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Conformational Spectroscopic Studies of Halogenated Cyclohexanes in Thiourea Clathrates

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The IR spectra of the monosubstituted compounds: chloro-, bromo-, iodo-, cyano- and isocyanatocyclohexane and the disubstituted compounds: *trans*-1,2-dichloro- and *trans*-1,2-dibromocyclohexane; *trans*-1,4-dichloro- and *trans*-1,4-dibromocyclohexane as thiourea clathrates were recorded as Nujol mulls between 1500 and 400 cm^{-1}. Raman spectra of the solid clathrates were also obtained.

From earlier assignments of these cyclohexane spectra it was clear that the conformational equilibrium was shifted towards the axial (diaxial) conformer compared to the liquid (dissolved) state in all the cyclohexanes. Semiquantitative calculations of the shift in conformational equilibrium were carried out, independently based upon IR bands situated around 1000 and 850 cm^{-1}. In iodocyclohexane and isocyanatocyclohexane considerable amounts of the equatorial conformer were present in the thiourea clathrate, for the other cyclohexanes negligible concentrations of this conformer were found.

Some reassignments of the previous work regarding equatorial and axial bands were carried out.

It was reported by Nishikawa from IR spectroscopy long time ago that certain halogenated cyclohexanes probably existed in the axial conformer when occluded in a thiourea adduct.[1] Very recently two independent studies were published; Allen *et al.*[2] studied the thiourea clathrates of chloro-, bromo- and iodocyclohexane by Raman spectroscopy, while Fukushima[3] extended the IR spectra of the chlorocyclohexane clathrate to the low frequency region. Both groups confirmed the earlier results[1] regarding the preference for the axial conformers in the clathrate.

It is well-known[4,5] that the conformational equilibrium in monosubstituted cyclohexanes is displaced towards the equatorial conformer in the vapour, in the liquid and in solution. Moreover, they crystallize in the equatorial conformer, including fluorocyclohexane,[6] at low temperature[7–9] as well as under high pressure.[8] Therefore, the predominance of the axial conformer in the thiourea clathrates[1–3] is quite unexpected and is probably related to the steric dimensions within the cavity of the host lattice.

We have studied the conformational equilibria of various mono- and dihalogenated (and pseudohalogenated) cyclohexanes for some time, and felt it would be of interest to investigate the clathrates of these compounds. In particular, we wanted to establish possible conformational preferences for these cyclohexanes in the thiourea clathrates. Better understanding of the host-guest interactions and the apparent preference for the axial conformers should be achieved when more cyclohexane derivatives have been investigated. In the present study we shall report our data for five monosubstituted cyclohexanes (including the three halocyclohexanes reported previously[1–3]), two *trans*-1,2-dihalo- and two *trans*-1,4-dihalocyclohexanes. Additional data for fluorocyclohexane,[6] other *trans*-1,4-dihalocyclohexanes and methylcyclohexanes will be given in a forthcoming paper.

EXPERIMENTAL

The monosubstituted cyclohexanes (chloro-, bromo-, iodo-, cyano- and isocyanatocyclohexane) as well as *trans*-1,4-dichlorocyclohexane were all commercial products; their supplier and methods of purification have been described in earlier papers. *trans*-1,2-Dichloro- and dibromocyclohexane[10] and *trans*-1,4-dibromocyclohexane[11] were purified sam-

ples from our earlier investigations. Thiourea was *puriss.* grade from Fluka AG., used without purification.

The thiourea clathrates of the liquid cyclohexanes were prepared[3] by adding the cyclohexane to a saturated methanol solution of thiourea, filtering and drying the precipitate. The *trans*-1,4-dihalocyclohexanes which are crystalline solids at room temperature, were dissolved in methanol and added to the methanolic thiourea solution and cooled. Excess of cyclohexane on the "outside" of the solid clathrate was removed by subsequent washing with carbon tetrachloride.

The clathrates were investigated as thick nujol mulls between KBr-plates in the region 1500–400 cm^{-1} with a Perkin-Elmer model 225 spectrometer. The Raman spectra were recorded with a Cary 81 spectrometer, modified[12] for 90° illumination, using the 5145 Å argon line for excitation.

