(246 mg, 0.50 mmol) with 8-hydroxypsoralen (222 mg, 1.10 mmol), K_2CO_3 (346 mg, 2.50 mmol) and KI (16 mg, 0.10 mmol) as described for the preparation of **6d** yielded 257 mg (70%) of **6e**. mp 81-82 ℃; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.72 (2H, d, J=9.6 Hz), 7.64 (2H, d, J=2.2 Hz), 7.31 (2H, s), 6.78 (4H, s), 6.77 (2H, d, J=2.2 Hz), 6.32 (2H, d, J=9.6 Hz), 4.45 (4H, t), 3.86 (4H, t), 1.87-1.65 (8H, m), and 1.55-1.37 (16H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.51 (CO), 153.10 (C), 148.16 (C), 146.55, 144.32, 143.39, 132.01, 125.91, 116.46, 115.31 (CH), 114.63, 112.90, 106.67, 74.04 (OCH_2), 68.54 (OCH_2), 30.01 (CH_2), 29.30 (CH_2), 29.24 (CH_2), 29.20 (CH_2), 25.92 (CH_2), and 25.60 (CH_2); IR (NaCl) cm^{-1} 3140, 3118, 3060, 2932, 2856, 1728, 1622, 1586, 1507, 1467, 1440, 1400, 1331, 1292, 1224, 1148, 1098, 1028, 870, 823, and 753; UV (MeOH) λ_{max} 297.1, 248.4, and 220.7 nm.

Preparation of Bis(C9HQ)Ps (6f). Reaction of **5f** (260 mg, 0.50 mmol) with 8-hydroxypsoralen (222 mg, 1.10 mmol) in the presence of K_2CO_3 (346 mg, 2.50 mmol) and KI (16 mg, 0.10 mmol) as described for the preparation of **6d** yielded 237 mg (62%) of **6f**. mp 75-77 ℃; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.72 (2H, d, J=9.6 Hz), 7.64 (2H, d, J=2.2 Hz), 7.30 (2H, s), 6.78 (4H, s), 6.77 (2H, d, J=2.2 Hz), 6.32 (2H, d, J=9.6 Hz), 4.44 (4H, t), 3.85 (4H, t), 1.86-1.64 (8H, m), and 1.54-1.33 (20H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.50 (CO), 153.07 (C), 148.13 (C), 146.52, 144.32, 143.36, 131.99, 125.89, 116.42, 115.28 (CH), 114.59, 112.89, 106.66, 74.04 (OCH_2), 68.52 (OCH_2), 30.01 (CH_2), 29.38 (CH_2), 29.30 (CH_2), 29.24 (CH_2), 29.20 (CH_2), 25.95 (CH_2), and 25.62 (CH_2); IR (NaCl) cm^{-1} 3138, 3118, 3055, 2929, 2855, 1728, 1622, 1586, 1507, 1467, 1440, 1399, 1331, 1292, 1224, 1179, 1148, 1098, 1029, 990, 871, 823, and 753; UV (MeOH) λ_{max} 297.3, 248.3, and 220.6 nm.

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Efficient Synthesis of Tetrathiol and Octathiacarceplex. First Attempt to Estimate Guest's Peak by ^{1}H NMR Data Comparison

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Cram and co-workers, container hosts are synthetic molecules having an enforced cavity capable of embracing guest ions or molecules.[1] Most of them are based on the derivatives of resorcarenes formed by acid-catalyzed cyclotetramerization between resorcinol (or its derivatives) and various aldehydes. The prototype carcerands **1** (tetrathiacarcerands, D_{4h} point group) were made by shell-closing reactions of compounds **7** and **8** (R=CH_3 or $(CH_2)_4CH_3$) obtained from tetrabromide **6** and revealed many unprecedented properties

as permanent molecular containers.[2] The second carcerand **2** (a octaoxacarcerand) was made of tetrol **9**.[3] Carcerands were generated as carceplex containing solvent whose role as template is known crucial.[4] Octaoxahemicarcerands **3**[5] or **4**[6] were also made of tetrol **9** and revealed controlled thermodynamic or chemical properties as molecular container or reactor. Triols **10** and diols **11** with various R groups are also important hemispheres toward hemicarcerands or carcerands.[7] Those new container hosts are being studied as a new phase of matters.[1,8]

Up to now the effects of the number and the length of bridges on the thermodynamic or chemical properties of hemicarceplexes or carceplexes have been exclusively scrutinized, but those of the functional groups on bridges or hemisphere have not. In these regards hemispheres having inherent functional groups such as thiol or amino groups would widen the scope of container host research and their applicability.

