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Design and Synthesis of Rhombohedral Clathrates for Containment of Small, Reactive Guest Species

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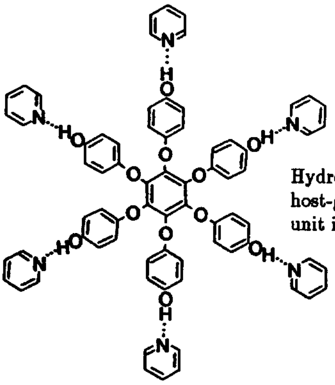
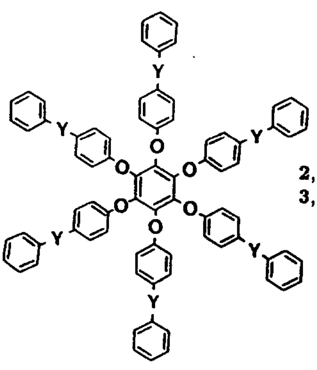
Abstract

The new hexa-hosts hexakis(*p*-phenoxyphenoxy)benzene **2** and its *p*-benzylphenoxy analogue **3**, targetted at rhombohedral clathrate packing, have been prepared. X-ray measurements have established that **2** and **3** form very similar rhombohedral closed-cage structures with common trigonal space group $R\bar{3}$. The cavities of these clathrates are potentially useful for the handling of reactive reagents, examples for **2** being phosgene, thiophosgene, thionyl chloride, and methyl iodide.

The idea of covalent fusion of several molecules previously linked only by hydrogen bonds in a molecular crystal has previously found effective application in the derivation of the hexa-host analogy [1] (new *hosts* deriving from formal combination of H-bond linked *hosts*); and in the efficient isolation [2] of *trans*-1,4-bis(hydroxymethyl)cyclohexane from a *cis,trans* mixture of isomers (new *guest* mimicking hydrogen-bonded, centrosymmetric *guest* aggregate 1,4-dioxane.$2H_2O$). The present work provides the first example of new, stable, covalently linked *hosts* which are modelled on a pre-existing hydrogen-bonded *host-guest* assembly. Potential uses of these new hosts are also described.



Hydrogen-bonded
host-guest
unit in **1**.6py



2, X = O
3, X = CH_2

The conspicuous voids in the hydrogen-bonded adduct [3] of hexakis(*p*-hydroxyphenoxy)benzene **1** with six pyridine guest molecules, **1**.6py, suggested to us the possibility of synthesis of analogous - but highly inert - covalently linked host counterparts retaining the trigonal space group $R\bar{3}$.

Suitable molecules without reactive functionality and with potentially analogous packing characteristics were selected, namely hexakis(*p*-phenoxyphenoxy)benzene **2** and hexakis(*p*-benzylphenoxy)benzene **3**. These were prepared in high yields (*ca.* 90%) from hexafluorobenzene by dipolar aprotic solvent-promoted complete nucleophilic substitution as previously described [4]. Both **2** and **3** were fully characterised spectroscopically: ^{1}H and ^{13}C NMR, IR, mass spectrometry.

Both **2** and **3** were found to form beautifully crystalline adducts with a wide range of volatile guest species. For evaluation of their suitability as media for reagent handling, it was of prime importance to establish the nature of the voids present in these structures. The relationship to the pre-cursor host structure **1**.6py was also of interest. The methyl iodide and phosgene adducts of **2** and the CCl_3CH_3 clathrate of **3** [5] were chosen for detailed X-ray study.[1] The adducts were prepared by recrystallisation of unsolvated **2** or **3** from the appropriate pure, dry solvent, or in the case of gases, from a solution of the gas in a suitable solvent (which was not included to any significant extent). For example, the 1:1 $COCl_2$ clathrate of **2** was prepared by recrystallisation from a 12.5% (by weight) solution of $COCl_2$ in toluene, in a sealed tube. Thermogravimetric analysis (TGA) showed no guest loss below 125°C (heating rate 10°C/min, N_2 atmosphere), the main weight loss occurring in the range *ca.* 150-200°C.

Crystal Data. [6] $C_{78}H_{54}O_{12}.CH_3I$: $M = 1325.2$, rhombohedral, space group $R\bar{3}$, $a = 22.311(5)$, $c = 11.005(2)$ Å, $U = 4744(2)$ Å^3, $Z = 3$, $D_c = 1.39$ g cm^{-3}, $T = 293K$, $R = 0.085$, $R' = 0.087$ for 844 independent reflections with $F_o^2 > 2\sigma(F_o^2)$.

$C_{78}H_{54}O_{12}.COCl_2$: $M = 1282.2$, rhombohedral, space group $R\bar{3}$, $a = 22.300(7)$, $c = 10.980(3)$ Å, $U = 4729(2)$ Å^3, $Z = 3$, $D_c = 1.35$ g cm^{-3}, $T = 293K$, $R = 0.082$, $R' = 0.100$ for 874 independent reflections with $F_o^2 > 2\sigma(F_o^2)$.

