

## Variation of Inclusion Properties by Structural Modification of a Clathrate Host

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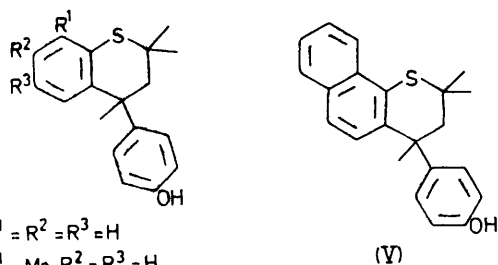
**Summary** By controlled modification of the structure of the selected clathrate host (I), it is possible to achieve a significant alteration in cavity geometry, accompanied by a striking change in selective clathration properties.

RECENTLY we have described the synthesis<sup>1</sup> of the versatile host compound, 4-*p*-hydroxyphenyl-2,2,4-trimethylthiachroman (I) which forms clathrates<sup>2</sup> in which the guest molecules are accommodated in approximately hour glass-shaped cavities. We sought to produce a new host giving voids of markedly altered geometry by an approach based on careful modification of a known host structure, taking into account crystal packing considerations, and now report preliminary results for selected analogues (II)—(V) of host (I). Compounds (II)—(V) were prepared<sup>1</sup> similarly to (I). The derived ketosulphide from the piperidine-cata-

lysed Michael addition of the appropriate arene thiol to mesityl oxide was cyclised in the presence of phenol with anhydrous HCl as catalyst: for (II), (III), and (IV) purification by gel permeation chromatography was necessary (200 × 2.5 cm column of Sephadex LH-20 modified<sup>3</sup> with Nedox 1114, elution with MeOH) while (V) crystallised readily without this further treatment. All compounds gave satisfactory elemental analyses, and had spectral properties (<sup>1</sup>H n.m.r., i.r., and m.s.) in keeping with their formulated structures.

Compound (V) which possesses an additional bulky fused benzene ring crystallised unsolvated from a range of solvents (*e.g.* benzene, EtOH, and *n*-pentane). However, the isomeric compounds (II), (III), and (IV) exhibited an interesting spectrum of behaviour dependent upon the position of the additional methyl group. Thus, (IV) forms

a cyclopentane clathrate (host:guest ratio of 6:1) with a crystal structure of space group  $R\bar{3}$  and with lattice constants, referred to a hexagonal unit cell, of  $a = 29.22$  and  $c = 10.82 \text{ \AA}$ ; these values were very similar to the corre-



I,  $R^1 = R^2 = R^3 = H$

II,  $R^1 = Me, R^2 = R^3 = H$

III,  $R^1 = R^3 = H, R^2 = Me$

IV,  $R^1 = R^2 = H, R^3 = Me$

sponding lattice parameters found for clathrates formed by the parent host (I), e.g.  $a = 27.81$  and  $c = 10.90 \text{ \AA}$  are found for the ethanol clathrate, and so imply fairly similar cage structures for (I) and (IV). Moving the position of the methyl substituent onto an adjacent carbon in the ring to give (III) completely eliminates any clathrate-forming properties, the unsolvated material (from cyclopentane or

cyclohexane) being found to crystallise in the enantiomorphous space group  $P2_12_12_1$ . Most significantly however, with the methyl group introduced *ortho* to sulphur, the crystal structure of compound (II) is markedly altered while it maintains the ability to form stable inclusion compounds. Shortening of the  $c$  dimension, referred to a hexagonal system of axes, to  $8.23 \text{ \AA}$  (measured for the cyclo-octane clathrate, host:guest ratio of 4:1) implies that this structural modification has effected a fundamental change in the dimensions and shape of the cavity. Consistently, a marked difference between the selective clathration properties of (I) and (II) is found; when (I) and (II) are separately recrystallised from an equimolar mixture of cyclopentane, cyclohexane, and cycloheptane, (I) exhibits a very strong preference for cyclopentane as shown by the respective percentages of 85, 10, and 5%, which were included, whereas (II) shows relatively increased tendency to include the larger cycloalkanes, the corresponding values, 20, 50, and 30%, reflecting† the altered cavity shape of (II).

A single crystal structure analysis of (II) is underway to determine the detailed geometry of the modified cavity.

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† A large alteration in cavity geometry such as found for (II) may not be required to produce dramatic changes in selective clathration behaviour, ratios of 12%:57%:31% being found for (IV) whose cavity shape is probably not greatly different from that of (I) (see text).

<sup>1</sup> D. D. MacNicol, *Chem. Comm.*, 1969, 836.

<sup>2</sup> D. D. MacNicol, H. H. Mills, and F. B. Wilson, *Chem. Comm.*, 1969, 1332; D. D. MacNicol and F. B. Wilson, *ibid.*, 1971, 786.

<sup>3</sup> J. Ellingboe, E. Nystrom, and J. Sjovall, *Biochim. Biophys. Acta*, 1968, 152, 803; *J. Lipid Res.*, 1970, 11, 266.