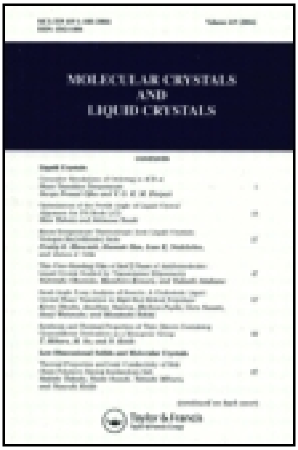

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Crystallization of Salts of Organic Acids from Non-Conventional Solvents

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Crystallization of sodium acetate trihydrate from water affords hexagonal plates. When crystallized from cyclohexane, a solvent in which this salt is completely insoluble but in which it may be solubilized by macrocyclic crown polyethers, needle-shaped crystals are produced. This habit change is consistent with selective solvation of hydrophilic vs. hydrophobic crystal faces by water and cyclohexane, respectively. Potassium hydrogen tartrate crystallizes from warm water in the form of prisms elongated along [001]. Crystallization at water/organic solvent (chlorinated hydrocarbon) interfaces, again mediated by the formation of organic solvent-soluble complexes with macrocyclic crown polyethers, affords distinctive prism forms. In these two-phase (aqueous/organic) solvent systems, the nature of the solvent and/or the crown polyether plays a significant role in determining crystal form.

Keywords: habit modification; crystal growth; complexation; nonaqueous

INTRODUCTION

Given the critical importance of crystal form to an astoundingly wide variety of technological applications, ranging from optoelectronic devices to pharmaceutical formulations, development of techniques for the control of the morphology of crystalline materials, be they bulk materials, thin films, or nanoparticles, is an area of intense and active exploration. Perhaps the most powerful and generally applicable developments have been in the use of additives as habit modifiers,[1] an effect known since at least the late 1700's, when de l'Isle reported the generation of octahedral sodium chloride crystals upon crystallization from aqueous solutions containing urea. Often, the effects of such additives may be ascribed to their selective interaction with particular crystal lattice planes, resulting in a slowing of the growth of these planes and therefore in their expression in the final crystal form.[2] Choice of crystallization solvent can also play a key role in the determination of crystal morphology, often due to the same underlying interactions as seen for additive effects. Thus, the selective interaction of various solvents with different crystal lattice planes has been reported to lead to the understandable and predictable alteration of crystal form for a variety of crystalline organic materials.[3] However, exploitation of solvent effects has only rarely been reported for the alteration of crystal morphology for highly polar organic and inorganic salts, for the simple reason that few solvents other than water are available in which such materials will dissolve.[4]

Since Pedersen's pioneering report in 1967 of the ability of macrocyclic polyethers to solubilize salts in nonaqueous media,[5] an extraordinary range of such macrocyclic complexes have been prepared, and a myriad of complexes have been crystallized and structurally characterized by single crystal x-ray diffraction and other solid-state techniques. In the course of attempting to obtain crystalline materials for such analyses, it is not infrequently found that the salt precipitates rather than the desired complex, particularly for those salts with comparatively high lattice energies. Rather than viewing this outcome as a problem to be circumvented, we have focused our attention on just these cases, as they represent the opportunity to exploit the often powerful effects of solvent on crystal morphology for the alteration of morphology of both hydrophilic salts and the solid-state materials derived therefrom via salt metathesis reactions.[6,7]

RESULTS AND DISCUSSION

Sodium Acetate Trihydrate

When sodium acetate trihydrate is crystallized from water, hexagonal tablet-like crystals are obtained, with the crystallographic *a*- and *b*-axes defining the plane of the tablets.[8] Several years ago, we reported the 15-crown-5 (1,4,7,10,13-pentaoxacyclopentadecane) mediated recrystallization of this salt from cyclohexane solution, which affords slender prismatic crystals elongated along the crystallographic *c*-axis.[9] Consideration of the crystal lattice of sodium acetate trihydrate (identical in the two crystal forms) provides a simple rationalization of this dramatic change in crystal habit. The salt crystallizes in the form of infinite chains of sodium ions joined by two bridging water ligands, with each sodium bearing an additional nonbridging water and a monodentate acetate ligand. These chains, oriented along the crystallographic *c*-axis, are packed in parallel to form the bulk crystalline material, and the parallel chains place the methyl groups of the acetate ligands in close proximity to one-another, suggesting that there is a hydrophobic component to the packing. For a growing nucleus of sodium acetate trihydrate in water, comparatively little interaction of the solvent with the hydrophobic chain surfaces is expected, leaving these surfaces free to grow and leading to the formation of the observed tablet-like crystals. In contrast, a growing nucleus in cyclohexane is expected to experience more significant interactions of this nonpolar solvent with the hydrophobic surfaces, slowing their growth while growth along the chain axis proceeds unfettered and resulting in the formation of slender prismatic crystals.

