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Enantioselective Fluorescent Sensors for Chiral Carboxylates Based on Calix[4]arenes Bearing an L-Tryptophan Unit

Guang-yan Qing,[a] Yong-bing He,*[a] Feng Wang,[a] Hai-juan Qin,[a] Chen-guang Hu,[a] and Xi Yang[a]

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Two-armed chiral calix[4]arenes (**3a–c**) functionalized at the lower ring with L-tryptophan units have been prepared and the structures of these receptors characterized by IR, MS, ^{1}H, and ^{13}C NMR spectroscopy and elemental analysis. The enantioselective recognition of these receptors has been studied by fluorescence titration and ^{1}H NMR spectroscopy. The receptors exhibited different chiral recognition abilities towards some enantiomers of chiral materials and formed 1:1 complexes between host and guest. Receptor **3a** exhibits excellent enantioselective fluorescent recognition ability towards the *N*-Boc-protected alanine anion and **3b** reveals good enantioselective recognition ability towards the enantiomers of mandelate.

Introduction

Chiral recognition of asymmetric compounds is an important subject not only in the field of supramolecular chemistry, but also in the field of medicinal and biomedical applications. In particular, supramolecular approaches to rapid sensing of the absolute configurations of asymmetric compounds are receiving increasing interest.[1]

The basis of any chiral recognition event is the formation of diastereomeric complexes composed of a chiral receptor and a chiral substrate possessing different stabilities.[2] The crucial points in the molecular design of chemosensors are how to achieve the specific recognition of a certain molecule and how to transduce the recognition event into a signal.[3] Many tools are available for the study of the structure and dynamics of multimolecular complexes with NMR spectroscopy being perhaps the most suitable method for a detailed examination of such complexes in solution.[4] The use of fluorescent molecular sensors for the detection of ions or molecules have attracted considerable interest in recent years because of their high sensitivity and potential applications in analytical, biological, clinical, and biochemical environments.[5] The development of molecular-based enantioselective fluorescence receptors has received more attention because such receptors potentially provide a real-time technique that can be used to determine the enantiomeric composition of chiral molecules.[6] Because of their unique cavity-shaped architecture and preorganized binding sites, calixarenes and their derivatives have been extensively used in the past few years as receptors to recognize a wide variety of ions or inorganic and organic guest molecules, forming host–guest or supramolecular complexes.[7] Although many chiral calixarenes have been synthesized that recognize a chiral guest,[1b,8] chiral calixarene receptors that give a fluorescence response upon chiral recognition of a guest are still rare.[9] In the synthesis of chiral receptors, amino acids or peptides can be employed as chiral sources in building the desired molecules because of their accessibility and biological relevance.[10a] L-Tryptophan is a natural amino acid that has both a fluorescent group and a binding unit, it has been used in chiral recognition, and has been shown to have a good fluorescence response.[10b]

The carboxylate group is an anionic entity of prime importance in nature. Enzymes, antibodies, amino acids, and metabolic intermediates contain a range of carboxylate functionalities that account for their characteristic biochemical behavior.[11] Enantioselective recognition of carboxylates is important in asymmetric synthesis and drug discovery.[12] Amino acid esters and salts have been widely researched owing to their important biochemical characteristics.[13]

Herein, we describe the development of three novel, chiral calix[4]arene derivatives bearing L-tryptophan residues that have similar two-armed structures; their chiral recognition ability towards chiral carboxylates, two amino acid anions, and two amino alcohols have been explored by fluorimetric titration and ^{1}H NMR study. Obvious changes in fluorescence and in NMR chemical shifts highlight the fact that compounds based on chiral L-tryptophan and calix[4]arene units have excellent chiral recognition ability towards the enantiomers of the *N*-Boc-protected alanine anion or mandelate.

[a] Department of Chemistry, Wuhan University, Wuhan 430072, P. R. China
Fax: +86-27-68754067
E-mail: ybhe@whu.edu.cn

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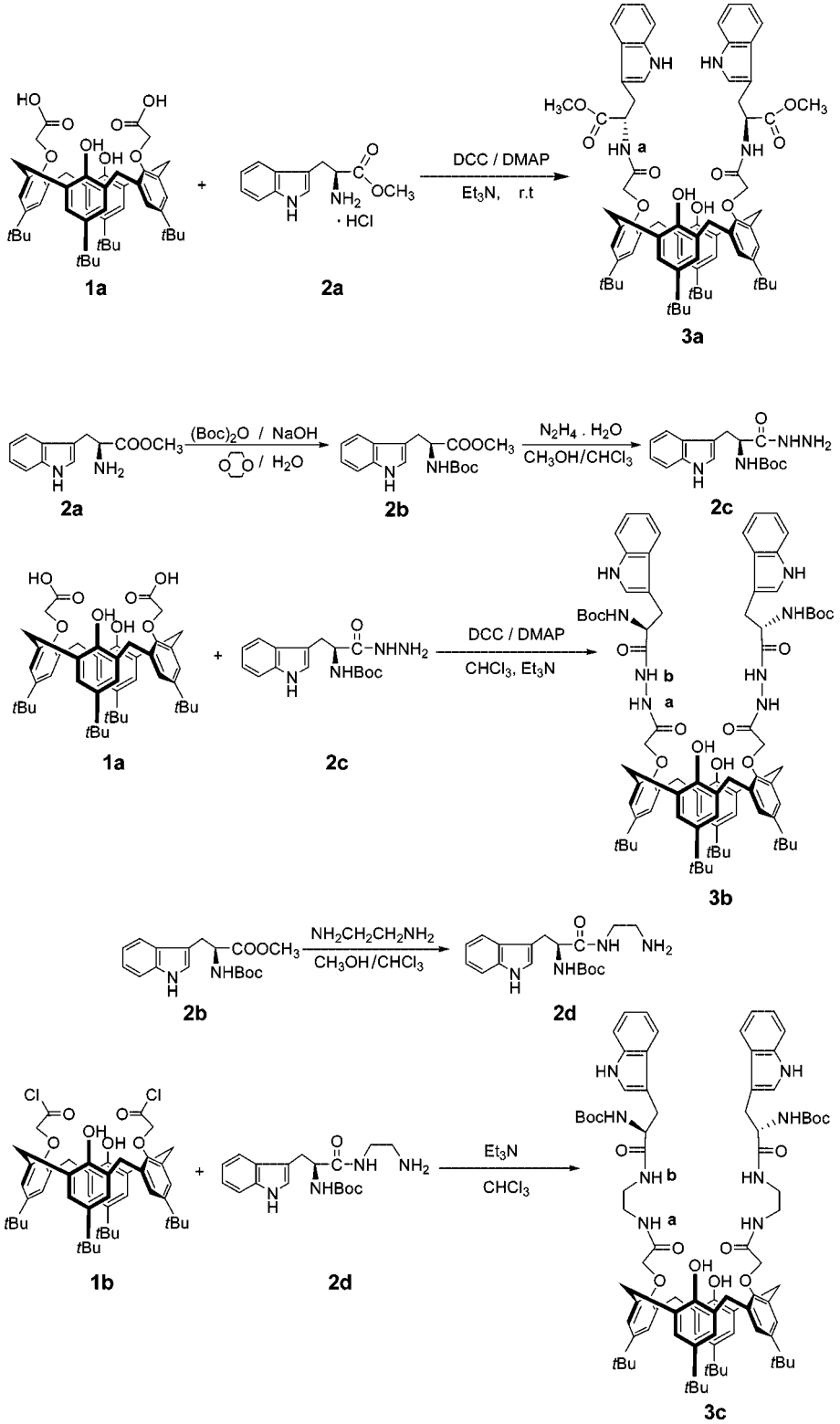
Results and Discussion

Synthesis

The synthesis of calix[4]arene receptors **3a**–**c** is outlined in Scheme 1. They are readily soluble in common organic solvents such as $CHCl_3$, CH_3OH, DMSO, and DMF. The structures of **3a**–**c** were characterized by IR, MS, ^1H, and ^{13}C NMR spectroscopy and by elemental analysis.

