Design and synthesis of novel C_2-symmetric chiral shift reagents derived from squaramide and their recognition of anions and chiral carboxylate anions

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Abstract

The novel, recyclable C_2-symmetric chiral shift reagents bearing both squaramide and indanol groups have been synthesized. These squaramides were examined as chiral shift reagents, and they have a wide recognition towards chiral carboxylate anions. The squaramide derived from (1*S*, 2*R*)-1-amino-2-indanol can distinguish the absolute configuration of the guest carboxylate anion.

Keywords: Chiral shift reagents, squaramide, carboxylic anions, recognition

Introduction

The design and synthesis of chiral receptors for molecular recognition has gained much interest due to the role of chirality in biological function and pharmaceutical molecules.[1-4] The study of molecular recognition can provide valuable information for understanding the interactions between biological molecules and small molecules and offer new perspectives with regard to the resolution of racemic mixtures, determination of the enantiomeric composition, screening of chiral catalysts and the development of useful molecular devices in pharmaceutical studies.[5] In particular, chiral recognition of carboxylic acids has gained considerable attention in recent years owing to their versatile biological applications.[6-8] There are several examples of chiral solvating agents (CSAs) for carboxylic acids such as amines, aminoalcohols, amides, macrocyclic compounds and ureas are explored in details in the past decades.[9-16] In 2012, Lisowski and coworkers developed macrocycles based binaphthyldiamine, that are effective chiral solvating agents for the carboxylic acids.[17] Gualandi's group reported the chiral hexaazamacrocycles as CSAs for α-substituted carboxylic acids.[18] More recently, Song and coworkers reported that a

chiral bisthiourea has been used as highly effective chemical solvating agent for diverse α-carboxylic acids in the presence of DMAP.[19] Despite important progress in this area, there is still room for improvement regarding this type of chiral artificial receptors for molecular recognition. For example, most of the CSAs are not practical and efficient. Therefore, the development of simple, highly effective CSAs for carboxylic acid derivatives recognition is still desirable.

The squaramide motif possesses remarkable hydrogen bonding capacity due to its propensity to increase the aromaticity of the four-membered ring upon bonding.[20-23] Many reports have shown that chiral squaramide compounds are efficient organocatalysts in diverse asymmetric transformations,[24-27] and squaramides are privileged members of an important group of molecules widely used as CSAs for anion recognition,[28-31] while the studies on the use of squaramides as CSAs for carboxylic acids are few, as part of our continuous efforts to design and synthesize novel chiral squaramides and their applications in asymmetric transformations,[32-35] we decided to explore the novel C_2-symmertric chiral shift reagents **1**-**3** based on squaramide and indanol moieties (Figure 1). We expected that the chiral indanol-based receptors bearing both the amino group and the hydroxyl group would be useful for the enantiomeric discrimination of carboxylic acids and could be used as chiral solvating agents (CSAs). The C_2-symmetric chiral shift reagents based on squaramide and indanol were derived from (1*R*, 2*R*)-1,2-diphenylethane-1,2-diamine using the corresponding reaction.

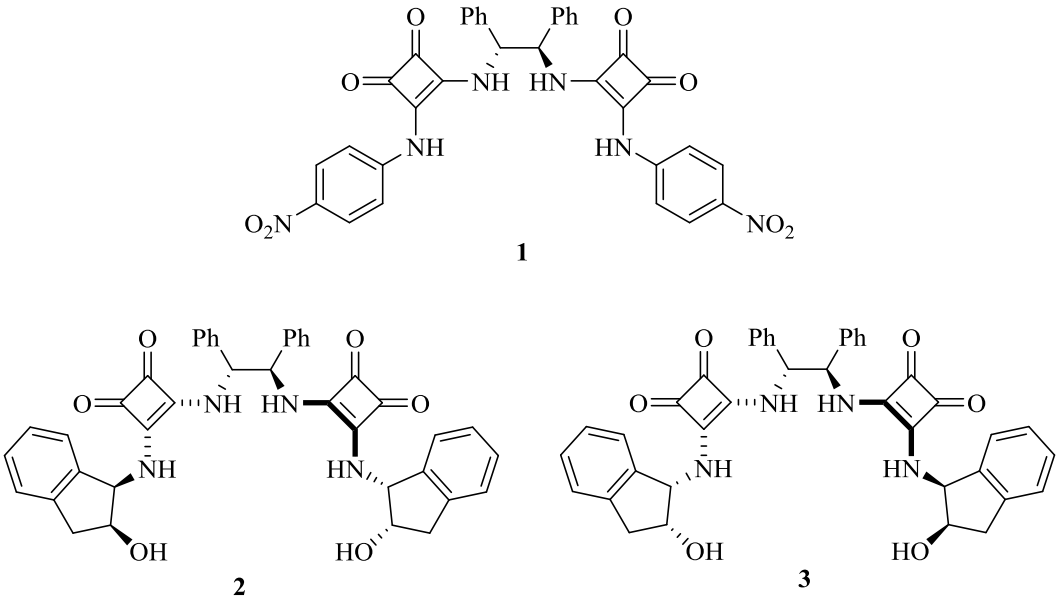
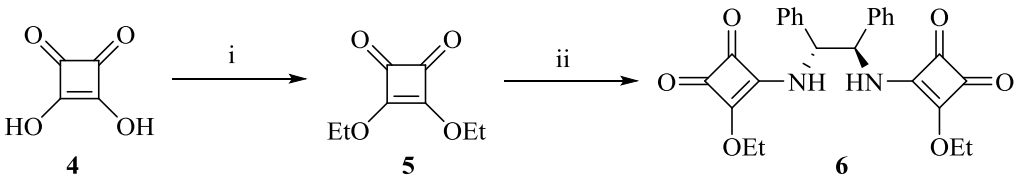


