Molecular Engineering. Part 12. Hemicarcerand Having a Metal Coordinating Ligand at a Hetero-Bridge

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Resorcin[4]arene-based container hosts such as carcerand,[1] hemicarcerand,[2] velcrand,[3] polyvelcraplex,[4] and self-assembled molecular capsule[5] have been characterized with the potential applications as molecular reactors, selective storage, delivery and controlled-releasing systems. Recently, the research fields of supramolecular systems are being expanded from single host-guest systems to high ordered macromolecular systems such as polymeric nanostructure[6] or self-assembly monolayer.[7]

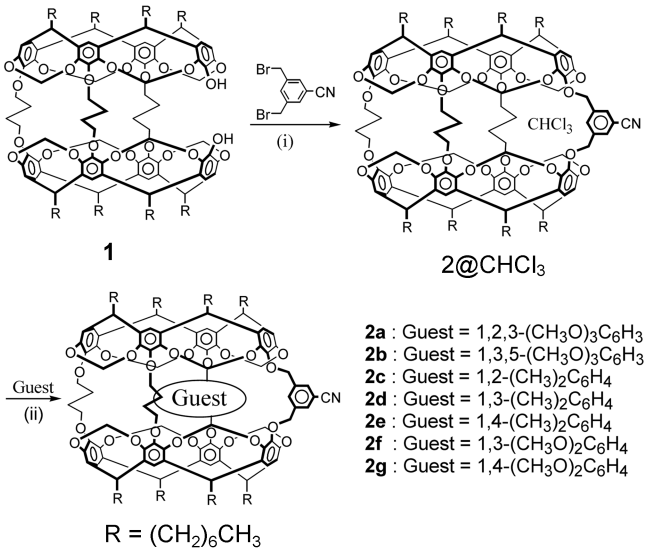
Dimeric container system could duplex the function of monomeric container molecule and a well-controlled manipulation of dimeric container system would result in a new highly accumulated information storage system. By Cram group, various heterobridged hemicarcerplexes were synthesized from diol **1**, in which the fourth bridging unit differs from the other three bridging units.[8] And a fourth bridging unit has been used to connect with another hemicarcerand to give various dimeric hemicarceplexes.[9]

Metal coordination to promote the self-assembly of high-ordered and well-defined supramolecular architectures has become an important synthetic strategy because it allows well defined geometry, coordination number, and a range of binding strengths.[10] Here we report on the synthesis and binding properties of hemicarcerand **2** which has a metal coordinating cyanophenyl unit and its preliminary characteristics as a dimeric self-assembly by metal coordination.

Diol **1**[8c] was synthesized in 44% yield from tetrol[11] using Sherman's templating procedure[12] (NMP, Cs_2CO_3, 3 equiv of $TsO(CH_2)_4OTs$, 25 °C, 12 h). Under the dilution condition, diol **1** was reacted with 3,5-bis(bromomethyl)-benzonitrile[13] in a mixture of Cs_2CO_3 and NMP at 60 °C to afford hemicarcerand **2**@$CHCl_3$ in 38% yield after chromatographic purification (hexane : $CHCl_3$ = 2 : 1) and recrystallization (CH_3OH). The initial product **2**@NMP seems to be changed to **2**@$CHCl_3$ by mass-driven exchange. Heterobridged hemicarcerand **2**@$CHCl_3$ was characterized by ^{1}H NMR, FT-IR and FAB+ Mass spectra. Hemicarceplexes **2a-g** were obtained by heating a mixture of **2**@$CHCl_3$ and an excess of guests. To a round bottom flask equipped with an argon gas inlet were added hemicarcerand **2**@$CHCl_3$ and various guests as solvents (> 1000 fold). The mixture was heated at 130-160 °C for 36-64 hours. The cooled reaction mixtures were flooded with CH_3OH and the precipitates were filtered and dried *in vacuo*.

