solution and clearly elucidated for the first time that the synthetic nanometer-sized magnetite was transformed to γ-Fe_2O_3 in air at room temperature by relatively fast oxidation. Therefore the previous studies of nanoparticle magnetites where the air oxidation was not considered have to be reconsidered in their characterization of the nanoparticles. In forthcoming papers we will investigate the size effect on the transformation and detailed studies of magnetic properties of nanoparticle magnetite under transformation to maghemite.

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Design and Synthesis of Amidine and Diphenyl Substituted Chiral Bispyridino-18-Crown-6 Ligands

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Enantiomeric recognition phenomena play an important role in a variety of physical, chemical, and biological process. Examples include sensing, determination of concentrations, separations of enantiomers, catalysis reactions, and incorporation of single enantiomeric forms of amino acids and sugars in biochemical pathways. It involves the discrimination between enantiomers of the guest by a chiral receptor or a chiral matrix. One area of recent interest is the enantiomeric recognition through interaction of macrocyclic ligands with chiral organic ammonium salts.[1-4]

Several research groups have carried out works involving these host-guest systems. Cram and his co-workers published their pioneering studies on the use of chiral macrocyclic ligands in enantiomeric recognition and a great number of chiral macrocycles have been synthesized and studied.[5] Izatt and his co-workers have reported chiral recognition of primary aromatic ammonium salts.[6] Echavarren and his co-workers have studied enantiomeric recognition of zwitter ionic hydrogen bonding of carboxylate and guanidine.[7]

The careful characterization of such synthetic systems could lead to a greatly improved understanding of natural systems.

Our research in this field has been focused on the design and synthesis of amidine and diaryl substituted chiral bispyridino-18-crown-6 ligand. The chiral host molecule should be designed in such a way that the interaction options available for the incoming chiral guest are limited. Preferably, the options would be limited to either "match" or "not match" interactions (Figure 1).

Designed synthetic chiral ligands have two hydrogen bonding donor which can interact with the carboxylate of