Figure 1. Structures of chiral shift reagents derived from squaramide.

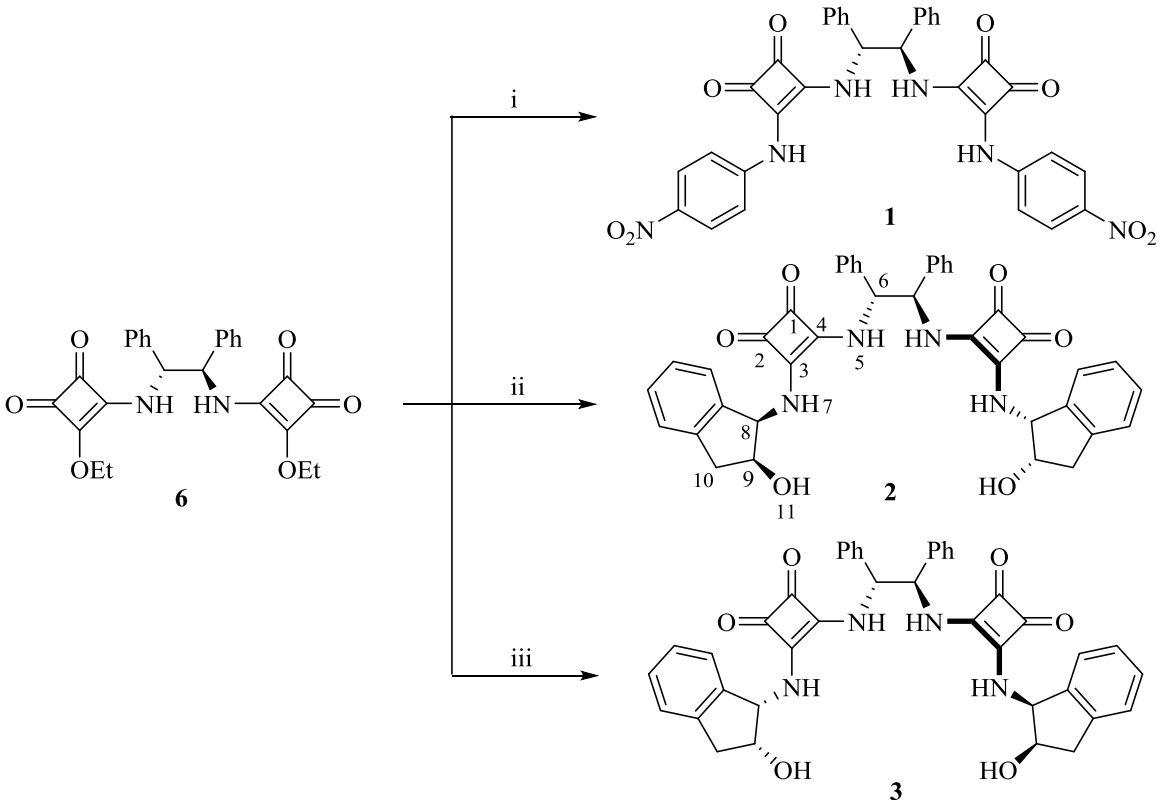
Results and Discussion

Synthesis of the C_2-symmetric chiral shift reagent derived from squaramide

C_2-symmetric chiral shift reagent was prepared from commercially available squaric acid and (1*R*, 2*R*)-(+)-1,2-diphenylethylenediamine. At first, the key intermediate **6** was synthesized from squaric acid **4** and (1*R*, 2*R*)-(+)-1,2-diphenylethylenediamine. The following coupling reaction of compound **6** with *p*-nitroaniline or 1-amino-2-indanol led to C_2-symmertric chiral shift reagents **1**-**3** in 78-90% yields (Scheme 2).[8b,8d] The structures of **1**-**3** were confirmed by ^{1}H, ^{13}C NMR spectra and mass spectrometry.



