Molecular Recognition of β-Ribofuranosides by Synthetic Polypyridine-Macrocyclic Receptors

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Abstract: Artificial ribofuranoside receptors were designed and synthesized. The design of the polypyridine-macrocyclic receptors was based on the multipoint hydrogen bond complementarity between the receptors and methyl β-D-ribofuranoside. The binding affinity of the receptors for the ribofuranoside in $CDCl_3$ was very high (up to $K_a = 5.2 \times 10^3\ M^{-1}$), so that even native ribose was extracted by them into such nonpolar solvents. Selective extraction of ribose by the receptors was observed: the extractabilities, or affinities to the receptors of various pentoses and hexoses decreased in the following order: ribose > deoxyribose ≅ lyxose ≅ xylose > fructose > arabinose > glucose ≅ mannose ≅ galactose. The selectivity is governed by the OH direction and the whole size of the sugars as well as their shapes. Furthermore, fluorescence emission of the receptors was largely enhanced in the presence of methyl β-D-ribofuranoside or ribose, and the degree for the fluorescence enhancement by the addition of various sugars was almost compatible with that of the extractabilities. The polypyridine-macrocycles represent rationally designed multifunctional artificial receptors for ribofuranosides.

Introduction

Selective complexation of polar molecules of biological origin is receiving much increased attention. The artificial receptors that recognize and bind to specific nucleobases and amino acids have been developed.[1] Among the many artificial receptors, however, only a few of those have been shown to be effective for the recognition of the third major class of natural building blocks, sugars.[2,3] This is possibly because of the three-dimensional complexity of sugar structures and of great difficulty for the distinction between the families of closely related stereoisomers. Aoyama et al. recently reported a notable example of selective complexation of sugars by synthetic polyhydroxy macrocycles, resorcinol/aldehyde cyclic tetramers, where ribose was bound highly selectively in the α-pyranose form.[4] On the other hand, Shinkai et al. and other research groups have exploited the interactions of boronic acids with sugars, from which remarkably strong interaction between the (methylene-*m*-phenylene)bis(boronic acid) and glucose through the formation of covalent bonds in protic solvents has been elucidated.[5] In view of biological importance of ribofuranosides such as the component of RNA and ATP, much attention should also be paid to the ribose binding in the furanose form. As part of our program aimed at the development of multifunctional artificial receptors for biologically important species,[6] we sought to construct receptors for β-ribofuranosides. In this paper we present the synthesis and strong complexation of rationally designed polypyridine-macrocyclic receptors for β-ribofuranosides.

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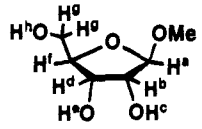
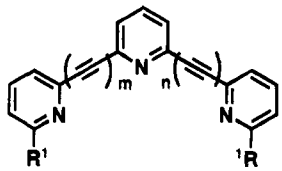
Scheme 1



Methyl β-(D)-ribofuranoside (1)

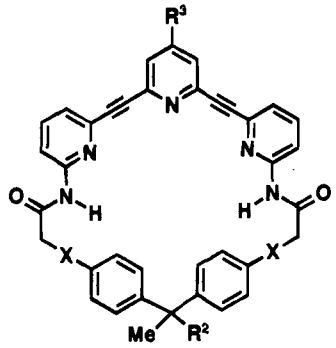


2a m = n = 0, R^1 = H

2b m = 0, n = 1, R^1 = H

2c m = n = 1, R^1 = H

3 m = n = 1, R^1 = $NHCO(CH_2)_{10}CH_3$



4 R^2 = Me, R^3 = H, X = O

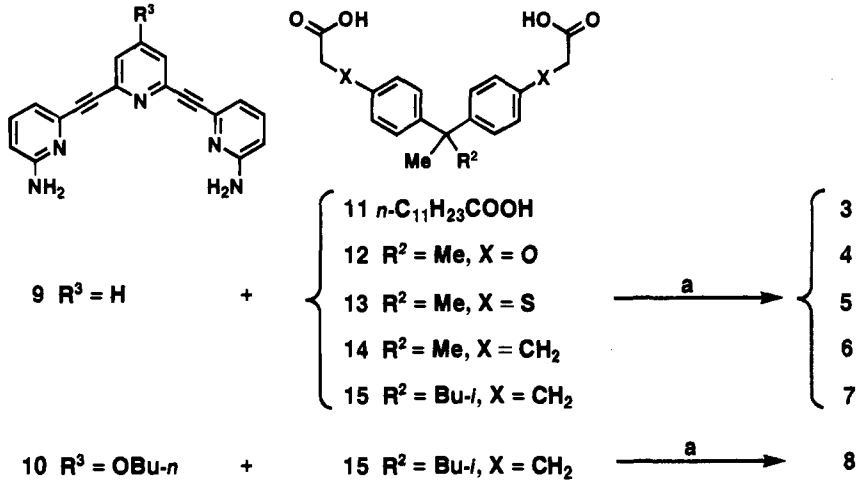
5 R^2 = Me, R^3 = H, X = S

6 R^2 = Me, R^3 = H, X = CH_2

7 R^2 = Bu-*i*, R^3 = H, X = CH_2

8 R^2 = Bu-*i*, R^3 = OBu-*n*, X = CH_2

Scheme 2[a]



[a] (a) 2-Chloro-1-methylpyridinium iodide, Et_3N, CH_3CN; (b) *n*-BuOH, concd H_2SO_4; (c) KOH, EtOH; (d) 1-hydroxy-2-pyridinethione, DCC, DMAP, $BrCCl_3$; (e) (trimethylsilyl)acetylene; (f) $PdCl_2(PPh_3)_2$, CuI, Et_2NH; (g) TBAF, H_2O, THF; (h) 2,6-dibromopyridine; (i) **19**; (j) *N,N*-dimethylthiocarbamoyl chloride, NaH, THF, DMF; (k) heat at 260 °C; (l) $ClCH_2CO_2Et$, K_2CO_3, NaI, acetone; (m) $(CF_3SO_2)_2O$, pyridine; (n) methyl acrylate, $PdCl_2(PPh_3)_2$, LiCl, DMF; (o) H_2 (30 atm), Pd/C, EtOH.

Molecular Design and Synthesis

As a starting point for the design of ribofuranoside receptors, we chose 2,2′:6′,2″-terpyridine skeleton with or without ethynediyl spacers as the binding site in the receptor molecules (Scheme 1).[7] The decision was based on (i) the utilization of strong OH···N hydrogen bonds, (ii) consideration for the direction of three ribofuranose-OH groups (2-C, 3-C, and 5-C), and (iii) incorporation of moderate rigidity and flexibility into the binding sites on the receptors. The sp-carbon spacers will allow flexibility for partial rotation about the pyridine−ethynediyl bonds maintaining linearity along the pyridine−pyridine axis, which would result in optimum for the expected hydrogen bonds.

The polypyridine-macrocyclic receptors **4**−**8** were synthesized from two key intermediates, diaminoterpyridine derivatives **9**−**10** and dicarboxylic acid derivatives **12**−**15** by Mukaiyama's macrocyclization in the final step (Scheme 2).[8] The diaminoterpyridine derivatives, the critical recognition moieties, were prepared from 2,6-dibromopyridine and its derivative **19** with 2-amino-6-ethynylpyridine (**22**) by Sonogashira reaction,[9] in which **19** was derived from the corresponding dicarboxylic acid by Barton-modified Hunsdieker reaction,[10] while **22** itself also by Sonogashira reaction (Scheme 3). The dicarboxylic acid derivatives **12**−**15**, the spacer components for the macrocyclic receptors, were all synthesized from bisphenol derivatives as a starting material. Ether- and thioether-linked dicarboxylic acids **12** and **13** were prepared by standard synthetic methods, whereas

(6) Inouye, M.; Ueno, M.; Kitao, T.; Tsuchiya, K. *J. Am. Chem. Soc.* **1990**, *112*, 8977−8979. Inouye, M.; Ueno, M.; Kitao T. *J. Org. Chem.* **1992**, *57*, 1639−1641. Inouye, M.; Ueno, M.; Tsuchiya, K.; Nakayama, N.; Konishi, T.; Kitao, T. *J. Org. Chem.* **1992**, *57*, 5377−5383. Inouye, M.; Kim, K.; Kitao, T. *J. Am. Chem. Soc.* **1992**, *114*, 778−780. Inouye, M.; Konishi, T.; Isagawa, K. *J. Am. Chem. Soc.* **1993**, *115*, 8091−8095. Inouye, M.; Noguchi, Y.; Isagawa, K. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1163−1166. Inouye, M.; Hashimoto, K.; Isagawa, K. *J. Am. Chem Soc.* **1994**, *116*, 5517−5518. Inouye, M. *Coord. Chem. Rev.* **1995**, in press.

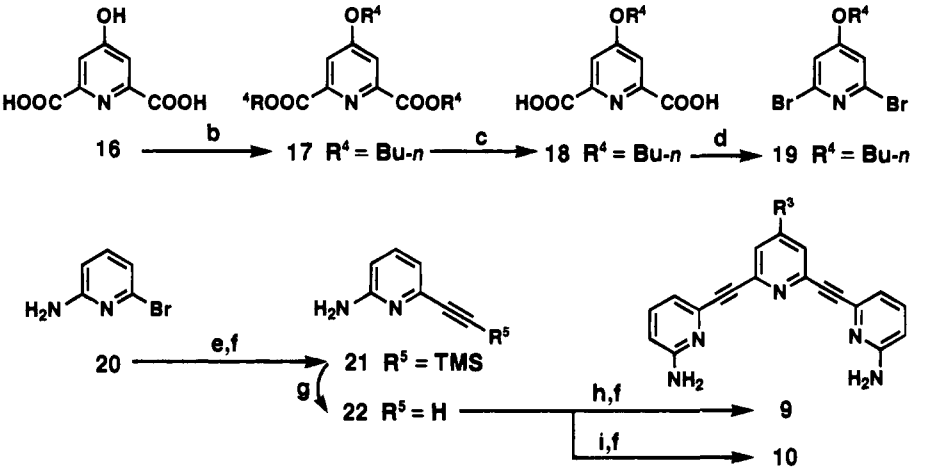
(7) The distances between the nitrogen atoms of two adjacent pyridines in the receptors were estimated to be ca. 0.3 (**2a**) and 0.5 (**2c**) nm (minimum) on the basis of the CPK models, while those between the 2-C/3-C and 3-C/5-C oxygen atoms in ribofuranose in the 0.3 to 0.6 nm region.

