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The Stabilization of Thermodynamically Disfavoured Conformers of Chlorocyclohexane in the Host Lattice of Tri-*ortho*-thymotide. Crystallographic and Infrared Spectroscopic Studies★

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Abstract. The clathrate compounds of tri-*o*-thymotide have been prepared with chlorocyclohexane, bromocyclohexane and 2-chlorotetrahydropyran. The cage-type inclusion complex $C_{33}H_{36}O_6 \cdot \frac{1}{2}C_6H_{11}Cl$ (trigonal, $P3_121$, $a = 13.604(1)$, $c = 30.605(1)$ Å, $Z = 6$) contains an axial-Cl chair and an axial-Cl boat conformation of the guest, distributed statistically in the ratio 2 : 1 over the available sites. The observed conformations have been compared with conformers calculated by force field methods. IR spectra are consistent with the crystal structure results for the tri-*o*-thymotide/chlorocyclohexane clathrate. They further demonstrate the similar preferential inclusion of axial isomers of bromocyclohexane and 2-chlorotetrahydropyran.

Key words: tri-*o*-thymotide clathrate, halocyclohexane guest species, host/guest conformational strain, constrained guest molecules, X-ray analysis, clathrate infrared absorption.

Supplementary Data relating to this article are deposited with the British Library as Supplementary Publication No. SUP 82023 (16 pages).

1. Introduction

Several studies of the monohalocyclohexanes in their thiourea inclusion compounds have been reported [1–3]. All these investigations, both theoretical and experimental, rely basically upon IR and Raman spectroscopy in the range 4000–30 cm^{-1}. With regard to the coexistence of axial and equatorial isomers in the host lattice it became clear that an axial conformer of chloro-, or bromocyclohexane, respectively, was largely predominant in the clathrate, in marked contrast with the prevalence of the equatorial isomer in the liquid phase. Unfortunately no X-ray crystallographic studies of these clathrates have been made and the conformation of the cyclohexane ring has not been examined.

In the present study clathrate compounds of tri-*o*-thymotide (**1**; Figure 1) have been prepared with, as guest molecules, monochlorocyclohexane (**2**), monobromocyclohexane (**3**) and 2-chlorotetrahydropyran (**4**). They have been investigated by X-ray diffraction (with **2**) and by IR spectroscopy.

★ Dedicated to Professor H. M. Powell.

★★ Corresponding author.

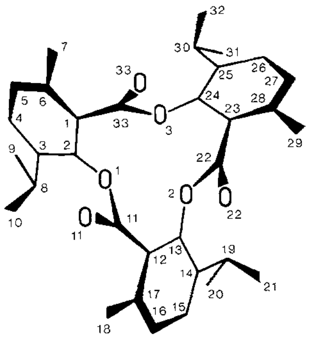

Fig. 1. Idealized view of the *M* configuration of (–)-tri-*o*-thymotide [21] and atom numbering used in the structure analysis.

