shown in XRD analysis. The orientation of acetate for HT(0) would be chelating-type. However, the acetate for HT(60) might be ligated to the zinc cation with unidentate type orientation and the calculated basal spacing from this orientation (12.8 Å) matches very well with the experimental one of 13.0 Å from the XRD analysis.

Therefore, it is concluded that the phase transformation reported in the XRD analysis is corresponding to the change in orientation of inserted acetate depending on the hydration rate. That is, deintercalation of water molecules in interlayer gives rise to the rotation and arrangement of acetates themselves into their stable structure of unidentate in a given hydration condition as shown in Figure 5. The lower wavenumber position of $\nu_{asym}(CO_2)$ band in HT(0) is due to the decrease of asymmetry in two C-O bonds, which could be induced from the steric hindrance and hydrogen bonding of water molecules in the more hydrated condition.

In TG-DTA for HT(60) and CP(60), a similar thermal behavior could be observed. The weight loss up to 150 °C (12 wt.%) corresponds to the removal of interlayer water molecules, which was confirmed by a decrease of 3 Å in the basal spacing. The basal spacing was increased again progressively when the samples were cooled down to room temperature and kept on in air at relative humidity of 60%. The phenomenon indicates the reversible deintercalation and intercalation of interlayer water molecules in the temperature range of 25-150 °C. Beyond 280 °C, the host LDSs readily decomposes itself along with a strong exothermic decomposition of interlayer acetates.[11]

According to the relative atomic ratios from the results of ICP and CHN analyses, and water content from thermogravimetric analyses, formulas could be proposed to be $Ni_{0.32}Zn_{0.36}(OH)_2(CH_3COO)_{0.30}(OH)_{0.06}(H_2O)_{0.98}$ for HT(60) and $Ni_{0.74}Zn_{0.42}(OH)_2(CH_3COO)_{0.42}(OH)_{0.16}(H_2O)_{1.10}$ for CP(60), respectively.

The supplementary hydroxyl groups are included to the interlayer space for satisfying the charge neutrality. The nominal Zn/Ni ratio, as in the starting nickel-zinc mixed acetate solution, is maintained only for the CP sample. This gives a good reliability to our theoretical volubility diagram used in the coprecipitation method. The structural stability of CP regardless of hydration rate is obviously due to higher layer charge (x =0.26), compared to HT (x =0.18), resulting in a stronger electrostatic interaction between layers.

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Synthesis of New Chiral, C_2 Symmetric Receptors Containing Quaternary Ammonium Salts

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Asymmetric synthesis by phase transfer catalysis using chiral ammonium salts has been extensively investigated by many groups.[1] The application of these catalysts has been mainly reported in the areas of chiral induction and kinetic resolution. However, in spite of their synthetic interest, most catalysts have proven to be ineffective in inducing asymmetry whereas the use of the catalysts derived from the naturally occurring cinchona alkaloids such as quinine, cinchonidine, etc. has been much more successful.[2,3]

Of several factors[4] influencing the Stereoselectivity in phase transfer reactions, the molecular structure of the catalyst seems to be the most important aspect: conformationally well-defined binding cavity sufficient to encapsulate appropriate substrates should be considered in the

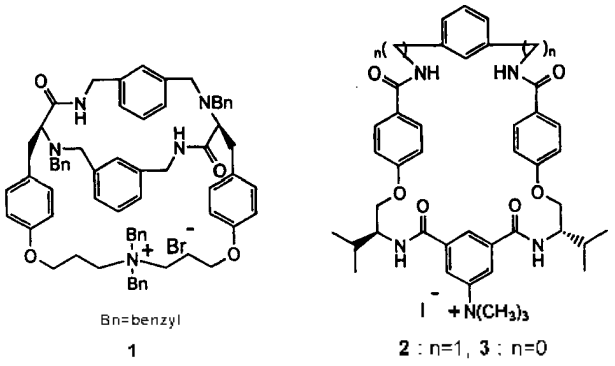


Figure 1.