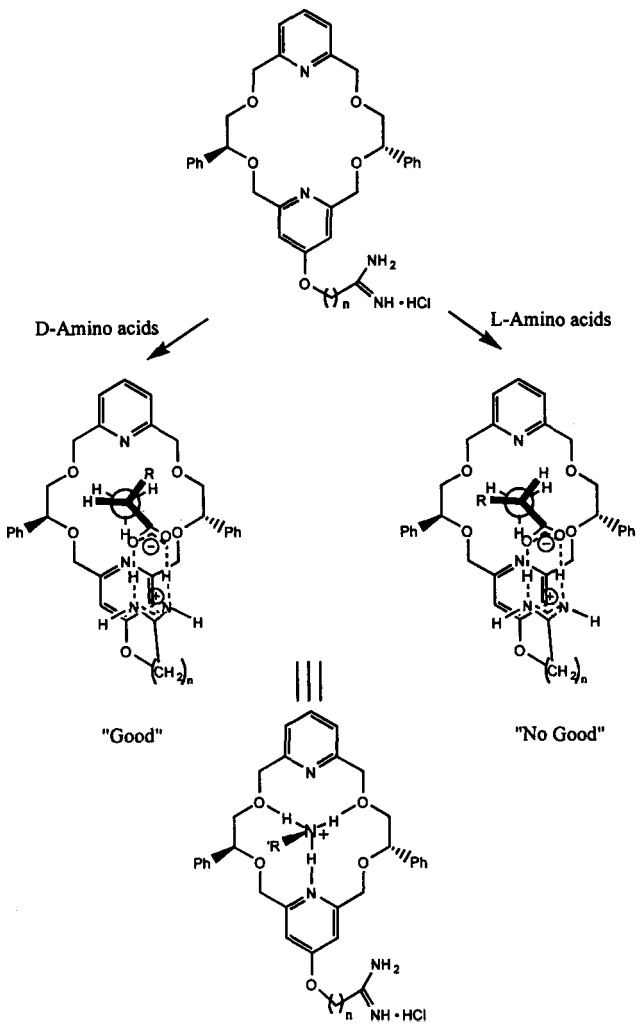
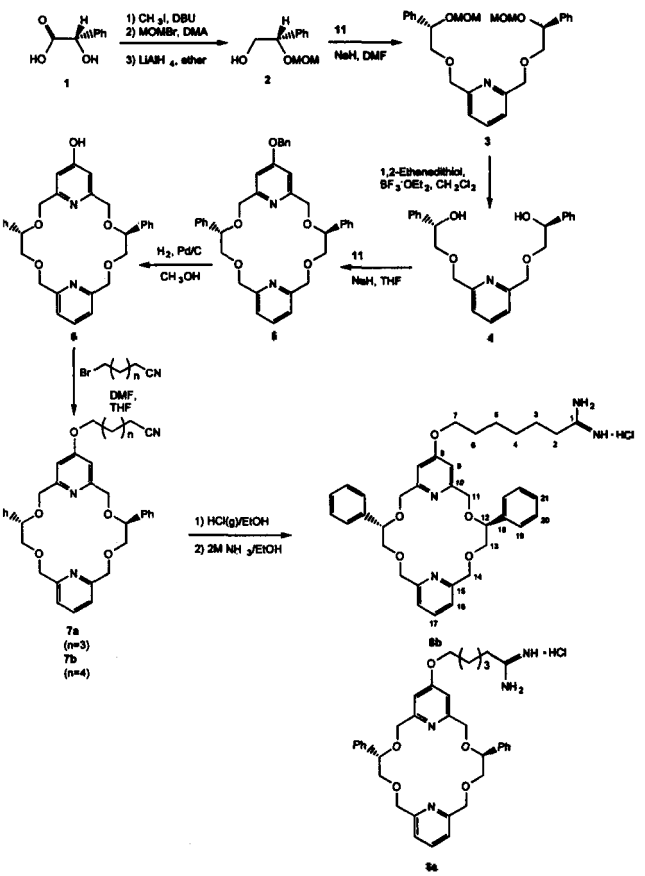


Figure 1. Illustration of possible interaction conformations between alkyl ammonium salt and amidine and diphenyl substituted chiral bispyridino-18-crown-6 ligand.

amino acids or carboxyl oxygen of the ester forms of amino acids. Carboxylate of amino acids could have zwitter ionic hydrogen bonding with amidine and primary ammonium salt of amino acids could have three point hydrogen bonding with two oxygen and one nitrogen of bispyridino-18-crown-6 ligand as shown Figure 1. The nitrogen atom of pyridine can provide one site of three hydrogen bonding interaction as forming complex with primary ammonium salt and stronger hydrogen bonding than oxygen atom.[8] Various functional group can be introduced easily at the position of 4-hydroxy of pyridine ring preserving C_2 symmetry. Amidine group has a strong binding ability with anionic moiety for its ability to be a cation in an extensive pH range. Therefore, it forms zwitter ionic hydrogen bonding of N^+-H--O form.[7] The length of the chains which connects the amidine and the macrocycle was chosen by HyperChem® for the optimal binding of the final macrocycles with the zwitter ions of amino acids.[9]

