

## The Tri-*o*-thymotide–2-Bromobutane (2:1) Clathrate at 125 K

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(Received 26 May 1981; accepted 16 November 1981)

### Abstract

$C_{33}H_{36}O_6 \cdot 0.5C_4H_9Br$  is trigonal,  $P3_121$ , with  $a = 13.620$  (8),  $c = 30.075$  (26) Å;  $Z = 6$ ;  $D_m = 1.192$  Mg  $m^{-3}$ .  $\mu = 0.719$   $mm^{-1}$ . Final  $R = 0.081$  for 2286 reflections at 125 K. The structure was determined by direct methods in space group  $P3_1$ . The geometry of the host structure is consistent with space group  $P3_121$  whereas the Hamilton test favours space group  $P3_1$ . The structure of the guest molecule and its axially disordered orientation within the cavity are discussed.

### Introduction

The complex presently investigated affords a simple model for a conformational approach to the chiral recognition of guest molecules in tri-*o*-thymotide (TOT) clathrates based on the calculation of packing energies (Gerdil & Allemand, 1980). The enantiomeric excess of 2-bromobutane is about 35% in a single crystal of the clathrate grown from racemic material. Lattice parameters and diffracted intensities were measured at 125 K on a four-circle Philips PW 1100 diffractometer (graphite monochromator, Mo  $K\alpha$  radiation,  $\omega$ - $2\theta$  scan). The space group was first assumed to be  $P3_1$ . Of the 4384 reflections measured in the range  $3 < \theta < 23^\circ$ , 3378 had  $|F_o| > 2\sigma(F_o)$  and  $|F_o| > 8.0$ , and were considered as observed at the beginning of the analysis. The phase problem was solved by direct methods using the XRAY (Stewart, 1976) adaptation of *MULTAN*. The *M* configuration was arbitrarily assigned to the two independent TOT molecules of the asymmetric unit (Fig. 1a). A difference synthesis disclosed, within the cavity, a constellation of peaks fitting the *R* configuration of 2-bromobutane (Fig. 1b). The resulting geometry was unsatisfactory; a minimum-energy conformation was therefore calculated by molecular mechanics methods (Kao & Allinger, 1977) and included as a rigid component in the model. An overall isotropic temperature factor was assigned to the guest together with

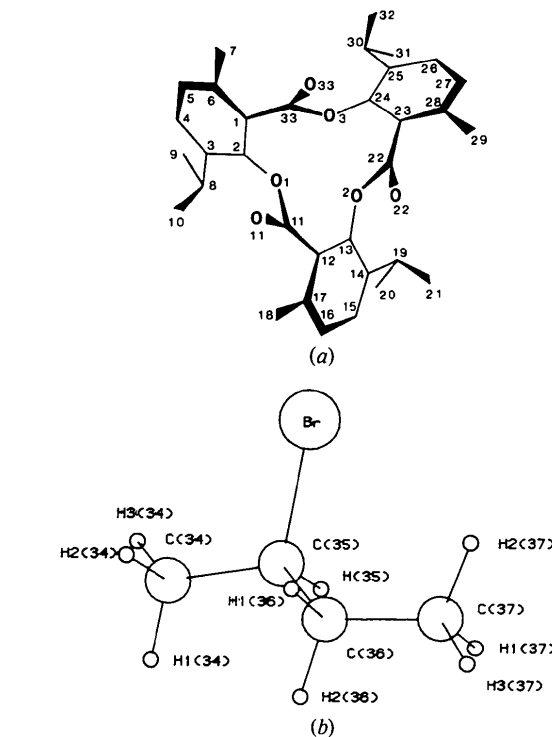


Fig. 1. The atom numbering system: (a) idealized view of the *M* configuration of (–)-tri-*o*-thymotide (Gerdil & Allemand, 1979); (b) minimum-energy conformation of (*R*)-2-bromobutane.

an occupancy factor of 1.0. Actually, an *average* guest occupancy factor of 0.74 was determined by NMR methods. This factor varied by more than 15% among crystals collected from the same crop. As was shown later, the arbitrary assignment of a unitary occupancy factor neither modifies the results of the refinement, nor affects the magnitude of the overall isotropic temperature factor of the rigid model.

