

Phase transitions in molecular crystals from a chemical viewpoint

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Abstract — Why do molecules pack in crystals as they do? The trivial answer: because they thereby achieve periodic arrangements corresponding to minimum potential energy. In general, for any given molecule, there must be many such arrangements of closely similar energy; experience accumulates to show that polymorphism is of widespread occurrence in the world of molecular crystals. It is often accompanied by radical changes in conformation and hydrogen bonding patterns. Indeed, as far as molecular crystals are concerned, there seems to be no clear cut boundary between polymorphic transitions and solid state chemical reactions. Of particular interest are those cases where crystal orientation is preserved during the structural change, for there, in principle, the atomic positions can be mapped quite precisely on both sides of the transition and mechanisms can be proposed for the molecular motions that are involved. Not all such processes occur under topochemical control, i.e., with a minimum amount of atomic or molecular movement from the known starting structure. Many seem to occur, or at least to be initiated, at crystal defects where the regular arrangement of molecules is interrupted. Examples of both types will be discussed, and the attempt will be made to describe these and related phenomena from a chemical point of view.

INTRODUCTION

A crystal is, in a sense, the supramolecule *par excellence*: a lump of matter, of macroscopic dimensions, millions of molecules long, held together in a periodic arrangement by just the same kind of interactions as are responsible for molecular recognition and complexation at all levels — ion-ion, ion-dipole, dipole-dipole interactions, hydrogen bonding, London forces, and so on. Indeed, crystallization from a solution containing several solutes is a most impressive self-organization process, involving specific molecular recognition at an amazing level of precision. It may seem all the more surprising that most compounds can exist in more than one crystalline form. The crystal structure of a compound is generally not unique but depends on the conditions of crystallization. Polymorphism is ubiquitous. Free energy differences between polymorphs are usually quite small, a matter of a few kcal mol⁻¹ or even less, and may have different temperature dependences. Thus, over quite a small range of temperature, and particularly between room temperature and the melting point, one polymorph or another can be the thermodynamically stable form. A metastable form can persist for years, or it can undergo spontaneous transformation to the stable form. Polymorphism can be thought of as a kind of higher form of isomerism, and a polymorphic transformation as a kind of isomerization reaction. You will not find much about such analogies in the textbooks about phase transitions in solids, for this is an area that seems to have been more or less annexed into the domain of physics.

Of course, one cannot ignore the physics, and, in particular, one has to pay due respect to thermodynamic considerations, especially those summed up in Gibbs's Phase Rule: $F = C - P + 2$, where F , the number of degrees of freedom of the system, is related to the number of components (C) and phases (P). For Gibbs, a phase is a portion of matter that is "uniform throughout, not only in chemical composition but also in physical state". "Uniform throughout" implies that the system is regarded as continuous rather than as molecular. From today's perspective, this kind of definition leaves much to be desired, but it is remarkable how often in modern textbooks we are referred back to Gibbs for the basic concepts involved in phase transitions. The freedom of the Phase Rule from all molecular assumptions is at the same time its strength and its weakness; its strength because of its generality, its weakness because precise, unambiguous definitions of the underlying concepts such as phase and component need ultimately to be expressed at the molecular level and must also involve kinetic factors.

At this stage we have to try to say what we mean by a polymorph. Following McCrone (ref. 1), we define a polymorph as "a solid crystalline phase of a given compound resulting from the possibility of at least two crystalline arrangements of the molecules of that compound in the solid state". What about the molecules having different conformations, or even different configurations, in the different crystalline phases? McCrone's criterion is that polymorphs are different in crystal structure but identical in the liquid and vapour states. This would mean that if crystals containing different molecular species are to be classed as polymorphs, the molecules concerned must interconvert rapidly in the melt or in solution. In phase rule terminology, we have a one-component system.

Although there are obviously borderline cases, the distinction is not merely a matter of semantics but may have subtle effects on the physical properties. Another question is whether different hydrates or solvates of a given compound should be classified as polymorphs. Again there is room for disagreement on this point.

According to the above, a racemate and a conglomerate are to be classed as polymorphs when the rate of interconversion in the melt or in solution is fast, but as different compounds when the interconversion rate is slow. A good example of how this may affect properties has recently come to light (ref. 2). According to Wallach's Rule (ref. 3) (based on 8 pairs of densities!), a racemic crystal generally has a denser packing than the corresponding crystal composed of homochiral molecules. Although this rule has not gone unchallenged (ref. 4), there does seem to be a fairly widespread opinion that a better packing can be achieved by a mixture of right- and left-handed objects than by a collection of all right- or left-handed ones.

With the help of the Cambridge Structural Database¹ we have made a new survey. In this, we distinguish between molecules that racemize rapidly and those that do not. The first group are one-component systems, the second two-component systems. For the 84 pairs in the first group $R = \langle V(\text{chiral})/V(\text{racemic}) \rangle$ is 1.001(3), not significantly different from unity, while for the 60 pairs in the second group $R = 1.009(3)$. The 3σ deviation from unity cannot be ignored, the probability of it having occurred by chance being about 0.001. Thus, Wallach's Rule appears to hold only for pairs where interconversion of enantiomers is slow. There is a simple thermodynamic explanation (ref. 2); the sample is biased — enough to say that there is no basis for the belief that a collection of right- and left-handed objects can be packed more efficiently than a collection of right- or left-handed ones.

