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Phase Changes and Chemical Reactions in Molecular Crystals

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Abstract

Changes in the attitude of crystallographers to phase changes and chemical reactions in molecular solids over the last 50 years are sketched. Various ways of classifying polymorphic modifications and structural changes in solids are discussed, and examples are given. The methods applied include multi-temperature crystal structure analysis, analysis of anisotropic displacement parameters, differential scanning calorimetry, solid-state NMR and visual observation. The importance of defects in influencing the kinetics of solid–solid phase changes is stressed.

Early experiences

When I began my apprenticeship 50 years ago in X-ray crystallography with J. Monteath Robertson at Glasgow, solid-state phase changes and chemical reactions were generally regarded as a nuisance rather than as an area worthy of serious study and attention. One hoped to avoid them but did not really know how, and all too often we were unwilling victims. It was disheartening to obtain the desired crystals after long efforts, only to see the tiny jewels fracture or change colour or undergo some other physical or chemical change on exposure to the laboratory atmosphere or to X-radiation or for no apparent reason. Crystals of acetylenedicarboxylic acid dihydrate (Dunitz & Robertson, 1947*a*) tended to lose water of crystallization on standing in the laboratory. Crystals of diacetylenedicarboxylic acid dihydrate (Dunitz & Robertson, 1947*b*) turned purple in light and almost black on exposure to X-rays. Although, in these two early examples, we were aware that some chemistry was occurring within these little crystal laboratories or at their interfaces with the outer world, we lacked both the time and the motivation to study the matter further.

These were, I believe, fairly typical experiences for anyone involved in crystal structure analysis around mid-century. As far as possible, we tried to avoid crystals that underwent phase transitions and chemical reactions. If we could not avoid them, we attempted to come to terms with them, but it was rare that anyone would actually set out to study them. This was true at least for those of us who were studying molecular crystals, which, before the flowering of organometallic chemistry, were mostly organic compounds.* The thermodynamic aspects of phase transitions were understood – or so we had been taught. There were two types: first-order changes, in which energy, volume and crystal structure change discontinuously; changes of higher order, in which the properties and the structure change continuously. The mineralogists, it seemed, were more interested in those of the first type; after all, the earth was one gigantic high-pressure laboratory. The solid-state physicists, on the other hand, seemed more concerned with those of the second type, for these were involved in the phenomena of ferromagnetism, ferroelectricity and, in general, with the onset and disappearance of order in crystalline substances. Thus, the literature on the chemistry and physics of the solid state at that time was almost entirely concerned with inorganic substances. One can see this trend continued into fairly recent times. For example, the excellent monograph by Rao & Rao (1978) on phase transitions in solids contains 3 out of 320 pages on transitions in organic solids.

Has anything changed? From my personal point of view, the organic field was opened up with the publication of the monumental two-volume '*Physics and Chemistry of the Organic Solid State*', edited by Fox, Labes & Weissberger (1963, 1965), still probably the best and most comprehensive book on the subject. This is a publication that has stood the test of time. Two chapters in particular are still required reading for anyone intending to enter the field today. One by Westrum & McCullough (1963) is an exemplary clear account of the thermodynamics of crystals, with a compilation of practically all experimental data on organic crystals available up to that time; the other is the chapter by McCrone (1965) on polymorphism.

From thermodynamics alone one cannot make any detailed statements about the actual structures involved in phase transitions or about the mechanisms involved. One of the early attempts to discuss phase transitions in structural rather than in thermodynamic terms was made by Buerger (1951), who classified the various types of transformation in terms of changes in the bonding

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* Of course there were exceptions. Robertson himself had studied the structural and thermodynamic aspects of the phase change in solid resorcinol (Robertson & Ubbelohde, 1938), and I recall that my fellow student at Glasgow, John G. White, prepared γ- or 'nacreous' sulfur in an undergraduate research project intended to study the properties and determine the crystal structure of this notoriously unstable and erratic substance (for details see Donohue, 1974).

network according to structural criteria. Buerger's discussion was directed mainly at inorganic mineral structures, and we do not have space to go into all the details, but one of the concepts that can be carried over into molecular crystals is the distinction he made between 'displacive' and 'reconstructive' transformations. The displacive transformation involves a mere distortion of one network into another, *i.e.* the initial structure can be imagined to deform continuously into the final one without any disruption. Buerger considered that, as a 'net distortion of this kind is opposed by no energy barrier', such transformations will proceed very rapidly, 'indeed with a speed equivalent to the transmission of heat in the structure undergoing transformation'. On the other hand, the reconstructive transformation involves the disruption of the old structure (network) and its subsequent reassembly into a new pattern, a process that would be associated with a very high energy barrier and would therefore 'proceed in a sluggish fashion indeed'. We know today that the kinetics of actual phase transformations cannot be explained as simply as Buerger imagined, but the emphasis on the possible mechanisms of structural changes represented a welcome change from pure thermodynamics.

What is polymorphism?

McCrone (1965) defined a polymorph as 'a solid crystalline phase of a given compound resulting from the possibility of at least two different arrangements of the molecules of that compound in the solid state'. McCrone concedes that the molecule itself may be of different shape in the two polymorphs – conformational polymorphism (Bernstein & Hagler, 1978; Bernstein, 1987) – but would exclude cases of dynamic isomerism. The proposed distinction is that polymorphs are different in crystal structure but identical in the liquid and vapour states, whereas dynamic isomers give melts of different composition that change only 'in time', *i.e.* slowly, to the equilibrium mixture with temperature-dependent composition. Crystals of isomers that interconvert rapidly in solution would thus be classed as polymorphs, while those of slowly interconverting isomers would be classed as different compounds. Thus, according to this distinction, a racemate and a conglomerate of enantiomeric crystals are to be classed as *polymorphs* when the rate of interconversion of the enantiomers in the melt or in solution is fast, but as three *different compounds* when the interconversion rate is slow. It all comes down to the definition of a component in the Phase Rule; components are 'chemically distinct constituents' or, otherwise expressed, constituents whose concentrations may be varied independently at the temperature concerned.

Wallach's rule

Does it matter whether two solids are to be regarded as two compounds or as two polymorphs? One example where the distinction may be relevant to a difference in physical properties concerns Wallach's rule, which states that a racemic crystal tends to have a denser packing than the corresponding crystal composed of homochiral molecules (Wallach, 1895). Although this rule has not gone unchallenged (see Jacques, Collet & Wilen, 1981, for a review of the evidence), there seems to have been 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 homochiral ones.

A few years ago, we decided to look into this. With the help of the Cambridge Structural Database, we found about 250 examples where the structures of a crystalline racemate and of its chiral counterpart had both been determined (Brock, Schweizer & Dunitz, 1991). The sample could be divided into two almost equal groups, one where the molecules racemize rapidly (polymorphs, one-component systems), the other where they do not (different compounds, multi-component systems). In the first group the average ratio of molecular volumes $R - \langle V(\text{chiral})/V(\text{racemate})\rangle$ was 1.002 (4), not significantly different from unity, whereas for the second group the average ratio was 1.009 (3), still close to unity, but now the 3σ deviation cannot be passed over. Is there a systematic difference between the two groups in the sample? And, if so, why should Wallach's rule appear to hold for pairs where the rate of interconverion of enantiomers is slow but not where it is rapid? One factor that needs to be considered is possible bias in the second group.

If interconversion is slow, the chiral crystal is always obtainable in principle (*e.g.* by chemical resolution of the racemic compound), even if it is thermodynamically unstable with respect to the crystalline racemate. But for the racemate it is different. For similar packing energies, the racemate will tend to have a lower melting point than its chiral counterpart because the racemic liquid has a higher entropy (by $R\ln 2$, entropy of mixing) and hence a lower free energy (Brock, Schweizer & Dunitz, 1991). If the racemate has a markedly lower melting point (or higher solubility) than the eutectic mixture of enantiomers, then it may not always be obtainable. Thus, the second group tends to contain pairs where the racemate packing energy is better than that of the enantiomer (assuming the enantiomers to be separable), but not where it is worse. The first group contains no such bias; for rapidly interconverting enantiomers, the racemic crystal may be more or less stable than its homochiral counterpart. Unfortunately, there is practically no information about the thermodynamic relationships among the polymorphs in this group. An experimental study to see if there are any systematic trends could lead to interesting results. In the absence of conclusive experimental evidence on the question of the greater thermodynamic stability of racemates in general over their chiral counterparts, one must admit that there are many more space groups available for the packing of a collection of right- and left-handed objects than for a collection of homochiral ones, and hence many more possible ways of packing in the racemic case. However, the small differences in internal energy and the importance of entropic factors at room temperature make any predictions difficult and unreliable.

