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Breaking the C_3-Symmetry of Chiral Tripodal Oxazolines: Enantio-Discrimination of Chiral Organoammonium Ions

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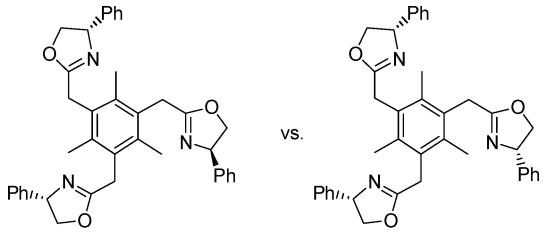

C_1-PhBTO C_3-PhBTO

A phenylglycinol-derived tripodal oxazoline with C_1-symmetry (C_1-PhBTO) was synthesized, and its enantioselective recognition behavior toward α-chiral primary organoammonium ions was studied. The C_1-PhBTO receptor showed higher selectivity with an opposite sense of enantio-discrimination compared to other C_1-symmetric analogues examined but lower selectivity with the same sense of enantioselection compared to its C_3-symmetric analogue. Binding studies indicated that the C_1-symmetric receptors, particularly C_1-PhBTO, interact with the guests in a 2:1 host−guest complex mode in stark contrast to its C_3-symmetric analogues.

Introduction

Chiral molecular recognition has attracted a continuing research interest for a better understanding of the recognition phenomena as well as for potential applications to separation processes, catalysis, and sensing.[1] The selective recognition of one enantiomer out of its racemic mixture requires an artificial receptor that provides an effective chiral environment toward one enantiomeric guest over another. Among a variety of chiral molecular receptors with different molecular symmetries, C_2-symmetric receptors have been widely used.[2] Recently, we introduced C_3-symmetric, benzene-based tripodal oxazolines (C_3-BTOs) as efficient and unique receptors for organoammonium ions.[3,4] Our tripodal oxazoline receptors, particularly C_3-PhBTOs, provide a C_3-symmetric "screw-sense" chiral environment toward α-chiral primary organoammonium ions. We have shown that this unique chiral discrimination in a C_3-symmetric environment actually occurs contrary to the previous perception.[3c] Although we proposed a plausible origin for the chiral discrimination, only a subtle structural difference exists between the diastereomeric inclusion complexes, and thus need for a further mechanistic study remained. In

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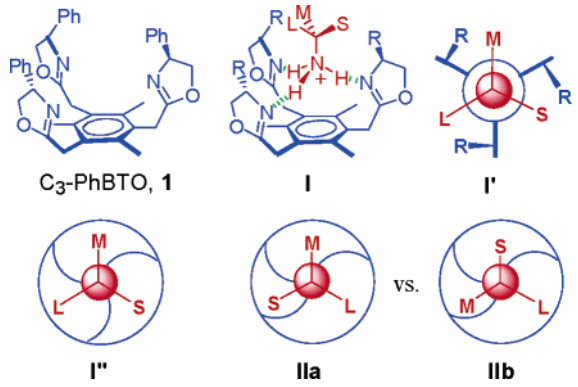


FIGURE 1. Schematic diagrams for supposed inclusion complexes of C_3- and C_1-BTOs with α-chiral organoammonium ions.

this context, we were interested in changing the symmetry of the chiral environment from C_3 to C_1 (no symmetry) to see its consequences on the enantiodiscrimination ability and binding mode. Herein, we report a new approach to the benzene-based tripodal oxazoline receptor with C_1-symmetry, C_1-PhBTO, and evaluation of chiral discrimination ability of the new receptor and its analogues toward α-chiral primary organoammonium ions.

Results and Discussion

What would be the chiral discrimination mode if we break the chiral environment of our BTOs from C_3- to non-C_3-symmetry, that is, C_1-symmetry? The inclusion complex between a C_3-BTO receptor and an enantiomeric α-chiral primary organoammonium ion, complex **I** in Figure 1, viewed from the top can be depicted in such a way that each of the oxazoline rings is almost perpendicular to the bottom benzene frame and its substituent R is pointing upward. In a top view, the α-substituents of the ammonium guest are in a screw-sense chiral environment,[3c] which can be simplified as diagram **I′** or **I″**; the latter shows three "chiral sectors" with equal space. We assumed that C_1-symmetric receptors, C_1-BTOs, would also show tripodal binding modes toward the ammonium ions similarly as that of the C_3-symmetric receptors. In this case, the α-substituents of an ammonium guest reside in different sectors; hence, we would expect different steric interactions between C_1-symmetric receptors and enantiomeric guests (**IIa** vs **IIb**) compared to the case of C_3-BTOs. This scenario, however, has found to be not true from the binding studies in the followings.