RESULTS

The IR spectrum of solid thiourea (orthorhombic) has a number of intense bands below 1500 cm^{-1},[13] which are considerably perturbed in the clathrates (rhombohedral). Several bands are shifted (Table 1), some are enhanced and, *e.g.*, the broad band at 630 cm^{-1} in thiourea is split into a sharp doublet at 654 and 615 cm^{-1} in the occlusion compounds. In the present series of clathrates the thiourea bands seemed practically identical for the various cyclohexane guest molecules.

The cyclohexane bands were negligibly displaced from their positions in the liquid (or solutions). Therefore, we have reported the same wave numbers in the clathrates as those previously observed for the free cyclohexane derivative.

The IR (and Raman) bands of the cyclohexane have generally lower intensities than those of the polar thiourea, and there are at least three times as many host molecules as guests in the clathrates. Therefore, only certain spectral regions are suitable for these studies. While Fukushima[3] focussed his attention on the far-IR region below 650 cm^{-1}, we preferred the region between the thiourea bands at 1058 and 761 cm^{-1}. For *trans*-1,2-dihalocyclohexanes many bands below 700 cm^{-1} were also useful for identification. Fairly complete lists of vibrational bands belonging to the equatorial, axial or both conformers are known for the present cyclohexanes from previous experimental work. We feel that it is highly preferable to base our present

Table 1. Infrared spectral data for thiourea and thiourea in cyclohexane clathrates (1500–400 cm^{-1}).

Thiourea (orthorhombic)	Thiourea clathrates (rhombohedral)
	1491 vs[a]
1412 s	1402 vs
1378 s	1378 vs
1200 m, br	1210 m, br
1082 vs	1086 vs
	1058 m
	955 vw
	888 w[b]
765 vw	761 s
731 s	723 s
630 s	654 s
	615 s
488 m, br	478 m
460 m, br	418 m
412 m	408 vw

[a] Abbreviations: s, strong; m, medium; w, weak; v, very; br, broad.
[b] Apparent in the spectra of the *trans*-1,4-dihalocyclohexanes only.

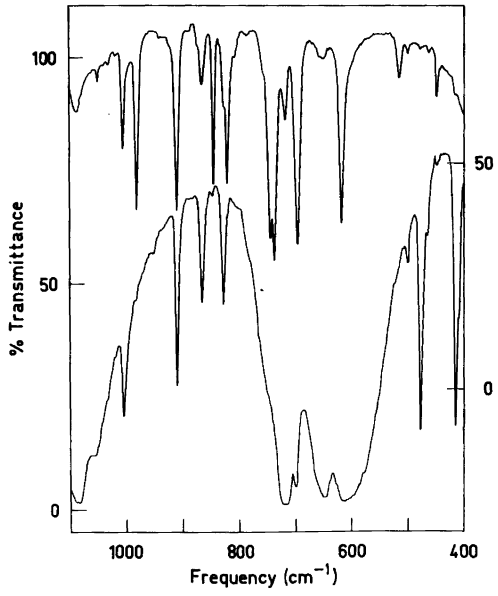

Fig. 1. Infrared spectra of liquid *trans*-1,2-dichlorocyclohexane (top, right ordinate axis) and crystalline thiourea clathrate (bottom, left ordinate axis) in the region 1100–400 cm^{-1}.

Table 2. Infrared spectral data for monosubstituted cyclohexane-thiourea clathrates (1400 – 400 cm^{-1}).

Cl[a]	Br[a]	I[a]	CN[b]	NCO[b]
1259 s	1252 s			1321 m,a
1214 vw	1191 m		1123 w,a	1262 w
1014 m,a	1010 m,a,	1006 m,a	1013 w,a	1020 w,a
993 vw,e	988 vw,e	988 m,e	935 m	1010 w,e
	919 m	920 w	920 w	928 w
				905 w
889 w,e[c]	885 w,e[c]	883 w,e[c]	892 vw,e	893 s,e
868 w,a	864 m,a	862 m,a	862 s,a	881 w,e
858 m	852 s[d]	848 s[d]		863 m,a
852 vw,e[c]			840 vw,e	839 m,e
817 w,e	810 vw,e			815 m,a
807 w,a	804 m,a	806 w,e		780 w,e
731 vw,e				759 w,a
684 m,a				
558 m,a	513 m,a	493 w,a	496 m,a	523 vw,e
472 m,a	458 m,a	445 s,a		

