Unusual Conformational Behaviour in the Chlorocyclohexane/Thiourea Inclusion Compound: a Theoretical Rationalization

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A theoretical approach, developed recently for the prediction and rationalization of structural properties of one-dimensional inclusion compounds, has been applied to the chlorocyclohexane/thiourea inclusion compound; the analysis provides theoretical justification for the observation that the preferred conformation of chlorocyclohexane within the thiourea tunnel structure is the axial conformation, and confirms that the optimum periodicity of the guest molecules along the tunnel is commensurate with the thiourea host structure.

Thiourea inclusion compounds comprise an extensively hydrogen bonded thiourea 'host' structure which contains parallel, one-dimensional tunnels[1-5]—this host structure is stable only when each tunnel contains a dense packing of 'guest' molecules. The chlorocyclohexane/thiourea inclusion compound represents a classic example of a molecule (chlorocyclohexane) being constrained to behave differently within a solid host structure from the way it behaves in its 'pure' solid phase or in dispersed phases. In the liquid and vapour phases there is an excess of the equatorial conformation;[6-8] in the solid state at sufficiently low temperature or high pressure it exists only in the equatorial conformation.[9] However, when included within the thiourea host tunnel structure, chlorocyclohexane exists predominantly as the axial conformation—these results (and similar findings for bromocyclohexane/thiourea and iodocyclohexane/thiourea) have been established from IR,[10,11] Raman[12] and high-resolution solid state ^{13}C NMR[13-15] techniques.

In this paper we rationalize this unusual conformational behaviour of chlorocyclohexane within the thiourea tunnel structure by applying a theoretical approach that we have developed recently[16,17] to predict and rationalize structural properties of real one-dimensional inclusion compounds. In such inclusion compounds, it is a good approximation to assume that the interaction between guest molecules in different tunnels is weak, and each tunnel of the inclusion compound can be considered to behave essentially independently. The periodic repeat distance of the guest molecules along the tunnel is denoted c_g and the periodic repeat distance of the host structure along the tunnel axis is denoted c_h.

Our theoretical approach allows potential energy functions (specifically, host–guest interaction, guest–guest interaction and intramolecular potential energies) computed for any one-dimensional inclusion compound of interest to be used to predict structural properties of the inclusion compound. Amongst these structural properties are the optimum value of
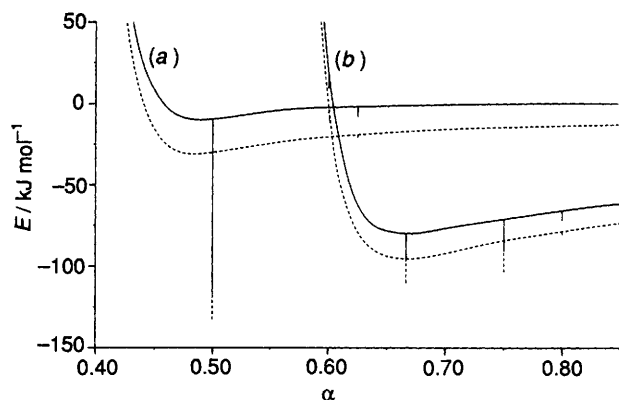
Fig. 1 Characteristic energy diagrams for (a) axial-chlorocyclohexane/thiourea and (b) equatorial-chlorocyclohexane/thiourea. The lowest point on the two characteristic energy diagrams is the 'downspike' at α = 1/2 for axial-chlorocyclohexane/thourea [the δ-neighbourhood (discussed fully in ref. 16) around this value of α is negligibly small ($\delta \approx 10^{-4}$)]. At this value of α, the axial-chlorocyclohexane/thiourea inclusion compound exhibits commensurate behaviour.

