Comparisons of Activation Energies for Guest Escapes from the Inner Phases of Hemicarcerands with Varying Numbers of Bowl-linking Groups

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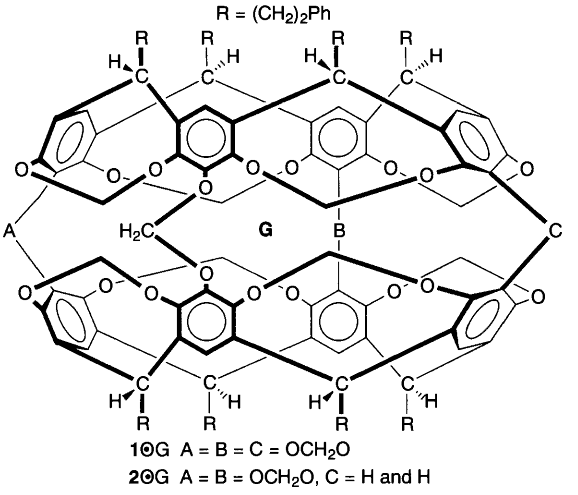
The syntheses and characterization of new hemicarcerands **3** and new complexes of **4** are described; the half-lives and activation energies for incarcerated Me_2NCHO and Me_2NCOMe escaping from the inner phases of **2** and **4** are compared.

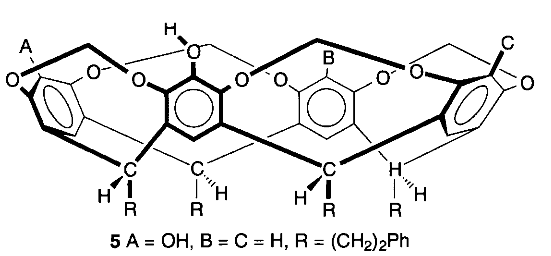
We wished to compare the binding properties of the series of hosts **1**–**4** in which the general rigidity of the shells defining the central cavity and the sizes and numbers of the portals were systematically varied. Carceplexes **1**⊙G,†[1] hemicarceplexes **2**⊙G[2] and **4**⊙Me_2NCOMe[2] have been reported, and here we describe the syntheses and constrictive binding properties of new complexes of **4**‡ and the new host **3**.‡ Polyols **5**–**8**, the immediate precursors of **3**, **4**, **2** and **1**, have been synthesized as mixtures separable by chromatography.[2] Whereas **7** and **8** were easy to purify directly, the isomeric diols **5** and **6** (as their dibenzoates) were difficult to separate from one another.[2]§ Therefore, we developed a new means of purifying the two diols which is interesting in its own right.

Treatment of a 1 : 2 ratio (^{1}H NMR) of the respective diols **5** and **6**[2] with 2 mol of dibromide **13**‡,¶ (Me_2NCOMe, Cs_2CO_3, 66 h, 25 °C, argon, high dilution) gave after chromatographic separation on silica gel–CH_2Cl_2–EtOAc a 35% yield of the mono-bridged cycle **9**‡ and a 10% yield of the doubly-bridged compound **10**.‡ Reduction of **9** and of **10** (Pd/C, H_2, EtOH) provided (after silica gel chromatography, EtOAc–hexanes) diols **5**[2] (77%) and **6**[2] (77%), respectively. Each of these diols was submitted to a shell-closure reaction with $BrCH_2Cl$ (Cs_2CO_3, argon, 60 °C, 12 h; then 100 °C, 48 h) in purified, degassed Me_2SO, Me_2NCOMe and Me_2NCHO as solvents to give, after chromatographic purification, free hemicarcerand **3**‡ (50, 38 and 20%, respectively), and the respective hemicarceplexes: **4**⊙Me_2NCOMe,[2] 20%; **4**⊙Me_2SO,‡ 28%; and **4**⊙Me_2NCHO,‡ 22% (procedures patterned after those in ref. 2). When **4**⊙Me_2NCHO was heated at 170 °C for 18 h in 2,4,6-$Cl_3C_6H_2Me$, a hundredfold excess of $MeOCH_2OMe$ was added, and the heating was continued for 24 h, **4**⊙$MeOCH_2OMe$‡ was produced (90%, evaporation and precipitation with MeOH).