The stereogenic centers of receptors **3a**–**c** disturb the planar symmetry of the parent rings, which results in more aromatic carbon signals appearing in the ^{13}C NMR spectra of the receptors. This pattern is similar to that observed for



Scheme 1. Synthesis of receptors **3**–**c**.

other chiral calix[4]arenes.[14] The ^{1}H NMR spectra of **3a**–**c** show two sets of doublets due to the bridging methylene protons and two sets of signals due to the *tert*-butyl groups. This indicates that these receptors adopt a cone conformation in $CHCl_3$. The ^{1}H NMR spectra of **3a**–**c** also exhibit one set of doublets due to the $ArOCH_2$ protons. This splitting pattern may be related to the introduction of chiral moieties into the molecules, as observed in other chiral calix[4]arenes.[14]

Fluorescence Spectra Study

Fluorescence spectra of solutions of **3a**–**c** were recorded in the absence and presence of various chiral carboxylates, such as mandelate, the α-phenylglycine anion, malate, and tartrate; *N*-Boc-protected alanine anions (Ala anions) and *N*-Boc-protected phenylalanine anions (Phe anions) were also examined as the guests. The amino groups were protected by the *tert*-butyloxycarbonyl functionality. In each case tetrabutylammonium was used as the counter cation. We also chose two amino alcohols, namely phenylglycinol and phenylalaninol, as guests to compare the associated abilities of the hosts to bind with neutral molecules. Considering the solubility of all the guests in various solvents, DMSO was chosen as the solvent in which receptors **3a**–**c** all have good fluorescence responses (see the Supporting Information).

Figures 1 and 2 show the fluorescence emission spectra of a mixture of **3a** and different concentrations of the L- or D-Ala anion in DMSO (λ_{ex} = 295 nm), respectively. The fluorescence emission of **3a** (at 346 nm) was slightly quenched by about 10% upon addition of 155 equiv. of L-Ala anions (Figure 1). Figure 2 shows the change in fluorescence emission of **3a** upon addition of D-Ala anions; the quenching efficiency (at 346 nm) was 48% for the addition of 155 equiv. of D-Ala anions. Satisfactory nonlinear curve fitting (the correlation coefficient is >0.99) confirmed that **3a** and the D-Ala anion formed a 1:1 complex (see the inset of Figure 2). For a complex of 1:1 stoichiometry, the association constant (K_{ass}) can be calculated by using Equation (1) from the Origin 7.0 software package,[15,16] where I represents the fluorescence intensity, C_H and C_G are the host and guest concentrations, 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.

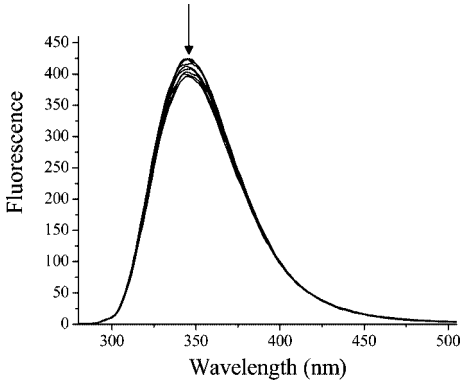


Figure 1. Fluorescence spectra of receptor **3a** (5.0×10^{-5} mol L^{-1}) with the L-Ala anion in DMSO. The anion equivalents are: 0, 1.5, 5.5, 11.5, 35.0, 55.0, 85.0, 115.0, and 155.0. λ_{ex} = 295 nm (EX: 5; EM: 10).

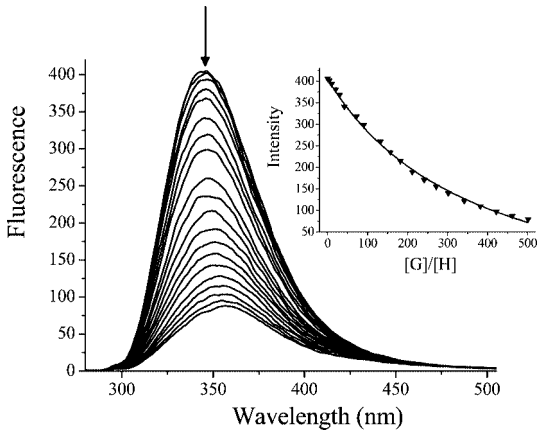


Figure 2. Fluorescence spectra of receptor **3a** (5.0×10^{-5} mol L^{-1}) with the D-Ala anion in DMSO. The anion equivalents are: 0, 4.0, 10.0, 20.0, 30.0, 40.0, 70.0, 90.0, 130.0, 155.0, 180.0, 210.0, 240.0, 270.0, 300.0, 340.0, 380.0, 420.0, 460.0, and 500.0. λ_{ex} = 295 nm (EX: 5; EM: 10). Inset: changes in the fluorescence intensity of **3a** at 346 nm upon addition of the D-Ala anion. The line shown is a line-fitted curve. The correlation coefficient (R) of the nonlinear curve fitting is 0.9982.

$$I = I_0 + \frac{I_{lim} - I_0}{2C_0}\{C_H + C_G + 1/K_{ass} - [(C_H + C_G + 1/K_{ass})^2 - 4C_HC_G]^{1/2}\} \quad (1)$$

The association constant for the interaction of **3a** with the D-Ala anion is 53.56 M^{-1}, whereas that for association of **3a** with the L-Ala anion could not be calculated from this equation owing to the weak response observed in the fluorescence spectra. The dramatically different fluorescent responses and quenching efficiencies observed for the two enantiomers indicate that **3a** has excellent enantioselective fluorescent recognition ability towards the Ala anion. When **3a** interacted with mandelate, no clear change in the fluorescence spectra was observed. Similar phenomena to that shown in Figure 2 were observed when other anion guests were added to the solution of **3a** (see the Supporting Information). However, the association constants for the interaction of **3a** with guests were rather small [ranging from 3.70 M^{-1} for L-phenylalaninol to 249.13 M^{-1} for L-malate (see Table 1)], which may be due to the rather weak hydrogen-bonding interaction between the host and guest.

Figures 3 and 4 show the fluorescence spectra of receptor **3b** (5.0×10^{-5} mol L^{-1}) with different concentrations of L- or D-mandelate in DMSO. Upon addition of D-mandelate, the fluorescence emission of **3b** decreased gradually, whereas addition of L-mandelate to the solution of **3b** led to a small change in the fluorescence emission. The quenching efficiency (at 345 nm) was 11% with 180.0 equiv. of L-man-

Table 1. Association constants (K_{ass}), correlation coefficients (R), enantioselectivities ($K_{ass(D)}/K_{ass(L)}$), Gibbs free energy changes ($-\Delta G_0$), and $\Delta\Delta G_0$ calculated from ΔG_0 for the complexation of receptors **3a**–**c** with L/D guests in DMSO at 25 °C.