Crystals as phases

The free energies of different polymorphic modifications differ usually by only a few kcal mol^{-1}, or even less, and have different temperature dependences so that 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. In relating structure to thermodynamic stability, one must keep in mind that although entropic factors are unimportant at temperatures close to 0 K, they are very relevant indeed to the relative stabilities at higher temperature. What determines the relative thermodynamic stability is not the packing energy alone but the free energy $G = PE + E(\text{vib}) - TS$ where $E(\text{vib})$, the vibrational energy, is usually only a small fraction of the packing energy and increases only slowly with temperature. At 0 K, the entropy S of a perfectly ordered crystal is zero; at higher temperature the entropy increases at a greater or smaller rate, depending on the vibrational frequencies of the crystal. Quite typically, there is a certain trade off between packing energy PE and entropy S; in general, the deeper the potential energy well, the greater is its curvature with respect to small displacements from equilibrium, the higher are the vibrational frequencies, and hence the lower are the vibrational contributions to the specific heat and entropy. This is the case for most types of assumed interatomic potentials, such as the Morse potential or the Lennard–Jones potential, where the curvature is directly proportional to the dissociation energy. Thus, a structure with a lesser packing energy will tend to have a greater entropy and will become the thermodynamically more stable form at a sufficiently elevated temperature T if the free energy *versus* temperature curves cross below the melting point (Fig. 1). The polymorphic form stable at low temperature has the largest possible packing energy, and this will tend to be associated with the highest density (although there are many exceptions where strongly directional interactions lead to an open structure with lower density, *e.g.* ice). At room temperature, this form may have been displaced by another form with lesser packing energy and lower density, as mentioned above.

Besides changes in energy, volume or crystal structure, a change in any physical property (such as electric conductivity) or in its derivatives with respect to temperature or pressure can serve as an indication of a phase change. With small changes, or with higher derivatives, it is sometimes difficult to know where to draw the line.

In this review I shall ignore order–disorder transitions and concentrate mainly on first-order transitions in molecular solids, an area where very little is known about kinetic aspects and almost nothing about the mechanisms. As far as these mechanisms are concerned, little can be said, except that first-order transitions are generally believed to occur by nucleation of the new phase within the other, followed by its growth. In many cases one can observe the coexistence of the two phases over quite a wide range of temperature. Superheating or supercooling, depending on the direction in which the transition is proceeding, seems to be necessary, which means that at the transition temperature T_t, where the free energies cross and the two phases are in thermodynamic equilibrium, nothing happens. On the high-temperature side of T_t the transformation rate can rise fairly steeply, whereas on the low-temperature side the rate first increases and then drops again to virtually zero (Fig. 2). Thus, if a high-temperature modification is cooled rapidly through T_t to very low temperatures, it may be kept indefinitely without reverting to the low-temperature modification. This makes it possible to make crystal structure analyses of high-temperature modifications at low temperatures, but not usually the other way around.

As we shall see from an example, the nucleation step, which is usually rate-limiting, is critically dependent on the presence of suitable defects, such as micro-cavities and other surface irregularities between crystal domains, as argued forcibly by Mynukh (1979). Depending on the nature of such defects, nuclei of the new phase may be formed at slightly different temperatures and grow at different rates. In many crystal transformations the phase boundary can be seen to advance with a sensible velocity across the crystal specimen (although examples are also

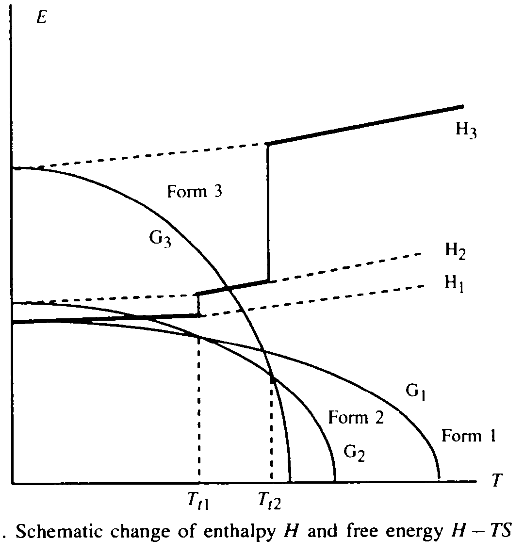


Fig. 1. Schematic change of enthalpy H and free energy $H - TS$ as a function of temperature for three phases, forms 1, 2 and 3. If form 3 is taken as the liquid phase then T_{12} is the melting point of the high-temperature form 2.

known where the phase transformation, once triggered, is practically instantaneous).

Crystals of a low-temperature phase that are free from defects can sometimes be warmed through the transition temperature without undergoing transformation to the high-temperature phase; on warming to the fusion temperature of the low-temperature phase, which is always lower than that of the high-temperature phase, the crystals then melt to yield the supercooled liquid. In this connection, although solid–liquid transitions are outside the scope of this article, it is worth noting that while a solid typically melts fairly sharply at its melting point to yield the liquid, the latter can often be supercooled to temperatures far below the thermodynamic freezing point: the change from the disordered to the ordered state does not happen as readily as the reverse. Here again, the formation of crystal nuclei in the melted liquid is the rate-limiting step.

Crystals as supramolecules

If the classical way of thinking about crystals is in terms of solid phases, a more fashionable view might be to regard them as supramolecules. And indeed, a molecular crystal is the very embodiment of a supramolecule – a lump of matter, of macroscopic dimensions, millions of molecules long, held together in a periodic arrangement by just the same type of non-covalent bonding interactions as are responsible for molecular recognition and complexation at all levels. The crystallization process itself is an impressive example of supramolecular self-assembly, involving molecular recognition at an amazing level of precision. Crystals are ordered supramolecular systems. If a crystal is a supramolecule, then polymorphic modifications are supra-isomers and polymorphism is a kind of supra-isomerism.

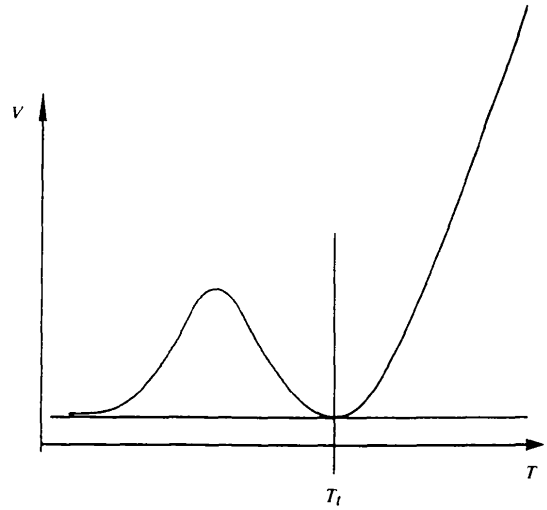


Fig. 2. Schematic representation of the rate of phase transformation as a function of temperature. The thermodynamic transition point is T_t.

There are, however, some obvious and important differences between phase transformations in solids and isomerization reactions in solution or the gas phase. One difference is that in a reversible chemical reaction there is at any temperature an equilibrium mixture of reactant and product, whereas in a crystal the transformation, once triggered on either side of the transition temperature (by nucleation of the new phase), usually goes practically to completion. In other words, either there is no reaction, or else one isomer is transformed completely into the other; the 'equilibrium constant' suddenly changes, so to speak, from zero to infinity. Secondly, there is the difference in the temperature dependence of the reaction rate. The rate constant of a 'normal' chemical reaction increases smoothly with temperature according to the Arrhenius relationship. With phase transformations, as mentioned above, superheating or supercooling of the 'reactant' is required before any 'product' is formed, but then the 'reactant' is transformed completely into 'product'. The defects required to initiate the transformation are, of course, catalysts in chemical parlance.