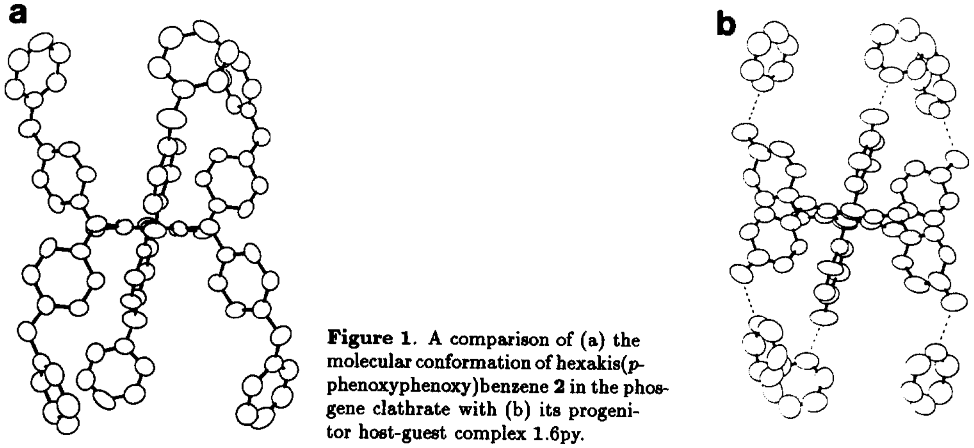


Figure 1. A comparison of (a) the molecular conformation of hexakis(*p*-phenoxyphenoxy)benzene **2** in the phosgene clathrate with (b) its progenitor host-guest complex **1**.6py.

Figure 1(a) shows the conformation of the host molecule, hexakis(*p*-phenoxyphenoxy)benzene **2**, which has exact C_{3i} ($\bar{3}$) symmetry, in its methyl iodide clathrate. This conformation is re-

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[1] The atomic coordinates for the CH_3I and $COCl_2$ adducts of **2** are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication. Supplementary data: structure factors. See Announcement to Authors, *Tetrahedron Letters*, **47**, 5154 (1983).

markably similar to the host-guest arrangement in the pre-cursor assembly **1**.6py, Figure 1(b). Whilst the central ring of **2** is effectively planar, the directly-attached oxygen atoms are alternately disposed above and below the ring plane by ±0.10(1) Å [±0.11(1) Å $COCl_2$ clathrate] in the opposite sense to that of the corresponding side chains. This may be compared with the corresponding value ±0.15(1) Å for **1**.

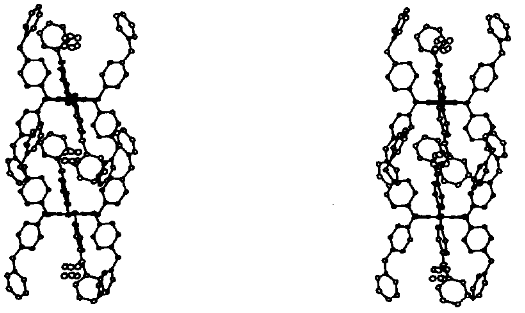

Figure 2. A stereoview normal to *c* illustrating a portion of the infinite columns along *c* in the methyl iodide clathrate of **2**. The guest's iodine atom, statistically disordered, appears in six positions close to the cage centre.

Figure 2 gives a stereoview of the infinite stacking of host molecules along the *c* axial direction, the cavities, possessing exact C_{3i} ($\bar{3}$) symmetry, being formed between adjacent host molecules. Only the iodine atom of the statistically-disordered methyl iodide could be located, and this can be seen, close to the cage centre, in Figure 2. The phosgene clathrate has a virtually identical host structure, but in this case it was not possible to locate unambiguously any guest atom. The efficient packing of columns is illustrated, for the phosgene clathrate, in Figure 3.

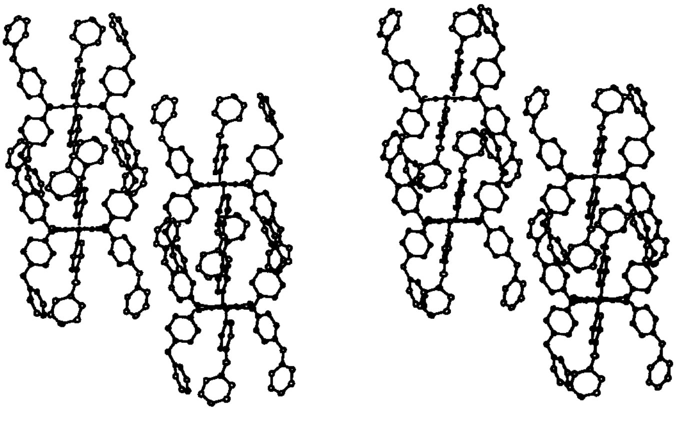

Figure 3. A stereoview illustrating the efficient packing of adjacent columns which extend infinitely along *c* in the 1:1 $COCl_2$ clathrate of **2**. The disordered phosgene molecule has been omitted for clarity.

