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Versatile cavitands for small molecules: the entropically driven ethanol selectivity

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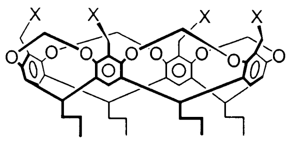
Abstract—Two new C_{2v} cavitands based on resorcin[4]arene were synthesized and their binding properties for nine small molecules were studied. The alcohol selectivity was in the order of $CH_3OH \sim CH_3CHOHCH_3 < CH_3CH_2CH_2OH \ll CH_3CH_2OH$ with the highest $K_a = 260$ M^{-1} at 23°C in $CDCl_3$. Their carceroisomerism was observed by ^1H NMR spectra and the quinone-capped cavitand's complexation of ethanol was driven entropically. © 2001 Elsevier Science Ltd. All rights reserved.

Various container hosts have been reported with potential applications as molecular reactor, selective storage, delivery or controlled-releasing systems as well as an information storage system.[1] However, the highly size- and shape-selective container hosts, even with a sensoring antenna, should be developed.

Tetrakis(resorcinolyl)tetrol **2** obtained from tetrabromide **1** by an excess of resorcinol has been studied as a diamine-selective host[2] or as a molecular vessel for various container molecules such as hemicarcerand **3**[3] and cavitand **4**.[4] Even though cavitand **4** has a defined cavity it showed only weak ($K_a = 73$ M^{-1} for THF) or nonbinding properties for various potential guests (toluene, dioxane, DMF, DMA and small alcohols) at −40°C in $(CD_2Cl_2)_2$ due to its low constrictability for the maximum contact between host and guest.[5]

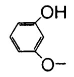
New type C_{2v} cavitands **5** and **6**,[6] which could electrochemically respond and have opposite electron density of cap, were both synthesized from tetrol **2** (Scheme 1) in 23 and 10%, respectively, using tetrafluoro-1,4-benzoquinone or tetrafluoroterephthalonitrile as capping agent.

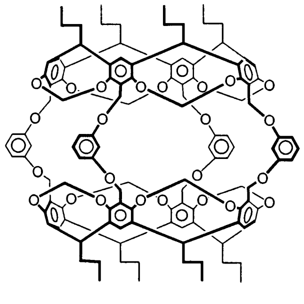
The CPK molecular model shows that host **5** and **6** can accommodate various small molecules. The complexations of host **5** or **6** with ethanol, *n*-propanol, ethylene glycol, acetaldehyde, nitromethane, acetonitrile and methylene chloride were observed by ^1H NMR spectra at 23°C in $CDCl_3$. Fig. 1 shows the spectral changes of host **5** upon complexation with ethanol. The resorcinol unit's singlet at 6.14 ppm was downfield-shifted to 6.50 ppm upon complexation with EtOH, which was further downfield-shifted to 6.78 ppm by complexation with CH_3CN. It is probable that the included EtOH might



1 : X = Br

2 : X =





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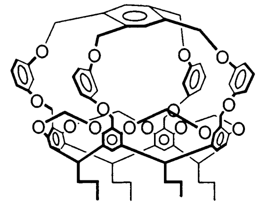

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Keywords: cavitand; resorcin[4]arenes; container molecule; carceroisomerism; alcohol selectivity.

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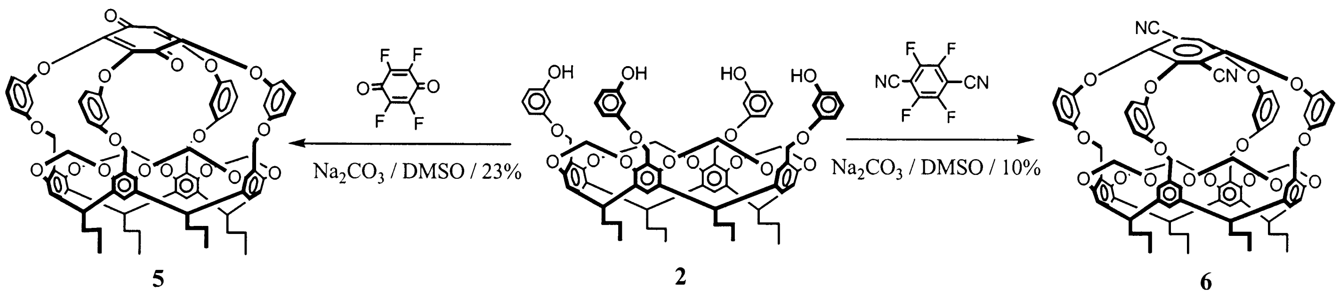

Scheme 1. Synthesis of new C_{2v} cavitands **5** and **6**.