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 a 'normal' chemical reaction, molecules react more or less independently of one another; what happens to one molecule has little effect on what happens to its neighbours. In the phase transformation, cooperativity is the essence. Within a crystal, every displacement of a molecule from its equilibrium conformation, position and orientation is immediately communicated to its immediate neighbours and thence to more distant neighbours, and so on, so that molecular motions are coupled in a set of lattice vibrations that extend through the entire crystal. In a liquid, on the other hand, although motions among neighbouring molecules are coupled, there is no long-range correlation between molecular positions or orientations; there are only local effects. It is this difference that is responsible for the different types of temperature dependence between normal reactions and the highly cooperative ones typical of phase transitions. From this point of view, polymorphic transitions are solid-state supramolecular chemical reactions involving a high degree of cooperativity.

Solid-state chemical reactions

Although there are borderline cases, solid-state chemical reactions are usually treated as being distinct from polymorphic transformations. The solid-state reaction can lead to an isolable product different from the starting material – different not just in the solid, but also in the melt or the vapour or in solution. Although cooperativity may play a role in thermally activated solid-state reactions, it is usually unimportant in photochemically activated ones, at least in the early stages where the product is formed initially in solid solution in the reactant crystal. Only when the concentration of product reaches a certain level can the product crystallize within the reactant. Besides, reaction is possible not only among molecules of the reactant but also between them and small molecules that may diffuse into the crystal from its surroundings. As with phase transitions, solid-state reactions may be triggered by crystal defects and may occur preferentially at crystal surfaces, voids and inclusions, as well as in the ordered bulk of the reactant crystal. Two recent multi-authored books (Desiraju, 1987; Ohashi, 1993) survey the state of knowledge in the general area of chemical reactivity in molecular solids.

Generally, any monomolecular chemical reaction that proceeds thermally in solution can also be expected to occur in the crystalline state. Its rate may be much slower in the crystal, because of greater limitations on molecular flexibility and atomic motion, or it may proceed 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 (Kohlschütter, 1919; Cohen & Schmidt, 1964; see Bürgi & Dunitz, 1993, for an account of the early history of this term).

A beautiful example of this type is the methyl transfer reaction that takes place in crystals of methyl 4-(dimethylamino)benzenesulfonate [(1); Sukenik, Bonopace, Mandel, Law, Wood & Bergman (1977)]. An intermolecular migration of the sulfonate methyl ester group yields the zwitterion (2). The crystal structure (Fig. 3) is such that this methyl migration can occur with a minimum of atomic motion – the methyl group of one molecule is close to the amino group of another – and not too far from the linear N···C—O arrangement required for the transition state of this S_N2 displacement reaction [the intermolecular N···C distance is 3.54 Å at room temperature, 3.47 Å at 193 K (Sarma & Dunitz, 1990) and the N···C—O angle is 147–151°]. 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. The anisotropic displacement parameters (ADP's) obtained from crystal structure analyses at 193 and 253 K (Sarma & Dunitz, 1990) suggest considerable librational motion of the molecules about their long axes, the r.m.s. libration amplitude of the sulfonate group about the C—S bond being *ca* 7 and 9° at the two temperatures mentioned and extrapolating to *ca* 12° at the melting point of the crystals. A coupled 10° rotation of neighbouring molecules would lead to a N···C distance less than 3 Å and to a nearly collinear approach of the reacting atoms (N···C—O angle ≈ 168°). Correlated libration of molecules within a given chain could then lead to concerted methyl migration from molecule to molecule along the chain. Such a mechanism eliminates the need for ion-pair intermediates, as have been postulated on the basis of energy calculations (Gavezzotti & Simonetta, 1977).

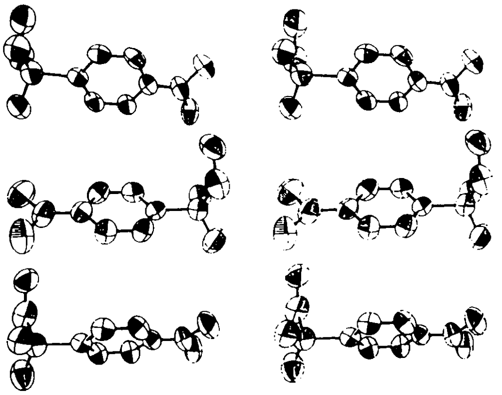
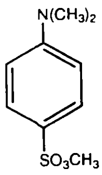


Fig. 3. *ORTEP* (Johnson, 1965) stereoview of a molecular stack in the crystal structure of (1) at 255 K, showing displacement ellipsoids at the 50% probability level (Sarma & Dunitz, 1990).



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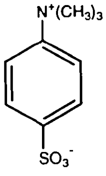

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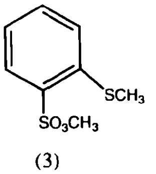

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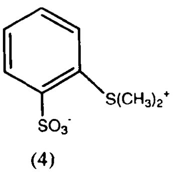

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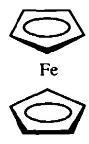

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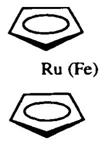

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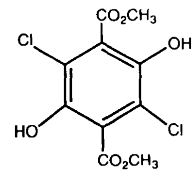

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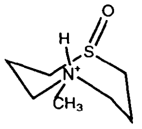

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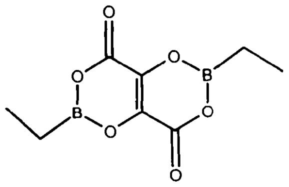

(9)

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 methyl 2-(methylthio)benzenesulfonate (3) to zwitterion (4). In solution the reaction proceeds intermolecularly, as shown more than 20 years ago by kinetic measurements; the intramolecular transfer of the methyl group is prevented by the difficulty of achieving the linear S···CH_3—O arrangement required in the transition state of this S_N2 type of reaction (Tenud, Farooq, Seibl & Eschenmoser, 1970). Much later, it was found that a remaining sample of solid (3) had been completely converted to (4) in the course of time (*ca* 25 years!). It was then confirmed that partial conversion of solid (3) to (4) occurs on heating to *ca* 315 K for a few days. The crystal structure of (3) is shown in Fig. 4. Contrary to the previous example, the arrangement of neighbouring molecules is not at all favourable for intermolecular methyl transfer; indeed, the molecular motions that are called for are such that they could hardly take place without disruption of the crystal structure. On the other hand, it is not possible (without extreme bond-angle distortions) to achieve a linear $S\cdots CH_3-O$ arrangement in the six-membered cyclic transition state that would be required for the intramolecular methyl transfer. The answer to this dilemma was provided by a double-labelling experiment, which showed clearly that the reaction in the solid is entirely intermolecular (Venugopalan, Venkatesan, Klausen, Novotny-Bregger, Leumann, Eschenmoser & Dunitz, 1991). Since this reaction cannot occur in the ordered crystal structure, it must take place preferentially at the crystal surface or at other crystal defects, where the regular arrangement of neighbouring molecules is interrupted; indeed, the reaction is found to run faster in powder than in single crystals, and still faster in the melt. Notice that a single intermolecular methyl transfer leads not to 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). As in the previous example, the ion-pair intermediate does not accumulate in the crystal; at least, attempts to detect its presence by spectroscopic analysis of solutions of the partially reacted material were unsuccessful.

In neither of these examples does the product of the solid-state reaction have a crystal structure that resembles that of the reactant. There are, however, other solid-state reactions where the crystal structures of reactant and product are very similar with respect to unit-cell dimensions, space group and molecular arrangement. Sometimes, a single crystal of reactant can even be converted into a single crystal of product, and sometimes the solid disintegrates into microcrystalline particles during the reaction. For single-crystal to single-crystal transformation to occur, it is important that, as the reaction proceeds, the product molecules are distributed statistically within the disordered single crystal. Otherwise, preferential crystallization of product in localized regions would set up strains that would lead to disruption of the parent crystal. It has recently been shown that for photochemical reactions, the single-crystal to single-crystal transformation can be produced if the irradiation is carried out not at the absorption maximum (where the intensity is high at the incident surface and drops off rapidly towards the inner regions), but with low-absorption light (more uniform absorption throughout the crystal). In this way the transformation can be made to occur more smoothly (Enkelmann, Wegner, Novak & Wagener, 1993).

