

# Organisation of long aliphatic monocarboxylic acids in $\beta$ -cyclodextrin channels: crystal structures of the inclusion complexes of tridecanoic acid and (Z)-tetradec-7-enoic acid in $\beta$ -cyclodextrin

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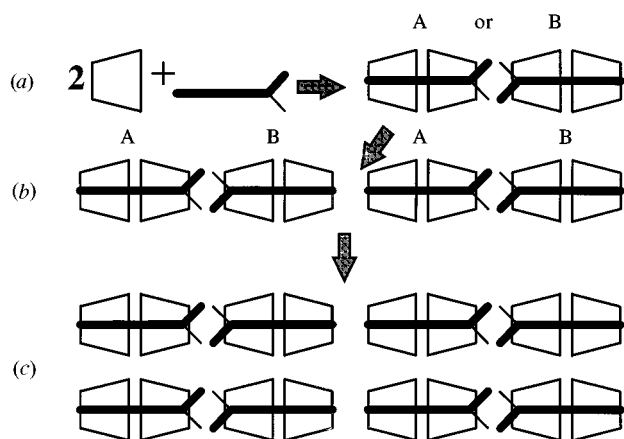
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**In the crystalline state, infinite channels of  $\beta$ -cyclodextrin dimers host infinite arrays of self associated linear aliphatic monocarboxylic acids, thus enclosing the hydrophilic carboxy ends inside the hydrophobic channels.**

Non-bonding interactions like H-bonds and hydrophobic interactions comprise the main routes for the assembly of supermolecules,<sup>1a,b</sup> entities detectable as distinct from the constituent molecules. Since the non-covalent bonding interactions are at least an order of magnitude weaker than covalent bonds, stable supermolecules require a large number of such interactions, *i.e.* the presence of a large area of complementary surface<sup>1c,d</sup> in order to compensate for the entropic loss due to organisation. This requirement is fulfilled in the formation of host-guest assemblies. Moreover, if the supermolecules possess groups capable of aggregation *via* non-covalent bonds, it is possible to synthesise supramolecular assemblies. Thus the latter can be generated by introducing groups with a tendency for specific interactions into strategic parts of the supermolecules.<sup>2</sup>

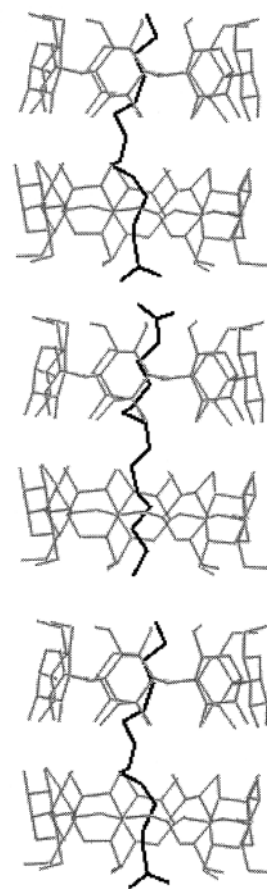
The systems reported here, which involve inclusion of one molecule of a long aliphatic mono-carboxylic acid (tridecanoic acid **1** and (Z)-tetradec-7-enoic acid **2**) into two molecules of  $\beta$ -cyclodextrin ( $\beta$ -CD), combine host-guest interactions and supramolecular synthon association of both host and guest to form supramolecular assemblies. They were designed to form three-component pseudo-rotaxanes and subsequent stacking of those into infinite channels. Indeed, such systems were prepared through precipitation from aqueous solutions of  $\beta$ -CD after the addition of a two-fold excess of the aliphatic acids at room temperature. The crystallographic analyses<sup>‡</sup> revealed that the above simple process allowed the formation of systems exhibiting many levels of supramolecular organisation.



