (0.73 g) was obtained by column chromatography on silica gel (eluant: $CHCl_3$/CH_3CH_2OH = 100:3 (v/v)) as a yellow powder in 35% yield; mp 200–202 °C; $[\alpha]_D^{20} = +8.7$ (c 0.5, $CHCl_3$); IR (KBr/cm^{-1})ν : 3428, 3290, 2958, 1655, 1484, 1458, 1341, 1203, 1166, 1148, 1047, 791; ^{1}H NMR ($CDCl_3$): δH 0.80 (d, J = 6.3 Hz, 6H, CCH_3), 1.08 (s, 18H, Bu^t), 1.20 (s, 18H, Bu^t), 2.69 (s, 12H, NCH_3), 3.13, (d, J = 15.3 Hz, 2H, OCH_2CO), 3.22 (d, J = 14.1 Hz, 2H, $ArCH_2Ar$), 3.35 (d, J = 14.1 Hz, 2H, $ArCH_2Ar$), 3.82–3.93 (m, 4H, $ArCH_2Ar$), 4.59 (d, J = 15.3 Hz, 2H, OCH_2CO), 4.74–4.79 (m, 2H, NCHCO), 6.86 (s, 2H, ArH), 6.93 (s, 6H, ArH), 7.10 (d, J = 7.5 Hz, 2H, H_6-naph), 7.41 (t, 2H, H_7-naph), 7.60 (t, 2H, H_3-naph), 7.70 (s, 2H, ArOH), 8.31 (d, J = 7.2 Hz, 2H, H_2-naph), 8.41 (d, J = 7.5 Hz, 2H, H_8-naph), 8.62 (d, J = 7.2 Hz, 2H, H_4-naph), 8.88 (br, 2H, CONHN), 9.35 (s, 2H, NNHS), 9.54 (d, J = 8.4 Hz,2H, CNHCO); ^{13}C NMR ($CDCl_3$): 171.5, 169.9, 149.9, 149.7, 147.9, 142.0, 133.2, 132.9, 132.7, 131.7, 131.4, 130.8, 129.6, 128.6, 127.0, 126.7, 125.7, 125.6, 125.2, 123.3, 115.2, 75.1, 46.3, 45.5, 34.3, 34.0, 32.5, 31.9, 31.3, 20.2; ESI-MS m/z (%): 1399 (M-1, 100); Elemental analysis calcd. (%) for $C_{78}H_{96}N_8O_{12}S_2$: C, 66.82; H, 6.92; N, 7.99; S, 4.56. Found: C, 66.75; H, 7.02; N, 7.89; S, 4.54.

4.2.6. 5,11,17,23-Tetra-4-*tert*-butyl-25,27-bis(*N*-(5-dimethylaminonaphthalene-1-sulfonyl)hydrazide-*N′*-L-phenylalanine-*N″*-carbonylmethoxy)-26,28-dihydroxycalix[4]arene 4b. Pure product (0.53 g) was obtained by column chromatography on silica gel (eluant: $CHCl_3$/CH_3CH_2OH = 100:3 (v/v)) as a yellow powder in 23% yield; mp 188–190 °C; $[\alpha]_D^{20} = -51.0$ (c 0.5, $CHCl_3$); IR (KBr/cm^{-1}) ν: 3415, 3287, 2957, 2867, 1701, 1655, 1536, 1483, 1458, 1342, 1203, 1166, 1248, 791; ^{1}H NMR ($CDCl_3$): δH 1.04 (s, 18H, Bu^t), 1.21 (s, 18H, Bu^t), 2.07 (d, J = 11.7 Hz, 2H, $ArCH_2CH$), 2.31 (d, J = 11.7 Hz, 2H, $ArCH_2CH$), 2.73 (s, 12H, NCH_3), 3.19, (d, J = 13.5 Hz, 2H, $ArCH_2Ar$), 3.22–3.46 (m, 4H, $ArCH_2Ar$), 3.60 (d, J = 14.7 Hz, 2H, OCH_2CO), 3.71 (d, J = 13.5 Hz, 2H, $ArCH_2Ar$), 4.58 (d, J = 14.7 Hz, 2H, OCH_2CO), 5.03–5.05 (m, 2H, NCHCO), 6.73–7.02 (m, 18H, ArH), 7.07 (d, J = 7.8 Hz, 2H, H_6-naph), 7.37 (t, 2H, H_7-naph), 7.53 (t, 2H, H_3-naph), 7.66 (s, 2H, ArOH), 8.28 (d, J = 7.5 Hz, 2H, H_2-naph), 8.43 (d, J = 7.8 Hz, 2H, H_8-naph), 8.63 (d, J = 7.5 Hz, 2H, H_4-naph), 9.06 (s, 2H, NNHS), 9.20 (br, 2H, CONHN), 9.57 (d, J = 9.0 Hz, 2H, CNHCO); ^{13}C NMR ($CDCl_3$): 171.7, 169.2, 149.9, 149.5, 147.8, 142.2, 135.9, 132.8, 132.7, 132.2, 131.5, 130.9, 129.7, 129.3, 128.6, 128.3, 126.9, 126.7, 126.1, 125.7, 124.9, 123.3, 115.2, 74.9, 50.0, 45.6, 38.9, 34.3, 34.0, 33.0, 32.5, 31.9, 31.3; ESI-MS m/z (%): 1551 (M−1, 100); Elemental analysis calcd. (%) for $C_{90}H_{104}N_8O_{12}S_2$: C, 69.55; H, 6.76; N, 7.21; S, 4.13. Found: C, 69.48; H, 6.81; N, 7.18; S, 4.08.

