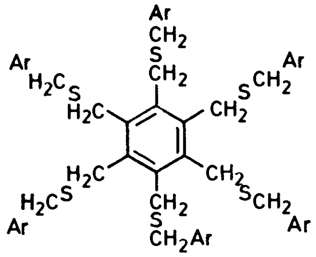
Design of Inclusion Compounds: Systematic Structural Modification of the Hexa-host Molecule Hexakis(benzylthiomethyl)benzene

By **Andrew D. U. Hardy, David D. MacNicol,* Stephen Swanson,** and **Derek R. Wilson,** Department of Chemistry, University of Glasgow, Glasgow G12 8QQ, Scotland

A study of the inclusion behaviour of the title compound (I) and eleven structurally related compounds (II)—(XII) is described. Substitution of each of the six outer aromatic rings of (I) with a single methyl group gives new hosts, the most general of which is the *meta*-analogue (III). A parallel situation is found for the hexachloro-compounds (X)—(XII) where inclusion is again favoured by *meta*-substitution. The versatile host (VII) favours inclusion of *o*-xylene from an equimolar mixture of *o*- and *p*-xylene, in contrast to host (III) which selectively includes the *para*-isomer. A detailed *X*-ray study of the 1,4-dioxan adduct of the parent (I) has been carried out. The crystals are monoclinic, space group $P2_1/c$, with a = 10.542, b = 20.863, c = 12.496 Å, β = 95.48°, and 2 host and 2 guest molecules in the unit cell. A true clathrate structure is found, the chair-shaped dioxan guest molecules being accommodated in effectively closed cages.

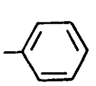
THE hexa-host analogy,[1-5] the key relationship between the hydrogen-bonded hexameric unit present in hydroxy-aromatic clathrates[6] and suitably hexa-substituted benzenes, has led to the discovery of many new host systems. In previous work[1-3,5] we have briefly described inclusion properties of hexakis(benzylthiomethyl)-benzene (I) and its hexamethyl counterparts (II)—(IV). We now report a detailed study of the host (I) and related molecules (II)—(XII) which have as a common structural feature a three-atom CH_2SCH_2 linkage between each side-chain aromatic ring and the central core of the molecule. Molecules (II)—(XII) were prepared analogously to (I), by base-promoted reaction of the appropriate arylalkanethiol with hexakis(bromomethyl)benzene, $C_6(CH_2Br)_6$ (see Experimental section). A detailed *X*-ray study of the 1,4-dioxan adduct of (I) has been carried out in order to define the molecular geometry of the host, as well as to elucidate the guest conformation and the nature of the voids available for guest accommodation.

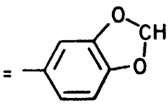


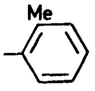
EXPERIMENTAL

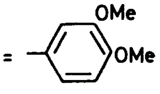
M.p.s were determined on a Kofler hot-stage apparatus and are uncorrected. I.r. spectra were run on a Perkin-Elmer 225 or 580 instrument, and ^1H n.m.r. spectra on Varian T-60 or Perkin-Elmer R32 90 MHz instruments with tetramethylsilane as internal standard.

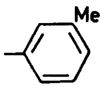
Hexakis(benzylthiomethyl)benzene (I). Compound (I) was prepared by a previously described method.[1] Results of inclusion experiments on (I) are given in Tables 1 and 2.

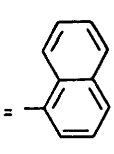
(I) Ar =


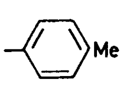
(VII) Ar =


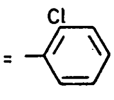
(II) Ar =


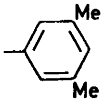
(VIII) Ar =


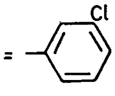
(III) Ar =


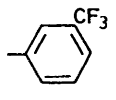
(IX) Ar =


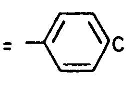
(IV) Ar =


(X) Ar =


(V) Ar =


(XI) Ar =


(VI) Ar =


(XII) Ar =


Hexakis-(2-methylbenzylthiomethyl)benzene (II). To dry ethanol (80 ml) was added finely cut metallic sodium (1.00 g, 0.043 mol) under dry, oxygen-free nitrogen. After hydrogen evolution had ceased, 2-methyltoluene-α-thiol (5.87 g, 0.042 mol) was added, forming a homogeneous solution, followed immediately by finely powdered hexakis(bromomethyl)benzene (3.0 g, 0.004 7 mol) with vigorous stirring. After stirring under reflux for 6 h, the mixture was allowed to cool, then added with stirring to ice–water (300 ml). The precipitate was collected by filtration, washed with water, dilute aqueous sodium hydroxide, and more water till neutrality, then dried *in vacuo*. Recrystallisation from toluene gave (II) (3.95 g, 85.4%), m.p. 171—175° (Found: C, 73.7; H, 6.75. $C_{60}H_{66}S_6$ requires C, 73.55; H, 6.78%), $\nu_{max.}$ (KBr) 3 015, 2 929, 1 492, 1 485, 1 238, 765, 727, and

681 cm^{-1}, τ(CDCl$_3$) 7.71 (18 H, s), 6.65br (12 H, s), 6.45br (12 H, s), and 2.87 (24 H, m). Nitromethane, acetone, furan, and *p*-chlorotoluene were not included by (II).