2. Experimental

2.1. CRYSTAL STRUCTURE ANALYSIS OF THE TRI-*o*-THYMOTIDE/CHLOROCYCLOHEXANE (2 : 1) CLATHRATE AT 158 K

Colourless hexagonal prisms of the clathrate grown from a solution of tri-*o*-thymotide in chlorocyclohexane (freshly distilled commercial sample; FLUKA), crystal sealed in Lindemann capillary, 0.31 × 0.31 × 0.31 mm; automatic four-circle Philips PW1100 diffractometer, graphite-monochromated Mo$K\alpha$ ($\lambda = 0.71069$ Å); 24 reflections within range $14 \leqslant 2\theta \leqslant 2\theta°$ used for measuring lattice parameters (crystal data reported in Table I); 4538 reflections scanned in the ω-2θ mode, scan width = 1.0°, scan speed 0.02° s^{-1}, $6.0 \leqslant 2\theta \leqslant 44°$, range of *hkl*: $-14 \leqslant h \leqslant 14$, $0 \leqslant k \leqslant 14$, $0 \leqslant l \leqslant 34$; three standard reflections monitored at 60 min. intervals showed insignificant intensity variations: $5\bar{3}2$, $\bar{4}1\bar{7}$ and 309 had average count rates and e.s.d.'s of 37765 (490), 15208 (225) and 28142 (297); no absorption correction applied; 2297 unique reflections after merging ($R_{\text{int}} = 0.021$), 2014 considered observed at the $3\sigma(I)$ level and used in the structure analysis. Host structure refined starting from the coordinates of non-hydrogen atoms taken from isomorphous tri-*o*-thymotide clathrate [4]; $R = 0.19$ with no guest included. Successive ΔF syntheses revealed two different guest conformations distributed statistically over the available cavities: a chair conformation and a boat conformation with approximate occupancy ratio of 2 : 1 based on the relative intensities of the Cl atoms peaks. Observed geometry for the boat conformation derived from a three-dimensional plot of a ΔF synthesis, with the chair conformation included in the F_c's. Both conformations have axial chloro-substitution. H atoms of **1** located from difference synthesis (one-third observable) and by calculation; block-diagonal least-squares refinement on F. Minimum-energy chair and boat guest conformations subsequently calculated by force field methods [5] and included as rigid bodies in the model with constant weights of 0.333 and 0.167 respectively; calculations carried out with anisotropic temperature factors for non-H atoms of **1**, isotropic factors for H atoms of **1**, and an overall isotropic factor for guest atoms; $\omega = 1$ if $F_0 \leqslant 24$, $\omega = (24/F_0)^2$ otherwise; final $R = 0.061$, $\omega R = 0.059$, $S = 2.0$, ratio of maximum least-squares shift-to-error = 5.8, average ratio = 0.7; no extinction correction; atomic scattering factors for C, O and Cl from [6]; for H from [7]; programs of the XRAY system [8]. The atomic coordinates are given in Tables II and III.

Table I. Crystal data

	(a)	(b)
Formula	$C_{33}H_{36}O_6 \cdot \frac{1}{2}C_6H_{11}Cl$	$C_{33}H_{36}O_6 \cdot \frac{1}{2}C_6H_{11}Br$
M_r	587.9	610.2
Crystal system	Trigonal	Trigonal
Space group	$P3_121$	$P3_121$
a	13.604(1) Å	13.794(1) Å
c	30.605(1) Å	30.876(1) Å
U	4905.2 Å^3	5087.8 Å^3
Z	6	6
μ	0.1249 mm^{-1}	0.7059 mm^{-1}
D_c	1.194 mg m^{-3}	1.195 mg m^{-3}

(a) Tri-*o*-thymotide/chlorocyclohexane at − 115°C
(b) Tri-*o*-thymotide/bromocyclohexane at room temperature

Table II. Atomic parameters for tri-*o*-thymotide (U_{eq}/U_{iso}(Å^2) × 10^3)

