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Host–Guest Complexation. 47. Carcerands and Carcaplexes, the First Closed Molecular Container Compounds[1,2]

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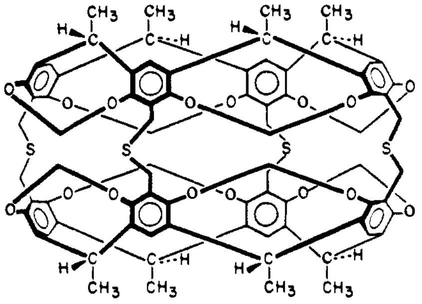
Abstract: The design, synthesis, and properties are reported for the first carcerand (**1**), a closed-surface container compound in whose interior are trapped simple organic molecules, a gas, and inorganic ions as permanent guests (G). A mixture of carcerand **1** and carcaplex **1**·G was formed by shell closure of two bowl-shaped cavitands, each containing a C_4 axis with four CH_2–X groups on their rims. The shell closure involved the reaction $(\sim CH_2{-}Cl)_4 + (\sim CH_2SCs)_4 \rightarrow (\sim CH_2SCH_2\sim)_4 + 4CsCl$ and was conducted in a mixture of $(CH_3)_2NCHO$, $(CH_2)_4O$, and Cs_2CO_3 under Ar. The insoluble carcerand–carcaplex mixture produced was purified by extensive extraction of byproducts with a variety of solvents (29% yield) and characterized. Elemental analysis demonstrated the following: the presence of N, indicating entrapped $(CH_3)_2NCHO$; the presence of Cs^+ and Cl^- in stoichiometric amounts, indicating the absence of CH_2–Cl bonds and the entrapment of at least one of these ions; carbon, hydrogen, nitrogen, and sulfur ratios compatible with **1**·G in which **1** is $C_{80}H_{72}O_{16}S_4$ and G is $(CH_3)_2NCHO$, $(CH_2)_4O$, CsCl, and Ar. An FT-IR spectrum indicated the presence of $(CH_3)_2NCHO$. The solid-state ^{13}C NMR spectrum was compatible with the structure of **1**. FAB-MS gave high-resolution *m/z* values (±10 ppm) corresponding to the carcerand and its various carcaplexes (relative intensities): $(M + H)^+$ (86); $(M + (CH_3)_2NCHO + H)^+$ (98); $(M + (CH_2)_4O + H_2O)^+$ (39); $(M + Cs)^+$ (100); $(M + Cs + H_2O)^+$ (61); $(M + (CH_3)_2NCHO + Ar)^+$ (28); $(M + (CH_3)_2NCHO + Cs)^+$ (32); $(M + Cs + Cs + H_2O + H)^+$ (14). Lower resolution peaks were observed as follows: $(M + Cs + {}^{35}Cl)^+$ (21); $(M + Cs + Cs + {}^{35}Cl)^+$ (4). No peaks were observed corresponding to masses for host–guest combinations that could not be made with CPK molecular models. Experiments with D_2O followed with FAB-MS indicated that H_2O can enter the interior of **1**. When the shell closure was conducted under an atmosphere of $ClCF_2CF_2Cl$ gas, **1**·G was shown to contain trace amounts of this gas.



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Although cubane,[3] pentaprismane,[4] and dodecahedrane[5] are closed-surface compounds, their interiors are much too small to contain simple organic compounds or inorganic ions. In 1983, we formulated what to our knowledge was the first closed-surface hydrocarbon sphere with an enforced interior of sufficient size to embrace simple organic compounds, inorganic ions, or gases. We also discussed the interesting questions that arose regarding the physical and chemical properties of imprisoned guests.[6]

In CPK models, the envisioned hydrocarbon (**2a** or **2b**, $C_{96}H_{72}$) appears essentially strain free and is about the size of a large cantalope, with an interior the size of a large orange. The surface is composed of 12 benzene rings woven together with 24 methylene groups substituted in the 1, 2, 4, and 5 positions of the benzenes in patterns that compose six macrorings of structure **3** and eight medium rings of structure **4**. In **2a** the eye views the interior through an expanded **3** unit, and in **4** through an expanded **4** unit. In CPK models these holes are much too small to allow entrance or egress of chemical entities larger than electrons or protons.

"Soccer ball", a conceptually new form of carbon (C_{60}), and its higher oligomers are also closed-surface, hollow spheres with potentially enough internal volume to contain small molecules or ions. The 1986 report of lanthanum encapsulated in C_{60}[7] has been

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(1) We warmly thank the National Science Foundation for NSF Grant CHE 21-09532, which supported the research at UCLA, and NASA Grant NAG 9-41, which supported the argon and thermal analysis at UCSD done by K. Marti and R. M. Sampson.

(2) A preliminary account of some of this work has appeared: Cram, D. J.; Karbach, S.; Kim, Y. H.; Baczynskyj, L.; Kalleymeyn, G. W. *J. Am. Chem. Soc.* **1985**, *107*, 2575–2576.

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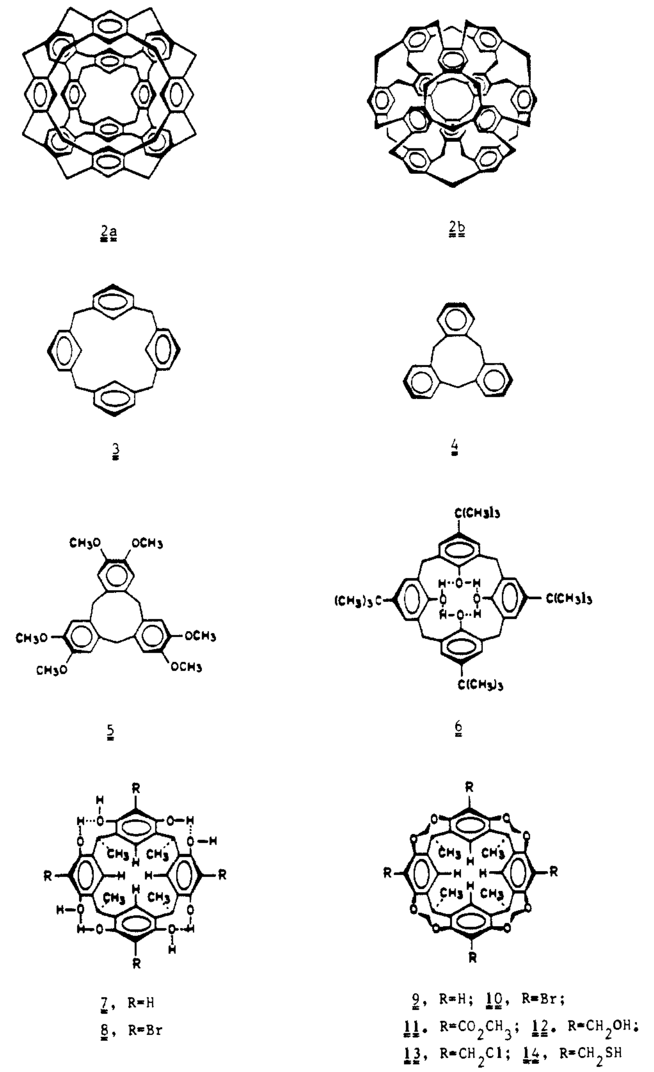
Chart I



questioned,[8] and the substances await rational syntheses and authentication.