The H atoms of TOT form a large part of the inner surface of the cavity and an accurate knowledge of their positions is of prime importance in calculating the non-bonded interactions with the guest molecule. When the *R* value was 0.13 a  $\Delta F$  synthesis revealed 13 out of 18 methyl H atoms and 30 out of 42 isopropyl H atoms of the asymmetric unit. The positions of the unobserved

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Table 1. Atomic coordinates and equivalent isotropic temperature factors ( $\text{\AA}^2$ ) ( $\times 10^3$  for non-H atoms,  $\times 10^2$  for H atoms) for tri-*o*-thymotide

The mean e.s.d.'s ( $\times 10^4$ ) for the  $x$ ,  $y$  and  $z$  coordinates of the H atoms are 98, 98 and 38 respectively.

$$U_{\text{eq}} = \frac{1}{3} \sum_i \sum_j U_{ij} a_i^* a_j^* (a_i \cdot a_j).$$

	$x$	$y$	$z$	$U_{\text{eq}}/U_{\text{iso}}$
O(1)	0.9815 (6)	0.3362 (6)	0.3930 (2)	37 (3)
O(2)	0.8809 (6)	0.4678 (6)	0.4057 (2)	37 (3)
O(3)	0.8178 (6)	0.3409 (6)	0.3279 (2)	33 (3)
O(11)	0.8900 (7)	0.2105 (7)	0.4477 (2)	52 (4)
O(22)	0.7161 (6)	0.3792 (8)	0.4436 (2)	57 (4)
O(33)	0.6932 (8)	0.1746 (8)	0.3579 (4)	108 (6)
C(1)	0.8742 (9)	0.2034 (9)	0.3354 (3)	34 (5)
C(2)	0.968 (1)	0.2524 (9)	0.3627 (3)	40 (5)
C(3)	1.0592 (9)	0.231 (1)	0.3578 (3)	38 (5)
C(4)	1.045 (1)	0.157 (1)	0.3228 (4)	46 (6)
C(5)	0.949 (1)	0.1051 (8)	0.2965 (4)	40 (5)
C(6)	0.8615 (9)	0.1263 (9)	0.3024 (4)	39 (5)
C(7)	0.755 (1)	0.068 (1)	0.2743 (4)	51 (6)
C(8)	1.1620 (9)	0.283 (1)	0.3873 (4)	47 (6)
C(9)	1.272 (1)	0.327 (1)	0.3632 (4)	54 (6)
C(10)	1.146 (1)	0.193 (1)	0.4228 (4)	63 (7)
C(11)	0.9392 (9)	0.306 (1)	0.4349 (4)	40 (5)
C(12)	0.9698 (9)	0.4105 (9)	0.4609 (3)	35 (5)
C(13)	0.9417 (9)	0.4893 (9)	0.4458 (3)	35 (5)
C(14)	0.9778 (9)	0.5931 (9)	0.4668 (4)	43 (5)
C(15)	1.0462 (9)	0.617 (1)	0.5047 (4)	44 (6)
C(16)	1.0724 (9)	0.537 (1)	0.5207 (3)	44 (5)
C(17)	1.0364 (9)	0.4339 (9)	0.4996 (3)	39 (5)
C(18)	1.070 (1)	0.350 (1)	0.5178 (4)	51 (6)
C(19)	0.950 (1)	0.680 (1)	0.4485 (4)	48 (6)
C(20)	1.061 (2)	0.792 (1)	0.4367 (6)	88 (9)
C(21)	0.880 (2)	0.704 (2)	0.4813 (5)	90 (10)
C(22)	0.7647 (9)	0.4152 (9)	0.4085 (3)	39 (5)
C(23)	0.7111 (8)	0.4151 (8)	0.3660 (3)	30 (5)
C(24)	0.7362 (8)	0.3746 (8)	0.3273 (3)	31 (5)
C(25)	0.6868 (9)	0.3724 (8)	0.2860 (3)	38 (5)
C(26)	0.6105 (9)	0.4107 (9)	0.2865 (3)	39 (5)
C(27)	0.5828 (9)	0.452 (1)	0.3239 (4)	44 (5)
C(28)	0.6340 (9)	0.4508 (9)	0.3652 (3)	40 (5)
C(29)	0.603 (1)	0.497 (1)	0.4051 (4)	49 (6)
C(30)	0.715 (1)	0.3293 (9)	0.2442 (3)	42 (6)
C(31)	0.775 (1)	0.426 (1)	0.2107 (4)	54 (6)
C(32)	0.607 (1)	0.231 (1)	0.2238 (4)	58 (6)
C(33)	0.7842 (9)	0.2345 (9)	0.3425 (4)	43 (5)
H(4)	1.1151	0.1408	0.3165	9 (5)
H(5)	0.9427	0.0473	0.2701	4 (3)
H1(7)	0.6809	0.0432	0.2951	5 (4)
H2(7)	0.7576	0.1255	0.2489	8 (4)
H3(7)	0.7479	-0.0067	0.2587	6 (4)
H(8)	1.1726	0.3568	0.4051	4 (3)
H1(9)	1.2725	0.2581	0.3449	11 (6)
H2(9)	1.2816	0.3926	0.3398	11 (5)
H3(9)	1.3481	0.3652	0.3847	7 (4)
H1(10)	1.0687	0.1698	0.4425	6 (3)
H2(10)	1.1359	0.1167	0.4069	6 (3)
H3(10)	1.2189	0.2297	0.4445	11 (5)
H(15)	1.0783	0.6976	0.5213	11 (5)
H(16)	1.1237	0.5565	0.5505	3 (3)
H1(18)	0.9944	0.2752	0.5299	10 (5)
H2(18)	1.1076	0.3264	0.4917	8 (4)
H3(18)	1.1286	0.3888	0.5448	8 (5)
H(19)	0.8991	0.6510	0.4183	17 (7)
H1(20)	1.1103	0.8246	0.4666	30 (10)
H2(20)	1.1048	0.7731	0.4117	20 (10)