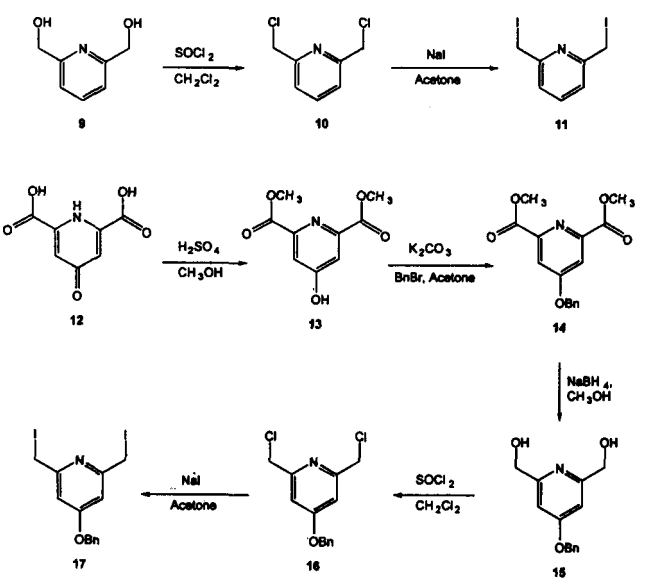
These new chiral ligands may provide a good chiral molecular recognition for the enantiomers of DL-amino acids and its derivatives. We herein report the design and synthesis of new chiral amidine and diphenyl substituted



Scheme 1.

bispyridino-18-crown-6 ligands.

The synthetic route of new chiral macrocycle **8b** began with conversion of (*s*)-(+)-mandelic acid **1** to alcohol **2** through esterification, protection of secondary alcohol with methoxymethyl bromide, and reduction of ester in 82% overall yield.[4,10] The resulting alcohol **2** was coupled with 2, 6-bis(iodomethyl)pyridine **11**, which was obtained by sub-



Scheme 2.

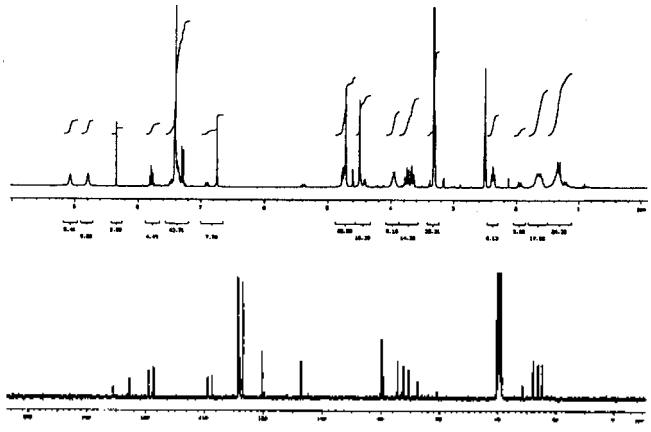


Figure 2. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra of chiral bispyridino-18-crown-6 ligand **8b** in DMSO-d_6 at 50 °C.

Table 1. ^{1}H NMR Data for Macrocycle **8b**

# of C	δ H	mult.	*J* (Hz)
1	–		
2	2.39	t	7.8
3,6	1.55-1.71	m	
4,5	1.22-1.42	m	
7	3.91-3.40	m	
8	–		
9	6.74	s	
10	–		
11	4.49	s	
12	4.75	dd	8.4, 3.0
13a	3.65	dd	10.6, 3.0
13b	3.75	dd	10.6, 8.4
14	4.72	s	
15	–		
16	7.29	d	7.8
17	7.79	t	7.8
18-21	7.39-7.47	m	
NHa	8.78	bs	
NHb	9.06	bs	

stitution of 2,6-pyridine dimethanol to iodide with thionyl chloride and sodium iodide in 77% yield as shown in Scheme 2, by using sodium hydride to give compound **3** in 58% yield. Deprotected diol **4** was obtained by reaction with 1,2-ethanedithiol and borontrifluoride dietherate in methylene chloride in 62% yield. The diol **4** was coupled with iodide **17** to obtain bispyridino-18-crown-6 **5** in 59% yield. The macrocycle **6** was obtained by deprotection of benzyl group with hydrogen in the presence of 5% palladium activated carbon catalyst in 83% yield. Iodide **17** was prepared from chelidamic acid **12** as shown in Scheme 2. Chelidamic acid **12** was treated with methanol and sulfuric acid for esterification, followed by benzylation of *p*-hydroxyl group with benzyl bromide in 80% yield. The resulting ester **14** was reduced to diol **15** by using sodium borohydride in 88% yield. The diol **15** was converted to iodide **17** by using thionyl chloride followed by sodium iodide in 77% yield.