(8) Bald, E.; Saigo, K.; Mukaiyama, T. *Chem. Lett.* **1975**, 1163−1166.

(9) Takahashi, S.; Kuroyama, Y.; Sonogashira, K.; Hagihara, N. *Synthesis* **1980**, 627−630.

(10) Barton, D. H. R.; Crich, D.; Motherwell, W. B. *Tetrahedron* **1985**, *41*, 3901−3924.

Scheme 3[a]



[a] See legend of Scheme 2.

for the synthesis of CH_2-linked **14** and **15**, Heck olefination of phenol triflate was used in the key step.[11] *i*-Bu groups in **7** and **8** were introduced for solubility problems instead of Me groups (Scheme 4). Other compounds were commercially available or easily synthesized.

Results and Discussion

Determination of the Hydrogen-Bonding Moiety. To determine the basic skeleton for the hydrogen-bonding region of ribofuranose receptors, we studied the interactions of three sets of 2,2′:6′,2″-terpyridine derivatives (**2a**−**c**) with $CDCl_3$-soluble methyl β-D-ribofuranoside (**1**). When the terpyridine derivative **2** was added incrementally to ca. 12 mM $CDCl_3$ solution of **1**, the ^1H NMR signals of all OH hydrogens of **1** were shifted downfield. The observed downfield shifts indicated that the all hydroxylic groups participate in the complexation with **2**. Titrations were carried out in $CDCl_3$ by following changes in the ^1H NMR resonances of **1**-H^c.[12] The titration curves in Figure 1 showed that **2c**-induced downfield shift of **1**-H^c exhibited much degree of saturation than those of **2a** and **2b**. Thus, we determined **2c** as a hydrogen-bonding moiety of our ribofuranose receptors.

Binding Studies with Methyl β-D-Ribofuranoside and Structural Modifications for the Ribofuranose Receptors. The interactions of ribofuranose receptors **3**−**8** in $CDCl_3$ with methyl β-D-ribofuranoside (**1**) were investigated by ^1H NMR. The basic recognition site **2c** chosen in the previous experiments was submitted to more functionalization. We synthesized an artificial ribofuranose receptor **3**, in which amide-type substituents were newly introduced at both the terminal pyridine rings of **2c** (6 and 6″ positions). For this structural modificaton, the pyridine nitrogen can serve as a hydrogen acceptor, while the amide-NH groups as a donor. Thus, 2-(acylamino)pyridine moiety can be expected to provide an additional hydrogen-bonding motif upon recognition of **1**.[3] Indeed, when 1 equiv of **3** was added to ca. 10 mM $CDCl_3$ solution of **1**, the ^1H NMR signals of not only three OH protons of **1** but also NH protons of **3** were shifted downfield. This finding suggested that all hydrogen acceptors and at least one donor of **3** take part in the complexation with **1**. A possible mode for the hydrogen-bonding between **1** and **3** is shown in Scheme 5. The 1:1 stoichiometry was confirmed by the continuous variation (Job) plots. Benesi−Hildebrand analysis of the shifts in δ_{NH} for **3** (under conditions of constant [**3**] with varying [**1**]) gave the association constant: $K_a = 3.0 \times 10^1\ M^{-1}$.[13]

In order to depress the free rotation about the pyridine−pyridine axis in **3**, which may be responsible for entropic disadvantage upon the recognition, we designed and synthesized a bisphenol-bridged polypyridine-macrocyclic receptor **4**. Formation of the 1:1 complex (**1**·**4**) was determined by Job's plots that contained a maximum at a mole ratio of 0.5 by monitoring both the chemical shifts of the **1**-H^c and **4**-NH protons (Figure 2). The association constant between **1** and **4** was approximately doubled ($5.0 \times 10^1\ M^{-1}$) compared to that of **3**. The increment of the binding constant was lower than that predicted by the factor that the free rotation of the receptor was forbidden. For this receptor **4**, intramolecular hydrogen bonds between amide-NH and phenol-O ether groups were observed. The resonance for the NH proton of **4** in $CDCl_3$ solution was independent of its concentration and occurred at 9.0 ppm at room temperature, while that of **3** showed dependence on the concentration: at ≤1.2 mM, the NH protons of **3** appeared at 7.9 ppm (Table 1). Thus, there is a strong presumption that the intramolecular hydrogen bonds may play a role in the reduced affinity of **4** for **1** (Scheme 6).

For suppression of the intramolecular hydrogen bonds in the receptors, the ether oxygen of **4** was substituted for sulfur to give **5**. The association constant between **5** and **1**, however, was only slightly higher than that for **4**.[14] On the other hand, the replacement of the oxygen by CH_2 groups produced a very large enhancement of the binding affinity of the receptors for **1**. Thus, **6** and **7** displayed K_a of $2.4 \times 10^3\ M^{-1}$ and $2.5 \times 10^3\ M^{-1}$, respectively, ca. 50-fold over **4**. Furthermore, increasing the electron density of the pyridine nitrogen, we anticipated a definite increase K_a due mainly to enthalpic factors. Indeed, alkoxy-substitution at the 4′ position of the central pyridine ring showed a further increment of the association constants.[15] Thus,

(11) Scott, W. J.; Peña, M. R.; Swärd, K.; Stoessel, S. J.; Stille, J. K. *J. Org. Chem.* **1985**, *50*, 2302−2308.

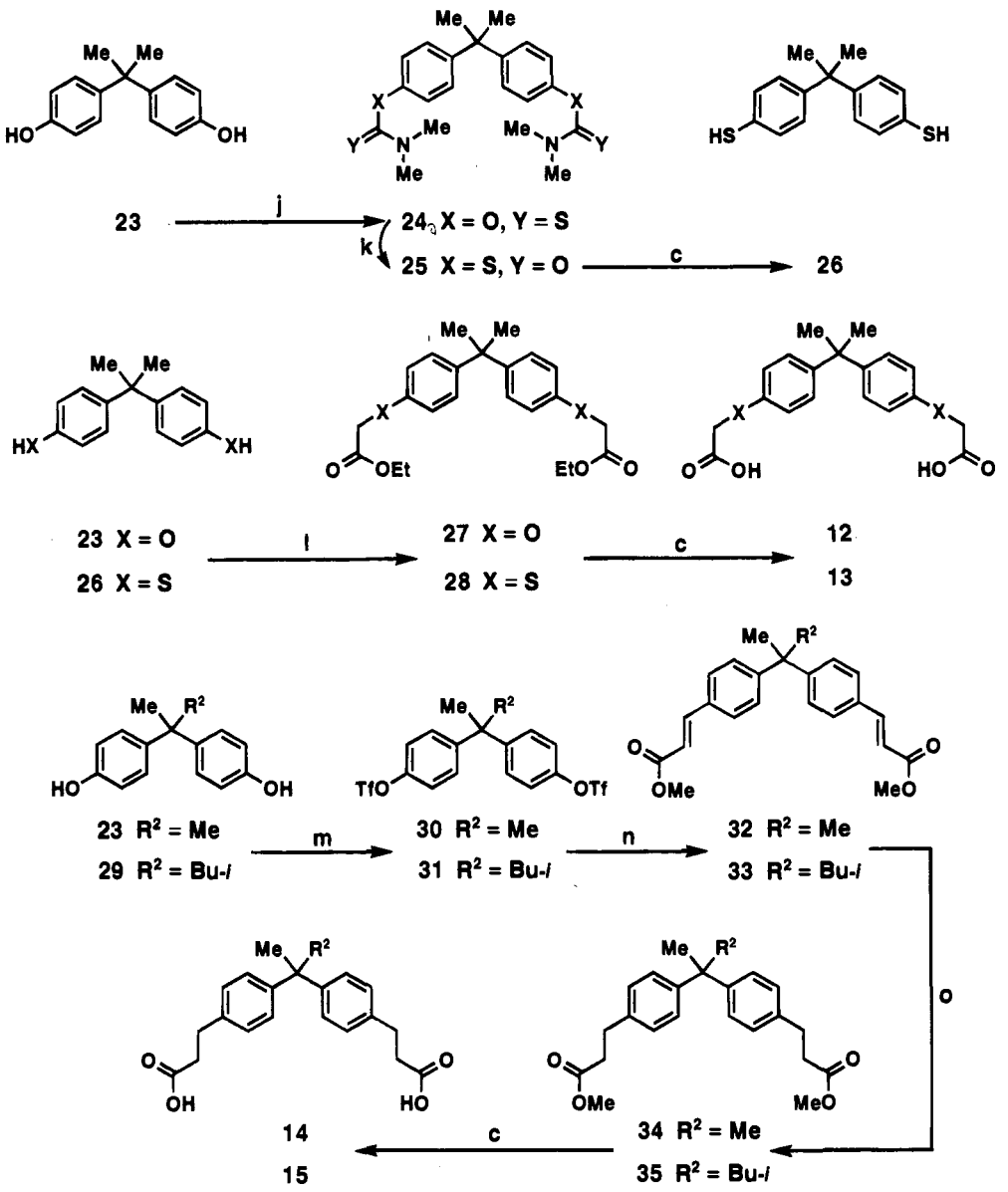
(12) The three OH protons (H^c, H^e, and H^h) of **1** were successfully assigned on the basis of $^1H-^1H$ COSY spectra. Carefully dried and acid-free $CDCl_3$ was used in order to assess all *CH*−*OH* correlations.

