Enantioselective Recognitions of Chiral Molecular Tweezers Containing Imidazoliums for Amino Acids

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ABSTRACT Two kinds of novel chiral molecular tweezers containing imidazoliums were synthesized from L-alanine, L-phenylalanine, and L-glutamic acid. They are constructed by the chiral imidazolium pincers and two different spacers which are 1,3-bis(bromomethyl)benzene and 2,6-bis(bromomethyl)pyridine, respectively. The enantioselective recognition of L- and D-amino acid derivatives by these molecular tweezers was investigated by UV spectroscopic titration experiments and good enantioselectivities were obtained, which are highly sensitive to whether the spacer has the binding site and the pincers has the other aromatic rings besides imidazolium ring. The host molecular 3b.2PF6 showed remarkable enantioselectivity for N-Boc protected histidine methyl ester, affording $K_I/K_D$ of 5.10. Chirality 21:539–546, 2009. © 2008 Wiley-Liss, Inc.

KEY WORDS: imidazolium; molecular tweezers; amino acid; chiral recognition; UV–vis titration

INTRODUCTION Molecular recognition, especially chiral recognition, is one of the significant processes for diverse chemical and biological phenomena. The study of synthetic modeling systems for chiral recognition is an area of ever increasing research activity. Such model systems can find potential applications in the development of pharmaceuticals, enantioselective catalysis, separation, and analysis of enantiomers. They can also contribute to better understanding of biological systems and their functions since chiral recognition is an essential phenomena in living systems. Continuing efforts creating chiral artificial receptors for enantioselective recognition have been made and the recognition mechanism has been gradually understood as the combined efforts of several noncovalent interactions such as hydrogen bonding, electrostatic interactions, hydrophobic interactions, cation–π interactions, π–π stacking interactions, and steric complementarity, etc.

Amino acids are the major components of proteins and have versatile abilities to form complexes with many hosts presenting various types of interaction modes. The development of new receptors capable of recognizing amino acids and their derivatives has attracted more interest in the recent past. A series of chiral artificial receptors, such as the binaphthol dimmers, the chiral macrocycles, the chiral crown ethers, the chiral metalloporpyrins and cyclodextrins derivatives, and cyclopeptides derivatives have been synthesized for enantioselective recognition of amino acids or their derivatives.

Imidazolium receptors have attracted widespread interest due to their recognition ability. A variety of imidazolium compounds, especially water-soluble bromide salts, have been synthesized and employed as excellent selective receptors for ions and molecules in aqueous solvents. At the same time, some other imidazolium salts which are easily soluble in organic solvents, such as hexafluorophosphate compounds, also showed recognition ability for anions and molecules. Imidazolium units display main structural motifs for the formation of unconventional (C–H)•••anion hydrogen bonding interactions and cation–π interactions for molecular recognition. As far as we are aware, there are few examples of chiral imidazolium compounds prepared and served as artificial receptors for chiral molecular recognition to date. We have focused our interest on the synthesis and application of imidazole and imidazolium compounds and have reported several chiral cyclophanes and chiral molecular tweezers containing imidazole and imidazolium residues as hosts for the enantioselective recognition toward amino acids or their derivatives.

We have recently reported a kind of chiral molecular tweezers constructed by the imidazolium and phenol spacer and hope to further find out whether the spacer has an immediate effect on the enantioselectivity of chiral molecular tweezers. Therefore we now report the effective synthesis of the chiral molecular tweezers spaced by 1,3-phenylenebis(methylene) and 2,6-pyridylenebis(methylene) spacer, respectively.
and their enantioselective recognition for L- and D-

amino acids and their derivatives. These chiral molecular
tweezers show strong 1:1 binding characteristic with

amino acids and good enantioselective recognition abilities
toward α-amino acids and their derivatives in water or
acetone.

**EXPERIMENTAL PROCEDURES**

**General Information**

1H NMR spectra were recorded on a Bruker DPX-300

instrument. 13C NMR spectra were recorded on a Bruker

DPX-200 instrument. Chemical shifts are given in δ (ppm)

relative to TMS as the internal standard. HRMS were

measured on Finnigan LCQDeca, IR and UV spectra were

obtained with the Nicolet FT-IR 170SX and the Tu-1600

UV/vis spectrophotometer, respectively. Amino acid

methyl esters and N-protected amino acid methyl

esters were prepared according to literature

procedure.35,39 (S)-2-(1-imidazolyl) propanol 1a, (S)-2-(1-imida-

zolyl)-3- phenylpropanol 1b, and (S)-2-(1-imidazolyl)-1,5-

pentanediol 1c were prepared from L-alanine, L-phenylala-

nine, and L-glutamic acid according to the procedure

recorded in the literature.35,40 Water was distilled before

use. Acetonitrile was purified according to the standard

method. All the other chemicals and reagents were

commercially available and used without further purification.