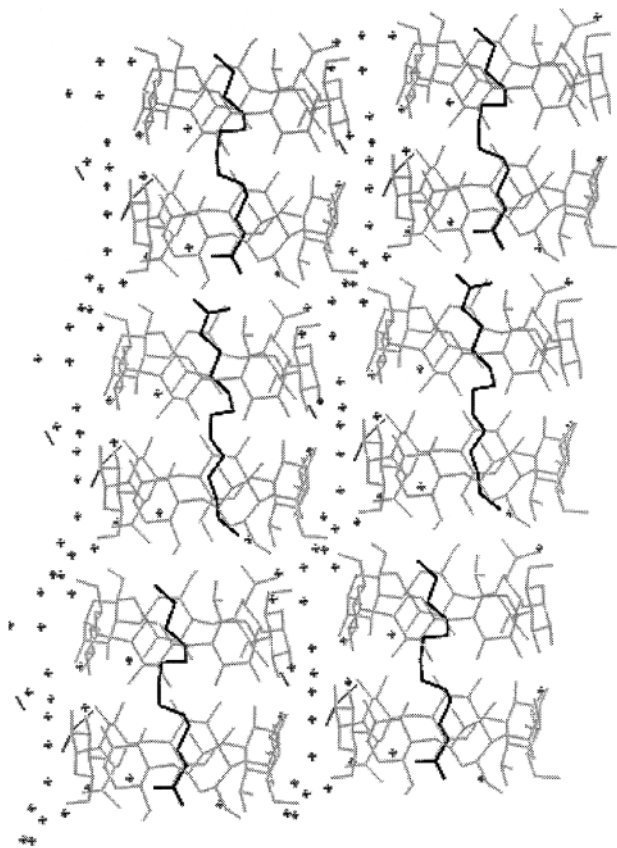
**Scheme 1** Schematic representation of (a) the self-assembly of two  $\beta$ -cyclodextrin molecules and an aliphatic acid molecule into [3]pseudorotaxanes, (b) the formation of a channel supramolecular array and (c) supramolecular arrays of higher order by channel association

Firstly,  $\beta$ -CD forms dimers *via* H-bonds between the O3 secondary hydroxy groups of the two monomers, as is common in  $\beta$ -CD inclusion complexes.<sup>3</sup> Each molecule of aliphatic acid threads into the long cavity of a  $\beta$ -CD dimer to form a [3]pseudorotaxane [Scheme 1(a)]. The aliphatic guests span the entire length of the  $\beta$ -CD dimer with the carboxylic groups slightly protruding from one primary face and the terminal methyl groups protected at the other end. Threading of two cyclodextrin units ( $\alpha$ -CD, permethylated  $\alpha$ -CD) onto one long aliphatic molecule has also been observed<sup>4</sup> in aqueous solutions and inter-cyclodextrin H-bonds have been invoked to account for the thermodynamic parameter measurements in solution studies of polypseudorotaxanes.<sup>5</sup>

At a second level, the supramolecular units align along the crystallographic *c* axis to form channels (Fig. 1). The crystallographic asymmetric unit contains one [3]pseudorotaxane in



**Fig. 1** Channel formation in the  $\beta$ -cyclodextrin complex of (Z)-tetradec-7-enoic acid. The two terminal guest molecules have the A orientation and the middle one the B orientation.



**Fig. 2** Organisation in three-dimensions of channels of  $\beta$ -cyclodextrin-tridecanoic acid complexes

which the aliphatic acid is disordered over two orientations (A and B) of almost equal probability (occupation factors for orientations A and B refined to: A = 52%, B = 48% for **1**, and A = 51%, B = 49% for **2**; considered as 50% each from the accuracy of the present data). Therefore, a  $\beta$ -CD dimer encloses one molecule of the acid in orientation A and the adjacent dimer along the channel in orientation B in order to form conventional carboxylic dimers [Scheme 1(b)]. The observed distances between the adjacent carboxylic oxygen atoms of orientations A and B are O1A...O1B = 2.50 and OA2...OB2 = 2.74 Å for **1** and OA1...OB1 = 2.70 and O2A...O2B 2.71 Å for **2**. The overall formation of the channel resembles an infinite pseudorotaxane where the  $\beta$ -CD molecules are not threaded onto a polymer chain but onto a linear assembly of aliphatic carboxylic acids held together by intermolecular interactions. In addition, the  $\beta$ -CD host assists in the formation of the supramolecular assembly *via* H-bonds between two primary hydroxy groups of consecutive dimers (O...O distances 2.93 and 2.98 Å for **1** and **2** respectively) that further strengthen the channel.

The supramolecular organisation extends to a third level, since the channels associate *via* H-bonds along the **a** and **b** axes [Scheme 1(c), Fig. 2]. The H-bonding interactions are either through direct association of primary and secondary hydroxy groups (five H-bonds at O...O distances 2.77–2.89 and 2.76–2.91 Å for **1** and **2** respectively) or through intervening water molecules.