(13) The self-association of methyl β-D-ribofuranoside (**1**) was judged to be negligible at ≤12.5 mM by ^1H NMR dilution experiments, so that all binding assays were carried out below that concentration.

(14) Examination of CPK molecular models for **5** indicated that introduction of sulfur caused the conformation of **5** to change because of the increasing size of S compared with O.

(15) Hamilton, A. D.; Little, D. *J. Chem. Soc., Chem. Commun.* **1990**, 297−300.

Scheme 4[a]



[a] See legend of Scheme 2.

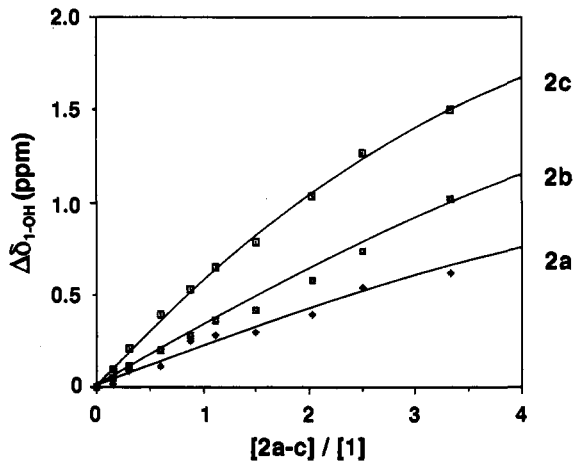
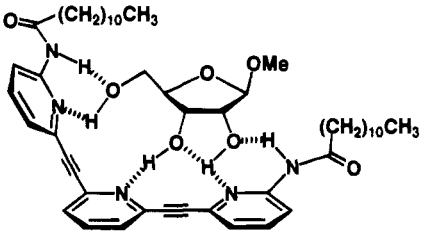


Figure 1. Complexation-induced shifts (positive value indicates a downfield shift) for **1**-H^c as a function of [**2a**−**c**]/[**1** = 12mM] in $CDCl_3$ at 23 °C.

8 revealed K_a value of $5.2 \times 10^3\ M^{-1}$, the highest value recorded for all the six ribofuranose receptors (Table 1).

Scheme 5



In the cases of **6**−**8**, useful information for the structures of the complexes was obtained by their ^1H NMR spectra. Treatment of a $CDCl_3$ solution of **1** (10 mM) with 1 equiv of **6** resulted in several characteristic changes in the spectrum (Figure 3). Downfield shifts were observed not only for the OH protons of **1** (H^c: 2.6, H^e: 2.5, and H^h: 0.4 ppm) and the NH proton of **6** (1.8 ppm) but also for CH protons of the furanose framework (H^a: 0.3, H^b: 0.2, H^d: 0.2, and H^f: 0.2 ppm). The former shifts reflect the formation of a multipoint hydrogen bonded complex, while the latter may be attributed to the influence of the diamagnetic anisotropy of **6** upon complexation: the positions of the CH protons of **1** were substantially near and

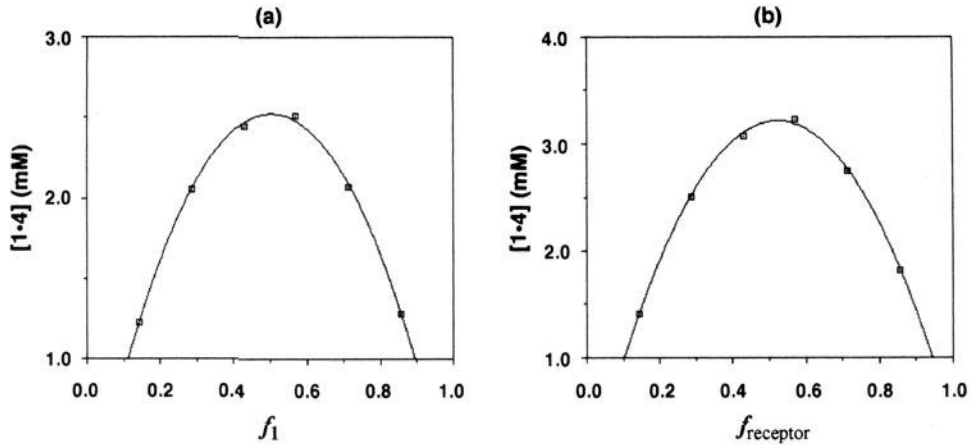


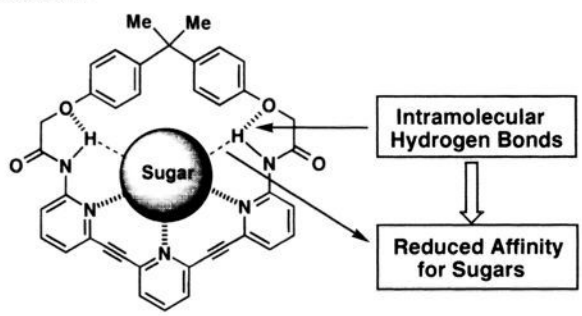
Figure 2. Job's plots of [complex] vs mole fractions of (a) **1** (f_1) and (b) **4** ($f_{receptor}$) for the complexation of **1** and **4** in $CDCl_3$ at 23 °C. For details, see Experimental Section.

Table 1. Association Constants and Thermodynamic Parameters Determined for the Binding of **1** to the Receptors in $CDCl_3$ at 23 °C[a]

receptor	K_a (M^{-1})	δ_{NH} (ppm)[a]	ΔG (kcal/mol)	ΔH (kcal/mol)	$T\Delta S$ (kcal/mol)
3	$3.0 \pm 0.4 \times 10^1$	7.90	–	–	–
4	$5.0 \pm 0.4 \times 10^1$	9.00	−2.3	−5.7	−3.4
5	$6.0 \pm 0.4 \times 10^1$	9.53	–	–	–
6	$2.4 \pm 0.2 \times 10^3$	7.55	−4.6	−10.0	−5.4
7	$2.5 \pm 0.2 \times 10^3$	7.65	–	–	–
8	$5.2 \pm 0.3 \times 10^3$	7.74	–	–	–

[a] δ_{NH} values indicate the chemical shifts for the receptor-NH in $CDCl_3$ at 23 °C under the same concentrations for determination of K_a values.

Scheme 6



parallel to the plane of the terpyridine moiety of **6**. On the other hand, OMe and CH_2OH protons were largely shifted upfield (OMe: 0.3 and CH_2OH: 0.4 and 0.2 ppm), indicating the hydrophobic moieties of **1** were placed on the diphenylpropane-bridge that is perpendicular to the terpyridine site. Furthermore, the receptor signals of aromatic (terpyridine and diphenylpropane moieties) and ethylene protons showed substantial changes after the recognition of **1**, suggesting that **6** employs the recognition strategy of substrate-induced organization of the conformation.[16] The induced-fit mechanism of this binding will be discussed in detail in the section of Molecular Modeling and Thermodynamic Studies. On the basis of the above results, a possible recognition mode for the complex **1·6** is shown in Scheme 7.

(16) Rebek, J., Jr.; Askew, B.; Ballester, P.; Jones, B. S.; Nemeth, D.; Williams, K. *J. Am. Chem. Soc.* **1987**, *109*, 5033−5035. Hamilton, A. D.; Van Engen, D. *J. Am. Chem. Soc.* **1987**, *109*, 5035−5036. Hamilton, A. D.; Pant, N.; Muehldorf, A. *Pure Appl. Chem.* **1988**, *60*, 533−538. Goswami, S.; Hamilton, A. D.; Van Engen, D. *J. Am. Chem. Soc.* **1989**, *111*, 3425−3426. Tjivikua, T.; Deslongchamps, G.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1990**, *112*, 8408−8414.

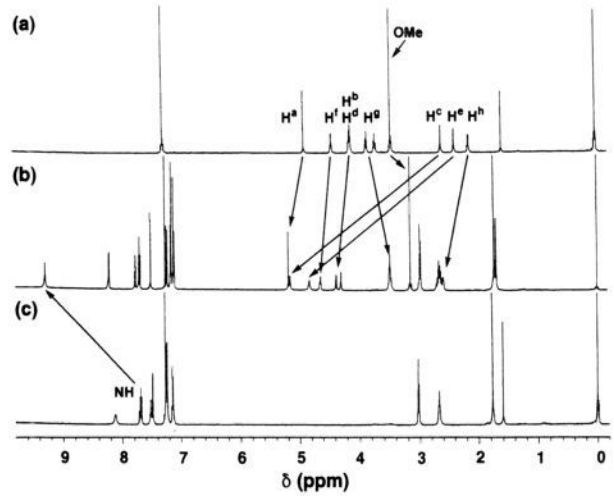
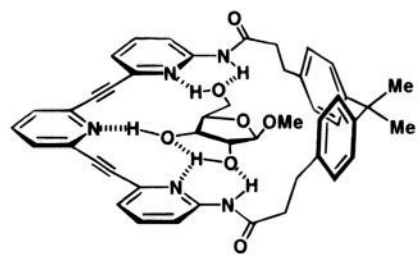


Figure 3. ^1H NMR spectra (500 MHz) of (a) **1**, (b) **1·6**, and (c) **6** in $CDCl_3$ at 23 °C.

