Dissymmetric new hemicarcerands containing four bridges of different lengths

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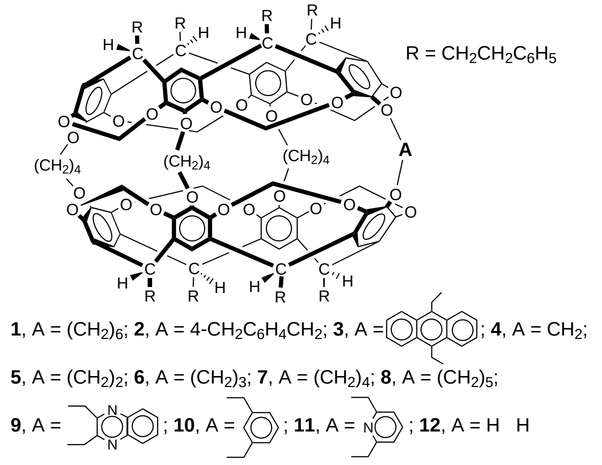
Three new hemicarcerands 1–3 each with one unique eight-atom-long bridge and three identical six-atom-long bridges are reported along with a crystal structure of 2⊙PhNO$_2$, a totally dissymmetric host with nitrobenzene as encapsulated guest.

A prior paper reported the syntheses and characterizations of seven new hemicarcerands **4–6**, **8–11** and 36 new hemicarceplexes with diol **12** as starting material.[1] The crystal structure of **8**⊙4-MeC$_6$H$_4$OMe indicated it to be somewhat disordered but essentially isostructural with more than 25 hemicarceplexes of **7**⊙guest containing 4 O(CH$_2$)$_4$O bridges.[2,3]



Examination of Corey–Pauling–Koltun (CPK) models of possible unique bridges whose lengths, steric requirements and rigidities would seriously disrupt the isostructural pattern of the standard [O(CH$_2$)$_4$O]$_3$ bridges provided O(CH$_2$)$_6$O, *p*-OCH$_2$C$_6$H$_4$CH$_2$O and 9,10-(OCH$_2$)$_2$-anthracene as candidate moieties. In *N*-methylpyrrolidinone (NMP) as solvent and Cs$_2$CO$_3$ as base, at temperatures of 55–70 °C, diol **12** reacted respectively with TsO(CH$_2$)$_6$OTs (Ts = tosyl), 4-ClCH$_2$C$_6$H$_4$CH$_2$Cl and 9,10-(ClCH$_2$)$_2$-anthracene to give after chromatographic purification (thick layer plate, CHCl$_3$/silica gel), **1**⊙CHCl$_3$ (78%), **2**⊙CHCl$_3$ (80%) and **3** (empty, 78%).†,‡ In **1–3** the unique bridges are all eight atoms long and of varying degrees of rigidity and steric requirements. Formally, the two portals that flank the unique bridge are 28-membered rings, while the other two are 26-membered rings.

The fact that **1** and **2** were isolated as their complexes with CHCl$_3$ rather than with NMP inside indicates either that the final bond-making process occurred in an empty cavity, or that guest exchange, host⊙NMP + CHCl$_3$ $\longrightarrow$ host⊙CHCl$_3$ + NMP, took place during the chromatographic purification conducted at 25 °C. In contrast, empty **3** was isolated as the product of completing the shell closure. In CPK models, both NMP and CHCl$_3$ easily enter and depart the inner phase of **1–3**, although the two benzo groups of the anthracene-containing bridge in **3** substantially narrow its two flanking portals. Experimentally a 400 MHz ^{1}H NMR spectrum of **3** in CDCl$_3$ at 25 °C gave two sets of host signals (OCH$_2$O protons) in an intensity ratio of 2.8 : 1 attributed to empty **3** (2.8) and **3**⊙CDCl$_3$ (1). When the solution was warmed to 55 °C, the signals due to **3**⊙CDCl$_3$ disappeared, but reappeared when the solution was cooled to 25 °C. When CDCl$_2$CDCl$_2$ and (CD$_2$)$_4$O were each substituted for CDCl$_3$ in similar experiments, only signals for empty **3** were observed at both 25 and 55 °C. Apparently, these two molecules are too large to enter **3** at these temperatures.