Table 1 (cont.)

	$x$	$y$	$z$	$U_{\text{iso}}$
H3(20)	1.0383	0.8538	0.4239	10 (5)
H1(21)	0.8030	0.6296	0.4882	8 (6)
H2(21)	0.9308	0.7401	0.5116	19 (8)
H3(21)	0.8620	0.7703	0.4681	6 (2)
H(26)	0.5702	0.4103	0.2551	5 (3)
H(27)	0.5241	0.4831	0.3220	7 (4)
H1(29)	0.5555	0.4282	0.4288	8 (4)
H2(29)	0.6790	0.5609	0.4211	9 (4)
H3(29)	0.5510	0.5321	0.3954	6 (3)
H(30)	0.7731	0.2980	0.2507	12 (6)
H1(31)	0.7202	0.4605	0.2025	8 (4)
H2(31)	0.8535	0.4928	0.2255	5 (3)
H3(31)	0.7953	0.3960	0.1804	7 (4)
H1(32)	0.5703	0.1622	0.2478	11 (6)
H2(32)	0.5487	0.2599	0.2159	7 (4)
H3(32)	0.6286	0.2010	0.1935	2 (2)

methyl H atoms were determined as follows: the C—C bond axis of a rigid C—CH<sub>3</sub> rotor having tetrahedral angles and C—H = 1.08 Å was brought into coincidence with the C<sub>Ar</sub>—C<sub>Me</sub> bonds of TOT and oriented so as to minimize, by least squares, the distances with the observed H atoms. The final orientation of the rigid group was considered as representative of that of the methyl group, from which the H atom positions were further independently refined. The orientations of the methyl components of the isopropyl groups were obtained by the same procedure. The 'optimized' H atom positions were refined in alternate cycles with those of the non-hydrogen atoms; their idealized positions are depicted in Fig. 2. At a later stage of the refinement the two TOT molecules of the asymmetric unit were found to be identical within the limits of experimental error and symmetrically related about a line parallel to the crystallographic  $a$  axis, suggestive of the presence of an intervening twofold axis. In addition, an axial twofold disorder was now distinctively apparent in the cavity, as shown by a  $\Delta F$  synthesis. Consequently, refinement was also carried out in space group  $P3_121$  using a weight of 1/2 for the atoms of the guest. Anisotropic temperature factors for the non-hydrogen atoms (isotropic for the H atoms) of TOT were included in the model during the latter stages. The condition for the inclusion of a reflection in the refinement was  $|F_o| > 2\sigma(F_o)$  and  $|F_o| > 8.0$ , and  $|F_o| \leq 2\sigma(F_o)$  and  $|F_o| \leq 8.0$  only if  $|F_c| > |F_o|$ . The agreement factors for symmetry  $P3_1$  were  $R = 0.065$ ,  $R_w = 0.065$  based on 4127 reflections; those for symmetry  $P3_121$  were  $R = 0.081$ ,  $R_w = 0.083$  based on 2286 reflections. Unit weights were used in the least-squares refinements. Unexpectedly, the Hamilton test (Hamilton, 1965) substantiated the refinement in  $P3_1$  at the 0.005 level. It will be noted that the opposite result was obtained with the TOT-2-butanol clathrate (Allemand & Gerdil, 1981) whose structure deter-

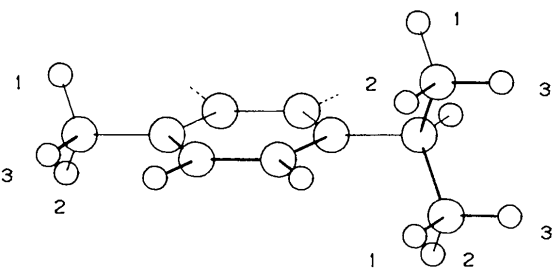


Fig. 2. Representative part of the tri-*o*-thymotide structure showing the mean rotational orientation of the alkyl substituents and the numbering of the H atoms. The carbonyl O atoms (not shown) are located above the ring plane.

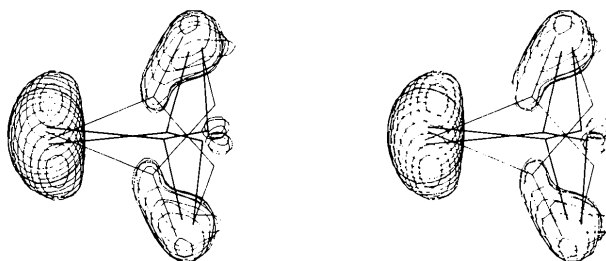


Fig. 3. Electron density distribution of 2-bromobutane in its average position of twofold disorder in a cage framework consisting of (*M*)-TOT molecules (calculated from a  $\Delta F$  synthesis). The contours include about 90% of the total electron population. Heavy line: *R* configuration of the X-ray model. Thin line: calculated position of the *S* enantiomer.

Table 2. Atomic coordinates ( $\times 10^4$ ) of the rigid model for 2-bromobutane

The overall isotropic temperature factor is  $0.066 (1) \text{ \AA}^2$ . The upper limits for the e.s.d.'s are 0.0019 for *x* and *y*, and 0.0008 for *z*.