TABLE 1

Representative inclusion compounds formed by hosts (I)—(XII)

Host	Guest	Mol ratio of host : guest [a]
(I)	Cyclohexane	1 : 1 [b]
	Toluene	1 : 1 [b]
	1,4-Dioxan	1 : 1 [b]
	Acetone	1 : 2 [b]
	1,1,1-Trichloroethane	1 : 1
	Ethyl acetate	1 : 1
	p-Chlorotoluene	1 : 1
	Benzene	1 : 1
(II)	1,1,1-Trichloroethane	1 : 6 [c]
(III)	1,4-Dioxan	1 : 1
	Benzene	1 : 1
	Acetone	1 : 2
	Cyclohexane	1 : 1
	p-Xylene	1 : 1
	o-Xylene	1 : 1
	Ethylbenzene	1 : 1
	Anisole	1 : 1
	Furan	1 : 2
	Ethyl acetate	1 : 1
(IV)	1,4-Dioxan	1 : 1
	Benzene	1 : 1
(V)	Benzene	1 : 1
	Cyclohexane	1 : 2
	1,1,1-Trichloroethane	1 : 2
(VI)	Anisole	1 : 1
	Toluene	1 : 1
(VII)	Toluene	1 : 1
	Benzene	1 : 1
	Anisole	1 : 1
	1,4-Dioxan	1 : 2
	Ethyl acetate	1 : 2
	Nitromethane	1 : 2
	Acetone	1 : 2
(VIII)	1,4-Dioxan	1 : 4
(IX)	Benzene	1 : 2
	1,4-Dioxan	2 : 3
(X)	Nitromethane	1 : 3
(XI)	Cyclohexane	1 : 1
	Benzene	1 : 1
	1,1,1-Trichloroethane	1 : 1
	1,4-Dioxan	1 : 1
	Toluene	1 : 1
	Ethyl acetate	1 : 1
(XII)	1,4-Dioxan	*ca.* 1 : 6 [c]

[a] Measured by multiple integration of the ^{1}H N.m.r. spectrum employing CDCl$_3$ as solvent, and given to nearest integral ratio. [b] Ratio from ref. 1. [c] Variable ratios have been obtained.

Hexakis-(3-*methylbenzylthiomethyl*)*benzene* (III).—Compound (III) was prepared by a similar method to (II). The reagents were dry ethanol (100 ml), sodium (2.28 g, 0.099 mol), 3-methyltoluene-α-thiol (12.8 g, 0.093 mol), and hexakis(bromomethyl)benzene (6.36 g, 0.01 mol). After the work-up described, drying *in vacuo* gave crude (III) (1 : 2, host : guest) (9.01 g, 91.9%), m.p. 130—133° (from acetone), thick needles (Found: C, 73.5; H, 6.55. C$_{60}$H$_{66}$S$_6$ requires C, 73.55; H, 6.8%), $\nu_{max.}$ (KBr) 3 020, 2 920, 1 610, 1 487, 1 227, 788, and 712 cm^{-1}, τ(CDCl$_3$) 7.65 (18 H, s), 6.69br (12 H, s), 6.48br (12 H, s), and *ca.* 2.7—3.1 (24 H, m). Results of inclusion experiments are given in Tables 1 and 2. Compound (III) crystallised insolvated from *m*-xylene.

Hexakis-(4-*methylbenzylthiomethyl*)*benzene* (IV).—The same procedure was used as in the preparation of (II). The reagents were dry ethanol (100 ml), sodium (2.27 g, 0.099 mol), 4-methyltoluene-α-thiol (12.5 g, 0.09 mol), and hexakis(bromomethyl)benzene (6.36 g, 0.01 mol). The standard work-up, followed by drying *in vacuo* gave (IV) (9.13 g, 93%), m.p. 181—186° (from dioxan 1 : 1), (Found: C, 73.3; H, 6.95. C$_{60}$H$_{66}$S$_6$ requires C, 73.55; H, 6.8%), $\nu_{max.}$ (KBr) 3 017, 2 909, 1 512, 1 242, 824, 803, and 731 cm^{-1}, τ(CDCl$_3$) 7.74 (18 H, s), 6.71br (12 H, s), 6.51br (12 H, s), and 2.88 (24 H, s). Results of inclusion experiments are given in Table 1. Acetyl chloride, nitromethane, acetone, and ethyl acetate did not give adducts with (IV).

Hexakis-(3,5-*dimethylbenzylthiomethyl*)*benzene* (V).—Compound (V) was prepared by a similar method as for (II), except that argon was used in place of nitrogen. The reagents were dry ethanol (80 ml), sodium (1.14 g, 0.05 mol), 3,5-dimethyltoluene-α-thiol [7] (7.54 g, 0.05 mol), and hexakis(bromomethyl)benzene (3.5 g, 0.005 5 mol). Recrystallisation of the crude product from toluene gave (V) (5.01 g, 85.5%), m.p. 165—170° (Found: C, 74.5; H, 7.6. C$_{66}$H$_{78}$S$_6$ requires C, 74.55; H, 7.4%), $\nu_{max.}$ (KBr) 3 020, 2 920, 1 606, 1 467, 1 229, 850, 721, and 690 cm^{-1}, τ(CDCl$_3$) 7.71 (36 H, s), 6.73br (12 H, s), 6.48br (12 H, s), and 3.15br (18 H, s). Inclusion compounds of (V) are given in Table 1. Acetone and toluene were not included by (V).

Hexakis-(3-*trifluoromethylbenzylthiomethyl*)*benzene* (VI).—Compound (VI) was prepared by a similar method to (II) with argon used in place of nitrogen. The reagents were dry ethanol (100 ml), sodium (1.17 g, 0.051 mol), 3-trifluoromethyltoluene-α-thiol (9.81 g, 0.051 mol), and hexakis(bromomethyl)benzene (3.60 g, 0.005 7 mol). The normal work-up procedure followed by drying *in vacuo* gave crude (VI) (6.89 g, 93.3%), m.p. 166—168° (from benzene) (Found: C, 55.25; H, 3.8; S, 14.55. C$_{60}$H$_{48}$S$_6$F$_{18}$ requires C, 55.3; H, 3.7; S, 14.75%), $\nu_{max.}$ (KBr) 1 451 1 331, 1 239, 1 161, 1 128, 1 072, 810, and 701 cm^{-1}, τ(CDCl$_3$) 6.66br (12 H, s), 6.52br (12 H, s), and *ca.* 2.4—2.7 (24 H, m). Adducts of (VI) are given in Table 1. Compound (VI) recrystallised unsolvated from 1,1,1-trichloroethane, nitromethane, ethyl acetate, and cyclohexane.