When **2**⊙CHCl$_3$ was heated in PhNO$_2$ as solvent at 150 °C for 3 days, **2**⊙PhNO$_2$ was formed.† The complex crystallized as **2**⊙PhNO$_2$·5PhNO$_2$, whose crystal structure was determined at −98 °C. The remarkable feature of the crystal structure is not that *R* (0.22) is so large, but that a solvated complex of molecular mass 3037 which contains no symmetry element and is disordered could be determined at all. Fortunately the disorder is concentrated in the least interesting parts of the structure (the eight feet and the five solvate molecules).§ In Fig. 1 are shown a stereo side-view of **2**⊙PhNO$_2$ (*a*) a stereo end-view of the bridges and guest (*b*), and a side-view of the bridges and guest (*c*). Included for comparison is a side-view of the bridges and guest of **7**⊙PhNO$_2$ (*d*), reported earlier.[2]

Substitution of one conformationally mobile, six-atom-long O(CH$_2$)$_4$O bridge in **7** by the relatively rigid eight-atom-long *p*-OCH$_2$C$_6$H$_4$CH$_2$O bridge in **2** both desymmetrizes and

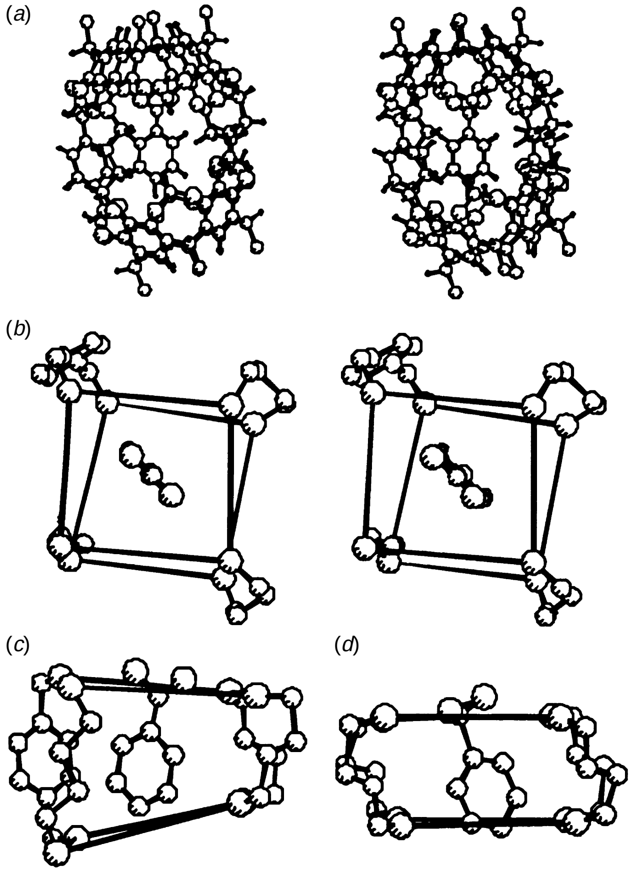
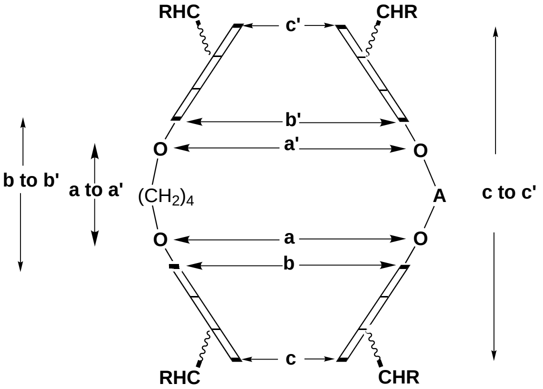


