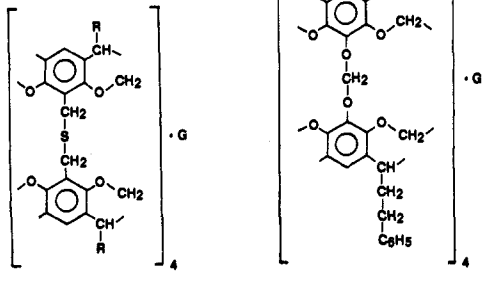
Guest Capture during Shell Closure[1a-c]

Judi A. Bryant,[†] Michael T. Blanda,[†] Marco Vincenti,[‡] and Donald J. Cram*,[†]

Contribution from the Department of Chemistry and Biochemistry, University of California at Los Angeles, Los Angeles, California 90024, and Department of Analytical Chemistry, Istituto Guido Donegani, Via G. Fauser 4, 28100 Novara, Italy. *Received July 25, 1990*

Abstract: The preparation and properties of seven new carceplexes **1–7** of general structure H·G are reported in which H is an enforced closed-shell molecule (carcerand) composed of linked anisyl moities to which are attached pendant R groups required to impart solubility to the complexes. The guest molecules (G) are incarcerated in the enforced hollow interior of the hosts: **1**, R = $CH_2CH_2C_6H_5$ and G = $CH_3OH{\cdot}HOCH_3$; **2**, R = $CH_2CH_2C_6H_5$ and G = $CH_3CN{\cdot}NCCH_3$; **3**, R = $CH_2CH_2C_6H_5$ and G = CH_3CN; **4**, R = $(CH_2)_4CH_3$ and G = $(CH_3)_2NCHO$; **5**, R = $(CH_2)_4CH_3$ and G = CH_3CH_2OH; **6**, R = $(CH_2)_4CH_3$ and G = $CH_3COCH_2CH_3$; and **7**, R = $(CH_2)_4CH_3$ and G = $CH_3CH_2COCH_2CH_3$. The complexes were all thermally stable except that $H{\cdot}CH_3CN{\cdot}NCCH_3$ when heated gave $H{\cdot}CH_3CN$ plus CH_3CN. The critical shell-closing reactions used to prepare **1–7** involved a 4-fold substitution in which four CH_2Cl groups attached to the rim of a cavitand reacted with a second cavitand with four CH_2SH groups attached to its rim. The M_2CO_3-catalyzed reactions were run in solvents whose molecules fitted well into the interiors of the carcerands on the basis of an inspection of Corey–Pauling–Koltun (CPK) molecular models. The nonpolar complexes were purified by chromatography. The yields were high for the 4-fold reactions: **1**, 22%; **2** + **3** mixture, 25%; **4**, 20%; **5**, 20%; **6**, 32%; and **7**, 23%. No shell closure occurred with benzene as solvent. When conducted in benzene–alcohol or benzene–acetonitrile, only the more polar component was incarcerated. All carceplexes except **2** gave strong molecular ions in their desorption chemical ionization mass spectra (DCI MS) ($(CH_3)_3CH$ was the reagent gas), in both their positive and negative ion modes. The proton signals of the guests in **1–7** occurred 1–4 ppm upfield in their ^1H NMR spectra in $CDCl_3$, while the chemical shifts of the inward-turned protons of the OCH_2O groups of the hosts were guest-sensitive. The ^1H NMR spectra of **1** and **3–5** indicated that the guests rotated about both the C_2 and C_4 axes of the host rapidly on the ^1H NMR time scales (360 and 500 MHz). The spectrum of **6** indicates the long axis of the $CH_3COCH_2CH_3$ guest is aligned with the C_4 axis of the host and rotates around this axis rapidly, but not about the shorter C_2 axes.

Previous papers reported that, in the synthesis of I·G in which R = CH_3, mixtures of carceplexes were produced in which G was Cs^+, $Cs^+{\cdot}H_2O$, $Cs^+{\cdot}(CH_3)_2NCHO$, $(CH_3)_2NCHO$, $(CH_2)_4O{\cdot}H_2O$, $(CH_3)_2NCHO{\cdot}Ar$, $(CH_3)_2NCHO{\cdot}CsCl$, and $CsCl{\cdot}Cs^+$. Most of the Cl^- was present in the unbound state. The carceplexes were purified by washing the non-shell-closed oligomers away from the desired products, which as a mixture was subjected to extensive elemental, mass spectral, infrared, and solid-state ^{13}C NMR spectral analyses. The extreme insolubility of these carceplexes in the 20 different solvents examined prohibited the isolation of the component complexes.[2]



I·G

II·G

In a subsequent study, three carceplexes were prepared of structure II·G in which G was $(CH_3)_2NCHO$, $(CH_3)_2NCOCH_3$, or $(CH_3)_2SO$. Each compound was purified by chromatography and fully characterized.[3] The respective shell closures gave excellent yields (49–61%) for reactions involving formation of eight new bonds (eq 1). No free carcerand was obtained in these shell

$$2(ArOH)_4 + 4CH_2BrCl + 4Cs_2CO_3 \rightarrow 4H_2O + (ArOCH_2OAr)_4 + 4CsBr + 4CsCl \quad (1)$$

closures or when $(CH_2)_5NCHO$ was used as solvent. In Corey–Pauling–Koltun (CPK) molecular models, $(CH_2)_5NCHO$ is too large to occupy the hollow interior of II. Thus, incarceration appears to be a condition of shell closure, suggesting that the shell closures are templated by the guests.[2]

The present paper reports the preparation and characterization of seven new carceplexes of the general structure I·G in which R = $CH_2CH_2C_6H_5$ or $(CH_2)_4CH_3$ and G is $CH_3OH{\cdot}HOCH_3$, $CH_3CN{\cdot}NCCH_3$, CH_3CN, CH_3CH_2OH, $(CH_3)_2NCHO$, $CH_3COCH_2CH_3$, or $CH_3CH_2COCH_2CH_3$. The study was conducted to answer the following questions. (1) Would substitution of eight β-phenylethyl or pentyl for eight methyl groups of I·G provide enough solubility to the product carceplexes to allow their isolation and characterization as single molecular entities? (2) Would the shell closures occur with molecular recognition of the guests with respect to both their numbers and their character? (3) Would the abilities of the guests to rotate with respect to the host follow expectations derived from CPK molecular model examination? (4) Could small guests be expelled thermally through the small openings defined by the aryl hydrogens of I·G?

In CPK molecular models of **1–7**, the host is shaped like a U.S. football, fattest at its equator (CH_2SCH_2 region) and narrowed at its poles. At the north and south poles are located small holes lined with four aryl hydrogens around which are gathered four pendant R groups. The eight H_a protons face inward toward the cavity, the eight H_b protons face outward away from the cavity, and the sixteen benzylic protons can face outward or along the surface of the globe, but not inward, and thus are not extremely sensitive to the guests' spatial orientation.

Results and Discussion

Syntheses of Cavitands. The syntheses of cavitands **12–21** (needed for the syntheses of **1–7**) involved as the first step the

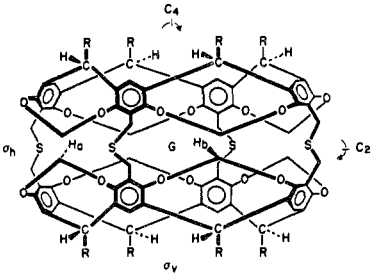
[†] University of California at Los Angeles.
[‡] Istituto Guido Donegani.

(1) (a) We thank the National Science Foundation for Grant CHE 88 02800, which supported this work. (b) Host–Guest Complexation. 55. (c) A preliminary account of some of these results has appeared in Bryant, J. A.; Blanda, M. T.; Vincenti, M.; Cram, D. J. *J. Chem. Soc., Chem. Commun.* **1990**, 1403–1405.

