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Facile synthesis and binding properties of C_{2v} container hosts based on resorcin[4]arene

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Abstract

Two new C_{2v} container hosts were synthesized by the capping of catechol- or resorcinol-fenced resorcin[4]arene with 1,2,4,5-tetrakis(bromomethyl)benzene and their K_a values were calculated directly from ^1H NMR spectra. These hosts showed the binding properties for alkyl alcohols, methylene chloride, and teterahydrofuran in $CDCl_3$ or $(CDCl_2)_2$ at -40 °C. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: container hosts; capped cavitands; resorcin[4]arenes; alcohol container.

Since the pioneering work of Professor Cram on container molecules numerous carceplexes and hemicarceplexes have been studied as a new phase of matter[1] and the mechanisms of the shell closing reaction[2] and the decomplexation process[3] are also scrutinized. Mainly three crude strategies have been adopted for the control of host-guest dynamics: the number of portal pillars, the length of portal pillars, and the dimension of hemispheres. But various tuning strategies on complexation-decomplexation dynamics between container hosts and guests are necessary for the practical application of these systems as analytical devices, timed release or delivery systems, radiation diagnostics or therapy, protected molecular reactor, or information storage devices.

Most of the resorcin[4]arene-based typical container hosts have two resorcin[4]arene moieties connected by $(\text{-O-bridge-O-})_n$ pillars (bridge = $(CH_2)_m$ or xylenyl and $n = 2 \sim 4$, $m = 1 \sim 6$). Recently C_{4v} carcerand by the coupling of calix[4]arene and resorcin[4]arene through amide bonds[4] as well as the chiral container hosts[5] are reported. To diversify and apply the nature of the so-called constrictive binding of container hosts, a mechanical inhibition of hemicarceplex decomplexation, various types of caps should be adopted and studied[6]. The

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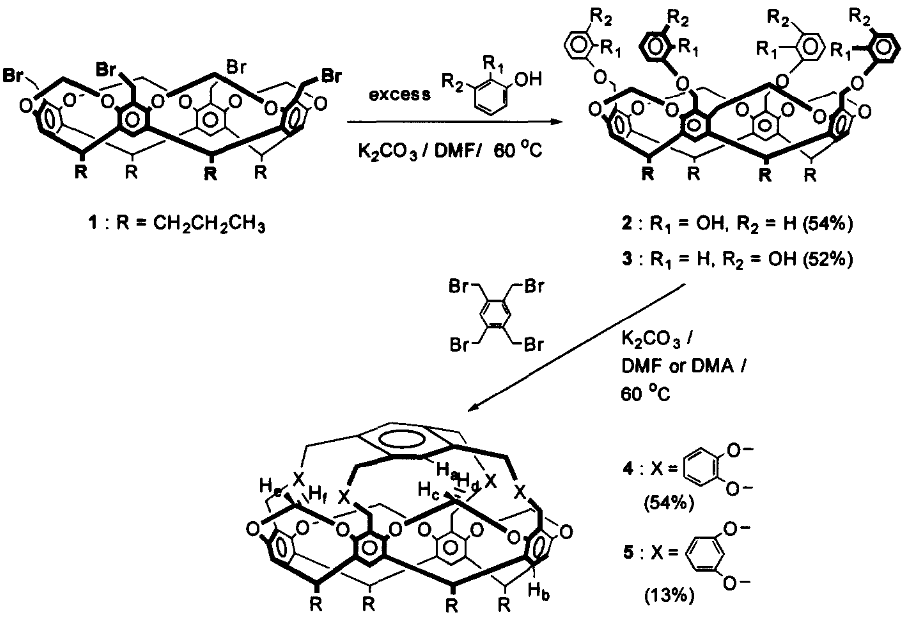
easy access to tetrabromide **1** allowed the synthesis of various hosts[7] and here a new stepwise route from tetrabromide **1** to C_{2v} container hosts **4** and **5** having a benzene cap and (-CH_2O-bridge-OCH_2-$)_4$ pillars and their preliminary binding properties are reported.