	<i>x</i>	<i>y</i>	<i>z</i>		<i>x</i>	<i>y</i>	<i>z</i>
Br	2049	23	3223	H3(34)	2485	-1780	2833
C(34)	3001	-1428	3134	H(35)	3861	313	2907
C(35)	3381	-170	3201	H1(36)	3617	-87	3916
C(36)	4120	336	3617	H2(36)	4801	123	3607
C(37)	4676	1627	3665	H1(37)	5180	2061	3369
H1(34)	3735	-1549	3097	H2(37)	4048	1898	3712
H2(34)	2512	-1932	3421	H3(37)	5244	1943	3954

mination was based on the same strategy as the present one. The listed positional and structural parameters (Tables 1–3)\* are those obtained for symmetry  $P3_121$ . The electron density distribution in Fig. 3 results from a  $\Delta F$  synthesis calculated with  $F_c$ 's from which the contribution of 2-bromobutane had been omitted.

\* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36552 (17 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 3. Bond lengths ( $\text{\AA}$ ) and angles ( $^\circ$ )

O(1)–C(2)	1.400 (15)	C(12)–C(13)	1.384 (20)
O(1)–C(11)	1.360 (13)	C(12)–C(17)	1.411 (15)
O(2)–C(13)	1.409 (12)	C(13)–C(14)	1.395 (16)
O(2)–C(22)	1.374 (13)	C(14)–C(15)	1.405 (16)
O(3)–C(24)	1.399 (16)	C(14)–C(19)	1.523 (22)
O(3)–C(33)	1.356 (14)	C(15)–C(16)	1.394 (22)
O(11)–C(11)	1.191 (14)	C(16)–C(17)	1.381 (17)
O(22)–C(22)	1.213 (12)	C(17)–C(18)	1.527 (22)
O(33)–C(33)	1.186 (14)	C(19)–C(20)	1.554 (17)
C(1)–C(2)	1.382 (15)	C(19)–C(21)	1.512 (28)
C(1)–C(6)	1.393 (16)	C(22)–C(23)	1.472 (15)
C(1)–C(33)	1.497 (20)	C(23)–C(24)	1.400 (15)
C(2)–C(3)	1.410 (22)	C(23)–C(28)	1.360 (20)
C(3)–C(4)	1.403 (17)	C(24)–C(25)	1.406 (15)
C(3)–C(8)	1.502 (16)	C(25)–C(26)	1.377 (21)
C(4)–C(5)	1.383 (16)	C(25)–C(30)	1.514 (17)
C(5)–C(6)	1.370 (21)	C(26)–C(27)	1.392 (18)
C(6)–C(7)	1.514 (16)	C(27)–C(28)	1.429 (17)
C(8)–C(9)	1.497 (18)	C(28)–C(29)	1.513 (18)
C(8)–C(10)	1.552 (20)	C(30)–C(31)	1.531 (16)
C(11)–C(12)	1.490 (17)	C(30)–C(32)	1.531 (15)
		Br–C(35)	1.960*
		C(34)–C(35)	1.535*
		C(35)–C(36)	1.537*
