Pergamon

Tetrahedron: Asymmetry, Vol. 7, No. 7, pp. 1891-1894, 1996
Copyright © 1996 Elsevier Science Ltd
Printed in Great Britain. All rights reserved
0957-4166/96 $15.00 + 0.00

PII: S0957-4166(96)00223-6

Chiral Recognition in Incommensurate One-dimensional Inclusion Compounds: A Computational Investigation

Lily Yeo and Kenneth D.M. Harris*

School of Chemistry, University of Birmingham, Edgbaston, Birmingham B15 2TT, U.K.

Abstract: Computational investigations of host-guest interaction between the chiral urea tunnel structure and chiral 2-bromoalkane guest molecules have been used as a basis for understanding the nature of chiral recognition in 2-bromoalkane/urea inclusion compounds.

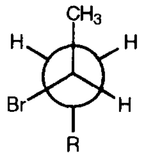
In recent years, significant progress has been made in understanding aspects of the structural and dynamic properties of solid one-dimensional inclusion compounds, typified by the urea inclusion compounds[1-3]. In the conventional urea inclusion compounds, the host structure[4,5] comprises an extensively hydrogen bonded arrangement of urea molecules; this host structure contains a series of parallel, linear tunnels, within which guest molecules are densely packed. The periodicity (denoted c_h) of the host substructure along the tunnel axis and the periodicity (denoted c_g) of the guest substructure along the tunnel axis are usually incommensurate. In classical terms, this means that it is not possible to find sufficiently small integers p and q for which $pc_g \approx qc_h$. A detailed discussion of commensurate and incommensurate behaviour in one-dimensional inclusion compounds is given in ref. 6.

To a first approximation[5-7], the space group of the urea tunnel structure in the conventional urea inclusion compounds is $P6_122$ or $P6_522$. The urea tunnel is constructed from a spiral arrangement of urea molecules, and a single crystal contains either only right-handed spirals ($P6_122$) or only left-handed spirals ($P6_522$). Thus, the urea tunnel represents a chiral environment. This chirality is generated spontaneously during crystal growth, and there is clearly considerable potential for exploiting this chirality in the properties and applications of these crystalline materials. For example, asymmetric synthesis could, in principle, be effected by carrying out reactions between achiral guest molecules to generate an enantiomeric excess (induced by the influence of the chiral host environment) of a chiral product guest molecule. The potential to exploit the chiral nature of the urea tunnel structure devolves upon the extent to which the interaction between a host tunnel of a given chirality (e.g. $P6_122$) differs for two enantiomers (R and S) of a chiral guest species. Depending on the application of interest, the chiral guest species could be a reactant, a transition state, or a reaction product. In spite of the potential for exploiting the chirality of urea inclusion compounds, virtually all reported studies of urea inclusion compounds have focused on achiral guest molecules, although an important exception is the work of Schlenk[8–10] which demonstrated experimentally that urea inclusion compounds can indeed exhibit some degree of chiral recognition.

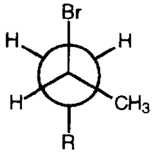
In view of the importance of developing a fundamental understanding of the nature of the chiral recognition between host and guest components in urea inclusion compounds, and with a view to assessing the potential for exploiting the chiral nature of the urea tunnel structure, we report preliminary computational investigations that have probed the characteristics of host-guest interaction between chiral 2-bromoalkane guest molecules and the urea tunnel structure. This represents a first step towards deriving a fundamental understanding of chiral recognition in urea inclusion compounds.

An important consequence of the incommensurate relationship between the host and guest substructures in the incommensurate urea inclusion compounds is that, within a given tunnel of the inclusion compound, each guest molecule will experience a different environment with respect to the host structure. For a sufficiently long tunnel, it can be assumed that the set of guest molecules within the tunnel will sample all values of z-coordinate within the unit cell of the host structure (where z defines the position of the guest molecule along the tunnel). For this reason, it is essential that investigations of chiral recognition in the conventional (incommensurate) urea inclusion compounds consider the host-guest interaction energy as a function of z.

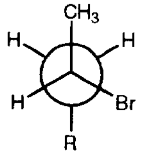
Our investigations of host-guest interaction in the 2-bromotridecane/urea ($C_{13}Br$/urea) and 2-bromotetradecane/urea ($C_{14}Br$/urea) inclusion compounds have considered a single guest molecule within the $P6_122$ urea tunnel structure (taken from the published crystal structure of hexadecane/urea[5]). Powder X-ray diffraction indicates that the $C_{13}Br$/urea and $C_{14}Br$/urea inclusion compounds have the conventional urea tunnel structure (as exemplified by hexadecane/urea). The $C_{13}Br$ and $C_{14}Br$ molecules were constructed according to standard geometries and were kept rigid throughout the calculations. For each guest molecule, both R and S enantiomers were considered, and for each enantiomer the following conformations of the end-group containing the Br atom were considered: (i) Br atom *trans* and CH_3 group *gauche*; (ii) Br atom *gauche* and CH_3 group *trans*. The notation used for the different enantiomer/conformation combinations is defined as follows:



