Mechanism of Several Solid−Solid Transformations between Dihydrated and Anhydrous Copper(II) 8-Hydroxyquinolinates. Proposition for a Unified Model for the Dehydration of Molecular Crystals

Samuel Petit and Gérard Coquerel*

Laboratoire de Modélisation Moléculaire, Centre Régional Universitaire de Spectroscopie,
I.F.R.M.P. No. 23, Université de Rouen, F 76 821 Mont Saint Aignan Cedex, France

Received January 23, 1996. Revised Manuscript Received June 5, 1996[⊗]

An attempt to describe, at a molecular level, solid−solid transformations between copper(II) oxinates of known structure is presented. On the basis of experimental data and by modeling the molecular movements, it is shown that the dehydration of the stable dihydrated form (β) takes place with the transmission of structural information from the parent to the daughter phase, so that a coherence is maintained. After the departure of water molecules through channels, the resulting unstable new anhydrous material (NAM) reorganizes rapidly toward one of the two closest energy minima: X′ or β', depending on whether an adduct is present or not in the parent structure. Polymorphic transitions from the anhydrous metastable forms (β', γ', X′) to the stable form (β'') are described by a nucleation and growth mechanism, with a complete loss of the structural information contained in the parent phase. Both proposed mechanisms (continuous and cooperative processes for the dehydration, and nucleation and growth mechanism for the polymorphic transitions) are consistent with available experimental results: crystal structures, routes of preparation, evolution of the crystal size distribution (CSD), specific surfaces, SEM photographs, and DSC results. An extension of this study together with several other examples led to a unified model for the dehydration mechanism of molecular crystals being proposed. Four decisive topological, energetic, and physical criteria are proposed. The mechanisms are related to the possible filiation of structural information and fall into two categories: class I mechanisms are associated with the absence and class II mechanisms correspond to the presence of structural filiation. Each class is divided into several subclasses according to the process of release of water molecules (cooperative or destructive) and to the eventual process of reorganization (cooperative or through a nucleation and growth process).

Introduction

Polymorphic transitions and decompositions of solvates are very common problems the organic chemist has to deal with. In both types of transformation, the organic or metal−organic compounds modify their molecular conformation and/or the packing of the molecules. The previous attempts to describe the mechanisms involved, for either organic or inorganic compounds, fall into two categories:[1,2]

(1) "Continuous" models[3−8] assume that transformations take place by means of a progressive reorientation and/or translation of the molecules in the crystals. It is supposed that these reactions are smooth and cooperative in the core of the crystal and involve molecular movements of weak magnitude.

(i) Decompositions of solvates are supposed to occur by the progressive evacuation of the solvent through interlayer planes or channels, controlled by an overall diffusion process. Therefore, the reorganization begins in the inner part of each particle, without loss of crystallinity. These reactions are said to be topotactic when the reaction proceeds throughout the entire volume of the crystal. For this type of transformation, the parent and daughter phases should be of great structural similarity, so that a filiation can be described between the two crystallographic lattices. (Hereafter, "filiation" is defined as a retention of structural information of the reactant in the product phase.) This model was applied for the dehydration study of molybdenum and tungsten oxides.[5] A mechanism of the same type was also proposed for other mineral compounds.[6]

(ii)Polymorphic transitions are termed displacive when atoms or molecules shift by small fractions of unit-cell dimensions, so that the topology of the molecular network is preserved. This type of transition was explained in terms of "soft" modes of lattice vibration and mainly applied to molecular crystals.[3]

Since contacts are continuously maintained between molecules during the transformation, this type of mechanism leads to at least part of the structural information contained in the parent phase being transmitted to the daughter phase. Furthermore, a simple orientation

---

[⊗] Abstract published in *Advance ACS Abstracts,* July 15, 1996.

(1) Galwey, A. K.; Laverty, G. M. *J. Chim. Phys., Phys.-Chim. Biol.* **1990**, *87*, 1207.

(2) Mnyukh, Yu. V. *Mol. Cryst. Liq. Cryst.* **1979**, *52*, 163.

(3) Munn, R. W. *Chem. Brit.* **1978**, *14* , 231.

(4) Reynolds, P. A. *Acta Crystallogr.* **1977**, *A33*, 185.

(5) Boudjada, N.; Rodriguez-Carvajal, J.; Anne, M.; Figlarz, M. *J. Solid State Chem.* **1993**, *105*, 211.

(6) Stoch, L. *J. Thermal Anal.* **1992**, *38*, 131.

(7) Bayard, F.; Decoret, C.; Royer, J.; Smeyers, Y. G.;Randez, J. J. *Int. J. Quantum Chem.* **1988**, *33*, 61.

(8) Le Bideau, J.; Bujoli, B.; Jouanneaux, A.; Payen, C.; Palvadeau, P.; Rouxel, J. *Inorg. Chem.* **1993**, *32*, 4617.

S0897-4756(96)00043-9 CCC: $12.00

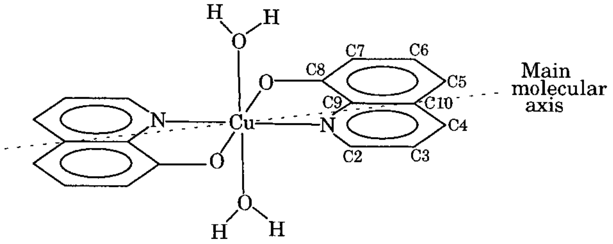


Figure 1. Molecular structure and atomic labels of dihydrated copper(II) oxinate.

relationship can exist between the two crystallographic lattices.[9]

(2) "Nucleation and growth" models[2,10−12] assume that transitions start on a particular site (generally crystal defects for polymorphic transitions and particle surface for dehydrations) and continue by a progressive propagation of a reaction interface.

(i) For decompositions of solvates, the most widely accepted model consists of the advancement of an interfacial zone of appreciable thickness, composed of amorphous materials. This induces a true recrystallization to yield the daughter phase. Dehydration is assumed to be started at crystal surfaces, so that nucleation and growth of the daughter phase proceed inward and gaseous product is evacuated in the opposite direction through the recrystallized layer. This model has been deduced from experimental work on ionic crystals.[11]

(ii) For polymorphic transitions, Mnyukh[2] has developed a model applied to molecular crystals, in which the nucleation is not the result of a random fluctuation but is fully predetermined by the crystal defects. At the interface between parent and daughter phases, a molecule-by-molecule mechanism is proposed. This presupposes a momentary "vaporized" state of the molecules. There is no intermediate layer of excited molecules between the two phases.

In these nucleation and growth models, there is a complete loss of the structural information during the transformation.

The experimental part of the present study deals with solid−solid transformations of metal−organic complexes formed between copper(II) and the deprotonated form of 8-hydroxyquinoline (oxine, Oxi hereafter). Copper(II) oxinates (Figure 1) present several dihydrated and anhydrous polymorphic varieties. Filiations are depicted in Figure 2, using the notation proposed by Suito et al.[13] Among the numerous complexes obtained in water between the oxinate anion and divalent metallic cations, such as Mg, Mn, Co, Ni, Zn, and Cd, the dihydrated β form is a ubiquitous structure. Copper(II) oxinates present a specific character since $Cu(Oxi)_2\cdot 2H_2O$ (β form) has the lowest dehydration temperature, close to 350 K, whereas the other oxinates (there are two polymorphic forms for $Zn(Oxi)_2\cdot 2H_2O$) must be heated to temperatures ranging from 410 to 450 K to be dehydrated. Some of the resulting anhydrous phases (with Mg, Mn, Co, and Cd) are quasi-amorphous solids.

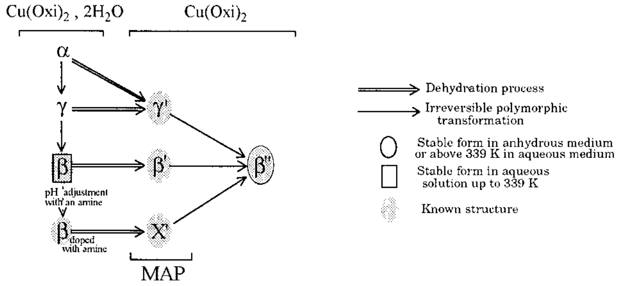


Figure 2. Filiations between dihydrated and anhydrous copper(II) oxinates (MAP stands for metastable anhydrous phase).

Another specificity of copper(II) oxinates is the ability of anhydrous phases to present polymorphism: until now, no less than three metastable anhydrous phases (MAP = β', γ', and X′) and one stable form (β'') have been identified.

Some of our recent works have brought new data, allowing an attempt to describe the mechanisms involved in the transitions between varieties of known structure. More precisely, we are interested here in the dehydration mechanism of $Cu(Oxi)_2\cdot 2H_2O$ (β form) toward $Cu(Oxi)_2$ (β' or X′ forms), and in the mechanism of the solid−solid transitions from the MAP toward the stable β'' form. Our aim is therefore to answer the following questions:

What type of model can be used in order to describe the dehydration of $Cu(Oxi)_2\cdot 2H_2O$ (β form)?