Scheme 1. Synthesis of key intermediate **6**: (i) Triethyl orthoformate, EtOH, reflux, 89%; (ii) (1*R*, 2*R*)-(+)-1,2-diphenylethylenediamine, EtOH, triethylamine, rt, 86%.



Scheme 2. Synthesis of chiral shift reagents: (i) Zinc trifluoromethanesulfonate toluene/DMF, *p*-nitroaniline, 100 °C, 78%; (ii) (1*R*, 2*S*)-1-amino-2-indanol, triethylamine, EtOH, reflux, 90%; (iii) (1*S*, 2*R*)-1-amino-2-indanol, triethylamine, EtOH, reflux, 88%.

Binding properties of chiral shift reagents toward anions

With the C_2-symmertric chiral shift reagents in hand, enantiomeric recognition abilities of compounds **1**-**3** for anions were studied under ^{1}H NMR controlled titrations at a constant concentration of receptor. In all cases, affinities were measured by complexation induced resonance shift change upon addition of guests in the form of tetrabutylammonium salts. Substantial changes in ^{1}H NMR spectra could be observed directly from the chemical shift of the protons of amides.

Based on our preliminary experimental results, we found that the C_2-symmertric chiral shift reagent **1** had the recognition ability towards anions such as chloride ion and bromide ion rather than carboxylic ion. We then turned our attention to chiral shift reagents **2** and **3**. The only difference between **2** and **3** is the absolute configuration of the 1-amino-2-indanol on the squaramide, although the existence of 1-amino-2-indanol may affect the configuration of the center part of the receptor, but will not affect the binding with the C_2-symmertric chiral shift reagents. At the beginning, their recognition ability toward anions was investigated. The recognition ability of these receptors can be seen directly from the ^{1}H NMR: due to the influence of nearby anions, there will be an obvious chemical shift of amide hydrogen bond toward anions, so the study of the binding properties of **2** and **3** toward anions is feasible. For this experiment, anions of different geometries and salts such as chloride, bromide, nitrate and acetate were used and the results were showed in Figure 2. The addition of tetrabutylammonium acetate to **2** causes a downfield shift for one of the amide NH proton. The proton that was the most downfielded the free ligand (δ 8.27 ppm) had the largest chemical shift after addition of **2** (δ 10.35 ppm). The results indicated that receptor **2** has good discrimination ability towards carboxylic anions. Thus C_2-symmertric chiral ligands **2** and **3** are potential chiral shift reagents for the recognition of carboxylic acids.

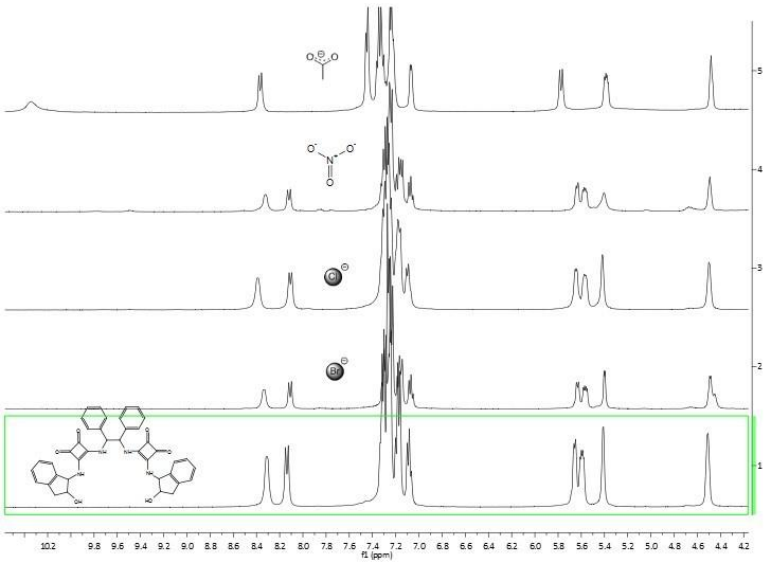


Figure 2. The binding study of chiral shift reagent **2** towards different anions detected by ^{1}H NMR (400 MHz) spectroscopy in DMSO-d_6 at 25 ºC. (1) ^{1}H NMR of receptor **2**; (2) receptor **2** with tetrabutylammonium bromide (mole ratio, n/n = 1: 3.2); (3) receptor **2** with

tetrabutylammonium chloride (mole ratio 1:0.9); (4) receptor **2** with tetrabutylammonium nitrate (molar ratio 1: 1.2); (5) receptor **2** with tetrabutylammonium acetate (mole ratio, 1: 0.83).