PHASE TRANSITIONS IN SOLIDS

In spite of the unmistakable analogies, there are important differences between phase transitions in solids, and chemical reactions in solution or the gas phase. First, there is the difference in the way the rates of these processes depend on the temperature. The rate constant of a chemical reaction increases smoothly with temperature; for a phase transition, nothing much happens on the "wrong" side of the transition temperature, but once this temperature is passed, the transformation rate may suddenly increase, especially when it is superheating that is involved (Fig. 1). Secondly, in a reversible chemical reaction there is an equilibrium mixture of reactant and product, whereas in a crystal, the transformation, once it is triggered on either side of the transition temperature, usually goes practically to completion. These differences between the "normal" chemical reaction and the crystal transformation result from the importance of cooperativity in the crystal but not in the liquid or gaseous states. In the latter, the molecules react virtually independently of one another, whereas in the crystal each molecule is influenced by what happens to its neighbours.

Phase transitions in solids have been classified in several ways, some of which are indicated in Table 1. According to the thermodynamic classification, first-order transitions involve a discontinuous change in the first derivatives of the free energy (e.g., volume, entropy) at a definite transition temperature T_0 ; here the two phases are supposed to be in equilibrium on opposite sides of an interface. In second-order transitions there is a change of slope, but no discontinuity in the temperature dependence of the volume or entropy. Such transitions are usually associated with a change in the degree of order in the solid (order-disorder transitions). A discontinuous change of any physical property with change in temperature is often taken as evidence of a first-order transition, while a continuous change is associated with a second-order one. As far as mechanisms are concerned, first-order transitions are generally believed to occur by nucleation of one phase within the other, followed by its growth. Second-order transitions are often supposed to occur in a concerted fashion by a so-called soft-mode mechanism. One of the lattice vibrations of the periodic crystal structure is supposed to soften gradually with change in temperature until the corresponding frequency becomes zero; correlated atomic motions then cause the crystal to change from one structure to another. In this type of transition, the two phases are expected to have a high degree of orientational relationship.

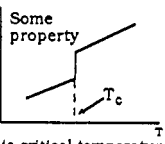
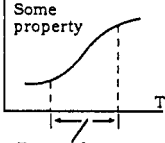
These classifications have been strongly criticized by Mnyukh (ref. 5), who regards polymorphic transformations as non-equilibrium phenomena. Superheating or supercooling is not only possible, it is necessary. In other words, at the temperature where the two phases are in thermodynamic equilibrium, nothing can happen. According to his view, all solid state transitions occur by a nucleation and growth mechanism, and the nucleation step is critically dependent on the presence of suitable defects, such as micro-cavities and other surface irregularities between crystal domains. Depending on the nature of these defects, nuclei of the new phase are formed at different temperatures and grow at different rates.

Although there is considerable evidence to support this picture, the factors that govern the rates of the nucleation and growth stages are little understood. Mnyukh claims that the absence of orientational relationships between the parent and daughter phases is a general rule (ref. 6) for nucleation and growth mechanisms, but there are too many exceptions. Sometimes an orientational relationship between the two phases is observed, sometimes not. The temperature range in which the transition occurs can be very variable, depending on what can be described as the "history of the sample". When suitable defects, such as micro-cavities of the right size and shape, are absent or, let us say, when their concentration is low, a crystal modification can sometimes be kept indefinitely at a temperature well outside its normal range of stability. Even when defects are present, rapid cooling of a phase to a temperature well below its transition temperature can completely inhibit growth of the stable modification. Sometimes the two phases can co-exist over a considerable temperature range. For most transitions, a phenomenological description is all that is possible.

As far as static aspects are concerned, there is no shortage of concepts for factorizing the potential energy of a crystal into component parts — electrostatic interactions, hydrogen bonds, donor-acceptor interactions, steric

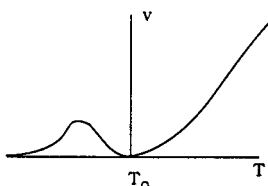
¹ Available through the Cambridge Crystallographic Data Centre (CCDC), University Chemical Laboratories, Lensfield Road, Cambridge, England.

TABLE 1. Different classifications of solid-solid phase transitions

Thermodynamic	Phenomenological	Mechanistic	
FIRST ORDER $\Delta V \neq 0; \Delta Q \neq 0$ Heterogeneous Nucleation and growth Hysteresis is inevitable $v = f(T)$	DISCONTINUOUS  T_c is critical temperature	RECONSTRUCTIVE By full reconstruct Crystal structures are not "similar" No orientational relationship Rate of transition: "sluggish" First order	
SECOND ORDER $\Delta V = 0; \Delta Q = 0$ Homogeneous Soft mode No hysteresis Symmetry change	CONTINUOUS  Range of transition	DISPLACIVE By displacement or distortion Crystal structures are "similar" Rate of transition: "rapid" "Almost second order" Continuous	MARTENSITIC Definite orientational relationships $v \neq f(T)$ $v = \text{velocity of sound}$ Relief on surface Sharp transition temperature

T is Temperature; ΔV is volume change; ΔQ is heat of transition; v is velocity

FIG. 1. Dependence of rate of growth of new phase as function of temperature. At the thermodynamic transition point T_0 nothing happens