Scheme 7



Selectivity for Native Sugars. Solid D-ribose, scarcely soluble in $CDCl_3$, was readily solubilized into such nonpolar solvents by addition of the artificial ribofuranose receptors. Thus, upon solubilization, the molar ratio of ribose/**6** in $CDCl_3$ was determined to be ca. 1, as judged by integrations of the spectrum (Figure 4). The NH proton on **6** was shifted downfield by 1.8 ppm, consisting of the data obtained for methyl β-D-ribofuranoside (**1**). The complexation was corroborated on the basis of FAB mass experiments. Before addition of ribose, the ion peak for $(M + H)^+$ was detected; after the addition the signal decreased, while the peak for $(M + \text{ribose} + Na)^+$ appeared (Figure 5). The solubilization of ribose was observed also with **7** and **8** in place of **6**, but never with **3**, **4**, and **5**. The $^{13}C\{^1H\}$ NMR spectrum for the $CDCl_3$ solution of the complex (ribose·**6**) revealed the ribose resonances at δ_c 95.7, 71.9, 69.6, 68.3, and 64.6, indicating that *free*-ribose was solubilized into the solvent

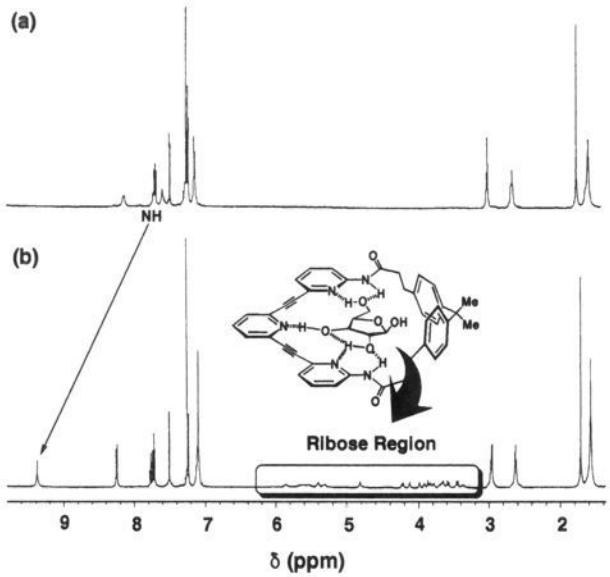


Figure 4. ^{1}H NMR spectra (500 MHz) of (a) **6** (5.0 mM), and (b) **6**·D-ribose in $CDCl_3$ at 23 °C.

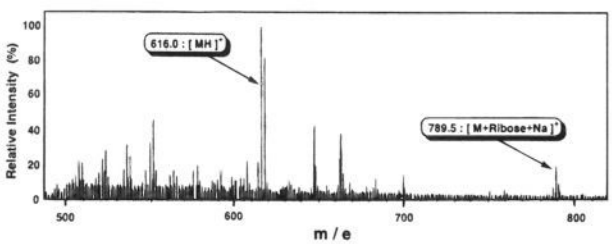


Figure 5. FAB mass spectrum of **6** with 3-nitrobenzyl alcohol matrix after addition of D-ribose.

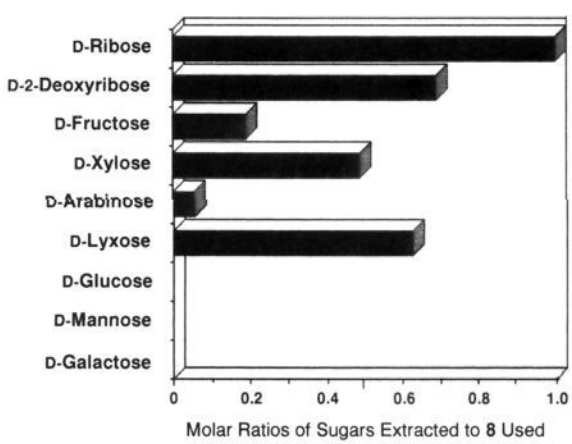


Figure 6. Extractabilities of various sugars with **8**. For details, see Experimental Section.

by the receptor mainly in the pyranose form, although the selectivity of the receptors for furanoside vs pyranoside remains to be clarified.

The extraction of various sugars into $CDCl_3$ containing **8** was carried out under similar conditions described above. The sugars extracted were estimated as above for ribose. The molar ratios of sugars extracted to **8** were summarized in Figure 6, in which selective extraction of ribose by the receptor was shown. Only a little or negligible extraction was observed in the cases of all of hexoses investigated (D-fructose, D-glucose, D-mannose, and D-galactose). D-Lyxose and D-xylose showed moderate affinities to **8**, and noteworthy is that extractability of D-ribose is higher than that of more lipophilic D-deoxyribose. These results

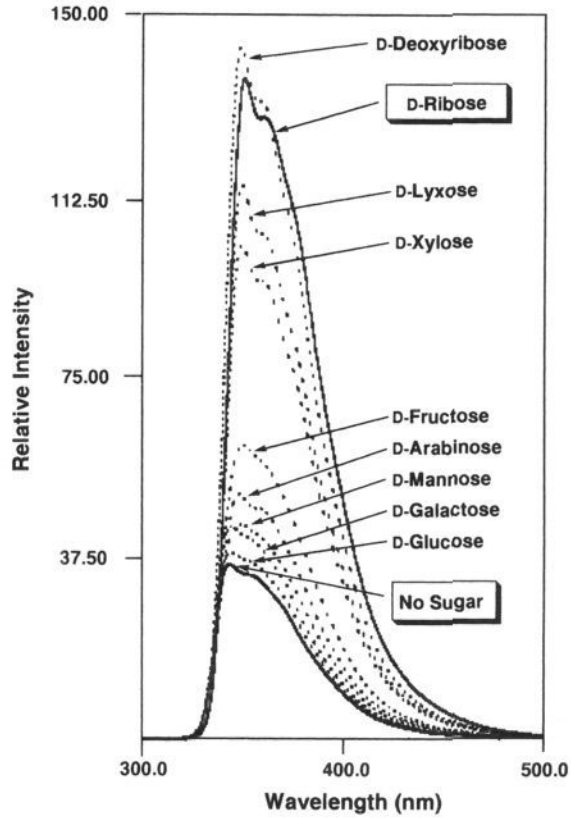


Figure 7. Fluorescence emission spectra of CH_2Cl_2 solutions of **8** in the presence of various sugars. The extinction wavelength was 333 nm. For details, see Experimental Section.

indicated that the binding affinities of the receptors for sugars were governed mainly by the whole size and the OH directions of sugars as well as their shapes.

UV and Fluorescence Changes upon Complexation. Most sugars are neither UV-active nor fluorescent, so that the changes for absorption or fluorescence spectra of the receptors upon complexation can be used directly to obtain the information for the sugar-binding. Conversely, there is great interest in the development of molecular sensors that change optical properties in response to the presence of specific sugars. The artificial ribofuranose receptors **6**−**8** showed almost similar absorption bands in CH_2Cl_2 ($\lambda_{max} = 320$ nm, $\epsilon = 3.6 \times 10^4$). When various sugars were added to a CH_2Cl_2 solution of **8**, small but significant changes in its absorption spectrum were observed. This recognition-induced bathochromic shift is explained by the stabilization of the polarized excited state of the terpyridine chromophore by the resulting highly polar hydrogen bonds. Indeed, the order of the bathochromic shifts of ribose, lyxose, deoxyribose, arabinose, fructose, mannose, xylose, galactose, and glucose, which decreased in that order, gave rough agreement for that of the extraction experiments above mentioned.

Fluorescence spectra of the receptors were much affected by addition of ribose. The receptor **8** displays a fluorescence emission at 346 nm in CH_2Cl_2. Addition of ribose to a CH_2Cl_2 solution of **8** produced a significant fluorescence increase. The same result was obtained for methyl β-D-ribofuranoside (**1**). The order of the degree for the fluorescence enhancement by the addition of sugars is also compatible with that of the extractabilities of sugars by **8** (Figure 7).

Molecular Modeling and Thermodynamic Studies. In searching for an ideal receptor for **1**, the structures **6**−**8** were developed. Their affinity for **1** was so high that they would

solubilize even quantities of ribose into $CDCl_3$. The large enhancement of the binding affinity of **6** for **1** compared with that of **4** was initially thought to be attributed only to the lack of the intramolecular hydrogen bonds that played a role in the reduced affinity of **4** to **1**. To confirm sure this assumption, computer modeling (MOPAC 93) was performed.[17] The preliminary results of the calculation, however, revealed that there was only a small gap in the electron density of the amide-NH between the two receptors. Furthermore, by comparison of the dominant low-energy structures between **1·6** and **1·4**, the definitive differences could not be obtained. Detailed calculation is now under way and will be reported elsewhere. On the other hand, thermodynamic parameters determined by VT-NMR gave significant information for the binding of **1** to **4** and **6** (Table 1). The entropy change of binding **1** by **4** was considerably smaller than that of **6**, in which one might postulate that the intramolecular hydrogen bonds in **4** made the receptor framework rigid. Indeed, upon complexation with **1**, the changes for ^1H NMR signals of **4**, other than NH, were very small than those of **6** (vide supra). Of course, introducing flexibility is introducing adjustability that results in entropic disadvantages and enthalpic advantages simultaneously for binding, while in the case of **6**, the favorable enthalpy change compensated for more than the unfavorable entropic change. Evaluation of the contents for the enthalpic change (hydrogen bond, van der Waals interaction, etc.) is still unknown and remains to be elucidated.

Conclusion

We developed polypyridine-macrocyclic structures as rationally designed artificial ribofuranose receptors. The binding affinity of the receptors for methyl β-D-ribofuranoside was very high, so that native ribose was extracted by them into nonpolar solvents. The driving force for the binding was found to be governed mainly by the whole size and the OH directions of sugars as well as their shapes. Furthermore, the fluorescence emission of the receptors was largely affected by recognition of ribose. We are currently investigating the design and synthesis of a nucleobase recognition site as well as connecting it to the ribofuranose receptors, which are expected to bind native nucleosides.

Experimental Section

Instrumentation. ^1H and ^{13}C NMR spectra were recorded at 270 and 67.8 MHz, respectively, unless otherwise noted. EI mass spectra were measured at 70 eV. For FAB mass experiments, Xe was used as the atom beam accelerated to 8 keV. Melting points are uncorrected.

Materials. The starting materials were all commercially available, and **2a**[18] and **20**[19] were prepared according to literature procedures. The preparation of **2c**[20] was carried out by a modification of the published procedure.