[a] For wavenumbers and conformers, see Ref. 8. [b] For wavenumbers and conformers, see Ref. 17. [c] For conformers, see Ref. 9. [d] Assigned as *e* in Ref. 9.

work upon experimental evidence, instead of on normal coordinate analyses.[3] Various such analyses have been performed on the monohalocyclohexanes,[3,14-16] but it seems unreliable to assign the vibrational bands to the conformers from these calculations alone.

The observed IR bands which were attributed to the guest molecules are listed in Tables 2 (halo and pseudohalo cyclohexanes), 3 (*trans*-1,2-dihalocyclohexane) and 4 (*trans*-1,4-dihalocyclohexanes). As examples, the infrared curves between 1100 and 400 cm^{-1} of the thiourea clathrates of *trans*-1,2-dichlorocyclohexane (Fig. 1) and iodocyclohexane (Fig. 2) are given with the corresponding liquid cyclohexane spectra.

We found the Raman spectra of the present clathrates to be generally less informative than the IR-spectra. Since the Raman spectra of the three halocyclohexane clathrates have recently been

Table 3. Infrared spectral data for *trans*-1,2-dihalocyclohexane – thiourea clathrates (1400 – 200 cm^{-1}).

ClCl[a]	BrBr[a]
	1255 w,aa
1214 m,aa	1195 w,aa
	1178 s,aa
1140 w,aa	1160 w,ee
	1032 w,aa
1005 s,aa	999 s,aa
980 vvw,ee	972 vw,ee
909 s[b]	903 s
865 s,aa	861 s,aa
845 vw,ee	840 vw,ee
826 s,aa	812 m,aa
	803 vw,aa
698 m,aa	685 vw,ee
498 m,aa	664 m,aa
462 w,aa	540 vs,aa
361 m,aa	
209 m,aa	

[a] For wavenumbers and conformers, see Ref. 10. [b] Assigned as ee in Ref. 10.

Table 4. Infrared spectral data for *trans*-1,4-dihalocyclohexane – thiourea clathrates (1400 – 400 cm^{-1}).

ClCl[a]	BrBr[a]
1363 vw,aa	
1270 m,aa	1245 m,aa
1006 m,aa	1003 m,aa
995 vw,ee	988 vw,ee
890 vw,ee	886 vw,ee
874 m,aa	869 m,aa
860 vw,aa	861 vw,aa
558 m,aa	495 m,aa

[a] For wavenumbers and conformers, see Ref. 11.

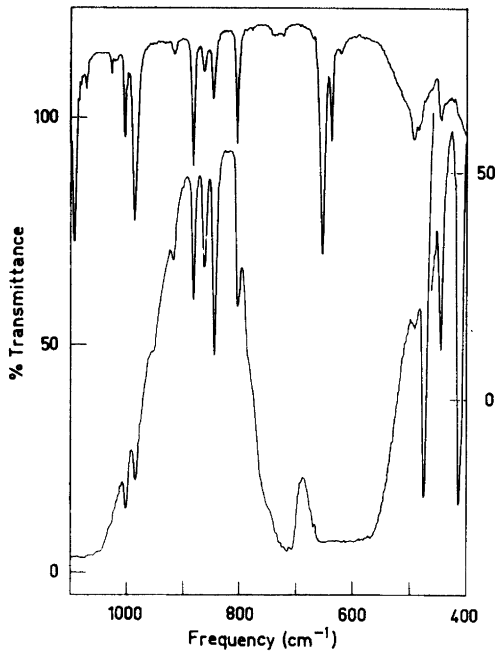

Fig. 2. Infrared spectra of liquid iodocyclohexane (top, right ordinate axis) and crystalline thiourea clathrate (bottom, left ordinate axis) in the region 1100–400 cm^{-1}.

reported,[2] our corresponding data will not be given. However, the Raman spectra of the clathrates served as a supplement to our IR values and confirmed in all the cases the conclusions drawn.

