Complexation-Mediated Crystallization. Crystallization of Sodium Acetate Trihydrate Needles from Cyclohexane Solution

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Abstract. The phenomenon of complexation-mediated crystallization is introduced and proposed as a new means for the preparation of novel forms of materials. Attempted crystallization of complexes of salts with crown ethers often results in the precipitation of the uncomplexed salt rather than the complex. In this study, a solution of the 15-crown-5 complex of sodium acetate in cyclohexane precipitated uncomplexed sodium acetate trihydrate as single crystals. The crystal morphology (long needles) of this crystalline sodium acetate stands in sharp contrast to the hexagonal plates known to form from aqueous solution. X-ray diffraction analysis revealed that sodium acetate as crystallized from cyclohexane 'solution' adc.pted a crystal lattice identical to that in sodium acetate crystallized from aqueous solution. Possible origins of the change in crystal morphology are discussed.

Key words. Sodium acetate, crystallization, non-aqueous, morphology.

1. Introduction

Literally hundreds if not thousands of crystalline complexes of organic and inorganic salts with crown ether type compounds have been prepared and characterized by X-ray crystallography. Indeed, X-ray structure determination has played a crucial role in the development of the field of complexation chemistry [2]. What is often found but rarely reported is that improper choice of solvent for crystallization of complexes of salts not infrequently results in precipitation of the *uncomplexed* salt [3]. Rather than appearing a nuisance, this phenomenon struck us as providing the most unusual opportunity for preparing potentially novel solid phases of salts through their precipitation or crystallization from solvents in which they are ordinarily completely insoluble (i.e., effectively *non*solvents). Accordingly, we have embarked on an exploration of the growth of single crystals from *non*solvents through the intermediacy of complex formation.

Herein we report the crystallization of sodium acetate trihydrate from *cyclohexane* solution and the X-ray crystallographic determination of its structure. Sodium acetate trihydrate is typically obtained from aqueous solutions in the form of hexagonal plates. Though some disputes have arisen through the years over the

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proper space group assignment and crystal lattice parameters, it now appears well settled that the hexagonal plate habit results from a $C2/c$ space group lattice [4–9]. An alternative morphology of crystalline sodium acetate trihydrate was obtained by Zelingher [10] through his technique of slow diffusion/evaporation of aqueous solutions through a cellulose acetate membrane. Though the resulting 'whiskers' of sodium acetate trihydrate were quite imperfect, containing extensive twinning, channeling, broadening, and branching, X-ray powder diffraction data were interpreted to demonstrate again a $C2/c$ space group, with lattice parameters essentially identical to those of the hexagonal plate form.

We have found that sodium acetate trihydrate may be crystallized from cyclohexane solution, through the intermediacy of its 15-crown-5 complex, in the form of long, slender needles. As this crystalline habit appeared distinct from both the hexagonal plate and whisker forms, we subjected this material to single crystal X-ray diffraction analysis. We herein report the details of these studies and discuss the implications of the phenomenon of complexation-mediated crystallization in the preparation of new crystalline habits or lattices.

2. Experimental Section

2.1. CRYSTALLIZATION

An excess of solid sodium acetate was shaken vigorously with a dichloromethane solution of 15-crown-5 (1, 4, 7, 10, 13-pentaoxacyclopentadecane) in a snap-cap vial for several minutes. The suspension was filtered through glass wool into a test tube, then excess cyclohexane was carefully layered onto the filtered solution. The tube was loosely capped and allowed to stand undisturbed for three months. The long, opaque needles which formed were isolated by decantation of the remaining mother liquor (composed of the sodium acetate complex of 15-crown-5 in cyclohexane) and air dried.

2.2. STRUCTURE DETERMINATION

Data were collected on an opaque needle-shaped crystal of approximate dimensions $0.7 \times 0.1 \times 0.1$ mm. No precautions were taken to avoid desolvation effects. The crystal was mounted in an arbitrary orientation on a glass fiber which was then fixed onto a copper pin and placed on a goniometer. Diffraction data were collected on a Syntex/Nicolet P2$_1$ diffractometer. Fifteen accurately centered reflections were used to obtain an orientation matrix for data collection. Unit cell parameters and data collection data are provided in the supplementary material. Two standard reflections [(4 0 −10) and (5 −3 −10)] were monitored at 50 reflection intervals as a check for decomposition; no variation in intensity was observed.

