# Hemicarcerands with Interiors Potentially Capable of Binding Large Guests

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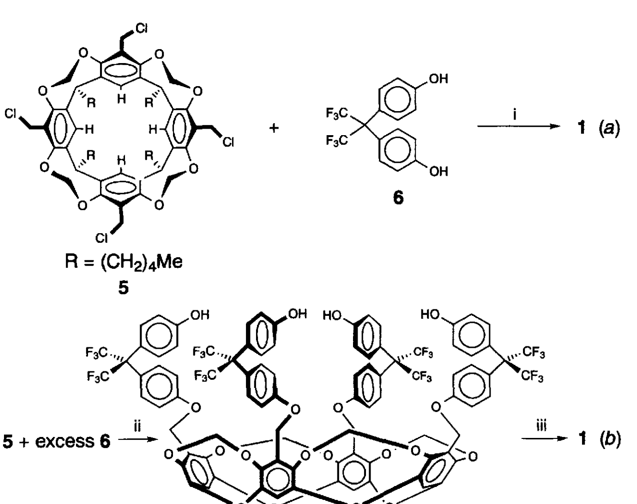
The synthesis and characterization of four new hemicarcerands (**1–4**) are reported, whose interiors in principle are large enough to embrace such guests as tetraphenylporphyrin or [60]fullerene.

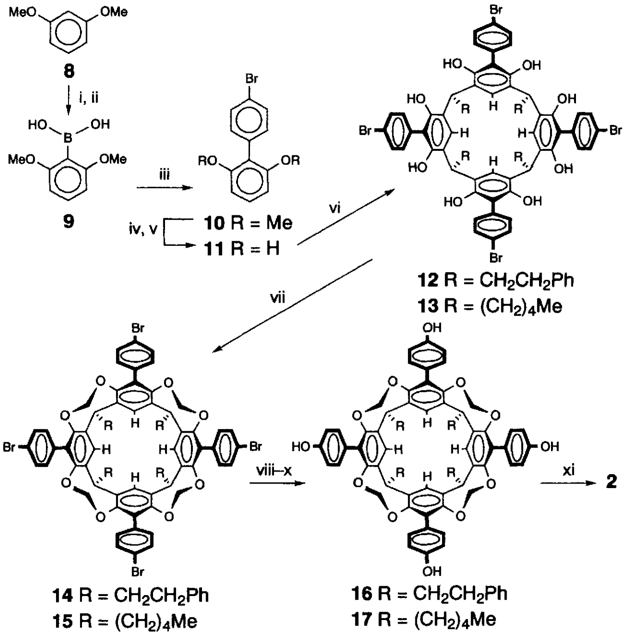
Prior publications report syntheses of hemicarcerands with large enough portals and interiors to allow guests like [3.3]-paracyclophane to be incarcerated at temperatures of 120–220 °C to give hemicarceplexes stable towards decomplexation in solution at ambient temperatures.[1] Mechanical inhibition of hemicarceplex decomplexation has been termed *constrictive binding*,[2] which coupled with host–guest attractive forces accounts for the stability to chemical[3] and physical[2] manipulation of hemicarceplexes. This paper addresses the question of whether hemicarcerands can be prepared with large enough enforced interiors to incarcerate guests such as tetraphenylporphyrin or [60]fullerene ($C_{60}$). A complex of the former might act as an oxidation catalyst stabilized by the shell, whereas the host of a capsular complex of $C_{60}$ should impart interesting new properties to that molecule. We have successfully synthesized hosts **1–4**, whose Corey–Pauling–Koltun (CPK) molecular models suggest that **1** and **2**, especially, might complex such large guests.

The synthesis of **1** was accomplished by the reaction sequence (*a*) starting with **5**[4] (Scheme 1), and in better yield using sequence (*b*). The synthesis of **2** is shown in Scheme 2.†

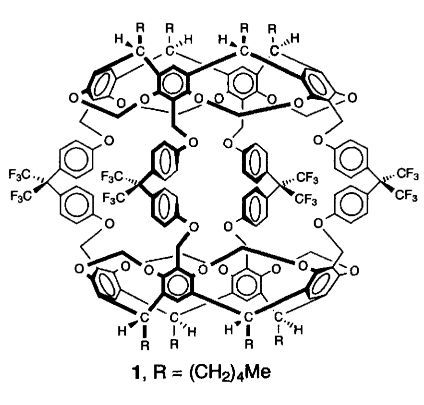
The respective extended-bowl cavitands, **13**, **15** and **17**,† similar to **12**, **14** and **16**, but with R = $(CH_2)_4Me$ instead of $CH_2CH_2Ph$ were prepared in comparable yields when Me-



