X-Ray Crystallographic Investigation of Guest Orientation and Conformation in a Clathrate Inclusion Compound

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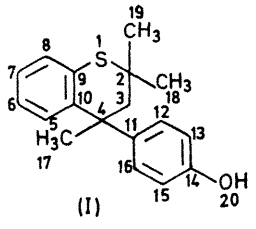
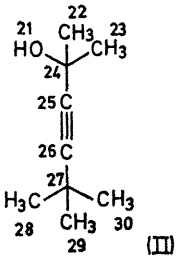
Summary An *X*-ray crystal structure analysis has unambiguously established the orientation and conformation of the guest molecule 2,5,5-trimethylhex-3-yn-2-ol (II) in the cage of the clathrate host 4-*p*-hydroxyphenyl-2,2,4-trimethylthiochroman (I).

THE thiochroman (I) forms clathrates[1-6] in which the guest molecule is accommodated in a cavity approximating to an hour-glass in shape and having the dimensions shown in Figure 1. We sought to define the orientation and conformation of a guest molecule when actually within the host and chose as guest the acetylene (II), on the basis of its molecular shape and volume.



(I)



(II)

The 2,5,5-trimethylhex-3-yn-2-ol clathrate† of (I) crystallises in the trigonal system with lattice constants referred to a hexagonal unit cell containing‡ 18 molecules of $C_{18}H_{20}OS$ and 3 molecules of $C_9H_{16}O$, $a = 27{\cdot}91$ Å and $c = 10{\cdot}99$ Å. The space group is $R\bar{3}$; some 2387 intensity data were estimated visually from equi-inclination Weissenberg photographs $hki0 \cdots hki9$ taken with Cu-K_α radiation at room temperature.

The structure of the host molecule (I) was obtained from an electron density map phased on the co-ordinates of (I)

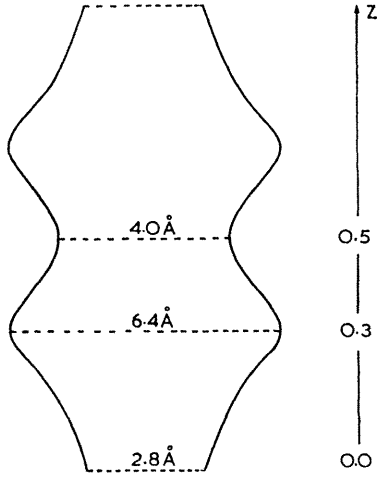


FIGURE 1. *A section through the van der Waals surface of the cavity.*

† Prepared by re-crystallisation of the thiochroman (I) from pure dry (II).
‡ The host : guest ratio (6 : 1) was determined by integration of the ^1H n.m.r. spectrum recorded for a $CDCl_3$ solution.

from a previous analysis.[6] An electron density map of the cavity with phases based on the co-ordinates of (I) revealed three, and only three, independent peaks. Two were situated along the *c*-axis and the third was a general peak; this means that *all* guest molecules adopt a staggered conformation with a statistical disorder of OH and CH_3 groups to conform with the imposed $\bar{3}$ symmetry of the cavity. The host and guest structures were refined by Fourier and isotropic least-squares methods and the *R*-factor is at present 0·15. Further refinement is in progress.

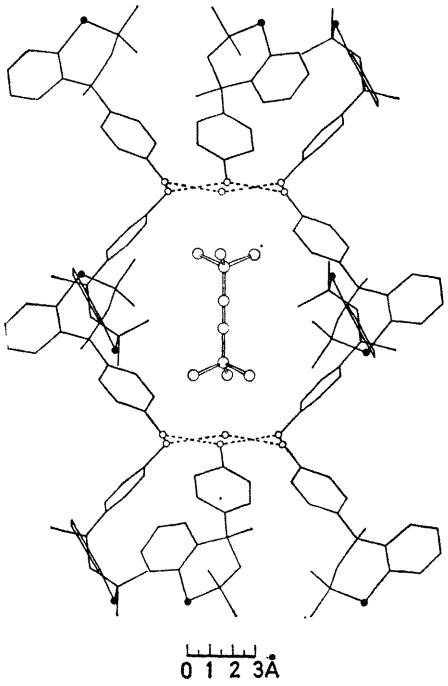


FIGURE 2. *The structure projected along the* a*-axis, showing the guest molecule* (II) *within the cavity. Two molecules of* (I), *which lie directly above and below the cavity as viewed in this direction, have been excluded apart from their hydroxy-oxygen atoms.*

Within the cavity (Figure 2) the acetylenic unit of the guest molecule (II) is collinear with the *c*-axis, the triple bond fitting neatly into the waist of the cavity, leaving a tetrahedral unit in the upper and lower halves of the cavity. The interaction between the tetrahedral unit of the guest molecule and the host molecules is shown in Figure 3.

This may be taken as an illustration of a "lock and key" type interaction in which the conformation of the guest molecule is governed by the host.

Although this study has unambiguously established the orientation and conformation of the guest molecule and the molecular dimensions of the collinear unit within the cavity (C≡C 1·20Å; C–C≡C 1·45 Å), the statistical disorder present does not allow the accurate dimensions of the tetrahedral unit within the cavity to be determined.§

The success of this analysis supports the view that detailed structural information on the guest molecule will

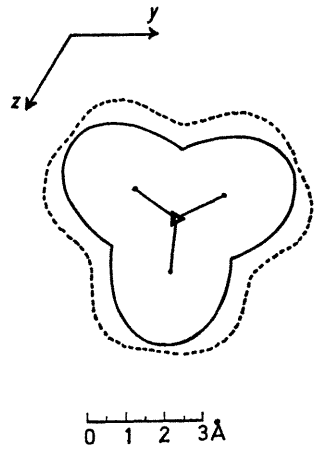


FIGURE 3. *The van der Waals contacts of host and guest as viewed along the* c*-axis; section at* z = 0·26, *the broken lines represent the van der Waals volumes of the atoms comprising the cage and the full lines the approximate van der Waals volume of the guest.*

only be obtained *directly* when the following requirements are met: (i) the molecular symmetry of the guest molecule(s) should be compatible with the symmetry of the cavity [*viz.* $C_{3i}(\bar{3})$]; (ii) the van der Waals model of the guest molecule should conform to the approximate shape and volume of the empty cavity.

We are at present studying the inclusion of di-t-butylacetylene (host:guest ratio‡ 6:1) in (I), with a view to defining accurately the dimensions of the guest molecule within the cavity.

We thank Dr. H. H. Mills for valuable discussion.

(*Received, May 5th,* 1971; *Com.* 708.)

§ However a weighted average based on the assumed bond lengths, C–C 1·54 Å; C–O 1·43 Å, gives 1·52 Å which agrees with the experimental value of 1·53 Å.

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