The space group was determined to be $C2/c$ from systematic absences and subsequent successful solution and refinement of the structure. The diffractometer data were then processed and corrected for absorption effects. Though there was some initial uncertainty about the composition of the crystals, the structure of $Na(OCOCH_3)(H_2O)_3$ repeatedly appeared as the correct structure in the direct methods solutions. Several cycles of least-squares refinement with anisotropic

temperature factors for all non-hydrogen atoms gave a final R factor of 5.2%. The program SHELX76 [11] was employed in the direct methods solutions; SHELX76 [12] was employed in all least-squares refinements. The final difference Fourier map was essentially featureless. Final atomic coordinates, bond distances and angles, anisotropic thermal parameters, and observed and calculated structure factors are provided in the supplementary material.

3. Discussion

Sodium acetate has been crystallized from a number of different solvents, including water, aqueous or alcoholic formamide, and aqueous acetic acid [13]. From aqueous solvents at lower temperatures, the trihydrate appears to be the dominant form, though the tetrahydrate has also been obtained. Of necessity, sodium acetate has never been crystallized from organic solvents such as dichloromethane or cyclohexane, as it is completely insoluble in such solvents.

Attempted crystallization of the 15-crown-5 complex of sodium acetate from methylene chloride/cyclohexane solution resulted in the deposition of pure, crystalline sodium acetate trihydrate. This general phenomenon, namely the deposition of inorganic phases rather than complexes upon attempted crystallization, has been recognized ever since the first reports of macrocyclic polyether complexation. To our knowledge, however, these inorganic phases have never been obtained in single crystal form, and no structural analyses of such deposited phases have ever been reported. This method of decomplexation/crystallization, which we refer to as *complexation-mediated crystallization*, would appear to allow almost routine formation of solid phases of organic or inorganic salts from their solutions, in the form of their complexes, in solvents in which they would ordinarily be completely insoluble. As even relatively subtle changes in solvent, concentration, temperature, or impurities are well-recognized for their ability to affect crystal morphology as well as internal lattice structure [14], we are quite intrigued by the prospect that the drastic alteration of crystallization conditions provided through complexation-mediated crystallization may result in the formation of new and unusual forms of otherwise common materials.