Methods for the Evaluation of Stoichiometry and Association Constants. Job's plot of [complex] vs mole fraction of the receptor ($f_{receptor}$) for the complexation of the receptor and **1** was obtained by ^1H NMR in $CDCl_3$ at 23 °C under conditions where [receptor] + [**1**] is maintained at 10, 5.0, and 3.0 mM for **3**−**5**, **6**, and **7**, **8**, respectively.[21] The concentration of a complex in $CDCl_3$ was evaluated from $\Delta\delta_{obsd}$ for the receptor-NH, according to the equation, $[complex] = [receptor]_t \cdot (\Delta\delta_{obsd}/\Delta\delta_{sat})$ (t = total; obsd = observed; sat = saturated).

Determination of binding constants (K_a) was carried out under Benesi−Hildebrand conditions at 23 °C in $CDCl_3$.[22] The receptor concentration for **3**−**5** was 0.5 mM, while that of **6** and **7**, **8** was 0.3 and 0.1 mM, respectively. The concentration of **1** was 4.6−10.0, 2.7−6.0, and 0.9−2.0 mM for **3**−**5**, **6**, and **7**−**8**, respectively. The chemical shifts of the receptor-NH protons were monitored as a function of **1** concentration. In every case, the double reciprocal plots according to the equation, $1/\Delta\delta_{obsd} = 1/\Delta\delta_{sat} + 1/\Delta\delta_{sat}K_a[\mathbf{1}]_t$, gave good linearity with a correlation coefficient $r \geq 0.97$. For every K_a, at least a 30−80% complexation was covered.

Computational Method. Molecular modeling was performed with WFW program (molecular modeling program: Butch Software std., NAA00705@niftyserve.or.jp). Geometry optimization for **1**, **4**, and **6** and for their binding structures were carried out by using PM3 level approximation on MOPAC 93 with EF PRECISE key words. The dominant binding structures for **1·4** and **1·6** were obtained by varing weight point coordinates and dihedral angles for three O−H bonds of **1** manually.

Determination of Thermodynamic Parameters. Van't Hoff plots were employed for evaluating the thermodynamics of complexation. Several K_a values were measured in the temperature range from 283 to 313 K as described above. Plotting $R \ln K_a$ versus $1/T$ gave a straight line and resulted in ΔH and then $T\Delta S$.

Extraction Experiments. A suspension of a large excess of each sugar (solid) and **8** (0.01 mmol) in $CDCl_3$ (1.0 mL) was sonicated with an ultrasonic generator at 25 °C for 2 h. The suspension was filtered, and the filtrate was analyzed directly by ^1H NMR. The molar ratio (sugar/**8**) of the solution was determined by integrations of the spectrum. Some sugars are slightly soluble in $CDCl_3$. In such cases, the extractability of each sugar by **8** was corrected for by subtracting the value obtained in a blank.

UV and Fluorescence Spectra. A suspension of a large excess of each sugar (solid) in a CH_2Cl_2 solution of **8** (0.04 mM for UV and 0.01 mM for fluorescence experiments) was sonicated with an ultrasonic generator at 25 °C for 2 h. The suspension was filtered, and the filtrate was measured with UV and fluorescence spectrophotometers.

6-(Pyrid-2-ylethynyl)-2,2′-bipyridine (2b). To an Et_2NH (15 mL) solution of 6-bromo-2,2′-bipyridine[23] (1.18 g, 5.0 mmol), $(PPh_3)_2PdCl_2$ (140 mg, 0.2 mmol), and CuI (19 mg, 0.1 mmol) was added an Et_2NH (5 mL) solution of 2-ethynylpyridine[24] (773 mg, 7.5 mmol) at room temperature. The reaction mixture was stirred at this temperature for 10 h. After removal of the solvent, the residue was dissolved in water and extracted with $CHCl_3$. The $CHCl_3$ extract was evaporated and chromatographed (silica gel; eluent, hexane:AcOEt = 1:1) to give **2b**: yield = 65% (836 mg); mp 88−89 °C; IR (KBr) 1578, 1467, 1431, 987, 779, 743 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.29−7.31 (m, 2 H), 7.63−7.72 (m, 3 H), 7.80−7.86 (m, 2 H), 8.42 (d, J = 7.9 Hz, 1 H), 8.50 (d, J = 7.9 Hz, 1 H), 8.65−8.69 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 87.53, 88.25, 120.87, 121.52, 123.34, 124.03, 127.69, 127.75, 136.20, 136.93, 137.11, 142.02, 142.79, 149.13, 150.19, 155.38, 156.68; MS *m/e* (rel intensity) 257 (M^+, 100%). Anal. Calcd for $C_{17}H_{11}N_3$: C, 79.35; H, 4.31; N, 16.34. Found: C, 79.76; H, 4.22; N, 15.99.

2,6-Bis(2-pyridylethynyl)pyridine (2c). To an Et_2NH (15 mL) solution of 2,6-dibromopyridine (1.18 g, 5.0 mmol), $(PPh_3)_2PdCl_2$ (140 mg, 0.2 mmol), and CuI (19 mg, 0.1 mmol) was added an Et_2NH (5 mL) solution of 2-ethynylpyridine[24] (1.55 g, 15 mmol) at room temperature. The reaction mixture was stirred at this temperature for 10 h. After removal of the solvent, the residue was dissolved in water and extracted with $CHCl_3$. The $CHCl_3$ extract was evaporated and chromatographed (silica gel; eluent, $CHCl_3$:EtOH = 40:1) to give **2c**: yield = 40% (563 mg). This product was identical to that synthesized by Dela Rosa et al.[20]

Dibutyl 4-Butoxypyridine-2,6-dicarboxylate (17). An *n*-BuOH (200 mL) suspension of chelidamic acid (**16**) (12.8 g, 70.0 mmol) and concd H_2SO_4 (2.0 mL) was refluxed with a Dean−Stark apparatus for 24 h. After removal of the solvent, the residue was subjected to column chromatography (silica gel; eluent, $CHCl_3$) to give **17**: yield = 70% (17.3 g); oil; IR (KBr) 3444, 2960, 1724, 1348, 1221, 1030, 787 cm^{-1};

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^{1}H NMR ($CDCl_3$) δ 0.96−1.04 (m, 9 H), 1.48 (sext, J = 7.9 Hz, 6 H), 1.81 (quint, J = 2.4 Hz, 6 H), 4.13 (t, J = 6.7 Hz, 2 H), 4.40 (t, J = 6.6 Hz, 4 H), 7.74 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.51, 18.83, 18.97, 30.37, 30.52, 65.77, 68.44, 113.94, 149.98, 164.58, 166.76; MS *m/e* (rel intensity) 352 (M^+, 2%).

4-Butoxypyridine-2,6-dicarboxylic Acid (18). To an EtOH (80 mL) solution of **17** (14.1 g, 40.0 mmol) was added an EtOH (30 mL) solution of KOH (9.0 g, 160.0 mmol) at room temperature. The reaction mixture became turbid, and the cloudy solution was allowed to stand for 4 h at the same temperature. After removal of the solvent, the residue was dissolved in water and washed with ether in order to remove the unreacted starting materials. The water phase was neutralized to pH 5 with 10% aqueous hydrochloric acid solution, and the resulting precipitate was filtered and washed with water. The precipitate was dried in vacuo to give **18**: yield = 70% (6.38 g); mp 143−144 °C; IR (KBr) 3088, 2958, 1726, 1603, 1458, 1304, 689 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 0.93 (t, J = 7.3 Hz, 3 H), 1.43 (sext, J = 7.3 Hz, 2 H), 1.73 (quint, J = 7.9 Hz, 2 H), 4.20 (t, J = 6.4 Hz, 2 H), 7.68 (s, 2 H); ^{13}C NMR (DMSO-d_6) δ 13.78, 18.70, 30.42, 68.65, 113.71, 149.89, 165.48, 166.95; MS *m/e* (rel intensity) 239 (M^+, 7%).

2,6-Dibromo-4-butoxypyridine (19). A $BrCCl_3$ (50 mL) suspension of **18** (4.54 g, 20.0 mmol), 1-hydroxy-2-pyridinethione (6.10 g, 48.0 mmol), dicyclohexylcarbodiimide (9.08 g, 44.0 mmol), and 4-(*N*,*N*-dimethylamino)pyridine (5.86 g, 48.0 mmol) was stirred at 70 °C for 6 h. After removal of the solvent, the residue was poured into a $CHCl_3$−water (1:1) mixed solvent, and the resulting precipitate was filtered through Celite. The $CHCl_3$ phase was separated, and the water phase was extracted with $CHCl_3$. The combined $CHCl_3$ extract was evaporated and chromatographed (silica gel; eluent, hexane:$CHCl_3$ = 6:1) to give **19**: yield = 33% (2.03 g); oil; IR (KBr) 2960, 2873, 1574, 1535, 1375, 1072, 764 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.98 (t, J = 7.3 Hz, 3 H), 1.47 (sext, J = 7.9 Hz, 2 H), 1.77 (quint, J = 8.4 Hz, 2 H), 4.00 (t, J = 6.4 Hz, 2 H), 6.97 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.60, 18.91, 30.57, 68.86, 113.68, 140.93, 167.07; MS *m/e* (rel intensity) 309 (M^+ + 2, 6%).

2-Amino-6-[(trimethylsilyl)ethynyl]pyridine (21). To an Et_2NH (60 mL) solution of 2-amino-6-bromopyridine[19] (**20**) (3.46 g, 20 mmol), $(PPh_3)_2PdCl_2$ (281 mg, 0.4 mmol), and CuI (38 mg, 0.2 mmol) was added (trimethylsilyl)acetylene (2.36 g, 24.0 mmol) dropwise at room temperature. The reaction mixture was stirred at this temperature for 10 h. After removal of the solvent, the residue was subjected to column chromatography (silica gel; eluent, hexane:AcOEt = 2:1) to give **21**: yield = 93% (3.56 g); mp 115−116 °C; IR (KBr) 3460, 3304, 3167, 2965, 2156, 1626, 1562, 1464, 1250, 845, 795 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.25 (s, 9 H), 4.49 (br s 2 H), 6.45 (d, J = 8.6 Hz, 1 H), 6.86 (d, J = 7.3 Hz, 1 H), 7.37 (t, J = 7.9 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ −0.19, 93.48, 104.06, 108.79, 118.07, 137.69, 140.93, 158.17; MS *m/e* (rel intensity) 190 (M^+, 58%).