Compound **5** has the same ring system as **4**, and **6–8** the same as **3**. Although **5–7** and their relatives have long been known, their exact structures and conformational propensities have been established only relatively recently.[9-11] Their ease of synthesis makes them attractive starting materials for adding extra bridges that rigidify them to form bowl-shaped cavitands **9** and **10**,[12,13] which are convenient starting points for the syntheses of carcerands. The present paper documents the first synthesis of a carcerand and its carcaplexes.[2,14]

Results and Discussion

Design. Molecular models (CPK) of **1** are easy to assemble and appear to be free of strain. The molecule is composed of two bowl-shaped cavitands of structure **9** coupled to each other at their rims through four CH_2–S–CH_2 groups occupying the four positions of R in **9–14**. The bridging carbons of the CH_2 groups are coplanar with their attached aryls, and the four sulfur atoms are turned inward in a square-planar arrangement, with the orbitals of their unshared electron pairs facing one another across a substantial gap. Each CH_2–S–CH_2 bridge is flanked by two O–CH_2–O bridges in a complementary packing arrangement leaving essentially no portals in this part of the shell of the molecular cell and little room for rotations about the Ar–CH_2 or CH_2–S bonds. Substitution of four O atoms for the four S atoms substantially compresses the model.

The molecule belongs to the D_{4h} point group and is shaped like an American football. Two small openings in the shell occur at the top and bottom of **1** between the four methyl groups that protrude from the molecule to form a tunnel, constricted at the inner end by four aryl hydrogens. In the crystal structures of cavitands **9** and **10**,[13] the diameters of the openings defined by these hydrogens were 2.56 and 2.62 Å. In CPK molecular models of **1**, **9**, and **10**, a model of a molecule of H_2O is the largest entity that can be forced through these holes without bond ruptures. An impression of the internal volume of **1** is gained by the fact that a model of **1** can be easily assembled around models of C_6H_6, $(CH_2)_6$, Et_2O, $(CH_2)_4O$, $(CH_3)_2NCHO$, CH_2Cl_2, $CHCl_3$, or up to six waters. A model of Freon 114 ($ClCF_2CF_2Cl$) in its anti conformation fits into a model of **1** and occupies essentially all of its internal volume.

A molecular model of **2** differs from that of **1** in several respects: that of **2** is more spherical, has a larger internal volume, and is essentially free of pores. The choice of **1** over **2** as the initial target carcerand was made because a potentially viable synthesis for **1** was readily envisioned, but those for **2** appeared much more problematic.

Synthesis. The synthesis of **1** employed either **9** or **10** as starting materials and **11–14** as intermediates. Metalation of **9**[13] with C_6H_5Li in Et_2O at 0 °C and treatment of the organometallic produced with $ClCO_2CH_3$ gave tetraester **11** (89%). Alternatively, tetrabromide **10** was metalated with BuLi and the product quenched with CO_2 to give the corresponding tetraacid, which without characterization was treated with CH_2N_2 to give **11** (40% overall). Tetraester **11** was reduced with $LiAlH_4$ in THF to give tetrol **12** (77%). Treatment of this compound with Ph_3P and *N*-chlorosuccinimide gave tetrachloride **13** (65%). Thiolation of **13** with thiourea in $(CH_3)_2SO$ and hydrolysis of the intermediate produced with base led to **14** (56%).

The critical shell-closing step involved making four carbon–sulfur bonds. A solution of stoichiometric amounts of tetrachloride **13** and tetrathiol **14** in $(CH_2)_4O$ was added under high dilution conditions to a mixture of $(CH_3)_2NCHO$ and pulverized Cs_2CO_3 stirred under an atmosphere of Ar at 60 °C under dry conditions. The finely divided mixture of **1** and **1·G** (G stands for incarcerated guest entities) produced was washed with large volumes of water, EtOH, CH_2Cl_2, $CHCl_3$, and EtOAc. The resulting material (~29%, a gray-white powder) proved to be essentially insoluble in hot naphthalene, anisole, nitrobenzene, pyridine, or xylene.

Elemental Analysis and IR Spectrum. The virtual insolubility and infusability (mp >360 °C) of this carcerand–carcaplex mixture prohibited further purification and separation into its components. Elemental analysis of the material showed the presence of C, H, N, S, Cl, Cs, and Ar, whose percentages added to 79.05%. The remaining 20.95% was treated as if it were oxygen. The Cs content was determined by neutron activation analysis.[15] The Ar analysis is discussed in a future section.

The source of nitrogen in the material was demonstrated to be due to $(CH_3)_2NCH{=}O$. An FT-IR spectrum of **1·G** as a mull gave a peak at 1680 cm^{-1} (medium intensity), which compares with the carbonyl band of 1670 cm^{-1} observed for a neat sample of $(CH_3)_2NCH{=}O$. The Cs and Cl analyses indicate these elements to be present in stoichiometric amounts and thus present only as CsCl. Thus none of the chloride can be covalently bound

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

Chart II

	C	H	N	O	S	Cl	Ar	Cs
found, %	62.25	4.86	0.34	20.95	7.93	0.78	0.016	2.87
theory, %	62.19	4.98	0.34	20.92	7.92	0.77	0.016	2.87

to carbon as it is in the starting material, **13**, but must have originated from Cl^- and Cs^+ ions produced during the reaction. The Cs^+ present is accounted for without HCO_3^- or CO_3^{2-}. The Ar present in **1**·G must have originated from the use of Ar as an inert atmosphere for the reaction, a small amount of which was dissolved in the medium.

Sulfur is unique to **1**, nitrogen to $(CH_3)_2NCHO$, chloride to CsCl, and Cs to CsCl. Argon ordinarily is nonbonded. The percentages of these elements in **1**·G allowed the numbers of atoms present to be calculated relative to those of S. Since **1** contains four sulfur atoms, eq 1 expresses the observed molecular formula

$$C_{83.84}H_{77.99}O_{21.18}S_4N_{0.39}Cl_{0.35}Cs_{0.35}Ar_{0.0065} \quad (1)$$

of **1**·G. The molecular formula for **1** itself is $C_{80}H_{72}O_{16}S_4$, which when applied to eq 2 gives eq 3, which separates the contributions

$$(C_{80}H_{72}O_{16}S_4)\cdot C_{3.84}H_{7.99}\cdot O_{5.18}\cdot N_{0.39}Cl_{0.35}Cs_{0.35}Ar_{0.0065} \quad (2)$$

$$(C_{80}H_{72}O_{16}S_4)\cdot 0.39[(CH_3)_2NCHO]\cdot C_{2.67}H_{4.66}O_{4.79}\cdot 0.35(CsCl)\cdot 0.0065(Ar) \quad (3)$$

of the host and guest atoms in the carcaplex. The values for N, Cl, Cs, and Ar directly provide measures of the equivalents of $(CH_3)_2NCHO$, CsCl, and Ar present as guests per equivalent of host, as indicated in eq 3. Carbon, hydrogen, and oxygen are common to **1**, $(CH_3)_2NCHO$, and $(CH_2)_4O$ (a potential guest), but of these elements, only carbon is absent from water, also a potential guest. Accordingly, the remaining carbon is accounted for in terms of $(CH_2)_4O$ as in eq 4, which also consumes all of

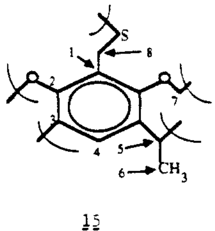
$$(C_{80}H_{72}O_{16}S_4)\cdot 0.39[(CH_3)_2NCHO]\cdot 0.67[(CH_2)_4O]\cdot 0.35(CsCl)\cdot 0.0065(Ar)\cdot O_{4.12} \quad (4)$$

the hydrogen, leaving only about four atoms of oxygen unaccounted for. Fritted glass plates were used for filtering the product during its extensive washing. Although great care was taken to avoid it, trace amounts of silica probably found their way into the analyzed sample. In the above treatment, any silica present would show up in the form of excess oxygen. The values calculated based on the composition derived from eq 4 and those actually observed are tabulated in Chart II.

