

Disappearing Polymorphs

JACK D. DUNITZ*,† AND JOEL BERNSTEIN*,‡

Organic Chemistry Laboratory, Swiss Federal Institute of Technology, ETH-Zentrum, CH 8092 Zurich, Switzerland, and Department of Chemistry, Ben-Gurion University of the Negev, Beer Sheva, Israel 84965

Received November 1, 1994

Introduction

When a compound exhibits polymorphism—the existence of more than one crystal structure—it may be important to obtain a particular polymorph under controlled and reproducible conditions. However, this is not always easy to achieve. Tales of difficulties in obtaining crystals of a particular known form or in reproducing results from another laboratory (or even from one's own!) abound. Indeed, there are cases where it was difficult to obtain a given polymorphic form even though this had previously been obtained routinely over long time periods. Several monographs contain explicit or passing references to these problems,¹ but much of this lore has gone undocumented, especially in the last 30 years or so. In this Account we present and discuss old and new examples.

Crystallization is a process taken for granted by most practicing chemists; the majority of the techniques were developed long ago and are described in all standard laboratory textbooks. It is the standard method for purifying solid compounds, and chemists generally believe that they can control the process, at least when it yields the desired product. What is disturbing about the phenomenon of disappearing or elusive polymorphs is the apparent loss of control over the process: we did the experiment last week and got this result, and now we cannot repeat it! This kind of statement can lead to raised eyebrows or even to outspoken expressions of disbelief. We have ourselves experienced the frustration of not being able to reproduce an experimental result that was undoubtedly obtained earlier.

Crystallization: Nucleation and Growth

The process of crystallization of a compound from solution or from the melt is poorly understood. At least two stages must be distinguished: the formation of a critical nucleus and its subsequent growth. The first step is decisive in that it can be regarded as being associated with a free energy of activation and is therefore rate limiting. Under suitable conditions, that step may be delayed almost indefinitely. For

instance, Faraday² observed that molten sulfur in a flask cooled to room temperature did not entirely solidify. When a drop of the fluid material was touched, it immediately crystallized; untouched, some drops were retained for a week in the fluid state. Faraday noted that this supercooled state of sulfur is analogous to that of water cooled below its freezing point, although the temperature difference is much greater (the freezing point of sulfur is 119 °C); De Coppet found that samples of salol (phenyl salicylate) could be kept in the liquid state at room temperature for periods of several years.³ When nucleation is rapid, the formation of many nuclei leads to many crystals, whereas slow nucleation tends to produce a smaller number of larger crystals. Of course, stirring, shaking, or other disturbances of the liquid phase during the crystallization process can affect the outcome.

A striking case where nucleation was decisive in determining the result of a crystallization experiment has been described recently.⁴ Sodium chlorate (NaClO₃) crystallizes in the chiral space group *P*2₁3; that is to say, individual crystals of this substance may occur in enantiomorphic forms. Normally, crystallization from solution produces the enantiomorphs in roughly equal numbers. Kondepudi, Kaufman, and Singh⁵ found, however, that stirring an aqueous solution of this substance leads to a predominance of

* Correspondence may be directed to either author.

† ETH.

‡ Ben-Gurion University.

(1) Buckley, H. E. *Crystal Growth*; Wiley: New York, 1951. Tipson, R. S. Crystallization and Recrystallization. In *Technique of Organic Chemistry*; Weissberger, A., Ed.; Interscience Publishers, Inc.: New York, 1956; Volume III, Part I, Chapter III, pp 395–562. Holden, A.; Singer, P. *Crystals and Crystal Growing*; Doubleday: New York, 1960.

(2) Faraday, M. *Experimental Researches in Chemistry and Physics*; Taylor and Francis: London, 1853; p 212. On the following page, Faraday apologized for not having acknowledged observations along similar lines made earlier (in 1813) by M. Bellani: "I very fully join in the regret...that scientific men do not know more perfectly what has been done, or what their companions are doing; but I am afraid the misfortune is inevitable. It is certainly impossible for any person who wishes to spend a portion of his time to chemical experiment, to read all the books and papers that are published in connection with his pursuit; their number is immense, and the labour of winnowing out the few experimental and theoretical truths which in many of them are embarrassed by a very large proportion of uninteresting matter, of imagination, and of error, is such, that most persons who try the experiment are quickly induced to make a selection in their reading, and thus, inadvertently, at times, pass by what is really good." Since Faraday's times, these difficulties have multiplied out of all proportion, but we may still use his words to apologize to any scientists whose works we may similarly have overlooked.