Fig. 1 (*a*) Side stereoview of **2**⊙PhNO$_2$. R groups in host **2** are represented by C atoms. (*b*) Top stereoview of bridges and guest. (*c*) Side-view of bridges and guest. (*d*) Side-view of bridges and guest of **7**⊙PhNO$_2$.

introduces strain into those parts of the host that define its cavity. Although strain distributes itself as evenly as possible, the polycyclic aryl-rich character of the bowls resists deformation more than the more linear bridges. The distances defined in diagram **13** substantiate this expectation. For example, the lengths (and maximum spread in values) of the four edges of the oxygen best planes **a** and **a′** visible in Fig. 1(*b*) average 6.25 (0.57) and 6.46 (0.49) Å, respectively, in **2**⊙PhNO$_2$, as compared to 6.31 (0.09) Å in **7**⊙PhNO$_2$. The lengths (and maximum spread in values) of the two diagonals of planes **a** and **a′** average 8.84 (0.47) and 9.12 (0.79) Å respectively in **2**⊙PhNO$_2$, as compared to 8.92 (0.07) Å for plane **a** (and **a′**) in **7**⊙PhNO$_2$. Thus the maximum spread in edge and diagonal distances for planes **a** and **a′** are 5 to 11 times larger for **2**⊙PhNO$_2$ than for **7**⊙PhNO$_2$. The **b**–**c** and **b′**–**c′** average bowl depths for **2**⊙PhNO$_2$ and **7**⊙PhNO$_2$ vary only from 2.47 and 2.44 for the former to 2.43 Å in the latter complex. Likewise, the maximum out-of-planes **a** and **a′** oxygen distances and spreads are small, 0.06 and 0.11 Å (spreads, 0.12 and 0.20 Å) respectively for **2**⊙PhNO$_2$, and 0.04 Å (spread, 0.08 Å) for **7**⊙PhNO$_2$.



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The bowl-to-bowl bridge lengths **b**–**b′** for **2**⊙PhNO$_2$ average 7.46 with a maximum spread of 2.00 Å, whereas **7**⊙PhNO$_2$ gives values of 6.46 and 0.14 Å, respectively. Thus the stressed **2**⊙PhNO$_2$ complex gives a factor of 14 more spread in its bridge lengths than does **7**⊙PhNO$_2$. More interestingly, one of the two O(CH$_2$)$_4$O bridges that flank the *p*-OCH$_2$C$_6$H$_4$CH$_2$O bridge (length, 8.51 Å) in **2**⊙PhNO$_2$ is 7.98 Å long, compared to the 6.46 Å average length of the four bridges in **7**⊙PhNO$_2$, and the other two O(CH$_2$)$_4$O bridges in **2**⊙PhNO$_2$ (6.51 and 6.82 Å). The two oxygen squares in the views of the bridges resemble a slightly opened book in **2**⊙PhNO$_2$, whereas in **7**⊙PhNO$_2$, the similar side-view resembles a closed book [Fig. 1(*b*)–(*d*)].