This treatment of the analytical data is reasonable, but not unique. Alternative methods in which water molecules are substituted for some of the $(CH_2)_4O$ also provide good agreement between found and theory.

Solid-State Nuclear Magnetic Resonance Spectra. The insolubility of **1**-**1**·G prevented the determination of its ^1H NMR spectrum. The natural-abundance (solid state) ^{13}C spectra of **1** were determined at 22.5-MHz field at ambient temperature with 90° pulse width, 2K data points, and a magic angle spinning at 3 kHz with a Kel-F rotor. The chemical shifts are given relative to that of the CH_3 carbon set at 14.4 ppm. Two spectra were run, one with the protons irradiated to remove residual dipole–dipole coupling, and a second without proton irradiation.[16]

The signals observed are assigned in Chart III to carbons 1–8 of drawing **15**. The assignments are based on their chemical shifts compared to those of known compounds, on their relative intensities, and on whether they were present in the nonirradiated spectrum. The signals assigned to carbons 4–8 without protons attached were not observed in the unirradiated spectrum. The intensities of the signals for carbons 2 and 3 were roughly twice those due to the other carbons, which were of approximately equal intensities. The signals were all somewhat broad. Those for the aromatic carbons were ca. 90–100 Hz and those of the aliphatic carbons 170–200 Hz full width at half-maximum. The structure of **1** indicates the presence of eight equivalent carbons of types C-1, C-4, C-5, C-6, C-7, and C-8 and of sixteen equivalent carbons of types C-2 and C-3. The signal-to-noise ratio was high enough and the concentration of guest carbons to host carbons low enough to render signals due to guests invisible. The concentrations of each guest carbon of $(CH_3)_2NCHO$ per average molecule would have been about $^1/_{24}$ that for C-1 and $^1/_{48}$ that for C-2. The important features of the spectra are that the structure assigned to **1** accommodates all of the observed peaks, and structure **1** does not require any peaks that were not observed. The most unusual chemical shift was found for C-5 at δ 29.6, which compares with δ 41.9 for the methylene carbon of $(C_6H_5)_2CH_2$. However, the methine carbon of the $Ar_2(CH_3)CH$ moiety of model compound **16**[17] gives δ 29.0, close to the peak at δ 29.6 assigned to C-5 of **1**. Thus the ^{13}C NMR spectrum of **1**-**1**·G supports the structure anticipated from its synthesis and elemental analysis.



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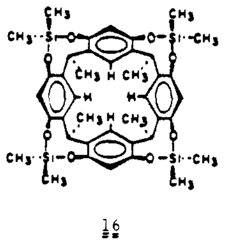

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Chart III

obsd peaks for 1-1·G (δ)	assignment	obsd peaks for models	assignment
120.6	C-1	*a*	^{13}C-aryl-CH_2
151.8	C-2	147.5	^{13}C-aryl-O of 1,3-benzodioxole[b]
137.1	C-3	*a*	^{13}C-aryl-CH_2
118	C-4	*a*	^{13}C-aryl-H
29.6	C-5	28.8	$Ar_2(CH_3)^{13}CH$ of **16**[c]
14.4	C-6	16.8	$ArCH_2{}^{13}CH_3$
100.7	C-7	100.6	$O^{13}CH_2O$ of 1,3-benzodioxole[b]
29.6	C-8	28.8	$C_6H_5{}^{13}CH_2SH$[b]

[a] Several close values for different model compounds. See: Strothers, J. B. *Carbon-13 NMR Spectroscopy*; Academic: New York, 1972; Vol. 24 of *Organic Chemistry: A Series of Monographs*; Blomquist, A. T., Wasserman, H. H., Eds. [b] Sadtler Research Laboratories Division of Bio-Rad Laboratories *Sadtler Standard Carbon-13 NMR Spectra*; Philadelphia, 1980. [c] Ph.D. Thesis of Kent D Stewart, UCLA Department of Chemistry and Biochemistry, 1984, p 150.

Table I. Fast Atom Bombardment High-Resolution Mass Spectra (Xe Gun,[a] Sample A)

ion	mass calcd	mass obsd	rel intens[b]	% of sum[c]
$(M + H)^+$	1417.378	1417.375	86	16
$(M + O + H)^+$	1433.373	1433.373	33	6
$(M + (CH_3)_2NCHO + H)^+$	1490.431	1490.422	98	19
$(M + (CH_2)_4O + H_2O)^+$	1506.438	1506.418	39	7
$(M + Cs)^+$	1549.276	1549.275	100	19
$(M + Cs + H_2O)^+$	1567.286	1567.270	61	12
$(M + Cs + 2O)^+$	1581.266	1581.245[d]	20	4
$(M + Cs + Ar)^+$	1589.238	1589.249	28	5
$(M + (CH_3)_2NCHO + Cs)^+$	1622.328	1622.333	32	6
$(M + 2Cs + H_2O + H)^+$	1701.199	1701.188	14	3
$(M - {}^{12}C + {}^{13}C + 2Cs + H_2O + H)^+$	1702.203	1702.186	14	3
$(M + 2Cs + HOD + H)^+$	1702.206			

[a] $(SCH_2CH_2OH)_2$ matrix. [b] By integration under peak clusters, arbitrary units. [c] Equal to 100 × (relative intensity)/(summed intensities of peaks listed). [d] Within 13 ppm.

Fast Atom Bombardment Mass Spectrum (FAB-MS). The carcerand–carcaplex mixture was submitted to high-resolution FAB-MS in a $(SCH_2CH_2SH)_2$ matrix with a xenon gun. Table I lists the m/z values of the eleven most prominent peaks and their

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(16) We warmly thank Dr. Charles M. Schramm for running this spectrum, and Drs. Jane Strouse and John E. Ericson for help in its interpretation.

(17) Cram, D. J.; Stewart, K. D.; Goldberg, I.; Trueblood, K. N. *J. Am. Chem. Soc.* **1985**, *107*, 2574–2575.