The recognition ability of chiral shift reagents toward chiral carboxylate anion

We next studied the enantiomeric discrimination ability of chiral shift reagents **2** and **3** towards different configuration of the guest carboxylate anions **7**-**12** (Figure 3). Since the shift reagents could affect the chemical shift of each enantiomer of chiral carboxylate anions, one of the enantiomers was added more than the other during the whole process, thus the enantiomeric discrimination properties of the receptors could be seen directly from the ^{1}H NMR. In fact, among the ammonium carboxylate salts **7**-**12**, there is good enantiomeric discrimination ability of **2** and **3** towards **7** and *N*-BOC-protected **10** and **11**, the results were summarized in Table 1.

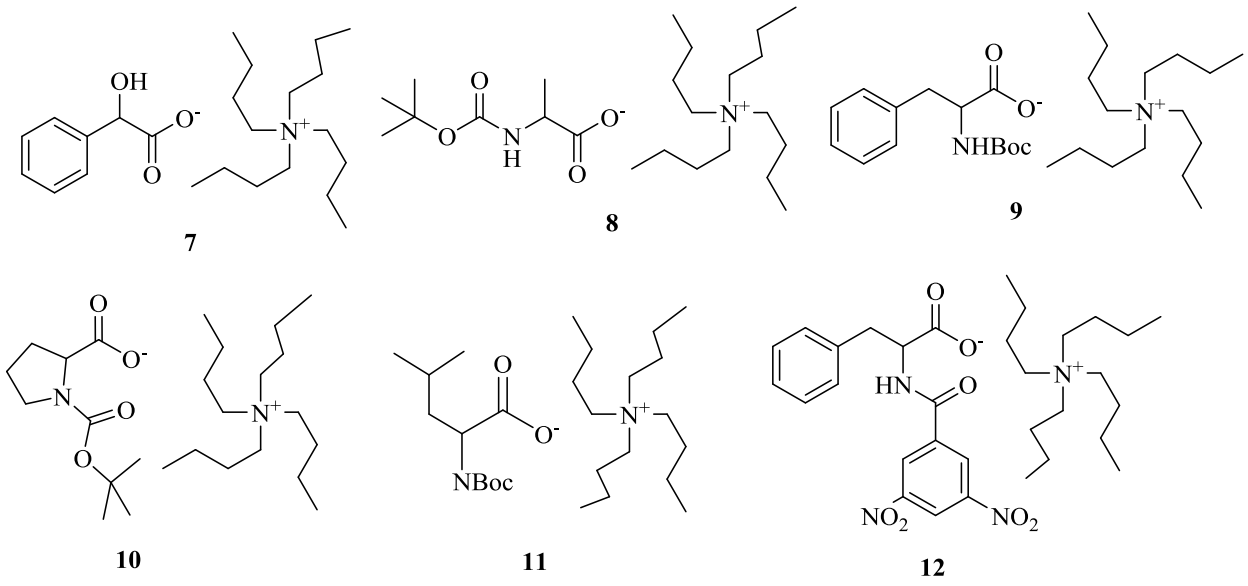
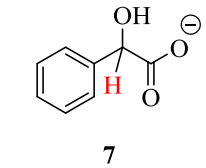
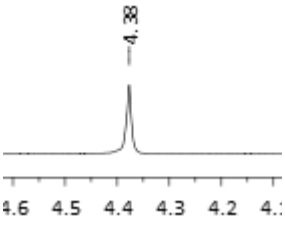
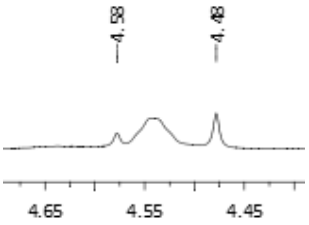
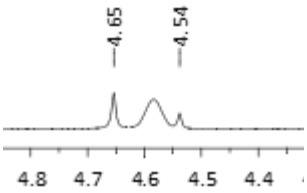
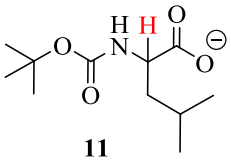
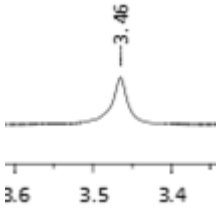
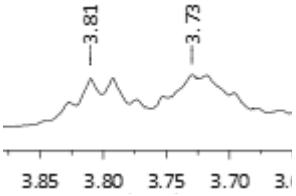
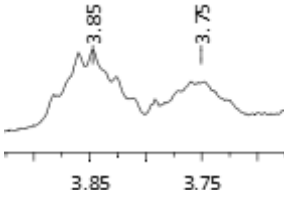


Figure 3. Structures of carboxylic acid and α-amino acid tetrabutylammonium salts.

It is presumed that there are three major factors possibly accounted for the binding ability of receptors **2** and **3**, which including the hydrogen bond, absolute configuration and the steric-hindrance effect of the ligands, in which the effect of hydrogen bond is very obvious. As shown in Table 1, chemical shift change of proton of CH (neighboring to the carbonyl group of carboxylic acid) can be fairly observed in the presence of receptors **2** or **3**. But receptor **3** shows better enantiomeric discrimination ability.

