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Reactivity of Organic Crystals

The geometric arrangement of the molecules in crystalline reagents leads to distinctive phenomena.

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Most studies of chemical reactions are concerned with the behavior of liquid or gaseous systems. This is not surprising, since reagent molecules must collide with each other to react, and such collisions are difficult in the crystalline state, where the mobility of the constituent particles is severely restricted. The notion that reactions might, nevertheless, take place in a crystalline phase seems to have been first advanced by Hedvall (*1*). He observed that the formation of calcium silicate from calcium oxide and silica proceeds at a reasonable rate at 1050°C, although the lowest-melting eutectic in this system solidified at 1418°C. Moreover, different crystalline forms of silica were found to have widely different reactivities. Later, extensive studies were concerned with reactions of alkaline earth oxides with alkaline earth salts, such as the reaction of barium oxide with calcium carbonate, sulfate, or phosphate to form the corresponding barium salts (*2*). It was shown that such processes take place far below the decomposition temperature of the salt and that the relative rates cannot be correlated with the decomposition temperatures of the salts participating in the reaction.

In spite of such early demonstrations, the existence of solid-state reactions remained controversial for a long time. An understanding of such processes became possible only when theories of crystal dislocations and an analysis of their role in transport processes provided a foundation for the interpretation of diffusion through crystals and when the availability of tracers permitted measurements of the diffusion coefficients. As might be expected, diffusion in solids is very slow and is characterized by a very high activation energy. For instance, in single crystals of pure sodium chloride, the self-diffusion coefficient of the chloride ions at 1000°K is 1.4×10^{-9} square centimeter per second, with an activation energy of 49 kilocalories per mole (*3*), and oxide ion in alumina at 2000°K has a diffusion coefficient as low as 1.9×10^{-4} square centimeter per second with the enormous activation energy of 152 kilocalories per mole (*4*). Also, it is characteristic that the mobility of various species through a crystal lattice may be drastically altered by an increase in the concentration of dislocations, caused either by mechanical damage or by the presence of impurities. For instance, the diffusion coefficient of oxide ions through alumina is increased a hundred fold when a single crystal of that substance is mechanically crushed (*4*), and the self-diffusion coefficient of chloride in sodium chloride is depressed by a factor of 5 to 10 by the introduction of as little as 0.01 mole percent of calcium chloride (*3*). The use of tracers in clarifying the mechanism of a solid-state reaction is exemplified by the reaction of magnesium oxide with aluminum oxide to form magnesium aluminate (*5*). By this technique it was proved that this reaction proceeds by an interdiffusion of the cations through a rigid lattice of the oxide ions.

The kinetic pattern of solid-state reactions is generally very complex. In the initial stages, a new solid phase has to be nucleated, so that the reaction typically exhibits an accelerating phase. It appears that the nucleation of a new phase in the interior of a perfect crystal is impossible and that nuclei are thus formed only at the crystal surface, or near crystal imperfections. The nucleation rate is very sensitive to the concentration of such imperfections (*6*) and may also be highly dependent on the composition of the atmosphere, particularly its content of water vapor (*7*). Once nuclei of the reaction-product phase have been formed, the reaction proceeds at the interface of the reagent and product phases, so that a quantitative interpretation of experimental data involves assumptions about the geometry of the interface. Also, the advance of the reaction front need not be isotropic, but may favor certain crystallographic directions. Since the nucleation rate of the reaction product usually varies widely from crystal to crystal, kinetic data obtained with a single crystal are usually meaningless, and polycrystalline samples have to be employed in which the special characteristics of individual crystals average out.

Problems with Organic Reagents

Studies of the reactivity of organic molecules in the crystalline state present entirely new problems. For instance, the reaction of magnesium oxide and aluminum oxide, referred to above, involves merely an interdiffusion of small ionic species, whereas in the case of organic reactions covalent bonds must be broken and formed. Thus organic reactions involve a much greater variety of phenomena which encompass, for

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instance, isomerizations, the possibility of alternate reaction paths, polymerizations, and the behavior of free radical reagents.

The nature of the mobility of the species participating in inorganic reactions is well understood; it involves their motion from lattice positions into interstitial positions or into lattice vacancies. When the relatively large molecules diffuse through molecular crystals, it may be assumed that only the vacancy mechanism is operative. The anisotropy of molecular mobility is illustrated by data obtained with anthracene, where the self-diffusion coefficients at 450°K in two different crystallographic directions were found to be 7.5×10^{-11} and 4×10^{-11} square centimeter per second, with activation energies of 22 and 24 kilocalories per mole, respectively (*8*). However, the kind of molecular motion needed to enable organic molecules to react in the solid state is quite different from that involved in diffusion, and measurements of diffusion coefficients will probably add little to our understanding of most reactions occurring in molecular crystals.

Many organic crystals have relatively low melting points and relatively high vapor pressures. Some convincing criteria are, therefore, necessary for proving that any observed reaction takes place in the solid rather than the liquid or gaseous state. Most valuable, in this context, are indications that the geometrical arrangement of the molecules in the crystal is of crucial importance in determining its reactivity. Wherever observed phenomena cannot be accounted for by the chemical properties of isolated molecules, but are clearly a consequence of their geometrical arrangement in the crystal structure, the process is said to be under "topochemical control." The following types of evidence will be valuable to establish the existence of such phenomena:

1) A reaction occurs in the solid state, when the liquid reagent is either totally unreactive or reacts at a much slower rate.