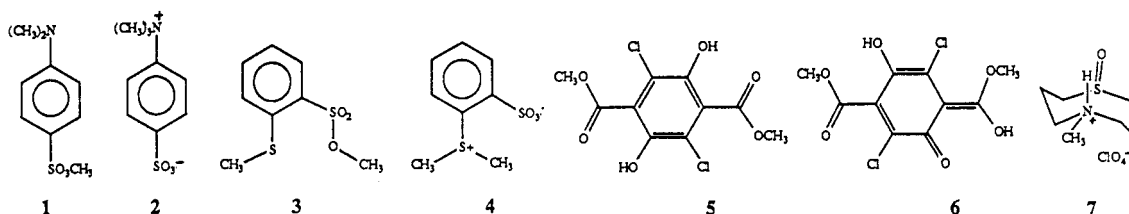
repulsions, van der Waals attractions — and several widely available computer programs can be applied to estimate the potential energy of any known crystal structure. Usually the observed structure corresponds to a calculated potential energy minimum, or is quite close to one. On the other hand, methods for predicting unknown crystal structures are still in their infancy. In general, we know very little about the possible crystal structures that a given molecule might adopt. Most potential functions in general use have been parametrized to reproduce room-temperature crystal structures. The calculated energies may be a fair approximation to free energies around this temperature, but they are not accurate to better than a kcal mol⁻¹ or so, and, hence, they can hardly be used for predicting the ranges of relative stability of polymorphs.

Given the crystal structures of the polymorphs, it is tempting to superimpose them and assume that the transition occurs by the simplest imaginable deformation of one structure into the other, involving translations and rotations of the individual molecules. Such an assumption might possibly be permissible for a single-crystal to single-crystal transformation, where unit cells of the two phases match closely and perfect crystal orientation is maintained. But even then, it would be suspect. In general, it seems likely that the molecules do not move appreciably within an existing phase but rather are transferred somehow, molecule by molecule, from the unstable phase to the growing, stable one, across the phase boundaries.

PHASE TRANSITIONS AND SOLID STATE REACTIONS

So far, we have avoided the question of distinguishing between phase transitions and solid-state reactions (ref. 7). There are obviously grey areas; for example, transitions that involve changes in hydrogen bonding patterns or in molecular conformation. The term "conformational polymorphism" has been coined to cover the latter case (ref. 8). A classification based on the phase rule would require that the various molecular species involved in different polymorphs interconvert rapidly in the melt or in solution. On the other hand, the "product" of a solid-state reaction should be separable from the starting material — not merely detectable. Also, the product of a thermally induced solid-state reaction can be expected to be considerably more stable thermodynamically than the starting material. Otherwise it could not be formed at all in the crystalline matrix designed to accommodate the molecules of the starting material, where it is an intruder. In the early stages of such reactions, the product presumably accumulates as a solid solution in the parent crystal until nucleation and growth of a separate phase becomes possible. The role of defects in initiating nucleation and growth of new phases in thermal reactions seems to be little understood, although their importance in certain photochemically induced solid-state reactions (ref. 9) has been established.

Generally, any monomolecular chemical reaction that proceeds thermally in solution can be expected to occur also in the crystalline state. Its rate may be much slower in the crystal, because of the greater limitations on molecular flexibility and atomic motion, but sometimes the reaction in the crystal proceeds faster because of an especially suitable packing arrangement, where the atomic motions needed to go from the starting structure to the final one are minimal. Such solid-state reactions are referred to as topochemical (ref. 10).



A beautiful example of this kind is the methyl transfer reaction studied by Bergman and his collaborators (ref. 11). On warming a crystal of *p*-*N,N*-dimethylaminobenzenesulphonic acid methyl ester **1**, there is an intermolecular migration of the methyl group to yield the zwitterion **2**. The crystal structure (Fig. 2) is such that this methyl migration can occur with a minimum of atomic motion — the sulphonic acid group of one molecule is close to the amino group of another — and not too far from the collinear orientation required for an S_N2 displacement (the intermolecular $N\cdots C$ distance is 3.54 Å and the $N\cdots C-O$ angle is 147°). On warming the crystals, the reaction rate gradually increases up to the melting point (364 K), when it abruptly drops. The ordered arrangement of molecules in the crystal is thus especially suitable for the methyl transfer. In our laboratory, we have recently analyzed the anisotropic displacement parameters (ADP's) (ref. 12) obtained from new crystal structure analyses (ref. 13) at 193 and 253 K. The molecules show considerable librational motion about their long axes, the mean square libration amplitude of the sulphonate group about the C-S bond being about 50 and 80 deg² at the two temperatures mentioned and extrapolating to about 140 deg² at the melting point of the crystals. A coupled 10° rotation of neighbouring molecules would lead to a $N\cdots C$ distance less than 3 Å and to a nearly collinear approach of the reacting atoms ($N\cdots C-O$ angle \approx 168°). Correlated libration of molecules within a given chain could then lead to concerted methyl migration from molecule to molecule along the chain, thus eliminating the need for a two-step mechanism involving an ion-pair intermediate, as postulated on the basis of energy calculations (ref. 14).

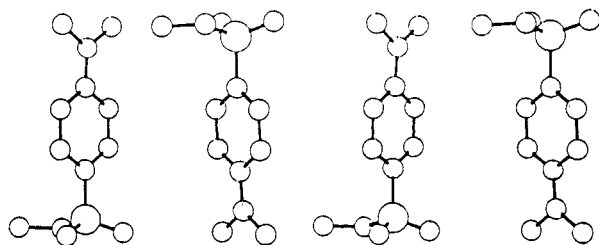


FIG. 2. Crystal structure of **1**.