2-Amino-6-ethynylpyridine (22). To a THF (120 mL) solution of **21** (2.63 g, 15.0 mmol) containing a small amount of H_2O (1.5 mL, 83.3 mmol) was added a THF (30 mL) solution of *n*-Bu_4NF (5.88 g, 22.5 mmol) dropwise at 0 °C. The reaction mixture was stirred at this temperature for 4 h. After removal of the solvent, the residue was subjected to column chromatography (silica gel; eluent, CH_2Cl_2) to give **22**: yield = 91% (1.60 g); mp 123−124 °C; IR (KBr) 3448, 3244, 3149, 2100, 1630, 1591, 1562, 1464, 795 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.06 (s, 1 H), 4.62 (br s, 2 H), 6.49 (d, J = 8.5 Hz, 1 H), 6.87 (d, J = 7.3 Hz, 1 H), 7.39 (t, J = 7.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 75.96, 83.08, 109.15, 117.94, 137.77, 140.10, 158.29; MS *m/e* (rel intensity) 118 (M^+, 100%).

2,6-Bis[(6-aminopyrid-2-yl)ethynyl]pyridine (9). To an Et_2NH (15 mL) solution of 2,6-dibromopyridine (1.18 g, 5.0 mmol), $(PPh_3)_2PdCl_2$ (140 mg, 0.2 mmol), and CuI (19 mg, 0.1 mmol) was added a Et_2NH (5 mL) solution of **22** (1.30 g, 11.0 mmol) dropwise at room temperature. The reaction mixture was stirred at this temperature for 6 h. After removal of the solvent, the residue was poured into $CHCl_3$, and the resulting precipitate was filtered. The precipitate was washed sequentially with MeOH, H_2O, MeOH, and $CHCl_3$ to give **9**: yield = 94% (1.47 g); mp > 260 °C dec; IR (KBr) 3412, 3302, 3180, 1624, 1470, 798 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 6.22 (br s, 4 H), 6.52 (d, J = 7.9 Hz, 2 H), 6.84 (d, J = 7.3 Hz, 2 H), 7.44 (t, J = 7.9 Hz, 2 H), 7.65 (d, J = 7.9 Hz, 2 H), 7.91 (t, J = 7.6 Hz, 1 H); ^{13}C NMR (DMSO-d_6) δ 85.38, 89.33, 109.62, 116.45, 127.29, 137.58, 137.92, 139.20, 142.71, 160.02; MS *m/e* (rel intensity) 311 (M^+, 100%).

2,6-Bis[(6-aminopyrid-2-yl)ethynyl]-4-butoxypyridine (10). To an Et_2NH (15 mL) solution of **19** (1.54 g, 5.0 mmol), $(PPh_3)_2PdCl_2$ (140 mg, 0.2 mmol), and CuI (19 mg, 0.1 mmol) was added an Et_2NH (5 mL) solution of **22** (1.30 g, 11.0 mmol) dropwise at room temperature. The reaction mixture was stirred at this temperature for 10 h. After removal of the solvent, the residue was poured into $CHCl_3$, and the resulting precipitate was filtered. The precipitate was washed with $CHCl_3$ to give **10**. Furthermore, the filtrate was evaporated and chromatographed (silica gel; eluent, AcOEt) to afford additional **10**: yield = 84% (1.60 g); mp 249−250 °C; IR (KBr) 3396, 3290, 3180, 2953, 1624, 1583, 1543, 1468, 1227, 1147, 797 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 0.94 (t, J = 7.6 Hz, 3 H), 1.47 (sext, J = 7.32 Hz, 2 H), 1.71 (quint, J = 6.9 Hz, 2 H), 4.15 (t, J = 6.4 Hz, 2 H), 6.21 (br s, 4 H), 6.51 (d, J = 8.5 Hz, 2 H), 6.82 (d, J = 7.3 Hz, 2 H), 7.24 (s, 2 H), 7.43 (t, J = 7.9 Hz, 2 H); ^{13}C NMR (DMSO-d_6) δ 13.78, 18.72, 30.43, 68.42, 85.55, 88.78, 109.56, 113.99, 116.45, 137.58, 139.26, 143.83, 160.00, 165.35; MS *m/e* (rel intensity) 383 (M^+, 100%).

Receptor 3. A mixture of **9** (311 mg, 1.0 mmol), 2-chloro-1-methylpyridinium iodide (1.02 g, 4.0 mmol), Et_3N (0.8 mL, 607 mg, 6 mmol), and lauric acid (**11**) (601 mg, 3.0 mmol) in CH_2Cl_2 (5 mL) was refluxed for 8 h. After removal of the solvent, the residue was dissolved in water and extracted with CH_2Cl_2. The CH_2Cl_2 extract was evaporated and chromatographed (silica gel; eluent, $CHCl_3$:AcOEt = 10:1) to give **3**: yield = 35% (236 mg); mp 147−148 °C; IR (KBr) 3853, 3440, 2914, 2848, 1678, 1578, 1470, 806 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.87 (t, J = 6.7 Hz, 6 H), 1.20−1.37 (m, 32 H), 1.73 (quint, J = 7.0 Hz, 4 H), 2.39 (t, J = 7.6 Hz, 4 H), 7.38 (d, J = 6.7 Hz, 2 H), 7.59 (d, J = 7.9 Hz, 2 H), 7.68−7.80 (m, 3 H), 7.94 (br s, 2 H), 8.27 (d, J = 8.6 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.05, 22.61, 25.28, 29.13, 29.27, 29.38, 29.43, 29.54, 31.84, 37.80, 87.14, 87.69, 114.35, 123.79, 127.22, 136.61, 138.70, 140.04, 142.99, 151.52, 171.93; MS *m/e* (rel intensity) 675 (M^+, 28%). Anal. Calcd for $C_{43}H_{57}O_2N_5$: C, 76.39; H, 8.50; N, 10.37. Found: C, 75.92; H, 8.85; N, 9.72.

Diethyl 4,4′-Isopropylidenebis(phenoxyacetate) (27). To an acetone (15 mL) solution of **23** (1.14 g, 5.0 mmol), K_2CO_3 (2.07 g, 15.0 mmol), and NaI (2.25 g, 15.0 mmol) was added $ClCH_2CO_2Et$ (1.84 g, 15.0 mmol) dropwise at room temperature. The reaction mixture was refluxed for 10 h and evaporated. The residue was dissolved in water and extracted with CH_2Cl_2. The CH_2Cl_2 extract was evaporated and chlomatographed (silica gel; eluent, CH_2Cl_2:hexane = 5:1) to give **27**: yield = 84% (1.69 g); mp 73−74 °C; IR (KBr) 3510, 2966, 1770, 1512, 1211, 1182, 1076 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.29 (t, J = 7.3 Hz, 6 H), 1.62 (s, 6 H), 4.27 (q, J = 7.3 Hz, 4 H), 4.58 (s, 4 H), 6.80 (d, J = 9.2 Hz, 4 H), 7.12 (d, J = 9.2 Hz, 4 H); ^{13}C NMR ($CDCl_3$) δ 14.15, 30.98, 41.75, 61.20, 65.51, 114.08, 127.81, 144.02, 155.75, 169.03; MS *m/e* (rel intensity) 400 (M^+, 18%).

4,4′-Isopropylidenebis(phenoxyacetic acid) (12). To an EtOH−THF (10 + 10 mL) mixed solution of **27** (1.20 g, 3.0 mmol) was added an EtOH (10 mL) solution of KOH (673 mg, 12.0 mmol) at room temperature. The reaction mixture became turbid, and the cloudy solution was allowed to stand for 4 h at this temperature. After removal of the solvent, the residue was poured into water and washed with ether in order to remove the unreacted starting materials. The water phase was neutralized to pH 5 with 10% aqueous hydrochloric acid solution, and the resulting precipitate was filtered and washed with water. The precipitate was dried in vacuo to give **12**: yield = 97% (1.00 g); mp 173−175 °C; IR (KBr) 3440, 2966, 1724, 1510, 1244, 824 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 1.58 (s, 6 H), 4.61, (s, 4 H), 6.79 (d, J = 8.6 Hz, 4 H), 7.10 (d, J = 9.2 Hz, 4 H), 12.93 (br s, 2 H); ^{13}C NMR (DMSO-d_6) δ 30.85, 41.34, 64.64, 113.97, 127.55, 143.18, 155.67, 170.43; MS *m/e* (rel intensity) 344 (M^+, 13%).

Receptor 4. To a CH_3CN (50 mL) solution of **9** (311 mg, 1.0 mmol), **12** (344 mg, 1.0 mmol), and Et_3N (0.6 mL, 405 mg, 4.0 mmol) was added a CH_3CN (10 mL) solution of 2-chloro-1-methylpyridinium iodide (562 mg, 2.2 mmol) dropwise at 60 °C. The reaction mixture was stirred at this temperature for 12 h. After removal of the solvent, the residue was dissolved in water and extracted with CH_2Cl_2. The CH_2Cl_2 extract was evaporated and chromatographed (silica gel; eluent, $CHCl_3$:AcOEt = 20:1) to give **4**: yield = 11% (69 mg); mp 328−330 °C dec; IR (KBr) 3381, 1714, 1570, 1504, 1452, 1225, 806 cm^{-1}; ^{1}H

NMR ($CDCl_3$) δ 1.65 (s, 6 H), 4.67 (s, 4 H), 6.94 (d, J = 8.5 Hz, 4 H), 7.16 (d, J = 8.6 Hz, 4 H), 7.31 (d, J = 7.3 Hz, 2 H), 7.50 (d, J = 7.9 Hz, 2 H), 7.65−7.80 (m, 3 H), 8.29 (d, J = 8.5 Hz, 2 H), 9.00 (br s, 2 H); ^{13}C NMR ($CDCl_3$) δ 30.70, 42.08, 68.04, 77.66, 87.28, 87.60, 113.96, 114.47, 123.38, 126.47, 128.37, 136.50, 138.66, 140.46, 145.25, 150.75, 155.40, 167.81; MS *m/e* (rel intensity) 619 (M^+, 21%).