Synthesis of C_1-Symmetric Tripodal Oxazoline Receptors. To change the C_3-symmetry of our oxazoline receptors into C_1-symmetry (asymmetry), several approaches are possible. One is to introduce three oxazoline rings with different substituents (R^1, R^2, R^3) but with the same sense of chirality, as the type I in Figure 2. This approach, however, poses a severe synthetic challenge of stepwise introduction of the three different oxazolines. Another approach to synthesize C_1-BTOs is to introduce one of the three oxazoline rings with a substituent of opposite stereochemistry to those of the other two. In this approach, we can use either different R-substituents (such as type IIa) or the same ones (type IIb).

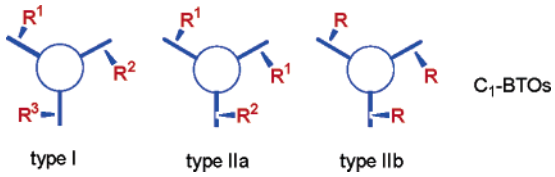
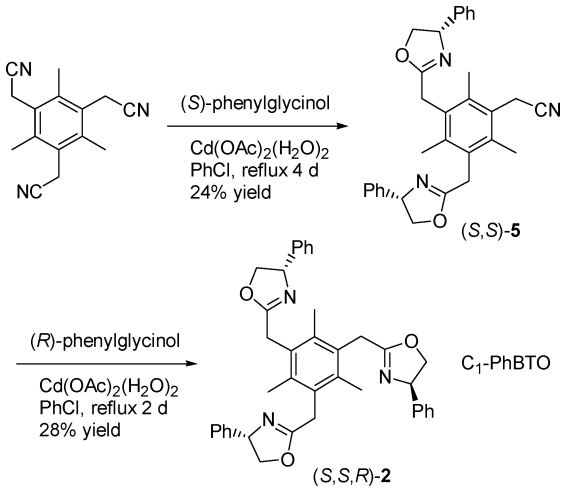


FIGURE 2. Schematic diagrams of different types of C_1-symmetric tripodal oxazolines.

SCHEME 1



Recently, we disclosed a novel method for the synthesis of the type IIa oxazolines through an oxazoline exchange reaction with amino alcohols mediated by $ZnCl_2$.[5] Using this novel method we were able to synthesize various C_1-BTOs. However, we found that the oxazoline exchange method was not effective for the synthesis of type IIb oxazolines, particularly C_1-PhBTO (R = Ph) which is the most required C_1-BTO analogue considering that its counterpart C_3-PhBTO is the most efficient receptor in the chiral discrimination among several C_3-BTOs examined.[3c] Experiments suggested that significant decomposition of phenylglycinol during the oxazoline exchange reaction might be the problem. Therefore, we envisaged that a Lewis acid milder than $ZnCl_2$ might solve this problem, under which condition phenylglycinol could survive. Thus, we reinvestigated the oxazoline formation starting from cyano-bis(oxazoline) **5** using $Cd(OAc)_2$ that is known to be a milder Lewis acid compared to $ZnCl_2$ (Scheme 1).[6]

The (*S*,*S*)-bis(oxazoline) **5** was prepared from tris(cyanomethyl)mesitylene by treatment with (*S*)-phenylglycinol in the presence of 5 mol % of $Cd(OAc)_2$ in refluxing chlorobenzene for 4 days in 24% isolated yield. Then, treatment of cyano-bis(oxazoline) **5** with (*R*)-phenylglycinol under otherwise identical conditions, to our delight, afforded C_1-PhBTO (*S*,*S*,*R*)-**2** in 28% isolated yield. Thus, using the milder Lewis acid in a catalytic amount, we were able to synthesize the most desired C_1-PhBTO **2**.

C_1-PhBTO thus synthesized, that is (*S*,*S*,*R*)-**2**, interestingly exhibited very simple ^1H and ^{13}C NMR spectra,

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(6) Gerisch, M.; Krumper, J. R.; Bergman, R. G.; Tilley, T. D. *J. Am. Chem. Soc.* **2001**, *123*, 5818−5819. $Cd(OAc)_2$ is a harmful and dangerous chemical for human and the environment, and thus, it should be handled with proper caution.