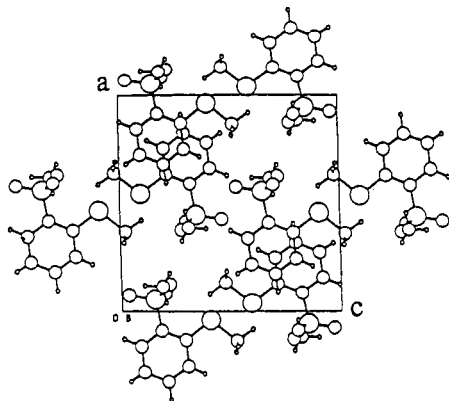


FIG. 3. Crystal structure of **3**.

Nevertheless, one cannot assume that all solid-state reactions occur under topochemical control. A striking example to the contrary concerns the apparently very similar rearrangement of *o*-methoxysulphonylthioanisole **3** to zwitterion **4**. In solution the reaction proceeds intermolecularly, as shown 20 years ago by kinetics; the intramolecular transfer of the methyl group is prevented by the difficulty of achieving the linear $S\cdots CH_3-O$ arrangement required in the transition state of this S_N2 type of reaction (ref. 15). Following an inquiry of Professor K. Venkatesan from the Indian Institute of Science in Bangalore, it was found that solid **3** had been completely converted to **4** in the course of time. Venkatesan then confirmed that partial conversion of solid **3** to **4** occurs (on heating to ca. 315 K for about a week) and determined the crystal structure of the starting material (Fig. 3). Contrary to the structure of **1**, the arrangement of neighbouring molecules in **3** is not at all favourable for intermolecular methyl transfer; indeed, the molecular motions that are called for are so large that they could hardly take place without disruption of the crystal structure. On the other hand, by making suitable rotations around the C-S and S-O bonds, a pathway for the intramolecular, endocyclic reaction could be imagined that was admittedly less-than-perfect but could not completely be ruled out. If the solid state reaction is indeed topochemical, then the methyl transfer would have to be intramolecular, contrary to what had been observed in solution. Topochemical control or stereoelectronic control? Which was operating here? The answer is that in this case stereoelectronic control wins. A double-labeling experiment showed clearly that the reaction in the solid is entirely intermolecular (ref. 16). It must be occurring preferentially on the crystal surface or at other crystal defects, where the regular arrangement of neighbouring molecules is interrupted; in support of this, the reaction is found to run faster in powder than in the single crystal, and still faster in the melt. Notice that a single intermolecular methyl transfer leads not to the zwitterionic product **4** but to an intermediate ion pair -- a trimethylated cation and a monomethylated anion. A second methyl transfer is needed to form **4**. Apparently, the ion-pair intermediate does not accumulate in the crystal; at least, its presence has not been detected by spectroscopic analysis of solutions of the partially reacted material.

EXAMPLES OF POLYMORPHIC TRANSITIONS

We shall now discuss three series of polymorphic transitions, of very different types, which we have studied recently. One is an example of conformational polymorphism, and the other two are examples where crystal orientation is maintained to a high degree on passing through the transitions in either direction. As we shall see, the first two seem to be best explained by nucleation of the new phases at pre-formed micro-cavities in the parent crystal, followed by their growth. The third example illustrates a special kind of order-disorder transition, where the disorder is in the stacking sequence of well defined, ordered layers.

THREE POLYMORPHS, THREE COLOURS

The dimethyl ester of 2,5-dihydroxy-3,6-dichloroterephthalic acid **5** yields three crystal forms, deep yellow (Y), light yellow (LY) and white (W), which can all be obtained together by crystallization in the same vessel. From their solubility behaviour, we know that at room temperature, Y is the most stable, W the least; at higher temperature, the order changes, W becoming the most stable, Y the least. The Y and W forms were recognized 75 years ago by Hantsch (ref. 17), who noted that the former transforms to the latter on heating to about 410 K; both types of crystal gave identical solutions, colourless in methanol and yellow in chloroform. Hantsch considered the two forms as tautomers, W as **5**, Y as the quinonoid enol isomer **6**. So the problem rested until 1969, when Curtin and Byrn made new spectral measurements in various solutions and interpreted the colour changes in terms of differences in hydrogen bonding, rather than keto-enol isomerism (ref. 18). The same authors, with Paul (ref. 19), then showed by crystal structure analysis that the Y and W forms are conformational isomers of **5**. In Y the molecules are almost coplanar, with intramolecular hydrogen bonds to carbonyl O atoms, while in W the ester groups are rotated nearly perpendicular to the plane of the other atoms (with intermolecular hydrogen bonds to carbonyl O atoms of different molecules).

During a sabbatical leave in my laboratory, Venkatesan noticed that the published (ref. 19) anisotropic displacement parameters (ADP's) (ref. 12) led to a large mean-square amplitude of libration (ca. 145 deg²) for the ester group about the exocyclic C-C bond in Y, whereas the corresponding amplitudes for the two independent molecules in W were not significantly different from zero. We wondered whether this large internal motion might be, so to say, a kind of harbinger of the transformation to W. Generally, one might ask about possible relationships between large-amplitude atomic motions, temperature and phase transitions in molecular crystals. We decided, for a start, to redetermine the Y and W crystal structures over as wide a temperature range as possible (ref. 20).