c_g, the question of whether the inclusion compound is commensurate or incommensurate, and the optimum conformation of the guest molecules. A rigorous development of the mathematics underlying the model has been published previously,[16] and the successful application of the model has been demonstrated[17,18] via predictions of the optimum c_g and the commensurate/incommensurate nature of alkane/urea inclusion compounds. This paper represents the first attempt to use this theoretical approach to assess the preferred conformation of the guest molecules within a one-dimensional inclusion compound. Within the model, the one-dimensional inclusion compound is considered to comprise an infinite, rigid, periodic, linear host tunnel containing a finite number n of equally spaced, rigid guest molecules. The unit of length is taken to be c_h, and the periodicity of the guest molecules along the tunnel is then denoted α (where $\alpha = c_g/c_h$). The conformation of each guest molecule is assumed to be the same; the structure of the host tunnel and the conformation of the guest molecules are assumed to be independent of α and n.

We defined a characteristic energy function $\hat{E}(\alpha,n)$ for the inclusion compound,[16] as in eqn. (1), with the entailment that the optimum guest structure in the inclusion compound corresponds to the minimum characteristic energy. In this expression, $E_h(t)$ represents the energy of an individual guest molecule, due to host–guest interaction, when the guest molecule is located at position t along the host tunnel, $\hat{E}_{guest}(\alpha)$ is the guest–guest interaction energy, per guest molecule, when the periodicity of the guest structure is α, and $\hat{E}_{intra}$ is the intramolecular potential energy of the guest molecule. A graphical method (construction of the 'characteristic energy diagram') has been developed[17] to allow the structural properties of the one-dimensional inclusion compound to be assessed from the potential energy functions $E_h(t)$, $\hat{E}_{guest}(\alpha)$ and $\hat{E}_{intra}$ for the inclusion compound of interest. While it is obvious that $\hat{E}_{intra}$ will depend critically on the conformation of the guest molecules, it is important to stress that $\hat{E}_{guest}(\alpha)$ and $E_h(t)$ will also depend on the conformation of the guest molecules. In order to assess the relative energetic favourability of two different conformations of a given guest molecule within the inclusion compound (such as comparing the axial and equatorial conformations of chlorocyclohexane discussed here) it is necessary to compare the characteristic energy at optimal α for one conformation of the guest with the characteristic energy at optimal α for the other conformation of the guest.

$$\hat{E}(\alpha,n) = \frac{1}{\alpha}\left\{ \inf_{\lambda}\left[\frac{1}{n}\sum_{k=0}^{n-1} E_h(k\alpha + \lambda)\right] + \hat{E}_{guest}(\alpha) + \hat{E}_{intra} \right\} \quad (1)$$

The potential energy functions $E_h(t)$, $\hat{E}_{guest}(\alpha)$ and $\hat{E}_{intra}$ for axial-chlorocyclohexane/thiourea and equatorial-chlorocyclohexane/thiourea were calculated using the CHEM-X program package.[19] Full details of the methods used to calculate $E_h(t)$ $\hat{E}_{guest}(\alpha)$ and $\hat{E}_{intra}$ will be given, together with a discussion of the main features of these potential energy functions, in a future publication. The potential energy parameterization used to compute $E_h(t)$, $\hat{E}_{guest}(\alpha)$ and $\hat{E}_{intra}$ was that embodied within the CHEM-X program package, and this parameterization was not specifically adapted or optimized for the particular system (chlorocyclohexane/thiourea) under investigation. However, the excellent agreement (vide infra) between the theoretical predictions reported in this paper and the known experimental information serves, inter alia, to vindicate the suitability of this potential energy parameterization for chlorocyclohexane/thiourea.

Characteristic energy diagrams (Fig. 1) for axial-chlorocyclohexane/thiourea and equatorial-chlorocyclohexane/thiourea inclusion compounds were constructed using the computed potential energy functions $E_h(t)$, $\hat{E}_{guest}(\alpha)$ and $\hat{E}_{intra}$ by following the methods developed previously[16–18] (the following parameters relating to construction of the characteristic energy diagram were used: ε = 10.5 kJ mol^{-1}; ε' = 4.2 kJ mol^{-1}; $N \approx$ 831 000 [results from the characteristic energy diagram can be related to the properties of real inclusion compounds provided the number of guest molecules in the real inclusion compound is greater than N (vide infra)]. In constructing the characteristic energy diagram, values of $\hat{E}_{intra}$ were taken relative to the intramolecular potential energy of the free equatorial-chlorocyclohexane molecule.