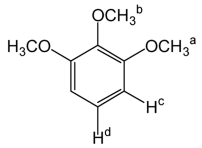
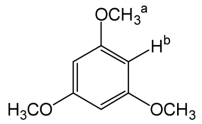
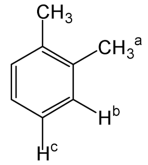
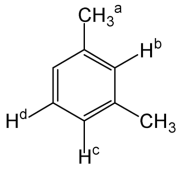
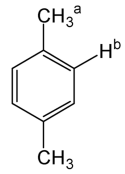
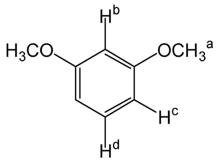
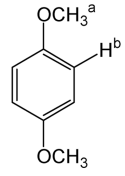
Table 1 shows the conditions and results for thermally induced complexation, and chemical shifts of ^{1}H NMR spectra for complexed guest in $CDCl_3$ at 25 °C. The sizes and shapes of guest candidates must be complementary enough to the host's portals and interiors so that constrictive and intrinsic binding taken together allow isolable and manipulable hemicarceplexes. The chemical shift changes of guest protons illustrate the relative orientation of guest in the interior of hemicarcerand. Due to the shielding effect of aromatic units, protons close to aromatic π-cloud shift to up-field. In general the upfield-shift of protons on *meta*- or *para*-substituent is larger than that of *ortho*-substituent. Trisubstitued benzenes enter slowly than disubstitued ones do. From the complexation ratio of disubstitued benzenes the complexation efficiency decreases in the order of *para*- > *meta*- >> *ortho*-disubstituted benzene. Interestingly methoxy group favors complextion than methyl group does.

Table 2 shows the half-lives for decomplexation. It is assumed that decomplexation exhibits the first order behavior in large excess of solvent over several half-lives. Decomplexation half-life for hemicarceplex **2a** is about 2.5 times longer than that for hemicarceplex **2b** whose half-life is about 17 times longer than that of hemicarceplex **2e**. Clearly the steric hindrance of guest imposes a large activation energy barrier to escape the portal of host.



Scheme 1. Conditions: (i) Cs_2CO_3/NMP, 60 °C, 38%, (ii) 130-160 °C, 3 days.

Table 1. Conditions and results for complexation and chemical shifts of complexed guest proton (400 MHz ^{1}H NMR, $CDCl_3$, 25 °C)

No	guest structure	T (°C)	t (hours)	isolation yield (%)	δ (ppm) of complexed guest		Δδ (ppm) ($\delta_{free}-\delta_{compl}$)	complexation ratio (%)
2a		160	36	86	H_a H_b H_c H_d	–0.56 –0.46 6.58 6.60	4.41 4.32 0 0.39	46%
2b		160	36	66	H_a H_b	–0.66 a	4.50 a	52%
2c		130	64	95	H_a H_b H_c	–1.74 a a	4.11 a a	44%
2d		130	64	95	H_a H_b H_c H_d	–2.00 5.92 5.92 5.92	4.32 0.93 1.07 1.21	59%
2e		130	64	95	H_a H_b	–1.99 5.92	4.31 1.15	66%
2f		130	64	76	H_a H_b H_c H_d	–0.60 4.80 4.80 4.80	4.40 1.70 1.74 2.40	64%
2g		130	64	65	H_a H_b	–0.46 5.30	4.23 1.35	74%

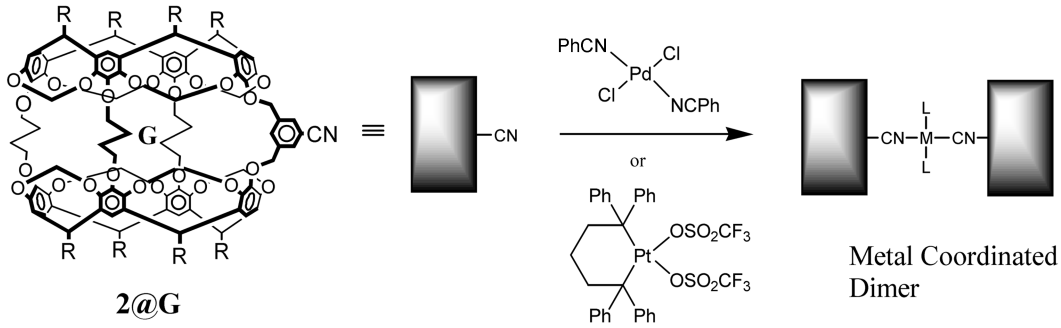
[a]Signal obscured by other peaks.