Atom	x	y	z	U_{eq}/U_{iso}
O(1)	0.9731(4)	0.3301(4)	− 0.11008(13)	43.3(23)
O(2)	0.8682(4)	0.4612(4)	− 0.09595(14)	48.2(24)
O(3)	0.8130(4)	0.3389(4)	− 0.17409(13)	38.7(22)
O(11)	0.8779(5)	0.2008(5)	− 0.05718(16)	70(3)
O(22)	0.7016(4)	0.3640(5)	− 0.06087(16)	69(3)
O(33)	0.6840(6)	0.1728(6)	− 0.1463(3)	109(4)
C(01)	0.8662(6)	0.1996(6)	− 0.16731(20)	38(3)
C(02)	0.9604(6)	0.2463(6)	− 0.14061(20)	43(4)
C(03)	1.0474(6)	0.2218(6)	− 0.14515(23)	47(4)
C(04)	1.0357(7)	0.1482(7)	− 0.17951(23)	55(4)
C(05)	0.9410(7)	0.1003(7)	− 0.20552(23)	53(4)
C(06)	0.8522(7)	0.1229(6)	− 0.19999(22)	49(4)
C(07)	0.7482(7)	0.0668(7)	− 0.22917(25)	57(4)
C(08)	1.1512(7)	0.2728(7)	− 0.1153(3)	63(5)
C(09)	1.2635(8)	0.3186(8)	− 0.1399(3)	75(5)
C(10)	1.1376(9)	0.1834(10)	− 0.0822(3)	85(6)
C(11)	0.9269(6)	0.2965(7)	− 0.06907(23)	51(4)
C(12)	0.9583(6)	0.4009(7)	− 0.04311(20)	46(4)
C(13)	0.9288(6)	0.4799(7)	− 0.05659(21)	45(4)
C(14)	0.9639(7)	0.5827(7)	− 0.03481(22)	53(4)
C(15)	1.0322(7)	0.6018(7)	0.00231(23)	53(4)
C(16)	1.0622(7)	0.5239(7)	0.01583(22)	57(4)
C(17)	1.0260(6)	0.4221(7)	− 0.00564(21)	52(4)
C(18)	1.0607(7)	0.3385(8)	0.01093(25)	62(5)
C(19)	0.9330(8)	0.6679(7)	− 0.0501(3)	63(5)
C(20)	1.0374(12)	0.7834(12)	− 0.0576(4)	126(9)
C(21)	0.8510(11)	0.6773(11)	− 0.0195(3)	111(9)
C(22)	0.7526(6)	0.4044(6)	− 0.09396(22)	46(4)
C(23)	0.7010(6)	0.4070(6)	− 0.13658(20)	38(3)
C(24)	0.7304(6)	0.3749(6)	− 0.17587(21)	39(3)
C(25)	0.6872(6)	0.3790(6)	− 0.21575(21)	42(3)
C(26)	0.6088(7)	0.4161(7)	− 0.21575(22)	50(4)
C(27)	0.5762(7)	0.4473(7)	− 0.17759(22)	50(4)
C(28)	0.6221(6)	0.4440(6)	− 0.13825(22)	48(4)

Table II (continued)

Atom	x	y	z	U_{eq}/U_{iso}
C(29)	0.5879(8)	0.4854(8)	− 0.0976(3)	65(5)
C(30)	0.7212(7)	0.3421(7)	− 0.25771(22)	53(4)
C(31)	0.7855(8)	0.4440(8)	− 0.2882(3)	64(5)
C(32)	0.6189(8)	0.2481(8)	− 0.2814(3)	77(5)
C(33)	0.7775(6)	0.2321(6)	− 0.16100(24)	50(4)
H(04)	1.101(6)	0.126(6)	− 0.1805(20)	89(24)
H(05)	0.934(5)	0.046(5)	− 0.2308(18)	59(20)
H(107)	0.681(4)	0.049(4)	− 0.2130(13)	50(13)
H(207)	0.750(8)	0.128(8)	− 0.258(3)	140(30)
H(307)	0.734(10)	− 0.006(10)	− 0.242(3)	150(50)
H(08)	1.151(6)	0.337(6)	− 0.0946(20)	63(24)
H(109)	1.263(4)	0.364(4)	− 0.1631(14)	31(13)
H(209)	1.337(7)	0.352(8)	− 0.1204(24)	130(30)
H(309)	1.265(7)	0.253(6)	− 0.1611(22)	80(30)
H(110)	1.053(4)	0.143(4)	− 0.0676(12)	60(11)
H(210)	1.196(9)	0.213(9)	− 0.055(3)	130(40)
H(310)	1.145(7)	0.126(7)	− 0.0951(24)	100(30)
H(15)	1.061(5)	0.670(5)	0.0156(17)	53(18)
H(16)	1.114(6)	0.547(6)	0.0428(19)	53(22)
H(118)	1.080(5)	0.307(5)	− 0.0125(17)	71(18)
H(218)	1.117(11)	0.374(11)	0.028(4)	140(60)
H(318)	1.001(9)	0.276(9)	0.026(3)	150(40)
H(19)	0.890(6)	0.650(6)	− 0.0860(19)	79(22)
H(120)	1.077(7)	0.779(7)	− 0.0781(22)	100(30)
H(220)	1.030(10)	0.850(11)	− 0.072(4)	230(50)
H(320)	1.058(7)	0.815(7)	− 0.0243(21)	90(30)
H(121)	0.782(5)	0.610(5)	− 0.0152(15)	58(16)
H(221)	0.900(7)	0.715(7)	0.0104(22)	140(30)
H(321)	0.821(7)	0.737(7)	− 0.0322(23)	130(30)
H(26)	0.575(6)	0.418(6)	− 0.2452(19)	63(21)
H(27)	0.515(6)	0.469(6)	− 0.1779(20)	84(23)
H(129)	0.550(6)	0.431(6)	− 0.0813(20)	74(22)
H(229)	0.665(6)	0.557(6)	− 0.0803(21)	110(30)
H(329)	0.538(7)	0.523(7)	− 0.1061(22)	110(30)
H(30)	0.789(5)	0.318(5)	− 0.2484(18)	54(19)
H(131)	0.730(6)	0.476(6)	− 0.2950(19)	84(22)
H(231)	0.858(6)	0.507(6)	− 0.2759(19)	104(22)
H(331)	0.806(6)	0.422(6)	− 0.3180(19)	67(21)
H(132)	0.574(3)	0.269(3)	− 0.2875(11)	12(10)
H(232)	0.639(6)	0.210(5)	− 0.3080(18)	60(21)
H(332)	0.570(5)	0.186(5)	− 0.2650(18)	60(19)

