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Effects of ring substituents on enantioselective recognition of amino alcohols and acids in uryl-based binol receptors

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ABSTRACT

The uryl-based binol aldehyde, (*S*)-2-hydroxy-2′-(3-phenyluryl-benzyl)-1,1′-binaphthyl-3-carboxaldehyde (**1**), binds 1,2-amino alcohols and amino acids stereoselectively by reversible formation of imine bond. Hydrogen bond (between uryl group and alcohol –OH moiety) plays an important role in the stereoselectivity of amino alcohols. Hence, any substituents on phenyl group in **1** are expected to affect H-bond ability of uryl group. To study the effects of ring substituents on the stereoselective recognition of amino alcohols, (substituted phenyl)uryl-based chiral binol receptors have been prepared. The receptors with electron-donating X substituents have been synthesized from (*S*)-2-methoxymethoxy-2′-hydroxy-1,1′-binaphthyl-3-carboxaldehyde and X-phenyluryl-benzyl bromide. The receptors with electron-withdrawing Y substituents, however, required a different synthetic strategy including transformation of an aldehyde to alcohol. The incorporation of the electron withdrawing groups slightly accelerated the stereoselective recognition property of the receptor. Though the acceleration is not so remarkable, this work demonstrates the versatile derivatization of **1** in achieving higher stereoselective recognition of 1,2-amino alcohols and stereoconversion of L-amino acids to D-amino acids.

1. Introduction

Pure enantiomers of chiral amino alcohols and amino acids are useful as intermediates for producing a wide variety of biologically active molecules[1] and also as chiral pool in ligand design for stereoselective catalysts.[2] In the past decades, there have been a number of publications on developing enantioselective receptors for amines, amino alcohols, and amino acids.[3–6] Most of these studies are mainly based on noncovalent interactions such as hydrogen bonding, metal coordination, and hydrophobic interactions.

Recently, we reported an uryl-derivatized binol aldehyde **1**, which binds stereoselectively with various 1,2-amino alcohols[7] and converts bound L-amino acids to D-amino acids[8] by reversible formation of imine bond with internal Resonance Assisted Hydrogen Bonding (RAHB).[9] The imine bond, compared to the noncovalent interactions, is much stronger and structurally well defined and is particularly desirable for developing stereoselective receptors. The hydrogen bond between uryl NH and OH/COOH of the guests exerts an important role in the stereoselective recognition of **1** as shown in Scheme 1. Hence, altering the strength of hydrogen bond of the uryl NH in the receptor might alter its behavior toward the enantioselectivity of amino alcohols and conversion efficiency of amino acids. In order to test this notion, we designed several derivatives of **1** with electron-donating (X) and withdrawing (Y) substituents at the uryl benzene ring. Here we report detailed synthetic procedures of those derivatives along with their stereoselectivities.

2. Results and discussion

2.1. Synthesis of uryl-based binol aldehydes, 1–5

The synthesis of the parent receptor involves a slight modified procedure from the previous one[7] as shown in Scheme 2. The selective mono protection of the enantiomerically pure (*S*)-2,2′-dihydroxy-1,1′-binaphthyl-3-carboxaldehyde with MOM chloride in DMF gave the mono-MOM-protected binol aldehyde **6**. Addition of 3-phenyluryl-benzyl bromide led to the MOM-protected uryl-based binol receptor **7** in 94% yield, which upon hydrolysis under acidic condition gave the optically pure uryl-based binol receptor **1** in quantitative yield. The same procedure was applied to the synthesis of the methoxy derivative **2**, using 3-(4-methoxyphenyl)uryl-benzyl bromide.

However, a (Y-phenyl)uryl-benzyl bromide with electron-withdrawing substituent Y is very unstable and decomposes so rapidly and cannot be isolated as pure form nor reacted directly with mono-MOM-protected binol aldehyde. Therefore, we followed up another synthetic strategy to obtain electron-withdrawing group substituted derivatives as shown in Scheme 3. The binol