The presence of phosgene in complexation with **2** was substantiated by microanalysis; [2] (found: C, 73.89%; H, 4.37%; Cl, 5.33%: $C_{78}H_{54}O_{12}.COCl_2$ requires: C, 74.00%; H, 4.25%; Cl, 5.53%), and confirmed by IR spectroscopy first by the presence [3] of a ν(C=O) (KBr disc) band at 1803 cm^{-1}, and then by release of the guest into a vapour phase IR cell, giving a spectrum in complete agreement with a reference vapour spectrum.

In summary, the present work represents a unique example of crystal design of highly inert crystalline host lattices [8, 9], successfully targetted at trigonal space group $R\bar{3}$, for the storage of volatile and reactive species potentially useful as synthetic reagents. The intriguing strategy of building permanent, consolidated analogues of hydrogen-bonded moieties, *cf.* ref. [1, 2] will undoubtedly lead to the synthesis of many new host lattices as well as other types of new material based on molecular crystals.

References

[1] See, for example, D.D. MacNicol in *Inclusion Compounds*, eds. J.L. Atwood, J.E.D. Davies and D.D. MacNicol, Academic Press, London, 1984, vol. 2, ch. 5.

[2] J.H. Gall, M. McCartney, D.D. MacNicol and P.R. Mallinson, *J. Incl. Phenom.* 1985, **3**, 421.

[3] D.D. MacNicol, P.R. Mallinson, A. Murphy, and C.D. Robertson, *J. Incl. Phenom.* 1987, **5**, 233.

[4] C.J. Gilmore, D.D. MacNicol, A. Murphy and M. Russell, *Tet. Lett.* 1983, **24**, 3269.

[5] The CCl_3CH_3.**3** adduct also has space group $R\bar{3}$ with closely similar lattice parameters a = 23.144, c = 11.247 Å, $Z = 3$. Current $R = 0.100$ for 851 independent reflections.

[6] X-ray intensity measurements were made by $2\theta - \omega$ scan on a Nonius CAD4 diffractometer using graphite-monochromated MoK_α radiation. Unit cell parameters were determined by least-squares refinement of diffractometer setting angles for 25 reflections. The principal computer programs used in structure solution and refinement are: MITHRIL, A Computer Program for the Automatic Solution of Crystal Structures from X-ray data, C.J. Gilmore, *J. Appl. Crystallogr.* 1984, **17**, 42; the GX Crystallographic Program System, P.R. Mallinson and K.W. Muir, *J. Appl. Crystallogr.* 1985, **18**, 51.

[7] Y. Ono and Y. Ueda, *Chem. Pharm. Bull.* 1970, **18**, 2013.

[8] We note the interesting use of crown complexes in the fixation, as crystalline complexes, of volatile, highly toxic molecules, for example N,N-dimethylnitrosamine, which have acidified CH_3-, $CH_2 <$ or analogous heteroatom groups (F. Vögtle and W.M. Müller, *Naturwiss.* 1980, **67**, 255).

[9] The effective storage of the volatile and extremely toxic dimethyl mercury in the clathrate cages of 4-*p*-hydroxyphenyl-2,2,4-trimethylthiacroman has previously been described (R.J. Cross, J.J. McKendrick and D.D. MacNicol, *Nature* (London) 1973, **245**, 146).

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[2] For some clathrates of **2** and **3** with halogenated guests, microanalysis for halogen consistently indicated host-guest ratios greater than 1:1, for example for the CCl_4 adduct of **2**. Since X-ray unit cell determination shows the cell (a = 22.420(10), c = 11.030(2) Å) analogous to the methyl iodide and phosgene clathrates, and CPK models show that an additional CCl_4 molecule cannot be accommodated in the cavity, it seems probable that excess guest may be situated in macroscopic defects in the crystal. For the $CSCl_2$ clathrate of **2**, obtained as golden-coloured crystals on recrystallisation of **2** from a 20% (by weight) solution of $CSCl_2$ in mesitylene, an excess over a 1:1 ratio is also obtained, and again this may be due to crystal imperfections, assuming an isostructural host lattice. Methods used to determine host-guest ratios were microanalysis, TGA, and ^{1}H NMR where appropriate.

[3] The ν(C=O) band of phosgene in the clathrate at 1803 cm^{-1} is somewhat lower than its value of 1813 cm^{-1} in CCl_4 solution. A similar effect is found for the 1:1 clathrate of CH_3COCl with **2** [7], where ν(C=O) is 1800 cm^{-1} compared to 1806 cm^{-1} in CCl_4.

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