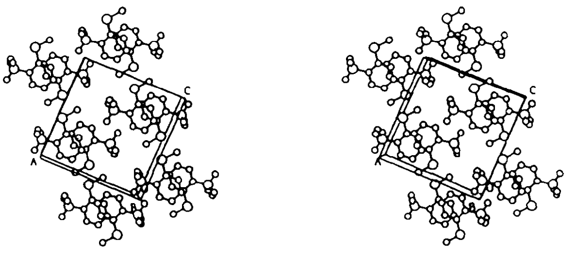

Fig. 4. Stereoview of the crystal structure of (3) at 190 K along a direction nearly normal to the benzene ring planes (Venugopalan, Venkatesan, Klausen, Novotny-Bregger, Leumann, Eschenmoser & Dunitz, 1991).

While the topochemical approach has been most helpful in clarifying the course of many solid-state reactions, it is limited to those that take place in the ordered crystal structure and without too great disruption of this structure as the reaction proceeds. The real solid has surfaces, grain boundaries, dislocations, substitutional impurities, occluded solvent and possibly other types of defect. Molecules at or close to these defects have a higher potential energy than those in the ordered regions and may be more reactive. Reactions at defects may sometimes merely lead to side reactions but they may also yield the only or the major product if the bulk crystal is unreactive.

Polymorphism of ferrocene

I want to turn now to the polymorphism of ferrocene, bis(cyclopentadienyl)iron, a topic that has been discussed from different standpoints in two recent reviews (Braga, 1992; Dunitz, 1993). The transition-metal metallocenes have very similar molecular shapes and might be expected to show very similar packing arrangements in their crystals. Three types of crystal structure are known. Most crystallize in a monoclinic form with space group $P2_1/a$, $Z = 2$. This was the form found initially for room-temperature ferrocene (Fischer & Pfab, 1952; Eiland & Pepinsky, 1952; Dunitz & Orgel, 1953; Dunitz, Orgel & Rich, 1956) and is the basis of the centrosymmetric, staggered molecular structure (5) (point group D_{5d}) usually shown in textbooks. Ruthenocene has long been known to crystallize in a different space group, $Pmna$, $Z = 4$, in which the molecules are required to have mirror symmetry, hence eclipsed (point group D_{5h}) (6) (Hardgrove & Templeton, 1959). Ferrocene undergoes an order–disorder phase transition at 165 K (Edwards, Kington & Mason, 1960) and is polymorphic (Clec'h, Calvarin, Bérar & Kahn, 1978; Seiler & Dunitz, 1979*a*; Ogasahara, Sorai & Suga, 1979). On cooling below 164 K, all three axes double and the crystals become triclinic $F\bar{1}$, $Z = 16$. The crystal structure (Seiler & Dunitz, 1979*b*) is closely related to the monoclinic one (Fig. 5), but there are now two independent molecules, which turn out to be neither eclipsed ($\alpha = 0$) nor staggered ($\alpha = 36°$) but intermediate, closer to eclipsed ($\alpha \approx 9°$). On cooling the monoclinic crystals from room temperature to the transition point, the apparent libration amplitude of the cyclopentadienyl rings hardly changes. This is an indication of disorder (Seiler & Dunitz, 1979*a*) that is corroborated by neutron-diffraction analysis (Takusagawa & Koetzle, 1979). The apparent centrosymmetry of the molecules in the high-temperature form of ferrocene is thus shown to be not necessarily a genuine molecular property but merely a manifestation of the statistical distribution of ring orientations in the centrosymmetric space group corresponding to the averaged structure. For example, each cyclopentadienyl ring, the unit of structure in the high-temperature form, might be regarded as an averaged superposition of the four symmetry-independent rings in the ordered low-temperature triclinic structure. Recent refinements of the neutron-diffraction data show, however, that still more elaborate models are needed (Brock & Fu, 1991; Fu, 1991).

In the meantime, a third crystalline form had been detected by cooling large ferrocene crystals until they disintegrated into powder, followed by annealing at 190 K (Ogasahara, Sorai & Suga, 1979). Although it was the last to be identified, this is the thermodynamically stable phase below 242 K, so that the triclinic–monoclinic transition at 164 K occurs between phases that are both metastable at this temperature. From its powder diffraction pattern, the new phase was found to be orthorhombic, isostructural with ruthenocene (Bérer, Calvarin & Weigel, 1980); from calorimetric measurements the enthalpy change for the orthorhombic to monoclinic phase transition is 4145 J mol^{-1} at 242 K, corresponding to an entropy change ΔS of 17.1 J mol^{-1} K^{-1}, much larger than the ΔS of 5.31 J mol^{-1} K^{-1} for the triclinic to monoclinic transition at 164 K (Edwards, Kington & Mason, 1960).

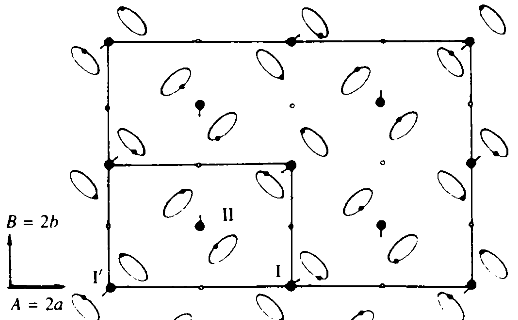

Fig. 5. Relation between the triclinic (full cell) and monoclinic (subcell) crystal structures of ferrocene. The ellipses represent projections of cyclopentadienyl rings and the dots identify symmetry-related rings in one layer of the triclinic structure. An equivalent layer is related to the one shown by the translation 0.5, 0, 0.5 (or 0, 0.5, 0.5) to produce an *F*-centred lattice. In the monoclinic structure (subcell) the molecules are formally centrosymmetric and all four rings are symmetry related (Seiler & Dunitz, 1979*a*).

Single crystals of this new orthorhombic modification could be obtained by crystallization from cryosolvents at temperatures around 100 K (Seiler & Dunitz, 1982). Crystallization at higher temperatures gave the other crystal forms, in spite of their thermodynamic metastability. Clearly, the crystallization process is under kinetic rather than thermodynamic control, the rate-limiting step being the formation of suitable nuclei. The single crystal analysis of the orthorhombic form confirmed the isomorphism with ruthenocene and showed, moreover, that the eclipsed molecules have much smaller vibrational parameters than in the triclinic form around the same temperature. The stable conformation of the ferrocene molecule is thus eclipsed, in agreement with the results from an early gas-phase electron-diffraction study (Haaland & Nilsson, 1968), and not staggered, as usually depicted in textbooks. The same eclipsed conformation has recently turned up in the C_{60}(ferrocene)$_2$ cocrystal (Crane, Hitchcock, Kroto, Taylor & Walton, 1992) – an unexpected corroboration!

Ferrocene can thus adopt three different crystal structures. They have different colours: monoclinic (room-temperature form, stable above 242 K, metastable from 164 to 242 K), orange; triclinic, metastable below 164 K, canary yellow; orthorhombic, stable below 242 K but difficult to obtain, brown. In contrast, as far as we know, the other sandwich-structure metallocenes are found only in one crystal form, monoclinic for most, orthorhombic for ruthenocene (Hardgrove & Templeton, 1959; Seiler & Dunitz, 1980) and osmocene (Jellinek, 1959; Boeyens, Levendis, Bruce & Williams, 1986). Orthorhombic crystals of nickelocene, together with monoclinic ones, can be obtained from solution at temperatures around 175 K, but only after seeding with ruthenocene (Seiler & Dunitz, 1982). Why these differences? What is so special about ferrocene?