How can the presence of a specific adduct induce, during dehydration, the formation of a new metastable form (X′) instead of the "usual" β' metastable form?

Why does the dehydration of a dihydrated variety systematically lead to a metastable anhydrous variety (β', X′, or γ') before the formation of the stable β'' phase?

Starting from these experimental results and additional data from the literature, an attempt to classify the different dehydration processes for molecular crystals will be proposed.

Experimental Section

Preparative routes for the different phases of copper(II) oxinate have been described recently.[14] Let us recall that when a hydroxylated base (NaOH, KOH, $Ca(OH)_2$) is used in order to obtain a quantitative yield of the dihydrated β form (pH adjustment), the subsequent dehydration of the β form leads to the metastable β' anhydrous form, whatever the route of dehydration: P_2O_5, vacuum, heating, MeOH, or acetone. When the pH adjustment is achieved using ammonia or an amine, the β phase is "doped" by the NHRR′ (R, R′ = H, Me, Et) compound and its dehydration, whatever the route used, leads to the X′ variety (Figure 2). Careful analyses have shown that about 0.5 mol % of the amine remains in the crystal of $Cu(Oxi)_2$ (X′ form). This gives evidence that the amine acts as a true adduct, inserted in the crystal lattice.

The crystal structures of the β dihydrated form[15] and of the anhydrous β'[16] and β''[17] forms were solved from Weissenberg photographs in 1964 and 1967. More recently, the structures of the γ' form[18] and of the X′ form[14] have been described.

---

(9) Ferg, E. E.; Levendis, D. C.; Schoening, F. R. L. *Chem. Mater.* **1993**, *5*, 1293.

(10) Royer, J.; Skalli, M.; Bayard, F.; Decoret, C. *J. Cryst. Growth* **1993**, *130*, 280.

(11) Galwey, A. K. *J. Thermal Anal.* **1992**, *38*, 99.

(12) Lyakhov, N. Z.; Boldyrev, V. V. *Russ. Chem. Rev.* **1972**, *41*, 919.

(13) Suito, E.; Arakawa, M.; Kobayashi, T. *Kolloid Z. Z. Polym.* **1966**, *212*, 155.

(14) Petit, S.; Coquerel, G.; Perez, G.; Louër, D.; Louër, M. *Chem. Mater.* **1994**, *6*, 116.

(15) Palenik, G. J. *Acta Crystallogr.* **1964**, *17*, 696.

(16) Hoy, R. C.; Morriss, R. H. *Acta Crystallogr.* **1967**, *22*, 476.

(17) Palenik, G. J. *Acta Crystallogr.* **1964**, *17*, 687.

(18) Ammor, S.; Coquerel, G.; Perez, G.; Robert, F. *Eur. J. Solid State Inorg. Chem.* **1992**, *29*, 445.

Stereoscopic projections of the structures along $\vec{b}$ were deposited as supporting information (Figure 1′). The molecular geometry is almost identical in all solids.[14] Therefore, no conformational polymorphism exists[19] and the solid−solid transitions mainly consist of a modification of molecular packings. A detailed analysis reveals that the main conformational variations concern the coordination polyhedron of the copper ion. In the dihydrated β form, the (Cu−O) and (Cu−N) bond lengths of the planar square are 0.13 ± 0.01 Å longer than in the anhydrous forms. UV−visible spectroscopic measurements (see Figure 2′ in the supporting information) have confirmed the decrease of the (Cu−O) and (Cu−N) bond lengths during the dehydration of the β variety. This decrease involves the Jahn−Teller effect and is consistent with the modification of the overlapping of the d_{z^2} orbital due to the departure of water molecules. Moreover, according to the spectroscopic results, the coordination polyhedron in the dihydrated α variety is similar to that of anhydrous varieties. We might therefore assume that the $\alpha \rightarrow \gamma \rightarrow \beta$ transformations consist of a stronger bonding of water molecules in the apical position of cupric ions, inducing an elongation of bond lengths in the square plane. In the anhydrous β'' form, an angular distortion of the planar square is observed, due to a weak fifth bond with an oxygen atom of a neighboring molecule ($d(\mathrm{Cu-O}) = 2.83$ Å). Therefore, the coordination polyhedron is of (4 + 1) type, and the main feature of the crystal structure is a centrosymmetric dimer unit.

Although they are essential data, crystal structures depict only the initial and final stages of transformations. The possible molecular movements and intermediate steps of the transitions can be simulated by molecular modeling. The SYBYL software[20] and the Tripos force field[21] have been used here for this purpose. Other experimental data which have contributed to this study are as follows:

(i) Scanning electronic microscopy (SEM) photographs of single crystals of the β phase after dehydration under vacuum (i.e., transformed into the anhydrous β' phase). Figure 3a shows that "single crystals" have become stacks of thin sheets parallel to the (100) plane of the initial β crystals (the indexes are referred to the unit cell of the β form). SEM observations have also been carried out for the β'' phase (Figure 3b) and showed that, for this stable anhydrous variety, crystal surfaces are smooth, with well-defined morphologies.

(ii) Crystal size distribution (CSD) and specific surface (BET type) measurements. Table 1 summarizes the values of mean diameter and specific surface for the phases considered here. The values presented in this table refer to consistent evaluations of CSD and specific surfaces since they were obtained with the same sample of the β variety successively transformed into β' and β'' varieties.

(iii) Differential scanning calorimetry (DSC) measurements (Setaram 101). In the DSC curve with a 2 K min^{-1} heating rate for the dihydrated β form (see Figure 3′ in the supporting information), the first peak (endothermic, $T_{\mathrm{onset}} = 349$ K) corresponds to the one-step departure of the two water molecules, and the second phenomenon (exothermic, $T_{\mathrm{onset}} = 454$ K) is due to the polymorphic transition between the anhydrous phases: $\beta' \rightarrow \beta''$. Table 2 contains the enthalpies and the activation energies associated with the transitions of the metastable anhydrous varieties toward the stable β'' variety. The activation energies have been calculated from DSC results and Kissinger's rule,[22] which establishes a relationship between the heating rate, the temperature of maximum deflection of the heat-transfer peak and the activation energy.

(iv) Powder X-ray diffraction patterns were systematically collected in order to check the crystallinity of each phase. This showed that the dihydrated β variety and all anhydrous phases are well crystallized.

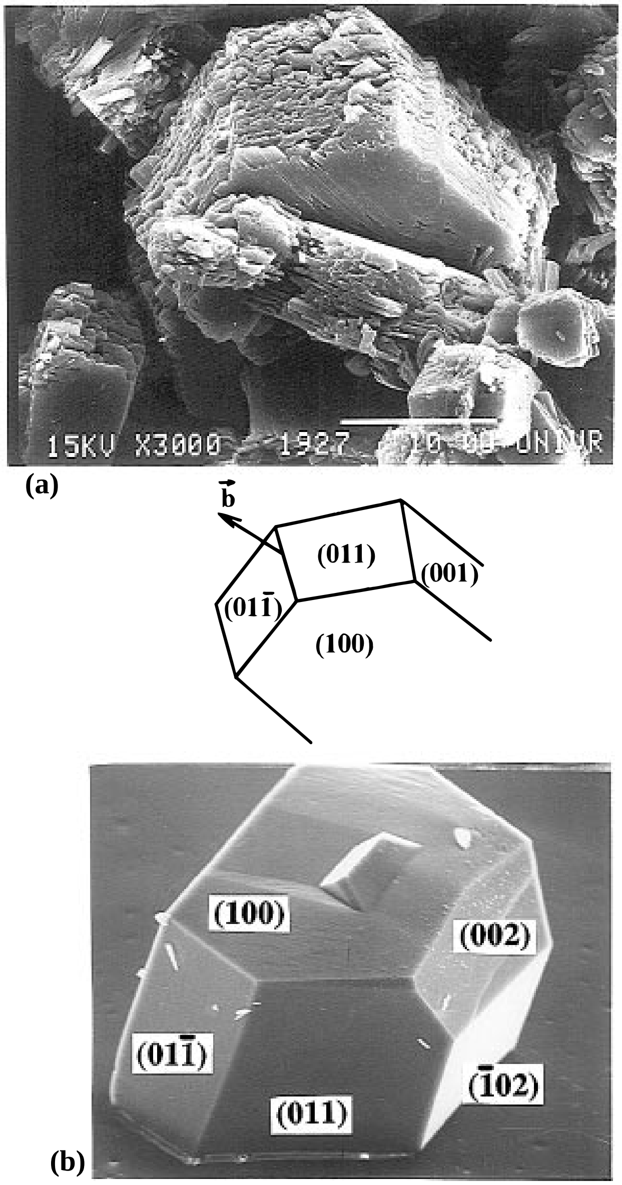


Figure 3. SEM photograph of single crystals of (a) $\mathrm{Cu(Oxi)_2 \cdot 2H_2O}$ (β form) after dehydration under vacuum (×3000) (the indexes correspond to the β form) and (b) $\mathrm{Cu(Oxi)_2}$ (β'' form) (×600).

