Synthesis of Novel H₈-Binaphthol-based Chiral Receptors and Their Applications in Enantioselective Recognition of 1,2-Amino alcohols and Chirality Conversion of L-Amino acids to D-Amino acids

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Novel H₈-binaphthol-based chiral receptors appended with an uryl moiety (**2a**) and a guanidinium moiety (**2b**) have been designed and synthesized for the enantioselective recognition of 1,2-amino alcohols *via* reversible imine formation. The selectivities ($K_R/K_S = 9.8 \sim 19.4$) of **2b** in imine formation with 1,2-amino alcohols are higher than those of **2a** ($K_R/K_S = 1.8 \sim 4.5$). Similar efficiency trend have been observed in the conversion of L-amino acids to D-amino acids, i.e., the efficiency of the receptor **2b** (D/L ratio: $4.3 \sim 10.1$) is superior to **2a** (D/L ratio: $4.0 \sim 8.7$).

Key Words: Octahydrobinaphthol, Chirality conversion, Amino acid, Amino alcohol, Enantioselective recognition

Introduction

Enantiomerically pure amino acids and amino alcohols are extremely useful starting materials or intermediates for the synthesis of a variety of biologically active chiral molecules.[1] They also serve as building blocks for ligand design in the development of chiral catalysts.[2] Over the years, different kinds of receptors for amines,[3] amino alcohols[4] and amino acids[5] have been developed to discriminate the enantiomeric pairs or to enrich one enantiomer from racemic mixtures.[6] In most of these studies, molecular recognition is based on non-covalent interactions such as hydrogen bonding, metal coordination, and hydrophobic interactions. In contrast, reversible covalent bond, more specifically imine formation has been rarely explored for the recognition studies. When compared to non-covalent interactions, imine bonds[7] are slower to form but have the advantage of being much stronger and structurally well-defined, which are the desirable feature for developing stereoselective receptors. We recently developed a new type of binaphthol-based chiral receptors **1a**,**b**[8] which dramatically increase the rate and equilibrium constants for imine formation through the internal resonance assisted hydrogen bonds (RAHB) (Figure 1a).[9] The receptors **1a**,**b** exhibited high efficiency in enantioselective recognition and resolution of 1,2-amino alcohols. These receptors are also good biomimetic chirality conversion reagents (CCRs), as they convert the L-form to D-form in amino acids[10] and peptides.[11] In nature, L-amino acids are racemized by pyridoxal phosphate (PLP) dependent enzymes.[12] The racemization is occurred through the acidification of the α proton of the amino acid in the Schiff base formed between the PLP and an amino acid.[13] The receptors **1a**,**b** have the capability to form Schiff bases like PLP. In contrast to PLP, the receptors **1a**,**b** deracemize the bound amino acids due to the chirality of binaphthyl moiety.

Though these receptors are effective for enantiomeric recognitions, for practical application of this system, it is still needed to improve the selectivities as well as the solubility of the receptors in organic solvents. However, replacement of the hydrogen bonding groups (uryl and guanidinium) to heterocyclic moieties capable of hydrogen bondings, such as pyrrole-, imidazole-, benzoimidazole-, and indole-carboxamides,[14] did not improve the efficiency in enantioselective recognition of 1,2-amino alcohols. In present work, we attempted to modify the binaphthyl chiral backbone by using the octahydro-1,1'-binaphthyl (H₈-binaphthyl) moiety. Although it can be expected that receptors **2a**,**b** would have similar working modes with **1a**,**b** favoring the formation of imines **B** over **A**,[8,10] the H₈-binaphthyl moiety[15] provide additional features such as a sufficiently enlarged dihedral angle for better stereo-discrimination, favorable solubility and modified electronic properties as compared to its binaphthyl analogues (Figure 1b). Herein we report the detailed synthetic procedures of the receptors **2a**,**b** and their efficacies in enantioselective recognition towards the amino alcohols and as CCRs in the conversions of L-amino acids to D-amino acids.