In the case at hand, complexation-mediated crystallization from cyclohexane solution, through the intermediacy of 15-crown-5 complexation, afforded sodium acetate trihydrate in the form of long, slender needles (Figure 1). This crystalline habit appears to represent a new morphology for sodium acetate trihydrate, which has previously been obtained in the form of hexagonal plates (Figure 2) or whiskers. X-ray diffraction analysis revealed that the trihydrate crystallized in the form of polymeric chains. The repeat unit of the chains, $Na(H_2O)_3(OCOCH_3)$, is depicted in Figure 3, while a segment of one chain, the dimeric unit, $Na_2(H_2O)_6(OCOCH_3)_2$, is shown in Figure 4. Each sodium ion is roughly octahedrally coordinated, with coordination by one terminal H_2O, four bridging H_2Os (two bridging to each adjacent sodium), and one acetate. Metrical parameters for the acetate ligands support simple, monodentate coordination, [15] with bond localization, giving average bond lengths for the C—O of 1.34 Å and for the C=O of 1.18 Å. More thorough discussions of the crystal and molecular geometries of sodium acetate trihydrate may be found in literature reports of the
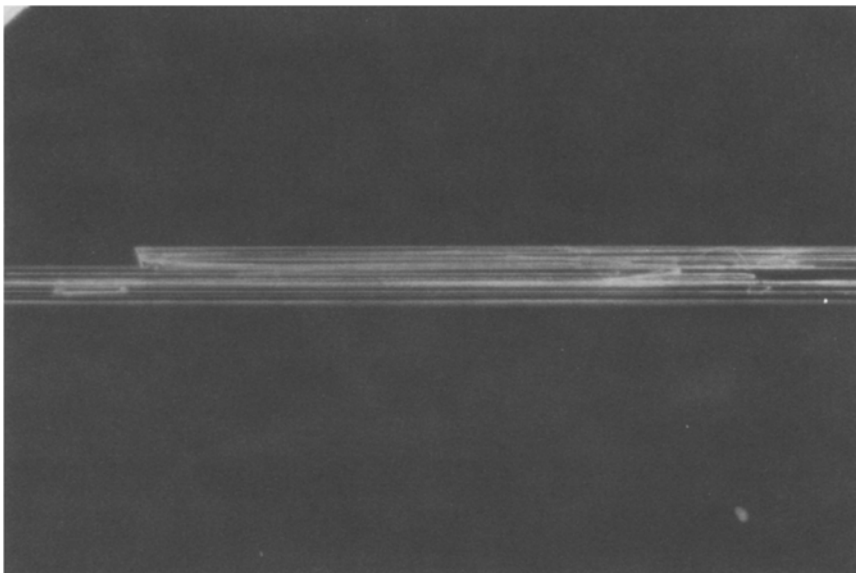
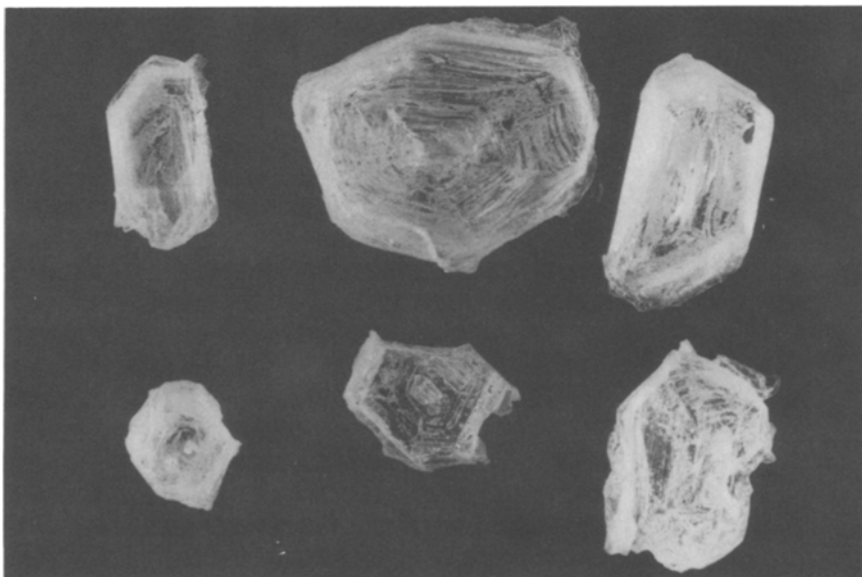Fig. 1.   Photomicrograph of $Na(H_2O)_3(OCOCH_3)$ needles (see [22]). The scale represents 1.0 mm.