Potassium Hydrogen Tartrate

Initial attempts to expand these studies of solvent effects on crystal form of salts of organic acids to the dipotassium salt of (*L*)-(+)-tartaric acid led to the isolation from chloroform solution of a peculiar 9-coordinate potassium complex of 18-crown-6 (1,4,7,10,13,16-hexaoxacyclooctadecane) containing chloride rather than tartrate as the counteranion.[10] This, together with the rather sparing solubility of dipotassium tartrate in nonaqueous solvents even in the presence of excess 18-crown-6, led to the study of a two-phase system, in which an aqueous solution of dipotassium tartrate was layered above a solution of 15-crown-5 in dichloromethane. This procedure, originally anticipated to provide access to a crystalline crown ether complex of dipotassium tartrate, does indeed result in slow growth of single crystals of good quality. However, x-ray diffraction analysis clearly indicates that the material is potassium hydrogen tartrate (potassium bitartrate), not dipotassium tartrate. Since dipotassium tartrate may be successfully recrystallized from water, the crystallization of potassium bitartrate in these two-phase crystallizations was unexpected. Its formation is apparently due to the desired initial solubilization of tartrate in the organic phase, followed by deprotonation of either the solvent or dissolved water by the tartrate ion, which is rendered more highly basic in the nonaquous environment. The resulting formation of the sparingly soluble potassium bitartrate then leads to its crystallization.

Crystallization of potassium hydrogen tartrate from warm water affords prismatic crystals elongated along [100] (Figure 1), while crystallization from hot water generally affords platelike forms with analogous features, but with more prominent (001) faces.[11] Alteration of the crystal form of potassium hydrogen tartrate as a function of solution pH has been noted.[12] The influence of organic additives on the nucleation and growth forms of this salt has been reported in the context of its crystallization in wine, wherein it represents a natural product whose formation as a crystalline solid is undesirable.[13]

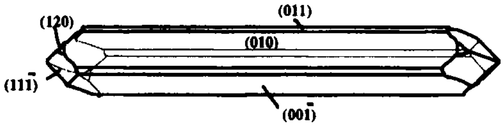

FIGURE 1 Crystal form of potassium hydrogen tartrate from warm water.

Somewhat surprisingly, given the presence of water in the two-phase crystallization, the resulting potassium hydrogen tartrate crystal form (Figure 2) is significantly different from that obtained in purely aqueous recrystallizations of this salt.

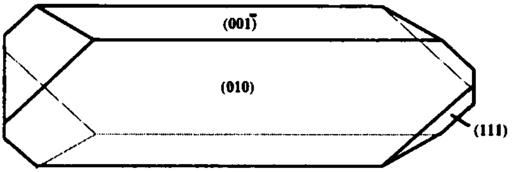

FIGURE 2 Crystal form of potassium hydrogen tartrate from aqueous dipotassium tartrate in contact with 15-crown-5 in CH_2Cl_2.

Given the expected strong interaction between 15-crown-5 and potassium ion, it seems likely that not only the solvent, but also the crown ether may exert an influence on the growth of the crystalline salt, since it presumably delivers the potassium ion to the growing crystal before releasing its chelating grip on it. In order to explore this possibility, a closely related crystallization was studied, differing only in the use of 18-crown-6 in place of 15-crown-5. Prismatic crystals were again obtained, but of distinctive form (Figure 3), suggesting that the crown ether does indeed actively participate in the process of crystal growth rather than serving merely to solubilize the salt.