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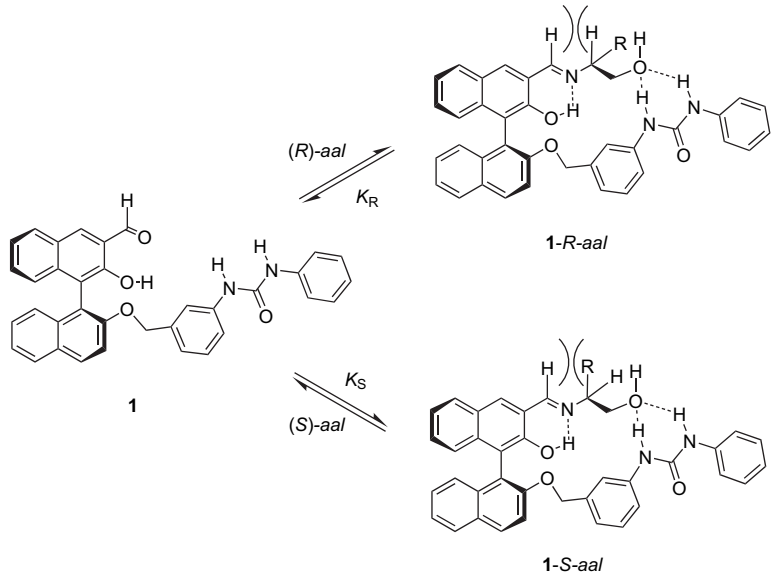
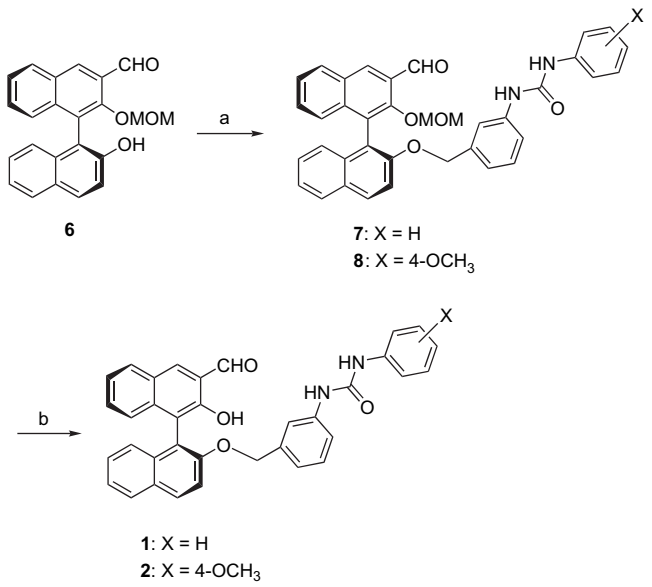


Scheme 1. Stereoselective imine formation of **1** with 1,2-amino alcohol (aal). Steric repulsions around imine bond are different between **1**-R-aal and **1**-*S*-aal.



Scheme 2. Reagents and conditions: (a) NaH, DMF, (Y-phenyl)uryl-benzyl bromide, rt, 5 h; (b) concd HCl, EtOH, reflux, 0.5 h.

amine **9** was reacted with appropriate (Y-phenyl)isocyanates in tetrahydrofuran to obtain the corresponding mom-protected uryl-based binol alcohols in good yields. These alcohols were treated with pyridinium chlorochromate (PCC) in methylene chloride and upon hydrolysis under acidic conditions gave the optically pure uryl-based binol receptors **3**–**5**.

2.2. Enantioselective recognition of receptors for chiral amino alcohols and amino acids

Stereoselectivity (K_R/K_S) in the imine formation shown in Scheme 1 can be assessed based on the following relations: K_R=[**1**-*R*-aa]/[**1**][(*R*)-aa], K_S=[**1**-*S*-aa]/[**1**][(*S*)-aa] and K_R/K_S=([**1**-*R*-aa][(*S*)-aa])/([**1**-*S*-aa][(*R*)-aa]). When 2 equiv of racemic amino alcohol is completely reacted with **1** to imine form, then [**1**-*R*-aa]/([**1**-*S*-aa]=[(*S*)-aa])/[(*R*)-aa] and K_R/K_S=([**1**-*R*-aa])/([**1**-*S*-aa])^2.