Results and Discussion

Synthesis of receptors 2a and 2b. The synthetic routes for the optically pure uryl-appended receptor **2a** and guanidinium-appended receptor **2b** are described in Scheme 1 and 2, respectively. The required common intermediate, mono MOM-protected carboxaldehyde **5**, can be synthesized in two steps, starting from the commercially available optically pure (*S*)-H₈-binaphthol **3**. The direct ortho formylation could be accomplished according to the reported procedure,[16] and thus, reaction of **3** with magnesium chloride and paraformaldehyde produced the mono aldehyde **4** in 69% yield. The selective mono protection of **4** with MOM chloride in DMF afforded the desired mono MOM protected H₈-binaphthyl aldehyde **5**. Addition of 3-phenyluryl-benzyl bromide led to the formation of the MOM protected compound **6**, which upon hydrolysis under acidic
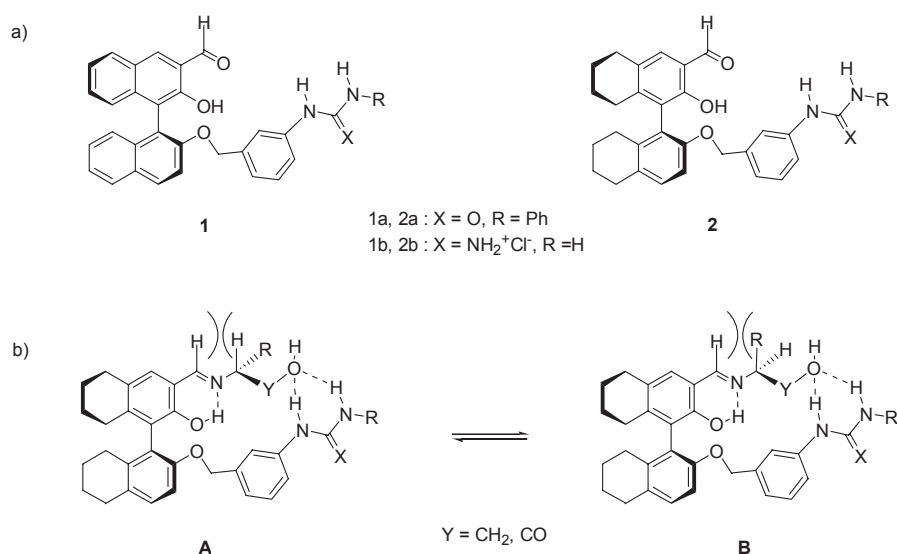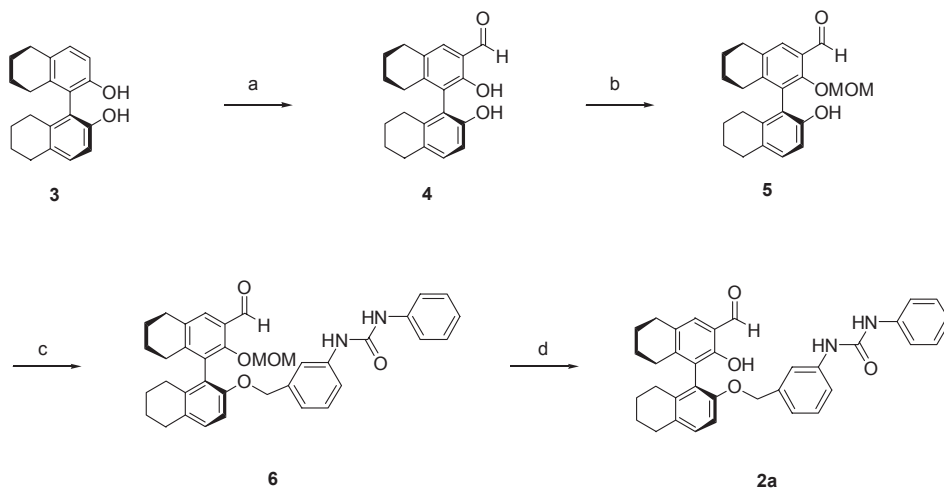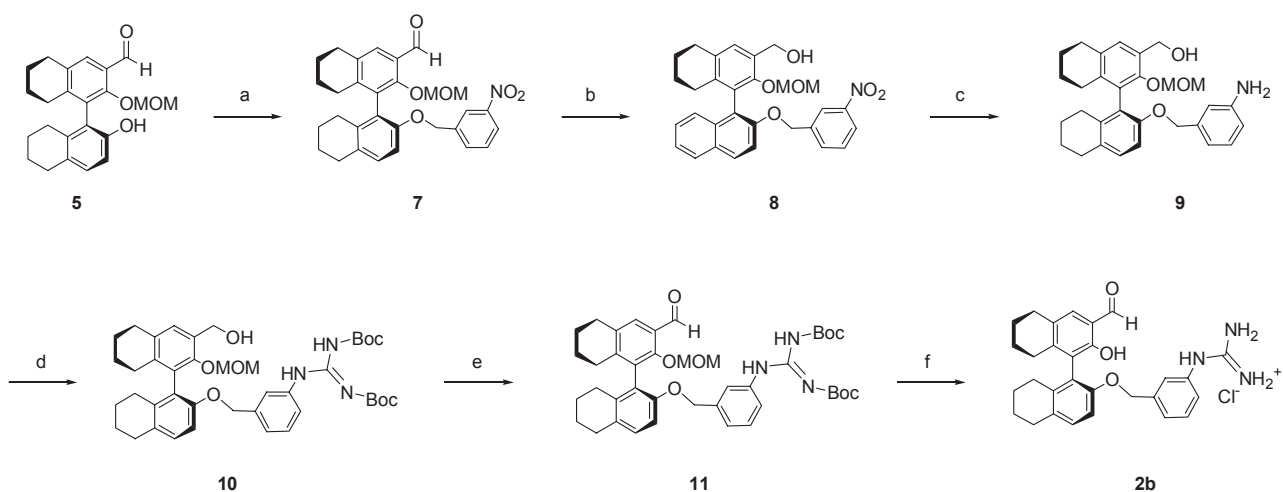
a)

1a, 2a : X = O, R = Ph
1b, 2b : X = NH₂⁺Cl⁻, R =H

b)

Y = CH₂, CO

Figure 1. a) The structures of chiral receptors **1** and **2** and b) imines of **2** formed with amino alcohols (Y=CH₂) and amino acids (Y=CO).