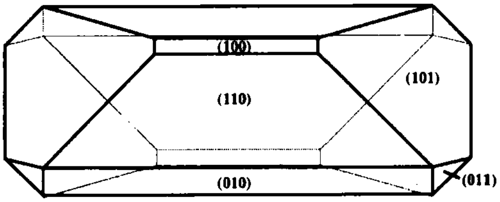

FIGURE 3 Crystal form of potassium hydrogen tartrate from aqueous dipotassium tartrate in contact with 18-crown-6 in CH_2Cl_2.

Although a number of morphological differences are apparent between the crystals obtained using 15-crown-5 (Figure 2) and 18-crown-6 (Figure 3), one of the most striking is the emergence of (100) faces in the 18-crown-6-mediated crystallization. The crystal lattice of potassium hydrogen tartrate may be considered to be comprised of two-dimensional sheets of intermolecularly hydrogen bonded bitartrate ions.[14] These sheets, separated by charge-balancing layers of potassium ions, stack along the crystallographic *a*-axis to form the bulk crystal. Given the absence of (100) surfaces in crystals obtained from aqueous solution, crystal growth along this potassium-mediated stacking direction is clearly comparatively rapid in water. Use of 15-crown-5 in the two-phase system does not demonstrably impact the relative growth rate of (100) surfaces. However, 18-crown-6 clearly slows the rate of growth of the (100) surfaces, leading to their appearance in the bulk crystal. This crown ether interacts more strongly than 15-crown-5 with potassium ion in homogeneous solution, and this stronger interaction is apparently expressed in a stronger interaction with the potassium ion layers of the crystal lattice as well, inhibiting growth in this direction.

The role of the nonaqueous solvent is clearly indicated by an analogous crystallization using 18-crown-6 in carbon tetrachloride in place of dichloromethane. Prismatic crystals with distinctive form are obtained (Figure 4), confirming that the solvent does assist in determination of crystal form even in these two-phase systems, in which water might have been expected to dominate in the growth process. The role of the solvent may parallel that proposed in the sodium acetate studies, with the less polar carbon tetrachloride interacting differently with various lattice planes than the more polar and potentially hydrogen bonding dichloromethane. Alternatively, the reduced polarity of carbon tetrachloride, providing a less supportive solution environment than dichloromethane for the potassium crown ether complex, is expected to result in an enhanced interaction of the crown ether with the potassium ion lattice planes, further slowing crystal growth along this crystallographic axis and consistent with the dramatically enhanced expression of (100) surfaces (Figure 4).

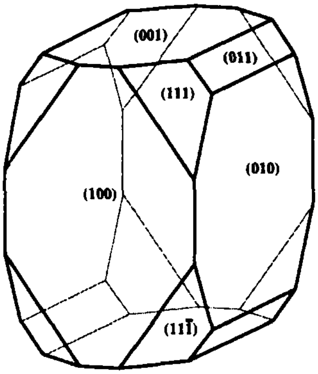

FIGURE 4 Crystal form of potassium hydrogen tartrate from aqueous dipotassium tartrate in contact with 18-crown-6 in CCl_4.

CONCLUSIONS

Complexation-mediated crystallization clearly offers the opportunity for dramatic alteration of the crystal morphology of salts of organic acids. Observed alterations in crystal morphology are apparently due to selective interactions of organic solvents and of the crown ethers used to solubilize the salts in them with various crystal lattice planes. Computational and experimental studies to address the molecular-level nature of the crown polyether and solvent interaction(s) responsible for the observed changes in growth form are currently under investigation.

EXPERIMENTAL

Above a solution of 15-crown-5 (1,4,7,10,13-pentaoxaxcyclopentadecane) in CH_2Cl_2 in a *ca.* 15 mm diameter test tube was placed an approximately equal volume of a saturated solution of dipotassium (2*R*,3*R*)-tartrate [(*L*)-(+)-tartrate] in water. The tube was tightly capped and allowed to stand for *ca.* 2 months, at which time the solvents were removed by pipette and the crystalline product was rinsed with water and with CH_2Cl_2. The product, mp 262-273 °C (dec), insoluble in dimethyl sulfoxide, was confirmed by single crystal x-ray diffraction analysis to be potassium hydrogen tartrate. Crystallographic data were in accord with those reported earlier for this compound, and are thus not provided here. Preparations of potassium hydrogen tartrate using CCl_4 and 18-crown-6 (1,4,7,10,13,16-hexaaoxaxcyclooctadecane) proceeded analogously. Crystal forms were recorded for archival purposes by photomicroscopy. The SHAPE program[15](version 4.2) was used to generate schematics of crystal morphology.