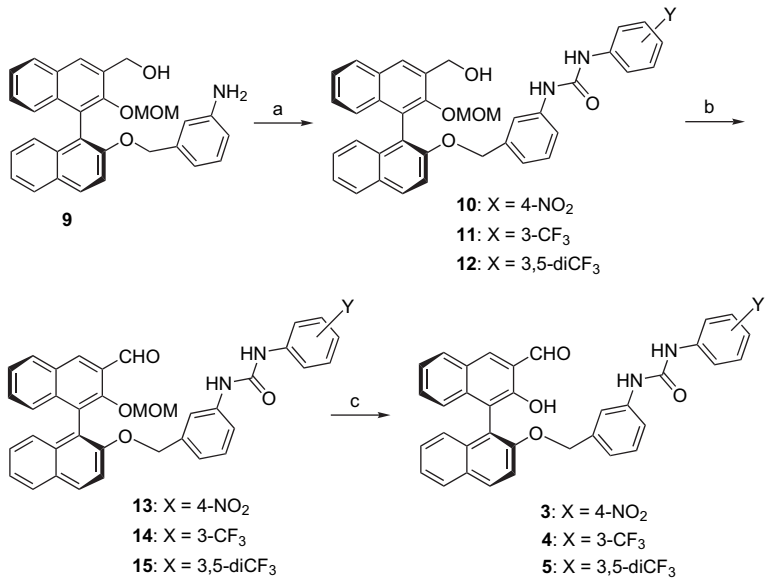
Figure 1a shows the ^{1}H NMR spectrum of **2** in benzene-d_6. Addition of (*S*)-2-aminopropanol ((*S*)-ap) to **2** results in complete and rapid decrease of the aldehyde signal at 9.51 ppm with concomitant increase of the signal at 8.13 ppm, which corresponds to imine C–H proton of **2**-*S*-ap (Fig. 1a). Similarly, addition of (*R*)-ap to **2** results in complete formation of imine **2**-*R*-ap with its C–H proton signal appearing at 8.21 ppm (Fig. 1c). These signals are markers for the two diastereomers. Aside from the imine C–H signals, the benzylic CH_2 signals are also useful for distinguishing **2**-*S*-ap and **2**-*R*-ap. The benzylic hydrogens are diastereotopic and appear as a doublet of doublet (dd) pattern at 4.6–5.0 ppm. The (*R*)-ap bound imine, **2**-*R*-ap, exhibits wider doublet of doublet than **2**-*S*-ap and **2**, which reflects the more rigid three-dimensional structure of **2**-*R*-ap.

Figure 1d shows the ^{1}H NMR spectrum for a mixture of **2**-*S*-ap and **2**-*R*-ap formed by the addition of 2 equiv of racemic ap to **2**. The ratio of **2**-*S*-ap and **2**-*R*-ap can be measured from the integration of imine C–H and benzylic hydrogen signals. Integration of the two peaks provides the ratio of **2**-*S*-ap and **2**-*R*-ap is 1:1.9 at equilibrium. This indicates the imine formation constant for **2**-*R*-ap (K_R) is larger than **2**-*S*-ap (K_S) by a factor of about 1.9^2=3.61. Even if **2**-*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 have compared the stereoselective imine formation (K_R/K_S) between the receptors **1**–**5** and four representative 1,2-amino alcohols, 2-aminopropanol (ap), 2-amino-1-butanol (ab), 2-amino-3-phenyl-1-propanol (app), and 2-amino-2-phenylethanol (ape), following the above mentioned protocol. The results are tabulated in Table 1. The stereoselectivities of the receptors are in similar range, high with **5** and low with **2**. Being an electron-withdrawing group, CF_3 seems to increase the hydrogen bonding donor ability of uryl –NH–, which in turn increases the stereoselectivity by stabilizing the two diastereomers as described in Scheme 1.

Furthermore, we have also studied the receptor activities for the conversion efficiency (epimerization) of amino acids from L-form to D-form according to the reported procedure.[8] In nature, L-amino acids are racemized by pyridoxal phosphate (PLP) dependent enzymes.[10] The receptors of this work form Schiff base like PLP, however, deracemize the bound amino acids unlike PLP due to the chirality of binol (Scheme 4).

A receptor is completely reacted in DMSO-d_6 with L-amino acids to form an imine, **1**-L-aa, which epimerizes to the imine of D-amino



Scheme 3. Reagents and conditions: (a) THF, (Y-phenyl)isocyanates, rt, 5 h; (b) PCC, CH_2Cl_2, rt, 5 h; (c) concd HCl, EtOH, reflux, 0.5 h.