(2) (a) Cram, D. J.; Karbach, S.; Kim, Y. H.; Baczynskyj, L.; Kalleymeyn, G. W. *J. Am. Chem. Soc.* **1985**, *107*, 2575–2576. (b) Cram, D. J.; Karbach, S.; Kim, Y. H.; Baczynskyj, L.; Marti, K.; Sampson, R.; Kalleymeyn, G. W. *J. Am. Chem. Soc.* **1988**, *110*, 2554–2560.

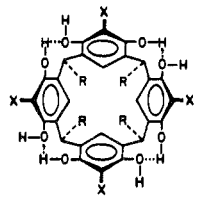
(3) Sherman, J. C.; Cram, D. J. *J. Am. Chem. Soc.* **1989**, *111*, 4527–4528.

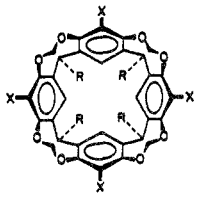
0002-7863/91/1513-2167$02.50/0



1, R = $CH_2CH_2C_6H_5$, G = $CH_3OH{\cdot}HOCH_3$
2, R = $CH_2CH_2C_6H_5$, G = $CH_3CN{\cdot}NCCH_3$
3, R = $CH_2CH_2C_6H_5$, G = CH_3CN
4, R = $(CH_2)_4CH_3$, G = CH_3CH_2OH
5, R = $(CH_2)_4CH_3$, G = $(CH_3)_2NCHO$
6, R = $(CH_2)_4CH_3$, G = $CH_3COCH_2CH_3$
7, R = $(CH_2)_4CH_3$, G = $CH_3CH_2COCH_2CH_3$

acid-catalyzed condensation of resorcinol with dihydrocinnamaldehyde to give octol **8** (55%) or with hexanal to give octol **9** (77%).[4] These octols were brominated with *N*-bromosuccinimide (NBS) to give **10** (75%) and **11** (77%), respectively. These





8, R = $CH_2CH_2C_6H_5$, X = H
9, R = $(CH_2)_4CH_3$, X = H
10, R = $CH_2CH_2C_6H_5$, X = Br
11 R = $(CH_2)_4CH_3$, X = Br

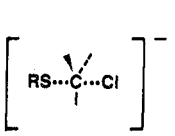
12, R = $CH_2CH_2C_6H_5$, X = Br
13, R = $(CH_2)_4CH_3$, X = Br
14, R = $CH_2CH_2C_6H_5$, X = CO_2CH_3
15, R = $(CH_2)_4CH_3$, X = CO_2CH_3
16, R = $CH_2CH_2C_6H_5$, X = CH_2OH
17, R = $(CH_2)_4CH_3$, X = CH_2OH
18, R = $CH_2CH_2C_6H_5$, X = CH_2Cl
19, R = $(CH_2)_4CH_3$, X = CH_2Cl
20, R = $CH_2CH_2C_6H_5$, X = CH_2SH
21, R = $(CH_2)_4CH_3$, X = CH_2SH

conformationally mobile bromo octols were rigidified by 4-fold cyclizations by treatment with CH_2BrCl–$(CH_3)_2NCHO$–K_2CO_3 to give cavitands **12** (53%) and **13** (56%), respectively. These compounds were lithiated with *n*-BuLi, and the organometallics were treated with $ClCO_2CH_3$ to give tetraesters **14** (82%) and **15** (80%), respectively. Reduction of **14** with $LiAlH_4$ gave tetrol **16** (85%), and similarly **15** gave **17** (90%). When **16** and **17** were treated with *N*-chlorosuccinimide–triphenylphosphine, **18** (72%) and **19** (65%) were produced, respectively. Treatment of **18** with thiourea (followed by base) gave tetrathiol **20** (80%), whereas **19** gave **21** (60%).

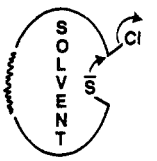
The critical shell-closure reactions were conducted at moderately high dilution in solvents whose molecules we wished to examine for their propensity for incarceration. Typically, Rb_2CO_3 was used as the base, although both Cs_2CO_3 and K_2CO_3 were also examined. The yield of neutral carceplex appeared to not be greatly affected by which base was used but was dependent on the solvent employed. The reactions were carried out by adding over a 24-h period equimolar solutions of tetrachloride **18** and tetrathiol **20** (or **19** and **21**) to a stirred solution of the carbonate salt heated at about 80 °C. The solvent was then evaporated under reduced pressure and the residue chromatographed on silica gel with 1:1 (v/v) pentane–chloroform as the mobile phase. Oligomers and any carcerands containing alkali-metal ions remained at the top of the column and were not examined in this study. In the shell closure conducted in each solvent, the following compounds were isolated: CH_3OH–C_6H_6, $H{\cdot}CH_3OH{\cdot}HOCH_3$ (**1**, 22%); CH_3CN–C_6H_6, $H{\cdot}CH_3CN{\cdot}NCCH_3$ (**2**, 14%) and $H{\cdot}CH_3CN$ (**3**, 11%) as a mixture; CH_3CH_2OH–C_6H_6, $H{\cdot}CH_3CH_2OH$ (**4**, 20%); $(CH_3)_2NCHO$, $H{\cdot}(CH_3)_2NCHO$ (**5**, 20%); $CH_3COCH_2CH_3$, $H{\cdot}CH_3COCH_2CH_3$ (**6**, 32%); $CH_3CH_2COCH_2CH_3$, $H{\cdot}CH_3CH_2COCH_2CH_3$ (**7**, 23%).

Molecular Recognition in Shell Closures. Since **18**–**21** were relatively insoluble in pure methanol, acetonitrile, or ethanol, the reactants were added dissolved in benzene to the carbonate solutions of the more polar solvents plus benzene. Only carceplexes containing the polar solvent molecules were isolated. No carceplex was isolated from a run in which benzene was the only solvent present. Thus, the shell closures showed high structural recognition for incarcerating the more polar molecules in the medium. We interpret this selection as follows.

The base-catalyzed reaction of thiol with the benzyl chloride very probably occurs by an S_N2 mechanism involving either solvated $ArCH_2S^-$ or ion-paired $ArCH_2S^-M^+$ as a nucleophile. The former would lead to solvating-solvent and the latter to M^+ or solvent + M^+ incarceration. In the prior paper,[2] which reported the synthesis of the insoluble I·G, the pendant R groups were methyls and the mixture of carceplexes formed included G = Cs^+ and $Cs^+{\cdot}(CH_3)_2NCHO$ as major incarcerated products.[2] We think it likely that similar products were formed in the shell closures reported here but that only the noncharged carceplexes formed could be chromatographed. Consequently, we isolated only products in which solvated $ArCH_2S^-$ acted as the nucleophile. Only the more polar alcohol or nitrile components in the benzene–cosolvent mixtures were likely to solvate the sulfide anion and thus end up incarcerated. Molecular model examination of the product-determining transition state (making the second or third S–CH_2 bond) indicates that a linear arrangement of the three atoms involved (as in **22**) is possible only when the solvated S^- is inside the cavity and the Cl^- is outside, as shown in **23**.



22



23

This explanation of guest recognition also explains why empty carcerand was never formed. Its presence among the products would require that RS^- be surrounded by a vacuum, the volume of which would have to equal that of the carcerand interior. Not only is RS^- likely to be too high in energy to be formed in a vacuum when solvent is available to solvate it, but also a vacuum the size of the carcerand interior is unlikely to occur on entropic grounds. Organic solvents have roughly 30% of their volume as "empty space", which occurs as "small spaces" between solvent molecules at places where solvent to solvent contacts are noncomplimentary.[5] Many such small spaces would have to be gathered in one place to create an empty carcerand, and such a concentration would have to overcome entropy of dilution of the small spaces.

