# *Communications to the Editor*

## Fine-Tuning the Crystal Morphology of Tunnel Inclusion Compounds: A General Strategy

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To explore several properties of crystalline solids and to exploit certain of their applications, it is often crucial to obtain single crystals of the material with a specific desired shape (morphology). However, the crystal morphology produced spontaneously by normal crystal growth procedures is often not the required morphology, and in such cases experimental strategies must be devised to bias the crystal growth toward the desired morphology.[1−8] In principle, mechanical techniques could be used either to constrain the preferred directions of growth or to change the morphology after crystal growth, although such approaches may introduce additional problems, not least the introduction of stresses within the crystals. An alternative strategy is to understand the molecular mechanisms that govern the crystal growth process and to devise techniques to produce the desired crystal morphology by altering aspects of these mechanisms at the molecular level.

In general, crystal growth is governed by kinetic factors, and the observed crystal morphology reflects the relative rates of growth of the crystal in different directions. To alter the crystal morphology, additive molecules (crystal growth inhibitors) may be introduced to interact selectively with certain crystal faces such that the growth of these crystal faces is inhibited. The choice of inhibitor molecule depends on the chemical nature (e.g., the types of functional group) and the structure (i.e., the arrangement of these functional groups) of each crystal face, such that the inhibitor molecule interacts in a selective manner with different crystal faces. Here we present a general strategy for controlling the crystal morphology of solid inclusion compounds that have tunnel host structures,[9] allowing the controlled preparation of crystals with specific morphologies within the broad spectrum ranging from long needle crystals to flat plate crystals. To illustrate the application of this strategy, we focus on urea inclusion compounds[10−14] as a prototypical example of tunnel inclusion compounds.

The host structure in conventional urea inclusion compounds[15,16] comprises a hydrogen-bonded array of urea molecules, based on a hexagonal structure (space group $P6_122$ or $P6_522$). This structure contains one-dimensional tunnels (parallel to the $6_1$ or $6_5$ axis; diameter ca. 5.5−5.8 Å) that are occupied by guest molecules. Appropriate guest molecules are based on an *n*-alkane chain, with only limited substitution allowed. Spontaneous crystal growth of conventional urea inclusion compounds produces a long hexagonal needle morphology (see Figure 2a), indicating that the rate of growth parallel to the tunnel ($k_{||}$) is substantially greater than the rate of growth perpendicular to the tunnel ($k_{\perp}$). We have shown[17] that crystals of alkane/urea inclusion compounds can be induced to grow as hexagonal flat plates, rather than long hexagonal needles, by using a selective crystal growth inhibitor (5-octadecyloxyisophthalic acid; 5-ODOIPA) to inhibit the rate of crystal growth along the tunnel direction, such that $k_{||} \ll k_{\perp}$. Details of the design strategy and mechanism of action of the 5-ODOIPA inhibitor are discussed in ref 17.

Here we demonstrate that the 5-ODOIPA inhibitor can be used in a significantly broader context to produce a broad spectrum of crystal morphologies under experimental control, by altering the concentration (denoted $c_{inh}$) of inhibitor in the crystallization solution. In addition to the two extreme situations corresponding to long needle crystals [for $c_{inh} = 0$; $k_{||} \gg k_{\perp}$] or flat plate crystals [for sufficiently large $c_{inh}$; $k_{||} \ll k_{\perp}$], we focus here on the growth of crystals with comparable dimensions parallel and perpendicular to the tunnel axis, the requirement for which is $k_{||} \approx k_{\perp}$.