**UV Spectral Measurements**

The chiral recognition of chiral molecular tweezers for

amino acids and their derivatives was investigated using

UV spectrophotometric titration. In the experiments, the cell

was kept at constant temperature (27°C ± 0.1°C) with

thermostated cell compartment. A 3.0 ml solution of host

was put into the cell, and 3.0 ml water or acetonitrile was

put into the reference cell. Guest solutions of the same

concentration were added to the sample cell and reference

cell. The different absorption spectra were obtained

directly using the instrument. The concentration of the

host is 5.0 × 10−5 mol dm−3, and that of the guest is 2.0

× 10−4 to 1.8 × 10−3 mol dm−3. The whole volume of the

guest solution added to the cell did not exceed 100 μl to
dispel the effect of volume change. All the titration experi-

ments were repeated three times.

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**Synthesis**

A series of novel chiral molecular tweezers were prepared

(Scheme 1). Chiral imidazoles 1a–c were obtained

according to the procedure recorded in the literatures.35,40

Water-soluble dibromide salts 2a–c.2Br− and 3a–c.2Br−

were obtained by direct quaternization of 1a–c with 1,3-

bis(bromomethyl)benzene or 2,6-bis(bromomethyl)pyr-

idine in dry acetonitrile at 65°C for 24–36 h. Hexafluoro-

phosphate salts 2a–c.2PF6− and 3a–c.2PF6− were

obtained by treating the aqueous solution of the corre-

sponding bromide salt with a saturated aqueous solution

of NH4PF6. All the compounds were obtained in good

yields (>70%). The structure of the new compound was

confirmed by 1H NMR, 13C NMR, IR, MS, and HRMS.

**General Procedures for the Synthesis of Chiral

Imidazolium Receptors**

A solution of 1a–c (2.20 mmol) and the corresponding

alkylating agent 1,3-bis(bromomethyl)benzene (1.00

mmol) or 2,6-bis(bromomethyl)pyridine (1.00 mmol) in

dry acetonitrile (10.0 ml) was stirred at 65°C for 24–36 h.

The insoluble oily material was separated by decantation

and wash several times with cool dry acetonitrile and THF
to give yellow oil 2a–c.2Br− and 3a–c.2Br−. To a solution

of bromide salts (0.5 mmol) in 10 ml water, a satu-

rated aqueous solution of NH4PF6 (1 ml) was added and

stirred for 1 h. The insoluble material was washed several

times with cool water and EtOH to give pale yellow oil,

affording hexafluorophosphate salts 2a–c.2PF6− and 3a–

−c.2PF6− as a pure product.

**Scheme 1.** Synthesis of chiral molecular tweezers.
(S,S)-3,3'-Bis(1-hydroxyl-3-phenyl-2-propanyl)-1,1'-[1,3-phenylenebis(methylene)] bis(imidazolium)

Bis(hexafluorophosphate) 2a.2PF$_6^-$

Yield: 240 mg (0.37 mmol, 73%). Pale yellow oil. $[\alpha]_D^{25} = +9.4$ (c 0.2, CH$_3$COCH$_3$). $^1$H NMR (300 MHz, DMSO-d$_6$) δ (ppm): 9.41 (s, 2H, ImH-2), 7.81 (m, 4H, Ar), 7.60 (s, 2H, ImH-4), 7.42 (s, 2H, ImH-5), 5.51 (m, 4H, ArCH$_2$), 4.58 (m, 2H, CH$_2$), 3.67 (m, 4H, CH$_2$O), 1.48 (d, 6H, J = 6.8 Hz, CH$_3$), 2.08 (s, 2H, OH). $^{13}$C NMR δ (ppm): 135.26, 136.54, 131.46, 129.35, 125.99, 123.03, 121.73, 60.31, 51.21, 40.39, 19.54, 18.87. IR: 3283, 3040, 2881, 1631, 1578, 1449, 1375, 1156, 741 cm$^{-1}$. ESI-MS m/z (rel, intensity) = 356 [M-HPF$_6$PF$_6$]. HRMS m/z calad for C$_{23}$H$_{36}$F$_{14}$N$_{10}$P$_2$ 501.4292 [M-PF$_6$$^-$], Found 501.4310.