TABLE 1. Enantioselective Extraction Experiments Using C_1-BTOs 2−4 toward α-Chiral Organoammonium Guests

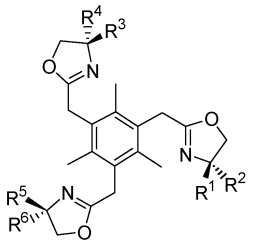
entry	receptor	ammonium guest[a]	enantioselectivity[b]	% extraction[c]
1[d]	**1**	$PhCH(NH_3^+)CH_3$	71 (*R*):29 (*S*)	82
2[d]	**1**	$PhCH(NH_3^+)CO_2Me$	78 (*S*):22 (*R*)	60
3	**2**	$PhCH(NH_3^+)CH_3$	64 (*R*):36 (*S*)	51
4	**2**	$PhCH(NH_3^+)CO_2Me$	70 (*S*):30 (*R*)	22
5[e]	**3a**	$PhCH(NH_3^+)CH_3$	59 (*S*):41 (*R*)	100
6[e]	**3a**	$PhCH(NH_3^+)CO_2Me$	62 (*S*):38 (*R*)	91
7[e]	**3b**	$PhCH(NH_3^+)CH_3$	58 (*S*):42 (*R*)	80
8[e]	**3b**	$PhCH(NH_3^+)CO_2Me$	69 (S):31 (*R*)	69
9	**3c**	$PhCH(NH_3^+)CH_3$	50 (S):50 (*R*)	-
10[e]	**4**	$PhCH(NH_3^+)CH_3$	50 (*S*):50 (*R*)	70

[a] Perchlorate salts. [b] Ratio of the enantiomeric guests extracted from a racemic mixture (0.5 M in D_2O) using the C_1-BTO (0.05 M in $CDCl_3$) at 25 °C. [c] Percentage of the extracted ammonium ions with respected to the receptor used (see the Experimental Section). [d] Taken from ref 3c. [e] Taken from ref 5.

showing little difference with respect to those of C_3-PhBTO **1**. To differentiate C_1-PhBTO from C_3- on NMR spectra, we compared their ammonium ion complexes. Thus, an equimolar mixture of $NH_4^+PF_6^-$ and (*S*,*S*,*R*)-**2** exhibited significant differences in their ^1H and ^{13}C NMR spectra, compared to those of the corresponding inclusion complex of (*S*,*S*,*S*)-**1**. For example, the inclusion complex of (*S*,*S*,*R*)-**2** exhibited more split peaks, particularly three peaks for the 2,4,6-trimethyl groups of the central benzene, while singlet for those of the (*S*,*S*,*S*)-**1** complex.[7] Surely, both PhBTOs showed much different physical properties such as their melting points and optical rotations [(*S*,*S*,*R*)-**2** vs (*S*,*S*,*S*)-**1**: 118−120 vs 125−126 °C; $[\alpha]_D$ −12 vs +77.8 (c = 1, $CHCl_3$)].

Chiral Discrimination of C_1-BTOs toward α-Chiral Organoammonium Ions. The chiral discrimination ability of C_1-PhBTO (*S*,*S*,*R*)-**2** was evaluated by the extraction experiment[8] described previously in the case of C_3-PhBTO **1**.[3c] Typically, the method involves extraction of a D_2O solution of the racemic organoammonium salt (0.5 M) with a $CDCl_3$ solution of (*S*,*S*,*R*)-**2** (0.05 M) in the presence of $NaPF_6$ (0.6 M) at 25 °C. This time, a direct NMR analysis for the organic layer did not give information on the degree of enantioselection; hence, the organic layer was further derivatized to the corresponding Mosher amides as described previously[3e] for assessing their percent diastereomeric excess. The percent extraction and enantioselection values are listed in Table 1, together with some previously determined values using structurally different C_1-BTOs.

Only those tripodal receptors that have two phenylglycinol-derived oxazolines exhibited appreciable enantioselectivity toward the racemic α-chiral ammonium ions examined (entries 1−8). In the case of C_1-BTO, **3c**, which has one phenyl-substituted oxazoline ligand, showed little enantioselectivity (entry 9). Other C_1-BTOs that have no phenyl substituents on the oxazoline ligands such as **4** did not show any chiral discrimination, although they extracted the ammonium guests well (entry 10). Interestingly, when we carried out the extraction experiment separately toward each of the enantiomeric guest ions, C_1-BTO **4** gave 50% extraction toward the (*R*)-guest and 26% extraction toward the (*S*)-guest. We do not know the reason for the discrepancy between the "separate" and "racemic mixture" experiments, but these results clearly warn that separate extraction experiments toward each enantiomeric guest to assess enantio-discrimination of a receptor could be misleading.