Billiard-Ball Effect. Elemental analyses were performed for all atoms (C, H, O, S, and N, when present) in carceplexes **1** and **3**–**7**. The analysis for each element in each compound was within 0.25% of theory, and the sum of the analyses for each compound was 100 ± 0.25%. Those data alone attested to their purity and established that the host:guest ratios of these complexes are 1:1,

(4) Tunstad, L.; Tucker, J.; Dalcanale, E.; Weiser, J.; Bryant, J.; Sherman, J.; Helgeson, R. C.; Knobler, C.; Cram, D. J. *J. Org. Chem.* **1989**, *54*, 1305–1312.

(5) We thank Dr. Raymond A. Firestone for the following references and for a discussion of this question: (a) Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*; Verlag Chemie: New York, 1988; p 5. (b) Reichardt, C. *Ibid.* p 280. (c) Cameron, C. *J. Phys. Chem.* **1988**, *92*, 3417–3421. (d) Asano, T.; leNoble, W. *Rev. Phys. Chem. Jpn.* **1973**, *43*, 82–91. (e) Nishimura, N. *Can. J. Chem.* **1987**, *65*, 2248–2253. (f) Firestone, R. A.; Smith, G. *Chem. Ber.* **1989**, *122*, 1089–1094. (g) Markus, Y. *Introduction to Liquid State Chemistry*; Wiley: New York, 1977; p 58.

except for $H{\cdot}CH_3OH{\cdot}HOCH_3$. Initially, **2** and **3** were isolated as a 1.2:1.0 mixture (see below), which was converted to **3** and free CH_3CN by heating the mixture at 110 °C in toluene for 72 h. Molecular model examination indicates this expulsion of one incarcerated CH_3CN from $H{\cdot}CH_3CN{\cdot}NCCH_3$ could occur only through one of the small portals centered at the north or south poles of the carceplexes. When $H{\cdot}CH_3CN$ (**3**) was heated in 1,2,4-trichlorobenzene at 215 °C for 5 days, no signs of further loss of CH_3CN were detected.

We attribute the difference in thermal stability of $H{\cdot}CH_3CN{\cdot}NCCH_3$ (**2**) and $H{\cdot}CH_3CN$ (**3**) to a *billiard-ball effect* that operates only in **2**. Examination of CPK models of **2** indicates the long axes of the two CH_3CN molecules must be roughly aligned along the north–south axis of the host. Thus, high-energy collisions between the two CH_3CN molecules would occur mainly along this axis, providing the proper aim for one CH_3CN to be driven out of the complex by the other CH_3CN. Collisions of a single CH_3CN molecule with the sides of its cage would not aim the rebounding molecule in the proper direction for ejection through the north–south portals.

The rates of the reaction **2** → **3** + CH_3CN were followed by the ^1H NMR integration techniques applied to the diminution of the δ −2.15 signal assigned the CH_3CN group of **2**, to the increases of the CH_3CN signals for free guest at δ 2.33, and to the increases of the incarcerated guest of **3** signals at δ −1.65 in $Cl_2CDCDCl_2$ at 110, 100, 90, and 80 °C. The starting material was the 1.2:1.0 mixture of **2** and **3** (respectively) isolated from the shell closure. A plot of log k vs $1/T$ provided an energy of activation of 20 kcal mol^{-1} for the unimolecular process. The respective temperatures (±1 K), first-order rate constants (min^{-1}), and half-lives (h) obtained are as follows: 383, 1.8, 0.5; 373, 0.13, 5; 363, 0.05, 13; 353, 0.02, 26. These data suggest that most, and probably all, of the $H{\cdot}CH_3CN$ (**3**) originally isolated in the mixture of **2** and **3** was produced by the reaction **2** → **3** + CH_3CN. The shell-closing reaction was conducted in 2:1 (v/v) CH_3CN–C_6H_6 and involved an addition time of 24 h and an additional period of 24 h at a reflux temperature of approximately 80 °C. Attempts to carry out the reverse reaction of **3** + CH_3CN → **2** by refluxing a solution of **3** in 2:1 (v/v) CH_3CN–$C_6H_5CH_3$ for 72 h failed to give any **2**.

In an attempt to observe the billiard-ball effect in the behavior of $H{\cdot}CH_3OH{\cdot}HOCH_3$ (**1**), this substance was heated at 110 °C for 5 days in $C_6D_5CD_3$. No loss of CH_3OH was observed (^1H NMR). Apparently the hydrogen bonding between the two methanol molecules was strong enough to overcome the billiard-ball effect. Furthermore, at temperatures where the monomers predominantly existed, the random collisions between them did not cause ejection of one methanol molecule.

Mass Spectra. All carceplexes except $H{\cdot}CH_3CN{\cdot}NCCH_3$ (**2**) gave strong molecular ions in their desorption chemical ionization mass spectra (DCI MS) with $(CH_3)_3CH$ as the reagent gas (pressure in the ion source was about 0.5 mbar) in both their positive and negative ion modes.[6] Carceplex **2** undoubtedly lost some of the first but not the second molecule of CH_3CN during the strong heating required for vaporization. Although very intense signals (80–100%) were observed for host plus guest for **1** and **3**–**7**, significant signals were also observed at masses that corresponded to host alone and to the host minus one or more of the eight pendant, solubilizing R groups of general formula I·G. These same phenomena were observed previously in the DCI MS of carceplexes of the II·G structure.[2] The carcerands are prone to cracking at their equatorial bridges to give $ArCH_2^+$–SCH_2Ar, $ArCH_2^{\bullet}$ $^{\bullet}SCH_2Ar$, or like species, which provide openings through which the incarcerated guests depart. Cracking of the bond between the pendant groups and the globes similarly provide Ar_2CH^+, Ar_2CH^-, or $Ar_2CH^{\bullet}$ species stabilized by delocalization effects.

Mass spectral analysis of $H{\cdot}CH_3OH{\cdot}HOCH_3$ confirmed that **1** contained 2 mol of CH_3OH, although masses of substantial intensity were observed that corresponded to $[H{\cdot}CH_3OH]^+$ but not to $[H{\cdot}CH_3OH]^-$. Possibly a small amount of CH_3OH escaped during the vaporization of the sample to give $H{\cdot}CH_3OH$. In the shell closures leading to **1**–**4**, benzene was a cosolvent. No mass peaks were observed that corresponded to $\mathbf{1}{\cdot}C_6H_6$, $\mathbf{1}{\cdot}C_6H_6{\cdot}CH_3OH$, $\mathbf{1}{\cdot}C_6H_6{\cdot}CH_3CN$, or $\mathbf{1}{\cdot}C_6H_6{\cdot}CH_3CH_2OH$ in the spectra of the carceplexes **1**, **3**, and **4**. These observations confirm the conclusions derived from elemental analyses.

Proton Nuclear Magnetic Resonance Spectra. The ^1H NMR spectra of **1**–**7** provided much information concerning both the structures and dynamics of the carceplexes. All proton resonances for the guests are shifted 1–4 ppm upfield from their normal positions. Thus, all guest parts are subject to large aryl-shielding effects, which are strongest in the temperate zones of the globe and weakest in the torrid and equatorial regions. The magnitudes of the upfield movements of the guests' signals depends on the locations of their molecular parts relative to these zones, which in turn depend partly on how completely the guests fill the cavity.