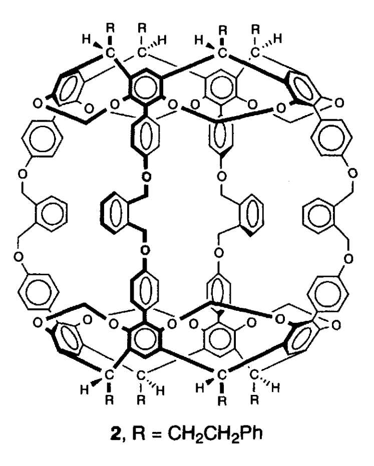
**Scheme 1** *Reagents and conditions*: i, $Cs_2CO_3$, $Me_2NCOMe$, 60 °C, 4 d, high dilution, 3%; ii, $Cs_2CO_3$, $Me_2NCOMe$, 60 °C, 7 d, 52%; iii, **5**, $Cs_2CO_3$, $Me_2NCOMe$, 60 °C, 4 d, 19%



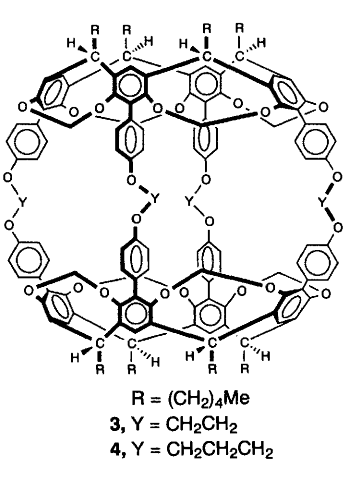
**Scheme 2** *Reagents and conditions*: i, $Bu^nLi$; ii, $B(OMe)_3$, $Et_2O$, 55%; iii, 1,4-$Br_2C_6H_4$, $Pd(PPh_3)_4$, $Cs_2CO_3$, MePh–MeOH, reflux, 24 h, 50%; iv, $BBr_3$, $CH_2Cl_2$, 0 °C, 5 h; v, $H_2O$, 25 °C, 2 h, $Et_2O$, 82%; vi, $PhCH_2CH_2CHO$, $MeCH_2CH_2OH$, HCl (aq. conc.), 85 °C, 7 d, 50%;‡ vii, $ClCH_2Br$, $Me_2NCHO$, $Na_2CO_3$, 100 °C, 12 h, 61%; viii, $Bu^nLi$–hexane, THF, −78 °C, 15 min; ix, $B(OMe)_3$, −78 then 25 °C, 3 h; x, $H_2O_2$ (15%), NaOH, −40 then 25 °C, 2 h, 47%; xi, 1,2-$(BrCH_2)_2C_6H_4$, $Me_2NCHO$, $Cs_2CO_3$, 70 °C, 76 h, high dilution, 17%



**1**, R = $(CH_2)_4Me$



**2**, R = $CH_2CH_2Ph$



R = $(CH_2)_4Me$
**3**, Y = $CH_2CH_2$
**4**, Y = $CH_2CH_2CH_2$

$(CH_2)_4CHO$ was substituted for $PhCH_2CH_2CHO$ in the fourfold condensation ring-closure reaction. Model procedures for the above conversions are detailed in the literature.[5–7] The two remaining shell closures were carried out as shown in Scheme 3.†

A crystal structure of 2⊙(unknown)§ was determined and is depicted in Fig. 1.¶ A partial stereoview is shown in Fig. 2 featuring only the four $C_6H_4OCH_2C_6H_4CH_2OC_6H_4$ hemisphere-linking groups whose eight terminal aryl carbon atoms are connected in two sets of four to form two squares about 10.1 Å apart. Each 'square' is 6.69 by 6.89 Å with angles of 87, 88, 91 and 94°. The least-squares planes of the squares are parallel, being related by the centre of symmetry in the hemicarcerand molecule, and one square is 'slipped' 2.15 Å with respect to the other. No atom in the square deviates from the plane by more than 0.1 Å.

$$\mathbf{17} + TsOCH_2CH_2OTs \rightarrow \mathbf{3}\ (32\%)$$

$$\mathbf{17} + TsO(CH_2)_3OTs \rightarrow \mathbf{4}\ (30\%)$$

**Scheme 3** *Reagents and conditions*: $Cs_2CO_3$, 70–80 °C, 96 h; 100 °C, 24 h, high dilution under argon, degassed $Me_2NCHO$ (Ts = toluene-*p*-sulfonyl)