3a: R^1 = Me, R^2 = R^3 = R^5 = H, R^4 = R^6 = Ph
3b: R^1 = R^2 = R^3 = R^5 = H, R^4 = R^6 = Ph
3c: R^1 = R^3 = Me, R^2 = R^4 = R^5 = H, R^6 = Ph
4: R^1 = R^2 = R^3 = R^4 = Me, R^5 = H, R^6 = *i*Pr

Table 1 shows that C_1-PhBTO **2** is more enantioselective than other C_1-BTOs, but less selective than C_3-PhBTO **1**. Interestingly, C_1-PhBTO **2** gave significantly lower % extraction values than other receptors. Another notable result was that type IIa C_1-BTOs **3** and **4** extracted (*S*)-α-phenylethylammonium ion preferentially over the (*R*)-guest, a reverse sense of chiral discrimination in comparison with that of C_3-PhBTO **1**, whereas C_1-PhBTO **2** showed the same sense of chiral discrimination as that of C_3-PhBTO **1**. The opposite sense of chiral discrimination observed between C_3-PhBTO **1** and C_1-BTOs **3** and **4** and between C_1-PhBTO **2** and C_1-BTOs **3** and **4** suggested that different binding modes might be involved. Also, the observation that two phenyl-substituted oxazolines are necessary for the chiral discrimination demonstrates again that the phenyl-substituted oxazolines provide more efficient chiral environments than do the alkyl-substituted oxazolines.[3c]

Studies on the Binding Modes. To get information on the binding mode, we determined thermodynamic parameters for the binding processes in the cases of C_1-BTOs **2**, **3a**, and **3b** toward each of the enantiomeric α-phenylethylammonium ions by isothermal titration calorimetry (ITC).[9] The results are summarized in Table 2. Interestingly, both C_1-BTOs **3a** and **3b** showed slightly larger association constants than that of C_3-PhBTO **1**, whereas C_1-PhBTO **2** showed smaller values than that of C_3-PhBTO **1**. These relative association constants are

(7) See the Supporting Information.
(8) Lein, G. M.; Cram, D. J. *J. Am. Chem. Soc.* **1985**, *107*, 448−455.
(9) (a) Christensen, J. J.; Wrathall, D. P.; Oscarson, J. O.; Izatt, R. M. *Anal. Chem.* **1968**, *40*, 1713−1717. (b) Smithrud, D. B.; Wyman, T. B.; Diederich, F. *J. Am. Chem. Soc.* **1991**, *113*, 5420−5476. (c) Rekharsky, M.; Inoue, Y. *J. Am. Chem. Soc.* **2000**, *122*, 4418−4435.