The data of Tables 2–4 clearly reveal that for all the present compounds except iodo- and isocyanatocyclohexane, the intense bands all belong to the *a* (*aa*) conformer or are common to both conformers, whereas the *e*-bands are missing or have very low intensities.

For iodo- and isocyanatocyclohexane the equatorial conformers were still present in the clathrates, although with less abundance than in the liquid state. Preliminary results on fluorocyclohexane,[6] *trans*-1,4-diiodo- and the unsymmetrical *trans*-1,4-dihalocyclohexanes suggest considerable amounts of the equatorial conformers present in their thiourea clathrates as well.

Conformational displacement. The shift of the conformational equilibria between the liquid (or dissolved) cyclohexane and the clathrate was estimated from the infrared band intensities. For this purpose we selected the characteristic pair of bands[10,17] around 1000 cm^{-1} which are intense in IR and well suited for quantitative studies. Also, the intense IR-bands in the region 900–800 cm^{-1}, discussed previously[17] were employed, but for the *trans*-1,4-dihalocyclohexanes a host lattice band around 890 cm^{-1} apparently interfered. The intense C–halogen stretching bands which have been the subject of several detailed studies[18] were completely covered by the host bands (Figs. 1 and 2) and therefore not useful for this purpose.

The ratio between the absorbances (A_a) of the *a* and the neighbouring *e* conformer bands (A_e) was calculated independently for both the 1000 and 850 cm^{-1} bands whenever feasible. These values are given for the liquids (A_a^l/A_e^l) and for the clathrates (A_a^c/A_e^c) in Table 5. Applying the Lambert-Beer's law for the liquid (I)

$$A_a^l/A_e^l = (\varepsilon_a/\varepsilon_e)C_a^l/C_e^l \quad \text{(I)}$$

$$A_a^c/A_e^c = (\varepsilon_a/\varepsilon_e)C_a^c/C_e^c \quad \text{(II)}$$

and the clathrate (II) we obtain eqn. (III), assuming that the molar absorbance indexes (ε_a and ε_e) are the same in the liquid and in the clathrate. (C_a and C_e)

$$\frac{A_a^c/A_e^c}{A_a^l/A_e^l} = \frac{C_a^c/C_e^c}{C_a^l/C_e^l} = \frac{K_c}{K_l} = f \quad \text{(III)}$$

are the concentrations of axial and equatorial conformer, respectively, $K_c = C_a^c/C_e^c$ and $K_l = C_a^l/C_e^l$). Values for f readily available from the IR-absorbance values, are listed in Table 5, and they represent the ratio between the equilibrium constants in the clathrate (K_c) and the liquid (K_l). The value of K_c (or K_l) cannot be derived from this simple arithmetic since the values of the absorbance indexes (ε_a and ε_e) are not known.

The independent values for f listed in Table 5 agree satisfactorily considering the low intensities of some of the IR-bands involved and the rather coarse approximation of constant $\varepsilon_a/\varepsilon_e$ in the liquid and clathrate.

Spectral interpretations. The vibrational bands of the present cyclohexanes were previously attributed to the respective conformers from various criteria, of which the most important was the spectral simplification upon crystallization. Most of the present cyclohexanes crystallize in the equatorial conformer at low temperature and high pressure (*vide infra*). For these compounds the axial bands

Table 5. Displacement of conformational equilibrium from liquid to thiourea clathrate of substituted cyclohexanes.

Substituent	IR bands	A_a/A_e [a]		$f=\frac{K_{clath.}}{K_{liq.}}$ [b]	IR bands	A_a/A_e [a]		$f=\frac{K_{clath.}}{K_{liq.}}$
		Liquid (solution)	Clathrate			Liquid (solution)	Clathrate	
	1014 *a*				868 a			
Cl		0.17	2.22	13		0.13	1.25	10
	993 *e*				889 e			
	1010 *a*				864 a			
Br		0.26	3.47	13		0.15	2.40	16
	988 *e*				885 e			
	1006 *a*				862 a			
I		0.40	0.90	2		0.16	0.74	5
	988 *e*				883 e			
	1013 *a*				862 a			
CN		0.95	10.85	11		0.53	6.17	12
	1042 *e*				892 e			
	1020 *a*				863 a			
NCO		0.48	0.81	2		0.20	0.54	3
	1010 *e*				839 e			
	1005 *aa*				865 aa			
1,2-*trans*-Cl_2		0.51	22.50	45		0.27	16.37	60
	980 ee				845 ee			
	999 *aa*				861 aa			
1,2-*trans*-Br_2		2.40	13.82	6		4.04	24.62	6
	972 *ee*				840 ee			
	1006 *aa*							
1,4-*trans*-Cl_2		0.85	28.00	33				
	995 *ee*							
	1003 *aa*							
1,4-*trans*-Br_2		1.21	8.24	7				
	988 *ee*							