		C(36)–C(37)	1.535*
C(2)–O(1)–C(11)	119.6 (8)	C(14)–C(15)–C(16)	120.1 (11)
C(13)–O(2)–C(22)	117.4 (8)	C(15)–C(16)–C(17)	122.3 (10)
C(24)–O(3)–C(33)	117.2 (8)	C(12)–C(17)–C(16)	118.0 (13)
C(2)–C(1)–C(6)	121.5 (13)	C(12)–C(17)–C(18)	121.6 (10)
C(2)–C(1)–C(33)	118.1 (10)	C(16)–C(17)–C(18)	120.3 (10)
C(6)–C(1)–C(33)	120.4 (10)	C(14)–C(19)–C(20)	109.8 (13)
O(1)–C(2)–C(1)	119.3 (13)	C(14)–C(19)–C(21)	111.3 (12)
O(1)–C(2)–C(3)	117.9 (9)	C(20)–C(19)–C(21)	110.4 (13)
C(1)–C(2)–C(3)	122.4 (11)	O(2)–C(22)–O(22)	121.2 (10)
C(2)–C(3)–C(4)	114.1 (10)	O(2)–C(22)–C(23)	112.9 (8)
C(2)–C(3)–C(8)	123.4 (11)	O(22)–C(22)–C(23)	125.8 (10)
C(4)–C(3)–C(8)	122.5 (14)	C(22)–C(23)–C(24)	120.2 (12)
C(3)–C(4)–C(5)	123.4 (14)	C(22)–C(23)–C(28)	119.1 (10)
C(4)–C(5)–C(6)	121.2 (12)	C(24)–C(23)–C(28)	120.7 (10)
C(1)–C(6)–C(5)	117.3 (10)	O(3)–C(24)–C(23)	120.5 (10)
C(1)–C(6)–C(7)	121.2 (13)	O(3)–C(24)–C(25)	117.0 (10)
C(5)–C(6)–C(7)	121.5 (11)	C(23)–C(24)–C(25)	122.3 (12)
C(1)–C(8)–C(9)	114.6 (10)	C(24)–C(25)–C(26)	115.2 (10)
C(3)–C(8)–C(10)	108.2 (9)	C(24)–C(25)–C(30)	122.2 (13)
C(9)–C(8)–C(10)	111.4 (13)	C(26)–C(25)–C(30)	122.6 (10)
O(1)–C(11)–O(11)	123.5 (11)	C(25)–C(26)–C(27)	124.7 (11)
O(1)–C(11)–C(12)	109.0 (9)	C(26)–C(27)–C(28)	117.8 (14)
O(11)–C(11)–C(12)	127.4 (10)	C(23)–C(28)–C(27)	119.2 (11)
C(11)–C(12)–C(13)	120.9 (10)	C(23)–C(28)–C(29)	120.3 (10)
C(11)–C(12)–C(17)	119.4 (12)	C(27)–C(28)–C(29)	116.4 (13)
C(13)–C(12)–C(17)	119.5 (10)	C(25)–C(30)–C(31)	110.2 (10)
O(2)–C(13)–C(12)	118.9 (10)	C(25)–C(30)–C(32)	110.8 (10)
O(2)–C(13)–C(14)	117.9 (12)	C(31)–C(30)–C(32)	110.7 (9)
C(12)–C(13)–C(14)	123.0 (10)	O(3)–C(33)–O(33)	122.5 (14)
C(13)–C(14)–C(15)	117.1 (13)	O(3)–C(33)–C(1)	111.8 (8)
C(13)–C(14)–C(19)	122.1 (10)	O(33)–C(33)–C(1)	125.7 (12)
C(15)–C(14)–C(19)	120.8 (11)	Br–C(35)–C(34)	109.6*
		Br–C(35)–C(36)	110.9*
		C(34)–C(35)–C(36)	112.8*
		C(35)–C(36)–C(37)	115.2*