Table II. Fast Atom Bombardment Low-Resolution Mass Spectra (Xe Gun, Sample A and B Comparisons)[a]

	mass		rel intens in samples	
ion	calcd	obsd	A	B
$(M + H - 3CH_3)^+$	1372	1372	18	3
$(M + H - 2CH_3)^+$	1387	1388	16	5
$(M + H - CH_3)^+$	1402	1402	28	6
$(M + H)^+$	1417	1417	86	13
$(M + O + H)^+$	1433	1434	33	5
$(M + Cs - 4CH_3)^+$	1489	1489	75	4
$(M + (CH_3)_2NCHO + H)^+$	1490	1490	98	5
$(M + (CH_2)_4O + H_2O)^+$	1506	1506	39	4
$(M + Cs)^+$	1549	1549	100	100
$(M + Cs + H_2O)^+$	1567	1567	61	11
$(M + Cs + 2O)^+$	1581	1581	20	9
$(M + Cs + Cl)^+$	1584	1584	21	6
$(M + Cs + 2H_2O)^+$	1585	1585	0	4
$(M + Cs + Ar)^+$	1589	1589 ± 1	28	10
$(M + (CH_3)_2NCHO + Cs)^+$	1622	1622	32	5
$(M + (CH_2)_4O + Cs + Cl)^+$	1655	1655	0	1
$(M + (CH_3)_2NCHO + Cs + Cl)^+$	1656	1657	0	4
$(M + 2Cs + 2H)^+$	1683	1683	0	3
$(M + 2Cs + H_2O)^+$	1700	1700	28	0
$(M + 2Cs + Cl)^+$	1717	1717	0	4

[a] $(SCH_2CH_2OH)_2$ matrix.

assigned elemental compositions. Of these, ten are within ±10 ppm of theory, and one is within −13 ppm. Also listed are the relative integrations of the clusters associated with each of these peaks, and the percent contribution that each integral makes to the sum of the integrals listed. Although many low-intensity peaks were observed between 1416 and 1717 (the lowest and highest masses listed), none were observed that could not be explained in terms of appropriate combinations of **1**, $(CH_3)_2NCHO$, $(CH_2)_4O$, Cs, CsCl, Ar, H_2O, O, or these peaks minus CH_3 groups. All of the combinations of host and guest shown in Table I (and of those not included) correspond to host–guest combinations that in CPK molecular models are compatible with carcaplexes constructed with the guests located inside the hosts. No peaks were observed with masses higher than 1717. The oxygen atoms listed in $(M + O + H)^+$ (6%) and (M + Cs + 2O) (4%) are probably covalently bonded to sulfur to provide inward-turned sulfoxide or sulfone groups. Their formation probably occurred before or during shell closure.

It is interesting to compare the mole fractions of the various species suggested by elemental analysis with those suggested by FAB-MS. Equation 4 derived from elemental analysis suggests the presence of 0.39 mol of $(CH_3)_2NCHO$, 0.67 mol of $(CH_2)_4O$, 0.35 mol of Cs, and 0.0065 mol of Ar per mol of total host. The data of Table I suggest the presence of 0.25 mol of $(CH_3)_2NCHO$, 0.07 mol of $(CH_2)_4O$, 0.49 mol of Cs, and 0.05 mol of Ar. The agreement is not bad except for $(CH_2)_4O$, whose estimate from elemental analysis depended on differences between numbers and was more arbitrary than the other assignments.

A second shell closure was conducted similarly to the first. The product from the first was labeled A and that from the second was labeled B. The same conditions were employed for both shell closures but involved different batches of **13** and **14** and different experimentalists. Both product A and product B were purified by extensive washing with the specified solvents, but larger volumes were applied to the purification of B as compared to A. Sample A was the one submitted to elemental analysis. Table II compares the low-resolution FAB-MS of the two samples.

The compositions of the two samples are qualitatively similar for the major ions, but quantitatively quite different. For both A and B, the parent ion is $(M + Cs)^+$, whose intensity is set at 100. Sample A, which was washed with smaller volumes of solvent than B, appears to be generally richer in species whose interiors do not carry a net positive charge. For example, peak intensity factors for sample A compared to B for prominent ions are as follows: 7 for $(M + H)^+$; 6 for $(M + O + H)^+$; 20 for $(M + (CH_3)_2NCHO + H)^+$; 8 for $(M + (CH_2)_4O + H_2O)^+$; 5 for $(M + Cs + H_2O)^+$; 3 for $(M + Cs + Cl)^+$.

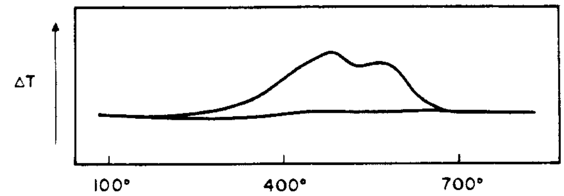


Figure 1. Differential thermal analysis of the combustion of **1**–**1**·G in air at atmospheric pressure by repeat analysis of 0.05–0.12-mg samples (temperature in °C) (ΔT in arbitrary units).

We conclude that the species presence in the **1**–**1**·G mixture produced were differentially soluble in the solvents used for purification, $(\mathbf{1}\cdot Cs)^+Cl^-$ being the least soluble of the major compounds present. In this material, the Cs^+ is inside the host, and the Cl^- is outside the host, the latter ion particularly being subject to solvation. This species gives rise directly to the $(\mathbf{1}\cdot Cs)^+$ ion in the FAB-MS, whose detection might be a more efficient process than that for those species that must undergo ionization to be detected.

Carcaplex $(\mathbf{1}\cdot Cs)^+Cl^-$ should be differentiated from carcaplex $\mathbf{1}\cdot Cs^+\cdot Cl^-$, in which both the Cs^+ and Cl^- ions are inside the carcerand and are shielded from solvation by the host. Thus $(\mathbf{1}\cdot Cs)^+Cl^-$ is a shell-separated ion pair, and $\mathbf{1}\cdot Cs^+\cdot Cl^-$ is a shell-encapsulated contact ion pair.

Other less prominent ions in the FAB-MS must have been derived from interesting carcaplexes. For example, $(M + (CH_3)_2NCHO + Cs^+)^+$ must come from $(\mathbf{1}\cdot(CH_3)_2NCHO\cdot Cs^+)Cl^-$, $(M + Cs + Ar)^+$ from $(\mathbf{1}\cdot Cs\cdot Ar)^+Cl^-$, $(M + 2Cs + Cl)^+$ from $(\mathbf{1}\cdot 2Cs\cdot Cl)^+Cl^-$, $(M + (CH_3)_2NCHO + Cs + Cl)^+$ from $\mathbf{1}\cdot(CH_3)_2NCHO\cdot Cs^+\cdot Cl^-$, and $(M + (CH_2)_4O + Cs + Cl)^+$ from $\mathbf{1}\cdot(CH_2)_4O\cdot Cs^+\cdot Cl^-$. *The striking feature of the results is that all of the entities present in the medium during the shell closure except* CO_3^{2-} *and* HCO_3^- *appear to have been incarcerated.* The absence of CO_3^{2-} and HCO_3^- probably reflects the very low solubility of Cs_2CO_3 in the medium.

Entrance of Water into the Host. Four of the molecular ions listed in Tables I and II must have come from carcaplexes containing encapsulated water. We had tried to ensure dryness during the shell closure. These facts suggested that water might enter the interior of the carcerand after it is formed. To examine this possibility, sample A of **1**·G was suspended in refluxing D_2O for 3 days, recovered, and submitted to FAB-MS. The peak intensity ratio $[(M + Cs + D_2O)^+, 1569]/[(M + Cs + H_2O)^+, 1571]$ changed from 0.34 before the treatment to 0.85 after the treatment, an increase in D_2O over H_2O by a factor of 2.5. The peak intensity ratio of $[(M + 2Cs + D_2O + H)^+, 1703]/[(M + 2Cs + H_2O + H)^+, 1701]$ went from 0.79 before the D_2O treatment to 1.87 after D_2O treatment, an increase in D_2O over H_2O by a factor of 2.4. We conclude that water molecules can at least enter the interior of **1**, probably with considerable activation energy. This possibility was suggested by an examination of CPK molecular models of **1** during the design phase of this research. The interesting question arises as to the magnitude of hydrogen–deuterium isotope effects for the water incarceration processes as a function of the character of the permanent resident guests present.