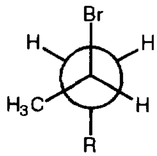
$\mathbf{R_g}$



$\mathbf{R_t}$



$\mathbf{S_g}$

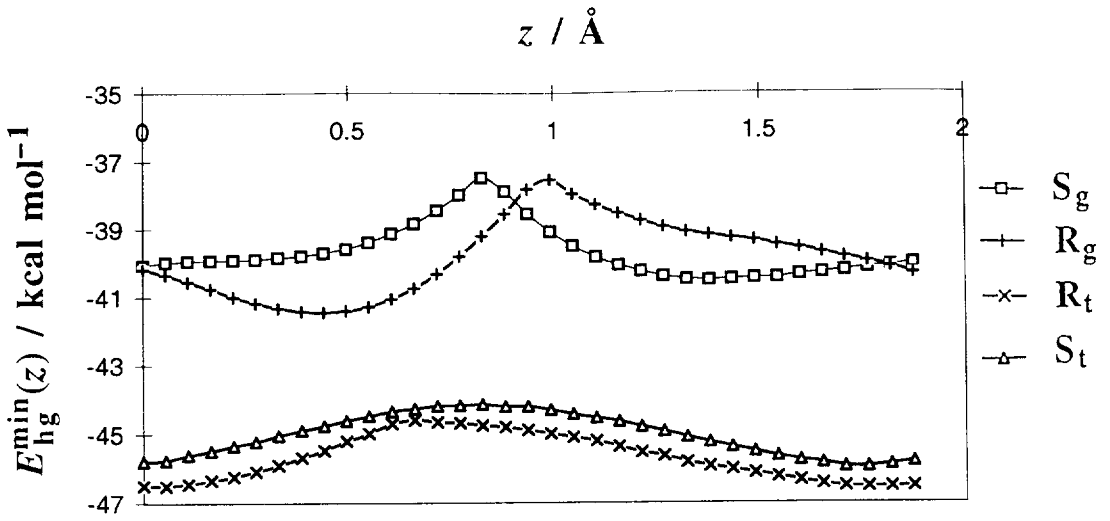


$\mathbf{S_t}$

Six parameters define the position (x,y,z) of the centre of mass and the orientation (θ,ϕ,γ) of the rigid 2-bromoalkane guest molecule with respect to the urea tunnel structure. The host-guest interaction energy $E_{hg}(x,y,z,\theta,\phi,\gamma)$ was calculated using a standard potential energy parameterization[11] based on the atom-atom approach, and for each value of z, the minimum host-guest interaction energy ($E_{hg}^{min}(z)$) was determined (by variation of x, y, θ, ϕ and γ) as:

$$E_{hg}^{min}(z) = \min_{x\,y\,\theta\,\phi\,\gamma} \{E_{hg}(x,y,z,\theta,\phi,\gamma)\}$$

Note that $E_{hg}^{min}(z)$ is periodic in z, with period equal to $c_h/6$. The graph of $E_{hg}^{min}(z)$ *versus* z (for the range $0 \leq z < c_h/6$) for $C_{13}Br$/urea is shown below (qualitatively similar behaviour is observed for $C_{14}Br$/urea):



For both $C_{13}Br$/urea and $C_{14}Br$/urea, $E_{hg}^{min}(z)$ is lower, at all values of z, for R_t and S_t than for R_g and S_g; thus, there is a distinct preference for the Br *trans*/CH_3 *gauche* conformation of the guest molecule over the Br *gauche*/CH_3 *trans* conformation. The energetic preference for the Br *trans*/CH_3 *gauche* conformation can be quantified by comparing the average values (denoted $\langle E_{hg}^{min}\rangle$) of $E_{hg}^{min}(z)$ for the two conformations:

$$\langle E_{hg}^{min}\rangle = \frac{6}{c_h}\int_0^{c_h/6} E_{hg}^{min}(z)\ dz$$

The difference in $\langle E_{hg}^{min}\rangle$ between R_t and R_g is 5.8 kcal mol^{-1} ($C_{13}Br$/urea) and 5.1 kcal mol^{-1} ($C_{14}Br$/urea) and the difference in $\langle E_{hg}^{min}\rangle$ between S_t and S_g is 5.3 kcal mol^{-1} ($C_{13}Br$/urea) and 4.9 kcal mol^{-1} ($C_{14}Br$/urea). The differences in intramolecular potential energy between R_t and R_g and between S_t and S_g are estimated to be only *ca.* 0.2 – 0.3 kcal mol^{-1}, and host-guest interaction is clearly the major factor discriminating the preferred conformation of the guest molecules. Experimental investigations of the conformational properties of the guest molecules in 2-bromoalkane/urea inclusion compounds are in progress.