(3) De Coppet, M. L.-C. *Ann. Chim. Phys.* **1907**, *10*, 457. "La surfusion dure donc depuis bientôt 6 ans." In another experiment, de Coppet reported that a sample of sodium sulfate, supersaturated with respect to the decahydrate, had still not crystallized after 25 years. In general, the higher the temperature to which the liquid was raised and the longer the time it was held at high temperature, the more resistant the liquid was to crystallization. Heating a liquid destroys residual order.

(4) McBride, J. M.; Carter, R. L. *Angew. Chem.* **1991**, *103*, 298; *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 293.

Jack D. Dunitz was born in Glasgow, Scotland, in 1923 and studied chemistry at Glasgow University. Following a decade of postdoctoral studies at Oxford, Caltech, NIH, and the Royal Institution, London, he moved to the ETH in Zurich as professor of chemical crystallography, a post he held until his retirement in 1990. He is the author of *X-Ray Analysis and the Structure of Organic Molecules* (1979) and (with E. Heilbronner) *Reflections on Symmetry in Chemistry... and Elsewhere* (1993).

Joel Bernstein was born in Cleveland, OH, in 1941. He received his B.A. in chemistry from Cornell University in 1962 and Ph.D. in physical chemistry from Yale in 1967. Following postdoctoral stints in chemical crystallography at UCLA with K. N. Trueblood and organic solid state chemistry at the Weizmann Institute with G. M. J. Schmidt he moved to the Ben-Gurion University of the Negev in Beer Sheva Israel, where he is now professor of chemistry. His research interests include a

crystals of one handedness, sometimes right, sometimes left, but not depending on the direction of stirring. In checking this result, McBride and Carter⁴ showed by video recording that a single nucleation event can produce almost all of the crystals formed: "...Crystals begin nucleating at random, but the first crystal to be struck by the stirrer clones hundreds or thousands of new nuclei. Growth of so many nuclei soon lowers the concentration of the solute below the threshold for spontaneous formation of primary nuclei, so that there is no way to begin crystallization of the enantiomer."

Seeding

One way of influencing the crystallization process is by seeding, and here we need to differentiate between what we may term intentional and unintentional seeding. Intentional seeding is a common practice among chemists who wish to coax crystallization of a compound from solution or from the melt; small crystals or crystallites of the desired material (seeds) are added to the system. In this way, the rate-limiting nucleation step, which may be extremely slow, is circumvented. For this method to be applied, it is of course necessary that a sample of the crystalline material is available; that is, the compound must have been already crystallized in a previous experiment. When polymorphic forms of a substance are known to occur, intentional seeding with one of the polymorphs is a useful and often the most successful way of preferentially producing it rather than the other.

Seeding may also occur if small amounts of the crystalline material are present as contaminants: unintentional seeding.⁶ Unintentional seeding is often invoked as an explanation of phenomena which otherwise are difficult to interpret. We shall argue in favor of this explanation, although there is no consensus about the size and range of activity of such seeds, which have never actually been directly observed.⁷ Estimates of the size of a critical nucleus range from a few tens of molecules to a few million molecules.⁸ With a size of about a million molecules, even a speck (10^{-6} g) of a compound of molecular weight 100 contains approximately 10^{16} molecules, sufficient to make 10^{10} such nuclei. One can think of local seeding, where the contamination may apply to the experimentalist's clothing, a portion of a room, an entire room, a building, or even, with increasing degrees of implausibility, to a district, a town, a country, a continent, and so on. In the limit we have what has been proposed as universal seeding (planetary seeding would be a more accurate expression), where the whole planet is assumed to be contaminated.⁹ A seed that promotes formation of a crystallization nucleus need not necessarily be composed of the same molecules as the compound that is to be crystallized. Specks of dust, smoke particles, and other small foreign bodies can act as seeds in promot-

ing crystallization, which is the reason laboratory chemists often scratch the walls of a glass vessel with a glass rod to encourage a solute to crystallize.¹⁰