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(S,S)-3,3'-Bis(1-hydroxyl-3-phenyl-2-propanyl)-1,1'-[1,3-phenylenebis(methylene)] bis(imidazolium)

Bis(hexafluorophosphate) 2b.2PF$_6^-$

Yield: 500 mg (0.75 mmol, 75%). Light brown oil. $[\alpha]_D^{25} = -12.0$ (c 0.2, CH$_3$OH). $^1$H NMR (300 MHz, DMSO-d$_6$) δ (ppm): 9.46 (s, 2H, ImH-2), 7.91 (m, 2H, ArH), 7.91 (s, 2H, ImH-4), 7.90 (s, 2H, ImH-5), 7.39 (m, 4H, CH$_2$C$_6$H$_4$CH$_2$), 7.19 (m, 4H, CH$_2$C$_6$H$_4$), 7.06 (s, 2H, OH), 5.41 (m, 4H, CH$_2$C$_6$H$_4$CH$_2$), 4.74 (m, 2H, CH$_2$), 3.12 (m, 4H, ArCH$_2$), 3.10 (m, 4H, CH$_2$O). IR: 3296, 2935, 1652, 1578, 1454, 1154, 1091, 1066, 752, 704, 662 cm$^{-1}$. ESI-MS m/z (rel, intensity) = 509 [M-HBr$^-$]. HRMS m/z calad for C$_{29}$H$_{38}$F$_{14}$N$_{10}$O$_2$ 588.5664 [M$^-$], Found 588.5617.

(S,S)-3,3'-Bis(1-hydroxyl-3-phenyl-2-propanyl)-1,1'-[1,3-phenylenebis(methylene)] bis(imidazolium)

Bis(hexafluorophosphate) 2c.2PF$_6^-$

Yield: 400 mg (0.77 mmol, 77.0%). Light brown oil. $[\alpha]_D^{25} = +8.5$ (c 0.2, CH$_3$OH). $^1$H NMR (300 MHz, DMSO-d$_6$) δ (ppm): 9.12 (s, 2H, ImH-2), 7.89 (t, 1H, J = 4.2 Hz, p-pyr), 7.76 (s, 2H, ImH-4), 7.60 (s, 2H, ImH-5), 7.41 (d, 2H, J = 7.7 Hz, m-pyr), 5.56 (m, 4H, CH$_2$pyrCH$_2$), 4.56 (m, 2H, CH$_2$), 4.02 (s, 2H, OH), 3.73 (m, 4H, CH$_2$O), 1.48 (d, 6H, J = 6.9 Hz, CH$_3$). IR: 3420, 3015, 2961, 1604, 1451, 1376, 1166, 741, 667 cm$^{-1}$. ESI-MS m/z (rel, intensity) = 357 [M-HBr$^-$. HRMS m/z calad for C$_{19}$H$_{27}$BrN$_2$O$_2$ 437.3593 [M$^-$], Found 437.3569.

(S,S)-3,3'-Bis(1,5-dihydroxy-2-pentanyl)-1,1'-[1,3-phenylenebis(methylene)] bis(imidazolium)

Bis(hexafluorophosphate) 3a.2PF$_6^-$

Yield: 250 mg (0.77 mmol, 77%). Pale yellow oil. $[\alpha]_D^{25} = +10.0$ (c 0.2, CH$_3$OH). $^1$H NMR (300 MHz, DMSO-d$_6$) δ (ppm): 9.22 (s, 2H, ImH-2), 7.99 (t, 1H, J = 4.2 Hz, p-pyr), 7.81 (s, 2H, ImH-4), 7.68 (s, 2H, ImH-5), 7.47 (d, 2H, J = 7.7 Hz, m-pyr), 5.57 (m, 4H, CH$_2$pyrCH$_2$), 4.55 (m, 2H, CH$_2$), 3.70 (m, 4H, CH$_2$O), 2.06 (s, 2H, OH), 1.46 (d, 6H, J = 6.9 Hz, CH$_3$). $^{13}$C NMR δ (ppm): 153.61, 138.36, 136.98, 123.1, 122.01, 121.18, 51.35, 46.37, 17.21, 16.84. IR: 3530, 3360, 2959, 1609, 1454, 1356, 1046, 742, 665 cm$^{-1}$. ESI-MS m/z (rel, intensity) = 357 [M-HPF$_6$PF$_6$]. HRMS m/z calad for C$_{19}$H$_{27}$BrN$_2$O$_2$ 502.4173 [M$^-$], Found 502.4135.