\* 2-Bromobutane rigid model.

## Discussion

The physical significance of the Hamilton (1965) test in favour of symmetry  $P3_1$  is questionable. Firstly, at convergence in  $P3_1$  the rigid guest model assumed a prohibitive  $U_{\text{iso}}$  value of  $0.150 (1) \text{ \AA}^2$  as opposed to the value  $0.066 (1) \text{ \AA}^2$  in  $P3_121$ . The former value points out the inadequacy of the single-position model in a

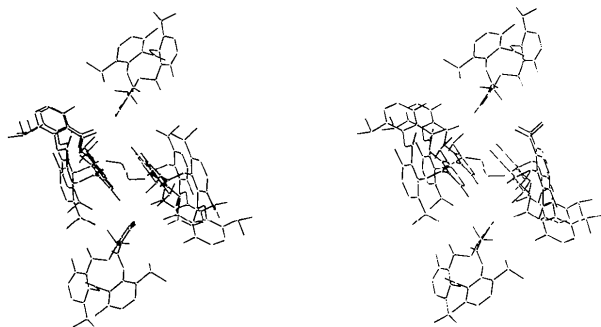


Fig. 4. A stereoscopic view along the twofold axis of the six proximal (*M*)-TOT molecules contributing to the formation of the cage. For clarity only the *R* enantiomer of 2-bromobutane is shown (the left rear molecule is the TOT molecule whose coordinates are listed in Table 1).