Table 1. Crystal Size Distribution (CSD) and Specific Surface Measurements for Copper(II) Oxinates

	CSD		
	mean diameter (μ)	σ (μ)	specific surface (m^2/g)
β	38	24	0.4
β'	28	19	2.8
γ'	4	4	8.6
X′	13	4.5	*a*
β''	31	18	1.2

[a] Not reproducible value (∼2.8 m^2/g as β'), due to inclusion of variable amount of β'' as an impurity.

Results and Discussion

I. Dehydration Mechanism of $\mathrm{Cu(Oxi)_2 \cdot 2H_2O}$ (β Form).

As outlined by Galwey et al.,[23] microscopic

---

(19) Bernstein, J.; Hagler, A. T. *Mol. Cryst. Liq. Cryst.* **1979**, *50*, 223.

(20) SYBYL, Molecular Modeling Software (vers. 6.03, 1994), Tripos Associates, St. Louis, MO.

(21) Clark, M.; Cramer, III, R. D.; Van Opdenbosch, N. *J. Comput. Chem.* **1989**, *10*, 982. Vinter, J. G.; Davis, A.; Saunders, M. R. *J. Comput.-Aided Mol. Design* **1987**, *1*, 31.

(22) Kissinger, H. E. *J. Res. Natl. Bur. Stand.* **1956**, *57*, 217; *Anal. Chem.* **1957**, *29*, 1702.

(23) Tanaka, H.; Koga, N.; Galwey, A. K. *J. Chem. Educ.* **1995**, *72*, 251.

Table 2. Enthalpies and Activation Energies for MAP → β'' Transitions (MAP: Metastable Anhydrous Phase)

phase	enthalpy ΔH kJ mol^{-1}	σ	activation energy (kJ mol^{-1})
β'	−3.7	0.26	131 ± 9
β'_{stab}	−3.4	0.25	172 ± 13
γ'_{stab}	−3.8	0.31	126 ± 8
X′	−2.3	0.36	158 ± 12

observations of dehydrated particles can provide decisive information in the understanding of the dehydration mechanism. The analysis of several SEM photographs (Figure 3a) indicates the following:

(i) During dehydration, the single crystals of the dihydrated β phase are altered but the global morphology of the initial particles remains recognizable. When dehydrated using P_2O_5 , single crystals are altered even less.

(ii) The various crystal surfaces are not altered in an identical way: the (100) faces are systematically much less affected than the (001) and (011) faces, so that stacks of thin plates are obtained.

These observations are not consistent with a nucleation and growth model since this model cannot explain the reproducible anisotropy of the surface alteration. Moreover, a reconstructive process of a well-crystallized product should lead to well-defined surfaces in order to minimize the surface energy, which is not observed. It can be seen from Table 1 that $\beta \rightarrow \beta'$ transformation (as well as $\beta \rightarrow$ X′) corresponds to a significant decrease in the mean crystallite size and to a sharp increase in specific surface. These data are also in favor of a continuous process.

Departure of Water Molecules. Hence, from the experimental results, a continuous mechanism of dehydration can be postulated. The one-step departure of water molecules is determined by topological constraints since it requires the possibility of a rapid and cooperative evacuation of water molecules. This implies a structural deformation which leads to the formation of planes or of channels. Nevertheless, this deformation should be of sufficiently low magnitude to maintain the structural cohesion.

Owing to the SEM photographs (Figure 3a), these channels or planes should be parallel to the (100) planes. This result is consistent with the crystal structure : Figures 1′a and 4a show that the (100) slice consists of a hydrophilic region (copper and oxygen atoms, water molecules) situated between two hydrophobic layers composed of aromatic rings. If we assume that water molecules are evacuated along a direction perpendicular to the $\vec{a}$ axis, two hypotheses for structural modification can be formulated, both consisting of rotations of the copper oxinate molecules around their main axis C10−C10′ (cf. Figure 1), but in opposite directions. Figure 4a−c presents the initial and resulting packings, obtained with an angular magnitude of 20° for the molecular rotations:

(i) In the first hypothesis (Figure 4b), molecular planes tend to become parallel to the (01$\bar{0}$) plane and channels appear along the [011] and [01$\bar{1}$] directions. The minimum section (bottle neck) in these channels is 3.8 Å wide, which is the distance between the oxygen atoms of neighboring molecules in the [011] rows.

(ii) In the second hypothesis (Figure 4c), rotations tend to make the molecular planes parallel to (001).

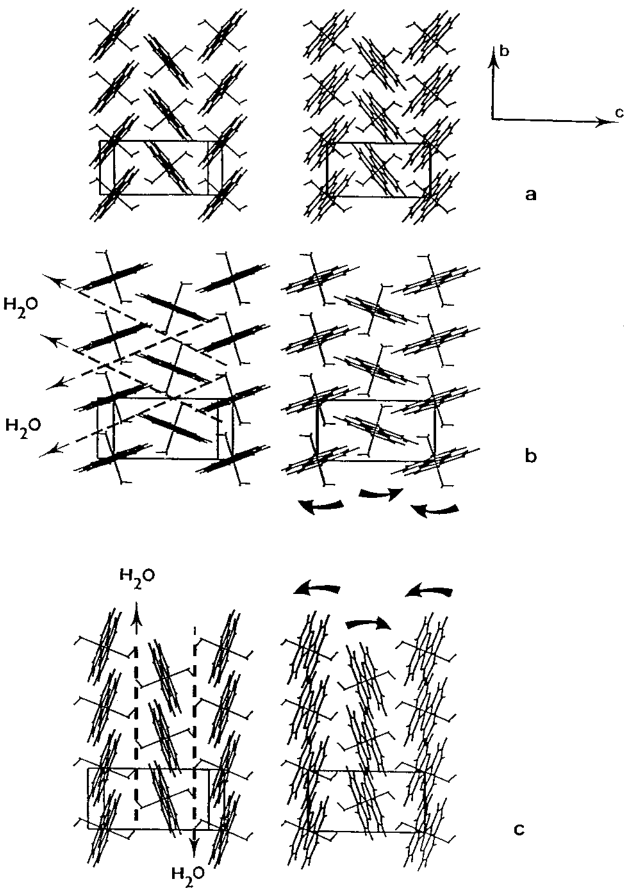


Figure 4. Projection along $\vec{a}$ of a slice (100) in Cu(Oxi)$_2$·2H_2O (β form) and modeling of the possible structural deformations leading to the formation of channels for a cooperative departure of water molecules.

Channels are formed along the [010] direction and their minimum diameter is 4.3 Å.

To evaluate the two hypotheses, a comparison in terms of energy, geometry, and dynamic process is envisaged.

(i) For an *energetic analysis*, the intermolecular interactions during the simulation of both structural deformations were computed with the SYBYL software. It has shown that steric constraints increase in a similar way in both hypotheses, so that no conclusion can be drawn. Due to the lack of parametrization for the copper atom, the energy of Cu−OH$_2$ bonds could not be computed with sufficient accuracy. Therefore, our modeling calculation was limited to an evaluation of van der Waals interactions.

(ii) The *geometric description* of the channels in the two hypotheses presents several features:

(1) Size of the channels. The values indicated above show that the minimum diameter is higher in the second hypothesis.

(2) Sinuosity of the channels. In the first hypothesis, they present a slight sinuosity, whereas they are strictly linear in the second one.

(3) Intermolecular links due to hydrogen bonds. In the β phase, the positioning of hydrogen atoms shows that the (100) slice cohesion is ensured by two hydrogen bonds between H atoms of water molecules and oxygen atoms of the oxinate ligand. During both deformations, the hydrogen bonds are elongated and could be replaced by hydrogen bonds between water molecules. Never-

theless, in the first hypothesis, the modification should only result in H-bonded dimers of water molecules, taking into account the distance between oxygen atoms. In the second hypothesis, it appears that hydrogen bonds between water molecules in the [010] direction can generate infinite chains, so that a cooperative departure in this direction of H-bonded chains is favored.

(iii) A *dynamic and cooperative analysis* reveals that a departure of water molecules along, for instance, the [011] direction in the first hypothesis might induce a closing of the channels parallel to the [01$\bar{1}$] directions, so that the number of possible departure directions is decreased. This is in relation with the crossing situation of the [011] and [01$\bar{1}$] channels (see Figure 4b). On the contrary, in the second hypothesis, the departure of water molecules in one channel maintains and even enhances the deformation, so that neighboring channels are kept open. This induces an easier departure in neighboring channels, and assuming that evacuation is achieved in opposite directions in two neighboring channels, this corresponds to a synergy and to a truly cooperative process.

From these geometric and dynamic points of view, the second hypothesis is therefore more favorable than the first one. Moreover, a careful observation of SEM photographs (Figure 3a) reveals that dehydrated "single crystals" are made of sheets which exhibit small cracks along the [010] direction. We can thus assume that water molecules are evacuated through channels parallel to the $\vec{b}$ axis, obtained from a structural deformation consisting of cooperative molecular rotations.