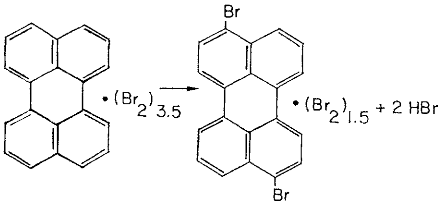
2) Pronounced differences, which cannot be accounted for by known chemical principles, are found in the reactivity of crystals of closely related compounds.

3) Different reaction products are obtained when the reaction is carried out in the solid and the liquid state.

4) The same reagent in different crystal modifications has a different reactivity or leads to different reaction products.

5) Reaction products are formed whose molecules have a preferred orientation in a crystallographic direction of the crystal of the parent reagent ("topotaxy").

If the interacting reagents are distributed between two phases, the interpretation of experimental data is greatly complicated by the need to define the interface. Studies of solid-state reactions have, therefore, generally been limited to processes which occur, at least initially, in a single phase. This introduces a very severe limitation on the types of reaction which may be studied, since organic molecules do not commonly form solid solutions with each other. Reactions involving two reagents may be investigated in the solid state if they form a crystallizable complex; an example of this type of reaction is the conversion of the charge-transfer complex of perylene with bromine to 3,9-dibromoperylene



as reported by Labes *et al.* (*9*). However, most studies of organic solid-state reactions involve processes of a single reagent.

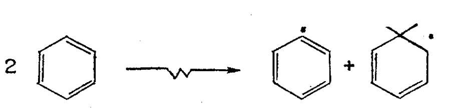
In the following paragraphs I shall try to illustrate some of the principles governing the reactivity of organic crystals. For more information, the reader is referred to a recent review (*10*).

Free Radicals in Organic Crystals

When a covalent bond is broken by homolytic scission in a rigid medium, the resulting radicals diffuse apart at a very low rate, unless one of the fragments is a hydrogen atom. This cage effect was first reported by Norman and Porter (*11*), who showed that ultraviolet irradiation of toluene incorporated in an organic glass yields relatively high concentrations of benzyl radicals, whereas similar treatment of bibenzyl (which would be expected to be cleaved more easily) led to no observable benzyl radicals. The result is easily explained as a consequence of the recombination of benzyl radical pairs. In a recent investigation by Claridge and Willard (*12*) the cage effect was demonstrated in a somewhat different manner: Radicals derived by scission of the C-X bond of alkyl halides embedded in an organic glass were observed by electron spin resonance (ESR) to decay by a first-order process—an unmistakable indication of the recombination of fragments derived from the same original molecule. The operation of the cage effect has the important consequence of stabilizing crystals of compounds which otherwise would be subject to thermal decomposition. For instance, *p*-chlorobenzoyl peroxide is decomposed, in solution, at an appreciable rate at 70°C, but remains stable over long periods of time in the crystalline state (*13*). At 80°C, the decomposition of the crystals was characterized by an accelerating phase, and this suggests that the formation of crystal imperfections increases the number of loci where the reaction can occur at an appreciable rate.

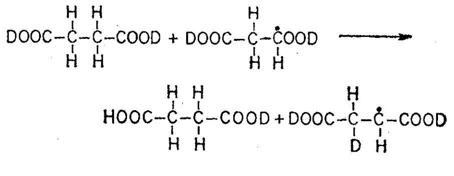
In the most commonly employed method for producing radicals in organic crystals the sample is exposed to ionizing radiation. The high energies of the quanta involved lead to a rather indiscriminate breaking of a variety of chemical bonds in the molecules of the sample, but the cage effect tends to bring about recombination of two heavy fragments, so that the ESR spectrum of the material frequently indicates a preponderance of a single radical species, particularly after a short annealing process which eliminates the less-stable radicals. Cole and Heller (*14*) have recently discovered that exposure of some organic crystals to fast hydrogen atoms leads to a highly selective abstraction of hydrogen, so that the method may be used to obtain specimens containing a single radical, entirely uncontaminated by other species of radicals.

Whatever the method by which radicals have been produced in an organic crystal, concentrations of an order of magnitude up to 10^{17} per gram frequently show negligible decay during many months at room temperature. This demonstrates the extremely low mobility of the radicals in the crystal matrix. In fact, not only translational, but even rotational mobility is severely restricted, so that the radicals produced in irradiated single crystals typically have ESR spectra highly dependent on the orientation of the specimen in the magnetic field and appear to retain a well-defined orientation in a crystallographic direction of the parent crystal (*15*). Usually, linear diffusion of the radicals embedded in a molecular crystal becomes appreciable at an absolute temperature that lies at about 90 percent of the melting temperature, and the radical concentration is then observed to decay by a second-order process (*16*). However, interesting differences may distinguish the mobilities of radicals of similar size in the same crystalline medium. Such a phenomenon was uncovered in a detailed study of the behavior of the radicals produced in irradiated benzene (*17*), where hydrogen atoms detached from one molecule are captured with high efficiency by a second benzene molecule so that the irradiated sample contains a mixture of phenyl and cyclohexadienyl radicals:



The bands in the ESR spectrum which are due to the cyclohexadienyl radical start to narrow at temperatures of about 100°K, where rotation around the sixfold symmetry axis of the benzene molecule sets in. At 241°K, that is, at 86.4 percent of the melting temperature of benzene, the cyclohexadienyl radicals disappear rapidly, whereas the phenyl radicals are still relatively stable, decaying only at temperatures very close to the melting point.