Polymorphism

We have mentioned the phenomenon of polymorphism, which is commonly understood as connoting the ability of a compound (or of an element) to crystallize in more than one distinct crystal structure. According to McCrone,¹¹ "A polymorph is 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." Because polymorphs have different structures, they may differ greatly in density, hardness, solubility, and optical and electrical properties; e.g., diamond and graphite are two polymorphic forms (allotropes) of carbon. Many compounds are known to crystallize in polymorphic forms. In the inorganic and mineralogical fields, these sometimes have different names, e.g., ZnS, wurtzite and sphalerite; CaCO₃, calcite, aragonite, and vaterite; TiO₂, rutile, brookite, and anatase; but, more generally, different polymorphic forms are denoted by letters, A, B, C or α , β , γ , etc., or by Roman numerals, I, II, III, etc., depending on the preference of the discoverer. McCrone¹¹ has provocatively suggested that "every compound has different polymorphic forms, and that, in general, the number of forms known for a given compound is proportional to the time and money spent in research on that compound." In support of this, McCrone observes that many compounds of industrial importance (i.e., those on which a great deal of time and money are spent) are known to exhibit polymorphism: silica, iron, calcium silicate, sulfur, soap, pharmaceutical products, dyes, and explosives. Such compounds, unlike the vast majority of compounds that are isolated, are prepared and crystallized not just once but repeatedly, under conditions that may vary slightly from time to time. Similarly, in the biomolecular area, where much time and effort is invested in attempts to crystallize proteins under many slightly different conditions, polymorphism is frequently observed.¹² The universality suggested by McCrone's statement may, however, be considerably tempered by the fact that fewer than 5% of the compounds in the Cambridge Structural Database (CSD) are known to be polymorphic (although it must be admitted that crystallographers typically choose one crystal specimen from their sample and leave it at that). Moreover, some very widely studied compounds have shown no evidence of polymorphic behavior, even though they have been crystallized and handled for many years under a far-ranging variety of conditions; naphthalene is an example that immediately comes to mind.

Here we shall be concerned exclusively with molecular crystals, where the molecule may have the same shape in the two polymorphs or it may have a different shape, resulting in what has been termed "conforma-

(6) It is well-known that it is often difficult to crystallize a newly synthesized compound. Subsequent crystallizations may be easier, because of the presence of suitable seeds.

(7) Chemists and physicists have long become accustomed to postulating models as explanations for phenomena that cannot be directly observed. The existence of atoms is perhaps the classic example.

(8) Mullin, J. W. *Crystallization*, 3rd ed.; Butterworth-Heinemann Ltd.: Oxford, 1993; pp 182-185.

(9) The claim for "universal seeding" taken literally is obviously

(10) "Auch das Reiben mit einem Glasstab an der Wandung des Gefässes schafft Keime, an deren Vorhandensein die Kristallisation gebunden ist." *Organikum*; VEB Deutscher Verlag der Wissenschaften: Berlin, 1977; p 46.

(11) McCrone, W. C. *Polymorphism In Physics and Chemistry of the Organic Solid State*; Fox, D., Laves, M. M., Weissberger, A., Eds.; Interscience: New York, 1965; Vol. II, pp 726-767.

(12) For example, according to the Protein Data Bank (distributed by Brookhaven National Laboratory, Upton, NY), the extensively studied