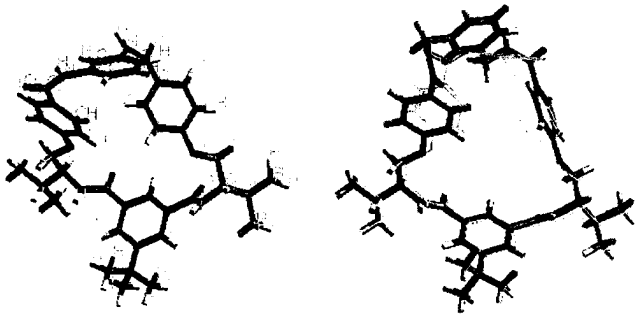
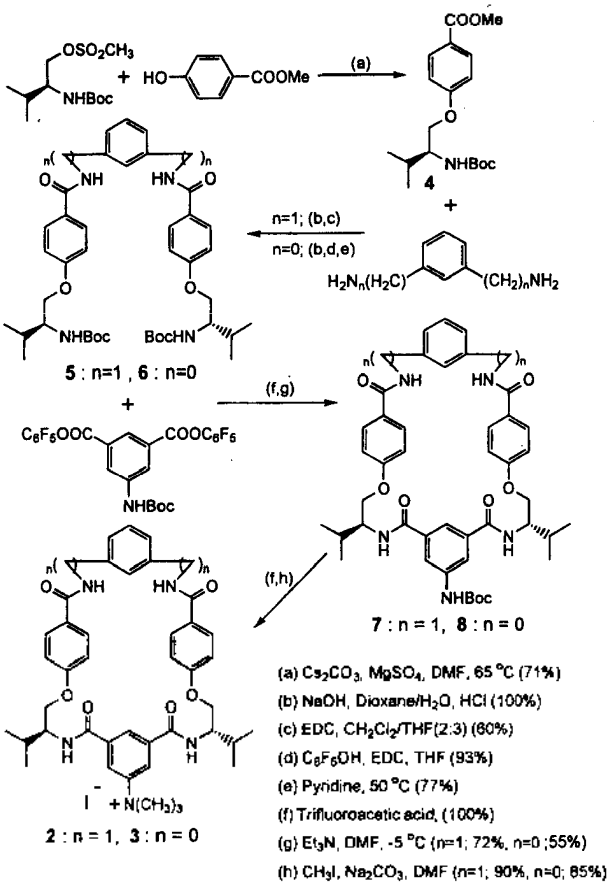


Figure 2.



Scheme 1.

design of effective chiral catalyst. The structural stability and volubility of the catalyst could be other crucial factors to satisfy various phase transfer catalyzed reaction conditions.

The chiral phase transfer catalyst **1** was previously synthesized by Still and the author. **1** generally showed low enantioselectivities in most asymmetric alkylations and reductions.[7] It could be estimated from the CPK model that conformational flexibility of linear aliphatic chain as a spacer and steric hindrance of either one of the two benzyl groups or counter anion (Br^-) blocking the binding cavity lead to poor recognition of substrates.

The C_2 symmetric receptors **2** and **3** were designed as the phase transfer catalysts to improve the enantioselective binding compared to **1** and investigate the binding efficiency according to the size variation of the binding cavity in **2** and **3**. They commonly show the following features from the CPK models as compared with **1**.

1. The amide functionalities for hydrogen bonds with small sized substrates are relatively better distributed around the periphery of the binding cavity.

2. The meta-substituted anilinium salt could be located rather outside the binding cavity to relieve steric encumbrance.

3. The sterically bulky isopropyl groups attached to the ring stereocenters keep the binding cavity conformationally rigid by restricting rotational freedom between the related bonds.

4. An inflexible binding cavity connected with the four substituted aromatic spacers may work as a π - π stacking site for properly arranged aromatic substrates.