An unexpected phenomenon was discovered by Pooley and Whiffen (*18*), who studied the behavior of crystals of succinic acid in which the carboxyl groups had been deuterated to obtain $DOOCCH_2CH_2COOD$. As would be expected, the methylene hydrogen of this substance cannot participate in isotopic exchange, either in the solid state or in solution. However, if the crystals are exposed to ionizing radiation, an isotopic exchange which may be represented by



$$\mathrm{DOOC{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}COOD + DOOC{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\dot{C}}OOD \longrightarrow}$$
$$\mathrm{HOOC{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}COOD + DOOC{-}\underset{D}{\overset{H}{C}}{-}\underset{H}{\dot{C}}{-}COOD}$$

may be observed by ESR spectroscopy. Pooley and Whiffen noted that the two β-methylene hydrogen atoms in the radical produced in the succinic acid crystal are magnetically nonequivalent and that only the hydrogen atom characterized by the larger hyperfine splitting constant can participate in the isotopic exchange. This is a striking demonstration that crystallographic nonequivalence may be used to induce chemical nonequivalence of two functions which would otherwise be identical. Miyazawa and Itoh (*19*) have observed a similar phenomenon with L-aspartic acid, and we may assume in this case that the dissymmetry of the crystal induces a stereospecific deuteration of one of the β-methylene positions. An even more surprising possibility may be conjectured. It is known that some organic substances, such as benzil and di-*O*-acetylphenolphthalein, whose molecules have no asymmetric centers, crystallize to give a mixture of levorotatory and dextrorotatory crystals (*20*). Such mixtures could be mechanically separated and the dissymmetry of one of the enantiomorphic crystals could then be used to obtain, by a solid-state reaction, an optically active reaction product.

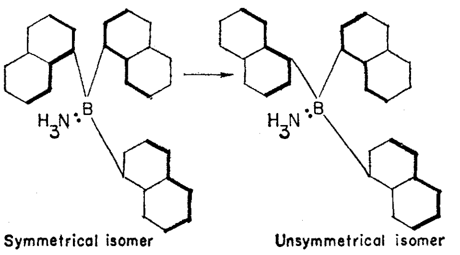
Radicals imbedded in organic crystals may also initiate chain reactions. I shall consider such processes again when discussing solid-state isomerizations and polymerizations; here I only refer to a study which constituted one of the early examples of topochemical control. In 1953, a chance observation was made at the Lawrence Radiation Laboratory of the University of California that C^{14}-labeled choline chloride, with a specific activity of 13 microcuries per milligram, is 60 percent decomposed as a result of self-irradiation after storage for 6 months (*21*). This finding was most surprising, since most organic compounds with such a low level of radioactivity would exhibit decomposition rates of only a fraction of 1 percent per year. Further study of the effect (*22*) showed that crystalline unlabeled choline chloride is highly susceptible to the effects of ionizing radiation, which induces decomposition according to

$$[(CH_3)_3NCH_2CH_2OH]^+\,Cl^- \longrightarrow [(CH_3)_3NH]^+\,Cl^- + CH_3CHO$$

The *G*-value (number of molecules decomposed per 100 electron volts of energy absorbed) was found to attain, under favorable conditions, values as high as 50,000, four orders of magnitude higher than *G*-values commonly observed for primary processes of radiation damage in organic molecules. It was concluded that the decomposition must proceed by a chain mechanism. Most significantly, choline chloride in solution is not unusually radiation-sensitive ($G=3$), and a number of other choline salts (the iodide, nitrate, sulfate, and cyanide) show none of the elevated reactivity of the crystalline chloride. These findings suggested that the chain reaction is possible only with the particular geometrical arrangement of the choline cations in crystals of the chloride. This interpretation was confirmed by the observation that the unusual radiation-sensitivity of choline chloride crystals is eliminated at higher temperatures (*23*), under conditions which bring about a phase transition to a form which is apparently incapable of supporting the chain reaction (*24*). It is also noteworthy that choline chloride crystals irradiated at 77°K exhibit negligible decomposition so long as they are kept at that temperature. The decomposition, which takes place after the sample has been warmed to room temperature, is independent of the length of prior storage. This indicates that the primary radicals, produced during the irradiation, are effectively trapped at low temperatures but can initiate the chain reaction whenever a temperature is attained which allows the chain propagation to proceed.

Isomerization and Dimerization

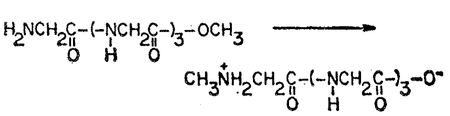
Isomerizations which proceed by a true monomolecular mechanism would be particularly interesting subjects for solid-state reaction studies, since they would not involve problems connected with the diffusion of the reactive species. A case of this type is apparently involved in the behavior of the ammonia adduct of tri-1-naphthylborine. Brown and Sujishi (*25*) found that the decomposition pressure of this compound tends to decrease with time above 100°C. For instance, when the compound was heated rapidly to 140°C, its dissociation pressure decayed gradually from 450 to 10 Torr. If the ammonia adduct was completely dissociated at 140°C and reformed at room temperature, the material with the high dissociation pressure was again obtained. These observations were interpreted by assuming an isomerization between a symmetrical and an unsymmetrical form of the tri-1-naphthylborine adduct:



Symmetrical isomer Unsymmetrical isomer

This interpretation is based on a very indirect inference, and a crystallographic study of this system would be most desirable.