Determination of the unit cells of crystals of  $\beta$ -CD complexes of aliphatic mono-acids with 12–16 carbon atoms show that they are isomorphous with the complexes reported here, showing that they also form [3]pseudorotaxanes aligned in channels. In contrast,  $\beta$ -CD complexes of aliphatic di-acids with 10–16 carbon atoms also form [3]pseudorotaxanes but they do

not align in channels,<sup>6</sup> preferring to interact with the polar environment. Therefore, in the case of the monocarboxylic acids we observe the remarkable fact that the carboxylic groups prefer to be enclosed inside the hydrophobic environment of the channel rather than interact with the aqueous environment in the periphery of the  $\beta$ -CD dimers, as in the case of the di-acids. We believe that what forces them inside the channel is the presence of the terminal methyl groups of the guest in the other primary face of the  $\beta$ -CD dimers. Due to the presence of the solvent in the lattice, these methyl groups would be exposed to the aqueous environment if channels were not formed. On the other hand, although the carboxylic groups prefer the polar environment, they can be stabilised by self-association into carboxylic dimers. The formation of the latter corresponds to an overall non-polar moiety<sup>7</sup> that can stay inside the hydrophobic channel.

Summarising, we have achieved the construction of an infinite channel structure, based on specific features of simple building blocks, with aliphatic mono-carboxylic acids threaded through two  $\beta$ -CD molecules. The tendency of cyclodextrins to form inclusion complexes and simultaneously to self-associate and form dimers is combined with the tendency of the guest molecules for self association through a very well known synthon, the carboxylic dimer. It is shown that the channel forming ability of similar systems is directly related to the degree of hydrophobicity/hydrophilicity of the end groups of the guest emerging from the primary faces, due to one more variable, the solvent, that influences the packing of the building blocks. Currently, we are exploiting the properties of the systems in order to design transitions between the packing modes<sup>8</sup> of dimeric  $\beta$ -CD complexes *via* the interplay of the aliphatic chain length and the nature of the end groups.

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## Notes and References

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‡ *Crystal data* for **1** (C<sub>42</sub>H<sub>70</sub>O<sub>35</sub>)<sub>2</sub>·(C<sub>13</sub>H<sub>26</sub>O<sub>2</sub>)·(H<sub>2</sub>O)<sub>19.5</sub>: triclinic, *P*1 *a* = 15.654(6), *b* = 15.650(6), *c* = 15.937(6) Å,  $\alpha$  = 101.585(12),  $\beta$  = 101.596(14),  $\gamma$  = 103.585(13)°, *V* = 3589(2) Å<sup>3</sup>, *Z* = 1,  $\rho_{\text{calc}}$  = 1.286 g cm<sup>-3</sup>,  $2\theta_{\text{max}}$  = 41°,  $\mu(\text{Mo-K}\alpha)$  = 0.1 mm<sup>-1</sup>, *T* = 293 K, *R*1 = 0.0862 for 5862 *F*<sub>o</sub> > 4 $\sigma$ (*F*<sub>o</sub>), *wR*2 = 0.2702 for 7565 independent reflections. 19.5 water molecules were located, distributed over 28 positions. For **2** (C<sub>42</sub>H<sub>70</sub>O<sub>35</sub>)<sub>2</sub>·(C<sub>14</sub>H<sub>26</sub>O<sub>2</sub>)·(H<sub>2</sub>O)<sub>14.6</sub>: triclinic, *P*1, *a* = 15.6259(9), *b* = 15.6226(10), *c* = 15.9349(10) Å,  $\alpha$  = 101.547(2),  $\beta$  = 101.555(2),  $\gamma$  = 103.642(2)°, *V* = 3576.4(4) Å<sup>3</sup>, *Z* = 1,  $\rho_{\text{calc}}$  = 1.283 g cm<sup>-3</sup>,  $\mu(\text{Mo-K}\alpha)$  = 0.1 mm<sup>-1</sup>, *T* = 293 K, *R*1 = 0.0862 for 6784 *F*<sub>o</sub> > 4 $\sigma$ (*F*<sub>o</sub>), *wR*2 = 0.2505 for 8004 independent reflections. 14.6 water molecules were located, distributed over 32 positions. A full description of the structures will be published elsewhere. CCDC 182/991.

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