Fig. 2.   Photograph of $Na(H_2O)_3(OCOCH_3)$ 'blocks' as obtained from slow evaporation of aqueous solutions. The crystal in the upper right corner has dimensions $12.0 \times 6.0 \times 2.3$ mm.
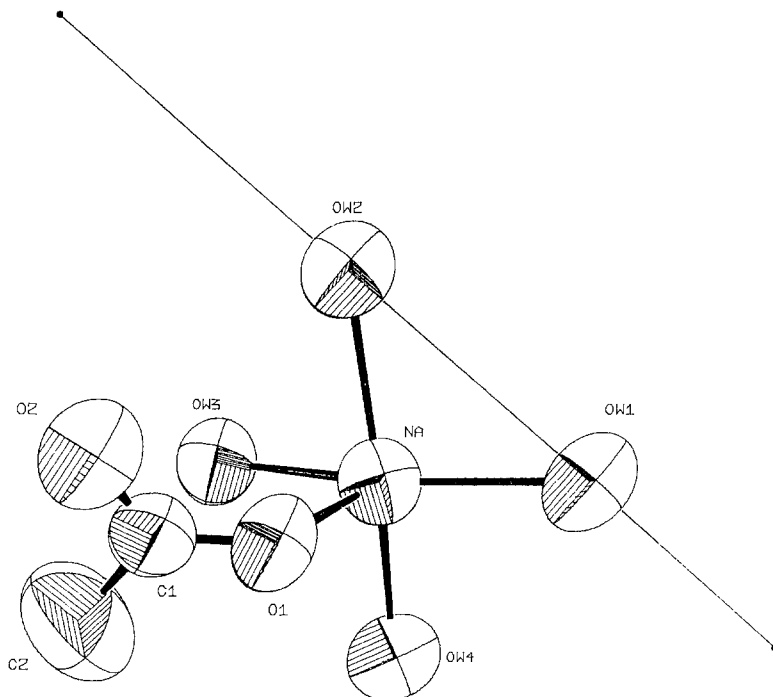
Fig. 3.   ORTEP view of the $Na(H_2O)_3(OCOCH_3)$ moiety which makes up the asymmetric unit. Atoms OW1 and OW2 lie on a crystallographic two-fold axis. Probability ellipsoids are at 75%.
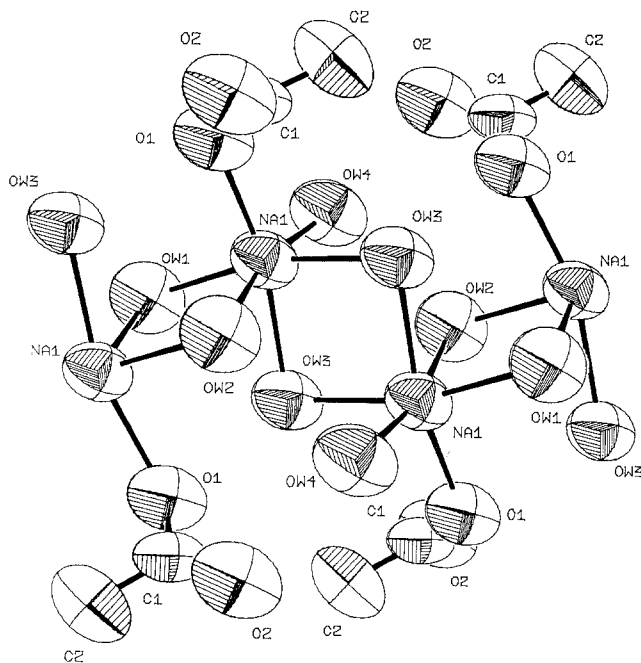
Fig. 4.   ORTEP view of a portion of the polymeric chain found in sodium acetate trihydrate crystallized from cyclohexane solution.

hexagonal plate form obtained through conventional crystallization from aqueous solution [4–9].

The solid state structure of sodium acetate was first explored as early as 1909, [16] and several reports of its three-dimensional structure have appeared in the literature through the years [4–9, 17]. Sodium acetate crystallized from cyclohexane with a different crystal habit, but, somewhat surprisingly, with an identical degree of hydration and crystal lattice environment as when it was crystallized from water. (Exposure to adventitious moisture evidently was responsible for hydration of the originally anhydrous sodium acetate used. Given the time required for the crystallization, atmospheric moisture appears the most likely source.) Clearly this sodium acetate structure is energetically compelling, as the compound finds this crystal lattice as it precipitates from either water or cyclohexane.

Addadi, Lahav, Leiserowitz, and coworkers have presented an exceptional series of studies on the use of additives to alter the habits of organic crystals [18]. As complexation-mediated crystallization also appears to provide a perhaps general opportunity for crystal habit alteration, it is instructive to compare this approach to that used by Addadi, *et al.*

Morphological changes induced by additives in the Addadi systems may be rationalized by a careful consideration of the interaction of the additive with growing crystal faces. If selective adsorption onto one (or several) face(s) of the crystal occurs, then growth of these faces may be slowed relative to the growth of faces on which the additive is not adsorbed. As crystal morphology appears to be largely a result of the relative rates of growth of crystal faces, understanding of these selective interactions of additives with faces can directly yield an understanding of the observed morphological changes. It is perhaps important to note that the adsorbing additives are incorporated within the crystals under these growth conditions. Solvents *may* in some cases be occluded within crystals grown under the conditions of complexation-mediated crystallization, though this was not observed in the present study of sodium acetate trihydrate.

Complexation-mediated crystallization may bear some resemblance to this additive modification process, in that the crown ether (15-crown-5 in this case) may interact selectively with sodium ions on one (or more) of the growing faces of the sodium acetate crystal. This interaction could well play a role in the determination of crystal morphology. Certainly the crown ether can interact with the surface of a crystal; this presumably is the first stage of solubilization of a salt in organic solution by crown ethers [19]. Given the observed crystal lattice of sodium acetate trihydrate, however (vide infra), one might reasonably expect any crown ether interactions with lattice sodium ions to be most pronounced along the *c*-axis. This interaction would be expected to slow crystal growth in this axis direction. In fact, the opposite is observed (vide infra); crystal *elongation* occurs preferentially along the *c*-axis.