Entry	Host	Guest	K_{ass} [M^{-1}][a,b]	R	$K_{ass(d)}/K_{ass(l)}$	$-\Delta G_0$ [kJ mol^{-1}]	$\Delta\Delta G_0$ [kJ mol^{-1}]
1	**3a**	L-mandelate	[c]				
2	**3a**	D-mandelate	[c]				
3	**3a**	L-α-phenylglycine	94.88 ± 7.76	0.9932		11.285	
4	**3a**	D-α-phenylglycine	231.84 ± 9.64	0.9972	2.44	13.499	–2.214
5	**3a**	L-*N*-Boc-Ala[d]	[c]				
6	**3a**	D-*N*-Boc-Ala[d]	53.56 ± 2.91	0.9982		9.867	
7	**3a**	L-*N*-Boc-Phe[d]	28.79 ± 2.97	0.9984		8.329	
8	**3a**	D-*N*-Boc-Phe[d]	32.24 ± 1.70	0.9991	1.12	8.609	–0.280
9	**3a**	L-malate	249.13 ± 5.85	0.9902		13.678	
10	**3a**	D-malate	84.37 ± 11.93	0.9913	0.34	10.994	2.684
11	**3a**	L-tartrate	13.59 ± 3.14	0.9945		6.468	
12	**3a**	D-tartrate	77.05 ± 8.69	0.9926	5.70	10.769	–4.301
13	**3a**	L-phenylglycinol	5.19 ± 0.66	0.9987		4.082	
14	**3a**	D-phenylglycinol	5.87 ± 0.70	0.9983	1.13	4.387	–0.305
15	**3a**	L-phenylalaninol	3.70 ± 0.68	0.9984		3.243	
16	**3a**	D-phenylalaninol	5.03 ± 0.92	0.9956	1.36	4.004	–0.761
					$K_{ass(d)}/K_{ass(l)}$		
17	**3b**	L-mandelate	[c]				
18	**3b**	D-mandelate	$(1.04 \pm 0.07) \times 10^3$	0.9928		17.220	
19	**3b**	L-α-phenylglycine	$(1.04 \pm 0.05) \times 10^4$	0.9927		22.928	
20	**3b**	D-α-pPhenylglycine	$(8.35 \pm 0.03) \times 10^3$	0.9957	0.80	22.384	0.544
21	**3b**	L-*N*-Boc-Ala[d]	411.37 ± 14.34	0.9983		14.921	
22	**3b**	D-*N*-Boc-Ala[d]	$(2.96 \pm 0.22) \times 10^3$	0.9910	7.20	19.813	–4.892
23	**3b**	L-*N*-Boc-Phe[d]	801.51 ± 23.63	0.9981		16.575	
24	**3b**	D-*N*-Boc-Phe[d]	674.99 ± 33.19	0.9966	0.84	16.149	0.426
25	**3b**	L-malate	$(1.39 \pm 0.08) \times 10^4$	0.9909		23.647	
26	**3b**	D-malate	$(3.87 \pm 0.15) \times 10^4$	0.9928	2.78	26.185	–2.538
27	**3b**	L-tartrate	$(1.02 \pm 0.05) \times 10^4$	0.9948		22.879	
28	**3b**	D-tartrate	$(8.45 \pm 0.06) \times 10^3$	0.9908	0.83	22.413	0.466
29	**3b**	L-phenylglycinol	62.63 ± 8.44	0.9929		10.255	
30	**3b**	D-phenylglycinol	67.10 ± 9.73	0.9921	1.07	10.426	–0.171
31	**3b**	D-phenylalaninol	177.54 ± 11.40	0.9919		12.838	
32	**3b**	D-phenylalaninol	192.89 ± 15.78	0.9907	1.09	13.044	–0.206
					$K_{ass(d)}/K_{ass(l)}$		
33	**3c**	L-mandelate	485.72 ± 39.70	0.9910		15.333	
34	**3c**	D-mandelate	788.67 ± 51.79	0.9912	1.62	16.535	–1.202
35	**3c**	L-α-phenylglycine	84.06 ± 12.87	0.9928		10.985	
36	**3c**	D-α-phenylglycine	65.36 ± 4.76	0.9947	0.78	10.298	0.687
37	**3c**	L-*N*-Boc-Ala[d]	66.56 ± 9.85	0.9918		10.406	
38	**3c**	D-*N*-Boc-Ala[d]	273.76 ± 25.31	0.9912	4.11	13.912	–3.506
39	**3c**	L-*N*-Boc-Phe[d]	59.35 ± 6.01	0.9947		10.122	
40	**3c**	D-*N*-Boc-Phe[d]	53.93 ± 7.24	0.9917	0.91	9.885	0.237
41	**3c**	L-malate	$(3.07 \pm 0.23) \times 10^3$	0.9927		19.904	
42	**3c**	D-malate	$(4.32 \pm 0.18) \times 10^3$	0.9975	1.41	20.750	–0.846
43	**3c**	L-tartrate	139.67 ± 13.56	0.9908		12.244	
44	**3c**	D-tartrate	163.72 ± 22.24	0.9914	1.17	12.637	–0.393
45	**3c**	L-phenylglycinol	[e]				
46	**3c**	D-phenylglycinol	[e]				
47	**3c**	L-phenylalaninol	24.99 ± 4.27	0.9913		7.978	
48	**3c**	D-phenylalaninol	123.74 ± 11.74	0.9903	4.95	11.943	–3.965

[a] The data were calculated from results of fluorescence titrations in DMSO. [b] All error values were obtained from nonlinear curve fitting. [c] The association constants could not be calculated precisely because the signal change was too small to provide reliable data with tolerable error. [d] *N*-Boc-alanine and -phenylalanine tetrabutylammonium salts, the amino group was protected by a *tert*-butyloxycarbonyl function. [e] The association is too small to be calculated.

delate, whereas it was 88% with 165.0 equiv. of D-mandelate. The different quenching efficiencies ($\Delta I_D/\Delta I_L$ = 8.0) indicate that **3b** has a good enantioselective fluorescent recognition ability towards mandelate.

Receptor **3b** also exhibits a good enantioselective fluorescence response to the enantiomers of the Ala anion (see Figures S3.9 and S3.10 of the Supporting Information). The fluorescence emission of **3b** was quenched by about

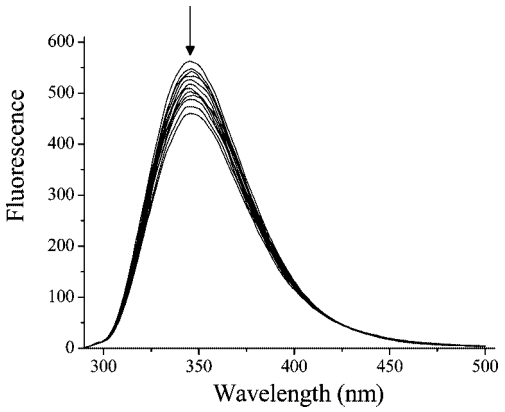


Figure 3. Fluorescence spectra of receptor **3b** (5.0×10^{-5} mol L^{-1}) with L-mandelate in DMSO. The anion equivalents are: 0, 0.2, 0.4, 3.0, 20.0, 50.0, 100.0, 130.0, 180.0, 230.0, 330.0, and 430.0. λ_{ex} = 296 nm (EX: 5; EM: 10).

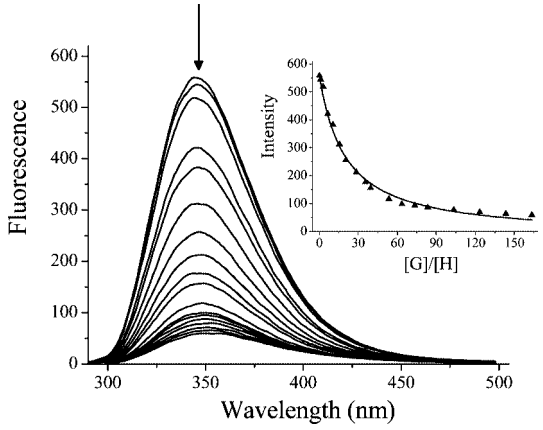


Figure 4. Fluorescence spectra of receptor **3b** (5.0×10^{-5} mol L^{-1}) with D-mandelate in DMSO. The anion equivalents are: 0, 1.0, 3.0, 6.5, 10.5, 15.0, 20.0, 28.0, 35.0, 40.0, 55.0, 65.0, 75.0, 85.0, 105.0, 125.0, 145.0, and 165.0. λ_{ex} = 296 nm (EX: 5; EM: 10). Inset: Changes in fluorescence intensity of **3b** at 345 nm upon addition of D-mandelate. The line shown is a line-fitted curve. The correlation coefficient (R) for the nonlinear curve fitting is 0.9928.

