A Tetrathiol Bowl-shaped Cavitand and a Derived Carceplex

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The syntheses and characterization of tetrathiol bowl **4**, its rearranged byproduct **6** and its derived carceplex **7**⊙$Me_2NCOMe{\cdot}4PhNO_2$ are reported, and the crystal structure of this carceplex is compared to that of its oxygen analogue, **8**⊙$Me_2NCOMe{\cdot}5CHCl_3$.

The first carceplexes to be reported were those whose hosts were prepared by rim-to-rim coupling reactions of two bowl-shaped compounds (*e.g.* **1**) through four bridges. The first types of bridges were CH_2SCH_2[1] and OCH_2O,[2] too short to provide gaps of molecular dimensions in the skin of the host. The coupling reactions were templated by solvent or solute molecules which, upon shell closure, became incarcerated guest molecules.[1–3] The mechanical containment of guest in host was referred to as *constrictive binding*.[4]

Here we report the syntheses of new compounds **3**–**7** and **9**,† **7** being characterized as its carceplex, 7⊙Me_2NCOMe.‡ This hollow compound with its imprisoned Me_2NCOMe was synthesized by the sequence **2**[3] → **3** → **4** → **5** → **7**⊙Me_2-NCOMe.§ The first two reactions were patterned after the conversion of 1,3-dimethoxybenzene to 2,6-dimethoxybenzenethiol.[5]

In unpublished work, the authors successfully formed hemicarceplexes in 50% yield by treatment of tetrol **1** with 1,3-$(ClCH_2)_2C_6H_4$ in *N*-methylpyrrolidinone–Cs_2CO_3 at 25–70 °C. In an attempt to synthesize the corresponding thiahemicarceplexes, 1 equiv. of tetrathiol **4** and 2 equiv. of 1,3-$(BrCH_2)_2C_6H_4$ in Me_2NCOMe–Cs_2CO_3 were stirred at 30 °C for 12 h and then at 65 °C for 12 h to produce after silica gel chromatography a 37% yield of **9**.† A Corey–Pauling–Koltun molecular model of **9** appears unstrained, while its oxygen analogue is difficult to assemble. Thus these models successfully correlate the directions taken by the reactions of the tetrol and tetrathiol with potential bridging agents.

Fig. 1 provides crystal-structure views involving complexes of **6**–**8**. Cavitand **6** contains a CH_2Cl_2 molecule with its CH_2 hydrogens pointing inward to provide guest-to-host H···C nonbonded distances as short as 2.9 Å. The host in 7⊙Me_2NCOMe is centrosymmetric in the crystal and its single Me_2NCOMe guest is disordered over 4 different orientations in the host cavity (two independent orientations, plus the two related orientations implied by the centre of symmetry). The host in **8**⊙Me_2NCOMe possesses noncrystallographic approximate D_4 symmetry with a C_4 long polar axis and four shorter C_2 axes.[2] Its Me_2NCOMe guest was well modelled with a single orientation in the host cavity, in contrast to the partial disorder of its sulfur analogue. In 7⊙Me_2NCOMe the plane of the guest in each of its orientations is roughly perpendicular to a line joining opposite bridges in the host, while in **8**⊙Me_2NCOMe the guest's plane is nearly perpendicular to a line joining opposite portals (see partial end views). Only one guest orientation is shown for **7** in Fig. 1. Whereas the two hemispheric caps of host **8** are rotated 25° with respect to one another about the common polar axis, this rotation is absent in **7**, and the northern and southern polar axes are parallel but displaced by a (perpendicular) distance of 1.72 Å. In both hosts, the heteroatoms' unshared electron pairs and the two hydrogens of the attached CH_2 groups generally face along the surface of the shell or outward, but not inward. A measure of the difference in size of the cavities is the average distance between the mean planes of 4 S atoms in **7**, 2.3 Å, and between planes of corresponding O atoms in **8**, 1.7 Å. Although the guest in 7⊙Me_2NCOMe does not completely fill the cavity, the sulfur to CH_3 carbon distances are as short as 3.0 Å, and the guest H to host C distances are as short as 2.4 Å. In **8**⊙Me_2NCOMe, host O to guest CH_3 carbon distances as short as 3.0 Å were observed.[2] Guest CH_3 carbon to host CH_2 carbon distances are also as short as 2.9–3.1 Å.

