Synthesis of a New Versatile Clathrate-host Compound: 4-*p*-Hydroxyphenyl-2,2,4-trimethylthiachroman

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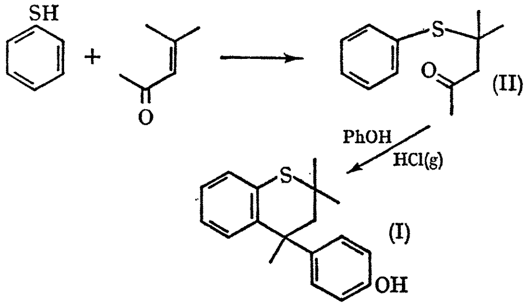
Summary The synthesis of a new versatile clathrate-host compound, 4-*p*-hydroxyphenyl-2,2,4-trimethylthiachroman (I), is described.

THE great scientific interest of clathrate compounds,† both from theoretical and practical standpoints, is now widely recognised. However, little systematic work in the organic field has been directed towards the preparation of new clathrate-host materials. As a first step in this direction,‡ 4-*p*-hydroxyphenyl-2,2,4-trimethylthiachroman (I), the thia-analogue of Dianin's compound,[1,2] has been synthesised by the route shown below.



Phenyl 2-(2-methyl-4-oxo)pentyl sulphide (II), prepared by the method of Tilak *et al.*,[3] was cyclised in presence of phenol, with anhydrous hydrogen chloride as catalyst, to give on work-up involving recrystallisation of the product from ethanol (details will be given in a future publication) the ethanol chathrate of (I) in fair yield (ratio of host/guest 3 : 1, see below). Slow sublimation of the ethanol clathrate *in vacuo* (*e.g.* 68° at 0·01 mm. Hg) yields a solvent-free form of (I) as colourless, hexagonal needles, m.p. 104—106° (uncorr.).

The structure of (I) as formulated, was substantiated§ by evidence accrued from ^{1}H n.m.r., i.r., and u.v. spectra as well as microanalysis and high-resolution mass spectrum. For example, the 100 MHz. ^{1}H n.m.r. spectrum of (I) in $CDCl_3$ has three singlets (3H each) at τ 8·90, 8·58, and 8·25 from the three methyl groups, an AB spectrum (2H) centred at τ 7·72 (δ_{AB} 0·32 p.p.m.; *J* 14 Hz.) from the nonequivalent methylene hydrogens, an AA′BB′ spectrum (4H) centred at τ 3·17 from the ring protons of the *p*-hydroxyphenyl group, and a tightly-coupled ABCD spectrum (4H, in approximate range τ 2·7—3·0) from the remaining aromatic hydrogens, and finally a concentration-dependent signal (1H, at *ca.* τ 5 for a near-saturated solution) from the phenolic OH proton. All other spectral evidence is also completely consistent with the formulated structure of (I).

The thiachroman (I) is remarkable in that it forms clathrates with all the many solvents tried, the clathrates being readily formed simply by recrystallisation of unsolvated (I) from the appropriate pure dry solvent. A selection of clathrates of (I) is given in the Table. The mole ratio of host to guest is dependent on the size of the guest molecule. For fairly small molecules, such as methanol, ethanol, and acetone the ratio is 3 : 1, whereas for larger molecules such as ethyl acetate, toluene, and *p*-xylene the ratio is 6 : 1. In the case of indane, the slightly higher ratio 7 : 1 observed may indicate that, in the specimen examined, some of the cavities were unoccupied.

A selection of molecules which can be enclathrated in the crystal lattice of 4-p-*hydroxyphenyl*-2,2,4-*trimethylthiachroman*

Guest	Mole ratio[a] of host to guest	Method of analysis
Methanol	3 : 1	b
Ethanol	3 : 1	b
Acetone	3 : 1	b
Acetic acid	3 : 1	b
Carbon tetrachloride	4 : 1	c
Ethyl acetate	6 : 1	b
Anisole	6 : 1	b
Toluene	6 : 1	b
p-Xylene	6 : 1	b
Indane	7 : 1	d
n-Heptane	e	–
3-Methylhexane	e	–

[a] The ratio is given as *n* : 1 where *n* is the nearest integer.
[b] Examined by integration of the high-resolution ^{1}H n.m.r. spectrum, several runs being averaged. All the clathrates were carefully dried *in vacuo* before analysis.
[c] Examined by microanalysis for chlorine.
[d] Single graphical integration of the ^{1}H n.m.r. spectrum using a planimeter.
[e] Ratio not determined.

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† For an excellent short review on clathrate compounds see S. M. Hagan, "Clathrate Inclusion Compounds," Reinhold, New York, 1962. A more general account of inclusion compounds is given in "Non-stoicheiometric Compounds,"ed. L. Mandelcorn, Academic Press, New York, 1964.

‡ Earlier attempts by W. Baker and co-workers (ref. 1) to prepare clathrate-host materials structurally related to Dianin's compound were unsuccessful.

§ A full three-dimensional *X*-ray crystallographic study of (I) is underway. It may be said here, however, that the unsolvated form of (I) described in the text is isomorphous with unsolvated Dianin's compound, the *molecular* structure of which has been unambiguously established by synthesis (see ref. 2).

[1] W. Baker, A. J. Floyd, J. F. W. McOmie, G. Pope, A. S. Weaving, and J. H. Wild, *J. Chem. Soc.*, 1956, 2010.
[2] W. Baker, J. F. W. McOmie, and A. S. Weaving, *J. Chem. Soc.*, 1956, 2018.
[3] B. D. Tilak, H. S. Desai, C. V. Deshpande, S. K. Jain, and V. M. Vaidya, *Tetrahedron*, 1966, **22**, 7.