2.2. CLATHRATES OF TRI-*o*-THYMOTIDE WITH BROMOCYCLOHEXANE AND 2-CHLOROTETRAHYDROPYRAN

On slow cooling of a saturated solution of tri-*o*-thymotide in bromocyclohexane (commercial sample; FLUKA) needle-shaped crystals of unsolvated host molecules were often obtained together with trigonal prismatic clathrate crystals. The **1**/**3** clathrate appeared to be stable at room temperature. The unit cell dimensions (Table I) were determined from the setting angles of 38 reflections with $14 > 2\theta \leqslant 24°$.

Table III. Atomic coordinates of the rigid models for chlorocyclohexane: (1) axial-chair, (2) axial-boat. The overall isotropic factor is 0.083 Å^2.

Atom^1	x	y	z	Atom^2	x	y	z
Cl(1)	0.1896	−0.0077	−0.1332	Cl(2)	0.1807	−0.1297	−0.1200
C(41)	0.3072	−0.0319	−0.1272	C(51)	0.3029	−0.1019	−0.1518
C(42)	0.2922	−0.1297	−0.1567	C(52)	0.4108	−0.0038	−0.1315
C(43)	0.3073	−0.0973	−0.2054	C(53)	0.4204	0.1120	−0.1396
C(44)	0.4222	0.0102	−0.2135	C(54)	0.4014	0.1307	−0.1878
C(45)	0.4350	0.1090	−0.1852	C(55)	0.3847	0.0323	−0.2173
C(46)	0.4200	0.0770	−0.1366	C(56)	0.2872	−0.0806	−0.2002
H(41)	0.3045	−0.0565	−0.0922	H(51)	0.3074	−0.1815	−0.1489
H(142)	0.2078	−0.2071	−0.1511	H(152)	0.4150	−0.0179	−0.0958
H(242)	0.3575	−0.1529	−0.1476	H(252)	0.4864	−0.0031	−0.1459
H(143)	0.2374	−0.0829	−0.2165	H(153)	0.3576	0.1200	−0.1186
H(243)	0.3012	−0.1688	−0.2253	H(253)	0.5059	0.1803	−0.1285
H(144)	0.4305	0.0341	−0.2489	H(154)	0.4742	0.2118	−0.2000
H(244)	0.4921	−0.0073	−0.2059	H(254)	0.3246	0.1401	−0.1905
H(145)	0.3710	0.1330	−0.1954	H(155)	0.4649	0.0288	−0.2190
H(245)	0.5203	0.1853	−0.1907	H(255)	0.3660	0.0473	−0.2514
H(146)	0.4279	0.1489	−0.1163	H(156)	0.2801	−0.1515	−0.2208
H(246)	0.4910	0.0632	−0.1265	H(256)	0.2064	−0.0798	−0.2050