Table 1 The enantiomeric discrimination recognition results of chemical shift nonequivalence ($\Delta\Delta\delta$) values of chiral shift reagents **2** and **3** toward representative carboxylate anions **7** and **11** [a]

Entry	Carboxylic acid	^{1}H NMR of carboxylic acid	^{1}H NMR of carboxylic acid and receptor **2** $\Delta\Delta\sigma$ (ppm)[b]	^{1}H NMR of carboxylic acid and receptor **3** $\Delta\Delta\sigma$ (ppm)[b]
1	 **7**			
2	 **11**			

[a] All samples were prepared by mixing the DMSO-d_6 solution of receptor **2** or **3** with carboxylic acid or α-amino acid tetrabutylammonium salts in NMR tubes at 25 ºC and were determined by ^{1}H NMR (400 MHz) spectroscopy. [b] $\Delta\Delta\delta$ values of the α-H methyl proton on the chiral centers of the acids.

As shown in Tables 1 and 2, in the presence of receptor **2** or **3**, there are obvious chemical shifts of appropriate signal for almost all the chosen carboxylate anions measured by ^{1}H NMR. But receptor **3** shows better enantiomeric discrimination ability (the overall chemical shift corresponding to each enantiomer $\Delta\Delta\delta$ > 0.1 ppm) than receptor **2**. Receptor **2** shows no enantiomeric discrimination towards *N*-BOC-Ala **8** and *N*-BOC-Phe **9**, which probably due to the fact that **3** possessing a (1*S*, 2*R*)-1-amino-2-indanol moiety which therefore could form a more wide binding site compared to that of receptor **2**, which had a (1*R*, 2*S*)-1-amino-2-indanol, thus the latter cannot bind well with bulky anions. In order to demonstrate the steric-hindrance effect of the substrate, *N*-DNB-protected amino acid **12** was designed. As expected, neither receptor **2** and **3** had discrimination ability toward the *N*-DNB-protected amino acid **12**.

Table 2 shows the detail values for the induced chemical shift ($\Delta\delta$) on the signals of the methenyl group after the addition of chiral receptor **2** or **3**. Combined with Table 1, the CH proton of *R*-enantiomers appeared at downfield with receptor **3** (entries 2 and 8), and the amide protons of *S*-enantiomers of all the carboxylic acids appeared at a low field with both receptors **2** and **3**.

Table 2. Chemical shift ($\Delta\delta$) of racemic carboxylic acids in the presence of receptor **2** or **3** [a]

Entry	isomers	Chemical shift caused by receptor **2** $\Delta\sigma$ (ppm)[b]	Chemical shift caused by receptor **3** $\Delta\sigma$ (ppm)[b]
1	***S*** **- 7**	0.20	0.16
2	***R*** **- 7**	0.10	0.27
3	***S*** **- 8**	0	0.32
4	***R*** **- 8**	0	0.43
5	***S*** **- 9**	0	0.15
6	***R*** **- 9**	0	0.27
7	***S*** **- 10**	0.10	0.08
8	***R*** **- 10**	0.09	0.14
9	***R*** **- 11**	0.33	0.29
10	***S*** **- 11**	0.26	0.39
11	***S*** **- 12**	0	0

[a] Determined by ^{1}H NMR (400 MHz) spectroscopy in DMSO-d_6 25 ºC. [b] $\Delta\delta$ values of the α-H methine proton on the chiral centers of the acids.

Possible mechanism for the recognition ability of *C*$_2$-symmertric chiral shift reagents toward carboxylate anion

In order to study the possible mechanism of the recognition of our C_2-symmertric chiral squaramide shift reagents towards carboxylate anions, the 2D NOESY spectra was analyzed in details (see supporting information). After all the chemical shifts were assigned, the ^{1}H NMR titrations was carried out by addition of tetrabutylammonium acetate to receptor **2**. As shown in **Figure 4**, with the increasing of tetrabutylammonium acetate, there was an obvious change of chemical shift of H_{N5} (δ > 2.5 ppm) but with a little change of H_{N7} (δ < 0.5 ppm), which indicated there was an intense hydrogen-bonding interaction between H_{N5} and carboxylic anions. While the disappearance of H_{O11} demonstrated that the deprotonation of N7 and bind with hydroxyl group through hydrogen-bond to form a five-membered ring (**Figure 5**), it is the principal factor for the mechanism during the reaction of carboxylic acids with receptors, while the hydrogen bond (2D structure, red color) is the secondary cause. Another evidence to demonstrate this hypothesis is the change of chemical shifts of protons of C6 (0.16 ppm) and C8 (0.25 ppm). The slightly change of chemical shift of H_{C6} to downfield and the obvious change of H_{C8} to high field is possibly due to the deshielding effect of electron negative N7.