These are short distances indeed!

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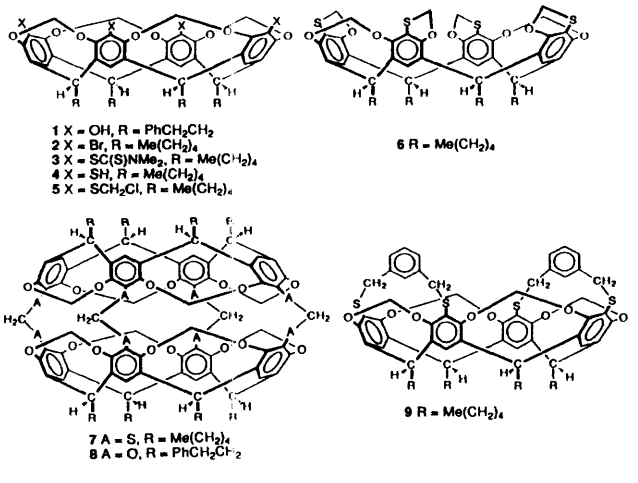


Footnotes

† These compounds all gave C and H elemental analyses within 0.30% of theory, M^+ *m/z* signals of substantial intensity in their MS or FAB MS, and ^1H NMR spectra consistent with their structures.

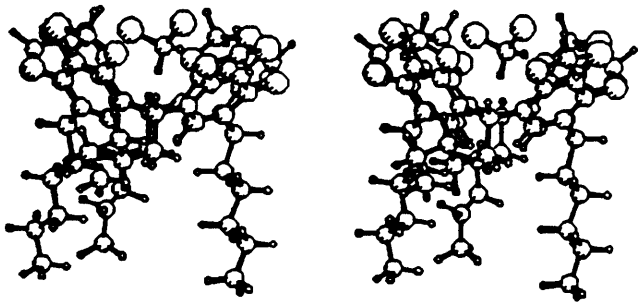
‡ We propose use of the symbol ⊙ to signify incarceration of guests in hosts, and the symbol ∪ for nesting, perching or partially encapsulated complexes such as **6**∪CH_2Cl_2.

§ In our syntheses, **2** was lithiated at −78 °C with Bu^nLi in THF and $Me_2NCS_2S_2CNMe_2$ was added to give **3** (84%). The reduction of **3** to **4** (55%) with excess $LiAlH_4$·THF required initial cooling of the reaction mixture to 0 °C followed by a 20 h reaction period at 25 °C. The excess $LiAlH_4$ had to be decomposed carefully at 0 °C with water. Attempts to convert tetrathiol directly to 7⊙Me_2NCOMe in Me_2NCOMe–K_2CO_3–CH_2ClBr at 70–100 °C only led to small amounts of compound **6**,† whose constitution was confirmed by crystal structure determination.

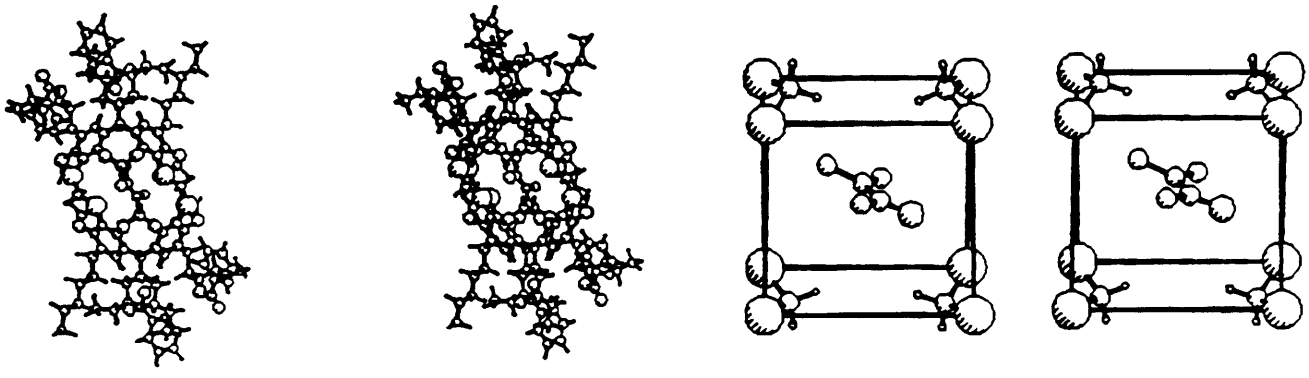
This compound probably was derived from precursor byproducts produced during the reduction of **3** to **4**. Accordingly, purified tetrathiol **4** was converted to tetrachloromethyl sulfide **5** (62%) with CH_2ClBr–$NEtPr^i_2$·Me_2CO at 25 °C for 10 h. The reaction of equivalent amounts of **5** with **4** in Me_2NCOMe–Cs_2CO_3–argon involved stirring the suspension for 24 h at 30 °C, 20 h at 60 °C and 3 h at 85 °C. The standard evaporative and extractive procedures[2] gave 7⊙Me_2NCOMe, which was purified by flash chromatography in silica gel–CH_2Cl_2–Et_2O to give pure carceplex† (22%). The constitution of 7⊙Me_2NCOMe was confirmed by its crystal structure.