The tri-*o*-thymotide/2-chlorotetrahydropyran clathrate was prepared by dissolving **1** in **4** (prepared according to [9]) at about 35 °C. Slow cooling below 0 °C produced large prismatic trigonal crystals which became brownish and opaque if not kept at low temperature in sealed capillaries. Despite the fact that **4** is isosteric with **2** and **3** it is surprising that the crystal morphology is unlike that of the usual cavity-type clathrates of **1**. The adduct crystallizes in a pseudohexagonal R system with axes $a = b = 17.142(3)$ and $c = 10.270(2)$ Å [10].

2.3. INFRARED SPECTRA

The spectra were recorded with a Perkin–Elmer Model 681 infrared spectrophotometer in the region 4000–600 cm^{-1}. The range 1000–600 cm^{-1} was re-measured with expanded scale (5 ×). The clathrates, as well as the mixtures of **1** with each solvent, were investigated as nujol mulls using Teflon spacers between KBr plates. The guest compounds were also investigated in their pure liquid state. Relevant vibration frequencies in the region 850–600 cm^{-1} are reported in Table IV.

3. Discussion

3.1. CONFORMATIONAL ANALYSIS OF ENCLATHRATED CHLOROCYCLOHEXANE

The cage-type clathrates of **1** form a wide class of isomorphous trigonal crystals whose host geometry is quasi independent of the guest molecule and has already been amply discussed [11, 12]. Consequently the discussion will be focused on the guest structure and its interaction with the host lattice. The relevant feature is the inclusion of two energetically disfavoured *axial* conformations of **2** in the host lattice, to the exclusion of the thermodynamically most stable equatorial isomer. Measured on the dimensions of the van der Waals envelope the overall

Table IV. Characteristic IR absorption bands in the region 850–600 cm^{-1} for the pure guest compounds and their clathrates (values in cm^{-1})

	eq.[1]	ax.[1]	*A*[3]	*B*	eq.[2]	ax.[2]	*C*
2	818	807	–	–	732	685	–
1/2	–	811	793	768	–	684[4]	662
3	810	804	–	–	687	658	–
1/3	–	804[5]	793	767	–	660[7]	–[6]
4	–	813	–	–	–	699	–
1/4	–	814[8]	794	769	–	696	660

[1] Ring stretching frequency [18].

[2] C—X stretching frequency [18].

[3] For *A*, *B* and *C* see Text and Figure 5.

[4] Low frequency component of a doublet (see Figure 5).

[5] Very weak band.

[6] Probable overlap with $\nu(\mathrm{C—X})_{\mathrm{ax}}$.

[7] Broad band.

[8] Shoulder.

length of **2** is about 8.3 Å for the equatorial conformer as compared to 7.1 Å for the axial one. The unlikely incorporation of the former conformer had previously been inferred [13] from an approximate estimation of the cavity size of **1**/2-chlorobutane [12] with dimensions 7.1 × 6.4 × 4.9 Å. A close, but more accurate estimation of the average space available to guest is given in [11].

The observation of the guest structure was obscured by the weighted superimposition of two conformations in addition to the local static 2-fold disorder (dissymmetric cage) and, in the first stage, the boat geometry was most unsatisfactory. A subsequent three-dimensional stacking of the contours-plots from a ΔF synthesis including the chair conformation in the F_c's was crucial in allowing a better delineation of the boat-shaped ring with a concomitant improvement of its atomic co-ordinates. Following the observed extensive overlap of the symmetry-equivalent C atoms, C_2 symmetry was imposed on the ring (Figure 2c). Refinement of the rigid guest model *without* the contribution of the boat conformer raises the *R* factor to 0.076 (ωR = 0.106) at convergence. This further supports the occurrence of the minor conformer. The ranges of observed bond lengths and angles were: $\mathrm{C—C_{chair}}$ = 1.50–1.66, $\mathrm{C—C_{boat}}$ = 1.43–1.52 Å; $\mathrm{C—C—C_{chair}}$ = 100–109, $\mathrm{C—C—C_{boat}}$ = 106–114°. The observed endocyclic dihedral angles are given in Figures 2a, c. For convenience in the discussion, the