Although the problem of predicting the crystal structure of a compound, given the molecular structure, is still far from being solved, the converse (and much simpler) problem can usually be answered: given the crystal structure, show that it is energetically stable, *i.e.* that it corresponds to an energy minimum with respect to small deformations. When Emily Maverick (unpublished work) calculated the energy of triclinic ferrocene with standard interatomic potentials, but with no allowance for a barrier hindering internal motion, she found that the observed structure did *not* correspond to an energy minimum. The inter-ring torsion angles in the observed structure (two independent molecules) were both *ca* 9°, whereas the energy minimum in the calculated structure occurred at considerably larger values – *ca* 15°. Each of the four symmetry-independent rings was rotated away from the orientation where it would be eclipsed with respect to its partner. In other words, when the internal barrier was set to zero, each ring was subjected to a net force pushing it away from its observed orientation. To counteract this force, to produce equilibrium at the observed structure, we need to introduce an intramolecular potential with its minimum at the eclipsed orientation of the rings; for a sinusoidal potential curve a barrier height of approximately 4 kJ mol^{-1} was required, roughly the same as the estimate from the earlier electron-diffraction study (Haaland & Nilsson, 1968).

In another computer experiment by Carol Brock (unpublished work), crystal-packing energy calculations were made for a range of metal–ring distances and atomic charges (again with no intramolecular barrier to ring rotation) for the three observed crystal structures of ferrocene. For all reasonable values of the metal–ring distance and atomic charges, these calculations gave the monoclinic structure with centrosymmetric molecules the lowest potential energy of the three, the orthorhombic structure with eclipsed rings the highest. However, the energy differences were small, and inclusion of an internal energy barrier of only a few kJ mol^{-1} favouring eclipsing was sufficient to make the orthorhombic structure the most stable of the three. Ruthenocene, which is believed to have the highest barrier (Carter & Murrell, 1980) occurs, as far as is known, only in the orthorhombic structure. For ferrocene, as mentioned above, the eclipsed arrangement is also favoured in the free molecule, but by a smaller amount. We assume that this preference is enough to make the orthorhombic structure the most stable by a small margin at 0 K. When the temperature is raised above 242 K the $T\Delta S$ term, arising from increased librational motion and/or disorder, overcomes the enthalpic preference and leads to a lower free energy for the monoclinic structure, which then becomes the thermodynamically stable form up to the melting point. On cooling the monoclinic structure, it does not revert to the orthorhombic structure at 242 K, but supercools and undergoes transformation at 164 K to the triclinic structure with its very similar packing but more ordered arrangement of the cyclopentadienyl rings in nearly eclipsed orientation. At temperatures below 164 K this has a lower free energy than the monoclinic form, but it is metastable with respect to the orthorhombic form throughout its entire existence range (Ogasahara, Sorai & Suga, 1981). Although single crystals of the triclinic form have been kept for weeks at temperatures between 100 and 164 K (long enough to measure extensive X-ray diffraction patterns), its thermodynamic instability is demonstrated by the fact that cooling below 164 K sometimes leads to crystal disintegration with explosive violence and a large evolution of heat (Naruse, Sorai & Sakiyama, 1983). Apparently, the thermodynamically driven transformations of the triclinic (below 164 K) and monoclinic (between 242 and 164 K) forms to the orthorhombic form can show very different kinetic behaviour, depending on factors that do not seem to be completely understood but must involve the uncertainties of nucleation processes. As mentioned, it is extremely difficult to obtain single crystals of the orthorhombic form from solution, even at temperatures where it is certainly thermodynamically favoured. [For nickelocene the internal barrier is believed to be very small, and here the structure remains monoclinic on cooling from room temperature at least down to 100 K (Seiler & Dunitz, 1980) and possibly down to 0 K, although there are indications that some sort of ordering process takes place (Azokpota, Calverin & Pommier, 1976)].

The interpretation given here of the relative stability of the ferrocene polymorphs leans on the temperature-dependent entropic contribution to the crystal free energy in stabilizing the disordered monoclinic form at higher temperature. An alternative view of the relationships among the polymorphs has been given by Braga & Grepioni (1992; see also Braga, 1992), who disregard internal rotation barriers and entropic factors and draw conclusions entirely from results of packing potential-energy calculations (Gavezzotti, 1983), based on the atomic coordinates derived in the various crystal structure analyses (in using the averaged atomic positions for the monoclinic structure, they treat this structure as if it were ordered). The ferrocene story is full of unexpected complications, and many aspects are still debatable. There seems no doubt that if the other metallocenes were to be studied as intensively as ferrocene has been, still more complications would appear.

Three polymorphs, three colours, from the same solution

Dimethyl 2,5-dihydroxy-3,6-dichloroterephthalate (7) yields three crystal forms, described as yellow (Y), light yellow (LY) and white (W). They can all be obtained together by crystallization in the same vessel. The Y and W forms were recognized 80 years ago by Hantzsch (1915), while the LY form was overlooked by everyone until recently (Yang, Richardson & Dunitz, 1989). From the solubility behaviour, we know that at room temperature Y is the most stable and W the least stable; at higher temperature, by *ca* 345 K, the order changes, W becoming the most stable and Y the least stable. As far as we know, LY is metastable at all temperatures. The three forms are conformational polymorphs. In Y the molecules are almost coplanar, with intramolecular hydrogen bonds from hydroxyl to carbonyl O atoms, in W the ester groups are rotated nearly perpendicular to the plane of the other atoms, with intermolecular hydrogen bonds from hydroxyl to carbonyl O atoms of different molecules (Byrn, Curtin & Paul, 1972), and in LY the ester groups are rotated *ca* 40° out of the plane (Yang, Richardson & Dunitz, 1989). Both inter- and intramolecular hydrogen bonds are formed in LY, but with less than optimal geometry. All three crystal structures (Fig. 6) have been measured at several temperatures between 100 and 350 K (Yang, Richardson & Dunitz, 1989).

We also studied the phase transformations with a device that allows simultaneous differential scanning calorimetry (DSC) measurements and microscopic observations recorded with a video camera (Wiedemann & Bayer, 1985). Visual observations can sometimes be more sensitive indicators of phase changes than the DSC measurements. On heating a sample through a given temperature range, for example, one can sometimes see that changes are happening in and on the surface of the crystals, while the DSC trace remains featureless. The video recorder secures the permanency of these ephemeral events. The phase transformation behaviour is complex (Richardson, Yang, Novotny-Bregger & Dunitz, 1990) and points to the overriding effect of defects as initiators of the phase transitions. For example, the Y→W transformation can occur between *ca* 370 and 419 K from one crystal to another and even at different temperatures in different portions of the same crystal. The DSC signal is typically broad and ragged, but from many experiments we estimate $\Delta H \approx 1.6\,\mathrm{kJ\,mol^{-1}}$, $\Delta S \approx 4\ \mathrm{J\,mol^{-1}\,K^{-1}}$; on further heating W melts at 453 K ($\Delta H \approx 9.7\,\mathrm{kJ\,mol^{-1}}$, $\Delta S \approx 21\,\mathrm{J\,mol^{-1}\,K^{-1}}$) to a yellow liquid. On cooling, the liquid does not always revert to W but often supercools, freezing around 430 K to Y (even though this is well above the usual Y→W transformation temperature). The Y material obtained in this way has the same crystal structure as Y from solution but it does not undergo the phase transition to W. On warming, it melts – some 20 K lower than the melting point of W – to the same yellow liquid as before. However, if the Y crystals are cooled rapidly and then reheated they transform normally to W. The most likely explanation is that the Y crystals obtained from the melt do not contain the type of defect that 'catalyses' the phase transformation. Rapid cooling can initiate such defects. We can also introduce defects by mechanical treatment. If the crystals are scratched by touching them with a sharp needle, then the Y→W transformation starts at the scratch and proceeds outwards from there.