Our first result was the recognition and identification of the LY form, which had apparently been overlooked by the earlier investigators. The new form proved to contain molecules in which the ester groups are neither coplanar with the benzene ring, as in Y, nor nearly perpendicular to it, as in W, but in an intermediate orientation with torsion angle about 40°. We made new crystal structure analyses of all three forms, Y and LY at five temperatures and W at three temperatures between 100 and 350 K. There are significant differences in bond lengths and angles as the molecular conformation changes, but the most striking difference between the three types of molecule comes from the analysis of the ADP's as function of temperature: the mean-square libration amplitude of the ester group about the exocyclic C-C bond rises much more steeply for Y than for the other two forms (Fig. 4).

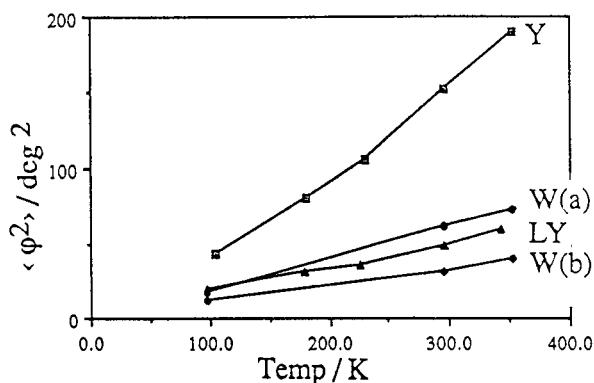


FIG. 4. Temperature dependence of libration of ester groups in **5**.

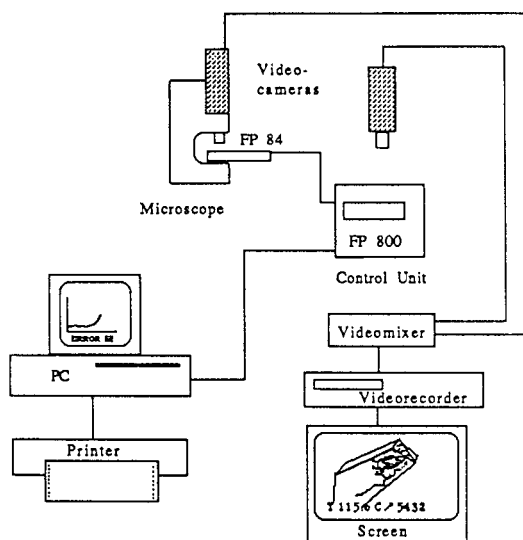


FIG. 5. Video-device

We also obtained much new information about the phase transformations. In this, we were greatly aided by a device (Fig.5) allowing simultaneous differential scanning calorimetry (DSC) measurements and microscopic observations recorded with a video-camera, as described by Wiedemann and Bayer (ref. 21). Visual observations can sometimes be more sensitive indicators of phase changes than the DSC measurements. On heating or cooling the sample, one can see that changes are happening in and on the surface of the crystals, while the DSC trace remains featureless. The video-record secures the permanency of these ephemeral events. The melting and phase transformation behaviour of a crystalline substance depends not only on the system itself, but also on such factors as crystal size and shape, thermal history, rate of heating, etc. The results (ref. 22) for **5** may be summarized as follows:

The Y to W transformation can occur between about 370 and 410 K. The broad, ragged endotherm in the DSC record is difficult to integrate, but from many experiments we estimate $\Delta H \approx +400 \text{ cal mol}^{-1}$, corresponding to $\Delta S \approx +1 \text{ cal deg}^{-1} \text{ mol}^{-1}$. On further heating, W melts at 453 K ($\Delta H_f \approx 9.5 - 9.9 \text{ kcal mol}^{-1}$, $\Delta S_f \approx 21 \text{ cal deg}^{-1} \text{ mol}^{-1}$) to a yellow liquid. This supercools and freezes around 430 K to give mainly Y, even though this is well above its usual range of stability. The Y material obtained in this way (sometimes as single crystals) does not revert to W on

rearming but melts — some 20 K lower than W. However, if the Y crystals are cooled rapidly to room temperature and then heated they transform normally to W. This kind of erratic behaviour points to the importance of crystal defects in initiating the various transformations. Indeed, if defects are introduced artificially, by touching the crystal surface with a sharp needle, the Y to W transformation starts at the scratch and proceeds outwards from there.

Crystals of LY usually transform to W, again over a wide temperature range, between 360 and 380 K ($\Delta H \approx 600$ cal mol⁻¹). Occasionally, however, a LY crystal (or part of one) may transform to Y. In contrast to the other transformations, which all yield polycrystalline products, this one sometimes yields quite large translucent regions of Y, an indication of a single-crystal to single-crystal transformation.

From visual observations during the Y to W transformation, one gets the impression that the colour change occurs in two stages, first a change from deep to light yellow, followed almost immediately by a second change to white, suggestive of the transient appearance of LY as an intermediate. As the transformation takes place over a wide temperature range, it can happen that in some regions of a crystal the Y \rightarrow LY \rightarrow W transition may be complete while other regions are still unreacted. The intermediacy of LY could be confirmed from the powder diffraction pattern of a crystal that had been heated until the first signs of transformation began to appear and then rapidly cooled.