Crystal growth of the urea inclusion compound containing hexadecane [$CH_3(CH_2)_{14}CH_3$] guest molecules was carried out in the presence of 5-ODOIPA at different guest/inhibitor molar ratios, but with all conditions otherwise identical. In all preparations, a fixed amount of urea ($1.667 \times 10^{-2}$ mol) was used, and the total number of moles of guest ($n_g$) and inhibitor ($n_{inh}$) was also fixed ($n_g + n_{inh} = 0.150 \times 10^{-2}$ mol). The inhibitor concentration ($c_{inh}$) is defined as: $c_{inh} = 100n_{inh}/(n_g + n_{inh})$. To prepare the crystals, hexadecane and 5-ODOIPA were added to a saturated solution of urea in methanol in a conical flask immersed in an ultrasonic bath at 55 °C. 2-Methylbutan-2-ol was added dropwise until the solution was homogeneous (any precipitate which formed at this stage was dissolved by further addition of a small amount of methanol). The flask was then placed in an incubator at 55 °C and cooled to 25 °C over 24 h. The crystals were collected and washed sparingly with 2,2,4-trimethylpentane. For $c_{inh}$ greater than ca. 5%, there is a tendency[17] to produce crystals of the pure phase of urea, rather than the urea inclusion compound, and we focus here only on cases with $c_{inh} \leq 5\%$.

As a quantitative measure of the crystal morphology of urea inclusion compounds, the conventional aspect ratio ($R$) is defined as $R = W/L$, where $W$ is the distance between opposite corners of the hexagonal {001} face and $L$ is the distance along the [001] direction (tunnel direction). However, this definition of aspect ratio is rather unsatisfactory as it is confined to the range 0−1 for needlelike crystals ($W < L$) and to the range 1 to ∞ for platelike crystals ($W > L$). Instead, a modified aspect ratio ($R_m$) that quantifies the shapes of both needlelike and platelike crystals

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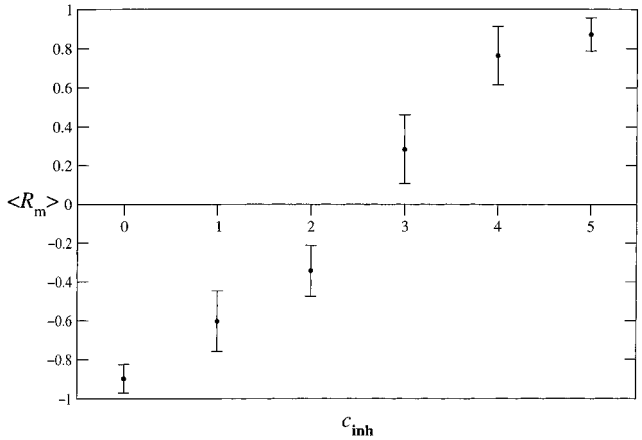


**Figure 1.** Graph of the mean value ($\langle R_m \rangle$) of the modified aspect ratio for crystals of hexadecane/urea versus the concentration ($c_{inh}$) of the 5-ODOIPA inhibitor in the crystal growth experiment. The error bars are estimated from the standard deviations in $\langle R_m \rangle$ (see Table 1), and represent $2\sigma(\langle R_m \rangle)$.

**Table 1.** Mean Values of the Aspect Ratios $R$ and $R_m$, and the Associated Standard Deviations, Measured from a Random Selection of 15 Crystals Taken from Each Preparation of Hexadecane/Urea Using Different Concentrations ($c_{Inh}$) of the 5-ODOIPA Inhibitor

| $c_{inh}$ (%) | $\langle R \rangle$ | $\sigma(\langle R \rangle)$ | $\langle R_m \rangle$ | $\sigma(\langle R_m \rangle)$ |
|---|---|---|---|---|
| 0 | 0.055 | 0.020 | −0.897 | 0.036 |
| 1 | 0.251 | 0.060 | −0.602 | 0.078 |
| 2 | 0.493 | 0.072 | −0.343 | 0.065 |
| 3 | 1.83 | 0.37 | 0.283 | 0.089 |
| 4 | 8.59 | 4.18 | 0.763 | 0.075 |
| 5 | 16.24 | 5.44 | 0.872 | 0.042 |

on the same scale would be more appropriate. Thus, we define a modified aspect ratio:

$$R_m = (R - 1)/(R + 1)$$

[note: $R_m = (W - L)/(W + L)$], with $R_m$ ranging from 0 to −1 for needlelike crystals and from 0 to +1 for platelike crystals.