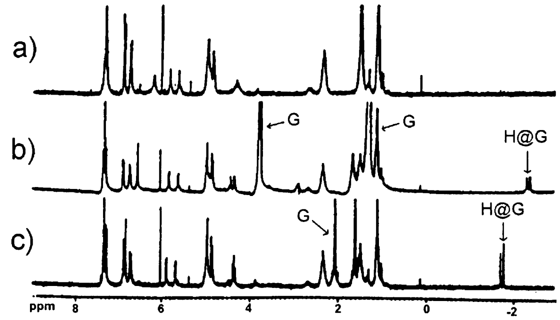

Figure 1. ^{1}H NMR spectra of (a) [host **5**] = 5.0×10^{-3} M; (b) addition of [CH_3CH_2OH] = 1.0×10^{-1} M; (c) addition of [CH_3CN] = 6.0×10^{-2} M in $CDCl_3$ at 23°C.

relocate the hydrogen from the shielding zone of the cavitand. The corresponding 2-hydrogen of 1,3-dimethoxybenzene appears at 6.50 ppm in $CDCl_3$. The further downfield-shift by CH_3CN is quite interesting, which is presumably due to the additional deshielding effect of C≡N bond. Similar phenomena to this hydrogen (CH_3CN; 5.92→6.64 ppm, EtOH; 5.92→6.33 ppm) were observed for host **6**.

The two peaks of the CH_3 group of complexed EtOH and CH_3CN in hosts **5** and **6** suggests the carceroisomerism at 23°C.[7] The two peak ratios of EtOH in **5** (0.84:1) or in **6** (0.71:1) and that of CH_3CN in **5** (0.99:1) or in **6** (0.71:1) may represent the ratios of carceroisomers due to the different orientation of guests through the C_2 axis and their slow inversion at 23°C. Also, the smaller ratio in **6** (~0.71) than that in **5** (0.84–0.99) suggests that, compared to **5**, the cavity of **6** is smaller and one carceroisomer is more populated than the other.

Table 1 shows the chemical shift difference ($\Delta\delta$ in ppm) of guest's starred hydrogen in $CDCl_3$ at 23°C, the association constants K_a (M^{-1}). The chemical shifts of methyl groups of ethanol, *n*-propanol and acetonitrile in host **6** are far upfield shifted ($\Delta\delta = 3.68$, 3.95 and 3.79, respectively) compared to that of protons of methylene chloride ($\Delta\delta = 1.04$), which means the methyl groups of alcohols and acetonitrile are far better nested in resorcin[4]arene moiety. The largest $\Delta\delta$ of 3.95 ppm was observed for *n*-propanol which accurately fits the CPK model.

The K_a value of ethanol in host **5** is the largest. The striking size selectivity for ethanol ($K_a = 260$ M^{-1}) versus methanol ($K_a = 0$ M^{-1}) and *n*-propanol ($K_a = 5$ M^{-1}) by host **5** is impressive. As far as we know host **5** is one of the smallest ethanol selective container hosts. However, the electronic conditions of caps (1,4-quinone versus 1,4-dicyanobenzene unit) seemed not to effect their binding properties, because the K_a values for EtOH by **5** and **6** ($K_a = 260$ M^{-1} versus 252 M^{-1}) and for CH_3CN ($K_a = 118$ M^{-1} versus 122 M^{-1}) are quite similar.

Table 2 shows thermodynamic parameters for complexation obtained by the Van't Hoff equation. It is quite

Table 1. ^{1}H NMR (300 MHz) spectral chemical shift changes of guest-hydrogen's (*) chemical shifts and the association constants K_a (M^{-1}) in $CDCl_3$ at 23°C of free and complexed guests in hosts **5** and **6**

Host	Guest	Free δ	Compl δ	$\Delta\delta$ (ppm)	K_a (M^{-1})
5	$C\overset{*}{H}_3OH$	1.11	–	–	–
5	$C\overset{*}{H}_3CH_2OH$	1.25	−2.40	3.68	260
5	$C\overset{*}{H}_3CH_2CH_2OH$	0.95	−3.00	3.95	5
5	$C\overset{*}{H}_3CHOHCH_3$	1.00	–	–	–
5	$HOC\overset{*}{H}_2CH_2OH$	3.75	−0.11	3.86	12
5	$CH_3C\overset{*}{H}O$	9.80	9.00	0.80	90
5	$C\overset{*}{H}_3NO_2$	4.34	0.52	3.82	56
5	$C\overset{*}{H}_2Cl_2$	5.32	4.28	1.04	208
5	$C\overset{*}{H}_3CN$	2.02	−1.77	3.79	118
6	$C\overset{*}{H}_3CH_2OH$	1.25	−2.51	3.76	252
6	$C\overset{*}{H}_3CN$	2.02	−1.88	3.90	122

Table 2. Thermodynamic parameters for complexation at 296 K in $CDCl_3$

Caviplex	$-\Delta G°$ (kcal mol^{-1})	ΔH (kcal mol^{-1})	ΔS (cal mol^{-1} K^{-1})
5@ethanol	3.47	3.75	23.80
5@acetonitrile	3.14	−3.56	−1.71
5@acetaldehyde	2.60	−1.16	5.32