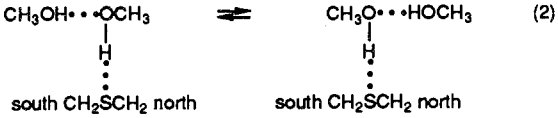
The host alone has a longitudinal polar C_4 axis and four equatorial C_2 (shorter) axes, as well as five mirror planes. The σ_h or equatorial plane passes through the four equatorial sulfur atoms, whereas the four σ_v or polar planes are defined by the two poles and two sulfur atoms (two such planes) or the two poles and two sets of OCH_2O moieties (two such planes). The multiplicities of the ^1H NMR signals due to H_a and H_b (see structure of **1**–**7**) provide indicator systems for possible constraints of the rotational degrees of freedom of guest relative to host. If rotations of guests around both the long polar and short equatorial axes are fast on the ^1H NMR time scale, the multiplicities of the H_a and H_b signals are the same as that expected for the host taken alone. If rotations of non-like-ended guests (e.g., $CH_3COCH_2CH_3$) around the long axis are fast but around the short axes are slow on the ^1H NMR time scale, the H_a and H_b signals of the northern and of the southern hemispheres might show different chemical shifts. In the unlikely event that rotations of the like-ended guests (e.g., $CH_3CH_2COCH_2CH_3$) should be slow around both the long and short axes, then only the H_a and H_b protons located in the eastern and western hemispheres might be different from one another. If such guests are non-like-ended and not rotating, then the H_a and H_b protons in both the northern and southern as well as the eastern and western hemispheres should have different environments and, therefore, might give different signals.

Some of these possibilities have been observed in the 360- and 500-MHz ^1H NMR spectra of the carceplexes in $CDCl_3$ at ambient temperature. The spectrum of $H{\cdot}CH_3COCH_2CH_3$ (**6**) provided two sets of H_a and H_b signals, one for the northern and one for the southern hemispheres. Thus, the long axis of the guest and that of the host are roughly coincident (the polar axis). The rotation of the guest around this axis is fast on the ^1H NMR time scale, and rotation around the short equatorial axis (end to end interchange) is slow on the ^1H NMR time scale. The spectrum of $H{\cdot}CH_3CH_2COCH_2CH_3$ (**7**) (the guest is like-ended) gave only one type of signal pattern for the H_a and H_b protons. Since $CH_3CH_2COCH_2CH_3$ has a longer carbon chain than $CH_3COCH_2CH_3$, the longer molecule cannot rotate about the equatorial axes if the shorter molecule cannot. Equally clear is the conclusion that both guest molecules can rotate about their longer polar axes. The ^1H NMR spectra of $H{\cdot}CH_3CH_2OH$ (**4**) and $H{\cdot}(CH_3)_2NCHO$ (**5**) also exhibit only one type of signal pattern for the H_a and H_b protons, but for a different reason. Molecular models (CPK) of **4** and **5** indicate there is plenty of room inside the carcerand for these guests to rotate rapidly around all axes and thus to give a single averaged environment for H_a and H_b.

The ^1H NMR spectrum of $H{\cdot}CH_3OH{\cdot}HOCH_3$ provided a single pattern of H_a and H_b signals. Furthermore, only one signal was observed for the CH_3OH proton at δ −0.75 and a second signal for the CH_3OH proton at δ −0.72. The $\Delta\delta$ for incarcerated CH_3OH vs nonincarcerated CH_3OH is 4.05 ppm, while $\Delta\delta$ for incarcerated CH_3OH vs nonincarcerated CH_3OH is 4.82 ppm based on δ values for 0.5 M CH_3OH in $Cl_2DCCDCl_2$ (acid-free) at room temperature. The most likely model for the orientation of the two incarcerated methanol molecules is one in which they

(6) (a) Baldwin, M. A.; McLafferty, F. W. *Org. Mass Spectrom.* **1973**, *7*, 1353–1356. (b) Cotter, R. J. *Anal. Chem.* **1980**, *52*, 1767–1770.

are hydrogen bonded to one another in the torrid zone (relatively low shielding) of the carcerand and the two methyl groups are located in the northern and southern temperate zones (high shielding) of the globe. In this suggested model, one of the methanol molecules is also hydrogen bonded to the inward-turned electron pairs of an S atom of the CH_2SCH_2 group (see eq 2).

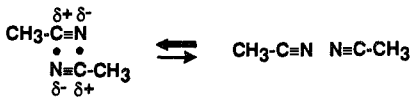


(2)

If this equilibration is slow on the ^1H NMR time scale, the dimer is non-like-ended and the north and south SCH_2 groups could have different chemical shifts. If the dimer rotates around the polar axis rapidly on the ^1H NMR time scale exchanging one H···S for another, then east and west CH_2S protons remain undifferentiated. For this model to apply, the two OH protons would have to have the same chemical shift and the H_a and H_b protons would have to be insensitive to the non-like-endedness of the methanol dimer.

In a variable-temperature ^1H NMR spectral study of H·C-H_3OH·$HOCH_3$ (**1**) over the range of −50 to +110 °C in Cl_2C-$DCDCl_2$, the OH signal shifted monotonically from the low field (δ −0.48 at −50 °C) to higher field (δ −0.72 at 22 °C) to highest field (δ −1.05 at 110 °C), indicating the OH···O hydrogen bond becomes stronger as the temperature is lowered, as expected.[7] The signals for H_a and H_b were little changed over the whole range.

Of the complexes involving acetonitrile (as guest), only H·C-H_3CN (**3**) was isolated in a pure state. It gave a CH_3CN signal at δ −1.65 ppm. By difference, the chemical shift of the protons due to the H·CH_3CN·$NCCH_3$ (**2**) in the 1.2:1.0 **2–3** mixture was easily identified. Thus, the protons of both methyls in **2** gave signals at δ −2.16. We interpret the higher field chemical shifts for the acetonitrile dimer as compared to monomer as being due to the methyls of the dimer being pushed by higher space occupation further into the temperate shielding zone of the carcerand. An attractive model for the acetonitrile dimer, which is compatible with CPK molecular model structure, is formulated as **24**, in which



24 **25**

the two dipoles compensate one another. This structure for the dimer would push the two methyl groups far into the most shielding temperate zone of the carcerand and, in effect, makes the dimer like-ended. This dimer is probably rotating rapidly around the long polar axis. This type of structure would also be compatible with the observation than only one type of H_a and H_b signal pattern is observed for **2**. Molecular models of **24** encapsulated in the carcerand indicate it unlikely that **25** or even other arrangements of the two CH_3CN molecules leave enough space for the $CH_3C{\equiv}N$ molecules to rotate about the equatorial axes of the carceplex rapidly on the ^1H NMR time scale. The observed billiard-ball effect, which allows one $CH_3C{\equiv}N$ molecule to drive out the second upon heating, can be explained by **24** being in equilibrium with a higher energy structure such as **25**, whose kinetic motions along the polar axis of the carceplex provide the driving force for the expulsion.

In the ^1H NMR spectrum of **3** (H·CH_3CN), the H_a and H_b patterns of signals were for a single environment for each of these protons. The spatial requirements of CH_3CN compared to $CH_3COCH_2CH_3$ are relatively small, and CH_3CN would be expected on steric grounds taken alone to rapidly rotate around all axes, as was observed for C_2H_5OH and $(CH_3)_2NCHO$.

Conclusions. We have synthesized seven new carceplexes involving two different hosts and six different guests that are soluble in organic solvents. They were prepared by shell closures of cavitands in 4-fold S_N2 reactions to give carcerands in 20–32% yields. High structural recognition for encapsulation of the more polar component in mixtures with benzene as a cosolvent was shown in the shell closures. Incarcerated molecules included two CH_3OH, two CH_3CN, CH_3CH_2OH, $(CH_3)_2NCHO$, CH_3COC-H_2CH_3, and $CH_3CH_2COCH_2CH_3$. Heating of H·CH_3CN·NC-CH_3 gave H·CH_3CN plus CH_3CN, the reaction going with E_a = 20 kcal mol^{-1}. All carcerands except H·CH_3CN·$NCCH_3$ (**2**) were fully characterized. The degrees of rotational freedom of the guests relative to the host were studied with ^1H NMR spectral techniques.