4.3. Tetrabutylammonium salts

All tetrabutylammonium salts were prepared by adding 1 equiv of tetrabutylammonium hydroxide in methanol to a solution of the corresponding *N*-protected (by Boc) amino acid derivatives (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, checked by NMR and stored in a desiccator.

4.4. Binding studies

The studies on the binding properties of **4a** and **4b** were carried out in $CHCl_3$ or $CDCl_3$. The fluorescence titration was performed with a series of 5×10^{-5} M solutions of receptor **4a** or **4b** containing different amounts of chiral anions (the excited wavelength was 361 or 363 nm, the excitation slit width was 1.5 nm and the emission slit width was 3 nm). ^{1}H NMR studies were recorded as adding equivalent racemic Ala or Phe anions into receptors (2.5×10^{-2} M).

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References

1. (a) Lehn, J.-M. *Supramolecular Chemistry. Concepts and Perspectives*; VCH: Weinheim, 1995; (b) Zhang, X. X.; Bradshaw, J. S.; Izatt, R. M. *Chem. Rev.* **1997**, *97*, 3313; (c) Finn, M. G. *Chirality* **2002**, *14*, 534.
2. (a) Murakami, Y.; Kikuchi, J.; Hisaeda, Y.; Hayashida, O. *Chem. Rev.* **1996**, *96*, 721; (b) Philp, D.; Stoddart, J. F. *Angew. Chem., Int. Ed.* **1996**, *35*, 1154.
3. (a) Roundhill, D. M. *Compr. Coord. Chem. II,* **2004**, *1*, 485; (b) Liu, S.-Y.; He, Y.-B.; Wu, J.-L.; Wei, L.-H.; Qin, H.-J.; Meng, L.-Z.; Hu, L. *Org. Biomol. Chem.* **2004**, *2*, 1552; (c) Liu, F.; Lu, G.-Y.; He, W.-J.; Liu, M.-H.; Zhu, L.-G. *Thin Solid Films* **2004**, *468*, 244; (d) Arturo, A.; Elisabetta, B.; Giovanna, G.; Andrea, P.; Andrea, S. *Tetrahedron* **2004**, *60*, 10747.
4. *Molecular Recognition: Chemical and Biochemical Problems*; Roberts, S. M. Ed.; RSC, Special Publication no.78, 1990.

