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SYNTHESIS OF A CHIRAL HEXA-HOST MOLECULE

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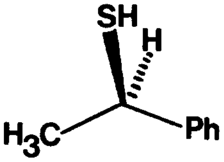
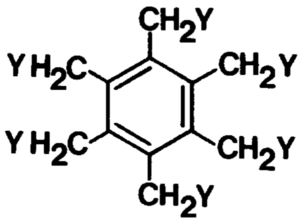
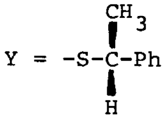
Summary. The synthesis of the first chiral hexa-host molecule (III) is described: an X-ray analysis of the acetic acid adduct of (III) allows the first direct observation of dimeric acetic acid.

Although a wide range of inclusion behaviour has been established for molecules of the hexa-host type, all the hexa-substituted benzene hosts described to date have been achiral.[1] In connection with current interest[2-6] in the design of chiral multimolecular host systems we now report the synthesis of the first chiral hexa-host molecule, hexakis(R-α-phenylethylsulphonylmethyl)benzene (III). In the present work we also briefly describe a single-crystal X-ray diffraction investigation of the inclusion compound formed by this novel host with acetic acid.

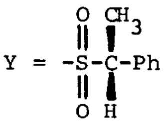


(I)



(II) 

$Y = -S-\overset{CH_3}{\underset{H}{C}}-Ph$

(III) 

$Y = -\overset{O}{\underset{O}{S}}-\overset{CH_3}{\underset{H}{C}}-Ph$

The precursor of hexasulphone (III), the chiral hexasulphide (II), was prepared by six-fold substitution of hexakis(bromomethyl)benzene, $C_6(CH_2Br)_6$, by the thiolate anion of (+)-1-phenylethanethiol (I)[7] generated in NaOEt/EtOH. The reaction was carried out under Ar, the thiol being kept in excess over base to minimise racemisation, and after a 1 h reflux, aqueous work-up gave optically pure (II) in 88% yield, m.p. 137-138°C (from benzene): $\tau(CDCl_3)$ 8.49 (18H, d, J 7 Hz), 6.42 (12H, diastereotopic CH_2, AB, δ_{AB} 0.19 p.p.m., J_{AB} 11 Hz), 6.37 (6H, q, J 7 Hz), and 2.70 (30H, m); ^{13}C n.m.r. (proton noise decoupled, 106K transients) showed only 8 singlets, $\delta_C(CDCl_3)$ 21.8, 29.7, 45.1, 127.1, 127.2, 128.4, 135.2 and 143.9; $[\alpha]_D^{25} = 135.6^{\circ}$ (c = 0.19, $CHCl_3$). The thiol (I) was assigned the R-(+)-configuration from the depolarised Raman c.i.d. spectrum,[8] this assignment being concordant with chemical correlation.[9] Accordingly, (II) has the absolute configuration formulated.

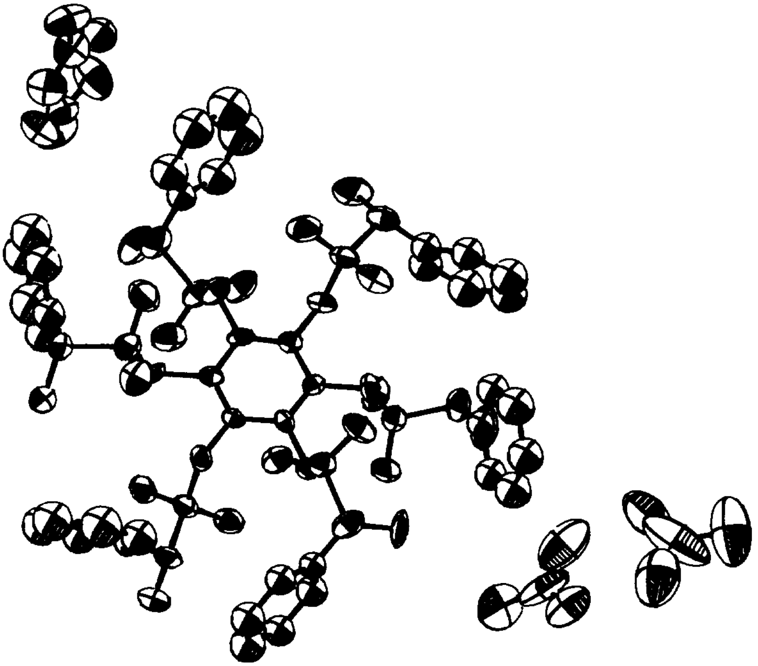
Oxidation of (II) was carried out employing a 2 h reflux with excess hydrogen peroxide in acetic acid, aqueous work-up (employing freeze drying in some runs), giving yields of (III) in excess of 90%: m.p. 255-260°, decomp., (from acetic acid, desolvated <u>in vacuo</u>), ν_{max}(KBr) 1314, 1137, 1123 cm^{-1}; $\tau(CDCl_3)$ 8.48 (18H, d, 7 Hz), 6.49 (6H, q, 7 Hz), 5.35 (12H, diastereotopic CH_2, AB, δ_{AB} 0.09 p.p.m., J_{AB} 15.5 Hz), 2.61 (30H, s); ^{13}C n.m.r. $\delta_C(CDCl_3)$ 13.6 (q), 48.0 (t), 65.4 (d), 129.0 (superposed d), 129.7 (d), 133.6 (s), 133.8 (s).

Chiral host hexakis(R-α-phenylethylsulphonylmethyl)benzene (III) forms an inclusion compound on recrystallisation from acetic acid, a host-guest ratio of 1:4 being determined by integration of the ^{1}H n.m.r. spectrum of a $CDCl_3$ solution of the adduct.

<u>Crystal data for (III)</u>: $C_{60}H_{66}S_6O_{12} \cdot 4(CH_3CO_2H)$, monoclinic space group $P2_1$, $Z = 2$; $a = 16.320(5)$, $b = 13.870(4)$, $c = 16.731(7)$ (Å), $\beta = 106.47(3)^{\circ}$. Cell dimensions and intensity data were obtained with an Enraf-Nonius CAD-4 diffractometer using monochromated Mo K_α radiation. The structure was solved by direct methods using a version of MULTAN 78 in which quartet and quintet invariants were incorporated. Full details will be published elsewhere. The current R factor is 0.076 for 3378 reflections having $I > 2.5\sigma(I)$. Refinement is still continuing.[10]

The figure shows a view of the molecular structure of the host (III), and also illustrates the acetic acid guest molecules. In the host molecule the $-SO_2-$ moieties in the chains linking the central ring to the phenyl groups are situated alternately above and below the mean plane of the central benzene ring. This disposition of the 'legs' of (III) is analogous to that found for hexakis-(benzylthiomethyl)benzene.[11] The four acetic acid guest molecules appear as hydrogen-bonded dimeric pairs which are crystallographically independent. These

FIGURE



A view illustrating the hexakis(R-α-phenylethylsulphonylmethyl)benzene (III) host molecule and the two crystallographically independent acetic acid guest dimers. Hydrogen atoms have been omitted for clarity.

discrete hydrogen-bonded units contrast with the infinite chains of hydrogen-bonded molecules found in the crystal structure of acetic acid[12,13] and also in the 1:1 complex of deoxycholic acid and acetic acid.[14] Each dimer consists of two planar acetic acid molecules whose mean planes intersect at an angle of approximately 18 degrees. The mean O.....O distance is 2.62(7) Å. The potential use of (III) for the optical resolution of racemates is currently being explored and related predesigned chiral host systems are also under investigation.

We thank the S.R.C. for support.

References

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