Reorganization of the Anhydrous Packing. After the departure of water molecules, the resulting unstable new anhydrous material (NAM) is composed of domains in which a structural order is maintained. This packing is similar to the one depicted in Figure 4c, without water molecules. Owing to its instability, it must evolve rapidly toward the closest energy minimum, and transforms into one of the two metastable β' or X′ forms of anhydrous copper(II) oxinate.

From a molecular point of view, the departure of water molecules induces a 13% decrease in the molecular volume. A relaxation of steric constraints caused by the dehydration process takes place and might correspond to molecular movements inverse to those associated with the formation of the channels. Hence, the relaxation might consist of rotations of the copper(II) oxinate molecules around their main axis. Taking into account the additional volume available, a modeling of this reorganization shows that the rotation can have a magnitude of 60°. Figure 5a presents the resulting packing, which is close to a (002) slice of Cu(Oxi)$_2$ (β' form). The molecular movements required for the evolution toward β' are of small magnitude and must occur by relative displacements between planes or rows which have high indexes of cohesion in the "relaxed" NAM. These movements can be described as follows:

(i) An alternating glide of successive [011]$_\beta$ rows along their axes, with a magnitude of 1.6 Å, leading to the packing presented in Figure 5b,

(ii) A molecular rotation of 30° around an axis parallel to the [031]$_\beta$ = [010]$_{\beta'}$ direction and containing copper atoms (Figure 5c).

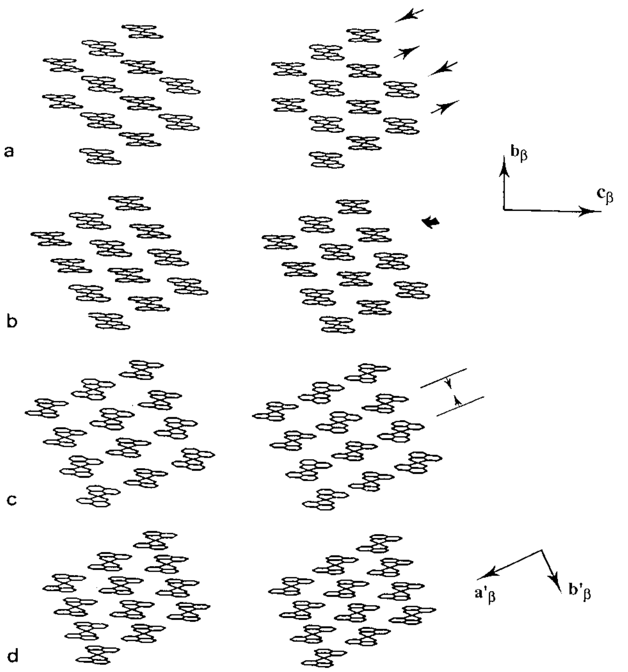


Figure 5. Modeling of the reorganization of the "flopped" NAM (a) toward Cu(Oxi)$_2$ (β' form) (d) (H atoms are omitted for clarity).

These cooperative movements are associated with a "compression" of the packing along [031]$_\beta$ = [010]$_{\beta'}$ direction ($d_{\mathrm{Cu-Cu}}$ is 5.04 Å in β and 3.84 Å in β'), whereas the intermolecular distances remain almost unchanged in the [0$\bar{1}$1]$_\beta$ = [100]$_{\beta'}$ direction ($d_{\mathrm{Cu-Cu}}$ is 7.60 Å in β and 7.40 Å in β'). This step of reorganization leads to the compact stacking of parallel molecules in the [010] rows observed in Cu(Oxi)$_2$ (β' form).

Hence, the reorganization of the unstable NAM toward the metastable β' form appears to be the shortest and easiest pathway for the relaxation of steric constraints due to water molecule departure. Considering the main molecular movements of Cu(Oxi)$_2$ molecules, both steps of the dehydration (departure of water molecules and reorganization) can be summarized by a "flip-flop" process, i.e., a succession of inverse rotations around the molecular axis C10−C10′.

In the case of the NAM → X′ transformation, the first step of the reorganization might be imposed by the same necessary relaxation of the strongest steric constraints, leading to the molecular packing presented in Figure 5a. All preparation routes for the X′ phase show that the insertion of residual amine molecules in the NAM is required. Thus the mechanism from NAM to X′ must take into account the presence of this adduct.

When an amine has been used during the preparation of the dihydrated β phase, we may assume that these adduct molecules are inserted in the crystal lattice of the β phase. Except in the case of ammonia, which has a molecular volume similar to water, the amine molecules should be responsible for the formation of crystal defects. The amine molecules are probably situated in the apical position of the copper atom since they are able to interact with the latter more strongly than water molecules. As a result, some of the amine molecules remain in the packing during dehydration and could hinder the departure of water molecules, inducing the formation of supplementary crystal defects.

It is likely that the formation of the X′ phase occurs because the reorganization toward the β' phase is impeded. The β' phase corresponds to the "natural" energy minimum closest to the "flopped" NAM, and this is consistent with the following statements:

(i) Experimentally, we often obtained a mixture of the X′ and β' phases, which is probably due to local fluctuations of amine concentration.

(ii) Our description of the NAM → β' reorganization revealed that similarities exist between the packing obtained after the relaxation of steric constraints and the β' structure.

Considering the "flopped" NAM → β' reorganization, the evolution toward β' could be impeded by the difficulty either of compressing the packing or shifting $[011]_\beta$ rows, because of steric hindrances due to the amine molecules.

It is likely that the NAM → X′ transformation occurs by means of a cooperative mechanism, for the following reasons:

(i) the CSD values (Table 1) indicate that the mean diameter for X′ powder is low, compared with the β and β' phases; (ii) chemical analyses (see above) have shown that amine molecules remain in Cu(Oxi)$_2$ (X′ form), whereas they should be evacuated during a reconstructive process; (iii) despite its good crystallinity checked by X-ray diffraction, SEM photographs of the X′ powder have shown irregular surfaces of the particles, similar to those observed for the β' powder, and, above all, clearly different from the regular and well-defined surfaces observed for the β'' crystallites.

Although the reorganization is mainly determined by kinetic factors, a reconstructive mechanism would have favored, from a thermodynamic point of view, the formation of the stable anhydrous variety, i.e., the β'' form.

Therefore, although the determining role of defects due to the amine molecules is established, these defects do not impede a cooperative process, but orientate the reorganization toward the formation of X′, since the β' packing cannot be reached. At a molecular level, the reorganization of the packing of Figure 5a toward X′ corresponds to the following molecular movements, depicted in Figure 6 (amine molecules are not represented):

(i) A "folding" of the packing by means of an alternating rotation of the molecules in successive $(100)_\beta$ slices, around an axis containing copper atoms and parallel to the $[001]_\beta$ direction (Figure 6 a,b). The magnitude of the rotation is 45°.

(ii) An opposite glide of one out of two consecutive $[\bar{1}02]$ planes in the $[201]_{X'}$ direction, with a magnitude equivalent to half a molecular slice, i.e., 5.5 Å (Figure 6 b,c).

It can be assumed that there is an advantage for the packing in evolving by means of folding (and consequently toward the X′ packing) when the easiest reorganization (toward β') is impeded. In particular, there is a higher flexibility of the X′ packing since $[\bar{1}02]$ slices consist of a succession of corrugated planes, so that this packing is more likely to bear deformations due to the presence of amine molecules. On the contrary, in (002) slices of the β' structure, the molecular planes are roughly coplanar, and localized deformations are made more difficult.

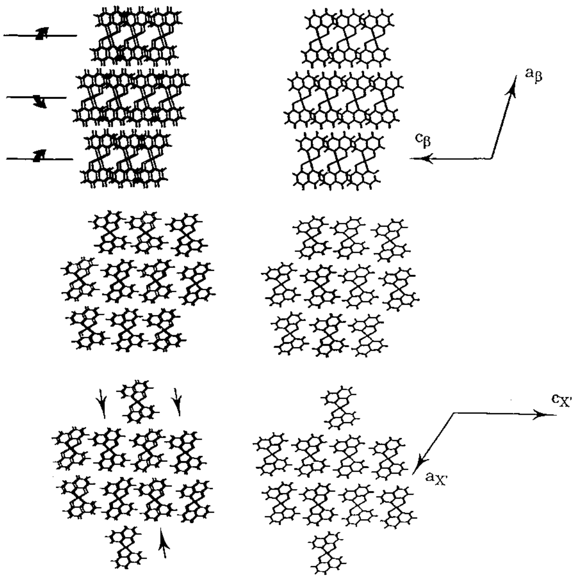


Figure 6. Modeling of the reorganization of the "flopped" NAM (a) toward Cu(Oxi)$_2$ (X′ form) (c).

Hence, the reorganization toward the X′ form is imposed by amine molecules which impede the formation of the β' packing by generating specific steric hindrances. The β → X′ dehydration also consists of a continuous mechanism involving cooperative molecular movements in the solid, associated with topological constraints: the permanence of the structural cohesion imposes successive steps in the order described above. This mechanism is consistent with experimental results, especially the evolution of CSD and specific surfaces during both dehydrations $\beta \rightarrow \beta'$ and β → X′.