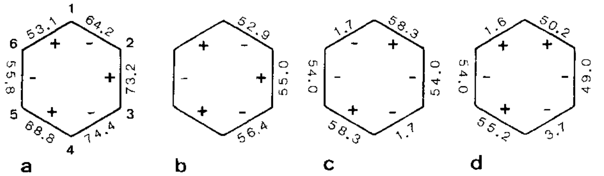

Fig. 2. Endocyclic torsion angles in various conformations of chlorocyclohexane as guest molecule. Ring conformations: (a) major observed; (b) major calculated, C_s molecular symmetry; (c) minor observed; (d) minor calculated [5]. The Cl atom is linked to atom C(1) and in axial-position in all conformations. The sequential ordering of the C atoms is similar to that used in Table III.

numbering of the guest atoms is that of Figure 2. A formalism for the quantitative measurement of the degree to which a given ring deviates from ideal symmetry (substituents are neglected) has been proposed [14]. Asymmetry parameters involving torsion angles are calculated, which result in a value of zero if the symmetry in question is present. The major conformer adopts a distorted chair conformation with asymmetry parameters [15]: $\Delta C_s(1) = 12{,}4$, $\Delta C_s(2) = 15.3$, $\Delta C_s(3) = 3.2°$; $\Delta C_2(1\text{–}2) = 19.4$, $\Delta C_2(2\text{–}3) = 13.2$, $\Delta C_2(3\text{–}4) = 6.7°$. It is shown that a 'fairly good' mirror plane, *not* containing the C—Cl bond, passes through atoms C(3) and C(6). The 'chair' is slightly puckered at C(3) and flattened at C(6). The minor conformer assumes a slightly distorted boat conformation exemplified by the parameters $\Delta C_s(2) = 3.3°$ and $\Delta C_s(3\text{–}4) = 4.3°$. The axial Cl atom points downwards, on the underside of the boat (see Figure 3), thus avoiding the strong 'flagpole' strain. Unfavourable interactions with axial H atoms are relieved by a moderate twisting of the ring.

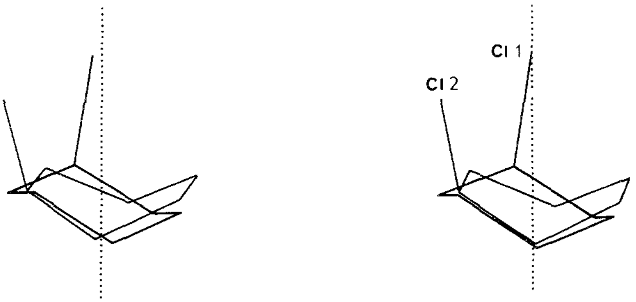

Fig. 3. Stereo view of the guest conformations along the *z*-axis. The dotted line denotes the crystallographic 2-fold axis. For clarity, the symmetry-equivalent molecular orientations have been omitted.

In order to improve the geometry of the observed guest structures further minimum energy conformations were calculated using force field methods [5]. Optimization of the internal coordinates of the major guest conformer, or of those of an 'ideal' chair conformation, converged to the same minimum energy conformation (strain energy $E_s = 30.1$ kJ mol^{-1}) displaying C_s molecular symmetry (Figure 2b). For the boat form several local energy minima could be located. The best fit (Figure 2d; $E_s = 58.9$ kJ mol^{-1}) with the observed geometry was reached from optimized internal parameters of an 'ideal' boat structure for the ring with additional axial Cl-substitution. The use of the observed boat geometry as a starting point resulted in a lower-energy conformation ($E_s = 52.7$ kJ mol^{-1}) which did not fit the observed ring parameters well, being closer to a twist-boat. Therefore it was not considered a valid substitute for the minor guest in the structure analysis. The refined orientations of the guest conformers relative to the crystallographic 2-fold axis are illustrated in Figure 3. The final positions of Cl(1) and Cl(2) are only shifted by 0.037 Å from their originally observed location. This result lends support to the use of a rigid guest model in the refinement.