How does the long O(CH$_2$)$_4$O bridge in **2**⊙PhNO$_2$ become that way, and what are the consequences for the cavity shape? In all but two [all four bridges were O(CH$_2$)$_5$O[5] or OCH$_2$CH$_2$OCH$_2$CH$_2$O[6]] of our prior crystal structures involving tetrol bowls of the type incorporated in **1**–**12**, the unshared electron pairs of the oxygens that terminate the four bridges face inward toward the cavity. This places their attached carbon chains outside the cube defined by the eight oxygens, as in **7**⊙PhNO$_2$. CPK molecular model examinations show that such conformations minimize bridge lengths, whereas when the electron pairs face outward, the carbon chains turn inward, the bridge lengths increase, and the cavities narrow in their equatorial dimensions because the methylenes encroach on the corners of the cavities. The top and side views of the bridges show that in contrast to the other three bridges of **2**⊙PhNO$_2$, two of the methylenes of the long O(CH$_2$)$_4$O bridge are turned inward to accommodate its adjacent, outward-turned but longer *p*-OCH$_2$C$_6$H$_4$CH$_2$O bridge. As a result of the longer bridge lengths (av., 7.46 Å) in **2**⊙PhNO$_2$ as compared to **7**⊙PhNO$_2$ (av., 6.46 Å), the average **c**–**c′** distance which measures cavity length in the former complex is 12.15 Å, significantly longer than the 11.28 Å length in the latter complex.

The PhNO$_2$ guest's best plane is diagonally arranged in the cavities so as to be roughly coplanar with the oxygens of diagonally located bridges. Molecular model examination indicates that diagonal arrangements avoid collisions of the guest atoms with the enforced inward-turned single hydrogens of the eight OCH$_2$O spanners. Of the two possible diagonal locations, the one including the *p*-OCH$_2$C$_6$H$_4$CH$_2$O bridge (length, 8.51 Å) is occupied by the PhNO$_2$ guest (see both top- and side-views in Fig. 1), thus avoiding the inward-turned O(CH$_2$)$_4$O bridge (length 7.98 Å).

The ways in which **2** modifies its structure to accommodate its single longer bridge provide insights about the degrees of freedom available to transition states for entries and exits of guests from the inner phases of hemicarcerands.

Attempts to obtain crystals suitable for structure determination of host **3** failed. However, a molecular model of **3** can be assembled only in a conformation whose 9,10-(OCH$_2$)$_2$-anthracene bridge resembles that found for the *p*-OCH$_2$C$_6$H$_4$CH$_2$O bridge of **2**⊙PhNO$_2$. A comparison of the complexing properties of hosts **1**–**3**, **8** and **10** will be reported in a future paper.

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Footnotes

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† These new compounds have elemental analyses within 0.30% of theory, and the expected ^{1}H NMR spectra and FAB (*m*/*z*, M$^+$ + H) mass spectra.

‡ These procedures were patterned after those leading to **4**–**6** and **8**–**11**.[1] Probably initially NMP solvent molecules served as guests during addition of the fourth bridge, but underwent exchange with CHCl$_3$ during chromatographic purification to provide **1**⊙CHCl$_3$ and **2**⊙CHCl$_3$.

§ *Crystal data*: the crystal structure of **2**⊙PhNO$_2$·5PhNO$_2$ (crystallized from CHCl$_3$–PhNO$_2$, determined at 175 K): triclinic, space group $P\bar{1}$, a = 20.241(5), b = 26.350(5), c = 15.143(3) Å, α = 98.84(2)°, β = 95.01(2)°, γ = 94.26(2)°, V = 7918(3) Å^3, Z = 2, 20676 unique reflections, 11944 > $4\sigma(F)$, maximum 2θ = 120°, Cu-Kα radiation, and was refined to R = 0.22 (SHELXL93[4a]). The precision of the intensities is severely affected by the high background, due to the capillary containing the crystal and the ice that collected on it. The structure was solved by direct methods (SHELXS90[4b]). All non-hydrogen atoms have been refined isotropically. All hydrogen atoms were refined with fixed C–H distances (0.93–0.98 Å) and with fixed displacement parameters (1.2 $U_{\rm iso}$ of the attached C atom). One molecule of PhNO$_2$ is located in the host cavity; there are five additional molecules of PhNO$_2$ per host molecule, two of which are probably disordered or low occupancy. In addition, high displacement parameters for three of the eight 'feet' (CH$_2$CH$_2$Ph groups) indicate disorder.

Atomic coordinates, bond lengths and angles, and displacement parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Information for Authors, Issue No. 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 182/466.

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