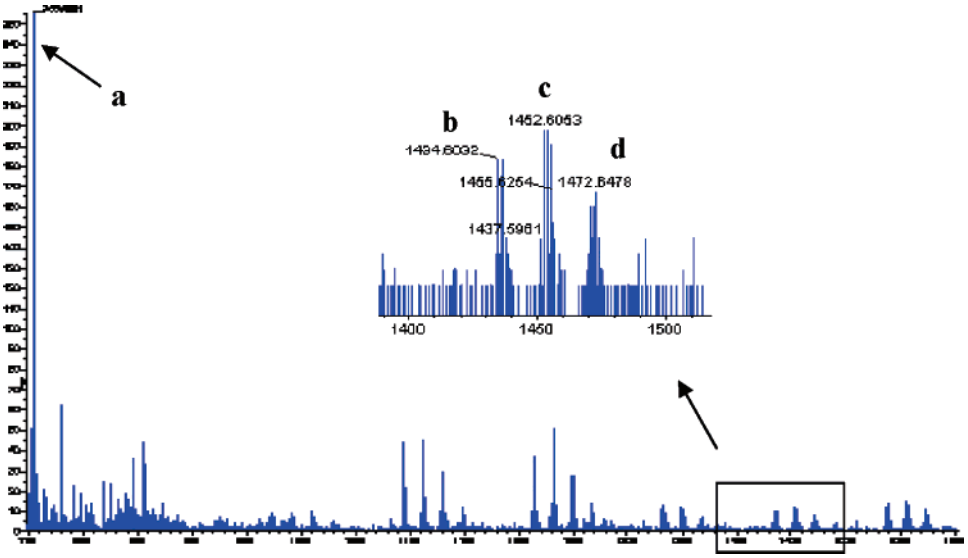


FIGURE 3. Enlarged portion of the ESI mass spectrum that shows 2:1 complexes of C_1-PhBTO **2** and (*R*)-α-PhCH(NH_2)CH_3·$HClO_4$ (the peaks b−d in the box): a, 719.4 [H_o + G_o + H^+]; b, 1434.8 [$2H_o$ + G_o + H^+ + H_2O + $HClO_4$]; c, 1452.6 [$2H_o$ + G_o + H^+ + $2H_2O$ + $HClO_4$]; d, 1470.7 [$2H_o$ + G_o + H^+ + $3H_2O$ + $HClO_4$]. H_o and G_o represent host **2** and the neutral amine guest PhCH(NH_2)CH_3, respectively. For a detailed analysis, see the Supporting Information.

TABLE 2. Thermodynamic Data for the Binding Process of C_1-BTOs 2, 3a, and 3b toward Enantiomeric α-Phenylethylammonium Ions, Determined by ITC in Acetonitrile at 30 °C

entry	receptor	guest[a]	*N* value	$\Delta H°$ (kcal·mol^{-1})	$-T\Delta S°$ (kcal·mol^{-1})	K_{assoc} (M^{-1})
1	**1**[b]	*S*	1.1	−7.3	1.7	1.1×10^4
2	**1**[b]	*R*	0.90	−9.0	2.7	3.3×10^4
3	**2**	*S*	0.53	−11.1	5.5	1.1×10^4
4	**2**	*R*	0.49	−11.9	6.0	1.8×10^4
5	**3a**	*S*	0.69	−12.0	5.7	3.5×10^4
6	**3a**	*R*	0.64	−10.8	4.8	2.4×10^4
7	**3b**	*S*	0.53	−12.3	5.7	5.5×10^4
8	**3b**	*R*	0.53	−13.4	6.8	5.4×10^4

[a] PhCH(NH_3^+)CH_3(ClO_4^-). [b] Taken from ref 3c.

correlated well with the percent extraction values listed in Table 1, which suggests that receptors with higher binding affinity toward the guests extract them better than receptors of lower binding affinity.

The results of ITC experiments confirm that both C_1- and C_3-PhBTOs form thermodynamically more stable inclusion complexes with the (*R*)-α-phenylethylammonium ion than with the (*S*)-guest ion, whereas C_1-BTOs **3a** and **3b** form more stable inclusion complexes with the (*S*)-α-phenylethylammonium ion. Of particular note is that the observed *N* values, stoichiometry of binding obtained from the nonlinear least-squares fit process, do not show values of near 1.0 but 0.49−0.53 in the cases of C_1-BTOs **2** and **3b**, and 0.64−0.69 in the case of C_1-BTO **3a**. These *N* values suggest that not a 1H:1G binding but a 2H:1G binding mode should be considered in these C_1-BTO cases, particularly in the cases of **2** and **3b** that show $N \approx 0.5$, which are in stark contrast to the 1H:1G binding mode proven in the case of C_3-PhBTO **1**.[3c] The *N* value of near 0.5 in the cases of C_1-BTOs **2** and **3b** argues well for the formation of 2H:1G complexes in these cases, which also provides a clue for the different sense of enantioselection and percent extraction observed depending on the receptors.

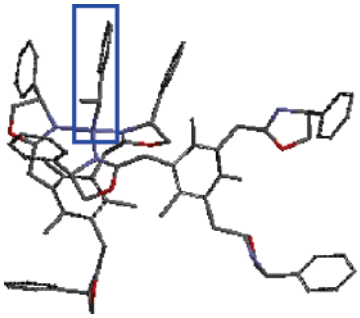


FIGURE 4. Modeled 2H:1G inclusion complex of C_1-PhBTO **2** and α-phenylethylammonium ion (indicated by the box).

To get supporting information on the 2H:1G complex, we performed the electrospray ionization (ESI) mass spectrometry for an equimolar mixture of C_1-PhBTO **2** and α-phenylethylammonium ion in a water−acetonitrile solution. The ESI mass data in Figure 3 shows several peaks responsible for the 2H:1G complexes, in addition to the large peak at $m/z = 719.4$ corresponding to 1H:1G inclusion complexes.