(S,S)-3,3'-Bis(1-hydroxyl-3-phenyl-2-propanyl)-1,1'-[2,6-pyridylenebis(methylene)] bis(imidazolium)

Bis(hexafluorophosphate) 3b.2Br$^-$

Yield: 500 mg (0.75 mmol, 75%). Brown oil. $[\alpha]_D^{25} = -38.0$ (c 0.2, CH$_3$OH). $^1$H NMR (300 MHz, DMSO-d$_6$) δ (ppm): 9.10 (s, 2H, ImH-2), 7.88 (t, 1H, J = 8.0 Hz, p-pyr), 7.78 (s, 2H, ImH-4), 7.54 (s, 2H, ImH-5), 7.35 (d, 2H, J = 8.0 Hz, m-pyr), 7.17 (m, 10H, PhH), 5.42 (m, 4H, CH$_2$pyrCH$_2$), 4.85 (s, 2H, OH), 4.78 (m, 2H, CH$_2$), 3.96 (m, CH$_2$)}
4H, PhCH₂), 3.27 (m, 4H, CH₂O). IR: 3358, 3007, 1602, 1460, 1146, 1062, 750, 659 cm⁻¹. ESI-MS m/z (rel. intensity) = 509 [M-HBr-Br⁻]. HRMS m/z calcd for C₃₁H₃₅BrN₅O₂ 589.1847 [M-Br⁻], Found 589.1821.

(5R,5S)-3,3′-Bis(1-hydroxy-3-phenyl-2-propanyl)-1,1′-[2,6-pyridylenebis(methylene)] bis[imidazolium]
Bis(hexafluorophosphate) 3b.2PF₆⁻

Yield: 310 mg (0.39 mmol, 78%) Pale yellow oil. [α]²⁵D = -31.8 (c 0.2, CH₂COCH₃). ¹H NMR (300 MHz, DMSO-d₆) δ (ppm): 9.20 (s, 2H, ImH-2), 7.91 (t, 1H, J = 7.7 Hz, p-pyr), 7.88 (s, 2H, ImH-4), 7.62 (s, 2H, ImH-5), 7.27 (d, 2H, J = 7.8 Hz, m-pyr), 7.16 (m, 10H, PhH), 5.41 (m, 4H, CH₂pyrCH₂), 4.74 (m, 2H, CH₂), 3.80 (m, 4H, PhCH₂), 2.07 (s, 2H, OH). ¹³C NMR δ (ppm): 154.31, 139.80, 136.93, 129.36, 129.10, 127.40, 127.32, 122.19, 121.66, 64.56, 62.67, 53.35, 36.51. HR: 3364, 3066, 1615, 1500, 1399, 1156, 1064, 756, 666 cm⁻¹. ESI-MS m/z (rel. intensity) = 509 [M-HPF₆⁻PF₆⁻]. HRMS m/z calcd for C₃₃H₃₅F₇N₆O₂P 654.2427 [M-PF₆⁻], Found 654.2386.

(5S,5S)-3,3′-Bis(1,5-dihydroxy-2-pentanoyl)-1,1′-[2,6-pyridylenebis(methylene)] bis[imidazolium]
Dibromide 3c.2Br⁻

Yield: 520 mg (0.86 mmol, 86.0%). Light brown oil. [α]²⁵D = +21.5 (c 0.2, CH₂OH). ¹H NMR (300 MHz, DMSO-d₆) δ (ppm): 9.24 (s, 2H, ImH-2), 7.95 (s, 2H, ImH-4), 7.41 (d, 2H, J = 8.1 Hz, p-pyr), 7.70 (s, 2H, ImH-5), 7.68 (s, 2H, ImH-4), 7.54 (d, 2H, J = 8.0 Hz, m-pyr), 5.49 (m, 4H, ArCH₂), 5.30 (s, 2H, CH₂CH₂OH), 4.85 (s, 2H, CH₂CH₂OH), 4.30-4.35 (m, 2H, CH₂), 3.72-3.76 (m, 4H, CH₂CH₂O), 1.80-1.85 (m, 4H, CH₂CH₂O), 1.31-1.40 (m, 4H, CH₂CH₂O), 1.22-1.27 (m, 6H, CH₂CH₂O). IR: 3310, 3005, 2927, 2857, 1349, 1149, 749 cm⁻¹. ESI-MS m/z (rel. intensity) = 445 [M-HBr⁻Br⁻]. HRMS m/z calcd for C₂₃H₂₃BrN₂O₂P 564.2247 [M-PF₆⁻], Found 564.2226.