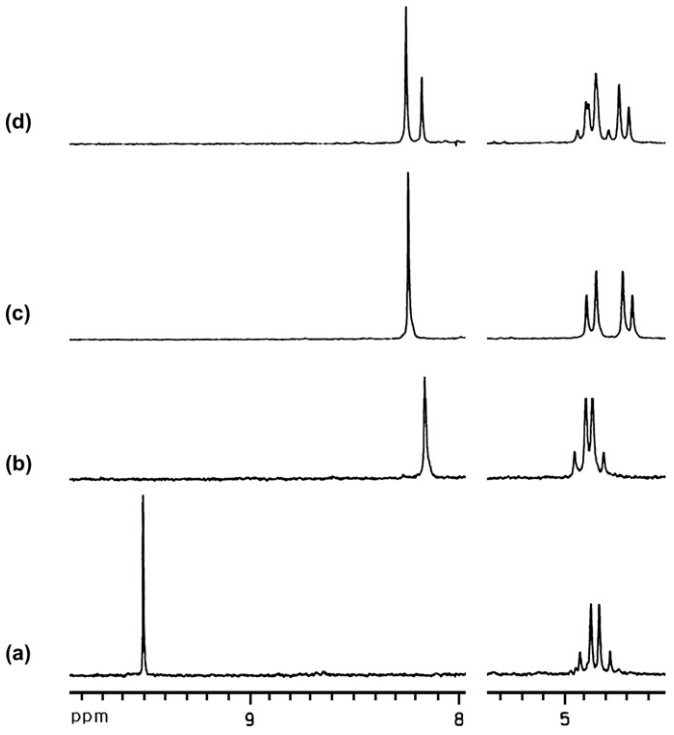


Figure 1. Partial ^{1}H NMR spectra in benzene-d_6 of (a) **2**, (b) **2**-*S*-ap, (c) **2**-*R*-ap, and (d) mixture of **2**-*S*-ap and **2**-*R*-ap formed from addition of 2 equiv of racemic ap to **2**.

Table 1
Stereoselective imine formation (K_R/K_S) between the receptors and amino alcohols as determined by ^{1}H NMR in benzene-d_6

Amino alcohols	Receptors				
	1	**2**	**3**	**4**	**5**
ap	3.70	3.61	3.68	3.82	3.88
ab	3.10	2.96	3.09	3.47	3.61
app	3.70	3.65	3.73	3.91	3.98
ape	4.80	4.84	4.82	4.87	5.10

acid, **1**-D-aa, in the presence of triethylamine. The ratios of (D-amino acid bound imine)/(L-amino acid bound imine) at equilibrium measured by integration of ^{1}H NMR spectra for representative four amino acids, alanine (Ala), phenyl alanine (Phe), histidine (His), serine (Ser) are listed in Table 2. The stereoselectivities show a similar pattern with those of the amino alcohol case. While all the receptors show similar efficiencies, receptor **5** exhibits the highest conversion efficiency and receptor **2** the lowest.

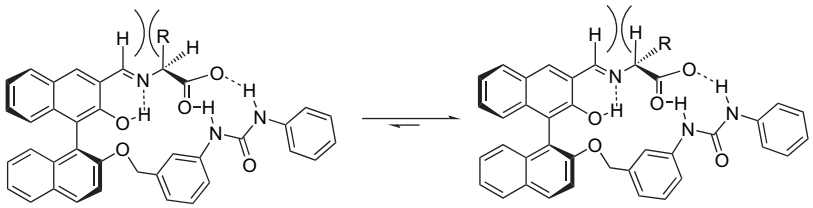
3. Conclusion

The enantioselective recognition of 1,2-amino alcohols has been studied using uryl-based chiral binol aldehyde receptors. Substituents are introduced at the aryl ring of the phenyluryl group by appropriate experimental protocols, which allow the investigation of their effect on stereoselective recognition process. Electron-withdrawing substituents, such as nitro and trifluoromethyl drive a slight improvement in chiral discrimination of amino alcohols and epimerization of amino acids. Electronegative methoxy group favor a weak recognition process compared to the parent receptor. This study demonstrates that the stereoselectiviy is, however, not remarkably affected by the derivatization of phenyl ring of uryl group, though slight improvement is observed in electron-withdrawing group substitution. This will be helpful in designing solid-supported receptors, which is required for facile recovery process in industrial application. Appropriate linkers may be derivatized at the phenyl ring position and connected to silica or other solid-supports without severe interference on the selectivity of the parent receptor.