We believe that a more global change in crystallization conditions is effected under the conditions of complexation-mediated crystallization, however. All questions of selective interaction with crown ether aside, the most significant change under these conditions would appear to be the dramatic change in solvent from water to cyclohexane. There is no question but that growing crystal faces are solvated to a greater or lesser extent during the crystallization process. One might

reasonably expect that this solvation, though perhaps more difficult to understand in a simple manner than selective adsorption, could play a role as significant as that of the adsorbing additives in the Addadi systems. Growing a crystal in cyclohexane medium rather than an aqueous one would appear to provide an *extremely* drastic alteration in face solvation. This ability to effect crystallization from solvents in which the crystallizing entity would ordinarily be completely insoluble, in fact, would appear to be one of the primary advantages of complexation-mediated crystallization over previously reported crystallization techniques. Though the effects of crown ether adsorption on faces cannot be readily dissected from our observations, it seems reasonable to focus on alteration of crystal face solvation as the major contributor to morphological alteration under the conditions of complexation-mediated crystallization.

Given this discussion, one must now question whether our observed change in morphology is explicable based upon solvation alteration. Again, crystal habit is largely the result of differing growth rates for different crystal planes, with the slowest growing faces dominating the appearance of the crystal [20]. One may speculate on the factors which may be responsible for the alteration in sodium acetate trihydrate crystal habit upon changing the crystallization medium from water (hexagonal plates) to cyclohexane (needles). One could perhaps view the sodium acetate trihydrate dimer repeat unit of the polymeric chain as an amphiphilic unit, with a rather polar, hydrophilic 'head' and 'tail', but relatively hydrophobic sides [21]. Three dimensional crystal growth then involves packing of these amphiphilic repeat units together, with newly depositing units having a choice of adding to the head or tail of a growing chain, thus extending the chain, or to the sides of an existing chain, thereby broadening the cross section of the growing crystal. In the case of crystallization from aqueous solution, one might expect aggregation of the comparatively hydrophobic sides of the units to be most thermodynamically compelling; extensive solvation of the hydrophilic ends of the growing chains would serve to slow further growth along this crystal axis. The net result of such enhanced lateral growth, at the expense of axial growth, would be the observed plate habit (Figure 5). Crystallization from cyclohexane solution, however, presents the growing crystal with a completely different environment. Now the solvent molecules find more beneficial interactions with the relatively hydrophobic *sides* of the growing chains rather than the ends. This solvation of the sides should slow lateral growth, while axial growth may continue unfettered by solvent molecules. Enhanced axial growth should lead to the elongated, needle-like crystalline habit observed to form under these conditions (Figure 5). Figure 6 displays a packing diagram for sodium acetate trihydrate which perhaps provides a more realistic depiction of these effects at work in the case at hand.

