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2

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6

deny occupancy to all but slim linear guests.

Treatment of **4** (conformationally mobile)[6] with appropriate dialkyldichlorosilanes in THF–Et$_3$N at high dilution closed four eight-membered rings to give **1**, **2**, and **3**[7] in 37%, 9%, and 7% yields, respectively. Although melting at >320 °C, **1–3** were soluble in nonpolar solvents. Evaporation of **1** in CS$_2$ gave crystalline **1·2CS$_2$** of X-ray quality.

The Benesi–Hildebrand method[8] for determining association constants (K_a) from ^{1}H NMR chemical shift changes[9] was applied to **1** (0.001 M) complexing CS$_2$ (0.1–2 M) in CDCl$_3$ (five to ten points per run). Upon complexation, protons "a" lining the well bottom in **1** moved upfield from 7.35 maximumly by 0.18 ppm. Protons "b" lining the upper sides in **1** moved downfield from –0.55 maximumly by 0.40 ppm. The outward-facing protons remained unchanged (±0.04 ppm). Similar experiments produced similar changes for protons "a", "b", and "c" of **2** and **3**. At 250 K, K_a (M^{-1}) values were, **1**, 0.82, **2**, 8.1, and **3**, 13.2.[10] From the differences in K_a values determined at 212, 250, 275, and 300 K for **1** binding CS$_2$, the following values were estimated (kcal mol^{-1} at 212 K): ΔG, –0.4; ΔH, –3.5; $T\Delta S$, –3.1. Thus enthalpy favors and entropy disfavors complexation. At 300 K, **1** binds CS$_2$ in CDCl$_3$ with ΔG = +0.91 and, in C$_6$D$_6$, with ΔG = +1.02 kcal mol^{-1}.[11] Even at 212 K in CDCl$_3$, the signals for free **1** and **1·CS$_2$** merged. Thus ΔG^* for decomplexation is <10 kcal mol^{-1}. Similar experiments with **1** and CH$_3$C≡CH in CDCl$_3$ produced similar spectral shifts. However, mixing C$_6$H$_6$, I$_2$, CH$_3$I, K$_3$Fe(CN)$_6$, *t*-BuNH$_3$SCN, H$_2$O, CO$_2$, or CH$_2$Cl$_2$ with **1** in CDCl$_3$ produced none, nor did mixing of CHCl$_3$ with solutions of **1** in C$_6$D$_6$. The signals for only protons "a" and "b" of **1** were significantly broadened when **1** in CDCl$_3$ was saturated with O$_2$ at 250 K.

Displacement of O$_2$ with N$_2$ reproduced sharp peaks. Thus **1–3** complex linear molecules CS$_2$, CH$_3$C≡CH, and O$_2$ but not detectably noncomplementary guest candidates.

In drawings **5** and **6** of the crystal structure of **1·2CS$_2$**[12a], the CS$_2$ molecule which lies between molecules of complex is omitted. The other CS$_2$ beautifully occupies the well of the host.[12b] The magnitudes and directions of the ^{1}H NMR resonance shifts in the spectra of **1·CS$_2$**, **2·CS$_2$**, and **3·CS$_2$** are consistent with the solution structures of these complexes being similar to the crystal structure of **1·CS$_2$**. Molecular model examination and the chemical shift patterns of the indicator protons at the bottom and top of the well in **1·HC≡CCH$_3$** require that the C≡CH end of CH$_3$C≡CH is inserted into the well. The existence of a totally organized organic complex for O$_2$ is unprecedented[13] and is striking considering the importance of the storage and transport of O$_2$ in biological systems.

Why do **1–3** complex slim linear molecules? In the cavitation model for dissolution, the free energy for cavity formation in the solvent (ΔG_c) is of opposite sign and similar magnitude to the free energy for solvent–solute interactions (ΔG_i).[14] Compounds **1–3** are the equivalent of benzene–alkane solvent molecules organized to form a cavity whose ΔG_c is supplied during synthesis, leaving ΔG_i unopposed.[15] Solvophobic driving forces[16] for expelling CS$_2$ from CDCl$_3$ are likely negligible, as are host–guest charge-transfer attractions between like species.[17] Thus ΔG_i appears composed of overall attractive dipole–dipole interactions. The fact that K_a^2 and $K_a^3 > K_a^1$ supports this conclusion, since host–guest interactions should increase with increasing areas of contact. Thus the principles of preorganization and complementarity[18] are applicable to designing complexes between lipophilic entities.