[a] A_a (A_e) absorbance of axial (equatorial) band. [b] $K_{clath.}$ and $K_{liq.}$ are equilibrium constants C_a/C_e in clathrate and liquid cyclohexane, respectively.

can be attributed with certainty while the distinction between equatorial bands and bands common to both conformers is uncertain. Obviously, the predominantly axial conformer observed in most of the clathrates gives added spectral information. Thus, the weak bands at 889, 885 and 883 cm^{-1} for chloro-, bromo- and iodocyclohexane, respectively, (Table 2) are probably equatorial[9] and not common to both conformers.[8] The strong bands at 852 (bromo-) and 848 cm^{-1} (iodocyclohexane) must be common to both conformers[8] and not equatorial,[9,17] whereas the 852 cm^{-1} band in chlorocyclohexane should be equatorial.[9] For isocyanatocyclohexane the equatorial and axial conformers were detected[17] in the low temperature and high pressure crystals, respectively, and no further results were obtained from the clathrate.

In *trans*-1,2-dichlorocyclohexane (Table 3) the intense 909 cm^{-1} band must be common to both conformers (as is the 903 cm^{-1} band in *trans*-1,2-dibromocyclohexane) and not diequatorial as reported.[10] In *trans*-1,2-dibromocyclohexane the crystals consist of molecules in the *aa*-conformer[10] and no further information was extracted from the present clathrate spectra. Finally, in the *trans*-1,4-dichloro- and dibromocyclohexane spectra the attributions to diequatorial and diaxial conformers are based upon very thorough data[11] and the agreement with the clathrate spectra (Table 4) is excellent.

DISCUSSION

The urea and thiourea molecules in the clathrates are linked together by hydrogen bonding,[19] leaving long channels[20] of hexagonal cross-sections in which the guest molecules are located.[19-22]

With the possible exception of cyano- and isocyanatocyclohexane, the present cyclohexanes are not hydrogen-bond acceptors and specific host-guest interactions are impossible. The preferred cross-sectional dimensions of adducts in thiourea are *ca.* 5.8–6.8 Å,[23] and parent cyclohexane falls well within these values. Therefore cyclohexane molecules can be stacked with the three-fold axis centred along the thiourea channel axis. In substituted cyclohexanes an equatorial substituent like, *e.g.*, chlorine, will increase the cyclohexane diameter to *ca.* 7 Å. An axial substituent, however, is ideally parallel to the cyclohexane three-fold axis and will therefore not increase the cyclohexane diameter significantly. The axially substituted cyclohexanes can therefore be stacked with the substituents directed parallel to the channels. Moreover, the axial conformers of mono- and 1,4-dihalocyclohexanes have smaller volumes than the equatorial conformers[24] which might independently favour the axial conformer in the clathrates.

Equatorial substituents can, if parallel or oblique to the channels, also be accomodated in the host lattice. The three-fold axis of the cyclohexane ring should then be oriented roughly perpendicular to the channels. Such packing of the guest molecules should be much less efficient than what is possible for the axially substituted cyclohexanes. Structure determinations by X-ray crystallography are needed to determine the guest molecule orientation.

The linear cyanogroup in cyanocyclohexane would also follow this pattern. Isocyanatocyclohexane has a non-linear side chain which apparently makes the axial conformer less favourable. The present and former[2] results for iodocyclohexane as well as preliminary[6] data for fluorocyclohexane clathrates indicate that the axial conformer is less preferable for these than for the chloro and bromo compounds. Hopefully, we shall be able to clarify the effects of the halogen size when the thiourea clathrates of more cyclohexanes have been investigated.

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