80% upon addition of 310 equiv. of L-Ala anions, whereas that of **3b** was quenched by about 90% with only 115 equiv. of D-Ala anions. Satisfactory nonlinear curve fitting (the correlation coefficient is >0.99) confirmed that receptor **3b** formed a 1:1 complex with the L- and D-Ala anion.[15] In addition, the association constants (K_{ass}) were different ($K_{ass(l)}$ = 411.37 M^{-1}, ΔG_0 = –14.921 kJ mol^{-1}; $K_{ass(d)}$ = 2.96×10^3 M^{-1}, ΔG_0 = –19.813 kJ mol^{-1}), yielding a D/L selectivity [$K_{ass(d)}/K_{ass(l)}$] of 7.20 for the Ala anion and a $\Delta\Delta G_0$ value of –4.892 kJ mol^{-1}, demonstrating that **3b** also has good chiral recognition ability towards the enantiomers of Ala anions.

Compared with **3a**, **3b** has a more rigid structure and more amides that are good hydrogen-bonding donors as a result of the introduction of hydrazine units into the calixarene arms, which causes the association constants for the interaction of **3b** with guests to be much higher than those of **3a**, ranging from 62.63 M^{-1} for L-phenylglycinol to 3.87×10^4 M^{-1} for D-malate.

In the absence of anions, photoinduced electron transfer (PET) between the indole group and the electron-withdrawing amide substituents might result in quenched fluorescence. When anions were introduced into a solution of either **3a** or **3b**, an anion–receptor complex was formed through hydrogen bonding, the reductive potential of the amide group increased along with electron transfer from the HOMO orbital of the receptors to the excited indole group, which in turn led to the intramolecular PET process being easier.[5a,5b,17] Therefore fluorescence quenching was observed.

Figures 5 and 6 show the fluorescence emission of receptor **3c** (5.0×10^{-5} mol L^{-1}) with different concentrations of the L- or D-Ala anion in DMSO. The fluorescence emission of **3c** (λ_{ex} = 375 nm) gradually increased upon addition of the L- or D-Ala anion. Satisfactory nonlinear curve fitting (the correlation coefficient is >0.99) confirmed that receptor **3c** and the L- or D-Ala anion formed a 1:1 complex[15] (see the insets in Figures 5 and 6). The association constants for the interaction of **3c** with the L- or D-Ala anion are 66.56 or 273.76 M^{-1}, respectively, which correspond to a D/L selectivity [$K_{ass(d)}/K_{ass(l)}$] of 4.11 for the Ala anion and a $\Delta\Delta G_0$ value of –3.506 kJ mol^{-1}.

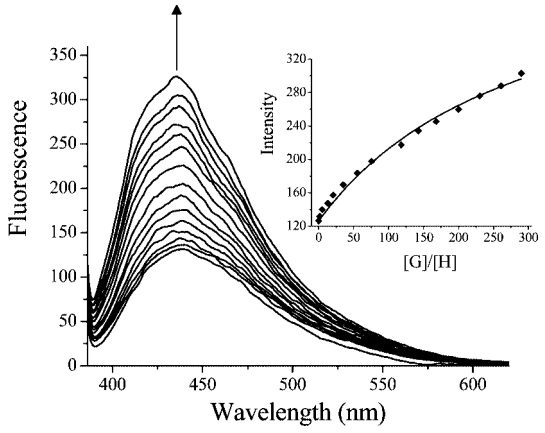


Figure 5. Fluorescence spectra of receptor **3c** (5.0×10^{-5} mol L^{-1}) with the L-Ala anion in DMSO. The anion equivalents are: 0, 1.5, 5, 12.0, 20.0, 35.0, 55.0, 75.0, 115.0, 145.0, 165.0, 200.0, 230.0, 260.0, and 290.0. λ_{ex} = 375 nm (EX: 5; EM: 10). Inset: Changes in the fluorescence intensity of **3c** at 445 nm upon addition of the L-Ala anion. The line shown is a line-fitted curve. The correlation coefficient (R) for the nonlinear curve fitting is 0.9918.

Intriguingly, the emission spectra of **3c** in DMSO are different to those of **3a** and **3b**: The emission peak of **3c** is at 445 nm, whereas those of **3a** and **3b** are both at 345 nm. Considering the similarities and differences in their structures, we presume that the more flexible ethylene chains of **3c** enable the intramolecular two indole moieties to approach, resulting in the formation of an excimer. In contrast, the much more rigid amide and hydrazine chains of **3a** and **3b** prevent the two indole groups from stacking together. Hence, only monomer emission peaks at 345 nm were observed. The monomer emission of **3c** could also be observed when the fluorescence of **3c** was excited at 291 nm, but the fluorescence intensity was much weaker than those

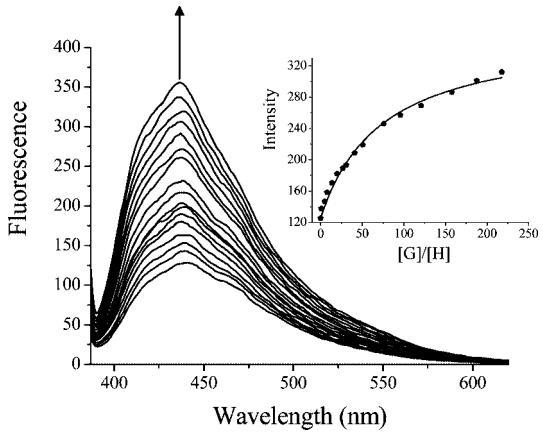


Figure 6. Fluorescence spectra of receptor **3c** (5.0×10^{-5} mol L^{-1}) with the D-Ala anion in DMSO. The anion equivalents are: 0, 1.0, 5.0, 8.0, 14.0, 20.0, 26.0, 30.0, 40.0, 50.0, 75.0, 95.0, 120.0, 155.0, 190.0, and 220.0. λ_{ex} = 375 nm (EX: 5; EM: 10). Inset: Changes in the fluorescence intensity of **3c** at 445 nm upon addition of the D-Ala anion. The line shown is a line-fitted curve. The correlation coefficient (R) for the nonlinear curve fitting is 0.9912.

of **3a** and **3b**, which may be due to the formation of an excimer causing a decrease in the emission of the monomer. The monomer emission was gradually quenched upon addition of the L- or D-Ala anions; the association constants calculated from the change in monomer emission is in accord with those calculated from the change in excimer emission (see Figures S3.25 and S3.26 of the Supporting Information).

The increase in fluorescence intensity of the excimer upon addition of the anion is similar to the anion-induced fluorescence enhancement reported previously.[18] In the absence of anions, the photoinduced electron transfer between the indole group and weak electron-withdrawing amide substituents might result in decreased fluorescence intensity. When anions were added to the solution, the interaction of the anion with the receptor unit could erase this specific PET process to increase fluorescence. Therefore anion-induced fluorescence enhancement was observed.[18] Similar phenomena were observed when other anions or neutral amino alcohol guests were added to the solution of receptor **3c** (see the Supporting Information). The association constants for the interactions of **3c** with the guests were smaller than those of **3b** with guests, ranging from 24.99 M^{-1} for L-phenylalaninol to 4.32×10^3 M^{-1} for D-malate (see Table 1). In particular, **3c** has good enantioselective recognition ability towards phenylalaninol, the association constants (K_{ass}) of **3c** with L- or D-phenylalaninol being 24.99 and 123.74 M^{-1}, respectively, with a corresponding D/L selectivity [$K_{ass(d)}/K_{ass(l)}$] of 4.95 for phenylalaninol and a $\Delta\Delta G_0$ value of –3.965 kJ mol^{-1} (Figure 7).