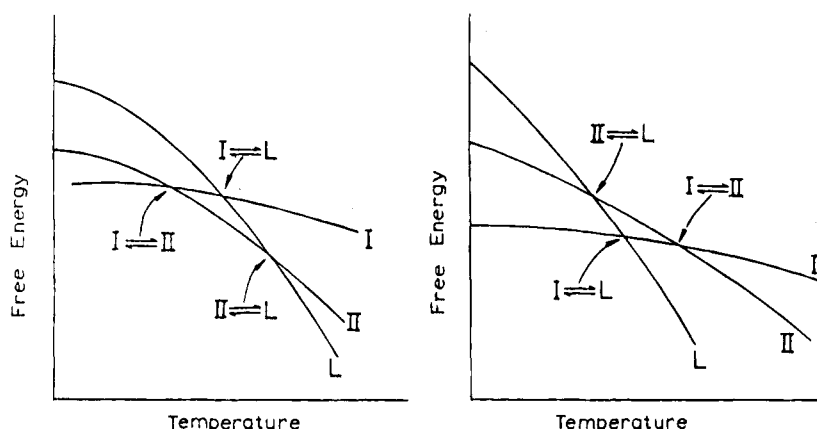


Figure 1. Free energy vs temperature diagrams for two polymorphs, with crossing points where their free energies cross: left, enantiotropic system; right, monotropic system.

tional polymorphism".¹³ McCrone's criterion¹¹ is that polymorphs are different in crystal structure but identical in the liquid or vapor states. This implies that crystals containing molecules with different atomic arrangements are to be classed as polymorphs if the molecules concerned interconvert rapidly in the melt or in solution to give the same equilibrium mixture. Thus, this definition would encompass not only conformational isomers but all kinds of isomers in dynamic equilibrium. In phase-rule terminology,¹⁴ the various polymorphs and the liquid obtained by melting them constitute a one-component system (or a two-component system if we consider solution of the polymorphs in a given solvent).

Clearly, this definition is not completely satisfactory and leaves several kinds of borderline cases open: are *syn*- and *anti*-oximes in the solid state to be classed as polymorphs or as separate compounds? What about the various molecular species involved in the complex equilibria among open-chain and cyclic forms of saccharides (constitutional and configurational polymorphs)? How long are we supposed to wait for equilibrium to be established? Should different hydrates or solvates of a given compound be classified as polymorphs? (The term pseudopolymorphism has been proposed to cover such cases.) Definitive answers to these and similar questions cannot be given; they depend on one's point of view. In the same way, there seems to be no unequivocal way of distinguishing between polymorphic transformations and solid-state chemical reactions. There are borderline cases that show characteristic features of both.

In molecular crystals, free energy differences between polymorphs are usually quite small, a matter of a few kilocalories/mole at most,¹⁵ and depend on temperature, mainly because of the entropic contribution to the free energy. Because of the thermodynamic relation $G = H - TS$, the form with the higher entropy will tend to become the thermodynamically more stable form as the temperature is raised (Figure 1). Thus, over a small temperature range, and particularly between room temperature and the melting point, one polymorph or another can change from being the stable form to being metastable. If the

thermodynamic transition temperature is below the melting point, the polymorphic system is known as enantiotropic (not to be confused with enantiotopic, a term applied to atoms or groups in a molecule that are related by an improper symmetry operation but not by a proper one, e.g., the two methylene H atoms in ethanol) and the transition is in principle reversible; if the transition temperature is above the melting point, then the system is monotropic and the transition can take place only in one direction. A metastable form can persist for years, or it can undergo spontaneous transformation to the stable form.

Mechanisms of Polymorphic Transformations

The title of this section promises more than it can deliver, because the mechanisms of polymorphic transformations in molecular crystals are largely unknown. The one type of transformation for which some level of understanding can be claimed is order-disorder transformations, where the high-temperature phase has essentially the same molecular arrangement as the low-temperature one and differs from it only by an increase in the crystallographic site symmetry of the structural units. This increase in apparent molecular symmetry is due to an increase in crystal disorder such that the space-averaged, time-averaged distribution of matter has a higher symmetry than the instantaneous distribution in an individual unit cell. The reverse transformation corresponds to the onset of an ordering process. Such transitions are usually classified as "second-order" from the thermodynamic point of view, and, since they are virtually the only ones that can be handled on a theoretical basis, they receive the most attention in textbooks. From reading, one might even get the impression that order-disorder transformations are the prototype of phase transitions in general, but this is not the case.