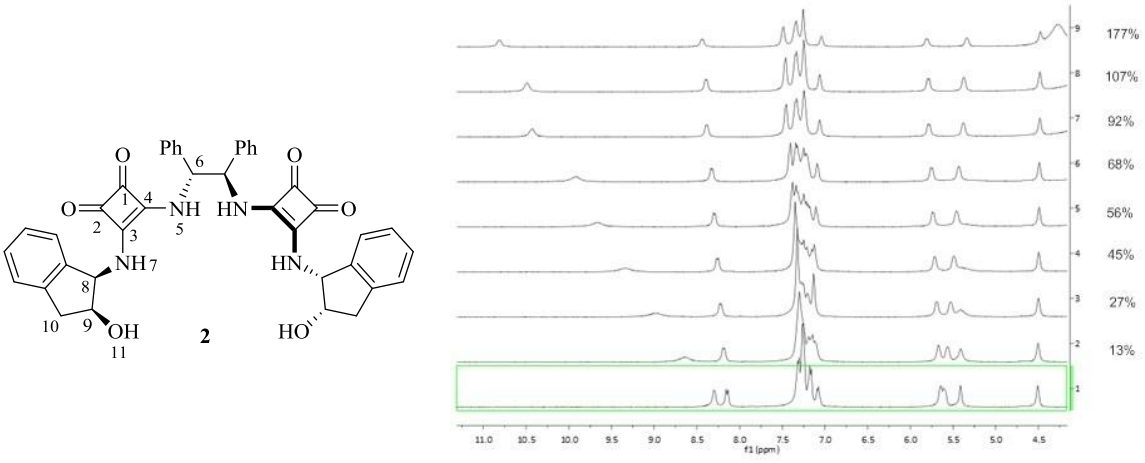


Figure 4. ^{1}H NMR titration of tetrabutylammonium acetate to C_2-symmertric chiral shift reagent **2** detected by ^{1}H NMR (400 MHz) spectroscopy in DMSO-d_6 at 25 ºC (1. Receptor **2**; 2-9. Different concentrations of tetrabutylammonium acetate).

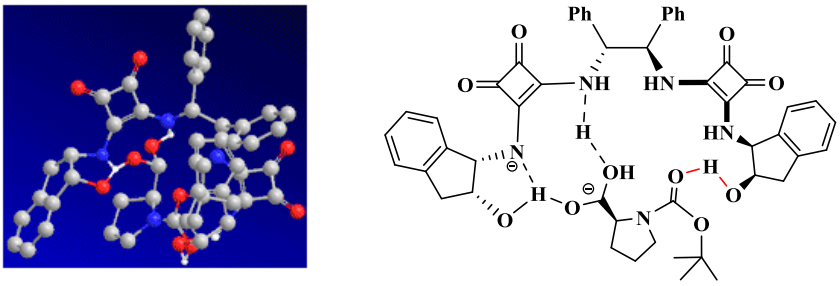


Figure 5. 2D and 3D structure for the probable mechanism of C_2-symmertric chiral shift reagent combined with acetate anions (receptor **2** and *N*-BOC-Pro tetrabutyl ammonium salt).

C_2-symmertric chiral shift reagent recovery

The poor solubility of the C_2-symmetric chiral shift reagent in organic solvents allows its easy recycling. The addition of common solvents such as EtOH and simple filtration will separate chiral shift reagent from system.

Conclusions

We have designed and synthesized the novel C_2-symmetric chiral shift reagents **2** and **3**. They can bind with carboxylic anions selectively. Compound **3** has a wide recognition towards chiral carboxylate anions and can distinguish the absolute configuration of the guest carboxylate anions. In addition, the poor solubility of the C_2-symmetric chiral shift reagent in organic solvents allows its recycling.

Experimental Section

General. Unless otherwise noted, reagents and materials were obtained from commercial suppliers and used without further purification. Tetrahydrofuran and toluene as well as ethanol were dried over Na and distilled prior to use. Dichloromethane was dried over CaH_2 and distilled prior to use. Glassware was oven-dried, assembled while hot, and cooled under an inert atmosphere. Unless otherwise noted, all reactions were conducted in an inert atmosphere. ^{1}H NMR and ^{13}C NMR spectra were obtained on Bruker Biospin AV400 (400 MHz) instrument. The chemical shifts are reported in ppm and are referenced to either tetramethylsilane or the solvent.