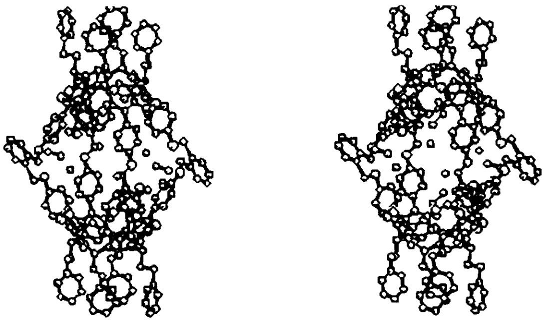


**Fig. 1** Crystal structure of stereoview of 2⊙unknown

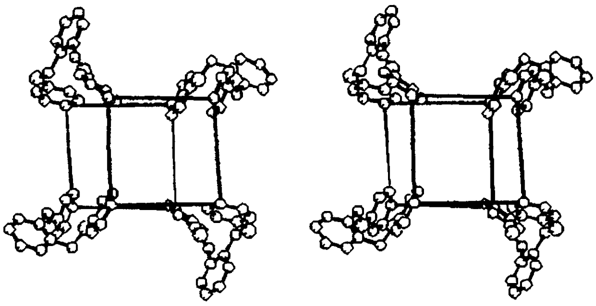


**Fig. 2** Partial stereoview of crystal structure of 2⊙unknown

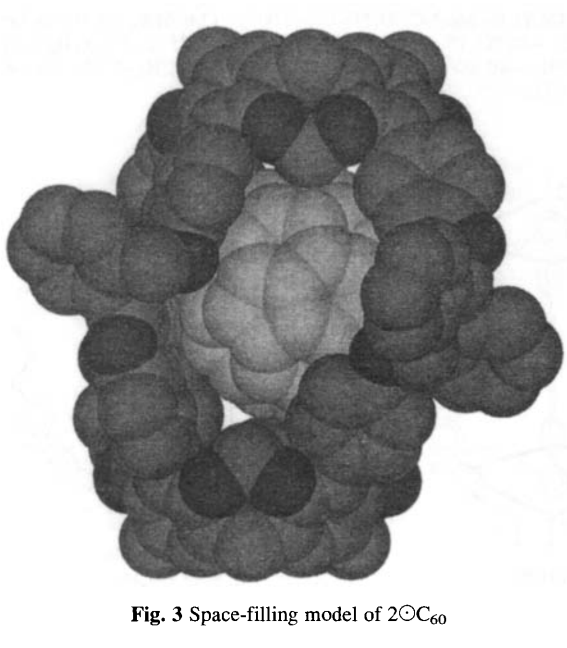


**Fig. 3** Space-filling model of $2\odot C_{60}$

Figs. 3 and 4 are perspective drawings of space-filling and ball-and-stick models of **2**, based on the crystal structure coordinates, as host complexing $C_{60}$. Phenethyl 'feet' (above and below in **2** and Fig. 1) have been replaced by H atoms and the complex has been rotated about the vertical axis to view $C_{60}$ through a portal. In CPK molecular models, **2** snugly surrounds a one-litre round-bottom flask, whose diameter on the host model scale corresponds roughly to that of $C_{60}$.[8] Calculations (Macromodel MM2 force field) were carried out for the energy-minimized structure (Fig. 3), and for a series of energy-minimized structures in which the $C_{60}$ was moved in small increments through one of the four equivalent portals and out to a decomplexed state. Fig. 5 depicts plots of these energy values against the displacement of the guest from its 12 Å position in the energy-minimized complex to 18 Å along the *x*-axis in the gas phase (upper line) and in $CHCl_3$ (lower line). The energy barrier for the egress was 56 kcal mol$^{-1}$ (1 cal = 4.184 J) in the gas phase and 57 kcal mol$^{-1}$ in $CHCl_3$, with the sum of the energies of isolated host and guest in $CHCl_3$ being 3 kcal mol$^{-1}$ lower than the energy of the complex. Experimentally, a solution of **2** and $C_{60}$ (large excess) was heated for 20 h at 130 °C in $CDCl_2CDCl_2$ without change of the $^1H$ NMR of the host, which indicates no detectable complexation occurred.