Acknowledgments

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References

[1.] See, e.g., I. Weissbuch, L. Leiserowitz, and M. Lahav, in *Crystallization Technology Handbook*, edited by A. Mersmann (Marcel Dekker, Inc., New York, 1995), p. 401.

[2.] A. Wells, *Phil. Mag., Ser. 7*, **37**, 184 (1946); I. Sunagawa, Ed., *Morphology of Crystals* (Terra Scientific Publishing Co., Tokyo, 1987).

[3.] Surface roughening: P. Bennema, *J. Cryst. Growth*, **122**, 110 (1992); J. R. Bourne and R. J. Davey, *J. Cryst. Growth*, **36**, 278 (1976). Surface inhibition: R. J. Davey, B. Milisavljevic, and J. R. Bourne, *J. Phys. Chem.*, **92**, 2032 (1988); F. C. Wireko, L. J. W. Shimon, F. Frolow, Z. Berkovitch-Yellin, M. Lahav, and L. Leiserowitz, *J. Phys. Chem.*, **91**, 472 (1987).

[4.] R. M. Hooper, B. J. McArdle, R. S. Narang, and J. N. Sherwood, in *Crystal Growth*, edited by B. R. Pamplin (Pergamon Press, New York, 1980), 2nd Edition, p. 397.

[5.] C. J. Pedersen, *J. Am. Chem. Soc.*, **89**, 7017 (1967).

[6.] K. M. Doxsee, D. S. Keegan, H. R. Wierman, J. Hagadorn, and M. Arimura, *Pure Appl. Chem.*, **65**, 429 (1993).

[7.] K. M. Doxsee, US patent 5,545,394, 13 August, 1996.

[8.] V. M. Padmanabhan, *Curr. Sci. (India)*, **21**, 97 (1952); A. Kalman, *Acta Crystallogr.*, **19**, 853 (1965); T. S. Cameron, Kh. M. Mannan, and Md. O. Rahman, *Acta Crystallogr., Sect. B*, **32**, 87 (1976); K.-T. Wei and D. L. Ward, *Acta Crystallogr., Sect. B*, **33**, 522 (1977); L. Y. Hsu and C. E. Nordman, *Acta Crystallogr., Sect. C*, **39**, 690 (1983); V. A. Efremov, N. O. Endeladze, V. M. Agre, and V. K. Trunov, *Zh. Strukt. Khim.*, **27**, 177 (1986) [*J. Struct. Chem.*, **27**, 498 (1986)].

[9.] K. M. Doxsee and R. C. Stevens, *J. Inclusion Phenomena*, **9**, 327 (1990).

[10.] K. M. Doxsee, H. R. Wierman, and T. J. R. Weakley, *J. Am. Chem. Soc.*, **114**, 5165 (1992).

[11.] S. Veintemillas-Verdaguer and R. Rodriguez-Clemente, *J. Cryst. Growth*, **99**, 211 (1990).

[12.] K. Aleksandrzyk, B. Wiktorowska, and B. Wojciechowski, *J. Cryst. Growth*, **52**, 868 (1981).

[13.] R. Rodriguez-Clemente and I. Correa-Gorospe, *Am. J. Enol. Vitic.*, **39**, 169 (1988); V. Gerbaud, N. Gabas, J. Blouin, and C. Laguerie, *J. Cryst. Growth*, **166**, 172 (1996); V. Gerbaud, N. Gabas, C. Laguerie, J. Blouin, S. Vidal, M. Moutounet, and P. Pellerin, *Chem. Eng. Res. Design*, **74**, 782 (1996); H. Tanahashi, H. Nishino, K. Tojo, and T. Nakai, *J. Chem. Eng. Jpn.*, **25**, 342 (1992).

[14.] M. Akkurt, T. Hökelek, and H. Soylu, *Z. Krist.*, **181**, 161 (1987); J. Buschmann and P. Luger, *Acta Cryst., Sect. C*, **C41**, 206 (1985).

[15.] E. Dowty and R. P. Richards, *SHAPE, A Computer Program for Drawing Crystals*, Macintosh v. 4.2, Shape Software, Kingsport, Tennessee, USA.