5. (a) Pirkle, W. H.; Pochapsky, T. C. *Chem. Rev.* **1989**, *89*, 347; (b) Welch, J. C. *J. Chromatogr. A* **1994**, *666*, 3.
6. (a) Samsone, E.; Barboso, S.; Casnati, A.; Fabbi, M.; Pochine, A.; Ugozzdi, F.; Ungaro, R. *Eur. J. Org. Chem.* **1998**, 897; (b) Xu, X.; He, J.; Chan, A. S. C.; Han, X.; Cheng, J.-P. *Tetrahedron: Asymmetry* **1999**, *10*, 2685; (c) Xu, H.; Kinsel, G. R.; Zhang, J.; Rudkevich, D. M. *Tetrahedron* **2003**, *59*, 5837.
7. (a) deSilva, A. P.; Gunaratne, H. Q. N.; Gunnlaugsson, T.; Huxley, A. J. M.; McCoy, C. P.; Rademacher, J. T.; Rice, T. E. *Chem. Rev.* **1997**, *97*, 1515; (b) Martínez, R.; Sancenón, F. *Chem. Rev.* **2003**, *103*, 4419.
8. (a) Pu, L. *Chem. Rev.* **2004**, *104*, 1687; (b) *Fluorescent and Luminescent Probes*; Mason, W. T., Ed.; Academic: San Diego, 1999.
9. (a) Corradini, R.; Sartor, G.; Marchelli, R.; Dossena, A.; Spisni, A. *J. Chem. Soc., Perkin Trans. 2* **1992**, 1979; (b) Yan, Y.; Myrick, M. L. *Anal. Chem.* **1999**, *71*, 1958; (c) Abe, Y.; Fukui, S.; Koshiji, Y.; Kobayashi, M.; Shoji, T.; Sugata, S.; Nishizawa, H.; Suzuki, H.; Iwata, K. *Biochim. Biophys. Acta* **1999**, *1433*, 188; (d) Pagliari, S.; Corradini, R.; Galaverna, G.; Sforza, S.; Dossena, A.; Marchelli, R. *Tetrahedron Lett.* **2000**, *41*, 3691.
10. (a) Schmidtchen, F. P.; Berger, M. *Chem. Rev.* **1997**, *97*, 1609; (b) Gale, P. A. *Coord. Chem. Rev.* **2003**, *240*, 191.
11. (a) Talanova, G. G.; Elkarim, N. S. A.; Talanov, V. S.; Bartsch, R. A. *Anal. Chem.* **1999**, *71*, 3106; (b) Métivier, R.; Leray, I.; Valeur, B. *Chem. Commun.* **2003**, 996; (c) Chen, Q.-Y.; Chena, C.-F. *Tetrahedron Lett.* **2005**, *46*, 165.
12. (a) He, Y.-B.; Xiao, Y.-J.; Meng, L.-Z.; Zeng, Z.-Y.; Wu, X.-J.; Wu, C.-T. *Tetrahedron Lett.* **2002**, *43*, 6249; (b) Yuan, H. S.; Huang, Z.-T. *Tetrahedron: Asymmetry* **1999**, *10*, 2685.
13. (a) Gunnlaugsson, T.; Davis, A. P.; O'Brien, J. E.; Glynn, M. *Org. Lett.* **2002**, *4*, 2449; (b) Amendola, V.; Fabbrizzi, L.; Mangano, C.; Pallavicini, P. *Acc. Chem. Res.* **2001**, *34*, 488.
14. Martínez, R.; Sancenón, F. *Chem. Rev.* **2003**, *103*, 4419.
15. Valeur, B.; Pouget, J.; Bourson, J. *J. Phys. Chem.* **1992**, *96*, 6545.
16. Collins, E. M.; Mckervey, M. A.; Madigan, E.; Moran, M. B.; Owens, M.; Ferguaon, G.; Harris, S. J. *J. Chem. Soc., Perkin. Trans. 1* **1991**, *2*, 3137.
17. Grady, T.; Harris, S. J.; Smyth, M. R.; Diamond, D. *Anal. Chem.* **1996**, *68*, 3775.
18. Krapcho, A. P.; Kuell, C. S. *Synth. Commun.* **1990**, *20*, 2559.
19. Du, C. P.; You, J. S.; Yu, X. Q.; Liu, C. L.; Lan, J. B.; Xie, R. G. *Tetrahedron: Asymmetry* **2003**, *14*, 3651.
20. Heng, X.; Gary, R. K.; Jiang, Z.; Meiling, L.; Dmitry, M. R. *Tetrahedron* **2003**, *59*, 5837.