TABLE 2

Guest-selectivity properties of hosts (I), (II), (VII), (VIII), and (IX) on recrystallisation from an equimolar mixture of *o*- and *p*-xylene

Host	Respective mole percentage of guest included [a]		Overall host : guest ratio
	o-Xylene	*p*-Xylene	
(I)	25	75	1 : 1
(III)	15	85	1 : 1
(VII)	80	20	1 : 1 [b]
(VIII)	70	30	2 : 3
(IX)	70	30	2 : 3

[a] Determined by integration of the ^{1}H n.m.r. spectrum and quoted to nearest 5%. [b] Variable host : guest ratios have been obtained in this case, owing to rapid guest loss *in vacuo.*

Hexakis-(3,4-*methylenedioxybenzylthiomethyl*)*benzene* (VII).—Compound (VII) was prepared in a similar manner to (II), argon being used in place of nitrogen. The reagents were dry ethanol (100 ml), sodium (1.41 g, 0.061 mol), 3,4-methylenedioxytoluene-α-thiol (9.91 g, 0.059 mol), and hexakis(bromomethyl)benzene (4.20 g, 0.006 6 mol). Normal work-up procedure followed by drying *in vacuo* gave crude (VII) (7.61 g, 99%), m.p. 169—180° (from toluene 1 : 1) (Found: C, 61.95; H, 4.9; S, 16.3. C$_{60}$H$_{54}$-

S_6O_{12} requires C, 62.15; H, 4.7; S, 16.6%), $\nu_{max.}$ (KBr) 2 888, 1 501, 1 488, 1 444, 1 256, 1 039, 927, and 811 cm^{-1} $\tau(CDCl_3)$ 6.62br (12 H, s), 6.46br (12 H, s), 4.13 (12 H, s), and *ca.* 3.15—3.25 (18 H, arom. H). Tables 1 and 2 give results of inclusion experiments for (VII). Compound (VII) did not include cyclohexane or 1,1,1-trichloroethane.

Hexakis-(3,4-*dimethoxybenzylthiomethyl*)*benzene* (VIII).—Compound (VIII) was prepared in a similar manner to (II), except for the use of argon in place of nitrogen. The reagents were dry ethanol (100 ml), sodium (1.35 g, 0.059 mol), 3,4-dimethoxytoluene-α-thiol (9.97 g, 0.054 mol), and hexakis(bromomethyl)benzene (3.80 g, 0.006 mol). After the normal work-up procedure, drying *in vacuo* gave (VIII) (7.28 g, 97%), m.p. 191—195° (from toluene) (Found: C, 63.3; H, 5.9; S, 15.5. $C_{66}H_{78}O_{12}S_6$ requires C, 63.15; H, 6.25; S, 15.3%), $\nu_{max.}$ (KBr) 1 515, 1 466, 1 262, 1 228, 1 155, 1 134, and 1 028 cm^{-1}, $\tau(CDCl_3)$ 6.66br (12 H, s), 6.47 (12 H, s), 6.23 (18 H, s), 6.12 (12 H, s), and *ca.* 3.1—3.3 (18 H, m). Results of inclusion experiments on (VIII) are given in Tables 1 and 2. Toluene and anisole did not give an adduct with (VIII).

Hexakis-(1-*naphthylmethylthiomethyl*)*benzene* (IX).—Compound (IX) was prepared in a similar manner to (II), argon being used in place of nitrogen. The reagents were dry ethanol (100 ml), sodium (1.30 g, 0.057 mol), 1-mercaptomethylnaphthalene (9.82 g, 0.056 mol), and hexakis(bromomethyl)benzene (4.01 g, 0.006 3 mol). After the normal work-up procedure, drying *in vacuo* gave crude (IX) (1 : 1) (6.81 g, 90.3%), m.p. 197—202° (from toluene) (Found: C, 78.6; H, 5.2. $C_{78}H_{66}S_6$ requires C, 78.35; H, 5.55%), $\nu_{max.}$ (KBr) 3 050, 1 598, 1 513, 1 400, 1 229, 802, 793, and 778 cm^{-1}, $\tau(CDCl_3)$ 6.91br (12 H, s), 6.72br (12 H, s), and *ca.* 2.0—3.5 (42 H, m). Results of inclusion experiments are given in Tables 1 and 2. Compound (IX) did not form an inclusion compound with cyclohexane.

Hexakis-(2-*chlorobenzylthiomethyl*)*benzene* (X).—Compound (X) was prepared in a similar manner to (II), the reagents being dry ethanol (100 ml), sodium (2.30 g, 0.1 mol), 2-chlorotoluene-α-thiol (14.28 g, 0.091 mol), and hexakis(bromomethyl)benzene (6.36 g, 0.01 mol). The crude product contained some unreacted hexakis(bromomethyl)benzene. Two recrystallisations from 1,4-dioxan gave (X) (6.0 g, 54.1%), m.p. 148—149° (Found: C, 58.55; H, 4.55; Cl, 19.4. $C_{54}H_{48}Cl_6S_6$ requires C, 58.85; H, 4.4; Cl, 19.3%), $\nu_{max.}$ (KBr) 1 483, 1 474, 1 444, 1 234, 1 053, 1 040, 758, and 732 cm^{-1}, $\tau(CDCl_3)$ 6.47br (12 H, s), 6.34br (12 H, s), and *ca.* 2.6—2.9 (24 H, m). Compound (X) formed an adduct with nitromethane (Table 1), but did not include toluene, dioxan, acetone, anisole, 1,1,1-trichloroethane, or cyclohexane.

Hexakis-(3-*chlorobenzylthiomethyl*)*benzene* (XI).—Compound (XI) was prepared in a similar manner to (II), argon being used in place of nitrogen. The reagents were dry ethanol (60 ml), sodium (0.78 g, 0.03 mol), 3-chlorotoluene-α-thiol [8] (5.01 g, 0.03 mol), and hexakis(bromomethyl)benzene (2.35 g, 0.003 7 mol). The normal work-up procedure followed by drying *in vacuo* gave crude (XI) (1 : 1) (3.8 g, 92.8%), m.p. 163—165° (from 1,1,1-trichloroethane) (Found: C, 58.95; H, 4.35; Cl, 19.35. $C_{54}H_{48}Cl_6S_6$ requires C, 58.85; H, 4.4; Cl, 19.3%), $\nu_{max.}$ (KBr) 1 598, 1 574, 1 479, 1 433, 1 200, 1 077, 791, 781, and 692 cm^{-1}, $\tau(CDCl_3)$ 6.66br (12 H, s), 6.52br (12 H, s), and *ca.* 2.6—3.0 (24 H, m). Results of inclusion experiments on (XI) are given in Table 1. Compound (XI) did not include nitromethane.