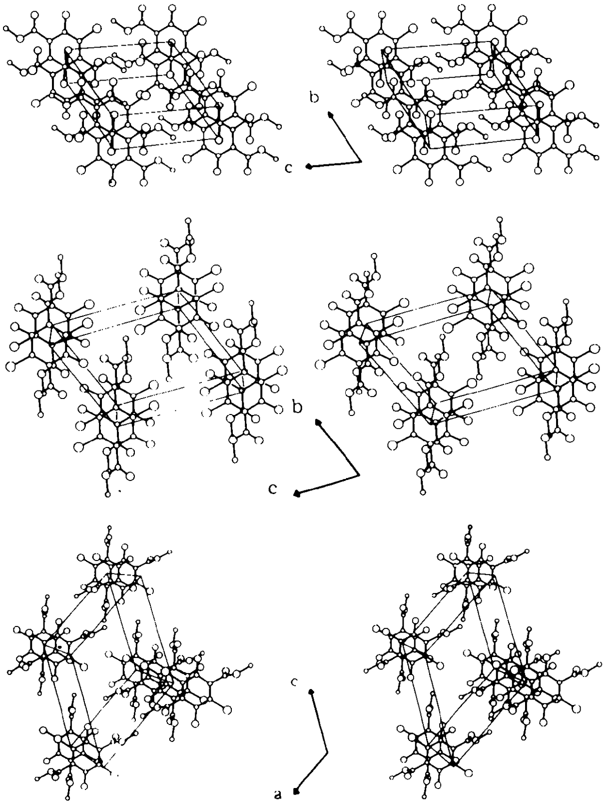

Fig. 6. Stereoviews of the three known crystal structures of dimethyl 2,5-dihydroxy-3,6-dichloroterephthalate (7). Y (top), LY (middle) and W (bottom), each projected on the plane of the benzene ring (Richardson, Yang, Novotny-Bregger & Dunitz, 1990).

Such observations underline the importance of kinetic rather than thermodynamic factors in controlling these processes. When the W crystal with its intermolecular hydrogen bonds is melted, the molecules in the liquid phase revert to the nearly coplanar conformation found in the Y crystal. Nucleation of the W form then requires a conformational change of the ester groups out of coplanarity, with an attendant activation energy, while nucleation of the Y form can occur without such a change. Thus, the Y crystals are preferentially formed even though they are thermodynamically unstable with respect to W at the temperature involved.

On warming crystals of LY they usually transform to W, again over a fairly wide temperature range from *ca* 360 to 380 K ($\Delta H \approx 2.5\,\mathrm{kJ\,mol^{-1}}$, $\Delta S \approx 7\,\mathrm{J\,mol^{-1}\,K^{-1}}$). Occasionally, however, a LY crystal (or even only 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. To make matters even more complicated, it could be shown that in the Y→W transformation, LY is sometimes (possibly always) formed as a transient intermediate. Although it cannot be measured directly, this Y→LY change must be exothermic. It would seem that LY is thermodynamically less stable than Y below 370 K, but more stable than Y at slightly higher temperature.

Fig. 7 shows the temperature dependence of the molecular volumes; the denser the crystal, the lower its

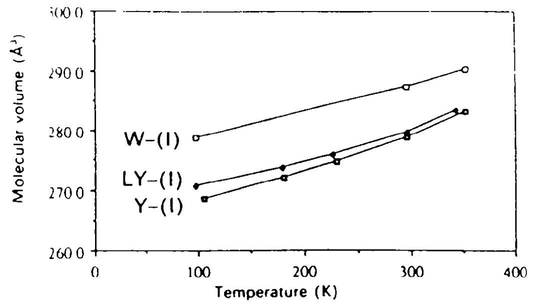

Fig. 7. Molecular volume of (7) in its three polymorphs as a function of temperature (Richardson, Yang, Novotny-Bregger & Dunitz, 1990).

internal energy (a general rule, although 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. 8). 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 the case. The Y→W transformation at around 390 K is endothermic and thus associated with an entropy increase. I do not have any explanation why the atomic ADP's should be largest in the crystal with the smallest entropy.

Two polymorphs with closely similar structures

The reversible transformation of *N*-methyl-1-thia-5-azacyclooctan-1-oxide perchlorate [TACO (8)] from a low-temperature α-phase (thermodynamically stable below *ca* 290 K) to a high-temperature β-phase with virtually complete retention of crystal orientation and outward morphology (Paul & Go, 1969; Duesler, Wiegers, Curtin & Paul, 1980) is remarkable. The unit-cell dimensions are closely related: on going to the β-phase the a-axis is doubled, the c-axis halved, while the b-axis remains the same. 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 the b-axis (Fig. 9). Sets of molecules related by glide reflection in the one phase are related by lattice translation in the other, and *vice versa*. The molecules occur in a chiral conformation, so the phase transformation involves a switch in the chirality sense of half the molecules. Neither DSC, optical microscopy nor solid-state NMR gives any indication of the phase transition, but it can be followed from the temperature dependence of intensities of reflections that are forbidden in one phase and allowed in the other (Novotny-Bregger, 1994). The intensity changes indicate that during the transformation, the disappearing phase disappears faster than the new phase forms. If the β-phase is cooled rapidly to 100 K, it can be kept there indefinitely, thus allowing the crystal structures of both phases to be determined over a wide temperature range up to the transition point. The ADP's of the two phases do not differ in any striking way and neither does the temperature dependence of these quantities. If one did not know from the diffraction evidence that a phase change had occurred, one could hardly have inferred it from other physical evidence.

It is difficult to see how alternate molecules in one phase can invert their sense of chirality and rotate cooperatively to produce the molecular arrangement in 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? One formal possibility is a cooperative defect-initiated 180° rotation of all centrosymmetric dimers in successive layers lying parallel to

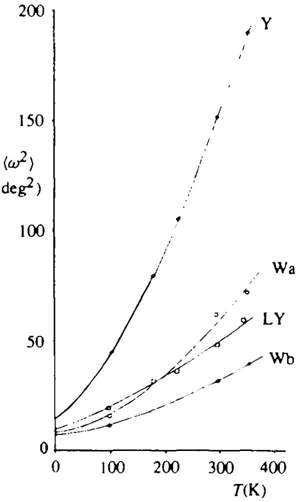

Fig. 8. Mean-square libration amplitude $\langle\omega^2\rangle$ of the ester group in the three polymorphs of (7) as a function of temperature (Yang, Richardson & Dunitz, 1989). The white form contains two independent molecules W_a and W_b.

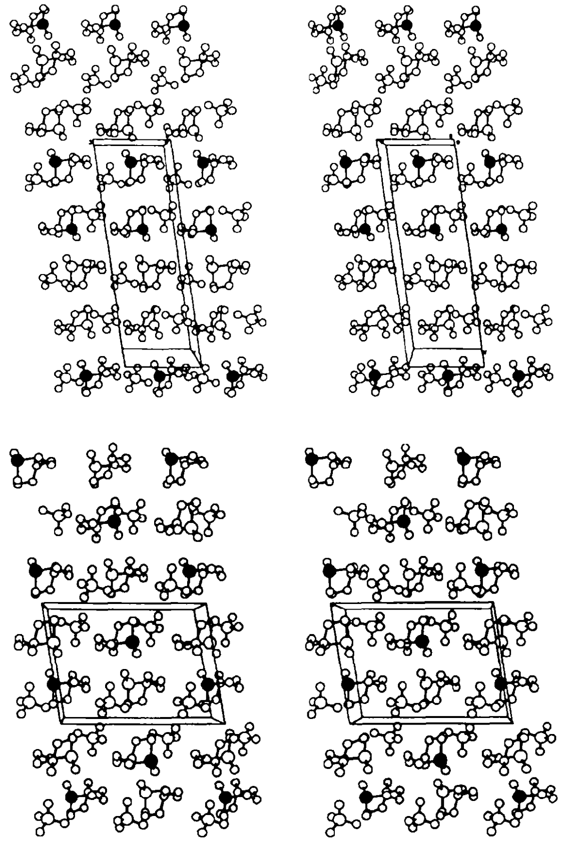

Fig. 9. Stereoviews of the α (top, space group $P2_1/c$) and β (bottom, space group $P2_1/a$) modifications of (8) projected down the b-axis. In both views the c-axis is horizontal and the a-axis is nearly vertical. The filled circles represent the S atoms of one set of homochiral molecules.

the [201] (α-form) or [102] direction (β-form) – one can distinguish such centrosymmetric dimers that retain almost exactly the same geometry in both polymorphs (Fig. 10). Subsequent rotation of the tetrahedral perchlorate groups should proceed with a relatively low activation energy. However, we lack evidence for this type of mechanism — or for any other type for that matter, such as the martensitic-like mechanism that has been proposed by Parkinson, Thomas, Gorings & Hobbs (1976).