RESULTS AND DISCUSSION

Among those various methods to characterize host-guest interaction, the UV-vis titration method is convenient and widely used for its high sensitivity to host-guest binding.⁴¹⁻⁴³ When the host absorbs light at different wavelengths in the free and host-guest complexed states, the difference in ultraviolet spectrophotometry may suffice for estimation of the enantioselective recognition between the host and guest molecules. In this article, recognition abilities of chiral molecular tweezers for amino acids or their derivatives were investigated at 27°C by UV-vis titration methods.

The chiral recognition ability of dibromide salts 2a-c.2Br⁻ and 3a-c.2Br⁻ was investigated in aqueous solvents. Meanwhile, hexafluorophosphate salts (2a-c.2PF₆⁻ and 3a-c.2PF₆⁻) and amino acid esters were insoluble in water, so acetonitrile was used as solvent. During the UV spectroscopic titration experiments, addition of varying concentration of guest resulted in a gradual decrease of the characteristic absorption of the host, illustrating that the host-guest interaction had happened and the host-guest complex could have formed. Typical UV spectral changes upon the addition of Boc-L-phenylalanine methyl ester to host 3a.2PF₆⁻ are shown in Figure 1, the characteristic absorption peak of the host at 213 nm gradually decreased with a slight bathochromic shift (about 10 nm).

The stability constant (K) of supramolecular system formed can be calculated according to the modified Hildebrand–Benesi equation,⁴⁴⁻⁴⁵ eq. 1.

\[ [G]_0[H]_0/\Delta\varepsilon = 1/K\Delta\varepsilon + [G]_0/\Delta\varepsilon \]

where [H]₀ represents the total concentration of host; [G]₀ denotes the total concentration of guest, Δε is the difference between the molar extinction coefficient for the free and the complexed chiral molecular tweezer, ΔA denotes the changes in the absorption of the host on adding amino acid derivatives. The binding constant was obtained by the curve fitting program of nonlinear least-squares (correlation coefficient > 0.99). The typical plot for the complexation of compound 3a.2PF₆⁻ with Boc-L-phenylalanine methyl ester is shown in Figure 2.

Association constants (K) and free-energy changes (ΔG₀) are shown in Table 1, along with enantioselectivity

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The chiral recognition ability of hosts is highly dependent on the substituted group on their pincers. The imidazolium moiety of the pincers might play an important role in the procedure of recognition. The cation-π or π-π stacking interactions between the imidazolium cation with the benzene groups of phenylalanine or the imidazole of histidine could be one of the key elements of the host–guest interaction.46,47 On the other hand, the C(2)-H in the imidazolium ring could offer proton to form hydrogen bonding with carboxylate.48 Hence, the imidazolium groups on the two pincers of hosts should take part in (C–H)···anion hydrogen bonding interactions with the carboxylate group of guests. At the same time, the hydroxyls at the terminal of the pincers could bond the guest molecule by the O–H···O or O–H···N hydrogen bonding interactions.

Our study clearly demonstrates that the spacer of tweezers-type hosts influences the chiral recognition for amino acids guests. Replacing the spacer of 3,6-m-xylylen with 2,6-bis(methylene)pyridine moiety, the binding ability and enantioselectivity of the receptors 3a-c for the desired guests strongly improve. As can be seen from Table 1, host 3a.2Br− shows much better chiral recognition for phenylalanine than 2a.2Br− (Entries 15–16 and 1–2). The 3b.2Br− also exhibits good chiral recognition for phenylalanine and histidine (Entries 19–20 and 21–22), but inferior result was observed while 2b.2Br− was used (Entries 5–6 and 7–8). Likewise, the regular results appeared while comparing the enantioselectivity of the host 3b.2PF6− with 2b.2PF6− for recognition of N-Boc protected histidine methyl ester, corresponding Kf/KD were 5.10 and 4.07, respectively (Entries 39–40 and 27–28). Herein, it might suggest that the hydrogen bond interaction between the nitrogen atom of the spacer of 2,6-bis(methylene)pyridine with NH2, NH, or COOH of guests are favorable for molecular recognition. The N–H···N or O–H···N hydrogen bonding interactions could be the very important driving force of the chiral recognition of hosts 3a–c for amino acids guests.