Table 2. Half-lives for decomplexation of **2**•Guest in $Cl_2CDCDCl_2$ at 80 °C

Complex No.	Guest	$t_{1/2}$ (h)
2a	1,2,3-$(CH_3O)_3C_6H_3$	167
2b	1,3,5-$(CH_3O)_3C_6H_3$	69
2e	1,4-$(CH_3)_2C_6H_4$	4

As shown in Scheme 2 metal coordinated dimeric container molecular system was attempted with hemicarceplex **2**@$CHCl_3$ and $Pd(PhCN)_2Cl_2$ or $Pt(dppp)OTf_2$. Figure 1 shows the partial FT-IR spectra of hemicarceplex **2**@$CHCl_3$ and their metal complexes. The stretching band of cyano group at 2231 cm^{-1} for hemicarcerand **2** was not changed significantly at 2 : 1 molar ration of **2** : $Pd(PhCN)_2Cl_2$. But at 2 : 1 molar ratio of **2** : $Pt(dppp)_2OT_{f2}$, new stretching band of cyano group at 2250 cm^{-1} was appeared with that of free host **2** at 2231 cm^{-1}.

But any chemical shift change of hemicarcerand **2** upon complexation by ^{1}H or ^{13}C NMR spectra couldn't be observed presumably due to the weak metal coordination strength of cyano group. The life time of metal coordinated complex seems too shorter than NMR time scale to be detected. The partial evidence of metal coordination by IR spectrum was possible due to the shorter IR time scale. It is desirable to adopt stronger ligand such as pyridyl to get stable metal-



Scheme 2. Proposed formation of metal coordinated dimeric container molecular system.

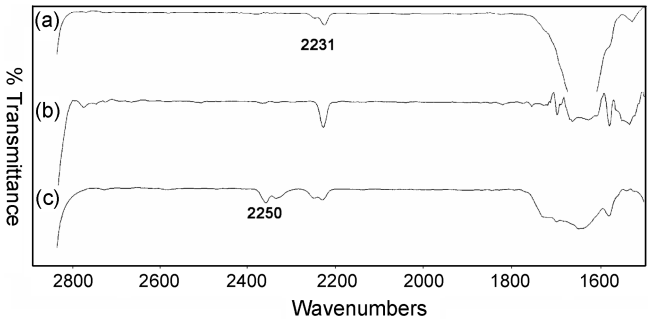


Figure 1. FT-IR spectra of (a) Hemicarceplex **2**@$CHCl_3$, (b) **2**@$CHCl_3$ + $Pd(NCPh)_2Cl_2$, (c) **2**@$CHCl_3$ + Pt(dppp)OTf_2.

coordinated dimeric container suprastructure. When container molecular systems with multi-ligands were developed, highly organized 2-D net-work of container molecular systems could be constructed.

Experimental Section

3,5-Bis(bromomethyl)-benzonitrile. A mixture of 3,5-dimethylbenzonitrile (1.0 g, 7.6 mmol), NBS (1.35 g, 3.8 mmol) and catalytic amount of AIBN in 50 mL of dry CH_2Cl_2 was stirred under visible light and argon atmosphere for 1 hr at 25 °C. To the mixture were added more NBS (1.35 g, 3.8 mmol) and catalytic amount of AIBN. After 1 day, the solvent was evaporated under vacuum. The residue was dissolved in CH_2Cl_2, wash with water and CH_2Cl_2 layer was dried over $MgSO_4$, and purified by silica gel chromatography with a mixture of CH_2Cl_2/Hexane (6 : 1) as a mobile phase to give 703 mg (32%) of product: FT-IR (KBr) 2230 cm^{-1} (ν_{CN}); ^1H NMR (400 MHz, $CDCl_3$) δ 4.45 (s, 6H, *CH_2*), 7.61 (s, 2H, *ArH*), 7.64 (S, 1H, *ArH*).