Presumably, as in the primary crystallization processes, the mechanisms of most solid-solid transformations involve the formation of critical nuclei of the new phase, followed by their growth. According to My-nukh,¹⁶ the nucleation step is critically dependent on the presence of "suitable" defects. Depending on the nature of these defects, nuclei of the new phase may be formed at different temperatures and grow at different rates. Thus, defects in the initial crystal structure may be necessary for initiating (or cata-

(13) Bernstein, J.; Hagler, A. T. *J. Am. Chem. Soc.* **1978**, *100*, 673.
Bernstein, J. Conformational Polymorphism In *Organic Solid State Chemistry*; Desiraju, G., Ed.; Studies in Organic Chemistry, Vol. 32; Elsevier: Amsterdam, 1987; pp 471-518.

lyzing) nucleation of the new phase. Indeed, in some cases, the transformation can be induced by mechanically introducing defects, for example, by scratching the surface of the crystal with a pinpoint. On the other hand, there are also examples where the transformation is virtually instantaneous (and in one case even reversible), causing the crystals to "jump".¹⁷

Solid-state transformations in molecular crystals often show a high degree of hysteresis. It may be necessary to heat the low-temperature form to a temperature well above the thermodynamic transition temperature before signs of phase transformation can be detected. Even when no solid-solid transformation of the low-temperature form occurs below the melting point, this is not sufficient proof that the system is monotropic; the transformation may simply be too sluggish to be observed. Similarly, transformations in the reverse direction, produced by cooling the high-temperature form, are also invariably accompanied by hysteresis. This can be so severe that a high-temperature form can sometimes be kept indefinitely at temperatures well below the transition point. Thus, X-ray structure analyses at 100 K have been made of crystal phases more than 200 K below their thermodynamic range of stability.¹⁸

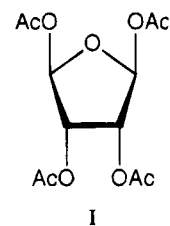
Vanishing Polymorphs

Woodard and McCrone¹⁹ described several cases where, after nucleation of a more stable crystal form, a previously prepared crystal form could no longer be obtained. Other examples were described by Webb and Anderson,²⁰ who wrote, "Within the fraternity of crystallographers anecdotes abound about crystalline compounds which, like legendary beasts, are observed once and then never seen again." In a sober comment on these views, Jacewicz and Nayler²¹ criticized some of the more exaggerated claims. While admitting the role of seeding in promoting nucleation, they argue that the disappearance of the metastable form is a local and temporary phenomenon and conclude that "any authentic crystal form should be capable of being re-prepared, although selection of the right conditions may require some time and trouble."

In most of the examples cited by these authors, relevant questions are left unanswered. Many chemists remain skeptical about a subject that calls into question the criterion of reproducibility as a condition for acceptance of a phenomenon as being worthy of scientific inquiry. Nevertheless, there are well-documented cases of crystal forms that were observed over a period of time but not thereafter, having been apparently displaced by a more stable polymorph. The relevant literature is scattered and almost impossible to find by subject searches. In the remaining space

we review published examples, present some new results, and try to put the subject into perspective. We begin with one of the best-studied examples.

1,2,3,5-Tetra-O-acetyl- β -D-ribofuranose (I). The early history of this compound reads like a mystery story. As first prepared in 1946 in Cambridge, England, by Howard, Lythgoe, and Todd,²² the compound had melting point 58 °C.



Virtually the same melting point was measured for material prepared by a different method in Jena by Brederick and Hoepfner.²³ When several batches of the same material were prepared soon afterward (1949) in a different laboratory on the other side of the Atlantic, in New York, by Davoll, Brown, and Visser,²⁴ the first three preparations had melting point 56–58 °C, but the fourth run yielded material with a distinctly higher melting point, 85 °C. Around the same time, in Jena, by direct acetylation of ribose, Zinner²⁵ obtained a mixture of two tetraacetyl derivatives, one the ribopyranose and the other the ribofuranose, with a melting point of 82 °C for the latter. The two high-melting compounds appeared to be identical, although the nature of the structural difference between them and the low-melting form was unknown. So far, so good; innumerable examples of polymorphism are known. The low-melting form can be called A, the high-melting one B.