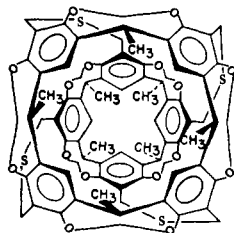(6) Högberg, A. G. S. *J. Org. Chem.* **1980**, *45*, 4498–4500.

(7) All new compounds gave C, H, and Si analyses within 0.20% of theory, MS molecular ions, and expected ^{1}H NMR spectra.

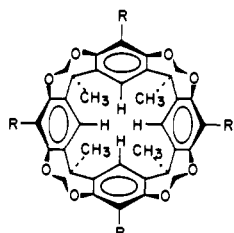(8) Benesi, H. A.; Hildebrand, J. H. *J. Am. Chem. Soc.* **1949**, *71*, 2703–2707.

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(10) Spectra were taken on a 200-MHz instrument. The R values of least-square plots were 0.98 or higher and the limit of error (twice the standard deviation) ranged from 2% to 7%.

(11) ±20%.

(12) (a) At 115 K, *a* = 11.233 Å, *b* = 20.018 Å, *c* = 10.069 Å, β = 90.84°, space group *P*2$_1$/*m*, *Z* = 2, *R* = 0.040. (b) The depth of the guest penetration into the well of the host is measured by these distances: the CS$_2$ carbon is located 0.47 Å below the plane defined by the C atoms of the four axial CH$_3$'s which form the upper rim of the cavity; the inserted sulfur lies 2.02 Å below this plane and 0.68 Å below the plane defined by the four Si atoms. The good steric fit between the complexing partners is reflected in the amplitudes of atomic thermal vibrations exhibited by the linear guest. They are relatively low and comparable to those of the rigid host. Details will be published elsewhere.

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(15) We warmly thank Professor J. Reisse, Universite Libre de Bruxelles, and Professor H. Reiss, University of California, Los Angeles, for helpful discussions of these ideas.

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Shell Closure of Two Cavitands Forms Carcerand Complexes with Components of the Medium as Permanent Guests[1]

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Absent among the over six million organic compounds reported are closed surface hosts with enforced interiors, large enough to imprison behind covalent bars guests (G) the size of ordinary solvents. We report here the shell closure of two hemispherical cavitands to form carcerand **1**, in whose interior are trapped

1

2, R = H; **3**, R = CO$_2$CH$_3$;
4, R = CH$_2$OH; **5**, R = CH$_2$Cl;
6, R = CH$_2$SH

molecular components of the medium.[2] Carcerand **1** belongs to the D_{4h} point group. Examinations of CPK molecular models reveal that the enforced cavity of **1** can easily embrace C$_6$H$_6$, (CH$_2$)$_6$, (Et)$_2$O, (CH$_3$)$_2$NCHO, (CH$_2$)$_4$O, CH$_2$Cl$_2$, CHCl$_3$, or up to six H$_2$O molecules. In models, only molecules as small as H$_2$O or O$_2$ can be forced without bond rupture into the interior of **1** through the narrow portals at the opposite ends of this egg-shaped, essentially rigid host.

Carcerand complexes, **1·G**, were prepared in seven steps (~2% overall) from resorcinol and acetaldehyde[3] through known compounds **2** and **3**[4] and new compounds **4–6**.[5] Elemental analysis of **1·G** (%): C, 62.25; H, 4.86; Cl, 0.78; Cs,[6] 2.87; N, 0.34; S, 7.93. Calcd: C, 62.51; H, 5.27; Cl, 0.78; Cs, 2.92; N, 0.34; S, 8.23; Ar, 0.24, based on a composition of (**1·**CsCl·3H$_2$O)$_{0.36}$(**1·**(CH$_3$)$_2$NCHO·2H$_2$O)$_{0.37}$(**1·**5H$_2$O)$_{0.18}$ (**1·**Ar·2H$_2$O)$_{0.09}$ in which **1** is C$_{80}$H$_{72}$O$_{16}$S$_4$.[7] This composition is only one of several model compositions consistent with the results. An FT-IR spectrum of **1·G** (mull) gave a peak at 1680 cm^{-1} (medium intensity) attributed to entrapped (CH$_3$)$_2$NCH=O, whose carbonyl band (neat) occurs at 1670 cm^{-1}.