4,4′-Isopropylidenebis[[(*N*,*N*-dimethylthiocarbamoyl)oxy]benzene] (24). To a THF (2 mL) suspension of NaH (880 mg, 22.0 mmol; commercial 60% dispersion was washed thoroughly with hexane prior to use) was added a DMF (2 mL) solution of 4,4′-isopropylidenediphenol (**23**) (2.28 g, 10.0 mmol) dropwise at 0 °C, and the reaction mixture was stirring for 30 min at the same temperature. A THF solution of *N*,*N*-dimethylthiocarbamoyl chloride (3.09 g, 25.0 mmol) was added dropwise to the solution at room temperature. The reaction mixture was stirred at room temperature for an additional 12 h. After removal of the solvent, the residue was dissolved in water and extracted with $CHCl_3$. The $CHCl_3$ extract was evaporated and chromatographed (silica gel; eluent, CH_2Cl_2) to give **24**: yield = 91% (3.6 g); mp 192−193 °C; IR (KBr) 2960, 1533, 1502, 1392, 1205, 1136, 837 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.70 (s, 6 H), 3.32 (s, 6 H), 3.45 (s, 6 H), 6.97 (d, J = 8.6 Hz, 4 H), 7.25 (d, J = 8.5 Hz, 4 H); ^{13}C NMR ($CDCl_3$) δ 30.98, 38.68, 42.54, 43.25, 122.05, 127.61, 147.90, 151.94, 187.77; MS *m/e* (rel intensity) 402 (M^+, 23%).

4,4′-Isopropylidenebis[[(*N*,*N*-dimethylcarbamoyl)thio]benzene] (25). Without solvent, **24** (3.22 g, 8.0 mmol) was heated at 260 °C for 3 h. The crude product was subjected to column chromatography (silica gel; eluent, CH_2Cl_2) to give **25**: yield = 90% (2.89 g); mp 140−141 °C; IR (KBr) 2962, 1657, 1356, 1261, 1014, 827 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.67 (s, 6 H), 3.05 (br s, 12 H), 7.24 (d, J = 8.6 Hz, 4 H), 7.38 (d, J = 7.9 Hz, 4 H); ^{13}C NMR ($CDCl_3$) δ 30.43, 36.70, 42.83, 125.69, 127.34, 135.19, 151.10, 166.84; MS *m/e* (rel intensity) 402 (M^+, 100%).

4,4′-Isopropylidenebis(thiophenol) (26). To an EtOH−THF (25 + 25 mL) mixed solution of **25** (2.82 g, 7.0 mmol) was added an EtOH (25 mL) solution of KOH (1.18 g, 21.0 mmol) at room temperature. The reaction mixture was stirred at 60 °C for 10 h. After removal of the solvent, the residue was poured into water and washed with CH_2Cl_2 in order to remove the unreacted starting materials. The water phase was neutralized to pH 5 with 10% aqueous hydrochloric acid solution and extracted with CH_2Cl_2. The CH_2Cl_2 extract was evaporated and chromatographed (silica gel; eluent, hexane:CH_2Cl_2 = 1:1) to give **26**: yield = 72% (1.31 g); mp 69−70 °C; IR (KBr) 3464, 2960, 2563, 1491, 1107, 1014, 822 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.61 (s, 6 H), 3.38 (s, 2 H), 7.08 (d, J = 8.5 Hz, 4 H), 7.18 (d, J = 8.5 Hz, 4 H); ^{13}C NMR ($CDCl_3$) δ 30.58, 42.36, 127.53, 127.59, 129.45, 148.17; MS *m/e* (rel intensity) 260 (M^+, 37%). Anal. Calcd for $C_{15}H_{16}S_2$: C, 69.09; H, 6.19. Found: C, 68.77; H, 6.05.

Diethyl 4,4′-Isopropylidenebis(thiophenoxyacetate) (28). To an acetone (15 mL) suspension of **26** (1.30 g, 5.0 mmol) and Cs_2CO_3 (977 mg, 3.0 mmol) was added $ClCH_2CO_2Et$ (1.84 g, 15.0 mmol) dropwise at room temperature. The reaction mixture was refluxed for 10 h and evaporated. The residue was poured into water and extracted with CH_2Cl_2. The CH_2Cl_2 extract was evaporated and chromatographed (silica gel; eluent, CH_2Cl_2:hexane = 5:1) to give **28**: yield = 91% (1.96 g); oil; IR (KBr) 2968, 1734, 1493, 1269, 1147, 1014, 825, 549 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.22 (t, J = 7.0 Hz, 6 H), 1.63 (s, 6 H), 3.60 (s, 4 H), 4.16 (q, J = 7.3 Hz, 4 H), 7.14 (d, J = 8.5 Hz, 4 H), 7.31 (d, J = 8.6 Hz, 4 H); ^{13}C NMR ($CDCl_3$) δ 14.08, 30.50, 36.88, 42.56, 61.46, 127.47, 129.97, 132.05, 149.34, 169.73; MS *m/e* (rel intensity) 432 (M^+, 39%).

4,4′-Isopropylidenebis(thiophenoxyacetic acid) (13). This compound was synthesized from **28** (1.21 g, 3.0 mmol) in a manner similar to that described for **12** except for the use of EtOH (20 mL) instead of EtOH−THF (10 + 10 mL) mixed solvent. **13**: yield = 99% (1.13 g); mp 139−140 °C; IR (KBr) 3018, 2966, 1707, 1284, 1136, 824 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 1.64 (s, 6 H), 3.62 (s, 4 H), 7.14 (d, J = 8.5 Hz, 4 H), 7.32 (d, J = 8.5 Hz, 4 H); ^{13}C NMR (DMSO-d_6) δ 30.26, 35.25, 42.08, 127.35, 127.88, 132.77, 148.11, 170.81; MS *m/e* (rel intensity) 376 (M^+, 29%). Anal. Calcd for $C_{19}H_{20}O_4S_2$: C, 60.60; H, 5.36. Found: C, 60.54; H, 5.40.

Receptor 5. This compound was synthesized from **9** (311 mg, 1.0 mmol) and **13** (376 mg, 1.0 mmol) in a manner similar to that described for **4**. **5**: yield = 8% (74 mg); mp 329−330 °C; IR (KBr) 3423, 3329, 1695, 1572, 1516, 1450, 808 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.61 (s, 6 H), 3.75 (s, 4 H), 7.23 (d, J = 8.6 Hz, 4 H), 7.30 (d, J = 8.6 Hz, 4 H), 7.33 (d, J = 8.5 Hz, 2 H), 7.50 (d, J = 7.9 Hz, 2 H), 7.65−7.80 (m, 3 H), 8.24 (d, J = 7.9 Hz, 2 H), 9.53 (br s, 2 H); ^{13}C NMR ($CDCl_3$) δ 30.84, 39.69, 42.99, 87.18, 87.80, 113.94, 123.32, 126.11, 128.33, 129.49, 131.14, 136.72, 138.52, 140.42, 143.11, 150.00, 151.04, 167.19; FABMS (in 3-nitrobenzyl alcohol) *m/e* (rel intensity) 652 (MH^+, 95%).

4,4′-Isopropylidenediphenyl Ditriflate (30). To a pyridine (50 mL) solution of **23** (3.42 g, 15.0 mmol) was slowly added $(CF_3SO_2)_2O$ (8.89 g, 31.5 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 5 min and then allowed to warm to room temperature and stirred at this temperature for 25 h. After removal of the solvent, the residue was dissolved in water and extracted with CH_2Cl_2. The CH_2Cl_2 extract was washed with 10% aqueous hydrochloric acid solution twice, dried over $MgSO_4$, and evaporated. The residue was subjected to column chromatography (silica gel; eluent, $CHCl_3$) to give **30**: yield = 96% (7.12 g); mp 58−59 °C; IR (KBr) 2976, 1502, 1431, 1201, 1140, 893, 600 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.69 (s, 6 H), 7.19 (d, J = 9.2 Hz, 4 H), 7.27 (d, J = 8.5 Hz, 4 H); ^{13}C NMR ($CDCl_3$) δ 30.77, 30.84, 42.91, 116.41, 121.06, 121.42, 128.62, 147.80, 150.21; MS *m/e* (rel intensity) 492 (M^+, 17%).

Dimethyl 4,4′-Isopropylidenebis(cinnamate) (32). To a DMF (30 mL) solution of **30** (4.92 g, 10.0 mmol), $(PPh_3)_2PdCl_2$ (351 mg, 0.5 mmol), LiCl (2.53 g, 60.0 mmol), and Et_3N (11.1 mL, 8.09 g, 80.0 mmol) was added methyl acrylate (3.44 g, 40.0 mmol) at room temperature. The reaction mixture was stirred at 70 °C for 10 h. After removal of the solvent, the residue was dissolved in water and extracted with CH_2Cl_2. The CH_2Cl_2 extract was evaporated and chromatographed (silica gel; eluent, hexane:AcOEt = 10:1) to give **32**: yield = 72% (2.61 g); mp 139−140 °C; IR (KBr) 3442, 2958, 1716, 1637, 1313, 1173, 827 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.69 (s, 6 H), 3.80 (s, 6 H), 6.40 (d, J = 15.9 Hz, 2 H), 7.24 (d, J = 7.9 Hz, 4 H), 7.44 (d, J = 7.9 Hz, 4 H), 7.67 (d, J = 16.5 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 30.35, 43.25, 51.66, 117.32, 127.32, 127.97, 132.09, 144.50, 152.65, 167.49; MS *m/e* (rel intensity) 364 (M^+, 28%). Anal. Calcd for $C_{23}H_{24}O_4$: C, 75.79; H, 6.64. Found: C, 75.46; H, 6.73.