At sufficiently low temperatures the relative free energies must have the same order as the internal crystal energies: Y < LY < W. Fig. 6 shows the temperature dependence of the molecular volumes; evidently, the denser the crystal, the lower its internal energy. (This can be considered as a general rule, but there are many exceptions.) The mean-square libration amplitude of the ester group in Y is much larger than in the two other forms, and so its temperature dependence (Fig. 4). In fact, all the atoms in the Y crystal have larger ADP's than the corresponding atoms in the other two forms. From this, one might guess that Y would have the largest entropy. However, this is not so. The Y to W transformation at around 390 K is endothermic and hence associated with an entropy increase. The relative molecular volumes seem to be a better guide. I do not know why the atomic ADP's should be smaller in the crystal with the greater entropy and leave this problem to the theoreticians.

The torsion angles about the exocyclic C-C bonds vary slightly with temperature for all three forms. From this information, together with the temperature dependence of the internal ester librations, we can construct a kind of potential energy diagram (Fig. 7). The horizontal lines represent $\phi \pm \langle \omega^2 \rangle^{1/2}$, ϕ being the mean twist angle of the ester groups. The relative displacements of the three curves along the energy coordinate have no well defined meaning; they have been drawn so that the positions of the energy minima correspond roughly to the relative thermodynamic stabilities around 375 K. The dashed curves that connect the three wells are purely hypothetical. Still, the diagram does include some experimental data, and it may be taken to portray, crudely, the energy dependence of ϕ at a suitable defect in the crystal, and, even more crudely, the energy profile for the phase transformations. Clearly, it cannot be more than a caricature of the actual process, but, like a caricature, it may convey an important component.

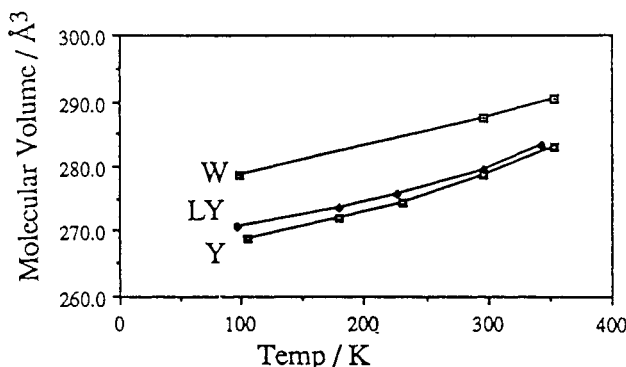


FIG. 6. Molecular Volumes versus Temperature

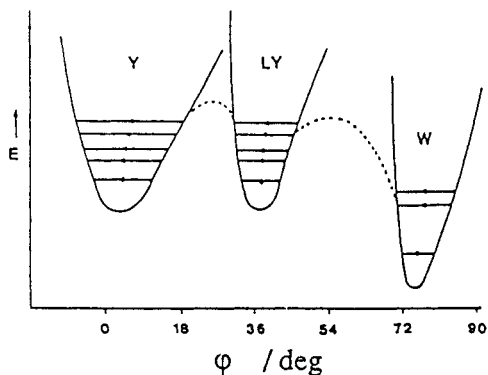


FIG. 7. Potential energy diagram

TWO POLYMORPHS WITH CLOSELY SIMILAR STRUCTURES

The reversible transformation of N-methyl-1-thia-5-azoniacyclooctane-1-oxide perchlorate **7** from a low-temperature α -phase (thermodynamically stable below about 290 K) to a high-temperature β -phase with almost complete retention of crystal orientation and outward morphology (ref. 23) is remarkable. The unit cell dimensions are closely related: in the β -phase the a axis is approximately doubled, the c axis approximately halved, while the b axis remains approximately constant. The space group switches from $P2_1/c$ (in the α -phase) to $P2_1/a$ (in the β -phase). The structures appear virtually identical when viewed down b (Fig. 8). The difference is that sets of molecules related by glide-reflection in one phase are related by lattice-translation in the other, and vice versa. The molecules occur in a chiral boat-chair conformation, so the phase transformation must involve a switch in the chirality sense of half the molecules. Every second molecule would need to undergo a conformational change, followed by a rotation (Fig. 9). The details of how this might be done are unclear. Quite another mechanism for the phase change has been suggested by Thomas and his co-workers (ref. 24). This dispenses with the need to invoke conformational changes and rotations of the molecules and postulates instead a cooperative shear of alternate (102) type planes in opposite directions.

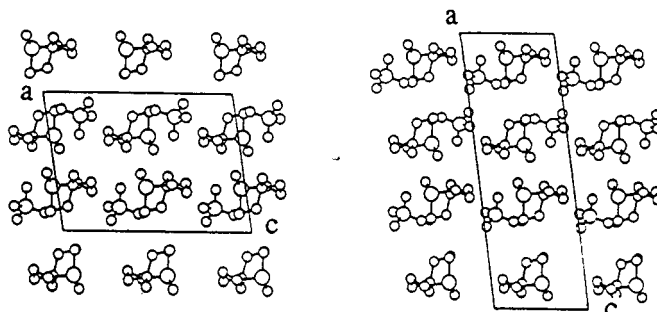


FIG. 8. Crystal structures of the two polymorphic forms of 7.