Differential Thermal Analysis of Combustion and Analysis for Argon. The presence of Ar as a guest was indicated by the peak at 1589.249 mass units in the FAB-MS, consistent with the calculated value of 1589.238 for $(M + Cs + Ar)^+$. The capture of a noble gas by an organic host was unusual enough to invite confirmation. Sample A first was submitted to differential thermal analysis of its combustion in air to give reproducible ΔT vs T plots typified by the one shown in Figure 1. The ΔT curves show a double peak with maxima at 490 and 580 °C. The lower of these temperatures may reflect partial decomposition of the material upon melting, and the higher temperature, decomposition by combustion. A more likely explanation is that combustion–fragmentation for some of the components in the mixture may occur from the "inside" via a mechanism operational at 490 °C, in which O_2 enters the host through the two portals and oxidizes the sulfide to sulfoxide or sulfone groups, which causes the molecular shell to crack open to spill its contents and become more exposed to conventional combustion mechanisms. The process visible at 580 °C may reflect oxidation which proceeds from the "outside", involving initial attack of oxygen on the methine and methylene oxygens. The high temperatures involved document the "refractory" properties of the carcerand–carcaplex mixture.

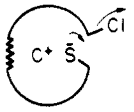
For argon analyses, sample A of **1**–**1**·G (1.3 mg) was degassed under vacuum at 100 °C and then burned at 600 °C in pure O_2. The Ar liberated was purified and its amount measured with a static noble gas mass spectrometer[18] to provide a value of 0.016% by weight Ar in **1**–**1**·G. The measured isotope ratio ($^{40}Ar/^{36}Ar = 290 \pm 10$) agrees with that of atmospheric Ar. Thus no isotopic fractionation was associated with its becoming a guest in **1**·G.

This analysis not only confirms the capture of Ar during the shell closure to form **1**·G but also indicates the inability of the noble gas to escape its prison during the extractions of **1**·G. The diameter of Ar is about 3.10 Å, somewhat greater than the diameter of 2.59 Å estimated for the portals at the constricted ends of host **1**. The amount of Ar present indicates that about 1 in every approximately 150 shell closures encapsulated a molecule of this noble gas. This value is consistent with the relative absence of Ar in most of the FAB-MS peaks detected (Tables I and II). Argon at saturation in the reaction medium is expected to be at pretty low concentrations. Its detection in the $(M + Cs + Ar)^+$ FAB-MS peak probably reflects a bias for detection of cesium ion containing carcaplexes over detection of originally neutral species.

Capture of Freon 114 by Shell Closure. Molecular model examination of **1** indicated that its cavity was complementary to the gas, $ClCF_2CF_2Cl$. To determine if this gas (Freon 114) could be imprisoned in **1**, a shell closure of **13** and **14** to produce carcerand was conducted as before except that the reaction was conducted in an atmosphere of Freon 114 in place of Ar. A FAB-MS of the well-washed product gave a faint peak for $(M + ClCF_2CF_2Cl)^+$ at 1584, not strong enough for a high-resolution spectrum. Consequently, the sample was decomposed at 120 °C in CF_3CO_2H, and the gases liberated were submitted to GC–MS analysis. Low-intensity peaks were detected at m/z 85 $(^{35}ClF_2C)^+$, 87 $(^{37}ClF_2C)^+$, and 135 $(^{35}ClF_2CCF_2)^+$. The same ions were produced by $ClCF_2CF_2Cl$ in a control run. Thus a small amount of Freon 114 appears to have been trapped inside the carcerand during the shell closure.

Liberation of Incarcerated Cs. The analysis of **1**·G for Cs was carried out by neutron activation to produce a radioactive sample of **1**·G, which was counted. This radioactive sample was also digested in CF_3CO_2H (120 °C, 3 h) to give a mixture that was flooded with water and filtered (Millipore). The solid was washed with water, dried, and found by counting to contain only 1.4% of the Cs^+ originally present in the sample of **1**·G. This treatment appears to efficiently decompose the carcerand and liberate its guests.

Differential Incarceration of Guests during Shell Closure. The elemental analysis of **1**–**1**·G indicated that equivalent amounts of Cs and Cl were present. FAB-MS indicated that Cs was largely inside and Cl largely outside the carcaplex. Furthermore, the amount of Cs incarcerated (~0.35 equiv per equiv of host) appears to be much greater than expectations based on the statistical presence of dissolved Cs^+ ions present during the shell closure. These facts taken in sum are readily explained as follows. The four S–C bonds made during the shell closure probably involve an S_N2 reaction mechanism between $\sim CH_2\text{–}S^-Cs^+$ contact ion pairs and $\sim CH_2\text{–}Cl$ groups. After three of the four $\sim CH_2\text{–}S\text{–}CH_2\sim$ bonds are in place, there is little room for escape of a Cs^+ located in the cavity of the incipient **1**·G. Examination of molecular models of the transition state for the intramolecular S_N2 reaction in which the fourth bond is made indicates that a linear arrangement of $S^{\delta-}\cdots C^{\delta+}\cdots Cl^{\delta-}$ is possible only in a conformation in which the nucleophile (S^-) is oriented toward the cavity and the leaving group (Cl^-) diverges from the cavity. If Cs^+ is ion-paired to the S^-, it must reside in the cavity, from which it cannot escape (as depicted in **17**). The 0.35 equiv of Cs^+ associated with **1**·G may measure the extent to which the S^- is ion-paired in the final reaction of the shell closure.



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Since $(CH_3)_2NCHO$ is the major component of the medium, its observed incarceration at the 0.39-equiv level per equiv of host in sample A is not surprising. Our best guess as to the relative levels of $(CH_3)_2NCHO$ and $(CH_2)_4O$ entrapped comes from the 4:1 peak intensity levels of the $(M + (CH_3)_2NCHO + Cs + Cl)^+$ and $(M + (CH_2)_4O + Cs + Cl)^+$ ions observed for sample B (Table II). Even this ratio of 4:1 exceeds the average mole fraction ratio of $(CH_3)_2NCHO$ to $(CH_2)_4O$ (about 24:1) that composed the medium during shell closure.

The best guess as to the amount of empty **1** produced relative to **1**·G comes from the percent contributed by $(M + H)^+$ to the sum of the peak intensities for sample A (Table II). The contribution is 12%. If anything, this value is surprisingly large since in the transition state leading to **1**, the S^- must exist in a microenvironment of very low dielectric constant.

Conclusions. This investigation for the first time reports the design and synthesis of the first molecular cell. Guest molecules and ions trapped inside the cell during shell closures include $(CH_3)_2NCHO$, $(CH_2)_4O$, Cs^+, Cl^-, Ar, and $ClCF_2CF_2Cl$. The discrimination shown in the shell closure (e.g., of Cs^+ over Cl^-) appears to relate to the mechanism of the shell-closing reaction. The two small pores in the molecular cell appear large enough to admit water to their interiors, at least when Cs^+ is trapped inside. The larger diameters of the organic guests and of Cs^+ (3.4 Å), Cl^- (3.62 Å), and Ar (3.10 Å) prevent these species from entering or departing their container. The chief limitation of the study relates to the extreme insolubility of **1**–**1**·G, which inhibited not only its separation into individual chemical entities but also an examination in solution of spectral properties of trapped guests in highly specialized combinations and environments.