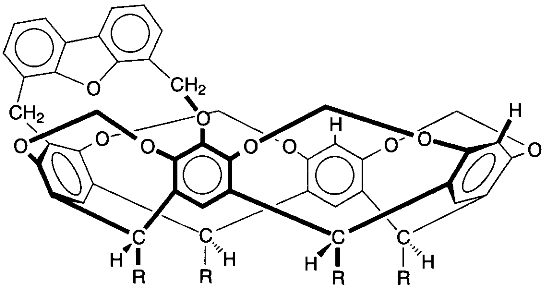
Preliminary ^{1}H NMR spectral experiments with **3** established that although **3**⊙Me_2NCOMe could briefly be detected at ambient temperature, the hemicarceplex decomplexed rapidly enough on the human time-scale to make kinetic experiments unfeasible. At the other extreme, **1**⊙G, with G = Me_2SO, Me_2NCOMe or Me_2NCHO, liberates its guest only at temperatures which cause host bond ruptures.[1] The decomplexation of **2**⊙Me_2SO in $C_6D_5NO_2$ was undetected after 18 h at 180 °C, the temperature limit for our Bruker AM500 ^{1}H NMR variable-temperature probe (calibrated with a $HOCH_2CH_2OH$ standard).



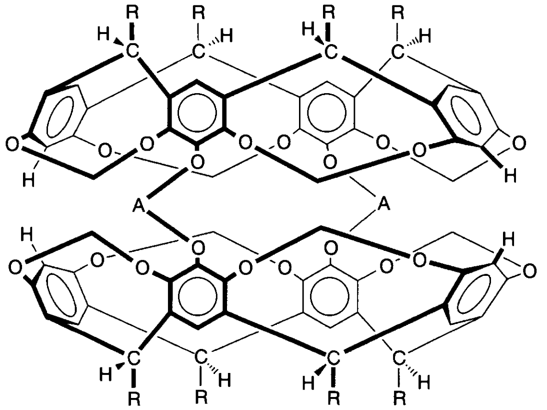
1⊙G A = B = C = OCH_2O
2⊙G A = B = OCH_2O, C = H and H
3⊙G A = OCH_2O, B = C = H and H
4⊙G B = OCH_2O, A = C = H and H



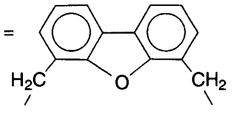
5 A = OH, B = C = H, R = $(CH_2)_2Ph$
6 A = C = H, B = OH, R = $(CH_2)_2Ph$
7 A = B = OH, C = H, R = $(CH_2)_2Ph$
8 A = B = C = OH, R = $(CH_2)_2Ph$

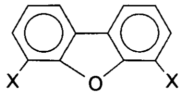


9 R = $(CH_2)_2Ph$



10 R = $(CH_2)_2Ph$, A =





11 X = CO_2H
12 X = CH_2OH
13 X = CH_2Br

However, the kinetics of decomplexation of 2⊙G and 4⊙G were conveniently followed in $C_6D_5NO_2$ as solvent at four temperatures in the range 130–170 °C with G = Me_2NCHO and Me_2NCOMe by watching the signal disappearance of the inward-pointing proton of the intrahemispheric bridges of the complex, and the appearance of the same proton's signals of the empty hosts. Good first-order rates were observed. Table 1 records the half-lives for decomplexation as a function of temperature and the derived activation energies for decomplexation. The kinetic techniques resemble those detailed in an earlier publication involving hemicarceplex **14**.[3]