In support of these assumptions, we have then carried out molecular mechanics and dynamics calculations to find the lowest energy structure of **2** and **3** using the universal force field[8] with the charge equilibration scheme[9] in the Cerius2 program by MSI. The calculation results also exhibited that the receptors may possess the features above (Figure 2). They additionally showed the binding cavities of **2** and **3** have some similarities. From these features, the designed C_2 receptors could be the selective binders for small sized substrates to achieve either asymmetric inductions or kinetic resolutions.

The synthesis of both **2** and **3** began with the coupling[8] between N-Boc-L-valinol methanesulfonate[10,11] and methyl 4-hydroxybenzoate in the presence of magnesium sulfate as shown in Scheme 1. Magnesium sulfate may work as an anti-oxidant not to produce the keto-form of methyl 4-hydroxy benzoate at all in the reaction condition described here. A considerable amount of the oxidized product was observed if it was not in use.[12] Ester hydrolysis of **4** and sequential DCC coupling with 1,3-xylenediamine afforded the diamide **5**. Similarly, direct substitution of a pentafluorophenyl ester, after EDC coupling of the hydrolyzed acid with pentafluorophenol, with 1,3-phenylenediamine in pyridine gave the diamide **6**. The Boc group removals of **5** and **6**, followed by the macrocyclizations between the corresponding amines and dipentafluorophenyl 5-(N-Boc-amino)-isophthalate (DPAI),[13] allowed to give **7** and **8** in 72% and 55% respectively. The structures of **7** and **8** were unambiguously iden-

tified by ^{1}H NMR, ^{13}C NMR and mass data (See experimental section). Treatments of **7** and **8** with trifluoroacetic acid and subsequent quaternizations of the corresponding amines with excessive methyl iodide produced the final receptors **2** and **3** in 90% and 85% separately. Although **2** and **3** were soluble in conventional organic solvents and aqueous media, they didn't seem to be the stable catalysts under several solid-liquid and liquid-liquid phase transfer reaction conditions. This is probably due to decomposition by nucleophilic attack to one of the three methyl groups in **2** and **3**.

In conclusion, we synthesized two chiral, C_2 symmetric receptors having restricted confirmational flexibility, sterically relieved binding cavity and appropriately distributed amide functionalities for possible hydrogen bonds with small sized substrates. Molecular modeling also supported these circumstances. Modification of quaternary anilinium salt parts maintaining the identical conformation of the cavities in **2** and **3** and their catalytic studies under phase transfer reaction conditions are in progress.

Experimental

General. Melting points were recorded on a Electrothermal 9100 without calibration. Infrared spectra were obtained using a Midac PRS-INT FTIR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Unity Plus 300, 600 and Varian Gemini 200, 300 BB spectrometer. All chemical shifts were reported on the δ scale using residual solvent as internal standard. Mass spectra were recorded on a VG70-VSEQ spectrometer using fast atom bombardment (FAB) techniques. TLC was carried out on glassplates coated with Merck silica gel $60F_{254}$. Compounds were visualized with UV light. Flash chromatography was carried out using Merck Kieselgel 60 flash silica gel. All commercially available solvents and chemicals were directly used without further purification.

Synthesis

Methylester (4). To a solution of N-Boc-L-valinol methanesulfonate (588 mg, 2.20 mmol) and methyl 4-hydroxybenzoate (642 mg, 4.22 mmol) in DMF (12 mL) were added Cs_2CO_3 (1.70 g, 5.22 mmol) and $MgSO_4$ (755 mg, 6.27 mmol). The reaction mixture was stirred at 65 °C for 81 h and filtered. The solvent was evaporated and the residue was dissolved in $CHCl_3$ to remove the excess insoluble solids by filtration. Solvent removal followed by chromatographic purification (ethyl acetate : Hexane, 1 : 2) produced the desired product **4** (525 mg, 71%) as a white solid.