Other examples of solid-state isomerization clearly involve a more complex mechanism. Some years ago it was observed that, when crystalline tetraglycine methyl ester is heated at 100°C, a slow transformation takes place which yields sarcosyl triglycine (*26*):



$$\mathrm{H_2NCH_2\underset{O}{\overset{\|}{C}}-(-\underset{H}{N}CH_2\underset{O}{\overset{\|}{C}}-)_3-OCH_3 \longrightarrow CH_3\overset{+}{N}H_2CH_2\underset{O}{\overset{\|}{C}}-(-\underset{H}{N}CH_2\underset{O}{\overset{\|}{C}}-)_3-O^-}$$

Such a migration of the methyl group from the ester end to the amino end of the oligopeptide would seem to be a most unlikely process, and it differs strikingly from the behavior of tetraglycine methyl ester in solution, where heating induces polycondensation to polyglycine. The results can only be understood by assuming that the reagent molecules are arranged in the crystal in such a manner that the ester end of one molecule lies next to the amine end of its nearest neighbor. Under these conditions, the transfer of a methyl group would involve very little motion and might take place, since the process would appear to be favored by a substantial decrease of free energy. Again, this interpretation of the experimental results is only hypothetical; it would be most desirable to obtain crystallographic data, so that its validity could be assessed.

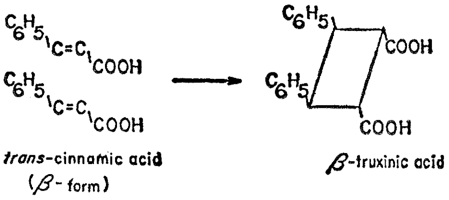
An interesting case of an isomerization process which may proceed in the solid state is represented by

$$\mathrm{RSO_2N\underset{R'}{\overset{CH_3}{C}}=CH_2 \longrightarrow HN\underset{R'}{\overset{CH_3}{C}}=CHSO_2R}$$

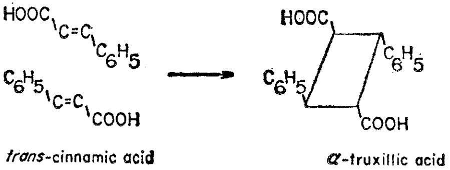
This reaction is known to proceed in solution by a radical-initiated chain mechanism. In comparing the relative rates for the process when it is initiated by ionizing radiation in the glassy state or in well-formed crystals, it was found that crystallization may favor or hinder the reaction, depending on the nature of the R and R′ substituent groups (*27*). For instance, with $R = CH_3C_6H_4-$, $R' = C_6H_5-$, no isomerization is detected in crystals irradiated at 50°C, whereas the glass reacts rapidly at 40° to 45°C. Conversely, with $R = C_6H_5-$, $R' = H-$, the irradiated crystals are isomerized rapidly at −75°C, but the substance is inert in the glassy state. These findings can only be rationalized by assuming that one of the substances has a crystal structure favoring the chain reaction, whereas such a chain reaction is incompatible with the structure of the crystals of the other reagent.

It is clearly most desirable to gain a detailed understanding of the relationship between the geometrical arrangement of molecules in a crystalline reagent and the chemical process which can take place in the solid state. This objective has been attained most satisfactorily for the photodimerization of a variety of substituted *trans*-cinnamic acids, which has been studied for a number of years at the Weizmann Institute under the leadership of G. M. J. Schmidt.

A total of 30 such derivatives were studied; of these, six existed in two, and one in three crystalline modifications (see *28*). Some of the crystals yielded a β-truxinic acid, others yielded an α-truxillic acid, and some failed to dimerize. Schmidt (*29*) showed that, in every case, the chemical result could be predicted from the crystal structure of the reagent. Where nearest-neighbor cinnamic acid molecules lie parallel to each other in the monomer crystal, the β-truxinic acid molecules characterized by a mirror plane are formed. Where the monomer molecules lie antiparallel, being related by a center of symmetry, the resulting dimer molecule also has a center of symmetry. The point may be illustrated for unsubstituted *trans*-cinnamic acid, which exists in both types of crystal modification and may be converted into either product by selecting the proper crystalline modification of the reagent:



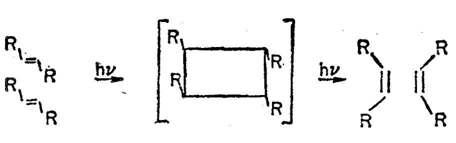
trans-cinnamic acid (β-form) β-truxinic acid



trans-cinnamic acid (α-form) α-truxillic acid

It was generally found that nearest-neighbor carbon-to-carbon double bonds in the dimerizing crystals were at a distance of less than 4.1 angstroms. In crystals where this distance exceeded 4.5 angstroms, no dimerization was possible. These studies demonstrate, in a most convincing manner, how the arrangement of the molecules in the reagent crystal determines not only the feasibility of a solid-state reaction, but also the nature of the product.

