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.

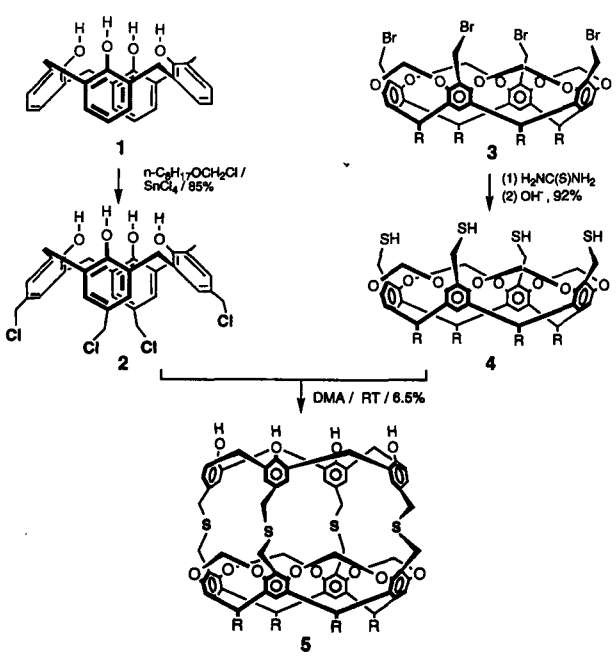
The high molecular order and the 2D or 3D confinement of heterocoupled host on solid surface or crystal lattice could lead to the possibility of switching the incarcerated guests by proper external forces without affecting the orientation of the host, which could be applied as information storage system. 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.

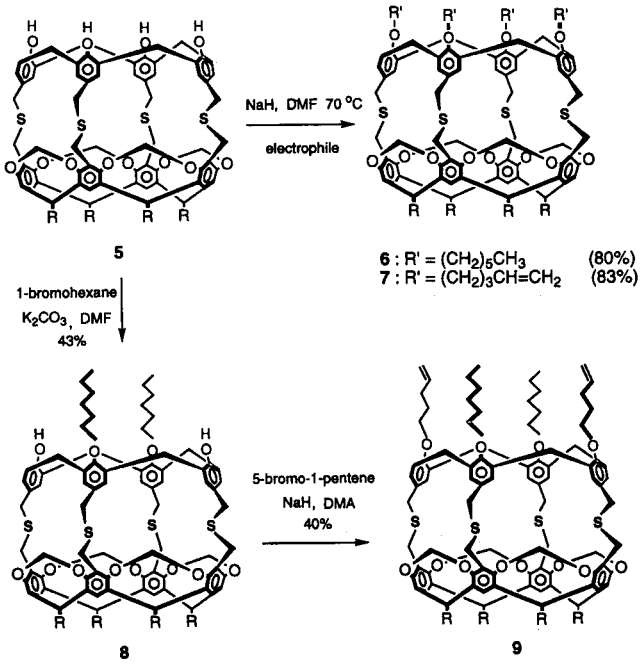
Calix[4]arene **1** was treated with *n*-$C_8H_{17}OCH_2Cl$ and $SnCl_4$ at −10 °C for 1 hour to give tetrakis(chloromethyl) calix[4]arene **2** in 85% yield.[6a] The cone conformation of tetrachloride **2** in $CDCl_3$ at room temperature was confirmed by ^{1}H NMR spectrum which shows two broad signals 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).



Scheme 2 (R=Propyl).

plation,[9] because ^{1}H NMR spectrum of the chromatographed but not recrystallized product showed that about 20% of the product is hemicarceplex **5**@DMA. FAB+ MS spectrum of this product also showed M^+ and $(M+DMA)^+$ peaks at m/z 1361 (74%) and 1448 (72%), respectively. But the chromatographed and then recrystallized product from a mixture of MeOH and CH_2Cl_2 appeared as a free host due to the low steric barrier against the escape of DMA at room temperature. The ^{1}H NMR spectrum of host **5** shows a sharp OH absorption at δ 9.94 ppm which indicates intramolecular H-bonding.

Since hemicarcerand **5** has nucleophilic hydroxyl groups, it can be modified purposefully to be hydrophilic or hydrophobic. Also anchors on polymer matrix or solid surface could be incorporated. Examples are shown in Scheme 2. Hemicarcerand **5** in NaH/DMF at 70 °C was treated with 1-bromohexane or 5-bromo-1-pentene to give hemicarcerand **6**[10] or **7** ($R_4R'_4$ type feet) in 80 or 83% yield, respectively. When the shell closing reaction for **5** and its hexylation to **6** in DMA were done in one-pot reaction, about 3 : 1 mixture of hemicarcerand **6** and hemicarceplex **6**@DMA was obtained. It seems that the escape of DMA from shell has much lower activation energy barrier than that of its entering into shell, which shifts the equilibrium in DMA solution at 70 °C to empty hemicarcerand. Hemicarcerand **5** is weakly soluble in chlorinated solvents, while hemicarcerands **6** and **7** are quite soluble in chlorinated solvents.