As for other simple halogenated guests [11, 12] the C—Cl(1) bond axis lies roughly parallel with the 2-fold axis direction. The Cl(1) atom is locked in position near the 2-fold axis through close contacts with atoms H(4), C′(10) and C″(20) of three symmetry-related host molecules, at distances 2.6, 3.40 and 3.44 Å, respectively. No particularly short contact distances of the ring atoms with the host molecules are to be noted. A good fit of the ring atoms of the boat conformation with the receptor is enabled at the expense of a concomitant displacement of Cl(2) by 1.65 Å from the more favorable location occupied by Cl(1) (Figure 4). As a

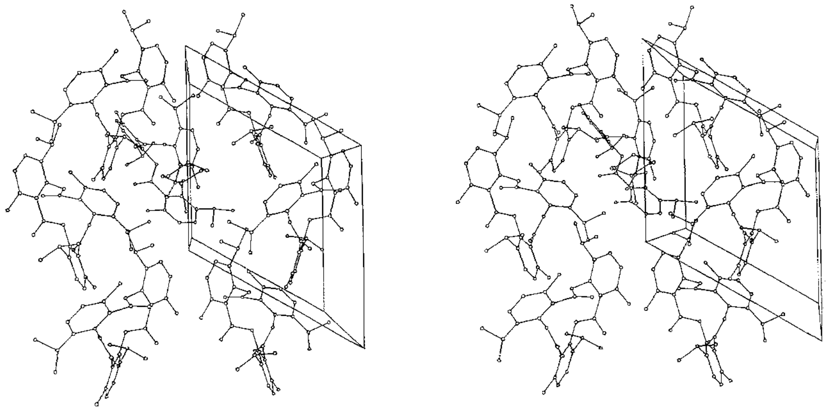

Fig. 4. Stereo view, down the z-axis, of the tri-*o*-thymotide molecules constituting the cage. For clarity the top host molecule and the minor guest conformer have been removed. The major guest conformer is shown single-positioned on a crystallographic 2-fold axis. A unit cell is depicted to indicate the crystallographic axis directions.

consequence a strong steric interaction ensues between Cl(2) and the methyl C(20) of an isopropyl group at a prohibitively short distance of 2.56 Å. This value bears no physical significance and rather reflects a local disorder. Indeed, the unduly large temperature factors (U_{eq}; Table II) of C(20) and C(21) are consistent with a disordered rotation of the isopropyl group about the C(14)—C(19) bond. Such a displacement releases the steric repulsion with Cl(2) and would be localized in those cavities enclosing the minor conformer.

A boat conformation of monochlorocyclohexane has never been detected in the liquid phase. As can be estimated on the basis of potential energy differences calculated by force fields methods, the population of the boat isomer in solution is roughly 10^{-6} times smaller than those of the chair conformations. The enhancement of the relative concentration of the boat form in the bimolecular compound is basically related to a free-energy change favorable to the growth of the clathrate crystal. A conclusion regarding the factors that influence this free-energy change cannot be reached at the present time. Let us note, however, that the packing coefficients [16] of the **1**/halocyclohexane clathrates, as well as that of the unsolvated host [17] have a common value of about 0.66–0.67.

3.2. BROMOCYCLOHEXANE AND 2-CHLOROTETRAHYDROPYRAN AS GUESTS IN TRI-*o*-THYMOTIDE CLATRHATES

The relative difficulty encountered in obtaining crystals of tri-*o*-thymotide/bromocyclohexane compared to the analogous chloro-clathrate may indicate that **3** is close to the limit of size of molecules which can be accommodated in the cavity. It cannot be due to the difficulty in attaining the axial conformation since the axial–equatorial energy difference is smaller than for chlorocyclohexane.