Dimethyl 4,4′-Isopropylidenebis(dihydrocinnamate) (34). An EtOH (30 mL) suspension of **32** (1.82 g, 5.0 mmol) and 5% Pd/C (180 mg) was stirred at room temperature for 8 h under hydrogen (at an initial pressure of 40 atm) in an autoclave. The reaction mixture was filtered through Celite, and the filtrate was evaporated to give **34**: yield = 99% (1.84 g); oil; IR (KBr) 3453, 2972, 1740, 1514, 839, 565 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.64 (s, 6 H), 2.61 (t, J = 8.5 Hz, 4 H), 2.91 (t, J = 8.5 Hz, 4 H), 3.67 (s, 6 H), 7.09 (d, J = 8.5 Hz, 4 H), 7.13 (d, J = 8.5 Hz, 4 H); ^{13}C NMR ($CDCl_3$) δ 30.31, 30.67, 35.49, 42.24, 51.46, 126.78, 127.75, 137.55, 148.55, 173.29; MS *m/e* (rel intensity) 368 (M^+, 15%).

4,4′-Isopropylidenebis(dihydrocinnamic acid) (14). This compound was synthesized from **34** (1.11 g, 3.0 mmol) in a manner similar to that described for **12**. **14**: yield = 91% (930 mg); mp 207−208 °C; IR (KBr) 3026, 2972, 2931, 1702.8, 1302, 829 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 1.59 (s, 6 H), 2.50 (t, J = 7.60 Hz, 4 H), 2.75 (t, J = 7.6 Hz, 4 H), 7.10 (s, 8 H), 12.09 (s, 2 H); ^{13}C NMR (DMSO-d_6) δ 29.96, 30.54, 35.27, 41.96, 126.52, 127.96, 138.04, 148.11, 173.93; MS *m/e* (rel intensity) 340 (M^+, 27%). Anal. Calcd for $C_{21}H_{24}O_4$: C, 74.08; H, 7.11. Found: C, 73.44; H, 7.13.

Receptor 6. This compound was synthesized from **9** (311 mg, 1.0 mmol) and **14** (340 mg, 1.0 mmol) in a manner similar to that described for **4**. **6**: yield = 10% (60 mg); mp 305−306 °C dec; IR (KBr) 3440, 1672, 1578, 1450, 1362, 802 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.76 (s, 6 H), 2.67 (t, J = 7.0 Hz, 4 H), 3.02 (t, J = 7.0 Hz, 4 H), 7.13 (d, J = 8.5 Hz, 4 H), 7.20−7.25 (m, 6 H), 7.48 (d, J = 7.9 Hz, 2 H), 7.60 (br s, 2 H), 7.62−7.80 (m, 3 H), 8.13 (d, J = 7.9 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 30.54, 31.34, 40.60, 42.62, 87.28, 87.80, 113.98, 122.73, 126.11, 127.49, 128.05, 136.48, 137.27, 138.46, 140.30, 143.21, 149.60, 151.30, 171.29; FABMS (in 3-nitrobenzyl alcohol) *m/e* (rel intensity) 616 (MH^+, 100%).

4,4′-(2-Methylpent-4-ylidene)diphenyl Ditriflate (31). This compound was synthesized from **29** (4.06 g, 15.0 mmol) in a manner similar to that described for **30**. **31**: yield = 93% (7.46 g); oil; IR (KBr) 2962, 1502, 1410, 1211, 1140, 889, 608 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ

0.72 (d, J = 6.7 Hz, 6 H), 1.40−1.58 (m, 1 H), 1.67 (s, 3 H), 2.05 (d, J = 4.9 Hz, 2 H), 7.19 (d, J = 9.2 Hz, 4 H), 7.25 (d, J = 9.2 Hz, 4 H); ^{13}C NMR ($CDCl_3$) δ 24.61, 24.94, 28.11, 46.55, 50.35, 116.43, 120.89, 121.16, 129.28, 147.76, 149.76; MS *m/e* (rel intensity) 477 (M^+ − Bu-*i*, 100%).

Dimethyl 4,4′-(2-Methylpent-4-ylidene)bis(cinnamate) (33). This compound was synthesized from **31** (5.345 g, 10 mmol) in a manner similar to that described for **32**. **33**: yield = 74% (3.01 g); oil; IR (KBr) 2953, 1714, 1633, 1169, 984, 827 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.74 (d, J = 6.7 Hz, 6 H), 1.46−1.59 (m, 1 H), 1.66 (s, 3 H), 2.07 (d, J = 5.5 Hz, 2 H), 3.80 (s, 6 H), 6.39 (d, J = 16.5 Hz, 2 H), 7.21 (d, J = 8.5 Hz, 4 H), 7.42 (d, J = 7.9 Hz, 4 H), 7.56 (d, J = 16.6 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 14.06, 22.61, 24.61, 25.06, 27.67, 31.53, 46.87, 49.94, 51.56, 117.24, 127.77, 127.91, 131.95, 144.45, 152.17, 167.41; MS *m/e* (rel intensity) 406 (M^+, 8%).

Dimethyl 4,4′-(2-Methylpent-4-ylidene)bis(dihydrocinnamate) (35). This compound was synthesized from **33** (2.03 g, 5.0 mmol), in a manner similar to that described for **34**. **35**: yield = 99% (2.02 g); oil; IR (KBr) 2952, 1739, 1510, 1436, 1365, 1169, 835 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.71 (d, J = 6.7 Hz, 6 H), 1.54 (m, 1 H), 1.62 (s, 3 H), 2.01 (d, J = 5.5 Hz, 2 H), 2.61 (t, J = 7.6 Hz, 4 H), 2.91 (t, J = 7.9 Hz, 4 H), 3.66 (s, 6 H), 7.09 (d, J = 4.9 Hz, 4 H), 7.10 (d, J = 8.6 Hz, 4 H); ^{13}C NMR ($CDCl_3$) δ 24.49, 25.00, 27.97, 30.27, 35.45, 45.88, 50.24, 51.32, 127.38, 127.53, 137.39, 147.90, 173.17; MS *m/e* (rel intensity) 410 (M^+, 3%).

4,4′-(2-Methylpent-4-ylidene)bis(dihydrocinnamic acid) (15). This compound was synthesized from **35** (1.23 g, 3.0 mmol) in a manner similar to that described for **12**. **15**: yield = 99% (1.13 g); mp 123−124 °C; IR (KBr) 3440, 2968, 1714, 1416, 1250, 941, 841 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.71 (d, J = 6.7 Hz, 6 H), 1.50 (m, 1 H), 1.62 (s, 3 H), 2.02 (d, J = 4.9 Hz, 2 H), 2.65 (t, J = 7.9 Hz, 4 H), 2.91 (t, J = 7.6 Hz, 4 H), 7.08 (d, J = 9.2 Hz, 4 H), 7.10 (d, J = 8.6 Hz, 4 H); ^{13}C NMR (DMSO-d_6) δ 24.44, 25.14, 27.81, 29.96, 35.29, 45.62, 49.87, 127.15, 127.84, 137.96, 147.55, 173.95; MS *m/e* (rel intensity) 382 (M^+, 1.5%).

Receptor 7. This compound was synthesized from **9** (311 mg, 1.0 mmol) and **15** (382 mg, 1.0 mmol) in a manner similar to that described for **4**. **7**: yield = 8% (52 mg); mp 181−182 °C; IR (KBr) 3415, 2953, 1701, 1572, 1452, 1389, 806 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.68 (d, J = 6.7 Hz, 6 H), 1.54−1.63 (m, 1 H), 1.64 (s, 3 H), 2.06 (d, J = 4.9 Hz, 2 H), 2.65 (t, J = 8.6 Hz, 4 H), 3.01 (t, J = 7.3 Hz, 4 H), 7.12 (d, J = 8.6 Hz, 4 H), 7.16 (d, J = 8.6 Hz, 4 H), 7.25 (d, J = 7.3 Hz, 2 H), 7.48 (d, J = 7.3 Hz, 2 H), 7.64−7.76 (m, 3 H), 7.79 (br s, 2 H), 8.15 (d, J = 7.9 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 24.60, 25.26, 28.20, 31.07, 40.52, 46.20, 49.80, 87.35, 87.85, 113.94, 122.61, 125.96, 127.80, 128.08, 136.54, 137.39, 138.51, 140.24, 143.17, 148.87, 151.35, 171.23; FABMS (in 3-nitrobenzyl alcohol) *m/e* (rel intensity) 658 (MH^+, 100%).

Receptor 8. This compound was synthesized from **10** (383 mg, 1.0 mmol) and **15** (382 mg, 1.0 mmol) in a manner similar to that described for **4**. **8**: yield = 8% (58 mg); mp 237−239 °C; IR (KBr) 3386, 2958, 1701, 1572, 1452, 1227, 804 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.71 (d, J = 6.7 Hz, 6 H), 1.00 (t, J = 7.3 Hz, 3 H), 1.42−1.85 (m, 8 H), 2.07 (d, J = 4.9 Hz, 2 H), 2.66 (t, J = 7.0 Hz, 4 H), 3.00 (t, J = 7.3 Hz, 4 H), 4.05 (t, J = 6.1 Hz, 2 H), 7.01 (s, 2 H), 7.11 (d, J = 8.6 Hz, 4 H), 7.14 (d, J = 8.6 Hz, 4 H), 7.23 (d, J = 7.3 Hz, 2 H), 7.69 (t, J = 7.9 Hz, 2 H), 7.95 (br s, 2 H), 8.16 (d, J = 9.2 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.76, 19.10, 24.71, 25.26, 27.34, 30.66, 30.80, 40.44, 45.84, 68.44, 87.36, 87.77, 112.93, 114.14, 122.29, 127.69, 127.77, 137.57, 138.72, 139.84, 143.74, 148.71, 151.62, 165.67, 171.41; FABMS (in 3-nitrobenzyl alcohol) *m/e* (rel intensity) 730 (MH^+, 100%).

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