Scheme 1. Reagents and conditions: (a) MgCl₂, triethylamine, paraformaldehyde, THF, 12 h, reflux, 69%; (b) MOMCl, NaH, DMF, −50 °C, 3 h, 79%; (c) 3-phenyluryl-benzyl bromide, DMF, NaH, 5 h, rt, 67%; (d) 1M HCl, EtOH, 60 °C, 3 h, 90%.

Scheme 2. Reagents and conditions: (a) 3-nitrobenzylbromide, NaH, DMF, rt, 4h, 90%; (b) NaBH₄, MeOH, 4h, rt, 95%; (c) Fe, NH₄Cl, EtOH, Dioxane, H₂O, 80 °C, 24 h, 95%; (d) 1,3-bis(BOC)-2-methyl-2-thiopseudourea, TEA, HgCl₂, DMF, rt, 24 h, 92%; (e) PCC, methylenechloride, 5 h, rt, 80%; (f) 0.1M HCl, THF, reflux, 6 h, 65%.
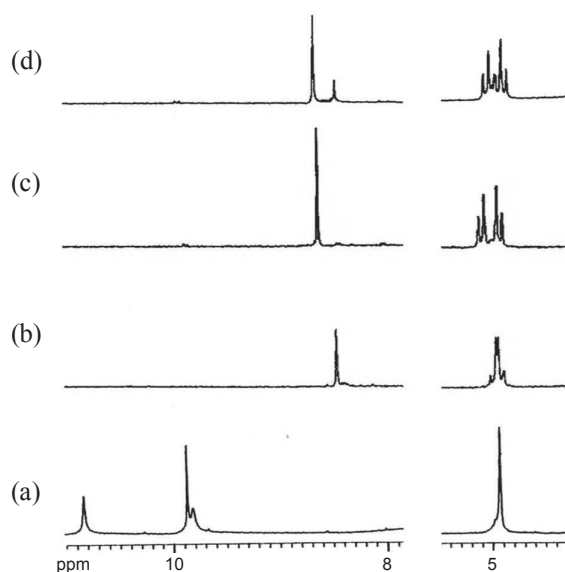
Figure 2. Partial ¹H NMR spectra in CDCl₃ of (a) **2b**, (b) **2b**-S-ap, (c) **2b**-R-ap and(d) mixture of **2b**-S-ap and **2b**-R-ap formed by the addition of 2 equiv of racemic *ap* to **2b**.
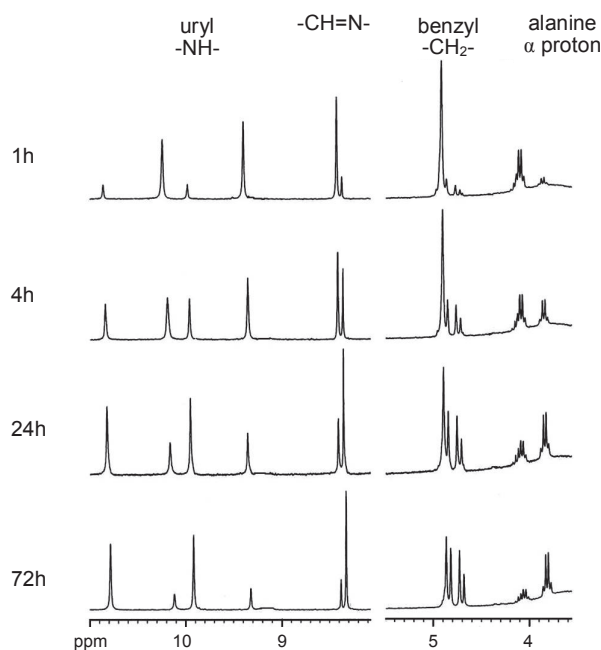

Figure 3. Time-dependent ¹H NMR of **2a**-L-Alanine in DMSO-d_6 in the presence of 4 equiv Et₃N.