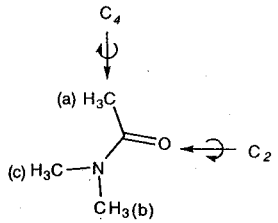
Tetrathiol **13** (R=pentyl) was efficiently synthesized (>85 %) by transmetallation of tetrabromide **6** (R=pentyl) with n-BuLi or s-BuLi followed by quenching with S_8 and then recrystallization from a mixture of MeOH/CH_2Cl_2. Cram *et al.* synthesized tetrathiol **13** *via* its dimethylthiocarbamyl sulfide **12** (46% for 2 steps).[9] Tetrol **9** has been obtained in <50% yield from tetrabromide **6** due to its multistep reaction.[3] Tetrathiol **13** was easily converted to tetrathiacavitand **15** in 72% yield using CH_3I/K_2CO_3/DMF.

One-pot shell-closing reactions of tetrathiol **13** were attempted with diiodomethane, 1,2-diiodoethane, or 1,3-diiodopropane in Cs_2CO_3/DMF or DMA at various temperatures using high dilution technique. Only diiodomethane/Cs_2CO_3/DMA/50 ℃ gave octathiahemicarceplex **5**@DMA in about 5% yield. Cram *et al.* synthesized **5**@DMA (22%) by stepwise shell-closing of tetrathiol **13** and its tetrachloromethyl sulfide **14**.[10] The 8-bond formation route for **5**@DMA caused low yield compared to 4-bond formation route. When α,α′-dibromo-o-xylene/Cs_2CO_3/DMA/70 ℃ was used, only intramolecularly bridged cavitand **16** was obtained (20%). Generally thia-type container hosts were formed in lower yields (<32%)[2b] compared to those of oxa analogues (<61%).[3] It might be attributable to the intrinsic low affinity as well as steric hindrance of sulfur atoms toward polar solvents, which causes low templation effect.

Table 1 shows the most probable orientation and ^{1}H NMR spectral data of DMA incarcerated in hosts **2-5**. It is known that cavity dimension through C_4 axis is longer than that through C_2 axis for hosts having D_{4h} point group.[1] Crystal structure of hemicarceplex **5**@DMA was reported[10] and the interior size could also be deduced by the comparison of upfield-shifted DMA peaks on ^{1}H NMR spectrum. Two peaks at −1.81 and -0.69 ppm can be assigned to those of acetyl (H(a)) and N-CH_3 (H(b)) which is cis to carbonyl oxygen. These are oriented through the long axis (C_4) of host **5** (see Figure 1) and accordingly located deeply into the two shielding zones formed by 4 aryls of each hemisphere. Another N-CH_3 (H(c), trans to carbonyl) is located around tropic (through C_2 axis) and accordingly less up-field shifted (This peak seems to be overlapped with those of alkyls of host **5**).

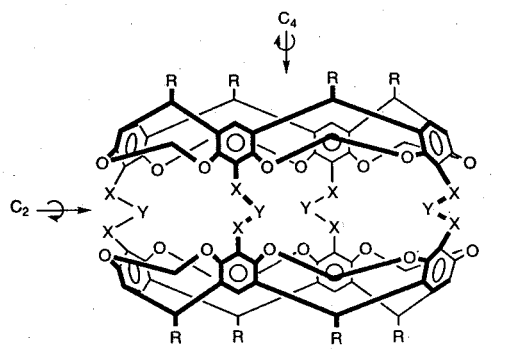
The up-field shift values (Δδ) suggest the compactness of inner sphere of host. For all hosts, Δδ values decrease in the order of H(a)>H(b)>H(c), which implies that H(a)s approach to the shielding zone in most proximity. Basically the shorter bridges make the tighter sphere and accordingly

Table 1. Comparison of ^{1}H NMR Spectral Data of Free or Incarcerated N,N-Dimethylacetamide in $CDCl_3$ ($\Delta\delta=\delta_{Free}-d_{Incarcerated}$, C_n axes belong to Hosts)

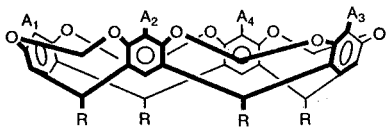


Host	δ (Δδ) in ppm		
	H(a)	H(b)	H(c)
Free	2.09	2.94	3.02
2[3]	−2.40 (4.49)	−1.46 (4.40)	1.04 (1.98)
3[5]	−2.19 (4.28)	−1.15 (4.09)	1.20 (1.82)
5	−1.81 (3.90)	−0.69 (3.63)	1.42 (1.60)*
4[8]	−1.64 (3.73)	−0.42 (3.36)	1.61 (1.41)

*Estimated values from graph in Figure 2.