4. Experimental

4.1. General

(X-Phenyl)uryl-benzyl bromides were prepared according to our earlier procedure.[7] All other chemicals were commercially available and used without further purifications. The solvents for dry reactions were dried with appropriate desiccants and distilled prior to use. NMR spectra were recorded on a Bruker AM 250 spectrometer in $CDCl_3$, DMSO-d_6, and benzene-d_6 solutions containing tetramethylsilane as internal standard. Melting points were



1-L-*aa* **1**-D-*aa*

Scheme 4. Epimerization of the imine formed between **1** and amino acid (aa).

Table 2
L to D conversion efficiency of the receptors for amino acid

Amino acids	Receptors				
	1	**2**	**3**	**4**	**5**
Ala	7	5.8	7.4	7.6	6.7
Phe	11	12	12	13	15
His	14	9.2	15	12	15
Ser	11	12	12	12	13

The diastereomeric ratio, (D-amino acid bound imine)/(L-amino acid bound imine), was determined by ^{1}H NMR in DMSO-d_6 at equilibrium.

measured with Electrothermal IA 9000 digital melting point apparatus and are uncorrected. HRMS spectra were obtained on FAB mode. EA was determined using vario EL Elemental Analyser. For column chromatography, silica gel of 230–400 mesh was used.

4.2. (*S*)-2-Methoxymethoxy-2′-(3-(4-methoxyphenyl)uryl-benzyl)-1,1′-binaphthyl-3-carbxaldehyde (8)

To an ice cooled solution of MOM-protected binol aldehyde **6** (1.0 g, 3.06 mmol) in 25 mL of DMF was added NaH (60%, 0.12 g, 3.06 mmol). After stirring for 1 h, 3-(4-methoxyphenyl)uryl-benzyl bromide (0.95 g, 3.1 mmol) was added and the resulting mixture was stirred overnight at ambient temperature. After the reaction completed (monitored by TLC), water was added to quench the reaction. Extraction with ethylacetate and silica gel column chromatography with EA/hexane (1:3, v/v) as eluent gave 1.1 g (65% yield) of the product **8**. Mp 143 °C. ^{1}H NMR ($CDCl_3$, 250 MHz): δ (ppm)=10.57 (s, 1H, CHO), 8.50 (s, 1H), 7.91–8.27 (m, 4H), 6.65–7.40 (m, 16H), 5.10–4.97 (dd, 2H, benzylic–CH_2), 4.72–4.64 (dd, 2H, OCH_2OCH_3), 3.91 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_2OCH_3). ^{13}C NMR ($CDCl_3$, 63 MHz): δ (ppm)=158.12, 157.23, 156.34, 152.10, 148.66, 136.13, 134.20, 132.13, 129.86, 129.69, 129.16, 128.35, 127.03, 126.35, 123.90, 120.10, 119.46, 119.14, 114.58, 95.69, 71.25, 58.92, 55.91, 55.68. Anal. Calcd for $C_{38}H_{34}N_2O_6$: C, 74.5; H, 5.26; N, 4.57. Found: C, 74.4; H, 5.38; N, 4.63.

4.3. (*S*)-3-Hydroxymethyl-2-methoxymethoxy-2′-(3-aminobenzyl)-1,1′-binaphthalene (9)

To an ice cooled solution of **6** (0.6 g, 1.67 mmol) in 5 mL of DMF was added NaH (0.081 g, 2.0 mmol). After stirring for a while, 3-nitrobenzylbromide (0.434 g, 2.0 mmol) was added and the resulting mixture was stirred for another 4 h at ambient temperature. Extraction with ethylacetate gave the product (*S*)-2-methoxymethoxy-2′-(3-nitrobenzyl)-1,1′-binaphthyl-3-carbxaldehyde, which was reduced by iron powder (0.504 g, 9.1 mmol) and ammonium chloride (0.126 g, 2.34 mmol) after converting aldehyde to alcohol with sodium borohydride. Silica gel column chromatography with EA and hexane 1:1 mixture provided the compound **9**. Overall yield 89% (mp 168 °C). ^{1}H NMR ($CDCl_3$, 250 MHz): δ (ppm)=8.03–8.78 (m, 4H), 7.49–7.24 (m, 7H), 6.96 (m, 1H), 6.48 (m, 2H), 6.13 (s, 1H), 5.04–4.86 (m, 4H), 4.60 (dd, 2H, OCH_2OCH_3), 3.51 (br, 3H), 3.18 (s, 3H, OCH_2OCH_3). ^{13}C NMR ($CDCl_3$, 63 MHz): δ (ppm)=154.261, 153.072, 146.653, 138.535, 134.867, 133.699, 133.386, 131.521, 130.409, 129.126, 129.706, 128.682, 128.157, 128.184, 127.021, 126.533, 125.981, 125.618, 125.236, 125.253, 124.205, 119.184, 116.757, 115.396, 114.348, 113.418, 99.374, 70.814, 62.140, 57.708. HRMS (FAB) calcd for $C_{30}H_{27}NO_4$: 465.1940; found: 465.1935.