From the data reported above, we find that the association constants for the interactions of **3b** with guests are larger than those of **3a** or **3c**, which maybe due to the more rigid structure and stronger hydrogen-bonding interactions between the host and guest (Figure 8). Receptor **3a** only has two amide groups and the NH group of indole that can participate in the association, which limits the effective hydrogen bonding between the host and guest; the rather small association constants confirm our conclusion. Compared with **3b**, receptor **3c** has the same number of amide groups and the NH group of indole, but the rigidity of the structure of **3c** is significantly lower owing to the flexibility of the CH_2CH_2 link; the acidity of the amide groups is also weakened by the separation of the two amide groups. These differences result in small association constants for the interaction of **3c** with guests, but they are larger than those of **3a**. In spite of the differences in structure, these three receptors all exhibit good chiral recognition ability towards the enantiomers of the Ala anion, which indicates that the

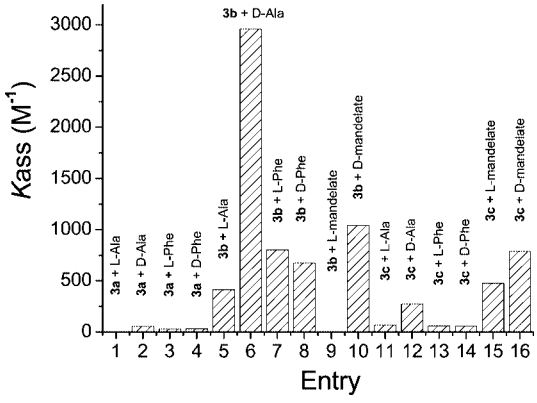


Figure 8. Bar plots of the association constants (K_{ass}) of receptors **3a**–**c** with Ala, Phe, and mandelate anions. [The $K_{ass(\mathbf{3a}+\text{l-Ala})}$ (Entry 1) and $K_{ass(\mathbf{3b}+\text{l-mandelate})}$ (Entry 9) could not be calculated owing to the fluorescence response being too low.].

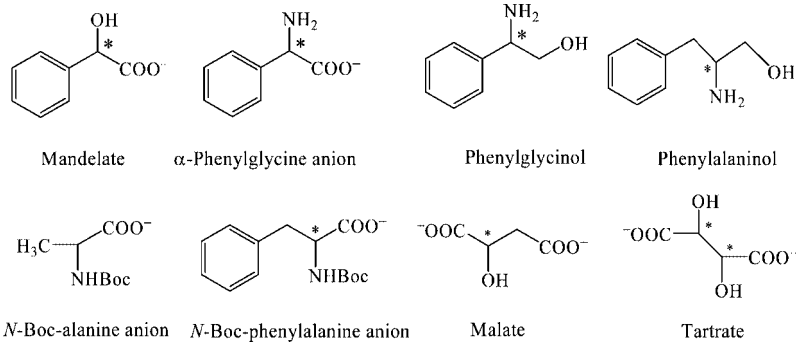


Figure 7. Structures of the guests.

preorganized structure of the calix[4]arene unit and the chiral center of L-tryptophan play important roles in the enantioselective recognition process.

The Phe anion has a structure similar to that of the Ala anion, but the association constants for the association of the receptors with the Phe anion are smaller than those for the Ala anion, which could be attributed to the greater steric hindrance of the phenyl ring relative to the methyl group. Interestingly, we found that the association constants for the interactions of **3a**–**c** with the D enantiomers were generally larger than those for the L enantiomers, which is probably due to the D enantiomers having a structure more complementary to the hosts. Further research is still being carried out to investigate these phenomena.

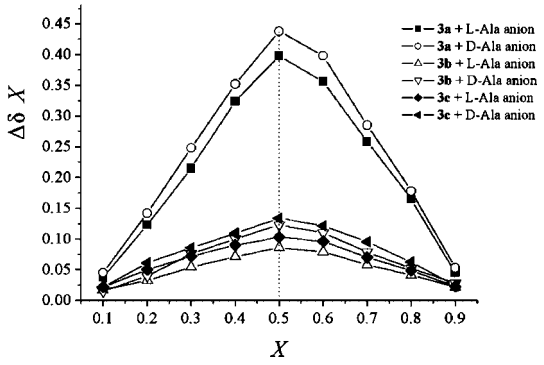


Figure 9. Job plots for receptors **3a**–**c** with the L- or D-*N*-Boc-Ala anion (X = mol fraction of the anion, $\Delta\delta$ = chemical shift change of the CH proton of the anion).

^{1}H NMR Study

^{1}H NMR experiments were undertaken to assess the chiral recognition properties between receptors **3a**–**c** and chiral anionic guests because NMR spectroscopy can provide structural and dynamic information directly.[9a,19] Chiral recognition studies were carried out with a 300 MHz NMR spectrometer using compounds **3a**–**c** as chiral solvating agents. $CDCl_3$ is the most common solvent used in the ^{1}H NMR study of chiral recognition, and herein we chose $CDCl_3$ as the solvent instead of [D_6]DMSO because of serious problems relating to the superposition of the signals of the chiral CH protons of guests (including *N*-Boc-protected alanine and mandelate) with the diagnostic signal of [D_6]-DMSO or the signals of the hosts leading to difficulties in clarifying the interaction properties. The ^{1}H NMR spectra of **3a**–**c** interactions with anionic guests in [D_6]DMSO are presented in the Supporting Information.

The ^{1}H NMR spectra of **3a**–**c** and the L- or D-Ala anion in a variety of ratios in $CDCl_3$ at a constant total concentration of 4.0×10^{-3} M were recorded. It was found that the CH proton signal of the Ala anion at δ = 3.834 ppm underwent a downfield shift when the Ala anion was treated with the three receptors. Figure 9 shows the Job plots of $\Delta\delta_X$ versus the mol fraction X of the L- or D-Ala anion in the mixture.[20] Maxima were observed at X = 0.5, indicating that the receptors **3a**–**c** all formed 1:1 complexes with the Ala anion under the conditions employed. Probably the two-armed structure based on calix[4]arene could associate with an anion effectively through multi-hydrogen-bonding interactions, which have been observed in other similar systems.[8a,8b,8g,14c,21]

When treated with equimolar amounts of receptor **3a**, the signal of the CH proton of the racemic Ala anion fragmented into a more complicated signal pattern (see the Supporting Information) with a downfield shift (changing from δ = 3.834 to 4.270 ppm), whereas the signal of the *CH proton of the host experienced an upfield shift (changing from δ = 5.092 to 5.081 ppm). The amide [N*H*(a)] of the host exhibited nearly no change; only the signal of the N*H* proton of the guest showed a small upfield shift from δ = 5.977 to 5.924 or 5.905 ppm for the L- or D-Ala anion, respectively.

