Constrictive Binding by an Octalactone Hemicarcerand

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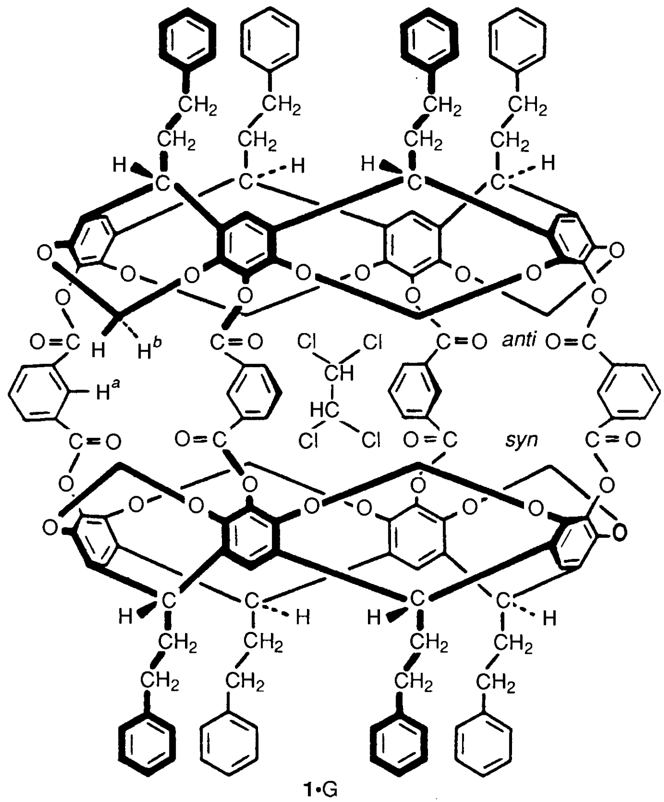
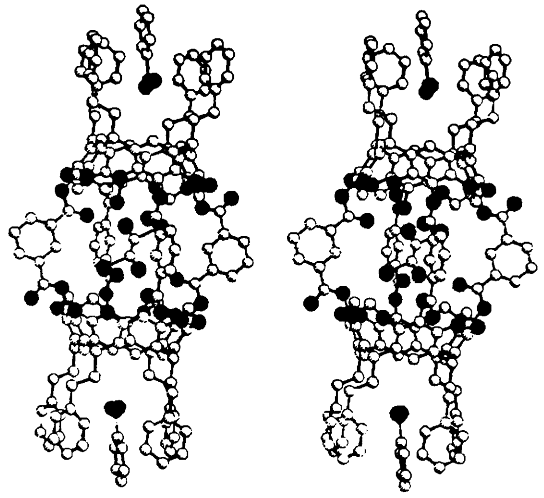
The synthesis, characterization (including a crystal structure determination) and constrictive binding properties of a hemicarcerand are described.

We reported previously the synthesis of a hemicarcerand with one opening in its shell through which guests such as Me_2NCOMe, Me_2NCHO and Me_2SO incarcerated during shell closures could be expelled at high temperatures. New guests of sizes complementary to or smaller than the hemicarcerand's interior were then introduced at appropriate temperatures to give isolable 1 : 1 complexes with guests such as MeCN, CS_2, pyridine, CH_2Br_2 and xenon.[1]

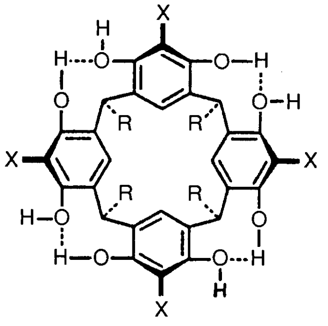
Here we report the synthesis, crystal structure and binding properties of hemicarcerand **1** with a cavity of much larger



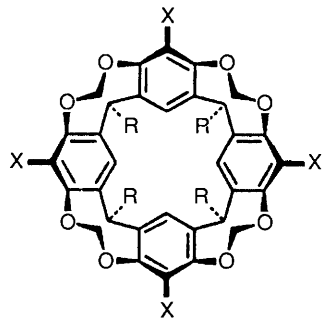
1•G



$1\cdot Cl_2CHCHCl_2\cdot 2PhNO_2$



2, X = H, R = CH_2CH_2Ph
3, X = Br, R = CH_2CH_2Ph



4, X = Br, R = CH_2CH_2Ph
5, X = OH, R = CH_2CH_2Ph

dimensions and with four large portals that can admit and accommodate larger guests. The synthetic sequence, resorcinol + dihydrocinnamaldehyde → **2** → **3** → **4** → **5**, has been reported.[1] Treatment of **5** with isophthaloyl dichloride–Cs_2CO_3–Me_2NCOMe (dry) at 65 °C under argon for four days gave **1**·G, which was purified by silica gel chromatography with CH_2Cl_2 as the mobile phase to give **1**·CH_2Cl_2 (5% yield; R_f 0.27, silica gel, CH_2Cl_2; FAB MS, M + H^+, *m/z* 2554, 100%; anal. calcd. for $C_{160}H_{120}O_{32}$ + CH_2Cl_2, dried at 120 °C for 12 h, C, 73.3 H, 4.7. Found: C, 73.4; H, 4.4%). When heated in $Cl_2HCCHCl_2$ at 110 °C under argon for 12 h, **1**·CH_2Cl_2 underwent guest exchange to give (after silica gel chromatography, $CHCl_3$) **1**·$Cl_2HCCHCl_2$ (90% yield; R_f 0.27, silica gel, $CHCl_3$; FAB MS, M·$Cl_2HCCHCl_2^+$, *m/z* 2720 cluster, 90%, M + H^+ *m/z* 2553 cluster, 100%; anal. calcd. for $C_{160}H_{120}O_{32}$ + $C_2H_2Cl_4$: C, 71.5, H, 4.5, found: C, 71.55, H, 4.5%)