Careful examination of the three-dimensional structure of the sodium acetate trihydrate lattice provides positive support for this admittedly simplistic analysis. Hydrogen bonding between acetate carbonyls and waters of hydration form sheets in the *ab*-plane of the crystal lattice, parallel to the (001) faces of the crystal, while edge sharing of oxygen coordination polyhedra build up the structure in the *c*-direction [7]. Additional interactions are also present in the *ab*-plane however, as first noted by Cameron *et al.* [6]. In particular, the methyl groups of the acetate ligands efficiently fill the center of the unit cell, with several quite short C—C
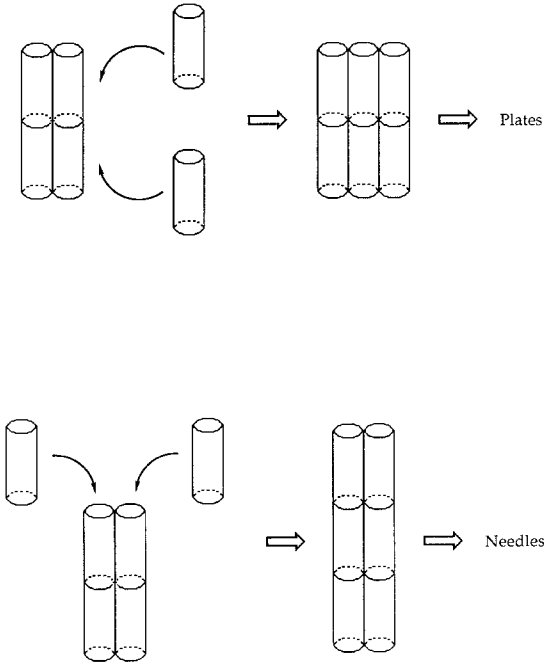
Fig. 5.   Schematic depiction of crystal growth processes leading to plate and needle habits of sodium acetate trihydrate (see text).
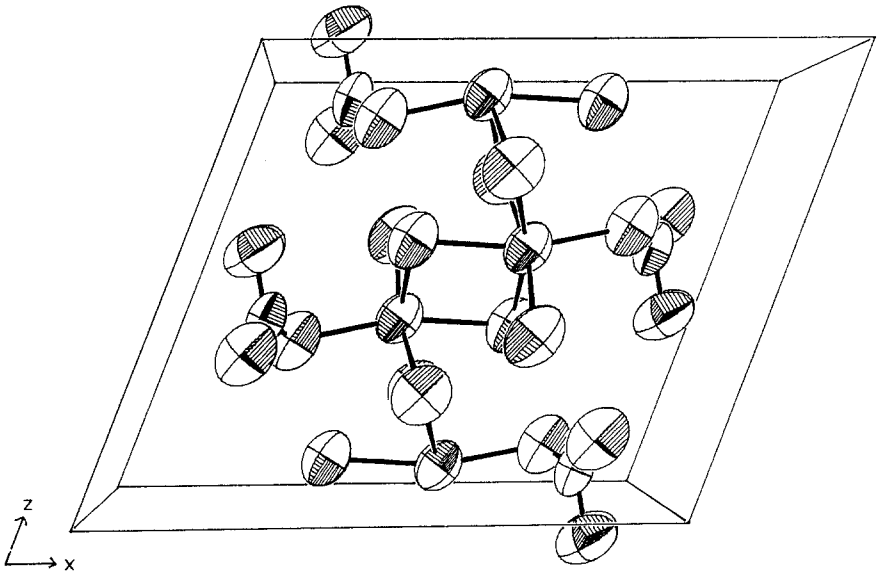

Fig. 6.   Packing diagram (looking down the y-axis) illustrating the intrastrand arrangement which allows sodium acetate trihydrate to crystallize in the form of needles from cyclohexane solution. Note the relatively hydrophobic surface of the strand, formed by the methyl groups of the acetate ligands.

distances of 3.6–3.8 Å. In other words, the *ab*-plane is built up through hydrogen bonding *and* hydrophobic interactions of the methyl groups, while the *c*-direction is built up primarily through ion-dipole interactions. Solvation by water might be expected to be rather significant on all growing faces of the crystal. However, cyclohexane solvation would appear to be most significant in the *ab*-plane, where interactions with the comparatively hydrophobic methyl groups are possible. These considerations, then, would lead one to suggest that crystallization from cyclohexane solution should lead to enhanced growth in the *c*-direction and in fact this is the case. The long axis of the needle crystals obtained from cyclohexane solution through complexation-mediated crystallization is indeed the *c*-axis, and the 'cartoon' depiction of crystal growth processes in Figure 5 would appear to have some heuristic value.

We are continuing our investigations into the phenomenon of complexation-mediated crystallization, and will report further developments in due course.

Acknowledgments

Notes and References

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19. A detailed understanding of such crown ether interactions may well prove extremely elusive, with any explanations really needing to go to the very heart of the nature of the complexation/decomplexation process.

20. See, for example: J. W. Mullin: *Crystallization*, 2nd edition. Butterworth: London (1972).

21. This of course represents an extreme simplification; sodium acetate ionic structures in aqueous solution most likely differ significantly from those of the complex in cyclohexane solution. Nevertheless, this discussion serves to suggest some of the *possible* factors entering into the alteration of crystal habit under the conditions of complexation-mediated crystallization.

22. Photographs of the needles obtained from cyclohexane solution were unfortunately not obtained. However, we have discovered that sodium acetate trihydrate trihydrate may be recrystallized from isopropanol in the form of needles of identical appearance. The photograph in Figure 1 is of these needles. Importantly, the discussion of selective solvation presented in the text appears completely consistent with needle formation from isopropanol.