^{1}H NMR spectra of **3b** in the absence and presence of Ala anions are shown in Figure 10. When treated with equimolar amounts of **3b**, the signal of the CH proton of the racemic Ala anion again fragmented into a more complicated signal pattern (Figure 10c) with a downfield shift (changing from δ = 3.834 to 3.918 ppm) and the signal of the *CH proton of the host also experienced a downfield shift (changing from δ = 5.269 to 5.327 ppm). The ^{1}H NMR spectra of **3b** show clear changes in the presence of the Ala anion. Upon addition of an equimolar amount of the L- or D-Ala anion to a solution of **3b**, the characteristic amide peaks [N*H*(a), N*H*(b)] nearly disappeared. But differences were found: The signal of the *CH proton of the host experienced a downfield shift from δ = 5.269 to 5.318 or 5.330 ppm for the L- or D-Ala anion, respectively, and the ^{1}H NMR titration illustrated that the change in chemical shift of the N*H*(b) signal of **3b** in the presence of the D-Ala anion occurred more quickly than with the L-Ala anion (see the Supporting Information). The signal of the amide group linked to the Boc moiety of the host was also clearly downfield-shifted from δ = 7.924 to 8.270 or 8.276 ppm for the L- or D-Ala anion, whereas the signal of the amide group (N*H*) of the guest was upfield-shifted from δ = 5.977 to 5.919 or 5.950 ppm for the L- or D-Ala anion, respectively, which suggested that the interaction between host and guest mainly happened through multiple hydrogen bonds.[14c,18a,18d,21] The above results indicate that **3b** has a stronger interaction with the D-Ala anion than with its L enantiomer.

Similar phenomena were found when **3b** interacted with mandelate (see the Supporting Information). The signals of the single CH protons of D- and L-mandelate were shifted downfield by about 0.071 and 0.038 ppm in the presence of **3b**, respectively. The signal intensities of the amide protons [N*H*(a), N*H*(b)] were much weaker; the signal of the amide group linked to the Boc moiety was also downfield-shifted when **3b** interacted with L- or D-mandelate. In particular, a downfield shift of the signal of the chiral proton of **3b** from δ = 5.269 to 5.302 or 5.289 ppm was observed for D- or L-mandelate, respectively, clearly indicating that the host's chiral centre has participated in the chiral recognition process.

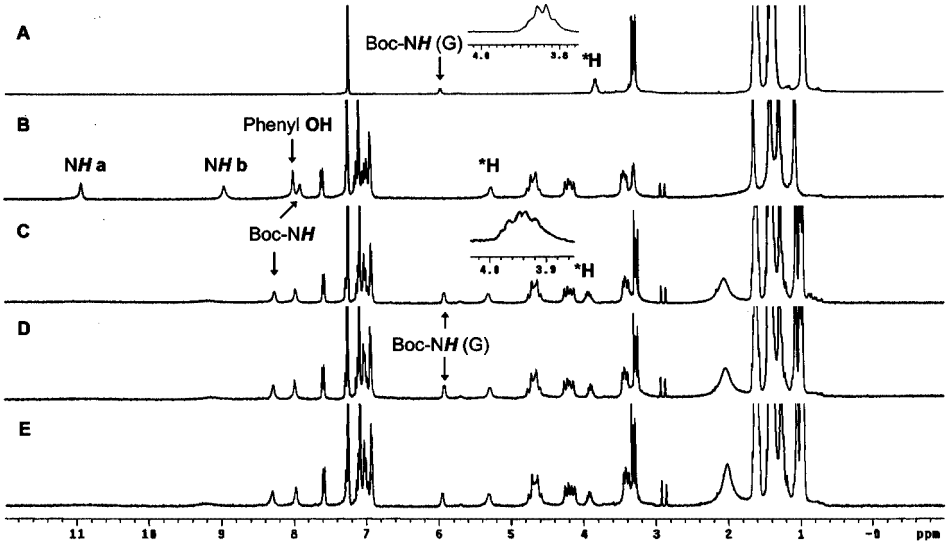


Figure 10. The ^{1}H NMR spectra of **3b** and its guest complexes at 25 °C ([**3b**] = [guest] = 2.0×10^{-3} M) in $CDCl_3$ at 300 MHz. A) Racemic *N*-Boc-Ala anion; B) receptor **3b**; C) receptor **3b** + racemic *N*-Boc-Ala anion; D) receptor **3b** + L-*N*-Boc-Ala anion; E) receptor **3b** + D-*N*-Boc-Ala anion.

Probably as a result of the flexibility of the CH_2CH_2 units, the ^{1}H NMR spectra of **3c** did not show such obvious changes as those of **3b** on interaction with the Ala anion (see the Supporting Information). The signals of the amide peaks [N*H*(a), N*H*(b), N*H*(c)] all have clear downfield shifts, but no signal disappeared, whereas the amide signal of the Ala anion was shifted upfield from δ = 5.977 to 5.917 or 5.902 ppm upon addition of the L- or D-Ala anion, suggesting that the amide group of the guest also participates in the association process.

We can draw similar conclusions from the ^{1}H NMR spectra of the interactions between hosts and anionic guests in [D_6]DMSO: The interactions mainly occur through multiple hydrogen bonds. Some differences were found, notably that the phenolic hydroxy groups of the calix[4]arene participates in the association process and exhibits different changes in chemical shifts upon addition of the L or D anion (see the Supporting Information).

The ^{1}H NMR spectra show that all the calix[4]arene derivatives retain the cone conformation in solution and we found it interesting that the amide groups of **3b** show the strongest acidity and the most obvious change on interacting with the anions, whereas the other two receptors show relatively weak changes, which is consistent with data obtained from the fluorescence titrations. In order to clarify the effect of the hydrazine amide groups of **3b**, receptor **3c** with a rather flexible CH_2CH_2 unit was designed; results indicate that the rigidity of a structure also has an important role in the association process.

The above results illustrate that the nature of the receptor, the structural rigidity, multiple hydrogen-bonding interactions, and complementary chiral-centre interactions may be responsible for the enantiomeric recognition of anionic guests.[22]

Conclusion

Three chiral fluorescent receptors (**3a**–**c**) were synthesized and their enantioselective recognition was studied by fluorescence titration and ^{1}H NMR spectroscopy. Receptors **3a**–**c** exhibit different chiral recognition abilities towards some enantiomers of chiral materials and form 1:1 complexes with the guest molecules. Receptor **3a** exhibits excellent enantioselective fluorescent recognition ability towards the *N*-Boc-protected alanine anion and **3b** reveals good enantioselective recognition ability towards the enantiomers of mandelate. It is clear that a relatively rigid structure, good structural preorganization, steric effects, and multiple hydrogen bonds induce the enantioselective recognition ability of **3a** and **3b**. The remarkably different fluorescent responses that result from complexation reveal that **3a** and **3b** could be used as fluorescent chemosensors for the *N*-Boc-protected alanine anion or mandelate in the future.

Experimental Section

General: Melting points were determined with a Reichert 7905 melting point apparatus and are uncorrected. Optical rotations were measured with a Perkin-Elmer Model 341 polarimeter. IR spectra were obtained with a Nicolet 670 FT-IR spectrophotometer. ^{1}H NMR spectra were recorded in $CDCl_3$ or [D_6]DMSO with a Varian Mercury VX spectrometer at 300 MHz. ^{13}C NMR spectra were recorded with a Varian Inova spectrometer at 600 MHz. Mass spectra were recorded with a Finnigan LCQ advantage mass spectrometer. Elemental analyses were determined with a Carlo-Erba 1106 instrument. Fluorescence spectra were obtained with a Shimadzu RF-5301 spectrometer. The UV/Vis spectra were recorded with a TU-1901 spectrophotometer. Ethylenediamine was distilled before use. $CHCl_3$ was washed with water and dried with $CaCl_2$, and Et_3N was dried and distilled from CaH_2. All other commer-

cially available reagents were used without further purification. The anions were used as their tetrabutylammonium salts. Compounds **1a**, **1b**, **2a**, and the *N*-protected (by the *tert*-butyloxycarbonyl functionality) amino acid derivatives were synthesized according to a literature method.[23]