Table 1. The stereoselectivities (K_R/K_S) for the imine formation of receptors **2a** and **2b** in CDCl₃ determined by ¹H NMR analysis

Amino alcohol	Selectivity (K_R/K_S)	
	2a (1a)[a]	**2b (1b)**[a]
2-amino-1-propanol	3.8 (3.7)	16.4 (11)
2-amino-1-butanol	4.5 (3.1)	13.2 (15)
Phenylalaninol	3.7 (3.7)	9.8 (8.3)
Valinol	3.1	19.4 (12)
Leucinol	1.8	14.4 (7.4)

[a]Data from reference 8b.

with pyridinium chlorochromate (PCC), followed by hydrolytic deprotection of the Boc group under acidic conditions provided the optically pure guanidnium based receptor **2b**. The structures of the receptors **2a** and **2b** were clearly confirmed by ¹H NMR, ¹³C NMR and HRMS analyses. It is also notable that they are freely soluble in various organic solvents including DMSO, CHCl₃ and benzene.

Enantioselective recognition of 1,2-amino alcohols with the receptors 2a and 2b. Figure 2a shows partial ¹H NMR spectra of **2b** in CDCl₃, where the aldehyde signal appears at 9.90 ppm, -OH signal at 9.85 ppm, and benzylic -CH₂ signal at 4.95 ppm. Addition of an equivalent of (*S*)-2-aminopropanol ((*S*)-*ap*) resulted in complete and rapid decrease of the intensity of aldehyde signal with concomitant increase of the signal at 8.55 ppm, which corresponds to the imine C-H proton of **2b**-S-ap (Figure 2b). On the other hand, addition of an equivalent of (*R*)-*ap* to **2b** showed complete formation of imine **2b**-R-ap with its C-H proton signal appearing at 8.65 ppm (Figure 2c). It has been also found that, aside from the imine C-H signals, the diastereotopic benzylic CH₂ signals are also useful for distinguishing **2b**-S-ap and **2b**-R-ap. The benzylic signal of **2b**-R-ap exhibits higher coupling constant for doublet of doublet than that of the **2b**-S-ap, which reflects the more rigid three-dimensional structure of **2b**-R-ap. Figure 2d shows the ¹H NMR spectrum for a mixture of **2b**-S-ap and **2b**-R-ap formed by the addition of 2 equiv of racemic *ap* to **2b**. The ratio of **2b**-R-ap and **2b**-S-ap can be measured from the integration of imine C-H and benzylic hydrogen signals. The observed 4.05:1 ratio of the two peaks indicated that the imine formation constant for **2b**-R-ap (K_R) is larger than **2b**-S-ap (K_S) by a factor of about $4.05^2 = 16.4$.[17] Even if **2b**-S-ap is first formed by the addition of 1 equiv of (*S*)-*ap*, the above equilibrium ratio is obtained within minutes upon addition of 1 equiv (*R*)-*ap*.

We studied the stereoselectivities in imine formation (K_R/K_S) of the two receptors **2a** and **2b** with five representative racemic 1,2-amino alcohols such as 2-amino-1-propanol, 2-amino-1-butanol, 2-amino-3-phenyl-1-propanol (phenylalaninol), 2-amino-3-methyl-1-butanol (valinol), and 2-amino-4-methyl-1-pentanol (leucinol) by ¹H NMR analysis. The results are summarized in Table 1, in which the selectivities obtained with binaphthol-based receptors **1a,b** were also included for comparison.[8b] As shown in Table 1, the pronounce positive effects of H₈-binaphthol have been observed, in both the uryl based **2a** and the guanidinium-based receptor **2b**, which exhibited

condition gave the optically pure **2a**.

For the synthesis of guanidinium-appended receptor **2b**, the mono MOM protected H₈-binaphthyl aldehyde **5** was reacted with 3-nitrobenzyl bromide to afford **7** (Scheme 2). Subsequent reductions of the aldehyde and nitro groups with sodium borohydride and iron, respectively, afforded the MOM protected alcohol **9**. Coupling of amine group of **9** with 1,3-bis(BOC)-2-methyl-2-thiopseudourea provided the di-BOC protected guanidine **10** in high yield (92%). Oxidation of benzyl alcohol **10**

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Table 2. The conversion efficiency of the receptors **2a**,**b** for amino acids determined by ^{1}H NMR anaylsis

Amino acid	D/L ratio	
	2a (1a)[a]	**2b (1b)**[a]
Alanine	4.0 (7)	4.4 (1.9)
Asparagine	8.1 (13)	10.1 (2.9)
Glutamine	6.1 (15)	8.0 (3.3)
Histidine	8.7 (14)	4.3 (12)
Phenylalanine	6.5 (11)	4.5 (2.2)
Serine	7.9 (11)	5.6 (2.2)
Tyrosine	8.4 (12)	4.9 (3.2)

[a]Data from reference 10c.

higher selectivities than their binaphthyl analogues **1a** and **1b**,[8b] may be due to the enlarged dihedral angle caused by the tetralin moieties. The higher selelectivities of the guadinium-based **1b** and **2b** than those of the uryl-based **1a** and **2a** are due to the charge reinforced hydrogen bonds of guanidinium-based receptors.[18,8b]