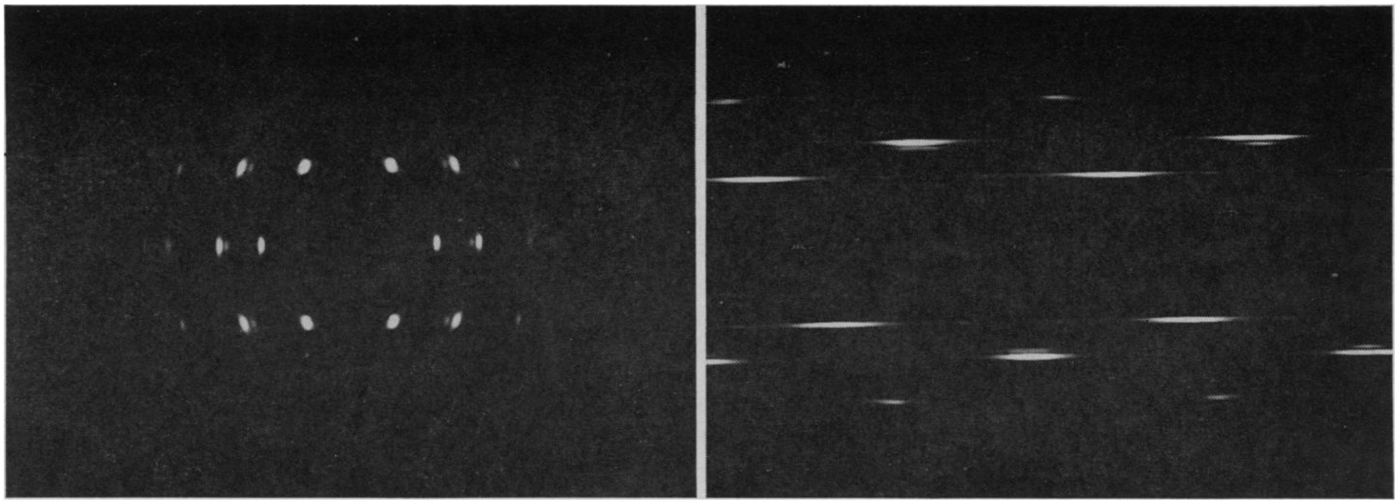
Some crystalline *cis*-cinnamic acids may be converted by a photochemical process into the *trans*-isomer, and several cases of this type have been studied by Bregman *et al.* (*30*). It appears that the feasibility of such isomerizations may also be correlated with the relative position of nearest-neighbor double bonds, and the authors suggest that the transition state of the *cis-trans* isomerization may be a complex of an excited *cis*-cinnamic acid with a neighboring molecule in the ground state. Another important principle was established in that study. In a photochemical solid-state reaction A →B, it is possible to obtain complete conversion of A into B although A is the thermodynamically more stable species, if B is "trapped" in a crystalline form which does not allow the molecules to react in the solid state. A similar reaction, the photoconversion of *trans*-dibenzoylethylene to the *cis*-isomer was studied by Griffin *et al.* (*31*). The possibility that the reaction might involve the cyclic dimer as an intermediate



has been ruled out by showing that, when the reagent crystal is a solid solution of *trans*-dibenzoylethylene with its deuterated analog, the product does not contain the half-deuterated species that the above mechanism would lead one to expect.

Oriented Chain Growth

More effort has been expended on studies of solid-state polymerizations than on any other class of solid-state organic reactions. The first observation in this field was made more than 30 years ago (*32*) when Kohlschütter discovered that trioxane crystals can be polymerized, on contact with formaldehyde vapor, to polyoxymethylene $(-CH_2O-)_n$ and proved by x-ray diffraction that the polymer chains are aligned parallel to the sixfold axis of symmetry of the parent trioxane crystal. He also emphasized that tetroxane which, on purely chemical grounds,



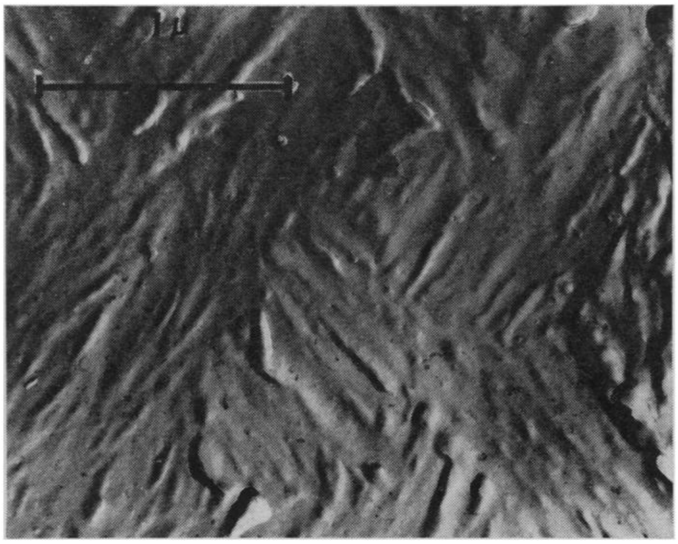


Fig. 1 (above). X-ray diffraction photographs of poly(methylene sulfide) obtained by irradiating a single crystal of trithiane with 10 megarads of γ-rays from a Co^{60} source, heating for 163 hours at 180°C and removing residual trithiane by sublimation. (Left) 180°C oscillation picture; rotation around *c*-axis of parent orthorhombic trithiane (the polymer chains are parallel to the *ab* diagonal). (Right) (hk0) Weissenberg photograph. [Courtesy Prof. J. B. Lando]

Fig. 2 (bottom left). Electron micrograph of surface of polymerized single crystal of ϵ-aminocaproic acid. [Courtesy Dr. E. W. Fischer and Mr. E. Macchi]

would be expected to be more reactive because of the strain in an eight-membered ring, is unreactive under comparable conditions. This was taken as an indication that the reactivity of the trioxane is caused by a favorable arrangement of the molecules in the crystal. It is hard to understand how this provocative report could have remained without any effect on the scientific community of its day, but it seems that it stimulated no further work in this area and was completely forgotten when, 20 years later, solid-state polymerization began to be investigated anew.