Potential uses of carcerands and carcaplexes are envisioned. Large metabolizable molecular cells might be used in drug or agricultural chemical delivery systems or in systems in which very slow release of compounds chemically shielded from their environments are needed. Metabolism-resistant carcerands containing appropriate radiation-emitting metal ions or atoms might be attached to immunoproteins that seek out cancer cells. Others might provide means of organ imaging. The shell of the host should inhibit deposition of heavy-metal salts in bones. The unusual thermal stability of **1**–**1**·G and its molecular shape suggest possible uses as molecular ball bearings. The demonstration that carcerands and their guests can be designed and synthesized is the most important feature of this study.

Experimental Section

General. Tetrahydrofuran (THF) and Et_2O were distilled from sodium benzophenone ketyl, and CH_3CN from CaH_2. Dimethylformamide (DMF) and dimethyl sulfoxide (DMSO) were stored at least 2 days with activated 3-Å molecular sieves and decanted. All glassware was carefully dried at high temperature either under vacuum or while purging with dry Ar. All reactions were carried out under Ar unless otherwise stated. Column chromatography was performed on silica gel 60 (E. Merck, particle size 0.063–0.200 nm, 70–230-mesh ASTM). Thin-layer chromatography was performed on silica gel, precoated plastic sheets (E. Merck, thickness 0.2 mm). Melting points were measured on either a Mel-Temp or a Thomas-Hoover melting point apparatus and are uncorrected. Proton NMR spectra were taken on a Bruker WP-200 spectrometer in $CDCl_3$, unless otherwise indicated. Mass spectra were taken on an AEModel MS 9 or a Hewlett-Packard diode array spectrometer with a 7470A plotter. FAB-MS were determined on a V. G. Analytical ZAB-2F instrument, with an ion gun from Ion Tech with Xe

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[18] Lightner, B. D.; Marti, K. *Geochim. Cosmochim. Acta* **1974**, *Suppl. 5*, 2023–2031.

as bombarding gas, beam energy 8.4 keV, accelerating voltage 7 kV, ion source pressure 5 × 10^{-5} mbar, and matrix $(HOCH_2CH_2S)_2$. FT-IR spectra were obtained on a Nicolet 60-SX spectrometer, carcerand **1**·G as a KBr pellet. The solid-state ^{13}C spectra were taken on a FXQ-90 console linked to a Chemagnetics magnet.

1,21,23,25-Tetramethyl-2,20:3,19-dimetheno-1*H*,21*H*,23*H*,25*H*-bis[1,3]dioxocino[5,4-*i*:5′,4′-*i*′]benzo[1,2-*d*:5,4-d′]bis[1,3]benzodioxocin-7,11,15,28-tetracarboxylic Acid Tetramethyl Ester (1*R,21*R**,23*S**,25*S**) (11).** Cavitand **9** was freed of CH_2Cl_2 or $CHCl_3$ by repeated evaporation of mixtures of **9** and toluene, followed by drying **9** at 75 °C under high vacuum. To a stirred suspension of 11.15 g (18.8 mmol) of **9** in 600 mL of dry ether was added 90 mL of a 1.6 M solution of C_6H_5Li in hydrocarbon (144 mmol, 1.9 equiv per position to be metalated, solution titrated before use) at 0 °C under Ar. The white suspension turned to a deep red-brown suspension after several hours. The mixture was stirred for 2 days at 25 °C and cooled to −78 °C, and 60 mL of dry CH_3OCOCl was added rapidly by syringe. The stirred mixture was allowed to slowly warm to 25 °C and kept there for 3 h. Excess CH_3OCOCl and ether were evaporated under reduced pressure, and the residue was dissolved in 2 L of EtOAc. The organic layer was washed with 500 mL of water–brine mixture, dried ($MgSO_4$), and evaporated under vacuum to about 200 mL and diluted with 200 mL of EtOH. The mixture was cooled to 4 °C, and the product was collected, washed, and dried to give 10.8 g (89%) of **11**. A small sample was recrystallized from CH_2Cl_2 and dried at 80 °C under high vacuum: mp >360 °C; MS, 824 (M^+); ^1H NMR ($CDCl_3$) δ 1.76 (d, 12 H, CH_3C, $J = 7.4$ Hz), 3.84 (s, 12 H, OCH_3), 4.58 (d, 4 H, inner of OCH_2O, $J = 7.4$ Hz), 4.98 (q, 4 H, CH_3CH, $J = 7.4$ Hz), 5.65 (d, 4 H, outer of OCH_2O, $J = 7.4$ Hz), 7.29 (s, 4 H, ArH). Anal. Calcd for $C_{44}H_{40}O_{16}$: C, 64.08; H, 4.99. Found: C, 64.07; H, 4.88.

1,21,23,25-Tetramethyl-2,20:3,19-dimetheno-1*H*,21*H*,23*H*,25*H*-bis[1,3]dioxocino[5,4-*i*:5′,4′-*i*′]benzo[1,2-*d*:5,4-*d*′]bis[1,3]benzodioxocin-7,11,15,28-tetramethanol Stereoisomer (12). To 13.1 g (15.9 mmol) of tetraester **11** stirred as a suspension in 300 mL of dry THF under Ar at −30 °C was added 6.8 g (179 mmol) of $LiAlH_4$ in small portions. After the addition was complete, the mixture was allowed to warm to 25 °C and stirred for 2 h. The mixture was cooled to 0 °C, the excess $LiAlH_4$ was destroyed with EtOAc, and 20 mL of H_2O was carefully added. The reaction mixture was shaken with a mixture of 200 mL of EtOAc and 300 mL of 6 N aqueous H_2SO_4. The aqueous layer was extracted with two 200-mL portions of EtOAc. The combined organic layers were washed with 100 mL of water, 100 mL of $NaHCO_3$-saturated aqueous solution, and 100 mL of brine and dried ($MgSO_4$). The solvent was evaporated under reduced pressure to about 50-mL volume. The mixture was cooled at 4 °C for 24 h, and the product that separated was collected, washed, and dried to give 8.7 g (77%) of **12**: TLC R_f 0.19 (SiO_2/10% MeOH in CH_2Cl_2); mp 360 °C; MS, 712 (M^+, very low intensity); ^1H NMR ($(CD_3)_2SO$) δ 1.80 (d, 12 H, CH_3C, $J = 7.4$ Hz), 4.29 (d, 8 H, $ArCH_2O$, $J = 4.8$ Hz), 4.45 (d, 4 H, inner of OCH_2O, $J = 7.7$ Hz), 4.70 (t, 4 H, OH, $J = 4.8$ Hz), 4.83 (q, 4 H, CH_3CH, $J = 7.4$ Hz), 5.81 (d, 4 H, outer of OCH_2O, $J = 7.7$ Hz), 7.70 (s, 4 H, ArH). Anal. Calcd for $C_{40}H_{40}O_{12}$: C, 67.40; H, 5.65. Found: C, 67.29; H, 5.54.