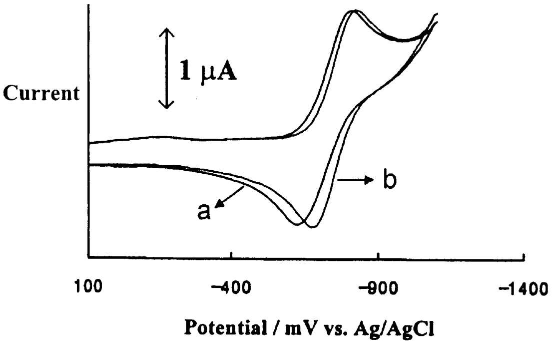

Figure 2. Cyclic voltammogram of **5**; (a) cavitand **5**, (b) cavitand **5**+acetonitrile (50 equiv.); [**5**] = 1.0 mM in $CHCl_3$ (+0.1 M TBAP), scan rate = 50 mV s^{-1}, gold working electrode, platinum counter electrode.

interesting that the complexation of EtOH is enthalpically disfavored, but entropically favored. However, the complexations of acetonitril or aldehyde are all enthalpically favored.

The electrochemical sensitivity of host **5**, a reversible one-electron process, was observed by cyclic voltammetry and its complexation with acetonitrile resulted in a faster oxidation compared to its reduction in $CHCl_3$ as shown in Fig. 2.

Water-solubilizing as well as functionalization with the photoluminescent chromophore of cavitands **5** and **6** are in progress.

Acknowledgements

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6. **5**: mp>356°C (dec.): FAB+MS *m*/*z* 1293.36 (M^+ 33%): FT-IR (KBr) 1611 cm^{-1} ($\nu_{C=O}$): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.12 (t, 12H, CH_3), 1.27–1.47 (m, 8H, $CH_2\mathit{CH_2}CH_3$), 2.29–2.31 (m, 8H, $\mathit{CH_2}CH_2CH_3$), 4.27 (m, 4H, inner $O\mathit{CH_2}O$), 4.84–4.94 (m, 12H, methine+ $Ar\mathit{CH_2}O$), 5.58 (d, 2H, outer $O\mathit{CH_2}O$), 5.78 (d, 2H, outer $O\mathit{CH_2}O$), 6.14 (s, 4H, catechol's H), 6.68 (d, J = 8.01, 4H, catechol's H), 6.85 (d, J = 8.31, 4H, catechol's H), 7.28 (m, 8H, $Ar\mathit{H}$+catechol's H): ^{13}C NMR (400 Hz, $CDCl_3$) δ 14.6 (CH_3), 22.5 ($CH_3\mathit{CH_2}CH_2$), 32.2 ($CH_3CH_2\mathit{CH_2}$), 36.8 (CH), 60.5 ($Ar\mathit{CH_2}$), 101.2, 102.4 ($O\mathit{CH_2}O$), 106.1, 111.1, 131.4, 144.3, 158.5, 160.1 (resorcinol's Ar*C*), 121.7, 123.8, 137.8, 138.5, 154.6, 155.1 (resorcin[4]aren's Ar*C*), 176.3 (cap C=O)
   6: mp>347°C (dec.): FAB+MS *m*/*z* 1313.13 (M^+ 100%): FT-IR (KBr) 2537 cm^{-1} ($\nu_{C\equiv H}$): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.06 (t, 12H, CH_3), 1.27–2.06 (m, 8H, $CH_2\mathit{CH_2}CH_3$), 2.23–2.30 (m, 8H, $\mathit{CH_2}CH_2CH_3$), 4.25 (m, 4H, inner $O\mathit{CH_2}O$), 4.81–4.93 (m, 12H, methine+ $Ar\mathit{CH_2}O$), 5.51 (d, 2H, outer $O\mathit{CH_2}O$), 5.87 (bs, 6H, catechol's H+outer $O\mathit{CH_2}O$), 6.64 (d, J = 3.57, 4H, catechol's H), 6.90 (d, J = 8.25, 4H, catechol's H), 7.28 (m, 8H, ArH+catechol's H): ^{13}C NMR (400 Hz, $CDCl_3$) δ 14.1 (CH_3), 20.9 ($CH_3\mathit{CH_2}CH_2$), 31.9 ($CH_3CH_2\mathit{CH_2}$), 36.3 (CH), 60.1 ($Ar\mathit{CH_2}$), 101.6, 103.4 ($O\mathit{CH_2}O$), 106.1, 111.7, 131.3, 147.9, 158.5, 159.7 (resorcinol's Ar*C*), 121.4, 123.2, 138.7, 154.6 (resorcin[4]aren's Ar*C*), 121.4 (cap C≡N).
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