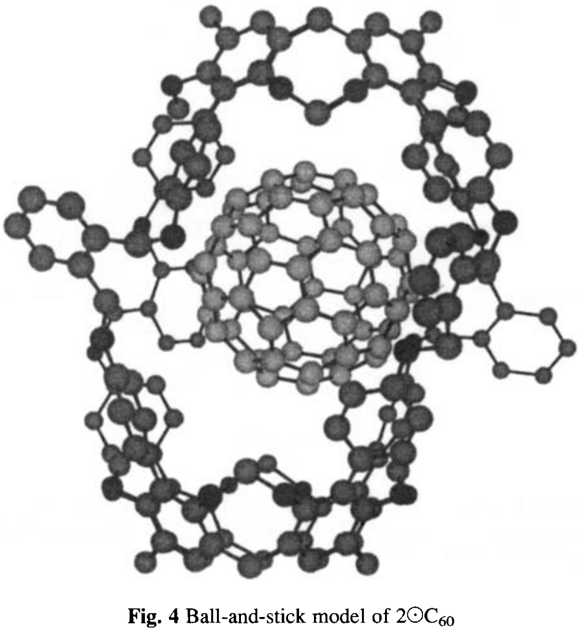


**Fig. 4** Ball-and-stick model of $2\odot C_{60}$

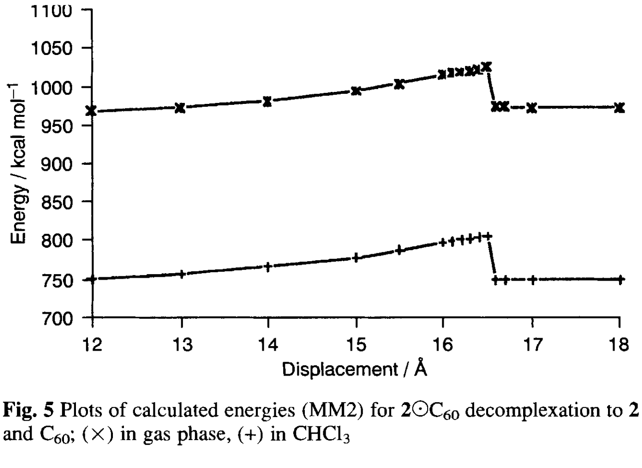


**Fig. 5** Plots of calculated energies (MM2) for $2\odot C_{60}$ decomplexation to **2** and $C_{60}$; (×) in gas phase, (+) in $CHCl_3$

A similar attempt to incarcerate tetraphenylporphyrin ($CDCl_3$, 60 °C, 3 d) in **2** failed, although a CPK model of **2**⊙tetraphenylporphyrin appears to be ideally shaped. The four phenyl groups of the guest nicely occupy the four portals of the host with room to spare. The activation energy for the encapsulation is probably too high for the guest to enter the host under the conditions employed.

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## Footnotes

† All new compounds 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 thank Roger C. Helgeson for first carrying out this reaction.

§ The symbol ⊙ signifies incarceration of guests in hosts, while ⊍ denotes nesting, perching or partially encapsulated complexes.

¶ *Crystal structure* of **2**⊙unknown: crystallized from $CH_2Cl_2$–pentane, determined at 25 °C; triclinic space group $P\bar{1}$, $a$ = 16.027(2), $b$ = 18.404(2), $c$ = 21.748 Å, $\alpha$ = 90.235(3), $\beta$ = 103.592(4), $\gamma$ = 109.586(3)°, $V$ = 5850 Å$^3$, $Z$ = 1, Syntex $P\bar{1}$, Cu-K$\alpha$ radiation, and was refined to $R$ = 0.23. Although, with the exception of the phenethyl 'feet', the host is reasonably well ordered, both guest and solvent are disordered. Solvent and guest have not been identified, although certain atoms of these have been included as carbon. The degree of disorder is evident in the data intensity distribution. Data were collected to $\sin \theta/\lambda$ = 0.46; of 9457 unique reflections, only 3391 measured intensities were greater than $2\sigma(I)$. At 1.1–1.2 Å resolution, of the 1527 unique reflections in this shell, only 178 measured greater than $2\sigma(I)$. When this fraction is one half or less, solution of the structure is unlikely.[9] The unit cell contains one host molecule plus an unknown quantity of solvent molecules in a volume of 5850 Å$^3$; if one applies the 'rule of 18' to 232 nonhydrogen atoms of the host molecule, the host should occupy approximately 4176 Å$^3$, or less than 3/4 of the total volume. Repeated attempts to get better crystals failed, as did exhaustive efforts to obtain a more refined structure. Accordingly, the main use of the structural parameters given here is to provide starting coordinates for the structural calculations. Given the degree of disorder in the 'feet', guests and interstitial solvent, the wonder is not that the refinement is so poor, but rather that the general outlines of the host's shape could be obtained at all.

Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

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