Synthesis of Compound 2b: NaOH (0.40 g, 10 mmol) and $(Boc)_2O$ (2.62 g, 12 mmol) were added to a solution of **2a** (2.55 g, 10 mmol) in water/dioxane (1:1, 40 mL). The mixture was stirred at room temperature for 24 h and then the pH was adjusted to 7.0 by adding 6 N HCl. The product was extracted with $CHCl_3$ (5 × 30 mL) and the solvent was evaporated under reduced pressure to give **2b** (2.71 g, 89%) as a pale yellow solid. M.p. 151–152 °C. $[\alpha]_D^{20}$ = +47.50 (*c* = 0.05, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3384, 3323, 2976, 1737, 1693, 1523, 1447, 1369, 1295, 1221, 1169, 1081, 1015, 752, 692 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.36 (s, 9 H, Boc-*t*Bu), 3.26–3.32 (m, 2 H, Indole-CH_2), 3.64 (s, 3 H, OCH_3), 4.58–4.60 (m, 1 H, NC**H*CO), 6.82 (s, 1 H, Indole-CH), 6.95 (s, 1 H, Indole-CH), 7.03–7.08 (m, 1 H, Indole-CH), 7.11–7.16 (m, 1 H, Indole-CH), 7.28 (d, *J* = 7.8 Hz, 1 H, Indole-CH), 7.52 (d, *J* = 7.8 Hz, 1 H, Indole-NH), 8.06 (s, 1 H, NHBoc) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 28.5, 29.2, 51.8, 54.5, 78.4, 110.8, 111.7, 118.8, 119.1, 121.5, 124.5, 127.7, 136.7, 155.8, 171.8 ppm. $C_{17}H_{22}N_2O_4$ (318.37): calcd. C 64.13, H 6.97, N 8.80; found C 64.15, H 7.02, N 8.69.

Synthesis of Compound 2c: Hydrazine hydrate (4 equiv. of **2b**) was added to a solution (20 mL) of **2b** (0.64 g, 2 mmol) in $CHCl_3$/CH_3OH (1:10, v/v). The reaction mixture was stirred at room temperature for 24 h. Then the solvent was evaporated under reduced pressure and water (40 mL) poured onto the residue. After filtration, the solid was dried in vacuo to obtain a pure white product (0.63 g) in 98.4% yield. M.p. 159–161 °C. $[\alpha]_D^{20}$ = –4.88 (*c* = 0.05, DMF). IR (KBr): $\tilde{\nu}$ = 3344, 2984, 2933, 1674, 1653, 1524, 1505, 1459, 1390, 1368, 1271, 1250, 1172, 1026, 738, 641 cm^{-1}. ^1H NMR ([D$_6$]DMSO): δ = 1.28 (s, 9 H, Boc-*t*Bu), 2.82–3.01 (m, 2 H, Indole-CH_2), 4.17 (m, 3 H, NC*HCO, NH_2), 6.67 (d, *J* = 8.1 Hz, 1 H, Indole-CH), 6.91 (m, 1 H, Indole-CH), 6.99 (m, 1 H, Indole-CH), 7.09 (s, 1 H, Indole-CH), 7.27 (d, *J* = 8.1 Hz, 1 H, Indole-CH), 7.54 (d, *J* = 7.2 Hz, 1 H, Indole-NH), 9.07 (s, 1 H, NHBoc), 10.74 (s, 1 H, CON*H*NH_2) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 28.4, 28.8, 54.3, 78.5, 110.8, 111.9, 118.8, 119.1, 121.5, 124.3, 127.9, 136.7, 155.7, 172.0 ppm. $C_{16}H_{22}N_4O_3$ (318.38): calcd. C 60.36, H 6.96, N 17.60; found C 60.34, H 7.03, N 17.58.

Synthesis of Compound 2d: Excess ethylene-1,2-diamine (0.72 g, 12 mmol) was added to a solution (20 mL) of **2b** (0.64 g, 2 mmol) in $CHCl_3$/CH_3OH (1:10, v/v). The reaction mixture was stirred at room temperature for 36 h. After evaporation of the solvent and the residual ethylenediamine under reduced pressure, a pale yellow solid (0.65 g) was obtained in 93.7% yield. M.p. 137–139 °C. $[\alpha]_D^{20}$ = +14.37 (*c* = 0.05, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3341, 2979, 2928, 1686, 1649, 1526, 1385, 1367, 1327, 1249, 1173, 1109, 741, 640 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.44 (s, 9 H, Boc-*t*Bu), 3.08–3.18 (m, 4 H, NCH_2C), 3.29–3.36 (m, 2 H, Indole-CH_2), 4.40 (d, *J* = 5.1 Hz, 2 H, NH_2), 5.25 (s, 1 H, NC*HCO), 6.07 (s, 1 H, NHBoc), 7.07 (s, 2 H, Indole-CH), 7.10–7.15 (m, 1 H, Indole-CH), 7.18–7.23 (m, 1 H, Indole-CH), 7.09 (s, 1 H, Indole-CH), 7.35 (d, *J* = 8.1 Hz, 1 H, Indole-CH), 7.65 (d, *J* = 7.8 Hz, 1 H, Indole-NH), 8.34 (s, 1 H, CONHC) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 28.5, 29.0, 40.5, 41.6, 54.4, 78.5, 110.7, 111.9, 118.9, 119.2, 121.5, 124.3, 127.8, 136.7, 155.8, 171.6 ppm. $C_{18}H_{26}N_4O_3$ (346.43): calcd. C 62.41, H 7.56, N 16.17; found C 62.39, H 7.59, N 16.14.

General Procedure for the Synthesis of Receptors 3a and 3b: DCC (0.41 g, 2.0 mmol) was added to a stirred and ice-cooled solution of **1a** (0.76 g, 1.0 mmol) in dry $CHCl_3$ (10 mL) and the mixture was stirred at room temperature for 2 h. Then a solution of **2a** (0.58 g, 2.0 mmol) or **2c** (0.64, 2.0 mol), Et_3N (0.1 mL) and DMAP [*p*-(dimethylamino)pydridine] (0.02 g) in dry $CHCl_3$ (20 mL, for **2c** 2 mL of DMF was added to increase the solubility) was added dropwise to the above solution under argon. After addition, the mixture was stirred at room temperature for 48 h and then at 55 °C for 5 h. The reaction mixture was washed with brine and the organic layer was collected and dried with anhydrous Na_2SO_4. After filtration, the solvent was removed under reduced pressure and the residue purified by column chromatography on silica gel.

Compound 3a: Chromatographic eluent: $CHCl_3$/CH_3CH_2OH = 200:1 (v/v). The pure product was obtained as a white powder (0.70 g, 60.0%). M.p. 152–154 °C. $[\alpha]_D^{20}$ = +45.71 (*c* = 0.05, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3420, 2958, 1746, 1666, 1540, 1484, 1439, 1362, 1207, 1124, 1046, 873, 741, 669 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.91 (s, 18 H, *t*Bu), 1.25 (s, 18 H, *t*Bu), 2.67 (d, *J* = 12.9 Hz, 2 H, $ArCH_2Ar$), 3.48 (d, *J* = 12.8 Hz, 2 H, $ArCH_2Ar$), 3.60 (d, *J* = 11.4 Hz, 6 H, OCH_3), 3.68 (d, *J* = 12.9 Hz, 2 H, $ArCH_2Ar$), 3.81 (d, *J* = 13.8 Hz, 2 H, $ArCH_2Ar$), 3.99 (d, *J* = 15.3 Hz, OCH_2CO), 4.81 (d, *J* = 15.3 Hz, 2 H, OCH_2CO), 5.03 (s, 2 H, NC*HCO), 6.85–6.97 (m, 4 H, ArH), 7.07 (d, *J* = 3.3 Hz, 4 H, ArH), 7.55 (s, 2 H, ArOH), 9.35 (d, *J* = 7.2 Hz, CON*H*CH) ppm. ^{13}C NMR ($CDCl_3$): δ = 25.6, 28.5, 29.4, 29.5, 29.6, 31.5, 31.6, 49.9, 50.0, 72.5, 107.7, 108.6, 116.1, 116.8, 119.4, 120.0, 122.4, 122.9, 123.1, 124.1, 125.3, 129.8, 129.9, 133.5, 139.7, 145.3, 147.5, 166.8, 169.7 ppm. ESI-MS: *m*/*z* (%) = 1187.6 (100) $[M - 1 + Na]^+$. $C_{72}H_{84}N_4O_{10}$ (1165.48): calcd. C 74.20, H 7.26, N 4.81; found C 74.15, H 7.31, N 4.78.