Experimental Section

General Methods. All air-sensitive reactions were performed under an inert atmosphere in flame-dried glassware. Compounds were dried according to the procedure that provided a correct elemental analysis. THF was freshly distilled from benzophenone ketyl. Benzene and DMF were dried over 3-Å molecular sieves for at least 3 days prior to use. Column chromatography was performed with E. Merck silica gel 60 (70–230 mesh). Silica thin-layer chromatography was done on E. Merck plates (silica gel 60, F254 0.2 mm). Fast atom bombardment (FAB) mass spectra of the cavitands and their precursors were determined on a ZAB SE instrument from VG Analytical with *m*-nitrobenzyl alcohol (NOBA) as the matrix. Mass spectra of the carceplexes were determined by desorption chemical ionization on a Finnigan-MAT 840 (SuperIncos data system) instrument with $(CH_3)_3CH$ as the reagent gas.[7] ^1H NMR spectra were recorded on Bruker instruments (AM 500, AM 360, or 200) and referenced to the solvent signal present or to internal $(CH_3)_4Si$ as 0.00 ppm.

Pentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacosa-1(25),3,5,7(28),9,11,13-(27),15,17,19(26),21,23-dodecaen-4,6,10,12,16,18,22,24-octol, 5,11,17,23-Tetrabromo-2,8,14,20-tetrakis(2-phenylethyl)-, Stereoisomer (10). To a solution of 100 g (110 mmol) of octol **8**[4] in 500 mL of 2-butanone was added with stirring 117 g (655 mmol) of solid *N*-bromosuccinimide. The mixture was stirred at room temperature for 8 h, and the precipitate formed was filtered and washed with cold 2-butanone. The product was dried in vacuo to give 100 g (75%) of **10**: ^1H NMR (360 MHz, $(CD_3)_2CO$) δ 2.50–2.75 (m, 16 H, CH_2CH_2), 4.52 (t, 4 H, methine), 7.11–7.25 (m, 20 H, ArH), 7.75 (s, 4 H, ArH), 8.36 (s, 4 H, ArH); MS (FAB, NOBA) *m/e* 1220 (M + H$^+$, 30%), 1115 (M + H$^+$ − CH_2CH_2Ph, 100%). Anal. Calcd for $C_{60}H_{52}Br_4O_8$: C, 59.04; H, 4.29. Found: C, 58.86; H, 4.20.

Pentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacosa-1(25),3,5,7(28),9,11,13-(27),15,17,19(26),21,23-dodecaen-4,6,10,12,16,18,22,24-octol, 5,11,17,23-Tetrabromo-2,8,14,20-tetrapentyl-, Stereoisomer (11). Application of the above procedure to 50.2 g (65.4 mmol) of **9**[4] and 72 g (404 mmol) of *N*-bromosuccinimide gave 54.2 g (77%) of **11**: ^1H NMR (200 MHz, $(CD_3)_2SO$) δ 0.85 (t, 12 H, CH_3), 1.19–1.32 (m, 24 H, $CH_2CH_2CH_2$), 2.17 (m, 8 H, CH_2 alpha to methine), 4.34 (t, 4 H, methine), 7.34 (s, 4 H, ArH), 9.07 (s, 8 H, OH); MS (FAB, NOBA) *m/e* 1084 (M$^+$, 6%), 1013 (M$^+$ − C_5H_{11}, 100%). Anal. Calcd for $C_{48}H_{60}Br_4O_8$: C, 53.16; H, 5.58. Found: C, 53.24; H, 5.74.

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-Tetrabromo-1,21,23,25-tetrakis(2-phenylethyl)-, Stereoisomer (12). To a solution of 40 g (33 mmol) of **10** in 500 mL of degassed $(CH_3)_2NCHO$ was added 60 g (220 mmol) of K_2CO_3 and 15 mL (230 mmol) of CH_2BrCl. The mixture was stirred at 40 °C for 24 h. The temperature was then increased to 80 °C, and the mixture was allowed to stir for an additional 48 h. The reaction mixture was cooled, and the solvent was evaporated in vacuo. The residue was dissolved in $CHCl_3$ (approximately 1 L) and filtered. The solution was concentrated to yield a crude solid material that was triturated with ethyl acetate. The tan solid obtained after filtration was chromatographed on 500 g of silica gel with methylene chloride–hexanes (4:1) as the mobile phase to provide 22 g (53%) of **12**: ^1H NMR (360 MHz, $CDCl_3$) δ 2.52–2.70 (m, 16 H, CH_2CH_2), 4.42 (d, 4 H, inner OCH_2, J = 7.2 Hz), 4.96 (t, 4 H, methine, J = 8 Hz), 5.98 (d, 4 H, outer OCH_2, J = 7.2 Hz), 7.08–7.25 (m, 24 H, ArH); MS (FAB, NOBA) *m/e* 1269 (M + H$^+$, 100%). Anal. Calcd for $C_{64}H_{52}Br_4O_8$: C, 60.59; H, 4.13. Found: C, 60.52; H, 4.04.

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-Tetrabromo-1,21,23,25-tetrapentyl-, Stereoisomer (13). Application of the above procedure to 54.1 g (52 mmol) of **11**, 33.5 mL (516 mmol) of CH_2BrCl, and 110 g (800 mmol) of K_2CO_3 gave, after crystallization from CH_2Cl_2–EtOH, 32.5 g (56%) of **13**: ^1H NMR (200 MHz, $CDCl_3$) δ 0.92 (t, 12 H, CH_3), 1.39 (m, 24 H, $CH_2CH_2CH_2$), 2.20 (m, 8 H, CH_2 α to methine), 4.39 (d, 4 H, inner OCH_2, J = 8 Hz), 4.85 (t, 4 H,

(7) Akitt, J. W. *NMR and Chemistry*; Chapman and Hall: New York, 1983; p 99.

methine, J = 8 Hz), 5.96 (d, 4 H, outer OCH_2, J = 8 Hz), 7.03 (s, 4 H, ArH); MS (FAB, NOBA) m/e 1133 (M^+, 100%). Anal. Calcd for $C_{52}H_{60}Br_4O_8$: C, 55.14; H, 5.34. Found: C, 55.01; H, 5.29.

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, 1,21,23,25-Tetrakis(2-phenylethyl)-, Tetramethyl Ester, Stereoisomer (14). To a solution of 9.0 g (7.4 mmol) of tetrabromide **12** in 500 mL of tetrahydrofuran stirred at −78 °C was added dropwise 50 mL of a 1.6 M mixture (80 mmol) of *n*-BuLi. The mixture was stirred at −78 °C for 2 h after the addition was complete, and then 6.5 mL (82 mmol) of CH_3O_2CCl was added. The mixture was allowed to warm (several hours) to 25 °C, 20 mL of H_2O was added, and the solvent was evaporated in vacuo. The residue was extracted with CH_2Cl_2–water, and the organic solution was dried over $MgSO_4$ and evaporated to dryness under vacuum. The crude solid material was chromatographed on silica gel with CH_2Cl_2–hexanes (80:20) to provide 7.2 g (82%) of the tetraester **14**: ^1H NMR (360 MHz, $CDCl_3$) δ 2.50–2.75 (m, 16 H, CH_2CH_2), 3.84 (s, 12 H, CO_2CH_3), 4.42 (d, 4 H, inner OCH_2, J = 7.5 Hz), 4.96 (t, 4 H, methine, J = 8 Hz), 5.96 (d, 4 H, outer OCH_2, J = 7.5 Hz), 7.08–7.26 (m, 24 H, ArH); MS (FAB, NOBA) m/e 1185 (M^+ + H, 82%), 1155 ($M^+ - OCH_3$, 100%). Anal. Calcd for $C_{72}H_{64}O_{16}$: C, 72.96; H, 5.44. Found: C, 72.90; H, 5.62.