4.4. (*S*)-3-Hydroxymethyl-2-methoxymethoxy-2′-(3-(4-nitrophenyl)uryl-benzyl)-1,1′-binaphthalene (10)

A mixture of binol amine **9** (0.2 g, 0.43 mmol) and 4-nitrophenyl isocyanate (0.085 g, 0.52 mmol) was dissolved in tetrahydrofuran and stirred for 5 h at room temperature. Evaporation of the solvent and silica gel column chromatography with EA and hexane 1:3 mixture afforded 0.20 g (81% yield) of the desired product **10**. Mp 141 °C. ^{1}H NMR ($CDCl_3$, 250 MHz): δ (ppm)=8.25–7.29 (m, 19H), 7.20 (br, 1H, NH), 6.80 (br, 1H, NH), 6.58 (br, 1H, OH), 5.34–5.02 (dd, 2H, benzylic–CH_2), 4.88–4.83 (dd, 2H, CH_2OH), 4.81–4.60 (dd, 2H, OCH_2OCH_3), 3.24 (s, 3H, OCH_2OCH_3). ^{13}C NMR ($CDCl_3$, 63 MHz): δ (ppm)=159.56, 157.45, 153.89, 147.57, 144.01, 142.04, 141.14, 136.34, 135.890, 131.68, 129.90, 129.15, 128.70, 128.26, 126.68, 124.18, 122.96, 121.37, 120.76, 118.45, 94.95, 70.93, 58.16, 54.85. Anal. Calcd for $C_{37}H_{31}N_3O_7$: C, 70.6; H, 4.96; N, 6.67. Found: C, 70.5; H, 4.89; N, 6.75.

4.5. (*S*)-3-Hydroxymethyl-2-methoxymethoxy-2′-(3-(3-(trifluoromethyl)phenyl)uryl-benzyl)-1,1′-binaphthalene (11)

It was prepared similar to **10**, but with α,α,α-trifluoro-*m*-tolyl isocyanate. Isolated yield: 85% (mp 182 °C). ^{1}H NMR ($CDCl_3$, 250 MHz): δ (ppm)=7.01–8.05 (m, 19H), 6.65 (d, 1H), 6.25 (s, 1H), 4.58–5.39 (m, 7H, three methylenes and OH), 3.3 (s, 3H, OCH_2OCH_3). ^{13}C NMR ($CDCl_3$, 63 MHz): δ (ppm)=158.68, 157.19, 151.54, 147.98, 143.58, 141.17, 136.51, 134.96, 131.29, 129.51, 129.25, 128.73, 128.04, 127.51, 126.49, 125.72, 124.38, 122.38, 122.09, 120.02, 117.94, 95.13, 71.89, 57.93, 55.49. Anal. Calcd for $C_{38}H_{31}F_3N_2O_5$: C, 69.9; H, 4.79; N, 4.29. Found: C, 69.8; H, 4.88; N, 4.21.

4.6. (*S*)-3-Hydroxymethyl-2-methoxymethoxy-2′-(3-(3,5-bis(trifluoromethyl)phenyl)uryl-benzyl)-1,1′-binaphthalene (12)

It was prepared similar to **10**, but with 3,5-bis(trifluoromethyl)phenyl isocyanate. Isolated yield: 82% (mp 203 °C). ^{1}H NMR ($CDCl_3$, 250 MHz): δ (ppm)=8.70–7.19 (m, 18H), 7.08–6.91 (m, 2H), 6.27 (s, 1H), 4.30–5.09 (m, 7H, three methylenes and OH), 3.31 (s, 3H, OCH_2OCH_3). ^{13}C NMR ($CDCl_3$, 63 MHz): δ (ppm)=159.45, 158.78, 157.30, 153.10, 148.64, 141.95, 136.52, 136.16, 134.19, 131.59, 129.94, 128.64, 128.24, 127.53, 126.89, 126.10, 125.39, 124.18, 123.90, 122.88, 120.78, 120.38, 118.73. Anal. Calcd for $C_{39}H_{30}F_6N_2O_5$: C, 65.0; H, 4.20; N, 3.89. Found: C, 65.2; H, 4.28; N, 3.97.