A fast atom bombardment mass spectrum (FAB-MS, Xe gun[8]) of **1·G** gave the high-resolution m/z values (relative intensities) listed, which correspond within ±10 ppm to those calculated for the formulas that follow: found, 1417.375 (13), (M + H)$^+$ 1417.378; 1490.422 (98), (M + (CH$_3$)$_2$NCHO + H)$^+$ 1490.431; 1506.418 (39), (M + (CH$_2$)$_4$O + H$_2$O)$^+$ 1506.438; 1549.275

(100), (M + Cs)$^+$ 1549.276; 1567.270 and 1567.404 doublet (61), (M + Cs + H$_2$O)$^+$ 1567.286; 1589.247 (10), (M + Cs + Ar)$^+$ 1589.238; 1622.333 (32), (M + (CH$_3$)$_2$NCHO + Cs)$^+$ 1622.328; 1701.188 (14), (M + Cs + Cs + H$_2$O + H)$^+$ 1701.200; 1702.186 (14), (M − ^{12}C + ^{13}C + Cs + Cs + H$_2$O + H)$^+$ 1702.203, (M + Cs + Cs + HOD + H)$^+$ 1702.206. Other interesting peaks (low resolution): 1433 (33), (M + O + H)$^+$ 1433; 1581 (20), M + Cs + O$_2$)$^+$ 1581; 1584 (21), (M + Cs + ^{35}Cl)$^+$ 1584; 1717 (4), M + Cs + Cs + Cl)$^+$ 1717. No peaks were observed above 1717, nor between 1416 and 1717, not explainable in terms of guest combinations of Cs, Cl, (CH$_3$)$_2$NCHO, (CH$_2$)$_4$O, Ar, H$_2$O, O$_2$, and H. No peaks were observed corresponding to masses for guest combinations which were uncomfortable in molecular models. When highly dried **1·G** was boiled in D$_2$O for 3 days, the peak intensity ratio for [(M + Cs + D$_2$O)$^+$ 1569]/[(M + Cs + H$_2$O)$^+$ 1567] went from 0.34 to 0.85. Thus H$_2$O can depart and enter the interior of **1**. The elemental and MS analyses taken together suggest that H$_2$O largely departs from **1·G** while in the MS spectrometer.[8]

Digestion in CF$_3$CO$_2$H (120 °C, 3 h) of **1·G** containing radioactive Cs[6] gave a mixture which was flooded with water and filtered (millipore). The solid was washed (H$_2$O), dried, and found to contain only 1.4% of the Cs$^+$ originally present. Shell closure[5] of **5** and **6** in an atmosphere of ClCF$_2$CF$_2$Cl gave **1·G** whose FAB-MS gave a faint peak for (M + ClCF$_2$CF$_2$Cl)$^+$ at 1586. The gas liberated when this complex was digested with CF$_3$CO$_2$H gave low-intensity peaks in its MS at 85 (^{35}ClF$_2$C)$^+$, 87 (^{37}ClF$_2$C)$^+$, and 135 (^{35}ClF$_2$CCF$_2$)$^+$; the same ions were produced by ClCF$_2$CF$_2$Cl in a control spectrum.

We conclude the following: (1) Carcerand complexes when formed contained components of the medium as permanent guests. Smaller mobile guests (H$_2$O or D$_2$O) subsequently entered or left the host through its small portals. The permanent guests were freed from their cells only by acid-catalyzed decomposition of the carcerand shells. (2) Ions Cs$^+$ and Cl$^−$ were immobilized in equivalent amounts[9] and out of proportion to their statistical presence in the medium. The FAB-MS coupled with the elemental analysis indicated the Cs was mainly inside and Cl mainly outside the shell of **1·G**. Models show that if the final covalent bond leading to **1·G** involves an intramolecular SN$_2$ linear transition state, Cs$^+$
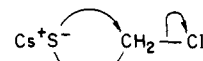
is trapped inside and Cl$^−$ is expelled from the cavity (**3**). The high-resolution MS for (M + Cs + Ar)$^+$ indicates enought argon was dissolved in the medium to be trapped during the shell closure. The MS peak intensity and the elemental analysis suggest the amount of argon is small. (4) Examinations of CPK molecular models reveal that the interior surface of **1** is complementary to the exterior surface of *anti*-ClCF$_2$CF$_2$Cl. The molecular immobilization of the latter indicates that a small amount of this Freon gas was dissolved in the medium and trapped inside the carcerand during shell closure.