The benzene rings on the pincers of the hosts (2b or 3b) contributed obviously to enantioselective recognition for aromatic amino acids and their derivatives. From the data in Table 1, it can be found that the hosts 2b or 3b, which contain phenyl side chains opposite to 2a or 3a, show stronger binding ability and better enantioselectivities for phenylalanine, histidine, and their derivatives. The binding constants of 3a.2Br− and 3b.2Br− for l-phenylalanine are 13,053 and 28,321, corresponding enantioselectivities of 2.51 and 3.35 (Entries 15–16 and 19–20). Similarly, the host 2b.2Br− exhibits stronger binding ability and better enantioselectivities than that of 2a.2Br− (Entries 5–6 and 1–2). For the guest N-Boc protected histidine methyl ester, the chiral recognition ability of the host 2b.2PF6− was also apparently superior to that of 2a.2PF6− (Entries 25–26 and 27–28). Moreover, the same trends were observed when compared the chiral recognition of 3b.2PF6− with 3a.2PF6− for both phenylalanine methyl ester (Entries 31–32 and 35–36) and N-Boc protected phenylalanine methyl ester (Entries 33–34 and 37–38). These differences indicate that the π-π stacking interaction between aromatic rings of hosts and guests is an important element for the molecular recognition. Comparatively, the second hydroxyl on the pincers of the hosts (2c or 3c) influences the enantioselectivity more inappreciably than the benzene ring of the hosts (2b or 3b). The regularity of recognition was not found when compared the chiral recognition of 2a.2Br− and 3a.2Br− with 2c.2Br− and 3c.2Br− for phenylalanine (Entries 1–2 with 9–10, Entries 15–16 with 23–24).

The aromatic functional groups of the guests influence the enantioselectivity similarly. It can be observed that the host 3a.2Br− showed better enantioselectivity for phenylalanine than alanine (Entries 11–12 and 15–16), and the host 3a.2PF6− also showed better enantioselectivity for phenylalanine methyl ester than alanine methyl ester similarly (Entries 29–30 and 31–32). The π-π stacking interaction might be expected to be favored for the recognition. Furthermore, the imidazole group of histidine not only takes part in the π-π stacking interaction, but involves the hydrogen bonding interactions as well. It can be deduced that the same host ought to show better enantioselectivity for histidine than phenylalanine and alanine. Of particular interest was that the experiment data agreed with the deduction. For the same host 3a.2Br−, the best enantioselectivity was obtained for histidine in all of the three amino acids; corresponding Kf/KD was 3.03, whereas the Kf/KD were 2.51 and 1.61 for phenylalanine and alanine, respectively (Entries 17–18, 15–16, and 11–12).

It is noteworthy that the bulky group of the guests, such as tert-butoxycarbonyl groups (Boc), may be in favor of the recognition of the chiral molecular tweezers. The host 3a.2PF6− shows better enantioselectivity toward N-Boc protected phenylalanine methyl ester than phenylalanine methyl ester, affording Kf/KD of 3.34 and 2.72, respec-
tively (Entry 33–34 and 31–32). The similar results were observed again while the host 3b.2PF₆ recognize N-Boc protected phenylalanine methyl ester and phenylalanine methyl ester (Entry 37–38 and 35–36). This might be ascribed to the steric hindrance of the bulky group of the guest and the steric complementarity interaction of host–guest. Because of its flexiblity, the host is able to organize itself in cleft-like structure according to the shape of the guest and bounds the guest well. So it was not surprising that the host 3b.2PF₆ showed remarkable enantioselectivity for N-Boc protected histidine methyl ester, affording $K_L/K_D$ of 5.10 (Entry 39–40).

**CONCLUSIONS**

In conclusion, we have successfully prepared two kinds of novel chiral molecular tweezers, which have two chiral imidazolium pincers and show good chiral recognition ability toward $\alpha$-amino acids and their derivatives in water or acetonitrile. The host containing benzene ring on the pincers shows better chiral recognition for aromatic guests because of the existence of $\pi-\pi$ stacking interaction. Meanwhile, when the spacer of the molecular tweezers has the binding site, the chiral recognition for all the amino acid guests are enhanced greatly. As for guests, the aromatic
function, especially imidazole ring, is an advantage factor for chiral recognition. These results show that the structures of hosts and guests, hydrogen bonding, π−π stacking, cation−π, steric complementarity, etc. may be responsible for the enantioselective recognition.

LITERATURE CITED


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