4.7. (*S*)-2-Methoxymethoxy-2′-(3-(4-nitrophenyl)uryl-benzyl)-1,1′-binaphthyl-3-carbxaldehyde (13)

A mixture of **8** (0.150 g, 0.24 mmol) and pyridinium chlorochromate (PCC, 0.11 g, 0.48 mmol) was dissolved in methylene chloride and stirred for 5 h. The reaction mixture was filtered and the filtrate after evaporation, on column chromatography with EA and hexane 1:2 mixture gave the compound **13**. Yield: 72% (mp 110 °C). ^{1}H NMR ($CDCl_3$, 250 MHz): δ (ppm)=10.46 (s, 1H, CHO), 8.51–7.09 (m, 19H), 6.99–6.79 (m, 2H), 5.20–4.96 (dd, 2H, benzylic CH_2), 4.84–4.64 (dd, 2H, OCH_2OCH_3), 2.64 (s, 3H, OCH_2OCH_3). ^{13}C NMR ($CDCl_3$, 63 MHz): δ (ppm)=191.04, 159.58, 152.84, 152.04, 144.59, 142.84, 141.48, 136.95, 135.79, 134.58, 132.39, 130.19, 129.84, 129.35, 128.48, 128.19, 126.83, 125.09, 124.38, 122.54, 121.10, 120.54, 119.64, 95.86, 71.63, 55.43. Anal. Calcd for $C_{37}H_{29}N_3O_7$: C, 70.8; H, 4.66; N, 6.69. Found: C, 70.8; H, 4.58; N, 6.76.

4.8. (*S*)-2-Methoxymethoxy-2′-(3-(3-(trifluoromethyl)-phenyl)uryl-benzyl)-1,1′-binaphthyl-3-carbxaldehyde (14)

Same procedures with **13**. Isolated yield: 75% (mp 95 °C). ^{1}H NMR ($CDCl_3$, 250 MHz): δ (ppm)=10.48 (s, 1H, CHO), 8.54 (s, 1H), 7.15–8.29 (m, 18H), 6.88 (d, 2H), 5.00–5.28 (dd, 2H, benzylic–CH_2), 4.61–4.89 (dd, 2H, OCH_2OCH_3), 2.57 (s, 3H, OCH_2OCH_3). ^{13}C NMR ($CDCl_3$, 63 MHz): δ (ppm)=192.31, 160.21, 158.19, 152.16, 141.43, 136.13, 134.52, 132.75, 132.15, 131.32, 129.84, 128.78, 128.02, 126.54, 125.85, 124.45, 124.10, 121.30, 120.87, 119.53, 117.45. Anal. Calcd for $C_{38}H_{29}F_3N_2O_5$: C, 70.1; H, 4.49; N, 4.31. Found: C, 70.3; H, 4.61; N, 4.43.

4.9. (*S*)-2-Methoxymethoxy-2′-(3-(3,5-bis(trifluoromethyl)-phenyl)uryl-benzyl)-1,1′-binaphthyl-3-carbxaldehyde (15)

It was prepared similar to **13**. Isolated yield: 78% (mp 133 °C). ^{1}H NMR ($CDCl_3$, 250 MHz): δ (ppm)=10.47 (s, 1H, CHO), 8.53–7.12 (m, 18H), 6.90–6.84 (m, 2H), 5.28–4.97 (dd, 2H, benzylic–CH_2), 4.89–4.56 (dd, 2H, OCH_2OCH_3), 2.53 (s, 3H, OCH_2OCH_3). ^{13}C NMR ($CDCl_3$, 63 MHz): δ (ppm)=193.12, 159.12, 157.56, 151.32, 142.68, 136.86, 135.72, 132.72, 132.15, 131.58, 129.78, 128.54, 128.15, 125.36, 124.18, 122.35, 121.10, 120.74, 120.18, 119.14, 118.76. Anal. Calcd for $C_{39}H_{28}F_6N_2O_5$: C, 65.2; H, 3.93; N, 3.90. Found: C, 65.2; H, 4.03; N, 3.78.