Conversion of L-Amino acid to D-amino acid by using 1 and 2 as CCRs. We also studied the activities of receptors **2a**,**b** for the conversion of amino acids from L-form to D-form. The conversion effficiency was determined by ^{1}H NMR analysis. Figure 3 shows the time-dependent change of ^{1}H NMR spectra of the imine **2a**-L-Ala formed between **2a** (10 mM) and L-Ala (10 mM) in the presence of 4 equiv triethylamine in DMSO-d_6. The mixing of the reagents and stirring for 1 h led to the complete imine formation. The peak at 9.33 and 10.13 ppm correspond to the two urea hydrogen signals, and the peak at 8.39 ppm is ascribed to the imine hydrogen signal of **2a**-L-Ala. The intensity of these peaks decrease as time goes, while new peaks corresponding to urea (9.92 and 10.80 ppm) and imine (8.31 ppm) signals of **2a**-D-Ala are growing. This clearly shows the chirality conversion of **2a**-L-Ala to **2a**-D-Ala. The apparent downfield shift of uryl NH protons of **2a**-D-Ala compared to **2a**-L-Ala is probably due to the stronger hydrogen bond between the uryl group of **2a** and carboxylate group of D-alanine. Besides urea and imine hydrogens, benzyl -CH$_2$- resonance signals at 4.90 for **2a**-L-Ala and 4.80 ppm for **2a-D-Ala, and alanine α proton signals at 4.05 for 2a**-L-Ala and 3.80 ppm for **2a**-D-Ala are also helpful to determine the chirality conversion. The intensities of the resonance signals reach the equilibrium in 72 h. The stereoselectivity defined by the ratio of (**2a**-D-Ala)/(**2a**-L-Ala) is measured by the integration of the corresponding signals.

After confirming the feasibility of the ^{1}H NMR analysis to determine the selectivity, we further investigated the efficiency of the receptors **2a**,**b** for representative seven amino acids such as alanine, asparagine, glutamine, histidine, phenyl alanine, serine and tyrosine. As shown in Table 2, conversion efficiencies of the uryl-based H$_8$-binaphthyl receptor **2a** is inferior to the corresponding binaphthyl receptor **1a**. In contrast, the conversion efficiencies of guanidinium-based receptor **2b** was dramatically increased compared to those of the corresponding **1a** for most amino acids tested except for histidine.[10c]

Conclusion

In summary, two novel H$_8$-binaphthol-derived uryl and guanidinium receptors **2a-b** have been synthesized and studied on the enantioselective imine formation of chiral 1,2-amino alcohols. Both the receptors showed higher selectivities than those of the previously reported binaphthol based receptors **1a-b**. The enlarged dihedral angle between the two phenyl rings in the H$_8$-binaphthyl group and modified electronic properties might have enhanced the enantioselectivities. Furthermore, compared to binaphthyl analogue **1b**, the guanidinium-based H$_8$-binaphthol receptor **2b** exhibited much improved conversion efficiency as CCRs towards the natural amino acids in converting their L-form to D-form. The higher solubility of these receptors in various solvents such as DMSO, CHCl$_3$ and benzene provides additional advantages in their usage as enantioselective recognition receptors.

Experimental

General. The (*S*)-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthol (**3**) was purchased from TCI. All chemicals were used as received without further purifications. The solvents were dried prior to use. NMR spectra were recorded on a Bruker AM 250 spectrometer in CDCl$_3$ and DMSO-d_6 solutions containing tetramethylsilane as internal standard. Chemical shifts are reported in δ unit. Melting points were measured with Electrothermal IA 9000 digital melting point apparatus and are uncorrected. HRMS spectra were obtained on FAB mode. For column chromatography, silica gel of 230 - 400 mesh was used.

(*S*)-2,2'-Dihydroxy-3-formyl-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthalene (4). To a solution of (*S*)-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthol **3** (12.0 g, 40.76 mmol) in anhydrous THF (300 mL), anhydrous magnesium chloride (7.76 g, 81.52 mmol), triethylamine (11.36 mL, 81.52 mmol) and paraformaldehyde (4.0 g) were successively added under nitrogen atmosphere, and the resulting mixture was refluxed for 12 h. The reaction was quenched by addition of 3 M HCl solution until the pH becomes 7. The solvent was evaporated and the residue was extracted with ethyl acetate. The combined organic layer was dried with MgSO$_4$ and evaporated. The resulting residue was purified by silica-gel column chromatography (EtOAc: hexane = 1:1) to yield the desired **4**. Yield: 8.5 g (69%); mp 146 - 147 °C; ^{1}H NMR (CDCl$_3$, 63 MHz) δ 10.89 (s, 1H, -CHO), 9.86 (s, 1H, -OH), 7.35-6.73 (s, dd, 3H), 4.37 (s, 1H, -OH), 2.82-1.66 (m, 16H); ^{13}C NMR (CDCl$_3$, 250 MHz) δ 192.3, 165.4, 157.3, 155.7, 148.6, 137.9, 136.3, 132.5, 128.5, 123.3, 120.3, 28.7, 27.9, 27.2, 27.0, 23.9, 23.5, 23.0, 22.9.