mp 83-85 °C; IR ($CHCl_3$) 3445 (NH), 1711 (C=O) cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.00 (d, J =6.8 Hz, 2H, ArH), 6.92 (d, J =6.8 Hz, 2H, ArH, 4.80 (d, J =8.8 Hz, 1H, BocNH), 4.08 (m, 2H, CH_2), 3.90 (s, 3H, $COOCH_3$), 3.72 (m, 1H, CH), 2.02 (m, 1H, $(CH_3)_2CH$), 1.45 (s, 9H, $C(CH_3)_3$), 1.00 (d, J =6.8 Hz, 6H, $2CH_3$).

Diamide (5). To a solution of **4** (607 mg, 1.80 mmol) in dioxane (10 mL) was added 0.5 N aqueous NaOH solution (5.0 mL, 2.50 mmol). The resulting solution was stirred at room temperature for 12 h and acidified with 1 N aqueous HCl solution (pH 3-4). The solvents were evaporated and the residue was dissolved in $CHCl_3$. The solution was washed with water, dried ($MgSO_4$) and concentrated to give the acid as an oil. To a solution of the acid (313 mg, 0.969 mmol) and 1,3-xylenediamine (67 mg, 0.485 mmol) in THF/CH_2Cl_2 (7.5 mL, v/v, 1 : 1.5) was added EDC (284 mg, 1.48 mmol) at − 10 °C. The reaction mixture was stirred at room temperature for 30 h and the solvents were removed. The resulting residue was partitioned between CH_2Cl_2 and 0.5 N aqueous HCl solution. The organic layer was washed with water, dried ($MgSO_4$) and concentrated to give a yellow solid. Purification by flash chromatography ($CHCl_3$: MeOH, 9: 1) gave the diamide **5** (219 mg, 60%) as a pale yellow solid.

mp 122-125 °C; IR ($CHCl_3$) 3449 (NH), 3349 (NH), 1707 (Boc C=O), 1651 (C=O) cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75 (d, J =7.5 Hz, 4H, ArH), 7.30 (m, 2H, ArH), 7.25 (m, 2H, ArH), 6.86 (d, J =7.3 Hz, 4H, ArH), 6.40 (t, J =5.5 Hz, 2H, 2NH), 4.78 (d, J =9.3 Hz, 2H, 2BocNH), 4.60 (d, J =5.6 Hz, 4H, $2ArCH_2$), 4.02 (m, 4H, $2CH_2$), 3.70 (m, 2H, 2CH), 2.00 (m, 2H, $2(CH_3)2CH$), 1.42 (s, 18H, $2C(CH_3)_3$), 1.00 (m, 12H, $4CH_3$).

Diamide (6). EDC (320 mg, 1.68 mmol) was added to a solution of pentafluorophenol (270 mg, 1.46 mmol) and the acid (450 mg, 1.40 mmol) obtained from the above hydrolysis of **4** in THF (17 mL) at 0 °C. The reaction mixture was stirred at room temperature for 16 h and the solvent was evaporated. The residue was partitioned between CH_2Cl_2 and 0.5 N aqueous HCl solution. The organic layer was washed with water, dried ($MgSO_4$) and concentrated to give the activated ester (637 mg, 93%). 1,3-Phenylenediamine (55 mg, 0.31 mmol) was added to a solution of the activated ester (300 mg, 0.61 mmol) in pyridine (8.0 mL). The reaction mixture was stirred at 50 °C for 60 h and the pyridine was evaporated. The resulting residue was partitioned between $CHCl_3$ and 0.5 N aqueous HCl solution. The organic layer was washed with water, dried ($MgSO_4$) and concentrated to give a white solid which was purified by flash chromatography ($CHCl_3$: MeOH, 20 : 1) to afford the desired product **6** (170 mg, 77%) as a white solid.