Regioselective 1,3-distal alkylation[11] of hemicarcerand **5** with 1-bromohexane and potassium carbonate in DMF gave a diol **8** ($R_4R'_2(OH)_2$ type) in 43% yield. ^{1}H NMR spectrum of **8** shows a high upfield shift (1.44 ppm) of the OH absorption at δ 8.50 ppm compared to that (9.94 ppm) of hemicarcerand **5** due to the cleavage of intramolecular hydrogen bondings. Distal diol **8** was converted to C_{2v} host **9**[12] using 5-bromo-1-pentene/NaH/DMA in 40% yield. Hemicarcerand **9** is the first container host having heterogeneous multifeet

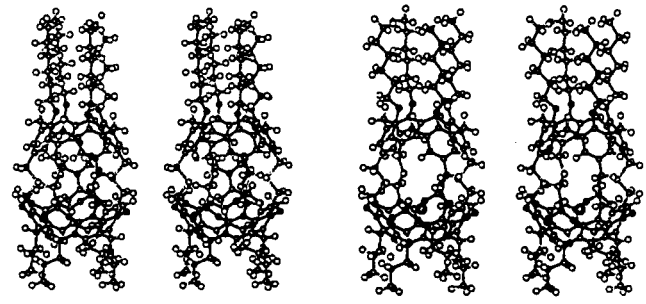


Figure 1. Computer-generated Energy-minimized Stereoviews of Hemicarceplexes **6**@DMA (Left) and **6**@Ag^+ (Right).

($R_4R'_2R''_2$ type). This step-wise feet incorporation strategy could be applied for the development of new functional membrane or polymeric materials.

The picrate extraction experiment shows that host **6** has a substantial affinity for Ag^+ (55% extractability at $[H]_{org}=[G]_{aq}=10^{-4}$ M) but not for other transition metal or alkali metal cations. Figure 1 shows the computer-generated energy-minimized stereo-views (MM+ force-field using HyperChem®) of hemicarceplexes **6**@DMA and **6**@Ag^+. Trans N-CH_3 of DMA is directing to roomy calix[4]arene hemisphere and Ag^+ ion is located to the center of resorcin[4]arene hemisphere. The molecular recognition and thermodynamic behaviors of these hosts in solution are being investigated.

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8. 5: mp >314 °C (decomposed); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.95 (m, 12H, CH_3), 1.27 (m, 8H, CH_2CH_2-CH_3), 2.22 (m, 8H, $CH_2CH_2CH_3$), 3.43 (d, *J*=13.7 Hz, 4H, exo $ArCH_2Ar$), 3.61 (s, 8H, SCH_2Ar), 3.80 (s, 8H, $ArCH_2S$), 4.15 (d, *J*=13.8 Hz, 4H, endo $ArCH_2Ar$), 4.30 (d, *J*=7.9 Hz, 4H, inner OCH_2O), 4.71 (t, 4H, $ArCHAr$), 5.85 (d, *J*=8.1 Hz, 4H, outer OCH_2O), 6.96 (m, 12H,

ArH), 9.94 (s, 4H, OH); FAB+ Mass m/z 1361 (M^+ 72%). Anal. Calcd for $C_{80}H_{80}O_{12}S_4 \cdot 2CH_2Cl_2$: C, 64.31, H, 5.53. Found: C, 64.41, H, 5.34.

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12. **9**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.98 (m, 18H, CH_3), 1.27 (m, 20H, $CH_2CH_2CH_3$ + $OCH_2CH_2(CH_2)_3CH_3$), 1.98 (m, 4H, $O(CH_2)_2CH_2CH{=}CH_2$), 2.17 (m, 16H, CH_2CH_2-CH_3 + $OCH_2CH_2(CH_2)_3CH_3$ + $OCH_2CH_2CH_2CH{=}CH_2$), 3.17 (d, J=12.0 Hz, 4H, exo $ArCH_2Ar$), 3.64 (s, 8H, -CH_2SCH_2-), 3.81 (m, 16H, -CH_2SCH_2- + OCH_2CH_2-), 4.39 (d, J=12.0 Hz, 4H, endo $ArCH_2Ar$), 4.48 (d, J=7.8 Hz, 4H, inner OCH_2O), 4.74 (t, 4H, ArCHAr), 5.05 (m, 4H, $CH{=}CH_2$), 5.91 (m, 6H, outer OCH_2O, $CH{=}CH_2$), 7.05 (m, 12H, ArH).