II. Polymorphic Transitions between Anhydrous Phases. *Structural Filiations.* The structural description of Cu(Oxi)$_2$ (X′ form)[14] has revealed analogies between X′ and β'' structures, which allowed the X′ → β'' filiation to be described by a two-step process (see Figures 4 and 5 in ref 14):

(i) A glide of $(100)_{X'}$ planes in $[001]_{X'}$ direction, with a magnitude of $c/2 = 7.6$ Å.

(ii) A glide of $[241]_{X'} = [110]_{\beta''}$ rows contained in $(\bar{1}02)_{X'} = (002)_{\beta''}$ slices, with a magnitude of 4.2 Å. A glide of $[\bar{2}41]_{X'} = [1\bar{1}0]_{\beta''}$ rows takes place symmetrically in neighboring slices. The angle between the two glide directions is 82°. This second step corresponds to the formation of the dimer units observed in β''.

The structural filiations $\beta' \rightarrow \beta''$ and $\gamma' \rightarrow \beta''$ cannot be described in such a simple way. In particular, the $\beta' \rightarrow \beta''$ filiation requires a three-step process, composed of two distinct molecular rotations (with angular magnitudes of 25° and 40°) and one glide of molecules in a direction parallel to their main axis.

Mechanism of the Transitions toward β'': Discussion. Our attempts to describe the structural filiations have shown that some of the polymorphic transitions MAP → β'' require, at a molecular level, high magnitude and/or complicated movements. On the contrary, the models presented in the literature for continuous mechanisms suppose that polymorphic transitions take place by means of cooperative molecular movements of weak magnitude,[3] so that filiations between the two crystal lattices can be decomposed into simple movements of low magnitude with weak activation energy.

From the experimental results of CSD and specific surface (Table 1), it can be seen that the mean size of the particles increases for all MAP → β'' transitions. This result is incompatible with a continuous mechanism since the relevant models cannot explain matter transport. It should also be noted that, when obtained from the X′ phase, the β'' phase does not contain residual quantities of amine.

It is therefore likely that the mechanism of the polymorphic transitions toward β'' is a nucleation and growth process, including matter transport. This means that transitions are not achieved simultaneously in the whole crystal but are initiated by a nucleation step on a particular site, followed by a propagation step through the particle and neighboring particles.

From energetic and steric considerations, the nucleation should preferentially take place on sites where molecules have the highest movement ability. In the model presented by Mnyukh,[24] it is postulated that the nucleation appears on crystal defects only. Nevertheless, the particle surfaces (especially edges, corners and anfractuosities, i.e., deep and irregular cavities) are also favorable regions since the corresponding molecules have an incomplete environment.

Although it must be outlined that the measured activation energies (Table 2) probably consist of a global evaluation of several phenomena, we may assume that the major part of these activation energies corresponds to a relative estimation of the nucleation difficulty. If we assume that particle surfaces are involved in the nucleation process, a relationship should exist between the mean size of the particles and the activation energies. Such a correlation is clearly observed for $\gamma' \rightarrow \beta''$: the lowest activation energy of this transition is associated with the smallest mean diameter and the highest specific surface. For X′ and β' varieties, the increase of the CSD is associated with an increase in activation energies. Further evidence for the relationship between the particle surface and the activation energy is obtained by the observation of a stabilization effect induced by an adduct[14] (here 5-sulfonic-8-hydroxyquinoline acid) adsorbed on the surface of the β' phase particles. The higher activation energy for $\beta'_{\text{stab.}} \rightarrow \beta''$ transition compared with $\beta' \rightarrow \beta''$ transition is consistent with a nucleation taking place at the particle surface.

If the nucleation is started on crystal defects, its mechanism should be related to the nature and the geometry of defects and therefore difficult to identify. If the nucleation occurs on the particle surface, two possible processes can be envisaged for the formation of nuclei:

(i) A mechanism involving cooperative molecular movements would result in a local deformation of the structure (Figure 7a). For instance, the two-step process proposed from a modeling study for the X′ → β'' transition[14] could in fact be responsible for the β'' nucleation only. In the same way, the structural filiations for MAP → β'' transitions could correspond to the nucleation step of these transitions.

(ii) Another possible mechanism, similar to the "molecule by molecule" mechanism proposed by Mnyukh,[2] would consist of a breaking of intermolecular links, followed by a "repositioning" of each molecule.

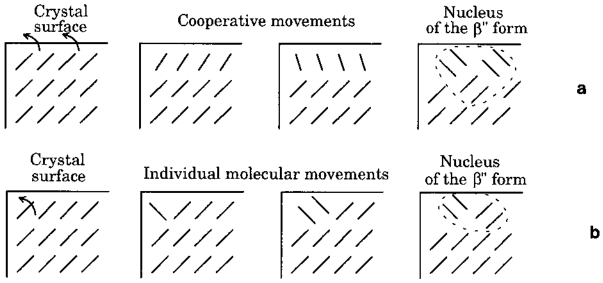


Figure 7. Schematic description of two possible mechanisms for the nucleation step of MAP → β'' polymorphic transitions.

Figure 8. Schematic description of the contamination of neighboring particles during the growth step of MAP → β'' polymorphic transitions.

Nevertheless, in this second hypothesis, a momentary "vapor state" does not necessarily occur: it can be supposed that each molecule preserves at least one intermolecular link with its neighbors throughout the nucleation step (Figure 7b).

Hence, although several features and hypotheses can be envisaged, the whole nucleation mechanism of these polymorphic transitions cannot be fully elucidated from the available experimental data.

A "contact mechanism" has been used by Mnyukh[2] in order to describe the growth step during polymorphic transitions of molecular crystals. This mechanism explains the increase of particle size during the MAP → β'' transitions by matter transport, i.e., propagation in every particle but also "contamination" of neighboring particles (Figure 8), inducing a stabilization due to the decrease in interfacial energy.

Conclusion of the Experimental Section. The study of the successive solid−solid transformations β → MAP → β'' (MAP: metastable anhydrous phase) between copper(II) oxinates has revealed that they occur by means of different mechanisms.

The dehydration process of the β phase is composed of two distinct steps, both involving cooperative molecular movements. The first step consists of a structural deformation leading to the formation of channels parallel to the $\vec{b}_\beta$ axis, in which water molecules are evacuated. The resulting unstable NAM (new anhydrous material) reorganizes rapidly toward the closest metastable packing, i.e., the β' phase when no adduct is inserted in the packing, and the X′ phase if a small amount of amine molecules are present as adduct. The reorganization toward X′ can be explained by considering the steric hindrances due to the amine molecules impeding the evolution of the NAM toward the β' structure. Figure 9 summarizes the dehydration process of $Cu(Oxi)_2 \cdot 2H_2O$ (β form). This cooperative mechanism induces a structural filiation from the parent phase to the metastable anhydrous phases (MAP).

The MAP → β'' polymorphic transitions have to be described by a nucleation and growth mechanism. Consequently, structural information is lost along the polymorphic transitions. The impossibility of a direct

---

[24] Mnyukh, Yu. V. *J. Cryst. Growth* **1976**, *32*, 371.

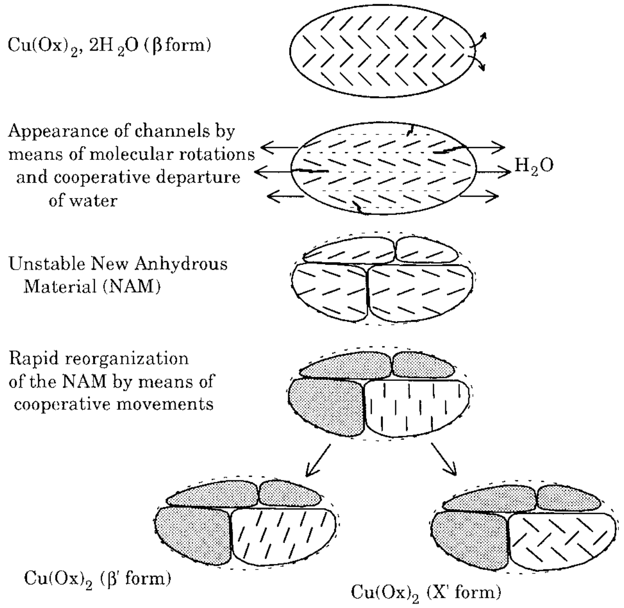


Figure 9. Schematic representation of the dehydration mechanism for the $\beta \rightarrow$ NAM $\rightarrow$ MAP transitions, leading to a decrease of the particle size.

$\beta \rightarrow \beta''$ transition is explained by considering the conditions of the reorganization step of the NAM after the departure of water molecules: the instability of the packing imposes a rapid evolution toward the closest energy minimum, whereas the formation of the β'' form requires high activation energy.

Extended Discussion

Proposition for a Unified Model for the Dehydration Mechanism of Molecular Crystals. In continuity with the above study on the dehydration mechanism of the dihydrated copper(II) oxinate (β form), the aim of this discussion is to propose a general and rationalized approach for the dehydration of molecular crystals. Whatever its mechanism, a dehydration includes a step in which the release of water molecules results in a New Anhydrous Material (NAM). In some cases, the whole dehydration process is limited to this step (one-step dehydrations) whereas in other cases, the release of water molecules is followed by a second step consisting of a reorganization of the NAM (two-step dehydrations).