Also, a Job plot was obtained by the continuous variations method, which excluded the 1H:1G complexation and indicated a 2H:1G binding mode between C_1-PhBTO **2** with α-phenylethylammonium ion.[7]

A model structure of the 2H:1G inclusion complex plausible in the case of C_1-PhBTO **2** is shown in Figure 4.[10]

Thus, the different sense of chiral discrimination and percent extraction values observed depending on receptors **1**−**4** are believed to be the consequence of the unusual binding modes. Although attempts to get single

(10) Molecular mechanics computation was performed using Spartan Windows '04 from Wavefunction, Inc. The computation used the MMFF94 force field and provided an isolated, equilibrium geometry at ground state. A geometry optimization could be readily done for the guest-bound region, for which region only a limited number of configurations resulted.

crystals of 2H:1G complexes have not been successful so far, the above experimental ITC, ESI, and Job plot data support the formation of 2H:1G complexes in the case of C_1-BTOs.

Conclusion

We have synthesized a phenylglycinol-derived tripodal oxazoline with C_1-symmetry (C_1-PhBTO) and studied its enantioselective recognition behavior toward α-chiral primary organoammonium ions. This C_1-PhBTO receptor showed higher selectivity with an opposite sense of enantio-discrimination compared to other C_1-symmetric analogues examined, but lower selectivity with the same sense of enantioselection compared to its C_3-symmetric analogue. Binding studies indicated that the C_1-symmetric receptors, particularly C_1-PhBTO, could interact with the guests in a 2:1 host−guest complex mode in stark contrast to its C_3-symmetric analogue. Thus, this study shows that changing receptor's symmetry, from C_3 to C_1, could lead to a dramatic modulation in the binding mode as well as the sense of enantioselection.

Experimental Section

(*S*,*S*)-{2,4,6-Trimethyl-3,5-bis[(4-phenyl-4,5-dihydrooxazol-2-yl)methyl]phenyl}acetonitrile (5). A three-necked flask was charged with $Cd(OAc)_2 \cdot 2H_2O$ (150 mg, 0.055 mmol), tris(cyanomethyl)mesitylene (3 g, 11.0 mmol), L-phenylglycinol (3.3 g, 24.1 mmol), and 35 mL of chlorobenzene. The mixture was heated at reflux for 4 days under argon. The solvent was removed under reduced pressure, giving an oily residue. The residue was purified by flash chromatography on silica gel (gradient elution: 30%-50% ethyl acetate/hexane) to afford the desired bis(2-oxazoline) **5** (1.26 g, 24%) as a white solid: mp 53−55 °C; $[\alpha]^{21}_D = +17.5$ ($c = 1.0$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34−7.17 (m, 10H), 5.15 (dd, 2H, $J = 10.1$, 8.4 Hz), 4.59 (dd, 2H, $J = 10.1$, 8.5 Hz), 4.05 (dd, 2H, $J = 8.5$, 8.3 Hz), 3.85 (s, 4H), 3.71 (s, 2H), 2.51 (s, 6H), 2.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.3, 143.1, 137.8, 135.8, 132.1, 129.3, 128.2, 127.2, 126.8, 78.1, 77.7, 77.3, 75.6, 70.2, 30.7, 19.8, 18.0, 17.8; MS (EI) *m/z* (rel intensity) 477 (M^+, 100), 447 (30), 356 (55)Anal. Calcd for $C_{31}H_{31}N_3O_2$: C, 77.96; H, 6.54; N, 8.80. Found: C, 77.24; H, 6.61; N, 8.64.