Its ^1H NMR spectrum (200 MHz) in $CDCl_3$ gave the following signals: δ, −1.75 (s, CH_3CO, 3H), −0.62 (s, NCH_3, *syn* to O, 3H), 0.90 (t, CH_2CH_3, 24H), 1.30 (m, $CH_2CH_2CH_2$ and NCH_3, *anti* to O, 51H), 2.13 (m, CH_2 α to methine, 16H), 4.16 (s, SCH_2S, 8H), 4.37 (d, inner OCH_2, J = 6.9 Hz, 8H), 4.76 (t, Ar_2CH, 8H), 5.92 (d, outer OCH_2, J = 6.9 Hz, 8H) and 7.06 (s, Ar *H*, 8H).

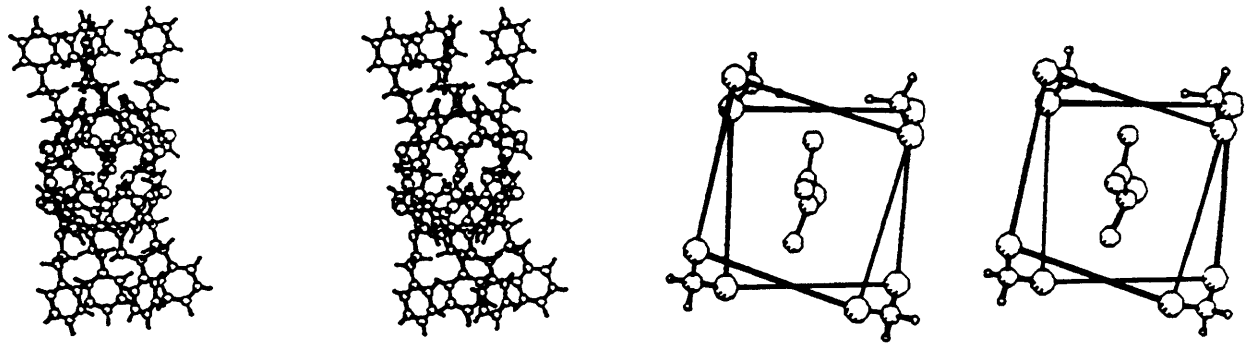
The crystal structure of **6**∪CH_2Cl_2 (**6** crystallized from CH_2Cl_2, determined at 25 °C) belongs to the triclinic space group $P\bar{1}$, refined to R = 0.071. The crystal structure of 7⊙$Me_2NCOMe{\cdot}4PhNO_2$ (crystallized from $PhNO_2$–$CHCl_3$, determined at 25 °C) also belongs to the triclinic space



Side view of crystal structure of 6⊃CH_2Cl_2



Side view of 7⊃Me_2NCOMe•4$PhNO_2$ Partial end view of 7⊃Me_2NCOMe



Side view of 8⊃Me_2NCOMe Partial end view of 8⊃Me_2NCOMe

Fig. 1 Stereoviews of crystal structures of **6–8**. Partial end views show an incarcerated Me_2NCOMe guest molecule and the S–CH_2–S (**7**) or O–CH_2–O (**8**) bridging groups, with the 4 S or O atoms belonging to the same hemisphere connected by solid lines.

group $P\bar{1}$ and was refined to R = 0.079. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

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