A chemical reaction showing high cooperativity

As an example of the grey area between polymorphic transitions and solid-state chemical reactions we can consider the remarkable solid-state polymerization and depolymerization of 2,6-diethyl-1,3,5,7-tetraoxa-1,6-dibora-4,8-octalindione [(9) Yalpani, Boese & Bläser, 1983; Yalpani, Scheidt & Seevogel, 1985]. At elevated temperature, above 313 K, the crystal structure (space group $P2_1/c$, $Z = 2$) is built from monomeric units (Fig. 11). On cooling, it transforms into a structure containing polymeric layers through the formation of additional bonds between B atoms and carbonyl O atoms of suitably placed neighbours. In the monomeric form, the molecular arrangement is such that a carbonyl O atom of one centrosymmetric molecule sits almost directly above the B atom of a neighbouring molecule (*i.e.* along the vacant p_z orbital direction) and only 2.84 Å from it, ideally poised for the addition reaction to give the new B—O bond. When this bond is formed, the coordination at the B atom changes from trigonal planar to tetrahedral, leading to a general tilting of the molecule to bring the other B atom closer to another carbonyl O atom. In the polymeric form (same space group, similar cell dimensions), the newly formed B—O bond is only slightly longer than the other formally single B—O bonds in the molecule [1.564 (5) *versus* 1.531 (5) Å] – in other words, there is little indication in the ground state structure of the polymer that this is a particularly weak or unusual bond.

DSC measurements showed a broad but unambiguous exotherm signal centred around 269 K on cooling the sample (with a minor signal some 40 K lower). The corresponding endotherm signals in the reverse warming cycle occur at higher temperatures. Polycrystalline samples give broad DSC signals, but with single crystals the transitions are more nearly isothermal. The hysteresis points to a first-order phase transformation but there is no question that chemical bonds are formed (on cooling) and broken (on warming). This is a clear case of a chemical reaction with cooperativity.

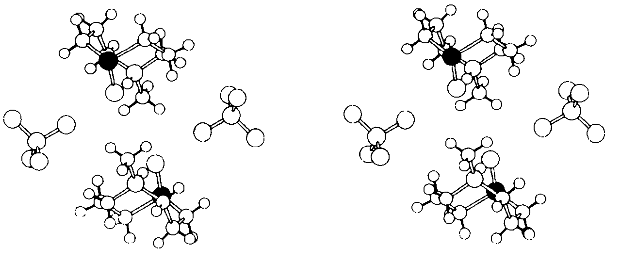

Fig. 10. Stereoview of a pair of centrosymmetrically related molecules of (8), which occurs almost unaltered in both crystal forms. The filled circles indicate the *S* atoms.

Concluding remarks

Are there any? Not really, except perhaps that there is no clear-cut distinction between solid-state phase transformations and chemical reactions, only differences in the degree of cooperativity. In studying the properties of matter and trying to understand them, one should not expect real systems to behave exactly like the simple models we use to describe them. It may be counterproductive to search for too exact definitions of the terms we use (such as phase, component, solid solution *etc.*) derived from models of ideal systems. Even at the microscopic level (1–10 μ) the solid state is much less perfect and homogeneous than was once imagined. The real world is complex, and if we insist on too precise definitions of terms, we shall find that there are no systems in the real world to which they can refer.

The traditional classifications of phase transitions in molecular crystals are not always very useful, and our understanding of the mechanisms involved is only at a very primitive level. By diffraction methods, we obtain an excellent picture of the time-averaged, space-averaged contents of a unit cell in a crystal, but very little

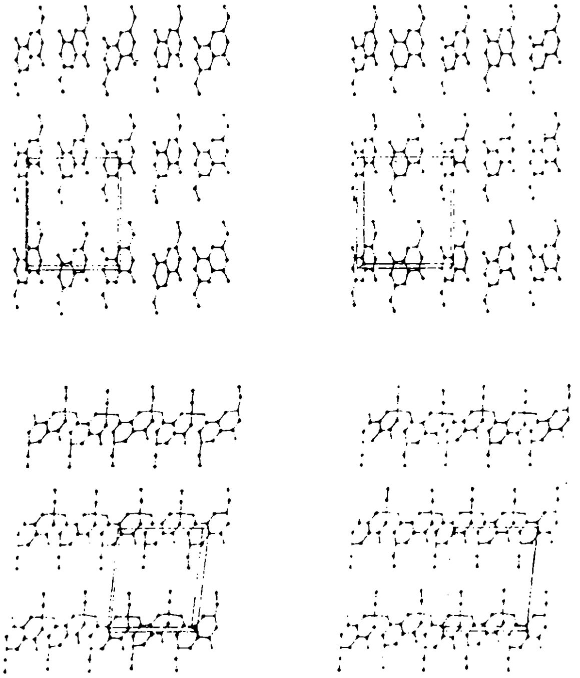

Fig. 11. Stereoscopic views of monomeric and polymeric forms of (9) (Yalpani, Scheidt & Seevogel, 1983, Figs. 8 and 9).

information about the nature of the fluctuations from the 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. We need better models, better theories, but above all we need better observations. Possibly, some insight may come from computer modelling – mainly molecular dynamics techniques, which seem more suitable than lattice dynamics for handling large-scale displacements of the atoms in molecular crystals.

Perhaps insights rather than understanding! When we think of chemical reactions in solution or in the gas phase, we normally focus attention on a single molecule of reactant and its interaction with its immediate neighbours. Often we can ignore all but one or two such interacting molecules. This kind of simplification is no longer useful when we come to deal with solid–solid phase transitions. In spite of the high degree of order shown by crystalline polymorphs, the transformation between them may resist simplification. Even when crystal orientation is maintained between the initial and final forms, the transformation probably involves a highly complex series of cooperative processes, in which order is first lost and then recrystallized out of chaos. With all the similarities between phase transitions and normal chemical reactions, perhaps we may have to give up the idea of *understanding* the mechanism of the former, except for a few simple types of order–disorder transitions. A molecular dynamics simulation may be the most we can ever expect to achieve. There is certainly much to be discovered and much to be learned.

An appeal to crystallographers who publish results of crystal structure analyses: please give the colour (easy to observe) and melting point of the crystals studied (easy to measure); if possible, also the heat of fusion and of any observed phase transitions (only slightly more difficult to measure): report also any 'unusual' behaviour, any observed change of physical properties or of the diffraction pattern. An appeal to journal editors and reviewers: please insist on this information. An appeal to the Cambridge Crystallographic Data Centre: please include this information in the database.

References

AZOKPOTA, C., CALVARIN, G. & POMMIER, C. (1976). *J. Chem. Thermodynam.* **8**, 283–287.

BÉRAR, J. F., CALVARIN, G. & WEIGEL, D. (1980). *J. Chem. Phys.* **73**, 438.

BERNSTEIN, J. (1987). *Organic Solid State Chemistry*, edited by G. R. DESIRAJU, pp. 471–58. Amsterdam: Elsevier.

BERNSTEIN, J. & HAGLER, A. T. (1978). *J. Am. Chem. Soc.* **100**, 673–681.

BOEYENS, J. C. A., LEVENDIS, D. C., BRUCE, M. I. & WILLIAMS, M. L. (1986). *J. Cryst. Spectrosc. Res.* **16**, 519–524.

BRAGA, D. (1992). *Chem. Rev.* **92**, 633–665.

BRAGA, D. & GREPIONI, F. (1992). *Organometallics*, **11**, 711–718.

BROCK, C. P. & FU, Y. (1991). *Program and Abstracts*, p. 68. American Crystallographic Association, Annual Meeting, 21–26 July 1991, paper C16.

BROCK, C. P., SCHWEIZER, W. B. & DUNITZ, J. D. (1991). *J. Am. Chem. Soc.* **113**, 9811–9820.