Synthesis of *C*$_2$-symmetric chiral shift reagents

Synthesis of compound 6. To a solution of diethyl squarate (374 mg, 2.2 mmol) in dry ethanol (15 mL) with triethylamine (228 μL, 2 mmol) were added a solution of (1*R*, 2*R*)-(+)-1,2-diphenylethylenediamine (212 mg, 1.0 mmol) in dry ethanol (10 mL) drop wise at 0 ºC under an argon atmosphere, the resulting reaction mixture was warmed to room temperature gradually, after 6 h, the reaction mixture was concentrated to about 15 mL, filtered, the resulting white residue was washed with ethanol (3 × 5 mL), compound **6** was obtained as a white solid, 86% yield, (mp 263 – 265 ºC). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.93 – 9.66 (br, 1H, NH), 9.65 – 9.34 (br, 1H, NH), 7.17 – 7.24 (m, 10H), 5.59 (br, 1H), 5.14 (s, 1H), 4.63 (br, 4H), 1.31 (br, 6H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 188.92, 182.42, 177.42, 172.54, 138.95, 128.36, 127.80, 127.19, 69.01, 68.91, 62.17, 61.37, 15.54. HRMS Calcd. for $C_{26}H_{24}N_2O_6$ $[M]^+$ 460.1634, Found 460.1642.

Synthesis of *C*$_2$-symmetric chiral shift reagent 1. To a solution of compound **6** (46 mg, 0.1 mmol) and zinc trifluoromethanesulfonate (7.3 mg, 0.02 mmol) in toluene and DMF (19:1, v/v) (3 mL) was added *p*-nitroaniline (34.5 mg, 0.25 mmol) at room temperature under an argon atmosphere, after 15 min, the reaction mixture was heated to 100 ºC and stirred for 12 h. The reaction mixture was cooled to room temperature and added methanol (5 mL), stirred for another 0.5 h and filtered, the precipitate was rinsed with hot MeOH (2 × 10 mL) to afford the pure compound **1** as a light yellow solid, 78% yield, (mp > 320 ºC). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.25 (s, 2H, NH), 8.36 (s, 2H, NH), 8.01 (d, *J* 8.9 Hz, 4H), 7.48 – 7.30 (m, 14H), 5.74 (d, *J* 6.5 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 185.55, 180.17, 169.87, 162.85, 144.63, 141.46, 137.23, 129.00, 128.51, 127.27, 125.30, 117.62, 63.39. HRMS Calcd. for $C_{34}H_{24}N_6O_8$ Na $[M + Na]^+$ 667.1553, Found 667.1545.

Synthesis of *C*$_2$-symmertric chiral shift reagent 2. To a solution of compound **6** (230 mg, 0.5 mmol) in ethanol with triethylamine (158 uL, 1.1 mmol) was added (1*R*, 2*S*)-1-amino-2-indanol (163 mg, 1.1 mmol) at one time, after stirred in room temperature for 6 h, the reaction mixture was refluxed for another 4 h, a white precipitate was obtained. After the mixture was cooled to room temperature, it was filtered and the residue was washed with ethanol (3 × 5 mL).

Compound **2** was obtained as a white solid, 90% yield, (mp > 360 ºC). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.31 (br, 2H, N_5H), 8.13 (d, *J* 8 Hz, 2H, N_7H), 7.27-7.06 (m, 18H), 5.65 (br, 2H), 5.59 (br, 2H), 5.41 (br, 2H, OH), 4.51 (s, 2H), 3.10 (d, *J* 12, 2H), 2.83 (d, *J* 16 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 182.89, 182.50, 167.54, 167.41, 141.51, 140.53, 138.21, 128.72, 127.98, 127.70, 127.18, 126.65, 124.94, 124.06, 72.96, 63.30, 61.11. HRMS Calcd. for $C_{40}H_{34}N_4O_6$ Na [M+ Na]$^+$ 689.2376, Found: 689.2364.

Synthesis of *C*$_2$-symmertric chiral shift reagent 3. Followed the synthesis method of compound **2**, compound **3** was obtained as white solid, 88% yield, (mp > 360 ºC). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.39 (s, 2H, N_5H), 7.97 (d, *J* 8.0 Hz, 2H, N_7H), 7.17 – 7.08 (m, 18H), 5.65 (s, 2H), 5.46 (br, 4H), 4.58 (s, 2H), 3.11 (d, *J* 12 Hz, 2H), 2.86 (d, *J* 12 Hz, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 183.39, 183.18, 168.19, 168.03, 142.43, 140.84, 139.40, 129.13, 128.28, 127.68, 127.10, 125.55, 124.63, 72.15, 62.89, 61.22. HRMS Calcd. for $C_{40}H_{34}N_4O_6$ Na [M+ Na]$^+$ 689.2376, Found: 689.2362.

Synthesis of chiral carboxylic acids

General procedure A. General procedure for the preparation of tetrabutylammonium carboxylic acid salts. Amino acid (1.0 eq) was dissolved in a solution of water and tetrahydrofuran (10:1, v/v), tetrabutylammonium hydroxide (1.0 eq) was added subsequently, and the resulting reaction mixture was stirred for 4 h. The reaction mixture was extracted with dichloromethane (2 × 5 mL) and the organic layer was washed with water (3 × 3 mL) and dried by Na_2SO_4, evaporated to afford the pure product.