4.10. (*S*)-2-Hydroxy-2′-(3-(4-methoxyphenyl)uryl-benzyl)-1,1′-binaphthyl-3-carbxaldehyde (2)

To MOM-protected binol aldehyde **8** in ethanol a few drops of concd hydrochloric acid was added and refluxed for 30 min. The solvent was evaporated and recrystallized with ethanol to afford the desired receptor **1**. Isolated yield: 99% (mp 85 °C). ^{1}H NMR ($CDCl_3$, 250 MHz) δ (ppm)=10.40 (s, 1H, OH), 10.02 (s, 1H, CHO), 8.43 (s, 1H), 7.84–8.14 (m, 3H), 6.60–7.36 (m, 17H), 4.74–5.00 (dd, 2H, benzylic–CH_2), 3.88 (s, 3H, OCH_3). ^{13}C NMR ($CDCl_3$, 63 MHz): δ (ppm)=197.34, 159.52, 158.34, 156.87, 143.58, 141.42, 136.14, 134.65, 132.97, 131.25, 130.78, 128.65, 128.10, 127.83, 126.95, 125.65, 124.58, 124.15, 123.69, 122.65, 121.35, 120.86, 114.57, 70.59, 54.89. HRMS (FAB) calcd for $C_{36}H_{28}N_2O_5$: 568.1998; found: 568.1991.

4.11. (*S*)-2-Hydroxy-2′-(3-(4-nitrophenyl)uryl-benzyl)-1,1′-binaphthyl-3-carbxaldehyde (3)

It was prepared similar to **2**. Isolated yield: 98% (mp 138 °C). ^{1}H NMR ($CDCl_3$, 250 MHz) δ (ppm)=10.62 (s, 1H, OH), 10.06 (s, 1H, CHO), 8.20–6.99 (m, 19H), 6.96–6.66 (m, 2H), 4.9 (s, 2H, benzylic–CH_2). ^{13}C NMR ($CDCl_3$, 63 MHz): δ (ppm)=197.16, 153.89, 152.23, 148.84, 143.67, 142.34, 138.67, 133.67, 133.00, 131.23, 130.96, 130.34, 129.61, 127.43, 126.86, 126.05, 124.62, 124.10, 123.58, 122.90, 121.76, 121.06, 117.89, 68.04. HRMS (FAB) calcd for $C_{35}H_{25}N_3O_6$: 583.1743; found: 583.1751.

4.12. (*S*)-2-Hydroxy-2′-(3-(3-trifluorophenyl)uryl-benzyl)-1,1′-binaphthyl-3-carbxaldehyde (4)

It was prepared similar to receptor **1**. Isolated yield: 99% (mp 176 °C). ^{1}H NMR ($CDCl_3$, 250 MHz) δ (ppm)=10.24 (s, 1H, CHO), 10.12 (s, 1H, OH), 8.27 (s, 1H), 7.85–8.0 (m, 3H), 7.63 (s, 1H), 7.05–7.55 (m, 12H), 6.77–6.85 (m, 3H), 6.41 (s, 1H), 5.01–5.13 (dd, 2H, benzylic–CH_2). ^{13}C NMR ($CDCl_3$, 63 MHz): δ (ppm)=196.83, 154.00, 152.88, 152.29, 140.54, 139.14, 138.00, 136.88, 136.64, 133.24, 130.23, 128.43, 128.00, 126.45, 125.85, 125.23, 124.69, 124.04, 123.72, 123.34, 122.38, 114.01, 69.95. HRMS (FAB) calcd for $C_{36}H_{25}F_3N_2O_4$: 606.1766; found: 606.1759.

4.13. (*S*)-2-Hydroxy-2′-(3-(3,5-di-trifluorophenyl)uryl-benzyl)-1,1′-binaphthyl-3-carbxaldehyde (5)

It was prepared similar to receptor **1**. Isolated yield 98% (mp 104 °C). ^{1}H NMR ($CDCl_3$, 250 MHz) δ (ppm)=10.48 (s, 1H, CHO), 10.07 (s, 1H, OH), 8.24–7.00 (m, 19H), 6.77–6.68 (m, 2H), 4.88 (s, 2H, benzylic CH_2). ^{13}C NMR ($CDCl_3$, 63 MHz): δ (ppm)=197.22, 153.95, 152.57, 151.98, 138.58, 137.45, 137.00, 134.67, 131.34, 129.93, 129.34, 127.87, 126.77, 126.22, 124.95, 124.36, 123.63, 123.24, 122.47, 115.23, 70.83. HRMS (FAB) calcd for $C_{37}H_{24}F_6N_2O_4$: 674.1640; found: 674.1649.

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