BUERGER, M. J. (1951). *Phase Transformations in Solids*, edited by R. SMOLUCHOWKSI, J. E. MAYER & W. A. WEYL, pp. 183–211. New York: Wiley.

BÜRGI, H.-B. & DUNITZ, J. D. (1993). *Helv. Chim. Acta*, **76**, 1115–1166.

BYRN, S. R., CURTIN, D. Y. & PAUL, I. C. (1972). *J. Am. Chem. Soc.* **94**, 890–898.

CARTER, S. & MURRELL, J. M. (1980). *J. Organomet. Chem.* **192**, 399–408.

CLEC'H, G., CALVARIN, G., BÉRAR, J. F. & KAHN, R. (1978). *C. R. Acad. Sci. Ser. C*, **286**, 315–317.

COHEN, M. & SCHMIDT, M. J. (1964). *J. Chem. Soc.* pp. 1996–2000.

CRANE, J. D., HITCHCOCK, P. B., KROTO, H. W., TAYLOR, R. & WALTON, D. R. M. (1992). *J. Chem. Soc. Chem. Commun.* pp. 1764–1765.

DESIRAJU, G. R. (1987). *Organic Solid State Chemistry*. Amsterdam: Elsevier.

DONOHUE, J. (1974). *The Structures of the Elements*, p. 342. New York: Wiley-Interscience.

DUESLER, E. N., WIEGERS, K. E., CURTIN, D. Y. & PAUL, I. C. (1980). *Mol. Cryst. Liq. Cryst.* **59**, 289–298.

DUNITZ, J. D. (1993). *Organic Chemistry: Its Language and its State of the Art*, edited by M. V. KISAKÜREK, pp. 9–23. Basel: Verlag HCA.

DUNITZ, J. D. & ORGEL, L. E. (1953). *Nature (London)*, **171**, 121–122.

DUNITZ, J. D. & ROBERTSON, J. M. (1947*a*). *J. Chem. Soc.* pp. 142–154.

DUNITZ, J. D. & ROBERTSON, J. M. (1947*b*). *J. Chem. Soc.* pp. 1145–1156.

DUNITZ, J. D., ORGEL, L. E. & RICH, A. (1956). *Acta Cryst.* **9**, 373–375.

EDWARDS, J. W., KINGTON, G. L. & MASON, R. (1960). *Trans. Faraday Soc.* **56**, 660–667.

EILAND, P. F. & PEPINSKY, R. (1952). *J. Am. Chem. Soc.* **74**, 4971.

ENKELMANN, V., WEGNER, G., NOVAK, K. & WAGENER, K. B. (1993). *J. Am. Chem. Soc.* **115**, 10390–10391.

FISCHER, E. O. & PFAB, W. (1952). *Z. Naturforsch. Teil B*, **7**, 377–379.

FOX, D., LABES, M. M. & WEISSBERGER, A. (1963). *Physics and Chemistry of the Organic Solid State*, Vol. 1. New York: Interscience.

FOX, D., LABES, M. M. & WEISSBERGER, A. (1965). *Physics and Chemistry of the Organic Solid State*, Vol. 2. New York: Interscience.

FU, Y. (1991). PhD Dissertation. Univ. of Kentucky, Lexington, USA.

GAVEZZOTTI, A. (1983). *J. Am. Chem. Soc.* **105**, 5220–5225.

GAVEZZOTTI, A. & SIMONETTA, M. (1977). *Nouv. J. Chim.* **2**, 69–72.

HAALAND, A. & NILSSON, J. E. (1968). *Acta Chem. Scand.* **22**, 2653–2670.

HANTZSCH, A. (1915). *Chem. Ber.* **48**, 797–816.

HARDGROVE, G. L. & TEMPLETON, D. H. (1959). *Acta Cryst.* **12**, 28–32.

JACQUES, J., COLLET, A. & WILEN, S. H. (1981). *Enantiomers, Racemates and Resolutions*. New York: Wiley.

JELLINEK, F. (1959). *Z. Naturforsch. Teil B*, **14**, 73–74.

JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee, USA.

KOHLSCHÜTTER, E. (1919). *Z. Anorg. Chem.* **105**, 1–25.

MCCRONE, W. C. (1965). *Physics and Chemistry of the Organic Solid State*, edited by D. FOX, M. M. LABES & A. WEISSBERGER, Vol. 2, pp. 725–767. New York: Interscience.

MYNUKH, YU. V. (1979). *Mol. Cryst. Liq. Cryst.* **52**, 163–200, 201–218.

NARUSE, M., SORAI, M. & SAKIYAMA, M. (1983). *Mol. Cryst. Liq. Cryst.* **101**, 219–234.

NOVOTNY-BREGGER, E. (1994). Doctoral Dissertation, ETH-Zurich.

OGASAHARA, K., SORAI, M. & SUGA, H. (1979). *Chem. Phys. Lett.* **68**, 457–460.

OGASAHARA, K., SORAI, M. & SUGA, H. (1981). *Mol. Cryst. Liq. Cryst.* **71**, 189–211.

OHASHI, Y. (1993). *Reactivity in Molecular Crystals*. Weinheim: VCH.

PARKINSON, G. M., THOMAS, J. M., GORINGS, M. J. & HOBBS, L. W. (1976). *J. Chem. Soc. Perkin Trans.* 2, pp. 836–838.

PAUL, I. C. & GO, K. T. (1969). *J. Chem. Soc. B*, pp. 33–42.

RAO, C. N. R. & RAO, K. J. (1978). *Phase Transitions in Solids*. New York: McGraw-Hill.

RICHARDSON, M. F., YANG, Q.-C., NOVOTNY-BREGGER, E. & DUNITZ, J. D. (1990). *Acta Cryst.* B**46**, 653–660.

ROBERTSON, J. M. & UBBELOHDE, A. R. (1938). *Proc. R. Soc. Ser. A*, **167**, 122–135, 136–147.

SARMA, J. A. R. P. & DUNITZ, J. D. (1990). *Acta Cryst.* B**46**, 780–784.

SEILER, P. & DUNITZ, J. D. (1979*a*). *Acta Cryst.* B**35**, 1068–1074.

SEILER, P. & DUNITZ, J. D. (1979*b*). *Acta Cryst.* B**35**, 2020–2032.

SEILER, P. & DUNITZ, J. D. (1980). *Acta Cryst.* B**36**, 2255–2260.

SEILER, P. & DUNITZ, J. D. (1982). *Acta Cryst.* B**38**, 1741–1745.

SUKENIK, C. N., BONOPACE, J. A. P., MANDEL, N. J., LAW, P. Y., WOOD, G. & BERGMAN, R. G. (1977). *J. Am. Chem. Soc.* **99**, 851–858.

TAKUSAGAWA, F. & KOETZLE, T. F. (1979). *Acta Cryst.* B**35**, 1074–1081.

TENUD, L., FAROOQ, S., SEIBL, J. & ESCHENMOSER, A. (1970). *Helv. Chim. Acta*, **53**, 2059–2069.

VENUGOPALAN, P., VENKATESAN, K., KLAUSEN, J., NOVOTNY-BREGGER, E., LEUMANN, C., ESCHENMOSER, A. & DUNITZ, J. D. (1991). *Helv. Chim. Acta*, **74**, 662–669.

WALLACH, O. (1895). *Liebigs Ann. Chem.* **286**, 90–143.

WESTRUM, E. F. & MCCULLOUGH, J. P. (1963). *Physics and Chemistry of the Organic Solid State*, edited by D. FOX, M. M. LABES & A. WEISSBERGER, Vol. 1, pp. 1–178. New York: Interscience.

WIEDEMANN, H. G. & BAYER, G. (1985). *J. Therm. Anal.* **30**, 1273–1281.

YALPANI, M., BOESE, R. & BLÄSER, D. (1983). *Chem. Ber.* **116**, 3338–3346.

YALPANI, M., SCHEIDT, W. R & SEEVOGEL, K. (1985). *J. Am. Chem. Soc.* **107**, 1684–1690.

YANG, Q.-C., RICHARDSON, M. F. & DUNITZ, J. D. (1989). *Acta Cryst.* B**45**, 312–323.