Assuming that dehydration mechanisms can be classified either as cooperative processes or as destructive and possibly reconstructive processes, our approach consists in trying to *identify the pertinent criteria* which determine how water molecules are released and the possible subsequent reorganization of the NAM. Considering each criterion, we also intend to show that there is a *limit* beyond which a cooperative mechanism is impeded. We are therefore interested in characterizing the *discontinuity* between these excluding situations. Scheme 1 is a summarized representation of the model developed hereafter.

This model can be applied to complete or partial dehydrations. Nevertheless, to facilitate the discussion, we will at first consider here only the simple case of a complete dehydration in a single step. To begin with, we will limit this study to dehydration processes which result in the formation of a single anhydrous solid phase. Thermodynamically, the reaction can be either irreversible or reversible. The following chemical equation describes an irreversible dehydration:

$$\langle A\cdot nH_2O\rangle \rightarrow \langle A\rangle + nH_2O\uparrow \qquad (1)$$

A reversible heterogeneous equilibrium is written:

$$\langle A\cdot nH_2O\rangle \rightleftarrows \langle A\rangle + nH_2O\uparrow \qquad (2)$$

Nevertheless, at a molecular level, this equilibrium does not necessarily imply the reversibility of the process. The latter situation, which must include the thermodynamic reversibility, could be symbolized by

$$\langle A\cdot nH_2O\rangle \leftrightarrow \langle A\rangle + nH_2O\uparrow \qquad (3)$$

In the case of thermodynamic reversibility (eqs 2 and 3) and provided that no domain of solid solution exists between A and H_2O,[25] there are, at equilibrium, two independent components and three phases so that the variance (v) of the system equals 1. At first, dehydrations will be considered to occur at (or very near) the equilibrium, i.e., in the smoothest conditions.

Unlike purely ionic or inorganic compounds (nonmolecular), molecular crystals are composed of discrete entities linked to each other by weak intermolecular bonds (hydrogen bonds and van der Waals contacts), so that deformations of packing can occur. They are commonly characterized by an alternation of hydrophilic and hydrophobic regions. A conformational flexibility can also exist, inducing intramolecular changes of the geometry upon dehydration. In the specific case of metal–organic compounds, water molecules can participate either as ligands or exclusively as entities involved in the packing cohesion. Another common characteristic of hydrated molecular crystals is the large volume of the anhydrous molecule, compared with the volume of the water molecule(s) to be released.

(1) Release of Water Molecules. *(1.1) Criteria for Pathway of H_2O Release.* At a molecular level, the mechanism of dehydration is dependent on the necessity to evacuate easily a great number of water molecules as soon as the temperature–pressure couple ($v = 1$) has reached the limit value of release. Both topological and energetic considerations are determining criteria:

(i) The first criterion (C1) is of a topological nature; it is related to the possibility of evacuating water molecules through channels or interlayer spaces of sufficient size ($\geq$3.5 Å) existing in the crystal structure of the hydrate, or the possible appearance of these exits by means of a simple and cooperative deformation of the structure.

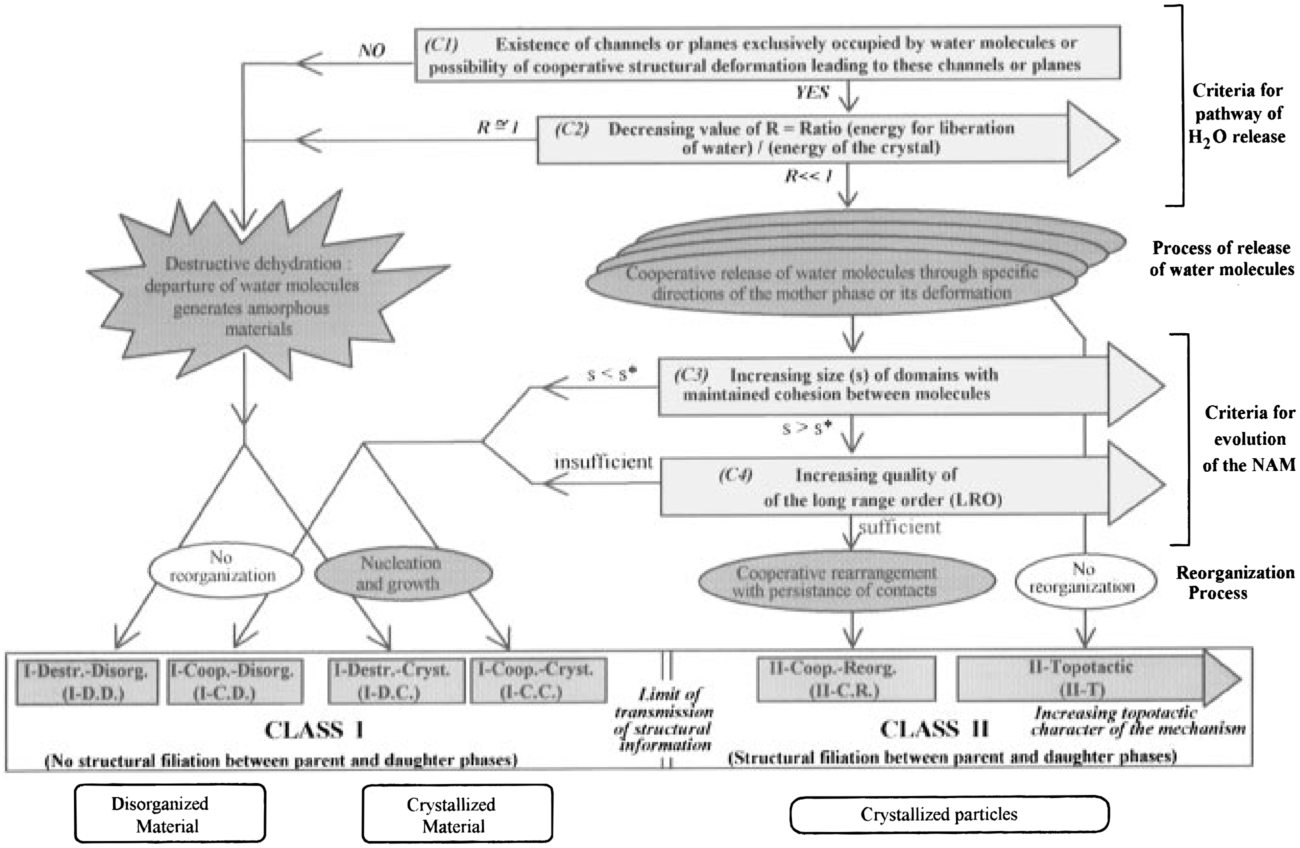
(ii) The second criterion (C2) concerns the value of the ratio R between the energy necessary for the liberation of water molecules and the energy of the crystal lattice. The liberation energy includes the energy of the bonds in which the water molecules are involved and the energy required for the eventual deformation of the packing.

(1.2) Process of Water Molecule Release and the Resulting Phase. If the first criterion (C1) is fulfilled and if the value of R (C2) is low enough ($R \ll 1$), water molecules can be released by means of a cooperative

---

(25) Cox, J. S. G.; Woodard, G. D.; McCrone, W. C. *J. Pharm. Sci.* **1971**, *60*, 1454.

Scheme 1. Organization Chart for Dehydration Mechanisms of Molecular Crystals



process through specific directions of the parent phase, usually corresponding to simple crystallographic directions. This process implies that all the water molecules are evacuated by similar and ordered displacements which maintain, if it exists, the structural deformation. Furthermore, this deformation should preferentially lead to noncrossing pathways of release. In numerous cases, uninterrupted chains of hydrogen-bonded water molecules can ease the cooperative process. Hence, the departure of water molecules is anisotropic. The first dehydrated region is the inner part of each particle since the molecules evacuated from the surface are rapidly replaced by water molecules from the deeper part of the particle. This phenomenon is related to an overall diffusion control allowed by close-to-equilibrium conditions. In that case, the NAM consists in dehydrated domains, defined hereafter as particles or parts of particles in which a structural cohesion is maintained throughout the dehydration process. This cohesion is due to hydrophobic (van der Waals) contacts and/or intermolecular hydrogen bonds in which the water molecules released were not involved.

If the first criterion is not fulfilled or if the value of R is too close to unity, the departure of water molecules must be destructive, i.e., it must occur by means of a complete destruction of the packing. The crystal lattice can be dismantled isotropically from the most brittle initialization site(s). The first dehydrated parts are therefore at the surface of the crystal and dehydrated materials progress inward through the displacement of a reacting interface. An amorphous NAM is generated, and the structural information is lost.

If we define as class I the mechanisms for which there is no transmission of structural information during dehydration and as class II the opposite situation, the cases of a destructive departure of water molecules necessarily correspond to a class I mechanism.