Figure 1 and Table 1 show the mean value (for a sample of 15 crystals selected at random) of $R_m$ for the hexadecane/urea inclusion compound as a function of the concentration ($c_{inh}$) of the 5-ODOIPA inhibitor, and demonstrate that the aspect ratio changes in a well-defined, monotonic manner as $c_{inh}$ is increased. Optical micrographs of representative crystals obtained from different preparations are shown in Figure 2. From the standard deviations in $R_m$ reported in Table 1, it is clear that a comparatively narrow distribution of crystal morphologies is obtained in each case. Clearly, to prepare crystals with comparable dimensions in directions parallel and perpendicular to the tunnel axis (i.e., $R \approx 1$, $R_m \approx 0$), we require that $c_{inh}$ is in the region of 2−3%, as illustrated in Figure 2b.

Our results demonstrate that, by controlling the concentration of the 5-ODOIPA inhibitor, a broad spectrum of crystal morphologies of alkane/urea inclusion compounds (encompassing long needles, crystals with comparable dimensions in each direction, and flat plates) can be obtained with a high degree of predictability

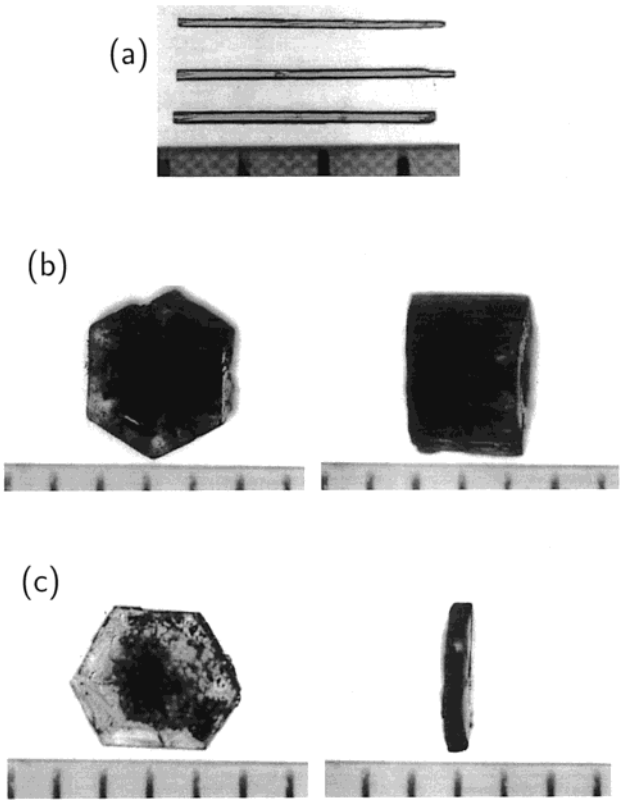


**Figure 2.** Optical micrographs (scale divisions = 1 mm) of crystals of the hexadecane/urea inclusion compound grown: (a) under conventional conditions with $c_{inh}$ = 0% (from top: $R$ = 0.029, $R_m$ = −0.94; $R$ = 0.035, $R_m$ = −0.93; $R$ = 0.045, $R_m$ = −0.91), (b) with $c_{inh}$ = 3% ($R$ = 1.41, $R_m$ = 0.17), (c) with $c_{inh}$ = 5% ($R$ = 8.60, $R_m$ = 0.79). In each of (b) and (c), the same crystal is viewed parallel (left side) and perpendicular (right side) to the tunnel direction.

and control, with the sample of crystals produced from a given preparation having a comparatively narrow distribution of aspect ratios. This crystal growth strategy should be generally transferable, at least in qualitative terms, to urea inclusion compounds containing other types of guest molecules, as well as to other families of solid inclusion compounds based on tunnel host structures (while recognizing that, in quantitative terms, the actual concentration of crystal growth inhibitor required to induce the formation of crystals with a given aspect ratio may be expected to vary from one system to another). This strategy creates the opportunity to prepare single crystals of these materials with the optimal morphology required for any specific application. In terms of the further design and development of crystal growth inhibitors for such applications, it is important to understand fundamental aspects of the mode of action of the crystal growth inhibitor, including issues such as the distribution of the inhibitor molecules at the crystal surface and the nature of their binding to the surface. A range of surface probes are being applied to address these issues as part of our ongoing research in this field.

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