1; X = CH_2, Y = S, R = CH_3 or $(CH_2)_4CH_3$
2; X = O, Y = CH_2, R = $CH_2CH_2C_6H_5$
3; X = O, Y = 1,2-$(CH_2)_2C_6H_4$, R = $CH_2CH_2C_6H_5$
4; X = O, Y = $(CH_2)_4$, R = $CH_2CH_2C_6H_5$
5; X = S, Y = CH_2, R = $(CH_2)_4CH_3$



6; $A_1 = A_2 = A_3 = A_4$ = Br
7; $A_1 = A_2 = A_3 = A_4 = CH_2Cl$
8; $A_1 = A_2 = A_3 = A_4 = CH_2SH$
9; $A_1 = A_2 = A_3 = A_4$ = OH
10; $A_1 = A_2 = A_3$ = OH, A_4 = H
11; $A_1 = A_3$ = OH, $A_2 = A_4$ = H
12; $A_1 = A_2 = A_3 = A_4 = SC(S)NMe_2$
13; $A_1 = A_2 = A_3 = A_4$ = SH
14; $A_1 = A_2 = A_3 = A_4 = SCH_2Cl$
15; $A_1 = A_2 = A_3 = A_4 = SCH_3$
16; $A_1 = A_2$ = 1,2-$(SCH_2)_2C_6H_4$, $A_3 = A_4$ = 1,2-$(SCH_2)_2C_6H_4$

Figure 1. Structures of Various Carcerands and Hemicarcerands Having D_{4h} Point group and Their Hemispheres.

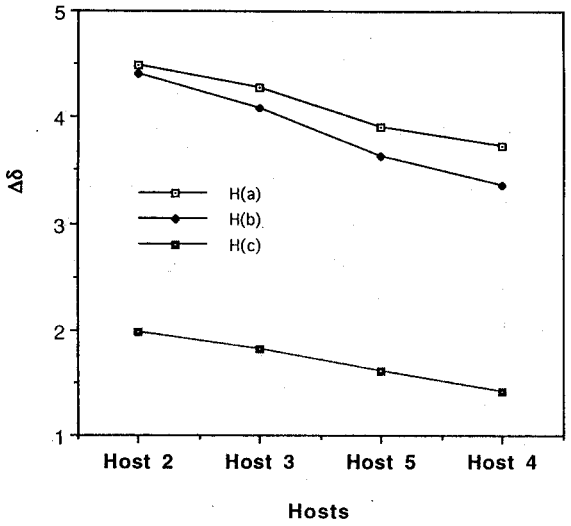


Figure 2. Comparison of Δδ Values of Each DMA Hydrogens Incarcerated in Host **2**, **3**, **4**, and **5**.

larger Δδ. Δδ values of **2**@DMA and **4**@DMA are very consistent with the effect of the length of bridges (3- *vs.* 6-atoms). When the length of bridges is similar, the constrictive wraping ability of portals determines Δδ.[5] Xylyldioxy groups of host **3** (6-atoms) seem to wrap-up core sphere better than butylenedioxy of host **4**. Even host **5** has 3-atom bridges, Δδ values caused by **5** are far less than those by host **2** and between those caused by **3** and **4**, which implies that host **5** constricts itself to embrace DMA much weakly compared to oxa analogues. It is presumable that the large sulfur atoms prevent bridges from dense constriction. The singlets for each methyls of DMA in **5** imply that DMA transits rapidly within the rather cylindrical cavity of host **5**. Also the simple peaks of host **5** imply DMA rotates freely through C_4 as well as C_2 axes on 400 MHz NMR time scale.

Figure 2 shows the graphic comparisons of Δδ values of incarcerated DMA hydrogens. All three kinds of hydrogens are responding in similar pattern; the larger the interior, the lesser the Δδ. H(b)s respond most sensitively, which implies that H(b)s are most sterically crowded in the sphere. H(c)s respond least sensitively, which is also consistent with the fact that H(c)s are located around tropic. These results are consistent to the decreasing order of Δδ values. From the graph chemical shift of H(c)s in host **5** was estimated to be 1.42 ppm.