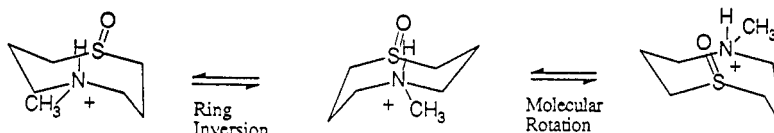
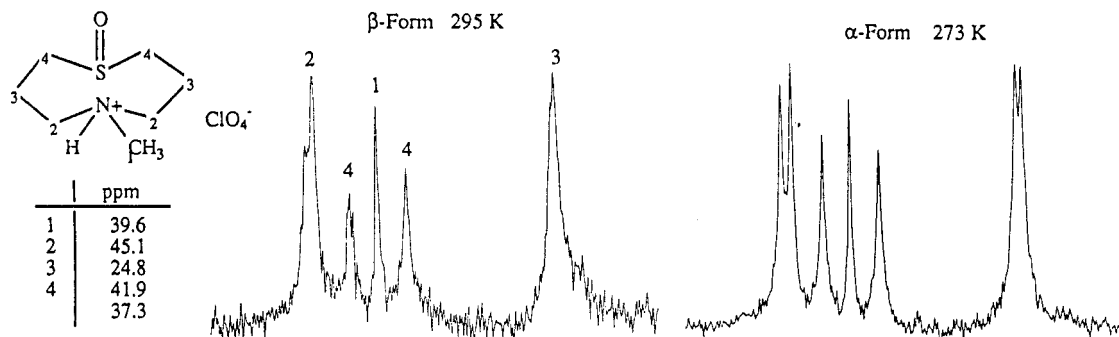


FIG. 9. Possible mechanism for inverting sense of chirality of 7.

We have taken up this problem again. Neither DSC curves nor optical microscopy give any indication of the phase transition, but it can be followed from the change in cell dimensions or in the intensities of reflections that are forbidden in one phase and allowed in the other. On warming a few degrees above 290 K the α to β transformation is completed within a few minutes; on cooling to 287 K the reverse transformation needs several days to go to completion. The transformation cycle can be repeated over and over again. The lower the temperature, the slower is the β to α transformation. If the β phase is cooled rapidly to 100 K, it can be kept indefinitely there. We have made new crystal structure determinations (ref. 25) of the α -phase at four temperatures (173, 213, 258 and 288 K) and of the β -phase at three (193, 290 and 298 K). In contrast to some of the other crystals we have studied, analysis of the ADP's gives no indication whatsoever of the nature of the atomic motions involved in the polymorphic changes. The ADP's of the β phase do not differ in any striking way from those of the α phase, and neither does the temperature dependence of these quantities, except for the ADP's of the oxygen atoms of the perchlorate groups, which indicate a greater degree of rotational disorder of this group in the β phase over the entire temperature range.

The results of the NMR study are also disappointing. The ^{13}C spectra at room temperature (β -phase) and below (α -phase) are shown in Fig. 10. The signals from the pair of C(4) atoms are resolved, those of the C(2) and C(3) pairs appear as unresolved peaks in the spectrum of the β -form. Apart from a small splitting of the signals from the unresolved C(2) and C(3) pairs, the changes in the spectrum as the temperature is lowered are very slight. In particular, there is no temperature range where the two resolved signals from the C(4) pair show any sign of broadening or coalescence. If one did not know from other evidence that a phase change had occurred, one could hardly have inferred it from the NMR spectra.

FIG. 10. Solid-state ^{13}C nmr spectra of 7.

Although the two structures are so similar, we do not believe that alternate molecules in one phase actually invert their sense of chirality and rotate cooperatively to produce the other phase. The energy required would be prohibitive. On the other hand, if the transformation occurs by nucleation at suitable defects, followed by growth of the new phase, how do the ionic species cross the phase boundaries? In any case, there seems to be no evidence for the martensitic-like mechanism proposed by Thomas and his co-workers (ref. 24)

A CASE OF STACKING DISORDER

When we tried to determine the crystal structure of the zwitterion **2** formed from **1** in the solid-state methyl transfer reaction discussed above, we found that its diffraction pattern changes with temperature (ref. 26). In their earlier study, Bergman and his collaborators (ref. 11) had reported unit cell dimensions ($a = 10.15$, $b = 9.69$, $c = 20.55$ Å, $Z = 8$) and possible space groups (No. 32, $Pc2a$, or No. 55, $Pcma$ —the axial orientation given in ref. 11 has been altered to conform with ours) for the crystalline product, but they did not attempt to determine the detailed structure. If they had done so, they would have run into difficulties. Neither space group is correct.

On cooling from room temperature (RT), reflections with l odd increase in intensity, indicating that some structural change is taking place. This appears to be complete by about 250 K. A full data set was collected at 193 K (unit cell dimensions 10.12, 9.42, 20.89 Å, close to the Bergman values) and the structure solved satisfactorily (R factor 0.04) in the polar space group $Pnc2$ (No. 30), quite different from the reported one. In this α -phase (Fig. 11) there are two symmetry-independent sets of molecules. In each set, molecules form polar chains running parallel to the c axis. The chains are held together by head-to-tail ionic interactions between the positively charged trimethylammonium group of one zwitterion and the sulphonate group of the next. All such groups in a given chain are "eclipsed" and have approximate mirror symmetry with respect to the planes $y = \pm 1/4$; in fact, apart from the central atoms of the phenylene groups, the molecules in a given chain are almost translationally equivalent. The phenylene groups, however, are inclined to these planes, and the inclination angle is different for the two sets of molecules. Each polar chain is surrounded by four chains of the opposite polarity. The structure can also be described in terms of layers perpendicular to the polar c axis (Fig. 12). The outsides of these layers are the regularly alternating arrays of cationic and anionic substituents, the insides are the nonpolar aromatic groups. As in **1**, the main atomic motion is libration about the long molecular axis, but, in addition to the rigid-body libration (mean-square amplitude circa 20 - 30 deg² at 193 K), the phenylene rings have a large internal motion (circa 20 - 50 deg²).