Tetrabromide **1** was treated with an excess of catechol and resorcinol in a mixture of K_2CO_3/DMF at 60 °C to give aryl-fenced cavitands **2** and **3** in 54% and 52% yields, respectively (Scheme 1). The capping of cavitands **2** and **3** with 1,2,4,5-tetrakis(bromomethyl)-benzene in a mixture of K_2CO_3/DMF at 60 °C gave container hosts **4** and **5** in 54% and 13% yields, respectively.[1] It is presumable that the higher yield of host **4** is mainly due to the entropic favor of intermediates for capping over those of **5**, because there is no noticeable steric congestion in either of hosts **4** and **5**.



Scheme 1

CPK molecular model shows that host **4** can accommodate DMA, DMF, MEK, THF, or pyrazine. But only the complexations with smaller guests such as methanol, ethanol, propanol and methylene chloride were detected by ^1H NMR spectra at -40 °C. Fig. 1 shows the sharpening of free host's spectrum (a) upon complexation with methanol and ethanol in $CDCl_3$ at -40 °C. Especially the peaks of benzylic (δ 5.11 - 4.73), dioxymethylenyl (δ 5.75 of H_c, 5.49 of H_e, 4.65 of H_d, and 4.37 of H_f), and aryl hydrogens (δ 7.70 of H_a and 7.16 of H_b) appeared clearly by complexation with ethanol (Spectrum c), which manifests that the complexed ethanol relieved various host's conformers. Moreover, the chemical shift values of H_a together with H_d and H_f were sensitive to the complexation of methanol and ethanol compared to those of free host. The H_a protons were shifted downfield up to 0.52 ppm, whereas the H_d and H_f protons were shifted upfield up to 0.20 ppm. The distinct peaks of free and complexed guests enable the direct calculation of K_a. The far upfield shifts of complexed guest's peaks (δ -2.61 of CH_3CH_2OH and δ -0.29 of CH_3OH) are typical to container hosts having aromatic shells. The 1:1 stoichiometry for the complex was assumed from the ^1H NMR spectral integration between host and guest at -40 °C, which showed less than 1:1 binding upto 100 equiv. of guest. For host **5** various potential guests such as DMA, DMF, dioxane, toluene, *m*-xylene, and *N*-methylpyrrolidinone were also tested, but only THF was complexed at -40 °C.

Table 1 shows the association constants K_a and the chemical shift differences ($\Delta\delta$) of guests in $CDCl_3$ or $(CDCl_2)_2$ at -40 °C. The chemical shifts of methyl groups of methanol, ethanol and propanol in host **4** are far upfield shifted ($\Delta\delta$ = 3.78, 3.82, and 3.53, respectively) compared to that of protons of methylene chloride($\Delta\delta$ = 1.89), which means the methyl groups of alcohols are far better nested in resorcin[4]arene moiety.

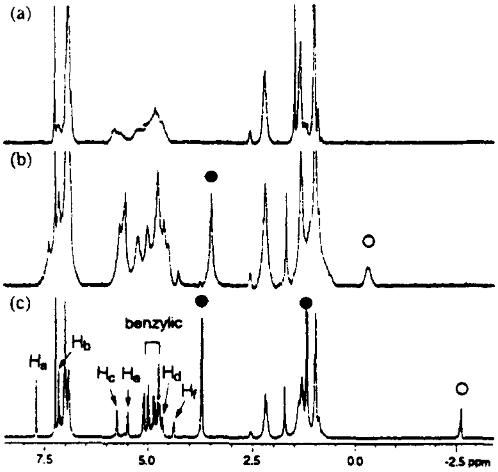


Fig. 1 ^1H NMR spectra of (a) host **4** (3 mM), (b) host **4** : MeOH = 1:2, and (c) host **4** : EtOH = 1:2 in $CDCl_3$ at -40 °C (● : free guest, ○ : complexed guest).

Table 1

The association constants (K_a, M^{-1}) and ^1H NMR spectral chemical shift differences ($\Delta\delta$ ppm in parenthesis)[a] of guest complexation in host **4** at -40 °C.

	Guest			
Solvent	CH_3OH	CH_3CH_2OH	$CH_3(CH_2)_2OH$	CH_2Cl_2
$CDCl_3$	238 (3.78)	190 (3.82)	3 (3.53)	45 (1.89)
$(CDCl_2)_2$	304 (3.81)	95 (3.85)	-[b]	nd[c]

[a] $\Delta\delta$ = δ of free guest − δ of complexed guest. [b] not complexed. [c] not determined.