After some time, however, the melting points of the early New York preparations had risen to 85 °C, and it was no longer possible to prepare the A form.²⁴ A sample of A was sent from Cambridge, but when it was exposed to the air in New York, in a laboratory that contained samples of B, the crystals of A rapidly became opaque and transformed to B. In the meantime, transformation of A to B was also found to have taken place in Cambridge. Since the A form could no longer be obtained in the New York laboratory, further experiments involving this form were moved to distant Los Angeles, where it was shown that when 1 g of A (melting point 57 °C) was inoculated with 1 mg of B (melting point 85 °C), the melting point of the sample was raised to 75–77 °C within 2 h and to 77–79 °C overnight.²⁴ Similar phenomena were observed in Manchester.²⁶ Low-melting A was first obtained, but when B was introduced into the laboratory, the whole of the material had the higher melting point and the low-melting form could no longer be prepared.²⁷

The scene now changes to Philadelphia, where Patterson and Groshens²⁸ (the same Patterson as in the Patterson function used in crystallography) took on the task of measuring X-ray diffraction data for the two crystalline forms. Low-melting A was found to be monoclinic, space group $P2_1$, and the crystal was

(17) Gigg, J.; Gigg, R.; Payne, S.; Conant, R. *J. Chem. Soc., Perkin Trans. 1*, **1987**, 2411. Ding, J.; Herbst, R.; Praefke, K.; Kohne, B.; Saenger, W. *Acta Crystallogr., Sect. B* **1991**, *47*, 739. Steiner, T.; Hinrichs, W.; Saenger, W.; Gigg, R. *Ibid.*, in press. Zamir, S.; Bernstein, J.; Greenwood, D. *J. Mol. Cryst. Liq. Cryst.* **1994**, *242*, 193. Etter, M. C.; Seidel, A. R. *J. Am. Chem. Soc.* **1983**, *105*, 641. Kohne, B.; Praefke, K.; Mann, G. *Chimia* **1988**, *42*, 139.

(18) For example, the white high-temperature modification of dimethyl 3,6-dichloro-2,5-dihydroxyterephthalate, unstable below about 340 K, crystal structure analysis at 98 K. Yang, Q.-C.; Richardson, M. F.; Dunitz, J. D. *Acta Crystallogr., Sect. B* **1989**, *45*, 312. Richardson, M. F.; Yang, Q.-C.; Novotny-Bregger, E.; Dunitz, J. D. *Ibid.* **1990**, *46*, 653.

(19) Woodard, G. D.; McCrone, W. C. *J. Appl. Crystallogr.* **1975**, *8*, 342.

(22) Howard, G. A.; Lythgoe, B.; Todd, A. R. *J. Chem. Soc.* **1947**, 1052.

(23) Brederick, H.; Hoepfner, E. *Chem. Ber.* **1948**, *81*, 51.