Compound 3b: Chromatographic eluent: $CHCl_3$/CH_3CH_2OH = 50:1 (v/v). The pure product was obtained as a white powder (0.30 g, 22.0%). M.p. 172–176 °C. $[\alpha]_D^{20}$ = –13.87 (*c* = 0.05, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3423, 2962, 1687, 1484, 1384, 1365, 1234, 1192, 1168, 1124, 1046, 1023, 871, 742 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.07 (s, 18 H, *t*Bu), 1.29 (s, 18 H, *t*Bu), 1.41 (s, 18 H, Boc-*t*Bu), 3.29–3.31 (m, 4 H, Indole-CH_2), 3.41 (d, *J* = 12.6 Hz, 2 H, $ArCH_2Ar$), 3.43 (d, *J* = 15.3 Hz, 2 H, $ArCH_2Ar$), 4.13 (d, *J* = 12.9 Hz, 2 H, $ArCH_2Ar$), 4.21 (d, *J* = 13.8 Hz, 2 H, $ArCH_2Ar$), 4.62 (d, *J* = 13.8 Hz, 2 H, OCH_2CO), 4.72 (d, *J* = 14.1 Hz, 2 H, OCH_2CO), 5.30 (br., 2 H, NC*HCO), 6.95 (s, 4 H, ArH), 7.00 (s, 4 H, Indole), 7.03 (d, *J* = 8.4 Hz, 2 H, Indole), 7.10 (s, 4 H, ArH), 7.14 (d, *J* = 7.8 Hz, 2 H, Indole), 7.60 (d, *J* = 7.2 Hz, 2 H, Indole-NH), 7.93 (d, *J* = 2.7 Hz, 2 H, NH-Boc), 8.01 (s, 2 H, ArOH), 8.98 (s, 2 H, CONHN), 10.94 (s, 2 H, CONHN) ppm. ^{13}C NMR ($CDCl_3$): δ = 25.5, 25.9, 28.6, 29.3, 29.9, 31.6, 31.8, 51.6, 64.7, 71.8, 77.9, 107.3, 108.8, 116.3, 117.0, 119.4, 121.5, 123.2, 123.4, 123.8, 124.0, 124.6, 124.8, 125.5, 129.9, 130.0, 133.6, 140.8, 146.1, 146.7, 147.1, 153.4, 163.7, 166.9 ppm. ESI-MS: *m*/*z* (%) = 1363.6 (100) $[M - 1]^+$. $C_{80}H_{100}N_8O_{12}$ (1365.72): calcd. C 70.36, H 7.38, N 8.20; found C 70.29, H 7.41, N 8.18.

Compound 3c: Compound **1b** (0.80 g, 1 mmol) in dry $CHCl_3$ (20 mL) was added dropwise to a solution of **2d** (0.69 g, 2 mmol) and triethylamine (2 equiv.) in dry $CHCl_3$ (25 mL) at 0 °C. After addition, the reaction mixture was stirred at room temperature for 2 d and then washed successively with an aqueous solution of citric acid (10%), sodium hydrogen carbonate (10%) and brine. The organic layer was collected and dried with anhydrous Na_2SO_4. After filtration, the solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel [eluent: $CHCl_3$/CH_3CH_2OH = 100:3 (v/v)]. The pure product was obtained as a white powder (0.26 g, 18.5%). M.p. 156–158 °C. $[\alpha]_D^{20}$ = +9.52 (*c* = 0.05, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3400, 2963, 1670, 1541, 1484, 1458, 1365, 1245, 1193, 1169, 1125, 1098, 1046, 873, 741 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.08 (s, 18 H, *t*Bu), 1.25 (s, 18

H, *t*Bu), 1.45 (s, 18 H, Boc-*t*Bu), 3.10–3.28 (m, 8 H, NCH_2C), 3.30–3.35 (m, 4 H, Indole-CH_2), 3.39 (d, J = 5.1 Hz, 2 H, $ArCH_2Ar$), 3.44 (d, J = 6 Hz, 2 H, $ArCH_2Ar$), 4.01 (d, J = 5.1 Hz, 2 H, $ArCH_2Ar$), 4.13 (d, J = 5.1 Hz, 2 H, $ArCH_2Ar$), 4.45 (d, J = 7.2 Hz, 2 H, OCH_2CO), 4.55 (d, J = 7.5 Hz, 2 H, OCH_2CO), 5.31(br, 2 H, NC*HCO), 6.23 (s, 2 H, NH-Boc), 6.83 (d, J = 10.2 Hz, 2 H, Indole), 6.96 (s, 4 H, ArH), 7.06 (s, 4 H, ArH), 7.10 (s, 4 H, Indole), 7.16 (m, 2 H, Indole), 7.38 (d, J = 8.1 Hz, 2 H, Indole), 7.63 (d, J = 7.5 Hz, 2 H, Indole-NH), 8.07 (s, 2 H, ArOH), 9.00 (s, 2 H, CONHC), 9.34 (s, 2 H, CONHC) ppm. ^{13}C NMR ($CDCl_3$): δ = 28.6, 28.9, 31.2, 31.7, 32.4, 34.1, 34.4, 38.5, 39.3, 55.6, 74.7, 80.2, 109.9, 111.7, 118.8, 119.6, 122.0, 124.3, 126.0, 126.5, 127.3, 127.7, 132.6, 136.5, 143.6, 148.8, 149.0, 149.3, 155.6, 169.3, 172.5 ppm. FAB-MS: *m/z* (%) = 1443.8 (100) $[M - 1 + Na]^+$. $C_{84}H_{108}N_8O_{12}$ (1421.83): calcd. C 70.96, H 7.66, N 7.88; found C 70.87, H 7.69, N 7.85.

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

Fluorescent Response Study: The host compounds **3a**–**c** were prepared as stock solutions (5×10^{-4} mol L^{-1}) in DMSO. All the anions used in this study were in the form of the tetrabutylammonium salt and stock solutions of the salts were prepared at concentrations of approximately 0.175 and 0.0175 mol L^{-1} in DMSO. The test solutions were prepared by adding different volumes of anion solution to a series of test tubes and then the same amount of stock solution of the host compound was added to each of the test tubes and diluted to 3.5 mL with DMSO. After being shaken for several minutes, the test solutions were analyzed immediately.

Job Plots: Stock solutions of the host (4 mM) and the tetrabutylammonium salts (4 mM) were prepared in $CDCl_3$. The ^1H NMR tubes were filled with 400 μL solutions of host and guest (the total concentrations were 4.0×10^{-3} M) in the following volume ratios: 40:360, 80:320, 120:280, 160:240, 200:200, 240:160, 280:120, 320:80, and 360:40. The resulting mixtures were allowed to stand at room temperature for 4 h before ^1H NMR measurements were taken.

Supporting Information (see footnote on the first page of this article): Characterization spectra, fluorimetric titration graphs of receptors **3a**–**c** with guests in DMSO, and ^1H NMR study of receptors with the *N*-Boc-protected Ala anion or mandelate in $CDCl_3$ and $[D_6]$DMSO.

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