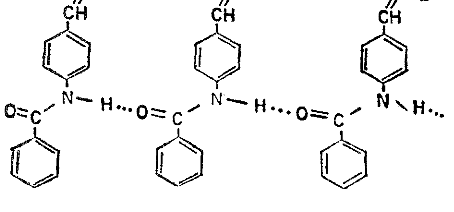
The field of solid-state polymerization has been adequately summarized elsewhere (*33*); here I should only like to draw attention to the phenomenon of oriented chain growth. The topotactic polymerization of trioxane was rediscovered by Okamura and his collaborators (*34*), who used ionizing radiation to induce the reaction in trioxane crystals. It is of interest that similar irradiation of liquid trioxane is without effect. It was later found that the polyoxymethylene chains are not only oriented in the direction of the chain axis, but that a single trioxane crystal is, in fact, converted into an assembly of polymer crystallites which are highly oriented in all crystallographic directions with respect to the original monomer crystal. The relation between the orientation of polymer and parent monomer has been fully clarified (*35*). The degree of orientation which may be achieved in this type of process is illustrated in Fig. 1, which shows x-ray diffraction oscillation and Weissenberg photographs of poly(methylene sulfide) $(\text{—CH}_2\text{S—})_n$ obtained by solid-state polymerization of an irradiated single crystal of trithiane (*36*). It may be noted that the orientation of the polymer crystallites is most perfect parallel to the *c*-axis of the monomer crystal from which they originated. Although the order in the other crystallographic directions is less well defined, the triaxial orientation achieved is superior to that attainable in a macroscopic polymer sample by any other means.

It might be assumed that oriented chain growth is particularly favored in the polymerization of cyclic monomers, where similar bonds are broken and formed, so that little energy is released by the reaction. The situation should be much less favorable in the case of vinyl monomers, which are characterized by strongly exothermic polymerizations. Nevertheless, various degrees of oriented chain propagation may be achieved in that case also, and a variety of techniques may be employed to demonstrate such phenomena. I have noted above that radicals produced by exposure of organic crystals to ionizing radiation generally retain a well defined orientation in the crystal from which they originate (*15*). The problem then arises as to the extent to which this preferred orientation is retained when a radical imbedded in a monomer crystal initiates a polymerization. The question may be settled by ESR spectroscopy, and this technique was used in a study of the radiation-initiated polymerization in a single crystal of barium methacrylate dihydrate (*37*). The initiating species here is $(CH_3)_2\dot{C}COO^-$, formed by the addition of a hydrogen atom to the C=C bond of the methacrylate ion. This radical, observed in irradiated crystals at −196°C, has six equivalent hydrogen atoms attached to the *β* carbons and is therefore characterized by seven absorption lines with a binomial intensity distribution. At 20°C, the spectrum changes very rapidly to one to be expected from the product of the reaction

$$CH_3\text{-}\overset{CH_3}{\underset{COO^-}{\dot{C}}} + CH_2\text{=}\overset{CH_3}{\underset{COO^-}{C}} \longrightarrow CH_3\text{-}\overset{CH_3}{\underset{COO^-}{C}}\text{-}CH_2\text{-}\overset{CH_3}{\underset{COO^-}{\dot{C}}}$$

where the unpaired electron now interacts with three methyl hydrogen atoms and two methylene hydrogen atoms. The significant finding is that the finestructure of the ESR spectrum of this new radical still depends on the orientation of the crystal in the magnetic field; that is, at least one monomer unit can be added to the initiating radical without loss of the preferred orientation within the monomer crystal.

A number of acylated derivatives of *p*-aminostyrene have been observed to polymerize spontaneously in the crystalline state at temperatures as much as 80°C below the melting point. The polymerization of a single crystal of one compound of this type, *p*-benzamidostyrene, was studied by infrared spectroscopy (*38*). The crystal has a layer structure with hydrogen-bonded sheets of molecules lying parallel to one another, as represented schematically by



so that the absorption due to the stretching vibration of the N−H bonds exhibits a very pronounced dichroism. By following changes in this dichroism as a function of the disappearance of the vinyl groups, it is possible to assess the extent to which the hydrogen-bonded network remains intact during the polymerization. It was found that the dichroism may be almost completely retained if the polymerization temperature lies below the glass transition temperature of the polymer.

In the case of vinyl stearate, the polymer exhibits "side-chain crystallization"; that is, the aliphatic hydrocarbon side chains seem to form paraffin-like crystallites, which leads to a characteristic x-ray diffraction ring. Crystallographic criteria may then be used in this case for deciding whether the parallel arrangement of the side chains in a single crystal of vinyl stearate is preserved during the radiation-induced polymerization. The evidence shows that the mutual orientation of these side chains indeed remains undisturbed (*39*). Although these results give no direct evidence concerning the direction of growth of the chain backbone, it is difficult to see how the arrangements of the side chains can remain so highly ordered unless the backbone chain propagates in a preferred crystallographic direction.

In the last two examples, the monomer crystal had a layer structure imposed by strong forces between bulky substituent groups—this layer structure was then shown to survive the polymerization process. However, it is possible to impose in a different way a restriction on the direction in which a growing chain can propagate, namely by enclosing the monomer inside its urea or thiourea clathrate (canal complex) (*40*). In such a complex, the urea (or thiourea) molecules are arranged along a hexagonal helix, and the monomer molecules are stacked up, end-to-end, in the central cavity of the helix. It is clear that any polymerization which does take place can proceed only along the axis of the cavity. It has, indeed, been found that the polymerization of vinyl chloride in a urea clathrate leads to parallel chains having an all-*trans* conformation of the chain backbone—a result which, incidentally, cannot be achieved by any other means (*41*).