(2) Possible Evolution of the NAM. In the case of a cooperative departure of water molecules, two situations must be envisaged for the evolution of the NAM:

(i) If this departure has occurred smoothly, easily, and without significant deformation of the crystal lattice, the NAM mainly consists of the hydrated structure deprived of water molecules. Therefore, the reorganization is almost nonexistent, and the resulting domains are crystallites of the same size as the initial particles. These situations correspond to topotactic or quasi-topotactic dehydrations and they are defined as class II topotactic (or class II-T) mechanisms since the structural information is strongly preserved. The absence of reorganization induces a topotactic dehydration through a one-step process with a great probability of reversibility of this process (cf. eq 3).

(ii) If the departure of water molecules does not have a topotactic character, the resulting domains are of smaller size than the initial particles, since the evacuation of water molecules and the consequent available volume induces a compression phenomenon and the appearance of cracks. The anisotropic character of the cooperative process influences, at a macroscopic level, the distribution of the domain sizes and the mean morphology exhibited by the domains. Hence, it should be considered that there is an interval in which the vast majority of the domain sizes lies. Furthermore, in each domain, the long-range order (LRO) could also be affected by an increased quantity of crystal defects due to the departure of water molecules. This means that the characterization of the NAM requires two additional criteria which determine a possible cooperative reorganization.

(2.1) Criteria for the Reorganization Process after a Cooperative Release of Water Molecules. The third criterion (C3) deals with the size of dehydrated domains. The inferior limit of the interval of the domain sizes defined above has to be compared with the critical size (s^*) of the daughter phase nucleus.

The quality of the LRO in each domain constitutes the fourth criterion (C4). The LRO can be altered, for instance, by ill-positioning or wrong conformation of molecules.

(2.2) Possible Reorganization Process after a Cooperative Release of Water Molecules. According to the (C3) criterion, when the cumulative percentage of particles which have a size greater than the critical size ($s > s^*$) is high enough and when the LRO is of sufficient quality (C4), the reorganization occurs in a cooperative way. It takes place by means of relative molecular displacements so that contacts between molecules are permanently maintained. Each domain reacts independently, due to the absence of nucleation and growth processes. Nevertheless, we may assume that very small particles can be incorporated in bigger particles by diffusion during the reorganization process. This incorporation allows a decrease of the surface energy.

A cooperative rearrangement process (following a cooperative release of water) leads to at least part of the information contained in the parent crystal being transmitted to the daughter phase. Hence, the whole dehydration mechanism, which includes two distinct steps, belongs to class II and is defined as a class II-Coop.-Reorg. (or class II-C.R.) mechanism.

When the size of the vast majority of the domains is too low ($s < s^*$), the (C3) criterion prevents the relaxation of the NAM through cooperative movements. Since the domains are very small, the surface energy is high and this dispersed system will tend to promote a nucleation. In other cases, even if the domains are of sufficient size, the (C4) criterion indicates that an insufficient quality of the LRO (i.e., too much “noise” during the structural information transmission) can also impede a cooperative reorganization process.

In such situations, the dehydration process as a whole occurs beyond the threshold of any information transmission (class I mechanisms) and the reorganization can be envisaged only through a nucleation and growth process. If this process takes place, the daughter phase results from the reconstruction of a crystal lattice from the NAM; a contamination phenomenon is likely to occur at contacts between domains. The dehydration thus consists of a two-step process and belongs to class I-Coop.-Cryst. (or class I-C.C.). If a nucleation and growth process does not occur, an amorphous-like material is obtained. The whole dehydration is limited to the single step of water molecule release and is classified as class I-Coop.-Disorg. (or class I-C.D.).

(2.3) Possible Reorganization Process after a Destructive Release of Water Molecules. When the release of water molecules has occurred through a destructive process, the situation is analogous to that existing when one of the (C3) or (C4) criteria are not fulfilled: if a nucleation and growth process can take place, the resulting phase is a crystallized material and the two-step mechanism is defined as class I-Destr.-Cryst. (or class I-D.C.). Otherwise, the anhydrous compound consists of an amorphous (or disorganized) material and, due to the absence of reorganization, the dehydration is limited to a single step. The mechanism is then defined as class I-Destr.-Disorg. (or class I-D.D.).

3. Additional Comments. Although in the previous sections we considered only quasi-equilibrium states, it must be emphasized that the imposed route and kinetics can influence the dehydration mechanism. In particular, if the process of water departure is not destructive, the size of resulting anhydrous domains and the quality of the LRO could be increased when using a smoother route and a slower rate of dehydration since the system remains close to the thermodynamic equilibrium. On the contrary, we might expect that using “hard” conditions could lead to a change of the reorganization process from class II-C.R. toward class I-C.D. or even I-C.C.

The presence of defects and/or impurities in the hydrate can either ease or hinder the departure of water molecules. In the case of a cooperative rearrangement (class II), impurities can influence the eventual reorganization by inducing a lower quality of the order in the domains. A specific impurity might also modify the cooperative rearrangement to such an extent that a different anhydrous phase is generated (see experimental part).

In connection with the determining role of kinetic factors and impurities, a cooperative rearrangement (class II) can induce the formation of a metastable anhydrous variety, as was observed above in the case of $Cu(Oxi)_2 \cdot 2H_2O$ (β form). Indeed it is quite common to observe polymorphism of anhydrous phases among organic hydrates undergoing dehydration. Nevertheless, the formation of a metastable phase can also result from a nucleation and growth process if the latter is kinetically favored for the metastable phase, compared with the stable phase.

Although we have considered only the most usual conditions of dehydrations (i.e., in a partial vacuum or in air), the above model could be adapted in order to consider dehydrations occurring in a saturated aqueous solution. Therefore, for a peritectic equilibrium, eq 2 becomes

$$\langle A \cdot nH_2O \rangle \rightleftarrows \langle A \rangle + \text{saturated solution} \qquad (2')$$

Similarly, an example of irreversible dehydration in an aqueous solution (corresponding to eq 1) is the case of the dihydrated β form of copper oxinate at 339 K, which leads to the anhydrous β' form. The latter is subsequently irreversibly transformed into the stable β'' form.

4. Experimental Data and Techniques for the Differentiation of Dehydration Mechanisms. The understanding of the dehydration mechanism of a molecular hydrate requires the use of several complementary types of experimental data which converge toward one of the mechanisms defined above. Hence, only a multitechnique approach can lead to an unambiguous elucidation of a given dehydration mechanism in known experimental conditions. A nonexhaustive list of the data and associated techniques useful for this purpose follows:

(1) Crystal structures for the hydrate but also for the anhydrous phase in order to detect a possible structural

filiation (preserved slices or ribbons). A detailed analysis of the hydrate structure should allow an evaluation of the first criterion (C1).

(2) Molecular modeling data concerning both (C1) and (C2) criteria, i.e., the possibility of an easy deformation of the hydrated structure (allowing water departure) and the computation of the energy for the release of water. The analysis of possible packing deformations could also allow the detection of a possible cooperative departure.

(3) The temperature and pressure conditions of dehydration, as well as the associated enthalpy variation (DSC measurements[26] and thermogravimetric analysis with or without an imposed p_{H_2O}). The higher the dehydration temperature, the higher the probability of a destructive mechanism (class I). Data on the reorganization process can also be obtained by the detection of a supplementary exothermic or endothermic peak (T_g, crystallization, polymorphic transition, etc.) after the departure of water molecules.

(4) SEM photographs of initial and final morphologies of indexed crystallites give insights into the mechanism and into the first criterion through the observation of possible surface alterations. In case of class I-D.C. or I-C.C., the resulting single crystals should present well-defined surfaces.

(5) Periodically or continuously collected powder X-ray diffraction patterns allow the identification of phases during dehydration. Furthermore, an estimation of the evolution of the crystallinity of the phases during dehydration can be achieved, and mainly deals with (C3) and (C4) criteria. If the diffraction peaks broaden during dehydration, this decrease of crystallinity may be caused by (i) a decrease in the LRO (C4 criterion), (ii) a sharp decrease in particle sizes inducing a Scherrer effect[27] (C3 criterion), or (iii) a dynamical disorder appearing after the departure of water molecules.

(6) The relative evolution of crystal size distribution (CSD) can establish the occurrence of a nucleation and growth mechanism when an increase of the mean size of the particles is observed. The relative evolution of specific surface measurements can confirm the CSD results since any decrease of specific surfaces is necessarily associated with a mechanism of class I-D.C. or I-C.C.

(7) Kinetic studies (generally obtained from DSC measurements or thermogravimetric analysis) can provide significant data concerning the influence of the rate of dehydration on the mechanism of dehydration. The physicochemical meaning of the value of n in the Avrami−Erofe'ev equation ($-\ln(1-\alpha) = (kt)^n$) has been extensively detailed by Galwey et al. (ref 23 and references therein). Nevertheless, the interpretation of kinetic studies must be undertaken carefully since the dependence of the kinetic law on the size of particles has been demonstrated by Byrn.[28] In some cases, a change of mechanism caused by using a high rate of dehydration can be detected.