In the characteristic energy diagram for axial-chlorocyclohexane/thiourea, optimal α corresponds to the large 'downspike' at α = 1/2 (the δ-neighbourhood[16,17] associated with this point is negligibly small), and represents commensurate behaviour of the inclusion compound. [It is important to recall[16] that the definition of commensurate vs. incommensurate behaviour is based upon energetic considerations (specifically, the choice of the parameter ε).] The results of the theoretical analysis are conditional on the tunnel length being greater than $N\alpha c_h$ = 0.52 mm—as required, this is shorter than the tunnel lengths found in practice (typically ca. 2 mm for a single crystal of the inclusion compound). The energy stabilization (giving rise to 'lock in' of host and guest structures) for axial-chlorocyclohexane/thiourea at α = 1/2 is 107.5 kJ mol^{-1} (assessed from the magnitude of the downspike at α = 1/2). This optimum α for axial-chlorocyclohexane/thiourea corresponds to a lower characteristic energy than any value of α for equatorial-chlorocyclohexane/thiourea. Thus, our theoretical analysis predicts correctly the preference for the axial conformation within the thiourea tunnel structure. The optimal guest periodicity (c_g = αc_h = c_h/2 = 6.24 Å) predicted for axial-chlorocyclohexane/thiourea is in good agreement with information inferred (but not proved) from X-ray diffraction data.[5] It is interesting to note that the minimum of the function $\hat{E}_{guest}(\alpha)$ for a pair of chlorocyclohexane molecules in the axial conformation and approaching each other in the manner that they are constrained to do within the thiourea tunnel structure corresponds to c_g = 5.95 Å.

On the basis of these results, we now discuss in more detail the energetic reasons underlying the preference for the axial conformation of chlorocyclohexane in the thiourea tunnel structure. Equatorial-chlorocyclohexane has a more negative $\hat{E}_{intra}$ than axial-chlorocyclohexane, and the observed preference for the axial conformation in the thiourea tunnel structure suggests that other factors are sufficient to outweigh the influence of $\hat{E}_{intra}$. From the results of the present study, the major factors to consider are $E_h(t)$ and the $1/\alpha$ term in the expression for $\hat{E}(\alpha,n)$.

For equatorial-chlorocyclohexane/thiourea the computed function $E_h(t)$ is relatively insensitive to the position of the

guest molecule along the tunnel, whereas for *axial*-chloro-cyclohexane/thiourea $E_h(t)$ contains significant fluctuations. Furthermore, although the average $E_h(t)$ is higher for *axial*-chlorocyclohexane/thiourea, there are specific sites for *axial*-chlorocyclohexane in the thiourea tunnel at which $E_h(t)$ is very favourable, and more negative than for any position of *equatorial*-chlorocyclohexane in the thiourea tunnel. Thus, a commensurate guest structure for *axial*-chlorocyclohexane/thiourea in which only these sites corresponding to minimum $E_h(t)$ are occupied should be particularly favourable.

Furthermore, detailed consideration of the functions $E_h(t)$ and $\hat{E}_{guest}(\alpha)$ indicates that *axial*-chlorocyclohexane can be packed much more efficiently (smaller α) within the constrained environment of the thiourea tunnel than can *equatorial*-chlorocyclohexane; this fact contributes to the more favourable characteristic energy for the axial conformation as a consequence of the factor $1/\alpha$ in the expression for the characteristic energy [this factor ensures that the characteristic energy refers to an energy per unit length of host tunnel rather than an energy per guest molecule].

Within the level of approximation inherent in the theoretical approach employed here (the assumptions underlying which are detailed in refs. 16–18), the results provide a clear and rigorous rationalization of the unusual conformational properties of chlorocyclohexane guest molecules within the thiourea tunnel structure.

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