(*S*)-2-Methoxymethoxy-2'-hydroxy-3-formyl-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthalene (5). To a solution of **4** (6.5 g, 21 mmol) in DMF (75 mL) was added 60 % NaH (0.79 g, 20 mmol) at 0 °C in portion by portion, and stirred for 1 h at room temperature. After addition of chloromethyl methyl ether (2.36 g, 31 mmol) at 0 °C, the reaction mixture was stirred for 3 h at room temperature. The reaction mixtrure was extracted with EtOAc/water. The organic layer was dried with MgSO$_4$, and evaporated. Recrystallization of the residue with EtOAc and hexane yielded the product **5**. Yield: 6.0 g (79%); mp 139 -

140 °C; ^{1}H NMR (CDCl₃, 250 MHz) δ 10.26 (s, 1H, -CHO), 7.66-6.76 (s, dd, 3H), 4.81-4.69 (dd, 2H, -OCH₂), 4.54 (s, 1H, -OH), 3.13 (s, 3H, -OCH₃), 2.86-1.65 (m, 16H); ^{13}C NMR (CDCl₃, 63 MHz) δ 190.9, 156.9, 155.9, 150.7, 148.0, 146.4, 136.1, 134.6, 130.0, 129.9, 127.3, 122.3, 100.2, 57.2, 29.5, 27.9, 27.8, 27.4, 27.1, 23.2, 23.0, 22.6, 22.4; [α]₍D₎ = -34.9 (*c* 18.6, CHCl₃).

(*S*)-2-Methoxymethoxy-2'-(3-phenyluryl-benzyloxy)-3-formyl-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthalene (6). To a suspension of NaH (0.1 g, 2.45 mmol) in DMF (5 mL) was added the solution of **5** (1.0 g, 2.73 mmol) in DMF (5 mL) at 0 °C over a period of 30 minutes. After stirring for 30 minutes, 3-phenylurylbenzyl bromide[8a] (0.58 g, 2.73 mmol) was added, and the stirring continued for an hour at room temperature. After quenching the reaction with aqueous sat. NH₄Cl solution, the reaction mixture was extracted with ethyl acetate. After evaporation of solvent, the residue was purified by silica column chromatography (EtOAc/hexane = 1:5) to afford **6**. Yield: 1.01 g (67%); mp 195 - 196 °C; ^{1}H NMR (CDCl₃, 250 MHz) δ 10.27 (s, 1H, CHO), 7.57-6.66 (m, 12H), 4.97-4.95 (d, 2H, OCH₂), 4.72-4.71 (dd, 2H, OCH₂O), 2.96 (s, 3H, OCH₃), 2.81-1.59 (m, 16H); ^{13}C NMR (CDCl₃, 63 MHz) δ 189.7, 162.1, 155.6, 154.7, 149.0, 139.1, 138.4, 137.5, 136.1, 135.4, 130.8, 129.9, 129.3, 128.4, 125.1, 123.7, 123.2, 121.3, 120.7, 119.3, 118.4, 118.0, 117.5, 72.4, 67.5, 31.3, 29.3, 29.8, 29.1, 28.6, 23.5, 23.2, 22.9, 22.6.

(*S*)-2-Methoxymethoxy-2'-(3-nitrobenzy)-3-fromyl-[5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthalene] (7). To a solution of **5** (3.0 g, 8.19 mmol) in DMF (50 mL) was added the 60% NaH (0.33 g, 8.19 mmol) at 0 °C, and the mixture was stirred for 30 minutes. After addition of the 3-nitrobenzylbromide (2.12 g, 8.19 mmol), the reaction mixture was stirred for 4 h and quenched with aqueous sat. NH₄Cl solution. The mixture was extracted with with ethyl acetate, and the combined organic layers was dried with MgSO₄, and evaporated. The resulting residue was purified by silica column chromatography (EtOAc/hexane = 1:5) to yield the desired **7**. Yield: 4.0 g (90%); mp 110 - 112 °C; ^{1}H NMR (CDCl₃, 250 MHz) δ 10.29 (s, 1H, -CHO), 8.10-6.74 (m, 7H), 5.09 (s, 2H, -OCH₂), 4.77-4.62 (dd, 2H, -OCH₂O), 3.08 (s, 3H, -OCH₃), 2.88-1.68 (m, 16H); ^{13}C NMR (CDCl₃, 63 MHz) δ 191.8, 163.4, 153.3, 141.8, 137.3, 136.7, 133.9, 132.5, 131.3, 129.2, 129.0, 128.8, 128.2, 127.5, 126.1, 122.4, 120.8, 109.3, 98.5, 72.5, 68.2, 31.5, 29.6, 28.7, 28.1, 27.3, 26.7, 22.8, 22.4, 21.7, 21.3.