7,11,15,28-Tetrakis(chloromethyl)-1,21,23,25-tetramethyl-2,20:3,19-dimetheno-1*H*,21*H*,23*H*,25*H*-bis[1,3]dioxocino[5,4-*i*:5′,4′-*i*′]benzo[1,2-*d*:5,4-*d*′]bis[1,3]benzodioxocin Stereoisomer (13). To a stirred mixture under Ar of 8.65 g (0.033 mol) of Ph_3P dissolved in 250 mL of dry THF at 0 °C was added over a 10 min period 4.72 g of *N*-chlorosuccinimide. The mixture was warmed to 25 °C and stirred for 0.5 h. Tetrol **12** (5.6 g, 0.0078 mol) dissolved in 100 mL of dry THF was added, and the reaction mixture was stirred for 10 h at 25 °C. Excess phosphonium salt was decomposed by addition of 0.5 mL of EtOH by syringe, and the solvent was evaporated under reduced pressure to a 50-mL volume. The product that separated was collected, washed, and dried at 78 °C under high vacuum to give 4.0 g (65%) of **13**: TLC R_f 0.25 ($SiO_2/CHCl_3$); MS, 786 (M^+); ^1H NMR ($CDCl_3$) δ 1.76 (d, 12 H, CH_3C, $J = 7.4$ Hz), 4.51 (d, 4 H, inner of OCH_2O, $J = 7.2$ Hz), 4.53 (s, 8 H. CH_2Cl), 5.02 (q, 4 H, CH_3CH, $J = 7.4$ Hz), 5.99 (d, 4 H, outer of OCH_2O, $J = 7.2$ Hz), 7.30 (s, 4 H, ArH). Anal. Calcd for $C_{40}H_{36}O_8Cl_4$: C, 61.08; H, 4.61. Found: C, 60.91; H, 4.56.

1,21,23,25-Tetramethyl-2,20:3,19-dimetheno-1*H*,21*H*,23*H*,25*H*-bis[1,3]dioxocino[5,4-*i*:5′,4′-*i*′]benzo[1,2-*d*:5,4-*d*′]bis[1,3]benzodioxocin-7,11,15,28-tetramethanethiol Stereoisomer (14). Thiourea (1.35 g, 0.018 mol) was added to a suspension of 3.37 g (0.0042 mol) of tetrachloride **13** in 80 mL of dry DMSO stirred at 25 °C until dissolution occurred (4 h), and stirring was continued for an additional 2 h. The solution was then added to a degassed solution of 400 mL of aqueous NaOH stirred at 0 °C under Ar. The mixture was stirred for 30 min and was then carefully acidified at 0 °C by the slow addition of 4 N aqueous HCl until a pH of 2 was reached. The white, gel-like precipitate that separated was filtered through Celite, and the pad was washed with water. The product and Celite were suspended in 300 mL of CH_2Cl_2 and 10 g of $MgSO_4$. The mixture was stirred for 3 h and filtered through a fritted glass funnel. The solid was washed with CH_2Cl_2. The combined filtrates were evaporated to a volume of 20 mL and flash chromatographed under medium pressure through silica gel with CH_2Cl_2 as the mobile phase. The column filtrates were evaporated under reduced pressure, and the residue was recrystallized from CH_2Cl_2/hexane to give 1.82 g (56%) of **14**: mp >360 °C; ^1H NMR ($CDCl_3$) δ 1.73 (d, 12 H, CH_3C, $J = 7.4$ Hz), 1.89 (t, 4 H, SH, $J = 7.5$ Hz), 3.57 (d, 8 H, CH_2S, $J = 7.5$ Hz), 4.49 (d, 4 H, inner of OCH_2O, $J = 7.0$ Hz), 4.98 (q, 4 H, CH_3CH, $J = 7.4$ Hz), 5.95 (d, 4 H, outer of OCH_2O, 7.0 Hz), 7.18 (s, 4 H, ArH). Anal. Calcd for $C_{40}H_{40}O_8S_4$: C, 61.83; H, 5.18. Found: C, 61.70; H, 5.13.

8,10,34,36,59,60,67,68-Octamethyl-5,19:31,45-(bis(epoxymethanoxy))-6,18:12,16:32,44:38,42-tetramethano-4,26:30,52-bis(methanethiomethano)-8*H*,10*H*,20*H*,22*H*,34*H*,36*H*,46*H*,48*H*-dibenzo[*d*,*n*]bisbenzo[4′,5′][1,3]dibenzodioxocino[9′,8′:4,5][1,3]benzodioxocino[10,9-*i*:10′,9′-*s*][1,3,11,13]tetraoxa[7,17]dithiacycloeicosin Stereoisomer (1–1·G). Dry Ar was bubbled 2–3 bubbles/s through a stirred mixture of 600 mL of dry DMF and 1.0 g of dry pulverized Cs_2CO_3 at 60 °C in an Ar atmosphere. A solution of 398 mg (50 mmol) of **13** and 400 mg (50 mmol) of **14** in 50 mL of pure dry THF was added by syringe pump over a 20-h period to the above stirred mixture. The reaction mixture was stirred an additional 10 h, and the solvents were evaporated under reduced pressure to leave a volume of about 30 mL, to which 500 mL of distilled water was added. The solid was collected by filtration through a sintered glass funnel and was in turn suspended in and filtered from 500 mL of H_2O, 500 mL of EtOH, 1 L of CH_2Cl_2, 1 L of EtOAc, 500 mL of H_2O, 100 mL of EtOH, and 100 mL of CH_2Cl_2. The remaining light gray solid was air-dried to give 232 mg (29%) of sample A of **1–1**·G: mp >360 °C; ^{13}C NMR (solid state, δ), FAB-MS, see Tables I and II; FT-IR spectrum (KBr pellet, cm^{-1}) 1245 ($ArOCH_2$), 1459 and 1590 (Ar), 1472 ($ArCH_2$), 1680 (C=O of $(CH_3)_2NCHO$).

Sample B of **1–1**·G was prepared in 20% yield by a procedure similar to that of sample A except that the reaction temperature was 70 °C, and the product after H_2O washes was submitted to Soxhlet extraction with EtOAc, CH_2Cl_2, and H_2O. Table II records the FAB-MS and Chart II, the elemental analysis. The Cs was analyzed by neutron activation analysis, and the Ar by the method described in the next section. The material after neutron activation to give radioactive Cs was heated in a sealed tube in CF_3CO_2H at 120 °C for 3 h to give a brown-colored mixture with a strong thiol smell. The solvent was evaporated and the residue was washed thoroughly with deionized water using a Millipore filter. The residue was dried and analyzed for radioactive Cs. The concentration of Cs had decreased to 1.4% of its value before the CF_3CO_2H treatment.