Hexakis-(4-*chlorobenzylthiomethyl*)*benzene* (XII).—Compound (XII) was prepared in a similar manner to (II). The reagents were dry ethanol (100 ml), sodium (2.30 g, 0.1 mol), 4-chlorotoluene-α-thiol (14.28 g, 0.091 mol), and hexakis(bromomethyl)benzene (6.36 g, 0.01 mol). Recrystallisation from 1,4-dioxan gave solvated (XII) (9.83 g, 88.7%, desolvated), m.p. 207—211° (from benzene) (Found: C, 58.95; H, 4.35; Cl, 19.55. $C_{54}H_{48}Cl_6S_6$ requires C, 58.85; H, 4.4; Cl, 19.3%), $\nu_{max.}$ (KBr) 1 492, 1 094, 1 023, 1 018, 836, 812, and 728 cm^{-1}, $\tau(CDCl_3)$ 6.68br (12 H, s), 6.59br (12 H, s), and *ca.*, 2.6—2.9 (24 H, m). Compound (XII) gave an adduct with 1,4-dioxan (Table 1), though crystallisation from cyclohexane or nitromethane gave unsolvated material.

X-Ray Crystal-structure Analysis of the 1,4-*Dioxan Adduct of Compound* (I).—*Crystal data.* $C_{54}S_6H_{54},C_4O_2H_8$, $M = 983.5$; a host : guest ratio of 1 : 1 was found by ^1H n.m.r. spectroscopy. Monoclinic, space group $P2_1/c$, $a = 10.542$, $b = 20.863$, $c = 12.496$ Å, $\beta = 95.48°$. $Z = 2$ (*i.e.* 2 host and 2 guest molecules), $U = 2\,735.7$ Å^3, $D_c = 1.19$ g cm^{-3}, $F(000) = 1\,044$, Mo-K_α radiation, $\lambda = 0.710\,7$ Å, μ(Mo-K_α) $= 2.79$ cm^{-1}. The crystal used was an almost colourless near-hexagon of approximate dimensions 0.97 × 0.72 × 0.36 mm. It was sealed in a thin-wall glass capillary (with a small amount of solvent) to prevent crystal decomposition during data collection.

Crystallographic measurements. Least-squares best cell dimensions were obtained by a treatment of the θ, χ, ϕ setting angles of 22 reflections measured on a Hilger and Watts automatic diffractometer. The intensities were measured by the θ—2θ step-scan procedure with Zr-filtered Mo-K_α radiation. Background counts were taken at each end of the scan range. The intensities of three reflections were monitored after every 60 intensity measurements and the results used to place the reflections on a common scale; the changes in the standard intensities during data collection were small (<8%). Reflections were surveyed out to $\theta \leqslant 27°$, with an option whereby those intensities with $I \leqslant 2\sigma(I)$ were not measured. The intensity values were corrected for Lorentz-polarisation effects, but not for absorption, and 2 495 independent reflections, with $I/\sigma(I) > 2.0$, were obtained.

Structure analysis. The structure was solved by direct phase-determining methods using MULTAN [9] and the 250 reflections having the largest $|E|$ magnitudes. An E map computed with that set of phases which gave the highest figure-of-merit and the lowest residual revealed 21 of the 30 host non-hydrogen atom positions in the asymmetric unit (*i.e.* one-half of a molecule). A subsequent electron-density distribution revealed the remaining nine atoms of the host molecule. These approximate atomic co-ordinates were adjusted by several cycles of full-matrix least-squares calculations employing the program CRYLSQ from the X-RAY 72 system,[10] and for anisotropic temperature factors for all the atoms R was reduced to 13.9%.

The three non-hydrogen atoms of the guest molecule and the 31 hydrogen atoms in the asymmetric unit were located in later difference electron-density distributions, and when included in subsequent cycles of least-squares calculations (with anisotropic temperature factors for the non-hydrogen atoms and isotropic temperature factors for the hydrogen atoms) the R value was lowered to a final value of 4.5% ($R' = 5.8\%$). The weighting scheme used through the least-squares calculations was $w = 1/\sigma^2(|F|)$.

Calculations were carried out on an IBM 370/168 computor at Newcastle. Observed and calculated structure factors, anisotropic thermal parameters, and the hydrogen atom co-ordinates and isotropic temperature factors are listed in Supplementary Publication No. SUP 22770 (20 pp.).* The scattering factors for S, O, and C atoms are those listed in ref. 11, those for H in ref. 12. The anomolous dispersion was allowed for in the least-squares calculations, with values for $\Delta f'$ and $\Delta f''$ for sulphur taken from ref. 13. Atomic fractional co-ordinates are listed in Table 3, and various parameters connected with the clathrate's molecular geometry are listed in Tables 4—7. The Figures show various aspects of the atomic and molecular packing arrangements in the crystal. Some atoms were found to exhibit large thermal motions, as shown by their very large anisotropic temperature factors (see ellipsoids in Figure 1).

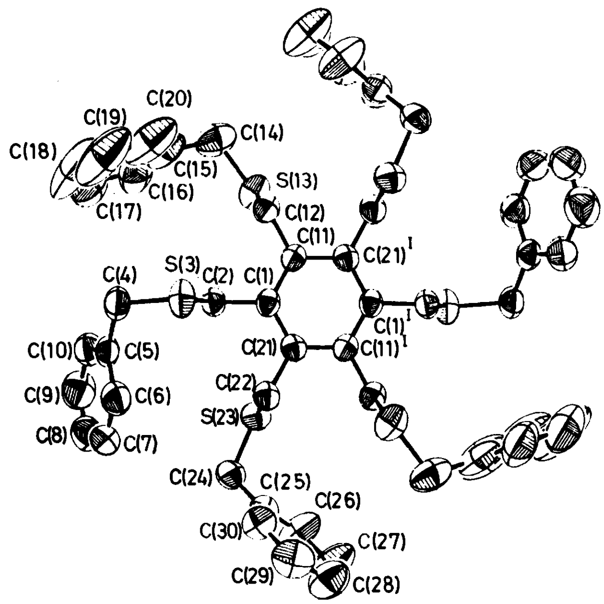


FIGURE 1 An ORTEP drawing with perspective normal to the plane of the central benzene ring of host molecule hexakis-(benzylthiomethyl)benzene (1) and its 1,4-dioxan clathrate. The hydrogen atoms have been omitted for clarity