It is particularly surprising that polycondensation reactions can take place in the solid state and that, even here, oriented chain growth is possible. This phenomenon has been demonstrated, so far, only for the case of 6-aminohexanoic acid, which condenses at 30° to 40°C below its melting point to polycapramide ("Nylon 6") (*42*). The polymer again has a high degree of three-dimensional orientation; the crystallites have two alternative orientations in which the chain axes are inclined at 110° to each other. This crystal twinning, deduced from x-ray diffraction data, is also clearly evident in the electron micrograph of the surface of a polymerized crystal, shown in Fig. 2.

Conclusion

The existence of reactions in molecular crystals is firmly established. The most convincing evidence is (i) the observation in crystals of reactions which do not take place in the liquid state; (ii) the isolation of different reaction products from different crystalline modifications of the same reagents; (iii) the correlation of the reaction path with geometric properties of the reagent crystal structure; and (iv) the existence to topotaxy. Progress in studying these reactions is greatly hampered by the lack of interest, on the part of organic chemists, in solid-state phenomena. It is clear that the detailed analysis of reactions which occur in organic crystals requires the application of a variety of experimental methods and the collaboration of organic chemists, physical chemists, and physicists.

References

1. J. A. Hedvall, *Z. Anorg. Allgem. Chem.* **98**, 57 (1916).
2. ——— and J. Heuberger, *ibid.* **122**, 61 (1922); **128**, 1 (1923); **135**, 49 (1925).
3. J. E. Hanlon, *J. Chem. Phys.* **32**, 1492 (1960).
4. Y. Oishi and W. D. Kingery, *ibid.* **33**, 480 (1960).
5. R. E. Carter, *J. Am. Ceram. Soc.* **44**, 116 (1961).
6. J. Benard, *Reactivity of Solids*, J. H. de Boer *et al.*, Eds. (Elsevier, Amsterdam, 1960), p. 362.
7. W. E. Garner and T. J. Jennings, *Proc. Roy. Soc. London Ser. A* **224**, 460 (1954); B. Topley and M. L. Smith, *J. Chem. Soc.* **1935**, 321 (1935).
8. C. H. Lee, H. K. Kevorkian, P. J. Rencroft, M. M. Labes, *J. Chem. Phys.* **42**, 1406 (1965).
9. M. M. Labes, H. W. Blakeslee, J. E. Bloor, *J. Am. Chem. Soc.* **87**, 4251 (1965).
10. H. Morawetz, in *Physics and Chemistry of the Organic Solid State*, D. Fox, M. M. Labes, A. Weissberger, Eds. (Interscience, New York), vol. 1 (1963), pp. 287–328; vol. 2 (1965), pp. 853–872.
11. I. Norman and G. Porter, *Proc. Roy. Soc. London Ser. A* **230**, 399 (1955).
12. R. F. C. Claridge and J. E. Willard, *J. Am. Chem. Soc.*, in press.
13. J. W. Breitenbach and H. Frittum, *J. Polymer Sci.* **29**, 565 (1956).
14. T. Cole and H. C. Heller, *J. Chem. Phys.* **42**, 1668 (1965).
15. See, for instance, I. Miyazawa and W. Gordy, *J. Chem. Phys.* **30**, 1590 (1959); D. K. Ghosh and D. H. Whiffen, *Mol. Phys.* **2**, 285 (1959); H. M. McConnell, C. Heller, T. Cole, R. W. Fessenden, *J. Am. Chem. Soc.* **82**, 766 (1960).
16. Ya. S. Lebedev, V. K. Ermolayev, Yu. D. Tsvetkov, Yu. N. Molin, N. Ya. Buben, V. V. Voevodsky, *Intern. Symp. Free Radical Stabilization, 5th, Uppsala, 1961*, paper No. 37.
17. S. Ohnishi, T. Tanei, I. Nitta, *J. Chem. Phys.* **37**, 2402 (1962).