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, 1,21,23,25-Tetrapentyl-, Tetramethyl Ester, Stereoisomer (15). Application of the above procedure to 10.7 g (9.4 mmol) of **13**, 700 mL of THF, 30.1 mL (2.5 M, 75.3 mmol) of *n*-BuLi, and 10.3 mL (152 mmol) of CH_3O_2CCl gave, after recrystallization from CH_2Cl_2–EtOH, 7.88 g (80%) of **15**: ^1H NMR (200 MHz, $CDCl_3$) δ 0.91 (t, 12 H, CH_3), 1.38 (m, 24 H, $CH_2CH_2CH_2$), 2.20 (m, 8 H, CH_2 α to methine), 3.83 (s, 12 H, CO_2CH_3), 4.57 (d, 4 H, inner OCH_2, J = 8 Hz), 4.75 (t, 4 H, methine, J = 8 Hz), 5.65 (d, 4 H, outer OCH_2, J = 8 Hz), 7.15 (s, 4 H, ArH); MS (FAB, NOBA) m/e 1049 (M^+ + H, 73%), 1019 ($M^+ - OCH_3$, 100%). Anal. Calcd for $C_{60}H_{72}O_{16}$: C, 68.69; H, 6.92. Found: C, 68.57; H, 7.00.

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, 1,21,23,25-Tetrakis(2-phenylethyl)-, Stereoisomer (16). A solution of 7.5 g (6.3 mmol) of **14** dissolved in 200 mL of THF was added with stirring to a mixture of 3 g (80 mmol) of $LiAlH_4$ and 300 mL of THF. The mixture was stirred at room temperature for 12 h, and the excess hydride was quenched by careful addition of 3 mL of H_2O, 3 mL of 10% NaOH, and 9 mL of H_2O. The inorganic salts were filtered, and the THF solution was dried over $MgSO_4$. The solvent was evaporated in vacuo to provide 5.74 g of tetrol **16** (85%): ^1H NMR (360 MHz, $CDCl_3$) δ 2.50–2.77 (m, 16 H, CH_2CH_2), 3.85 (d, 8 H, CH_2OH), 4.42 (d, 4 H, inner OCH_2, J = 7 Hz), 4.95 (t, 4 H, methine, J = 8 Hz), 5.94 (d, 4 H, outer OCH_2, J = 7 Hz), 7.11–7.30 (m, 24 H, ArH); MS (FAB, NOBA) m/e 1080 (M + Li^+, 100%). Anal. Calcd for $C_{68}H_{64}O_{12}$: C, 75.62; H, 5.97. Found: C, 75.53; H, 5.88.

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, 1,21,23,25-Tetrapentyl-, Stereoisomer (17). Application of the above procedure to 8.4 g (8.0 mmol) of tetraester **15**, 250 mL of THF, and 3.0 g (80 mmol) of $LiAlH_4$ gave 6.7 g (90%) of **17**: ^1H NMR (200 MHz, $CDCl_3$) δ 0.91 (t, 12 H, CH_3), 1.38 (m, 24 H, $CH_2CH_2CH_2$), 2.20 (m, 8 H, CH_2 α to methine), 3.84 (s, 8 H, CH_2OH), 4.57 (d, 4 H, inner OCH_2, J = 8 Hz), 4.75 (t, 4 H, methine, J = 8 Hz), 5.65 (d, 4 H, outer OCH_2, J = 8 Hz), 7.16 (s, 4 H, ArH); MS (FAB, NOBA) m/e 943 (M + Li^+, 60%). Anal. Calcd for $C_{56}H_{72}O_{12}$: C, 71.77; H, 7.74. Found: C, 71.53; H, 7.53.

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-Tetrakis(chloromethyl)-1,21,23,25-tetrakis(2-phenylethyl)-, Stereoisomer (18). A solution of *N*-chlorosuccinimide (8.4 g, 63 mmol) and triphenylphosphine (15.7 g, 60 mmol) in 300 mL of THF were stirred at room temperature for 45 min. Tetrol **16** (6.8 g, 6.3 mmol) was dissolved in 200 mL of THF and added to the reaction mixture. The mixture was stirred an additional 8 h at room temperature, and then 100 mL of absolute EtOH was added. The solvents were evaporated in vacuo, and the crude solid was recrystallized from CH_2Cl_2–EtOH to provide tetrachloride **18**, 5.14 g (72%): ^1H NMR (360 MHz, $CDCl_3$) δ 2.50–2.77 (m, 16 H, CH_2CH_2), 4.48–4.52 (overlapping s and d, 12 H, CH_2Cl and inner OCH_2), 4.80 (t, 4 H, methine, J = 8 Hz), 5.96 (d, 4 H, outer OCH_2, J = 7.3 Hz), 7.08–7.33 (m, 24 H, ArH); MS (FAB, NOBA) m/e (four-Cl isotope pattern centered at 1148, 100%). Anal. Calcd for $C_{68}H_{68}Cl_4O_8$: C, 71.19; H, 5.27. Found: C, 71.22; H, 5.42.

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-Tetrakis(chloromethyl)-1,21,23,25-tetrapentyl-, Stereoisomer (19). Application of the above procedure to 9.6 g (72 mmol) of *N*-chlorosuccinimide, 16.2 g (62 mmol) of triphenylphosphine, and 6.70 g (7.2 mmol) of tetrol **17** in 200 mL of THF gave, after recrystallization from CH_2Cl_2–EtOH, 4.73 g (65%) of **19**: ^1H NMR (200 MHz, $CDCl_3$) δ 0.91 (t, 12 H, CH_3), 1.38 (m, 24 H, $CH_2CH_2CH_2$), 2.20 (m, 8 H, CH_2 α to methine), 4.49–4.53 (overlapping s and d, 12 H, CH_2Cl and inner OCH_2), 4.99 (t, 4 H, methine, J = 8 Hz), 5.99 (d, 4 H, outer OCH_2, J = 8 Hz), 7.16 (s, 4 H, ArH); MS (FAB, NOBA) four-Cl isotope pattern centered at m/e 1010 (M^+, 100%). Anal. Calcd for $C_{56}H_{68}Cl_4O_8$: C, 66.53; H, 6.78. Found: C, 66.66; H, 6.88.

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, 1,21,23,25-Tetrakis(2-phenylethyl)-, Stereoisomer (20). Tetrachloride **18** (6.5 g, 5.6 mmol) was partially dissolved in 500 mL of degassed $(CH_3)_2NCHO$. Thiourea (3.1 g, 40 mmol) was added, and the solution was heated to 80 °C for 12 h. After it cooled to room temperature, the solution was poured into 600 mL of degassed aqueous 1 N NaOH. This mixture was stirred for 45 min and neutralized to pH 4–5 with HCl. The product was extracted into CH_2Cl_2 and solvent was evaporated in vacuo. Crystallization of the residue from CH_2Cl_2–EtOH provided tetrathiol **20**: 4.64 g (80%); ^1H NMR (360 MHz, $CDCl_3$) δ 1.90 (t, 4 H, SH, J = 8 Hz), 2.50–2.75 (m, 16 H, CH_2CH_2), 3.56 (d 8 H, CH_2SH, J = 8 Hz), 4.45 (d, 4 H, inner OCH_2, J = 8 Hz), 4.78 (t, 4 H, methine, J = 8 Hz), 5.93 (d, 4 H, outer OCH_2, J = 7.2 Hz), 7.11–7.30 (m, 24 H, ArH); MS (FAB, NOBA) m/e 1138 (M^+ + H, 100%). Anal. Calcd for $C_{68}H_{64}S_4O_8$: C, 71.82; H, 5.67. Found: C, 71.95; H, 5.93.

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, 1,21,23,25-Tetrapentyl-, Stereoisomer (21). Application of the above procedure to 4.7 g (4.7 mmol) of tetrachloride **19**, 2.1 g (28 mmol) of thiourea, and 500 mL of $(CH_3)_2NCHO$ (degassed) gave, after recrystallization from CH_2Cl_2–EtOH, 2.00 g of **21** (60%): ^1H NMR (200 MHz, $CDCl_3$) δ 0.91 (t, 12 H, CH_3), 1.38 (m, 24 H, $CH_2CH_2CH_2$), 1.90 (t, 4 H, SH, J = 8 Hz), 2.20 (m, 8 H, CH_2 α to methine), 3.84 (d, 8 H, CH_2SH, J = 8 Hz), 4.47 (d, 4 H, inner OCH_2, J = 8 Hz), 4.75 (t, 4 H, methine, J = 8 Hz), 5.96 (d, 4 H, outer OCH_2, J = 8 Hz), 7.16 (s, 4 H, ArH); MS (FAB, NOBA) m/e 1001 (M + H, 100%). Anal. Calcd for $C_{56}H_{72}S_4O_8$: C, 67.17; H, 7.25. Found: C, 67.27; H, 7.19.