(8) The reversibility (eq 3) is likely to be associated with a class II-T mechanism, meaning that the bond network is not significantly modified during dehydration. In the extreme case, water molecules can move freely in and out of the crystal. Topotactic dehydrations are also favored when high-energy slices or ribbons exist in the crystal structure of the hydrate (see examples).

When the thermodynamic reversibility (eq 2) does not correspond to the reversibility of the processes, the equilibrium point is linked to a balance between two destructive/constructive mechanisms at the dehydration temperature.

5. Examples and Field of Application. Generally, dehydration studies of molecular crystals in the literature do not contain sufficient data for a complete elucidation of molecular mechanisms. Nevertheless, some of the criteria and processes mentioned above can be illustrated by examples obtained from the literature or from our previous research.

In Byrn's review,[28] it is shown that in the structure of the monohydrated forms of caffeine, theophylline, thymine, and cytosine, water molecules are contained in channels parallel to one of the crystallographic axes, indicating that their departure is likely to occur along these channels. This statement is confirmed by visual (microphotographic) observations of indexed single crystals upon dehydration. The existence of large and linear channels has also been described in the crystal structure of biological macromolecules.[29]

Several data illustrate the major importance of the energetic (C2) criterion.[28] Although both structures are quasi-isomorphous, the higher dehydration temperature of theophylline (between 308 and 323 K) with regard to caffeine (room temperature) can be explained by the presence in the theophylline molecule of one supplementary hydrogen-bond site which can interact with the oxygen atom of water molecules. Quantitative estimations of hydrogen bond energies (hydration sites) have been achieved for purines and pyrimidines, including thymine and cytosine.[30]

The crystal structure and the thermal behavior[31] of the tetrahydrated variety of copper(II) sulfoxinate (copper(II) 5-sulfonic-8-hydroxyquinolinate, CuSu hereafter) have shown that a two-step dehydration occurs, according to the following scheme:

$$\mathrm{CuSu\cdot 4H_2O} \underset{293\ \mathrm{K,\ in\ water}}{\overset{347\ \mathrm{K,\ in\ air}}{\rightleftarrows}} \mathrm{CuSu\cdot 2H_2O}\ (\text{form III}) \xrightarrow{400\ \mathrm{K}} \mathrm{CuSu}\ (\text{form IV})$$

The analyses of the crystal structure and of SEM photographs have indicated that the first step corresponds to the departure of interlayer water molecules in directions parallel to the (100) plane. This release is reversible (eq 3) and does not alter the (100) slice, made up of hydrogen-bonded dimers associated in a two-dimensional polymeric structure. Hence, a partial topotactic character exists in the first dehydration step, and due to this mechanism, the {100} surfaces remain smooth, whereas the {011} surfaces are ill-defined. Therefore, the dehydration mechanism of this step corresponds to class II-T, with an extensive transmission of structural information. The dehydration for the

---

[26] Cammenga, H. K.; Epple, M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1171.

[27] Azároff, L. V.; Buerger, M. J. *The powder method in X-ray crystallography*; McGraw-Hill: New York, 1958.

[28] Byrn, S. R. Loss of Solvent of Crystallization In *Solid-State Chemistry of Drugs*; Academic Press: New York, 1982.

[29] Persichetti, R. A.; St. Clair, N. L.; Griffith, J. P.; Navia, M. A.; Margolin, A. L. *J. Am. Chem. Soc.* **1995**, *117*, 2732.

[30] Port, G. N. J.; Pullman, A. *F.E.B.S. Lett.* **1975**, *31*, 70.

[31] Ammor, S.; Coquerel, G.; Perez, G.; Robert, F. *Eur. J. Solid State Inorg. Chem.* **1992**, *29*, 131.

second step, however, is fully destructive and nonreversible. The release of the two water molecules involved in the square-planar coordination of the copper atom requires too much energy ((C2) criterion), so the structural filiation cannot be preserved and the mechanism corresponds to class I-D.C. since the anhydrous product is crystallized.

When a destructive departure of water molecules is not followed by a nucleation and growth process, the resulting phase is a disorganized solid (class I-D.D.). This situation is illustrated by the family of dihydrated metallic oxinates $M^{2+}(Oxi^-)_2 \cdot 2H_2O$ (β form). Among this family, the dehydration (except with Cu^{2+}) occurs at high temperature ($T > 410$ K) and leads, for some of them (M = Mg, Mn, Co, Cd), to quasi-amorphous compounds. These high dehydration temperatures indicate that the departure of water molecules is destructive, and the mechanism belongs to class I-D.D., whereas metastable anhydrous copper(II) oxinates (β' and X′ forms) correspond to class II-C.R. Hence, it appears that isotypic hydrated structures can present different dehydration mechanisms. This situation can be explained by the Jahn−Teller effect of the copper atom, since the modification of the coordination polyhedron requires less energy in this case than for other metals. Therefore, the change of mechanism is induced by the inability of the other β ($M^{2+} \neq Cu^{2+}$) hydrated structures to satisfy the second criterion (C2).

The above interpretation of the dehydration mechanism of $CuSu \cdot 4H_2O$ illustrates that water molecules can play very different roles in a crystal structure. In some cases, they may be involved only in intramolecular interactions, so that their role is to reinforce the conformational cohesion (for instance, in proteins) or to occupy an empty volume. The latter situation is common in macrocyclic molecules such as cyclodextrins.[32] In biomolecules such as proteins, some water molecules are weakly bonded, so that they can easily be evacuated without significant loss of structural cohesion.[33] These situations, which correspond to quasi-topotactic and reversible dehydrations (class II-T), can also occur in the case of small molecules. For instance, cephalosporin, cephaloridine, and cephalexin are compounds for which hydrated and anhydrous structures are unchanged,[28] meaning that anhydrous crystals contain voids and cavities. These examples of quasi-topotactic dehydrations should be related to the field of concerted molecular movements in the solid state[34] and to single-crystal-to-single-crystal reactions.[35,36]

An extension of the above model to other types of hydrates (inorganic [8] and ionic[11,37] compounds, clay materials,[38] zeolites,[39] polymers, etc.) or to other solvates should be undertaken by means of a preliminary analysis of several structural and energetic characteristics, using the four criteria defined above. This extension also requires the specific characteristics of molecular crystals to be reexamined and adapted for these materials. For solvates which present distinct characteristics according to the four criteria, this analysis could predict whether the desolvation will be either destructive (class I) or not completely destructive (class II) for smooth desolvation conditions.

Conclusion

A unified model that describes the possible dehydration mechanisms of molecular crystals shows that four necessary and sufficient criteria must be taken into account. The first two criteria are topological and energetic; they determine the process of water molecule release, resulting in a NAM. In the case of cooperative departure of water molecules, the two other criteria (size of the anhydrous domains and quality of the long-range order (LRO)) are decisive factors for the evolution of the NAM toward the anhydrous phase.

From these statements, it appears that two types of mechanism (called class I and class II) exist. In class I, there is no filiation of structural information either because the release of water molecules is destructive or due to the impossibility of a cooperative reorganization process of a highly defective material. In these cases, if the resulting material (NAM) does not undergo a nucleation and growth process, a quasi-amorphous solid is obtained, and the mechanism corresponds to one of the subclasses I-Destr.-Disorg. (I-D.D.) or I-Coop.-Disorg. (I-C.D.). If the NAM undergoes a nucleation and growth process, the resulting phase is a crystallized solid, and the mechanism corresponds to one of the subclasses I-Destr.-Cryst. (I-D.C.) or I-Coop.-Cryst. (I-C.C.).

In class II, the filiation of structural information results from a cooperative and anisotropic release of water molecules, followed (class II-Coop.-Reorg. or II-C.R.) or not (class II-topotactic or II-T) by a correlated rearrangement of the molecules in each domain. According to this model, the occurrence of class II requires that the four successive criteria be satisfied; the system evolves toward class I if one of them is not satisfied.

CM9600438

---

(32) Lindner, K.; Saenger, W. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 694. Betzel, C.; Saenger, W.; Hingerty, B. E.; Brown, G. M. *J. Am. Chem. Soc.* **1984**, *106*, 7545.

(33) McPherson, A. *The Preparation and Analysis of Protein Crystal*; John Wiley and Sons: New York, 1982.

(34) Toda, F. *Pure Appl. Chem.* **1996**, *68*, 285.

(35) Novak, K.; Enkelmann, V.; Kohler, W.; Wegner, G.; Wagener, K. B.; Kaftory, Y. *Mol. Cryst. Liq. Cryst. A* **1994**, *242*, 1.

(36) Nakanishi, H.; Jones, W.; Thomas, J. M.; Hursthouse, M. B.; Motevalli, M. *J. Phys. Chem.* **1981**, *85*, 3636.

(37) Cammenga, H. K.; Epple, M.; Blaschette, A.; Näveke, M. *Thermochim. Acta* **1989**, *151*, 171.

(38) Grim, R. E. *Clay Mineralogy*; McGraw-Hill: New York, 1968.

(39) Thomas, J. M. *Eur. J. Solid State Inorg. Chem.* **1994**, *31*, 651.