The debenzylated macrocycle **6** was reacted with 7-bromoheptanenitrile to afford alkylated product **7b** in 75% yield. Utilizing the known methodology of amidine formation from nitrile,[11] the nitrile **7b** was treated with hydrogen chloride gas in ethanol to generate the ethyl imidate, followed by 2.0 M solution of ammonia in ethanol to provide amidine **8b**[12a] in 64% yield. Compound **8a**[12b] was prepared using the analogous procedure with comparable yield. The structures of new chiral macrocycles are confirmed by spectroscopic data of ^{1}H NMR and ^{13}C NMR analysis (Figure 2 and Table 1).

Applications of synthesized new chiral ligands **8a-b** for chiral recognition of amino acids and its derivatives by ^{1}H NMR titration are underway and will be reported in the future. Further applications of these new macrocycles for HPLC stationary phase and mobile phase for capillary electrophoresis are under investigation.

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12. (a) **8b**: White Powder; mp 201 °C; MS (FAB) m/z 625.1 (M^+); ^{1}H NMR (300 MHz, DMSO, 50 °C) δ 1.22-1.42 (m, 4H), 1.55-1.71 (m, 4H), 2.39 (t, 2H, *J*=7.8 Hz), 3.65 (dd, 2H, *J*=10.6 Hz, *J'*=3.0 Hz), 3.75 (dd, 2H, *J*=10.6 Hz, *J'*=8.4 Hz), 3.91-4.0 (m, 2H), 4.49 (s, 4H), 4.72 (s, 4H), 4.75 (dd, 2H, *J*=8.4 Hz, *J'*=3.0 Hz), 6.74 (s, 2H), 7.29 (d, 2H, *J*=7.8 Hz), 7.39-7.47 (m, 10H), 7.79 (t, 1H, *J*=7.8 Hz), 8.78 (bs, 2H), 9.06 (bs, 2H); ^{13}C NMR (75

MHz, DMSO, 50 °C) δ 24.7, 26.1, 27.8, 28.0, 31.5, 67.5, 70.6, 72.3, 74.3, 79.7, 107.0, 120.4, 126.9, 127.9, 128.5, 137.2, 138.6, 157.2, 158.9, 165.4, 170.9. (b) **8a**: White Powder; mp 244 °C; MS (FAB) m/z 611.2 (M^+); ^{1}H NMR (300 MHz, DMSO, 50 °C) δ 1.37-1.43 (m, 2H), 1.61-1.78 (m, 4H), 2.39 (t, 2H, *J*=7.5 Hz), 3.64 (dd, 2H, *J*=10.8 Hz, *J'*=3.0 Hz), 3.74 (dd, 2H, *J*=10.8 Hz, *J'*=10.1 Hz), 3.95-4.02 (m, 2H), 4.49 (s, 4H), 4.72-4.79 (m, 6H), 6.75 (s, 2H), 7.28 (d, 2H, *J*=7.5 Hz), 7.33-7.48 (m, 10H), 7.80 (t, 1H, *J*=7.6 Hz), 8.83 (bs, 2H), 9.11 (bs, 2H); ^{13}C NMR (75 MHz, DMSO, 50 °C) δ 24.5, 25.8, 27.6, 31.4, 67.4, 70.4, 72.2, 74.2, 79.8, 107.1, 120.4, 126.8, 128.0, 128.5, 137.3, 138.4, 157.0, 158.8, 165.4, 171.0.

C_{4v} Tetrahydroxyhemicarcerand from Heterocoupling of *p*-Tetrakis(chloromethyl) calix[4]arene and Tetrakis(thiomethyl)resorcin[4]arene

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The correlations of structures with binding properties of carcerands and hemicarcerands have been reported since Cram's pioneering work on 1985,[1] which demonstrated their potential applicabilities such as separation or analytical devices, timed release or delivery system, radiation diagnostics or therapy, and protected molecular reactor.[2] The intrinsic properties of these container hosts can also be materialized if the controls over the molecular interactions and orientation in a matrix are achieved using the self-assembly or the covalent incorporation in organized patterns.