(24) Davoll, J.; Brown, B. B.; Visser, D. W. *Nature (London)* **1952**,

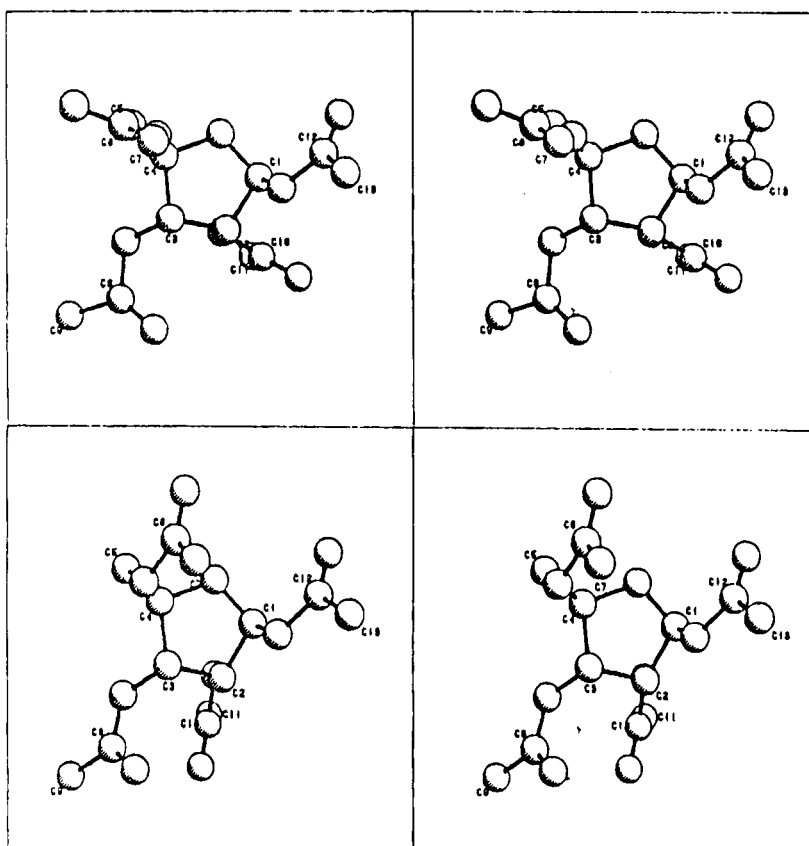


Figure 2. Stereoviews of the two forms of **I**. In both cases the view is on the plane of C1–O–C4 of the furanose ring: upper, monoclinic A form; lower, orthorhombic B form. For clarity, only carbon atoms are labeled.

sufficiently stable to last for 7 weeks. At the end of this time, crystals of B were introduced into the room. After three days, the A crystal was unchanged, but when powdered B was sprinkled over the A crystal, the latter transformed completely to B in a few minutes. The transformed material still had the external shape of the original A crystal, but it was opaque and polycrystalline with no preferred orientation of the crystallites. Crystals of B were found to be orthorhombic, space group $P2_12_12_1$, with quite different cell dimensions from A. Patterson and Groshens noted that the molecular volume increased by about 2% during the A to B transformation (A, 383.9 \AA^3 ; B, 392.5 \AA^3).

In the early 1950s it would have been a major undertaking to determine the atomic arrangement in these noncentrosymmetric crystals by X-ray analysis, and it was only some 20 years later that the crystal structure of form B was determined.²⁹ The authors made no mention of the other polymorph. Essentially the same structure was found by Poppleton,³⁰ who commented that an attempt to prepare the "rare" A form by application of high pressure was unsuccessful.

Comparison of the structures of the two forms only became possible when the elusive A form was obtained

in Budapest and its crystal structure determined.³¹ There is no simple structural relationship between the two polymorphs; the crystal packing is quite different, and although the ribose ring and its directly attached atoms are nearly superimposable, the molecules adopt different conformations with respect to the orientations of the acetyl groups about the bonds C2–O2, C3–O3, and C5–O5 (Figure 2).

According to force-field calculations³¹ the intramolecular nonbonded potential energy of the form A conformation is lower than that of the B conformation by 15.7 kJ mol^{-1} ; that is, the more stable molecular structure is found in the low-melting polymorph. This is reasonable, because, as mentioned earlier, the thermodynamic stability of a high-temperature form must be due to its higher entropy rather than to its lower potential energy (see Figure 1). The increase in molecular volume on going from the A to the B form is consistent with this.

In spite of all the work done on this system, we still do not know the thermodynamic transition point, where the two free energy curves cross. From the many instances where A has been reported to transform spontaneously to B, we can infer that the transition point lies somewhat below normal laboratory temperature. Thus, form A is likely to have been present as a metastable species during most of its existence. In spite of its thermodynamic instability with respect to form B, it may have tended to crystallize first from solution because of a more rapid rate of nucleation, a kinetic factor. Once formed, the crystals of A may endure for a longer or shorter period, depending on the local temperature and other factors.

(27) The state of affairs was summarized by Brown et al. (Brown, G. B.; Davoll, J.; Lowy, B. A. *Biochem. Prep.* **1955**, *4*, 70) as follows: "The form first reported melted at 58° or 56° and the form melting at 84° was initially termed the B form. A number of laboratories have observed the transformation of the low melting into the high melting form and once the latter is obtained the former is not encountered." For another contemporary account of the confusion, see: Overend, W. G.; Stacey, M. In *The Nucleic Acids*; Chargaff, E., Davidson, J. N., Eds.; Academic Press: New York, 1955; Vol. 1, p. 44.

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.