DISCUSSION

Inclusion Properties of Compounds (I)—(XII).—Table 1 gives the host : guest ratios of adducts of parent (I) and related molecules (II)—(XII); these inclusion compounds were formed on recrystallisation of un-

TABLE 3

Atomic co-ordinates ($\times 10^4$), with standard deviations in parentheses

	X	*Y*	*Z*
Hexa-host molecule (I)			
C(1)	−0 177(3)	0 629(1)	0 344(2)
C(2)	−0 340(4)	1 315(1)	0 693(2)
S(3)	−1 153(1)	1 347(0)	1 902(1)
C(4)	−1 307(4)	2 210(2)	2 032(3)
C(5)	−2 079(4)	2 522(2)	1 107(3)
C(6)	−3 291(5)	2 321(2)	0 776(4)
C(7)	−4 020(5)	2 635(3)	−0 048(5)
C(8)	−3 508(8)	3 146(3)	−0 541(4)
C(9)	−2 320(7)	3 342(2)	−0 241(4)
C(10)	−1 606(4)	3 034(2)	0 583(3)
C(11)	0 904(4)	0 291(2)	0 731(3)
C(12)	1 857(4)	0 592(2)	1 557(3)
S(13)	3 058(1)	1 035(1)	0 929(1)
C(14)	3 866(6)	1 413(3)	2 124(5)
C(15)	3 126(6)	1 937(4)	2 594(6)
C(16)	3 030(8)	2 527(5)	2 068(7)
C(17)	2 320(11)	3 014(5)	2 533(13)
C(18)	1 862(14)	2 851(10)	3 505(14)
C(19)	1 779(13)	2 289(8)	3 897(8)
C(20)	2 564(10)	1 836(5)	3 506(7)
C(21)	−1 105(3)	0 337(1)	−0 368(2)
C(22)	−2 326(4)	0 678(2)	−0 730(3)
S(23)	−2 165(1)	1 132(0)	−1 947(1)
C(24)	−3 805(4)	1 397(2)	−2 231(3)
C(25)	−4 735(4)	0 861(2)	−2 457(3)
C(26)	−4 858(5)	0 553(3)	−3 416(3)
C(27)	−5 704(6)	0 056(3)	−3 611(4)
C(28)	−6 470(5)	−0 131(3)	−2 856(5)
C(29)	−6 357(5)	0 168(3)	−1 898(4)
C(30)	−5 494(4)	0 667(2)	−1 693(3)
1,4-Dioxan guest			
O(31)	0 028(13)	−0 182(6)	3 949(7)
C(32)	1 032(13)	0 177(8)	4 525(12)
C(33)	−0 502(10)	−0 587(4)	4 757(12)

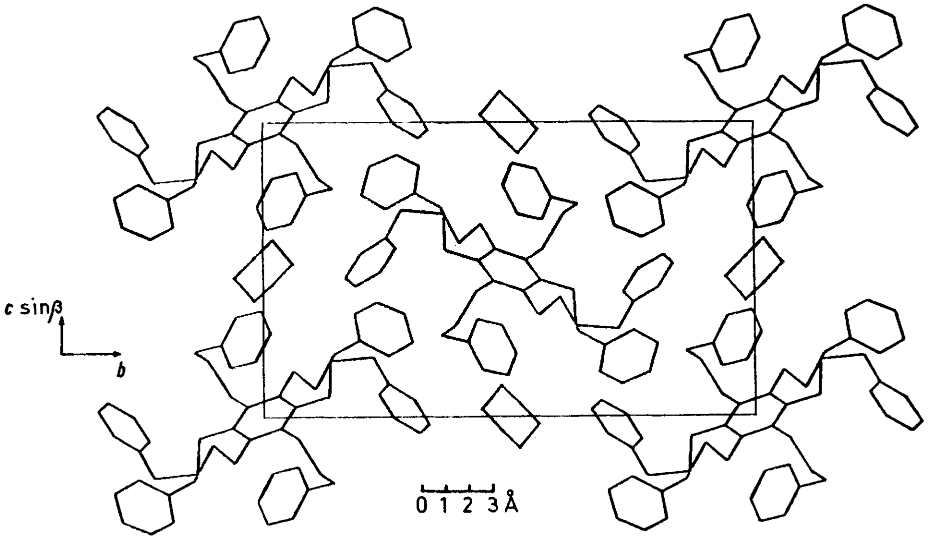


FIGURE 2 An illustration of host to guest packing in the crystal of the 1,4-dioxan clathrate of (I), as viewed along the *a*-axis

---

* For details of supplementary publications see Notice to Authors No. 7, in *J.C.S. Perkin II*, 1979, Index issue.

solvated material from the appropriate pure solvent. Substitution of each of the six outer aromatic rings of (I) with a single methyl group gives the new hosts (II)—(IV), the most general being the *meta*-analogue (III).

TABLE 4

Interatomic distances (Å) and valency angles (°), with standard deviations in parentheses

(a) Bond lengths

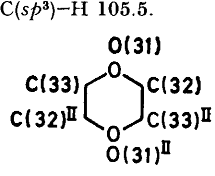
C(1)–C(2)	1.509(4)	C(15)–C(16)	1.395(12)
C(1)–C(11)	1.387(5)	C(15)–C(20)	1.351(12)
C(1)–C(21)	1.398(5)	C(16)–C(17)	1.419(15)
C(2)–S(3)	1.809(3)	C(17)–C(18)	1.392(23)
S(3)–C(4)	1.816(4)	C(18)–C(19)	1.277(25)
C(4)–C(5)	1.498(5)	C(19)–C(20)	1.376(18)
C(5)–C(6)	1.371(7)	C(21)–C(22)	1.502(5)
C(5)–C(10)	1.371(5)	C(22)–S(23)	1.813(3)
C(6)–C(7)	1.388(8)	S(23)–C(24)	1.817(4)
C(7)–C(8)	1.369(9)	C(24)–C(25)	1.495(5)
C(8)–C(9)	1.337(10)	C(25)–C(26)	1.355(6)
C(9)–C(10)	1.376(7)	C(25)–C(30)	1.365(6)
C(11)–C(12)	1.507(6)	C(26)–C(27)	1.375(9)
C(12)–S(13)	1.807(5)	C(27)–C(28)	1.357(9)
S(13)–C(14)	1.826(7)	C(28)–C(29)	1.345(8)
C(14)–C(15)	1.493(10)	C(29)–C(30)	1.391(7)
C(11)–C(21)$^{\mathrm{I}}$	1.410(5)	O(31)–C(33)	1.468(17)
O(31)–C(32)	1.435(19)		
C(32)–C(33)$^{\mathrm{II}}$	1.394(20)		

Means: C(sp^3)–H 0.94, C(sp^2)–H 0.96.