A sample of **1**·$Cl_2HCCHCl_2$ was recrystallized from $PhNO_2$ to give **1**·$Cl_2HCCHCl_2$·$2PhNO_2$ to give crystals suitable for crystal structure determination (*R* = 0.12).† Notice in the stereoview of the result that $Cl_2HCCHCl_2$ resides in the cavity with its long axis roughly coincident with the long axis of the host. One molecule of $PhNO_2$ solvate is inserted between the four CH_2CH_2Ph groups attached to the top, and a second between those attached to the bottom of the central globe-shaped container.

The 360 MHz ^1H NMR spectrum of **1**, whose H^a and H^b protons protrude into the cavity, is complicated since each of the four bislactone bridging groups contains one *syn* and one

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† *Crystal data* for: **1**, triclinic, space group $P\bar{1}$, a = 15.884(7), b = 15.985(7), c = 21.691(11) Å; α = 101.878(8); β = 108.085(9), γ = 96.142(9)°, U = 5036 Å^3, Z = 1; 10347 reflections; 3630 with $I > 3\sigma(I)$ used in structure solution, $2\theta_{max}$ = 100°, Cu-Kα radiation, Syntex $P\bar{1}$ diffractometer. Final R 0.125, R_w 0.165. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre See Notice to Authors, Issue No. 1.

anti conformation. The δ values of H^a (singlets) are guest-sensitive, while those of H^b (doublets) are both conformation- and guest-sensitive. For example, in $CDCl_3$, the H^a protons of **1**·$CDCl_3$ give δ 8.55, whereas those of **1**·$Cl_2HCCHCl_2$ give δ 8.85. The eight H^b protons of **1**·$CDCl_3$ give three types of signals, δ 5.07 (2H), 4.72 (4H) and 4.62 (2H). The corresponding eight H^b protons of **1**·$Cl_2HCCHCl_2$ signals are δ 4.39 (2H), 4.67 (4H) and 4.39 (2H). We conclude that the H^b chemical shifts are moved upfield by the shielding carbonyl groups whose positions are rigidified by the larger $Cl_2HCCHCl_2$ as compared to the smaller $CDCl_3$ guest solvent. The two sets of two H^b protons that provide the larger Δδ values (0.23 to 0.68 ppm) are those located between the two inward-turned carbonyl groups. The one set of four H^b protons that provides the smallest Δδ value (0.05) is flanked by one inward- and one outward-turned carbonyl group. This interpretation is consistent with **1**·$Cl_2HCCHCl_2$ having the same conformational arrangement of lactone linkages in the crystal as it has in solution. The proton signal of the guest at δ 6.13 in **1**·$Cl_2HCCHCl_2$ is 0.17 ppm downfield of free $Cl_2HCCHCl_2$ dissolved in $CDCl_3$. At higher temperature, the lactone conformations of **1**·$Cl_2HCCHCl_2$ in $Cl_2DCCDCl_2$ equilibrate to provide a symmetrical time-average ^1H NMR spectrum with T_c for H^b of 80 °C, and a $\Delta G^\ddagger$ value for the transition of *ca.* 18 kcal mol^{-1} (1 cal = 4.184 J).[2]

Complex **1**·$Cl_2HCCHCl_2$ is stable indefinitely at room temperature as a solid or in solution, but slowly decomplexes at 100–134 °C. The first-order rate constants for decomplexation of **1**·$Cl_2HCCHCl_2$ in $Cl_2DCCDCl_2$ to give **1**·$Cl_2DCCDCl_2$ were followed by the disappearance of the ^1H NMR signal for the guest protons at δ 6.13 (7 points per run) at 100, 112, 122 and 134 °C, whose van't Hoff plot provided $E_a = 24.6 \pm 4.7$ kcal mol^{-1} for the decomplexation. At 100 °C the $t_{1/2}$ value was 18 h. We believe the complex is held together largely by steric interactions that inhibit decomplexation. We propose the term, *constrictive binding*, to describe this type of interaction which holds host–guest complexes together. It probably accounts for a major part of the activation free energy for dissociation of **1**·$Cl_2HCCHCl_2$.

A survey employing ^1H NMR and TLC criteria for complex formation was conducted for **1**·CH_2Cl_2 when dissolved in potential guests as solvents. Of those tried, acetylmorpholine and *o*-dichlorobenzene formed characterizable complexes at 110–125 °C, whereas *p*-dichlorobenzene, *p*-xylene, tetrabromoethane, *p*-cyanotoluene, nitrobenzene and triethyl phosphate failed to provide isolable complexes.

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References

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2 J. Sandström, *Dynamic NMR Spectroscopy*, Academic Press, New York, 1982, p. 96.