(*S*)-2-Methoxymethoxy-2'-(3-nitrobenzyloxy)-3-hydroxymethyl-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthalene] (8). To a solution of **7** (4.0 g, 8.0 mmol) in methanol was added sodium borohydride (0.36 g, 9.57 mmol), and the reaction mixture was stirred for 4 h at room temperature. The reaction was quenched by addition of water, and the solvent is evaporated. The product was extracted with ethyl acetate, and evaporation of ethyl acetate afforded the pure **8**. Yield: 3.8 g (95%); mp 138 - 139 °C; ^{1}H NMR (CDCl₃, 250 MHz) δ 8.09-6.73 (m, 7H), 5.09 (s, 2H, -OCH₂), 4.73-4.5 (m, 2H, CH₂OH), 4.69-4.49 (dd, 2H, -OCH₂O), 3.26 (s, 3H, -OCH₃), 3.1 (t, 1H, -OH), 2.82-1.63 (m, 16H); ^{13}C NMR (CDCl₃, 63 MHz) δ 151.8, 150.4, 147.3, 138.8, 136.3, 135.7, 132.9, 131.2, 130.7, 129.8, 129.6, 129.1, 128.3, 128.0, 125.1, 121.4, 120.2, 108.4, 97.9, 67.5, 60.5,

55.8, 30.9, 28.6, 28.4, 28.3, 26.3, 26.0, 22.0, 21.9, 21.6, 21.2; [α]₍D₎ = -23.3 (*c* 6.88, CHCl₃).

(*S*)-2-Methoxymethoxy-2'-(3-aminobenzyloxy)-3-hydroxymethyl-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthalene (9). To a solution of **8** (4.5 g, 8.94 mmol) in a mixture of ethanol/1,4-dioxane/water (1:1:1) was added the iron powder (3.5 g, 62.6 mmol) and ammonium chloride (0.86 g, 16 mmol) successively. After reflux for 24 h, the solvent was evaporated. The residue was purified by silica gel column chromatography (EtOAc/hexane = 1:5) to afford **9**. Yield: 4.23 g (95%); mp 132 - 133 °C; ^{1}H NMR (CDCl₃, 250 MHz) δ 7.10-6.35 (m, 7H), 4.80-4.70 (m, 2H, CH₂OH), 4.49-4.44 (dd, 2H, -OCH₂O), 4.92 (s, 2H, -OCH₂), 3.28 (s, 3H, -OCH₃), 2.79-1.61 (m, 16H); ^{13}C NMR (CDCl₃, 63 MHz) δ 163.8, 163.5, 153.5, 151.4, 138.7, 138.5, 137.0, 136.9, 136.6, 133.6, 131.6, 130.9, 130.1, 129.9, 129.0, 125.8, 122.9, 121.8, 120.1, 119.9, 109.6, 99.1, 98.9, 69.4, 61.5, 56.8, 29.7, 29.5, 29.4, 28.1, 27.3, 27.2, 23.1, 23.0, 22.9; [α]₍D₎ = -19.8 (*c* 7.58, CHCl₃).

(*S*)-2-Methoxymethoxy-3-hydroxymethyl-2′-[(3-(*N*,*N*′-di(tert-butoxycarbonyl)-guanidino)-benzyloxy)-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthalene (10). To a stirred solution of **9** (2.5 g, 5.31 mmol) and 1,3-bis-BOC-2-methyl-2-thiopseudourea (1.57 g, 5.31 mmol) in dry DMF at 0 °C under nitrogen was added triethylamine (3.0 mL, 21.24 mmol) and HgCl₂ (1.58 g, 5.84 mmol). The resulting suspension was stirred at 0 °C for 3 h, and then at room temperature for overnight. The mixture was diluted with EtOAc and filtered through Celite. Evaporation of the solvent followed by silica column chromatography (EtOAc/hexane = 1:3) gave **10**. Yield: 3.5 g (92%); mp 174 - 175 °C; ^{1}H NMR (CDCl₃, 250 MHz) δ 11.65 (s, 1H, NH), 10.21 (s, 1H, NH), 7.62-6.73 (m, 7H), 4.99 (s, 2H, OCH₂), 4.71-4.69 (m, 2H, CH₂OH), 4.48-4.46 (dd, 2H, OCH₂O), 3.25 (s, 3H, OCH₃), 2.79-1.62 (m, 16H), 1.55-1.49 (m, 18H); ^{13}C NMR (CDCl₃, 63 MHz) δ 163.6, 155.1, 153.5, 152.9, 151.3, 145.2, 137.8, 136.6, 135.4, 133.7, 133.1, 130.5, 129.7, 129.1, 127.3, 126.7, 123.7, 122.2, 120.4, 119.8, 109.4, 99.4, 83.7, 69.5, 54.9, 28.3, 28.1, 27.8, 27.0, 26.6, 26.1, 22.8, 21.5, 21.2.