(*S*,*S*,*R*)-2-{3,5-Bis[(4-phenyl-4,5-dihydrooxazol-2-yl)methyl]-2,4,6-trimethylphenyl}methyl-4-phenyl-4,5-dihydrooxazole (2). A three-necked flask was charged with $Cd(OAc)_2 \cdot 2H_2O$ (11 mg, 0.042 mmol), bis(2-oxazoline) **5** (400 mg, 0.84 mmol), D-phenylglycinol (170 mg, 1.26 mmol), and 5 mL of chlorobenzene. The mixture was heated at reflux for 2 days under argon. The solvent was removed under reduced pressure, giving an oily residue. The residue was purified by flash chromatography on silica gel (gradient elution: 40%-60% ethyl acetate/hexane) to afford the desired tris(oxazoline) **2** (140 mg, 28%) as a white solid: mp 118−120 °C; $[\alpha]^{22}_D = -12.0$ ($c = 1.00$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34−7.21 (m, 15H), 5.16 (dd, 3H, $J = 10.1$, 8.3 Hz), 4.59 (dd, 3H, $J = 10.1$, 8.5 Hz), 4.05 (dd, 3H, $J = 8.5$, 8.3 Hz), 3.87 (s, 6H), 2.51 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.0, 142.5, 135.9, 130.7, 128.6, 127.4, 126.5, 74.8, 69.5, 30.1, 17.3; MS (EI) *m/z* (rel intensity) 597 (M^+, 100), 576 (28). Alal. Calcd for $C_{39}H_{39}N_3O_3$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.13; H, 6.70; N, 7.41.

C_3-PhBTO 1-$NH_4^+PF_6^-$ complex: ^{1}H NMR (300 MHz, acetone-d_6) δ 7.35−7.26 (m, 10H), 7.06 (d, $J = 7.9$ Hz, 5H), 4.97 (t, $J = 7.6$ Hz, 3H), 4.86 (dd, $J = 10.1$, 8.3 Hz, 3H), 4.19 (t, $J = 7.9$ Hz, 3H), 3.93 (s, 6H); ^{13}C NMR (75 MHz, acetone-d_6) δ 167.5, 144.4, 136.4, 132.0, 129.6, 128.0, 127.4, 75.4, 70.4, 30.5, 17.4.

C_3-PhBTO 2-$NH_4^+PF_6^-$ complex: ^{1}H NMR (300 MHz, acetone-d_6) δ 7.34−7.02 (m, 15H), 5.01−4.81 (m, 6H), 4.22−3.88 (m, 9H), 2.45 (s, 3H), 2.39 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (75 MHz, acetone-d_6) δ 170.8, 170.6, 143.2, 143.0, 136.6, 136.4, 132.2, 132.0, 129.6, 129.2, 128.5, 128.4, 128.3, 127.4, 127.1, 127.0, 126.9, 76.6, 76.5, 76.4, 69.3, 69.1, 32.3, 23.3, 17.1, 17.0, 14.3.

Determination of Enantioselective Binding. Binding experiments were carried out by extracting a D_2O solution (0.5 mL) of a racemic alkylammonium chloride (0.5 M) and $NaPF_6$ (0.6 M) with a $CDCl_3$ solution (0.5 mL, 0.05 M) of the tris(oxazoline) host. A D_2O solution of a racemic guest salt and a host solution were placed in a centrifuge tube equipped with a screw cap and equilibrated for 1 h in a thermostat at 25 °C. After 1 h, the whole mixture was extracted with a Vortex-Genie for 1 min and then centrifuged at 1500 rpm for 1 min. The organic layer was separated and treated with triethylamine (4 molar equiv) followed by (*R*)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (4 molar equiv). The Mosher's amide was purified by passing through a short pad of silica gel and subjected to ^{1}H and ^{19}F NMR analysis to determine the diastereomeric ratios.

Binding Study by Isothermal Titration Calorimetry. All binding experiments were performed on an isothermal titration calorimeter. A solution of the tris(oxazoline) in CH_3CN (1.5 mL, 0.2 mM) was added to the calorimetry cell. A solution of perchlorate salt of (*R*)- or (*S*)-α-phenylethylamine in CH_3CN (2.5 mM) was introduced by 40 5 μL injections, a total of 200 μL of the guest added. The solution was kept at an operating temperature of 303 K. Analysis and curve fitting using the software Origin afforded the binding affinities. The dilution of the guest solution in neat solvent was corrected.

ESI MS Analysis. The analysis was performed for an equimolar mixture of C_1-PhBTO **2** and (*R*)-(α)-$PhCH(NH_2)CH_3 \cdot HClO_4$ dissolved in water−acetonitrile (1:1 by volume; ∼0.2 mM solution) using a QSTAR XL Quadrupole TOF equipped with a nanospray tip at a flow rate of 10 $\mu L \cdot min^{-1}$ and electrospray ionization voltage of 700 V.

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Supporting Information Available: NMR spectra of new compounds, ammonium complexes of C_1- and C_3-PhBTOs, the Job plot, selected ITC data, and ESI MS data. This material is available free of charge via the Internet at http://pubs.acs.org.

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