We anticipate that unusual physical and chemical properties will provide unusual uses for carcerand complexes, particularly when their design renders them soluble and separable.

(1) We warmly thank the National Science Foundation for NSF Grant CHE 21-09532 which supported this research.

(2) *Carcer* in Latin and English means *prison*. The closest structural relatives of carcerands are the cavitands (Cram, D. J. *Science (Washington, D.C.)* **1983**, *219*, 1177–1183 and references therein), which *complex reversibly* small molecules such as CH$_2$Cl$_2$ (Canceill, J.; Lacombe, L.; Collet, A. *C. R. Acad. Sci. Ser. 2* **1984**, *298*, 39–42) or CS$_2$ (Cram, D. J.; Stewart, K. D.; Goldberg, I.; Trueblood, K. N. *J. Am. Chem. Soc.*, preceding paper in this issue), but not the solvent (CHCl$_3$ or C$_6$H$_6$).

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(5) All new compounds gave elemental analyses within 0.20% of theory and expected MS and ^{1}H NMR spectra. Reduction of **3** with LiAlH$_4$ gave **4** (77%), mp >360 °C. When treated with (CH$_2$CO)$_2$NCl and (C$_6$H$_5$)$_3$P, **4** gave **5** (99%), mp >360 °C dec. Thiolation of **5** with thiourea in Me$_2$SO and hydrolysis of the product with NaOH followed by acid gave **6** (71% after chromatography), mp >360 °C. To 600 mL of dry DMF containing 1.0 g of Cs$_2$CO$_3$ stirred under Ar at 60 °C was added (20 h) by syringe pump 50 mL of dry THF containing 0.398 g of **5** and 0.400 g of **6**. After an additional 10 h at 60 °C, solvent was evaporated (vacuum) to 30 mL, and 500 mL of water was added. The precipitate was collected, washed with 0.5 L of H$_2$O, 0.5 L of EtOH, 1 L of CH$_2$Cl$_2$, 1 L of EtOAc, 0.5 L of H$_2$O, 0.5 L of EtOH, and 0.1 L of CH$_2$Cl$_2$, and air dried to provide **1·G** (0.232 g, ~29%) as a white powder, mp >360 °C. The material was insoluble in hot naphthalene, C$_6$H$_5$OCH$_3$, C$_6$H$_5$NO$_2$, pyridine, and xylene.

(6) Neutron activation analysis. We warmly thank Dr. John Wasson for advice and facilities.

(7) This composition of **1·G** accommodates the observed analyses for the elements unique to G (Cs, Cl, and N) to the one element unique to **1** (S). The amount of bound water and Ar reconcile the C and H analyses common to **1** and G and the relative peak heights in the FAB-MS of those ions not containing Cs.

(8) Instrument, V. G. Analytical ZAB-2F; ion gun from Ion Tech.; bombarding gas, xenon; beam energy, 8.4 keV; accelerating voltage, 7 kV; ion source pressure, 5 × 10^{-5} mbar; matrix (HOCH$_2$CH$_2$S)$_2$.

(9) Evidence that **1·G** is not contaminated with substantial amounts of noncarcerand condensation products of **5** and **6** is as follows. (1) None were detected up to 2000-MW by FAB-MS. (2) The equivalent amounts of Cs and Cl present indicate the absence of impurities containing covalently bound Cl. (3) The S analysis suggests the absence of disulfides. (4) The elemental analyses for Cs and N indicate that ~73% of the sample contains immobilized Cs or DMF. (5) FAB-MS peak intensity comparisons between (M + (C-H$_3$)$_2$NCHO + H)$^+$ on the one hand, and (M + H)$^+$ and (M + (CH$_2$)$_4$O + H$_2$O)$^+$ on the other, coupled with the N analysis, suggest the latter complexes could account for the remaining ~27% of **1·G**. Others (Johnstone, R. A. W.; Rose, M. E. *J. Chem. Soc., Chem. Commun.* **1983**, 1268–1270) have found FAB-MS peak intensities for chorand–metal complexes to roughly measure relative amounts of complexes in a glycerine matrix.[6] The (M + O + 4)$^+$ and (M + Cs + O$_2$)$^+$ FAB–MS peaks are attributed to small amounts of carcerand sulfoxide and sulfone, respectively.