mp 97-99 °C; IR ($CHCl_3$) 3445 (NH), 3321 (NH), 1705 (Boc C=O), 1668 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (s, 1H, Ar'H), 7.90 (s, 2H, 2NH), 7.83 (d, J =8.8 Hz, 4H, ArH), 7.42 (dd, 2H, Ar'H), 7.35 (m, 1H, Ar'H), 6.95 (d, J =8.8 Hz, 4H, ArH), 4.80 (d, J =9.6 Hz, 2H, 2 BocNH), 4.10 (m, 4H, $2CH_2$), 3.72 (m, 2H, 2CH), 2.00 (m, 2H, $2(CH_3)_2$ CH), 1.45 (s, 18H, $2C(CH_3)_3$), 1.00 (m, 12H, $4CH_3$).

Cyclized amide (7). A solution of **5** (90 mg, 0.121 mmol) in trifluoroacetic acid (3.0 mL) was stirred at room temperature for 1.5 h and the solvent was removed. To a solution of the amine salt (97 mg, 0.125 mmol) and triethylamine (62 mg, 0.605 mmol) in DMF (40 mL) was added DPAI (77 mg, 0.125 mmol) at − 10 °C. The reaction mixture was stirred for 1 h at the same temperature and the solvent was evaporated *in vacuo*. The crude mixture was dissolved in CH_2Cl_2 and the solution was washed with 2 N aqueous NaOH solution, water and dried (Na_2SO_4). Solvent removal followed by chromatographic purification ($CHCl_3$: MeOH, 15 : 1) allowed to give **7** (71 mg, 72%) as a white solid.

mp 116 °C; IR ($CHCl_3$) 3437 (NH), 3322 (NH), 1711 (Boc C=O), 1651 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (s, 2H, Ar"H), 7.72 (s, 1H, Ar"H), 7.65 (d, J =8.6 Hz,

4H, ArH),7.35 (s, 1H, Ar'H),7.27 (m, 3H, Ar'H), 6.85 (d, J=8.7 Hz, 4H, ArH), 6.55 (d, J=8.8 Hz, 2H, 2NH), 6.35 (t, J=5.0 Hz, 2H, $2CH_2NH$), 4.85 (brs, 1H, BocNH), 4.57 (d, J=5.1 Hz, 4H, $2Ar'CH_2$), 4.15 (m, 6H, $2CH_2$+2CH), 2.05 (m, 2H, $2(CH_3)_2CH$), 1.55 (s, 9H, $C(CH_3)_3$), 1.10 (m, 12H, $4CH_3$); ^{13}C NMR (300 MHz, $CDCl_3$) δ 167.3, 167.1, 161.4, 152.9, 139.7, 139.3, 135.9, 128.9, 128.7, 127.8, 127.1, 126.6, 120.0, 119.1, 114.2, 81.0, 67.7, 54.7, 43.8, 29.1, 28.0, 19.3; MS (FAB, Glycerol) m/z 792 (M^++1, 2%), 692 (10%).

Cyclized amide (8). The compound **8** (35 mg, 55%) was prepared from **6** (60 mg, 0.084 mmol) and DAPI (51 mg, 0.084 mmol) as described above.

mp 190 °C; IR (KBr) 3435 (NH), 3328 (NH), 1709 (Boc C=O), 1650 (C=O) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 10.2 (s, 2H, Ar"H), 9.60 (s, 1H, Ar"H), 8.45 (m, 2H, 2NH), 8.30 (s, 1H, Ar'H), 8.05 (d, J=6.3 Hz, 2H, 2NH), 7.95 (d, J=8.3 Hz, 4H, ArH), 7.45 (m, 2H, Ar'H), 7.25 (dd, J=7.5, 2.5 Hz, 1H, Ar'H), 7.05 (m, 4H, ArH), 4.75 (brs, 1H, BocNH), 4.20 (m, 6H, $2CH_2$+2CH), 2.10 (m, 2H, $2(CH_3)_2CH$), 1.47 (s, 9H, $C(CH_3)_3$), 1.05 (d, J=5.6 Hz, 12H, $4CH_3$); MS (FAB, m-NBA) m/z 764 (M^++1, 2%), 664 (10%).