In conclusion, versatile tetrathiol **13** was efficiently synthesized. Also one-pot synthesis of octathiahemicarceplex **5**@DMA from tetrathiol **13** was successful. The first attempt to estimate the incarcerated guest's peak by comparing guest's peaks in analogous hosts was also successful, which could be an supplementary method to characterize 3D hosts and its guest.

Experimental Section

General Procedure. Chemicals were reagent grade (Aldrich), and used as received, unless otherwise noted. THF was stored under CaH_2 for several days and then distilled under N_2 fron sodium benzophenone ketyl. All anhydrous reaction were conducted under an atmosphere of argon. Melting points were measured on a electrothermal 9100 apparatus. The ^1H NMR spectra were run on a Bruker Aw-80 (80 MHz) or Jeollamda-400 (400 MHz) spectrometer. Spectra taken in $CDCl_3$ were referenced to residual $CHCl_3$ at about 7.26 ppm. FAB^+ MS spectra were determined on a VG70-VSEQ spectrometer with 3-nitrobenzyl alcohol as a matrix. Gravity chromatography was performed on E. Merck silica gel 60 (70-230 mesh). Thin-layer chromatography was done on plastic sheets silica gel 60 F254 (E. Merck, 0.2 mm).

Tetrathiol (13). A solution of n-BuLi (1.6 M) in hexane (44 mL, 70.4 mmol) under argon was slowly added at −78 ℃ to a solution of **6** (8 g, 7.06 mmol) in THF (400 mL). The mixture was stirred for 1 min, and then S_8 (4.6 g, 17.5 mmol) was added. After further stirring at −78 ℃ for 1h, the mixture was allowed to RT for 2h, and then 3 N HCl (30 mL) was added. THF was removed *in vacuo*, and the residue was dissolved in CH_2Cl_2, washed with brine, and then dried over $MgSO_4$. After addition of MeOH (15 mL), the mixture was slowly concentrated to give a crystalline product (6.06 g, 90.7%): mp 279-281 ℃; ^1H NMR (80 MHz, $CDCl_3$) δ 0.95 (t, J=11.2 Hz, 12H, CH_3), 1.35 (bs, 24H, $(CH_2)_3CH_3$), 2.00-2.35 (m, 8H, $CHCH_2$), 3.65 (s, 4H, ArS*H*), 4.35 (d, J=11.2 Hz, 4H, H-C-H_{in}), 4.75 (t, J=15.2 Hz, 4H, $CHCH_2$), 5.95 (d, J=11.2 Hz, 4H, H-C-H_{out}), 6.90 (s, 4H, Ar*H*); FAB MS m/z 943 (M^+, 100%).

Octathiacarceplex (5@DMA). Tetrathiol **13** (200 mg, 0.211 mmol) and CH_2I_2 (0.14 g, 0.53 mmol) were dissolved in 60 mL of dry, degassed anhyrdous DMA. This solution was added dropwise over 30 min to a mixture of 40 mL of DMA and 0.7 g of Cs_2CO_3 at 50 ℃. After 24 h, additional 0.25 mmol of CH_2I_2 (0.08 g) dissolved in 10 mL of DMA was added to the reaction mixture over 30 min. After 12 h, the mixture was partitioned between CH_2Cl_2 (30 mL) and 3 N HCl (100 mL) three times. The organic phase was washed with H_2O, brine, and then dried over $MgSO_4$. The product was crudly purified by silica gel gravity column chromatography using Hexane : EtOAc=6 : 1. The best portions were purified by an additional column chromatography using Hexane : CH_2Cl_2=3 : 1, which gave product **5** (18 mg, 5%): ^1H NMR (400 MHz, $CDCl_3$) δ −1.81 (s, 3H, CH_3C=O), −0.69 (s, 3H, NCH_3), 0.80 (t, J=16.0 Hz, 24H, CH_2CH_3), 1.19-1.53 (m, 51H, $(CH_2)_3CH_3$ and NCH_3), 1.94-2.30 (m, 16H, $CHCH_2$), 4.15 (s, 8H, S-CH_2-S), 4.30 (d, J=7.0 Hz, 8H, H-C-H_{in}), 4.69 (t, J=15.9 Hz, 8H, $CHCH_2$), 5.85 (d, J=7.0 Hz, 8H, H-C-H_{out}), 6.99 DMA (s, 8H, Ar*H*); FAB MS m/z 1938 ($(M\text{-}DMA)^+$, 3%), 967 ($(M\text{-}DMA)^{2+}$, 100%).