The sole detectable conformer of 2-chlorotetrahydropyran in the liquid phase is that with the Cl atom in the axial position [9]. The incorporation of **4** as an 'unstrained' axial guest molecule in a clathrate of **1** enhanced our interest in view of the results gathered with **2** and **3**. The presence of axial **4** in the **1**/**4** clathrate is clearly demonstrated by inspection of the IR spectra. The surprising outcome obtained with **4** as a guest molecule was the formation of a new clathrate species of **1** (see 2.2).

3.3. INFRARED SPECTRA

The assignment of absorption bands in the IR spectrum of pure **1** has not been attempted at the present time. On the other hand the IR spectra of the monohalogeno-cyclohexanes are well documented [18, 19]. Owing to the stoichiometric ratio, the absorption bands associated with the guests are relatively weak in the spectra of the clathrates. A useful band for identification of the guest conformation is that corresponding to the C—X stretching mode. IR spectra of interest for the **1**/**2** clathrate are qualitatively compared in Figure 5. The axial-chair conformation of **2** absorbs at 685 cm^{-1} and this band persists with no frequency shift in the clathrate spectrum, where it forms part of an asymmetrical doublet (Figure 5). The less intense component of the doublet occurs at 694 cm^{-1} and might tentatively be assigned to the stretching vibration of the more strained C—Cl bond of the boat conformer. A very weak absorption of the equatorial-isomer near 732 cm^{-1} would probably be obscured by the broad bands of **1** in this region. However, in view of the X-ray crystallographic results the presence of equatorial-**2** can be safely excluded.

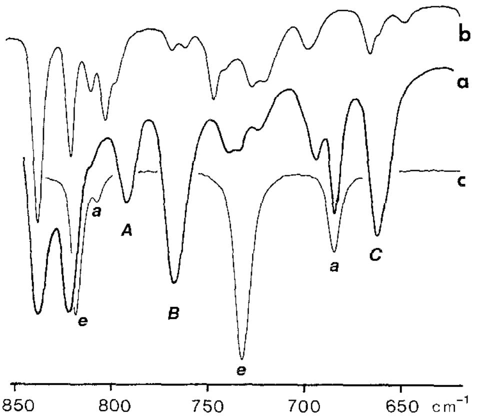

Fig. 5. Graphical comparison of the IR spectra of tri-*o*-thymotide (**1**) and chlorocyclohexane (**2**) with that of their inclusion complex. (a) **1**/**2** clathrate; (b) **1**; (c) **2**. The characteristic bands assigned to the axial and equatorial isomers [18, 19] are denoted by **a** and **e** respectively in the spectrum of **2**.

The overall appearance of the **1**/**3** clathrate spectrum resembles that of **1**/**2**. The axial C—X stretching mode occurs at a lower frequency and no equatorial absorption can be observed, thus suggesting the preferential inclusion of one (or several) axial conformation(s). A similar favoured inclusion is expected in the **1**/**4** clathrate. In the region of 800–600 cm^{-1}, the IR spectrum of **4** displays a single strong absorption band at 699 cm^{-1}. The same band is strongly apparent in the spectrum of the clathrate, indicating the persistence of an axial conformation.

Only small shifts in frequency are observed for the absorption bands in the region 4000–1000 cm^{-1}. Below 1000 cm^{-1} the differences are more noticeable. The characteristic bands denoted by A, B and C in Figure 5 are usually observed in cavity type clathrates of **1** [20] and do not result from halogen substituents of the guest molecules. The intense band B seems to be derived from a weak doublet in the pure host spectrum, whereas the other intense band C might be associated with the broad band of **1** near 670–660 cm^{-1}. Since the IR spectra of the three clathrates have most of their characteristic features in common it appears that the host–guest interactions are probably very similar from one clathrate to another despite the different crystal system of **1**/**4**.

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