1*H*,7*H*,9*H*,21*H*,29*H*,35*H*,37*H*,47*H*,49*H*-Bis[1,3]benzodioxocino[9,8-*d*:9′,8′-*d*″][1,3,11,13,7,17]tetraoxadithiacycloeicosino[4,5-*j*:10,9-*j*′:14,15-*j*″:20,19-*j*‴]tetrakis[1,3]benzodioxocin, 1,19,21,29,47,49,57,62,-octapentyl-, Stereoisomer Containing 2-Butanone (6). Rubidium carbonate (3.7 g, 16 mmol) was dissolved in 500 mL of 2-butanone and the resultant mixture heated to reflux. Tetrathiol **21** (1.32 g, 1.32 mmol) in 175 mL of 2-butanone and tetrachloride **19** (1.33 g, 1.32 mmol) in 175 mL of 2-butanone were mixed and added dropwise over 24 h via a constant-rate addition funnel to the stirred mixture at reflux. After the addition was complete, the mixture was refluxed an additional 48 h and cooled to room temperature. Water and CH_2Cl_2 were added, and the layers were separated. A large amount of white solid persisted, which was dissolved by additional $CHCl_3$. The organic layers were combined, and the solvent was evaporated in vacuo. Chromatography of the residue on silica gel with 50% pentane in $CHCl_3$ as the mobile phase yielded 0.81 g of carceplex **6** ($H{\cdot}CH_3COCH_2CH_3$) in 32% yield: ^1H NMR (360 MHz, $CDCl_3$) δ −3.08 (t, 3 H, $CH_3COCH_2CH_3$), −1.94 (s, 3 H, $CH_3COCH_2CH_3$), 0.74 (q, 2 H, $CH_3COCH_2CH_3$), 0.88 (t, 24 H, CH_3), 1.31–1.38 (m, 48 H, $CH_2CH_2CH_2$), 2.15 (m, 16 H, CH_2 α to methine), 3.85 (s, 16 H, $(CH_2)_2S$), 4.52 (d, 4 H, half of inner OCH_2), 4.71 (overlapping t and d, 12 H, methine and half of inner OCH_2), 5.87 (two overlapping d, 8 H, outer OCH_2), 7.03 (s, 8 H, ArH); MS (DCI positive ion) m/e 1939 (M + H^+, 100%), 1866 (empty **6**, 30%); MS (DCI negative ion) m/e 1938 (M^-, 100%), 1866 (empty **6**, 30%). Anal. Calcd for $C_{116}H_{144}S_4O_{17}$ (dried at 150 °C, 10^{-5} Torr, 6 h): C, 71.87; H, 7.49; S, 6.61; O, 14.03. Found: C, 71.86; H, 7.45; S, 6.48; O, 14.13; sum 99.92.

Carceplex 7 ($H{\cdot}CH_3CH_2COCH_2CH_3$). Potassium carbonate (0.85 g, 6.1 mmol) was dissolved in 500 mL of 3-pentanone. Tetrathiol **21** (0.61 g, 0.61 mmol) in 150 mL of 3-pentanone and tetrachloride **19** (0.62 g, 0.62 mmol) in 150 mL of 3-pentanone were combined and added dropwise over 24 h via a constant-rate addition funnel to the mixture stirred at reflux. The mixture was refluxed for an additional 12 h, and the solvent was evaporated in vacuo. The residue was extracted with $CHCl_3$–H_2O, and the organic layer was concentrated under reduced pressure. Chromatography of the residue on silica gel with 50% pentane in $CHCl_3$ yielded 0.27 g (23%) of **7**: ^1H NMR (360 MHz, $CDCl_3$) δ −3.39 (t, 6 H, $CH_3CH_2COCH_2CH_3$), 0.9 (t, 24 H, $(CH_2)_4CH_3$), 1.36 (m, 48 H, $CH_2CH_2CH_2$), 2.17 (m, 16 H, CH_2 α to methine), 3.86 (s, 16 H, $(CH_2)_2S$), 4.64 (d, 8 H, inner OCH_2), 4.73 (t, 8 H, methine), 5.87 (d, 8 H, outer OCH_2), 7.03 (s, 8 H, ArH), quartet of $CH_3CH_2COCH_2CH_3$

obscured; MS (DCI positive ion) m/e 1952 (M^+, 100%), 1866 (empty **7**, 50%); MS (DCI negative ion) m/e 1952 (M^-, 100%). Anal. Calcd for $C_{117}H_{142}S_4O_{17}$ (dried at 150 °C, 10^{-5} Torr, 6 h): C, 71.97; H, 7.54; S, 6.57; O, 13.93. Found: C, 71.91; H, 7.67; S, 6.49; O, 13.74; sum, 99.81.

Carceplex 4 ($H{\cdot}CH_3CH_2OH$). Cesium carbonate (1.2 g, 3.5 mmol) was dissolved in 100 mL of ethanol and 200 mL of benzene at reflux. Tetrathiol **21** (0.35 g, 0.35 mmol) and tetrachloride **19** (0.35 g, 0.35 mmol) in 100 mL of benzene were added dropwise over 24 h via a constant-rate addition funnel to the mixture stirred at reflux. The mixture was refluxed for an additional 24 h, and the solvent was evaporated in vacuo. The residue was extracted with $CHCl_3$-H_2O, and the organic layer was concentrated under reduced pressure. Chromatography of the residue on silica gel with 50% pentane in $CHCl_3$ as the mobile phase gave 0.13 g (20%) of **4**: ^1H NMR (360 MHz, $CDCl_3$) δ -3.33 (t, 1 H, CH_3CH_2OH), -1.18 (t, 3 H, CH_3CH_2OH), 0.59 (m, 2 H, CH_3CH_2OH), 0.91 (t, 24 H, CH_3), 1.34 (m, 48 H, $CH_2CH_2CH_2$), 2.18 (m, 16 H, CH_2 α to methine), 3.86 (s, 16 H, $(CH_2)_2S$), 4.47 (d, 8 H, inner OCH_2), 4.71 (t, 8 H, methine), 5.87 (d, 8 H, outer OCH_2), 7.03 (s, 8 H, ArH); MS (DCI positive ion) m/e 1913 ($M + H^+$, 100%), 1866 (empty **4**, 20%); MS (DCI negative ion) m/e 1912 (M^-, 100%), 1866 (empty **4**, 30%). Anal. Calcd for $C_{114}H_{142}S_4O_{17}$ (dried at 150 °C, 10^{-5} Torr, 6 h): C, 71.59; H, 7.48; S, 6.69; O, 14.22. Found: C, 71.97; H, 7.12; S, 6.46; O, 14.45; sum 100.02%.