Tetrathiacavitand (16). Tetrathiol **13** (200 mg, 0.21 mmol) and α,α′-dibromo-o-xylene (0.14 g, 0.53 mmol) were dissolved in 30 mL of dry degassed DMA. This solution was moved into a dropping funnel and added dropwise over 12 h to a mixture of Cs_2CO_3 (0.70 g, 2.11 mmol) and DMA (30 mL) at 70 ℃. The mixture was further stirred for 24 h, and then partitioned between CH_2Cl_2 (30 mL) and 3 N HCl (70 mL) three times. The organic phase was washed with H_2O, brine, and then dried over $MgSO_4$. The product was crudly purified by silica gel gravity column chromatography using Hexane : EtOAc=6 : 1. The best portions were purified by an additional column chromatography using Hexane : CH_2Cl_2

=2 : 1, which gave 50 mg (20%) of **16**: mp 186.5-186.9 ℃; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.90 (t, J=12.0 Hz, 6H, CH_3), 0.99 (t, J=12.0 Hz, 6H, CH_3), 1.15-1.70 (m, 24H, $(CH_2)_3CH_3$), 2.00-2.15 (m, 4H, $CHCH_2$), 2.30 (d, J=12.0 Hz, 4H, SCH_2), 2.30-2.40 (m, 4H, $CHCH_2$), 4.13 (d, J=12.0 Hz, 4H, SCH_2), 4.17 (d, J=8.1 Hz, 2H, H-C-H_{in}), 4.67 (t, J=18.0 Hz, 2H, $CHCH_2$), 4.86 (d, J=8.0 Hz, 2H, H-C-H_{in}), 5.40 (t, J=20.0 Hz, 2H, $CHCH_2$), 5.50 (d, J=8.1 Hz, 2H, H-C-H_{out}), 6.20 (d, J=8.0 Hz, 2H, H-C-H_{out}), 7.16 (s, 4H, ArH), 7.15-7.25 (m, 8H, ArH); FAB MS m/z 1149 (M^+, 100%).

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A Synthetic Route to a C_2-Symmetrical Alkoxyketone

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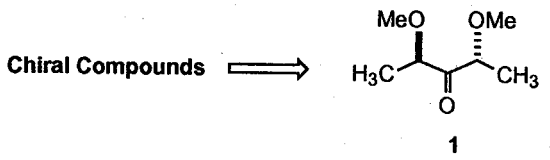
Asymmetric induction is one of the most tackling targets in the area of organic synthesis. For this purpose, chiral auxiliaries have been frequently employed and are being developed increasingly.[1] Among various classes of auxiliaries, C_2-symmetry chiral ligands,[2] whether natural or synthetic, play a critical role in the scenario, providing exceedingly high levels of absolute stereochemical control.[3] Therefore, searching for better ligands is an unabating endeavor in terms of better economy as well as higher efficiency.

For this purpose, we became interested in C_2-symmetrical ketones.[4] C_2-Symmetric ketones have been quite rarely utilized in the area, probably because those compounds are not naturally abundant or have not been elaborated enough for useful reactions.[4f] However, we envisioned that chiral C_2-symmetric ketones could be served as distinctive chiral auxiliaries, and designed a simple dialkoxyketone derivative **1** as a trial entrant. First we decided to secure a potentially divergent pathway to this class. In this note, we briefly describe a reliable route to **1** from a natural chiral source.

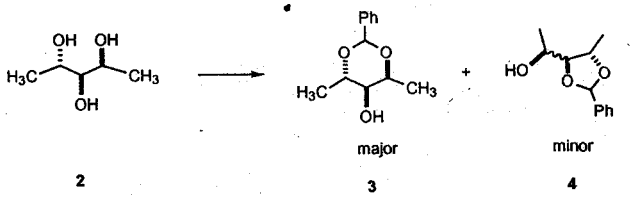
Initial attempts to differentiate hydroxy groups of **2**[5] *via* selective protections proved to be impractical (Scheme 1).[6] 6-Membered benzylidene **3** was formed as a major product over **4** in *ca.* 4 : 1 to 6 : 1 ratios,[7] however, difficulties in separation of the two made us seek an alternative pathway.

We counted that diepoxide **7** should be an appropriate precursor for the ketone **1**. Selective epoxide opening from the less hindered site would provide the desired hydroxy groups at the proper positions. Amberite resin treatment of bischloride **5** and the corresponding regioisomers formed



1

Figure 1.



2 **3** **4**

Scheme 1.

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