We now compare the energetics of host-guest interaction for the R_t and S_t guest molecules. For both $C_{13}Br$ and $C_{14}Br$ in the $P6_122$ urea tunnel structure, $E_{hg}^{min}(z)$ is lower for R_t than S_t at all values of z (as evident from the graph (shown above) of $E_{hg}^{min}(z)$ *versus* z for $C_{13}Br$/urea). [In contrast, it is interesting to note that for the R_g and S_g guest molecules, $E_{hg}^{min}(z)$ is lower for R_g than S_g at some values of z and lower for S_g than R_g at other values of z]. Thus, for the preferred conformation (Br *trans*/CH_3 *gauche*) of the 2-bromoalkane guest molecules, the urea tunnel structure discriminates clearly between the two enantiomers of the guest, and will result in the inclusion of an overall excess of the R enantiomer of the guest within the $P6_122$ urea tunnel structure.

To assess the relative proportions of the two enantiomers, we consider a two-state model in which the guest molecule at position z along the tunnel is either R_t (with energy $E_{hg}^{min}(z,R_t)$) or S_t (with energy $E_{hg}^{min}(z,S_t)$). Within this model, the probabilities at temperature T that a guest molecule at position z along the tunnel is R_t or S_t are given *via* the Boltzmann distribution by:

$$p(z,\mathrm{R_t},T) = \frac{\exp[-E_{hg}^{min}(z,\mathrm{R_t})/RT]}{\exp[-E_{hg}^{min}(z,\mathrm{R_t})/RT] + \exp[-E_{hg}^{min}(z,\mathrm{S_t})/RT]} \quad ; \quad p(z,\mathrm{S_t},T) = 1 - p(z,\mathrm{R_t},T)$$

And for an incommensurate inclusion compound, the overall proportions of R_t and S_t guest molecules within the tunnel at temperature T are given by:

$$P(\mathrm{R_t},T) = \frac{6}{c_h}\int_0^{c_h/6} p(z,\mathrm{R_t},T)\,\mathrm{d}z \quad ; \quad P(\mathrm{S_t},T) = 1 - P(\mathrm{R_t},T)$$

From our results, the value of $P(\mathrm{R_t}, 300\ \mathrm{K})$ is 0.75 for C_{13}Br/urea and 0.82 for C_{14}Br/urea. In both cases, there is a significant preference for the R enantiomer of the guest molecule within the $P6_122$ urea tunnel, and the corresponding enantiomeric excesses should have a significant bearing on properties of the inclusion compounds. The predicted enantiomeric excess is larger for the guest molecule with the longer alkane chain, although from the evidence available we cannot assess whether this is a general feature; a detailed investigation of this issue for a wide range of chain lengths (including consideration of the odd/even character of the chain) is in progress.

In summary, our computational investigations predict significant chiral preferences for 2-bromoalkane guest molecules within the urea tunnel structure. Importantly, the same enantiomer of the guest molecule is preferred for all positions of the guest molecule along the tunnel. While these investigations have focused on the key interaction (i.e. host-guest interaction) responsible for chiral recognition in these solids, it is important to note that certain other factors may also influence the exact proportions of the two enantiomers of a chiral guest molecule. These factors include the guest-guest interaction, which may be expected to exert some influence in cases when adjacent guest molecules are oriented such that their chiral head groups come together; we are currently investigating this issue as part of our experimental investigations of urea inclusion compounds containing these chiral guest molecules.

Acknowledgement: We thank Ciba Geigy plc and the Nuffield Foundation for support.

References:

1 Takemoto, K.; Sonoda, N. *Inclusion Compounds* (Editors: Atwood, J.L.; Davies, J.E.D.; MacNicol, D.D.), Volume *2*, Academic Press, New York, **1984**, p. 47.
2 Harris, K.D.M. *J. Solid State Chem.*, **1993**, *106*, 83.
3 Harris, K.D.M. *J. Mol. Struct.*, **1996**, *374*, 241.
4 Smith, A.E. *Acta Crystallogr.*, **1952**, *5*, 224.
5 Harris, K.D.M.; Thomas, J.M. *J. Chem. Soc., Faraday Trans.*, **1990**, *86*, 2985.
6 Rennie, A.J.O.; Harris, K.D.M. *Proc. Royal Soc. A*, **1990**, *430*, 615.
7 van Smaalen, S.; Harris, K.D.M. *Proc. Royal Soc. A*, **1996**, 452, 677.
8 Schlenk, W. *Experientia*, **1952**, *8*, 337.
9 Schlenk, W. *Justus Liebigs Ann. Chem.*, **1973**, *7*, 1145, 1156, 1179, 1195.
10 Arad-Yellin, R.; Green, B.S.; Knossow, M.; Tsoucaris, G. *Inclusion Compounds* (Editors: Atwood, J.L.; Davies, J.E.D.; MacNicol, D.D.), Volume *3*, Academic Press, New York, **1984**, p. 263.
11 BIOSYM Technologies Inc., 9685 Scranton Rd., San Diego, California, U.S.A.

(*Received in UK* 29 *April* 1996)