Sample C of **1–1**·G was prepared by the same procedure as that applied to the preparation of sample A except for the following differences. One liter of DMF and 2 g of Cs_2CO_3 were placed under vacuum, and Freon 114 was bubbled through the mixture. Again, vacuum was applied, and again, Freon 114 was bubbled through the mixture at a 2–3 bubbles/s rate. A solution of 415 mg (53 mmol) of **13** and 413 mg (53 mmol) of **14** in 50 mL of THF was added at 50–70 °C over a 24-h period to give 200 mg of **1–1**·G after submission to the same washing procedure applied to sample A. Sample C was submitted to the same CF_3CO_2H digestive procedure applied to sample B except that the ampule was broken in a closed and evacuated latex tube and the gases liberated were submitted to GC–MS with Bu-5 as a stationary phase. The major gaseous product was $CF_2{=}CF_2$ produced from CF_3CO_2H. Although $ClCF_2CF_2Cl$ (Freon 114) was not detected directly as M^+, low-intensity fragments at mass 85 (100), 87 (10), 135 (45), and 137 (5) were observed. In a control experiment, Freon 114 gave zero retention time on the GC, and the following peaks: 85 ($^{35}ClF_2C^+$, 100%), 87 ($^{37}ClF_2C^+$, 36%), 135 ($^{35}ClCF_2CF_2^+$, 20%), 137 ($^{37}ClCF_2CF_2^+$, 6%). In an attempt to use *p*-$CH_3C_6H_4SO_3H$ as the digesting medium for **1–1**·G, only CH_3CH_2Cl was observed in the GC–MS analysis, whose origins are probably the $CH_3CH(Ar)_2$ groups of the carcerand, which produce CH_3CHO, which in turn goes to CH_3CH_2Cl.

Entrance of D_2O into 1–1·G. A 20-mg sample of **1–1**·G (sample A) was mixed with 20 mL of D_2O, and the mixture was heated at reflux at 100 °C for 3 days in a closed system. The sample of **1–1**·G was recovered, air-dried, and submitted to FAB-MS in an $(SCH_2CH_2OH)_2$ matrix. The ratio of peak intensities for masses 1569/1567 was 0.34 before the D_2O treatment and increased to 0.85 after D_2O treatment. The ratio of peak intensities for masses 1702/1700 was 0.79 before D_2O treatment and 1.87 after D_2O treatment.

Analysis of Sample A of 1–1·G for Argon. A combustion system of 1-L volume was placed on-line with a gas clean-up system and a static noble gas mass spectrometer.[18] The combustion system, including a 1.3-mg sample of **1–1**·G in a preheated quartz finger, was briefly heated to ~100 °C under vacuum and then filled with 2.0 Torr of O_2 (generated from CuO at 750 °C). The system was closed off and the sample was heated to 600 °C. The total pressure in the reaction system began to drop at 550 °C and remained at 0.85 Torr at 600 °C when the heat was cut off. Residual O_2 (about one-third of the pressure) was removed by CuO at 600 °C. A glass capillary at the temperature of liquid N_2 reduced the pressure to $\sim 10^{-3}$ Torr. The Ar was adsorbed on charcoal at liquid N_2 temperature, isolated from the combustion system, and cleaned on Ti sponge, on Ti foil, and in two additional steps on Ti–Pd getters. The Ar was then admitted to the mass spectrometer. The amount of Ar was determined by calibrating the instrument with known air pipets to give $(1.14 \pm 0.1) \times 10^{-4}$ cm^3 at standard temperature and pressure (STP) obtained from the 1.3 mg of **1–1**·G. The procedure was repeated by heating a finger without sample. The total procedural blank was 1.0×10^{-6} cm^3 (STP), or 0.9% of the Ar from the sample. Thus 1 g of **1–1**·G would have provided 8.8×10^{-2} cm^2 (STP) of Ar, or 0.016% of the weight of the sample was Ar.

Registry No. 1, 95841-28-4; **9**, 83136-19-0; **10**, 83136-20-3; **11**, 83136-21-4; **12**, 95799-47-6; **13**, 95799-48-7; **14**, 95799-49-8; Cs_2CO_3, 534-17-8; D_2O, 7789-20-0; freon 114, 76-14-2; argon, 7440-37-1.

Boron, Aluminum, and Gallium Tris(trifluoromethanesulfonate) (Triflate): Effective New Friedel–Crafts Catalysts[1]

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Abstract: Boron, aluminum, and gallium tris(trifluoromethanesulfonate) (triflate) were prepared from the corresponding chlorides (bromides) and triflic acid. The group IIIA triflates were isolated in pure form and fully characterized (elemental analysis, molecular weight, and NMR and IR spectroscopy). Boron tris(triflate) is a monomeric, relatively volatile compound [mp 43–45 °C, bp 68–73 °C (0.5 Torr)], whereas aluminum and gallium triflate are associated, high-melting associated solids. Boron, aluminum, and gallium tris(triflate) are efficient new Friedel–Crafts catalysts as shown in alkylation, isomerization, and acylation reactions. Alkylation of benzene and toluene with methyl, ethyl, isopropyl, and *tert*-butyl halides (fluoride, chloride, and bromide) were carried out with boron, aluminum, and gallium tris(triflate) as catalyst in CH_2Cl_2 and CH_3NO_2 solvent at room temperature. Substrate (k_T/k_B) and positional selectivity (isomer distribution) were determined by GLC. Boron triflate shows the highest catalytic activity followed by gallium and aluminum triflate as reflected by overall yields in the alkylation reactions and tendency of accompanying isomerization, causing substantially increased meta substitution and disproportionation.

In the course of more than 100 years of Friedel–Crafts chemistry,[2] two catalysts achieved preeminence. Anhydrous aluminum trichloride was introduced by Friedel and Crafts themselves and maintained its wide use ever since despite some unfavorable properties such as being a subliming solid (limiting its use to solution chemistry) and only limited solubility in apolar or hydrocarbon solvents. Boron trifluoride became a significant catalyst since the 1920s following fundamental studies by Meerwein, Nieuwland, and others.[2,3] Because it is a low-boiling gas (bp −101 °C), some of its more convenient complexes, albeit reduced in reactivity, are frequently used, such as ether complexes. Although a significant number of other Lewis acid halide (and pseudohalide) catalysts are also used, none of them achieved similar wide application. Since the 1960s, some superacid catalysts such as antimony pentafluoride gained significance.[4]

The most widely used Lewis acids in Friedel–Crafts chemistry are halides of different metals.[2] Other derivatives are more seldom used. Following the discovery of trifluoromethanesulfonic (triflic) acid by Haszeldine and Kidd[5] in 1954, there has been a rapid growth in the chemistry of triflic acid and its metal derivatives.[6] Many metal triflates have been successfully used in various types of chemical transformations. The triflates of group IIIA elements remained, however, less studied.

Boron tris(triflate) was first prepared by Engelbrecht and Tschager[7] in trifluoromethanesulfonic (triflic) acid solution in the form of its conjugate Brønsted–Lewis superacid, $2CF_3SO_3H–B(OSO_2CF_3)_3$. The catalytic activity of this superacid was subsequently explored by Olah, Laali, and Farooq.[8] Boron tris(triflate) was obtained free of protic acids only in our recent work and was used in the preparation of stable carbocations.[8] It was, however, till now not studied concerning its Friedel–Crafts catalytic activity. Reports on the study of the triflates of aluminum and gallium are even more scanty. Although Cheradame et al. reported[9a] the preparation of aluminum tris(triflate) from triethylaluminum and triflic acid, no details were given, nor was the compound characterized or its catalytic activity studied, except in some olefin polymerizations.[9a,b]

We report now that in our continued study of Friedel–Crafts chemistry boron, aluminum, and gallium tris(trifluoromethanesulfonate) (triflate) were found to be convenient and effective new Friedel–Crafts catalysts.[10] We report their preparation, char-

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