Examination of Corey–Pauling–Koltun molecular models of **1**–**4** in those conformations found in the crystal structures of **1**⊙Me_2NCOMe[1] and **2**⊙Me_2NCHO[2] led to the following conclusions: (*a*) The cavity dimensions of all four hosts are very similar; (*b*) host **1** contains no portal, the portal dimensions and shapes of **2** and **4** are very similar to one another, whereas those of **3** are less well defined; (*c*) the four host models differ the most in the flexibility of their portals in the order **3** $\gg$ **4** $\geqslant$ **2** $\gg$ **1**. This order corresponds to that of the stability of the complexes; (*d*) the degree of freedom in **3** absent in the other hosts lies in the ability of its two hemispheres to bend back from one another and to rotate away from the long axis of the host common to those two hemispheres. Both movements open the portal; (*e*) intuitively, one might conclude that **4** with only two OCH_2O bridges should be much more flexible than **2** with three rigidifying bridges. Model examination of **4** indicates that steric repulsions between atoms lining one of the two portals inhibits opening of the opposite portal, almost as much as substituting a OCH_2O group for two hydrogens as in **2**. Thus the constraints on the two portals of **4** resemble those of the single portal of **2**. The activation energies (E_a) for decomplexation of **2**⊙Me_2NCHO and **4**⊙Me_2NCHO are indistinguishable at 100 kJ mol^{-1}, whereas those of **2**⊙Me_2NCOMe and **4**⊙Me_2NCOMe are within error of one another at 84 and 92 kJ mol^{-1}, respectively. Thus, the activation energies are host independent but guest dependent, the larger guest possessing the lower activation energy for decomplexing. We attribute this to greater compression in the complexes of Me_2NCOMe than in those of the smaller Me_2NCHO. A CPK model of the former guest's complex is difficult to assemble compared to the latter. This compression appears to be released in going to the respective transition states for decomplexation.

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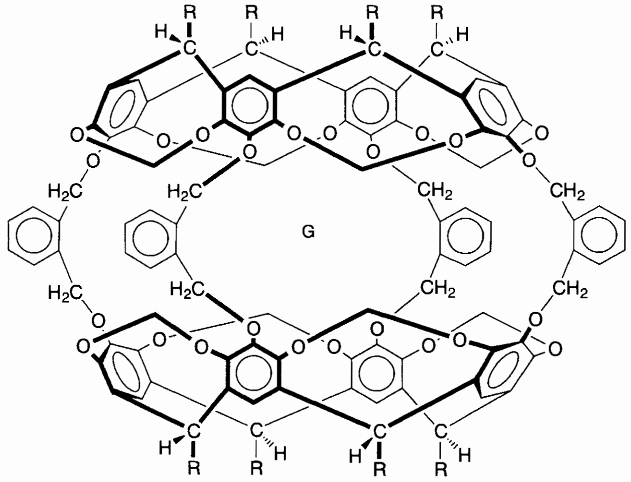
Table 1 Half-lives for decomplexation of 2⊙G and 4⊙G in $C_6D_5NO_2$

	$t_{1/2}$/h					E_a/
Complex	130 °C	140 °C	150 °C	160 °C	170 °C	kJ mol$^{-1\,a}$
2⊙Me_2NCHO	3.6	2.1	1.2	0.4		100 (16)
4⊙Me_2NCHO	3.1	2.4	1.2	0.4		100 (22)
2⊙Me_2NCOMe		5.1	2.8	1.9	0.9	84 (5)
4⊙Me_2NCOMe		5.5	3.6	2.1	1.1	92 (9)

[a] Calculated from least-squares fit to straight line.



14⊙G R = $(CH_2)_2Ph$

Footnotes

† The symbol ⊙ signifies incarceration of guests in hosts, and the symbol ◡ is used for nesting, perching or partially encapsulated complexes.

‡ These compounds gave C + H elemental analyses within 0.30% of theory, M^+ *m*/*z* signals of substantial intensity in their MS or FAB-MS, and ^1H NMR spectra consistent with their structures; **4**⊙Me_2SO was an exception—only the ^1H NMR spectrum was taken.

§ Reinhoudt *et al.*[4] reported a superior synthesis of an analogue of **5** with four n-$C_{11}H_{23}$ groups in place of our $(CH_2)_2Ph$ groups. They also shell-closed their diol to give the corresponding hemicarcerand analogue of **3**.

¶ Dibromide **13**‡ was synthesized by the sequence dibenzofuran → **11** → **12** → **13** as follows. Dibenzofuran was dimetallated with *sec*-BuLi, tetramethylethylenediamine and Et_2O under argon for 36 h at 25 °C, and the product was carbonated with CO_2 to give **11** (characterized only by ^1H NMR, 30%). Reduction of **11** with $BH_3{\cdot}O(CH_2)_4$ at 25 °C for 3 h gave diol **12** (74%), which when treated with PBr_3 in C_6H_6 under argon at 25 °C for 15 min gave **13** (88%). Examples of model conversions are found in E. B. Schwartz, C. B. Knobler and D. J. Cram, *J. Am. Chem. Soc.*, 1992, **114**, 10775.

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