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[1] Host **4** and **5** were completely characterized with elemental analyses and ^1H NMR and FAB (m/z, M^+) mass spectra. *Selected data for* **4**: mp 218 °C; Anal. Calcd for $C_{82}H_{78}O_{16}$: C, 74.64; H, 5.96. Found: C, 74.34; H, 5.96. ^1H NMR (400 MHz, $CDCl_3$) δ 0.95 (t, 12H, CH_3), 1.43 (m, 8H, $CH_2CH_2CH_3$), 2.24 (m, 8H, $CH_2CH_2CH_3$), 4.09-4.34 (two br s, 4H, inner OCH_2O), 4.48-4.88 (m, 12H, ArC*H* and $ArCH_2O$), 5.16 (m, 8H, $ArCH_2O$), 5.64-5.79 (two br s, 4H, outer OCH_2O), 6.87-6.97 (m, 16H, catechol's H), 7.14 (s, 4H, Ar*H*), 7.55 (s, 2H, Ar*H*); FAB(+) MS, m/z 1320 (M^+, 100%).

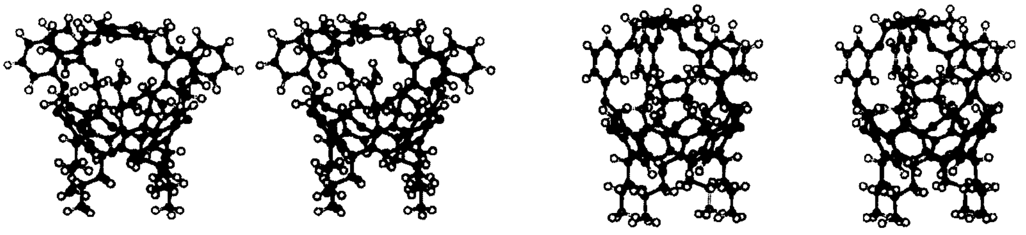

Fig. 2 The energy minimized (MM+ force-field) stereoviews of **4** · EtOH (left) and **5** · THF (right).

K_a value of methanol by host **4** is the largest among guest alcohols. Especially the size selectivity for methanol over ethanol or propanol by host **4** is larger in $(CDCl_2)_2$ than in $CDCl_3$. As far as we know host **4** is one of the smallest human-made alcohol container[8]. The THF complexation by host **5** in $(CDCl_2)_2$ at -40 °C gave K_a as 14 M^{-1}. The peaks of complexed THF protons were also shifted upfield showing the chemical shift differences of 2.40 and 1.61 ppm.

Fig. 2 shows the energy-minimized (MM+ force-field using HyperChem®) stereoviews of complexes **4** · EtOH and **5** · THF. The bridging units, catechol and resorcinol moieties, are paired to obtain maximum π - π interactions which resulted in two large and two small portals. The guest orientation of **4** · EtOH matches well with the guest's chemical shifts and the direction of hydroxyl group to the center of benzene cap is meaningful.

In conclusion, two C_{2v} container hosts were synthesized and the binding properties for various potential guests were characterized. Currently the complexation properties of these hosts for a wide spectrum of potential guests are being tested and the water-solubilization of these container hosts is also in progress.

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REFERENCES

[1] Cram DJ, Cram JM: Container Molecules and Their Guests: Stoddart JF, editor. Monographs in Supramolecular Chemistry. Cambridge: The Royal Society of Chemistry, 1994.

[2] Chapman RG, Sherman JC. J. Org. Chem. 1998; 63: 4103.

[3] Houk KN, Nakamura K, Sheu C, Keating AE. Science 1996; 273: 627.

[4] Timmerman P, Verboom W, van Veggel FCJM, van Duynhoven JPM, Reinhoudt DN. Angew. Chem., Int. Ed. Engl. 1994; 33: 2345.

[5] Yoon J, Cram DJ. J. Am. Chem. Soc. 1997; 119: 11796.

[6] Helgeson RC, Knobler CB, Cram DJ. J. Am. Chem. Soc. 1997; 119: 3229.

[7] Lee J, Choi K, Paek K. Tetrahedron Lett 1997; 38: 8203

[8] Hamaskai K, Ueno A, Toda F. J. Chem. Soc., Chem. Commun. 1993: 331.