(b) Valency angles

C(1)–C(2)–S(3)	110.6(2)	C(22)–S(23)–C(24)	99.2(2)
C(2)–S(3)–C(4)	99.5(2)	S(23)–C(24)–C(25)	113.8(3)
S(3)–C(4)–C(5)	114.1(2)	C(24)–C(25)–C(26)	121.8(4)
C(4)–C(5)–C(6)	121.5(3)	C(25)–C(26)–C(27)	121.4(5)
C(5)–C(6)–C(7)	120.9(4)	C(26)–C(27)–C(28)	120.8(5)
C(6)–C(7)–C(8)	119.2(5)	C(27)–C(28)–C(29)	118.5(5)
C(7)–C(8)–C(9)	120.8(6)	C(28)–C(29)–C(30)	120.8(5)
C(8)–C(9)–C(10)	119.8(5)	C(29)–C(30)–C(25)	120.7(4)
C(10)–C(5)–C(6)	117.7(4)	C(30)–C(25)–C(26)	117.7(4)
C(9)–C(10)–C(5)	121.6(4)	C(30)–C(25)–C(24)	120.5(3)
C(10)–C(5)–C(4)	120.7(4)	C(1)–C(11)–C(12)	120.0(3)
C(11)–C(12)–S(13)	111.4(3)	C(1)–C(21)–C(22)	120.8(3)
C(12)–S(13)–C(14)	99.1(3)	C(2)–C(1)–C(11)	119.5(3)
S(13)–C(14)–C(15)	114.6(5)	C(2)–C(1)–C(21)	120.3(3)
C(14)–C(15)–C(16)	118.5(7)	C(11)–C(1)–C(21)	120.1(3)
C(15)–C(16)–C(17)	117.2(9)	C(1)–C(11)–C(21)$^{\mathrm{I}}$	120.3(3)
C(16)–C(17)–C(18)	115.0(12)	C(1)–C(21)–C(11)$^{\mathrm{I}}$	119.5(3)
C(17)–C(18)–C(19)	127.0(16)	C(12)–C(11)–C(21)$^{\mathrm{I}}$	119.7(3)
C(18)–C(19)–C(20)	115.3(12)	C(22)–C(21)–C(11)$^{\mathrm{I}}$	119.7(3)
C(19)–C(20)–C(15)	121.3(10)	C(33)–O(31)–C(32)	105.4(10)
C(20)–C(15)–C(16)	121.1(8)	O(31)–C(32)–C(33)$^{\mathrm{II}}$	108.8(11)
C(20)–C(15)–C(14)	120.3(8)	O(31)–C(33)–C(32)$^{\mathrm{II}}$	106.9(10)
C(21)–C(22)–S(23)	110.7(2)		

Means: H–C(sp^3)–H 114.0, C(sp^2)–C(sp^2)–H 111.4, C(sp^2)–C(sp^3)–H 109.6, S–C(sp^3)–H 105.5.



Numbering scheme of 1,4-dioxan guest

The superscripts refer to the following transformations of the atomic co-ordinates (Tables 4—7):

I $-x, -y, -z$ II $-x, -y, 1-z$

This situation is paralleled for the hexachloro compounds (X)—(XII) where inclusion is again favoured by *meta*-substitution. Interestingly, compound (VI), which closely resembles host (III) in structure, shape, and molecular volume, does not match the general inclusion properties of (III), suggesting that the size and polarity of the *meta*-substituent are important. The dodecamethyl counterpart of (I), compound (V), possessing a methyl group in both *meta*-positions of each outer ring, is also an inclusion host. Fusion of a methylenedioxy-unit onto each outer aromatic ring, as in (VII), leads to a new host with more general inclusion properties than have been found for the related molecule (VIII). The versatile host (VII) selectively includes *o*-xylene when unsolvated (VII) is recrystallised from an equimolar mixture of *o*- and *p*-xylene (see Table 2). In contrast, the general host (III) exhibits marked selectivity for the *para*-isomer from the above binary mixture, the *p*-xylene

