

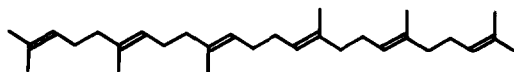
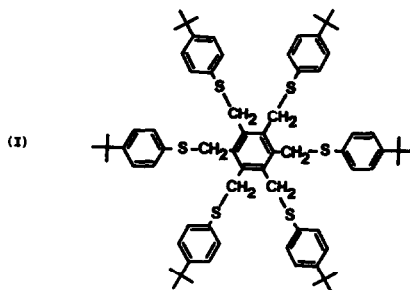
CRYSTAL AND MOLECULAR STRUCTURE OF A NOVEL HEXA-HOST
INCLUSION COMPOUND WITH SQUALENE AS GUEST

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Summary. An X-ray study of the adduct formed by hexakis(*p-t*-butylphenylthiomethyl)benzene (I) with squalene (II) establishes the first example of channel-type inclusion behaviour for a hexa-host molecule, the guest triterpene (II) being observed in a novel conformation controlled by host-guest interactions.

In recent studies,¹⁻⁴ X-ray crystallographic methods have revealed the conformations of small guest molecules accommodated in the cages of clathrate inclusion compounds.⁵ We now report the determination of the structure of the large guest species squalene C₃₀H₅₀, (II), present in a novel channel-type adduct with the versatile hexa-host molecule, hexakis(*p-t*-butylphenylthiomethyl)benzene (I).^{3,6} The present work is notable in that it provides the first unambiguous



(II)

structural information concerning a channel-type⁷ hexa-host inclusion compound. Another important aspect of this study is the direct observation of a squalene conformation distinct from that found in the normal molecular crystal (at -110°C) of this biologically important triterpene.⁸

The squalene adduct of (I) is triclinic, space group $P\bar{1}$ with a unit cell [$a = 14.710(5)$, $b = 15.773(6)$, $c = 20.417(5)$ Å, $\alpha = 107.40(2)$, $\beta = 113.90(3)$, $\gamma = 81.93(3)^\circ$] containing two host molecules and one squalene guest molecule.⁹ The structure was solved by direct methods using a version of MULTAN 78 into which quartet and quintet invariants were incorporated. A total of 4230 independent reflections having $I > 2.50\sigma(I)$ were measured on an Enraf-Nonius CAD-4 diffractometer using $\text{MoK}\alpha$ radiation. The current R -factor is 0.108. Full details of the structure analysis will be published elsewhere.

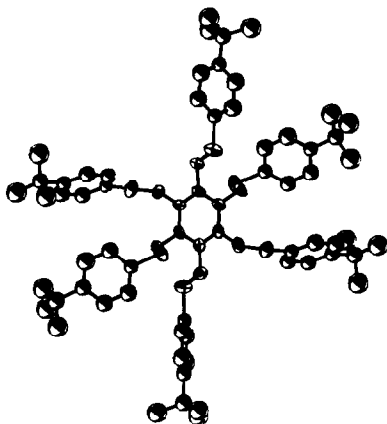


Figure 1. An ORTEP drawing showing a general view of the molecular structure of the host molecule (I) in the crystal of the squalene adduct.

Figure 1 shows a general view of the host molecule (I) which occupies a general position in the unit cell with a centroid at approximately $(0, \frac{1}{4}, \frac{3}{4})$. In common with other hexa-host molecules,²⁻⁴ the 'legs' of the molecule point alternately above and below the plane of the central benzene ring.¹⁰

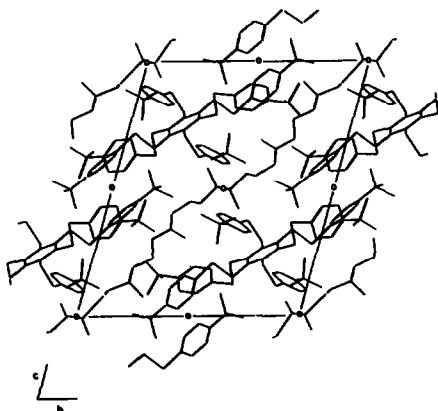


Figure 2. A view looking onto the bc plane illustrating the host to guest packing in the adduct of (I) with squalene.

The host-guest packing arrangement is illustrated in Figure 2, the squalene guest being accommodated in continuous channels running through the crystal. The location of the centre of either of the double bonds adjacent to the molecular centre of (II) at the crystallographic centre $(0, \frac{1}{2}, \frac{1}{2})$ leads to the existence of the squalene as a pair of enantiomeric conformations belonging to the point group C_1 , with the squalene appearing as continuous chain. This overlap of disordered squalene molecules causes the methyl groups close to points $(0, 0, 0)$ and $(0, \frac{1}{2}, \frac{1}{2})$ to appear with half statistical weight.¹¹

A comparison of the guest squalene conformation with that found^{8,12} in the molecular crystal of pure squalene is given in Figure 3. As can be seen these conformations differ markedly, the new squalene guest conformation being

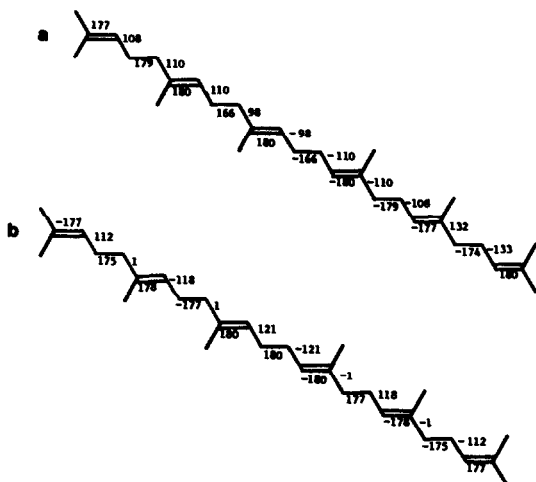


Figure 3. A comparison of main chain torsion angles for (a) squalene in its inclusion compound with host (I); and (b) squalene in its molecular crystal at -110°C (ref.8).

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accurately controlled by host-guest interactions. This direct observation and production of pure conformations not normally accessible is not only of theoretical interest but suggests the exciting possibility, currently under investigation, of specific reaction of guests which have been subjected to "conformational selection".

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References and Notes

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7. For structural information relating to clathrates formed by hexa-host molecules see, for example, refs. 2-5.
8. J. Ernst, W.S. Sheldrick, and J.-H. Fuhrhop, Angew. Chem. Int. Ed. Engl., 1976, 15, 778.
9. The first indication of phase coherence between host and guest components came from the exact 2.0:1 host-guest ratio determined by multiple ^1H n.m.r. integration of a CDCl_3 solution of the adduct.
10. In the present case, each of the six crystallographically distinct t-butyl groups exhibits rotational disorder, though for clarity secondary orientations are not shown in Figure 1. (This disorder will be described in detail in the full paper.)
11. The absence of additional 'ghost' peaks in appropriate electron density difference maps allows further guest disorder to be excluded, that is, a non-central squalene double bond cannot be located close to the point $(0, \frac{1}{2}, \frac{1}{2})$.
12. We thank Dr. W.S. Sheldrick for kindly providing detailed structural information of (II) in its molecular crystal.
13. For the first direct observation of dimeric acetic acid, cf. A. Freer, C.J. Gilmore, D.D. MacNicol, and S. Swanson, Tetrahedron Letters, 1980, 205.

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