(*S*)-2-Methoxymethoxy-2'-[(3-(*N*,*N*'-di(tert-butoxycarbonyl)-guanidino)-benzyl)-3-formyl-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthalene (11). To a solution of **10** (3.5 g, 4.89 mmol) in methylene chloride (50 mL) was added at room temperature the PCC (2.1 g, 9.78 mmol). After stirring for 12 h, the mixture was passed through a short pad of celite. The filtrate was concentrated and purified by column chromatography (EtOAc/hexane = 1:5) to give **11**. Yield: 2.7 g (80%); mp 86 - 88 °C; ^{1}H NMR (CDCl₃, 250 MHz) δ 11.65 (s, 1H, NH), 10.36 (s, 1H, CHO), 10.24 (s, 1H, NH), 7.63-6.75 (m, 7H), 5.00 (s, 2H, OCH₂), 4.78-4.61(dd, 2H, OCH₂O), 3.09 (s, 3H, OCH₃), 2.85-1.64 (m, 16H), 1.55-1.49 (m, 18H); ^{13}C NMR (CDCl₃, 63 MHz) δ 189.9, 162.5, 154.3, 152.5, 152.2, 144.3, 137.2, 136.0, 135.8, 133.1, 133.0, 130.8, 129.1, 128.3, 126.9, 126.4, 123.6, 121.7, 120.7, 118.9, 108.5, 98.9, 82.7, 78.6, 68.3, 56.1, 28.6, 28.4, 28.3, 27.0, 26.9, 26.3, 22.0, 21.8, 21.6; [α]₍D₎ = -13.2 (*c* 18.2, CHCl₃).

(*S*)-2-Hydroxy-2'-(3-phenyluryl-benzyl)-3-formyl-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthalene (2a). The solution of **6** (1 g, 1.829 mmol) in ethanol was treated with aqueous HCl (0.48 mL, 5.49 mmol) for 3 h at reflux temperature. After evaporation of the solvent, the residue was purified by silica column

chromatography (EtOAc/Hex = 1:5) to afford the receptor **1**. Yield: 0.89 g (90%); mp 117 - 118 °C; ^{1}H NMR (CDCl$_3$, 250 MHz) δ 10.73 (s, 1H, CHO), 9.69 (s, 1H, OH), 7.43-6.70 (m, 12H), 4.88 (s, 2H, OCH$_2$), 2.75-1.65 (m, 16H); ^{13}C NMR (CDCl$_3$, 63 MHz) δ 196.4, 156.1, 153.7, 153.3, 147.3, 138.5, 138.2, 138.1, 136.8, 133.2, 130.4, 129.7, 129.4, 128.9, 125.6, 123.9, 123.4, 121.8, 120.3, 119.7, 118.9, 118.7, 110.7, 70.0, 29.3, 29.0, 28.1, 27.0, 23.0, 22.9, 22.7, 22.5; HRMS (FAB) calcd for C$_{35}$H$_{36}$N$_2$O$_4$: 548. 2675; found: 548.2669; [α]$_D$ = -54.8 (*c* 6.02, CHCl$_3$).

(*S*)-2-Hydroxyl-2'-(3-guanidyl-benzyloxy)-3-formyl)-5,5', 6,6',7,7',8,8'-octahydro-1,1'-binaphthalene (2b). To a solution of **11** (0.3 g, 0.42 mmol) in THF (5 mL) was added the 0.1 M aqueous HCl (0.84 mL) at 0 °C. The temperature was slowly raised to room temperature, and then refluxed at 70 °C for 6 h. The solvent was evaporated and the residue was extracted with EtOAc. The combined organic layers were washed with 0.1M aqueous HCl. Evaporation of the solvent yielded the pure receptor **2**. Yield: 0.15 g (65%); mp 159 - 160 °C; ^{1}H NMR (CDCl$_3$, 250 MHz) δ 10.83 (s, 1H, NH), 9.90 (s, 1H, CHO), 9.85 (s, 1H, OH), 7.42-6.77 (m, 7H), 4.95 (s, 2H, OCH$_2$), 2.86-1.67 (m, 16H); ^{13}C NMR (CDCl$_3$, 63 MHz) δ 196.7, 156.6, 156.1, 152.9, 147.0, 140.0, 136.9, 133.9, 133.4, 130.8, 130.1, 129.6, 129.3, 125.9, 125.3, 124.6, 124.5, 123.5, 118.6, 111.1, 69.5, 29.3, 29.0,28.1, 27.0, 23.0, 22.9, 22.7, 22.6, 21.0; HRMS (FAB) calcd for C$_{29}$H$_{34}$N$_3$O$_3$: 472.2595; found: 472.2588; [α]$_D$ = 1.09 (*c* 18.3, CHCl$_3$).

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