Carceplex 5 ($H{\cdot}(CH_3)_2NCHO$). Rubidium carbonate (1.2 g, 4.5 mmol) was dissolved in 200 mL of degassed $(CH_3)_2NCHO$ at 80 °C. Tetrathiol **21** (0.35 g, 0.35 mmol) and tetrachloride **19** (0.35 g, 0.35 mmol) in 200 mL of $(CH_3)_2NCHO$ were added dropwise over 24 h via a constant-rate addition funnel. The mixture was stirred for an additional 24 h, and the solvent was evaporated in vacuo. The residue was extracted with $CHCl_3$-H_2O, and the organic layer was concentrated under reduced pressure. Chromatography of the residue on silica gel with 50% pentane in $CHCl_3$ yielded 0.14 g (20%) of **5**: ^1H NMR (360 MHz, $CDCl_3$) δ -0.33 (s, 3 H, CH_3NCH_3CHO), -0.10 (s, 3 H, CH_3NCH_3CHO), 0.89 (t, 24 H, CH_3), 1.32 (m, 48 H, $CH_2CH_2CH_2$), 2.18 (m, 16 H, CH_2 alpha to methine), 3.85 (s, 16 H, $(CH_2)_2S$), 4.47 (d, 8 H, inner OCH_2), 4.87 (t, 8 H, methine), 5.78 (s, 1 H, $(CH_3)_2NCHO$), 5.87 (d, 8 H, outer OCH_2), 7.03 (s, 8 H, ArH); MS (DCI positive ion) m/e 1939 (M^+, 100%), 1866 (empty **5**, 45%); MS (DCI negative ion) m/e 1939 (M^-, 100%), 1867 (empty **5**, 30%). Anal. Calcd for $C_{115}H_{143}NS_4O_{17}$ (dried at 150 °C, 10^{-5} Torr, 6 h): C, 71.22; H, 7.43; N, 0.72; S, 6.60; O, 14.03. Found: C, 71.41; H, 7.08; N, 0.92; S, 6.58; O, 14.24; sum 100.24.

Carceplex 1 ($H{\cdot}CH_3OH{\cdot}HOCH_3$). Rubidium carbonate (1.0 g, 4.3 mmol) was dissolved in 200 mL of methanol and 100 mL of benzene at reflux. Tetrathiol **20** (0.35 g, 0.35 mmol) and tetrachloride **18** (0.35 g, 0.35 mmol) in 100 mL of benzene were added dropwise to the stirred refluxing mixture over 24 h via a constant-rate addition funnel. The mixture was refluxed for an additional 24 h, and the solvent was evaporated in vacuo. The residue was extracted with $CHCl_3$-H_2O, and the organic layer was concentrated under reduced pressure. Chromatography of the residue on silica gel with 50% pentane in $CHCl_3$ as the mobile phase yielded 0.17 g (22%) of **1**: ^1H NMR (360 MHz, $CDCl_3$) δ -0.75 (d, 6 H, CH_3OH), -0.72 (d, 2 H, CH_3OH), 2.50-2.75 (m, 32 H, CH_2CH_2), 3.86 (s, 16 H, CH_2SH), 4.45 (d, 8 H, inner OCH_2), 4.75 (t, 8 H, methine), 5.96 (d, 8 H, outer OCH_2), 7.11-7.35 (m, 48 H, ArH); MS (DCI positive ion) m/e 2203 ($M + H^+$, 100%), 2171 ($M + H^+ - CH_3OH$, 75%), 2139 (empty **1** + H^+, 20%); MS (DCI negative ion) m/e 2202 (M^-, 100%), 2170 ($M^- - CH_3OH$, <10%), 2139 (empty carcerand, 20%). Anal. Calcd for $C_{138}H_{128}S_4O_{18}$ (dried at 150 °C, 10^{-5} Torr, 6 h): C, 75.24; H, 5.85; S, 5.83; O, 13.07. Found: C, 75.01; H, 5.97; S, 5.88; O, 13.13; sum, 99.99.

Carceplex 3 ($H{\cdot}CH_3CN$). Rubidium carbonate (1.0 g, 4.3 mmol) was dissolved in 200 mL of acetonitrile and 100 mL of benzene at reflux. Tetrathiol **21** (0.35 g, 0.35 mmol) and tetrachloride **19** (0.35 g, 0.35 mmol) in 100 mL of benzene were added dropwise over 24 h via a constant-rate addition funnel. The mixture was refluxed for an additional 24 h, and the solvent was evaporated in vacuo. The residue was extracted with $CHCl_3$-H_2O, and the organic layer was concentrated under reduced pressure. Chromatography of the residue on silica gel with 50% pentane in $CHCl_3$ yielded a mixture of **3** ($H{\cdot}CH_3CN$) and **2** ($H{\cdot}CH_3CN{\cdot}NCCH_3$) in 1:1.2 proportions, respectively, by proton counting of $H{\cdot}CH_3CN$ at δ -1.64 due to **3** and $H{\cdot}CH_3CN{\cdot}NCCH_3$ at δ -2.15 due to **2** (^1H NMR spectra in $CDCl_3$ at 25 °C). The mixture was dissolved in toluene and refluxed for 72 h during which time the 1:2 complex was converted to 0.19 g (25%) of the 1:1 carceplex (**3**) that was characterized: ^1H NMR (360 MHz, $CDCl_3$) δ -1.64 (s, 3 H CH_3CN), 2.50-2.75 (m, 32 H, CH_2CH_2), 3.86 (s, 16 H, $(CH_2)_2SH$), 4.45 (d, 8 H, inner OCH_2), 4.75 (t, 8 H, methine), 5.96 (d, 8 H, outer OCH_2), 7.11-7.35 (m, 48 H, ArH); MS (DCI positive ion) m/e 2180 ($M + H^+$, 100%) 2139 ($M + H^+ - CH_3CN$, 50%); MS (DCI negative ion) m/e 2179 (M^-, 50%), 2139 ($M^- + H - CH_3CN$, 50%). Anal. Calcd for $C_{138}H_{123}NS_4O_{16}$ (dried at 150 °C, 10^{-5} Torr, 6 h): C, 76.06; H, 5.69; N, 0.64; S, 5.87; O, 11.74. Found: C, 75.92; H, 5.88; N, 0.61; S, 5.72; O, 11.62; sum, 99.75.

Rates of Decomplexation of 2 To Give 3. A 3-mmol solution of **2** was prepared by dissolving the carceplex in tetrachloroethane-d_2. Samples of this solution were placed in NMR tubes, and the tubes were immersed in a thermostated oil bath (±1 °C) at 353 and 363 K. Spectra (^1H NMR) were recorded at 298 K. A series of 7-10 spectra were obtained over a 40-h period. The kinetic data at 373 and 383 K were derived from a series of spectra taken over 15- and 6-h periods, respectively. The experiments at 373 and 383 K were performed on a Bruker AM 500-MHz spectrometer equipped with a variable-temperature probe regulated to within ±1 °C of the desired temperature. The probe temperature was calibrated with an ethylene glycol standard. Spectra at 373 and 383 K were obtained via an automated data acquisition program, which recorded spectra at prescribed time intervals. The relative concentrations ([**2**]:[**3**]) in all experiments were calculated from the integrals of the distinct singlets unique to each species.

Use of ^{17}O NMR in a Stereochemical Study of the Alkaline Hydrolysis of Cyclic Six-Membered 2-Aryl Phosphates

Barbara Gordillo and Ernest L. Eliel*

Contribution from the William Rand Kenan Laboratories, Department of Chemistry, CB No. 3290, University of North Carolina, Chapel Hill, North Carolina 27599-3290.
Received August 17, 1990

Abstract: The alkaline hydrolysis of the title compounds **1-5** (Chart II) with $^{17}OH^-$ has been studied. The labeled cyclic phosphate salts produced by hydrolysis of **1-5** were converted to a mixture of the corresponding methyl esters **9** (Scheme III) by treatment with diazomethane. The resulting mixture was analyzed by ^{31}P NMR or GC for the epimeric OCH_3 ratio and by ^{17}O NMR for the ^{17}O axial to equatorial ratio in the P=^{17}O moiety. Nucleophilic displacement of ArO^- by $^{17}OH^-$ at phosphorus is nonstereospecific. The results can be rationalized by postulating that the direct displacement process involving inversion competes with pseudorotation of pentacoordinate intermediates involving retention.

Several years ago, we described[1] the use of ^{17}O NMR as a tool in the assignment of configuration of cyclic phosphates. In conformationally locked systems (Chart I) the axial phosphoryl oxygen nucleus is shifted downfield from the equatorial one by

0002-7863/91/1513-2172$02.50/0