TABLE 5

Torsion angles (°), with standard deviations in parentheses

C(11)–C(1)–C(2)–S(3)	−89.6(3)
C(2)–C(1)–C(11)–C(12)	4.7(5)
C(2)–C(1)–C(21)–C(22)	−5.0(5)
C(1)–C(2)–S(3)–C(4)	−175.6(2)
S(3)–C(4)–C(5)–C(6)	54.3(5)
C(4)–C(5)–C(6)–C(7)	176.7(4)
C(4)–C(5)–C(10)–C(9)	−177.4(4)
C(5)–C(6)–C(7)–C(8)	0.9(8)
C(7)–C(8)–C(9)–C(10)	−0.9(9)
C(1)–C(11)–C(12)–S(13)	−89.5(4)
C(12)–S(13)–C(14)–C(15)	−72.1(5)
S(13)–C(14)–C(15)–C(20)	105.1(8)
C(20)–C(15)–C(16)–C(17)	0.1(13)
C(16)–C(15)–C(20)–C(19)	6.1(15)
C(16)–C(17)–C(18)–C(19)	−15.8(24)
C(18)–C(19)–C(20)–C(15)	−16.1(19)
C(21)–C(22)–S(23)–C(24)	174.0(2)
S(23)–C(24)–C(25)–C(26)	−77.0(5)
C(24)–C(25)–C(26)–C(27)	179.1(5)
C(24)–C(25)–C(30)–C(29)	−179.8(4)
C(25)–C(26)–C(27)–C(28)	1.8(9)
C(27)–C(28)–C(29)–C(30)	1.3(9)
C(22)$^{\mathrm{I}}$–C(21)$^{\mathrm{I}}$–C(11)–C(1)	175.4(3)
C(22)$^{\mathrm{I}}$–C(21)$^{\mathrm{I}}$–C(11)–C(12)	−5.7(5)
C(21)$^{\mathrm{I}}$–C(11)–C(12)–S(13)	91.6(4)
C(21)$^{\mathrm{I}}$–C(11)–C(1)–C(21)	3.2(5)
C(33)–O(31)–C(32)–C(33)$^{\mathrm{II}}$	−65.6(14)
C(32)–O(31)–C(33)–C(32)$^{\mathrm{II}}$	64.3(13)
C(21)–C(1)–C(2)–S(3)	90.8(3)
C(21)–C(1)–C(11)–C(12)	—175.7(3)
C(11)–C(1)–C(21)–C(22)	175.4(3)
C(2)–S(3)–C(4)–C(5)	61.5(3)
S(3)–C(4)–C(5)–C(10)	−127.8(4)
C(10)–C(5)–C(6)–C(7)	−1.3(7)
C(6)–C(5)–C(10)–C(9)	0.6(7)
C(6)–C(7)–C(8)–C(9)	0.2(10)
C(8)–C(9)–C(10)–C(5)	0.5(8)
C(11)–C(12)–S(13)–C(14)	172.2(3)
S(13)–C(14)–C(15)–C(16)	−74.8(8)
C(14)–C(15)–C(16)–C(17)	179.9(8)
C(14)–C(15)–C(20)–C(19)	−173.7(9)
C(15)–C(16)–C(17)–C(18)	3.6(16)
C(17)–C(18)–C(19)–C(20)	21.7(24)
C(1)–C(21)–C(22)–S(23)	90.6(3)
C(22)–S(23)–C(24)–C(25)	−63.1(3)
S(23)–C(24)–C(25)–C(30)	103.1(4)
C(30)–C(25)–C(26)–C(27)	−0.9(7)
C(26)–C(25)–C(30)–C(29)	0.3(7)
C(26)–C(27)–C(28)–C(29)	−2.0(9)
C(28)–C(29)–C(30)–C(25)	−0.5(8)
C(21)$^{\mathrm{I}}$–C(11)–C(1)–C(2)	−176.4(3)
C(12)$^{\mathrm{I}}$–C(11)$^{\mathrm{I}}$–C(21)–C(1)	−175.7(3)
C(11)$^{\mathrm{I}}$–C(21)–C(1)–C(2)	176.5(3)
C(11)$^{\mathrm{I}}$–C(21)–C(1)–C(11)	−3.1(5)
O(31)–C(32)–C(33)$^{\mathrm{II}}$–O(31)$^{\mathrm{II}}$	66.6(14)

selectivity of (III) being greater than that of the parent (I) (see Table 2).

Structural Properties of the 1,4-*Dioxan Adduct of* (I).—A view looking directly onto the plane of the central benzene ring of the host molecule (I) is shown in Figure 1. The molecule is located on a crystallographic centre of inversion and is therefore constrained to be centrosymmetric. This situation may be compared with the exact three-fold symmetry found[4] for a clathrate of hexakisphenylthiobenzene, $C_6(SPh)_6$. The sulphur atoms in the ' legs ' of (I) are situated alternatively above and below the plane of the central benzene ring. Consideration of the torsion angles C(21)^{I}–C(11)–C(12)–S(13), C(11)–C(1)–C(2)–S(3), and C(1)–C(21)–C(22)–S(23), which have the respective values 92, −90, and 91°, and also C(1)–C(2)–S(3)–C(4), C(11)–C(12)–S(13)–C(14), and C(21)–C(22)–S(23)–C(24) (−176, 172, and 174°), reveal approximate three-fold ' core ' symmetry. Deviations from three-fold symmetry become more marked for the remainder of the molecule. In each of the three independent terminal phenyl groups, half the ring atoms lie above the central benzene ring plane, while the other half lie below. At the periphery of the molecule thermal motion effects cause apparent bond shortening, this being especially pronounced for the bond lengths C(8)–C(9), C(18)–C(19), and C(28)–C(29) (see Table 4). The central benzene ring is planar to ±0.01 Å, but the directly attached atoms C(2), C(12), and C(22) are displaced from this plane by −0.06, 0.09, and 0.09 Å respectively.

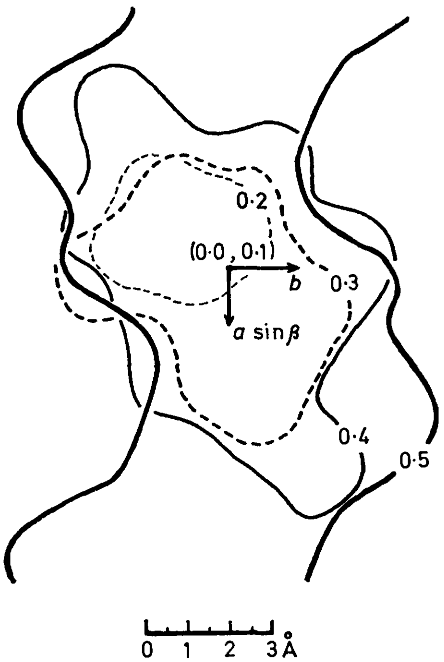


FIGURE 3 The space available in the cage of (I) in cross section at various fractional levels perpendicular to the *c*-axis. The contours shown represent only half the centrosymmetric cage

TABLE 6

Some short intramolecular separations (<3.8 Å)

C(22)–C(30)	3.44	S(13)–C(22)^{I}	3.66
C(12)–S(23)^{I}	3.64	C(12)–C(20)	3.59
S(3)–C(22)	3.68	S(3)–C(12)	3.61
C(2)–S(23)	3.68	C(2)–S(13)	3.61

TABLE 7

Displacements (Å) of atoms from planes through various sets of atoms

Plane (A): C(5)—C(10)