Generally, container hosts consist of northern, southern hemispheres, and bridges of these hemispheres. Most of them hitherto synthesized have the same hemispheres (homocoupled hosts). Different orientations of a unsymmetric guest through the long axis of homocoupled host do not lead to isomeric structures (so-called translational isomer[3] or carcerostereoisomer[4]) even at low temperature. But when a container host has different hemispheres (heterocoupled host), translational isomers can be obtained.

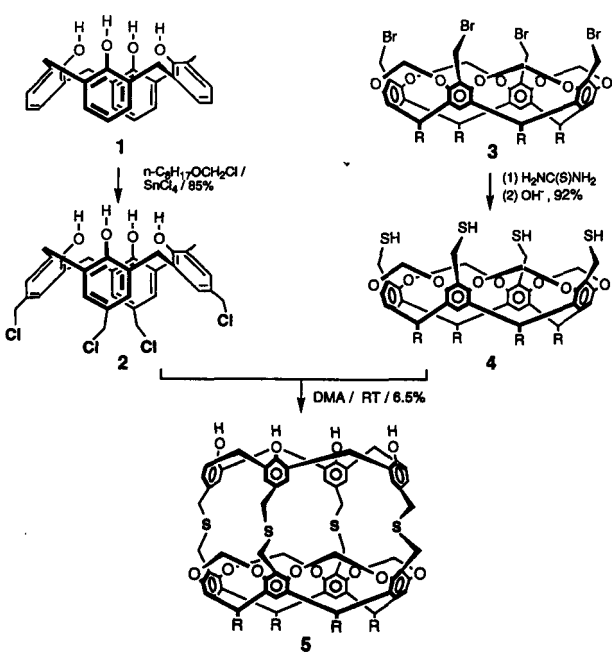
The high molecular order and the 2D or 3D confinement of heterocoupled host on solid surface or crystal lattice could lead to the possibility of switching the incarcerated guests by proper external forces without affecting the orientation of the host, which could be applied as information storage system. Reinhoudt *et al.* reported the successful confinement of a resorcin[4]arene-based carceplex in a self-assembled monolayer on gold.[5a] The driving force is the formation of very stable Au-S bonds and van der Waals interactions between the four dialkylsulfide chains, which function as pillars on the Au surface.[5b]

In this paper we report the synthesis and derivatives of a new manipulable C_{4v} tetrahydroxyhemicarcerand constructed on two different hemispheres.

Calix[4]arene **1** was treated with n-$C_8H_{17}OCH_2Cl$ and $SnCl_4$ at −10 °C for 1 hour to give tetrakis(chloromethyl) calix[4]arene **2** in 85% yield.[6a] The cone conformation of tetrachloride **2** in $CDCl_3$ at room temperature was confirmed by ^{1}H NMR spectrum which shows two broad signals at δ 3.54 and 4.17 ppm ($ArCH_2Ar$) and a sharp OH signal at δ 10.1 ppm which indicates intramolecular H-bonding. Tetrachloride **2** easily looses HCl, especially under basic conditions, to give a reactive *p*-quinone methide.[6b]

Tetrabromide **3** was efficiently obtained by three step-reaction from 2-methylresorcinol and butanal in overall 69% yield.[7] It was easily transformed to tetrathiol **4** with thiourea followed by basic hydrolysis in 92% yield.

Tetrahydroxyhemicarcerand **5**[8] which has $R_4(OH)_4$ type feet and two different hemispheres connected through four thia bonds was prepared in low yield (6.5%) by [1 + 1] shell-closing reaction of tetrachloride **2** and tetrathiol **4** without base at room temperature. It is presumable that this shell formation reaction also proceeds *via* solvent (DMA) tem-



Scheme 1 (R=Propyl).