C_2 receptor (2). A solution of **7** (77 mg, 0.097 mmol) in trifluoroacetic acid (3.0 mL) was stirred at room temperature for 1 h. The solvent was evaporated and the residue was dissolved in DMF (5.0 mL), neutralized with 1 N aqueous NaOH (2.0 mL). After removal of the solvents, the resulting residue was partitioned between $CHCl_3$ and water. The organic layer was dried (Na_2SO_4) and concentrated to give the free amine. A solution of the corresponding amine (50 mg, 0.072 mmol) and Na_2CO_3 (21 mg, 0.192 mmol) were dissolved in DMF/CH_3I (6.0 mL, v/v, 1 : 2) at room temperature for 6 h. The solvents were removed *in vacuo* and purification of the residue by washing with water (2 x 2 mL), drying produced **2** (67 mg, 90%) as a pale yellow solid.

mp 210 °C (Dec.); IR (KBr) 3449 (NH), 3296 (NH), 1652 (C=O) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 8.82 (t, J=5.2 Hz, 2H, $2CH_2NH$), 8.72 (d, J=8.0 Hz, 2H, 2NH), 8.45 (s, 1H, Ar"H), 8.38 (s, 2H, Ar"H), 7.72 (d, J=8.5 Hz, 4H, ArH), 7.25 (m, 4H, Ar'H), 6.93 (d, J=8.6 Hz, 4H, ArH), 4.40 (d, J=5.1 Hz, 4H, $2Ar'CH_2$), 4.15 (m, 6H, $2CH_2$+ 2CH), 3.70 (s, 9H, $3N(CH_3)_3$), 2.00 (m, 2H, $2(CH_3)_2CH$), 1.02 (m, 12H, $4CH_3$); ^{13}C NMR (300 MHz, DMSO-d_6) δ 167.8, 166.6, 148.0, 141.0, 137.7, 132.5, 129.8, 129.5, 128.5, 127.8, 127.3, 125.9, 122.9, 114.9, 68.2, 57.3, 49.5, 43.4, 31.6, 20.2; MS (FAB, Glycerol) m/z 734 (M^+, 100%).

C_2 receptor (3). **3** was synthesized from **8** (22 mg, 0.030 mmol) by an identical procedure to that described above. Treatment of the residue with $CHCl_3$/MeOH (2 mL, v/v, 9 : 1) gave a hydroscopic pale yellow solid, **3** (17 mg, 85%).

^1H NMR (300 MHz, DMSO-d_6) δ 10.07 (brs, 2H, 2NH), 8.77 (d, J=6.2 Hz, 2H, 2NH), 8.59 (s, 1H, Ar"H), 8.46 (s, 2H, Ar"H), 7.94 (d, J=8.1 Hz, 4H, ArH), 7.60 (m, 1H, Ar'H), 7.38 (d, J=7.2 Hz, 2H, Ar'H), 7.25 (m, 1H, Ar'H), 7.03 (d, J=8.5 Hz, 4H, ArH), 4.22 (m, 6H, $2CH_2$+2CH), 3.69 (s, 9H, $3N(CH_3)_3$), 2.00 (m, 2H, $2(CH_3)_2CH$), 1.01 (m, 12H, $4CH_3$); MS (FAB, Glycerol) m/z 706 (M^+, 15%).

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12. The similar result was generated when the coupling between phloroglucinol dihydrate and benzylic bromide was carried out with or without magnesium sulfate.
13. DPAI was commonly prepared from dimethyl 5-aminoisophthalate via amine protection, diester hydrolysis and activated ester formation in overall 70% yield.