C(5) −0.004, C(6) 0.007, C(7) −0.003, C(8) −0.006, C(9) 0.005, C(10) 0.001, C(4) −0.068

Plane (B): C(15)—C(20)

C(15) −0.002, C(16) 0.014, C(17) 0.000, C(18) −0.107, C(19) 0.086, C(20) −0.028, C(14) 0.014

Plane (C): C(25)—C(30)

C(25) 0.000, C(26) −0.004, C(27) 0.010, C(28) −0.007, C(29) 0.002, C(30) 0.000, C(24) 0.004

Plane (D): C(1), C(11), C(21)^{I}, C(1)^{I}, C(11)^{I}, C(21)

C(1) −0.009, C(11) 0.014, C(21)^{I} −0.009, C(1)^{I} 0.009, C(11)^{I} −0.014, C(21) 0.009, C(2) −0.065, C(12) 0.091, C(22) 0.087, S(3) 1.603, S(13) −1.555, S(23) −1.573

Angles (°) between plane normals: (A)–(B) 76.4, (A)–(C) 62.8, (B)–(C) 120.6, (A)–(D) 58.9, (B)–(D) 95.7, (C)–(D) 97.7

The host–guest packing arrangement in the crystal is illustrated in Figure 2, the host and guest molecules above and below those shown being directly superposed in this view. All the host and guest molecules are situated at crystallographic centres of symmetry on the *b*–*c* plane. The acute angle between the plane normal to the central benzene ring and the *c*-axis is 36°. The space available for guest accommodation may be appreciated from the contours shown in Figure 3, which are at various fractional levels perpendicular to the *c*-axis, and

TABLE 8

Some selected crystal data for adducts of hexakis(benzylthiomethyl)benzene (I) and related molecules (III) and (IV), and for unsolvated (IV)

Host	Guest (host : guest ratio *)	Space group	Lattice parameters
(I)	1,4-Dioxan (1 : 1)	$P2_1/c$ Monoclinic	a = 10.542, b = 20.863, c = 12.496 Å, β = 95.48°, Z = 2 (host), U = 2 735.7 Å^3
(III)	*p*–*o*-Xylene † (1 : 1)	$P2_1/c$ Monoclinic	a = 9.62, b = 15.45, c = 22.72 Å, β = 111.0°, Z = 2 (host), U = 3 152.6 Å^3
(IV)	None ‡	$P2_1/c$ Monoclinic	a = 8.66, b = 23.69, c = 13.50 Å, β = 92.9°, Z = 2, U = 2 766.1 Å^3
(IV)	1,4-Dioxan (1 : 1)	$Pcab$ Orthorhombic	a = 18.67; b = 14.18, c = 23.22 Å, Z = 4 (host), U = 6 147.3 Å^3

* Ratio determined by ^1H n.m.r. employing $CDCl_3$ as solvent. † Crystals prepared by recrystallisation from an equimolar mixture of *o*- and *p*-xylene; a marked selectivity for the *para*-isomer is found (see text). ‡ Unsolvated material produced by recrystallisation from cyclohexane (solvated crystals have also been obtained from this solvent).

represent only half the centrosymmetric cage. These contours were obtained after allowing for the van der Waals volumes of the cage wall atoms, and represent the greatest degree of freedom for a hydrogen atom at each fractional level. The cavity may be considered to be of the closed cage type, there being only a narrow interconnection between cages. Despite this, however, solvent loss does in fact occur slowly in air.

The 1,4-dioxan guest molecule has a chair conformation, though its pronounced thermal motion gives rise to some unrealistic structural parameters (see Tables 4 and 5). There are no intermolecular contacts which are significantly shorter than the sum of the appropriate van der Waals radii.

Table 8 gives a comparison of selected crystal data for (I) and methyl derivatives. In contrast to the monoclinic adducts of (I) and (III), host compound (IV) forms solvated orthorhombic crystals from 1,4-dioxan with an approximate doubling of the unit cell volume.

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

[9/1215 *Received, 1st August, 1979*]

REFERENCES

[1] A. D. U. Hardy, D. D. MacNicol, and D. R. Wilson, *J.C.S. Perkin II*, 1979, 1011.

[2] D. D. MacNicol and D. R. Wilson, *J.C.S. Chem. Comm.*, 1976, 494.

[3] D. D. MacNicol and D. R. Wilson, *Chem. and Ind.*, 1977, 84.

[4] D. D. MacNicol, A. D. U. Hardy, and D. R. Wilson, *Nature*, 1977, **266**, 611.

[5] A. D. U. Hardy, D. D. MacNicol, S. Swanson, and D. R. Wilson, *Tetrahedron Letters*, 1978, 3579.

[6] For recent reviews of clathrates see, for example, D. D. MacNicol, J. J. McKendrick, and D. R. Wilson, *Chem. Soc. Rev.*, 1978, 65; J. E. D. Davies, in ' Molecular Spectroscopy,' eds. J. Sheridan, D. A. Long, and R. F. Barrow, Specialist Periodical Reports, The Chemical Society, London, 1978, vol. 5, ch. 2; S. G. Frank, *J. Pharm. Sci.*, 1975, **64**, 1585.

[7] W. E. Truce and D. W. Onken, *J. Org. Chem.*, 1975, **40**, 3200.

[8] J. G. Lombardini and E. H. Wiseman, *J. Medicin. Chem.*, 1970, **13**, 206.

[9] G. Germain, P. Main, and M. M. Woolfson, ' MULTAN, a Computer Program for the Automatic Solution of Crystal Structures,' University of York, 1973.

[10] ' *X*-Ray 72 ' suite of programs, eds. J. M. Stewart, G. J. Kruger, M. L. Ammon, C. Dickinson, and S. R. Hall, 1972. Technical Report TR192, Computer Science Centre, University of Maryland.

[11] D. T. Cromer and J. B. Mann, *Acta Cryst.*, 1968, **A24**, 321.

[12] R. F. Stewart, E. R. Davidson, and W. T. Simpson, *J. Chem. Phys.*, 1965, **42**, 3175.

[13] ' International Tables for *X*-Ray Crystallography,' Kynoch Press, Birmingham, vol. III, 1962.