cage whose twofold symmetry has been clearly established. Secondly, the *R* factor for symmetry  $P3_121$  could be substantially lowered, in a somewhat artificial manner, by fixing the Br atom on the twofold axis (this implies only a small conformational distortion) and refining its temperature factor anisotropically. The overall scale factor was also adjusted while the rest of the asymmetric unit was kept invariant. Following this procedure the *R* factor dropped from 0.081 to 0.067, in qualitative agreement with the strongly anisotropic contribution of the Br atom to the scattering of the disordered guest molecule.\* This demonstrates how static disorder can be mimicked by a magnified thermal motion. The elongated electron density distribution at the Br site (Fig. 3) is due to the weighted overlap of four atoms displaced from each other and related in pairs by the twofold axis. Each pair of equivalent atoms

\* In addition to any dynamic disorder there are two kinds of static disorder which severely impair the precise localization of the guest atoms: (i) two enantiomeric molecules are present (enantiomeric excess = 35%); (ii) the distribution of the atoms must conform with the twofold symmetry.

*Acta Cryst.* (1982). **B38**, 1476–1480

## The Structures of *m*-Cyanoaniline and *p*-Cyanoaniline\*

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(Received 28 November 1980; accepted 27 November 1981)

### Abstract

*m*-Cyanoaniline,  $C_7H_6N_2$ ,  $M_r = 118.14$ , is orthorhombic,  $Pna2_1$ , with  $Z = 4$ ,  $a = 8.27$  (1),  $b = 16.94$  (2),

\* 3- and 4-aminobenzonitrile.

is associated with one of the enantiomers of 2-bromobutane. However, the minor enantiomer, (*S*)-2-bromobutane, has not been experimentally located. Its calculated orientation, fitting the minimum of the van der Waals energy in a rigid cage (Gerdil & Allemand, 1980), is depicted in Fig. 3.

According to the NMR and chiroptical observations the situation prevailing in a single crystal can be roughly described as follows: the cavities are vacant in the ratio 1:4 and the same enantiomer is present in two out of three filled cavities. *The introduction of an occupancy factor of 0.75, and of a  $\frac{1}{3}$  contribution of the S enantiomer in the refinement did not, however, bring about any significant improvement.* Inspection of the host-guest intermolecular contacts suggests that the enclosed component fits tightly into the cage and has only little motional freedom. A detailed analysis of the host-guest interactions will be presented elsewhere together with that for related clathrates [see preliminary account (Gerdil & Allemand, 1980)]. A stereoscopic view of the packing arrangement is shown in Fig. 4.

Financial support for this work by the Swiss National Science Foundation is gratefully acknowledged.

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$c = 4.89$  (1) Å,  $V = 685.1$  Å<sup>3</sup>,  $D_c = 1.14$  g cm<sup>-3</sup>,  $\mu(\text{Cu } K\alpha) = 5.9$  cm<sup>-1</sup>. *p*-Cyanoaniline,  $C_7H_6N_2$ ,  $M_r = 118.14$ , is monoclinic,  $P2_1/c$ , with  $Z = 4$ ,  $a = 7.35$  (1),  $b = 5.56$  (1),  $c = 16.10$  (2) Å,  $\beta = 102.0$  (1)°,  $V = 643.6$  Å<sup>3</sup>,  $D_c = 1.22$  g cm<sup>-3</sup>,  $\mu(\text{Cu } K\alpha) = 6.3$  cm<sup>-1</sup>.