18. D. Pooley and D. H. Whiffen, *J. Chem. Soc.* **1962**, 366 (1962).
19. I. Miyazawa and K. Itoh, *J. Chem. Phys.* **43**, 2915 (1965).
20. T. M. Lowry, *Optical Rotatory Power* (Dover, New York, 1964), p. 338.
21. B. M. Tolbert, P. T. Adams, E. L. Bennett, A. M. Hughes, M. R. Kirk, R. M. Lemmon, R. M. Noller, R. Ostwald, M. Calvin, *J. Am. Chem. Soc.* **75**, 1867 (1953).
22. R. M. Lemmon, M. A. Parsons, D. M. Chin, *ibid.* **77**, 4139 (1955); R. M. Lemmon, P. K. Gordon, M. A. Parsons, F. Mazetti, *ibid.* **80**, 2730 (1958); R. O. Lindblom, R. M. Lemmon, M. Calvin, *ibid.* **83**, 2484 (1961).
23. I. Serlin, *Science* **126**, 261 (1957).
24. R. L. Collin, *J. Am. Chem. Soc.* **79**, 6086 (1957).
25. H. C. Brown and S. Sujishi, *ibid.* **70**, 2793 (1948).
26. L. A. Ae. Sluyterman and H. J. Veenendaal, *Rec. Trav. Chim.* **71**, 137 (1952); L. A. Ae. Sluyterman and M. Kooistra, *ibid.*, p. 277.
27. F. W. Stacey, J. C. Sauer, B. C. McKusick, *J. Am. Chem. Soc.* **81**, 987 (1959).
28. M. D. Cohen, G. M. J. Schmidt, F. I. Sonntag, *J. Chem. Soc.* **1964**, 2000 (1964).
29. G. M. J. Schmidt, *ibid.*, p. 2014.
30. J. Bregman, K. Osaki, G. M. J. Schmidt, F. I. Sonntag, *ibid.*, p. 2021.
31. G. W. Griffin, E. J. O'Connell, J. M. Kelliher, *Proc. Chem. Soc.* **1964**, 337 (1964).
32. H. W. Kohlschütter, *Ann. Chem.* **482**, 75 (1930); ——— and L. Sprenger, *Z. Phys. Chem. Abt. B* **16**, 284 (1932).
33. P. G. Garrett, *Polymer* **3**, 325 (1962); M. Magat, *ibid.*, p. 449; H. Morawetz, *J. Polymer Sci. Part C* **1**, 65 (1963); V. A. Kargin and V. A. Kabanov, *Zh. Vses. Khim. Obshchestva im. D. I. Mendeleeva* **9**, No. 6, 602 (1964); A. Chapiro, *J. Polymer Sci. Part C* **4**, 1551 (1964); see also *10*.
34. S. Okamura, K. Hayashi, Y. Kitanishi, *J. Polymer Sci.* **58**, 925 (1962); S. Okamura, E. Kobayashi, M. Takeda, K. Tomikawa, T. Higashimura, *J. Polymer Sci. Part C* **4**, 827 (1964).
35. G. Carazzolo, S. Leghissa, M. Mammi, *Makromol. Chem.* **60**, 171 (1963).
36. J. B. Lando and V. Stannett, *J. Polymer Sci. Part A* **3**, 2369 (1965).
37. J. H. O'Donnell, B. McGarvey, H. Morawetz, *J. Am. Chem. Soc.* **86**, 2322 (1964).
38. S. Z. Jakabhazy, H. Morawetz, N. Morosoff, *J. Polymer Sci. Part C* **4**, 805 (1964).
39. N. Morosoff, H. Morawetz, B. Post, *J. Am. Chem. Soc.* **87**, 3035 (1965).
40. J. F. Brown and D. M. White, *ibid.* **82**, 5671 (1960); D. M. White, *ibid.*, p. 5678.
41. S. Krimm, J. J. Shipman, V. L. Folt, A. R. Berens, *J. Polymer Sci. Part B* **3**, 275 (1965).
42. N. Morosoff, D. Lim, H. Morawetz, *J. Am. Chem. Soc.* **86**, 3167 (1964).

Chromosome Variability and Geographic Distribution in Insects

Chromosome rather than gene variations provide the key to differences among populations.

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There is no group of organisms in which the analysis of chromosome variation in relation to geographical distribution has been carried further than in the Insecta. This kind of variation has tended to be neglected by many and ignored by some. Yet, in reality, it is more spectacular and, though less understood, at least as important as either the external variation or indeed the remaining genetic variation that exists in natural populations.

The chromosome complement is not just another character. To regard it as such is to misunderstand the nature of phylogenetic change and thus the whole basis of biological evolution. The material of the genotype itself forms part of the structure of the chromosomes. For this reason the chromosome phenotype is far less influenced by external factors than is the morphological or the physiological phenotype. Moreover, the chromosome phenotype is often a much more sensitive indicator of biological change and biological distinctiveness.

Chromosome variation of different kinds has been described within or between many natural insect populations (Table 1). In most cases, however, no analysis of this variation has been undertaken. The detailed study of chromosome variation in different geographical areas was initiated in the United States by the pioneer investigation of Dobzhansky and Sturtevant (*1*). They studied the polymorphism obtaining in the banding sequence of the giant polytene chromosomes of *Drosophila*. Their approach, that of comparing patterns of polymorphism within and between populations, has since been used by many workers in many lands and with many species. The *Drosophila* studies, however, still represent the most comprehensive and formidable body of data available on chromosome variation in geographically defined areas, for they have been in progress now for almost 30 years. Let us begin, then, by considering the extent, the validity, and the applicability of the conclusions reached from these studies.

The Drosophila Affair

Populations of many, though by no means all, species of *Drosophila* are mixtures of individuals with differently constructed chromosomes. In particular, a large number of distinct paracentric inversions (Fig. 1) of the band sequences in the giant polytene chromosomes have been found in the heterozygous state, and each inversion tends to have its own definite range. A few of these inversions occur throughout most of the species area, but most are restricted to varying degrees and some are quite local. The frequencies of some of the more abundant types vary along regular geographical clines and, since the clines do not coincide, each region is characterized by different frequencies of its principal chromosome types.

Different geographical populations of the same species may vary considerably with regard to their degree of polymorphism. Some are structurally monomorphic, some are moderately polymorphic, and others highly so. Moreover, in *D. subobscura* the inversions show a pronounced tendency to overlap, so forming complex heterozygotes, whereas in *D. willistoni* many of the inversions are small and independent.

Four main correlations have been established in relation to these varying patterns of polymorphism:

1) In species such as *D willistoni*, whose geographical races differ in the extent of their polymorphism, the chromosome variability of natural populations is highly correlated with environmental conditions. Populations in heterogeneous environments are more variable than those living in more homogeneous habitats (*2*). This suggests that chromosome polymorphism allows for a more efficient exploitation of the environment.

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