New Strategy for the Design of Inclusion Compounds: Discovery of the 'Hexa-hosts'

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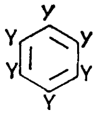
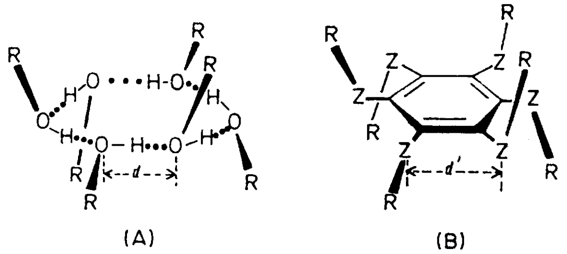
Summary A novel concept for the design of inclusion compounds, which has lead to the discovery of a series of hosts, is described.

IN previous studies[1] we have described the marked changes in cavity geometry and guest selectivity which may be produced by the judicious modification of the structure of clathrate host molecules. We now report a new approach which has lead to the synthesis of inclusion hosts not directly related to any known host.



(I), Y = SPh (V), Y = $CH_2OC_6H_4Bu^t$-*p*
(II), Y = CH_2OPh (VI), Y = $CH_2SC_6H_4Bu^t$-*p*
(III), Y = CH_2SPh (VII), Y = CH_2SCH_2Ph
(IV), Y = CH_2SePh

An intrinsic factor involved in the molecular packing of the clathrates formed by Dianin's compound[2] and related systems[1,3] and also those formed by hydroquinone[4] and phenol[5] is the linking of the OH groups of six host molecules by a network of hydrogen bonds such that the oxygen atoms form a hexagonal arrangement (A), shown in the Figure. Struck by the parallel between this temporary unit, which is subject to collapse as the groups R are varied, and the permanent consolidated structure of a benzene (B), we have prepared a number of suitable hexa-substituted benzenes, *e.g.* (I)—(VII) in order to ascertain if these latter compounds might possess an increased tendency to crystallise forming non-close-packed structures with possible inclusion properties. It may be noted that unit (A) corresponds to (B) both in terms of overall geometric aspects and 'hexamer' dimensions (*cf.* distances *d* and *d'* in the Figure, where Z denotes a general atom or group attached directly to the central benzene ring).



(A) (B)

FIGURE. Comparison of (A) hydrogen-bonded hexamer unit with (B) hexa-substituted benzene analogue.

Compound (I) was prepared[6] by reaction of hexachlorobenzene with PhSCu, and compounds (II)—(VII)† by the action[7] of the appropriate phenol, thiol, or selenol on hexakis(bromomethyl)benzene, $C_6(CH_2Br)_6$, in the presence of base. All compounds gave satisfactory microanalysis, and had spectroscopic properties in keeping with their formulated structure: full details will be given in a future publication. On crystallisation from suitable solvents, a wide range of inclusion behaviour was found, illustrative examples, with

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† Encouragingly (see ref. 7), a number of these materials had been found to retain certain solvents, though at the time of publication the nature of inclusion compounds was less well understood. While the present work was in progress, a number of 'octopus' molecules, based on a hexa-substituted benzene nucleus, have been shown to be capable of binding metal cations in solution (see ref. 8).

Table. Prospective 'hexa-host' compounds and representative guests

Compound	Guest molecules^a (host:guest ratio)
(I)	CCl_4 (1:2), CCl_3Br (1:1)
(II)	PhMe (1:2), dioxan (1:3), xylene^b (1:2)
(III)	PhMe (1:1), dioxan (1:2)
(IV)	c
(V)	c
(VI)	PhMe (1:2), cycloheptane (1:2), cyclo-octane (1:2), PhC≡CH (1:2), $CHBr_3$ (1:2), PhI (1:2)
(VII)	PhMe (1:1), cyclohexane (1:1), dioxan (1:1), acetone (1:2)

[a] The host–guest ratios (given to nearest integer) were determined by ^1H n.m.r. and/or by microanalysis for halogen. Where necessary, crystals were washed with n-pentane to remove surface liquid. Retention of toluene by compounds (II), (III), (VI), and (VII) had previously been reported (ref. 7). [b] Recrystallised from an equimolar mixture of *o*- and *m*-xylene, these guests being included to essentially the same extent. [c] No inclusion behaviour found to date.

host–guest ratios, being given in the Table. Compound (I) in which sulphur is linked directly to the central ring, retains CCl_4 and CCl_3Br but these are lost slowly on standing in air. Interesting differences are found among the compounds (II)—(IV). Whereas hexakis(phenoxymethyl)benzene (II) and its sulphur analogue (III) retain toluene and other guests, no parallel behaviour has yet been found for the related selenium compound (IV). Compound (VI) exhibits the widest range of inclusion properties found so far, though in marked contrast its oxygen counterpart (V) gives no evidence of inclusion compound formation. Generally speaking, escape of guest is slow at room temperature, but more rapid when the adducts are heated under reduced pressure, suggesting the possibility of channel-type inclusion.

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