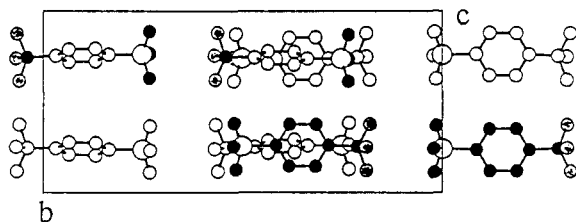


FIG. 11. Chains of molecules of **2** (view down a)

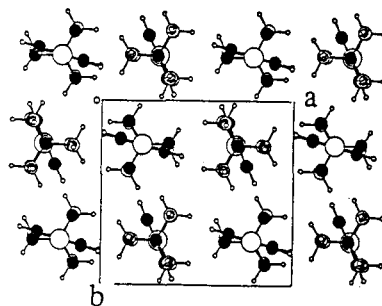


FIG. 12. Layers of molecules of **2** (view down c)

As the temperature is raised, reflections with l odd weaken and many show diffuse streaks or satellites, an indication of errors in the layer stacking. At the same time, $hk0$ reflections with h odd, and also $0kl$ reflections with k odd, weaken and disappear by about 335 K. With the c axis halved and the new glide planes present, the space group becomes No. 57 ($Pbma$, $Z = 4$). Successive molecules along the chains are now translationally equivalent, and the a/c glide plane relates the two formerly independent sets of chains. Moreover, the molecules are now formally mirror symmetric. However, the detailed structure analysis of RT data (ignoring the superfluous reflections) yields atomic positions corresponding to an averaged superposition of the four orientations of the phenylene groups in the α -phase, two close to the mirror plane and two nearly perpendicular to it. The space group $Pbma$ refers, of course, only to the contents of the space-averaged, time-averaged unit cell. The disordered structure, lacking three-dimensional periodicity, does not have a space group.

A further transformation, first detected by DSC, occurs at about 385 K (382 K in the cooling cycle). Above this temperature, the crystal becomes tetragonal (cell dimensions circa 7.2, 7.2, 10.5 Å, space group $P4/nmm$, $Z = 2$). Now it is not only the phenylene groups that are disordered about the chain axis but also the two orientations of the polar substituents. But the polar chains still retain their characteristic head-to-tail succession of dipolar molecules, and each chain is still surrounded by four others of opposite polarity, as in the α -phase.

Both transformations have characteristics associated with order-disorder transitions: the structures are closely related and differ only in their formal symmetry, the atomic motions involved are very small, and crystal orientation is maintained. But the second shows an abrupt change in cell dimensions, and the temperature range of about 50 K for completion of the first transition seems abnormally large. At room temperature, this process is not yet complete; reflections from the α -phase are still present, indicating that domains free from stacking faults must still co-exist with disordered domains.

CONCLUSIONS

Our first example was one of conformational polymorphism — three polymorphs, each with a distinctive colour; three crystal structures, each showing a different molecular conformation. As far as we can tell, there is no "mechanism" for the solid-state interconversions. At high enough temperatures, the new phase simply starts to grow within the old one, presumably at defects or other domain boundaries.

The second example involves two phases that look extremely similar, with similar arrangements of virtually isometric molecules. There is no obvious change in colour or in the NMR spectrum, and no observed specific heat anomaly. Only the diffraction pattern tells us that a phase transformation has occurred, but it tells us it unmistakably. The phase change involves extensive reorganization of the crystal structure, but, as in the previous example, we can find no plausible "mechanism". The new phase starts to grow within the old one, and, at least on the cooling cycle, if the cooling rate is chosen appropriately, we can see the co-existence of both phases.

In the third example, stacking faults arise from the reorientation of phenylene groups within layers built from a framework of ionic groups. Above about 335 K the layers are disordered, below about 255 K they have a double-layer periodicity, and in between we have some kind of co-existence of order and disorder. Here, perhaps, one can talk about a mechanism. As the temperature increases, the librational motion of the phenylene groups becomes large enough to flip the groups in a given layer from the "right" orientation characteristic of the double-layer structure into a "wrong" orientation. On warming, the frequency of such mistakes increases.

Are there any conclusions to be drawn? They are mostly negative, I am afraid: for various reasons, the traditional classifications of phase transitions in molecular crystals are often unsatisfactory, and our understanding of the mechanisms involved in these transformations is only at a very primitive level. The main trouble is that as long as our main tool is X-ray diffraction, we obtain an excellent picture of the time-averaged, space-averaged contents of a unit-cell in a crystal but very little information about the nature of the fluctuations from this averaged structure. In our experience, solid-state NMR has also not been particularly informative about the details of the atomic motions involved in phase transitions. Improved insight is likely to be obtained not only from better observations or better theories but also from computer modelling — I am thinking mainly of molecular dynamics techniques, which seem much more suitable than lattice dynamics for handling large scale displacements of the atoms in molecular crystals. Once we learn to know what to look for, important insights should be forthcoming from this approach. There is certainly much to be discovered.

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