General procedure B. General procedure for the di-*tert*-butyl dicarbonate protected amino acids. Amino acid (1.0 eq) was dissolved in a solution of water and tetrahydrofuran (10:1, v/v), sodium carbonate (2.0 eq) was added subsequently, the reaction mixture was then cooled to 0 ºC, di-*tert*-butyl dicarbonate (1.1 eq) was added drop wise, after the addition completed, the reaction mixture was warmed to room temperature gradually and stirred for another 16 h. After the reaction completed, the pH of the reaction mixture was adjustment to 2.0 by adding of 9% hydrochloride aqueous and was then extracted with dichloromethane (2 × 15 mL), the organic layer was dried by Na_2SO_4, evaporated to afford the pure product.

General procedure C. General procedure for the 3,5-dinitrobenzoyl protected amino acids

To a solution of amino acid (1.0 eq) in dry tetrahydrofuran was added 3,5-dinitrobenzoyl chloride (1.0 eq) and 1,2-epoxypropane (1.1 eq), the reaction mixture was stirred at room temperature for 3 h and filtered to remove the amino acid, the resulting filtrate was concentrated to afford the crude product.

Mandelic acid tetrabutyl ammonium salt 7. Followed general procedure A, this compound was obtained as colorless oil in 88% yield. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.36 (d, *J* 8 Hz, 2H), 7.21 (t, *J* 8 Hz, 2H), 7.12 (t, *J* 8 Hz, 1H), 4.38 (s, 1H), 3.21 – 3.12 (m, 8H), 1.57 (t, *J* 8 Hz, 8H), 1.37 – 1.25 (m, 8H), 0.94 (t, *J* 8 Hz, 12H).

***N*-BOC-Ala tetrabutyl ammonium salt 8.** Followed general procedure B and then procedure A, this compound was obtained as colorless oil in 77% yield over two steps. ^{1}H NMR (400 MHz,

DMSO-d_6) δ 6.00 (d, *J* 4 Hz, 1H), 3.38 – 3.30 (m, 1H), 3.29 – 3.12 (m, 8H), 1.66 – 1.51 (m, 8H), 1.49 – 1.20 (m, 17H), 1.11 (d, *J* 8 Hz, 3H), 0.94 (t, *J* 8 Hz, 12H).

***N*-BOC-Phe tetrabutyl ammonium salt 9.** Followed general procedure B and then procedure A, this compound was obtained as colorless oil in 81% yield over two steps. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.15 (m, 5H), 5.73 (br, 1H), 3.78 – 3.72 (m, 1H), 3.23 – 3.10 (m, 8H), 3.03 (br, 1H), 2.92 (br, 1H), 1.62 – 1.50 (m, 8H), 1.40 – 1.23 (m, 17H), 0.93 (t, *J* 8 Hz, 12H).

***N*-BOC-Pro tetrabutyl ammonium salt 10.** Followed general procedure B and then procedure A, this compound was obtained as a white solid in 82% yield over two steps. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.16 – 4.04 (m, 1H), 3.59 – 3.51 (m, 1H), 3.35 – 3.30 (m, 10H), 2.10 – 2.03 (m, 1H), 1.72 – 1.60 (m, 10H), 1.53 – 1.37 (m, 17H), 1.00 (t, *J* 8 Hz, 12H).

***N*-BOC-Leu tetrabutyl ammonium salt 11.** Followed general procedure B and then procedure A, this compound was obtained as a white solid in 86% yield over two steps. ^{1}H NMR (400 MHz, DMSO-d_6) δ 5.82 (br, 1H), 3.75 (m, 1H), 3.22 – 3.14 (m, 8H), 1.62 – 1.54 (m, 8H), 1.50 – 1.40 (m, 2H), 1.38 – 1.28 (m, 17H), 0.94 (t, *J* 8 Hz, 2H), 0.84 (d, *J* 8 Hz, 6H).

DNB-Ala tetrabutyl ammonium salt 12. Followed general procedure C and then procedure A, this compound was obtained as colorless oil in 69% yield over two steps. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.03 – 8.74 (m, 4H), 4.20 – 4.12 (m, 1H), 3.19 (br, 8H), 1.54-1.61 (m, 8H), 1.36 – 1.16 (m, 11H), 0.93 (t, *J* 8 Hz, 12H).

Discrimination ability of CSAs 2 and 3 toward racemic guests 7-12

1 equiv of CSA and 1 equiv of guest were mixed in NMR tube, to which the DMSO-d_6 was added. The ^{1}H NMR spectra of all samples were recorded on a 400 MHz spectrometer at room temperature.

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