Hemicarcerand 2@$CHCl_3$. A mixture of diol **1** (100 mg, 0.04 mmol) and Cs_2CO_3 (60 mg, 0.12 mmol) in 20 mL of degassed NMP. The reaction mixture was stirred at 60 °C, and 3,5-bis(bromomethyl)-benzonitrile were added (0.67 mg, 0.12 mmol) and stirred for 36 hr. 3 N HCl was added and the mixture was extracted with CH_2Cl_2. The organic layer was washed with water and brine, and then dried over $MgSO_4$. The product was purified by silica gel chromatography with a mixture of Hexane : $CHCl_3$ (2 : 1) as a mobile phase, and recrystallized by CH_3OH to give **2** (40 mg, 38%): FAB+ MASS (NOBA) m/e 2298 (2·Na^+, 25), 2397 (**2**@$CHCl_3$ + H^+, 100); ^1H NMR (400 MHz, $CDCl_3$) δ 6.76-6.82 (m, 11H, *ArH*), 5.64-5.83 (2d, 8H, outer O*CH_2*O), 4.69 (m, 8H, methine), 4.16 (m, 8H, inner O*CH_2*O), 3.90 (d, 12H, O*CH_2*), 3.81 (m, 12H, *CH_2*), 2.17 (s, 8H, CH*CH_2*), 1.90 (d, 18H, *CH_3*), 1.25-1.37 (m, 40H, *$(CH_2)_5$*), 0.90 (t, 12H, *CH_3*).

General procedure for the guest complexation. All complexations-decomplexations were carried out in an argon atmosphere. The guests were used as the solvent for complexation experiments. Table 1 record the structures and the labels of the guests, reaction time and temperature, the isolated yield, and the percent complexed. In each complexation, 10 mg of host dissolved in the following specified molar excesses of guest were heated to the specified time and temperature. To the reaction mixture was added 40 mL of CH_3OH, and the precipitate was filtered, washed, and dried, and its ^1H NMR spectrum in $CDCl_3$ taken at 25 °C. In a separate experiment, the ^1H NMR of the pure guest was taken under the same conditions.

Hemicarcerplex 2a. 1.3 g (7.93 mmol) of 1,2,3-trimethoxybenzene. **2a** was obtained in 86% of isolation yield (8.6 mg). The complex guest ^1H NMR δ −0.56 (s, 6H, O*CH_3*), −0.46 (s, 3H, O*CH_3*).

Hemicarcerplex 2b. 1.0 g (5.95 mmol) of 1,3,5-trimethoxybenzene. **2b** was obtained in 66% isolation yield (5.6 mg). The complex guest ^1H NMR δ −3.28 (t, 9H, O*CH_3*).

Hemicarcerplex 2c. 1.0 mL (8.15 mmol) of *o*-xylene. **2c** was obtained in quantitative isolation yield. The complex guest ^1H NMR δ −1.74 (s, 6H, *CH_3*).

Hemicarcerplex 2d. 1.0 mL (8.15 mmol) of *m*-xylene. **2d** was obtained in quantitative isolation yield. The complex guest ^1H NMR δ5.92 (s, 3H, *ArH*), −2.00 (s, 6H, *CH_3*).

Hemicarcerplex 2e. 1.0 mL (8.15 mmol) of *p*-xylene. **2e** was obtained in quantitative isolation yield. The complex guest ^1H NMR δ5.92 (s, 3H, *ArH*), −1.99 (s, 6H, *CH_3*).

Hemicarcerplex 2f. 1.0 mL (7.25 mmol) of 1,3-dimethoxybenzene. **2f** was obtained in 76% of isolation yield (2.6 mg). The complex guest ^1H NMR δ 4.80 (m, 4H, *ArH*), −0.60 (s, 6H, O*CH_3*).

Hemicarcerplex 2g. 1.0 mL (7.25 mmol) of 1,4-dimethoxybenzene. **2g** was obtained in 65% of isolation yield (5.5 mg). The complex guest ^1H NMR δ 5.30 (m, 4H, *ArH*), −0.46 (s, 6H, O*CH_3*).

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